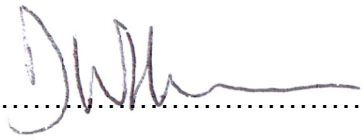
Investigating the Epidemiology of Bovine Tuberculosis in the European Badger

Submitted by David Hudson, to the University of Exeter as a thesis for the degree of Doctor of Philosophy in Biological Sciences, October 2021.

I certify that all material in this thesis which is not my own work has been identified and that any material that has previously been submitted and approved for the award of a degree by this or any other University has been acknowledged.

(Signature)  ……

Acknowledgements

I would like to take this opportunity to thank the fantastic support and guidance of my supervisors Dave Hodgson and TJ McKinley without which I would not have been able to get to this point. Thanks for your enthusiasm and patience and I hope to work with you again in the future.

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A further thank you to the data collection team at Woodchester Park (badgers) and on the Mweya Peninsula in Queen Elizabeth National Park, western Uganda (banded mongoose).

Abstract

Global health is becoming increasingly reliant on our understanding and management of wildlife disease. An estimated 60% of emerging infectious diseases in humans are zoonotic and with human-wildlife interactions set to increase as populations rise and we expand further into wild habitats there is pressure to seek modelling frameworks that enable a deeper understanding of natural systems.

Survival and mortality are fundamental parameters of interest when investigating the impact of disease with far reaching implications for species conservation, management and control. Survival analysis has traditionally been dominated by non- and semi-parametric methods but these can sometimes miss subtle yet important dynamics. Survival and mortality trajectory analysis can alleviate some of these problems by fitting fully parametric functions that describe lifespan patterns of mortality and survival. In the first part of this thesis we investigate the use of survival and mortality trajectories in epidemiology and uncover novel patterns of age-, sex- and infection-specific mortality in a wild population of European badgers (*Meles meles*) naturally infected with *Mycobacterium bovis*, the causative agent of bovine tuberculosis (bTB). Limitations of dedicated software packages to conduct such analyses led us to investigate alternative methods to build models from first principles and we found the NIMBLE package to offer an attractive blend of flexibility and speed. We create a novel parameterisation of the Siler model to enable more flexible model specification but encounter the common problem of competing models having comparable fits to the data. Multi-model inference approaches can alleviate some of these issues but require efficient methods to carry out model comparisons; we present an approach based on the estimation of the marginal likelihood through importance sampling and demonstrate its application through a series of simulation- and case-studies. The approach works well for both census and capture-mark-recapture (CMR) data, both of which are common within ecological research, but we uncover challenges in recording and modelling early life mortality dynamics that occur as a result of the CMR

sampling process. The final part of the thesis looks at another alternative approach for model comparison that doesn't require direct estimation of the marginal likelihood, Reversible Jump Markov Chain Monte Carlo (RJMCMC), which is particularly efficient when models to be compared are nested and the problem can reduce to one of variable selection. In the final chapter we carry out an investigation of age-, sex-, infection- and inbreeding-specific variation in survival and mortality in a wild population of European badgers naturally infected with bovine Tuberculosis. Using the methods and knowledge presented through the earlier chapters of this thesis we uncover patterns of mortality consistent with both the mutation accumulation and antagonistic pleiotropy theories of senescence but most interestingly uncover antagonistic pleiotropic effects of inbreeding on age-specific mortality in a wild population for the first time.

This thesis provides a number of straightforward approaches to Bayesian survival analysis that are widely applicable to ecological research and can offer greater insight and uncover subtle patterns of survival and mortality that traditional methods can overlook. Our investigation into the epidemiology of bovine Tuberculosis and in particular the effects of inbreeding have far-reaching implications for the control of this disease. This research can also inform future conservation efforts and management strategies as all species are likely to be at increasing risk of inbreeding in an age of dramatic global change, rapid habitat loss and isolation.

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Authors Declaration

I had no involvement in the collection of any field data. The badger data used throughout this thesis was collected by the Woodchester Park team, including all badger trapping, sampling, release and compilation of trapping records. Mongoose data used in chapter 4 was collected by the field team based on the Mweya Peninsular in Queen Elizabeth National Park, western Uganda.

My supervisors commented on earlier drafts of this work. With the additional contribution from other co-authors who provided comments on manuscripts that have formed chapters 2 and 4. All of whom are credited in the acknowledgements.

With these exceptions, I declare that the work contained in this thesis is my own and has not been submitted for any other degree or award.

Chapter 1: Inbreeding, ageing and disease: a challenge for wildlife disease epidemiology

Wildlife disease epidemiology

Wildlife disease is increasingly recognised as being of critical importance to global health. The impacts are rarely confined to the conservation and management of a particular species (Blanchong et al., 2016) because many of the pathogens involved have important implications for the health of humans and domestic animals (Daszak et al., 2000; Morens & Fauci, 2013). An estimated 60% of emerging infectious diseases in humans are zoonotic; the majority with an identified wildlife reservoir (Jones et al., 2008). Future levels of human-nature interaction are set to rise, driven by population increase, environmental encroachment and climate change, all of which will likely accelerate the emergence of future zoonotic diseases (Hassell et al., 2017). It is widely accepted that ignoring wildlife hosts of a shared infectious disease will render any potential eradication program ineffective (Martin et al., 2011). Infectious diseases rank among the most important and common environmental challenges faced by both species and individual animals (Daszak et al., 2001; Robinson et al., 2010; Weatherall, 2003). Governments and policy-makers are faced with the challenge of minimising the knock-on economic and health impacts of wildlife disease and to be successful requires an understanding of the complete system including routes of transmission and infection combined with knowledge of how wildlife populations are affected (McKnight et al., 2017). For these reasons there has been an increase in the number of studies focused on epidemiological modelling, with developments in both life-course (Ben-Shlomo & Kuh, 2002; Mishra et al., 2015) and multi-level hierarchical models (Gomes et al., 2014; Lanzas & Chen, 2015).

Mathematical and statistical modelling of infectious diseases allows for exploration of the variability, interactions and complexities of disease systems, and has contributed to improved understanding and changes in policy and management (Lanzas & Chen, 2015). Typically such models focus on specific aspects of population or individual level health such as mortality or fecundity to

assess disease impact, yet accurate modelling of such complex systems in wild populations remains an ongoing challenge; limited data availability, incomplete capture histories and substantial heterogeneity from various sources are all typical issues associated with wildlife disease research. Much of the recent research in wildlife disease epidemiology has focused on identifying sources of variation both within and among wild populations to better target management strategies. Modelling wildlife disease systems obliges researchers to make decisions about model complexity which satisfy both academic scrutiny and managers' desire to be suitably system-specific (Joseph et al., 2013). Bovine tuberculosis is a globally important infectious disease with economic and health impacts for humans, livestock and wildlife. In the United Kingdom the European badger (*Meles meles*) is believed to be the primary wild maintenance host for the disease and is involved in the persistence of the disease in cattle populations (Donnelly et al., 2006). This disease system has been the subject of extensive research (for a review see Gallagher & Clifton-Hadley, 2000) and highlights the complexities involved with wild disease systems such as the sparse nature and quality of the data (often incomplete or censored), diagnostic uncertainty and the multiple sources of heterogeneity common in the natural world (Stallknecht, 2007).

Success in the modelling of disease systems in wild populations requires an acceptance that the natural world is essentially a stochastic system (Heesterbeek et al., 2015) but researchers should seek explanations of observed variation to better understand complex disease interactions. Here we review the literature on three major sources of variation observed in infectious disease epidemiological research: sex, inbreeding and ageing; and present current modelling approaches that can deal with the complexity of such systems.

Sex Variation & Disease:

In humans, sex difference in lifespan is well documented with females displaying lower mortality rates throughout life (Austad, 2011). This is a common phenomenon across other mammalian and avian species (e.g. Badgers - Rogers et al., 1997; Red deer - Loison et al., 1999; Cotton-tail rabbits - Bond et al., 2001; Common grackle - Howe, 1977) and explanatory

hypotheses focus on sexual-selection theory and the increased cost that males incur for attempting to ensure reproductive success (Moore & Wilson, 2002). For example, Kraus et al. (2008) demonstrated how increased risk-taking behaviours and biased movement patterns of male grey mouse lemurs (Microcebus murinus) led to a reduction in survival; Owen-Smith (1993) found an increased rate of male predation in Greater kudos (Tragelaphus strepsiceros); and Roberts et al. (2004) highlighted the immunosuppressant effects of testosterone which leaves males more susceptible to infectious diseases in reptiles (also in Hau, 2007). Wilkinson et al. (2000) identified higher mortality rates in male European badgers and demonstrated an increase in mortality as a result of infection with bovine tuberculosis that was stronger in males than females suggesting that there may be sex differences in the mode of disease spread and their ability to cope. This study highlights some of the issues associated with wildlife disease research in that they struggled with small sample sizes in certain categories of disease state and failed to mention the poor sensitivity of the diagnostic tests and subsequent impact of false-negative badgers. Life-table analysis was used to produce fixed mortality rates that were assumed to be time independent, with any disease impact being simply viewed as an elevation of these static rates at particular life stages. An increase in the number of epidemiological studies looking at sex-related differences in host-pathogen interactions in humans resulted in two fundamental hypotheses being used to explain the often male-biased disease incidence: the physiological hypothesis which points at differences in sex hormones and genetic make-up; and the behavioural hypothesis which suggests sex differences in exposure (Brabin, 1992). A meta-analysis of ten major pathogens in humans showed that physiological differences was the primary driver of sex differences with differences in behaviour playing a lesser role (Guerra-Silveira & Abad-Franch, 2013).

Similar investigations have been carried out in both laboratory and wild animal populations looking at specific pathogens and the drivers of any observed sex differences. McDonald et al. (2014) inferred the drivers of sex-specific variation in disease response by using mortality trajectories which allow for age-specific effects. In doing so they identified a faster rate of increase in mortality, post-

infection, in male badgers from the point of infection suggesting differences in immunological responses between the sexes. An alternative explanation includes the possibility that infection modifies male host behaviour, potentially increasing aggression which could then explain the increased rate of bite wounding in infected male badgers (Jenkins et al., 2012) which in turn affects survival. Often disease prevalence shows no pattern of sex variation (e.g. devil facial tumour disease in Tasmanian devils (Sarcophilus harrisii) - Lachish et al., 2009; chronic wasting disease in White-tailed Deer (Odocoileus virginianus) - Samuel & Storm, 2016) with male-female differences only becoming apparent after the point of infection. The subsequently recorded disease effects are often then categorised into different age classes (i.e. juvenile/adult) which can then be compared against known physiological changes in an attempt to reveal the driving forces behind the observed phenomena. The importance of age-specific effects have been highlighted across a variety of different wild species (e.g. Hagen et al., 2007; Loison, Festa-Bianchet, et al., 1999) but the common approach in wildlife disease epidemiology is to categorise age (e.g. Samuel & Storm, 2016) which often fails to capture the complexities of potential age- and sex-specific impacts.

Inbreeding depression & disease:

The effects of inbreeding on the demography and persistence of wild populations has often been questioned, and evidence for inbreeding effects in this field is scarce (Keller & Waller, 2002). Wild populations are often assumed to be outbred with high genetic variation creating likely effective immune responses (Abolins et al., 2011) and a lack of inbreeding depression (ID). ID refers to a decline in fitness of offspring of related individuals (Charlesworth & Charlesworth, 1987), usually expressed in comparison to outbred individuals. It was long believed that inbreeding and ID would not be evident in wild populations as a result of the many inbreeding avoidance mechanisms that have been identified (Pusey & Wolf, 1996), and because populations that were subject to strong inbreeding could have purged deleterious mutations through selection (Robinson et al., 2018). Recent research has shown inbreeding and ID to be more common than previously thought, with many wild populations exhibiting genome-wide homozygosity displaying exaggerated age-dependent

mortality trajectories (Keller et al., 2008; Swindell & Bouzat, 2006). Studies comparing inbred and outbred white-footed mice (*Peromyscus leucopus nooeboracensis*) demonstrated significantly lower survival for inbred individuals and found that the difference between inbred and outbred individuals was far greater when released into the wild compared to those kept in laboratory conditions (Jiménez et al., 1994). Evidence remains contradictory, with some wild inbred populations showing relatively little sign of ID (e.g. Bilde et al., 2005; Kalinowski & Hedrick, 1998) which may suggest that animals are able to overcome the deleterious genetic effects before they manifest on a phenotypic level through behavioural or physiological means. For example, a study on burying beetles (*Nicrophorus vespilloides*) found evidence of behavioural buffering by showing that inbred males increased their competitive effort for a reproductive opportunity. They were more risk taking and willing to suffer greater injury whilst defending their brood than their outbred counterparts, resulting in no difference in the number of grand offspring between the two groups (Richardson & Smiseth, 2017). The possible explanations for this behaviour are time/life-stage dependent, revolving around the idea that inbred individuals are more likely to invest in current reproductive opportunities as the likelihood of future opportunities is diminished through potentially worsening future health. However there is some evidence to suggest that inbred individuals that survive beyond a period of increased juvenile mortality may be fitter than outbred individuals (Lacy et al., 1993). Although this may in part be due to knock-on impacts of inbred individuals on their outbred counterparts: in the case of the burying beetles researchers found outbred individuals had to expend more energy to repel inbred intruders with detrimental effects on its own brood's survival.

There is a high degree of variation in the magnitude of ID both within and among populations and although it is often reported as being experienced most strongly in juvenile life stages, there is evidence to suggest that deleterious effects for adults can be just as severe but harder to detect (Huisman et al., 2016). The lack of consensus within the research into ID may result from the different measures of inbreeding used: traditional pedigree-based coefficients are an estimate of genome-wide homozygosity from identity by descent

information but are generally not available for wild populations as pedigrees of sufficient detail are difficult to construct. This will often result in the exclusion of large cohorts of individuals which may bias results. A more common approach in wild populations is using average homozygosity at certain genetic markers; this approach is often constrained to limited microsatellite data which can produce estimates of marker homozygosity which are poorly correlated with the more traditional genome-wide measures (Slate et al., 2004) and any correlations with phenotypic traits are typically very small. Recent advances in genome-wide high density marker data has improved detection of ID across life stages by reducing much of the error variance inherent when only small numbers of marker loci are analysed (Hoffman et al., 2014). Research looking at ID in adult life-stages is relatively rare mainly due to the difficulty of monitoring wild populations and the evidence is far from conclusive: for example, no evidence of ID in mandrills (Mandrillus sphinx) (Charpentier et al., 2006) yet clear ID present in red-cockaded Woodpeckers (Picoides borealis) (S. J. Daniels & Walters, 2000) for post-juvenile life-history stages. Recent arguments suggest that ID research should consider complete life-histories with greater effect sizes being correlated with the inclusion of an increasing number of life-stages resulting in underestimates when research is limited to a specific life-stage (Szulkin et al., 2007).

The inconsistent effects of inbreeding and ID across different life-stages highlights the importance of considering potential age-specific disease impacts. Studies looking at the relationship between age, inbreeding and disease in wild populations are rare (Benton et al., 2018) but this is likely due to problems associated with data collection and the construction of inbreeding measures rather than a lack of relationship. With recent advances in statistical and genomic methods these challenges are being overcome revealing evidence for interactions between sex, age, inbreeding and disease in wild badgers (Benton et al., 2018).

Age effects

Senescence (the deterioration of physiological function with increasing age) is an ongoing evolutionary problem with no universally accepted theory for its explanation. The most established theories are the mutation accumulation (MA)

(Medawar, 1957), disposable soma (DS) (Kirkwood, 1977) and antagonistic pleiotropy (AP) (Williams, 1957) theories. MA and AP both rely on the declining force of selection with age: MA suggests that any deleterious mutations that have effects felt later in life will be harder for natural selection to eliminate whereas AP believes that late life damaging mutations could have been favoured in early life if they were initially advantageous. DS is sometimes considered a special case of AP but suggests that organisms have to trade-off between committing energy to reproduction or investing in maintenance of their somas. Senescence is a complex problem and it can affect a variety of different traits including fecundity (Reid et al., 2003), behaviour (Chen et al., 2005) and physiology (Angelier et al., 2007) yet most commonly it refers to an increase in mortality with age known as actuarial senescence (Ricklefs, 2008).

Most non-human studies assessing senescence hypotheses have involved fruit flies (*Drosophila*) and it was long believed that individuals in wild populations did not senesce as they would succumb to environmental pressures (e.g. predation, starvation) long before any age-related decline in survival would manifest. However, the recent emergence of several exemplary, long-term demographic studies, along with some statistical and theoretical advances has revealed patterns of actuarial senescence in a variety of wild populations (e.g. Beirne et al., 2016; Nussey et al., 2013) and shown previous conclusions to be specious. Despite many studies failing to detect senescence in wild populations there is now ample evidence to suggest that it exists for a variety of species with differing life-histories (see Nussey et al. (2008) for a summary). This has prompted an increase in research focused upon understanding the high degree of heterogeneity in longevity and ageing rates which is observed between and among species in the wild. For example, a study into the survival of female red-deer used measures of recent and longer-term reproductive effort as individual- and time-dependent covariates to model survival (Moyes et al., 2006). Although environmental covariates explained a large amount of the variance the inclusion of previous reproductive effort significantly improved the model. Successful reproduction in repeated seasons had previously been shown to have a cumulative and detrimental effect on a variety of health measures (Boyd et al., 1995; Hanssen et al., 2003), but in this study long-term reproductive effort

varied in its effect on survival between different age categories. This study highlights the need to include time-varying individual level covariates to accurately model and understand complex systems. Although studies focused on age related disease effects in wild populations are relatively common (e.g.Beirne et al., 2014; Calvete et al., 2004; Childs et al., 1989; McDonald et al., 2014) very few include age as a continuous variable and in doing so risk losing valuable information.

Modelling complex disease systems

Modelling has been used extensively in epidemiological studies to focus on a variety of different aspects such as disease propagation (Keeling & Rohani, 2011), transmission (Craft, 2015), host survival (McDonald et al., 2014) or to inform management strategies (Levin et al., 2011). Wildlife systems present a unique set of challenges to statisticians and ecologists which are often rooted in the difficulties associated with monitoring wild populations. Any model is a simplified representation of reality (Maunder, 2004) yet to avoid misleading inferences requires an appreciation of environmental and/or demographic stochasticity, differential susceptibility to infection, individual level covariates and the potential for non-constant mortality. Observational data are commonly sourced from long-term capture-mark-recapture (CMR) monitoring projects which rely on accurate identification of individuals within a given population. The benefits of applying CMR methods to epidemiological studies are well reported (e.g. Chang et al., 1995) with the aim being to repeatedly capture and record individuals' disease status along with demographic information to build a picture of species survival and disease effects. As a result of imperfect observation (which is almost unavoidable in the collection of ecological data) most modern statistical methods within this field use a hierarchical structure to separate a latent state from the observed data. This state-space model formulation can then account for the ecological process being partially hidden (King, 2014) (i.e. when individuals are not recaptured). Epidemiological models focus on calculating survival rates from CMR data and are often developed from the Cormack-Jolly-Seber (CJS) (Cormack, 1964; Jolly, 1965; Seber, 1965) structure which defines the probability of capture and survival separately. CJS models make a number of assumptions: every marked animal in the population at

sampling period i has the same probability p_i of being captured; every marked animal present in the population at sampling period i has the same probability φ_i of survival until sampling period $i + 1$; marks are neither lost nor overlooked and always recorded correctly; sampling periods are instantaneous and recaptured individuals are released immediately; all emigration from the sampling area is permanent; the fate of each animal with respect to capture and survival probability is independent of the fate of any other animal. Violations can bias estimates of survival (e.g. Smout et al., 2011) but developments of the CJS modeling framework have overcome some of these assumptions. Of particular relevance here, capture and survival probabilities can vary as functions of environmental and individual covariates (for a review see Pollock, 2002) which has led to the emergence of two main approaches: Generalised Linear Models (GLMs) and multi-state models (MS) (for a comparison see Bonner & Schwarz, 2006). Both model structures can incorporate the effects of continuous covariates that are both individual- and time-dependent and each can be implemented in a frequentist (maximum likelihood) or Bayesian framework.

The nature and complexity of wild populations has promoted Bayesian methods that more readily integrate multiple sources of data and directly model uncertainties in the values of model parameters (Heesterbeek et al., 2015). Bayesian statistical inference explicitly encapsulates our uncertainty about the values of parameters-of-interest through the use of probability distributions. If we have some data that we wish to fit a model to, then we begin by specifying a prior distribution, $f(\theta)$ for the parameters θ, which captures our uncertainty about their values before we fit the model to the current data y. Then we calculate the posterior distribution, $f(\theta|y)$ for the parameters, where:

$$f(\theta \mid y) \propto f(y \mid \theta) f(\theta).$$

The posterior then represents how much our prior beliefs change in the presence of the observed data, where the information about the parameters contained by the data is captured through the likelihood function $f(y|\theta)$. In this way, Bayesian analysis provides a probabilistic representation of our uncertainty in the true values of the model parameters. Further support and use of Bayesian approaches has been driven by statistical advances and

implementation of algorithms such as Markov chain Monte Carlo (MCMC) (Diaconis, 2009; Kass et al., 1997), which produce empirical estimates of the posterior distribution using random sampling. Within wildlife disease epidemiology Bayesian methods have come to the fore as they can provide a probabilistic distribution for unobserved infection statuses (Buzdugan et al., 2016), which can improve lifetime tracking of disease status whilst mediating an underestimation of uncertainty into the analysis (McDonald et al., 2018). For example, Olive et al. (2017) reconstructed the transmission of Rift Valley Fever in Madagascar using Bayesian modelling to estimate the force-of-infection. The nature of this system required links to be made between the results of serological tests, the true serological status of each individual and the annual force of infection; the combination of uncertainties (in terms of true infection status) and the hierarchical structure is well suited to the Bayesian framework. Pradel (2005) extended the MS framework presenting multi-event models based on hidden Markov chains (MacDonald & Zucchini, 1997), which consider imperfect state classification when an individual is captured. Conn & Cooch (2009) used this approach to study the dynamics of conjunctivitis in the house finch (Carpodacus mexicanus) and demonstrated that the inclusion of data with unknown disease states dramatically improved parameter estimates. The influx of studies using Bayesian approaches has led to comparisons of the different methodologies and increasing discussion of the limitations of p values and advantages of Bayesian hypothesis testing (for a review see Marden, 2001) particularly in wildlife disease epidemiology. For example, McDonald et al. (2014) used Bayesian survival trajectory analysis to infer the drivers of sex-specific epidemiology of bovine tuberculosis in a wild population of European badgers showing that sex differences were linked to a greater increase in male mortality following infection.

Many studies have demonstrated the importance of including individual heterogeneity (Lloyd-Smith et al., 2005; VanderWaal & Ezenwa, 2016) within model structures. Although achieved in a variety of ways, the simplicity of adding random effects (that can be individual- and time-varying) in the Bayesian framework is often the preferred approach. This is because all parameters are treated as random variables in a Bayesian model, and thus there is no

theoretical difference between a fixed and random effect in the Bayesian framework, it's simply that the latter has parameters that are dependent on other parameters. This is referred to as a Bayesian hierarchical model – in this way it is possible to account for all sorts of dependence structures between parameters, and the uncertainties involved are treated in a straightforward manner. The ease of modelling time-varying covariates at the individual-level in MS models has led to their predominant use in studies of infectious diseases, as it intuitively allows modelling of time-specific progression through different disease states. The emergence and subsequent development of a number of software packages has simplified the process of implementation for many ecologists and enabled increasingly complex dynamics to be modelled; for example, in a maximum-likelihood framework through programme MARK (White & Burnham, 1999) and software such as E-SURGE (Choquet et al., 2009), and for Bayesian models in WinBUGS (Lunn et al., 2000; Thomas et al., 1992), JAGS (Plummer, 2003), NIMBLE (de Valpine et al., 2017) or Stan (Carpenter et al., 2017) and software such as BaSTA (Colchero et al., 2012). The demand for ever more flexible models to deal with increasingly complex systems requires ecologists to clarify hypotheses and determine when greater complexity is appropriate (Bailey et al., 2014). Over recent years there has been increasing interest in studying disease impacts over complete life courses (Hall et al., 2002) with efforts to include age-specific effects. Commonly this is completed using age categories (e.g. juvenile vs adult) rather than using age as a continuous variable (e.g. Graham et al., 2013) but this risks masking subtle but potentially important mortality dynamics and can lead to potentially erroneous inference. The decision over which approach should be taken will depend on the question being asked, the study system and the quality of the data. Broad comparisons between adults and juveniles may suffice when researchers are less concerned about age-specific effects that occur within a given age class such as senescence. Collecting longitudinal data that allows detailed age-specific effects to be investigated is costly and can require many years (for slow lived species) which will often result in researchers being forced to crudely group information into age classes to retain statistical power. It is important to not overlook the potential drawbacks of using discrete age classes; Colchero et

al. (2018) demonstrated that categorisation can produce markedly different age-specific demographic rates and in the 24 species they studied assuming constant adult mortality was never appropriate. Mortality trajectory analysis considers rates of mortality throughout the entire lifespan, but until recently has been difficult to implement in wild populations. It can provide additional understanding of complex disease systems and identify age-specific effects but requires appropriate selection of a particular mortality function (see following section for examples and explanation). The implementation of this approach has been made easier with the development of software BaSTA (Colchero et al., 2012) but as with many packages its application is limited by its flexibility to accommodate the intricacies of specific systems.

Pressure from policy makers for more detailed understanding of complex epidemiological systems has elevated the importance of this area of research – to help solve these problems we need to better integrate data from a variety of sources. Integrated population models (IPMs) are a recently developed approach used for the estimation of population trends and demographic parameters which combine multiple independent sources of data into a single statistical framework (Besbeas et al., 2002; Tempel et al., 2014). They can offer increased parameter precision and potentially improve conservation modelling (Fitsum et al., 2010) but so far their use in 'real-world' situations has been rare (but see Tempel et al., 2014). The next step for wildlife disease epidemiological research is to use IPM style frameworks that can utilise data and analysis from a range of different sources to build models of disease systems that include all sources of possible variation; this approach has the potential to narrow the possibility/expectation gap between academic researchers and disease managers.

Commonly used mortality functions

A range of different functions have been used to model mortality; the simplest of which is the exponential model (Cox & Oakes, 1984) which describes constant mortality throughout life. The Gompertz model (Gompertz, 1825) is arguably the most commonly used function and although developed to describe human mortality has been used extensively across a wide variety of species. It uses 2

parameters and describes mortality as increasing exponentially (rate = b_1) from an initial level (b_0), with b_1 often being interpreted biologically as the senescence parameter. The British actuary William Makeham felt that the Gompertz model could be improved by partitioning causes of death into age dependent (intrinsic) and age independent (extrinsic) sources through the addition of a single parameter: the Makeham term (which represents age-independent mortality) leading to the Gompertz-Makeham mortality model (Makeham, 1867). The partitioning of mortality was further developed by William Siler who developed the competing risks model for animal mortality by splitting lifetime mortality into 3 competing functions (Siler, 1979). The first (a declining Gompertz) describes an early life decline in mortality from birth through to the second: a baseline level which describes adult mortality (the Makeham term) before the third: a senescent increase in mortality dominates in later life (the standard Gompertz function) – put together this model describes the classic 'bathtub' shape. At a similar time Pinder et al. (1978) suggested using the 2 parameter Weibull distribution to describe survivorship data. The shape parameter controls the rate of change of the age-specific mortality rate and together with the scale parameter it allows a wide variety of shapes to be modelled and compared. All of these functions have faced some criticism for not accommodating individual heterogeneity which led to the development of the logistic model (Vaupel et al., 1979) which uses a specific scaling parameter which then allows for heterogeneity in frailty to be modelled, this is often categorised by a levelling of mortality rates in very late life. Although many other models have been used to describe survivorship data those outlined here are the most common and will constitute those used in this thesis.

Implications and future research

Modelling wildlife disease has informed management policy in a variety of different contexts across the globe (e.g. rabies - for a review see Sterner & Smith, 2006; chronic wasting disease - Wasserberg et al., 2009; bovine tuberculosis - Stringer & Linklater, 2014) and remains an ongoing challenge with the understanding that human, animal and ecosystem health are intrinsically linked with regard to emerging zoonotic disease (Alexander et al., 2012). Accurate modelling of infectious disease allows for the identification and

evaluation of management strategies which can broadly be grouped by their overall aim: prevention of disease transmission to humans or livestock, or conservation of host species and research. In the United States managers attempted to eradicate chronic wasting disease in white-tailed deer through culling and an extension of the hunting season, whilst still contending with uncertainties in certain aspects of the disease system. After five years prevalence of the disease was still on the increase (Heisey et al., 2010) confirming previous models of the system to be inadequate and highlighting the need for a more complete understanding of the system whilst promoting evolution of the epidemiological models.

Here we have identified and reviewed three major sources of variation in response to infectious diseases in wild populations. Senescence and inbreeding depression have historically been thought of as redundant topics when investigating species in the wild, yet recent research has revealed that they cannot be ignored. Modelling wildlife disease has seen many advances in recent years and consistently identifies age effects as a notable source of variation yet the majority of studies continue to model age in discrete categories which we believe results in information loss and potentially biased inferences. There is an increasing body of evidence for links between inbreeding and ageing, inbreeding and disease and sex and disease but very few studies have considered the interaction between age, sex, inbreeding and disease particularly in a natural population. The monitoring of a population of wild badgers naturally infected with bovine Tuberculosis in Woodchester Park, Gloucestershire provides an exceptional longitudinal dataset (1975–present) describing a wild reservoir of an economically important zoonotic disease. This dataset provides the unique opportunity to investigate age- and sex-specific effects of inbreeding on an infectious disease in a wild population to better inform management strategies whilst advancing epidemiological modelling approaches.

Aims and structure of thesis

In this thesis we explore and develop a number of innovative modelling frameworks to conduct Bayesian survival and mortality analysis to investigate the epidemiology of bovine Tuberculosis in a natural population of European badgers.

In chapter 2 we use a dedicated software package that introduces Bayesian survival trajectory analysis and the benefits that it potentially offers. Here we investigate sex- and infection-specific variation in survival and mortality but uncover limitations in the flexibility of the software.

Chapter 3 charts the development of flexible modelling techniques to carry out Bayesian survival and mortality trajectory analysis from first principles. We also conduct a detailed analysis of the Siler (Siler, 1979) competing risks model of mortality which describes the classic ‘bathtub’ shape of lifetime mortality.

In chapter 4 we employ the modelling framework of chapter 3 to analyse survival data. Here we focus on model comparison and develop an efficient approach based on importance sampling that enables multi-model inference techniques such as Bayesian model averaging to be used.

Chapter 5 extends the approaches presented in chapter 4 making them applicable to capture-mark-recapture (CMR) data, common within ecological research. We also take a focused look at the challenges of recording and reporting early life survival and mortality dynamics using CMR.

In chapter 6 we compare our importance sampling approach to model comparison to another Bayesian method that is rare within ecological research: Reversible Jump Markov Chain Monte Carlo (RJMCMC). We demonstrate the straightforward nature of its use and highlight potential benefits.

We then utilise the RJMCMC approach in chapter 7 to investigate inbreeding effects on age-, sex- and infection-specific mortality in the same wild population of European badgers that we analysed in chapter 2. We provide evidence for the two dominant evolutionary theories of senescence with implications for wildlife disease management and conservation strategies.

Finally in chapter 8 I provide a synthesis of results, discuss potential implications and suggest possible directions for future work.

Throughout this thesis I use the term "*we*" as per publication standard and for consistency. It does not mean that any part of this thesis is not my own work.

Chapter 2: Analysis of Lifetime Mortality Trajectories in Wildlife Disease Research: BaSTA and Beyond

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Abstract:

Wildlife hosts are important reservoirs of a wide range of human and livestock infections worldwide, and in some instances, wildlife populations are threatened by disease. Yet wildlife diseases are difficult to monitor, and we often lack an understanding of basic epidemiological parameters that might inform disease management and the design of targeted interventions. The impacts of disease on host survival are generally associated with age, yet traditional epidemiological models tend to use simplistic categories of host age. Mortality trajectory analysis provides the opportunity to understand age-specific impacts of disease and uncover epidemiological patterns across complete life histories. Here, we use Bayesian survival trajectory analysis (BaSTA) software to analyse capture-mark-recapture data from a population of wild badgers (*Meles meles)* naturally infected with *Mycobacterium bovis*, the causative agent of tuberculosis in badgers and cattle. We reveal non-constant mortality trajectories and show that infection exaggerates an age-dependent increase in late-life mortality. This study provides evidence for actuarial senescence in badgers, a species previously believed to display constant mortality throughout life. Our case study demonstrates the application of mortality trajectory analysis in wildlife disease research, but also highlights important limitations. We recommend BaSTA for mortality trajectory analysis in epidemiological research, but also suggest combining approaches that can include diagnostic uncertainty and the movement of hosts between disease states as they age. We recommend future combinations of multi-state and multi-event modelling frameworks for complex systems incorporating age-varying disease states.

Introduction

Investigating the epidemiology of any disease in wild populations is challenging because of the practical difficulties in monitoring both infections and their wild hosts (Delahay et al., 2009), yet wildlife hosts are important contributors to many emergent and widespread infections of humans and livestock worldwide (Gortázar et al., 2007). Consequently, any improvements in our understanding of wildlife disease epidemiology can be beneficial to human health, animal welfare and productivity, as well as to biodiversity conservation (Delahay et al., 2009; Wiethoelter et al., 2015). Disease-related mortality is a critical parameter

in any epidemiological model (Heisey et al., 2006) and methods for its estimation, developed for the study of human populations, are now commonly used in studies of wildlife (Samuel et al., 2015). Disease can increase rates of host mortality (Frick et al., 2010; Kilpatrick et al., 2010) and in extreme cases can contribute to decline and risks of species' extinction (Berger et al., 2016; van Riper et al., 1986). Disease-induced mortality is commonly modelled as a simple increase in otherwise fixed mortality rates at particular life stages (Samuel & Storm, 2016; Wilkinson et al., 2000) but the reality can be much more complex. Mortality trajectories reveal patterns in age-specific mortality that are often missed when using fixed rates in discrete age classes, yet the inclusion of these trajectories in epidemiological models is rare. The ability to accurately model factors that influence mortality is fundamental to any demographic investigation and the inclusion of mortality trajectories could offer greater precision whilst uncovering subtle variations in the patterns of age-specific mortality. Here we show that the inclusion of disease status, alongside full mortality trajectory analysis, can reveal disease-induced changes in the shape of lifetime schedules of mortality.

Predicted increases in the proportion of the global human population living over the age of 80 (Fontana et al., 2014) have attracted substantial economic investment and scientific interest (Hayflick, 2000) in age-associated diseases in humans. Disease effects have been shown to vary with age in both humans (Haas et al., 2008) and now non-human animals (Jorgenson et al., 1997). While such variation can have a direct impact on population size (Larsen et al., 2007), empirical studies of age-specific causes of mortality in wild populations are scarce (Koons et al., 2014). The decline of physiological function with age (i.e. senescence) can affect fecundity (Reid et al., 2003), morphological traits (Reimers et al., 2005), behaviour (Chen et al., 2005) and physiology (Angelier et al., 2007) but most commonly it refers to an increase in the rate of mortality with age, known as actuarial senescence (Ricklefs, 1998). A long-standing belief that environmental factors would result in an animal's death long before the impact of senescence became manifest, has now been shown to be false (Nussey et al., 2013). The emergence of several high-quality, long-term demographic studies, combined with theoretical and statistical advances, have

since revealed senescence in many wild populations of various species, and have promoted the study of factors affecting senescence in the wild. Traditional approaches in wildlife epidemiology have focused on estimating fixed mortality parameters for a finite and predetermined number of age categories (e.g., cubs versus adults - Graham et al., 2013) which results in the loss of information and risks unnecessarily coarse conclusions. Mortality trajectory analysis, which considers rates of mortality through the entire lifespan is a means of mitigating some of these problems, but until recently has been difficult to employ with wildlife populations. This is because of several statistical challenges (Nussey et al., 2008) as well as the requirement to monitor marked individuals through entire life histories (Nussey et al., 2013). Furthermore, the accurate interpretation of mortality trajectories and their associated parameters requires ecological understanding of a species' behaviour and life strategies (Ricklefs & Scheuerlein, 2002), as well as suitable model selection through comparisons of model fit. If an inappropriate model is fitted to the data, then subsequent conclusions are often specious.

Several mathematical functions have been used to describe lifetime trajectories of age-specific mortality. Historically the preferred choice was the Gompertz curve (Gompertz, 1825) which describes mortality as increasing exponentially with age from an intercept representative of an initial baseline risk of death. The more flexible Weibull distribution (Pinder et al., 1978) has recently been used in survivorship analysis and can accommodate accelerating increase, decelerating increase, decreasing and constant mortality (Colchero & Clark, 2012) but can fail to capture early decelerations in mortality rates. Makeham (Makeham, 1867) proposed that death could be separated into age-dependent and age-independent sources, resulting in the addition of a 'Makeham' term (a constant) to established mortality functions (e.g. Gompertz-Makeham, Weibull-Makeham etc.). Criticism of these models has focused on the omission of individual heterogeneity, leading to potentially flawed statistical inference (Cam et al., 2016): development of the logistic model has been proposed as a solution (Vaupel et al., 1979). This model accommodates individual variation as a decrease in mortality at advancing ages (i.e. individual frailty; frail individuals tend to die younger, leaving more robust individuals as survivors) (Jones et al.,

2014; Pletcher, 1999; Vaupel et al., 1998). Although these functions have been applied across a variety of species (e.g. Barthold et al., 2016; Ricklefs & Scheuerlein, 2001), support for them is mixed and it is often difficult to deduce whether uncertainty in parameter estimates is evidence of absence (the parameter is not important) or absence of evidence (the data do not provide sufficient signal to help infer the parameter). Life histories can be split into distinct phases each with an individual mortality signature. Caughley (1966) identified 3 stages: juvenile (characterised by relatively high mortality), adult (with relatively low mortality), and senescent (increasing rates of mortality in later life). When combined these stages form a 'U' shape or 'bathtub' mortality curve which can capture complex patterns of mortality over complete life histories (e.g. the Siler function - Siler, 1979). The use of mortality trajectories and the separation of life stages allows us to unravel subtle changes in mortality and identify actuarial senescence, hereafter referred to as senescence. This combining of mortality models to accommodate different life stages has found support in a variety of species (Bebbington et al., 2007; Klutke et al., 2003; Snoke & Promislow, 2003) and has helped to reveal some of the drivers (McDonald et al., 2014) of age-specific patterns of mortality and senescent variation.

To evaluate the use of mortality trajectories and investigate patterns of age-specific mortality, we use data from a long-term study of a population of European Badgers (*Meles meles*) naturally infected with *Mycobacterium bovis*, the causative agent of bovine tuberculosis (bTB). In the United Kingdom, badgers are the primary wild maintenance host for bTB (Delahay et al., 2013) and in some locations contribute to the persistence of infection in cattle populations (Donnelly et al., 2006). Being able to discern patterns of mortality and distinguish between groups in terms of disease susceptibility may help inform approaches to managing infection in badgers, thereby reducing risks of onward transmission to cattle. The epidemiology of bTB in badgers has been the focus of many studies (for a review see Gallagher & Clifton-Hadley, 2000) yet the use of mortality trajectories, using age as a continuous variable, has to our knowledge been implemented only once. McDonald et al. (2014) used Bayesian survival trajectory analysis (BaSTA) (Colchero et al., 2012) to identify

sex differences in mortality from the point of infection and infer the mechanisms underpinning them. Increased mortality as a result of bTB infection in male badgers is already known (Graham et al., 2013; Wilkinson et al., 2000) but this was further dissected to identify where in the infection process the sex differences arose (McDonald et al., 2014). These analyses, however, do not capture the full lifetime trajectory of mortality in badgers and cannot reveal actuarial senescence. Here we study mortality trajectories by using cubs of known age and known infection status to analyse disease-related mortality trajectories across entire life histories. Previous analyses of badger mortality have suggested that badgers show no evidence of actuarial senescence (Wilkinson et al., 2000) but these conclusions were based on static life table data so may not be an authentic representation of badger life histories.

In the following analyses, we use Bayesian approaches to demonstrate the benefits of using age-specific mortality trajectories to reveal when and how sex differences in disease-induced mortality occur. Research employing mortality trajectory analysis commonly recognises sex and individual heterogeneity (Colchero et al., 2017; Tidière et al., 2015) as critical drivers of mortality although environmental variation has also been considered (Lemaître et al., 2013; Nussey et al., 2013). Males are often more susceptible to infection (Klein, 2000), have a weaker immune response (Møller, 1987) and greater disease induced mortality (Graham et al., 2013; Wilkinson et al., 2000) stemming from physiological variation (Zuk & McKean, 1996) or behavioural and ecological differences that result in males being more likely to become infected (McDonald et al., 2014). Sex differences are not consistent across all species and our understanding of the complex nature of sex-influences on ageing patterns is far from complete (Berger et al., 2016). Long-lived species are more likely to display negligible or negative patterns of senescence (Baudisch, 2011) but by using BaSTA to assess mortality trajectories we uncover complex age- and sex-specific patterns of mortality that vary with infection status. We also reveal important limitations of standard mortality trajectory analysis for epidemiological research, including age-dependent predictors (disease state changes with age) and diagnostic uncertainty (tests for infection vary in their sensitivity and specificity towards the target pathogen (McDonald & Hodgson, 2018). We

discuss alternative modelling strategies that will help to deal with these limitations.

Materials and Methods

Ecological data

We used capture-mark-recapture (CMR) data from a population of wild badgers naturally infected with *Mycobacterium bovis* in Woodchester Park, Gloucestershire. Data for the present study consisted of badgers trapped from 1982 to 2015 inclusive. The badger population was sampled using live-traps on (usually) four occasions per year. All trapped badgers are anesthetised and subjected to several diagnostic tests for bTB before being released (for a more detailed account of the trapping and testing procedures, see Delahay et al., 2000; McDonald et al., 2018). On first capture each badger is given a unique identifying tattoo so that it can be identified at subsequent captures. Although difficult to test completely due to behavioural differences between individual badgers, previous studies have shown the probability of recapturing marked individuals is no different to unmarked individuals (i.e. no evidence of trap shyness/dependence) (Rogers et al., 1997).

Diagnostic tests

Samples of sputum, faeces, urine and swabs of any abscesses or wounds were taken for *M.bovis* culture (Gallagher & Horwill, 1977) as well as blood samples obtained for antibody tests as follows:

Brock ELISA (Goodger et al., 1994) - used from 1982 to 2006

BrockTB Stat-Pak lateral flow immunoassay – Chembio Diagnostics Systems, USA; (Chambers et al., 2008) - used from 2006 to 2015

We used badgers of known age (i.e. badgers caught as cubs) and categorised them as ‘cub-positive’ if they tested positive to either the Brock ELISA, Stat-Pak or culture during the first year of their lives, and ‘never-positive’ if they never tested positive to any test throughout their lives (sex was also included as a categorical covariate for each group). The distinction between these two groups allows for the comparison of disease effects on mortality trajectories across entire life histories, and identification of where variations occurred. The analysis

of age-dependent acquisition of disease requires a more complex modelling framework, but for this analysis we filtered out any badgers that acquired test-positive status beyond the first year of life (see discussion for commentary on the risk of bias). We also recognise that the diagnostic tests employed in this study have limitations in terms of their sensitivity (Brock ELISA: 40.7% - Clifton-Hadley et al., 1995; Stat-Pak: 97%; culture: 10% - Drewe et al., 2010), yet all the tests used are highly specific (Brock ELISA – 94-98% - Goodger et al., 1994; Stat-Pak – 97% - Buzdugan et al., 2016; Culture – 100% - Drewe et al., 2010). As a result, we are confident that individuals diagnosed as infected are very rarely truly uninfected, but can be rather less confident that individuals diagnosed as uninfected are truly uninfected. Our classification of 'never-positive' removes some of this uncertainty, as an individual is required to have tested negative throughout their capture history and is not reliant on a single diagnostic test result - (see discussion for implications).

Ongoing research seeks to clarify links between diagnostic outcomes and infection status (Buzdugan et al., 2016; Wawegama et al., 2016) but for the purposes of our analyses here, we worked with diagnostic results rather than true infection status.

Badgers caught and identified as cubs were assigned a birth occasion as the first trapping season for the year of first capture, as the majority of cubs are born between February and March each year (Kullback & Leibler, 1951). Badgers recovered dead were assigned a known death occasion as the time of the *post-mortem* examination.

Analysis

To understand age-specific mortality patterns in badgers and how their mortality trajectories are affected by diagnosis of bTB infection we used the package BaSTA (Colchero et al., 2012) in R (R Core Team, 2019). This package implements a hierarchical Bayesian model (for full details and likelihood functions see Colchero & Clark, 2012) and draws inference on age specific survival from CMR data when large portions of the data consist of unknown birth and death years. Age-specific survival analysis requires the definition of mortality or hazard rate (for continuity we use the term mortality throughout the

remainder of the thesis): we define a random variable X for ages-at-death, where $X > 0$, with any given age represented by (lower case) x. Standard theory of survival models defines the *mortality function* (i.e. the instantaneous rate of death (Kalbfleisch & Prentice, 2002), given survival to age x) as

$$\mu(x \mid \mathbf{b}) = \lim_{\Delta x \to 0} \frac{\Pr(x < X < x + \Delta x \mid X > x, \mathbf{b})}{\Delta x}, \tag{2.1}$$

where $\mathbf{b}$ is a vector of mortality parameters to be estimated and Δx is some very small time period. The *cumulative mortality function* H, at age x, t years later is then defined as

$$H(x \mid \mathbf{b}) = \int_0^x \mu(t \mid \mathbf{b})\, dt. \tag{2.2}$$

From equation (2.1) and (2.2) it is possible to derive the survival function, S as

$$S(x \mid \mathbf{b}) = \Pr\{X > x \mid \mathbf{b}\} = \exp\left[-H(x \mid \mathbf{b})\right] \tag{2.3}$$

and the probability density function (pdf) of ages at death as

$$f(x \mid \mathbf{b}) = \Pr\left(x \le X < (x + \Delta x)\right) = S(x \mid \mathbf{b})\, \mu(x \mid \mathbf{b}) \tag{2.4}$$

BaSTA allows for comparison of four different functional forms of the mortality function in equation (2.1) (Exponential, Gompertz, Weibull and Logistic) as well as the extension of the latter three to incorporate more complex shapes. The inclusion of a 'Makeham' (Makeham, 1867) term models the effect of age-independent mortality c. The further addition of a declining Gompertz function then allows the exploration of 'bathtub' mortality shapes. In total we compared ten different forms of mortality function (Table 2.1).

Table 2.1 Basic mortality and survival probability functions available to test in BaSTA, namely: exponential, Gompertz, Weibull and logistic. Additional terms can be added to each model (except exponential) to test different shapes, namely: 'Makeham' and bathtub. Parameter constraints are also indicated.

	Mortality rate	***Survival probability***	***Parameters***
	$\mu_b(x\|\boldsymbol{b})$	$S_b(x\|\boldsymbol{b})$	
Exponential	b_0	e^{-bx}	$b_0 > 0$
Gompertz (Gompertz, 1825)	$exp(b_0 + b_1 x)$	$exp\left[\frac{e^{b_0}}{b_1}(1 - e^{b_1 x})\right]$	$-\infty < b_0, b_1 < \infty$
Weibull (Pinder et al., 1978)	$b_0 b_1 (b_1 x)^{b_0 - 1}$	$exp[-(b_1 x)^{b_0}]$	$b_0, b_1 > 0$
Logistic (Vaupel et al., 1979)	$\frac{exp(b_0 + b_1 x)}{1 + \left(\frac{e^{b_0}}{b_1}\right) b_2 (e^{b_1 x} - 1}$	$\left(1 + b_2 \frac{e^{b_0}}{b_1}(e^{b_1 x} - 1)\right)^{-1/b_2}$	$b_0, b_1, b_2 > 0$

The Makeham structure consists of adding a constant c to the mortality:

$$\mu_b\left(x\,|\,\mathbf{b},c\right) = c + \mu_b\left(x\,|\,\mathbf{b}\right) \tag{2.5}$$

$$S_b\left(x\,|\,\mathbf{b},c\right) = e^{-cx} S_b\left(x\,|\,\mathbf{b}\right) \tag{2.6}$$

with $c > 0$ if $\mu(x)$ is declining or $c > -\mu(0)$ otherwise. The bathtub structures are constructed by adding a declining Gompertz function and a constant to the basic mortality:

$$\mu_b\left(x\,|\,\mathbf{b},a,c\right) = e^{a_0 - a_1 x} + c + \mu_b\left(x\,|\,\mathbf{b}\right) \tag{2.7}$$

$$S_0\left(x\,|\,b,a,c\right) = \exp\left[\frac{e^{a_0}}{a_1}\left(e^{-a_1 x} - 1\right) - cx\right] S_b\left(x\,|\,\mathbf{b}\right) \tag{2.8}$$

with $-\infty < a_0, < \infty$, $a_1 > 0$, and $c > -[e^{a_0 - a_1 x_{min}} + \mu_b(x_{min}|\mathbf{b})\,]$, where x_{min} is the age at which equation 5 is at its lowest values.

Examples of the shapes of mortality trajectory that can be defined by these models are shown in Figure 2.1.

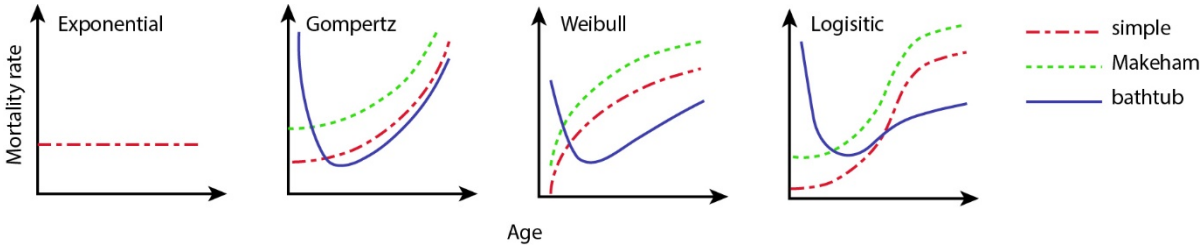


Figure 2.1 Possible mortality trajectories, $\mu(x|\boldsymbol{\theta})$ when $\boldsymbol{\theta}$ is a vector of mortality parameters to be estimated, resulting from the four models included in BaSTA. Mortality rate is shown on the *y*-axis, with age as a continuous variable on the *x*-axis. The line styles represent examples of each model shape that are possible to test: simple, Makeham, and bathtub. The exponential model is only applicable in a simple format.

The models in Table 2.1 define parameters and describe mortality in four different ways: 1) exponential, in which the model assumes mortality to be constant and independent of age; 2) Gompertz (Gompertz, 1825) in which the model describes baseline mortality ($\boldsymbol{b_0}$) and an exponential increase with age ($\boldsymbol{b_1}$); 3) Weibull (Pinder et al., 1978) in which $\boldsymbol{b_0}$ is the shape parameter and $\boldsymbol{b_1}$ is the scale parameter, the model assumes that mortality increases (or decreases) as a power function of age; and 4) logistic (Vaupel et al., 1979) in which the model consists of an initial exponential increase in mortality that decelerates to a plateau after a particular age. The $\boldsymbol{b_2}$ parameter describes the degree of deceleration in mortality with age. Bathtub variants of the models include a declining Gompertz function $\boldsymbol{e^{a_0 - a_1 x}}$ where $\boldsymbol{a_0}$ represents initial mortality rate at birth and $\boldsymbol{a_1}$ is the exponential decrease in age-dependent mortality from birth.

Badger sex and infection status ('cub-positive' or 'never-positive) were included as categorical covariates and incorporated into the models as linear functions of the survival parameters, for example in a Gompertz mortality function:

$$\mu(\boldsymbol{x}\,|\,\boldsymbol{\theta}) = \exp\left[\overbrace{\left(\boldsymbol{a}^T\boldsymbol{z}\right)}^{b_0} + \overbrace{\left(\boldsymbol{\beta}^T\boldsymbol{z}\right)}^{b_1} x\right] \tag{2.9}$$

where $\boldsymbol{\alpha^T}$ and $\boldsymbol{\beta^T}$ are transposed vectors of linear coefficients that link the covariate $\boldsymbol{z}$ with the survival parameters $\boldsymbol{b_0}$ and $\boldsymbol{b_1}$ such that $\boldsymbol{\theta} = (\boldsymbol{\alpha}, \boldsymbol{\beta})$. Covariates are included for all parameters in each model structure.

To ensure model convergence, initial trials of four Markov Chain Monte Carlo (MCMC) chains were run for each model followed by 1,000,000 iterations, with a burn-in of 10,001 iterations and thinning every 100 iterations (Gelman et al., 2014). Convergence was assessed visually ensuring mixing of the chains and formally within each model using the potential scale reduction ($\widehat{\boldsymbol{R}}$) (Colchero & Clark, 2012). Convergence is reasonable when $\widehat{\boldsymbol{R}} \approx \mathbf{1}$. We assessed the sensitivity of the mortality parameters to the choice of prior distributions (Kass & Raftery, 1995) by running the analysis under four different prior structures and found there to be no differences in the selection or identification of parameters as a result.

The fits of the ten models were compared using their deviance information criterion (DIC) (Spiegelhalter et al., 2002) which is a measure of predictive power and criterion for model fit akin to the Akaike information criterion and the Bayesian information criterion (for a review of its use see Spiegelhalter et al., 2014). To evaluate the impact of categorical covariates BaSTA uses an adapted version of the Kullback-Liebler discrepancy (Kullback & Leibler, 1951; McCulloch, 1989) which estimates the degree of overlap in the posterior distributions of the parameter estimates. This indicator provides a value for $\boldsymbol{k_\beta} \in [\mathbf{0.5}, \mathbf{1}]$ for a given parameter $\boldsymbol{\beta}$ (0.5 indicating full overlap, 1 meaning no overlap); $\boldsymbol{k_\beta} \approx \mathbf{0.65}$ is generally interpreted as indicative of a difference between means that is unlikely to occur if the distributions of the two variables were the same (Larson et al., 2016).

Recapture probabilities were modelled as fully time-dependent, allowing the parameter estimate to vary for each occasion. Sample sizes for each type of datum are provided in Table 2.2.

Table 2.2 Summary of capture-mark-recapture datasets describing badgers in one of two health states: “cub-positive” (badgers that tested positive in the first year of their lives) and “never-positive” (badgers that have never tested positive throughout their lives). Known birth years refers to cubs captured and identified as being within the first year of their lives. Known death years refers to badgers who were recovered dead and subjected to post-mortem. Detections are the total number of capture events that took place over the duration of the study.

	Cub-positive	**Never-positive**
Total number badgers	428 (M 191; F 237)	1768 (M 833; F 935)
Number of known birth years	428	1768
Number of known death years	13	323
Total number of detections	2515	7588

Results

The Gompertz bathtub or Siler (Siler, 1979) function was the most supported mortality model across both the ‘cub-positive’ (Figure 2.2a) and ‘never-positive’ (Figure 2.2b) badger datasets with substantial support as the ‘best’ model and clear difference in DIC to the nearest rival model (Table 2.3). The Siler model is the sum of three different mortality models: the first describing a decrease in mortality over the initial phase of life with e^{a_0} being the initial level and a_1 modelling the rate of decrease. The central ‘Makeham’ term is a constant mortality which is independent of age and the final term is a Gompertz function which describes mortality as increasing exponentially with a rate of b_1 from an initial level e^{b_0}.

Table 2.3 Ranked list of proposed mortality functions fitted to data from a wild population of European badgers naturally infected with *bovine tuberculosis*. Badgers were separated into two health states (cub-positive – tested positive in the first year of their lives; never-positive – never tested positive throughout their lives). Deviance information criterion (DIC) values given for each model and corresponding differences (ΔDIC) from the 'best' model. Substantial support for the 'best' model is indicated when rival models have ΔDIC > 3 (Bronikowski et al., 2011).

Cub-Positive (in rank order by DIC)				**Never-Positive**			
Model	**Shape**	**DIC**	**△DIC**	**Model**	**Shape**	**DIC**	**△DIC**
Gompertz	Bathtub	4622	0	Gompertz	Bathtub	25678	0
Gompertz	Simple	4642	20	Exponential	Simple	25693	15
Logistic	Bathtub	4661	39	Weibull	Bathtub	25695	17
Weibull	Bathtub	4669	47	Weibull	Makeham	25954	276
Weibull	Makeham	4675	53	Logistic	Makeham	25975	297
Logistic	Makeham	4682	60	Logistic	Simple	25982	304
Weibull	Simple	4689	67	Gompertz	Makeham	26004	326
Logistic	Simple	4697	75	Logistic	Bathtub	26048	370
Gompertz	Makeham	4710	88	Gompertz	Simple	26136	458
Exponential	Simple	4741	119	Weibull	Simple	26235	557

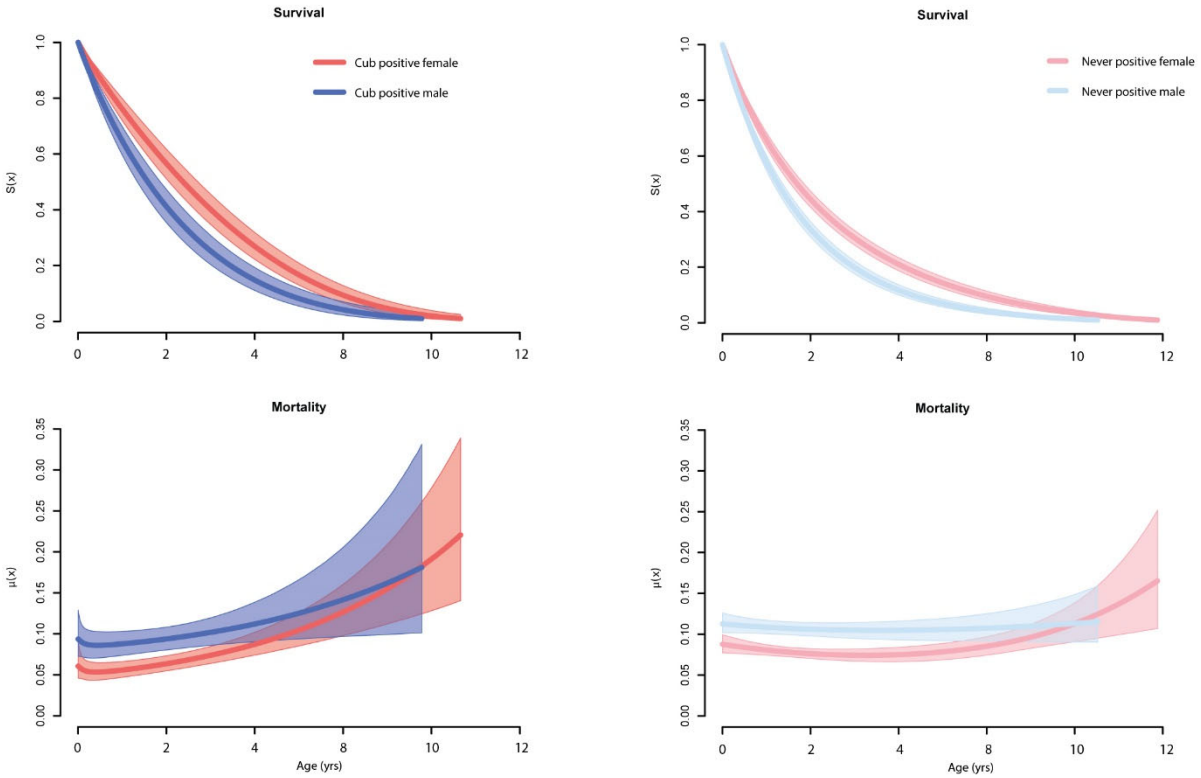


Figure 2.2 Age-specific survival and mortality trajectories of European badgers from a wild population naturally infected with *bovine tuberculosis*. (a) 'cub-positive' individuals (badgers that tested positive in the first year of their lives). (b) 'never infected' individuals (badgers that never tested positive throughout their lives). Female (red) and male (blue) estimated survival and mortality curves of the Siler function. Coloured areas surrounding the curve represent 95% credible intervals. Age in ¼ years.

Having revealed sex-, disease- and age-specific patterns of mortality we then analysed the entire dataset using the Siler function with disease status and sex as individual level categorical covariates creating four different groups (cub-positive male, cub-positive female, never-positive male, never-positive female). We assessed model fit by producing Kaplan-Meier plots of observed survival against predicted survival trajectories (Appendix 1) and were satisfied that the Siler function and posterior parameter estimates were appropriate. We compared the posterior distributions between groups for each mortality parameter both visually and using an adapted version of the Kullback-Liebler discrepancy (Kullback & Leibler, 1951) proposed by McCulloch (McCulloch, 1989) (Figure 2.3). The discrepancy measure works on the log of estimated

probabilities and due to the posterior densities of the a_1 parameters between 'cub-positive' and 'never-positive' female badgers being so different the estimated probability produced zeroes which in turn produced NA in the Kullback-Liebler calculations.

Badgers diagnosed as infected shared very similar patterns of age-dependent mortality with the only gender difference in mortality trajectories lying within the Makeham/age-independent parameter (c). 'Never-positive' badgers displayed a greater degree of dissimilarity between the sexes. Male badgers had greater age independent mortality (c) and initial 'at birth' mortality rates (a_0) which follows previous research (Delahay et al., 2006; Wilkinson et al., 2000); however, we also uncovered sex variation in the senescent phase (b_0 and b_1) of the mortality trajectory. 'Never-positive' male badgers fail to display any evidence of a senescent decline in survival whereas female badgers spend the majority of their lives with a comparatively lower mortality rate until the later phase of their lives, when they display a much clearer pattern of senescence. Infection raised the initial mortality rate (a_0) and intensified the senescent decline (b_1) in survival for both sexes, inducing a pattern of senescence in male badgers.

The parameter estimates also uncovered a lack of any real decline in mortality during the juvenile phase of the life history (a_1) for 'never-positive' individuals (male a_1 = 0.05, female a_1 = 0.06) as well as extremely flat posteriors for 'cub-positive' individuals suggesting a lack of certainty. This pattern of mortality is further supported by the second 'best' model being the simple exponential ('never-positive') and simple Gompertz ('cub-positive'), neither of which define an initial phase of reducing mortality for uninfected badgers.

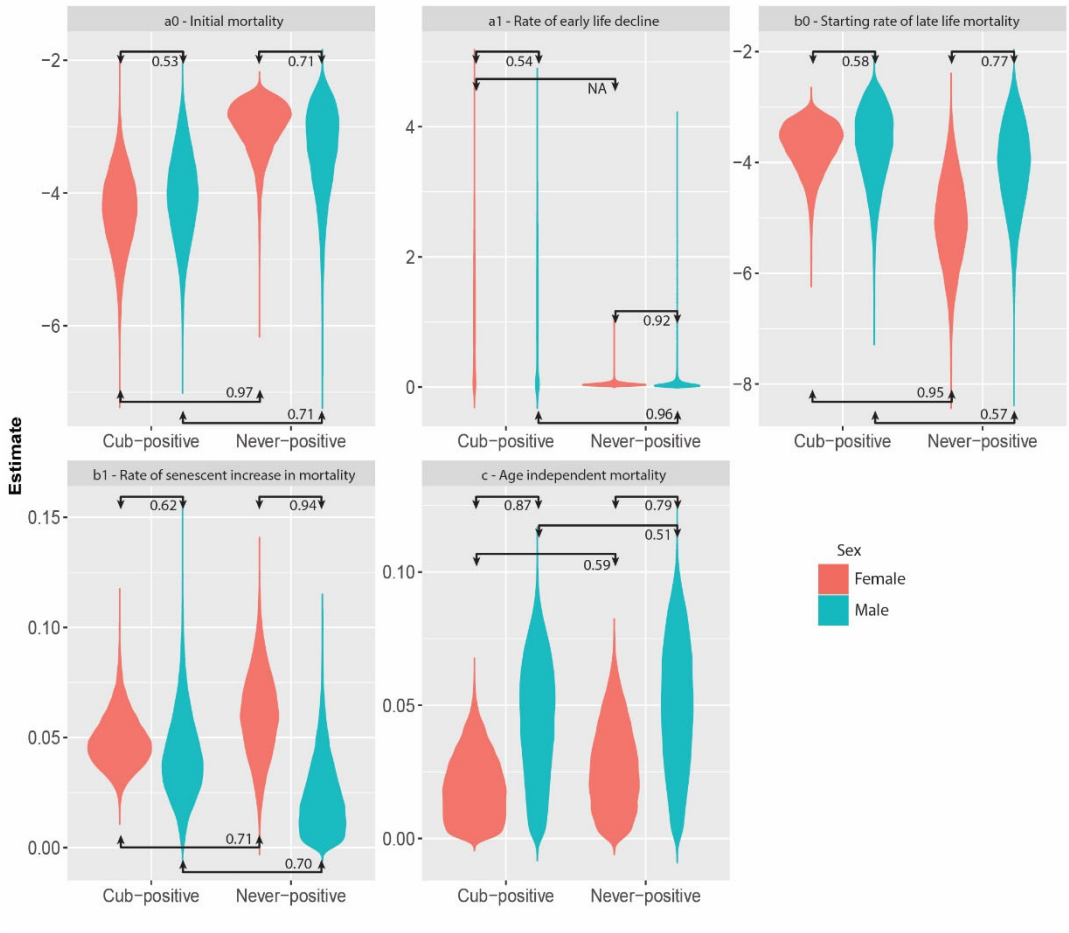


Figure 2.3. Posterior distributions of mortality trajectory parameter estimates for a population of wild European badgers naturally infected with bovine tuberculosis. Female (red) and male (blue) posterior distributions of mortality parameters of the Siler function, split by infection status. “Cub-positive” refers to individuals who tested positive in the first year of their life. “Never-positive” refers to individuals who never tested positive throughout their lives. Adapted Kullback–Liebler discrepancy measures are shown in black, indicating the degree of distribution overlap between classifications of sex and disease status. Measures over 0.65 are considered important (0.5 = distributions are identical, 1 = no overlap). Iterations = 1,000,000; burn in = 10,001; thinning = 200; number of chains = 4. (For table of estimates and 95% confidence intervals, see Appendix 1)

Discussion

Mortality trajectory analysis has revealed complex, age-specific patterns of mortality, and provided evidence of actuarial senescence in badgers, a species previously believed to display near-constant rates of mortality throughout life. Our results discern the impact of bTB infection on wild badgers and has allowed us to estimate where in a species' life history disease- and sex-differences occur.

The inclusion of age as a continuous variable enabled us to generate mortality trajectories and clarify age-specific sex differences. In our case study, we found "never positive" male badgers to have a higher initial mortality rate (compared to females), which appears to decline with age, yet "never-positive" females show a more intense increase in later life (senescence). Higher rates of mortality in males resemble the sex bias evidenced across other mammalian species (Bronikowski et al., 2011). Explanations for higher rates of mortality among males include differences in intra-sexual reproductive competition (Beirne et al., 2015), physiology (Zuk & McKean, 1996) and behaviour (Byrnes et al., 1999) and ecology (Delahay et al., 2006). In addition to an age-independent sex difference, the male bias in juvenile mortality hints at differences in physiology being the key driver: although behavioural differences could appear, ecological explanations are unlikely to have come into effect at this early stage of a badger's life. An unanticipated result was the more intense senescent increase in mortality with age found in female badgers. Males do not live as long as females (11% reduction in lifespan irrespective of infection status), and it is possible that this reduced lifespan removes or reduces the potential to exhibit detectable signs of senescence. There is a growing body of evidence reporting sex differences in senescence (e.g. Descamps et al., 2008; Greiner et al., 2014) with the majority indicating a greater effect in males. A number of reasons have been proposed, mostly associated with a greater impact of sexual selection in males, although this has been challenged in a study of herbivores (Lemaitre & Gaillard, 2013). The pattern of 'never-positive' male mortality found here is more in line with previous findings that show negligible actuarial senescence in badgers (McDonald et al., 2014).

It was already known that bTB infection, as indicated from several diagnostic tests, results in increased male mortality in badgers (Graham et al., 2013; Wilkinson et al., 2000), but our analysis provides evidence for a similar effect in females. Mortality trajectories of the 'cub-positive' individuals revealed novel patterns of senescence and indicated that infection promotes a senescent increase in late-life mortality, this effect being more pronounced in male badgers thus homogenizing the shape of the mortality trajectories and removing any signature of age-dependent sex differences. Recent work has revealed a diversity of age specific patterns of mortality both within and amongst species (Jones et al., 2014) with sex and individual differences in frailty being highlighted as the most important sources of variation in survival parameters (Noonburg et al., 2015). Our analyses found only limited support for individual heterogeneity amongst badgers, indicated by the low ranking of the logistic model (3rd for infected badgers and 5th for uninfected). Males and females on the other hand do display differences in individual heterogeneity and may in fact be better described by sex-specific models (Wilson, 1994). Our combined sex analysis may have masked such variation suggesting that any reduction in mortality with advancing age could be representative of real change (Pletcher, 1999) or be an artefact of heterogeneity among individuals in the population (Vaupel et al., 1979). Previous studies have suggested that ignoring frailty may result in biased parameter estimates (e.g. Vaupel & Yashin, 1985), but with only moderate support for the logistic mortality model it is difficult to draw any firm conclusions. Should individual heterogeneity in frailty exist then the more frail individuals with higher mortality should be removed from the population as a result of within-cohort selection (Dahlgren et al., 2016). The lack of evidence for individual heterogeneity in the present study may in part be due to aspects of badger ecology. Most badgers give birth between mid-January and mid-March (Kynaston et al., 2006) then cubs spend their first few weeks underground and unavailable for capture. Previous research has estimated pre-capture mortality at 24% (Rogers et al., 1997) and perhaps it is at this stage when the majority of weaker individuals are lost from the population. Pre-capture mortality has not been included in our analysis and with trapping not taking place during March and April cubs may be upwards of 6 months old when they are first captured

and tested for bTB. Consequently, our estimates of initial mortality are likely to be underestimates and in reality the downward curve assumed in the juvenile phase of the Siler function would be more pronounced than presented here.

We used the package BaSTA with age-specific survival data and a hierarchical structure within a Bayesian framework to draw inference from censored CMR data in order to investigate survival and mortality in a badger population naturally infected with bTB. Our study has demonstrated the benefits of this approach to mortality trajectory analysis for the study of wildlife disease epidemiology and clarified age-specific sex and disease variation in patterns of mortality. There are however inherent weaknesses in our modelling framework, and to overcome them will require a more flexible modelling approach.

BaSTA dictated our categorisation of badgers into two fixed groups of 'cub-positive' and 'never positive' individuals, as it is unable to assess the influence of time-varying disease states on mortality parameters. This restriction meant filtering out badgers first that tested positive after their first year of life and leaves unanswered questions regarding the mortality trajectories of such individuals. The inability to model time-varying disease states also forced us to use a binary disease classification. Recent research into the epidemiology of bTB in badgers has identified at least four different states of infection (susceptible, test positive, single site excretor, multi-site/occasion excretor) with differing mortality rates at each stage (Wilkinson et al., 2000) and high levels of individual heterogeneity in disease progression over time (Graham et al., 2013). This adds further complexity and suggests the potential for differing mortality trajectories at each disease state, as well as for each age-at-infection/state if for example, older badgers are more likely to become infected and experience more rapid disease progression. To model this system more completely will require a more flexible multi-state framework that allows for time-varying transition through multiple disease states. Further complications relevant to studies of bTB are the limitations of diagnostic tests and changes in the prevailing tests employed in studies over time (Clifton-Hadley et al., 1995; Dalley et al., 2008). False positive diagnosis would potentially weaken the signal of mortality in 'cub-positive' badgers whereas the more likely false negatives could strengthen the signal in the 'never-positive' individuals. Our

results may therefore be more conservative for ‘cub-positive’ yet potentially overstated for ‘never-positive’ individuals. We are confident that any impact is minimal due to tests being highly specific (low chance of false positive) and recapture being common, with an average 5.9 capture/testing occasions per badger (therefore reducing the chance of any individual being wrongly included in either category). There was no bias in the recapture rate between categories which reduces any impact of selective disappearance. The issue of test performance could be explicitly addressed by the further development of mixture models that can incorporate diagnostic uncertainty generated from false-positive and false-negative test results (McDonald & Hodgson, 2018). Multi-event methods have been developed to deal with such problems (Conn & Cooch, 2009; Koons et al., 2014; Pradel et al., 1997) often implementing the software package E-Surge (Choquet et al., 2009). To fully address all the difficulties outlined here requires the combination of these methods and a need to develop more complex hierarchical state-space models developed from first principles using MCMC software such as BUGS, JAGS, NIMBLE or Stan which also allow for the inclusion of age as a continuous covariate.

