

1 **Industrial bees: the impact of apicultural intensification on local disease**  
2 **prevalence.**

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## 15 Abstract

- 16 **1)** It is generally thought that the intensification of farming will result in higher disease prevalences,  
17 although there is little specific modelling testing this idea. Focussing on honeybees, we build multi-  
18 colony models to inform how ‘apicultural intensification’ is predicted to impact honeybee pathogen  
19 epidemiology at the apiary scale.
- 20 **2)** We used both agent-based and analytical models to show that three linked aspects of apicultural  
21 intensification (increased population sizes, changes in population network structure, and increased  
22 between-colony transmission) are unlikely to greatly increase disease prevalence in apiaries.  
23 Principally this is because even low-intensity apiculture exhibits high disease prevalence.
- 24 **3)** The greatest impacts of apicultural intensification are found for diseases with relatively low  $R_0$  (basic  
25 reproduction number), however, such diseases cause little overall disease prevalence and therefore  
26 the impacts of intensification are minor. Furthermore, the smallest impacts of intensification are for  
27 diseases with high  $R_0$  values, which we argue are typical of important honeybee diseases.
- 28 **4) *Policy Implications:*** Our findings contradict the idea that apicultural intensification by crowding  
29 honeybee colonies in large, dense apiaries leads to notably higher disease prevalences for  
30 established honeybee pathogens. More broadly, our work demonstrates the need for informative  
31 models of all agricultural systems and management practices in order to understand the implications  
32 of management changes on diseases.

33 **Key Words:** apiculture, beekeeping, agriculture, intensification, infectious disease, mathematical model,  
34 agriculture, disease prevalence

## 35 Introduction

36 Infectious diseases have significant impacts on agricultural sustainability (Brijnath, Butler, & McMichael,  
37 2014) and profitability (James, 1981). A key question is how agricultural intensification and novel agricultural  
38 practices impact the emergence and epidemiology of infectious disease (Cressler, McLeod, Rozins, Hoogen,  
39 & Day, 2016; Gandon, Hochberg, Holt, & Day, 2013). It is generally assumed that intensification increases  
40 vulnerability to severe disease outbreaks (Jones et al., 2013; Kennedy et al., 2016; Mennerat, Nilsen, Ebert,  
41 & Skorping, 2010), but there is relatively little empirical data and therefore epidemiological theory is needed  
42 to address this problem (Atkins et al., 2013; Rozins & Day, 2016). Here we build specific models of apiary-  
43 level intensification in commercially farmed honeybees to examine the impact of industrial-scale  
44 management practices on honeybee infectious disease prevalence.

45 Honeybee health and the apicultural industry are under threat from a variety of pressures (Ghazoul, 2005;  
46 vanEngelsdorp & Meixner, 2010), including parasites and pathogens (Budge et al., 2015; De la Rúa, Jaffé,  
47 Dall'Olio, Muñoz, & Serrano, 2009; Potts et al., 2010). There is a growing body of literature documenting the  
48 damage that emerging or re-emerging diseases (Wilfert et al., 2016) are causing in apiculture (Jacques et al.,  
49 2017; Kielmanowicz et al., 2015) and native pollinators (Cohen, Quistberg, Philpott, & DeGrandi-Hoffman,  
50 2017; Fürst, McMahon, Osborne, Paxton, & Brown, 2014; Graystock, Blane, McFrederick, Goulson, &  
51 Hughes, 2016; Manley, Boots, & Wilfert, 2015; McMahon et al., 2015; McMahon, Wilfert, Paxton, & Brown,  
52 2018). Evidence exists supporting a link between the risk of these diseases and specific apicultural practices  
53 (Giacobino et al., 2014; Mõtus, Raie, Orro, Chauzat, & Viltrop, 2016; Pacini et al., 2016). However, the  
54 evidence is geographically limited, lacking in mechanistic underpinning, or contradictory even within this  
55 small collection of studies. For example, Mõtus et al. (2016) report that larger apiaries show marginally  
56 higher incidence of ectoparasitic *Varroa* mites in Estonia, whilst Giacobino et al. (2014) did not find this  
57 association in a similar study in Argentina. It is therefore critical that we learn how different apicultural  
58 practices impact disease outcomes (Brosi, Delaplane, Boots, & de Roode, 2017). The need for an  
59 epidemiological framing of honeybee diseases has been frequently discussed (Brosi et al., 2017; Fries &

60 Camazine, 2001) in both empirical (van Engelsdorp et al., 2013) and modelling (Becher, Osborne, Thorbek,  
61 Kennedy, & Grimm, 2013) studies, but we lack a modelling framework for disease ecology in honeybees at a  
62 scale larger than a single colony.

63 Honeybees are typically managed in apiaries, which are associated colonies placed together for beekeeping  
64 convenience at a single site. Pathogen dynamics at the apiary level are determined both by pathogen  
65 transmission within and between colonies. Intensification of apiculture changes apiary ecology in a number  
66 of ways, all potentially relevant to disease (Brosi et al., 2017). In particular, increasing the number of  
67 colonies and changing the arrangement of those colonies influences epidemiology through changes in both  
68 the size and network structure of the population. They both may also increase the rate at which transmission  
69 between colonies occurs via more frequent 'drifting' of honeybees (Free, 1958; Neumann, Radloff, Pirk, &  
70 Hepburn, 2003). Drift is a key mechanism of between-colony pathogen transmission (Goodwin, Perry, &  
71 Houten, 1994; Roetschi, Berthoud, Kuhn, & Imdorf, 2008) and has been invoked as an explanatory  
72 mechanism accounting for higher parasite prevalences in larger apiaries (Mötus et al., 2016).

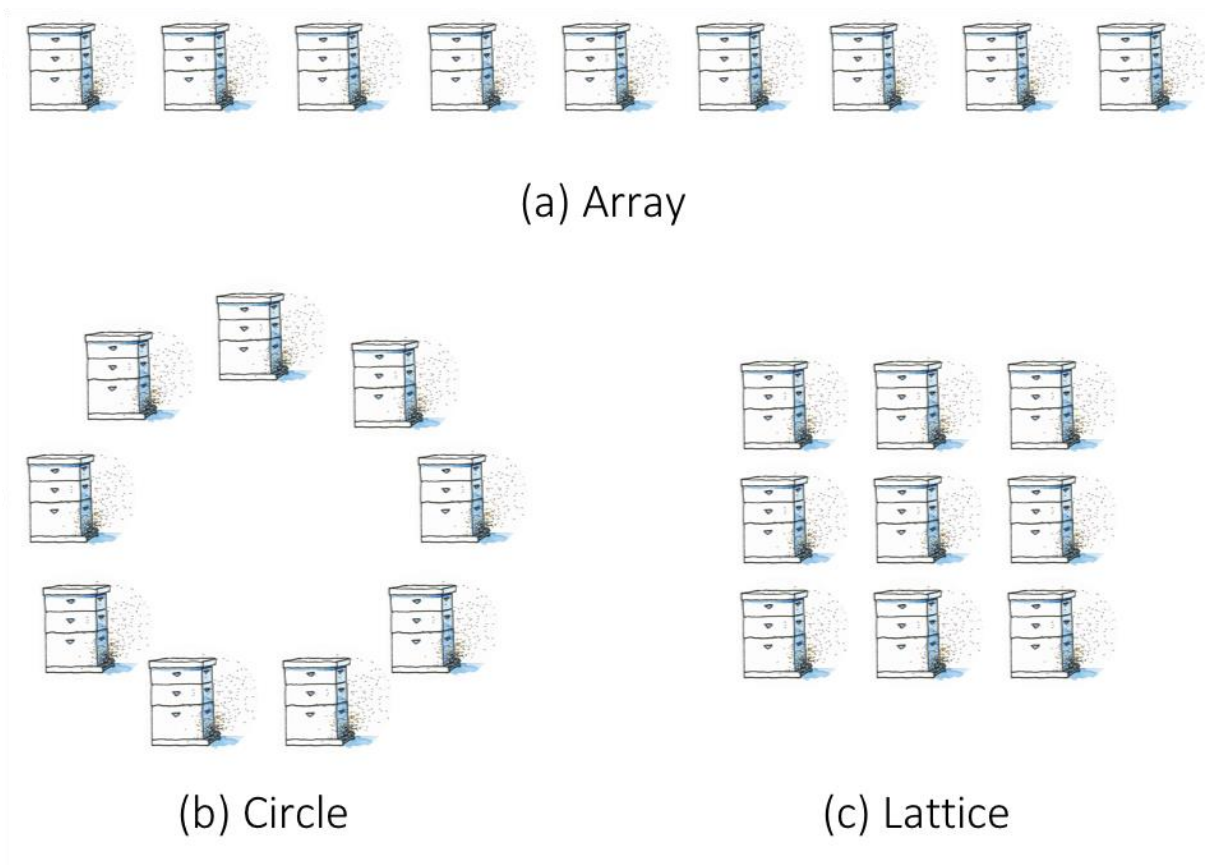
73 The intensification of agricultural systems generally means larger, denser population sizes and greater  
74 pathogen transmissibility at local (within a population, such as a farm) and landscape (between populations,  
75 such as neighbouring farms) scales. To understand these effects in honeybees we build multi-colony models  
76 to examine how apicultural intensification is predicted to impact honeybee pathogen epidemiology. We  
77 examine the epidemiological consequences of increasing the number of colonies within an apiary, changing  
78 colony configurations, and increasing between-colony pathogen transmission.