We have demonstrated the use of relatively simple mortality trajectory analysis in the study of wildlife disease epidemiology. We recommend widespread use of this approach, in systems that have sufficient information to infer patterns of mortality across the whole life cycle. Despite senescence being notoriously difficult to detect in wild populations (Nussey et al., 2008), the present study has provided credible evidence of actuarial senescence in badgers. Furthermore, it has revealed that senescence can be intensified in diseased individuals. Understanding the physiological, evolutionary and ecological drivers of these mortality trajectories remains an ongoing challenge (Nussey et al., 2013). BaSTA is a powerful tool to begin exploration whilst accommodating many of the problems associated with CMR data. However, there are limitations associated with age-dependence and diagnostic uncertainty of disease states, and we are now developing similar Bayesian methods with more complex hierarchical and multi-state frameworks.

Chapter 3: Flexible model specification for Bayesian survival analysis

Abstract

Estimating survival in wild systems relies on robust monitoring strategies such as capture-mark-recapture (CMR) but without consideration of the sampling process within the modelling framework results will be inaccurate. A variety of software packages have been developed to accommodate such data, each with advantages and disadvantages but often they lack the flexibility and transparency that researchers require. We advocate the use of NIMBLE (de Valpine et al., 2017) which has been shown to perform well against competing software and offers a plethora of adjustments to suit specific requirements. Survival analysis in wild systems presents a number of specific challenges to modellers (e.g. censorship, incomplete records) which are often overcome by fitting parametric models and constructing survival and mortality trajectories. Data regarding young individuals are generally scarce meaning research often focuses on later life dynamics such as senescence and *bathtub* shaped mortality trajectories are overlooked as researchers strive for parsimony. We highlight the potential for erroneous conclusions should early life patterns of mortality be ignored and recommend the fitting of bathtub shaped functions, such as the Siler function to survival data (should the data allow). Having presented a novel parameterisation of the Siler function we conclude with a case study analysis of CMR data to expose the competing nature of the Siler parameters highlighting the need for caution when interpreting parameter estimates independently.

Modelling survival in the wild

Our knowledge of survival gleaned from laboratory studies and captive populations is restricted in the depth of understanding it can provide of wild systems as environmental pressures cannot be easily replicated. It is therefore important to utilise methods that have been designed for monitoring species in their natural environment despite the challenges that can be presented in the wild (Cooch et al., 2012; Delahay et al., 2009). The possibility to collect census data are rare within ecological research and more commonly a Capture-Mark-Recapture (CMR) study design is employed which involves the repeated sampling of a population – at first capture individuals are marked and released, on subsequent sampling occasions individuals are either recaptured, not

detected or recovered dead (Catchpole et al., 1998). CMR has been extensively used across ecological research (see Lindberg, 2012 for a review of CMR study design) but the data generated requires diligent modelling strategies to ensure accurate inference and predictions (Conn & Cooch, 2009).

There exists a variety of different software programs for the analysis of CMR data. Program MARK (White & Burnham, 1999) is often considered one of the most comprehensive (Laake et al., 2013), using maximum-likelihood techniques. There is also a large number of more specialised stand-alone packages or libraries for R (R Core Team, 2019) which target specific applications. BaSTA (Colchero et al., 2012) focuses on a Bayesian approach to the analysis of CMR data, recognising the inherent uncertainty common within ecological data which makes the Bayesian methodology attractive (Durban & Elston, 2005). These dedicated packages generally aim to simplify statistical or programming challenges and in doing so broaden the analyst's toolbox, leading to widespread usage that is evident from the high number of citations that associated explanatory articles have received. Despite the benefits, these software packages do have potential drawbacks: first, a proportion of the code and analysis remains 'under-the-hood' and happens automatically (although source code is available) meaning it is possible to overlook elements of the analysis such as 'default' inputs leading to potentially specious inference (e.g. see Warner et al., 2016 and comment from Keevil, n.d.). Second, the specific niche to which a given package is targeted may not offer the full flexibility required by the researcher leading to potentially restricted analysis (Hudson et al., 2019) and a reduced depth of understanding of the system in question (de Valpine et al., 2017). The solution is to construct models from first principles. Within the Bayesian paradigm this is generally completed using a dedicated model-specification language such as that from the BUGS project (Bayesian inference Using Gibbs Smpling - Gilks et al., 1994) which has been widely implemented through a number of different programs (e.g. WinBUGS - Lunn et al., 2000; OpenBUGS - Spiegelhalter et al., 2007). Despite the utility of Bayesian methods, a key challenge is that the posterior distribution can often not be evaluated analytically. Instead numerical algorithms such as Markov Chain Monte Carlo (MCMC) can be used, in which empirical estimates of the

posterior distributions can be derived through random sampling. The development of more efficient and effective MCMC algorithms (and other alternative numerical methods) remains an ongoing area of methodological research. The goal of the BUGS project was to provide flexible software to allow straight-forward Bayesian analysis of complex statistical models using MCMC methods. A number of other software platforms have developed the BUGS language or used it as inspiration for their own model specification language (e.g. JAGS - Plummer, 2003; Stan - Carpenter et al., 2017; NIMBLE - de Valpine et al., 2017) and although there are differences among them, all share the common goal of providing efficient running of MCMC analyses.

The continued development of software has coincided with increases in computing power and enabled huge improvements in the efficiency of fitting complex Bayesian models using a variety of MCMC algorithms and optimisers. These programmes are continually being developed and there now exists a wide range of algorithms each with strengths and weaknesses in different areas. The challenge for developers is balancing increased flexibility without sacrificing computational performance. NIMBLE (de Valpine et al., 2017) is a recently developed software package which makes use of the flexible BUGS language (and extends it) for model specification, but also allows a variety of different MCMC algorithms to be used, and the ability to customise algorithms if required. Separating model specification and model computation into higher- and lower-level languages has meant that flexibility and efficiency have not been compromised. Numerous speed comparisons have been carried out between the different programmes but the majority are confined to statistical blogs and usually restricted to very specific situations. Beraha et al. (2021) carried out a more comprehensive comparison of NIMBLE, JAGS and Stan, finding NIMBLE to be considerably faster in terms of runtime and iterations per second across a variety of different situations. They did temper this with a warning of autocorrelation among samples noting the number of effective samples was lower than the other programmes. This comparative analysis was conducted using only the default samplers within NIMBLE, thus ignoring the modular nature of the package, which further adds to its appeal. NIMBLE offers a broad range of sampling algorithms and fine-tuning options that allows the

user to overcome a spectrum of different issues (including autocorrelation) without sacrificing computational efficiency. In our analyses we have found NIMBLE to outperform OpenBUGS and JAGS, meanwhile the flexibility and control offered by NIMBLE's sampling setup is straight-forward to utilise and has overcome many mixing issues that we have come across with a variety of different datasets. Stan uses a specific MCMC sampler called Hamiltonian Monte Carlo, which can be very efficient for a wide-variety of models, but cannot be applied to sample discrete parameters (such as the various latent indicator variables required for our models). For these reasons we have transferred to NIMBLE for our remaining analyses.

Survival Analysis & Mortality Trajectories

With increased modelling flexibility comes the ability to fit more complex models and better understand complex natural systems. For survival analysis, complexity can come from additional explanatory variables, incorporating individual- and time-specific variations and in the structure chosen to fit these variables. Our understanding of ageing and mortality in wild populations has developed in recent years with a move away from life-table methods which failed to fully accommodate the complex dynamics of wild systems (Coulson et al., 2004; Gimenez et al., 2015), but there are many questions relating to the evolutionary, ecological and physiological causes of variation that remain unanswered (see e.g. Nussey et al., 2013). Virtually all survival analysis requires the accommodation of censored data, but when analysis is focused upon wild populations, especially CMR studies, there are additional considerations such as imperfect detection that must be incorporated to ensure unbiased survival estimates (George et al., 2014; Gimenez et al., 2015). The non-parametric Kaplan-Meier method to estimate survival (Kaplan & Meier, 1958) and semi-parametric Cox proportional hazards model (Cox, 1972) have both been used extensively but fitting fully-parametric models remains less common despite offering several advantages (Nardi & Schemper, 2003).

The ability to describe the complete lifetime mortality functions means that estimation of survival and mortality is more straightforward, projected trajectories are smoother as they draw information from the whole data, and the insight offered can be greater when compared to alternative methods. The main

drawback of the fully parametric approach revolves around how to choose an appropriate function that best describes the survival and mortality of individuals in a population, and how this choice can be validated. Many distributions may fit the data well, making the task of selecting between mortality models a challenge. Increased numbers of parameters may improve fit but often penalised metrics such as the Bayesian information criterion (Schwarz, 1978) or deviance information criterion (Spiegelhalter et al., 2002) are used to select between mortality models, thus selecting the model that best balances model fit with model parsimony according to the specific criterion of interest. The use of such metrics remains controversial (Spiegelhalter et al., 2014) but when different models provide comparable fits to the data, analysts should avoid methods that simply select one 'best' model: with such methods, any uncertainty in model choice is immediately ignored leading to overconfidence and greater potential for statistical bias (Parrish et al., 2012). Multi-model inference (Burnham & Anderson, 2002; Harrison et al., 2018) can alleviate issues of model uncertainty and has the potential to offer greater insight (Hobbs et al., 2006). Within the Bayesian paradigm this can be achieved by averaging across candidate models in a technique known as Bayesian Model Averaging (Kass & Raftery, 1995); this requires the additional calculation of posterior model weights and there is yet to be a consensus on the most appropriate method to use, and in the following chapters we explore a number of alternatives.

Mortality models and exploration of the Siler function

Ageing and mortality has historically been modelled by the Gompertz (Gompertz, 1825) or Gompertz-Makeham (Makeham, 1867) distributions and both have been shown to adequately fit the survival data for a broad range of wild species (Kirkwood, 2015) despite the fact they ignore early life changes. The view that mortality follows a 'bathtub' shape (initially decreasing, then approximately constant and finally increasing) is well established in humans and many animals but the early life decrease remains poorly understood (Levitis, 2011).

When considering natural populations, the practical difficulties of monitoring species in the wild are well known (e.g. Delahay et al., 2009). Sampling

strategies such as CMR together with statistical methods to deal with imperfect detection have helped alleviate some of these issues (e.g. Cormack Jolly Seber (CJS) models - Cormack, 1964; Jolly, 1965; Seber, 1965) but the challenge of monitoring and thus estimating survival is amplified for younger individuals: birthing events are often hidden from observers (e.g. within subterranean dens), live trapping is often suspended during birthing seasons to avoid disturbance and in general, encounters with very young individuals are rare. Without the ability to accurately monitor the number of births taking place it is impossible to estimate the number of deaths occurring, deaths will go undetected as individuals die prior to any capture event taking place and mortality rates for early life stages are likely underestimated. The Siler model (Siler, 1979) considers mortality across individuals' complete life history, and encompasses early life decreases that describe the classic 'bathtub' shape. However, its use has been sporadic. The majority of research focused upon age-specific mortality has centred on late-life changes and senescence (e.g. Carnes et al., 2006; Snoke & Promislow, 2003) which has resulted in researchers overlooking the importance of early life dynamics for later-life mortality. The Gompertz and Gompertz-Makeham models both assume ageing to begin at the age of first reproduction (Hamilton, 1966; Williams, 1957) and ignore early life changes prior. The Siler model with additional parameters relevant to early life is often overlooked as researchers strive for parsimony and often lack signal in the data from this period of individuals' lives. Recent research has demonstrated considerable variation in when ageing commences among mammals (Gaillard & Lemaître, 2017), questioning previous analyses and advocating for models that consider complete life history (when data are available) no matter what life stage is being focused upon (Ronget et al., 2020 and e.g. Lemaître et al., 2020).

The Siler model is somewhat unique in its structure: by combining three different functions (a declining Gompertz, a 'Makeham' constant and a Gompertz) it presents a 5-parameter model for mortality with each parameter having an explicit biological interpretation.

$$h(t) = a_1 e^{-b_1 t} + c + a_2 e^{b_2 t} \tag{3.1}$$

Here we slightly adjust Siler's original notation for additional clarity: a_1 represents the 'at-birth' mortality rate, b_1 is the exponential rate at which mortality decreases from birth into maturity, c is the age-independent mortality rate (notation adopted from the Gompertz-Makeham model) with the final term then describing senescence: a_2 being the intercept for the senescent increase (set at time = 0) and b_2 representing the exponential rate of senescent increase in mortality in later life (Fig. 3.1).

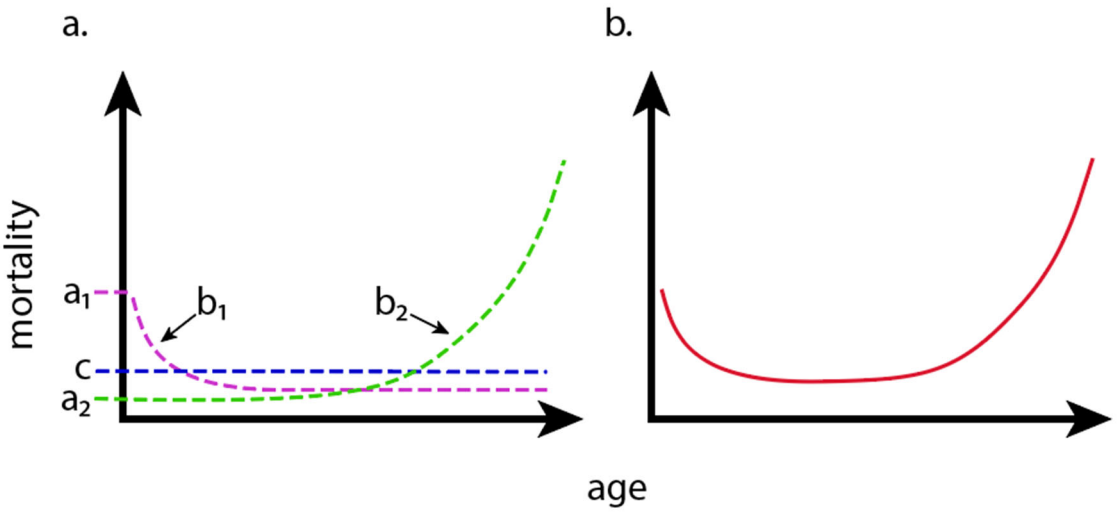


Figure 3.1. The Siler (Siler, 1979) competing risks mortality model; a. showing the 5 parameters and their influence on the resulting mortality curve b.

The ability to interpret each parameter has led researchers to view them independently and it is common to see comparisons of individual parameter estimates using statistical tests such as Kullback-Leibler (Kullback & Leibler, 1951) discrepancy measures to indicate the impact of covariates (e.g. Spagopoulou et al., 2020). In Siler's original paper (Siler, 1979) he describes the model as 'A competing-risk model for animal mortality' but often the competing element is overlooked. The correlated structure of the Siler parameters means that parameters will *compete* to describe mortality during a specific life phase. If parameter estimates are taken and used independently then there is potential for inaccurate conclusions to be drawn. To demonstrate this point we constructed a Shiny app (*Web Application Framework for R [R Package Shiny Version 1.6.0]*, 2021) to allow a full exploration of the Siler

mortality models (Hudson, 2019) and it is clear that the influence of each individual parameter is not necessarily constrained to a specific age-specific portion of the mortality trajectory. Figure 3.1a. shows that for much of the mortality curve the mortality rate could be described by a number of competing parameters - in the example below (Fig. 3.2) we demonstrate that a change in one parameter can have an impact on the overall shape of the mortality trajectory.

By adjusting a_2 it is clear to see that the scope of its influence extends across a large proportion of the mortality curve. In this way it is possible to see that when fitting the Siler function to *real* data the parameters will compete with one another to describe underlying mortality patterns. Inference from studies where parameter estimates are analysed independently should thus be treated with

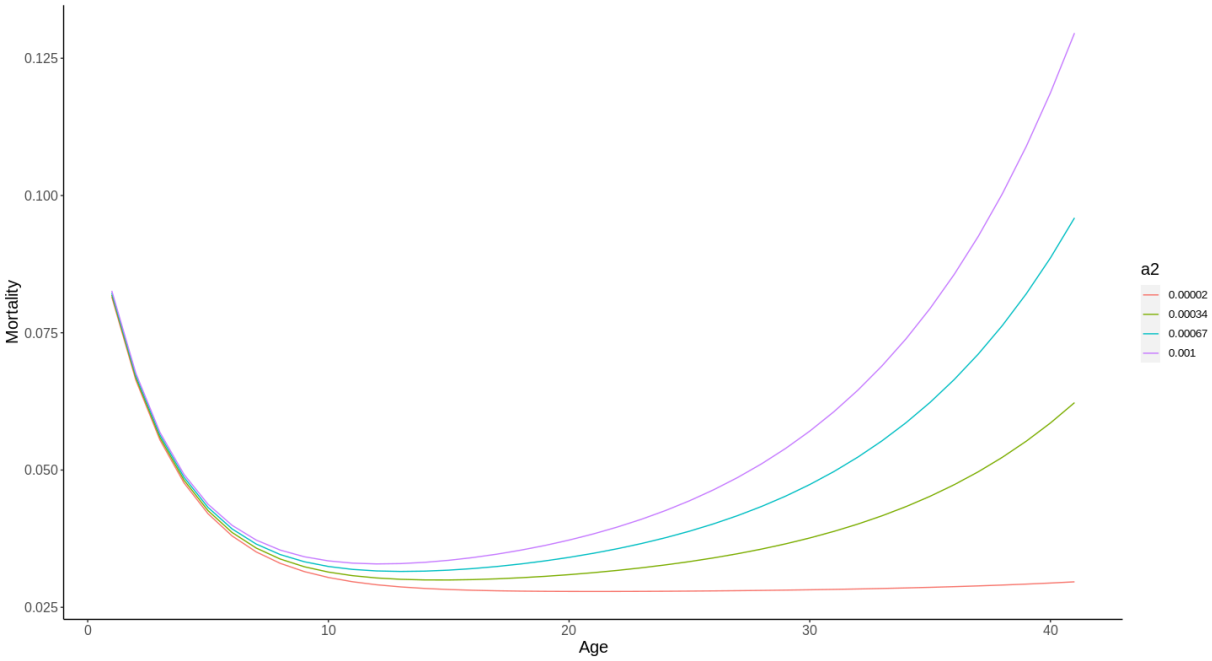


Figure 3.2: Mortality trajectories constructed using the Siler (Siler, 1979) function with fixed parameter values for a_1, b_1, b_2 and c, and adjusting a_2.

caution. Parameter estimates need to be considered as part of a 'set' and interpreted as such—an increase in one parameter may correspond to a compensatory decrease in a different parameter meaning summary statistics of posterior distributions may not accurately reflect the dynamics of the underlying mortality trajectory. The safest method to analyse survival and mortality inferred

from the Siler model is to use the 5 parameter estimates from each iteration of the MCMC process to calculate estimates of age-specific mortality and/or survival and then combine these to form median survival/mortality rates and associated credible intervals to be interpreted accordingly. Covariates may differentially impact individual parameters but unless all 5 parameters are considered together then the subtleties of the processes involved may go undiscovered.

Parameterising the Siler function

Straight-forward yet flexible model specification requires definition of the accompanying probability distributions. The bathtub nature of the Siler function with a combination of increasing and decreasing exponential rates make this a non-trivial computational task when considering the quantile (and random number generator) function. The inverse transform method is the most straight forward method to produce random samples from a probability distribution given its cumulative distribution function (CDF) which also defines its survivor function. Inverse sampling takes samples from a uniform distribution between 0 and 1 and returns the largest number x from the given distribution $P(X)$ where $P(-\infty < X < x)$. To use this method requires a closed-form expression for the quantile function which to our knowledge is absent in the literature for the Siler distribution. We instead made use of the Lambert W function in a similar way to Jodrá (2009) who constructed a closed-form expression for the quantile function of the Gompertz-Makeham distribution to provide a novel method of producing random samples from the Siler distribution.

The full Siler survivor function can be defined as:

$$S(t) = \exp\left(\frac{a_1}{b_1}\left[e^{-b_1 t} - 1\right] - ct + \frac{a_2}{b_2}\left[1 - e^{b_2 t}\right]\right), \tag{3.2}$$

where $a_1, a_2, b_1, b_2, c > 0$. Since the survivor function is not monotonic with respect to t, it cannot be analytically inverted to allow a simple use of inverse transform sampling. It is possible to invert this numerically, but at an additional computational cost and the requirement to monitor the convergence of the

numerical optimiser. Instead, there is a trick that we can consider if it is possible to write a survivor function as a product of M independent survivor functions, i.e.

$$S(t) = S_1(t)...S_M(t). \tag{3.3}$$

In this case, if we are then able to take random samples, $t_1, \dots, t_M$ from distributions $1, \dots, M$ independently, then $t^* = min(t_1, \dots, t_M)$ will be a random draw from a distribution with survivor function $S(t)$ as required. The proof of this is as follows. For sample t^* generated as above, we have:

$$\begin{aligned} P(t > t^*) &= P(\min[t_1,...,t_M] > t^*) \\ &= P(t_1 > t^* \cap t_2 > t^* \cap ... \cap t_M > t^*) \\ &= P(t_1 > t^*)...P(t_M > t^*) \qquad \text{since } t_1,...,t_M \text{ independent} \\ &= S_1(t^*)...S_M(t^*) \\ &= S(t^*) \end{aligned} \tag{3.4}$$

from (3.3) and since the survivor function uniquely determines a probability distribution, the proof is complete.

In the case of the Siler distribution, the survivorship function given in equation (S1) can be decomposed into a product of three independent functions where $S_1(t) = \exp\left(\frac{a_1}{b_1}[e^{-b_1 t} - 1]\right)$, $S_2(t) = \exp(-ct)$ and $S_3(t) = \exp\left(\frac{a_2}{b_2}[1 - e^{b_2 t}]\right)$ as per the original derivation in Siler (1979). The final two components are straightforward to sample from using inverse transform sampling (the second being a standard exponential survivor function and the third being a standard Gompertz survivor function). However, as noted in Siler (1983), $S_1(t)$ is not a proper survivor function, and thus does not define a proper probability distribution when considered independently of $S_2(t)$ and $S_3(t)$, despite the product survivor function $S(t)$ being proper. We can see this most evidently by taking the limit as $t \to \infty$:

$$\lim_{t\to\infty} S_1(t) = \lim_{t\to\infty} \exp\left(\frac{a_1}{b_1}\left[e^{-b_1 t} - 1\right]\right) = \exp\left(-\frac{a_1}{b_1}\right) \neq 0 \tag{3.5}$$

as expected. Hence we cannot decompose the composite survivor function (2) into three independent proper survivor functions. Instead we choose to

decompose into two components, such that $S_1(t) = exp\left(\frac{a_1}{b_1}[e^{-b_1 t} - 1] - ct\right)$ and $S_2(t) = exp\left(\frac{a_2}{b_2}[1 - e^{b_2 t}]\right)$. In this case the second component is a standard Gompertz survivor function as before, and the first component now defines a proper survivor function. Hence if we can generate independent random samples from distributions 1 and 2, then the minimum of the two samples will be a draw from the desired Siler distribution (as proved above). Distribution 2 is straightforward to sample from using inverse transform sampling, but distribution one is trickier. Jodrá (2009) provides a clever approach for evaluating the quantile function for a Gompertz-Makeham distribution using Lambert's W function, and we adapt that approach here that enables us to use inverse transform sampling to sample from distribution 1.

Drawing from distribution 1:

The Lambert W function is defined as the solution of the equation:

$$W(z)e^{W(z)} = z \tag{3.6}$$

where z is a complex number. For real values of $W(z)$ the Lambert W function has only two real branches and $z \geq -1/e$. Here we restrict attention to the principal branch, $W_0(z)$ where $-1 \leq W_0(z) < \infty$.

If we consider an equation of the form

$$x - ae^{-bx} = c \tag{3.7}$$

where $a, b > 0$ and $-\infty < c < \infty$, then we can rearrange this as:

$$\begin{aligned} x - c &= ae^{-bx} \\ (x - c)e^{bx} &= a \\ b(x - c)e^{b(x-c)} &= abe^{-bc} \end{aligned} \tag{3.8}$$

Since $a, b > 0$, the right hand side is > 0 always, and the equation is thus of the form

$$W(z)e^{W(z)} = z \tag{3.9}$$

and a solution is provided by Lambert's W function. Since $z > 0$ this has only one real solution, given by the principal branch, such that:

$$\begin{aligned} \mathrm{W}_0\left(abe^{-bc}\right) &= b\left(x-c\right) \\ x &= c+\frac{1}{b}\mathrm{W}_0\left(abe^{-bc}\right) \end{aligned} \tag{3.10}$$

For a detailed and clear description of this approach, the reader is referred to Jodrá (2009).

For inverse transform sampling, at some probability, p , we wish to determine the quantile function to allow us to invert the relationship:

$$\begin{aligned} F\left(t\right) &= p \\ 1-S\left(t\right) &= p \\ S\left(t\right) &= 1-p \end{aligned} \tag{3.11}$$

Substituting in the survivor function for distribution 1 we have:

$$\begin{aligned} \exp\left[\frac{a_1}{b_1}\left(e^{-b_1 t}-1\right)-ct\right] &= 1-p \\ \frac{a_1}{b_1}\left(e^{-b_1 t}-1\right)-ct &= \log\left(1-p\right) \\ \frac{a_1}{b_1}\left(e^{-b_1 t}\right)-\frac{a_1}{b_1}-ct &= \log\left(1-p\right) \\ ct-\frac{a_1}{b_1}e^{-b_1 t} &= -\log\left(1-p\right)-\frac{a_1}{b_1} \\ t-\frac{a_1}{b_1 c}e^{-b_1 t} &= -\frac{1}{c}\left[\log\left(1-p\right)+\frac{a_1}{b_1}\right] \end{aligned} \tag{3.12}$$

This has the form of (3.6), and thus has solution

$$t=-\frac{1}{c}\left[\log\left(1-p\right)+\frac{a_1}{b_1}\right]+\frac{1}{b_1}W_0\left[\frac{a_1}{c}\exp\left(\frac{b_1}{c}\left[\log\left(1-p\right)+\frac{a_1}{b_1}\right]\right)\right] \tag{3.13}$$

Therefore we can sample $u_1 \sim \mathrm{U}\left(0,1\right)$ and generate a random sample

$$t=-\frac{1}{c}\left[\log\left(1-u_1\right)+\frac{a_1}{b_1}\right]+\frac{1}{b_1}W_0\left[\frac{a_1}{c}\exp\left(\frac{b_1}{c}\left[\log\left(1-u_1\right)+\frac{a_1}{b_1}\right]\right)\right], \tag{3.14}$$

and t is distributed according to distribution 1 as required.

Sampling from distribution 2:

Now if we consider:

$$S_2(t) = \exp\left[\frac{a_2}{b_2}\left(1 - e^{b_2 t}\right)\right] \tag{3.15}$$

which is a proper Gompertz survivor function that can be sampled from using the inverse transform method.

Hence, if $u_2 \sim \mathrm{U}(0,1)$, then calculate

$$\begin{aligned} u_2 &= \exp\left[\frac{a_2}{b_2}\left(1 - e^{b_2 t_2}\right)\right] \\ 1 - e^{b_2 t_2} &= \frac{b_2 \log(u_2)}{a_2} \\ e^{b_2 t_2} &= 1 - \frac{b_2}{a_2}\log(u_2) \\ t_2 &= \frac{1}{b_2}\log\left[1 - \frac{b_2}{a_2}\log(u_2)\right] \end{aligned} \tag{3.16}$$

and thus t_2 will be a random sample from the required Gompertz distribution. A random sample from the Siler distribution can be calculated as: $t = \min(t_1, t_2)$.

We have used the above method to construct R code (R Core Team, 2019) for the full set of Siler probability distribution functions. These can be registered and used in NIMBLE (de Valpine et al., 2017) as custom distribution functions allowing complete flexibility in model specification and removing the constraints felt within the BaSTA analysis of the previous chapter.

Case Study: Analysis of Capture Mark Recapture (CMR) data from a natural population of European Badgers (*Meles meles*)

To demonstrate, using the above parameterisation, the true competing nature of the Siler parameters we carried out a brief analysis of CMR data from a long-term monitoring project of a natural population of European badgers in Woodchester Park, Gloucestershire. Data analysed here consists of badgers (n = 2754) trapped from 1977 to 2020 inclusive; (live) trapping events occur

(usually) four times per year and upon first capture each badger is given an identifying tattoo (for a more complete account of the trapping procedure see Delahay et al., 2000; McDonald et al., 2018). The capture history of each individually marked badger makes up the CMR data and forms the basis for the survival analysis carried out here – the full statistical process is omitted for clarity and to allow the reader to focus on the internal correlation structure of the Siler parameters (for a comprehensive account of the statistical procedure used see Chapter 5). We used Bayesian methods to generate posterior parameter samples which can be used to infer estimates of age-specific mortality and survival from the badger CMR data. Of importance here is the correlation structure of the parameter samples. The pairs plots (Fig. 3.3) indicate a strong correlation between a_1 and c, and between a_2 and b_2 which clearly demonstrates how the parameters compete with one-another to describe the underlying mortality patterns. When using a more complex model, such as when assessing the effects of covariates, it may be that e.g. sex (being male or female) is associated with an increase in the mean parameter estimates for both a_1 and $c$which could, if viewed independently, be interpreted as males/females having a higher rate of mortality at birth *and* higher age-independent mortality throughout life. However, when considered together, an increase in a_1 may be associated with a decrease in c, and so it is important to consider differences in the estimated survival and mortality trajectories as a whole in order to get a feel for where biological differences in survival lie.

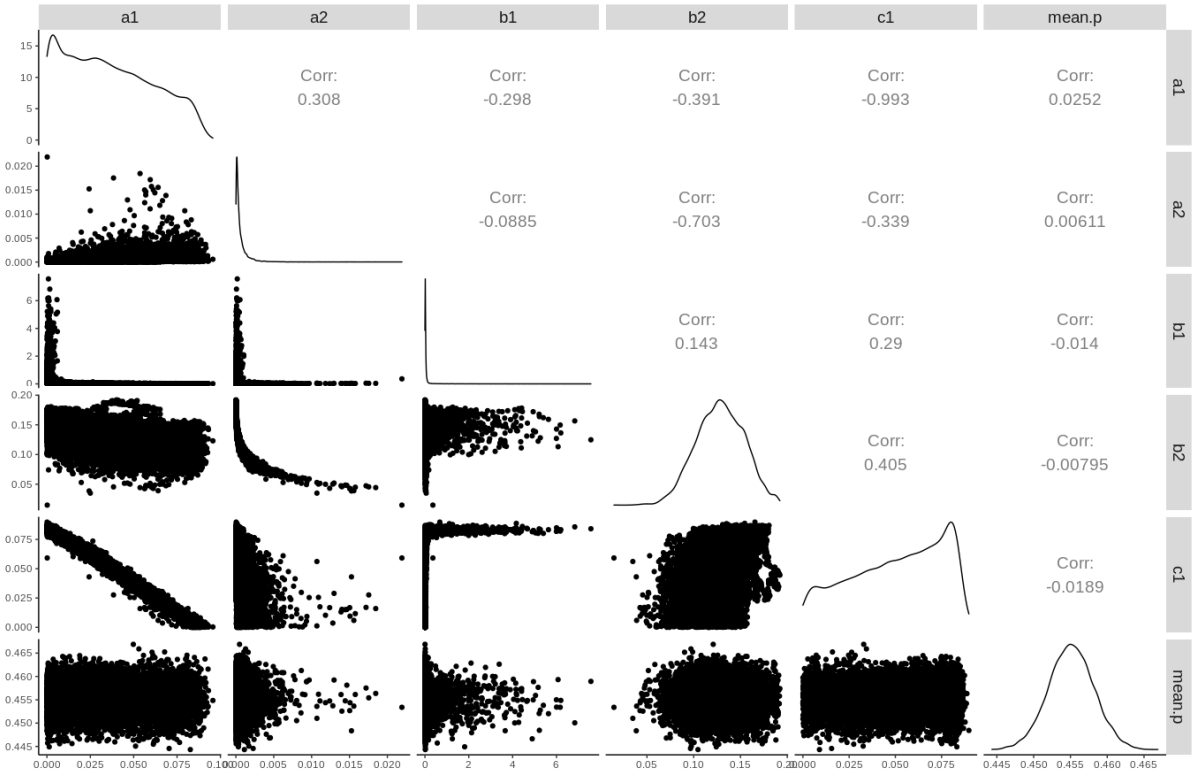


Figure 3.3: Pairs plots of posterior parameter samples from the analysis of CMR data from a natural population of European badgers (*Meles meles*) fitted to the Siler model.

For these reasons it is important to assess posterior parameter estimates with due care, linking with and drawing from suitably calculated (i.e. from *sets* of posterior samples) survival and mortality trajectories will ensure any inferences made are as appropriate as possible.

Concluding remarks

Accurately estimating survival and mortality in the wild is a challenge but it remains a critical parameter within evolutionary and conservation biology. Having demonstrated that early-life mortality dynamics can have impacts in later life – despite potentially weak signal within data, we recommend researchers fit 'bathtub' shaped models (when analysing lifespan data) that allow early life changes to occur as they may have impacts felt later in life. The Siler model describes the classic 'bathtub' shape and we present a novel parameterisation that can be implemented in the flexible software package NIMBLE which we hope will broaden its appeal and allow more complex models to be constructed. But, it is important that the Siler function be employed with heed to Siler's

original description as a '*competing risks*' model for animal mortality. In our case-study analysis we have highlighted the often overlooked correlated structure of the parameters which can lead to erroneous inferences when parameter estimates are viewed independently. Armed with appropriate tools and a deeper understanding of lifetime mortality and survival trajectories, in particular the Siler model, we can focus our future analyses on developing straightforward methods to carry out robust survival analysis and uncovering subtle variations that may help inform our evolutionary understanding of mortality changes such as senescence.

Abstract

Empirical research in ecology and evolution usually relies on model-comparison techniques to investigate competing hypotheses. Many traditional approaches target one ‘best-fitting’ model to explain particular phenomena, which ignores model uncertainty and can lead to overconfident inference and prediction. Multi-model inference has become more popular as a method to account for model uncertainty.

Despite a variety of model comparison techniques being available to the Bayesian ecologist there remains a lack of consensus on the most appropriate tools to use. Bayes’ Factors and posterior model weights are powerful options, but remain underused, usually due to complexities associated with calculation of the required marginal likelihood terms. Here we present a straightforward and efficient approach to estimate the marginal likelihood using importance sampling, and in turn calculate Bayes’ Factors and posterior model weights that can be used to guide e.g. Bayesian model averaging.

Survival analysis is a vital tool in population biology but is often plagued by incomplete data, censoring and latency. Through simulations of censused and censored survival data we demonstrate the efficacy of Bayesian model selection to deal with such situations. We conclude with a case study investigation of sex-specific survival in banded mongooses, which highlights the power of these approaches.

Ignoring model uncertainty can lead to inaccurate inferences which adds weight to arguments in favour of model averaging but also focuses attention on the lack of agreement for which model comparison technique is most applicable. We introduce a clear and flexible approach which is particularly efficient when dealing with missing data and so lends itself to ecological studies, particularly survival analysis, where missingness and censoring are prevalent.

Introduction

The fields of ecology and evolution now rely heavily on model comparison techniques (Johnson & Omland, 2004) which allow the researcher to formulate a set of competing statistical models and then evaluate the relative strength of evidence in the data supporting different hypotheses (Plummer, 2008). Many

traditional approaches tend to target the ‘best-fitting’ model from a pre-determined set of models, but this is known to overestimate confidence and increase the statistical bias of forecasts if some of the competing models are similarly supported under the data (Parrish et al., 2012). Recent approaches use multi-model inference to account for uncertainty in model choice (Burnham & Anderson, 2002; Harrison et al., 2018). This development has broadened the range of questions that ecologists can address and has led to a deeper understanding of complex ecological systems (Hobbs et al., 2006). Ecological research is often based on data from field observations which results in large amounts of missing or incomplete data, varying degrees of unknown measurement error, or data uncertainty (Martin et al., 2005). Bayesian statistical inference is regularly advocated as a powerful approach when dealing with missing data, since it provides a coherent framework to account for and characterise the uncertainties associated with the missing information (Durban & Elston, 2005). There are various ways to approach the challenge of Bayesian multi-model inference, and here we focus on Bayes’ Factors and posterior model weights as a flexible and powerful paradigm.

Bayesian model selection

Common approaches to model selection include the use of e.g. Akaike information criterion (AIC) (Akaike, 1974) or Bayesian information criterion (BIC) (Schwarz, 1978). However, these both rely on maximum likelihood point estimates and hence have limited utility in a Bayesian context where we consider distributions (Hooten et al., 2015; Millar, 2009). The deviance information criterion (DIC) (Spiegelhalter et al., 2002) is a popular analogous Bayesian metric that is straightforward to calculate, and hence is a popular choice (for example it is used for model comparison by the survival analysis software BaSTA, Colchero et al., 2012). However, it can perform poorly when dealing with missing-data models (Celeux et al., 2006). Watanabe proposed the Watanabe-Akaike or Widely Applicable information criterion (WAIC) (Watanabe, 2010) for Bayesian models, which has received support for its use on hierarchical models (e.g. Gelman et al., 2014). However, the calculation of WAIC depends on an independence assumption of the data given the parameters so has faced criticism for spatial models where this assumption is

often violated (Hooten et al., 2015; although see Ando & Tsay, 2010, for a method to relax the assumption).

The Bayesian paradigm offers an alternative approach to model choice through consideration of the *marginal likelihood* of the data for a given model (Jeffreys, 1961). This is sometimes known as the *model evidence*. Model comparison can then be conducted either by calculating Bayes' Factors (Jeffreys, 1961) or posterior model weights. Although this approach is not new, it is often overlooked due to complexities in calculating the marginal likelihood, which we address in this paper by employing a straightforward and flexible approach using importance sampling.

For a given model, Bayesian statistical inference estimates a posterior probability distribution, $f(\boldsymbol{\theta}|\boldsymbol{y})$, for parameters $\boldsymbol{\theta}$ given data $\boldsymbol{y}$. The posterior distribution satisfies:

$$f(\boldsymbol{\theta}|\boldsymbol{y}) = \frac{f(\boldsymbol{y}|\boldsymbol{\theta})f(\boldsymbol{\theta})}{f(\boldsymbol{y})} \tag{4.1}$$

where $f(\boldsymbol{y}|\boldsymbol{\theta})$ is the likelihood function (the distribution of the data given the parameters) and $f(\boldsymbol{\theta})$ is the prior distribution (representing our belief in the values of the parameters in the absence of data). The denominator, $f(\boldsymbol{y})$, is the *marginal likelihood*, and is defined as the (multidimensional) integral of the numerator of equation (1) with respect to all parameters:

$$f(\boldsymbol{y}) = \int_{\theta} f(\boldsymbol{y}|\boldsymbol{\theta})f(\boldsymbol{\theta})d\theta \tag{4.2}$$

This is only solvable analytically for very simple models, and so to avoid evaluation of $f(\boldsymbol{y})$ it is common to derive an empirical estimate of the posterior distribution $f(\boldsymbol{\theta}|\boldsymbol{y})$ using numerical techniques such as Markov Chain Monte Carlo (MCMC) (see e.g. Kass et al., 1997; Kéry & Royle, 2009). However, the marginal likelihood is fundamental to various forms of Bayesian model comparison, since it represents the probability density of the data given the model after integrating (averaging) over the parameter space (as opposed to

methods like AIC that ignore uncertainty in the parameters). For clarity we can make explicit that all inferences from equation (4.1) are in fact dependent on some model M i.e.

$$f(\boldsymbol{\theta} \mid \boldsymbol{y}, M) = \frac{f(\boldsymbol{y} \mid \boldsymbol{\theta}, M) f(\boldsymbol{\theta} \mid M)}{f(\boldsymbol{y} \mid M)} \tag{4.3}$$

Bayes' Factors (Jeffreys, 1961) are defined as the ratio of the posterior odds to prior odds, which equates to the ratio of marginal likelihoods from the competing models:

$$B_{i,j} = \frac{f(\boldsymbol{y} \mid M_i)}{f(\boldsymbol{y} \mid M_j)} \tag{4.4}$$

Where $B_{i,j}$ is the Bayes' Factor for $M_i$versus M_j. Bayes' Factors are very general, not requiring competing models to be nested, but are also naturally parsimonious, and will select simpler models when more complex models offer little or no gain in predictive power therefore acting as a fully automatic Occam's razor (Smith & Spiegelhalter, 1980). An alternative approach to model comparison is to calculate posterior model weights, which can also be used as weighting probabilities in Bayesian model averaging (Hoeting et al., 1999; Kass & Raftery, 1995). Consider K competing models denoted $M_1, \ldots, M_K$. We can derive a posterior probability for model M_k as:

$$P(M_k \mid \boldsymbol{y}) = \frac{f(\boldsymbol{y} \mid M_k) P(M_k)}{\sum_{i=1}^{K} f(\boldsymbol{y} \mid M_i) P(M_i)} \tag{4.5}$$

where $f(\boldsymbol{y} \mid M_k)$is the marginal likelihood given in equation (4.2), and $P(M_k)$is the prior probability weight for model M_k such that $\sum_{k=1}^{K} P(M_k) = 1$. It is common to set $P(M_k) = 1/K$, thus assuming that there is no *a priori* reason to prefer one model over another (although this can be changed).

It is sensible to apply the *Occam's window* approach of Madigan & Raftery (1994) to select a subset of the models initially considered. If a model is far less likely *a posteriori* than the most likely model, it is discredited and should no

longer be considered thus reducing the number of models to average over and allowing straight forward communication of model uncertainty.

The key challenge to using these approaches is the computation of the marginal likelihood terms. There exists a wide range of competing methods, e.g. the Gelfand-Dey estimator (Gelfand & Dey, 1994); harmonic mean (Newton & Raftery, 1994); bridge sampling (Meng & Wong, 1996) and importance sampling (see e.g. Geweke, 1989) among others. Methods have been compared for varying situations (e.g. Bhat et al., 2010; Bos, 2002; Touloupou et al., 2018; Zeng et al., 2018) but there remains no definitive consensus on the optimal method to use. Here we advocate importance sampling (IS), which is straightforward to implement, and has been shown to work well compared to competing methods, in particular when dealing with large amounts of missing data, which is common in certain areas of ecological research (Mckinley et al., 2020; Touloupou et al., 2018; Tran et al., 2014).

Importance sampling

IS belongs to a collection of Monte Carlo methods where a mathematical expectation with respect to a target distribution is approximated by a weighted average of random draws from another distribution (see e.g. Tokdar & Kass, 2010). We follow the two-stage approach of Touloupou et al. (2018) in which a model is fitted to observed data via MCMC to collect posterior samples, which are then used to inform a tractable importance distribution from which we can estimate the marginal likelihood. Hence—with a slight abuse of notation—we draw n random samples from the importance distribution, $\boldsymbol{\theta}_i \sim q(\cdot)$, for $i = 1,\ldots,n$, where $q(\cdot)$ denotes the probability density function for the importance distribution. We then estimate the marginal likelihood of a given model as:

$$\hat{f}(\boldsymbol{y} \mid M_k) = \frac{1}{n}\sum_{i=1}^{n} \frac{f(\boldsymbol{y} \mid \boldsymbol{\theta}_i, M_k) f(\boldsymbol{\theta}_i \mid M_k)}{q(\boldsymbol{\theta}_i \mid M_k)} \tag{4.6}$$

Posterior model weights for all competing models can then be estimated by substituting estimates from (4.6) into (4.5). For this approach to work well, we need to choose an importance distribution, $q(\cdot)$, that a) is straightforward to

sample from; b) has a tractable probability density function; and c) is a good, but overdispersed, representation of the posterior distribution. This last requirement can be difficult to achieve; Vehtari et al. (2015) developed the idea of Pareto-smoothed importance sampling (PSIS) to stabilize the importance weights when aspects of the target distribution are not well captured by the approximating distribution but here we illustrate that finite mixture modelling - a process which approximates a non-standard probability distribution through a mixture of simpler parametric distribution functions—can provide a flexible and easily implementable approach to finding a suitable form for $q(\cdot)$.

Survival analysis

Estimation of demographic parameters is key to any investigation in population biology of wildlife species (Sandercock, 2020) hence survival analysis remains a highly active area of research with the objective often being to understand factors that affect the timings of particular events of interest (commonly death) (Wang et al., 2019). Survival data are frequently *censored*, when measurements or observations are only partially known. For example, if some deaths occur after the study period has ended, then those individuals provide only partial information about mortality by surviving at least to the end of the study (so-called right-censoring). Similarly for left- and interval-censoring. Failing to account for missingness in the data correctly can lead to biased inferences and potentially ill-advised conservation management strategies (Martin et al., 2005).

In survival analysis the problem of censoring is generally overcome by fitting a parametric model that adequately describes the data (Wilson, 1994), which can then be used to generate probabilities of events happening at some point during the censoring period. Many models have been developed for this purpose (e.g. Gompertz - Gompertz, 1825; Gompertz-Makeham - Makeham, 1867; Weibull - Pinder, Wiener, & Smith, 1978; logistic – Vaupel et al., 1979; Siler - Siler, 1979; used by e.g. Bronikowski et al., 2011; Damos & Soulopoulou, 2015; Hudson, et al., 2019; Gao & Dong, 2020) yet historically the Gompertz model was assumed to provide an adequate fit for most mammalian species (Pletcher, 1999; Kirkwood, 2015; although see Ronget et al., 2020). Best-fit parameter estimates

for a single model will often be compared between populations to determine survival differences as a result of genetic or environmental manipulation but the data from these different groups may be better fit by altogether different functions (Wilson, 1994). This realisation has led to researchers needing efficient and reliable methods to compare the fit of competing survival models (e.g. Larson et al., 2016).

The aim of this paper is threefold: (1) to broaden the appeal of model comparison via marginal likelihoods (specifically estimated using IS) to ecologists and conservation biologists for whom imperfect detection and sampling methodologies often result in incomplete data; (2) develop case studies and provide open code that performs survival model comparisons; and (3) demonstrate through simulations the impact that varying degrees of censorship have on the inferences made.

Material and methods

Complete annotated code is available via our GitHub repository and can be found in Appendix 3. (https://github.com/davehudson67/BayesianModelComparisonsRCode).

Survival Models

Mortality trajectories describe the pattern of mortality through an organism's lifespan, using age as a continuous predictor, with actual longevity an emergent property of avoiding, and then not avoiding, these age-dependent hazards. The use of mortality trajectories can allow greater precision and uncover subtle variations in patterns of age-specific mortality that can be missed when using comparisons of fixed rates of mortality in lumped age classes (Hudson et al., 2019). We used four different mortality functions to simulate longevity data: (i) Exponential (Cox & Oakes, 1984); (ii) Gompertz (Gompertz, 1825); (ii) Gompertz Makeham (Makeham, 1867); and (iv) Siler (Siler, 1979). These functions are hierarchical in nature and vary in their complexity, allowing a range of different mortality curves to be described.

Table 4.1: Mortality functions used as proposal models to simulate and fit data.

Model	**Mortality rate** $\mu(x\mid\theta)$	**Parameters**
Exponential	r	$r>0$
Gompertz	ae^{bx}	$a,b>0$
Gompertz-Makeham	$ae^{bx}+c$	$a,b,c>0$
Siler	$a_1e^{-b_1x}+c+a_2e^{b_2x}$	$a_1,a_2,b_1,b_2,c>0$

The models in Table 4.1 define parameters and describe mortality in four different ways: (1) the exponential model assumes constant mortality throughout life, independent of age; (2) the Gompertz model describes mortality as exponentially increasing with age; (3) the Gompertz-Makeham is an extension of the Gompertz model that aims to capture near-constant early- to mid-life mortality, followed by exponentially increasing mortality due to senescence; and (4) the Siler model which extends the Gompertz-Makeham model with an additional declining early-life mortality—leading to "bathtub-shaped" mortality curves. The basic forms of each model are conceptualised in Fig. 4.1.

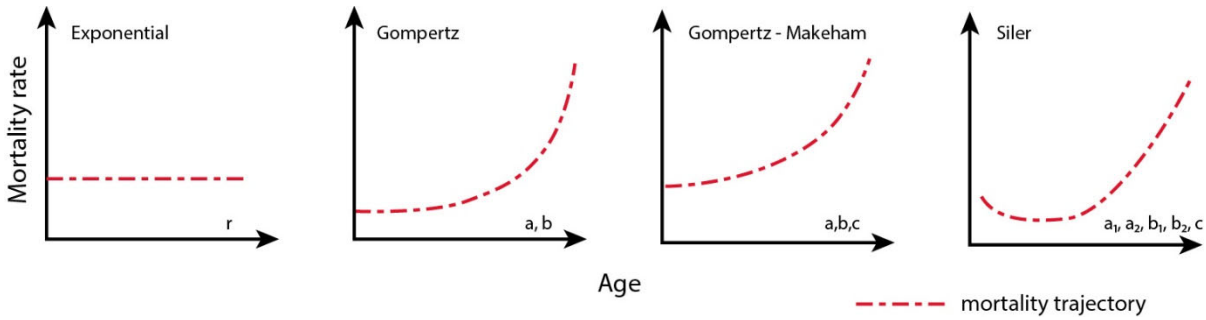


Figure 4.1: Possible mortality trajectories $\mu(x\mid\theta)$ where x is age and θ is a vector of mortality parameters to be estimated, resulting from the four models we compared. The set of parameters required by each model is shown in each plot.

We created custom probability distributions for the Gompertz, Gompertz-Makeham and Siler functions that could be implemented in package NIMBLE (de Valpine et al., 2017) in R (R Core Team, 2019). Making use of the Lambert W function in a similar fashion to Jodrá (2009) enabled us to create a random number generator for the Siler model which we believe is new to the literature (see derivation and proof in chapter 3). We can use this approach to generate simulated survival times from Siler distributions without having to use discrete-time approximations.

Simulations

Parameter Values

We chose parameter values for each of the mortality models that generated distinctive shapes of mortality trajectory and were also representative of values from real populations. As a result we expect our posterior model probability analysis to find clear evidence for the data-generating model for sufficient data, and reduce to less complex models otherwise. The exponential model was simulated with constant mortality rate of 0.01 (Hydra - Schaible et al., 2015); the Gompertz model used values of $a = 0.121$ and $b = 0.105$ (bighorn sheep - Gaillard et al., 2004); the Gompertz-Makeham model used values of $a = 6.7 \times 10^{-6}$, $b = 0.125$ and $c = 0.011$ (*Homo sapiens* - Gurven & Kaplan, 2007); and the Siler model used $a_1 = \exp(-2)$, $a_2 = \exp(-11)$, $b_1 = 1.2$, $b_2 = 0.11$ and $c = \exp(-5)$ (*Homo sapiens* - derived from Engelman, et al., 2014).

Uncensored data

We randomly simulated a vector $\boldsymbol{y}$ of individual survival times for 10 different homogenous populations of varying size (*n* = 1000, 500, 100) using each of the four mortality functions described above. The exponential and Gompertz models can be simulated using simple inverse-transform sampling (Devroye, 1986); the Gompertz-Makeham model uses the approach of Jodrá (2009), and the Siler model uses a novel approach that uses the ideas of Jodrá (2009)—see chapter 3 for details.

Right-censored data

We randomly simulated a vector $\boldsymbol{y}$ of survival times for a homogeneous population (n = 500) and then adjusted the number of right censored individuals (censorship rate = 0.1, 0.2, 0.5). Censoring times were generated by randomly selecting an occasion between birth and death times. We then have two vectors: (1) indicating whether individuals are censored or not; and (2) a vector of times consisting of either times of death or the times the individual was last seen alive. This could represent individuals who survive beyond the end of a study or are lost during the study.

Case study: banded mongoose survival

We modelled life history data from a habituated population of wild banded mongooses (*Mungos mungo*) living on and around the Mweya Peninsula in Queen Elizabeth National Park, western Uganda. This population has been continuously monitored since 1995, with some individual records going back to 1992 (for full details of the field site and population see Cant, Vitikainen, & Nichols, 2013). Each monitored group is visited for at least 20 minutes every 1–3 days to record the presence and absence of individuals in each group. Animals disperse in same sex cohorts, usually after violent evictions, allowing death to be distinguished from dispersal as a cause for permanent absence from a group (Thompson et al., 2016). We only included records with a known birth date (removing 140 individuals from a total of 3380), and all death dates were modelled as right- or interval-censored. Individuals with a recorded death date were considered interval-censored with the lower boundary being 3 days prior to the recorded death date; individuals with no recorded death date were considered right censored from the last seen alive date.

We then conducted two separate analyses: first we fitted four different mortality functions to the life-history data of 3,240 individuals assuming no sex differences and applied Occam's Window to select any models with a log-marginal likelihood value within log(20) of the best model (Kass & Raftery, 1995). Second, we took the selected model(s) and fitted variations allowing sex-specific differences in survival on each of the parameters in turn. Pups that died prior to being sexed were included in the model, with the unknown sex

becoming an additional latent variable inferred by the model. In this instance it is reasonable to assume that the probability of a pup not being sexed was independent of its sex, and as such we used a Bernoulli distribution to capture whether individuals were male or female, and used a Uniform(0, 1) prior distribution on the probability of being male. The ability to include missing covariate information and robustly characterise the uncertainty associated with the missing information emphasises the flexibility of the Bayesian approach and avoids data being unnecessarily discarded. For both analyses we also calculated the DIC and WAIC of each model and compared the subsequent ranking of the proposed models to the results from our IS approach.

Process

Step 1: Fit the proposal model M_1 to the data $\boldsymbol{y}$, estimating the posterior distribution $f\left(\boldsymbol{\theta} \mid \boldsymbol{y}, M_1\right)$ using MCMC.

Step 2: Find a suitable importance distribution by fitting a series of multivariate finite Gaussian mixture models of increasing complexity to the posterior samples from Step 1. Find the best-fitting mixture model using e.g. BIC, and check that this gives a good approximation of the posterior density (see Fig. 2). To do this step, we used the R package “mclust” (Scrucca et al., 2016). It is sensible in practice to ensure that the importance distribution is overdispersed with respect to the target distribution to ensure that the variance of the importance sample estimator is finite; we do this here by using a “defensive mixture” (Hesterberg, 1995) of the form:

$$q\left(\theta \mid M_1\right) = pq_M\left(\theta \mid M_1\right) + \left(1-p\right) f\left(\theta \mid M_1\right) \qquad (4.7)$$

where $q_M\left(\theta \mid M_1\right)$ is the p.d.f. of the finite Gaussian mixture model described above, and $f\left(\theta \mid M_1\right)$ is the prior distribution. We set the mixing proportion $p = 0.95$.

Step 3: Estimate the marginal likelihood of the model $f(y|M_1)$ using the defensive mixture importance distribution and equation (4.6).

Step 4: We then repeat Steps 1–3 for any number of alternate proposal models $M_2,...,M_K$ and compare the posterior model probabilities as defined in equation (4.5). We use uniform prior model weights for each competing model such that $P(M_k) = \frac{1}{K}$. The process for right-censored data is the same but requires an adjustment to the likelihood function (Kalbfleisch & Prentice, 2002).

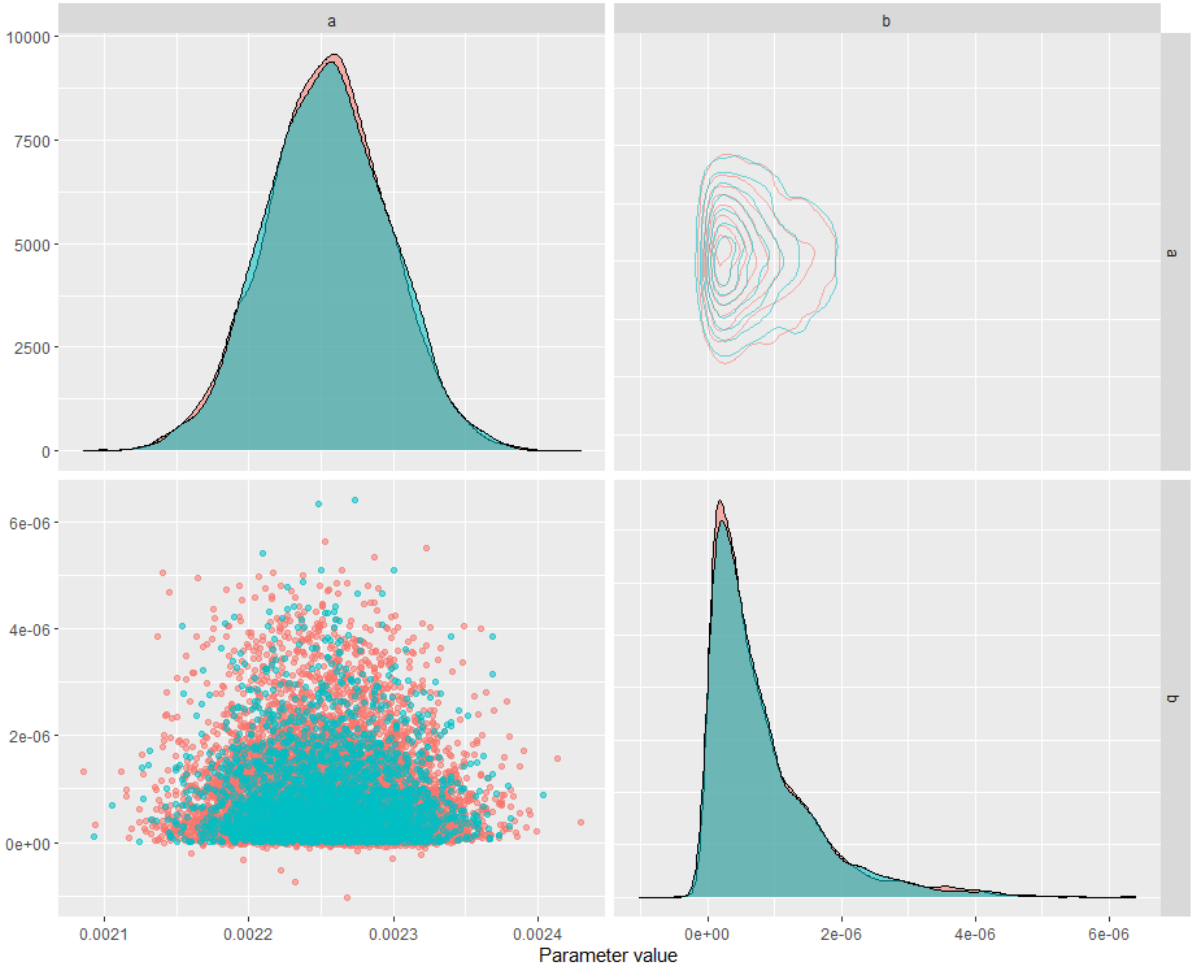


Figure 4.2: Example pairs plot of the posterior samples from MCMC (blue) showing sample values and distribution density from the importance distribution $q_M(\cdot)$ (red) generated from the selected mixture model overlayed. This example is for the Gompertz model fitted to the entire banded mongoose data.

Priors

We specified weakly informative exponential distributions (rate = 1) for the priors of the model parameters. Bayes' Factors are sometimes criticised for their sensitivity to the priors used so we repeated the mongoose analysis using more diffuse exponential distributions (rate = 0.1); this had negligible effect on any outcomes of the model comparisons, so we present the Exp(1) results here.

Results

When applying Occam's Window, we generate confidence intervals for the log-marginal likelihood estimates using bootstrapping, and to be conservative we retain any model that has an upper confidence interval within log(20) (Kass & Raftery, 1995) of the lower confidence interval of the most supported model.

Simulations

For log marginal likelihood plots see Appendix 3.

Uncensored data

Across 120 simulated datasets, there was only one occasion when the data generating model was not selected as the 'best fitting' (see Table 4.2). The one occasion occurred with Gompertz-Makeham simulated data and a small population size ($n = 100$). In this instance the data more closely resembled a Gompertz mortality curve given the small sample size; the data-simulating model was however within the threshold to be included in any further analysis. The distinctive shape of the exponential and Siler mortality models meant that there was only one occasion where any other model was retained by the Occam's Window threshold. The Gompertz and Gompertz-Makeham models are much harder to accurately distinguish, particularly with small sample sizes, which explains the increased number of plausible models suggested within the threshold of the 'best' fitting, since simpler models can fit the data similarly well for certain parameter values.

Table 4.2: Results from repeated model comparisons of uncensored data. Each population size (n = 1000, 500, 100) simulated 10 times for each of the 4 data simulating models (Exponential, Gompertz, Gompertz-Makeham, Siler). Threshold represents the log marginal likelihood value within log(20) of the best fitting model.

Data simulating model	Population size	Proportion of times correct model selected as 'best' fitting	Simulating model within threshold if not chosen as 'best'	Proportion of times alternate models are within threshold
Exponential	1000	10/10	Best	1/10
Exponential	500	10/10	Best	0
Exponential	100	10/10	Best	0
Gompertz	1000	10/10	Best	5/10
Gompertz	500	10/10	Best	5/10
Gompertz	100	10/10	Best	8/10
Gompertz-Makeham	1000	10/10	Best	0
Gompertz-Makeham	500	10/10	Best	4/10
Gompertz-Makeham	100	9/10	1/1	9/10
Siler	1000	10/10	Best	0
Siler	500	10/10	Best	0
Siler	100	10/10	Best	0

Censored data

The addition of censoring saw little change in the accuracy of our approach (see Table 4.3), the data generating model being selected as the 'best' fitting on every occasion (120 simulated datasets). The exponential and Siler models were almost exclusively selected without another model within the threshold value but as censorship increased with the Gompertz and Gompertz-Makeham simulated data so too did the variety of models suggested within the threshold.

Table 4.3: Results from repeated model comparisons of right censored data. Each censorship rate (0.2, 0.5, 0.7) simulated 10 times for each of the 4 data simulating models (Exponential, Gompertz, Gompertz-Makeham, Siler). Threshold represents the log marginal likelihood value within log(20) of the best fitting model, population size was kept constant throughout (*n* = 500).

Data simulating model	Censorship rate	Proportion of times correct model selected as 'best' fitting	Proportion of times alternate models are within threshold
Exponential	0.1	10/10	0
Exponential	0.2	10/10	0
Exponential	0.5	10/10	1/10
Gompertz	0.1	10/10	0
Gompertz	0.2	10/10	0
Gompertz	0.5	10/10	2/10
Gompertz-Makeham	0.1	10/10	1/10
Gompertz-Makeham	0.2	10/10	3/10
Gompertz-Makeham	0.5	10/10	4/10
Siler	0.1	10/10	0
Siler	0.2	10/10	0
Siler	0.5	10/10	0

Case study: banded mongoose survival

We applied the methodology to life history data from a long-term monitoring project of banded mongooses. NIMBLE allows for different sampling algorithms to be employed: we achieved satisfactory mixing and convergence of chains using a combination of slice and adaptive slice samplers on different parameters (see appendix 3 for details of R code). The initial mortality model comparisons using our IS approach clearly selected the Siler model as the best fitting model (see Fig. 4.3a) – this result was supported by both the DIC and WAIC scores which indicated the Siler model as substantially better than any other competing models (see table 4.2). As before, we employed Occam's Window to exclude any competing models that have a difference in log marginal likelihood greater than log(20) , which is indicated on the plot with a dashed line. The predicted survival trajectory from the Siler model matched the Kaplan-Meier

plot of actual survival (Fig 4.3b.) very closely, further validating the result of the model comparison process.

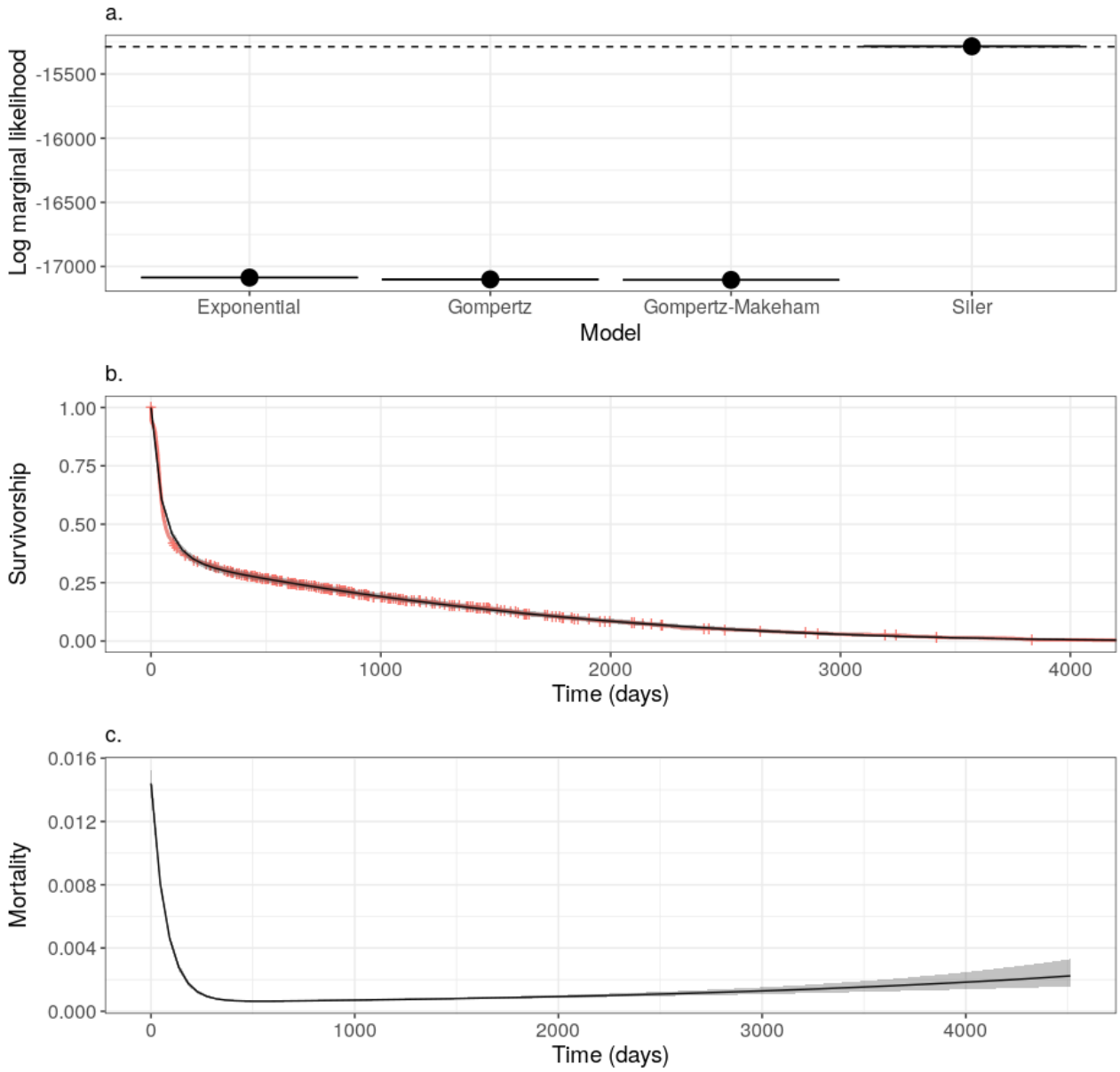


Figure 4.3 a. Comparison of log marginal likelihood values of 4 competing mortality models: Exponential, Gompertz, Gompertz-Makeham and Siler fitted to survival data from a population of banded mongoose. Dashed line represents a value log(20) less than the most supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals. b. Kaplan-Meier plot of mongoose survival with predicted survival curve from the most supported model from the comparison process overlaid. c. Mortality curve for the banded mongoose generated by the Siler model.

Table 4.4. Deviance Information Criterion (DIC) and Widely Applicable Information Criterion (WAIC) scores for competing models. Substantial support for one model over another is considered when the ΔDIC / ΔWAIC > 3 – this refers to the difference in DIC or WAIC score compared to the next best model.

Model	DIC	Rank	ΔDIC	WAIC	Rank	ΔWAIC
Siler	30493	1		30494	1	
Gompertz-Makeham	34109	2	3616	34159	2	3665
Exponential	34156	3	47	34158	3	1
Gompertz	34158	4	2	34160	4	2

We then carried out an analysis of sex-specific survival differences within the mongoose data, carrying out a comparison of 6 variants of the Siler model: first with no sex-specific differences and then allowing sex-specific differences to occur on each of the 5 parameters in turn (Fig. 4.4a).

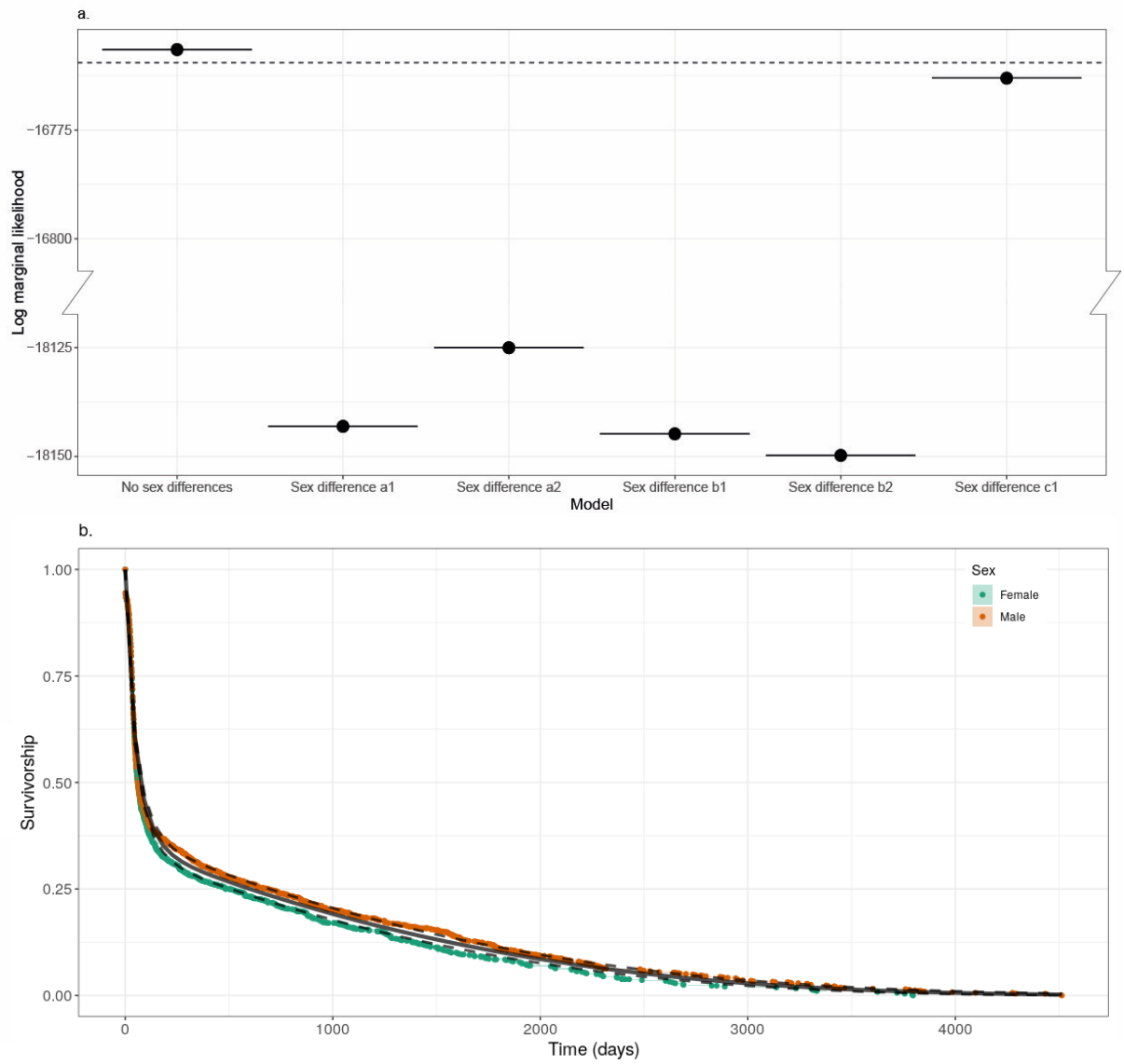


Figure 4.4a: Comparison of log marginal likelihood values of 6 competing mortality models fitted to survival data from a population of banded mongoose; all are variants of the Siler model firstly with no sex-specific differences and then allowing sex-specific differences on each parameter in turn. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals. Please note the collapsed Y-axis. b. Kaplan-Meier plot of sex specific survival with survival curve from the most supported model from Fig. 4a. overlaid.

The best supported model was the Siler model with no sex-specific differences, no other model was within the required threshold, although a model allowing sex-specific differences in the c_1 parameter was extremely close. To assess the

model fit but accounting for the unknown sex individuals we took random samples from the posterior distributions for each missing sex variable, and then generated an empirical Kaplan-Meier curve for each set of samples. The points shown in Fig 4.5b are the posterior means from this posterior predictive K-M curve. The predicted survival trajectory from our parametric model fits very well to these data, further supporting the selected model as a reasonable descriptor of the data – we have omitted the mortality curve from this plot as it is the same as Fig 4.4c.

We calculated DIC and WAIC scores for the competing sex-specific models (see Table 4.3) – the results from both methods were very similar to that of our IS approach. Neither DIC or WAIC suggested that the model allowing sex-specific differences on c_1 performed substantially better than one that allowed no sex-specific differences, but both of these models scored considerably better than all other competing models which mirrors our IS approach.

Table 4.5: Deviance Information Criterion (DIC) and Widely Applicable Information Criterion (WAIC) scores for competing sex-specific survival models. Models have been ranked and the Δ score represents the difference to the next best mode. Substantial support for one model over another is considered when the ΔDIC or ΔWAIC > 3.

Model	**DIC**	**Rank**	**ΔDIC**	**WAIC**	**Rank**	**ΔWAIC**
Siler sex diff c_1	33432.66	1	2.46	33432.51	1	2.38
Siler no sex diff	33435.12	2	2727.7	33434.89	2	2737.13
Siler sex diff a_1	36162.82	3	3.98	36172.02	3	46.15
Siler sex diff a_2	36166.80	4	7.29	36218.17	4	2.04
Siler sex diff b_1	36174.09	5	39.39	36220.21	5	0.46
Siler sex diff b_2	36213.48	6		36220.67	6	

Discussion

In this chapter we have introduced an accurate and accessible method to carry out Bayesian model comparisons through the use of an efficient two-stage approach to the estimation of the marginal likelihood which can be used to

calculate posterior model weights. For ecologists and evolutionary biologists, this makes the now-familiar techniques of multi-model inference more accessible for Bayesian models. We have demonstrated the straightforward nature of the method and provide annotated code in the hope that it can be adapted to suit a wide range of situations and datasets. Our analyses have focused on survival trajectory analysis where datasets will often include missing or incomplete data. We have developed a novel random sampling algorithm for the Siler function (to accompany similar ones for other standard survival models) and implemented all of these ideas in the open-source R statistical language using the NIMBLE MCMC package.

With no censoring the method correctly selected the data-simulating model in all but one of our replicated simulations, even when population size was small. We took parameters from previously published research on real populations where authors had selected a particular model to represent the survival or mortality (Gaillard et al., 2004; Gurven & Kaplan, 2007; Schaible et al., 2015), but for nested models the ability to select more complex model forms will also depend on the parameters used in the simulations. The shape of the exponential and Siler models are distinctive and it is perhaps no surprise that when simulating data from these models with appropriate parameters that on only one occasion is a rival model selected within threshold of the correctly selected simulating model. When the data are simulated from the Gompertz and Gompertz-Makeham models with the chosen parameters, then there is more uncertainty in the model form, with simpler models providing similar fits in some cases. Makeham (1867) and Gompertz (1871) acknowledged that their original equations may not apply to the entire age range, but despite this many researchers have continued to use them in this way (e.g. Pietrzak et al., 2015). Although the c parameter in the Gompertz-Makeham model represents age-independent extrinsic mortality it will compete with the a_1 parameter to describe the baseline mortality level. The results from the Gompertz and Gompertz-Makeham simulations offer support for the idea that ignoring model uncertainty and simply selecting a single model to describe mortality could lead to overconfident inferences when compared to model averaging approaches; unless there is overwhelming evidence in favour of a single model over all

others compared (as is the case with the mongoose investigation carried out here).

The naturally parsimonious nature of the method is shown by our investigation into the Gompertz-Makeham simulated data: although the GM model was correctly selected on every occasion the number of times other models fell within threshold was greater, when the survival and mortality curves for the competing models are very similar. The introduction of right-censoring to the simulated data mimics ecological data more closely and demonstrates the flexibility of this approach. As the censoring rate increases, a greater number of models are proposed within the threshold value of the most supported model indicating a greater degree of model uncertainty. Despite the loss of information as a result of censoring this method still correctly selected the data simulating model on every replication for these parameters.

The mongoose data are censused in nature which greatly reduces the risk of under-estimating prematurity mortality but as the interval in recording/sampling increases in length then this risk will increase. We found only limited support for models that allow sex specific differences in survival with none of the alternative models returning a marginal likelihood estimate within the threshold to be included. The model allowing sex-specific variation in the c parameter did come close suggesting there may be a difference in the underlying age-independent mortality but there is not enough information within the data to support the inclusion of the additional parameter. Although this is contrary to previous analyses (see Cant et al., 2016) where longevity was compared for individuals who had survived over a year our predictions are based on entire life history and match parametric tests on the same data (see appendix 3). We compared the IS results with more traditional model comparison techniques (i.e. DIC and WAIC) and in both the initial model and sex-specific investigations they supported the results of our IS approach. In the sex-specific analysis, DIC and WAIC selected a model allowing sex-specific variation on $c_1$as the best fitting model but the difference in score suggested that the fit was not considerably better than the model that allowed no sex-specific variation. In this instance it would be left to the researcher to decide on which model would be most

appropriate. There remains no justified method to approximate model weights using DIC or WAIC scores (Hooten et al., 2015 - although see Hoeting et al., 1999) meaning BMA is not possible when using these model selection approaches. The slight difference in the results of DIC/WAIC when compared to our IS approach suggest that they penalise model complexity (i.e. the number of parameters) differently although this requires further investigation.

Predicted survival curves from the best fitting models match Kaplan-Maier plots of recorded survival (Fig. 4.3b and 4.4b) suggesting they are suitable predictive models. Had the situation arisen whereby the marginal likelihood value for any of the competing models was within the threshold of the best fitting model, then the posterior model probabilities calculated would be available for Bayesian model averaging, and this is much more likely to happen in smaller data sets with less information available to distinguish between models.

Criticisms of the Bayes' Factor approach often focus on their sensitivity to the choice of priors (Kass, 1993) and challenges in their calculation (Xie et al., 2011). We found negligible differences with alternative priors when investigating the banded mongoose data but would recommend this safety check in any analyses. Efficient calculation of the marginal likelihood remains an ongoing area of research in statistics (Wang et al., 2018) but here we demonstrated the straightforward nature of our two-stage approach and the flexibility with which competing models can be compared. It also demonstrates the ability to model time of death on a continuous scale by assuming that all the data are censored to some extent (in addition to right censored individuals, those with a known dead record are considered interval censored). In this way we remove issues and inaccuracies relating to discretisation of the data. We are currently working on an extension of this method which can investigate capture-mark-recapture data which inherently contains greater proportions of missing data.

Concluding remarks:

Developments in computing power and software flexibility has meant that complex models are now routinely fitted using Bayesian approaches (Friel & Wyse, 2012). Ignoring model uncertainty can lead to inaccurate inferences (Parrish et al., 2012) which inevitably adds weight to arguments in favour of

model averaging but also focuses attention on the lack of agreement for which model comparison technique is most applicable. We have introduced a clear and flexible method to estimate the marginal likelihood via importance sampling which then allows simple and interpretable model comparison through the calculation of Bayes' factors or posterior model probabilities. This approach is particularly efficient when dealing with missing data (Touloupou et al., 2018) and so lends itself to ecological studies, particularly survival analysis, where missingness and censoring are prevalent.

Chapter 5: Bayesian Model Comparison of Capture Mark Recapture data for Survival Analysis

Abstract

Survival analysis is of increasing importance in wildlife research. The challenges of monitoring wild populations are often alleviated by using sampling strategies such as capture-mark-recapture (CMR), but this must be correctly accounted for to ensure accurate survival estimates. It is widely recognised that multiple models can have comparable fits to data leading to an increased use of multi-model inference techniques such as Bayesian model averaging (BMA). These techniques require efficient methods to compare models and having previously introduced a straightforward Bayesian approach that estimates the marginal likelihood based on importance sampling, here we extend this method to deal with CMR data – common within ecological research. Through a series of simulations we demonstrate the accuracy of the approach in identifying the data generating model in most situations but also uncover previously unreported difficulties of detecting 'bathtub' shaped mortality from CMR data. We explore different situations that affect the detection of the Siler function and comment on its use in ecological research. Finally, we carry out a case-study investigation of sex-specific mortality in a natural population of European badgers (*Meles meles*) using CMR data – we advocate the use of 'bathtub' shaped functions when analysing life-history data and comment that early-life mortality rates detected by CMR data are likely underestimates of true values.

Introduction

The modelling and accurate estimation of survival is critical to many areas of wildlife research (e.g. evolutionary pressures in the wild - Roulin et al., 2010; conservation of populations - Morris & Doak, 2002; wildlife disease - Benton et al., 2018). Emergence and re-emergence of a variety of pathogens of wild origin that cause disease in both humans and livestock (Ostfeld & Holt, 2004; Webster et al., 2006) has resulted in increased pressure to improve our understanding of the demography of wild populations. Any estimation of demographic parameters (e.g. survival, dispersal, fecundity) requires the analysis of individual observation data (Dey et al., 2019) which can be challenging to obtain due to the practical difficulties involved in monitoring wild populations (Delahay et al., 2009). A common approach is to use capture-mark-recapture (CMR) which requires the repeated sampling of a population in which individuals are first

marked and released, and, at each subsequent occasion they are either recaptured, not detected, or recovered dead (Catchpole et al., 1998).

Studying survival rates in this manner presents a number of key challenges. First, detection is often far from perfect so there are many occasions when we are unaware of individuals' fates (Kery & Schaub, 2012). Second, the duration of monitoring projects often does not span the entire life of many individuals, resulting in relatively few records of old individuals (Metcalf et al., 2009). Third, a proportion of individuals are likely to have unknown times of birth and/or death (Frederiksen et al., 2004) and fourth, juveniles are especially hard to monitor resulting in imprecise records of early-life deaths making survival estimates for this age category particularly challenging. To ensure survival estimates are as accurate as possible it is essential to consider the observation process in any analysis of CMR data. The prevailing approach is to jointly estimate survival and recapture probabilities using an open population capture-recapture model such as a Cormack-Jolly-Seber (CJS) model (Cormack, 1964; Jolly, 1965; Seber, 1965 and see Lebreton et al., 1992). Models of this class utilise information from individual capture histories generated by the CMR process to estimate survival rates which can then be compared among groups or against environmental conditions to uncover subtleties within demographic ecological processes. CJS models rely on a number of assumptions that can bias estimates, some of which can be addressed through study design: marks/tags must not be lost; capture should be instantaneous; individuals are identified without error; individuals are a random sample from the population. There are a further set of assumptions that can appear as a consequence of model specification (e.g. individuals from a specific age class have the same survival and recapture probabilities) but most can be dealt with in the modelling process (e.g. Pradel et al., 1997). The frequency of resampling occasions will often depend on the research question or target species but as mortality and permanent emigration are generally confounded, survival can only be reported as *apparent* survival which will be lower than true survival when permanent emigration is non-zero (Kery & Schaub, 2012 although see Schaub & Royle, 2014). The most appropriate method to achieve unbiased estimates of survival remains an area of ongoing debate (see e.g. Abadi et al., 2013; Cooch et al.,

2012) particularly when inferring demographic parameters (Gimenez & Choquet, 2010).

Ecological data, and in particular CMR data, is plagued by varying degrees of unknown measurement error and missingness (Cressie et al., 2009) which if not accounted for correctly can result in biased estimates of population parameters and cause general problems with inference to the target population (Williams et al., 2002). Within survival analysis this usually manifests in the form of censorship where measurements or observations are only partially known (see Fig.5.2 for further explanation): some births will occur before the study begins (left truncation); some deaths may occur after the study has ended (right censored); some deaths occur between a certain interval and we lack precise information (interval-censored). Although records from individuals that fall into one of these 3 categories suffer from missing information they can all contribute to survival estimates albeit in different ways. Bayesian approaches accommodate uncertainty from missing and/or incomplete data in a natural way (Daniels & Hogan, 2008) and the recent proliferation of Markov Chain Monte Carlo (MCMC) approaches and software makes it possible to analyse complex likelihood and prior structures. The Bayesian approach has thus become the default for many applied problems (Fragoso et al., 2018) particularly for the analysis of ecological systems (Clark et al., 2005). It is common within survival analysis to fit a parametric model to the data to overcome problems associated with censorship (Wilson, 1994) and there now exists a variety of survival trajectory models that have been applied variously to different species (e.g. Gompertz - Gompertz, 1825; Gompertz-Makeham - Makeham, 1867; Weibull - Pinder, Wiener, & Smith, 1978; logistic – Vaupel et al., 1979; Siler - Siler, 1979; used by e.g. Bronikowski et al., 2011; Damos & Soulopoulou, 2015; Hudson, et al., 2019; Gao & Dong, 2020)

Multiple models can often provide comparable descriptions of the distributions that may have generated the observed data (Fragoso et al., 2018) and for these reasons multi-model inference (Burnham & Anderson, 2002) has become a widely accepted approach. Incorporating model uncertainty has broadened the range of questions ecologists can address and deepened our understanding of complex ecological systems (Hobbs et al., 2006), but requires efficient methods

to compare the fits of competing models. Adopting a Bayesian approach to model comparison methods is well supported (e.g. see Berger & Pericchi, 2001) and has led to the use and development of methods such as the deviance information criterion (DIC) (Spiegelhalter et al., 2002), the Watanabe-Akaike or widely-applicable information criterion (WAIC) (Watanabe, 2010), reversible jump MCMC (RJMCMC) (Green, 1995) and Bayes Factors (Kass & Raftery, 1995). Despite the attention received there is yet to be a consensus on the most appropriate method to use and we point the reader to several reviews; see Alston et al., 2004; Hooten et al., 2015 for more in depth comparisons.

Bayes' Factors (BF) are defined as the ratio of posterior odds to prior odds which equates to the ratio of marginal likelihoods from competing models if the models are equally supported *a priori*. The complexity of calculating the marginal likelihood has resulted in comparatively limited use of BF within the ecological literature as researchers lean towards more off-the shelf solutions such as DIC which are simpler to compute although not suitable for all types of model. The interpretation of BF with respect to support for particular models remains contentious (Hoijtink et al., 2019). An alternative approach is to use the marginal likelihoods to calculate posterior model weights which can be used as weighting probabilities in Bayesian model averaging (BMA) leading to lower risk predictions that can be averaged over all considered models (Fragoso et al., 2018). The marginal likelihood is fundamental for model comparisons when calculating either BF or posterior model weights but its calculation is non-trivial. This has led to the development of many competing methods for its estimation e.g. Gelfand-Dey estimator (Gelfand & Dey, 1994), harmonic mean (Newton & Raftery, 1994), bridge sampling (Meng & Wong, 1996) and importance sampling (see e.g. Geweke, 1989) but there remains no consensus as to which should be considered the preferred option. In previous work analysing census data, we implemented the straightforward two-stage approach of Touloupou, et al. (2018), demonstrating the flexibility and efficiency of Importance sampling (IS) for marginal likelihood estimation particularly when dealing with missing data (See Chapter 4 and Touloupou et al. (2018) for full details of the algorithm). Here we extend our IS approach for CMR data in an effort to further broaden its appeal to ecologists and conservation biologists. We first

demonstrate the efficiency of the approach through simulations and then its flexibility with a case study investigation of long-term monitoring data from a wild population of European badgers (*Meles meles*) naturally infected with bovine tuberculosis.

Materials and Methods

Survival Models

The basis for our approach is to model time of death as a latent random variable in continuous time that we assume can be described by one of four different mortality models (Table 5.1).

Table 5.1: Mortality functions used as proposal models to simulate and fit data.

Model	Mortality rate $\mu(x \mid \theta)$	Parameters
Exponential	r	$r>0$
Gompertz	ae^{bx}	$a,b>0$
Gompertz-Makeham	$ae^{bx}+c$	$a,b,c>0$
Siler	$a_1e^{-b_1x}+c+a_2e^{b_2x}$	$a_1,a_2,b_1,b_2,c>0$

The models in Table 5.1 define parameters and describe mortality in four different ways: (1) the exponential model (Cox & Oakes, 1984) assumes constant mortality throughout life, independent of age; (2) the Gompertz model (Gompertz, 1825) describes mortality as exponentially increasing with age; (3) the Gompertz-Makeham (Makeham, 1867) is an extension of the Gompertz model that aims to capture near-constant early- to mid-life mortality, followed by exponentially increasing mortality due to senescence; and (4) the Siler model (Siler, 1979) which extends the Gompertz-Makeham model with an additional

declining early-life mortality—leading to “bathtub-shaped” mortality curves. The basic forms of each model can be seen in Fig. 5.1.

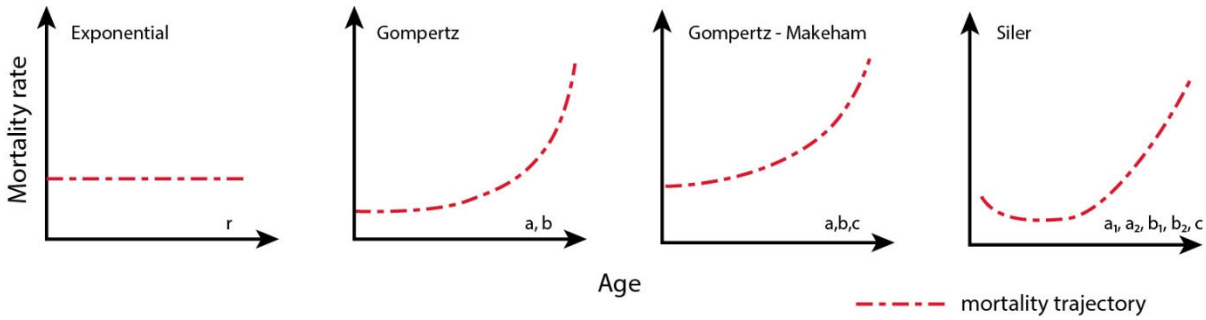


Figure 5.1: Possible mortality trajectories $\mu(x|\theta)$ where x is age and θ is a vector of mortality parameters to be estimated, resulting from the four models we compared. The set of parameters required by each model is shown in each plot.

Importance sampling for model comparisons

For a more detailed explanation of the theory behind the Importance Sampling method we refer the reader to the previous chapter; here we focus on a step-by-step guide. To summarise, first consider for a given model M, standard Bayesian statistical inference estimates a posterior probability distribution $f(\boldsymbol{y}|\boldsymbol{\theta},M)$, for parameters $\boldsymbol{\theta}$ given data $\boldsymbol{y}$. The posterior distribution satisfies:

$$f(\boldsymbol{\theta}|\boldsymbol{y},M)=\frac{f(\boldsymbol{y}|\boldsymbol{\theta},M)f(\boldsymbol{\theta}|M)}{f(\boldsymbol{y}|M)} \tag{5.1}$$

where $f(\boldsymbol{y}|\boldsymbol{\theta},M)$ is the likelihood function (the distribution of the data given the parameters) and $f(\boldsymbol{\theta}|M)$ is the prior distribution (representing our belief in the values of the parameters in the absence of any data). The denominator, $f(\boldsymbol{y}|M)$, is the marginal likelihood and defined as the (multidimensional) integral of the numerator of equation (5.1) with respect to all parameters

$$f(\boldsymbol{y}|M)=\int_{\theta} f(\boldsymbol{y}|\boldsymbol{\theta},M)f(\boldsymbol{\theta}|M)d\theta \tag{5.2}$$

and represents the probability density of the data given the model, *averaging* over the parameter space. This is in contrast to criteria such as AIC that fix the parameters at the maximum likelihood estimates and thus ignore parameter uncertainty. The posterior distribution is only solvable analytically for very simple models so it is common to sample from the posterior distribution using numerical techniques such as Markov Chain Monte Carlo (MCMC) (see e.g. Kass et al., 1997; Kéry & Royle, 2009) and this forms step one:

Step 1: Fit a proposal model M_1 to the data $\boldsymbol{y}$, estimating the posterior parameter distributions $f(\boldsymbol{\theta} \mid \boldsymbol{y}, M_1)$ using MCMC.

Step 2: Fit a series of multivariate finite Gaussian mixture models of increasing complexity to the posterior samples from Step 1 and find the best-fitting model using e.g. BIC and check that this gives a good approximation of the posterior density. The exact form of the distribution is unimportant as long as it is a good representation of the posterior; hence, it is appropriate to use BIC to choose a parsimonious but well-fitting distribution. We make use of R package mclust (Scrucca et al., 2016) to do this. It is sensible in practice to ensure that the importance distribution is overdispersed with respect to the target distribution to ensure that the variance of the importance sample estimator is finite; we do this here by using a "defensive mixture" model (Hesterberg, 1995) of the form:

$$q(\theta \mid M_1) = pq_M(\theta \mid M_1) + (1-p) f(\theta \mid M_1), \tag{5.3}$$

where $q_M(\theta \mid M_1)$ is the p.d.f. of the finite Gaussian mixture model described above, and $f(\theta \mid M_1)$ is the prior distribution. We set the mixing proportion $p = 0.95$.

Step 3: Take n random samples from the defensive mixture distribution (5.3), and then estimate the marginal likelihood of the model $f(y \mid M_1)$ using the defensive mixture importance distribution as

$$\hat{f}(\boldsymbol{y} \mid M_1) = \frac{1}{n} \sum_{i=1}^{n} \frac{f(\boldsymbol{y} \mid \theta_i, M_1) f(\theta_i \mid M_1)}{q(\theta_i \mid M_1)}. \tag{5.4}$$

Step 4: We then repeat Steps 1–3 for any number of alternate proposal models $M_2,...,M_k$ and compare the posterior model probabilities

$$P(M_k \mid \boldsymbol{y}) = \frac{f(\boldsymbol{y} \mid M_k) P(M_k)}{\sum_{i=1}^{K} f(\boldsymbol{y} \mid M_i) P(M_i)}. \tag{5.5}$$

We use uniform priors for each competing model such that $P(M_k) = \frac{1}{K}$.

Incorporating the CMR sampling process

Extending our previous work, the sampling process inherent in any CMR model must be correctly incorporated within the likelihood function. Individual capture histories provide information on the number of times each individual is captured (y_i). If we assume a constant capture probability p, given that an individual is alive at some time point t, then the likelihood reduces to a function of y_i and tM, where tM is the final time point of the study. If we then assume that capture events occur at each discrete time point t (in units of 1), then the likelihood contribution for individual i with known birth and death times, tB and tD respectively can be written as:

$$p^{y_i}(1-p)^{\min(\lfloor tD_i - tB_i \rfloor, \lfloor tM - tB_i \rfloor) - y_i} \times f(tD_i - tB_i \mid \boldsymbol{\theta}) \tag{5.6}$$

where the notation $\lfloor x \rfloor$ corresponds to rounding x down to the nearest integer. Here $f(tD_i - tB_i \mid \boldsymbol{\theta})$ is the p.d.f of the survival distribution. This is of the general form:

$$P(y_i \mid tD_i, tB_i, tM, \boldsymbol{\theta}) f(tD_i - tB_i \mid \boldsymbol{\theta}) \tag{5.7}$$

If survival time is right-censored then the only information we have is tL_i, the time point when the individual was last captured. In these cases we can model tD_i as a latent variable and the likelihood contribution becomes:

$$\int_{tL_i}^{\infty} P(y_i \mid tD_i, tB_i, tM, \boldsymbol{\theta}) f(tD_i - tB_i \mid \boldsymbol{\theta}) dtD_i. \tag{5.8}$$

We can numerically estimate (5.8) by including tD_i as a latent variable in our MCMC. Alternatively, this integral can be calculated analytically. In our analyses we model time of death as a continuous variable and consider all the data to be censored - adjusting the likelihood accordingly. Those individuals recovered dead at time tU_i are considered interval censored with $tL_i < tD_i < tU_i$ requiring only a minor adjustment to (5.8):

$$\int_{tL_i}^{tU_i} P(y_i \mid tD_i, \boldsymbol{\theta}) f(tD_i \mid \boldsymbol{\theta}) dtD_i \,. \tag{5.9}$$

Fig.5.2 represents the different individual scenarios that appear in our analysed dataset: individuals 1, 3 and 4 are captured and identified as cub (which enables time of birth to be estimated and an age calculated); individual 2 dies prior to being captured and so contributes nothing to survival estimation; individuals 1 and 4 are both considered right censored as we only have information about survival up to a certain point (last captured alive). Individual 3 contributes the most information and is considered interval censored (died at some point between interval 6 and 7).

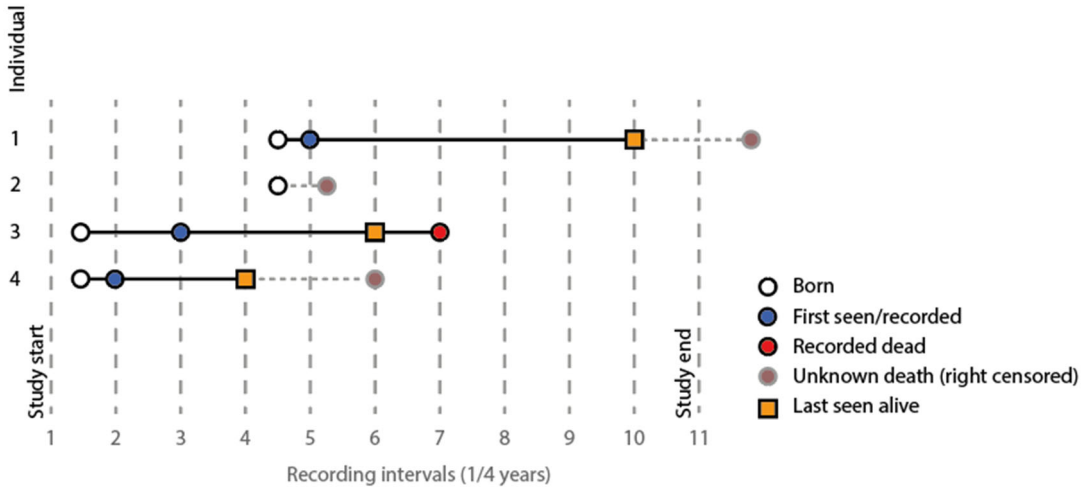


Figure 5.2: Representation of the types of censorship evident in the badger dataset. Individual 1 and 4 are both right censored, individual 3 is interval censored, individual 2 is never recorded.

Our analysis is split into 2 sections: First, we generate survival data from four different known distributions and format it to represent CMR data with known recapture probability. Any records where the individual has died prior to being captured are removed from the analysis to correspond with *real* data where these individuals would never have been recorded. Using our IS approach we then analyse the remaining capture histories, comparing the fits of the four mortality models to identify the data generating model. Second, we analyse CMR data originating from a wild population of European badgers fitting and comparing a variety of models to investigate sex-specific differences in survival and mortality.

Simulations

Parameter Values

We chose parameter values for each of the mortality models that generated distinctive shapes of mortality trajectory and were also representative of values from real populations. As a result we expect our posterior model probability analysis to find clear evidence for the data-generating model for sufficient data, and reduce to less complex models otherwise. The exponential model was simulated with constant mortality rate of 0.01 (Hydra - Schaible et al., 2015); the Gompertz model used values of $a = 0.121$ and $b = 0.105$ (bighorn sheep - Gaillard et al., 2004); the Gompertz-Makeham model used values of $a = 6.7 \times 10^{-6}$, $b = 0.125$ and $c = 0.011$ (*Homo sapiens* - Gurven & Kaplan, 2007); and the Siler model used $a_1 = exp(-2)$, $a_2 = exp(-11)$, $b_1 = 1.2$, $b_2 = 0.11$ and $c = exp(-5)$ (*Homo sapiens* - derived from Engelman, et al., 2014).

Capture-Mark-Recapture data

We randomly simulated a vector $\boldsymbol{y}$ of individual survival times for 10 different homogenous populations of varying size (*n* = 1000, 500) using each of the four mortality functions. The exponential and Gompertz models can be simulated using simple inverse-transform sampling; the Gompertz-Makeham model uses the approach of Jodrá (2009), and the Siler model uses a novel approach that

we previously introduced (see Chapter 4) that also uses the ideas of Jodrá (2009).

We then set a population recapture rate ($p = 0.7$) and dead recovery rate ($r = 0.1$) to create a capture history for each individual and removing any that failed to be captured (i.e. dying before an alive capture occasion - these individuals would never have been recorded in a wild situation). This resulted in a series of vectors corresponding to each individual:

$\boldsymbol{y}$ Number of alive captures

$\boldsymbol{tM}$ Maximum possible number of captures (from birth until dead recovery or end of study)

$\boldsymbol{tL}$ Last alive capture occasion

$\boldsymbol{tU}$ Recovered dead occasion

Case Study

We used data from badgers trapped between 1982 and 2020 inclusive. The badger population is sampled using live traps on (usually) four occasions per year with all trapped badgers anaesthetized and subjected to several diagnostic tests for bTB before being released (for a detailed account of the trapping and testing procedures see Wilkinson et al., 2000). On first capture, each badger is given a unique tattoo so it can be identified without error on subsequent capture occasions. We used badgers of known age (i.e. badgers caught and identified as cubs or yearlings which is readily identifiable from size, pelage and tooth wear; (Delahay et al., 2013) and then completed a series of different analyses. First, we fitted the 4 mortality models to the entire data set; then, using the best fitting model(s) we then allowed sex variation on combinations of parameters to determine a set of one or more models that describes sex differences (or similarities) in lifetime survival and mortality trajectories.

Simulations:

In the analysis of the exponential and Gompertz simulated survival data our approach correctly selected the data generating model on every occasion at both population sizes with no other model coming within the threshold to be considered. The Gompertz-Makeham model was correctly selected as the best fitting model on every occasion for the Gompertz-Makeham simulated data at both population sizes but the Siler model was suggested as a plausible option, coming within the threshold of the best fitting model on 5 occasions, once with a population of 500 and 4 times with a population of 1000. The accuracy of these results contrasts with the investigation of the Siler simulated data. The Siler model was only selected as the optimal model on one occasion out of the 20 replications. With population size at 500 individuals the Siler model was within the threshold of the optimal model on only 3 occasions and with a population of 1000 the Siler model was within threshold on 7 occasions (Gompertz-Makeham selected as the optimal model on every occasion).

To investigate the detection of the Siler model further we adjusted the dead recovery rate (r = 0.4, 0.6, 0.8; p = 0.7; n = 1000) and found it to have little impact on the Siler model being selected as the optimal model. At all dead recovery rates the Gompertz-Makeham was consistently favoured with the Siler model being within threshold on 4, 6 and 5 occasions at recovery rates of 0.4, 0.6 and 0.8 respectively. We then adjusted the recapture probability (p = 0.4, 0.6, 0.8; r = 0.1; n = 1000) and again the Gompertz-Makeham model was favoured on all but one occasion at p = 0.6 and one occasion at p = 0.8. The Siler model was within threshold on 1, 5 and 7 occasions at recapture rates of 0.4, 0.6 and 0.8 respectively. Throughout these simulations the Gompertz-Makeham model was chosen as the best fitting model or at least suggested within the threshold of the optimal model, suggesting that the early-life mortality changes were failing to be detected. We elevated the a_1 parameter to accentuate the early-life downtick in mortality and when set at 0.2 (originally 0.1353) the Siler model was within the threshold of the optimal model on every occasion and selected as the optimal on 5 occasions (dead recovery = 0.1,

recapture = 0.7). We then set a_1 at 0.25 which resulted in the Siler model being selected as the optimal model on every occasion and the Gompertz-Makeham being within threshold on 6 occasions. Finally we adjusted the b_1 parameter (originally 1.2) by 0.5 thus increasing and decreasing the rate at which early life mortality decays. With the rate decreased the Siler model was selected as the optimal model on every occasion (with no other model within threshold) and with the rate sped up the Gompertz-Makeham model remained the preferred model throughout with no other model within threshold.

Case Study: Badger Analysis

We initially compared the fit of the four different mortality models to all the badgers together (n = 2617) and found the best fitting model to be the Gompertz-Makeham with the Siler model selected within the threshold. Having demonstrated that the Siler model is difficult to detect and yet in this case still within the threshold value of the best fitting model, our further analyses used the Siler model to allow the opportunity for early life mortality patterns to be inferred. We therefore investigated sex specific differences in lifetime mortality trajectories using the Siler model. It is worth noting that as the parameters a_1 and b_1 reduce towards zero the shape of the Siler becomes more similar to a Gompertz-Makeham shape, so by using the Siler model we are not preventing the data from fitting this shape. We used a regression style model construction to allow parameters to vary according to sex, for example:

$$\begin{aligned} tD_i &\sim \text{Siler}(a_1 \times a_1^M, a_2, b_1, b_2, c) \\ \log(a_1^M) &= \beta \times \text{sex}_i \end{aligned}, \qquad (5.10)$$

where tD is actual time of death on a continuous scale and described by the Siler model allowing sex specific variation on a_1. The parameter a_1^M is modelled on the log scale to ensure the resulting parameter is positive and represents a multiplier of any difference between males and females in the parameter a_1. We constructed the 32 different models that allow sex specific variation on every possible combination of the 5 parameters, and compared the resulting log marginal likelihoods, see Fig.5.3.

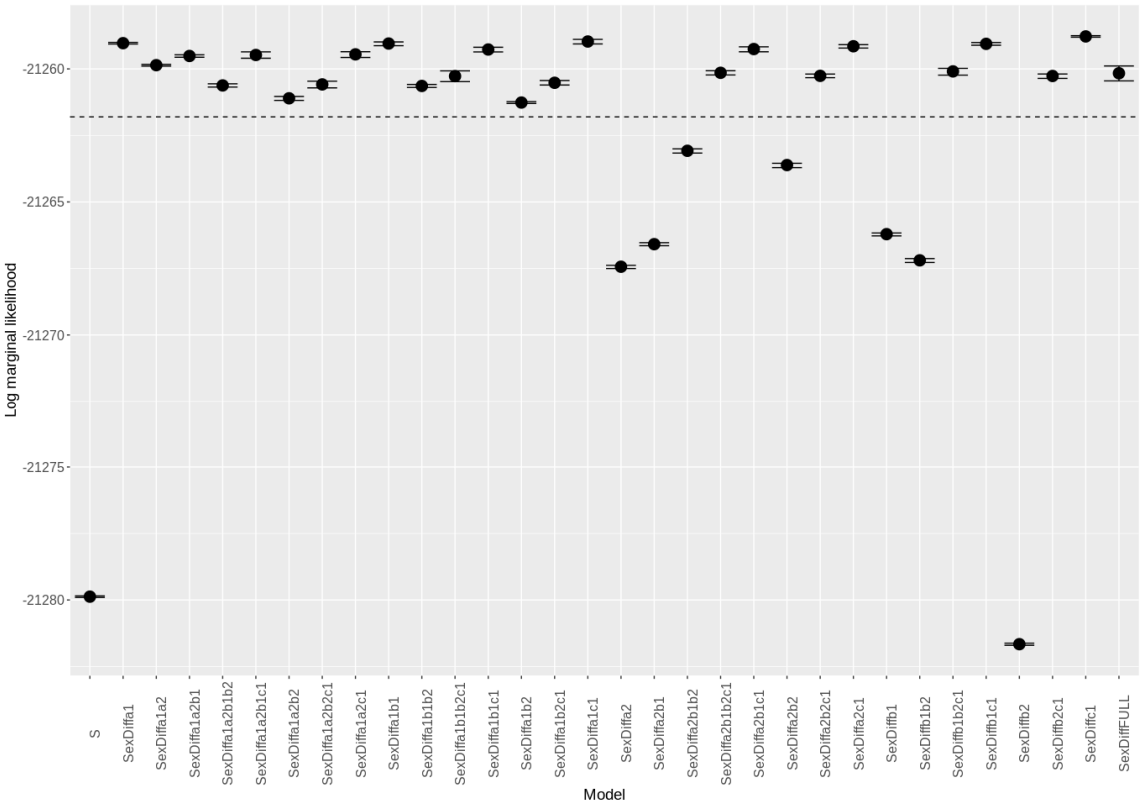


Figure 5.3: Log marginal likelihoods for all proposed models used to fit the badger data. Dotted line represents a value log(20) from the lower credible interval of the most supported model: following Kass & Raftery (1995) we consider all models lying above this threshold to be credible models that can be used in BMA.

The best fitting model chosen by the importance sampling approach was one allowing for sex specific variation on c1, suggesting that there is evidence for an underlying age independent difference in mortality between males and females. Several models were within the threshold of the best fitting model but the Siler model with no sex-specific variation was dismissed, suggesting that there is strong evidence for some sex specific variation in mortality across the lifespan of badgers. We calculated DIC and WAIC scores for all models compared (see Table 5.2) and found WAIC to be in support of the results of our IS approach – no clear 'best model' and multiple models within 3 points of one another. The DIC scores were slightly different and suggested strong support for a model allowing sex-specific variation on b_2 – a model that in all other model comparisons had performed poorly.

Table 5.2: Deviance Information Criterion (DIC) and Widely Applicable Information Criterion (WAIC) scores for competing models. Substantial support for one model over another is considered when the ΔDIC / ΔWAIC > 3 – this refers to the difference in DIC or WAIC score compared to the next best model. All of the competing models are variants of the Siler model with each allowing sex specific variation on a combination of parameters.

Parameter	DIC	Rank	ΔDIC	WAIC	Rank	ΔWAIC
a1	42434.02	12	0.46	42469.48	1	
c1	42438.32	15	2.01	42469.54	2	0.07
a1c1	42390.43	4	21.01	42469.88	3	0.34
a1a2	42433.56	11	9.26	42469.90	4	0.02
a1b1	42447.28	17	2.55	42470.34	5	0.44
a2b1c1	42453.58	19	3.62	42470.44	6	0.10
a1a2b1c1	42417.14	8	0.06	42470.55	7	0.11
a1a2b1	42456.93	23	0.96	42470.76	8	0.21
a1b2	42457.26	24	0.32	42470.76	9	0.00
a1b1c1	42404.84	5	14.41	42470.84	10	0.08
a2b2c1	42444.73	16	6.40	42471.12	11	0.28
a2c1	42461.53	26	3.09	42471.21	12	0.09
a1a2c1	42455.39	20	1.81	42471.25	13	0.05
b1c1	42458.44	25	1.19	42471.32	14	0.07
b2c1	42455.50	21	0.11	42471.52	15	0.19
a2b1b2c1	42449.95	18	2.67	42471.80	16	0.28
b1b2c1	42424.30	10	6.92	42471.88	17	0.09
a1b1b2	42455.97	22	0.48	42471.92	18	0.04
a1a2b1b2	42436.31	14	1.05	42472.05	19	0.12
a1b1b2c1	42369.42	3	91.83	42472.61	20	0.57
a1a2b2	42417.38	9	0.25	42472.63	21	0.02
ALL	42417.08	7	7.01	42473.06	22	0.43
a1a2b2c1	42277.59	2	81.08	42473.84	23	0.78
a2b1b2	42470.07	28	2.03	42477.85	24	4.01
a2b2	42468.05	27	6.52	42478.85	25	1.00
b1b2	42477.55	29	7.48	42487.98	26	9.12
b1	42435.26	13	1.24	42489.05	27	1.07
a2b1	42410.06	6	5.22	42493.86	28	4.81
a2	42492.04	31	13.05	42494.31	29	0.45
No sex diff.	42478.99	30	1.44	42516.19	30	21.88
b2	42196.52	1		42521.50	31	5.31
a1b2c1	42700.47	32	208.43	42756.72	32	235.21

We then used three different approaches to produce survival and mortality trajectories (Fig. 5.4). First, we chose the most complicated model that was within threshold of the best fitting model (this was the full model allowing sex specific variation on all parameters); second we chose the outright optimal

model (one that allows sex specific variation on c) and finally we conducted Bayesian model averaging across all models that were within threshold of the best fitting model. There are negligible differences between the approaches in the shape of the survival and mortality curves for both sexes, with all indicating sex specific variation across the entire lifetime trajectory.

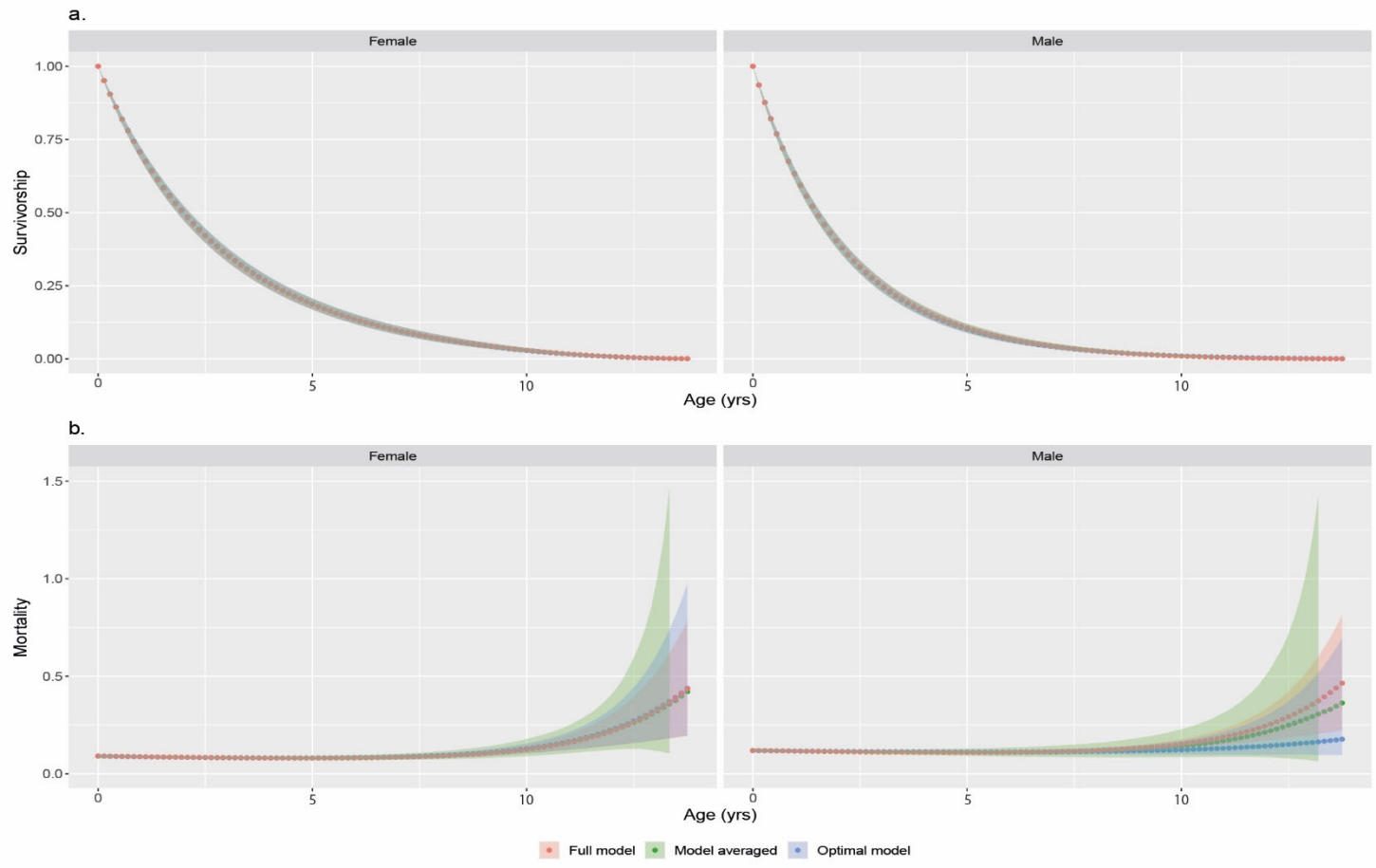


Figure 5.4: Sex specific predicted (a) Survival and (b) Mortality curves using models selected using our Importance sampling approach. Colour indicates different sex and the model selection method: Most complicated model alone (Siler model allowing sex specific variation on all parameters); the most supported model (Siler model allowing sex specific variation on c_1); Bayesian model averaged (parameters averaged according to posterior model probabilities across all models within log(20) of the most supported model).

The only major difference lies within the male mortality curves, here the Siler model with sex specific variation on all parameters suggests a reduced rate of senescence as compared to the other approaches. This is the only model which allowed any variation on the b_2 parameter which primarily describes this region of the curve. Whilst analysing the badger data we also studied the underlying structure of the Siler model to detect the dynamics of the model parameters. The correlated nature of some of the parameters suggests that the parameters compete with one another to describe the patterns of survival and mortality. This is most evident between a_1, which describes 'at birth' mortality rates and c, which describes age-independent mortality (see Fig.5.5).

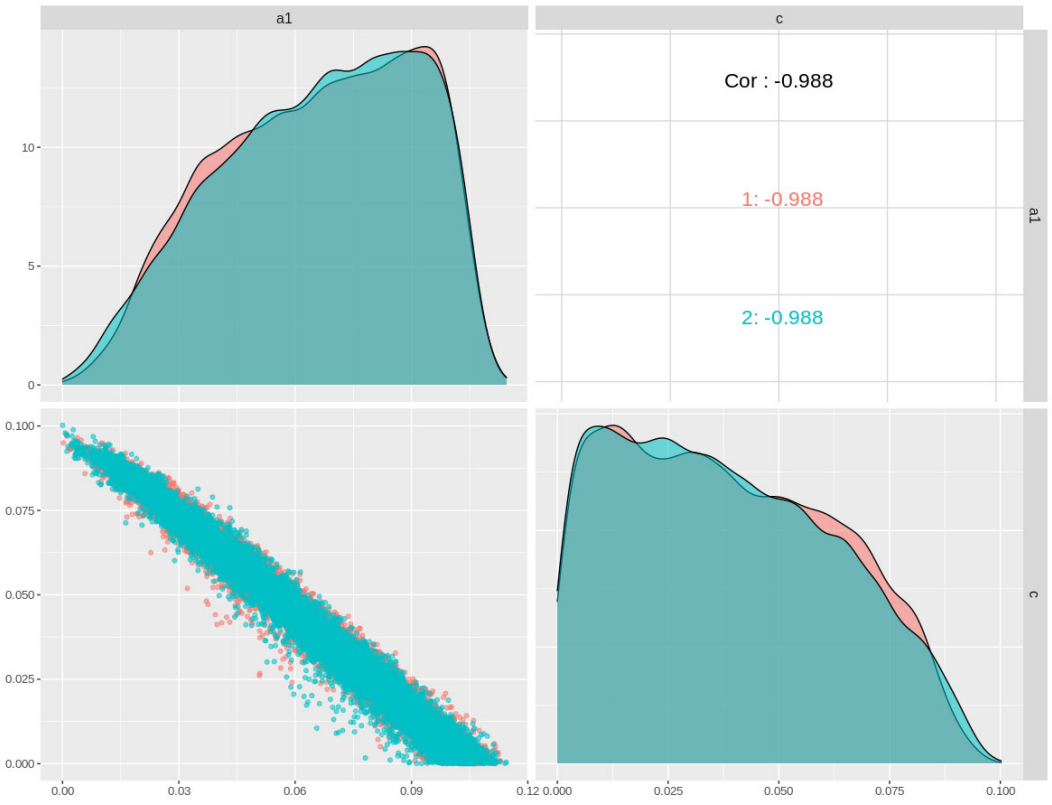


Figure 5.5: Pairs plot of a_1 and c MCMC samples when fitting a Siler model with no sex-specific variation to the badger data, colour representing the 2 chains run.

Discussion

In this chapter we have developed a straightforward Bayesian approach for the estimation of the marginal likelihood that we introduced in chapter 4 and made it applicable to CMR data which is common in ecological research. We openly provide all code in the hope that this will allow researchers to adapt it to suit individual requirements and research questions.

Through the investigation of simulated data we demonstrated the accuracy of the approach particularly when the shape of the mortality and survival curves are distinctive and there is little change in early life mortality (i.e. when simulating from the exponential and Gompertz models). The impacts of the CMR sampling process become more apparent when attempting to detect early life changes in mortality. Any early life downtick in mortality is suppressed by individuals failing to survive long enough for an initial capture event to take place, so their existence goes unrecorded and initial mortality estimates are underreported. The resulting lack of signal within the data in support of bathtub shaped mortality trajectories explains why our approach had difficulty in correctly selecting the Siler model as the data generating model, instead choosing the Gompertz-Makeham. This result has wider implications for survival analysis when using CMR data and offers a potential explanation as to why bathtub shaped mortality (e.g. Siler model) is rarely reported in wild systems, with simpler models generally being favoured (e.g. Dukas, 2008). We demonstrated that increasing recapture and/or dead recovery rates (even to levels unlikely to be achievable in the wild) had little impact on the detection of early life mortality changes, suggesting that truly accurate descriptions of lifetime mortality requires detailed information on juvenile survival which remains difficult to achieve in the field (Delahay et al., 2009). Directly adjusting the parameters that describe early mortality (a_1 and b_1) allows a deeper understanding of the challenge involved in inferring the Siler parameters. An increase in the initial mortality rate a_1 serves to extend the length of time that the early life downtick in mortality lasts, this allows some individuals to survive long enough to be captured and therefore adds information that can inform parameter estimates. A similar effect can be seen when adjusting b_1- the Siler model only became the optimal model when the b_1 parameter was reduced, not

increased. Again, this serves to elongate the shape of the mortality decrease through early life and thus increases the chance of individuals surviving long enough to be captured. When analysing data from natural populations it is important to remember that the two parameters will interact so there are no set limits which can be deemed truly detectable and likely to infer a Siler or bathtub shaped mortality curve. To accurately estimate the dynamics of early life mortality it is crucial to consider the frequency of capture events in conjunction with the speed of life history of the target species. Researchers will need to balance data collection with the potential negative impacts of repeated captures if they are to accurately estimate the shape of early life survival and mortality. In some simple situations it may be possible to utilise remote/ less invasive recording/capture methods (e.g. camera traps, photographic ID, radio frequency identification) to alleviate potential negative impacts of increased captures but often the research question will require physical capture (e.g. to carry out diagnostic tests on the individual).

A further complication associated with the Siler model is caused by the correlated structure of the model parameters and in particular a_1 and c. These two parameters are often highly correlated (see Fig. 5.5) and compete against each other to describe underlying mortality levels albeit with differing explanations: set at birth (in the case of a_1) or acting across entire lifetime but independently of age (in the case of c). Distinguishing between the origins of survival and mortality rates requires high quality data and the issue will have greatest impact when information regarding births and early life deaths is sparse, as is often the case with CMR data. When carrying out model comparisons in these instances it is unsurprising that the Gompertz-Makeham model is chosen over more complicated bathtub shaped models (here the Siler model) as even moderate levels of early life mortality can be absorbed by the age-independent parameter c rendering the additional parameters redundant.

We warn against dismissing mortality models that ignore the potential for early life variation, for accurate descriptions of mortality and survival trajectories we recommend bathtub shaped models be considered as a matter of course when analysing lifetime CMR data. Should analysis identify only subtle changes in

early life mortality then it is feasible that these changes are being underreported and more complicated models are dismissed speciously. Pre-capture mortality has been estimated in the past (e.g. Cheesman et al., 1987; Harris & Cresswell, 1987) which could be readily incorporated into Bayesian analyses with biological justification as a result of our investigations here.

When analysing the badger data the Gompertz-Makeham model was identified as optimal but the Siler model remained within the threshold to be included and returned a posterior model probability of approximately 10%. For the reasons outlined above we chose to use the Siler model to investigate sex specific differences in mortality which although more complicated could still allow a Gompertz-Makeham shape to be described if necessary (when parameters a_1 and a_2 reduce towards 0). We found considerable evidence for sex specific variation in mortality with all 23 of the models within threshold of the best fitting model allowing sex specific variation on at least one parameter and a Siler model with no sex variation dismissed with a posterior model probability of zero. Our results from the badger analysis matches previous investigations into sex specific differences in badgers (Rogers et al., 1997; Hudson et al., 2019). The results from our IS approach were mirrored by the WAIC scores but the DIC scores were less consistent. DIC has faced some criticism in the literature, and is known not to work well for some types of model due to the fact it relies on point estimates of the parameters, whereas WAIC uses measures that average over the posterior distribution, and our posterior model weights use the marginal likelihood averaged over the prior distribution (see e.g. Plummer, 2008; Celeux et al., 2006 and summarised in Spiegelhalter et al., 2014). We investigated the posterior parameter distributions of the model with sex-specific variation included and found some evidence of multi-modality (see Appendix 4 for an example), suggesting that a single point estimate (i.e. the posterior mean) is unlikely to be a robust choice in this case. The WAIC analysis highlights a fundamental issue of using WAIC (and DIC) for model comparisons. When there is no clear ‘best’ model the researcher is left with a judgement call as to which model is most appropriate to select and there is no justified method to generate model weights to allow e.g. BMA to incorporate this uncertainty (Hooten et al., 2015 - although see Hoeting et al., 1999), although

there is interesting work being done towards this using Bayesian predictive stacking (Yao et al. 2018), which we do not explore here.

Conclusions

Survival and mortality research often focuses on a particular life phase and commonly the focus is upon senescence. Historically the Gompertz equation has been the most commonly used model to describe age-specific mortality (Pletcher, 1999) and is often the choice when comparing mortality across species (e.g. Tidière et al., 2015). Although this has been a result of data recorded often consisting only of individuals that have reached maturity, as monitoring projects improve the quality and depth of information available it is crucial to not overlook early life mortality changes that could be impacting other phases of life. An over-reliance on the Gompertz model may result in erroneous inference as it ignores early life mortality changes but the Siler model or in more general terms ‘bathtub’ shaped mortality curves are difficult to detect and remain rare when describing wild populations (although see e.g. Hudson et al., 2019; Lemaître et al., 2020 and the recommendations of Ronget et al. (2020). The frequency of capture events should be given careful consideration in the planning of any monitoring project to ensure the dynamics of early life mortality can be recorded and accurate estimates of survival and mortality inferred, including the detection of bathtub shapes. In our analysis we chose to compare a series of nested models of increasing complexity (the Siler model has the exponential, Gompertz and Gompertz-Makeham models nested within it) which allows a wide range of mortality curves to be described. We highlighted the correlated structure of the parameters and show that only minor changes in one parameter value can impact the entire mortality trajectory (see Hudson, 2019) further emphasising the need to assess mortality over entire lifespan to gain the most accurate estimate of mortality at any chosen stage of life.

Chapter 6: Efficient Bayesian model comparisons for nested models – from importance sampling to reverse jump Markov chain Monte Carlo

Abstract

Model comparison is a fundamental aspect of statistical analysis. Being able to quantify the weight of support in the data for a particular model is increasingly important as researchers favour multi-model inference techniques such as Bayesian model averaging (BMA) which reduce bias by incorporating model uncertainty. Methods usually require estimation of the marginal likelihood of each competing model – the so-called *model evidence*, from which posterior model probabilities can be calculated. A variety of methods, of differing complexity have been proposed and we previously presented a straightforward and flexible approach based on importance sampling. Reverse Jump Markov chain Monte Carlo (RJMCMC) is an alternative method that avoids direct estimation of the marginal likelihood and instead naturally offers posterior model probabilities which can be used for model comparison and BMA. RJMCMC is particularly efficient for comparing nested models or in variable selection, survival analysis provides a suitable situation to implement this method. Here we present a comparison of our IS approach with RJMCMC in an analysis of sex-specific variation in mortality from capture-mark-recapture data from a natural population of European badgers (*Meles meles*). The results show that both methods produce comparable results but the RJMCMC is notably faster and requires less coding effort. We therefore advocate the use of RJMCMC for survival analysis when model comparison can reduce to a variable selection problem.

Introduction

Comparing the fits of potential models to data remains a core element of statistical analyses, whether researchers are attempting to select one optimal model or wanting to estimate the strength of support in favour of a range of models, thus allowing multi-model inference (Burnham & Anderson, 2002; Harrison et al., 2018; Kass & Raftery, 1995) techniques to be employed. Adopting a Bayesian approach to model selection and comparison has many natural advantages (see Berger & Pericchi, 1996, 2001) which has led to a variety of different methods being proposed, yet there is no consensus over which performs best (Robert & Wraith, 2009). Penalised loss functions such as the deviance information criterion (DIC) (Spiegelhalter et al., 2002) and

Watanabe-Akaike information criterion (WAIC) (Watanabe, 2010) are straightforward to calculate which has led to widespread use despite some criticism (e.g. Plummer, 2008; and see chapter 4). Both these methods can be viewed as approximations to different versions of a process known as cross-validation (Stone, 1977) – a resampling method that uses different portions of the data to train and then test a proposed model. The goal of cross-validation (CV) is to evaluate a model's predictive ability (usually measured using the mean-squared error) and highlight problems like overfitting or selection bias (Cawley et al., 2010). A popular version of CV is leave-one-out CV (LOO-CV) which repeatedly uses all but one observation as training data – the left out observation then being used to test the proposal model. CV is a popular choice but can be computationally expensive and is not always well defined in dependent data settings (Gelman et al., 2013). An alternative approach within the Bayesian paradigm requires consideration of the marginal likelihood of the data given a model (Jeffreys, 1961) – sometimes referred to as the *model evidence*. Calculating the marginal likelihood is computationally intractable for all but the most trivial models, meaning it is often approximated using numerical methods (Xie et al., 2011 and see Llorente et al., 2020 for a comprehensive review). Having estimated the marginal likelihood, model comparisons can then be carried out by calculating Bayes' Factors (Jeffreys, 1961), which equates to the ratio of marginal likelihoods of competing models, or by calculating posterior model probability weights that can also be used in Bayesian model averaging (BMA) to efficiently incorporate any model uncertainty into inference and prediction (Fragoso et al., 2018). In the previous two chapters we presented a method for the accurate estimation of a model's marginal likelihood based on importance sampling (IS), which performs well when dealing with a large amount of missing data (Touloupou et al., 2018; and see chapters 4 & 5) – a common feature of ecological research. This versatile approach has a wide range of applications and is not limited by models having to be nested. However, as the number of competing models increases the time taken to calculate the marginal likelihoods for each and every model can quickly become prohibitively large.

An alternative approach to calculating posterior model weights is to use reversible jump Markov Chain Monte Carlo (RJMCMC) (Green, 1995). RJMCMC is a flexible technique that computes the joint posterior distribution of a latent model indicator and associated parameters given the data by extending the posterior space and allowing the Markov chain to jump between models with potentially different dimensions (Green & Hastie, 2009). The number of iterations when the chain is within a particular model space is proportional to the marginal likelihood of that particular model and equates to posterior model probabilities (Hastie & Green, 2012). RJMCMC has faced some criticism (Brooks et al., 2003) as the MCMC can be difficult to tune and suffer with poor mixing, particularly as competing models become more distinct (in terms of the number and interpretation of parameters). However, if well tuned it can often perform more efficiently than other approaches (O'Hara & Sillanpaa, 2009). It is becoming a more popular choice in recent years, partly due to the availability of general-purpose software to facilitate its implementation (Hooten et al., 2015). In many instances model selection problems can reduce to a simpler framework of variable selection, where the question becomes: which subset of variables should be included within a model? A variety of algorithms have been proposed to complete this task (see O'Hara & Sillanpaa, 2009 for a review) but RJMCMC performs particularly well in these instances where models are nested and transition rules are simpler to define (Touloupou et al., 2018). A common approach for variable selection involves defining the most complex model with latent binary indicators attached to each explanatory variable – the RJMCMC algorithm then includes (and excludes) different combinations of explanatory variables by switching the indicators 'on' and 'off' (see e.g. Dellaportas et al., 2002). A "model" is then defined by each unique combination of indicator variables, whereas the marginal posterior probabilities of inclusion for each variable can also be directly calculated (Hoeting et al., 1999; Kass & Raftery, 1995; Viallefont et al., 2001).

Survival analysis often involves the exploration of potential impacts of explanatory variables on individuals' survival and therefore presents a situation well suited to RJMCMC analysis. Our previous analysis investigated sex-specific effects on age-specific survival of the European badger (*Meles meles*)

using the Siler (Siler, 1979) mortality model. Our IS approach required the construction and analysis of 32 different versions of the 5-parameter Siler model to fully analyse the potential impact of sex. As the number of explanatory variables increases, the number of models that are required increases exponentially and thus reduces the efficiency of the process. Framed within a RJMCMC variable selection problem the same investigation only requires the construction of one large model, which is not dependent on the number of potential explanatory variables to be investigated. Here we introduce RJMCMC as a variable selection tool that is simpler to implement than our IS approach particularly as the number of explanatory variables increases and when the models to be compared are nested.

Methods

To demonstrate the accuracy of the RJMCMC process we chose to repeat the analysis of the previous chapter – investigating sex-specific variation in age-specific mortality in a population of European badgers (*Meles meles*). The data are collected as part of a long-term monitoring project of a natural population of badgers in Woodchester Park, Gloucestershire; the analysis here consists of capture history records from individuals sampled on (usually) four occasions each year between 1982–2020 inclusively. For a detailed account of the trapping and testing procedures see Wilkinson et al. (2000). We have previously completed the same analysis using our IS method in chapter 5 so omit the methodology used to generate the posterior model probabilities using that approach here and focus instead on the RJMCMC. All our analysis is carried out using software package NIMBLE (de Valpine et al., 2017) implemented in R (R Core Team, 2019). We provide full model code in Appendix 5 and describe the steps taken here.

We first define the full model

$$tD_i \sim \text{Siler}(a1a1_i^M, a2a2_i^M, b1b1_i^M, b2b2_i^M, cc_i^M) \quad (6.1)$$

where tD_i is the latent variable 'age at death' and each parameter multiplier is described by e.g.

$$\log(a1_i^M) = \beta_{a1} \times \text{sex}_i \times z_{a1} \quad (6.2)$$

where z_{a_1} is the binary indicator variable that switches the effect of sex on parameter a_1 (in this example), on and off. Similarly for the other parameters. The setup and run code remains the same as a standard MCMC analysis in NIMBLE except for the configuration of the samplers. The reversible jump sampler is an extension of the Metropolis-Hastings algorithm and must be used to update the indicator variable (and corresponding coefficient) within the MCMC chain.

We ran two MCMC chains for 50,000 iterations with a burn in of 10,000 and no thinning. We confirmed satisfactory mixing and convergence by visually inspecting the posterior trace plots and calculating the Gelman-Rubin Rhat value for each parameter. The total computation time for this method was recorded at 2284 seconds as compared to 3091 seconds taken to estimate the marginal likelihood for the simplest of the 32 models using the IS approach, meaning that the full IS analysis would require approximately 27 hours to complete. The MCMC chain produces a point estimate for each posterior model weight, and so we bootstrapped the posterior samples to generate 95% confidence intervals to give us some idea about the uncertainty of the estimates.

Priors

For the RJMCMC analysis we set weakly informative exponential (rate = 1) priors on the Siler parameters, the recapture rate had a uniform prior (min = 0, max = 1), the inclusion indicators were set with a Bernoulli (p = 0.5) distribution and all beta coefficients were set with an uninformative Normal (mean = 0, sd = 1) prior which in turn acts as a regularisation method.

Interpretation

We make use of the posterior probability categorisations outlined by Kass & Raftery (1995) to correspond to the strength of association between two variables.

Table 6.1: Bayesian model averaging: categorisation of posterior probabilities from (Kass & Raftery, 1995)

Evidence for an association with Y	Posterior probability
Weak	50-75%
Positive	75-95%
Strong	95-99%
Very strong	> 99%

Results

Having already calculated the posterior model probabilities (and confidence intervals) using our IS approach in the previous chapter, we combined the estimates with those generated here via RJMCMC (Fig. 6.1). Figure 6.1 shows good agreement across the two methods with every confidence interval overlapping to some degree and many with near identical ranges given the finite number of samples.

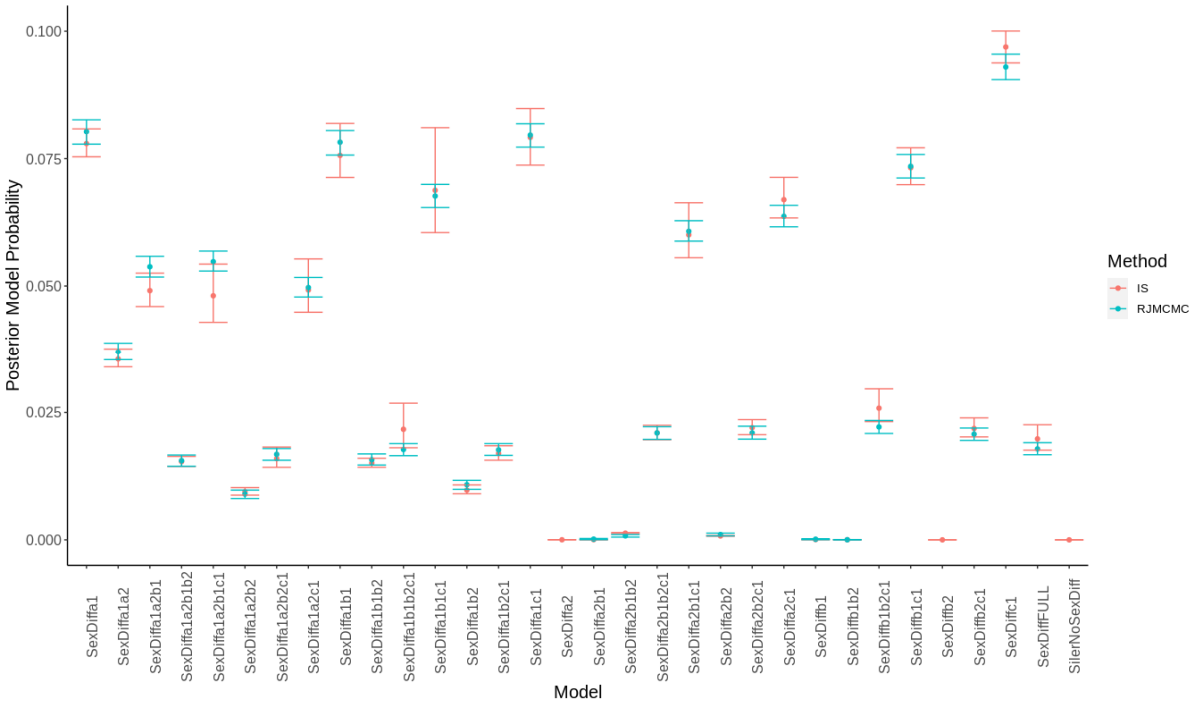


Figure 6.1: Comparison plot of median posterior model probabilities and 95% credible intervals generated via importance sampling (red) and reversible jump Markov chain Monte Carlo (blue) methods. Competing models are investigating sex-specific variation in age specific mortality for a natural population of European badgers fitted to the Siler (Siler, 1979) function.

These approaches should converge to the same answer in probability. There are three models that do not appear in the RJMCMC analysis (SexDiffa2, SexDiffb2, SilerNoSexDiff) – this is a result of the RJMCMC sampler not accepting any *jumps* into the posterior space for these models as the posterior probability was deemed too low. This corresponds with the negligible posterior model probability generated by the IS approach.

Discussion

Model comparison is a fundamental part of data analysis and there are a wide variety of methods that have been proposed to complete this task (Plummer, 2008). Variable selection is a special case of model comparison and a fundamental part of survival analysis, where the list of potential explanatory variables can be long (Li et al., 2005). Analysts will often begin with a large number of possible predictors but aim for a more parsimonious model to improve interpretation and to prevent possible overfitting. Therefore having

efficient methods to select important variables is vital for model building. Here we have presented a comparison of our previously introduced IS approach and RJMCMC. In cases where the models to be compared are nested and the problem can be reduced to one of variable selection we have found implementation of the RJMCMC analysis to be the more efficient method. The results from both analyses are comparable with only minor differences in posterior model probabilities which are due to numerical sampling error, and we expect these differences to disappear if we increased the number of samples in each case. The main advantage of the RJMCMC approach is in the amount of time taken to carry out the analysis as compared to the IS approach. With appropriate sampling strategies employed, running the full RJMCMC analysis of the maximal model takes comparable time to the analysis of one proposed model when using IS, as the number of predictors increases the time saving can quickly become palpable. Variable selection via RJMCMC is straightforward to implement within the software package NIMBLE (de Valpine et al., 2017) which offers a range of sampling algorithms that can be explored to ensure satisfactory mixing of the MCMC chains. Output is interpretable and a transparent reflection of model uncertainty. This model uncertainty is easily dealt with through the use of multi-model inference techniques such as BMA but it is also possible to calculate posterior inclusion probabilities (i.e. in our example, the proportion of iterations that are within models that include sex variation) for each predictor which may be more interpretable in such situations. BMA and more specifically model comparison using marginal likelihoods has faced criticism due to the sensitivity to the specific prior specification in each model. This has led to alternatives being developed – e.g. Yao et al. (2018) extended the idea of stacking from minimising the squared error to maximising scoring rules therefore making the approach applicable to combining posterior predictive distributions generated using LOO-CV techniques. CV methods will fail if the current data are not representative of future data or if the observations are not exchangeable conditional on the model parameters – for this reason CV must be used with caution when assessing models with temporal, spatial or multi-level structure (Vehtari et al., 2018). The stacking (using PSIS LOO-CV) approach has faced some criticism (Gronau & Wagenmakers, 2019) and in

future work we hope to carry out a more in-depth comparison of these techniques for survival analysis. Throughout this thesis we have focused our attention on model comparisons based on marginal likelihoods and always recommend to fit proposal models with different prior specifications to check for any inherent sensitivity. Marginal likelihood methods, such as those we propose, weight the proposed models in a probabilistic way conditional on the given dataset and will always select the model which best fits the data – it is then up to the researcher to determine if this fit is adequate.

Survival analysis is increasingly important within conservation and population ecology but the understanding that has come from laboratory studies or captive populations is often not reflective of wild systems. Uncovering the subtle dynamics of various predictors in natural populations remains an ongoing challenge. There is an increasing demand for tools that can facilitate variable selection over many predictors particularly as data rich monitoring projects of wild populations are becoming more common. RJMCMC is not new and we do not claim RJMCMC to be the panacea of Bayesian model comparison – in many cases IS, for example, can solve problems that are difficult to implement using RJMCMC (Touloupou et al., 2018). Applications of RJMCMC are diverse but it is yet to reach mass appeal with the majority of research implemented by 'experts' (Green & Hastie, 2009) and confined to statistical journals. Using RJMCMC as a variable selection tool for survival analysis is rare (although see Karapanagiotis et al., 2018; Newcombe et al., 2014) and we believe this to be the first instance of its use on data from a wild population. We hope that by providing the complete code for the analysis carried out here we can further broaden its appeal and use in applied settings.

Chapter 7: Investigating the impact of inbreeding on lifetime survival and mortality trajectories of European badgers

Abstract

Inbreeding depression (ID) is a fundamental concept in evolutionary biology and refers to a decrease in fitness caused by inbreeding. Traditionally, ID has been studied under laboratory conditions or with captive populations but the environmental stressors present in wild systems are difficult to replicate so comparisons to natural populations can lead to specious inference. The use of large scale molecular genetic data is in its infancy but has removed the necessity to conduct parentage analysis to provide a measure of inbreeding and shown the effects of ID to be dynamic across life stages and more severe and widespread in the wild than first thought. Our understanding of ID in the wild remains limited as studies generally focus on individual traits (as indicators of fitness) at specific phases of life – full life course effects are often overlooked.