## 79 **Materials and Methods**

80 We combine mathematical models and agent-based model (ABM) simulations to make predictions on how  
81 intensification affects disease risk, spread, and endemic prevalence within an apiary. The key to our  
82 approach is that we capture pathogen transmission both within and between colonies.

83 We generalise colony arrangements to three unique configurations drawn from experience, classic  
84 apicultural literature (Jay 1966) and current experimental work (Dynes, Berry, Delaplane, Brosi, & de Roode,  
85 2019): array, circular and lattice (Fig. 1). We restrict between-colony pathogen transmission to nearest  
86 neighbours (see discussion), those in closest proximity to each other (connected by an arrow in Fig. 2).  
87 Between-colony transmission is always assumed to be at a lower rate than within colony transmission. The  
88 mathematical model allows us to obtain tractable analytical results while the ABM simulations allow us to  
89 model disease at the level of the individual bee and consider stochastic effects.

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93 **Figure 1.** Colony configurations, demonstrated for apiaries with nine colonies.

94 We first derive a compartmental SI (Susceptible, Infected) model for pathogen transmission within an apiary.  
 95 The model treats each colony as an individual population and allows for within colony as well as between-  
 96 colony transmission (for nearest neighbours). Within a colony, honeybees are either susceptible to infection  
 97 or infected (and infectious). We denote the number of susceptible honeybees in colony  $i$  at time  $t$  as  $S_i(t)$ .  
 98 Likewise, we denote the number of honeybees in colony  $i$  infected with the pathogen at time  $t$  as  $I_i(t)$ .  
 99 Susceptible honeybees in colony  $i$  become infected at rate  $\beta_{ij}$  following contact with an infected bee that  
 100 resides in colony  $j$ . We assume that honeybees do not recover from infection. Honeybees are born at rate  $\phi$ ,  
 101 have a natural mortality rate of  $m$ , and an additional mortality rate of  $v$  if infected. The following  $2n$   
 102 differential equations, [1], model disease transmission within and between  $n$  colonies in an apiary.

$$\frac{dS_i}{dt} = - \sum_{j=1}^n \beta_{ij} S_i I_j - m S_i + \phi \quad 103$$

104

$$\frac{dI_i}{dt} = \sum_{j=1}^n \beta_{ij} S_i I_j - (m + v) I_i \quad [1] \quad 105$$

106

107

108 The matrix  $\beta=[\beta_{ij}]$  will depend on the colony arrangement (see Fig. 1; and S.I. Section 1). The transmission  
 109 rate between a susceptible and infected honeybee within the colony is  $a$ , and transmission between  
 110 neighbouring colonies is  $b$ . For example, for a 9-colony apiary, the transmission matrices for an array,  
 111 circular and lattice configured apiary (respectively) are as follows:

$$112 \begin{bmatrix} a & b & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ b & a & b & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b & a & b & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & b & a & b & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & b & a & b & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & b & a & b & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & b & a & b & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & b & a & b \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & b & a \end{bmatrix}, \begin{bmatrix} a & b & 0 & 0 & 0 & 0 & 0 & 0 & b \\ b & a & b & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b & a & b & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & b & a & b & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & b & a & b & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & b & a & b & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & b & a & b & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & b & a & b \\ b & 0 & 0 & 0 & 0 & 0 & 0 & b & a \end{bmatrix}, \begin{bmatrix} a & b & 0 & b & 0 & 0 & 0 & 0 & 0 \\ b & a & b & 0 & b & 0 & 0 & 0 & 0 \\ 0 & b & a & 0 & 0 & b & 0 & 0 & 0 \\ b & 0 & 0 & a & b & 0 & b & 0 & 0 \\ 0 & b & 0 & b & a & b & 0 & b & 0 \\ 0 & 0 & b & 0 & b & a & 0 & 0 & b \\ 0 & 0 & 0 & b & 0 & 0 & a & b & 0 \\ 0 & 0 & 0 & 0 & b & 0 & b & a & b \\ 0 & 0 & 0 & 0 & 0 & b & 0 & b & a \end{bmatrix}$$

113

114 The corresponding network structures for the above transmission matrices can be seen in Fig. S1. We  
115 assume that honeybees are much more likely to become infected by a honeybee that resides within its home  
116 colony than by a honeybee from a neighbouring colony (i.e.  $a \gg b$ ). Note that for each apiary configuration to  
117 be possible and unique, the number of colonies ( $n$ ) must be a perfect square,  $n=L^2$  where  $L \geq 3$  (see Fig. 1).  
118 Therefore, the minimum number of colonies per apiary is 9, which has been observed to be the mean size of  
119 a hobbyist or small beekeeping operation (Mötus et al., 2016; Pocol, Marghitas, & Popa, 2012).

120 We complement our mathematical model [1] with the ABM; our ABM simulates pathogen spread, through  
121 individual bee movements, across an apiary. Apiaries are differentiated by the same characteristics as in the  
122 mathematical model; a description of the ABM is available in the S.I. (Section 2) and the model is publicly  
123 available (see S.I.). We use the ABM to simulate disease dynamics for both different pathogen phenotypes  
124 (varying both pathogen virulence and transmissibility) and different apiary ecologies (varied as previously  
125 described in the number of colonies per apiary, layout, and likelihood of bees moving between colonies) (S.I.  
126 Figs. S3 & S4); we compare the ABM to the analytical model and use it to test assumptions made elsewhere  
127 in the study (Fig. 4a, S.I. Fig. S6).

128 We can understand the dynamics presented by our models by focussing on the basic reproduction number,  
129  $R_0$ .  $R_0$  is a fundamental concept in infectious disease ecology, defined as the average number of secondary  
130 infections caused by one infectious individual in an otherwise entirely susceptible population (Anderson &  
131 May, 1992). We derive  $R_0$  expressions, using model [1], for each of the apiary configurations.  $R_0$  derivations  
132 using model [1] allow us to characterise the relationship between  $R_0$  and pathogen prevalence, defined as  
133 the proportion of honeybees within an apiary that are infected at the endemic equilibrium. The  $R_0$   
134 expressions for apiaries with  $n > 1$  colonies were calculated using the next generation method (van den  
135 Driessche & Watmough, 2002), (see S.I. Section 1).

$$R0_{Array} = \frac{\phi}{m(m+v)} \left( a - 2b \cos \frac{n\pi}{n+1} \right) \quad [2a]$$

$$R0_{Circle} = \frac{\phi}{m(m+v)}(a+2b) \quad [2b]$$

$$R0_{Lattice} = \frac{\phi}{m(m+v)}\left(a - 4b \cos \frac{\sqrt{n}\pi}{\sqrt{n}+1}\right) \quad [2c]$$