Here we employ Bayesian techniques and make use of microsatellite data to investigate the effects of inbreeding on age-, sex- and infection-specific survival and mortality in a wild population of European badgers (*Meles meles*) naturally infected with bovine Tuberculosis. We use survival and mortality trajectory analysis to view life course effects and uncover antagonistic pleiotropic effects of inbreeding on mortality in a wild species for the first time. Our analysis provides evidence for both the mutation accumulation and antagonistic pleiotropy evolutionary theories of senescence suggesting they are not mutually exclusive mechanisms. The results of this study can help inform wildlife disease management strategies as well as potential conservation efforts and we provide full annotated code in the hope that other systems can be analysed to help improve our understanding of ID in wild populations.

Introduction

Evidence for the damaging effects of inbreeding is both widespread (Bozzuto et al., 2019; Charlesworth & Willis, 2009; Crnokrak & Roff, 1999; Keller & Waller, 2002) and controversial (e.g. Bulger & Hamilton, 1988; Hoogland, 1992). Decreased fitness caused by inbreeding, known as inbreeding depression (ID), has been a fundamental premise of evolutionary ecology since the writings of Darwin (1876). ID is caused by an increase in homozygosity at loci that carry rare recessive deleterious alleles or exhibit overdominance as a result of mating between relatives (Charlesworth & Charlesworth, 1987).

Empirical research into inbreeding depression has traditionally focused upon captive animals (Boakes et al., 2006; Ralls & Ballou, 1986) or laboratory populations (e.g. Bijlsma, Bundgaard, & Boerema, 2000; Swindell & Bouzat, 2006) and generally concentrates upon specific life stages or single components of fitness (Hoeck et al., 2015; Ralls et al., 1988). Artificial conditions have the capacity to affect the strength and genetic architecture of ID (Bijlsma et al., 1999) making any comparisons to wild populations, where environmental conditions will likely be more stressful, potentially specious. Our understanding of the mechanisms at play in the wild is limited and requires critical attention: from a conservation perspective, continued habitat destruction and fragmentation are making many wild populations smaller, more isolated (Haddad et al., 2015) and likely more susceptible to inbreeding (Stoffel et al., 2021). In evolutionary terms, improving our understanding of how genetic variation affects individual fitness in populations is paramount to our core understanding of evolution (Ellegren & Sheldon, 2008; Merilä & Crnokrak, 2001). Analysis of ID in the wild has demonstrated its detrimental impact on a variety of traits such as juvenile survival, adult longevity, fecundity, birth weight and egg-hatching rates (for a review see Keller & Waller, 2002) but whole life-course effects are generally overlooked meaning our understanding of some of the fundamental principles remains limited (Kardos et al., 2016; Stoffel et al., 2021).

Analyses of associations between inbreeding and fitness have traditionally relied on pedigree based measures of inbreeding (e.g. Pemberton, 2004) but the generation of large-scale molecular genetic data has presented alternatives and removed the need to conduct parentage analysis over many generations, which can be challenging in natural populations. The use of genomic data for the analysis of ID is still in its infancy but studies have shown that ID is both more severe and more widespread in natural populations than had originally been thought and the effects can be state-dependent and dynamic across life stages (Bérénos et al., 2016; Chen et al., 2016; Harrisson et al., 2019; Hoffman et al., 2014; Huisman et al., 2016; Niskanen et al., 2020). One state of particular interest is individual age (Brooks & Kemp, 2001) and the understanding that

fitness often declines in old age, a process known as senescence (Partridge & Mangel, 1999).

Evolutionary theories of senescence are based on the assumption that the force of selection declines with age and hence will be more efficient at eliminating genetic variants (alleles) that have detrimental effects in early life than those whose detrimental effects are not felt until later life (Hamilton, 1966; Medawar, 1957). These alleles then accrue in populations, causing age-related effects on fitness. The two leading genetic explanations are *mutation-accumulation* (MA): which refers to the process of accumulation of late acting deleterious mutations by any organism, caused by weak selection against late-acting genes; and *antagonistic pleiotropy* (AP): which assumes that detrimental mutations affecting late-life survival or reproduction are retained in populations thanks to pleiotropic effects that are beneficial in early life. Efforts to tease apart AP and MA as alternative genetic mechanisms responsible for senescence have generally been confined to laboratory studies (e.g. Hughes et al., 2002) which have found greater support for AP (Nussey et al., 2013). Despite an increasing number of information-rich demographic-monitoring projects contributing to our understanding of age related declines in mortality and other fitness related traits in wild populations (for a review see Nussey et al., 2013) comparatively few have made links with ID (although see e.g. Charmantier et al., 2006; Wilson et al., 2007; Keller et al., 2008; Harrison et al., 2011; Benton et al., 2018). These isolated studies of wild populations generally focus on changes in a specific fitness related trait (e.g. fecundity) across life-course rather than age-specific survival, and evidence in favour of AP and/or MA is less conclusive with support for both theories and suggestions that the mechanisms may co-exist (Harrison, et al., 2011).

Inbreeding is challenging to study in the wild (Huisman et al., 2016) particularly as evolutionary mechanisms such as inbreeding avoidance (Pusey & Wolf, 1996) make inbred individuals rare. The most straightforward approach to measuring inbreeding, in the absence of pedigree information, is to consider the prevalence of heterozygosity/homozygosity across multiple loci in each individual's genome. Large scale studies tend to use single-nucleotide polymorphisms or microsatellite data to measure multiple-locus heterozygosity

and then look for statistical associations with specific fitness traits (Marta Szulkin et al., 2010) although the compliment to multiple-locus heterozygosity – multiple-locus homozygosity has also been used (e.g. Benton et al., 2018). The validity of marker-based measures of inbreeding has been questioned (Slate et al., 2004) but many of the early studies utilising the approach used only a small numbers of markers: the utility of the approach depends on both the number of loci used and their expected heterozygosity (Miller et al., 2013). More recent research has found that fitness traits are more strongly correlated with marker-based measures of inbreeding, compared to pedigree-based measures (e.g. Forstmeier et al., 2012).

Survival is a key fitness trait when assessing animal population size yet it remains a difficult parameter to estimate in the wild (Murray & Paterson, 2006; Mccallum, 2008; Delahay, Smith, & Hutchings, 2009). Some of the issues associated with traditional life-table methods of monitoring survival (e.g. accommodating individual variability in mortality risk; discretisation of continuous time) are being overcome by the use of survival and mortality trajectories (Jones et al., 2008; Colchero & Clark, 2012). Lifetime trajectories can be used to describe survival and mortality patterns across entire lifespans in continuous time and often allow a deeper understanding of life history through the uncovering of subtle variations that could be missed by alternative approaches (Gaillard et al., 1994; and e.g. McDonald et al., 2014). Several functions have been used to describe mortality trajectories (e.g. Gompertz - Gompertz, 1825; Gompertz-Makeham - Makeham, 1867; Siler - Siler, 1979) and in humans and laboratory animals the standard shapes are well established (Bebbington et al., 2007; Eberhardt, 1985). The typical pattern for many species is a ‘bathtub’ shape: an initial drop in mortality risk from high early-life mortality, followed by a flat phase of relatively low mortality through early adult life and finally an accelerating, senescent increase in mortality in late life, also known as actuarial senescence. Evidence for bathtub shapes in natural populations is less prevalent particularly as research generally focuses solely on senescence (e.g. Nussey et al., 2008) often relying on the Gompertz function (Ronget et al., 2020), but may potentially be due to sampling procedures used to collect data. For example, Capture Mark Recapture (CMR) studies will miss individuals that

die prior to being caught (see chapter 5), and commonly suffer small sample sizes of older individuals. Even if wild populations tend to have bathtub-shaped mortality trajectories, as described by the Siler function, they are difficult to detect.

Our aim here is to employ a combination of statistical techniques to uncover novel patterns in the effects of ID on survival across the entire life-history of a free-living mammal and in doing so improve our understanding of how ID evolves. Employing survival (and mortality) trajectory analysis on data from a long-term monitoring project of a wild population of European badgers (*Meles meles*), naturally infected with the pathogen *Mycobacterium bovis* which is responsible for bovine tuberculosis (bTB), we investigate the influence of ID on the risk of mortality throughout the lifespan. Age-, sex-, and infection-specific variations in badger mortality have previously been evidenced (McDonald et al., 2014) including the detection of a senescent increase in mortality in later life (Hudson et al., 2019). We have shown elsewhere that the risk of acquiring disease increases with increasing multi-locus homozygosity (Benton et al., 2018). Here we ask, using Bayesian approaches to survival-trajectory analysis, whether multi-locus homozygosity influences survival during early-, mid- or late-life. If ID exists among badgers, then the MA hypothesis provides the prediction of a positive association between late-life increases in mortality and increasing multi-locus homozygosity. If AP plays a role, we predict a similar association in late-life, coupled with a negative association between early-life mortality and multi-locus homozygosity (MLH).

Materials and Methods:

Badger sampling

Data used in these analyses were collected from a long-term CMR study of a wild population of badgers at Woodchester Park in Gloucestershire (Delahay et al., 2013). Badgers are live trapped up to four times a year and on the occasion of first capture are given a unique identifying tattoo. All captured badgers were anaesthetised and subjected to several diagnostic tests for bTB before being released (for a detailed account of capture and testing procedures see Delahay et al., 2000; McDonald et al. 2018). A range of clinical samples (sputum, faeces,

urine, swabs of bite wounds or abscesses) have been routinely taken for the detection of *M. bovis* by culture (Gallagher & Horwill, 1977) as well as blood samples obtained for antibody tests. Between 1990 and 2005 the Brock ELISA (enzyme-linked immunosorbent assay) test was used (Goodger et al., 1994), this was replaced with the Brock TB Stat-Pak lateral flow immunoassay (Chembio Diagnostics Systems, USA - Chambers et al., 2008) test in 2006. A gamma-interferon assay for the cytokines associated with the cell mediated response to M. bovis (Dalley et al., 2008) was also used from 2006.

We only used badgers of known age (i.e. first trapped and identified as cubs or yearlings) and for which we had a genotype. Although difficult to test completely due to behavioural differences between individual badgers, previous studies have shown the probability of recapturing marked individuals is no different to unmarked individuals (i.e. no evidence of trap shyness/dependence) (Rogers et al., 1997). Limitations in the sensitivity of the diagnostic tests are well known (Drewe et al., 2010) but all tests are highly specific and so we are confident that those individuals who do test positive in this study are not truly uninfected. We created two distinct infection categories: Cub-positive (individuals that tested positive to at least one diagnostic test during the first year of their life) and Never-positive (individuals that never tested positive to any diagnostic test throughout their life). For the purpose of our analyses we worked with diagnostic test results rather than true infection status, ongoing research seeks to clarify the link between the two (Buzdugan et al., 2016; Wawegama et al., 2016)

Genotyping and measures of inbreeding

A hair sample was taken at first capture and stored in 80% ethanol prior to DNA extraction and genotyping (Carpenter et al., 2005). Genotyping involved the use of 22 microsatellite markers, each with 4-7 alleles.

All data processing and analysis was completed in R (R Core Team, 2019). We used the MicroDrop Programme (Wang & Rosenberg, 2012) to impute missing microsatellite data and tested for deviations from Hardy-Weinberg equilibrium for each of the 22 microsatellite makers using the *hwtest* function in R package Adegenet (Jombart, 2008) with none being found. There has been considerable

debate questioning whether a subset of molecular markers can accurately reflect genome wide homozygosity (DeWoody & DeWoody, 2005) but this uncertainty can be partially addressed through calculation of the parameter g^2 (David et al., 2007) which measures the degree to which a set of markers reflects variation in inbreeding among individuals. We calculated the parameter using the *g2_microsats* function in R package inbreedR (Stoffel et al., 2016) and for our set of markers g^2 was significantly different from zero ($g^2 = 0.002$, $p < 0.001$) meaning that the marker set can be said to reflect genome-wide effects of homozygosity (Szulkin et al., 2010).

We calculated a number of different measures of inbreeding: initially being inferred using a measure of multi-locus heterozygosity (Keller & Waller, 2002) using the *MLH* function in the InbreedR package (Stoffel et al., 2016). An individual inbreeding coefficient can also be estimated directly from the microsatellite data – defined as the probability of an individual inheriting 2 identical alleles from a single ancestor (calculated using the Adegenet package in R - Jombart, 2008). Finally we calculated a measure of multi-locus homozygosity – the proportion of genotyped loci that are homozygous. We checked the robustness of our analysis by repeating with each different measure of inbreeding and found negligible differences.

Statistical modelling

All R code is provided in Appendix 6.

We jointly estimate survival and recapture probabilities in a similar fashion to Cormack-Jolly-Seber (CJS) (Cormack, 1964; Jolly, 1965; Seber, 1965) models which accounts for the sampling process and subsequent missing data inherent in CMR studies. We made use of the Siler (Siler, 1979) mortality function to model age at death in continuous time. The Siler function consists of 5 parameters that describes the mortality rate μ at age x

$$\mu(x) = a_1 e^{-b_1 x} + c + a_2 e^{b_2 x} \quad (7.1)$$

with parameters $a_1, a_2, b_1, b_2, c > 0$. We have previously coded the full Siler function as a custom distribution function (chapter 3) that can be implemented in the package NIMBLE (de Valpine et al., 2017) which allows flexible and straight forward model specification. We employed a Reversible Jump Markov Chain Monte Carlo (Green, 1995) (RJMCMC) approach to variable selection to investigate sex-, infection- and inbreeding-specific effects by constructing a maximal model with indicator nodes attached to each variable. RJMCMC is a general framework in which the dimension of the parameter space can vary between iterations of the Markov-chain; this allows variables to be *switched* on and off by the reverse jump sampler and thus included or excluded from the model as the chain runs. The amount of time (number of iterations) that the MCMC chain spends within a given model space can then be used to calculate posterior model probabilities in favour of any possible model and inform model comparisons/choice. In models that include a large number of possible combinations of included variables the posterior model probabilities can quickly become diluted by the sheer volume of possible models unless the signal within the data is particularly strong in favour of a small number of models. In these instances it is more straightforward and interpretable to generate posterior inclusion probabilities for each of the variables and use the posterior model probabilities to inform multi-model inference techniques such as Bayesian model averaging (BMA) to account for the uncertainty in model choice when constructing survival and mortality trajectories.

Priors

We used weakly informative exponential distributions (rate = 1) for the priors of the five Siler parameters. We specified uninformative normal distributions (mean = 0, sd = 1) for all of the sex-, infection- and inbreeding-specific coefficients and used Bernoulli distributions (p = 0.5) for the inclusion probabilities giving each variable equal prior chance of being included in a model.

Model Specification

We set the core structure of the model such that age at death is distributed according to the Siler model with each parameter then allowing for combinations of sex-, infection- and inbreeding specific variations. For example, in a model allowing effects of sex-, infection- and inbreeding-specific variation (and 2-way interactions)

$$tD_i \sim \text{Siler}(\text{a1}_i^M, \text{a2}_i^M, \text{b1}_i^M, \text{b2}_i^M, \text{c}_i^M) \tag{7.2}$$

where tD is age at death and each parameter is then described

$$\begin{aligned}\log(\text{a1}_i^M) = \log(a_1) &+ beta_{\text{sex}}^{a1} \times \text{sex}_i \\ &+ \beta_{\text{infection}}^{a1} \times \text{infection}_i \\ &+ \beta_{\text{inbreeding}}^{a1} \times \text{inbreeding}_i \\ &+ \beta_{\text{inbreeding:sex}}^{a1} \times \text{inbreeding}_i \times \text{sex}_i \\ &+ \beta_{\text{inbreeding:infection}}^{a1} \times \text{inbreeding}_i \times \text{infection}_i \\ &+ \beta_{\text{infection:sex}}^{a1} \times \text{infection}_i \times \text{sex}_i\end{aligned} \tag{7.3}$$

We ensured the interaction terms could not be included in the model unless both associated main effects were included by using the constraint function in NIMBLE. This returns a probability of zero for the set of parameter estimates should the constraint not be true (i.e. we set the z indicator for the interaction term such that it must be less than or equal to the multiplication of the z terms of the main effects).

Results

We began our investigation with the maximal model which includes main effects of sex, infection and inbreeding and interaction terms for sex:infection, sex:inbreeding, infection:inbreeding (Eq. 7.2 & 7.3). To judge the importance of each variable we used the inclusion probability levels as described in Viallefont et al., (2001), who consider anything over p = 0.5 to be informative. Sex (male, female), infection (test positive cub, never positive) and inbreeding (greater than or equal to median, lower than median) are fitted as categorical variables. When estimating the effects of inbreeding depression the consensus has been to perform a linear regression with a fitness component as the response (Keller & Waller, 2002; Morton et al., 1956). When estimating survival from CMR data the only information we have details individual capture histories and we infer the

latent, unseen variable – age at death, which informs survival estimates. Although our measure of inbreeding is continuous and we are able to run the analysis using inbreeding as a continuous variable in doing so we are then assuming a linear relationship is correct. For this reason we now split the analysis into two sections, first treating inbreeding as a categorical variable which ensures we don't make assumptions regarding the relationship between inbreeding and the Siler parameters; and second, modelling inbreeding as continuous accepting that we are then assuming a linear relationship is correct.

Categorical inbreeding

With over 3000 different models visited by the RJMCMC algorithm and no one model having a posterior probability greater than 1% it is sensible to look at the proportion of models that include each variable and calculate posterior inclusion probabilities (Fig. 7.1).

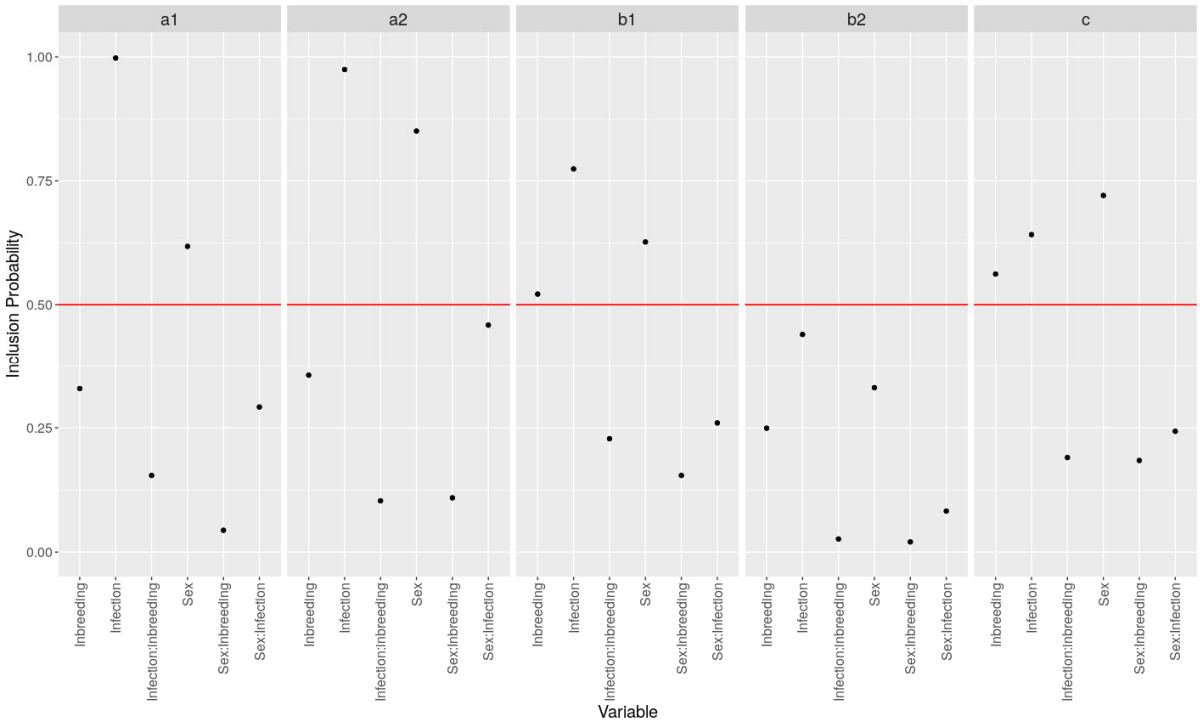


Figure 7.1: Posterior variable inclusion probabilities from all possible models allowing main effects of sex, infection and inbreeding and interactions between sex:infection, sex:inbreeding and infection:inbreeding. Sex, infection and inbreeding fitted as categorical variables.

Figure 7.1 indicates that main effects of sex and infection are important across all parameters except b_2, none of the interaction effects are informative and inbreeding is only of importance for parameters b_1 (exponential rate of decrease in mortality from birth) and c(age-independent mortality). We also constructed violin plots to highlight the impact of the covariates on the five Siler parameters (Fig. 7.2), these are drawn using only the sample estimates when the particular covariate is included in the model as indicated by the associated indicator node. With reference to the two parameters considered important by the inclusion

probabilities, figure 7.2 suggests that being inbred reduces the b_1 and c parameters.

As we have shown in previous chapters (see Ch.3 & Ch.5), the Siler parameters compete with one another to describe the patterns of mortality and this is particularly apparent with parameters $a1$ and c. As a result it is difficult to accurately interpret the effects of the coefficients independently and it is more appropriate to view the model-averaged survival and mortality trajectories (Fig.

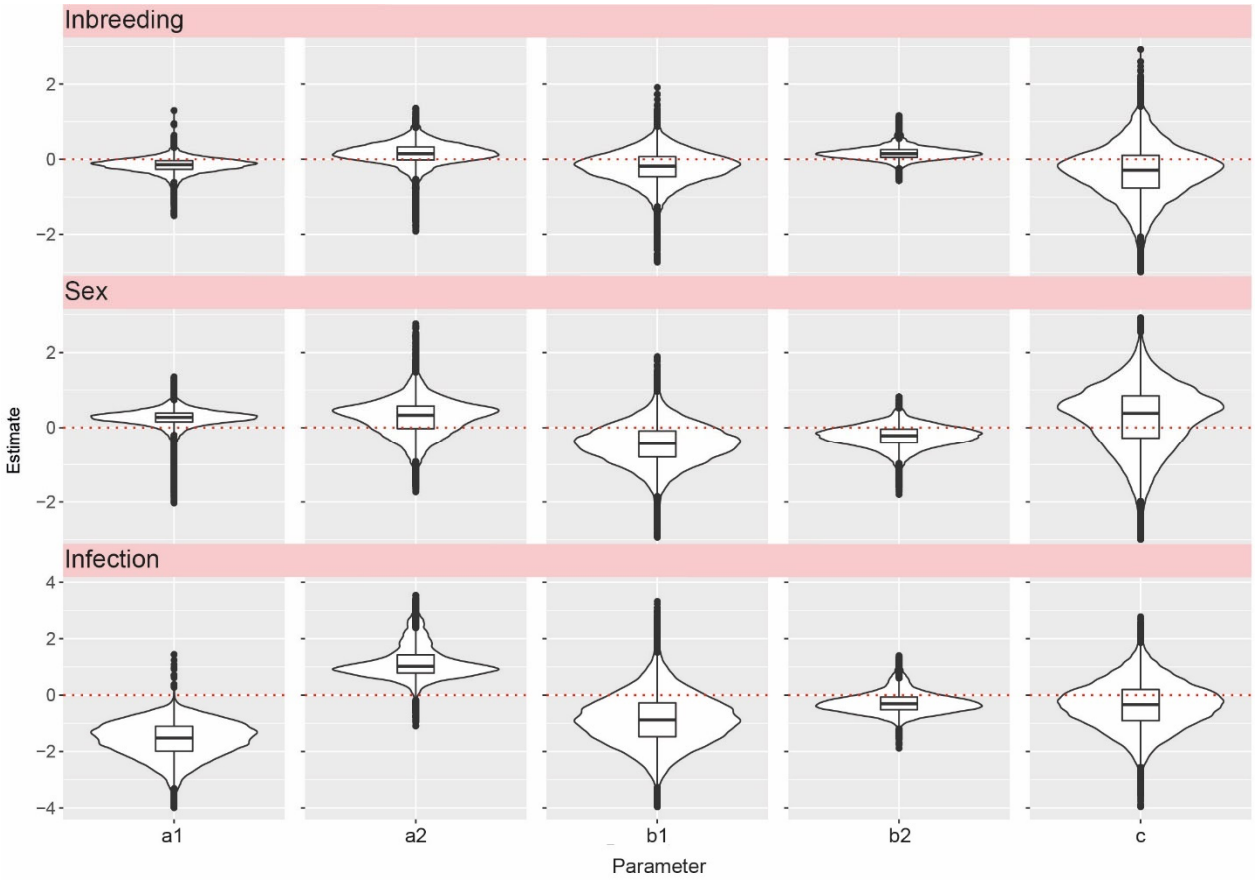


Figure 7.2: Posterior distributions of coefficient estimates from a Reverse Jump Markov chain Monte Carlo (RJMCMC) analysis of capture-mark-recapture data from a population of wild European badgers naturally infected with bovine tuberculosis. The coefficient estimates refer to the additional effect of being: 1. Inbred; 2. male and 3. cub positive, on each of the five Siler parameters. The distributions consist only of samples from the RJMCMC chain when the covariate is included within the model as indicated by the associated indicator node.

7.3). Figure 7.3 highlights the subtle impacts of inbreeding with little difference in age-specific survival between the inbred and outbred individuals.

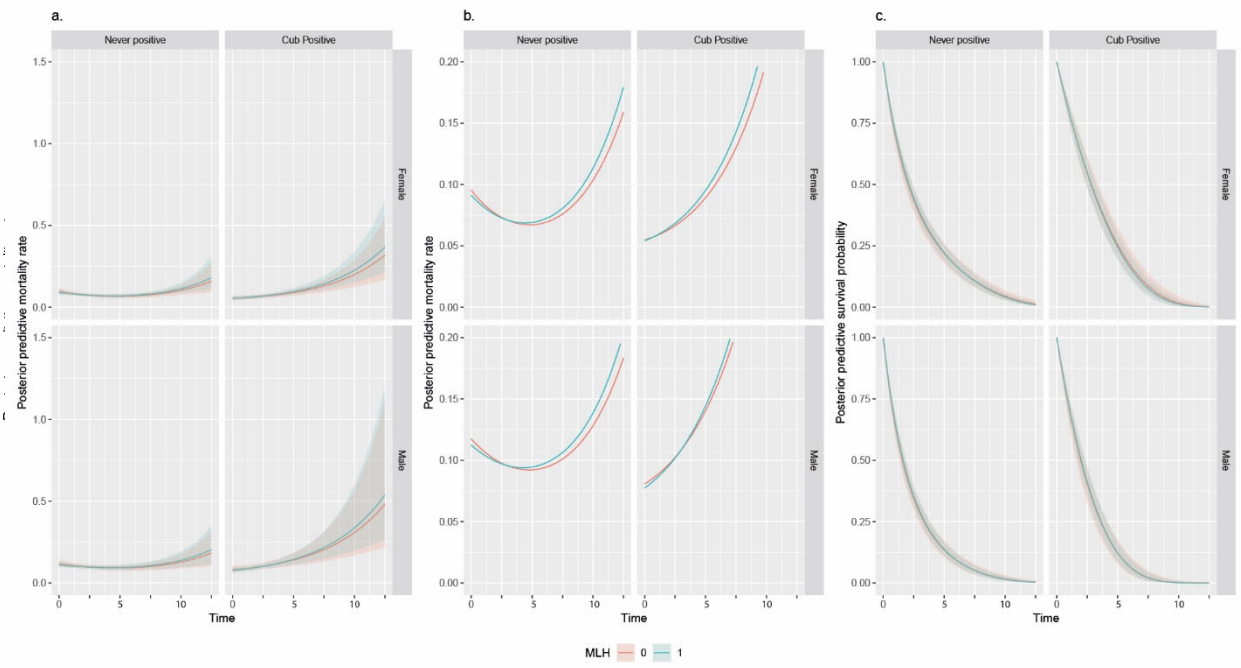


Figure 7.3. Model averaged, posterior predictive mortality (a. and b.) and survival trajectories (c.) of a natural population of European badgers (*Meles meles*). Badgers have been split by sex and 'infection' status (infected (cub) = test positive for bTB during first year of life; uninfected = never tested positive for bTB throughout life). Inbreeding fitted as a categorical covariate (above and below population median level of inbreeding). Time is in years. Shaded areas in (a.) and (c.) represent 95% credible intervals. Plot (b.) is focused on the early changes in mortality and is a zoomed in version of (a.).

The mortality trajectories are more sensitive and suggest that there are several inbreeding-specific differences in the dynamics of mortality across entire lifespan. The slower reduction in mortality from birth shown by parameter b_1 for inbred individuals suggests a negative impact of inbreeding in the early stages of life. The importance of inbreeding on parameter c also suggests that there are age-independent effects throughout life. The coefficient distribution of the effect of inbreeding on parameter c (Fig. 7.2) is centred just below zero suggesting that being inbred reduces age-independent mortality. This effect is not clearly visible in the mortality trajectories with the inbred trajectory generally

displaying higher rates of mortality except for the very early stages of life – further highlighting the correlated structure of the parameters and the importance of viewing the model averaged trajectories. It is worth noting here that c does not affect the shape of the trajectory; it only serves to raise or lower the underlying mortality rates. Despite the posterior inclusion probabilities indicating the effect of inbreeding is unimportant for parameter a_1, a_2, and b_2, the model averaged trajectories reveal a number of subtle variations: a lower initial, 'at-birth' mortality rate among inbred badgers; and a more intense increase in mortality throughout life (from approximately age 3 for uninfected badgers and from birth for infected badgers). The results here show that inbreeding has both age-specific and age-independent effects on mortality across badgers lifespan. If we consider the model-averaged mortality trajectories as well then we find that the effects of inbreeding can be both positive and negative at different times of life.

Continuous inbreeding

We approach this analysis with some caution because we have no clear method to judge the validity of the assumption of linearity in the relationship between our latent parameter and inbreeding.

The posterior inclusion probabilities (Fig. 7.4) indicate that, when modelled as a continuous variable, inbreeding has an important impact across all 5 of the Siler parameters and therefore both age-dependent and age-independent effects across the entire lifespan of badgers. None of the interactions are considered important and the main effects of sex and infection mirror that of the previous analysis. The trajectories (Fig. 7.5) demonstrate the impact of inbreeding across a badger's lifetime and are similar in shape to that of the previous categorical analysis. The survival curves (Fig. 7.5c) indicate reduced survival with increased inbreeding throughout life for all groups of badger but the effect is most pronounced for the cub positive badgers. The shape of each trajectory describes a similar pattern of survival and mortality to that of the categorical analysis but the posterior inclusion probabilities indicate a stronger relationship with inbreeding across all 5 Siler parameters.

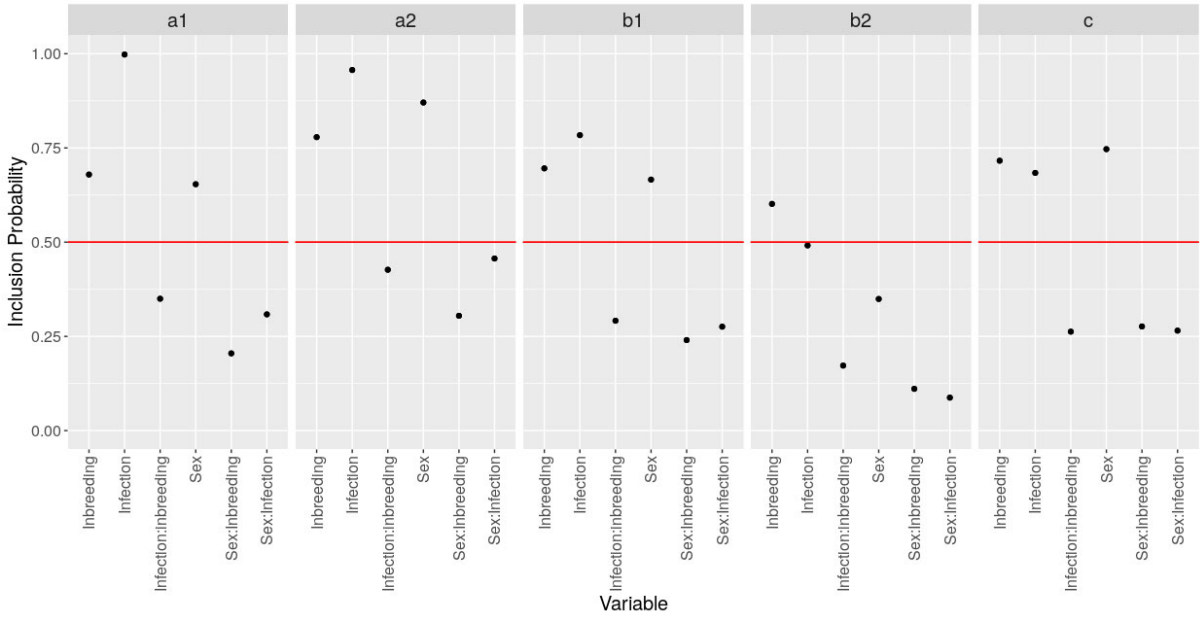


Figure 7.4: Posterior variable inclusion probabilities from all possible models allowing main effects of sex, infection and inbreeding and interactions between sex:infection, sex:inbreeding and infection:inbreeding. Sex and infection fitted as categorical variables, inbreeding fitted as a continuous variable.

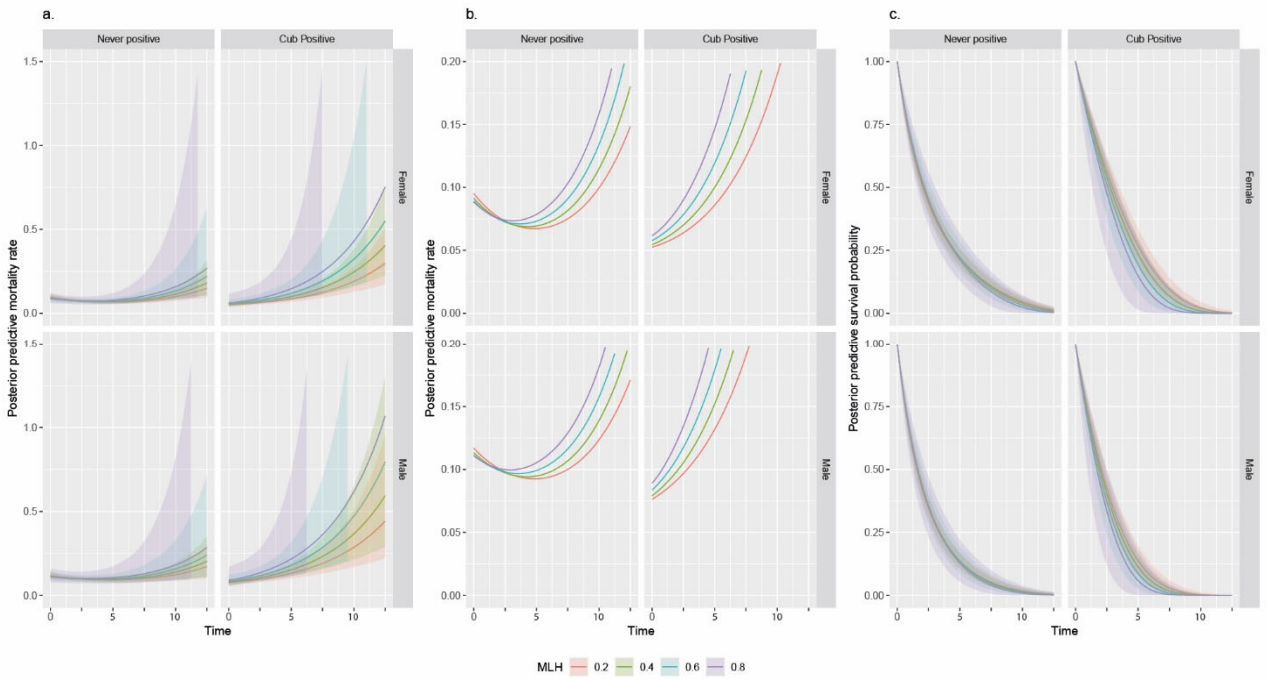


Figure 7.5: Model averaged, posterior predictive mortality (a. and b.) and survival trajectories (c.) of a natural population of European badgers (*Meles meles*). Badgers have been split by sex and 'infection' status (infected (cub) = test positive for bTB during first year of life; uninfected = never tested positive for bTB throughout life). Inbreeding fitted as a continuous covariate, trajectories drawn at 4 different levels of increasing inbreeding (0.2, 0.4, 0.6, 0.8). Time is in years. Shaded areas in (a.) and (c.) represent 95% credible intervals. Plot (b.) is focused on the early changes in mortality and is a zoomed in version of (a.).

Traditional model validation tools to check the linear assumption, such as residual checks, cannot be employed here since the linearity assumptions affects variables other than the mean and in complex ways. There are a number of supportive analyses that we can complete. An argument against assuming a linear relationship is that there could be a number of outliers that have high leverage and thus falsely provide support for the linear relationship, or indeed simply that the relationship to inbreeding coefficient is not linear on the log-scale for these parameters. Figure 7.6 indicates an approximately normal distribution of inbreeding scores for the badger population suggesting the chance of any individual having high leverage is small.

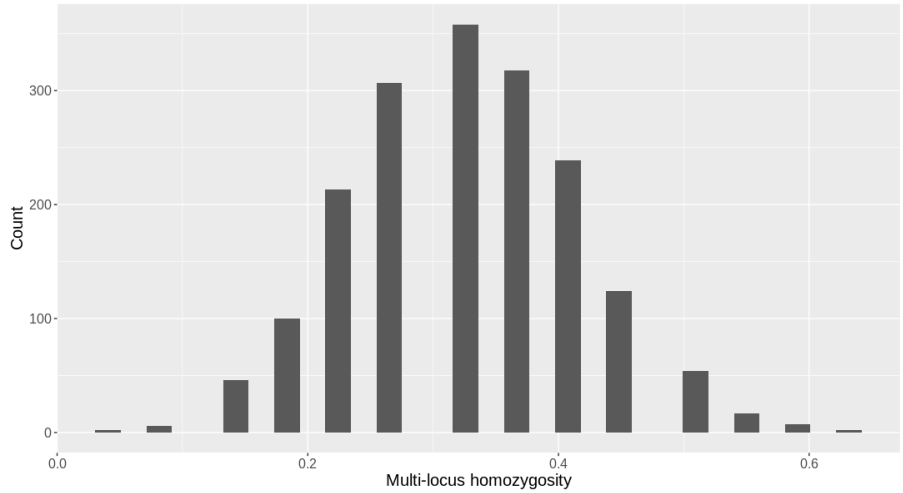


Figure 7.6: Distribution of individual inbreeding scores from the population of European badgers (*Meles meles*) used in this analysis.

As a final more focused check we looked specifically at the effect of inbreeding on what is considered the senescence parameter b_2. The Bayesian paradigm offers the advantage of being able to extract posterior distributions for each individual's age at death – another latent variable, which we generate (and then use the median as inferred age at death) using a model that allows sex- and infection-specific variation with an individual level random effect but does not include inbreeding. Judging the mortality trajectories (Fig. 7.3 & 7.5) it appears that the senescent increase in mortality begins to take effect when badgers are approximately 8 years of age, so we are only concerned with those individuals we believe have died after this age. We attempt here to validate our linear regression between b_2 and inbreeding by plotting the inferred age at death of each individual against MLH and comparing the model averaged predictions of age at death from models that also include inbreeding as a categorical or continuous covariate (Fig. 7.7).

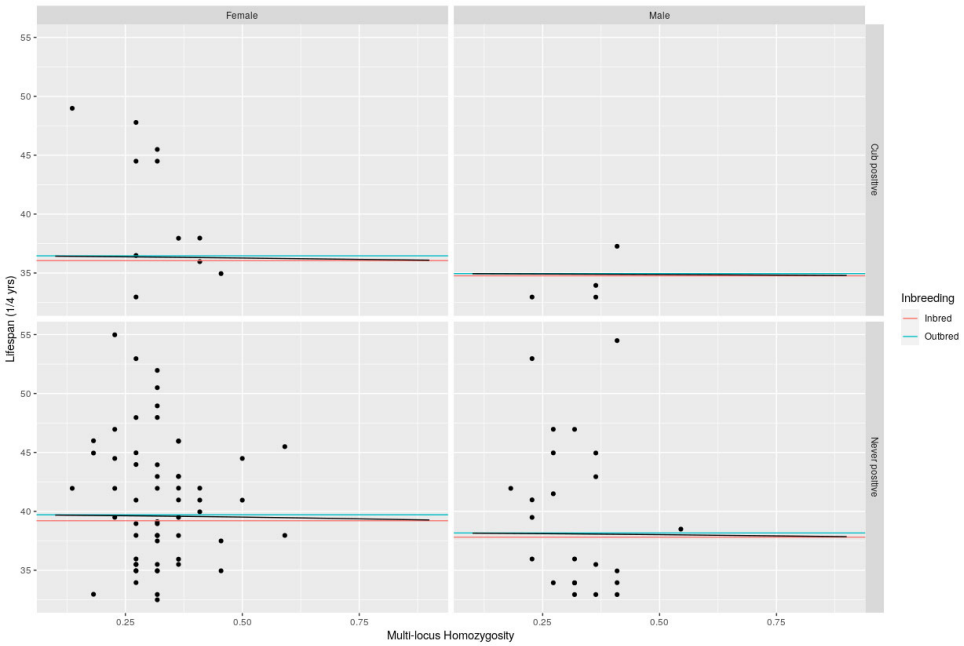


Figure 7.7: Plot of inferred age at death against multi-locus homozygosity for a population of wild European badgers naturally infected with bovine Tuberculosis. Plot only shows individuals who survive beyond age 8. Inferred ages at death are generated from a Bayesian investigation of capture mark recapture data and a model allowing sex- and infection-specific variation and an individual level random effect. Fitted lines indicate predicted age at death generated from models that allow sex-, infection- and inbreeding-specific variation fitted to the same dataset and conditional on having survived to age 8. Red (inbred) and blue (outbred) lines are generated from a model that fits inbreeding as a categorical covariate, the black line is generated from a model that fits inbreeding as a continuous covariate.

Figure 7.7 suggests that a linear assumption is not unreasonable when attempting to explain the relationship between inbreeding and senescence, or at least that there is no discernible difference in the goodness of fit of the continuous vs categorical treatment of MLH.

Discussion

A number of studies have linked inbreeding with juvenile or fitness-related traits in wild populations but comparatively few have investigated impacts across lifespan (although see Keller, 1998; Slate et al., 2000; Szulkin et al., 2007). Here we have found evidence for novel impacts of inbreeding on age-, sex- and

infection-specific mortality in a population of wild badgers using a measure of inbreeding derived from genome-wide data. The Siler (Siler, 1979) model allows assessment of the impacts of inbreeding across entire lifespan but should be carefully investigated through the posterior inclusion probabilities in conjunction with the model averaged mortality trajectories. Although the Siler parameters can be interpreted biologically and related to a specific phase of life: early, late, and independent of age, due to the correlated structure of the function (see Ch.3 & 5) their influence can be felt across much larger age ranges.

The RJMCMC analysis generated posterior inclusion probabilities that indicated an important effect of inbreeding on parameters b_1 and c suggesting both age-dependent and age-independent effects (Fig. 7.1). Although interpretation of the parameters independently can help suggest where in an individual badgers lifetime the impacts of being inbred maybe felt, it is safer to accommodate model uncertainty (Raftery et al., 1994) and produce model averaged survival and mortality trajectories (Fig. 7.3). The survival trajectories show little variation between groups but the mortality trajectories are better able to capture subtle differences. As suggested by the inclusion probabilities, the impacts of being classed as inbred can be felt across individuals' complete life history and is not limited to the phases of life that are primarily connected with parameters b_1 and c . For the 'never-positive' individuals the initial mortality rate appears to be lower at birth (for inbred individuals), the drop from this rate is slower (b_1) but is followed by an earlier onset of senescence. The rate of senescent increase in mortality is similar for both inbred and outbred individuals but it occurs sooner for the inbred badgers. The shape of mortality trajectory for the 'cub-positive' individuals is markedly different with no initial downtick in mortality from birth, instead characterised by a consistent increase in mortality rate from birth with only minor differences between the inbred and outbred individuals being evident with the female badgers where there is a slightly lower rate of mortality at birth but an earlier onset of senescence for inbred individuals. The patterns of 'infection' -specific differences in mortality have been evidenced previously (Hudson et al., 2019) – a more intense senescent increase in mortality although previously we had uncovered a small downtick in early mortality that was not found here for this group of badgers. We found no evidence for any

two-way interactions between sex, infection and inbreeding indicating any effects were being felt independently from one another. Previous research has found evidence for sex:inbreeding interactions but analyses have been confined to older individuals (Fox et al., 2006; Reid et al., 2007). Harrisson et al. (2019) analysed lifetime fitness costs of inbreeding and found, as we have, no evidence for an interaction between homozygosity and sex. Evidence for inbreeding:disease interactions are less common, particularly in wild populations. The research generally focuses on the impact of inbreeding on susceptibility to disease – using this as a measure of fitness as opposed to looking for links with survival and mortality (Benton et al., 2018; Queirós et al., 2016; Trinkel et al., 2011) as we have done here.

Having noted the caveat that we are unable to conclusively validate the linearity assumption when fitting inbreeding as a continuous variable it is still important to view these results. The posterior inclusion probabilities for inbreeding increased consistently across all the five parameters (Fig. 7.4) but more crucially, the model averaged survival and mortality curves (Fig. 7.5) were supportive of the previous categorical analysis showing similar relationships across the badger's lifespan which adds weight to our analysis and conclusions.

Although we have demonstrated support for both evolutionary models of senescence, strengthening the argument that they may co-exist in natural populations (Wilson et al., 2007; also shown in laboratory experiments - Service et al., 1988; Snoke & Promislow, 2003), the mortality trajectories indicate a stronger influence of inbreeding consistent with AP. MA theory suggests that ID will increase with age (Charlesworth & Hughes, 1996) which can be seen in the earlier onset of senescence across all inbred badgers and the more intense increase in the rate of senescence, although this is only weakly apparent and confined to the 'cub-positive' badgers. Support for AP is stronger with differential impacts of inbreeding on survival felt across lifespan – beneficial initially and then detrimental. Previous research has generally made use of recorded trade-offs (Stearns, 1989) among life-history traits as evidence for AP with most focused on negative associations between lifespan and reproduction (e.g. Robinson et al., 2006; Marshall et al., 2017). But these results do not cleanly support AP (Austad & Hoffman, 2018) and can also be attributed to the

disposable soma theory (Kirkwood, 1977) which suggests organisms have to trade-off between committing energy to reproduction or investing in maintenance of their somas. To our knowledge our analysis has for the first time demonstrated antagonistic pleiotropic effects of inbreeding on individual mortality in a wild population – highlighted by the beneficial, lower rate of mortality at birth followed by the negative effects of a slower reduction in mortality, earlier onset of senescence and more intense senescent increase in mortality in later life. These effects are not easily attributable to a trade-off scenario and therefore suggest that late-acting deleterious mutations may have been favoured by selection as they have early-acting beneficial effects as Williams (1957) originally described. The beneficial effects are only apparent in the very early phase of life however and are quickly overtaken by the detrimental slow rate of reduction in mortality towards maturity. It is possible that the apparent early benefit of being inbred may be a result of differential levels of maternal care provided to offspring that are more similar to the parents. Pilakouta et al. (2015) demonstrated that parental care can moderate the severity of ID in burying beetles (*Nicrophorus vespilloide*) and a similar study indicated that ID could be buffered by either parental care or group living in a subsocial spider (*Anelosimus cf. jucundus*, currently *Anelosimus arizona*) (Avils & Bukowski, 2005). Although experimental investigations of this hypothesis found no support for maternal care reducing the impact of inbreeding in the European earwig (*Forficula auricularia*) (Meunier & Kölliker, 2013).

Here we have provided further evidence that ID can vary across life-history stages as has been shown in different species (e.g. Huisman et al., 2016; Harrisson et al., 2019) but for the first time we have uncovered antagonistic pleiotropic effects on individual mortality in a wild population consistent with the AP evolutionary theory of senescence. We are unable to dismiss the alternative MA theory having also identified some age-dependent effects of inbreeding and therefore believe that the two theories should not be considered mutually exclusive – each playing its part in the evolution of senescence. Any beneficial effects of inbreeding are quickly overtaken by the detrimental effects which take control as early as aged 3 for ‘never-positive’ badgers. We also highlighted the

additional effect of being a ‘test-positive’ cub: here the detrimental effects of inbreeding occur much sooner (aged 1). The magnitude of ID across life history has rarely been quantified (Trask et al., 2021) and our understanding of the processes involved remains limited (Kardos et al., 2016). We have demonstrated a straightforward method for the analysis of life-history impacts of inbreeding in a natural population which we hope will encourage further similar research on other species. Of greatest importance is understanding how ID at the individual level effects population growth and viability, particularly due to the rapid progression of global change and habitat fragmentation (Stoffel et al., 2021) which will likely lead to increased levels of inbreeding across a large proportion of wild species.

Overview

Wildlife disease is of increasing importance to conservation biology and recognised as a critical factor in ongoing global health. Survival analysis conducted on wild populations is unsurprisingly a very active area of research as it has the potential to uncover subtleties of complex epidemiological interactions that often exist in natural systems. Within this thesis I have presented a number of different Bayesian approaches to survival analysis that are well suited to the challenges posed by wild populations.

We made use of the software package BaSTA (Bayesian Survival Trajectory Analysis - Colchero et al., 2012) to uncover previously unreported sex- and infection-specific patterns of age-specific mortality in the European badger – *Meles meles* (Chapter 2); for the first time reporting 'bathtub' shaped mortality patterns across all groups of badger. Cubs categorised as 'test-positive' (used as an indicator of disease status) displayed a more intense senescent increase in mortality in later life but to investigate this relationship further required a more flexible modelling approach than that offered by BaSTA. We investigated a number of different programmes (e.g. WinBUGS, JAGS, NIMBLE) that allow models to be built from first principles and analysed within the Bayesian framework (Chapter 3). We settled on NIMBLE which we found offered the flexibility required without compromising efficiency. We developed a novel algorithm, new to the literature, for generating random samples from the Siler (Siler, 1979) distribution, extending the ideas in Jodrá (2009). This facilitates more straightforward simulation studies and allows for more straightforward predictions. We carried out an in-depth investigation of the Siler function, creating a Shiny (*Web Application Framework for R [R Package Shiny Version 1.6.0]*, 2021) app (Hudson, 2019); noting an internal correlation structure that is often overlooked in the literature.

Having established a framework that allows flexible model construction the challenge became one of model comparison and how best to select the most credible model or set of rival models. It is widely recognised that a variety of models can often provide comparable fits to the data. This has led to the development of multi-model inference techniques such as Bayesian model averaging (BMA) (Kass & Raftery, 1995; Burnham & Anderson, 2002; Harrison

et al., 2018) which readily accommodate model uncertainty. Despite a wide range of methods used for model comparison, there is no consensus over which should be preferred. We presented a method for the estimation of the marginal likelihood based on importance sampling which works well when proportions of the data are missing – a common feature of ecological research. The process enables straightforward model comparisons to be made via the calculation of Bayes' Factors or posterior model probabilities which can also act as weighting probabilities in BMA. We demonstrated the efficiency and accuracy of this approach through a series of simulations and case studies: first, on censused data and banded Mongoose (Chapter 4) and second, on capture-mark-recapture (CMR) data and European badgers (Chapter 5). Our analysis of CMR data highlighted the difficulties of recording dynamics of early-life mortality suggesting why 'bathtub' shaped mortality such as the Siler function remain underused in wildlife research and why the reported levels of early-life mortality are likely underestimates.

Datasets from long-term monitoring projects of wild populations are recording an increasing number of potential explanatory variables, allowing more complex models to be fitted to the data. Although caution should be taken to avoid over-fitting, many model comparison problems can reduce to variable selection. In these instances our IS approach can become time consuming, due to the large number of potential covariate combinations. This led us to investigate Reverse Jump Markov chain Monte Carlo (RJMCMC) (Green, 1995) methods as an alternative approach to generate posterior model probabilities. We compared our IS analysis of sex-specific variation in age-specific mortality in badgers from Chapter 5 with an RJMCMC analysis of the same data and found the results to be comparable, but with a considerable time saving (Chapter 6). Finally, we presented a detailed analysis of the effects of inbreeding on age-, sex- and infection-specific mortality in badgers using RJMCMC methods. Our understanding of the characteristics underlying the Siler model allowed us to identify antagonistic pleiotropic effects of inbreeding on individual mortality rates in a wild population for the first time (Chapter 7).

Methodological advances for Survival Analysis

Studies completing survival analysis within the Bayesian paradigm are still relatively rare compared to the number using frequentist methodologies (Brard et al., 2016). Survival analysis generally focuses on non-parametric (e.g. Kaplan-Meier survival plots) or semi-parametric (e.g Cox proportional hazards framework) modelling, but both methods can struggle with increasing levels of censorship – something that is common when monitoring wild populations. Adopting a Bayesian approach has both advantages and disadvantages which have been widely discussed (e.g. Berry, 2006; Gelman, 2008) but the natural ability to incorporate and quantify all levels of uncertainty make it particularly well suited to datasets from systems that are challenging to monitor perfectly. There can be confusion between the interpretation of survival and mortality rates (Ellis et al., 2014), and although linked it is often the mortality rates that exhibit higher sensitivity to subtle changes and therefore have the potential to add greater depth to our understanding of the underlying processes involved. Traditionally, mortality rates have been analysed using static life tables which give mortality at given ages or discrete life phases, but these are limited in the information they offer and can mask subtle mortality patterns. Mortality (and survival) trajectories offer a greater depth of information when describing the dynamics of natural systems and as a result may offer a deeper level of understanding. The challenge for analysts wishing to employ survival and mortality trajectory analysis lies in the comparison and selection of potential mortality functions. Within this thesis we have presented two different approaches that perform well with the types of data common within ecological research. Our IS approach allows straightforward comparison of any competing models that the analyst deems appropriate and the RJMCMC approach can offer significant time savings when the models to be compared are nested or the investigation can be reduced to one of variable selection. Both approaches utilise the benefits of working within the Bayesian paradigm and its natural handling of multiple sources of uncertainty and include the option to generate posterior model probabilities that facilitate multi-model inference techniques such as BMA. Posterior predictive, model averaged survival and mortality trajectories can then offer straightforward graphical representations of covariate

effects that are easy to interpret. We hope that by providing annotated code for all methods and analysis included within this thesis we can broaden the statistical toolbox of the ecological researcher.

Evolutionary perspective on Senescence

Our analysis of the impacts of inbreeding on age-, sex- and infection-specific survival and mortality in badgers suggested it to be an important explanatory covariate. Using our knowledge of the Siler function (specifically the correlated nature of its parameters), survival and mortality trajectory analysis allowed us to uncover full life history effects of ID. Our approach revealed antagonistic-pleiotropic effects on mortality previously unreported in wild populations. Although there is a weight of evidence that argues in favour of the antagonistic pleiotropy (AP) evolutionary theory of senescence (Williams, 1957) they are generally based on trade-offs among life-history traits (Stearns, 1989) and cannot be exclusively attributed to AP as Kirkwood's (1977) disposable soma theory cannot be dismissed. Our results also offered some support for the alternative evolutionary theory of senescence, mutation accumulation (MA), adding weight to the argument that the two theories may co-exist in natural populations (Harrison et al., 2013).

Future Research - *Left censoring*

Survival analyses conducted on natural systems will always suffer from some degree of censorship where the fate of certain individuals is unknown. Censoring can occur in three different ways for a given event of interest: left-censoring – the event happens prior to the start of a study; right-censoring – the event happens after the end of the study; and interval-censoring – the event occurs within a given timeframe. In this thesis we have accommodated right- and interval-censored death times in our modelling framework (Chapters 4 & 5) to infer survival and mortality estimates. However, when analysing longitudinal monitoring data in this manner there are two events of interest: birth and death. If we do not have information regarding an individual's birth (i.e. it occurred prior to the study start and is therefore left-censored) then we cannot easily calculate an age at death to inform survival and mortality estimates. This is a common problem and often results in researchers having to discard valuable data (as we did after Chapter 2) and lose statistical power in their analyses.

In Chapter 2 we used the software package BaSTA (Colchero & Clark, 2012) which addresses this problem in the same manner as it handles right-censoring – by adding birth time as a latent variable and estimating it within the model. As we began building models from first principles to achieve the flexibility we required (Chapter 3) we initially stripped back the complexity and chose to focus on right- and interval- censoring. The dataset that we primarily make use of throughout this thesis (CMR data from a natural population of European badgers at Woodchester Park, Gloucestershire) has relatively few left-censored records; over 85% of the badgers available for our analyses were of known age, thus to some degree mitigating potential bias. We developed our models without incorporating left-censoring although we have written some preliminary code that places a prior distribution on the unknown birth time and estimates it within the model which can accommodate such records. We hope to have the opportunity to develop this further but provide our code in Appendix 7 for reference. Gilbert et al. (2014) carried out an investigation into left-censoring and found it can have considerable impact on survival estimates, this is something we comment on in Chapter 5 when we address the difficulties in monitoring the early stages of life and the problem of individuals dying prior to detection. Improving study design and increasing the frequency of sampling occasions can reduce the impact of left-censoring but it is unlikely to be possible to solve the issues without causing detrimental levels of disturbance to the target population. Through careful consideration of the demographics of the sample population together with average recapture rates it is quite feasible to construct a model that could better estimate initial mortality and survival rates but we have not been able to explore this avenue further.

Future Research - *Life-course analysis*

Survival and mortality rates are often the basis of demographic analysis and often key in decisions regarding population management (Servanty et al., 2011) so any improvement in the accuracy of our estimations may be critical to effective conservation or control. As we have discussed throughout this thesis, survival analysis is often focused on a particular life phase with the dynamics of survival and mortality generally considered independent of other periods of an individual's life. This may be generating specious inferences. The majority of

studies looking at late life mortality have used the Gompertz function (Gompertz, 1825), particularly when carrying out cross-species comparisons (e.g. Nussey et al., 2008). This may seem a logical choice as the Gompertz model ignores any early-life changes in mortality and just describes an exponential increase from a particular intercept level but as we have demonstrated this may be an important oversight. Datasets from intensive long-term monitoring projects are becoming more common and the depth of information concerning the demographics of natural populations more detailed, but by using models that ignore some of this information researchers risk oversimplified pictures of reality and inaccurate conclusions. We have shown in Chapter 3 and again in Chapter 5 that changes in mortality rates through early stages of life can have impacts that are felt in later life. We used the Siler model throughout our analyses, and compared the fit of this function to others that ignore early life changes (e.g. Gompertz, exponential, Gompertz-Makeham); despite the difficulties in recording very young individuals the Siler model was consistently selected as either the optimal model, or within a pre-determined threshold value of the optimal model. This supports the idea that the additional parameters describing mortality changes in early life can have an impact in later life – something we demonstrated in Chapter 3. We strongly recommend the use of bathtub shaped mortality functions when analysing full life-course data (see Ronget et al. (2020) for additional arguments in favour of this approach), even if the signal within the data is only weakly supportive of early life changes they may be having an impact not felt until later life stages. Rather than simply focusing on, for example, senescent increases in mortality in later life researchers should be considering life-course analysis as the optimal approach to any analysis of mortality and survival.

Future Research - *Latent variable model validation*

Survival analysis of wild populations will always be hampered by the fact that the parameter of interest, survival, is an unseen latent variable inferred from monitoring information such as CMR. Right-censoring compounds the problem as crucial information that could provide bounds on individual survival times are missing. In Chapter 2 we were able to compare predictive survival trajectories with Kaplan-Meier plots of actual survival as levels of censorship were relatively

low, as the proportion of censored records increases Kaplan-Meier plots become increasingly poor representations of true survival rendering them an ineffective tool for model validation. This issue presented itself in Chapter 7 where we had the ability to fit inbreeding as a continuous variable but no method to validate our model and the assumed linear relationships. This led us to the more conservative approach of categorising the inbreeding measure. Within our analysis in Chapter 7 we chose to investigate potential relationships between inbreeding and the individual parameters of the Siler model to allow for a more detailed assessment of the age-specificity of any effects. By not modelling a more general relationship between inbreeding and mean survival rates (as would be the case in e.g. a Cox proportional hazards framework) we added further layers of complexity and difficulties in potential validation of any linearity assumptions. Survival analyses have used an individual's Martingale (Therneau et al., 1990) or deviance residual in a similar fashion to a residual measure in linear regression but neither are applicable here. This is an area of ongoing research (e.g. Vieland et al., 2020) but we have been unable to find a workable solution. In Chapter 7 we adopted the conservative approach through the construction and assessment of model averaged posterior predictive mortality and survival trajectories which incorporate our uncertainty and illustrates any effects of inbreeding on the patterns of age-specific life-time mortality and survival.

Implications for future epidemiological modelling

Effective epidemiological modelling is a critical tool within health policy development and disease prevention and control (Garner & Hamilton, 2011). Methods presented here have been developed primarily for ecological research where data often suffers from different degrees of missingness, but are transferable to many other fields including human epidemiological research. Fitting parametric models to survival data remains an underused approach to estimate survival and mortality but has the potential to uncover subtle patterns that can be missed by alternative approaches. We have favoured the Siler model throughout our research as it offers the flexibility to describe a variety of different patterns but this is also an underused function. Throughout this thesis we have demonstrated the appeal of parametric models and specifically the

Siler function when investigating impacts of a variety of explanatory variables on survival and mortality. Working within the Bayesian paradigm offers the opportunity to incorporate all levels of uncertainty in the modelling process and the resulting, model averaged posterior predictive survival and mortality trajectories offer interpretable representations of the effects of any number of covariates. We hope that by providing all code throughout, that the approaches demonstrated here will not only become more widespread within ecology but within all epidemiological research.

Concluding remarks

The aim of this thesis was to investigate the effects of inbreeding on the epidemiology of bovine tuberculosis in the European badger. At the core of this research is a focused development of an appropriate modelling framework to carry out survival analysis on naturally occurring populations that is widely applicable beyond ecological research. Inbreeding is an important factor in the mortality and survival of badgers having apparently antagonistic pleiotropic effects that are beneficial in early life and detrimental in later life. Inferred infection (i.e. test positive) is well known to increase mortality rates and our analysis indicates that increased inbreeding further intensifies this relationship. Inbreeding rates are relatively low within our study population but effects are still detected. In our rapidly changing world with habitats becoming increasingly isolated, inbreeding levels will likely increase. The full impact of current bTB control measures on population levels of inbreeding are unknown but if badgers are completely removed from certain areas leaving isolated populations then inbreeding rates are set to increase further.

Appendices

Appendix 1 – Supplementary material from Chapter 2: Analysis of lifetime mortality trajectories in wildlife disease research: BaSTA and beyond.

- *Figure A1.1*: Kaplan-Meier plots of observed survival on top of predicted survival trajectories
- *Table A1.1*: Posterior parameter estimates, standard deviations and lower/upper 95% confidence intervals of mortality trajectories
- R code - BaSTA analysis

Appendix 2 – Supplementary material from Chapter 3: Flexible model specification for Bayesian survival analysis

- R code - Case Study investigation
- R code - Siler distribution

Appendix 3 – Supplementary material from Chapter 4: Bayesian model selection for survival analysis.

- Uncensored simulations Log Marginal Likelihood plots.
  - SF1 – Exponential simulated data
  - SF2 – Gompertz simulated data
  - SF3 – Gompertz-Makeham simulated data
  - SF4 – Siler simulated data
- Censored simulations Log Marginal Likelihood plots.
  - SF5 – Exponential simulated data
  - SF6 – Gompertz simulated data
  - SF7 – Gompertz-Makeham simulated data
  - SF8 – Siler simulated data
  - SF9 - Kaplan-Meier sex specific survival plot with log rank comparison of survival curves
- R code – Example R code to carry out investigation of sex-specific variation on parameter a1 using census data of banded mongoose.

Appendix 4 – Supplementary material from Chapter 5: Bayesian model comparison of capture-mark-recapture data for survival analysis

- R code – Example R code to carry out investigation of sex-specific variation on parameter a1 using CMR data of European badgers.

Appendix 5 – Supplementary material from Chapter 6: Efficient Bayesian model comparisons for nested models: from importance sampling to reversible jump Markov chain Monte Carlo.

- R code – RJMCMC analysis of sex-specific variation in badger mortality

Appendix 6 – Supplementary material from Chapter 7: Investigating the impact of inbreeding on lifetime survival and mortality trajectories of European badgers.

- R code – RJMCMC analysis of age-, sex-, infection- and inbreeding-specific survival and mortality trajectories of European badgers.

Appendix 1 – Supplementary material from Chapter 2 :Analysis of lifetime mortality trajectories in wildlife disease research: BaSTA and beyond.

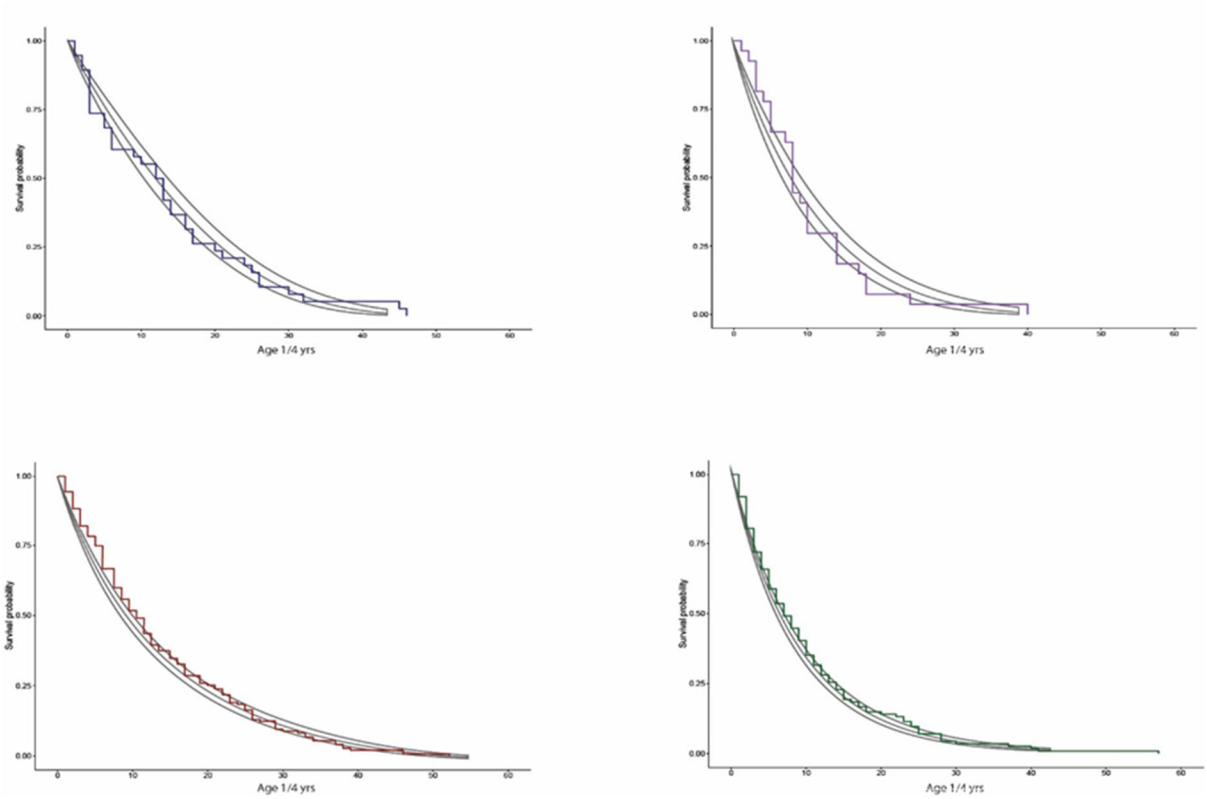


Figure A1.1 Kaplan-Meier plots (in red) of observed survival on top of predicted survival trajectories and 95% confidence intervals for a population of European badgers naturally infected with *bovine tuberculosis*. Split by sex and infection status (a) Cub-positive females; (b) Cub-positive males; (c) Never-positive females; (d) Never-positive males.

Table A1.1 Posterior parameter estimates, standard deviations and lower/upper 95% confidence intervals of mortality trajectories for a population of wild European badgers naturally infected with *bovine tuberculosis*.

Parameter	Status	Gender	Estimate	S.D	Lower	Upper
a0	**Cub positive**	**Female**	-4.29	0.59	-5.52	-3.22
		Male	-4.07	0.65	-5.41	-2.90
	Never positive	**Female**	-2.35	0.15	-2.70	-2.13
		Male	-2.57	0.36	-3.41	-2.06
a1	**Cub positive**	**Female**	1.02	0.85	0.01	2.85
		Male	0.95	0.88	0.00	2.82
	Never positive	**Female**	0.06	0.02	0.03	0.09
		Male	0.05	0.02	0.02	0.11
c	**Cub positive**	**Female**	0.02	0.01	0.00	0.05
		Male	0.04	0.02	0.00	0.08
	Never positive	**Female**	0.02	0.01	0.00	0.05
		Male	0.04	0.02	0.00	0.09
b0	**Cub positive**	**Female**	-3.72	0.45	-4.76	-3.07
		Male	-3.66	0.65	-5.14	-2.69
	Never positive	**Female**	-5.32	0.68	-6.71	-4.04
		Male	-4.30	0.79	-5.93	-2.90
b1	**Cub positive**	**Female**	0.05	0.01	0.03	0.07
		Male	0.04	0.02	0.01	0.08
	Never positive	**Female**	0.07	0.02	0.04	0.10
		Male	0.03	0.02	0.00	0.07

R Code for BaSTA analysis

```
library(tidyverse)
library(BaSTA)
library(data.table)
library(snowfall)
```

Load Data

The following code shows the steps to analyse the entire badger data set. In the journal article we first analyse 'Cub-positive' and 'Never positive' individuals separately. The steps are the same as below.

```
CH.data<- read.table("Hudson_2019_MTA_Data.txt", header = TRUE)
CH.data<- as.data.frame(CH.data)
```

Prepare matrices for BaSTA

Create capture history

Using BaSTA function CensusToCaptureHist and specifing ID and date column.

```
Y.full<- CensusToCaptHist(ID=CH.data[,1], d=CH.data[,2])
```

Create birth and death year matrix

Keep only single entry per badger and create birth and death year matrix.

```
CH.data<- data.table(CH.data)
CH.data<- distinct(CH.data, CH.data$ID, .keep_all = TRUE)
CH.data <- droplevels(CH.data)
BirthDeath.full<- CH.data[,c(1,8:9)]
```

Create co-variate matrix

Specify model co-variate as status. (This is a 4 category co-variate: 1. Cub positive female; 2. Cub positive male; 3. Never positive female; 4. Never positive male)

```
CovMat.full<- MakeCovMat(x=~status, CH.data)
```

Create input matrix

Combine the birth/death matirx, co-variate matrix and full capture history.

```
inputMat.aim <- as.data.frame(cbind(BirthDeath.full, Y.full[,-1], CovM
at.full[,-1]))
```

Data check

```
newData.aim <- DataCheck(inputMat.aim, studyStart = 2,studyEnd = 173,
autofix = rep(1, 7),silent = FALSE)
```

```
## No problems were detected with the data.
##
## *DataSummary*
## - Number of individuals         =    2,957
## - Number with known birth year  =    2,228
## - Number with known death year  =     764
## - Number with known birth
##  AND death years                =     335
##
## - Total number of detections
##  in recapture matrix            =   11,420
##
## - Earliest detection time       =       2
## - Latest detection time         =     173
## - Earliest recorded birth year  =       6
## - Latest recorded birth year    =     170
## - Earliest recorded death year  =       6
## - Latest recorded death year    =     173
```

Begin BaSTA analysis

All Badgers:

Analyse all badgers together specifying all models to compare. Recapture probabilities allowed to vary on each occasion. The following code takes approximately 10 days to run.

```
All.badgers.out <- multibasta(object = inputMat.aim, studyStart = 2, s
tudyEnd = 173, nsim = 4, niter = 1000000, burnin = 10001, thinning = 1
00, parallel = TRUE, ncpus = 4, models = c("EX", "GO", "LO"), shapes =
c("simple","Makeham", "bathtub"), recaptTrans = 2:173)
```

Most supported model

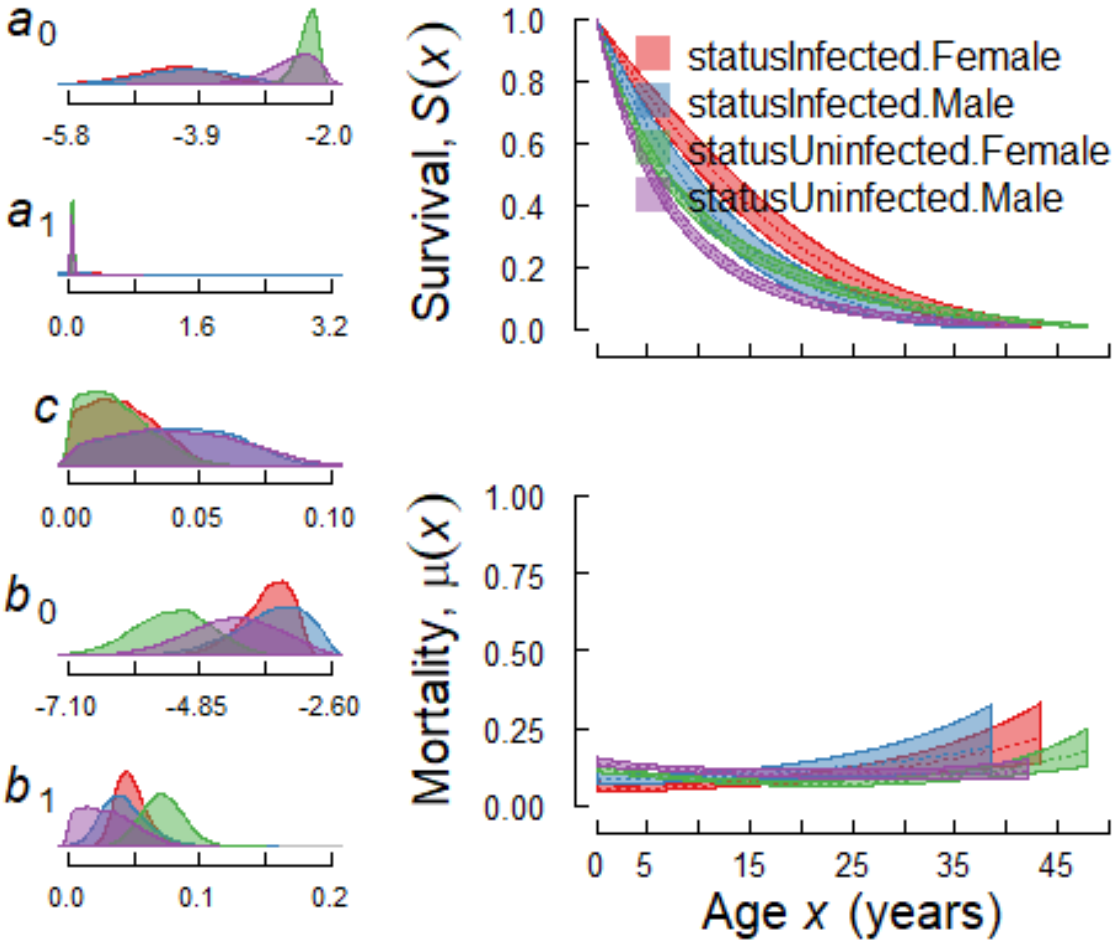
The output from the multi-Basta above for the most supported model has been saved in the additional file “All.badger.out.GObt”. Load the output and view the summary.

```
load(file="All.badger.out.GObt")
summary(All.badgers.Go.Bt.long)

##
## Output from BaSTA version 1.9.5
##
## Call:
## Model                    : GO
## Shape                    : bathtub
## Covars. structure        : fused
## Minimum age              : 0
## Cat. covars.             : statusInfected.Female, statusInfected.Ma
le, statusUninfected.Female, statusUninfected.Male
## Cont. covars.            :
##
## Model settings:
```

```
##    niter   burnin thinning     nsim
##  1000000    10001      200        4
##
## Jumps and priors:
##                                Jump.sds Prior.means Prior.sds
## a0.statusInfected.Female   2.44055916       -2.00         1
## a0.statusInfected.Male     2.38855868       -2.00         1
## a0.statusUninfected.Female 0.19053737       -2.00         1
## a0.statusUninfected.Male   0.30052001       -2.00         1
## a1.statusInfected.Female   4.31114061        0.01         1
## a1.statusInfected.Male     3.65705130        0.01         1
## a1.statusUninfected.Female 0.02281527        0.01         1
## a1.statusUninfected.Male   0.05147027        0.01         1
## c.statusInfected.Female    0.02483013        0.00         1
## c.statusInfected.Male      0.03606863        0.00         1
## c.statusUninfected.Female  0.01566606        0.00         1
## c.statusUninfected.Male    0.01889691        0.00         1
## b0.statusInfected.Female   0.51199928       -3.00         1
## b0.statusInfected.Male     0.68933530       -3.00         1
## b0.statusUninfected.Female 0.48099634       -3.00         1
## b0.statusUninfected.Male   0.86294360       -3.00         1
## b1.statusInfected.Female   0.02548119        0.01         1
## b1.statusInfected.Male     0.05096491        0.01         1
## b1.statusUninfected.Female 0.01379019        0.01         1
## b1.statusUninfected.Male   0.04614644        0.01         1
##
## Mean Kullback-Leibler
## discrepancy calibration (KLDC):
##                                                          a0     a1
c     b0     b1
## statusInfected.Male - statusInfected.Female     0.5350 0.5008 0.827
0 0.5689 0.5897
## statusUninfected.Female - statusInfected.Female 0.9996    NaN 0.505
2 0.9855 0.8917
## statusUninfected.Female - statusInfected.Male   0.9973    NaN 0.852
9 0.9773 0.8764


SOME ROWS HAVE BEEN REMOVED


## pi.173                      0.03919 0.02235  0.0080401    0.09345
5.382e-03     1.0000        0.9999
##
## Convergence:
## Appropriate convergence reached for all parameters.
##
## DIC:
## 30300.98
```

Plot mortality trajectory and posterior distributions of parameters.

```
plot(All.badgers.Go.Bt.long, fancy = TRUE)
```


a 0
-5.8
-3.9
-2.0
a 1
0.0
1.6
3.2
c
0.00
0.05
0.10
b 0
-7.10
-4.85
-2.60
b 1
0.0
0.1
0.2
Survival, S(x)
1.0
0.8
0.6
0.4
0.2
0.0
statusInfected.Female
statusInfected.Male
statusUninfected.Female
statusUninfected.Male
Mortality, μ(x)
1.00
0.75
0.50
0.25
0.00
0
5
15
25
35
45
Age x (years)

Appendix 2 – Supplementary material from Chapter 3: Flexible model specification for Bayesian survival analysis

R code for Case study analysis

Setup

Load libraries, data, additional functions and seed

```
## load libraries
library(nimble)
library(tidyverse)
library(boot)
library(lamW)
library(GGally)
library(coda)
library(data.table)

## load data
load("badgerALL.RData")

## load distributions and register with NIMBLE
source("Dist_Siler.R")
source("Dist_SilerNim.R")
```

```
## Registering the following user-provided distributions: dsilerNim
```

```
## load required additional functions
source("ModelComparison_FUNCTIONS.R")

## set seed
set.seed(42)
```

Prepare for Nimble analysis

Define model, set constants, data and initial values. The initial values are generated inside a function and we add them to the compiled model a little later.

```
code <- nimbleCode({

  ## survival components for dead badgers
  for (i in 1:nind) {

    ## likelihood for interval-truncated siler
    censored[i] ~ dinterval(tD[i], cint[i, ])
    tD[i] ~ dsilerNim(a1, a2, b1, b2, c1)

    ## sampling component
    pd[i] <- exp(y[i] * log(mean.p) + (min(floor(tD[i]), tM[i]) - y[i]
) * log(1 - mean.p))
```

```
    dind[i] ~ dbern(pd[i])
  }

  ## priors
  a1 ~ dexp(1)
  a2 ~ dexp(1)
  b1 ~ dexp(1)
  b2 ~ dexp(1)
  c1 ~ dexp(1)
  mean.p ~ dunif(0, 1)

})

## set up data
consts <- list(nind = nind, tM = tM)

data <- list(
  y = y, cint = cint, censored = censored, tD = tD, dind = dind)

## find overdispersed initial values
tinitFn <- function(cint, censored) {
  apply(cbind(cint, censored), 1, function(x) {
    if(x[3] == 2) {
      y <- x[2] + rexp(1, 1)
    } else {
      y <- runif(1, x[1], x[2])
    }
    y
  })
}
initFn <- function(cint, censored, model) {
  ## get ML estimates as initial values
  optFn <- function(pars, t) {
    if(any(pars[1:5] < 0)) {
      return(NA)
    }
    ll <- sum(dSiler(t, a1 = pars[1], a2 = pars[2], b1 = pars[3], b2 =
pars[4], c1 = pars[5], log = TRUE))
  }
  valid <- 0
  while(valid == 0) {
    pars <- list(convergence = 1)
    k <- 0
    while(pars$convergence != 0 & k < 20) {
      ## sample missing values
      tD <- tinitFn(cint, censored)
      pars <- optim(rexp(5, 10), optFn, t = tD, control = list(fnscale
= -1))
      k <- k + 1
    }
    if(k == 20) {
      stop("Can't sample initial values")
    }
```

```
    pars <- pars$par

    ## output initial values
    inits <- list(
      tD = tD,
      a1 = pars[1],
      a2 = pars[2],
      b1 = pars[3],
      b2 = pars[4],
      c1 = pars[5],
      mean.p = runif(1, 0, 1)
    )
    model$setInits(inits)
    valid <- ifelse(!is.finite(model$calculate()), 0, 1)
  }
  return(inits)
}
```

Build the model in NIMBLE.

We do not supply the initial values here. This will throw an initialization error at this stage but do not worry, it is safer to add them to the compiled model in a few steps time.

```
## build the model
model <- nimbleModel(code, constants = consts, data = data)

## defining model...

## building model...

## setting data and initial values...

## running calculate on model (any error reports that follow may simpl
y reflect missing values in model variables) ... Error in if (a1 < 0 |
a2 < 0 | b1 < 0 | b2 < 0 | c1 < 0) { :
##   missing value where TRUE/FALSE needed
##
## checking model sizes and dimensions... This model is not fully init
ialized. This is not an error. To see which variables are not initiali
zed, use model$initializeInfo(). For more information on model initial
ization, see help(modelInitialization).
## model building finished.
```

Compile the model

We now compile the model into C++ and then add the initial values argument.

```
## compile the model
cModel <- compileNimble(model)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.
```

```
## compilation finished.

## find list of valid initial values (needs compiled model)
inits <- list()
for(k in 1:2) {
  inits[[k]] <- initFn(cint, censored, cModel)
}
```

Configure the MCMC

We can now make adjustments to the default sampler settings in NIMBLE.

```
## define the configuration
config <- configureMCMC(model)

## ===== Monitors =====
## thin = 1: a1, a2, b1, b2, c1, mean.p
## ===== Samplers =====
## RW sampler (2760)
##   - a1
##   - a2
##   - b1
##   - b2
##   - c1
##   - mean.p
##   - tD[]  (2754 elements)

## remove default samplers
config$removeSamplers(c("a1", "a2", "b1", "b2", "c1"))

## add required samplers
config$addSampler(target = c("a1","a2", "b2", "c1"), type = 'AF_slice'
)
config$addSampler(target = c("b1"), type = 'slice', control = list(sli
ceWidth = 1.5, adaptInterval = 50))
```

Build and compile

We now build our model with the updated configuration and compile again.

```
knitr::opts_chunk$set(echo = TRUE)
# load in custom RJ-MCMC samplers
rMCMC <- buildMCMC(config)
cMCMC <- compileNimble(rMCMC, project = model)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.

## compilation finished.
```

Run the MCMC

Here we set our MCMC options: iterations, burnin, chains etc.

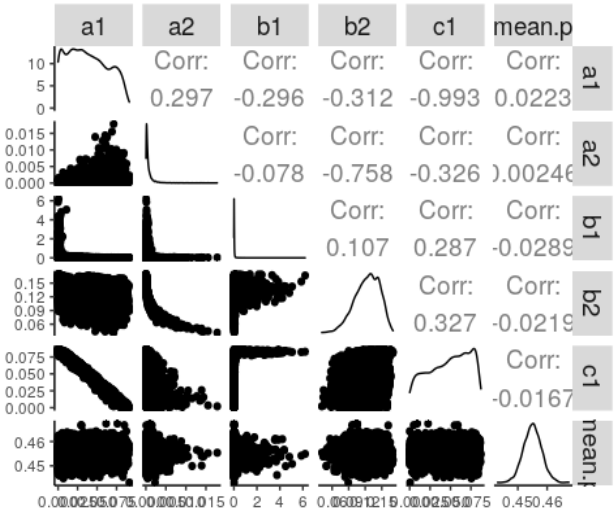
```
run <- runMCMC(cMCMC,
                            niter = 50000,
                            nburnin = 20000,
                            nchains = 2,
                            inits = inits[[1]],
                            progressBar = TRUE,
                            summary = TRUE,
                            samplesAsCodaMCMC = TRUE,
                            thin = 1)

## running chain 1...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|

## running chain 2...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|
```

Now save the output samples as a matrix

```
samples <- as.matrix(run$samples)
```

And plot

```
samples <- samples[sample.int(nrow(samples), ceiling(nrow(samples) * 0
.1)), ]
samples %>%
  as.data.frame() %>%
  ggpairs(upper = list(continuous = wrap("cor", size = 5))) +
  theme(panel.grid.major = element_blank(), panel.grid.minor = element
_blank(),
        panel.background = element_blank(), axis.line = element_line(c
olour = "black")) +
  theme(strip.text = element_text(size = 14))
```



Siler Distribution

```
# Truncated Siler distribution:

## zL = lower truncation point
## zU = upper truncation point

## load libraries
library(lamW)

## R function to run optimiser
optimiseR <- function(interval, a1, a2, b1, b2, c1, zL, zU, p) {
  silerRootFn <- function(x, a1, a2, b1, b2, c1, zL, zU, p) {
    abs(pSiler(x, a1, a2, b1, b2, c1, zL, zU) - p)
  }
  optimise(silerRootFn, interval, a1, a2, b1, b2, c1, zL, zU, p)$minim
um
}

## probability density function
dSiler <- function(x, a1, a2, b1, b2, c1, zL = NA, zU = NA,
                   log = FALSE) {

  ## all parameters length = 1 or length(x)
  ntot <- length(x)
  if ((length(a1) != 1 & length(a1) != ntot) |
      (length(a2) != 1 & length(a2) != ntot) |
      (length(b1) != 1 & length(b1) != ntot) |
      (length(b2) != 1 & length(b2) != ntot) |
      (length(c1) != 1 & length(c1) != ntot)) {
    stop("Length of parameters must be = 1 or length(x)")
  }
  if ((length(zL) != 1 & length(zL) != ntot) |
      (length(zU) != 1 & length(zU) != ntot)) {
    stop("Length of zL/zU must be = 1 or length(x)")
  }

  ## expand entries
  x <- cbind(x, zL, zU, a1, a2, b1, b2, c1)
  colnames(x) <- NULL

  ## run checks (first column of checkPass corresponds to invalid
  ## inputs [so should return NA]; second column is x outside range
  ## [so should return 0 p.d.f. outside the range])
  checkPass <- (is.na(x[, 2]) | is.na(x[, 3]) | x[, 2] < x[, 3])
  checkPass <- checkPass & (rowSums(x[, -c(1:3), drop = FALSE] > 0) ==
5)
  checkPass <- cbind(checkPass, (x[, 1] >= 0) & (is.na(x[, 2]) | x[, 1
] >= x[, 2]) & (is.na(x[, 3]) | x[, 1] <= x[, 3]))

  ## extract vectors as needed
  zL <- x[, 2]
  zU <- x[, 3]
```

```
  a1 <- x[, 4]
  a2 <- x[, 5]
  b1 <- x[, 6]
  b2 <- x[, 7]
  c1 <- x[, 8]
  x <- x[, 1]

  ## No truncation
  logS <- rep(NA, length(x))
  logH <- rep(NA, length(x))
  zN_ind <- which(checkPass[, 1] & checkPass[, 2])
  logS[zN_ind] <- (a1[zN_ind] / b1[zN_ind]) * (exp(-b1[zN_ind] * x[zN_
ind]) - 1) -
      c1[zN_ind] * x[zN_ind] + (a2[zN_ind] / b2[zN_ind]) * (1 - exp(b2
[zN_ind] * x[zN_ind]))
  logH[zN_ind] <- log(a1[zN_ind] * exp(-b1[zN_ind] * x[zN_ind]) + c1[z
N_ind] + a2[zN_ind] * exp(b2[zN_ind] * x[zN_ind]))
  logProb <- logH + logS

  ## Left truncation
  zL_ind <- which(!is.na(zL) & is.na(zU) & checkPass[, 1] & checkPass[
, 2])
  if(length(zL_ind) > 0) {
      logS_zL <- (a1[zL_ind] / b1[zL_ind]) * (exp(-b1[zL_ind] * zL[zL_
ind]) - 1) - c1[zL_ind] * zL[zL_ind] + (a2[zL_ind] / b2[zL_ind]) * (1
- exp(b2[zL_ind] * zL[zL_ind]))
      logProb[zL_ind] <- logProb[zL_ind] - logS_zL
  }

  ## Right truncation
  zU_ind <- which(is.na(zL) & !is.na(zU) & checkPass[, 1] & checkPass[
, 2])
  if(length(zU_ind) > 0) {
      logS_zU <- (a1[zU_ind] / b1[zU_ind]) * (exp(-b1[zU_ind] * zU[zU_
ind]) - 1) - c1[zU_ind] * zU[zU_ind] + (a2[zU_ind] / b2[zU_ind]) * (1
- exp(b2[zU_ind] * zU[zU_ind]))
      logProb[zU_ind] <- logProb[zU_ind] - log(1 - exp(logS_zU))
  }

  ## Interval truncation
  zI_ind <- which(!is.na(zL) & !is.na(zU) & checkPass[, 1] & checkPass
[, 2])
  if(length(zI_ind) > 0) {
      logS_zL <- (a1[zI_ind] / b1[zI_ind]) * (exp(-b1[zI_ind] * zL[zI_
ind]) - 1) - c1[zI_ind] * zL[zI_ind] + (a2[zI_ind] / b2[zI_ind]) * (1
- exp(b2[zI_ind] * zL[zI_ind]))
      logS_zU <- (a1[zI_ind] / b1[zI_ind]) * (exp(-b1[zI_ind] * zU[zI_
ind]) - 1) - c1[zI_ind] * zU[zI_ind] + (a2[zI_ind] / b2[zI_ind]) * (1
- exp(b2[zI_ind] * zU[zI_ind]))
      S_zL <- exp(logS_zL)
      S_zU <- exp(logS_zU)
      logProb[zI_ind] <- logProb[zI_ind] - log(S_zL - S_zU)
  }
```

```
  ## return correctly
  logProb[!checkPass[, 2]] <- -Inf
  logProb[!checkPass[, 1]] <- NA

  if(log) {
      return(logProb)
  } else {
      return(exp(logProb))
  }
}

## cumulative distribution function (and survivor function)
pSiler <- function(q, a1, a2, b1, b2, c1, zL = NA, zU = NA,
                   lower.tail = TRUE, log.p = FALSE) {

  ## all parameters length = 1 or length(x)
  ntot <- length(q)
  if ((length(a1) != 1 & length(a1) != ntot) |
      (length(a2) != 1 & length(a2) != ntot) |
      (length(b1) != 1 & length(b1) != ntot) |
      (length(b2) != 1 & length(b2) != ntot) |
      (length(c1) != 1 & length(c1) != ntot)) {
    stop("Length of parameters must be = 1 or length(q)")
  }
  if ((length(zL) != 1 & length(zL) != ntot) |
      (length(zU) != 1 & length(zU) != ntot)) {
    stop("Length of zL/zU must be = 1 or length(q)")
  }

  ## expand entries
  x <- cbind(q, zL, zU, a1, a2, b1, b2, c1)
  colnames(x) <- NULL

  ## run checks (first column of checkPass corresponds to invalid
  ## inputs [so should return NA]; second column is x below lower
  ## bound and third column is x above upper bound
  ## [so should return 0 c.d.f. before the lower bound and 1 above
  ## the upper bound])
  checkPass <- (is.na(x[, 2]) | is.na(x[, 3]) | x[, 2] < x[, 3])
  checkPass <- checkPass & (rowSums(x[, -c(1:3), drop = FALSE] > 0) ==
5)
  checkPass <- cbind(checkPass, (x[, 1] >= 0) & (is.na(x[, 2]) | x[, 1
] >= x[, 2]))
  checkPass <- cbind(checkPass, is.na(x[, 3]) | x[, 1] <= x[, 3])

  ## extract vectors as needed
  zL <- x[, 2]
  zU <- x[, 3]
  a1 <- x[, 4]
  a2 <- x[, 5]
  b1 <- x[, 6]
  b2 <- x[, 7]
```

```
  c1 <- x[, 8]
  q <- x[, 1]

  ## No truncation
  logS <- (a1 / b1) * (exp(-b1 * q) - 1) - c1 * q + (a2 / b2) * (1 - e
xp(b2 * q))
  S <- exp(logS)

  ## Left truncation
  zL_ind <- which(!is.na(zL) & is.na(zU) & checkPass[, 1] & checkPass[
, 2] & checkPass[, 3])
  if(length(zL_ind) > 0) {
      logS_zL <- (a1[zL_ind] / b1[zL_ind]) * (exp(-b1[zL_ind] * zL[zL_
ind]) - 1) - c1[zL_ind] * zL[zL_ind] + (a2[zL_ind] / b2[zL_ind]) * (1
- exp(b2[zL_ind] * zL[zL_ind]))
      logS[zL_ind] <- logS[zL_ind] - logS_zL
  }

  ## Right truncation
  zU_ind <- which(is.na(zL) & !is.na(zU) & checkPass[, 1] & checkPass[
, 2] & checkPass[, 3])
  if(length(zU_ind) > 0) {
      logS_zU <- (a1[zU_ind] / b1[zU_ind]) * (exp(-b1[zU_ind] * zU[zU_
ind]) - 1) - c1[zU_ind] * zU[zU_ind] + (a2[zU_ind] / b2[zU_ind]) * (1
- exp(b2[zU_ind] * zU[zU_ind]))
      S_zU <- exp(logS_zU)
      logS[zU_ind] <- log(S[zU_ind]-S_zU) - log(1 - S_zU)
  }

  ## Interval truncation
  zI_ind <- which(!is.na(zL) & !is.na(zU) & checkPass[, 1] & checkPass
[, 2] & checkPass[, 3])
  if(length(zI_ind) > 0) {
      logS_zLi <- (a1[zI_ind] / b1[zI_ind]) * (exp(-b1[zI_ind] * zL[zI
_ind]) - 1) - c1[zI_ind] * zL[zI_ind] + (a2[zI_ind] / b2[zI_ind]) * (1
- exp(b2[zI_ind] * zL[zI_ind]))
      logS_zUi <- (a1[zI_ind] / b1[zI_ind]) * (exp(-b1[zI_ind] * zU[zI
_ind]) - 1) - c1[zI_ind] * zU[zI_ind] + (a2[zI_ind] / b2[zI_ind]) * (1
- exp(b2[zI_ind] * zU[zI_ind]))
      S_zLi <- exp(logS_zLi)
      S_zUi <- exp(logS_zUi)
      logS[zI_ind] <- log(S[zI_ind] - S_zUi) - log(S_zLi - S_zUi)
  }

  ## return correctly
  logS[!checkPass[, 2]] <- 0
  logS[!checkPass[, 3]] <- -Inf
  logS[!checkPass[, 1]] <- NA

  if(!lower.tail) {
    if(log.p) return(logS)
    else return(exp(logS))
  } else {
```

```
    p <- 1 - exp(logS)
    if(!log.p) return(p)
    else return(log(p))
  }
}

## quantile function
qSiler <- function(p, a1, a2, b1, b2, c1, zL = NA, zU = NA,
                   lower.tail = TRUE, log.p = FALSE) {
  ## all parameters length = 1 or length(x)
  ntot <- length(p)
  if ((length(a1) != 1 & length(a1) != ntot) |
      (length(a2) != 1 & length(a2) != ntot) |
      (length(b1) != 1 & length(b1) != ntot) |
      (length(b2) != 1 & length(b2) != ntot) |
      (length(c1) != 1 & length(c1) != ntot)) {
    stop("Length of parameters must be = 1 or length(p)")
  }
  if ((length(zL) != 1 & length(zL) != ntot) |
      (length(zU) != 1 & length(zU) != ntot)) {
    stop("Length of zL/zU must be = 1 or length(p)")
  }

  ## check log and lower tail arguments and
  ## adjust p accordingly
  if(log.p) p <- exp(p)
  if(!lower.tail) p <- 1 - p

  ## expand entries
  x <- cbind(p, zL, zU, a1, a2, b1, b2, c1)
  colnames(x) <- NULL

  ## run checks (first column of checkPass corresponds to invalid
  ## inputs [so should return NA]; second column is p outside range
  ## [so should return NA if p not in (0, 1)])
  checkPass <- (is.na(x[, 2]) | is.na(x[, 3]) | x[, 2] < x[, 3])
  checkPass <- checkPass & (rowSums(x[, -c(1:3), drop = FALSE] > 0) ==
5)
  checkPass <- cbind(checkPass, x[, 1] >= 0 & x[, 1] <= 1)

  whichPass <- which(checkPass[, 1] & checkPass[, 2])
  if(length(whichPass) > 0) {
    ## extract valid entries
    x <- x[whichPass, , drop = FALSE]

    ## extract vectors as needed
    zL <- x[, 2]
    zU <- x[, 3]
    a1 <- x[, 4]
    a2 <- x[, 5]
    b1 <- x[, 6]
    b2 <- x[, 7]
    c1 <- x[, 8]
```

```
    p <- x[, 1]

    ## Left truncation
    zL_ind <- which(!is.na(zL) & is.na(zU))

    ## Right truncation
    zU_ind <- which(is.na(zL) & !is.na(zU))

    ## Interval truncation
    zI_ind <- which(!is.na(zL) & !is.na(zU))

    ## No truncation
    zN_ind <- which(is.na(zL) & is.na(zU))

    ## set lower bound
    qL <- rep(0, times = length(p))
    qL[zL_ind] <- zL[zL_ind]
    qL[zI_ind] <- zL[zI_ind]

    ## set/find upper bound
    qU <- qL + 10
    qU[zU_ind] <- zU[zU_ind]
    qU[zI_ind] <- zU[zI_ind]

    ## amend upper bound if necessary
    zNo_ind <- c(zN_ind, zL_ind)
    while(length(zNo_ind) > 0) {
      pTarget <- p[zNo_ind]
      pU <- pSiler(qU[zNo_ind], a1[zNo_ind], a2[zNo_ind], b1[zNo_ind],
b2[zNo_ind], c1[zNo_ind], zL[zNo_ind], zU[zNo_ind])
      zNo_ind <- zNo_ind[pU < pTarget]
      pU <- pU[pU < pTarget]
      if(length(zNo_ind) > 0) {
        qU[zNo_ind] <- qU[zNo_ind] + 10
      }
    }

    data <- cbind(qL, qU, a1, a2, b1, b2, c1, zL, zU, p)
    out <- rep(NA, ntot)
    out[whichPass] <- apply(data, 1, function(x) {
      optimiseR(x[1:2], x[3], x[4], x[5], x[6], x[7], x[8], x[9], x[10
])
    })
  } else {
    out <- rep(NA, ntot)
  }
  return(out)
}


## combined function
rSiler <- function(n, a1, a2, b1, b2, c1, zL = NA, zU = NA) {
```

```
  ## all parameters length = 1 or length(x)
  if(length(n) > 1) {
    n <- length(n)
    message("Since 'n' is a vector, 'length(n)' is taken to be the num
ber of samples required.")
  }
  if ((length(a1) != 1 & length(a1) != n) |
      (length(a2) != 1 & length(a2) != n) |
      (length(b1) != 1 & length(b1) != n) |
      (length(b2) != 1 & length(b2) != n) |
      (length(c1) != 1 & length(c1) != n)) {
    stop("Length of parameters must be = 1 or n")
  }
  if ((length(zL) != 1 & length(zL) != n) |
      (length(zU) != 1 & length(zU) != n)) {
    stop("Length of zL/zU must be = 1 or n")
  }

  ## expand entries
  x <- cbind(zL, zU, a1, a2, b1, b2, c1)
  if(n == nrow(x)) {
      x <- cbind(1, x)
  } else {
      if(nrow(x) != 1) {
          stop("Error we're not catching")
      } else {
          x <- matrix(rep(c(1, x[1, ]), n), nrow = n, byrow = TRUE)
      }
  }
  colnames(x) <- NULL

  ## run checks (corresponds to invalid
  ## inputs [so should return NA])
  checkPass <- (is.na(x[, 2]) | is.na(x[, 3]) | x[, 2] < x[, 3])
  checkPass <- checkPass & (rowSums(x[, -c(1:3), drop = FALSE] > 0) ==
5)

  ## extract vectors as needed
  zL <- x[, 2]
  zU <- x[, 3]
  a1 <- x[, 4]
  a2 <- x[, 5]
  b1 <- x[, 6]
  b2 <- x[, 7]
  c1 <- x[, 8]

  ## set up output vector
  rs <- rep(NA, n)

  ## no truncation and/or left-truncation
  zN_ind <- which(is.na(zL) & is.na(zU) & checkPass)
  zL_ind <- which(!is.na(zL) & is.na(zU) & checkPass)
  zNL_ind <- c(zN_ind, zL_ind)
```

```
  nNL <- length(zNL_ind)
  if(nNL > 0) {
    ## sample from distribution 1
    u1 <- runif(nNL, 0, 1)
    u2 <- runif(nNL, 0, 1)

    ## distribution 1
    logS_zNL <- (a1[zNL_ind] / b1[zNL_ind]) * (exp(-b1[zNL_ind] * zL[z
NL_ind]) - 1) - c1[zNL_ind] * zL[zNL_ind]
    S_zNL <- exp(logS_zNL)

    ## distribution 2
    logS_zNL2 <-  (a2[zNL_ind] / b2[zNL_ind]) * (1 - exp(b2[zNL_ind] *
zL[zNL_ind]))
    S_zNL2 <- exp(logS_zNL2)

    ## left truncation
    zL_ind1 <- match(zL_ind, zNL_ind)
    if(length(zL_ind1) > 0) {
      u1[zL_ind1] <- u1[zL_ind1] * S_zNL[zL_ind1]
      u2[zL_ind1] <- u2[zL_ind1] * S_zNL2[zL_ind1]
    }

    ## sample from distribution 1
    w0 <- (a1[zNL_ind] / c1[zNL_ind]) * exp((log(u1) + a1[zNL_ind] / b
1[zNL_ind]) * (b1[zNL_ind] / c1[zNL_ind]))
    w0 <- lambertW0(w0)
    x1 <- (-1 / c1[zNL_ind]) * (log(u1) + a1[zNL_ind] / b1[zNL_ind]) +
w0 / b1[zNL_ind]
    ## sample from distribution 2
    x2 <- log(1 - log(u2) * (b2[zNL_ind] / a2[zNL_ind])) / b2[zNL_ind]

    rs[zNL_ind] <- ifelse(x1 < x2, x1, x2)
  }

  ## Right truncation
  zU_ind <- which(is.na(zL) & !is.na(zU) & checkPass)
  if(length(zU_ind) > 0) {
    rs[zU_ind] <- qSiler(runif(length(zU_ind), 0, 1), a1[zU_ind], a2[z
U_ind], b1[zU_ind], b2[zU_ind], c1[zU_ind], zL[zU_ind], zU[zU_ind])
  }

  ## Interval truncation
  zI_ind <- which(!is.na(zL) & !is.na(zU) & checkPass)
  if(length(zI_ind) > 0) {
    rs[zI_ind] <- qSiler(runif(length(zI_ind), 0, 1), a1[zI_ind], a2[z
I_ind], b1[zI_ind], b2[zI_ind], c1[zI_ind], zL[zI_ind], zU[zI_ind])
  }

  ## return correctly
  return(rs)
}
```

Appendix 3 – Supplementary material from Chapter 4: Bayesian model selection for survival analysis

Uncensored simulations Log Marginal Likelihood plots.

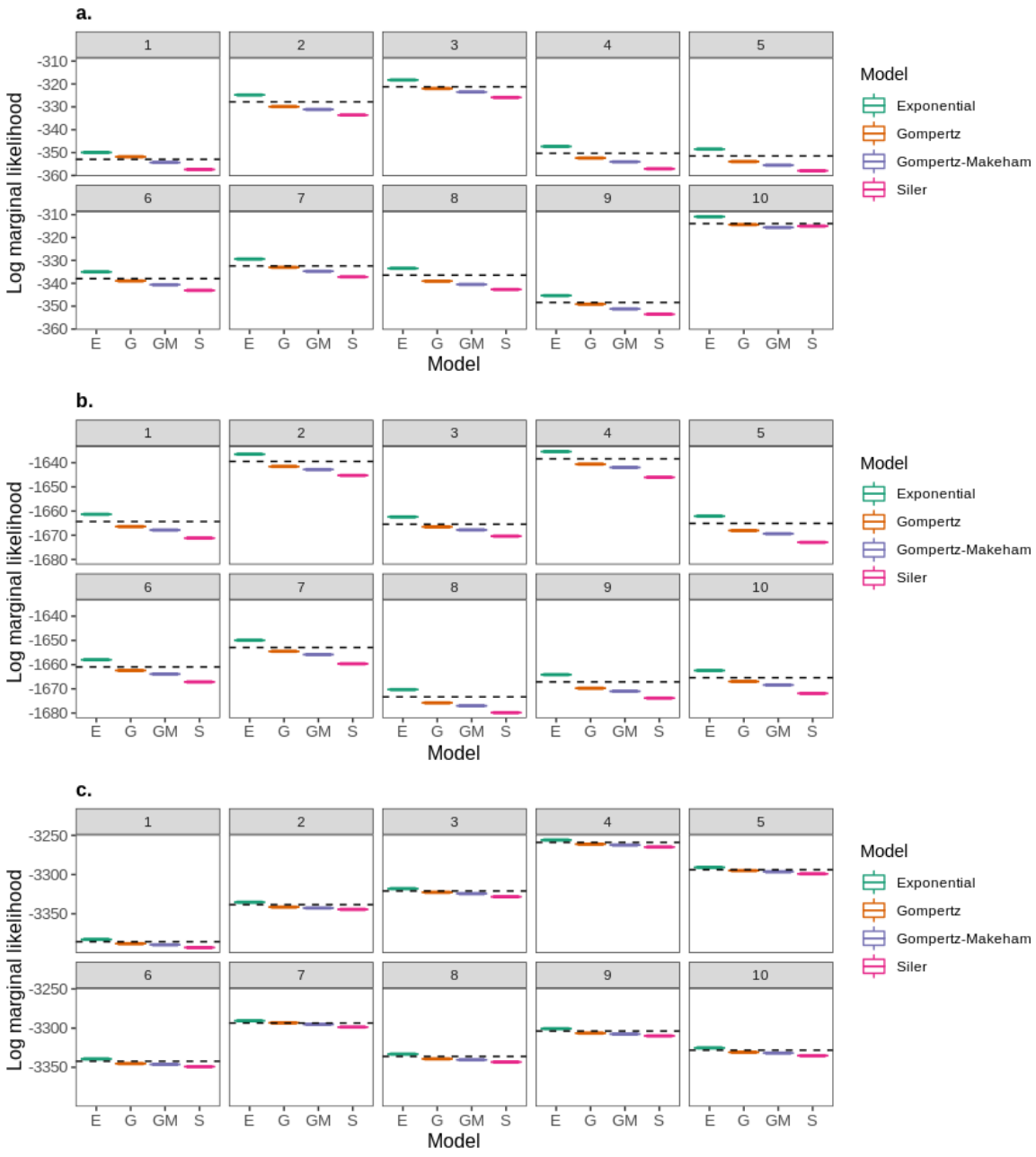


Figure A3.1: Log marginal likelihood plots of fitted mortality models to exponential simulated survival data of various population size: a. $n=100$; b. $n=500$; c. $n=1000$. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

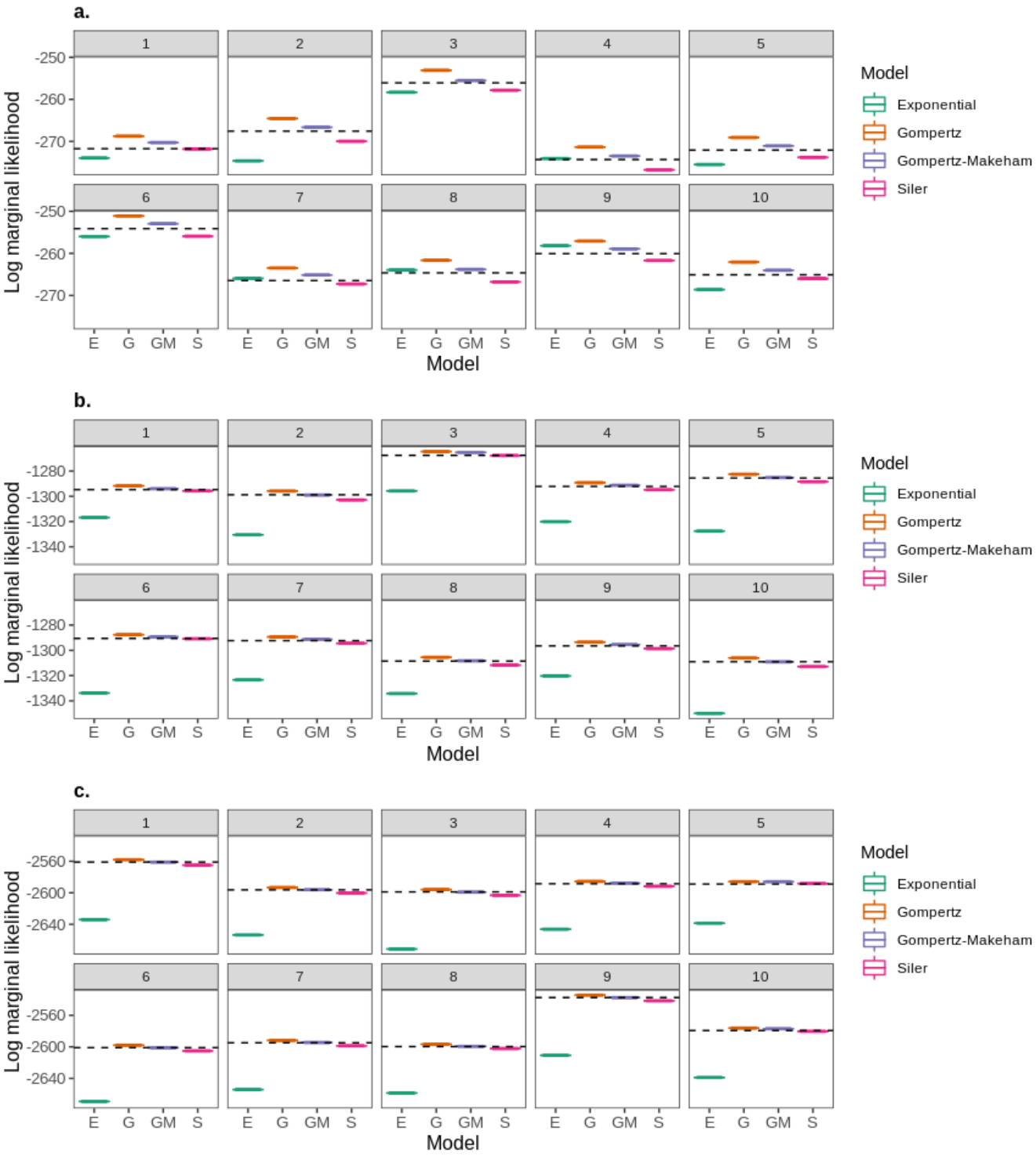


Figure A3.2: Log marginal likelihood plots of fitted mortality models to Gompertz simulated survival data of various population size: a. $n=100$; b. $n=500$; c. $n=1000$. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

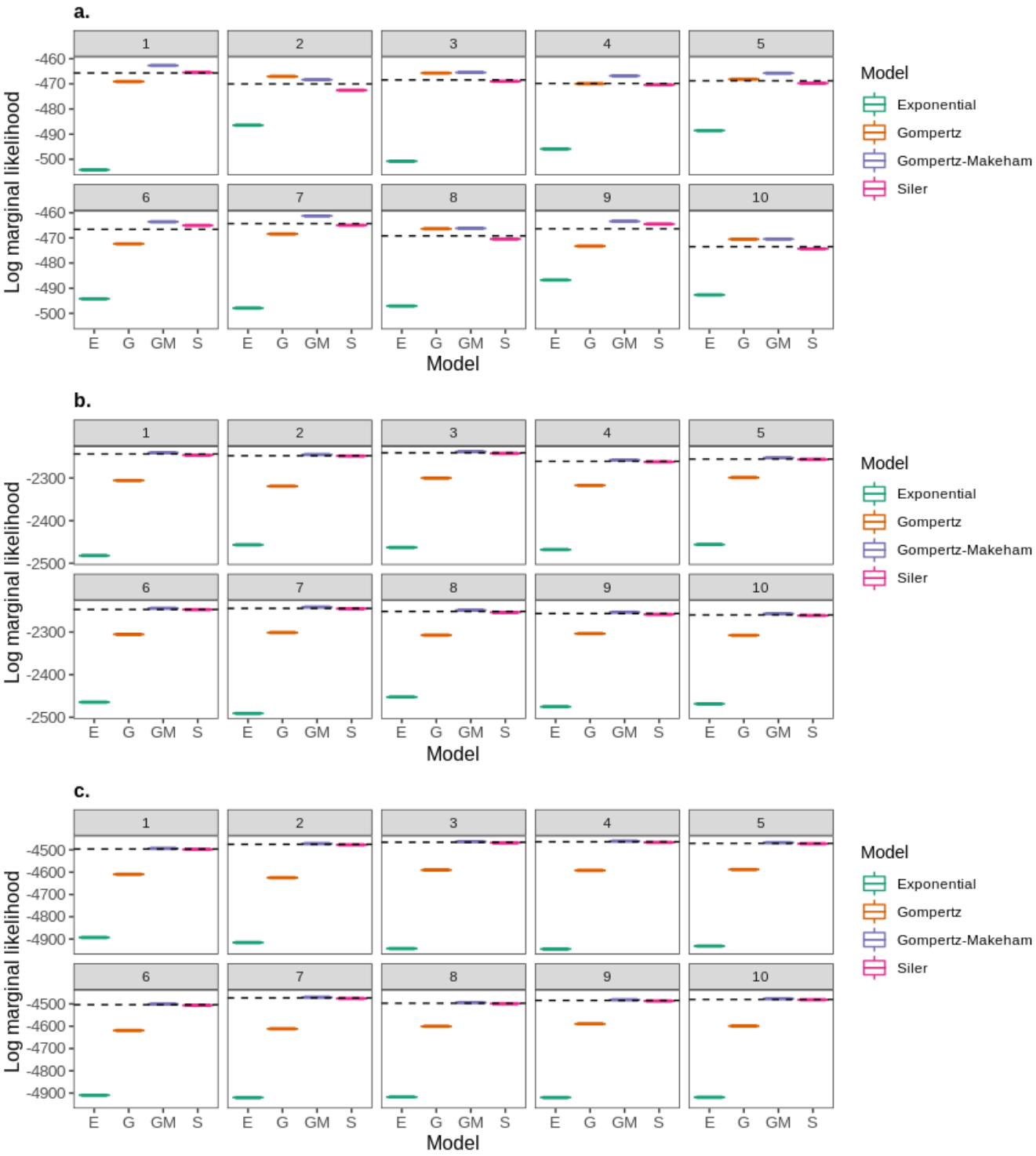


Figure A3.3: Log marginal likelihood plots of fitted mortality models to Gompertz-Makeham simulated survival data of various population size: a. $n=100$; b. $n=500$; c. $n=1000$. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

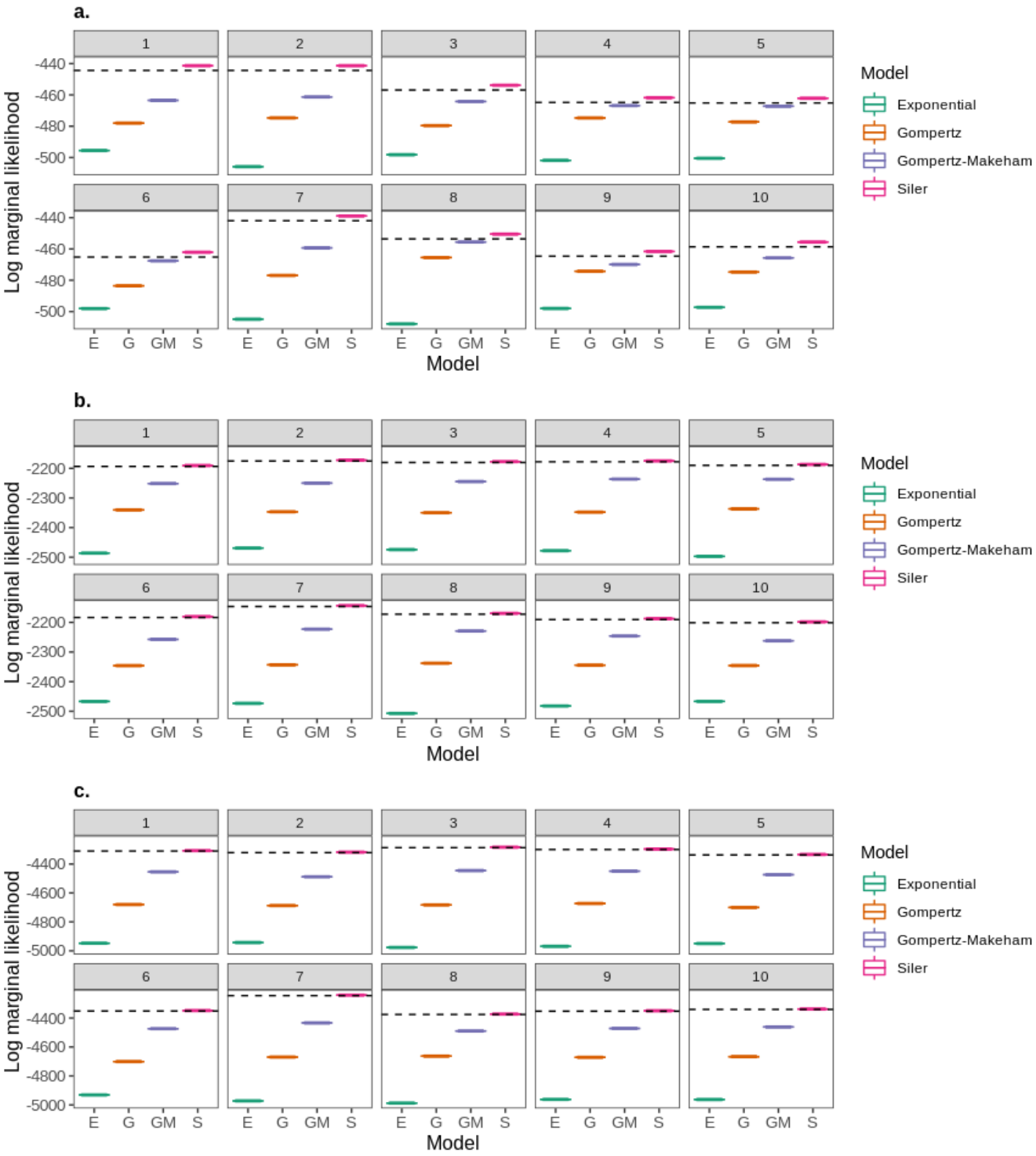


Figure A3.4: Log marginal likelihood plots of fitted mortality models to Siler simulated survival data of various population size: a. $n=100$; b. $n=500$; c. $n=1000$. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

Censored simulations Log Marginal Likelihood plots.

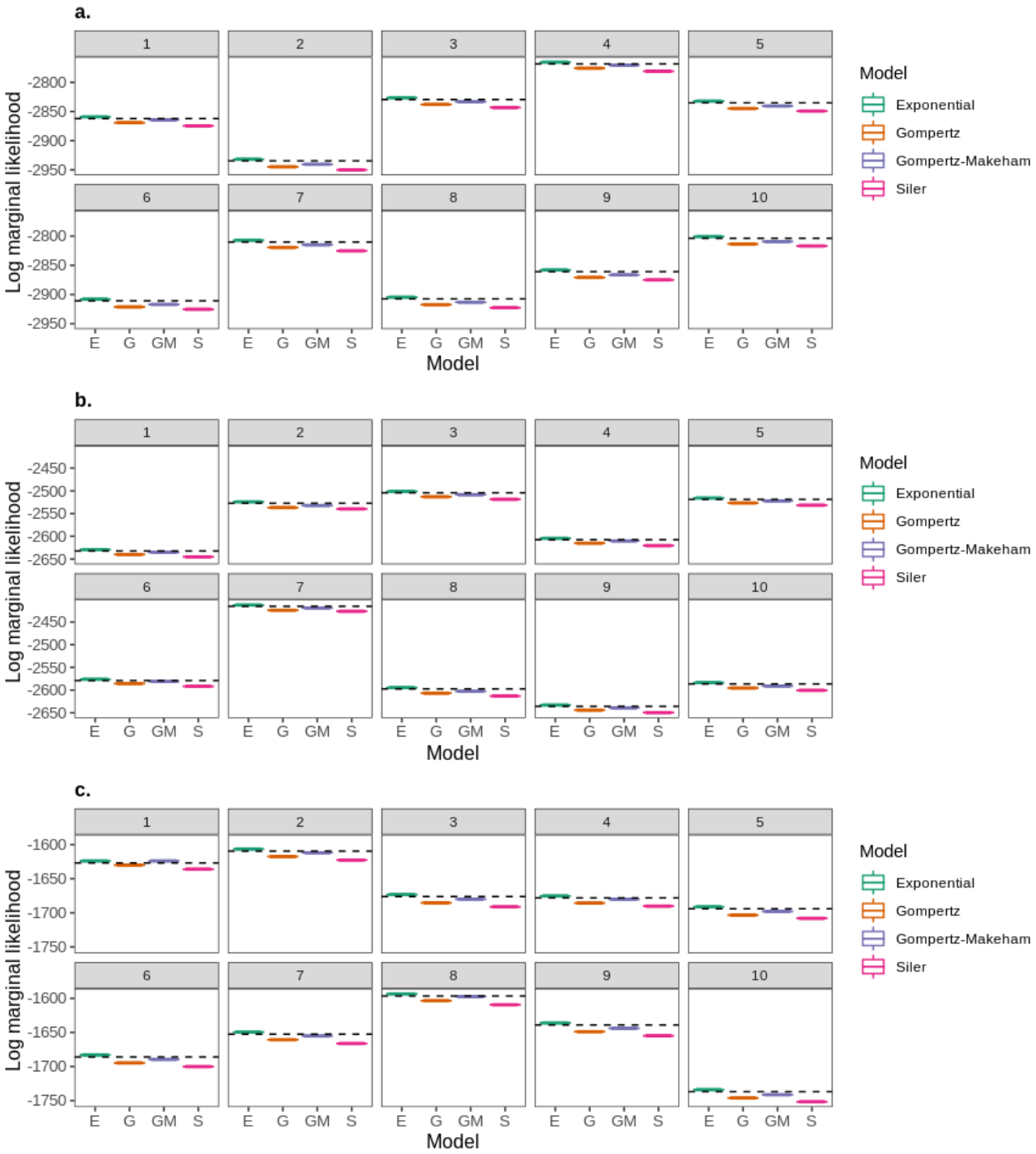


Figure A3.5: Log marginal likelihood plots of fitted mortality models to exponential simulated survival data with different censorship rates: a. censorship = 0.1; b. censorship = 0.2; c. censorship = 0.5. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

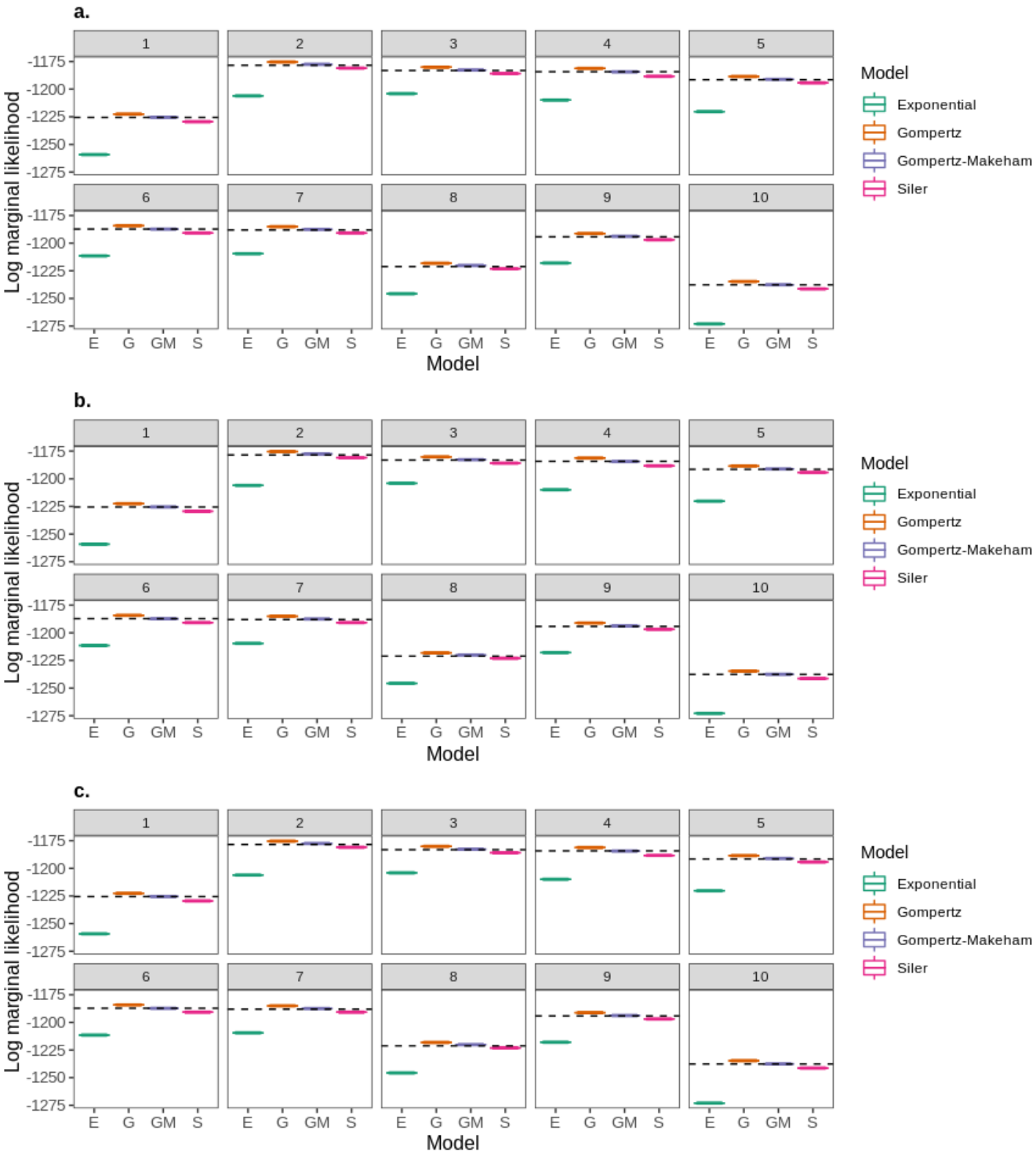


Figure A3.6: Log marginal likelihood plots of fitted mortality models to Gompertz simulated survival data with different censorship rates: a. censorship = 0.1; b. censorship = 0.2; c. censorship = 0.5. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

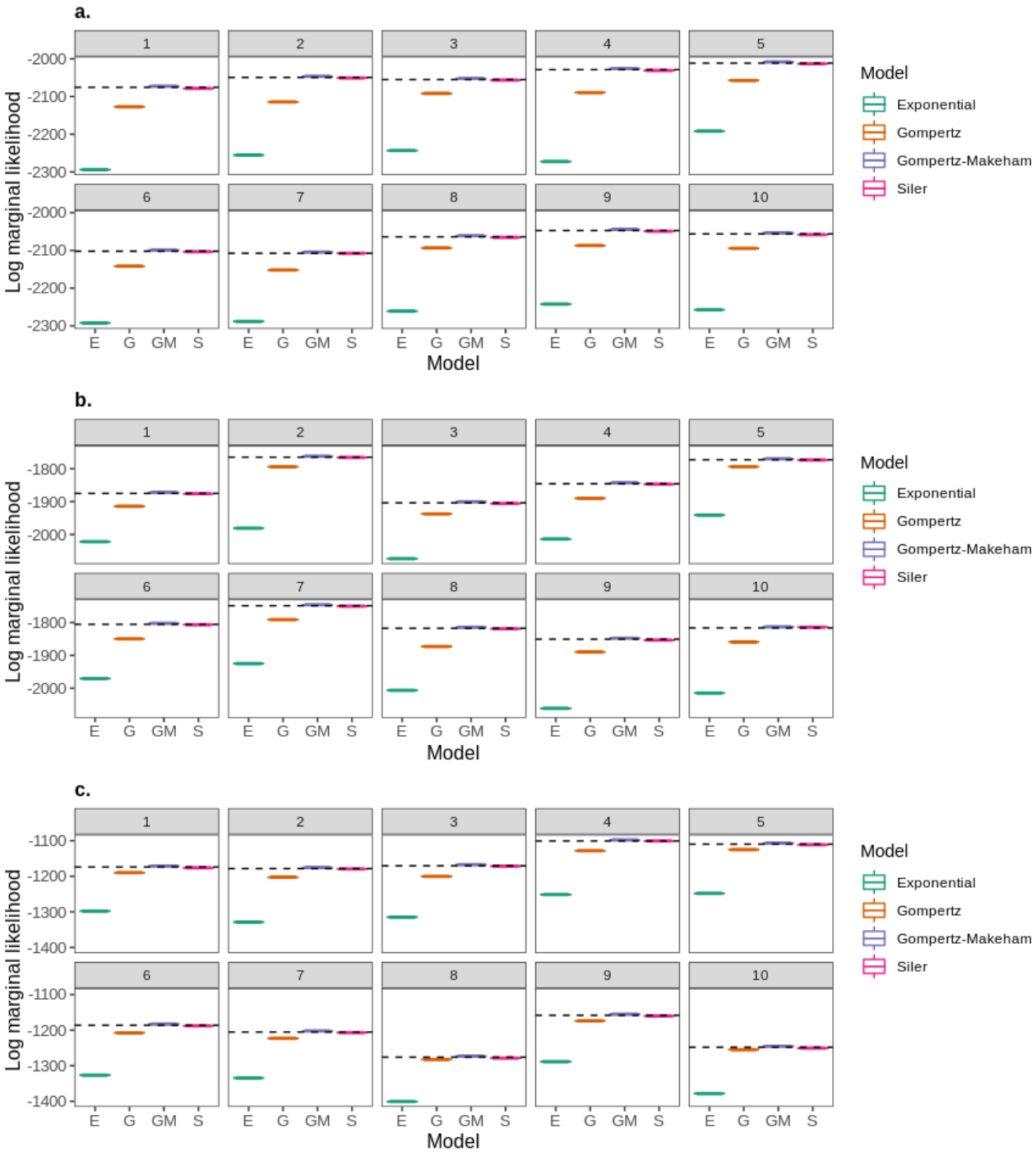


Figure A3.7: Log marginal likelihood plots of fitted mortality models to Gompertz-Makeham simulated survival data with different censorship rates: a. censorship = 0.1; b. censorship = 0.2; c. censorship = 0.5. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

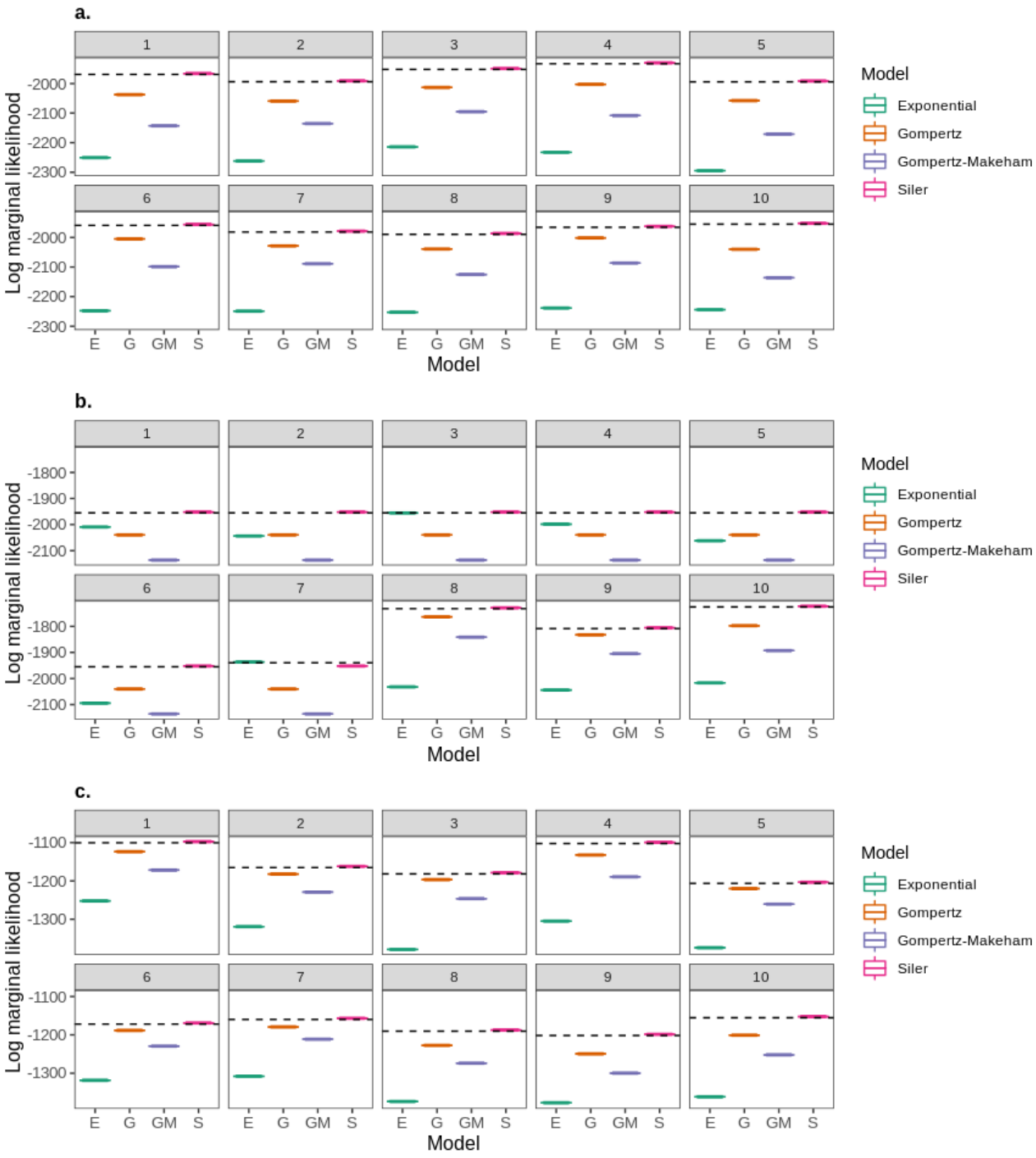


Figure A3.8: Log marginal likelihood plots of fitted mortality models to Siler simulated survival data with different censorship rates: a. censorship = 0.1; b. censorship = 0.2; c. censorship = 0.5. Dashed line represents a value log(20) less than the best supported model. Samples bootstrapped 1000 times to provide 95% confidence intervals.

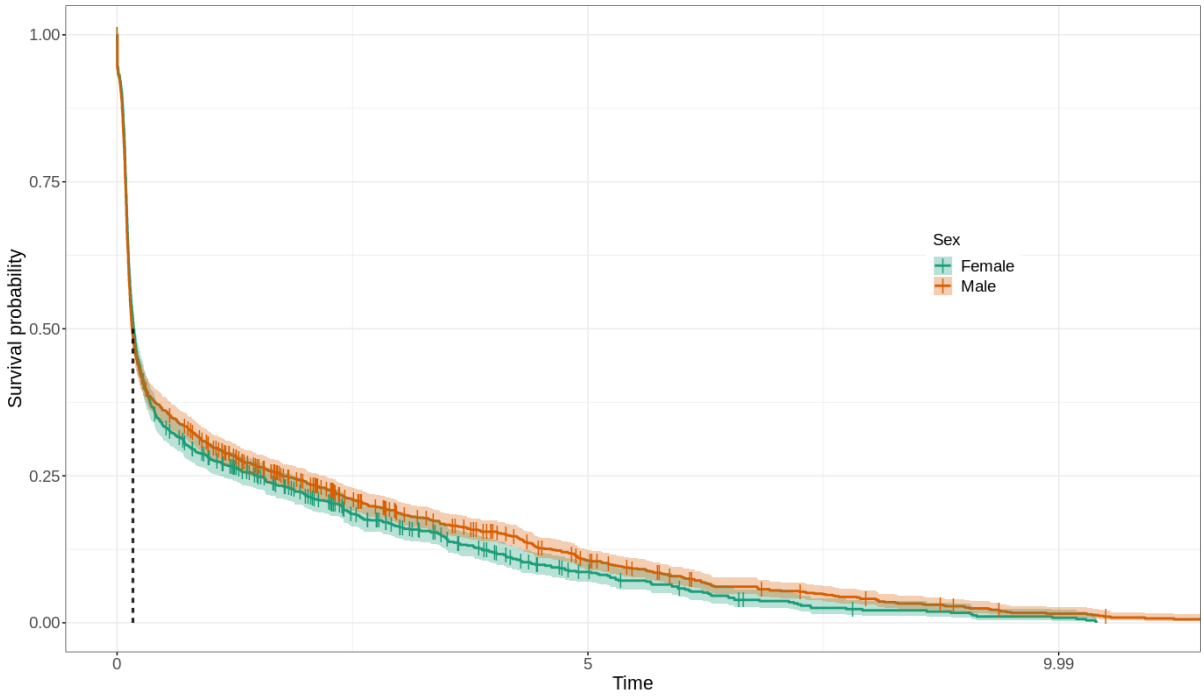


Figure A3.9: Kaplan-Meier plot of mongoose sex specific survival, vertical lines correspond to right-censored individuals, dashed line indicates median age. Survival curves compared using log-rank comparison - $\chi^2\left(1, N=3240\right)=1.7, p=0.2$.

Example R code – This code calculates the log marginal likelihood of a model that allows sex-specific variation on parameter a1.

Setup

Load libraries, data, additional functions and set seed

```
## load libraries
library(nimble)
library(tidyverse)
library(mvtnorm)
library(boot)
library(lamW)
library(GGally)
library(coda)
library(mclust)
library(parallel)
library(survminer)
library(survival)
rm(list = ls())

## source necessary R distributions
source("../../Distributions/Dist_Gompertz.R")
source("../../Distributions/Dist_GompertzNim.R")

## Registering the following user-provided distributions: dgompzNim

source("../../Distributions/Dist_GompertzMakeham.R")
source("../../Distributions/Dist_GompertzMakehamNim.R")

## Registering the following user-provided distributions: dgompzMakeNi
m

source("../../Distributions/Dist_Siler.R")
source("../../Distributions/Dist_SilerNim.R")

## Registering the following user-provided distributions: dsilerNim

source("../../Distributions/Dist_Expo.R")

## source additional R functions
source("../../ModelComparison_FUNCTIONS.R")

## load data
load("mong.RData")

## set seed according to model
set.seed(42)
```

Prepare for Nimble analysis

Define model, set constants, data and initial values.

```
code <- nimbleCode({
  ## survival components for dead badgers
  for (i in 1:nind) {
    ## likelihood for interval-truncated Siler
    censored[i] ~ dinterval(tD[i], cint[i, ])
    tD[i] ~ dsilerNim(a1[sex[i] + 1], a2, b1, b2, c1)
    sex[i] ~ dbern(Pm)
  }

  for (j in 1:g){
    ## priors
    a1[j] ~ dexp(1)
  }

  a2 ~ dexp(1)
  b1 ~ dexp(1)
  b2 ~ dexp(1)
  c1 ~ dexp(1)
  Pm ~ dunif(0,1)

})

## set up other components of model
consts <- list(nind = nind, g = g)

data <- list(cint = cint, censored = censored, tD = tD, sex = sex)

## find overdispersed initial values
tinitFn <- function(cint, censored) {
  apply(cbind(cint, censored), 1, function(x) {
    if(x[3] == 2) {
      y <- x[2] + 1
    } else {
      y <- runif(1, x[1], x[2])
    }
    y
  })
}
initFn <- function(cint, censored, sex) {
  ## get ML estimates as initial values
  optFn <- function(pars, t, sex) {
    if(any(pars < 0)) {
      return(NA)
    }
    llM <- sum(dSiler(t[sex == 0], a1 = pars[1], a2 = pars[3], b1 = pa
rs[4], b2 = pars[5], c1 = pars[6], log = TRUE))
    llF <- sum(dSiler(t[sex == 1], a1 = pars[2], a2 = pars[3], b1 = pa
rs[4], b2 = pars[5], c1 = pars[6], log = TRUE))
```

```
    llM + llF
  }
  pars <- list(convergence = 1)
  k <- 0
  while(pars$convergence != 0 & k < 20) {
    ## sample missing values
    tD <- tinitFn(cint, censored)
    ## sample sex proportion
    Pm <- runif(1, 0.4, 0.6)
    ## sample missing sex indicators
    sexI <- rbinom(length(censored), size = 1, prob = Pm)
    sexI[!is.na(sex)] <- sex[!is.na(sex)]
    ## optimise to interval-censored only
    pars <- optim(rexp(6, 100), optFn, t = tD, sex = sexI, control = l
ist(fnscale = -1))
    k <- k + 1
  }
  if(k == 20) {
    stop("Can't sample initial values")
  }
  pars <- pars$par
  ## check log-likelihoods
  ll <- sum(dSiler(tD[sexI == 0], a1 = pars[1], a2 = pars[3], b1 = par
s[4], b2 = pars[5], c1 = pars[6], log = TRUE))
  ll <- ll + sum(dSiler(tD[sexI == 1], a1 = pars[2], a2 = pars[3], b1
= pars[4], b2 = pars[5], c1 = pars[6], log = TRUE))
  stopifnot(is.finite(ll))
  ## reformat sex initial conditions correctly
  sexI[!is.na(sex)] <- NA
  ## output initial values
  list(
    tD = tD,
    sex = sexI,
    Pm = Pm,
    a1 = c(pars[1], pars[2]),
    a2 = pars[3],
    b1 = pars[4],
    b2 = pars[5],
    c1 = pars[6]
  )
}
```

Build the model in NIMBLE

```
## compile the model
## define the model, data, inits and constants

model <- nimbleModel(code = code, constants = consts, data = data, ini
ts = initFn(cint, censored, sex))

## defining model...

## building model...
```

```
## setting data and initial values...

## running calculate on model (any error reports that follow may simpl
y reflect missing values in model variables) ...
## checking model sizes and dimensions...
## model building finished.
```

Compile the model

We now compile the model into C++.

```
## compile the model
cmodel <- compileNimble(model)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.

## compilation finished.
```

Configure the MCMC

We can now make adjustments to the default sampler settings in NIMBLE.

```
## set monitors
config <- configureMCMC(cmodel, monitors = c("a1", "a2", "b1", "b2", "
c1", "Pm"), thin = 1)

## ===== Monitors =====
## thin = 1: a1, a2, b1, b2, c1, Pm
## ===== Samplers =====
## RW sampler (3247)
##   - a1[]  (2 elements)
##   - a2
##   - b1
##   - b2
##   - c1
##   - Pm
##   - tD[]  (3240 elements)
## binary sampler (1097)
##   - sex[]  (1097 elements)

## remove default samplers and add the required ones
config$removeSamplers(c("a1", "a2", "b1", "b2", "c1"))
config$addSampler(target = c("a1", "b1"), type = 'AF_slice')
config$addSampler(target = c("a2", "c1"), type = 'AF_slice')
config$addSampler(target = c("b2"), type = 'slice')

#Check monitors and samplers
config$printMonitors()

## thin = 1: a1, a2, b1, b2, c1, Pm

config$printSamplers(c("a1", "a2", "b1", "b2", "c1", "Pm"))
```

```
## [1]    RW sampler: Pm
## [4339] AF_slice sampler: a1, b1
## [4340] AF_slice sampler: a2, c1
## [4341] slice sampler: b2
```

Build and compile

We now build our model with the updated configuration and compile again.

```
#Build the model
built <- buildMCMC(config)
cbuilt <- compileNimble(built)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.

## compilation finished.
```

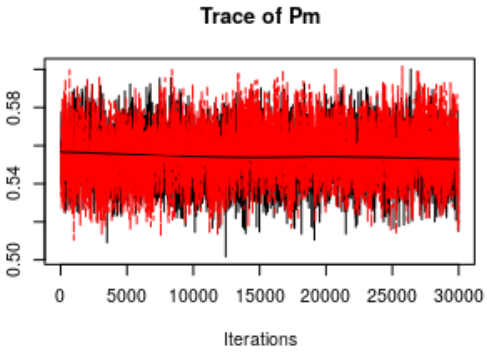
Run the MCMC Here we set our MCMC options: iterations, burnin, chains etc.