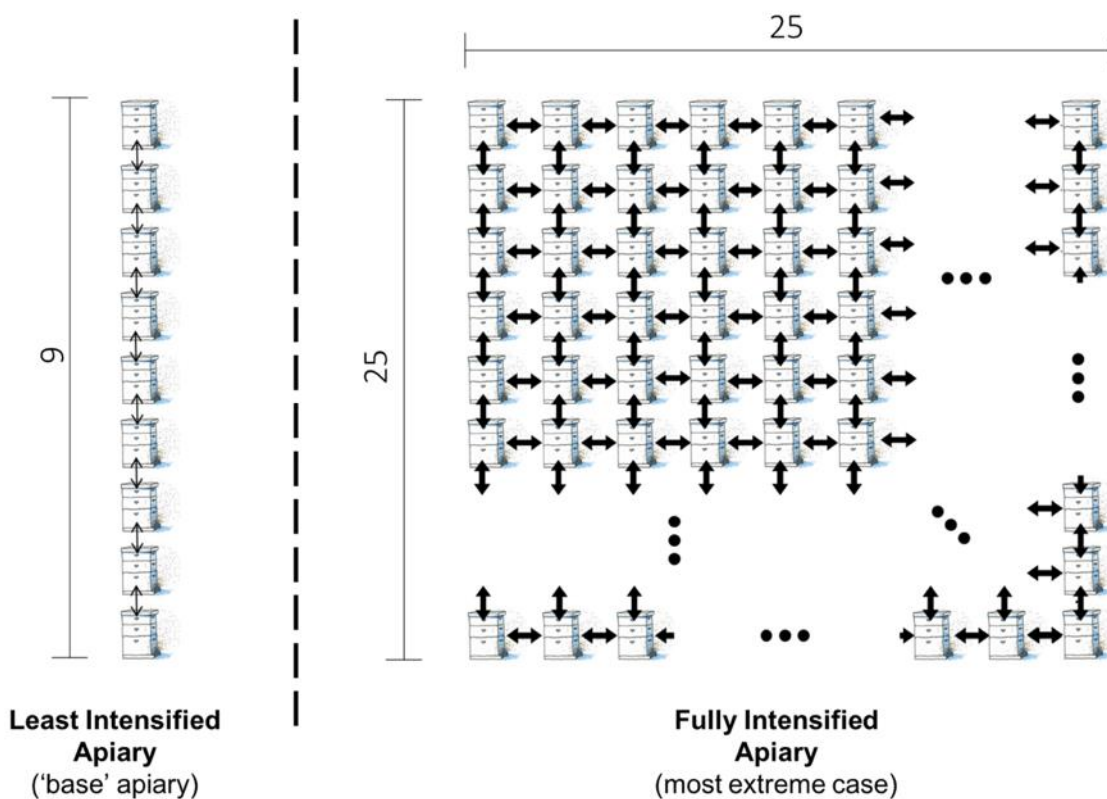
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137 For the ABM we estimate  $R_0$  values for particular parameter combinations by treating simulation outputs as  
 138 ideal empirical data (Keeling & Rohani, 2008) and track the number of infections following the index case.

139 The term ‘base  $R_0$ ’ is used throughout the remainder of this paper and refers to a value of  $R_0$  for a specific  
 140 pathogen phenotype in a least intensified apiary, an array with nine colonies (see Fig. 2). We determine how  
 141 intensification affects  $R_0$  by separating  $R_0$  into a ‘base  $R_0$ ’ and an ‘additional  $R_0$ ’. The term ‘additional  $R_0$ ’  
 142 refers to the observed difference in  $R_0$  for a given pathogen phenotype when comparing a ‘lower intensity’  
 143 apiary to a ‘high intensity’ one (Fig. 2)

144 An extreme, but plausible, example of intensification is used for these comparisons. Specifically, an increase  
 145 in colonies per apiary from 9 to 225 colonies, a change to a lattice configuration, and a tenfold increase in  
 146 between-colony infection (0.015 to 0.15 per bee per day), demonstrated in Fig. 2. The difference in the  $R_0$   
 147 before and after intensification is how we estimate ‘additional  $R_0$ ’. This permits the interaction (non-  
 148 additive) effects of our three aspects of intensification. The ‘additional  $R_0$ ’ can then be used in combination  
 149 with the analytically derived relationship between  $R_0$  and prevalence (see model [1] and equations [2a-c]) to  
 150 characterise how intensification affects disease prevalence. We focus on disease prevalence as both models  
 151 show rapid pathogen spread across apiaries, such that infection prevalence at the endemic equilibrium was  
 152 the major result differentiating modelling scenarios (S.I. Figs. S4 & S5).



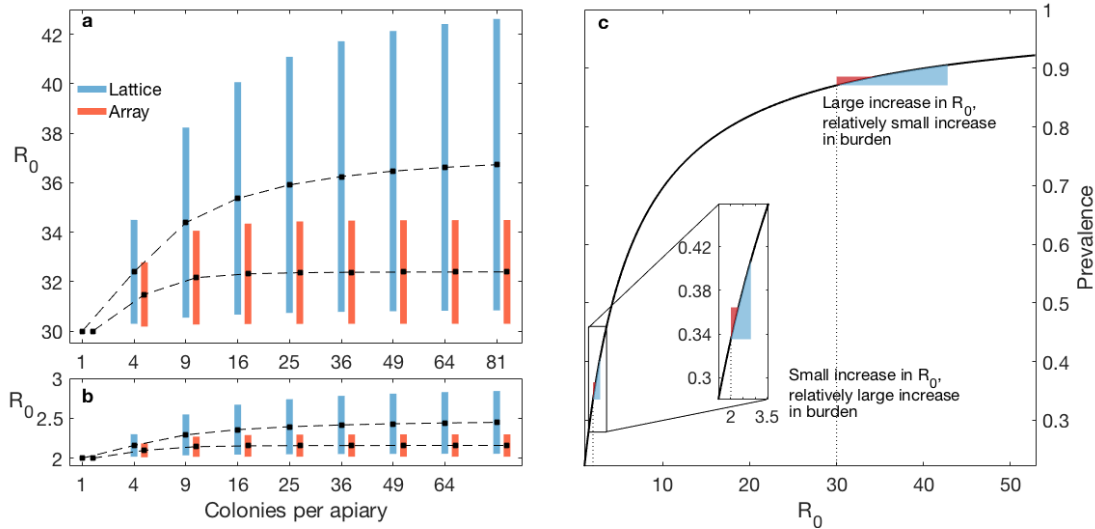


153 **Figure 2.** Illustrative schematic of the ‘intensification’ treatment as it is used in parts of this manuscript. We show the  
 154 apiary used to estimate ‘base  $R_0$ ’ (left) compared to the intensified apiary (right) reflecting an increase in number of  
 155 colonies from 9 to 225, a change from an array to a lattice, and a tenfold increase in movement of honeybees between  
 156 colonies (illustrated using arrow weight) from a likelihood of 0.015 per bee per day to 0.15. Note that for the intensified  
 157 apiary, not all 225 colonies are shown, with missing colonies denoted by ellipses (...).

158

## 159 Results

160 Our main results constitute three main characterisations of this system: the relationship between  $R_0$  and  
 161 pathogen prevalence; the effects of intensification on  $R_0$ ; and by combination of these relationships, the  
 162 effect of intensification on pathogen prevalence. The relationship between  $R_0$  and pathogen prevalence is  
 163 principally derived from the analytical model (presented first in these results) but is confirmed to broadly  
 164 agree with the agent-based model (presented second). The relationship between intensification and  $R_0$  is  
 165 principally derived from the ABM, presented second, but is partly explored in the analytical model presented  
 166 first. The critical overall result is the combination of these relationships, presented last and visualised in Fig.  
 167 5, demonstrating how intensification impacts disease prevalence. Detailed derivation, exploration, and  
 168 testing of both models is detailed in the Supplementary Information.



169

170 **Figure 3:** Relationships between number of colonies,  $R_0$ , and prevalence from model (1). Figures 3a and 3b demonstrate  
 171 that the effect on  $R_0$  for different degrees of intensification rapidly asymptotes, justifying our ‘single intensification’  
 172 treatment (Fig. 2). Figure 3c defines the relationship between  $R_0$  and prevalence, the shape of which critically  
 173 determines our main result (see Fig. 5). Technical description: **a)** When  $R_0=30$  for a single colony-apiary, the addition of  
 174 colonies yields a maximum increase in  $R_0$  of 12.7 for the lattice and 4.5 for the array. **b)** When  $R_0=2$  for a single colony,  
 175 there is a maximum increase in  $R_0$  of 0.85 for the lattice and 0.29 for the array, when colonies are added. Recall that the  
 176  $R_0$  for the circle is independent of  $n$  (see [2b]), and hence absent from the figure. Parameter values are set to:  $v=0.1$ ,  
 177  $m=0.0272$ ,  $\phi=1600$  and in a)  $a+b = 4.32485 \times 10^{-6}$  and in b)  $a+b = 6.48725 \times 10^{-5}$ . The transmissibility is what affects base  
 178  $R_0$ . Black dots are values where between-colony transmission is held at 10% of total transmission, with the bottom and  
 179 top of the bars representing 1% and 20% of the total transmission being between hives, ‘b’, respectively. **c)** The  
 180 relationship between  $R_0$  and disease prevalence. The range of  $R_0$  values is generated by varying the overall transmission  
 181 rate (i.e.  $a+b$ ) from  $2.143 \times 10^{-6}$  to  $1.178 \times 10^{-4}$  as reported by Roberts & Hughes (2015) for *Nosema ceranae*.