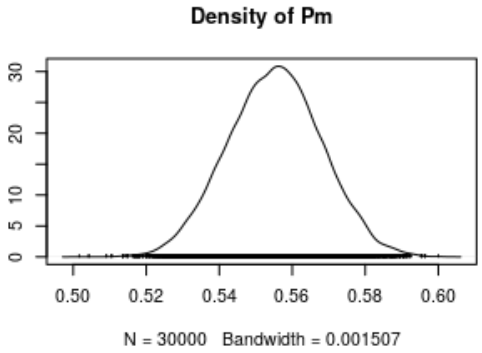
```
#Run the model
run <- runMCMC(cbuilt,
                            niter = 50000,
                            nburnin = 20000,
                            nchains = 2,
                            progressBar = TRUE,
                            summary = TRUE,
                            samplesAsCodaMCMC = TRUE,
                            thin = 1)

## running chain 1...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|

## running chain 2...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|
```

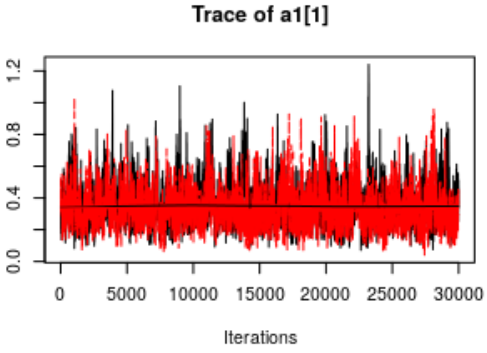
Plot trace plots to check mixing etc

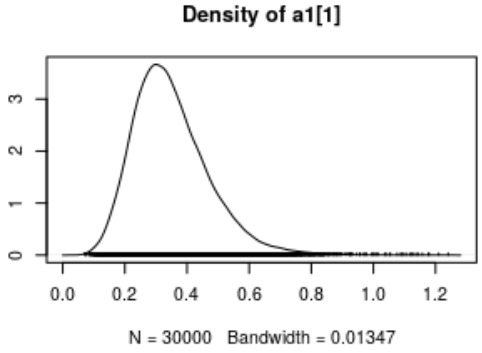
Need to check mixing here, you may need to adjust configuration of samplers and re-run.

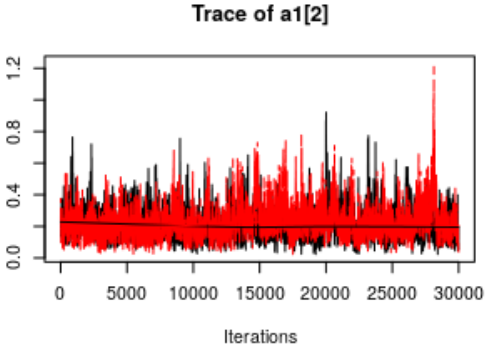
```
#Plot mcmcm
samples <- run$samples
plot(run$samples)
```

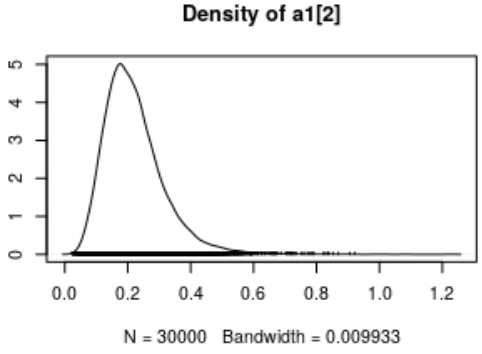

Trace of Pm
0.50
0.54
0.58
0
5000
10000
15000
20000
25000
30000
Iterations


Density of Pm
0
5
10
20
30
0.50
0.52
0.54
0.56
0.58
0.60
N = 30000 Bandwidth = 0.001507

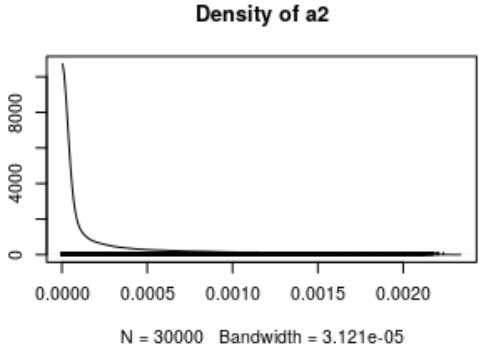

Trace of a1[1]
0.0
0.4
0.8
1.2
0
5000
10000
15000
20000
25000
30000
Iterations

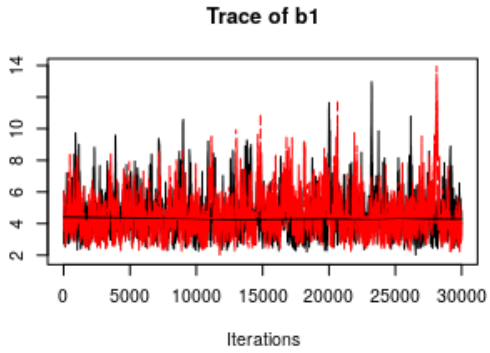

Density of a1[1]
0
1
2
3
0.0
0.2
0.4
0.6
0.8
1.0
1.2
N = 30000 Bandwidth = 0.01347

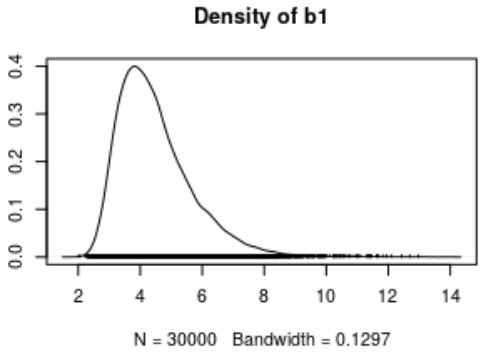

Trace of a1[2]
0.0
0.4
0.8
1.2
0
5000
10000
15000
20000
25000
30000
Iterations

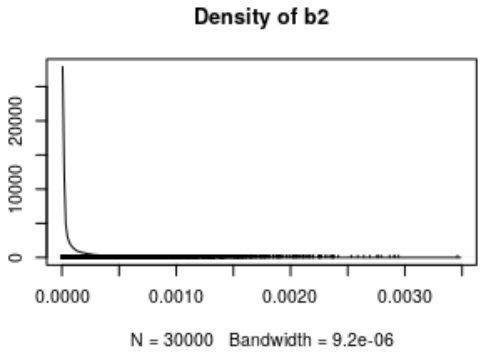

Density of a1[2]
0
1
2
3
4
5
0.0
0.2
0.4
0.6
0.8
1.0
1.2
N = 30000 Bandwidth = 0.009933

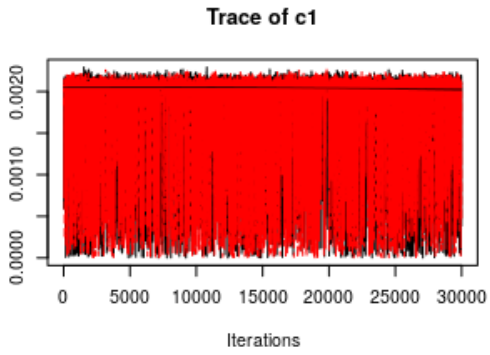

Trace of a2
0.0000
0.0010
0.0020
0
5000
10000
15000
20000
25000
30000
Iterations

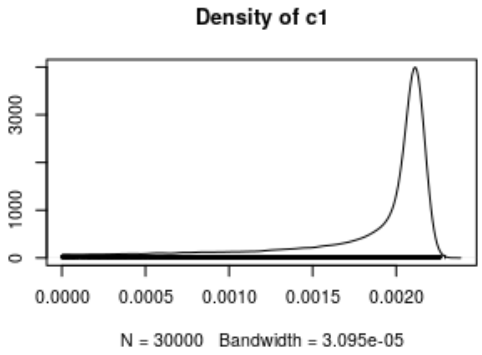

Density of a2
0
4000
8000
0.0000
0.0005
0.0010
0.0015
0.0020
N = 30000 Bandwidth = 3.121e-05







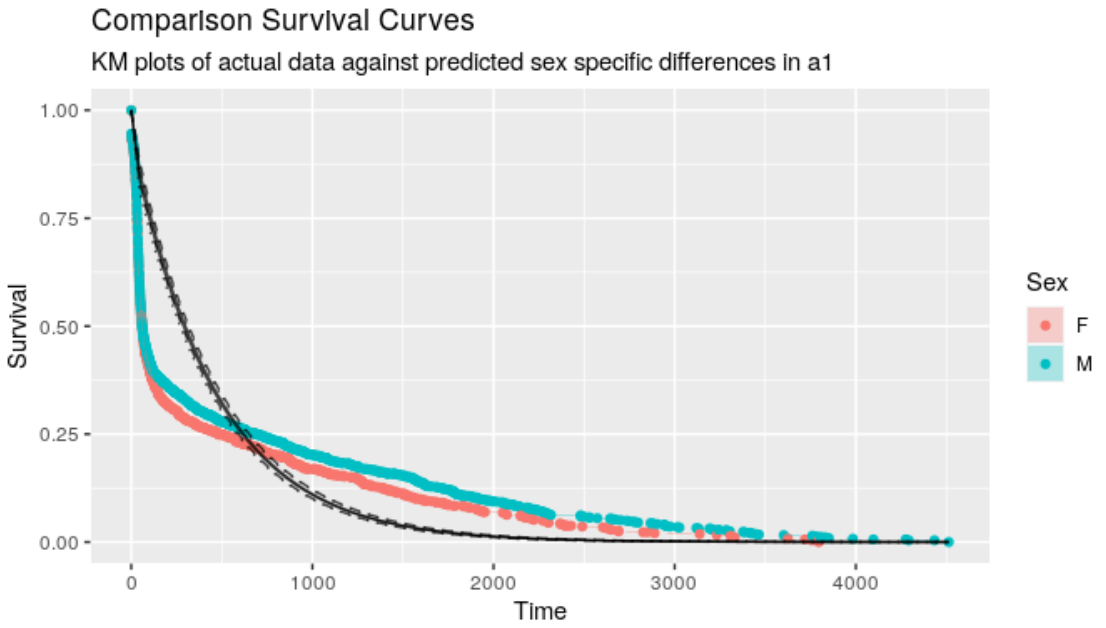




Predictive plots against the data

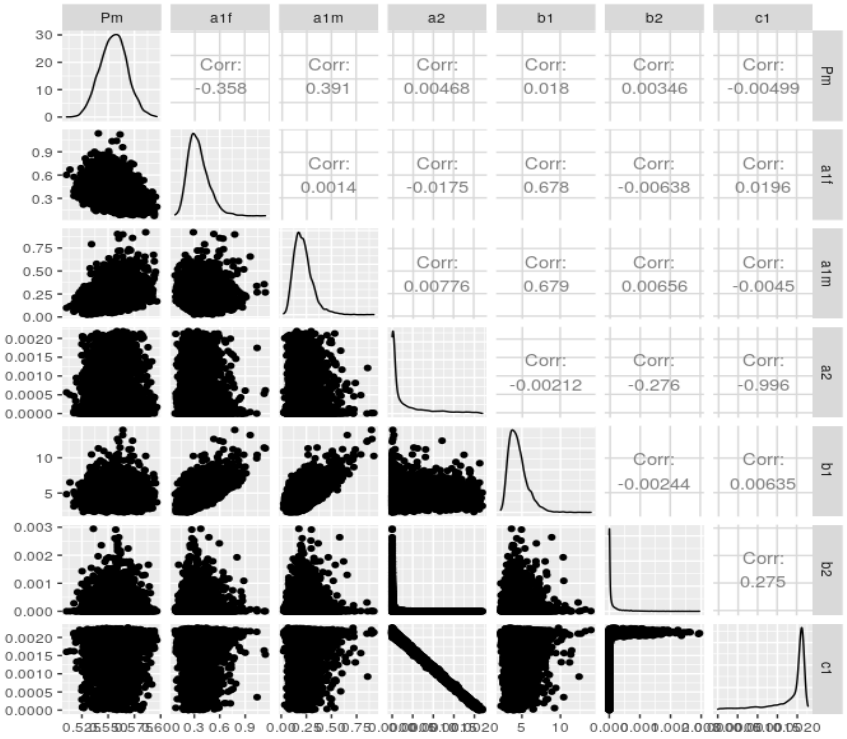
```
## predictive plot against data
t_pred <- seq(0, max(cint), length.out = 100)

predsM <- as.matrix(samples)[1:2000, -1] %>%
  apply(1, function(pars, t) {
    pSiler(t, a1 = pars[2], a2 = pars[3], b1 = pars[4], b2 = pars[5],
c1 = pars[6], lower.tail = FALSE)
  }, t = t_pred) %>%
  apply(1, function(x) {
    quantile(x, probs = c(0.025, 0.5, 0.975))
  }) %>%
  t() %>%
  as_tibble() %>%
  set_names(c("LCI", "Median", "UCI")) %>%
  mutate(t = t_pred, )
```

```r
predsF <- as.matrix(samples)[1:2000, -1] %>%
  apply(1, function(pars, t) {
    pSiler(t, a1 = pars[1], a2 = pars[3], b1 = pars[4], b2 = pars[5],
c1 = pars[6], lower.tail = FALSE)
  }, t = t_pred) %>%
  apply(1, function(x) {
    quantile(x, probs = c(0.025, 0.5, 0.975))
  }) %>%
  t() %>%
  as_tibble() %>%
  set_names(c("LCI", "Median", "UCI")) %>%
  mutate(t = t_pred, )

## plot posterior predictive K-M plots against the posterior predictiv
e survival curve
pred_sex <- mclapply(as.matrix(samples)[1:2000, 1], function(p, temp_d
at) {
  temp_dat$sex[temp_dat$sex == "P"] <- ifelse(rbinom(sum(temp_dat$sex
== "P"), size = 1, prob = p) == 1, "M", "F")
  temp_dat$sex <- factor(as.character(temp_dat$sex))
  temp_fit <- surv_fit(Surv(tD, cens) ~ sex, data = temp_dat)
  tibble(time = temp_fit$time, surv = temp_fit$surv, sex = rep(names(t
emp_fit$strata), temp_fit$strata))
}, temp_dat = mong_km_dat, mc.cores = 20) %>%
  bind_rows() %>%
  mutate(sex = ifelse(sex == "sex=F", "F", "M")) %>%
  group_by(time, sex) %>%
  summarise(
    Median = median(surv),
    LCI = quantile(surv, probs = 0.025),
    UCI = quantile(surv, probs = 0.975)
  )
pred_plot <- ggplot(pred_sex, aes(x = time)) +
  geom_point(aes(y = Median, colour = sex)) +
  geom_ribbon(aes(ymin = LCI, ymax = UCI, fill = sex), alpha = 0.3) +
  geom_line(aes(x = t, y = Median), data = predsM, alpha = 0.7) +
  geom_line(aes(x = t, y = LCI), data = predsM, linetype = "dashed", a
lpha = 0.7) +
  geom_line(aes(x = t, y = UCI), data = predsM, linetype = "dashed", a
lpha = 0.7) +
  geom_line(aes(x = t, y = Median), data = predsF, alpha = 0.7) +
  geom_line(aes(x = t, y = LCI), data = predsF, linetype = "dotted", a
lpha = 0.7) +
  geom_line(aes(x = t, y = UCI), data = predsF, linetype = "dotted", a
lpha = 0.7) +
  xlab("Time") + ylab("Survival") + labs(colour = "Sex", fill = "Sex")
+
  ggtitle("Comparison Survival Curves", subtitle = "KM plots of actual
data against predicted sex specific differences in a1")
pred_plot
```



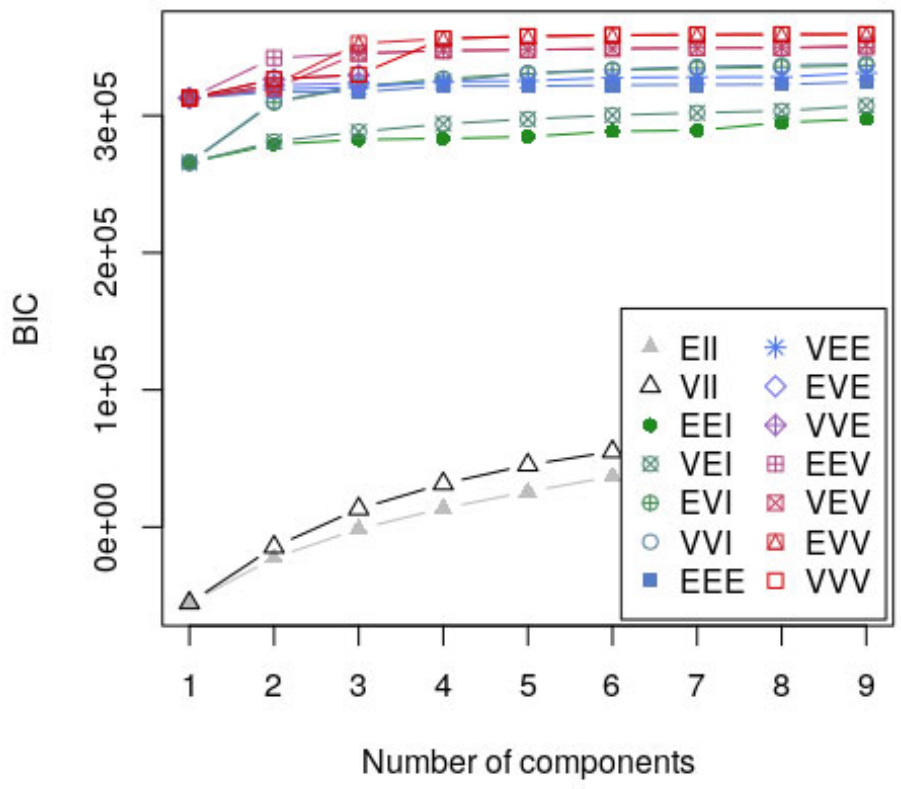
Pairs plot to check for correlations among parameters

```
## pairs plot
samples <- as.matrix(samples)
colnames(samples) <- c("Pm", "a1f", "a1m", "a2", "b1", "b2", "c1")
samples <- samples[sample.int(nrow(samples), ceiling(nrow(samples) * 0
.1)), ]
samples %>%
  as.data.frame() %>%
  ggpairs()
```



Find suitable mixture models to match posteriors

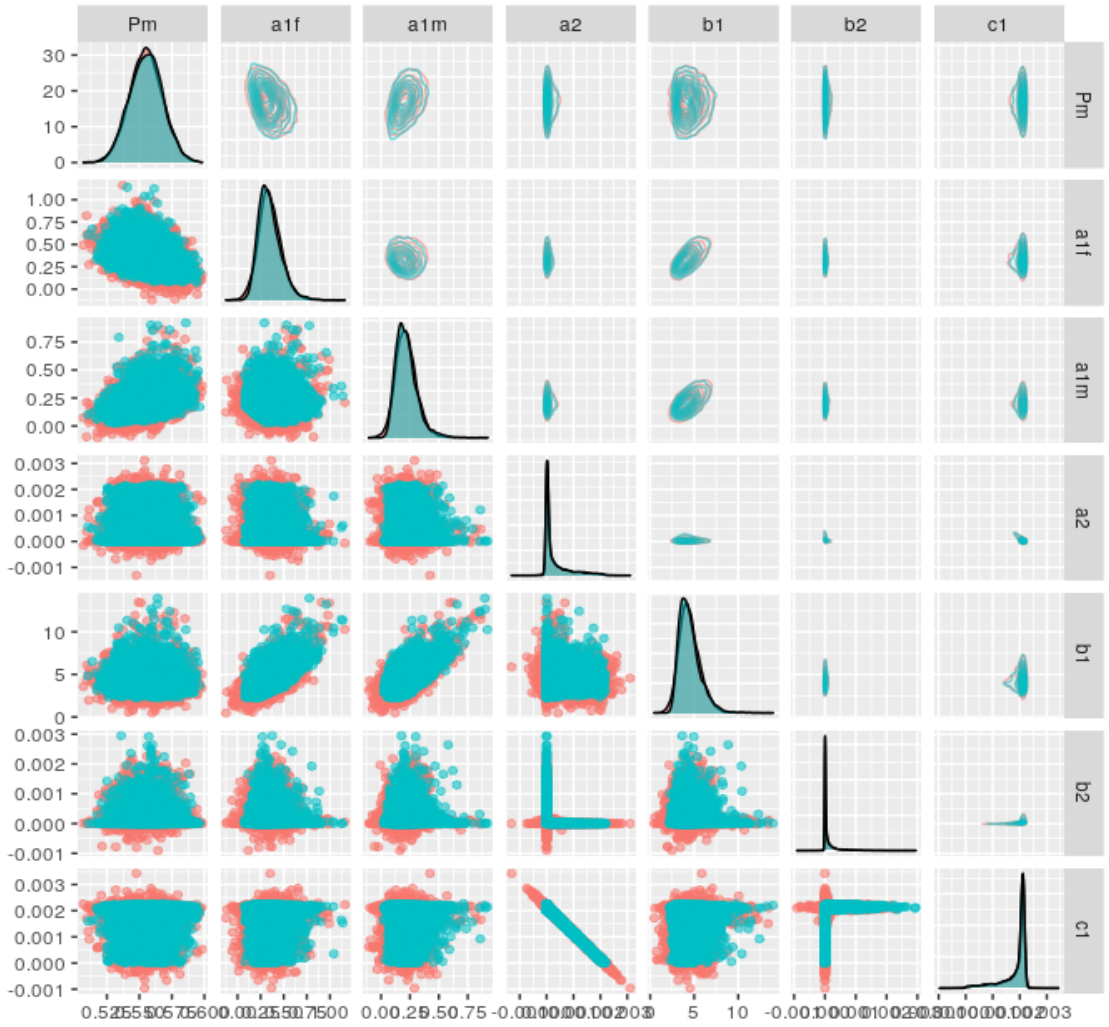
```
## fit range of finite mixture models
mod <- densityMclust(samples)

## summary of finite mixture models
summary(mod)

## ------------------------------------------------------
## Density estimation via Gaussian finite mixture modeling
## ------------------------------------------------------
##
## Mclust VVV (ellipsoidal, varying volume, shape, and orientation) mo
del with 9
## components:
##
##  log-likelihood    n  df      BIC      ICL
##        181110.1 6000 323 359410.3 356233.7

plot(mod, what = "BIC")
```



Create importance distribution and check against posteriors

```
## take random samples from mixture
nimp <- 10000
```

```r
nmix <- rbinom(1, size = nimp, prob = 0.95)
props <- sim(mod$modelName, mod$parameters, nmix)
props <- props[, -1]
colnames(props) <- c("Pm", "a1f", "a1m", "a2", "b1", "b2", "c1")

## take random samples from prior (to create defense mixture)
defense <- matrix(runif(nimp - nmix, 0, 1), ncol = 1)
defense <- cbind(defense, matrix(rexp(6 * (nimp - nmix), 1), ncol = 6)
)
colnames(defense) <- c("Pm", "a1f", "a1m", "a2", "b1", "b2", "c1")

## check IS distribution against posterior samples
as.data.frame(props) %>%
  mutate(type = "IS") %>%
  rbind(as.data.frame(samples) %>%
          mutate(type = "Post")) %>%
  ggpairs(mapping = aes(colour = type, alpha = 0.5), upper = list(cont
inuous = "density"), columns = 1:7)
```



Create defensive mixture

```
## combine defense and importance samples
props <- rbind(props, defense)
```

Generate importance weights

```
## generate importance weights

## log-likelihood function
## REQUIRES BOTH RIGHT- AND INTERVAL-CENSORED INDIVIDUALS
## AND MISSING SEX INDIVIDUALS
stopifnot(all(dim(table(sex, censored)) == 2))
stopifnot(length(table(is.na(sex))) == 2)
log.like <- function(zL, zU, censored, sex, pars) {
  ## calculate log-likelihoods

  ## interval-censored, known sex
  llI_f <- log(pSiler(zU[censored == 1 & sex == 0 & !is.na(sex)], pars
[2], pars[4], pars[5], pars[6], pars[7]) - pSiler(zL[censored == 1 & s
ex == 0 & !is.na(sex)], pars[2], pars[4], pars[5], pars[6], pars[7]))
+ log(1 - pars[1])
  llI_m <- log(pSiler(zU[censored == 1 & sex == 1 & !is.na(sex)], pars
[3], pars[4], pars[5], pars[6], pars[7]) - pSiler(zL[censored == 1 & s
ex == 1 & !is.na(sex)], pars[3], pars[4], pars[5], pars[6], pars[7]))
+ log(pars[1])

  ## right-censored, known sex
  llR_f <- pSiler(zL[censored == 2 & sex == 0 & !is.na(sex)], pars[2],
pars[4], pars[5], pars[6], pars[7], log = TRUE, lower.tail = FALSE) +
log(1 - pars[1])
  llR_m <- pSiler(zL[censored == 2 & sex == 1 & !is.na(sex)], pars[3],
pars[4], pars[5], pars[6], pars[7], log = TRUE, lower.tail = FALSE) +
log(pars[1])

  ## interval-censored unknown sex
  llI_miss <- (1 - pars[1]) * (pSiler(zU[censored == 1 & is.na(sex)],
pars[2], pars[4], pars[5], pars[6], pars[7]) - pSiler(zL[censored == 1
& is.na(sex)], pars[2], pars[4], pars[5], pars[6], pars[7]))
  llI_miss <- llI_miss + pars[1] * (pSiler(zU[censored == 1 & is.na(se
x)], pars[3], pars[4], pars[5], pars[6], pars[7]) - pSiler(zL[censored
== 1 & is.na(sex)], pars[3], pars[4], pars[5], pars[6], pars[7]))
  llI_miss <- log(llI_miss)

  ## right-censored unknown sex
  llR_miss <- (1 - pars[1]) * pSiler(zL[censored == 2 & is.na(sex)], p
ars[2], pars[4], pars[5], pars[6], pars[7], lower.tail = FALSE)
  llR_miss <- llR_miss + pars[1] * pSiler(zL[censored == 2 & is.na(sex
)], pars[3], pars[4], pars[5], pars[6], pars[7], lower.tail = FALSE)
  llR_miss <- log(llR_miss)

  ## return log-likelihood
```

```
  sum(llI_f) + sum(llR_f) + sum(llI_m) + sum(llR_m) + sum(llI_miss) +
sum(llR_miss)
}

## calculate log-likelihoods in parallel
logimpweight <- apply(props, 1, list)
logimpweight <- purrr::map(logimpweight, 1)
logimpweight <- mclapply(logimpweight,
                         function(pars, zL, zU, censored, sex) {
                           log.like(zL, zU, censored, sex, pars)
                         }, zL = zL, zU = zU, censored = censored, sex
= sex, mc.cores = 24)
logimpweight <- reduce(logimpweight, c)
```

Add priors and importance distributions

```
## priors
logimpweight <- logimpweight + dunif(props[, 1], 0, 1, log = TRUE)
for(j in 2:ncol(props)) {
  logimpweight <- logimpweight + dexp(props[, j], 1, log = TRUE)
}

## importance distributions
logimpweight <- logimpweight -
  log(0.95 * dens(mod$modelName, props, FALSE, mod$parameters) + 0.05
* exp(dunif(props[, 1], 0, 1, log = TRUE) +

dexp(props[, 2], 1, log = TRUE) + dexp(props[, 3], 1, log = TRUE) +

dexp(props[, 4], 1, log = TRUE) + dexp(props[, 5], 1, log = TRUE) +

dexp(props[, 6], 1, log = TRUE) + dexp(props[, 7], 1, log = TRUE)))
```

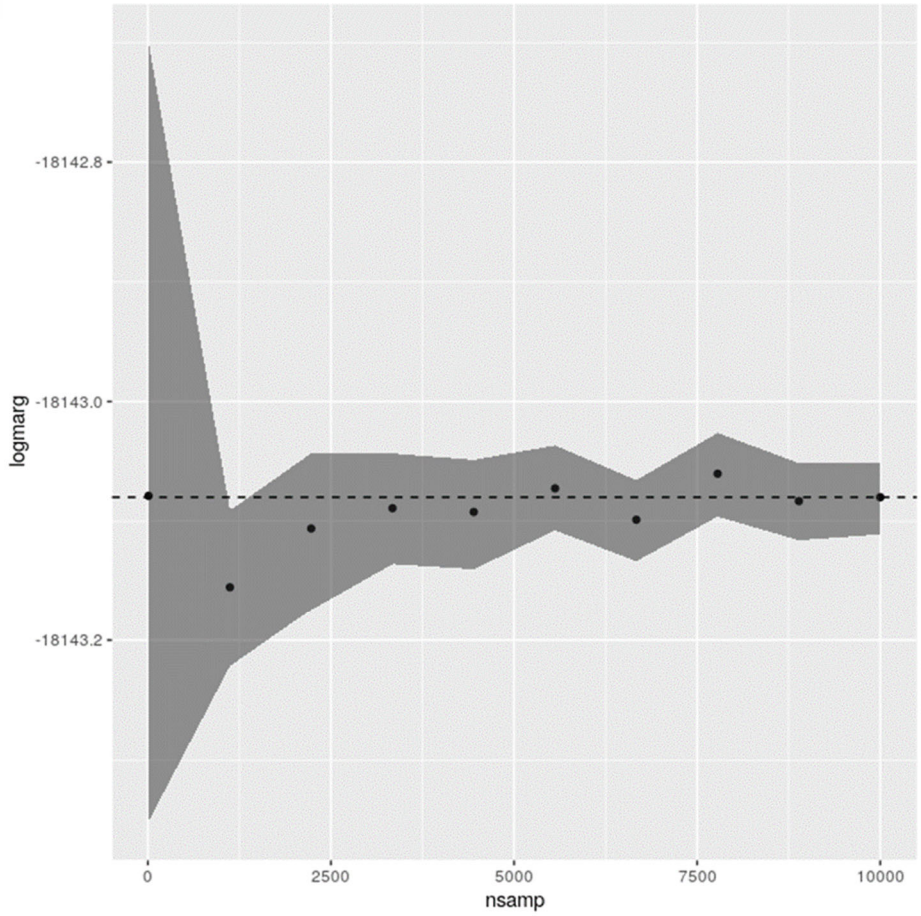
Run final checks, calculate log-marginal likelihoods and then bootstrap and create plots

Plots are created by additonal functions sourced at the start, this code is accessible via our github repository.

```
## final checks
summary(props[is.finite(logimpweight), ])

##        Pm               a1f                 a1m                  a2
##  Min.   :0.5095   Min.   :0.007838   Min.   :0.001196   Min.   :7.0
00e-10
##  1st Qu.:0.5468   1st Qu.:0.270042   1st Qu.:0.157081   1st Qu.:1.0
53e-05
##  Median :0.5551   Median :0.341982   Median :0.212694   Median :6.9
35e-05
##  Mean   :0.5552   Mean   :0.349762   Mean   :0.218974   Mean   :3.0
01e-04
##  3rd Qu.:0.5636   3rd Qu.:0.423980   3rd Qu.:0.272534   3rd Qu.:4.0
```

```
65e-04
##  Max.   :0.5982   Max.   :0.981793   Max.   :0.861547   Max.   :2.2
58e-03
##        b1                b2                  c1
##  Min.   : 0.5535   Min.   :2.000e-10   Min.   :7.789e-06
##  1st Qu.: 3.6925   1st Qu.:3.553e-06   1st Qu.:1.724e-03
##  Median : 4.3715   Median :2.060e-05   Median :2.054e-03
##  Mean   : 4.4930   Mean   :1.252e-04   Mean   :1.836e-03
##  3rd Qu.: 5.1778   3rd Qu.:1.146e-04   3rd Qu.:2.118e-03
##  Max.   :12.2479   Max.   :2.300e-03   Max.   :2.265e-03

summary(props)

##        Pm                a1f               a1m                a2
##  Min.   :0.001414   Min.   :-0.1232   Min.   :-0.1059   Min.   :-0.
001306
##  1st Qu.:0.546048   1st Qu.: 0.2692   1st Qu.: 0.1568   1st Qu.: 0.
000009
##  Median :0.555009   Median : 0.3451   Median : 0.2149   Median : 0.
000072
##  Mean   :0.552962   Mean   : 0.3827   Mean   : 0.2511   Mean   : 0.
046040
##  3rd Qu.:0.563994   3rd Qu.: 0.4345   3rd Qu.: 0.2802   3rd Qu.: 0.
000515
##  Max.   :0.999932   Max.   : 8.4542   Max.   : 5.9753   Max.   : 7.
114943
##        b1                  b2                  c1
##  Min.   : 0.001389   Min.   :-0.000907   Min.   :-0.000961
##  1st Qu.: 3.553864   1st Qu.: 0.000003   1st Qu.: 0.001761
##  Median : 4.285046   Median : 0.000020   Median : 0.002071
##  Mean   : 4.314832   Mean   : 0.048251   Mean   : 0.047489
##  3rd Qu.: 5.126025   3rd Qu.: 0.000139   3rd Qu.: 0.002132
##  Max.   :13.456856   Max.   : 7.695171   Max.   : 5.107370
```

```r
## calculate log-marginal likelihood
logmarg <- log_sum_exp_marg(logimpweight)

## bootstrap the importance weights and create 95% intervals
BootsPlot(logimpweight, 5000, trace = TRUE)
```




```
##     logmarg       LCI       UCI
## 1 -18143.08 -18143.11 -18143.05
```

Appendix 4 – Supplementary material from Chapter 5: Bayesian model comparison of capture-mark-recapture data for survival analysis

SilerSexDiffa1BadgerCMR

Setup Load libraries, data, additional functions and seed

```
## load libraries
library(nimble)
library(tidyverse)
library(mvtnorm)
library(boot)
library(lamW)
library(GGally)
library(coda)
library(mclust)
library(parallel)
library(survminer)
library(survival)
rm(list=ls())

## source necessary R functions
source("../../../FirstPaperFiles/Distributions/Dist_Gompertz.R")
source("../../../FirstPaperFiles/Distributions/Dist_GompertzNim.R")

## Registering the following user-provided distributions: dgompzNim

source("../../../FirstPaperFiles/Distributions/Dist_GompertzMakeham.R"
)
source("../../../FirstPaperFiles/Distributions/Dist_GompertzMakehamNim
.R")

## Registering the following user-provided distributions: dgompzMakeNi
m

source("../../../FirstPaperFiles/Distributions/Dist_Siler.R")
source("../../../FirstPaperFiles/Distributions/Dist_SilerNim.R")

## Registering the following user-provided distributions: dsilerNim

source("../../../FirstPaperFiles/Distributions/Dist_Expo.R")
source("../../../FirstPaperFiles/ModelComparison_FUNCTIONS.R")

## load data
load("badgerSex.RData")

## set seed
set.seed(42)
```

Prepare for Nimble analysis Define model, set constants, data and initial values.

```
code <- nimbleCode({

  ## survival components for dead badgers
  for (i in 1:nind) {

    ## likelihood for interval-truncated Siler
    censored[i] ~ dinterval(tD[i], cint[i, ])
    tD[i] ~ dsilerNim(a1[sex[i] + 1], a2, b1, b2, c1)
    sex[i] ~ dbern(Pm)

    ## sampling component
    pd[i] <- exp(y[i] * log(mean.p) + (min(floor(tD[i]), tM[i]) - y[i]
) * log(1 - mean.p))
    dind[i] ~ dbern(pd[i])

  }

  ## priors
  for (j in 1:g){
    a1[j] ~ dexp(1)
  }
  a2 ~ dexp(1)
  b1 ~ dexp(1)
  b2 ~ dexp(1)
  c1 ~ dexp(1)
  mean.p ~ dunif(0, 1)
  Pm ~ dunif(0,1)

})

## set up other components of model
consts <- list(nind = nind, tM = tM)
data <- list(y = y, cint = cint,
             censored = censored, tD = tD, dind = dind, sex = sex)

## find overdispersed initial values
tinitFn <- function(cint, censored) {
  apply(cbind(cint, censored), 1, function(x) {
    if(x[3] == 2) {
      y <- x[2] + 1
    } else {
      y <- runif(1, x[1], x[2])
    }
    y
  })
}
initFn <- function(cint, censored, sex) {
  ## get ML estimates as initial values
  optFn <- function(pars, t, sex) {
```

```
    if(any(pars < 0)) {
      return(NA)
    }
    llM <- sum(dSiler(t[sex == 0], a1 = pars[2], a2 = pars[3], b1 = pa
rs[4], b2 = pars[5], c1 = pars[6], log = TRUE))
    llF <- sum(dSiler(t[sex == 1], a1 = pars[1], a2 = pars[3], b1 = pa
rs[4], b2 = pars[5], c1 = pars[6], log = TRUE))
    llM + llF
  }
  pars <- list(convergence = 1)
  k <- 0
  while(pars$convergence != 0 & k < 20) {
    ## sample missing values
    tD <- tinitFn(cint, censored)
    ## sample sex proportion
    Pm <- runif(1, 0.4, 0.6)
    ## sample missing sex indicators
    sexI <- rbinom(length(censored), size = 1, prob = Pm)
    sexI[!is.na(sex)] <- sex[!is.na(sex)]
    ## optimise to interval-censored only
    pars <- optim(rexp(6, 100), optFn, t = tD, sex = sexI, control = l
ist(fnscale = -1))
    k <- k + 1
  }
  if(k == 20) {
    stop("Can't sample initial values")
  }
  pars <- pars$par
  ## check log-likelihoods
  ll <- sum(dSiler(tD[sexI == 0], a1 = pars[1], a2 = pars[3], b1 = par
s[4], b2 = pars[5], c1 = pars[6], log = TRUE))
  ll <- ll + sum(dSiler(tD[sexI == 1], a1 = pars[2], a2 = pars[3], b1
= pars[4], b2 = pars[5], c1 = pars[6], log = TRUE))
  stopifnot(is.finite(ll))
  ## reformat sex initial conditions correctly
  sexI[!is.na(sex)] <- NA
  ## output initial values
  list(
    tD = tD,
    sex = sexI,
    Pm = Pm,
    a1 = c(pars[1], pars[2]),
    a2 = pars[3],
    b1 = pars[4],
    b2 = pars[5],
    c1 = pars[6],
    mean.p = runif(1, 0, 1)
  )
}
```

Build the model in NIMBLE

```
## define the model, data, inits and constants
model <- nimbleModel(code = code, constants = consts, data = data, ini
ts = initFn(cint, censored, sex))

## defining model...

## building model...

## setting data and initial values...

## running calculate on model (any error reports that follow may simpl
y reflect missing values in model variables) ...
## checking model sizes and dimensions...
## model building finished.
```

Compile the model We now compile the model into C++.

```
## compile the model
cModel <- compileNimble(model, showCompilerOutput = TRUE)

## compiling... this may take a minute. On some systems there may be s
ome compiler warnings that can be safely ignored.

## compilation finished.
```

Configure the MCMC We can now make adjustments to the default sampler settings in NIMBLE.

```
## try with adaptive slice sampler
config <- configureMCMC(cModel, monitors = c("a1", "a2", "b1", "b2", "
c1", "mean.p", "Pm"), thin = 1)

## ===== Monitors =====
## thin = 1: a1, a2, b1, b2, c1, mean.p, Pm
## ===== Samplers =====
## RW sampler (2625)
##   - a1[]  (2 elements)
##   - a2
##   - b1
##   - b2
##   - c1
##   - mean.p
##   - Pm
##   - tD[]  (2617 elements)
## binary sampler (9)
##   - sex[]  (9 elements)

config$removeSamplers(c("a1", "a2", "b1", "b2", "c1"))
config$addSampler(target = c("a1", "a2", "b1", "b2", "c1"), type = 'AF
_slice')
```

Build and compile We now build our model with the updated configuration and compile again.

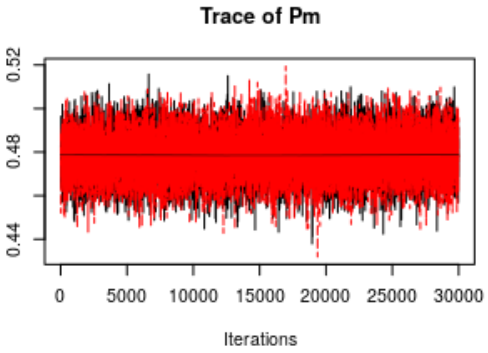
```
#Build the model
built <- buildMCMC(config)
cbuilt <- compileNimble(built)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.

## compilation finished.
```

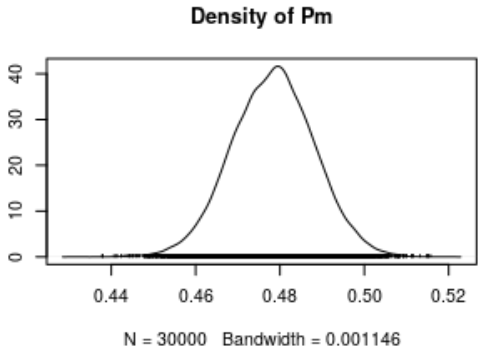
Run the MCMC Here we set our MCMC options: iterations, burnin, chains etc.

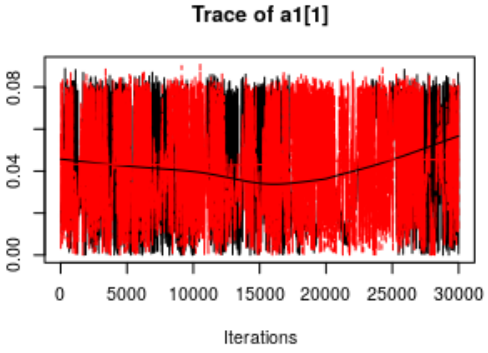
```
#Run the model
run <- runMCMC(cbuilt,
                            niter = 50000,
                            nburnin = 20000,
                            nchains = 2,
                            progressBar = TRUE,
                            summary = TRUE,
                            samplesAsCodaMCMC = TRUE,
                            thin = 1)

## running chain 1...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|

## running chain 2...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|
```

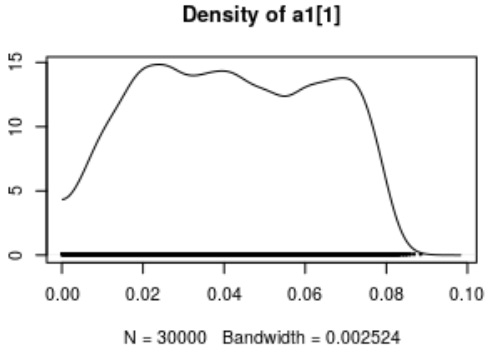
Plot trace plots to check mixing etc

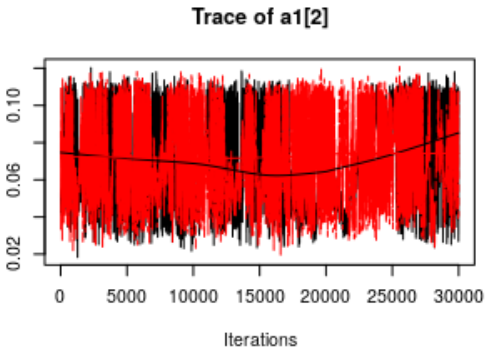
```
#Plot mcmcm
samples <- run$samples
plot(run$samples)
```

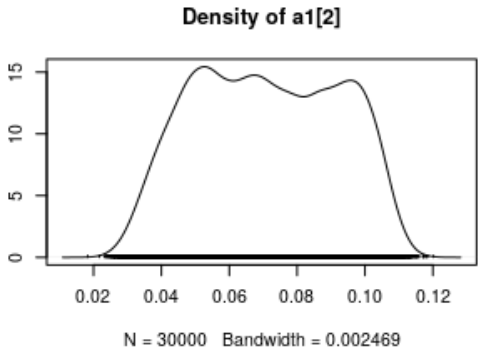

Trace of Pm
0.44
0.48
0.52
0
5000
10000
15000
20000
25000
30000
Iterations

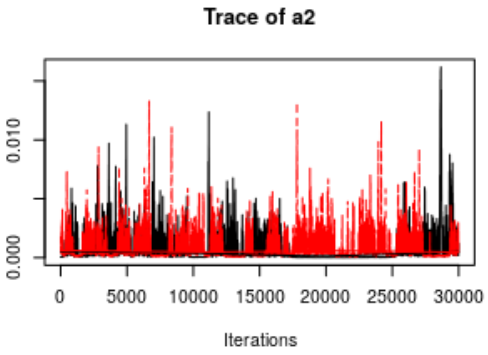

Density of Pm
0
10
20
30
40
0.44
0.46
0.48
0.50
0.52
N = 30000 Bandwidth = 0.001146

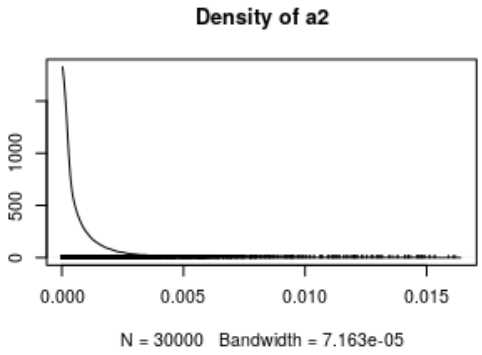

Trace of a1[1]
0.00
0.04
0.08
0
5000
10000
15000
20000
25000
30000
Iterations

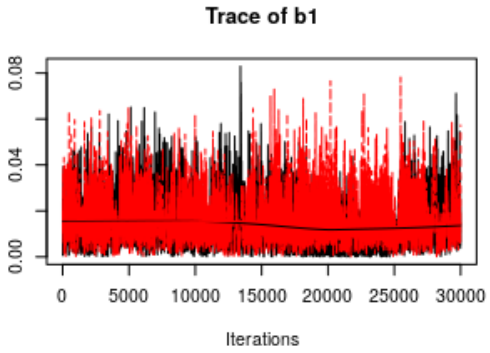

Density of a1[1]
0
5
10
15
0.00
0.02
0.04
0.06
0.08
0.10
N = 30000 Bandwidth = 0.002524

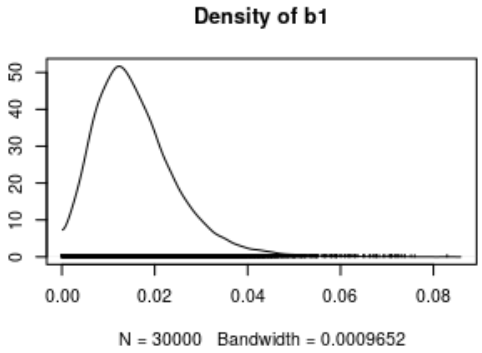

Trace of a1[2]
0.02
0.06
0.10
0
5000
10000
15000
20000
25000
30000
Iterations

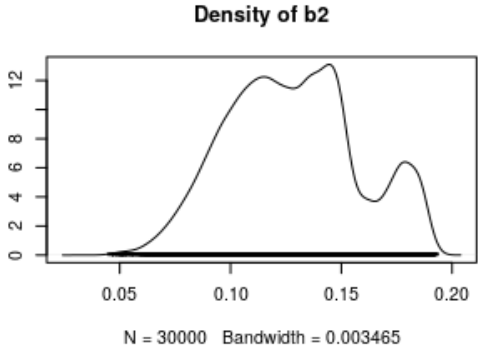

Density of a1[2]
0
5
10
15
0.02
0.04
0.06
0.08
0.10
0.12
N = 30000 Bandwidth = 0.002469

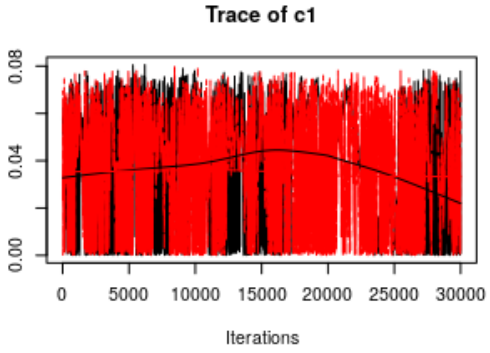

Trace of a2
0.000
0.010
0
5000
10000
15000
20000
25000
30000
Iterations

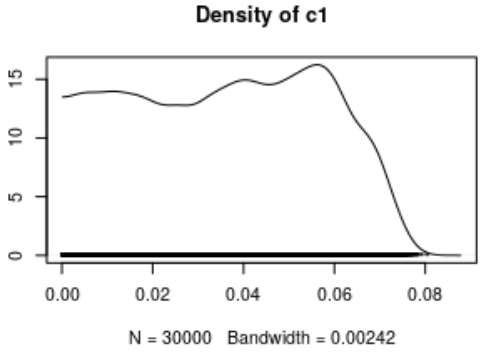

Density of a2
0
500
1000
0.000
0.005
0.010
0.015
N = 30000 Bandwidth = 7.163e-05

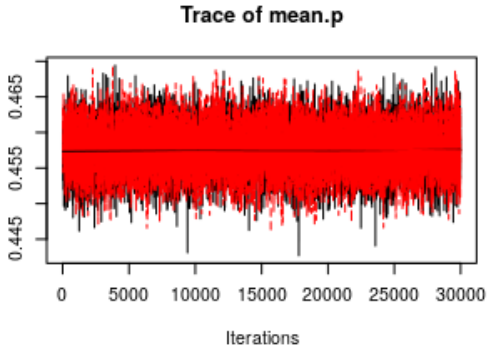


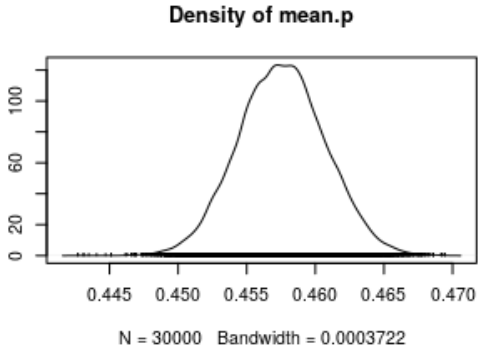








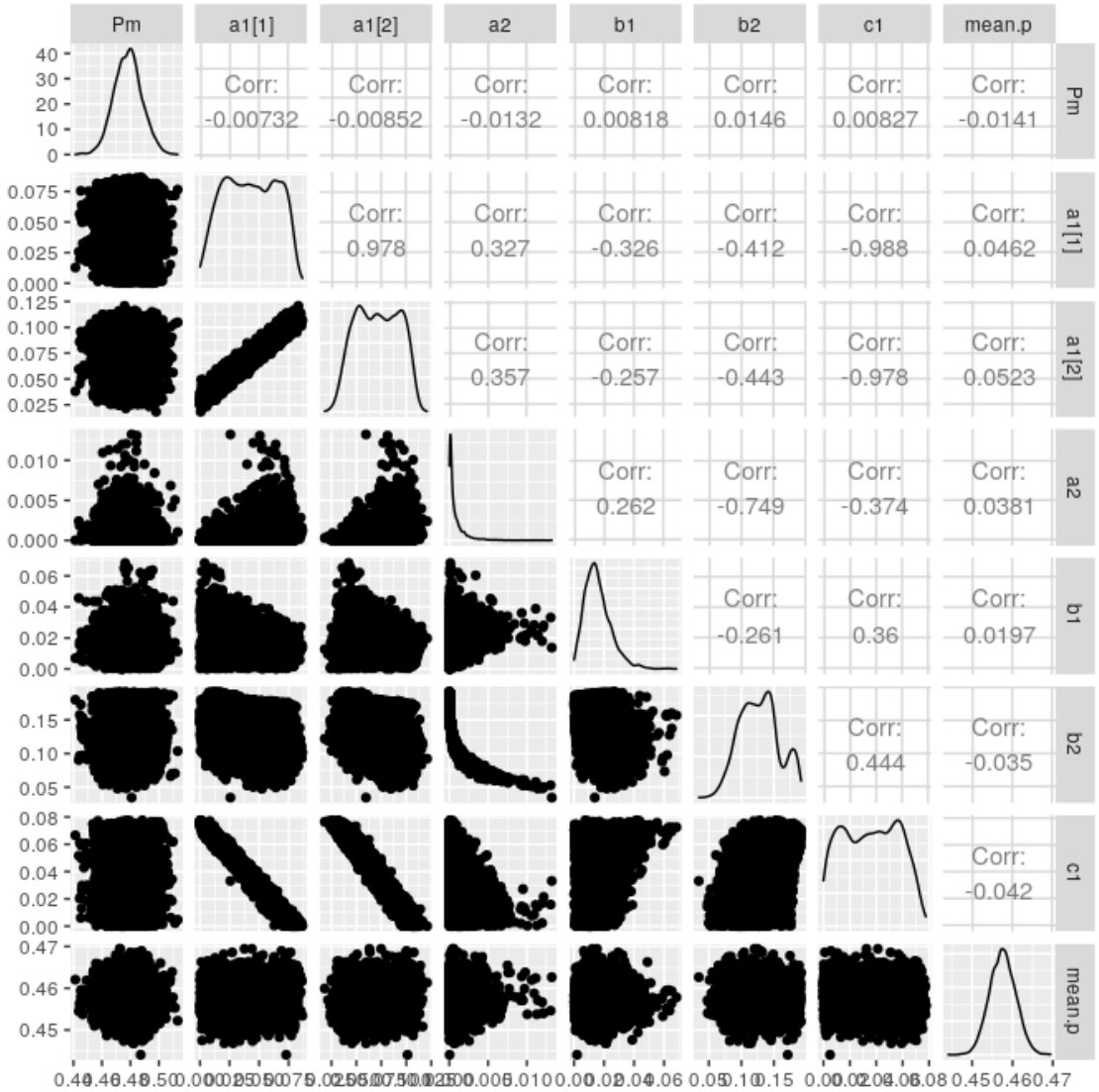




Pairs plot to check for correlations among parameters

```
## pairs plot
samples <- as.matrix(samples)
```

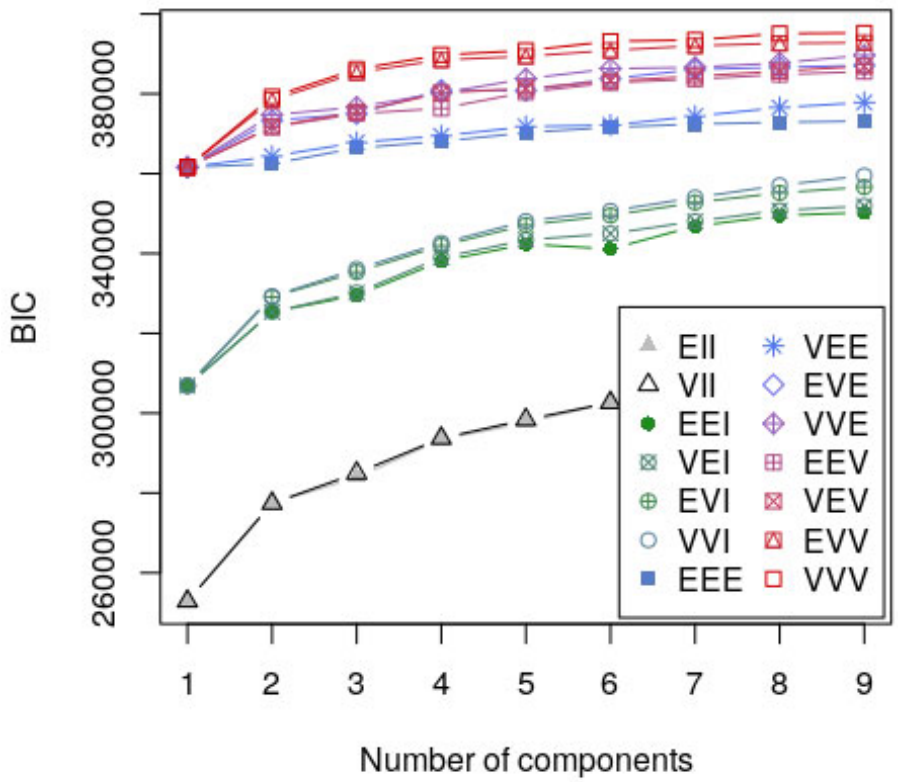
```
samples <- samples[sample.int(nrow(samples), ceiling(nrow(samples) * 0
.1)), ]
samples %>%
  as.data.frame() %>%
  ggpairs()
```



Find suitable mixture models to match posteriors

```
## fit range of finite mixture models
mod <- densityMclust(samples)

## summary of finite mixture models
summary(mod)

## ------------------------------------------------------
## Density estimation via Gaussian finite mixture modeling
## ------------------------------------------------------
##
## Mclust VVV (ellipsoidal, varying volume, shape, and orientation) mo
del with 9
```

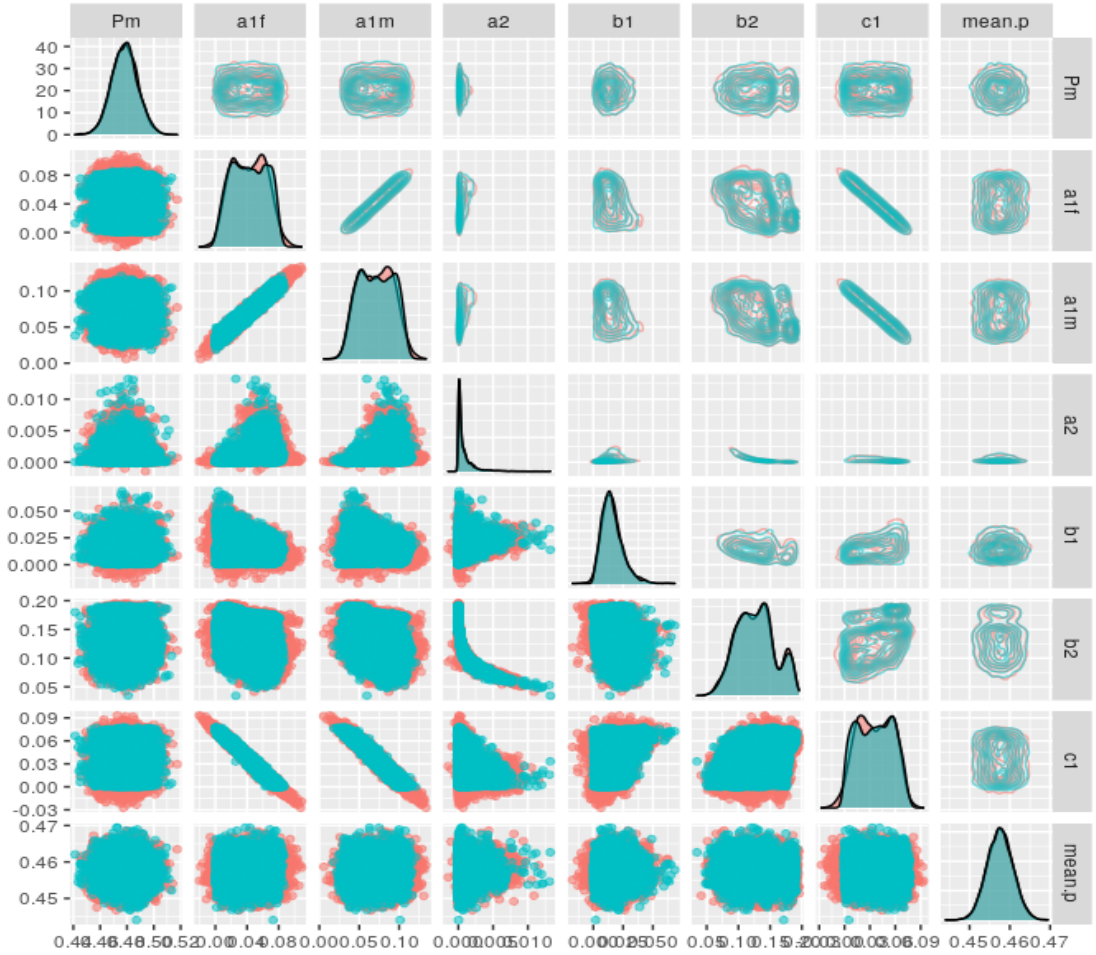
```
## components:
##
##  log-likelihood    n  df      BIC      ICL
##          199384 6000 404 395253.4 393403.8

plot(mod, what = "BIC")
```



Create importance distribution and check against posteriors

```
## take random samples from mixture
nimp <- 10000
nmix <- rbinom(1, size = nimp, prob = 0.95)
props <- sim(mod$modelName, mod$parameters, nmix)
props <- props[, -1, drop = FALSE]
colnames(props) <- c("Pm", "a1f", "a1m", "a2", "b1", "b2", "c1", "mean
.p")

## take random samples from prior (to create defense mixture)
dmp <- runif((nimp - nmix), 0, 1)
dpm <- runif((nimp - nmix), 0, 1)
defense <- as.data.frame(matrix(rexp(6 * (nimp - nmix), 1), ncol = 6))
defense <- defense %>%
  mutate(mean.p = dmp) %>%
  mutate(pM = dpm)
colnames(defense) <- c("a1f", "a1m", "a2", "b1", "b2", "c1", "mean.p",
```

```
"Pm")

## adjust column names of samples to match IS
colnames(samples) <- c("Pm", "a1f", "a1m", "a2", "b1", "b2", "c1", "me
an.p")

## check IS distribution against posterior samples
as.data.frame(props) %>%
  mutate(type = "IS") %>%
  rbind(as.data.frame(samples) %>%
          mutate(type = "Post")) %>%
  ggpairs(mapping = aes(colour = type, alpha = 0.5), upper = list(cont
inuous = "density"), columns = 1:8)
```



Create defensive mixture

```
## combine defense and importance samples
props <- rbind(props, defense)
```

Generate importance weights

```
## this next function takes vectors for y, zL, zU, and censored
## and scalar tM and parameters and calculates log-likelihood
loglike <- function(y, zL, zU, censored, tM, a1f, a1m, a2, b1, b2, c1,
```

```
p, sex, Pm) {
  ## loop over individuals
  fsurv1 <- pmap_dbl(list(y, zL, zU, censored, tM, sex), function(y, z
L, zU, censored, tM, a1f, a1m, a2, b1, b2, c1, p, sex, Pm) {

    ll <- y * log(p) + (zL - y) * log(1 - p)

    if(censored == 1){                              #interval
      t <- (zL + 1):zU
      if (sex == 0 & !is.na(sex)){                 #female
        temp <- pSiler(t, a1f, a2, b1, b2, c1) - pSiler(t - 1, a1f, a2
, b1, b2, c1)
        temp1 <- log(temp) + (t - 1 - zL) * log(1 - p)
        ll <- ll + log_sum_exp_marg(temp1, mn = FALSE)
        ll <- ll + log(1 - Pm)
      } else {
        if (sex == 1 & !is.na(sex)){          #male
          temp <- pSiler(t, a1m, a2, b1, b2, c1) - pSiler(t - 1, a1m,
a2, b1, b2, c1)
          temp1 <- log(temp) + (t - 1 - zL) * log(1 - p)
          ll <- ll + log_sum_exp_marg(temp1, mn = FALSE)
          ll <- ll + log(Pm)
        } else {                                    #unknown
          t <- (zL + 1):zU
          temp <- Pm * (pSiler(t, a1m, a2, b1, b2, c1) - pSiler(t - 1,
a1m, a2, b1, b2, c1))
          temp1 <- (1 - Pm) * (pSiler(t, a1f, a2, b1, b2, c1) - pSiler
(t - 1, a1f, a2, b1, b2, c1))
          temp2 <- log(c(temp, temp1)) + (t - 1 - zL) * log(1 - p)
          ll <- ll + log_sum_exp_marg(temp2, mn = FALSE)
        }
      }
    } else {                                       #right censored
      if(zL < tM) {
        t <- (zL + 1):tM
        if (sex == 0 & !is.na(sex)){                 #female
          temp <- pSiler(t, a1f, a2, b1, b2, c1) - pSiler(t - 1, a1f,
a2, b1, b2, c1)
          temp1 <- log(temp) + (t - 1 - zL) * log(1 - p)
          ## tail component (after last capture time)
          temp <- pSiler(tM, a1f, a2, b1, b2, c1, lower.tail = FALSE)
          temp <- log(temp) + (tM - zL) * log(1 - p)
          temp1 <- c(temp1, temp)
          ll <- ll + log_sum_exp_marg(temp1, mn = FALSE)
          ll <- ll + log(1 - Pm)
        } else {
          if (sex == 1 & !is.na(sex)){          #male
            temp <- pSiler(t, a1m, a2, b1, b2, c1) - pSiler(t - 1, a1m
, a2, b1, b2, c1)
            temp1 <- log(temp) + (t - 1 - zL) * log(1 - p)
            ## tail component (after last capture time)
            temp <- pSiler(tM, a1m, a2, b1, b2, c1, lower.tail = FALSE
)
```

```
            temp <- log(temp) + (tM - zL) * log(1 - p)
            temp1 <- c(temp1, temp)
            ll <- ll + log_sum_exp_marg(temp1, mn = FALSE)
            ll <- ll + log(Pm)
          } else {                                        #unknown
            temp <- Pm * pSiler(t, a1m, a2, b1, b2, c1) - pSiler(t - 1
, a1m, a2, b1, b2, c1)
            temp1 <- (1 - Pm) * pSiler(t, a1f, a2, b1, b2, c1) - pSile
r(t - 1, a1f, a2, b1, b2, c1)
            temp2 <- log(c(temp, temp1)) + (t - 1 - zL) * log(1 - p)
            ## tail component (after last capture time)
            temp <- (1 - Pm) * pSiler(tM, a1f, a2, b1, b2, c1, lower.t
ail = FALSE)
            temp1 <- Pm * pSiler(tM, a1m, a2, b1, b2, c1, lower.tail =
FALSE)
            temp3 <- log(c(temp, temp1)) + (tM - zL) * log(1 - p)
            temp4 <- c(temp2, temp3)
            ll <- ll + log_sum_exp_marg(temp4, mn = FALSE)
          }
        }
      } else {                                            #zL = tM
        if (sex == 0 & !is.na(sex)){                      #female
          temp <- pSiler(tM, a1f, a2, b1, b2, c1, lower.tail = FALSE)
          ll <- ll + log(temp) + (tM - zL) * log(1 - p)
          ll <- ll + log(1 - Pm)
        } else {
          if (sex == 1 & !is.na(sex)){          #male
            temp <- pSiler(tM, a1m, a2, b1, b2, c1, lower.tail = FALSE
)
            ll <- ll + log(temp) + (tM - zL) * log(1 - p)
            ll <- ll + log(Pm)
          } else {                                        #unknown
            temp <- (1 - Pm) * pSiler(tM, a1f, a2, b1, b2, c1, lower.t
ail = FALSE)
            temp <- Pm * pSiler(tM, a1m, a2, b1, b2, c1, lower.tail =
FALSE)
            ll <- ll + log(temp) + (tM - zL) * log(1 - p)
          }
        }
      }
      ll}
  }, p = p, Pm = Pm, a1f = a1f, a1m = a1m, a2 = a2, b1 = b1, b2 = b2,
c1 = c1)
  sum(fsurv1)
}

## calculate log-likelihoods in parallel
logimpweight <- apply(props, 1, list)
logimpweight <- purrr::map(logimpweight, 1)
logimpweight <- mclapply(logimpweight,
                         function(pars, y, zL, zU, censored, tM, p, se
x, Pm) {
                           loglike(y, zL, zU, censored, tM, pars[2], p
```

```
ars[3], pars[4], pars[5], pars[6], pars[7], pars[8], sex, pars[1])
                          }, y = y, zL = zL, zU = zU, censored = censor
ed, tM = tM, sex = sex, mc.cores = 24)
logimpweight <- reduce(logimpweight, base::c)
```

Add priors and importance distributions

```
## add prior densities
logimpweight <- logimpweight + dunif(props[, 1], 0, 1, log = TRUE) +
  dexp(props[, 2], 1, log = TRUE) + dexp(props[, 3], 1, log = TRUE) +
  dexp(props[, 4], 1, log = TRUE) + dexp(props[, 5], 1, log = TRUE) +
  dexp(props[, 6], 1, log = TRUE) + dexp(props[, 7], 1, log = TRUE) +
  dunif(props[, 8], 0, 1, log = TRUE)

## importance distributions
logimpweight <- logimpweight -
  log(0.95 * dens(mod$modelName, props, FALSE, mod$parameters) + 0.05
* exp(dunif(props[, 1], 0, 1, log = TRUE) +

dexp(props[, 2], 1, log = TRUE) +

dexp(props[, 3], 1, log = TRUE) +

dexp(props[, 4], 1, log = TRUE) +

dexp(props[, 5], 1, log = TRUE) +

dexp(props[, 6], 1, log = TRUE) +

dexp(props[, 7], 1, log = TRUE) +

dunif(props[, 8], 0, 1, log = TRUE)))
```

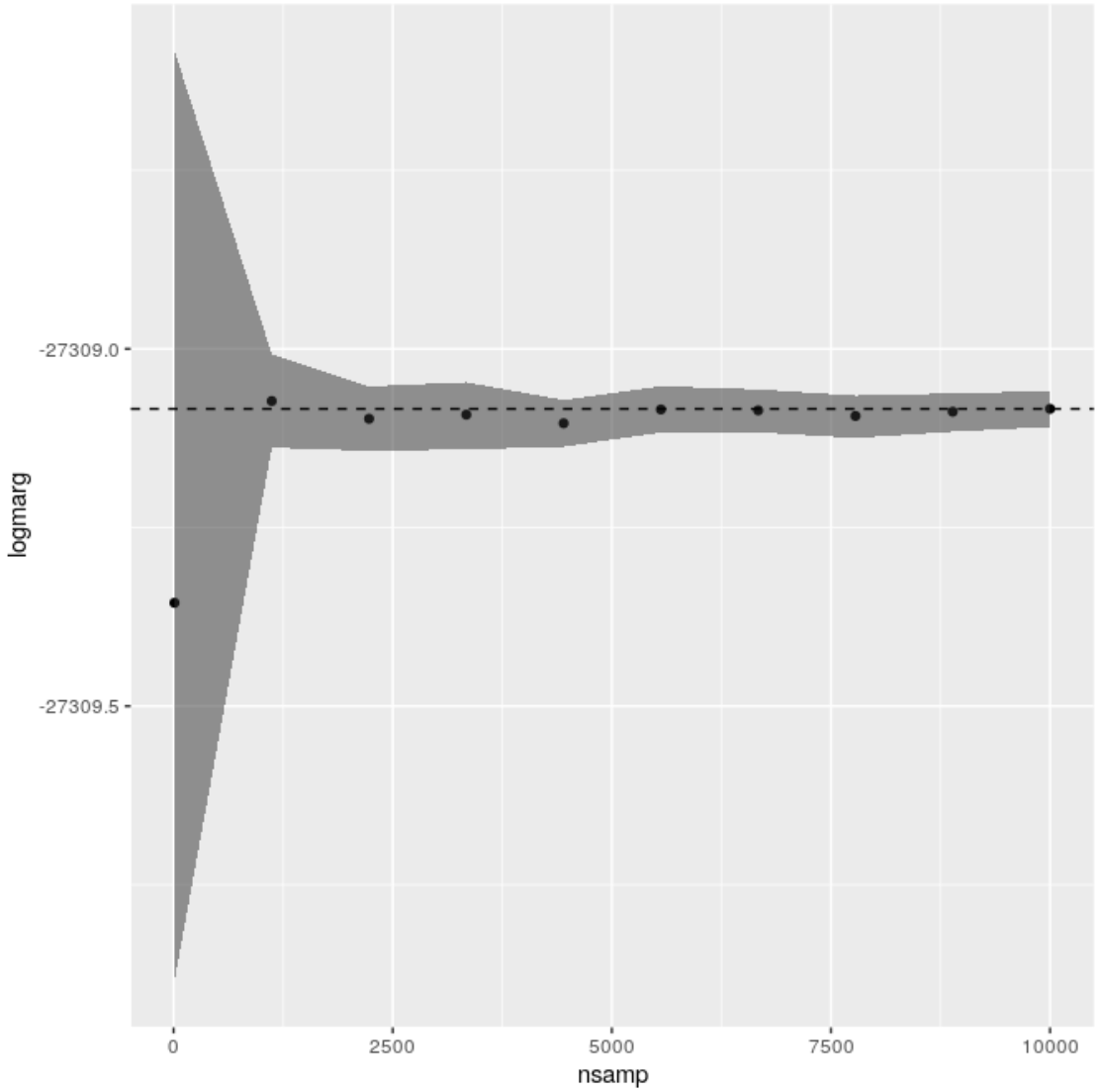
Run final checks, calculate log-marginal likelihoods and then bootstrap and create plots

Plots are created by additonal functions sourced at the start, this code is accessible via our github repository.

```
## final checks
summary(props[is.finite(logimpweight), ])
```

```
##        Pm               a1f                  a1m                 a2
##  Min.   :0.1393   Min.   :0.0000914   Min.   :0.02327   Min.   :0.0
000007
##  1st Qu.:0.4718   1st Qu.:0.0246238   1st Qu.:0.05389   1st Qu.:0.0
001470
##  Median :0.4784   Median :0.0421031   Median :0.07096   Median :0.0
003638
##  Mean   :0.4783   Mean   :0.0419307   Mean   :0.07080   Mean   :0.0
008811
##  3rd Qu.:0.4849   3rd Qu.:0.0585973   3rd Qu.:0.08674   3rd Qu.:0.0
```

```
010152
##  Max.   :0.5174   Max.   :1.7944641   Max.   :1.51321   Max.   :0.4
200564
##        b1                  b2                c1                mean
.p
##  Min.   :0.0000022   Min.   :0.01221   Min.   :0.0000203   Min.   :
0.4467
##  1st Qu.:0.0101653   1st Qu.:0.10416   1st Qu.:0.0201834   1st Qu.:
0.4554
##  Median :0.0150729   Median :0.12649   Median :0.0364165   Median :
0.4576
##  Mean   :0.0165196   Mean   :0.12725   Mean   :0.0367010   Mean   :
0.4576
##  3rd Qu.:0.0206587   3rd Qu.:0.14663   3rd Qu.:0.0532918   3rd Qu.:
0.4597
##  Max.   :2.2588190   Max.   :0.19551   Max.   :0.0793902   Max.   :
0.5043

summary(props)

##        Pm                 a1f                a1m                 a2
##  Min.   :0.0005045   Min.   :-0.02013   Min.   :0.004153   Min.   :
-0.001451
##  1st Qu.:0.4714270   1st Qu.: 0.02529   1st Qu.:0.054315   1st Qu.:
0.000149
##  Median :0.4783599   Median : 0.04476   Median :0.073040   Median :
0.000392
##  Mean   :0.4793485   Mean   : 0.08853   Mean   :0.117193   Mean   :
0.046985
##  3rd Qu.:0.4852523   3rd Qu.: 0.06196   3rd Qu.:0.090202   3rd Qu.:
0.001202
##  Max.   :0.9997140   Max.   : 6.38471   Max.   :7.826938   Max.   :
9.854459
##        b1                 b2                c1                mean.p
##  Min.   :-0.01741   Min.   :0.00122   Min.   :-0.02746   Min.   :0.
001932
##  1st Qu.: 0.01008   1st Qu.:0.10504   1st Qu.: 0.01978   1st Qu.:0.
455281
##  Median : 0.01532   Median :0.12860   Median : 0.03770   Median :0.
457586
##  Mean   : 0.06558   Mean   :0.16666   Mean   : 0.08800   Mean   :0.
459599
##  3rd Qu.: 0.02176   3rd Qu.:0.15007   3rd Qu.: 0.05561   3rd Qu.:0.
459848
##  Max.   : 5.97225   Max.   :6.88589   Max.   : 8.75672   Max.   :0.
999376

## bootstrap the importance weights to create 95% intervals
imp.boot <- BootsPlot(logimpweight, 5000, TRUE)
```


-27309.0
-27309.5
logmarg
0
2500
5000
7500
10000
nsamp

Appendix 5 – Supplementary material from Chapter 6: Efficient Bayesian model comparison for nested models: from importance sampling to reversible jump Markov chain Monte Carlo.