182

183 Both model [1] and the ABM simulations show that, for a given number of colonies per apiary,  $R_0$  is always  
 184 greatest for the lattice arrangement — the most highly connected configuration. As the number of colonies  
 185 per apiary increases (increasing  $n$ ), the values of  $R_0$  in both the array and lattice configurations increase (Fig.  
 186 3a & 3b), while the  $R_0$  for the circular configuration remains unchanged (see  $R_0$  equations). The increase in  $R_0$   
 187 from the addition of colonies asymptotes quickly due to convergence in the mean number of neighbours  
 188 across the apiary; this is also why the  $R_0$  for the circular apiary is independent of number of colonies as the  
 189 number of neighbours per colony remains two. This explains why  $R_0$  for an array arrangement approaches  
 190 the  $R_0$  value for a circular arrangement as the number of colonies increases.

191 If  $R_0 > 1$ , the pathogen will rapidly invade (see S.I. Section 1 &, Fig. S5) and each colony will reach a stable  
 192 population size and infection prevalence, called the endemic equilibrium (See S.I. Section 1). Mathematically

193 the disease prevalence at equilibrium for colony  $j$  is  $I_j^*/(I_j^*+S_j^*)$ , where  $S_j^*$  is the number of susceptible  
 194 honeybees and  $I_j^*$  is the number of infectious honeybees in colony  $j$  at equilibrium. The endemic equilibrium  
 195 for the circular configuration model can be solved explicitly (see S.I. Section 1). Due to symmetry, all colonies  
 196 within the circular apiary have disease prevalence at the endemic equilibrium of:

$$197 \quad \frac{\phi(a + 2b) - m(m + v)}{\phi(a + 2b) + v(m + v)}$$

198 We can approximate the endemic equilibrium for the lattice and array configured models using perturbation  
 199 theory, assuming  $0 < b \ll 1$  (See S.I. Section 1). The approximate disease prevalence in colony  $j$  at  
 200 equilibrium for a colony in the array or lattice configurations is:

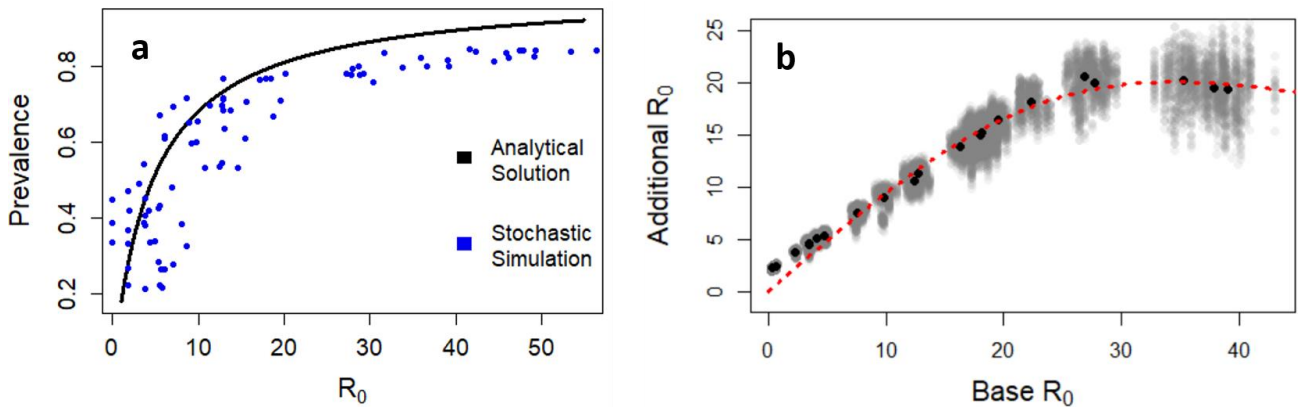
$$201 \quad \frac{\phi a^2 + lbm(m + v)}{\phi a^2 + a(m + v)^2 - blv(m + v)}$$

202 where  $l$  is the number of neighbours that colony  $j$  has. For any given set of parameters, we can therefore  
 203 formulate both  $R_0$  and prevalence, allowing us to characterise the relationship shown in Fig. 3c.

204 We show analytically, and in the ABM (S.I. Section 3) that intensification in the form of an increase in  
 205 colonies or an increase in movement between colonies increases  $R_0$  (Fig. 3a & 3b). Figure 4b shows the  
 206 additional  $R_0$  caused by our most extreme plausible changes in apiary management. The change in  $R_0$  caused  
 207 by increasing apiary size rapidly asymptotes (Fig. 3 a & b).

208 The effect of intensification is dependent on the base  $R_0$  – for small base  $R_0$ , intensification causes little  
 209 additional  $R_0$ , but at intermediate or high base  $R_0$ , intensification leads to large additional  $R_0$  (Fig. 4b). While  
 210 the increase in  $R_0$  is largest for an already large base  $R_0$ , this relationship saturates and the relative increase  
 211 in  $R_0$  for a given base  $R_0$  stays relatively constant for large base  $R_0$  values. The relationship shows a strong  
 212 nonlinearity when examining all three aspects of intensification in combination.

213



215 **Figure 4:** Results from the ABM. Figure 4a demonstrates the agreement between the ABM and analytical model; figure  
 216 4b presents the critical relationship estimated from the ABM relating base  $R_0$  to the increase in  $R_0$  following  
 217 intensification (see Fig. 2), the shape of which critically determines our main result (see Fig. 5). Technical description: **a)**  
 218 shows agreement between the stochastic simulations (ABM) and analytical model (Fig. 3c); using the following  
 219 equivalent model parameterisation to that for Fig. 3c: Circular configuration,  $n = 9$ ,  $M = 58200$ ,  $\phi = 1600$ ,  $5 \times 10^{-6} \leq \beta \leq$   
 220  $1 \times 10^{-4}$ ,  $v = 0.1$ ,  $\rho = 0.1$  (see S.I. Section 2). **b)** examines how an extreme example of intensification (see Fig. 2) alters  $R_0$   
 221 across a range of different ‘base  $R_0$ ’ values determined by pathogen phenotype using the ABM. Grey points represent  
 222 individual simulation comparisons, black points represent mean values. Base  $R_0$  values are unevenly distributed across  
 223 the range due to  $R_0$  being an emergent property of the system in both plot panels. We derive a non-linear relationship  
 224 between ‘base  $R_0$ ’ and ‘additional  $R_0$ ’ for panel **b**, corresponding to Fig. 2 (see Fig. 2 for panel **b** parameterisation,  
 225 otherwise as listed for **a**, plotted as a dashed red line. Variation within clusters is a result of the stochastic simulations.