R code for RJMCMC analysis

Setup Load libraries, data, additional functions and seed

```
## load libraries
library(nimble)
library(tidyverse)
library(mvtnorm)
library(boot)
library(lamW)
library(GGally)
library(coda)
library(mclust)
library(parallel)
library(survminer)
library(survival)
library(data.table)
rm(list=ls())

## source necessary R functions
source("../../../FirstPaperFiles/Distributions/Dist_Siler.R")
source("../../../FirstPaperFiles/Distributions/Dist_SilerNim.R")

## Registering the following user-provided distributions: dsilerNim

source("../../../FirstPaperFiles/ModelComparison_FUNCTIONS.R")

## load data
load("badgerSex.RData")

## set seed
set.seed(42)
```

Prepare for Nimble analysis Define model, set constants, data and initial values.

```
code <- nimbleCode({

  ## survival components for dead badgers
  for (i in 1:nind) {

    ## likelihood for interval-truncated gompertz
    censored[i] ~ dinterval(tD[i], cint[i, ])
    tD[i] ~ dsilerNim(a1 * a1mult[i], a2 * a2mult[i], b1 * b1mult[i],
b2 * b2mult[i], c1 * c1mult[i])
```

```
    log(a1mult[i]) <- beta[1] * sex[i] * z[1]
    log(a2mult[i]) <- beta[2] * sex[i] * z[2]
    log(b1mult[i]) <- beta[3] * sex[i] * z[3]
    log(b2mult[i]) <- beta[4] * sex[i] * z[4]
    log(c1mult[i]) <- beta[5] * sex[i] * z[5]

    ## sampling component
    pd[i] <- exp(y[i] * log(mean.p) + (min(floor(tD[i]), tM[i]) - y[i]
) * log(1 - mean.p))
    dind[i] ~ dbern(pd[i])
  }

  for (j in 1:5) {
    beta[j] ~ dnorm(0, sd = 1)
    z[j] ~ dbern(0.5)
#    psi[j] <- dunif(0, 1)
  }

  a1 ~ dexp(1)
  a2 ~ dexp(1)
  b1 ~ dexp(1)
  b2 ~ dexp(1)
  c1 ~ dexp(1)
  mean.p ~ dunif(0, 1)


})

## set up data
consts <- list(nind = nind, tM = tM, sex = sex)
data <- list(y = y, cint = cint,
             censored = censored, tD = tD, dind = dind)

## find overdispersed initial values
tinitFn <- function(cint, censored) {
  apply(cbind(cint, censored), 1, function(x) {
    if(x[3] == 2) {
      y <- x[2] + rexp(1, 1)
    } else {
      y <- runif(1, x[1], x[2])
    }
    y
  })
}

initFn <- function(cint, censored, sex) {
  ## get ML estimates as initial values
  optFn <- function(pars, t, sex) {
    if(any(pars[c(1:5)] < 0)) {
      return(NA)
    }
    llM <- sum(dSiler(t[sex == 1], a1 = pars[1] * exp(pars[6]), a2 = p
```

```
ars[2] * exp(pars[7]), b1 = pars[3] * exp(pars[8]),
                      b2 = pars[4] * exp(pars[9]), c1 = pars[5] * exp(
pars[10]), log = TRUE))
    llF <- sum(dSiler(t[sex == 0], a1 = pars[1], a2 = pars[2], b1 = pa
rs[3], b2 = pars[4], c1 = pars[5], log = TRUE))
    llM + llF
  }
  pars <- list(convergence = 1)
  k <- 0
  while(pars$convergence != 0 & k < 50) {
    ## sample missing values
    tD <- tinitFn(cint, censored)
    pars <- optim(c(rexp(5, 10), rnorm(5, 0, 1)), optFn, t = tD, sex =
sex, control = list(fnscale = -1))
    k <- k + 1
  }
  if(k == 50) {
    stop("Can't sample initial values")
  }
  pars <- pars$par
 list(
    tD = tD,
    a1 = pars[1],
    a2 = pars[2],
    b1 = pars[3],
    b2 = pars[4],
    c1 = pars[5],
    mean.p = runif(1, 0, 1),
    beta = c(pars[6], pars[7], pars[8], pars[9], pars[10]),
    z = rep(0, times = 5)
  )
}
```

Build the model in NIMBLE

```
## define the model, data, inits and constants
rIndicatorModel <- nimbleModel(code, constants = consts,
                               data = data,
                               inits = initFn(cint, censored, sex))

## defining model...

## building model...

## setting data and initial values...

## running calculate on model (any error reports that follow may simpl
y reflect missing values in model variables) ...
## checking model sizes and dimensions...
## model building finished.
```

Configure the MCMC We can now make adjustments to the default sampler settings in NIMBLE.

```
## try with adaptive slice sampler
config <- configureMCMC(rIndicatorModel) #, monitors = c("beta0a1", "b
eta1a1", "a2", "b1", "b2", "c1", "mean.p"), thin = 1)

## ===== Monitors =====
## thin = 1: beta, z, a1, a2, b1, b2, c1, mean.p
## ===== Samplers =====
## RW sampler (2399)
##   - beta[]  (5 elements)
##   - a1
##   - a2
##   - b1
##   - b2
##   - c1
##   - mean.p
##   - tD[]  (2388 elements)
## binary sampler (5)
##   - z[]  (5 elements)

config$removeSamplers(c("a1", "a2", "b1", "b2", "c1"))
config$addSampler(target = c("a1", "a2", "b1", "b2", "c1"), type = 'AF
_slice', control = 50)
config$addSampler(target = c("a1", "c1"), type = 'AF_slice', control =
20)
config$addSampler(target = c("b2"), type = 'slice')

## Add reversible jump
configureRJ(conf = config,   ## model configuration
            targetNodes = c("beta[1]", "beta[2]","beta[3]", "beta[4]",
"beta[5]"),    ## coefficients for selection
            indicatorNodes = c("z[1]", "z[2]", "z[3]", "z[4]", "z[5]")
,    ## indicators paired with coefficients
            control = list(mean = 0.5, scale = .5))

config$addMonitors("beta[1]", "beta[2]","beta[3]", "beta[4]", "beta[5]
", "z[1]", "z[2]", "z[3]", "z[4]", "z[5]")

## thin = 1: beta, z, a1, a2, b1, b2, c1, mean.p
```

Build and compile We now build our model with the updated configuration and compile again.

```
rIndicatorMCMC <- buildMCMC(config)
cIndicatorModel <- compileNimble(rIndicatorModel)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.

## compilation finished.

cIndicatorMCMC <- compileNimble(rIndicatorMCMC, project = rIndicatorMo
del)
```

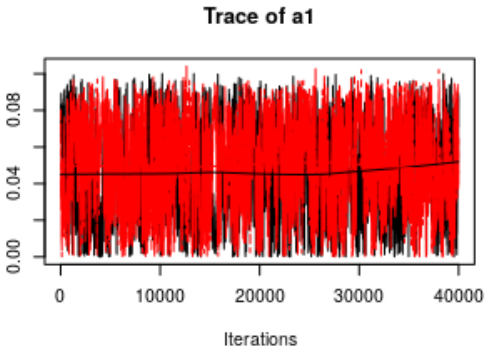
```
## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.
## compilation finished.
```

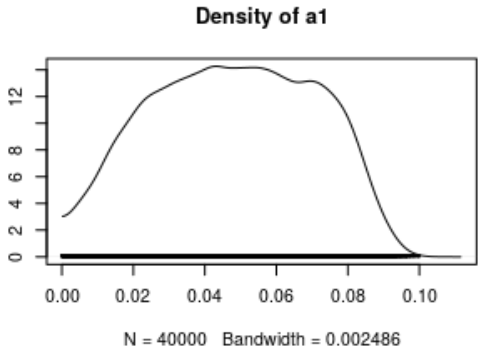
Run the MCMC Here we set our MCMC options: iterations, burnin, chains etc.

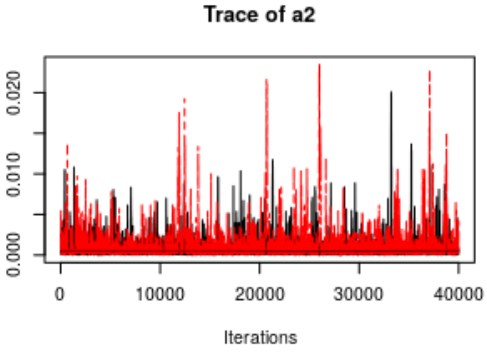
```
#Run the model
run <- runMCMC(cIndicatorMCMC,
                            niter = 50000,
                            nburnin = 10000,
                            nchains = 2,
                            progressBar = TRUE,
                            summary = TRUE,
                            samplesAsCodaMCMC = TRUE,
                            thin = 1)

## running chain 1...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|

## running chain 2...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|
```

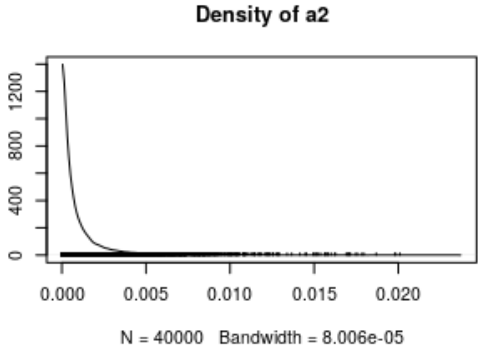
Plot trace plots to check mixing etc

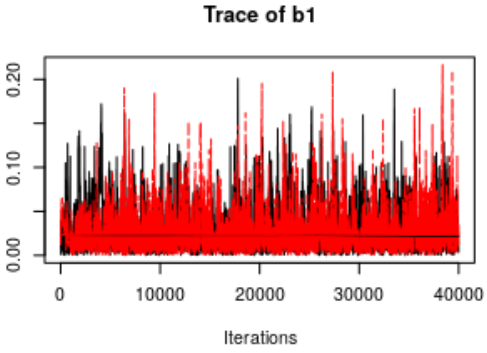
```
#Plot mcmcm
samples <- as.matrix(run$samples)
plot(run$samples)
```

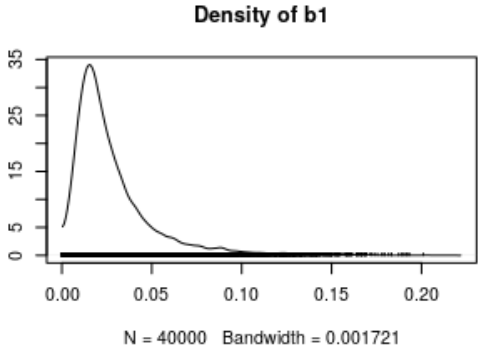

Trace of a1
0.00
0.04
0.08
0
10000
20000
30000
40000
Iterations


Density of a1
0
2
4
6
8
12
0.00
0.02
0.04
0.06
0.08
0.10
N = 40000 Bandwidth = 0.002486

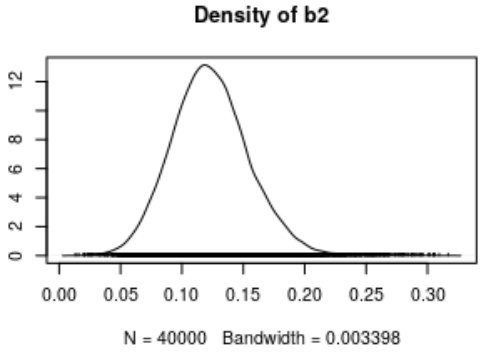

Trace of a2
0.000
0.010
0.020
0
10000
20000
30000
40000
Iterations

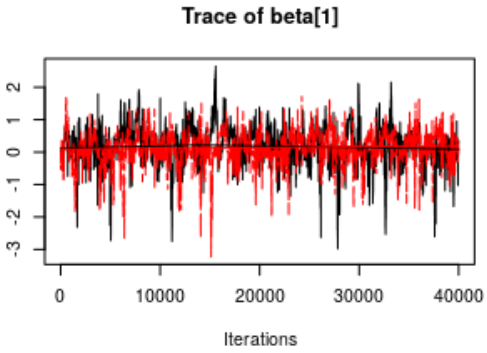

Density of a2
0
400
800
1200
0.000
0.005
0.010
0.015
0.020
N = 40000 Bandwidth = 8.006e-05

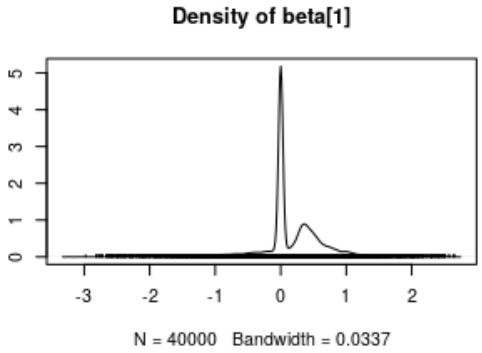

Trace of b1
0.00
0.10
0.20
0
10000
20000
30000
40000
Iterations

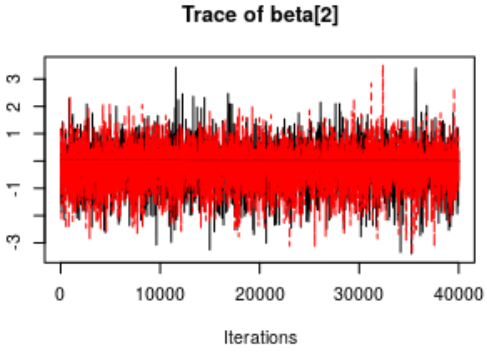

Density of b1
0
5
15
25
35
0.00
0.05
0.10
0.15
0.20
N = 40000 Bandwidth = 0.001721

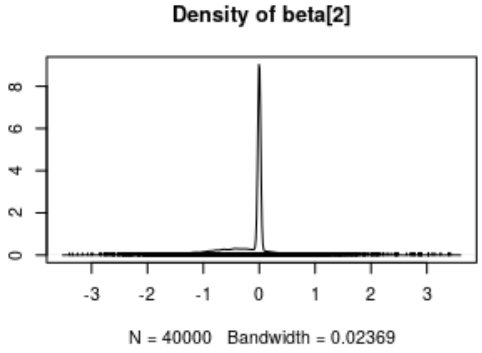

Trace of b2
0.05
0.15
0.25
0
10000
20000
30000
40000
Iterations

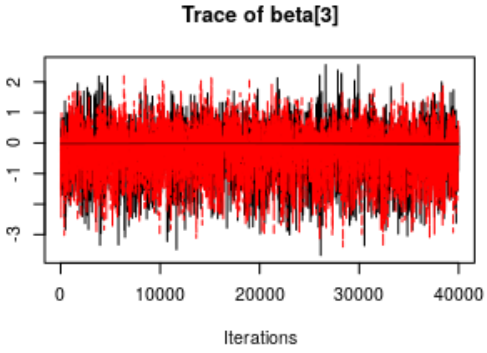

Density of b2
0
2
4
6
8
12
0.00
0.05
0.10
0.15
0.20
0.25
0.30
N = 40000 Bandwidth = 0.003398

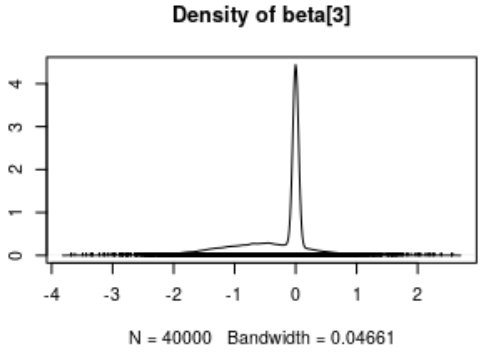

Trace of beta[1]
Iterations

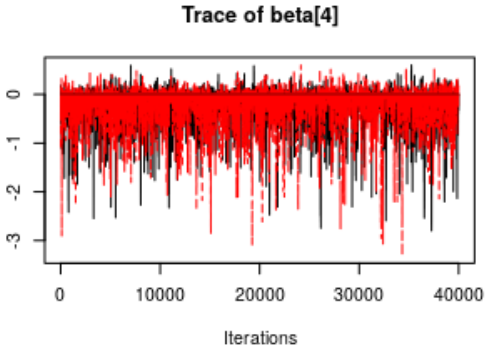

Density of beta[1]
N = 40000 Bandwidth = 0.0337

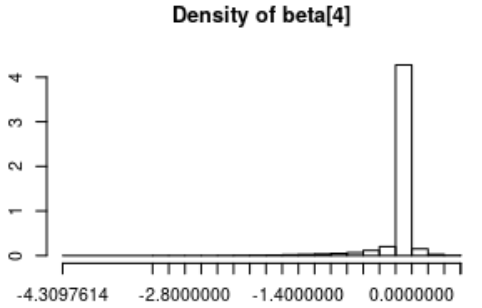

Trace of beta[2]
Iterations

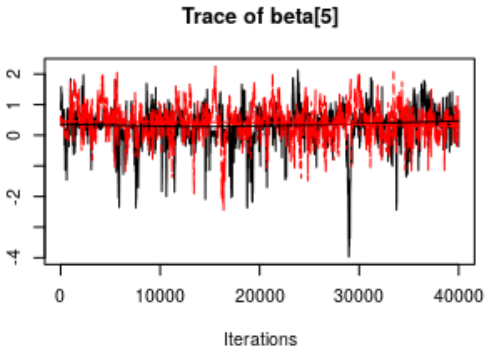

Density of beta[2]
N = 40000 Bandwidth = 0.02369

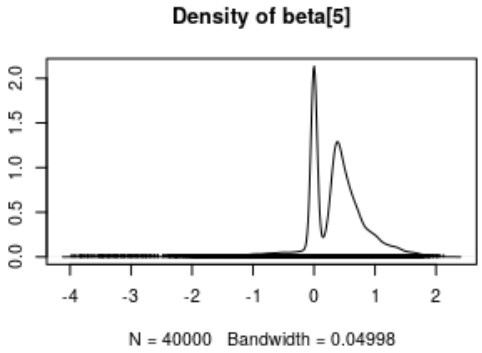

Trace of beta[3]
Iterations

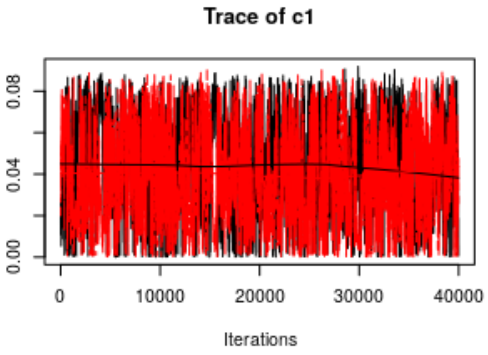

Density of beta[3]
N = 40000 Bandwidth = 0.04661

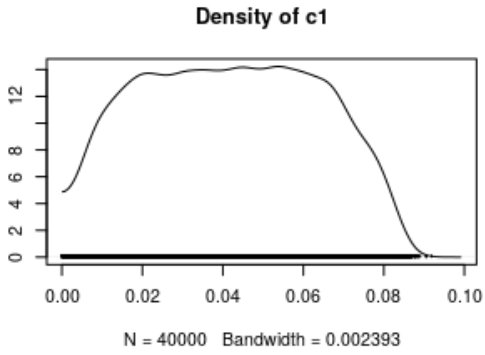

Trace of beta[4]
Iterations

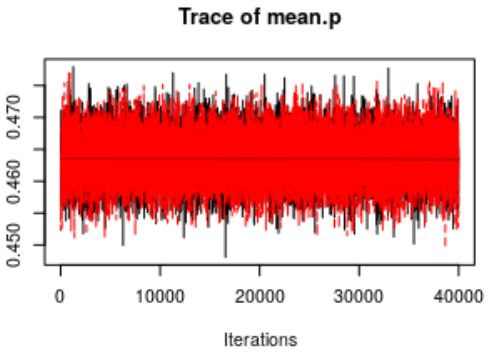

Density of beta[4]
-4.3097614
-2.8000000
-1.4000000
0.0000000

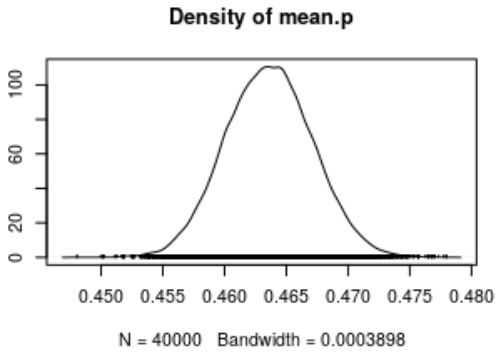

Trace of beta[5]
Iterations

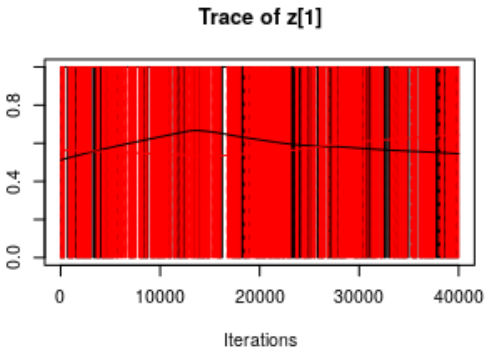

Density of beta[5]
N = 40000 Bandwidth = 0.04998

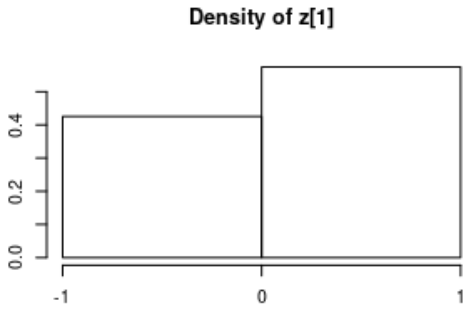

Trace of c1
Iterations

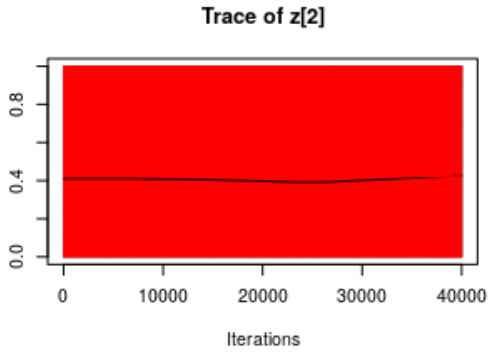

Density of c1
N = 40000 Bandwidth = 0.002393

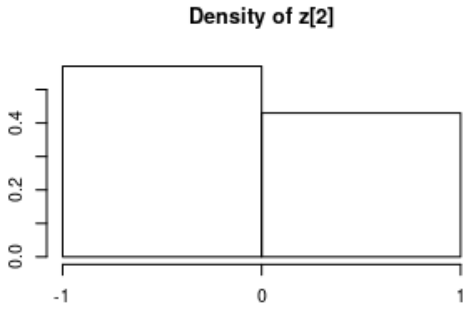

Trace of mean.p
Iterations

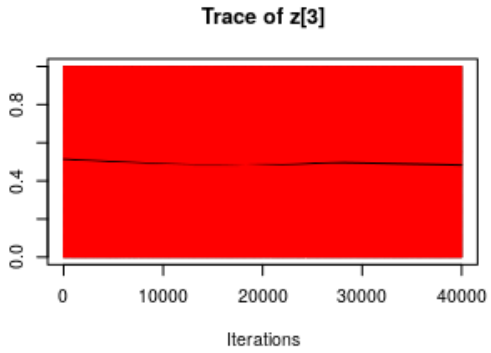

Density of mean.p
N = 40000 Bandwidth = 0.0003898

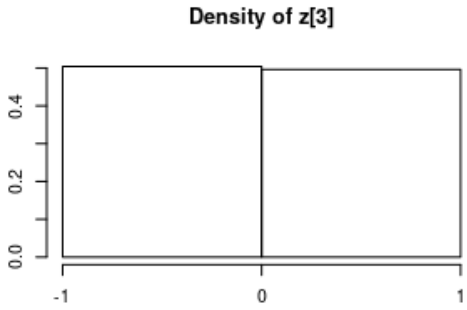

Trace of z[1]
Iterations

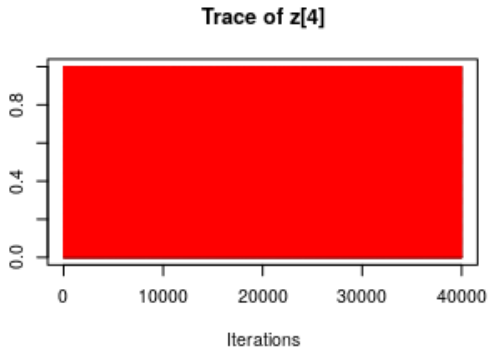

Density of z[1]

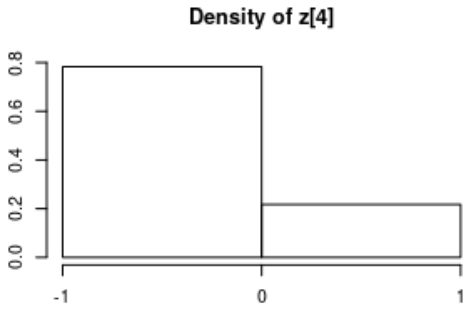


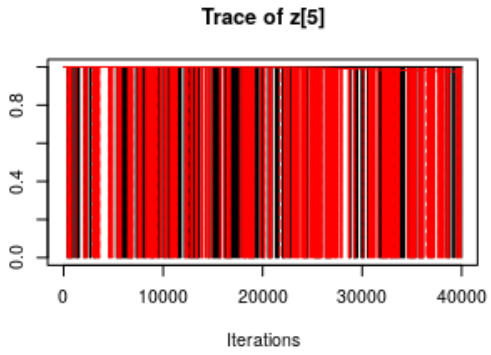


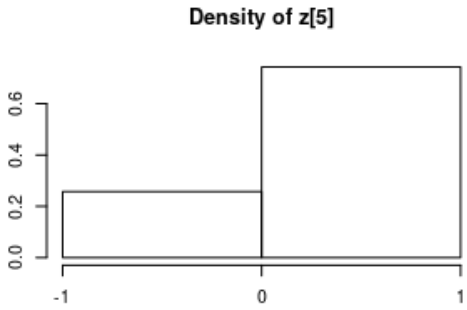












Look at posterior inclusion probabilities and bootstrap for CIs Extract indicator information

```
## Marginal probabilities of inclusion for each variable
zNames <- c("z[1]", "z[2]", "z[3]", "z[4]", "z[5]")
```

```
zCols <- which(colnames(samples) %in% zNames)
binary <- as.data.table((samples[, zCols] != 0) + 0)
colnames(binary) <- c("a1", "a2", "b1", "b2", "c1")
```

Set up bootstrapping functions

```
boots <- function(samples, nboot){
  lists <- list()

  for(i in 1:nboot) {
    samp_ints <- sample(1:50000, 50000, replace = TRUE)
    temp_post <- binary[samp_ints, ]
    res <- temp_post[ , .N, by=names(temp_post)]
    res <- res[order(N, decreasing = T)]
    res <- res[, prob := N/dim(temp_post)[1]]
    res$model <- paste(res$a1, res$a2, res$b1, res$b2, res$c1)
    res$bootn <- i
    res <- select(res, prob, model, bootn)
    lists[[i]] <- res
  }

  t <- as.data.frame(do.call(rbind, lists))
  l <- pivot_wider(t, names_from = model, values_from = prob)

  return(l)
}

## run function
out <- boots(samples, 1000)
out
```

```
## # A tibble: 1,000 × 29
##    bootn `0 0 0 0 1` `0 0 1 0 1` `1 0 0 0 1` `0 1 0 0 1` `1 0 1 0 1
` `0 1 1 0 1`
##    <int>       <dbl>       <dbl>       <dbl>       <dbl>       <dbl
>       <dbl>
##  1     1       0.105      0.0799      0.0779      0.0724      0.069
1      0.0676
##  2     2       0.108      0.0809      0.0793      0.0717      0.067
7      0.0665
##  3     3       0.105      0.0827      0.0807      0.0713      0.067
4      0.0666
##  4     4       0.105      0.0812      0.0811      0.0722      0.068
8      0.0692
##  5     5       0.107      0.0783      0.0810      0.0717      0.070
1      0.0655
##  6     6       0.106      0.0816      0.0801      0.0728      0.066
7      0.0686
##  7     7       0.106      0.0815      0.0813      0.0725      0.066
5      0.0683
##  8     8       0.107      0.0810      0.0798      0.0714      0.066
3      0.0673
##  9     9       0.105      0.0817      0.0811      0.0711      0.067
```

```
7      0.0691
## 10    10       0.106      0.0805      0.0816      0.0737      0.068
2      0.0685
## # … with 990 more rows, and 22 more variables: 1 0 1 0 0 <dbl>,
## #   1 0 0 0 0 <dbl>, 1 1 1 0 1 <dbl>, 1 1 0 0 1 <dbl>, 1 1 1 0 0 <d
bl>,
## #   1 1 0 0 0 <dbl>, 0 0 1 1 1 <dbl>, 0 1 1 1 1 <dbl>, 0 0 0 1 1 <d
bl>,
## #   0 1 0 1 1 <dbl>, 1 1 1 1 1 <dbl>, 1 1 0 1 1 <dbl>, 1 0 0 1 1 <d
bl>,
## #   1 1 1 1 0 <dbl>, 1 0 1 1 1 <dbl>, 1 0 1 1 0 <dbl>, 1 0 0 1 0 <d
bl>,
## #   1 1 0 1 0 <dbl>, 0 1 1 1 0 <dbl>, 0 1 0 1 0 <dbl>, 0 0 1 0 0 <d
bl>,
## #   0 1 1 0 0 <dbl>

out[is.na(out)] <- 0
```

Create CIs

```
## create CIs
ModProbs <- out[-1] %>%
  apply(2, function(x) {
    quantile(x, probs = c(0.025, 0.5, 0.975))
  }) %>%
  t() %>%
  as_tibble() %>%
  set_names(c("LCI", "Median", "UCI")) %>%
  mutate(model = colnames(out[-1]))

m <- ModProbs$model #extract model codes
m <- gsub(" ", "", m) #remove spaces
```

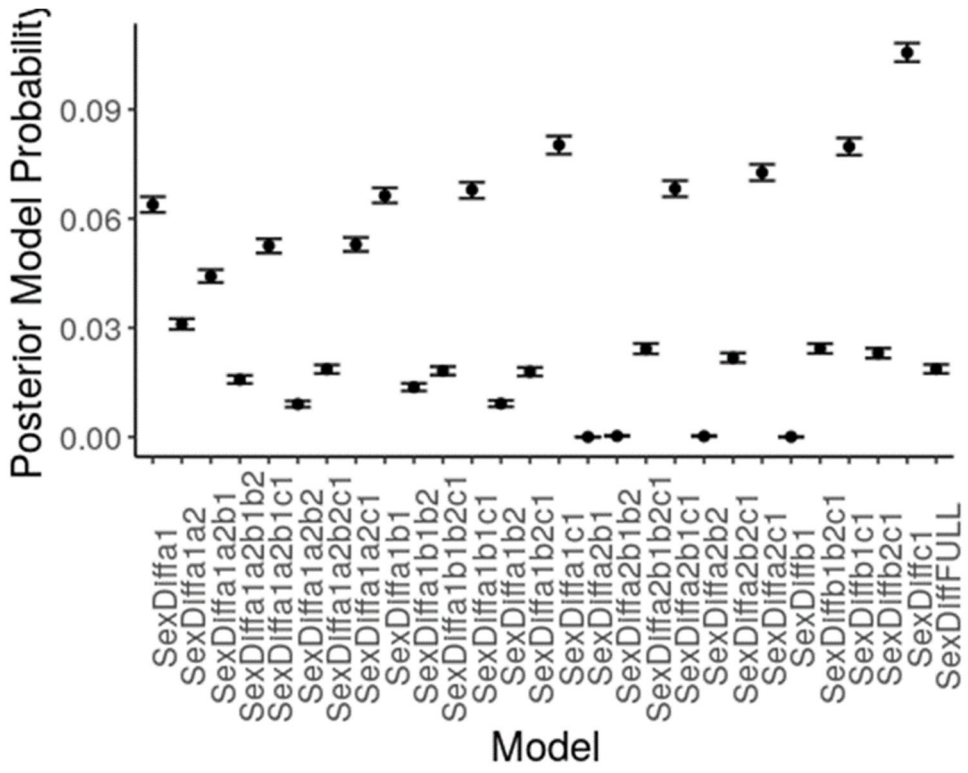
Adjust names

```
## create function to convert codes to names
names <- function(codes){
  lists <- list()

    for (i in 1:length(codes)){
    name <- rep(NA,5)
    name[1] <- ifelse(substr(codes[i], 1, 1) == 1, "a1", "")
    name[2] <- ifelse(substr(codes[i], 2, 2) == 1, "a2", "")
    name[3] <- ifelse(substr(codes[i], 3, 3) == 1, "b1", "")
    name[4] <- ifelse(substr(codes[i], 4, 4) == 1, "b2", "")
    name[5] <- ifelse(substr(codes[i], 5, 5) == 1, "c1", "")
    name <- str_c(name, collapse = "")
    lists[[i]] <- name
    }
  names <- unlist(lists)
  return(names)
}
```

```
## run function
out <- names(m)

## add "SexDiff" to each code
out <- paste("SexDiff", out, sep = "")
FULL <- which(out == "SexDiffa1a2b1b2c1")
out[FULL] <- "SexDiffFULL"

## add to df
ModProbs$model <- out
ModProbs$Method <- "RJMCMC"
```

Plot results

```
ggplot(ModProbs,aes(x = model, y = Median)) +
  geom_point() +
  geom_errorbar(data = ModProbs, aes(ymax = UCI, ymin = LCI)) +
  theme(axis.text.x = element_text(angle = 90)) +
  xlab("Model") + ylab("Posterior Model Probability") +
#  scale_colour_discrete(name = "Method", labels = c("IS", "RJMCMC"))
+
  theme(axis.text=element_text(size=12)) +
  theme(axis.title=element_text(size=15)) +
  theme(legend.text=element_text(size=10)) +
  theme(legend.title=element_text(size=15)) +
  theme(panel.grid.major = element_blank(), panel.grid.minor = element
_blank(),
        panel.background = element_blank(), axis.line = element_line(c
olour = "black"))
```



Appendix 6 – Supplementary material from Chapter 7: Investigating the impact of inbreeding on lifetime survival and mortality trajectories of European badgers

R code for Inbreeding Analysis

Setup Load libraries, data, additional functions and seed

```
## load libraries
library(nimble)
library(tidyverse)
library(mvtnorm)
library(boot)
library(lamW)
library(GGally)
library(coda)
library(mclust)
library(parallel)
library(survminer)
library(survival)
library(coda)
library(mcmcplots)
library(MCMCvis)
library(scales)
library(data.table)

rm(list=ls())

## load data
load("Data/badgerSexInb_ICubvUninf.RData")

## load distributions
source("../SimulationStudy/FirstPaperFiles/Distributions/Dist_Siler.R"
)
source("../SimulationStudy/FirstPaperFiles/Distributions/Dist_SilerNim
.R")

## Registering the following user-provided distributions: dsilerNim

source("../SimulationStudy/FirstPaperFiles/ModelComparison_FUNCTIONS.R
")

## set seed
set.seed(seeds[15])
```

Prepare for Nimble analysis Define model, set constants, data and initial values.

```
code <- nimbleCode({

  ## survival components for dead badgers
  for (i in 1:nind) {

    ## likelihood for interval-truncated siler
    censored[i] ~ dinterval(tD[i], cint[i, ])
    tD[i] ~ dsilerNim(a1mult[i], a2mult[i], b1mult[i], b2mult[i], c1mu
lt[i])

    log(a1mult[i]) <- log(a1) + betaSEX[1] * sex[i] * zSEX[1] +
      betaINFCUB[1] * infection[i] * zINF[1] +
      betaSEXINFCUB[1] * sex[i] * infection[i] * zSEXINF[1] +
      betaINBR[1] * inbr[i] * zINBR[1] +
      betaSEXINBR[1] * sex[i] * inbr[i] * zSEXINBR[1] +
      betaINFINBRCUB[1] * infection[i] * inbr[i] * zINFINBR[1]

    log(a2mult[i]) <- log(a2) + betaSEX[2] * sex[i] * zSEX[2] +
      betaINFCUB[2] * infection[i] * zINF[2] +
      betaSEXINFCUB[2] * sex[i] * infection[i] * zSEXINF[2] +
      betaINBR[2] * inbr[i] * zINBR[2] +
      betaSEXINBR[2] * sex[i] * inbr[i] * zSEXINBR[2] +
      betaINFINBRCUB[2] * infection[i] * inbr[i] * zINFINBR[2]

    log(b1mult[i]) <- log(b1) + betaSEX[3] * sex[i] * zSEX[3] +
      betaINFCUB[3] * infection[i] * zINF[3] +
      betaSEXINFCUB[3] * sex[i] * infection[i] * zSEXINF[3] +
      betaINBR[3] * inbr[i] * zINBR[3] +
      betaSEXINBR[3] * sex[i] * inbr[i] * zSEXINBR[3] +
      betaINFINBRCUB[3] * infection[i] * inbr[i] * zINFINBR[3]

    log(b2mult[i]) <- log(b2) + betaSEX[4] * sex[i] * zSEX[4] +
      betaINFCUB[4] * infection[i] * zINF[4] +
      betaSEXINFCUB[4] * sex[i] * infection[i] * zSEXINF[4] +
      betaINBR[4] * inbr[i] * zINBR[4] +
      betaSEXINBR[4] * sex[i] * inbr[i] * zSEXINBR[4] +
      betaINFINBRCUB[4] * infection[i] * inbr[i] * zINFINBR[4]

    log(c1mult[i]) <- log(c1) + betaSEX[5] * sex[i] * zSEX[5] +
      betaINFCUB[5] * infection[i] * zINF[5] +
      betaSEXINFCUB[5] * sex[i] * infection[i] * zSEXINF[5] +
      betaINBR[5] * inbr[i] * zINBR[5] +
      betaSEXINBR[5] * sex[i] * inbr[i] * zSEXINBR[5] +
      betaINFINBRCUB[5] * infection[i] * inbr[i] * zINFINBR[5]

    ## sampling component
    pd[i] <- exp(y[i] * log(mean.p) + (min(floor(tD[i]), tM[i]) - y[i]
) * log(1 - mean.p))
    dind[i] ~ dbern(pd[i])
```

```
  }

  ## priors
  for (k in 1:5) {
    betaSEX[k] ~ dnorm(0, sd = 1)
    betaINFCUB[k] ~ dnorm(0, sd = 1)
    betaINBR[k] ~dnorm(0, sd = 1)
    betaSEXINFCUB[k] ~ dnorm(0, sd = 1)
    betaSEXINBR[k] ~ dnorm(0, sd = 1)
    betaINFINBRCUB[k] ~ dnorm(0, sd = 1)
    zSEX[k] ~ dbern(0.5)
    zINF[k] ~ dbern(0.5)
    zINBR[k] ~ dbern(0.5)
    zSEXINF[k] ~ dbern(0.5)
    zSEXINBR[k] ~ dbern(0.5)
    zINFINBR[k] ~ dbern(0.5)
    constraint_dataSEXINF[k] ~ dconstraint(zSEXINF[k] <= zSEX[k] * zIN
F[k])
    constraint_dataSEXINBR[k] ~ dconstraint(zSEXINBR[k] <= zSEX[k] * z
INBR[k])
    constraint_dataINFINBR[k] ~ dconstraint(zINFINBR[k] <= zINF[k] * z
INBR[k])

  }
  a1 ~ dexp(1)
  a2 ~ dexp(1)
  b1 ~ dexp(1)
  b2 ~ dexp(1)
  c1 ~ dexp(1)
  mean.p ~ dunif(0, 1)

})

## set up data
consts <- list(nind = nind, tM = tM, sex = sex, infection = infection,
inbr = inbrCAT)

data <- list(
  y = y, cint = cint, censored = censored, tD = tD, dind = dind,
  constraint_dataSEXINF = rep(1, 5), constraint_dataSEXINBR = rep(1, 5
),
  constraint_dataINFINBR = rep(1, 5))

## find overdispersed initial values
tinitFn <- function(cint, censored) {
  apply(cbind(cint, censored), 1, function(x) {
    if(x[3] == 2) {
      y <- x[2] + rexp(1, 1)
    } else {
      y <- runif(1, x[1], x[2])
    }
    y
  })
```

```
}
initFn <- function(cint, censored, sex, model) {
  ## get ML estimates as initial values
  optFn <- function(pars, t, sex, infection3) {
    # browser()
    if(any(pars[1:5] < 0)) {
      return(NA)
    }
    ll <- sum(dSiler(t, a1 = pars[1], a2 = pars[2], b1 = pars[3], b2 =
pars[4], c1 = pars[5], log = TRUE))
  }
  valid <- 0
  while(valid == 0) {
    pars <- list(convergence = 1)
    k <- 0
    while(pars$convergence != 0 & k < 20) {
      ## sample missing values
      tD <- tinitFn(cint, censored)
      pars <- optim(rexp(5, 10), optFn, t = tD, sex = sex, control = l
ist(fnscale = -1))
      k <- k + 1
    }
    if(k == 20) {
      stop("Can't sample initial values")
    }
    pars <- pars$par

    ## output initial values
    inits <- list(
      tD = tD,
      a1 = pars[1],
      a2 = pars[2],
      b1 = pars[3],
      b2 = pars[4],
      c1 = pars[5],
      mean.p = runif(1, 0, 1),
      betaSEX = rnorm(5, 0, 1),
      betaINFCUB = rnorm(5, 0, 1),
      betaSEXINFCUB = rnorm(5, 0, 1),
      betaINBR  = rnorm(5, 0, 1),
      betaSEXINBR = rnorm(5, 0, 1),
      betaINFINBRCUB = rnorm(5, 0, 1),
      zSEX = rep(0, 5),
      zINF = rep(0, 5),
      zSEXINF = rep(0, 5),
      zINBR = rep(0, 5),
      zSEXINBR = rep(0, 5),
      zINFINBR = rep(0, 5)
    )
    model$setInits(inits)
    valid <- ifelse(!is.finite(model$calculate()), 0, 1)
  }
```

```
  return(inits)
}
```

Build the model in NIMBLE

```
## build the model without initial values
## (will throw an initialisation warning)

model <- nimbleModel(code, constants = consts, data = data)

## defining model...

## building model...

## setting data and initial values...

## running calculate on model (any error reports that follow may simpl
y reflect missing values in model variables) ... Error in if (a1 < 0 |
a2 < 0 | b1 < 0 | b2 < 0 | c1 < 0) { :
##   missing value where TRUE/FALSE needed
##
## checking model sizes and dimensions... This model is not fully init
ialized. This is not an error. To see which variables are not initiali
zed, use model$initializeInfo(). For more information on model initial
ization, see help(modelInitialization).
## model building finished.
```

Compile the build and calculate the inits

```
## compile the model
cIndicatorModel <- compileNimble(model)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.

## compilation finished.

## find list of valid initial values (needs compiled model
## for some reason)
inits <- list()
for(k in 1:2) {
  inits[[k]] <- initFn(cint, censored, sex, cIndicatorModel)
}
```

Configure the MCMC We can now make adjustments to the default sampler settings in NIMBLE.

```
## configure MCMC
config <- configureMCMC(model)

## ===== Monitors =====
## thin = 1: betaSEX, betaINFCUB, betaINBR, betaSEXINFCUB, betaSEXINBR
, betaINFINBRCUB, zSEX, zINF, zINBR, zSEXINF, zSEXINBR, zINFINBR, a1,
a2, b1, b2, c1, mean.p
```

```
## ===== Samplers =====
## RW sampler (1642)
##   - betaSEX[]  (5 elements)
##   - betaINFCUB[]  (5 elements)
##   - betaINBR[]  (5 elements)
##   - betaSEXINFCUB[]  (5 elements)
##   - betaSEXINBR[]  (5 elements)
##   - betaINFINBRCUB[]  (5 elements)
##   - a1
##   - a2
##   - b1
##   - b2
##   - c1
##   - mean.p
##   - tD[]  (1606 elements)
## binary sampler (30)
##   - zSEX[]  (5 elements)
##   - zINF[]  (5 elements)
##   - zINBR[]  (5 elements)
##   - zSEXINF[]  (5 elements)
##   - zSEXINBR[]  (5 elements)
##   - zINFINBR[]  (5 elements)

config$removeSamplers(c("a1", "a2", "b1", "b2", "c1"))
config$addSampler(target = c("a1"), type = 'slice', control = list(sli
ceWidth = 0.5, adaptInterval = 50))
config$addSampler(target = c("a2"), type = 'slice', control = list(sli
ceWidth = 1.5, adaptInterval = 20))
config$addSampler(target = c("b1"), type = 'slice', control = list(sli
ceWidth = 0.5, adaptInterval = 50))
config$addSampler(target = c("b2"), type = 'slice', control = list(sli
ceWidth = 1.5, adaptInterval = 20))
config$addSampler(target = c("c1"), type = 'slice', control = list(sli
ceWidth = 0.5, adaptInterval = 50))

configureRJ(conf = config,   ## model configuration
                  targetNodes = c("betaSEX", "betaINFCUB", "betaINBR",
"betaSEXINFCUB", "betaSEXINBR", "betaINFINBRCUB"),
                  indicatorNodes = c("zSEX", "zINF", "zINBR", "zSEXINF
", "zSEXINBR", "zINFINBR"),
                  control = list(mean = 0, scale = 1))

config$addMonitors("betaSEX", "betaINFCUB", "betaINBR", "betaSEXINFCUB
", "betaSEXINBR", "betaINFINBRCUB")

## thin = 1: betaSEX, betaINFCUB, betaINBR, betaSEXINFCUB, betaSEXINBR
, betaINFINBRCUB, zSEX, zINF, zINBR, zSEXINF, zSEXINBR, zINFINBR, a1,
a2, b1, b2, c1, mean.p

config

## ===== Monitors =====
## thin = 1: betaSEX, betaINFCUB, betaINBR, betaSEXINFCUB, betaSEXINBR
, betaINFINBRCUB, zSEX, zINF, zINBR, zSEXINF, zSEXINBR, zINFINBR, a1,
```

```
a2, b1, b2, c1, mean.p
## ===== Samplers =====
## slice sampler (5)
##   - a1
##   - a2
##   - b1
##   - b2
##   - c1
## RW sampler (1607)
##   - mean.p
##   - tD[]  (1606 elements)
## RJ_toggled sampler (30)
##   - betaSEX[]  (5 elements)
##   - betaINFCUB[]  (5 elements)
##   - betaINBR[]  (5 elements)
##   - betaSEXINFCUB[]  (5 elements)
##   - betaSEXINBR[]  (5 elements)
##   - betaINFINBRCUB[]  (5 elements)
## RJ_indicator sampler (30)
##   - zSEX[]  (5 elements)
##   - zINF[]  (5 elements)
##   - zINBR[]  (5 elements)
##   - zSEXINF[]  (5 elements)
##   - zSEXINBR[]  (5 elements)
##   - zINFINBR[]  (5 elements)
```

Build and compile We now build our model with the updated configuration and compile again.

```
rIndicatorMCMC <- buildMCMC(config)
cIndicatorMCMC <- compileNimble(rIndicatorMCMC, project = model)

## compiling... this may take a minute. Use 'showCompilerOutput = TRUE
' to see C++ compilation details.

## compilation finished.
```

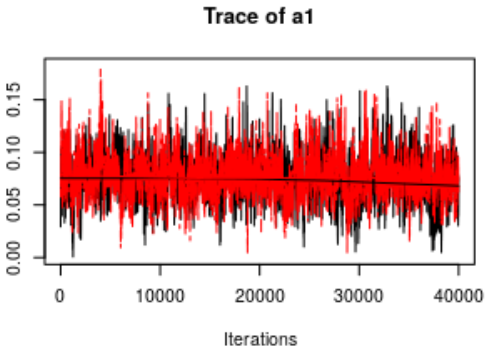
Run the MCMC Here we set our MCMC options: iterations, burnin, chains etc.

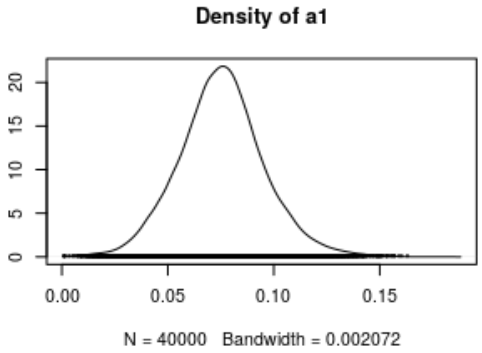
```
#Run the model
run <- runMCMC(cIndicatorMCMC,
                            niter = 50000,
                            nburnin = 10000,
                            nchains = 2,
                            inits = inits[[1]],
                            progressBar = TRUE,
                            summary = TRUE,
                            samplesAsCodaMCMC = TRUE,
                            thin = 1)

## running chain 1...

## |-------------|-------------|-------------|-------------|
## |-------------------------------------------------------|
```

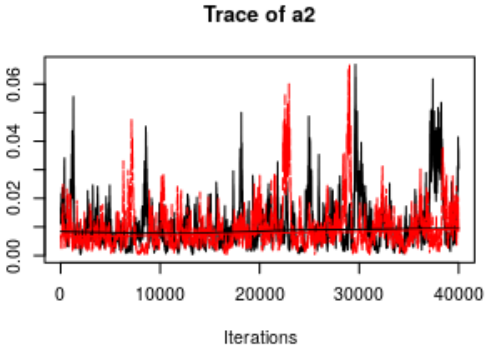
```
## running chain 2...

## |-------------|-------------|-------------|-------------|
## |-----------------------------------------------------|
```

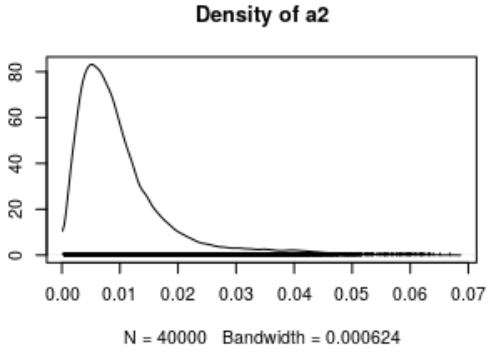
Plot trace plots to check mixing etc

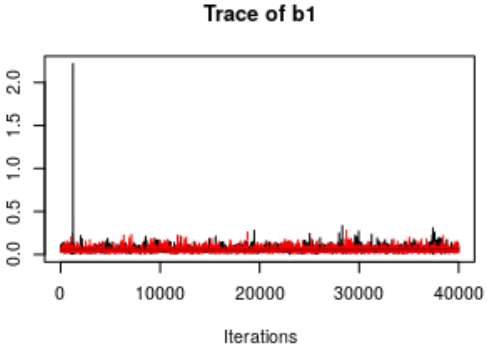
```
#Plot mcmcm
run <- readRDS("outputs/FullModel_z_all_runsamples_infCubVuninfLife_INBRCont.rds")

samples <- as.matrix(run$samples)
plot(run$samples)
```

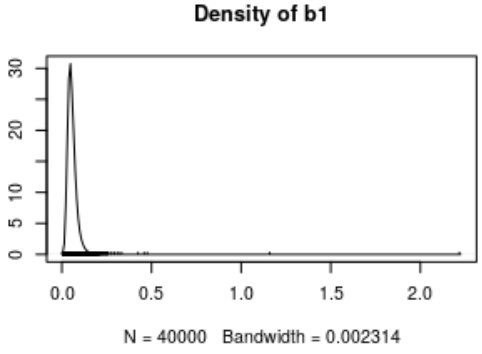

Trace of a1
0.00
0.05
0.10
0.15
0
10000
20000
30000
40000
Iterations

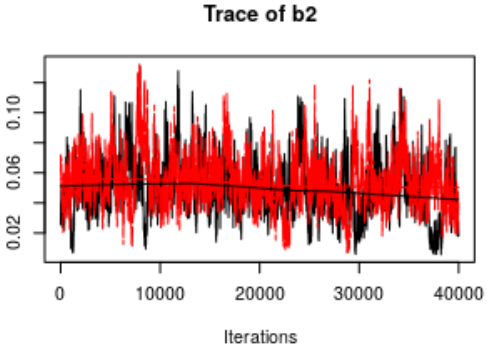

Density of a1
0
5
10
15
20
0.00
0.05
0.10
0.15
N = 40000 Bandwidth = 0.002072

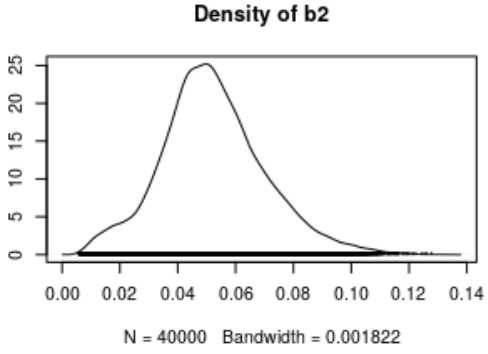

Trace of a2
0.00
0.02
0.04
0.06
0
10000
20000
30000
40000
Iterations

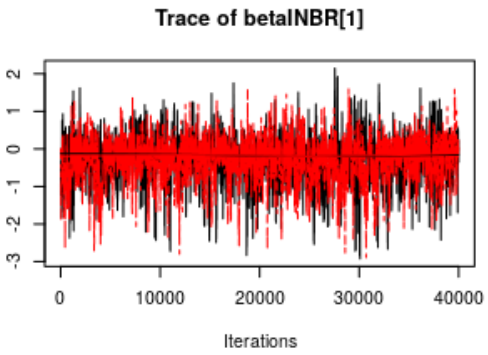

Density of a2
0
20
40
60
80
0.00
0.01
0.02
0.03
0.04
0.05
0.06
0.07
N = 40000 Bandwidth = 0.000624

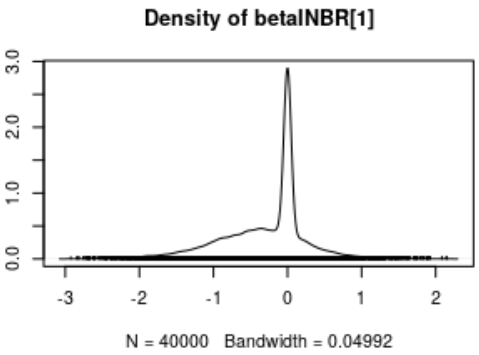

Trace of b1
0.0
0.5
1.0
1.5
2.0
0
10000
20000
30000
40000
Iterations

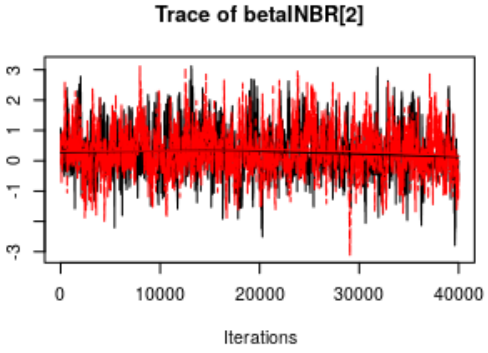

Density of b1
0
5
10
20
30
0.0
0.5
1.0
1.5
2.0
N = 40000 Bandwidth = 0.002314

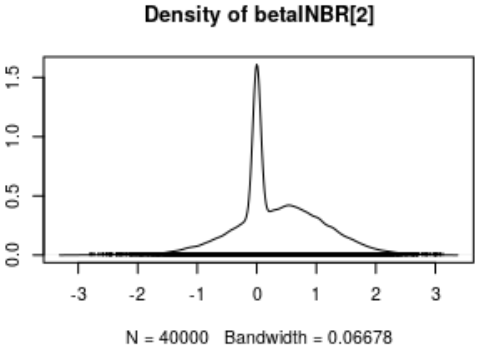

Trace of b2
0.02
0.06
0.10
0
10000
20000
30000
40000
Iterations

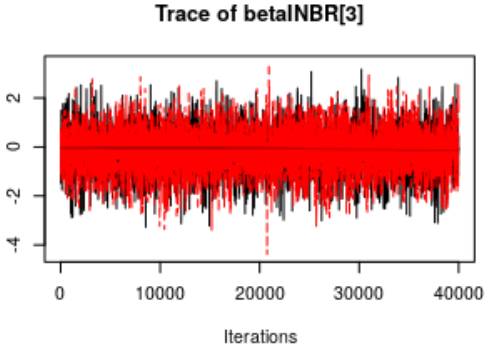

Density of b2
0
5
10
15
20
25
0.00
0.02
0.04
0.06
0.08
0.10
0.12
0.14
N = 40000 Bandwidth = 0.001822

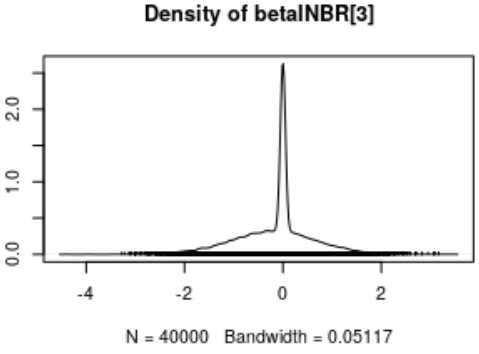

Trace of betaINBR[1]
Iterations

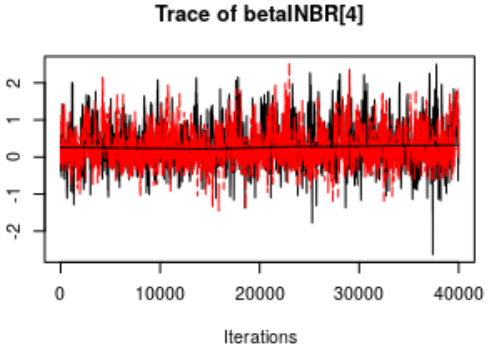

Density of betaINBR[1]
N = 40000 Bandwidth = 0.04992

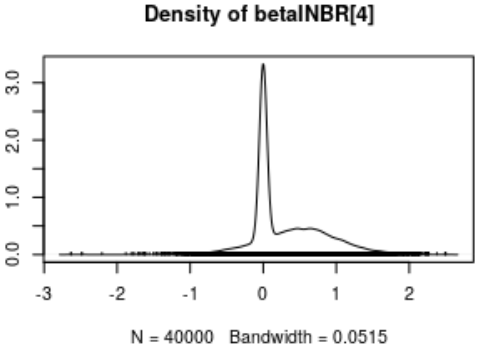

Trace of betaINBR[2]
Iterations

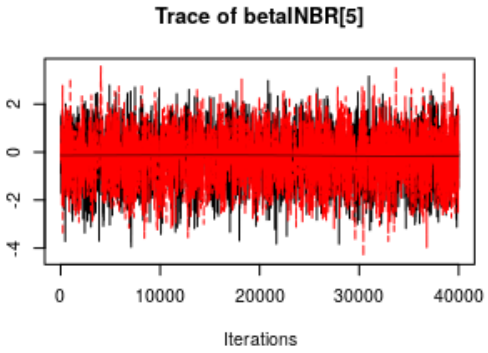

Density of betaINBR[2]
N = 40000 Bandwidth = 0.06678

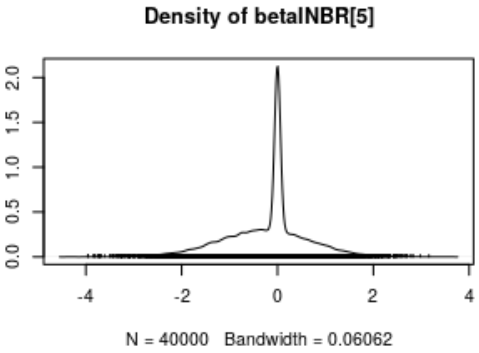

Trace of betaINBR[3]
Iterations

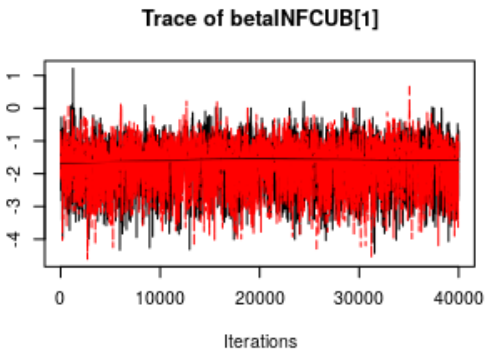

Density of betaINBR[3]
N = 40000 Bandwidth = 0.05117

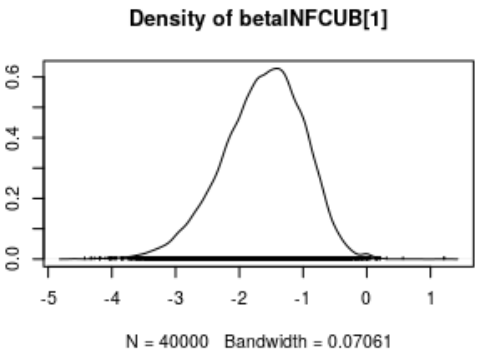

Trace of betaINBR[4]
Iterations

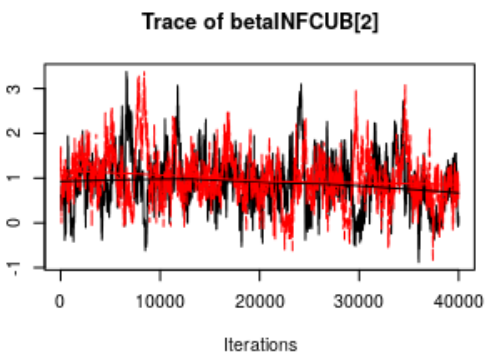

Density of betaINBR[4]
N = 40000 Bandwidth = 0.0515

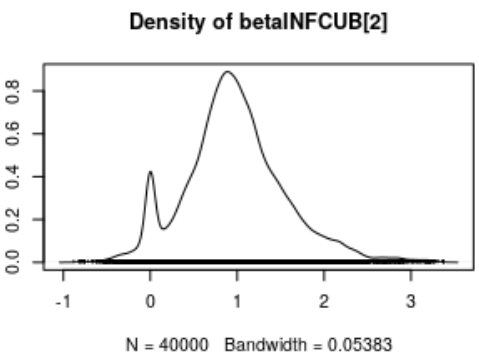

Trace of betaINBR[5]
Iterations

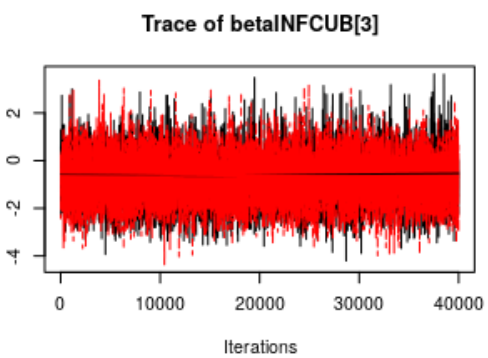

Density of betaINBR[5]
N = 40000 Bandwidth = 0.06062

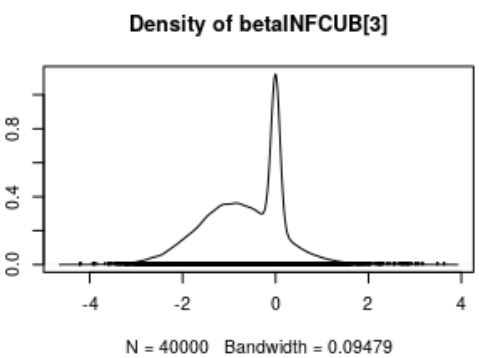

Trace of betaINFCUB[1]
Iterations

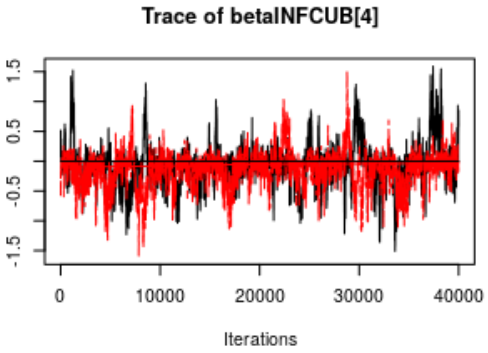

Density of betaINFCUB[1]
N = 40000 Bandwidth = 0.07061

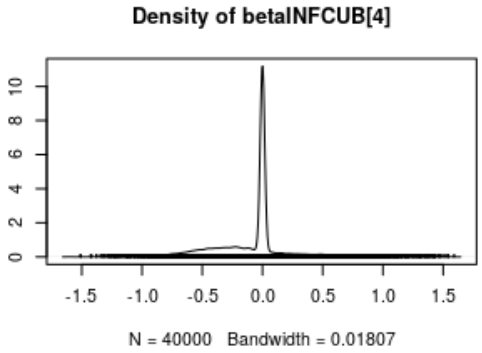

Trace of betaINFCUB[2]
Iterations

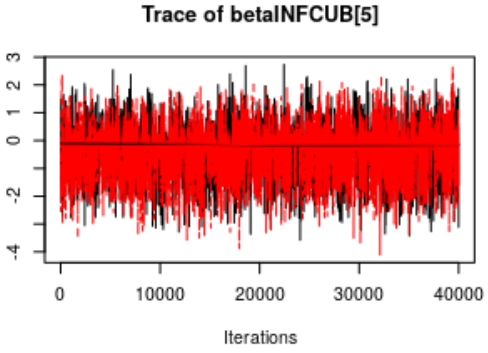

Density of betaINFCUB[2]
N = 40000 Bandwidth = 0.05383

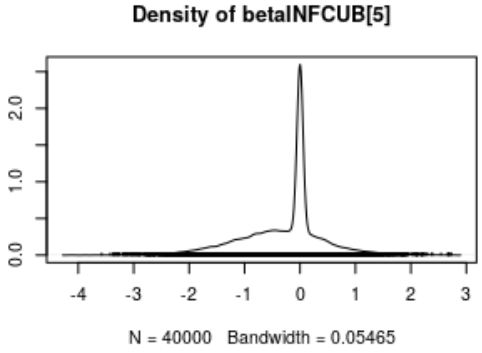

Trace of betaINFCUB[3]
Iterations

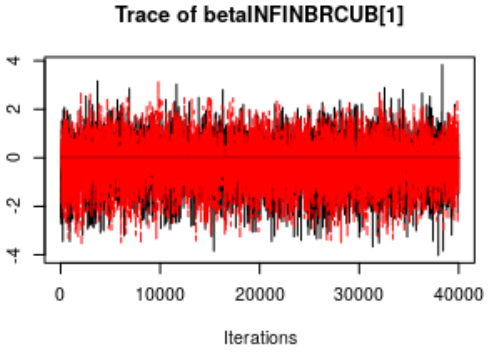

Density of betaINFCUB[3]
N = 40000 Bandwidth = 0.09479

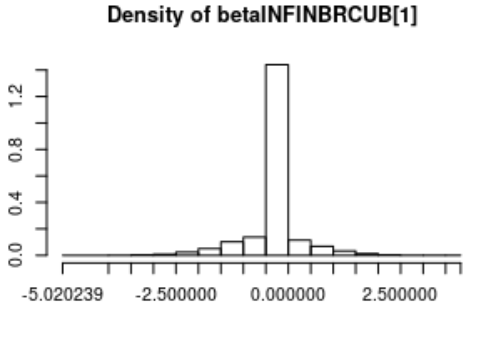

Trace of betaINFCUB[4]
1.5
0.5
-0.5
-1.5
0
10000
20000
30000
40000
Iterations

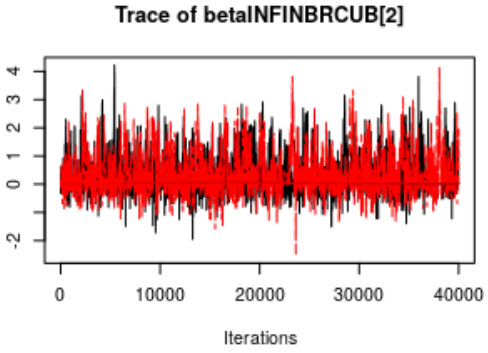

Density of betaINFCUB[4]
10
8
6
4
2
0
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
N = 40000 Bandwidth = 0.01807