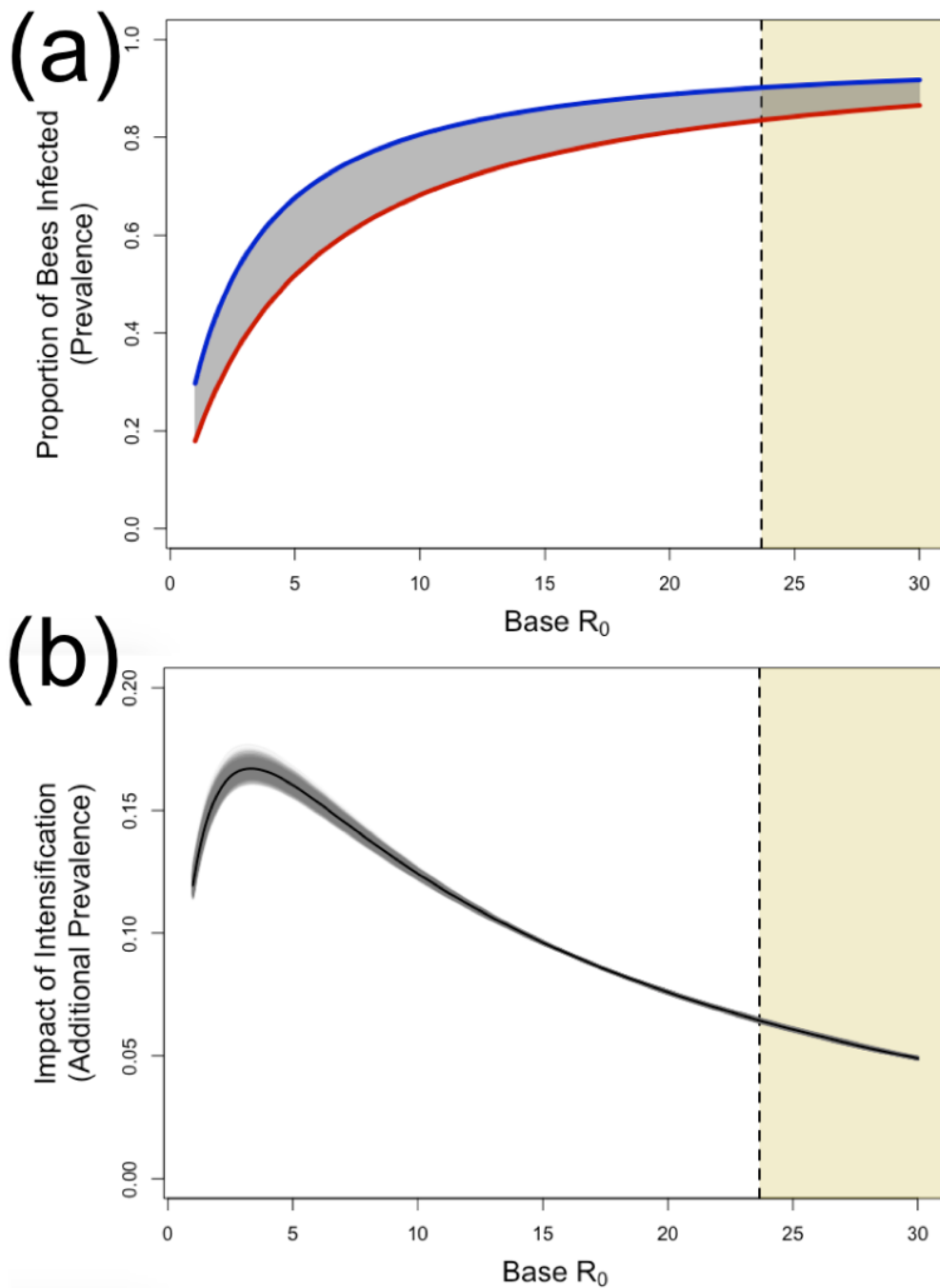
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227 By understanding the effect of intensification on  $R_0$  (Fig. 4b) and by characterising the relationship between  
 228  $R_0$  and disease prevalence (Fig. 3c, Fig. 4a), we can show how intensification impacts disease prevalences.  
 229 We approximate the non-linear relationship between ‘base  $R_0$ ’ (pathogen phenotype) and the ‘additional  $R_0$ ’  
 230 (effect of intensification) in Fig. 4b. We use a bootstrapping approach to create 1000 subsamples (subsample  
 231 size = 10% of full sample with replacement) of our combined approach. Each subsample is used to generate  
 232 a non-linear model of the form  $y = ax / (b + x^c)$ , where  $y$  is ‘additional  $R_0$ ’ and  $x$  is ‘base  $R_0$ ’, using a nonlinear  
 233 least squares approach in R (v 3.3.1). The relationship generated using the full sample is plotted in Fig. 4b.

234 We combine this relationship characterising how base  $R_0$  affects intensified additional  $R_0$  (Fig. 4b) with the  
 235 derived relationship between  $R_0$  and pathogen prevalence shown in Fig. 3c, allowing us to predict how  
 236 intensification impacts prevalences (Fig. 5). Fig. 5a shows the proportion of bees infected by a given (base  $R_0$ )  
 237 pathogen for the two apiaries in Fig. 2. The difference in disease prevalence between these lines is the  
 238 impact of intensification and is plotted in Fig. 5b. Fig. 5b shows a distinctly peaked relationship between base

239  $R_0$  and the impact of intensification, with the impact of intensification peaking around base  $R_0 = 3.3$ , and  
240 then rapidly declining. Even at its peak, the effect of intensification (which is as extreme as plausible), leads  
241 to an additional ~18% of bees infected at disease equilibrium. We present figure 5 as a the most important  
242 graphic for understanding the overall conclusions of this study, as the apparent ‘small’ shift in  $R_0$  required to  
243 double prevalence (Fig. 3c and 4a) is actually very difficult to achieve for low  $R_0$  pathogens (see Fig. 3b, 4b),  
244 resulting in the ‘maximum plausible’ change shown by the peak in Fig. 5b (~18.5%).

245 We contextualize these results by calculating an estimate of the lower-bound of  $R_0$  value for a honeybee  
246 pathogen (see highlighted regions in Fig. 5). We identified this region based on empirical data for the  
247 microsporidian pathogen *Nosema ceranae*; this was the only pathogen for which experimentally derived  
248 transmission rates as well as robust information on mortality due to infection is available (Martín-Hernández  
249 et al., 2011; Paxton, Klee, Korpela, & Fries, 2007; Roberts & Hughes, 2015). To estimate the plausible  $R_0$   
250 boundary in our model for this pathogen, we parameterised our mathematical model using the lowest  
251 empirically supported transmission value with the highest supported additional mortality, and fixed  
252 movement of honeybees between colonies at its lowest supported natural rate (Currie & Jay, 1991). We  
253 then calculated the  $R_0$  for a circular apiary due to its scale independence.



254

255 **Figure 5:** Depictions of our critical finding characterising the maximum (peak), and likely (shaded region),  
 256 increases in prevalence of a pathogen following local intensification of apiculture. High prevalence even in ‘low  
 257 intensity’ (see Fig. 2) systems yields little opportunity for large increases in prevalence. Panel (a) shows the  
 258 proportion of bees infected (prevalence) in non-intensified apiaries (lower red line) compared to intensified  
 259 apiaries (upper blue line), take from the mean values derived in Fig. 4b and the relationship shown in Fig. 3c.  
 260 The shaded grey area between these curves is the additional prevalence caused by intensification – the  
 261 ‘impact of intensification’. This is plotted in panel (b) where the black line represents the mean relationship,  
 262 and the grey lines represent 1000 bootstrapped samples. The vertical dashed line and yellow-shaded region of  
 263 the graphs to the right of the dashed line show a lowest estimated value of  $R_0$  for *Nosema ceranae*. Figures  
 264 start at  $R_0 = 1.0008$ .

## 265 Discussion

266 Our results present a counterintuitive picture of apicultural intensification and its consequences on  
267 disease prevalence within apiaries. Even in their most plausibly extreme cases, changes in the  
268 number of colonies, their spatial arrangement, and transmission rates between colonies (reflecting  
269 management intensification (Brosi et al., 2017)) had only a small effect on the severity of disease at  
270 the apiary level for pathogens of interest. Apicultural intensification leads to large gains in  $R_0$  when  
271  $R_0$  is initially high and small gains in  $R_0$  when  $R_0$  is initially low (Fig. 4b). However, increases in  $R_0$   
272 cause large increases in prevalence only when  $R_0$  is initially low (Fig. 3c, 4a). Pathogens with a base  
273  $R_0 \approx 3$  benefit most from intensification in terms of increased prevalence (Fig. 5); As discussed below,  
274 we argue that there is likely to be a high base  $R_0$  in important honeybee diseases and therefore our  
275 models suggest that there is likely to be little effect of apiary-scale intensification on disease  
276 prevalences. However, if a pathogen emerges with a relatively low  $R_0$ , our model does indicate that  
277 extreme intensification could lead to a significant increase in prevalence of approximately 18.5%.  
278 Therefore, if intensification increases the risk of novel pathogen emergence, then these newly  
279 emerged pathogens would benefit from intensification, as it would significantly increase their  
280 disease prevalence, relative to the pre-intensified apiary.

281 Our models most closely resemble the ecology of a directly transmitted microparasite able to infect  
282 individual honeybees at any life stage, conceptually similar to the microsporidian pathogens *Nosema*  
283 spp. (Fantham & Porter, 1912). *Nosema* is a major concern to beekeepers worldwide (Higes et al.,  
284 2008, 2009; Paxton, 2010), and has a minimum estimated base  $R_0$  of 23 (Fig. 5) when modelled here.  
285 We found that apicultural intensification, in the context of a pathogen with an initial  $R_0$  of 23, leads  
286 to a maximum 6.6% increase in disease prevalence. Our models predicted disease prevalences of up  
287 to 90% (Fig. 3, Fig. 5; S.I. Section 3), which while high, are empirically supported for the honeybee  
288 system (Higes et al., 2008; Kielmanowicz et al., 2015), and feature in other modelling studies that  
289 use similar transmission parameters to ours (Betti, Wahl, & Zamir, 2014). *Nosema* was the only

290 pathogen for which there are direct empirical studies characterising its transmissibility, however,  
291 other honeybee pathogens such as deformed wing virus are also well studied. While estimating an  
292  $R_0$  for DWV is difficult due to active management by beekeepers, maximum reported prevalences  
293 that may be indicative of its true ‘unmanaged’  $R_0$  are high, for example 73% in Natsopoulou et al.  
294 (2017), 80% in Budge et al. (2015), and 100% in Stamets et al. (2018). These high prevalences are  
295 consistent with high  $R_0$  values (Fig. 3c, Fig. 4a, & S.I. (Section 3)).

296 We additionally explored the behaviour of a more specific model, using an age-structured approach  
297 to infection dynamics, where only larvae are vulnerable to infection and develop into infectious  
298 adults with a high pathogen-associated mortality (as might be appropriate for pathogens such as the  
299 acute paralysis virus complex (Martin, 2001)), presented in the S.I. (Section 3). Convergence to  
300 equilibrium happens more slowly than the main model presented here, but still occurs quickly  
301 (within a single beekeeping season; see S.I. 3 Fig. S7). However adult-bee infection prevalence is far  
302 lower than seen in our SI model (S.I. Fig. S7) – this is in agreement with observations of lower  
303 prevalence of paralysis viruses (Budge et al., 2015). Notably, the endemic equilibrium prevalence  
304 increases only by small magnitudes as movement between colonies or apiary sizes are drastically  
305 increased (S.I. Fig. S7), in agreement with our main general result. This equivalence in behaviour  
306 between different models reflecting large disparities in infection mechanics and different endemic  
307 prevalences demonstrates that these results are likely generalisable to many honeybee pathogens.

308 We find rapid spread of a given pathogen across an apiary, which quickly reaches endemic  
309 equilibrium (S.I. Figs. S4-S6). While pathogens with a higher  $R_0$  reach this equilibrium more quickly,  
310 there is universally rapid spread. Given this result, we mainly focussed on the disease prevalence  
311 experienced at endemic equilibrium. Despite assuming transmission only to nearest neighbours,  
312 pathogen spread occurs rapidly, and the nearest neighbour assumption alters this very little when  
313 removed or relaxed (see S.I. Fig. S6). The rate at which epidemics are established in our model is also  
314 in agreement with other honeybee pathogen models. For example, Jatulan, Rabajante, Banaay,



315 Fajardo, & Jose (2015) show a single infectious adult causes an American Foulbrood (*Paenibacillus*  
316 *larvae*) epidemic that peaks within 50 days. Whilst they do not explicitly find an  $R_0$  for *P. larvae*, the  
317 short timescales characterising their epidemics are in line with ours (S.I. Section 3), suggesting high  
318  $R_0$  values and that their model would behave similarly to ours at an apiary scale.

319 Our inter-colony transmission can be understood to capture multiple processes arriving from  
320 beekeeper management such as brood transplantation or reduced distance between colonies (Brosi  
321 et al., 2017) as well as recognised transmission routes such as honeybee drift (Jay, 1965). Our  
322 approach was informed by studies which have focussed on how changes in the number of colonies  
323 and apiary configurations (Jay, 1966, 1968) alter drift (Dynes et al., 2017). Links between drift-  
324 mediated pathogen transmission and colony numbers have been documented for a variety of  
325 pathogens (Seeley & Smith, 2015) – including brood specialised and non-specialised, micro- and  
326 macro- parasites (Belloy et al., 2007; Budge et al., 2010; Dynes et al., 2017; Nolan & Delaplane,  
327 2017). Larger numbers of colonies per apiary are a driver of higher drift (Currie & Jay, 1991), as are  
328 changes in apiary arrangement (Jay, 1966; Dynes, Berry, Delaplane, Brosi, & Roode, 2019). While  
329 beekeepers typically maintain equal distances between their colonies regardless of how many  
330 colonies are in the apiary (such that larger apiaries have a bigger area footprint), our approach of  
331 increasing between-colony transmission in larger apiaries would also capture any additional  
332 transmission from spatial crowding.

333 Two clear candidates for future development of this model include seasonality and demography,  
334 which are closely linked. Honeybee demography within a colony influences epidemiology (Betti,  
335 Wahl, & Zamir, 2016) due in part to the temporal polyethism of task allocation influencing exposure  
336 and immunity (Calderone & Page, 1996), as well as the flexible ability of honeybees to regain  
337 immune function when they revert roles (Amdam et al., 2005; Robinson, Page, Strambi, & Strambi,  
338 1992). However, patterns in how age and immunosenescence in honeybees relates to survival and  
339 infectiousness remain complicated (Roberts & Hughes, 2014). Analytically tractable models

340 accounting for the role of this complex demography in understanding stress in a colony have only  
341 recently been developed (Boaton, Iwasa, Marshall, & Childs, 2017), and extending these models to  
342 incorporate diseases at the apiary scale is challenging. However, notable phenomena worth pursuing  
343 include: the role of male bees, which are known to be more easily infected, more infectious, and  
344 more likely to drift between colonies (Currie & Jay, 1991; Roberts & Hughes, 2015); as well as the  
345 role of robbing – where honeybees invade other colonies to steal food (Fries & Camazine, 2001;  
346 Lindström, Korpela, & Fries 2008).

347 At broader scales, overstocking of colonies may lead to resource limitation and consequently  
348 impaired immune function (Al-Ghamdi, Adgaba, Getachew, & Tadesse, 2016; Pasquale et al., 2013).  
349 These effects are important for a broader understanding of honeybee epidemiology, but should be  
350 separated from the within-apiary processes studied here. Additionally, most honeybee infectious  
351 diseases are caused by multi-host pathogens shared with other wild bees (Fürst et al., 2014; Manley  
352 et al., 2015; McMahon et al., 2015, 2018). Honeybee colony density across a landscape therefore has  
353 implications for wild pollinator health (Cohen et al., 2017; Graystock et al., 2016), however our  
354 results suggest that increased stocking of honeybees may have smaller impacts on local pollinator  
355 infectious disease dynamics than may have been previously thought.

356 Other industrialised agricultural livestock systems reflect extreme host densities similar to those in  
357 this study. However, the  $R_0$  for honeybee diseases may exceed that of other livestock diseases. We  
358 compare our lower threshold estimate for the  $R_0$  of *N. ceranae* to all available  $R_0$  values for livestock  
359 diseases that we could readily find in the literature (Fig. S9, see S.I. Section 4). Notably, all other  
360 livestock diseases for which  $R_0$  estimates exist show minimum  $R_0$  values far below our honeybee  
361 estimate, however examples of agricultural  $R_0$  values as high or higher than those we present for  
362 honeybees do also exist. There is therefore a clear need to develop explicit models of agricultural  
363 intensification scenarios for important agricultural disease.

364 Overall, our findings represent the first stage in developing robust epidemiological models for  
365 studying honeybee pathogens at an apiary scale. In the face of increasing challenges to global  
366 apiculture, our models predict that the size of apiaries *per se* is not causing notable increases in  
367 disease prevalence for important established bee pathogens, while it may increase the risk of  
368 pathogen emergence. Finally, this study demonstrates that conventional thought on how  
369 agricultural intensification influences disease may not be robust in the face of system-specific  
370 ecological nuance.

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### 377 **Authors' Contributions**

378 All authors contributed to conceptualisation and scope definition of the study. LJB, CR, MB  
379 developed approach. Mathematical modelling was undertaken by CR, AW, and MB. Computational  
380 modelling by LJB, KD, and MB. Model scope and parameterisation by LJB, KD, JCdR, BJB, LW. LJB and  
381 CR created figures, interpreted results and drafted manuscript with guidance and input from all  
382 authors. All authors contributed to further drafting, revision, and finalisation. All authors approved  
383 the final version for publication.

### 384 **Data Accessibility**

385 The agent-based model is made available in association with this manuscript via Dryad Digital  
386 Repository doi:10.5061/dryad.rn2j5p0 (Bartlett et al. 2019).

### 387 **References**

388 Al-Ghamdi, A., Adgaba, N., Getachew, A., & Tadesse, Y. (2016). New approach for determination of  
389 an optimum honeybee colony's carrying capacity based on productivity and nectar secretion  
390 potential of bee forage species. *Saudi Journal of Biological Sciences*, 23(1), 92–100.  
391 doi:10.1016/j.sjbs.2014.09.0209

392 Amdam, G. V., Aase, A. L. T. O., Seehuus, S.-C., Kim Fondrk, M., Norberg, K., & Hartfelder, K. (2005).  
393 Social reversal of immunosenescence in honey bee workers. *Experimental Gerontology*,  
394 40(12), 939–947. doi:10.1016/j.exger.2005.08.004

395 Anderson, R. M., & May, R. M. (1992). *Infectious diseases of humans: dynamics and control* (Vol. 28).  
396 Wiley Online Library.