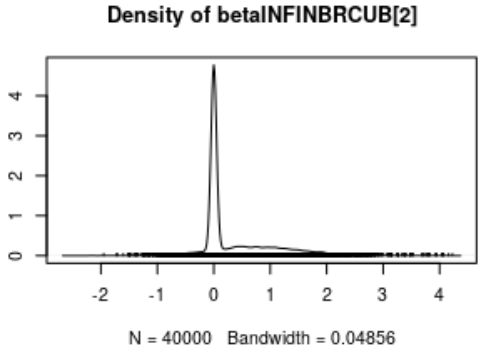

Trace of betaINFCUB[5]
3
2
1
0
-2
-4
0
10000
20000
30000
40000
Iterations

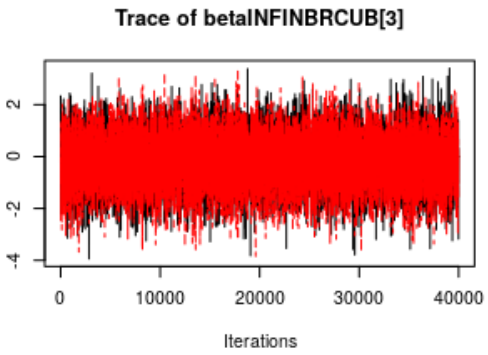

Density of betaINFCUB[5]
2.0
1.0
0.0
-4
-3
-2
-1
0
1
2
3
N = 40000 Bandwidth = 0.05465

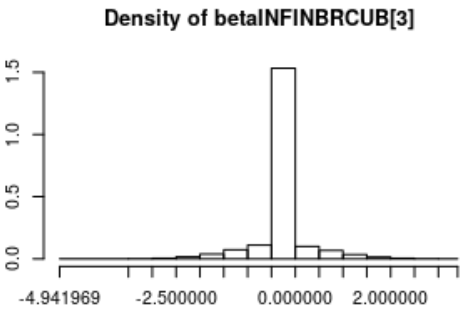

Trace of betaINFINBRCUB[1]
4
2
0
-2
-4
0
10000
20000
30000
40000
Iterations

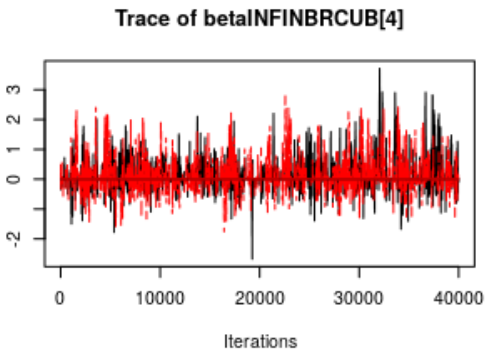

Density of betaINFINBRCUB[1]
1.2
0.8
0.4
0.0
-5.020239
-2.500000
0.000000
2.500000

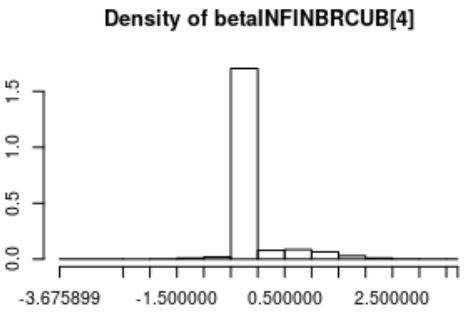

Trace of betaINFINBRCUB[2]
4
3
2
1
0
-2
0
10000
20000
30000
40000
Iterations

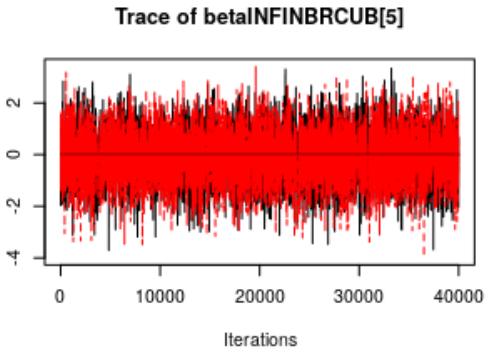

Density of betaINFINBRCUB[2]
4
3
2
1
0
-2
-1
0
1
2
3
4
N = 40000 Bandwidth = 0.04856

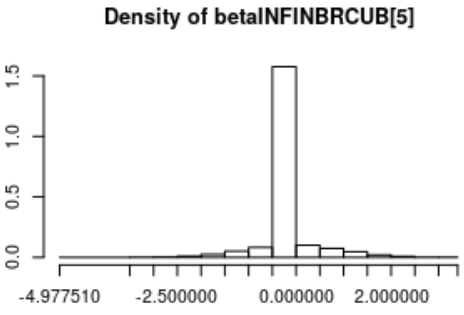

Trace of betaINFINBRCUB[3]
Iterations

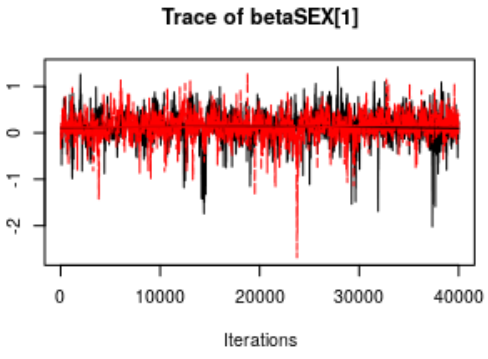

Density of betaINFINBRCUB[3]

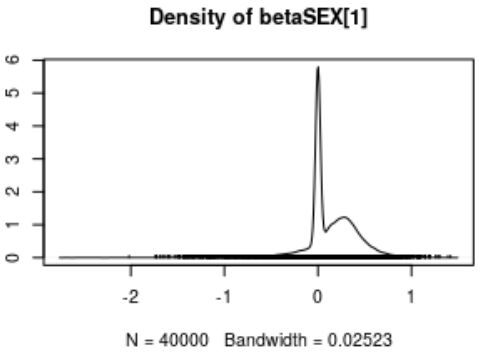

Trace of betaINFINBRCUB[4]
Iterations

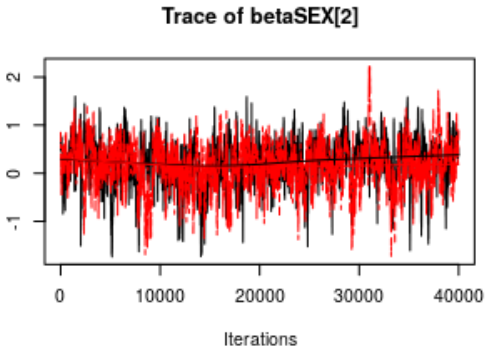

Density of betaINFINBRCUB[4]

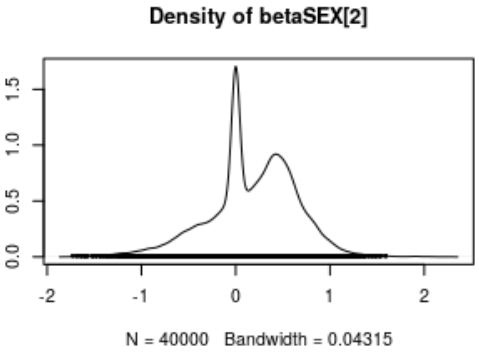

Trace of betaINFINBRCUB[5]
Iterations

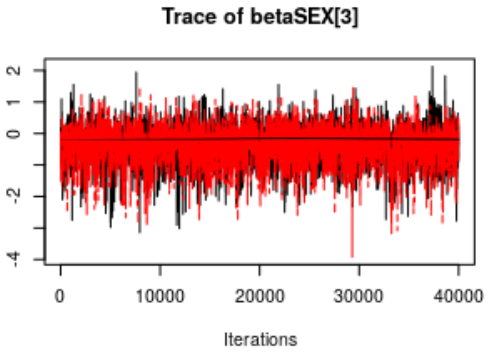

Density of betaINFINBRCUB[5]

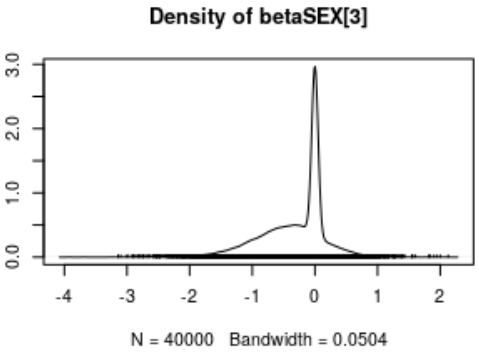

Trace of betaSEX[1]
Iterations

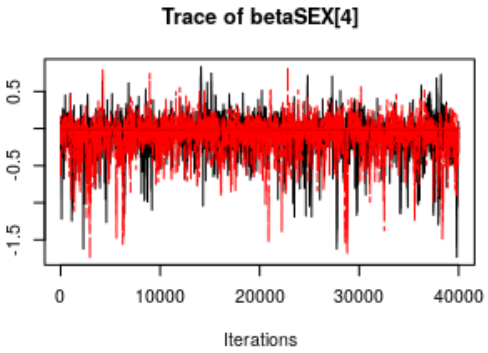

Density of betaSEX[1]
N = 40000 Bandwidth = 0.02523

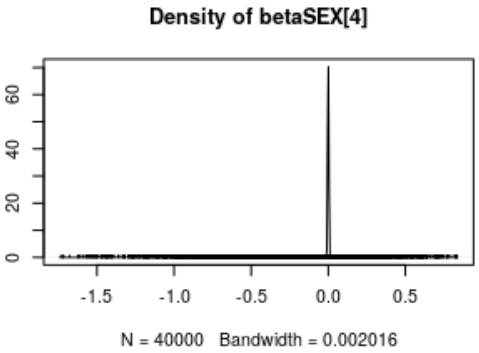

Trace of betaSEX[2]
Iterations

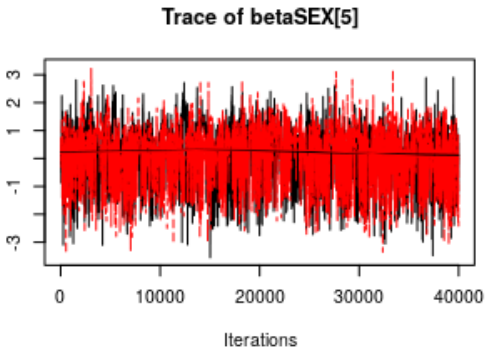

Density of betaSEX[2]
N = 40000 Bandwidth = 0.04315

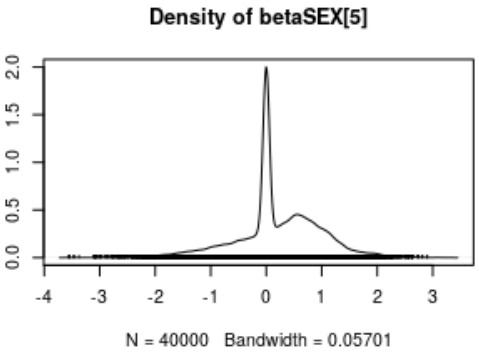

Trace of betaSEX[3]
Iterations

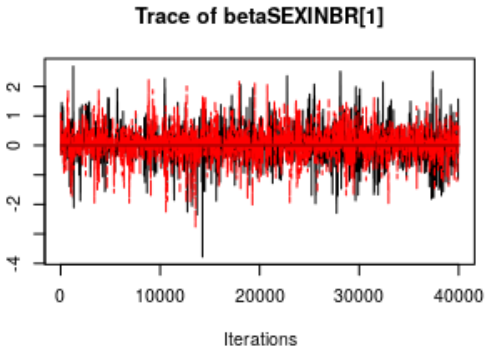

Density of betaSEX[3]
N = 40000 Bandwidth = 0.0504

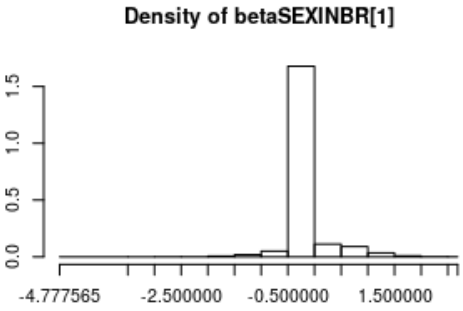

Trace of betaSEX[4]
Iterations

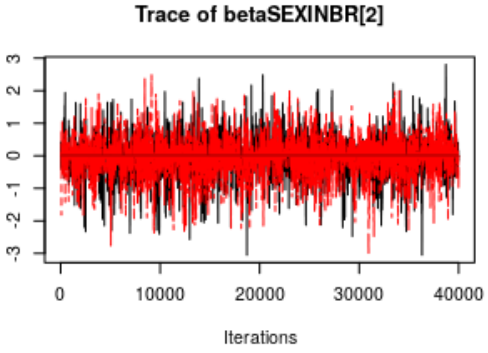

Density of betaSEX[4]
N = 40000 Bandwidth = 0.002016

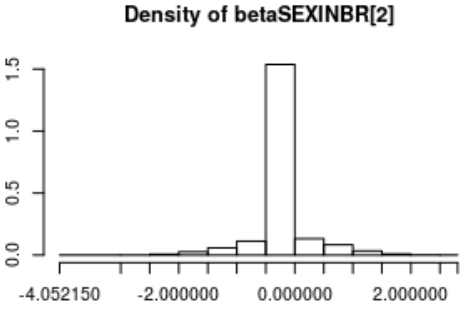

Trace of betaSEX[5]
Iterations

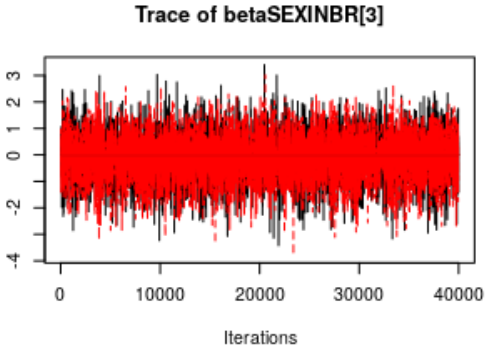

Density of betaSEX[5]
N = 40000 Bandwidth = 0.05701

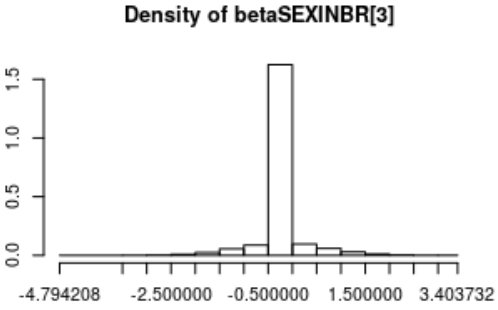

Trace of betaSEXINBR[1]
-4
-2
0
1
2
0
10000
20000
30000
40000
Iterations


Density of betaSEXINBR[1]
0.0
0.5
1.0
1.5
-4.777565
-2.500000
-0.500000
1.500000


Trace of betaSEXINBR[2]
-3
-2
-1
0
1
2
3
0
10000
20000
30000
40000
Iterations


Density of betaSEXINBR[2]
0.0
0.5
1.0
1.5
-4.052150
-2.000000
0.000000
2.000000


Trace of betaSEXINBR[3]
-4
-2
0
1
2
3
0
10000
20000
30000
40000
Iterations


Density of betaSEXINBR[3]
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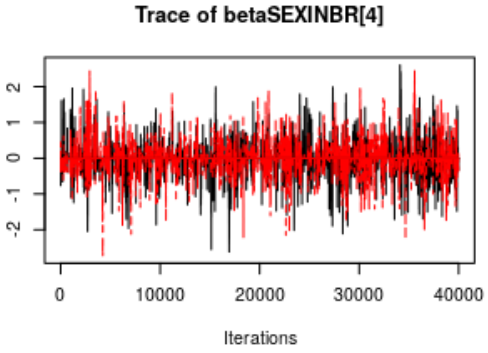
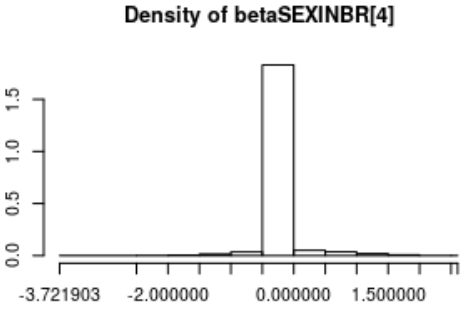
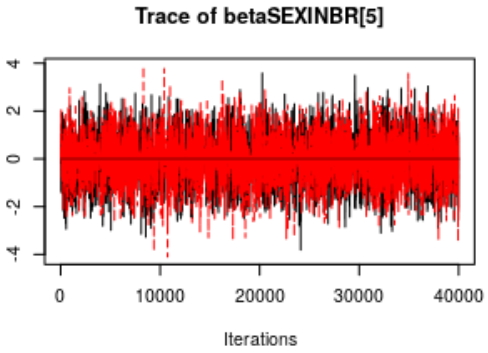
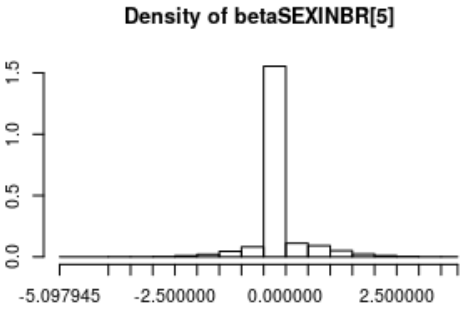
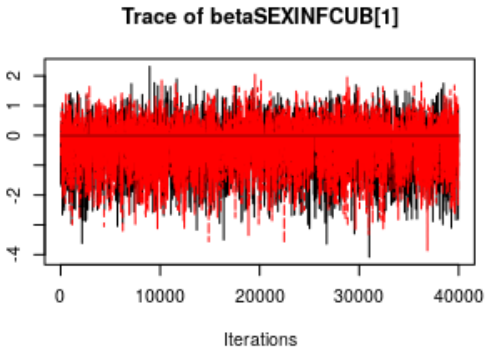
0.5
1.0
1.5
-4.794208
-2.500000
-0.500000
1.500000
3.403732

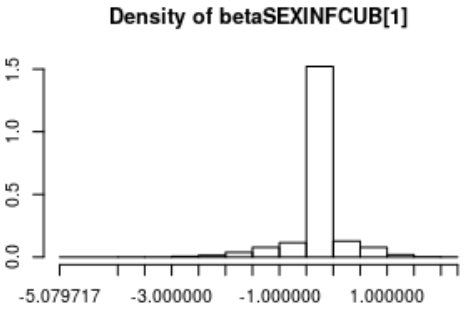

Trace of betaSEXINBR[4]
-2
-1
0
1
2
0
10000
20000
30000
40000
Iterations

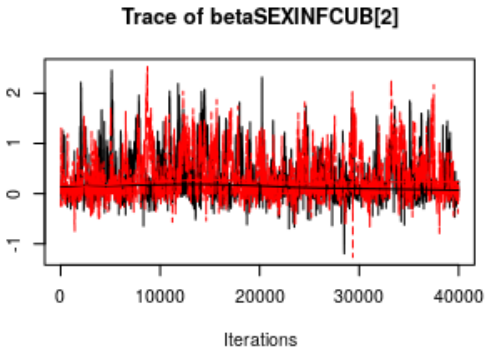

Density of betaSEXINBR[4]
0.0
0.5
1.0
1.5
-3.721903
-2.000000
0.000000
1.500000

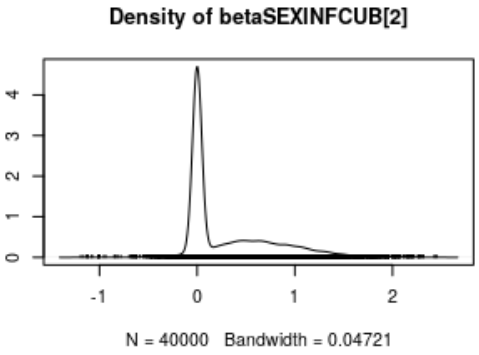

Trace of betaSEXINBR[5]
Iterations

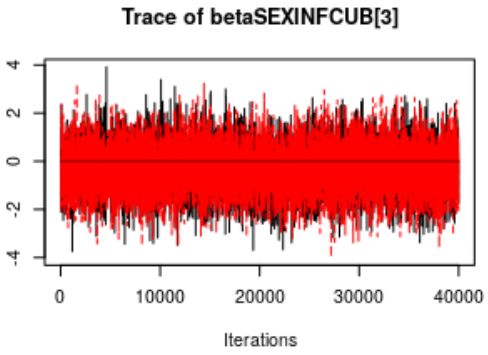

Density of betaSEXINBR[5]

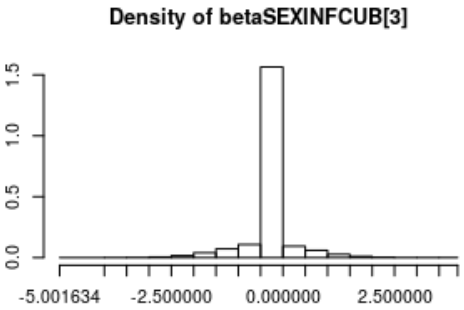

Trace of betaSEXINFCUB[1]
Iterations

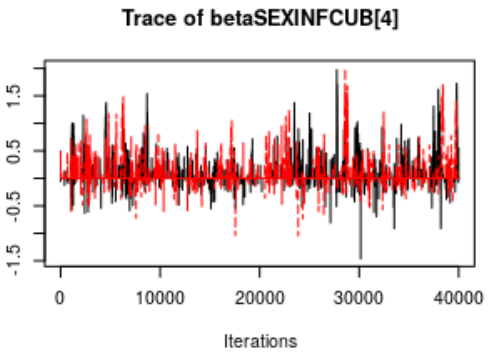

Density of betaSEXINFCUB[1]

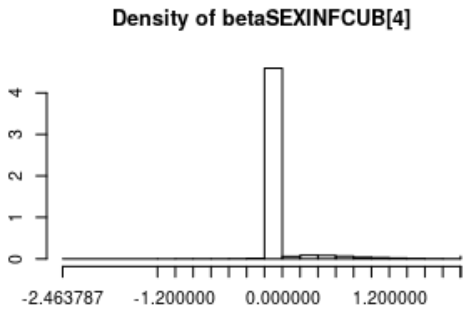

Trace of betaSEXINFCUB[2]
Iterations

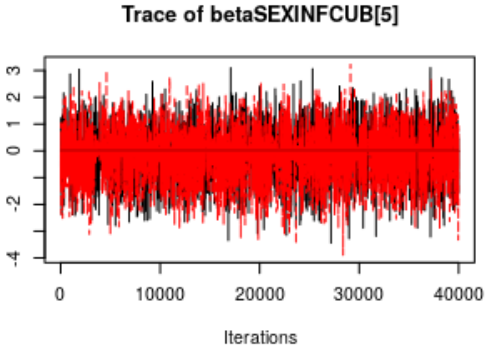

Density of betaSEXINFCUB[2]
N = 40000 Bandwidth = 0.04721

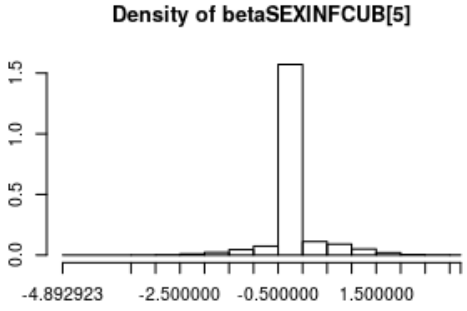

Trace of betaSEXINFCUB[3]
Iterations


Density of betaSEXINFCUB[3]


Trace of betaSEXINFCUB[4]
-1.5
-0.5
0.5
1.5
0
10000
20000
30000
40000
Iterations


Density of betaSEXINFCUB[4]
0
1
2
3
4
-2.463787
-1.200000
0.000000
1.200000


Trace of betaSEXINFCUB[5]
-4
-2
0
1
2
3
0
10000
20000
30000
40000
Iterations


Density of betaSEXINFCUB[5]
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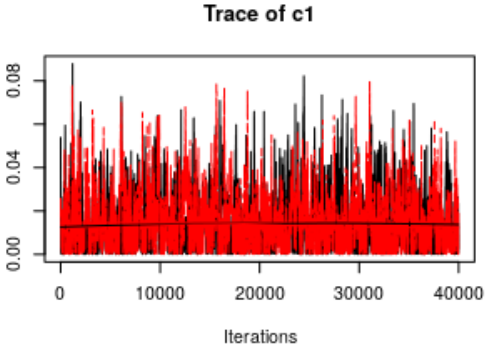
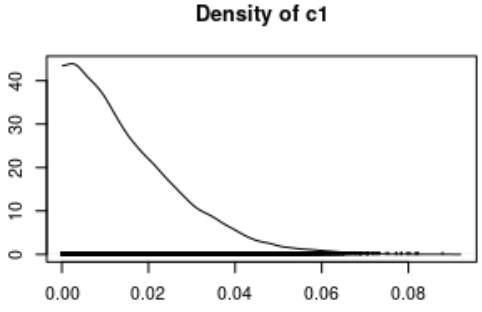
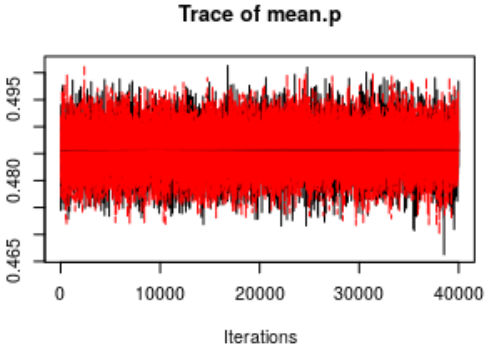
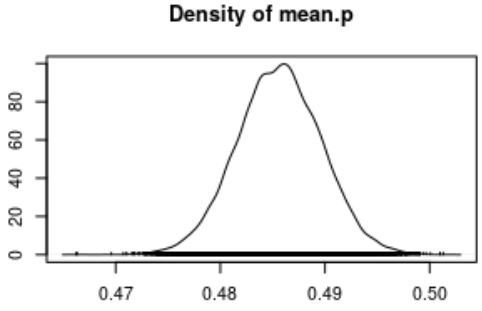
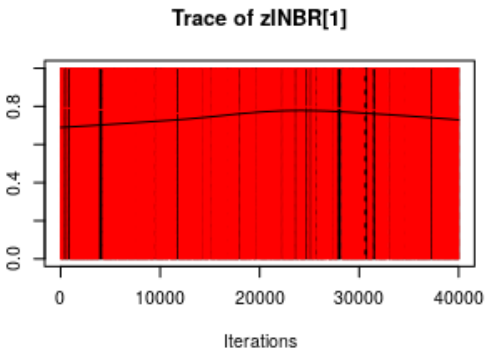
0.5
1.0
1.5
-4.892923
-2.500000
-0.500000
1.500000

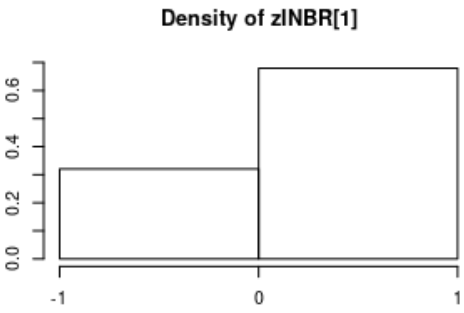

Trace of c1
0.00
0.04
0.08
0
10000
20000
30000
40000
Iterations

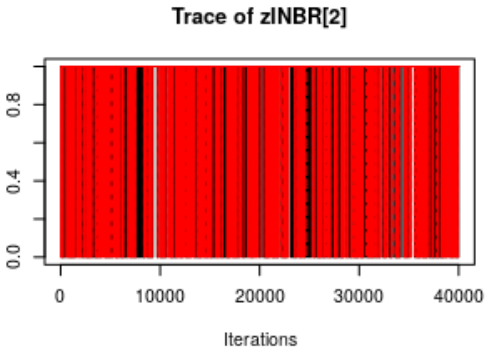

Density of c1
0
10
20
30
40
0.00
0.02
0.04
0.06
0.08
N = 40000 Bandwidth = 0.00139


Trace of mean.p
0.465
0.480
0.495
0
10000
20000
30000
40000
Iterations

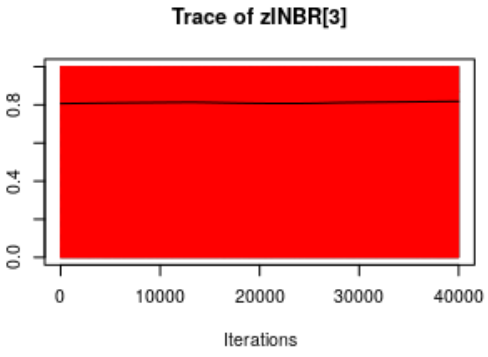

Density of mean.p
0
20
40
60
80
0.47
0.48
0.49
0.50
N = 40000 Bandwidth = 0.0004449


Trace of zINBR[1]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations

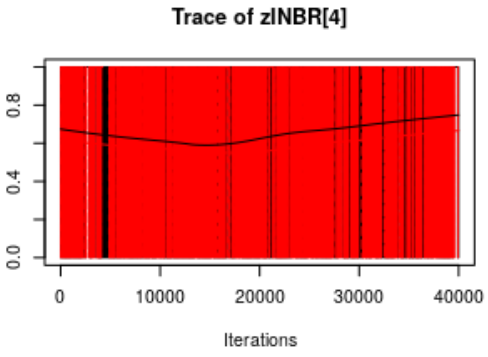

Density of zINBR[1]
0.0
0.2
0.4
0.6
-1
0
1

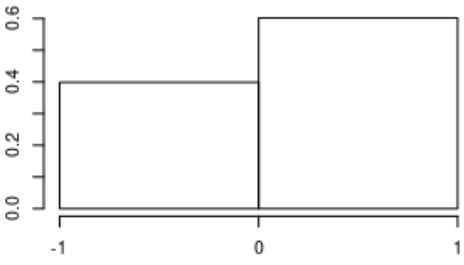

Trace of zINBR[2]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations

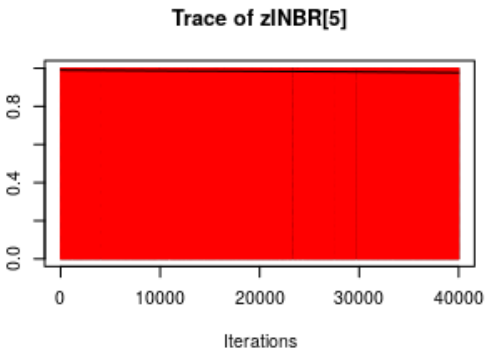

Density of zINBR[2]
0.0
0.2
0.4
0.6
0.8
-1
0
1


Trace of zINBR[3]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations

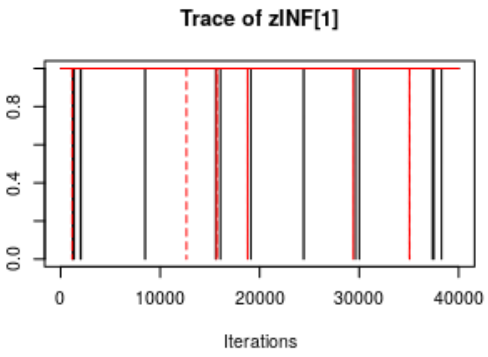

Density of zINBR[3]
0.0
0.2
0.4
0.6
-1
0
1

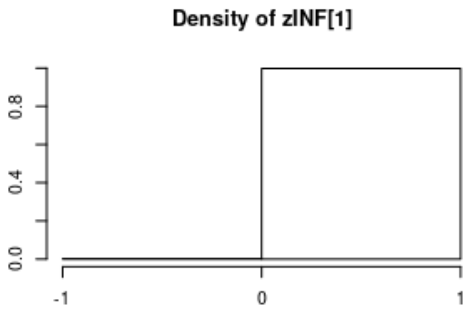

Trace of zINBR[4]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations

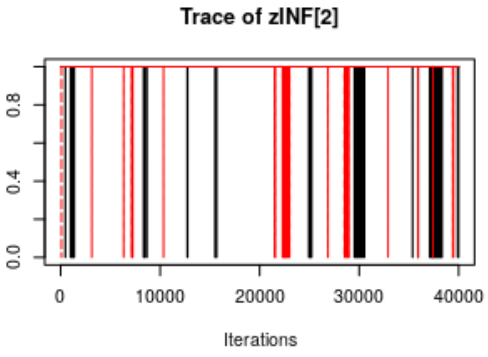

Density of zINBR[4]
0.0
0.2
0.4
0.6
-1
0
1

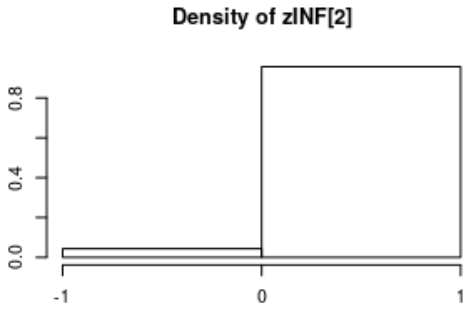

Trace of zINBR[5]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations

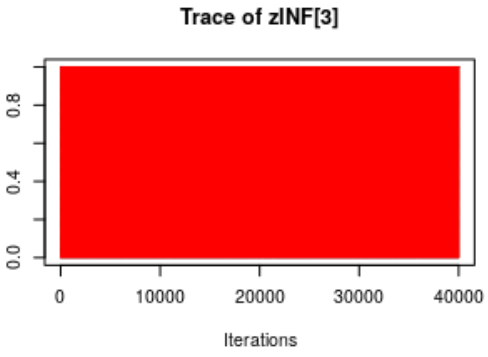

Density of zINBR[5]
0.0
0.2
0.4
0.6
-1
0
1

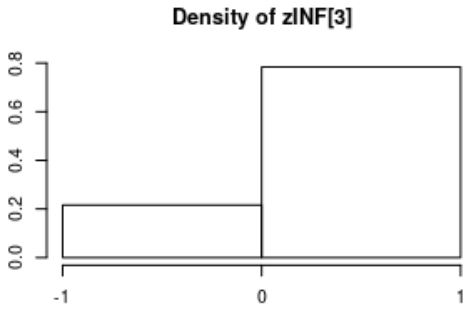

Trace of zINF[1]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations


Density of zINF[1]
0.0
0.4
0.8
-1
0
1


Trace of zINF[2]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations


Density of zINF[2]
0.0
0.4
0.8
-1
0
1


Trace of zINF[3]
0.0
0.4
0.8
0
10000
20000
30000
40000
Iterations


Density of zINF[3]
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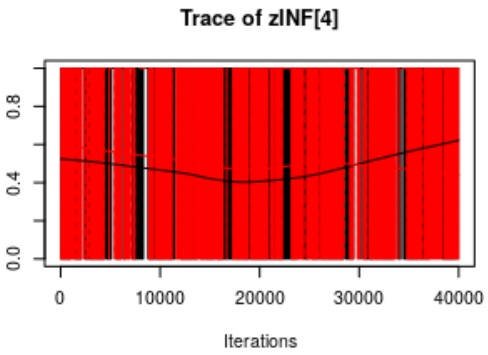
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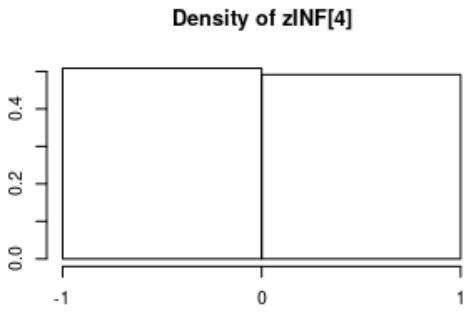
Iterations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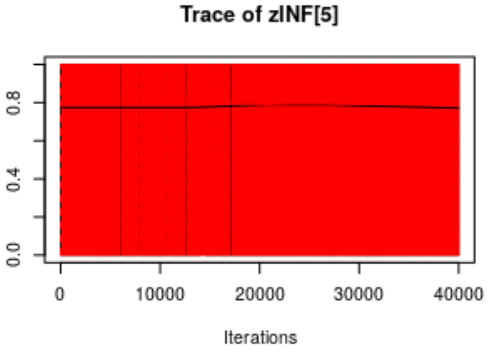
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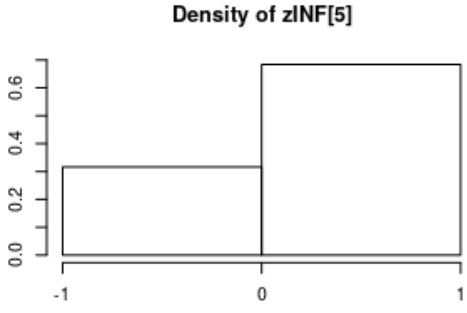
Iterations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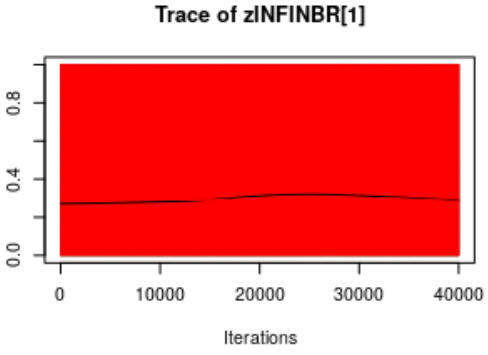
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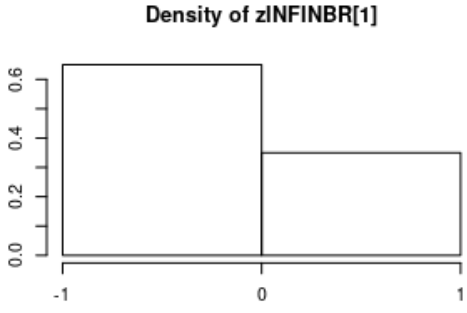
Iterations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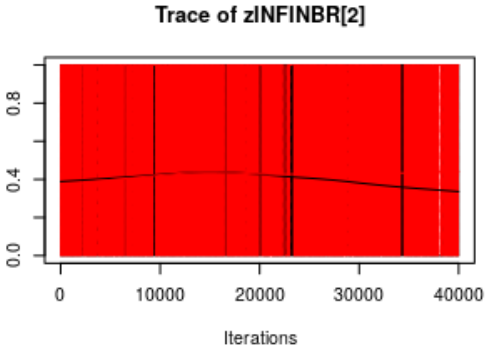
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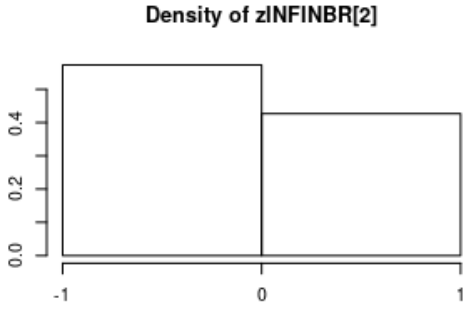
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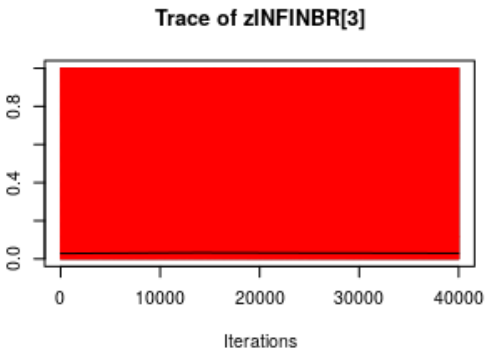
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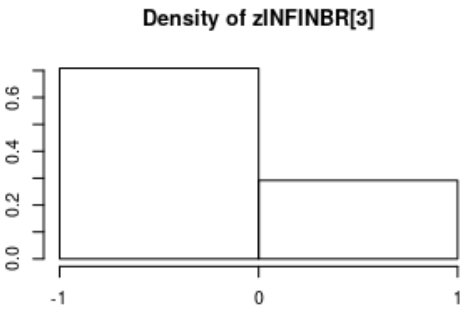
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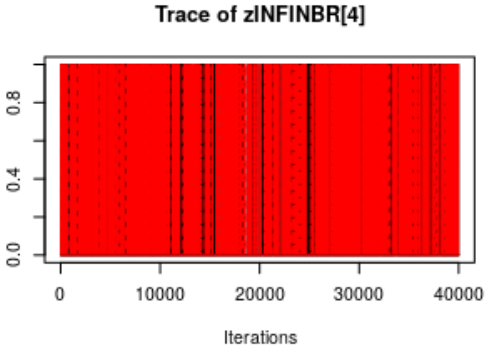
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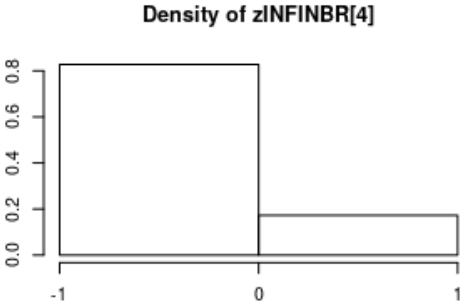
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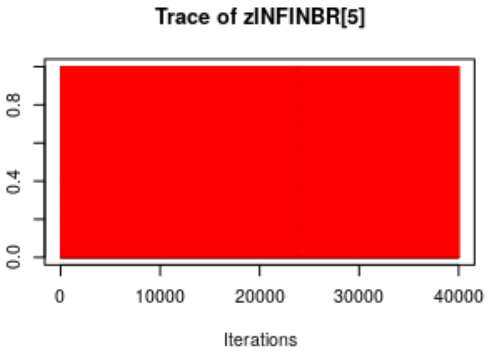
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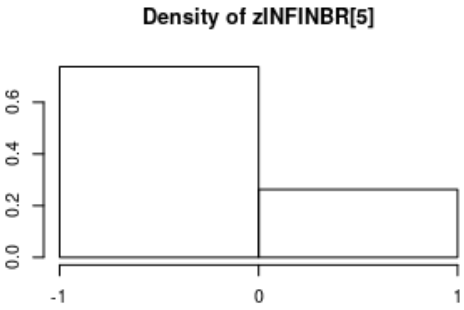
Iterations


Density of zINFINBR[5]
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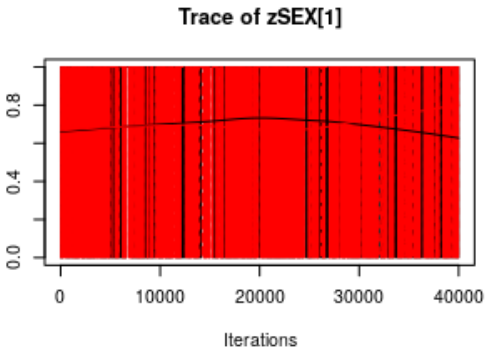
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10000
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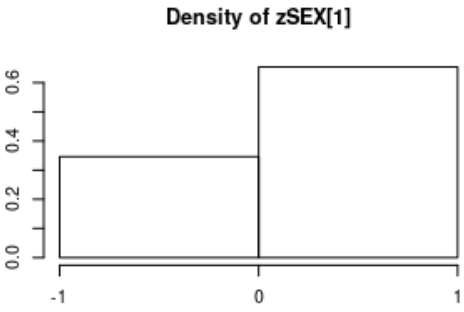
Iterations


Density of zSEX[1]
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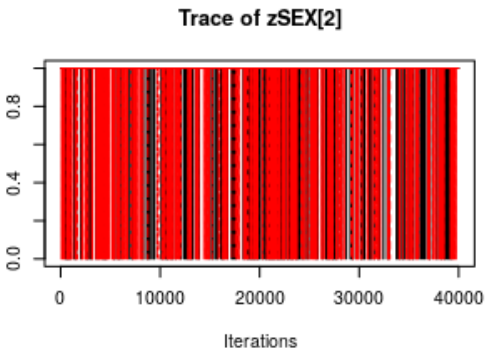
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10000
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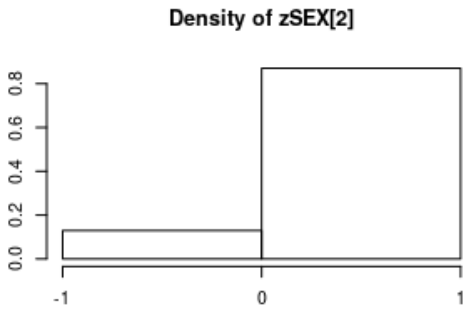
Iterations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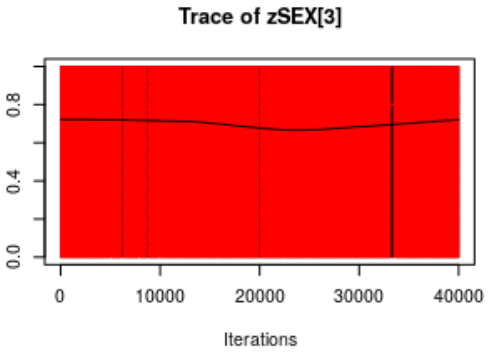
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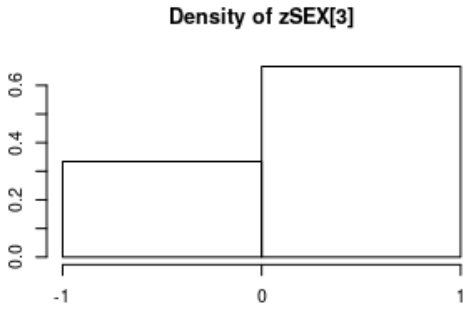
Density of zSEX[3]
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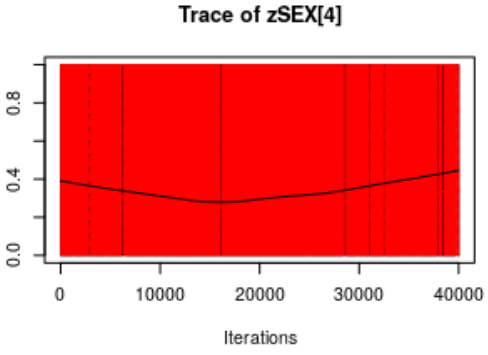
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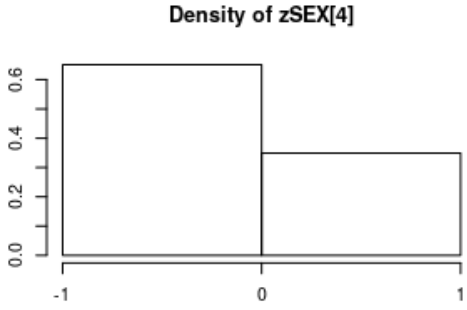
Iterations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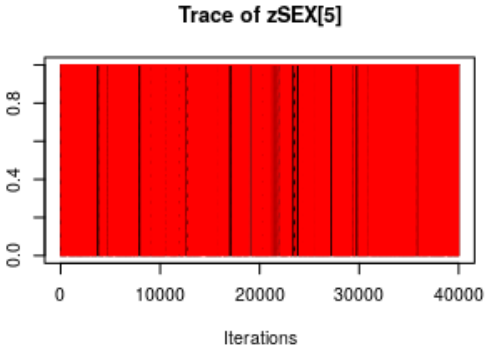
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30000
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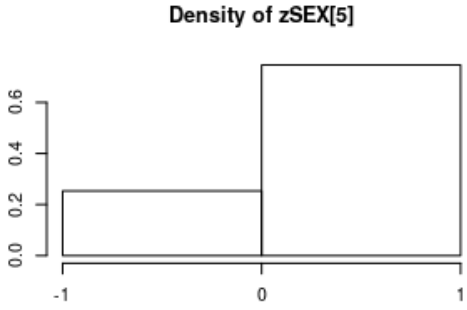
Iterations


Density of zSEX[5]
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0.4
0.6
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0
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Trace of zSEXINBR[1]
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10000
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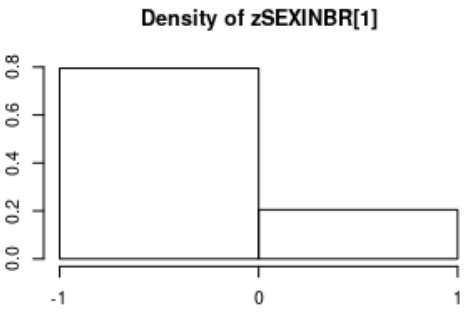
30000
40000
Iterations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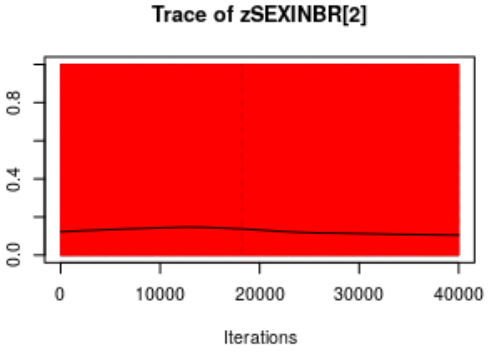
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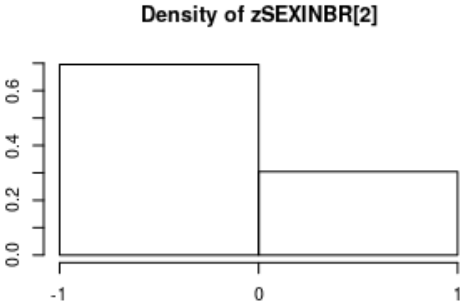
Iterations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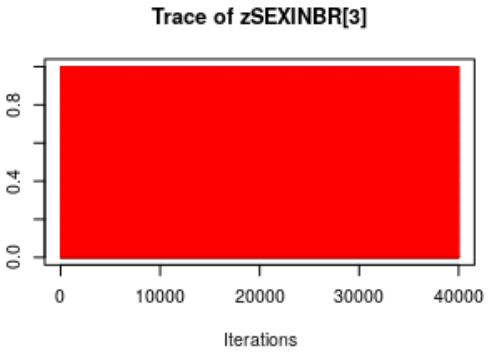
Trace of zSEXINBR[3]
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10000
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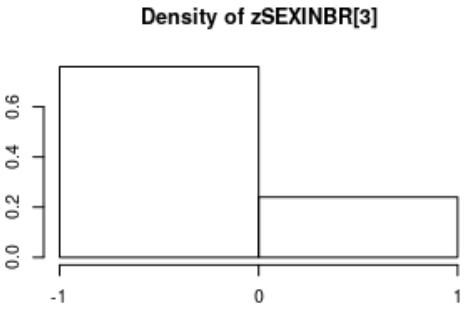
Iterations


Density of zSEXINBR[3]
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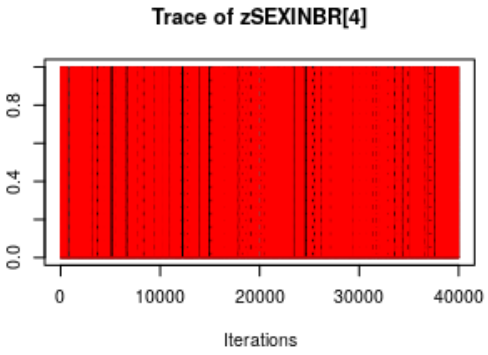
1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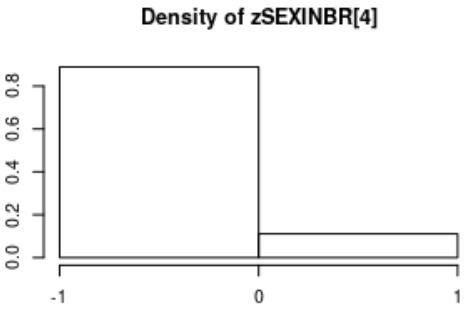
Iterations


Density of zSEXINBR[4]
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Trace of zSEXINBR[5]
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10000
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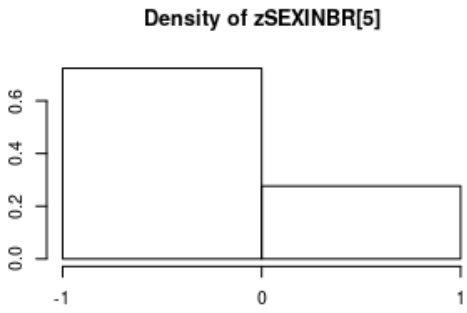
30000
40000
Iterations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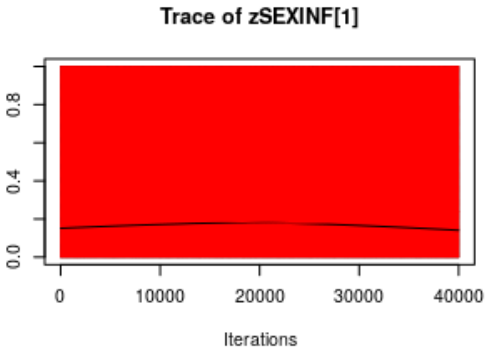
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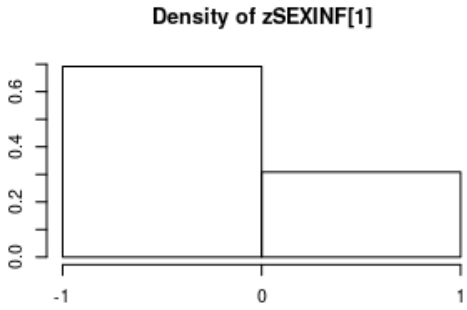
Iterations


Density of zSEXINF[1]
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0
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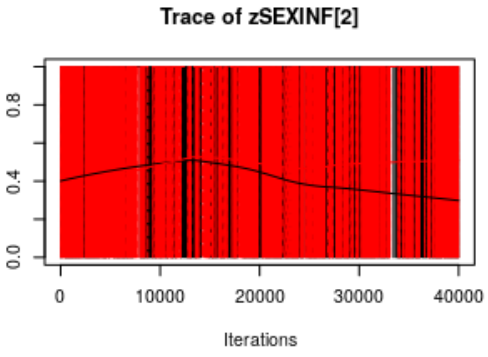
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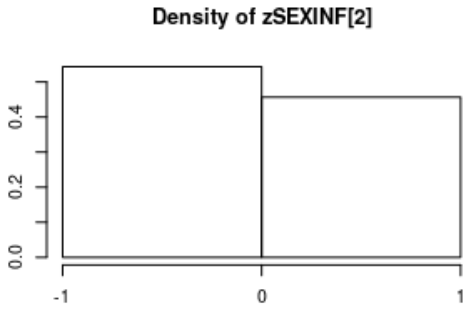
Iterations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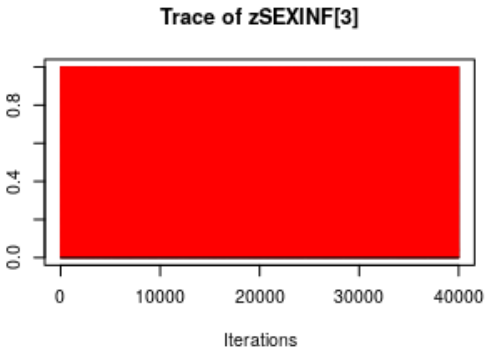
Trace of zSEXINF[3]
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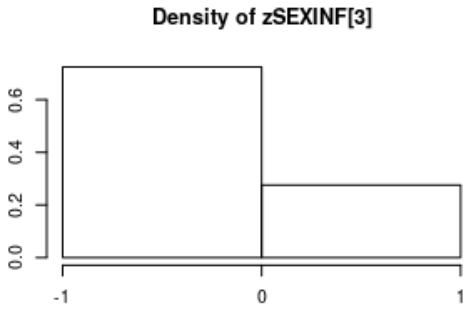
Iterations


Density of zSEXINF[3]
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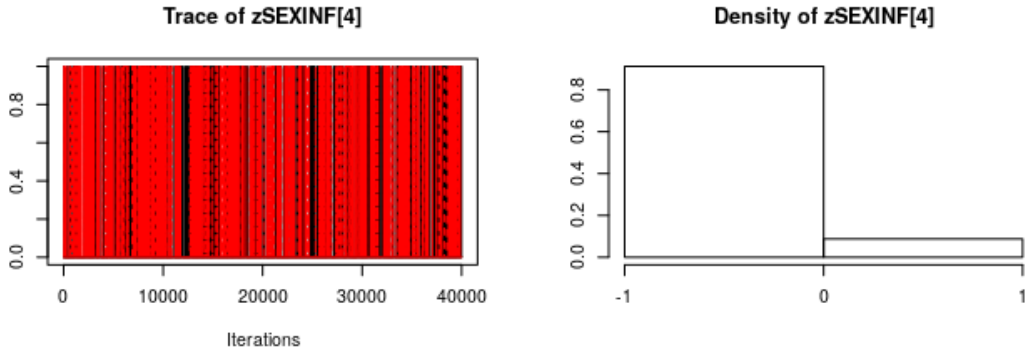
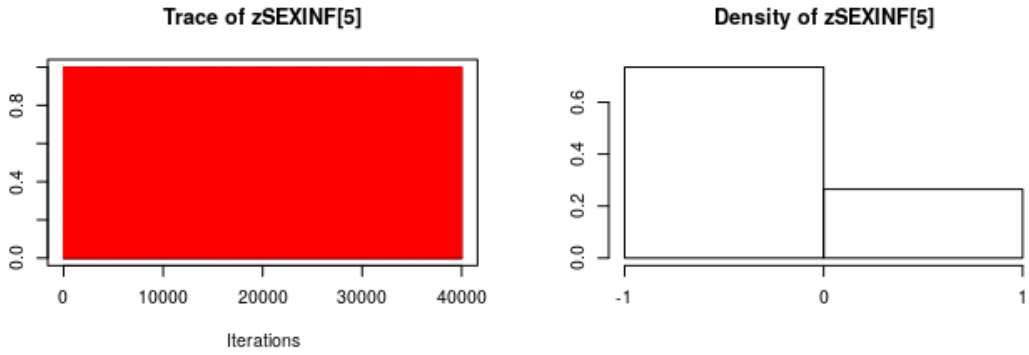




Look at posterior inclusion probabilities

Extract indicator information

```
## Marginal probabilities of inclusion for each variable
zNames <- model$expandNodeNames(c('z', 'zSEX', 'zINF', 'zINBR', 'zSEXI
NF', 'zSEXINBR', 'zINFINBR'))
zCols <- which(colnames(samples) %in% zNames)
binary <- as.data.table((samples[, zCols] != 0) + 0)
res <- binary[ , .N, by=names(binary)]
res <- res[order(N, decreasing = T)]
res <- res[, prob := N/dim(samples)[1]]
```

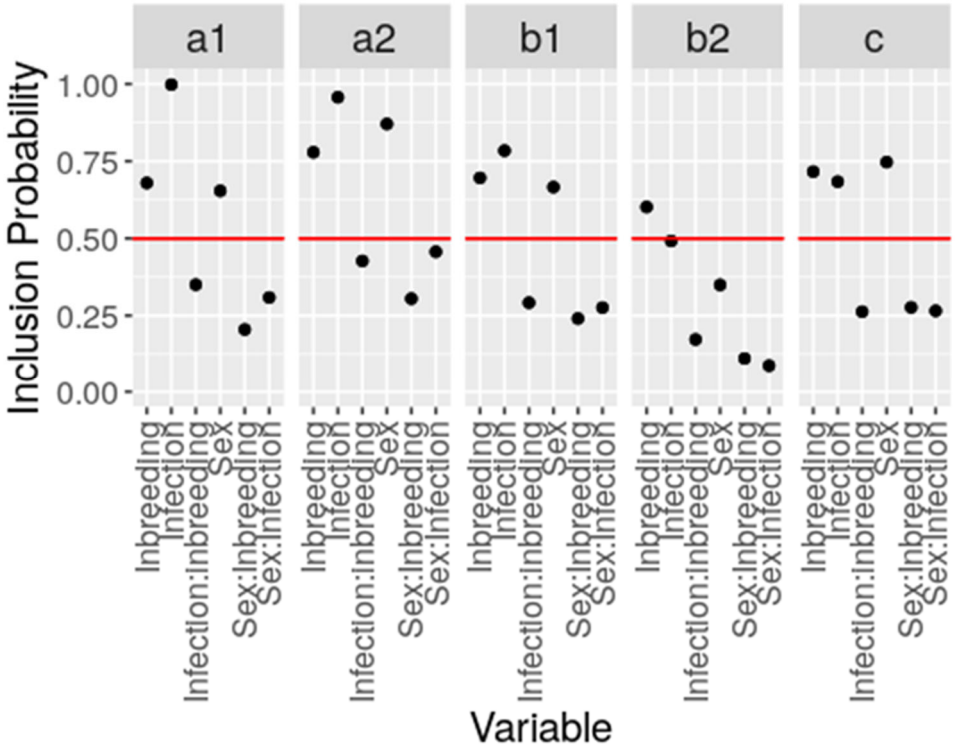
Prepare for plot

```
samples <- as.data.frame(samples)

z_indicators <- samples %>%
  select(c(37:66)) %>%
  colSums()

z_indicators <- data.frame(z_indicators/sum(res$N))

z_indicators$z <- rownames(z_indicators)
colnames(z_indicators) <- c("Inclusion_Prob", "z")
z_indicators$variable <- rep(c("Inbreeding", "Infection", "Infection:i
nbreeding", "Sex", "Sex:Inbreeding", "Sex:Infection"), each = 5)
```

```
z_indicators$Parameter <- rep(c("a1", "a2", "b1", "b2", "c"), times =
6)
```

Plot results

```
ggplot(z_indicators, aes(x = variable, y = Inclusion_Prob)) +
  geom_point() +
  geom_hline(yintercept = 0.5, colour = "red") +
  scale_y_continuous(limits = c(0,1)) +
  theme(axis.text.x = element_text(angle = 90)) +
  geom_point() +
  facet_grid(~Parameter) +
  geom_hline(yintercept = 0.5, colour = "red") +
  theme(strip.text.x = element_text(size = 15)) +
  theme(axis.text=element_text(size=12)) +
  theme(axis.title=element_text(size=15)) +
  theme(legend.text=element_text(size=10)) +
  theme(legend.title=element_text(size=15)) +
  labs(y = "Inclusion Probability", x = "Variable") +
  theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust=1))
```



Appendix 7 – Supplementary material from Chapter 8: General Discussion

R code for double censored individuals

```
## load libraries

library(nimble)

library(coda)

library(mcmcplots)

library(GGally)


## run simulation

rm(list = ls())

source("SimulateData/SimSilerCMRdata_500indiv.R")


## load custom distributions

source("../../Distributions/Dist_Siler.R")


## read in data

tKD <- readRDS("tKD.rds")

CH <- readRDS("CH.rds")

tKB <- readRDS("cub.rds")

CH[is.na(CH)] <- 0


## extract last alive time

tL <- apply(CH, 1, function(x) max(which(x == 1)))
```

```
names(tL) <- NULL

## extract first alive time
tF <- apply(CH, 1, function(x) min(which(x == 1)))
names(tF) <- NULL

## define censoring matrices for birth time
cintB <- cbind(tF - 4, tF)
cintB[is.na(tKB), 1] <- cintB[is.na(tKB), 2]
cintB[is.na(tKB), 2] <- cintB[is.na(tKB), 2] + 1
colnames(cintB) <- NULL
censoredB <- ifelse(is.na(tKB), 0, 1)
tB <- rep(NA, length(tKB))

## define censoring matrices for death time
cintD <- cbind(tL, tKD)
cintD[is.na(tKD), 2] <- cintD[is.na(tKD), 1]
cintD[is.na(tKD), 1] <- 0
colnames(cintD) <- NULL
censoredD <- ifelse(!is.na(tKD), 1, 2)
tD <- rep(NA, length(tKD))

## extract max possible capture time
tM <- ifelse(is.na(tKD), ncol(CH), tKD)
```

```
## extract min possible capture time
tm <- ifelse((tF - 3) < 0, 0, tF - 3)

## some checks
stopifnot(all(tL >= tF))
stopifnot(all(tKD[!is.na(tKD)] > tL[!is.na(tKD)]))
stopifnot(all(tM >= tL))
stopifnot(all(tm <= tF))

## set up dummy variables
dind <- rep(1, length(tKD))

## extract number of captures
y <- apply(CH, 1, sum)
names(y) <- NULL

## some checks
stopifnot(all(tM - tm >= y))

## set up nind
nind <- length(y)

## code for NIMBLE model with censoring
```

```
code <- nimbleCode({

  ## survival components for dead badgers
  for (i in 1:nind) {

    ## likelihood for interval-truncated Siler
    censoredB[i] ~ dinterval(tB[i], cintB[i, ])
    tB[i] ~ dflat()
    censoredD[i] ~ dinterval(tD[i], cintD[i, ])
    tD[i] ~ dsiler(a1, a2, b1, b2, c, tB[i])

    ## sampling component
    nm[i] <- max(ceiling(tB[i]), tm[i])
    nM[i] <- min(floor(tD[i]) - nm[i], tM[i] - nm[i])
    pd[i] <- exp(y[i] * log(mean.p) + (nM[i] - y[i]) * log(1 - mean.p))
    dind[i] ~ dbern(pd[i])
  }

  ## priors
  a1 ~ dexp(1)
  a2 ~ dexp(1)
  b1 ~ dexp(1)
  b2 ~ dexp(1)
  c ~ dexp(1)
```

```
    mean.p ~ dunif(0, 1)

  })

  ## set up other components of model
consts <- list(nind = nind, tM = tM, tm = tm)
data <- list(y = y, cintB = cintB, cintD = cintD,
             censoredB = censoredB, censoredD = censoredD,
             tD = tD, tB = tB, dind = dind)

    ## set initial values
    tBinit <- apply(cbind(cintB, censoredB), 1, function(x) {
      if(x[3] == 0) {
        y <- x[1] - rexp(1, 0.1)
      } else {
        y <- runif(1, x[1], x[2])
      }
      y
    })
    tDinit <- apply(cbind(cintD, censoredD), 1, function(x) {
      if(x[3] == 2) {
        y <- x[2] + rexp(1, 0.1)
      } else {
        y <- runif(1, x[1], x[2])
```

```
    }
    y
  })
inits <- list(
    tD = tDinit,
    tB = tBinit,
    a1 = 0.1,
    a2 = 0.1,
    b1 = 0.1,
    b2 = 0.1,
    mean.p = runif(1, 0, 1),
    c = 0.05
  )

## define the model, data, inits and constants
model <- nimbleModel(code = code, constants = consts, data = data, inits =
inits)

## compile the model
cModel <- compileNimble(model)

## try with adaptive slice sampler
config <- configureMCMC(cModel, monitors = c("a1", "a2", "b1", "b2", "c",
"mean.p", "tB", "tD"), thin = 1)
config$removeSamplers(c("a1", "a2", "b1", "c","b2"))
```

```
config$addSampler(target = c("a1", "b1"), type = 'AF_slice')
config$addSampler(target = c("a2", "c", "b2"), type = 'AF_slice')

#Check monitors and samplers
config$printMonitors()
config$printSamplers(c("a1", "a2", "b1", "b2", "c"))

#Build the model
built <- buildMCMC(config)
cBuilt <- compileNimble(built)

#Plot mcmcm0
system.time(runAF <- runMCMC(cBuilt,
                             niter = 10000,
                             nburnin = 2000,
                             nchains = 2,
                             progressBar = TRUE,
                             summary = TRUE,
                             samplesAsCodaMCMC = TRUE,
                             thin = 1))

## extract birth and death times
samples <- runAF$samples
```

```
tBpost <- as.matrix(samples) %>%
  as_tibble() %>%
  select(starts_with("tB"))
tDpost <- as.matrix(samples) %>%
  as_tibble() %>%
  select(starts_with("tD"))

## examine first few just to check
tBpost[, 1:6] %>%
  gather(ind, value) %>%
  ggplot(aes(x = value)) +
  geom_density() +
  facet_wrap(~ ind)

tBpost[, 1:6] %>%
  gather(ind, value) %>%
  group_by(ind) %>%
  summarise(min = min(value), max = max(value))

tDpost[, 1:6] %>%
  gather(ind, value) %>%
  ggplot(aes(x = value)) +
  geom_density() +
  facet_wrap(~ ind)
```

```
tDpost[, 1:6] %>%
  gather(ind, value) %>%
  group_by(ind) %>%
  summarise(min = min(value), max = max(value))

## plot mcmcm
samples <- runAF$samples[, 1:6]
#mcmcplot(samples)
# png("traceAF%d.png")
plot(samples)
# dev.off()
## throw away burnin
samples <- window(samples, start = 4000)
plot(samples)
## compare posteriors to true parameters
p1 <- samples %>%
  as.matrix() %>%
  as_tibble() %>%
  gather(parameter, value) %>%
  ggplot(aes(x = value)) +
  geom_density() +
  facet_wrap(~parameter, scales = "free")
truepars <- as.data.frame(t(readRDS("simpars.rds"))) %>%
```

```
  rename(`mean.p` = mean_p) %>%
  gather(parameter, value)
p1 <- p1 + geom_point(aes(x = value, y = 0), data = truepars)
p1 + ggtitle(paste0("Mean.p = ", truepars$value[truepars$Parameter ==
"mean.p"]))
ggsave("comppost.pdf")

## joint posteriors
p1 <- samples %>%
  as.matrix() %>%
  as_tibble() %>%
  ggpairs(lower = list(continuous = "density"), upper = list(continuous = "points"))
p1
ggsave("jointpost.png") ## just png here to save on file size
## save samples
saveRDS(samples, "newSiler.rds")
#Set age variable (quarter years)
x <- 0:80
## extract samples
samples <- as.matrix(samples)[, 1:5]
#Siler survival function
surv <- apply(samples, 1, function(pars, x) {
  ## extract pars
  a1 <- pars[1]
```

```
  a2 <- pars[2]
  b1 <- pars[3]
  b2 <- pars[4]
  c <- pars[5]

  ## return predictions
  psiler(x, a1, a2, b1, b2, c, lower.tail = 0)
}, x = x)
#Siler Mortality rate
mort <- apply(samples, 1, function(pars, x) {
  ## extract pars
  a1 <- pars[1]
  a2 <- pars[2]
  b1 <- pars[3]
  b2 <- pars[4]
  c <- pars[5]

  ## return predictions
  dsiler(x, a1, a2, b1, b2, c)
}, x = x)
mort <- mort / surv
## extract mean and 95% intervals
mort <- apply(mort, 1, function(x) {
```

```
  c(mean = mean(x), LCI = quantile(x, probs = 0.025), UCI = quantile(x, probs =
0.975))
})
## extract mean and 95% intervals
surv <- apply(surv, 1, function(x) {
  c(mean = mean(x), LCI = quantile(x, probs = 0.025), UCI = quantile(x, probs =
0.975))
})
## produce plots
pdf("survcurves.pdf", width = 10, height = 5)
par(mfrow = c(1, 2))
#Draw mortality curve
plot(x, mort[1, ], type = 'l', main = "Hazard function")
lines(x, mort[2, ], lty = 2)
lines(x, mort[3, ], lty = 2)
#Draw survival curve
plot(x, surv[1, ], type = "l", main = "Survivor function")
lines(x, surv[2, ], lty = 2)
lines(x, surv[3, ], lty = 2)
```

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