397 Atkins, K. E., Read, A. F., Savill, N. J., Renz, K. G., Islam, A. F., Walkden-Brown, S. W., & Woolhouse,  
398 M. E. J. (2013). Vaccination and Reduced Cohort Duration Can Drive Virulence Evolution:  
399 Marek's Disease Virus and Industrialized Agriculture. *Evolution*, 67(3), 851–860.  
400 doi:10.1111/j.1558-5646.2012.01803.x

401 Bartlett, L. J., Rozins, C., Brosi, B. J., Delaplaine, K. S., de Roode, J. C., White, A., Wilfert, L., Boots, M.  
402 (2019) Data files: ABM Simulation Code from: Industrial bees: the impact of apicultural  
403 intensification on local disease prevalence. Dryad Digital Repository  
404 doi:10.5061/dryad.rn2j5p0

405 Becher, M. A., Osborne, J. L., Thorbek, P., Kennedy, P. J., & Grimm, V. (2013). REVIEW: Towards a  
406 systems approach for understanding honeybee decline: a stocktaking and synthesis of  
407 existing models. *Journal of Applied Ecology*, 50(4), 868–880. doi:10.1111/1365-2664.12112

408 Belloy, L., Imdorf, A., Fries, I., Forsgren, E., Berthoud, H., Kuhn, R., & Charrière, J.-D. (2007). Spatial  
409 distribution of *Melissococcus plutonius* in adult honey bees collected from apiaries and  
410 colonies with and without symptoms of European foulbrood. *Apidologie*, 38(2), 136–140.

411 Betti, M. I., Wahl, L. M., & Zamir, M. (2016). Age structure is critical to the population dynamics and  
412 survival of honeybee colonies. *Royal Society Open Science*, 3(11), 160444.  
413 doi:10.1098/rsos.160444

414 Betti, Matt I., Wahl, L. M., & Zamir, M. (2014). Effects of Infection on Honey Bee Population  
415 Dynamics: A Model. *PLOS ONE*, *9*(10), e110237. doi:10.1371/journal.pone.0110237

416 Booton, R. D., Iwasa, Y., Marshall, J. A. R., & Childs, D. Z. (2017). Stress-mediated Allee effects can  
417 cause the sudden collapse of honey bee colonies. *Journal of Theoretical Biology*, *420*, 213–  
418 219. doi:10.1016/j.jtbi.2017.03.009

419 Brijnath, B., Butler, C. D., & McMichael, A. J. (2014). In an interconnected world: joint research  
420 priorities for the environment, agriculture and infectious disease. *Infectious Diseases of*  
421 *Poverty*, *3*, 2. doi:10.1186/2049-9957-3-2

422 Brosi, B. J., Delaplane, K. S., Boots, M., & de Roode, J. C. (2017). Ecological and evolutionary  
423 approaches to managing honeybee disease. *Nature Ecology & Evolution*, *1*(9), 1250.  
424 doi:10.1038/s41559-017-0246-z

425 Budge, G. E., Barrett, B., Jones, B., Pietravalle, S., Marris, G., Chantawannakul, P., ... Brown, M. A.  
426 (2010). The occurrence of *Melissococcus plutonius* in healthy colonies of *Apis mellifera* and  
427 the efficacy of European foulbrood control measures. *Journal of Invertebrate Pathology*,  
428 *105*(2), 164–170. doi:10.1016/j.jip.2010.06.004

429 Budge, G. E., Pietravalle, S., Brown, M., Laurenson, L., Jones, B., Tomkies, V., & Delaplane, K. S.  
430 (2015). Pathogens as Predictors of Honey Bee Colony Strength in England and Wales. *PLOS*  
431 *ONE*, *10*(7), e0133228. doi:10.1371/journal.pone.0133228

432 Calderone, N. W., & Page, R. E. (1996). Temporal polyethism and behavioural canalization in the  
433 honey bee, *Apis mellifera*. *Animal Behaviour*, *51*(3), 631–643. doi:10.1006/anbe.1996.0068

434 Cohen, H., Quistberg, R. D., Philpott, S. M., & DeGrandi-Hoffman, G. (2017). Vegetation Management  
435 and Host Density Influence Bee–Parasite Interactions in Urban Gardens. *Environmental*  
436 *Entomology*. doi:10.1093/ee/nvx155

437 Cressler, C. E., McLeod, D. V., Rozins, C., Hoogen, J. V. D., & Day, T. (2016). The adaptive evolution of  
438 virulence: a review of theoretical predictions and empirical tests. *Parasitology*, *143*(7), 915–  
439 930. doi:10.1017/S003118201500092X

440 Currie, R. W., & Jay, S. C. (1991). Drifting behaviour of drone honey bees (*Apis mellifera* L.) in  
441 commercial apiaries. *Journal of Apicultural Research*, 30(2), 61–68.  
442 doi:10.1080/00218839.1991.11101235

443 De la Rúa, P., Jaffé, R., Dall’Olio, R., Muñoz, I., & Serrano, J. (2009). Biodiversity, conservation and  
444 current threats to European honeybees. *Apidologie*, 40(3), 263–284.  
445 doi:10.1051/apido/2009027

446 Dynes, T. L., Roode, J. C. D., Lyons, J. I., Berry, J. A., Delaplane, K. S., & Brosi, B. J. (2017). Fine scale  
447 population genetic structure of *Varroa destructor*, an ectoparasitic mite of the honey bee  
448 (*Apis mellifera*). *Apidologie*, 48(1), 93–101. doi:10.1007/s13592-016-0453-7

449 Dynes, T. L., Berry, J. A., Delaplane, K. S., Brosi, B. J., & Roode, J. C. de. (2019). Reduced density and  
450 visually complex apiaries reduce parasite load and promote honey production and  
451 overwintering survival in honey bees. *PLOS ONE*, 14(5), e0216286. doi:  
452 10.1371/journal.pone.0216286

453 Fantham, H. B., & Porter, A. (1912). The Morphology and Life History of *Nosema Apis* and the  
454 Significance of its Various Stages in the so-called ‘Isle of Wight’ Disease in Bees  
455 (Microsporidiosis). *Annals of Tropical Medicine & Parasitology*, 6(2), 163–195.  
456 doi:10.1080/00034983.1912.11687060

457 Free, J. B. (1958). The drifting of honey-bees. *The Journal of Agricultural Science*, 51(3), 294–306.  
458 doi:10.1017/S0021859600035103

459 Fries, I., & Camazine, S. (2001). Implications of horizontal and vertical pathogen transmission for  
460 honey bee epidemiology. *Apidologie*, 32(3), 199–214. doi:10.1051/apido:2001122

461 Fürst, M. A., McMahon, D. P., Osborne, J. L., Paxton, R. J., & Brown, M. J. F. (2014). Disease  
462 associations between honeybees and bumblebees as a threat to wild pollinators. *Nature*,  
463 506(7488), 364. doi:10.1038/nature12977

464 Gandon, S., Hochberg, M. E., Holt, R. D., & Day, T. (2013). What limits the evolutionary emergence of  
465 pathogens? *Philosophical Transactions of the Royal Society of London B: Biological Sciences*,  
466 368(1610), 20120086. doi:10.1098/rstb.2012.0086

467 Ghazoul, J. (2005). Buzziness as usual? Questioning the global pollination crisis. *Trends in Ecology &*  
468 *Evolution*, 20(7), 367–373. doi:10.1016/j.tree.2005.04.026

469 Giacobino, A., Cagnolo, N. B., Merke, J., Orellano, E., Bertozzi, E., Masciangelo, G., ... Signorini, M.  
470 (2014). Risk factors associated with the presence of *Varroa destructor* in honey bee colonies  
471 from east-central Argentina. *Preventive Veterinary Medicine*, 115(3–4), 280–287.  
472 doi:10.1016/j.prevetmed.2014.04.002

473 Goodwin, R. M., Perry, J. H., & Houten, A. T. (1994). The effect of drifting honey bees on the spread  
474 of American foulbrood infections. *Journal of Apicultural Research*, 33(4), 209–212.  
475 doi:10.1080/00218839.1994.11100873

476 Graystock, P., Blane, E. J., McFrederick, Q. S., Goulson, D., & Hughes, W. O. H. (2016). Do managed  
477 bees drive parasite spread and emergence in wild bees? *International Journal for*  
478 *Parasitology: Parasites and Wildlife*, 5(1), 64–75. doi:10.1016/j.ijppaw.2015.10.001

479 Higes, M., Martín-Hernández, R., Botías, C., Bailón, E. G., González-Porto, A. V., Barrios, L., ... Meana,  
480 A. (2008). How natural infection by *Nosema ceranae* causes honeybee colony collapse.  
481 *Environmental Microbiology*, 10(10), 2659–2669. doi:10.1111/j.1462-2920.2008.01687.x

482 Higes, M., Martín-Hernández, R., Garrido-Bailón, E., González-Porto, A. V., García-Palencia, P.,  
483 Meana, A., ... Bernal, J. L. (2009). Honeybee colony collapse due to *Nosema ceranae* in  
484 professional apiaries. *Environmental Microbiology Reports*, 1(2), 110–113.  
485 doi:10.1111/j.1758-2229.2009.00014.x

486 Jacques, A., Laurent, M., Consortium, E., Ribière-Chabert, M., Saussac, M., Bougeard, S., ... Chauzat,  
487 M.-P. (2017). A pan-European epidemiological study reveals honey bee colony survival  
488 depends on beekeeper education and disease control. *PLOS ONE*, 12(3), e0172591.  
489 doi:10.1371/journal.pone.0172591

490 James, C. (1981). The cost of disease to world agriculture. *Seed Science and Technology*  
491 *(Netherlands)*. Retrieved from <http://agris.fao.org/agris->  
492 [search/search.do?recordID=XE8280339](http://agris.fao.org/agris-search/search.do?recordID=XE8280339)

493 Jatulan, E. O., Rabajante, J. F., Banaay, C. G. B., Fajardo, A. C., & Jose, E. C. (2015). A Mathematical  
494 Model of Intra-Colony Spread of American Foulbrood in European Honeybees (*Apis mellifera*  
495 L.). *PLOS ONE*, *10*(12), e0143805. doi:10.1371/journal.pone.0143805

496 Jay, S. C. (1965). Drifting of Honeybees in Commercial Apiaries 1. Effect of Various Environmental  
497 Factors. *Journal of Apicultural Research*, *4*(3), 167–175.  
498 doi:10.1080/00218839.1965.11100119

499 Jay, S. C. (1966). Drifting of Honeybees in Commercial Apiaries. III. Effect of Apiary Layout. *Journal of*  
500 *Apicultural Research*, *5*(3), 137–148. doi:10.1080/00218839.1966.11100147

501 Jay, S. C. (1968). Drifting of Honeybees in Commercial Apiaries. IV. Further Studies of the Effect of  
502 Apiary Layout. *Journal of Apicultural Research*, *7*(1), 37–44.  
503 doi:10.1080/00218839.1968.11100185

504 Jones, B. A., Grace, D., Kock, R., Alonso, S., Rushton, J., Said, M. Y., ... Pfeiffer, D. U. (2013). Zoonosis  
505 emergence linked to agricultural intensification and environmental change. *Proceedings of*  
506 *the National Academy of Sciences*, *110*(21), 8399–8404. doi:10.1073/pnas.1208059110

507 Keeling, M. J., & Rohani, P. (2008). *Modeling Infectious Diseases in Humans and Animals*. Princeton  
508 University Press.

509 Kennedy, D. A., Kurath, G., Brito, I. L., Purcell, M. K., Read, A. F., Winton, J. R., & Wargo, A. R. (2016).  
510 Potential drivers of virulence evolution in aquaculture. *Evolutionary Applications*, *9*(2), 344–  
511 354. doi:10.1111/eva.12342

512 Kielmanowicz, M. G., Inberg, A., Lerner, I. M., Golani, Y., Brown, N., Turner, C. L., ... Ballam, J. M.  
513 (2015). Prospective Large-Scale Field Study Generates Predictive Model Identifying Major  
514 Contributors to Colony Losses. *PLOS Pathogens*, *11*(4), e1004816.  
515 doi:10.1371/journal.ppat.1004816



516 Lindström, A., Korpela, S., & Fries, I. (2008). Horizontal transmission of *Paenibacillus* larvae spores  
517 between honey bee (*Apis mellifera*) colonies through robbing. *Apidologie*, *39*(5), 515–522.  
518 doi:10.1051/apido:2008032

519 Manley, R., Boots, M., & Wilfert, L. (2015). REVIEW: Emerging viral disease risk to pollinating insects:  
520 ecological, evolutionary and anthropogenic factors. *Journal of Applied Ecology*, *52*(2), 331–  
521 340. doi:10.1111/1365-2664.12385

522 Martin, S. J. (2001). The role of *Varroa* and viral pathogens in the collapse of honeybee colonies: a  
523 modelling approach. *Journal of Applied Ecology*, *38*(5), 1082–1093. doi:10.1046/j.1365-  
524 2664.2001.00662.x

525 Martín-Hernández, R., Botías, C., Barrios, L., Martínez-Salvador, A., Meana, A., Mayack, C., & Higes,  
526 M. (2011). Comparison of the energetic stress associated with experimental *Nosema*  
527 *ceranae* and *Nosema apis* infection of honeybees (*Apis mellifera*). *Parasitology Research*,  
528 *109*(3), 605–612. doi:10.1007/s00436-011-2292-9

529 McMahon, D. P., Fürst, M. A., Caspar, J., Theodorou, P., Brown, M. J. F., & Paxton, R. J. (2015). A sting  
530 in the spit: widespread cross-infection of multiple RNA viruses across wild and managed  
531 bees. *Journal of Animal Ecology*, *84*(3), 615–624. doi:10.1111/1365-2656.12345

532 McMahon, D. P., Wilfert, L., Paxton, R. J., & Brown, M. J. F. (2018). Emerging Viruses in Bees: From  
533 Molecules to Ecology. In *Advances in Virus Research*. Academic Press.  
534 doi:10.1016/bs.aivir.2018.02.008

535 Mennerat, A., Nilsen, F., Ebert, D., & Skorping, A. (2010). Intensive Farming: Evolutionary  
536 Implications for Parasites and Pathogens. *Evolutionary Biology*, *37*(2–3), 59–67.  
537 doi:10.1007/s11692-010-9089-0

538 Mötus, K., Raie, A., Orro, T., Chauzat, M.-P., & Viltrop, A. (2016). Epidemiology, risk factors and  
539 varroa mite control in the Estonian honey bee population. *Journal of Apicultural Research*,  
540 *55*(5), 396–412. doi:10.1080/00218839.2016.1251081

541 Natsopoulou, M. E., McMahon, D. P., Doublet, V., Frey, E., Rosenkranz, P., & Paxton, R. J. (2017). The  
542 virulent, emerging genotype B of Deformed wing virus is closely linked to overwinter  
543 honeybee worker loss. *Scientific Reports*, 7(1), 5242. doi:10.1038/s41598-017-05596-3

544 Neumann, P., Radloff, S. E., Pirk, C. W. W., & Hepburn, R. (2003). The behaviour of drifted Cape  
545 honeybee workers (*Apis mellifera capensis*): predisposition for social parasitism? *Apidologie*,  
546 34(6), 585–590. doi:10.1051/apido:2003048

547 Nolan, M. P., & Delaplane, K. S. (2017). Distance between honey bee *Apis mellifera* colonies  
548 regulates populations of *Varroa destructor* at a landscape scale. *Apidologie*, 48(1), 8–16.  
549 doi:10.1007/s13592-016-0443-9

550 Pacini, A., Giacobino, A., Molineri, A., Bulacio Cagnolo, N., Aignasse, A., Zago, L., ... Signorini, M.  
551 (2016). Risk factors associated with the abundance of *Nosema* spp. in apiaries located in  
552 temperate and subtropical conditions after honey harvest. *Journal of Apicultural Research*,  
553 55(4), 342–350. doi:10.1080/00218839.2016.1245396

554 Pasquale, G. D., Salignon, M., Conte, Y. L., Belzunces, L. P., Decourtye, A., Kretzschmar, A., ... Alaux, C.  
555 (2013). Influence of Pollen Nutrition on Honey Bee Health: Do Pollen Quality and Diversity  
556 Matter? *PLOS ONE*, 8(8), e72016. doi:10.1371/journal.pone.0072016

557 Paxton, R. J. (2010). Does infection by *Nosema ceranae* cause “Colony Collapse Disorder” in honey  
558 bees (*Apis mellifera*)? *Journal of Apicultural Research*, 49(1), 80–84.  
559 doi:10.3896/IBRA.1.49.1.11

560 Paxton, R. J., Klee, J., Korpela, S., & Fries, I. (2007). *Nosema ceranae* has infected *Apis mellifera* in  
561 Europe since at least 1998 and may be more virulent than *Nosema apis*. *Apidologie*, 38(6),  
562 558–565. doi:10.1051/apido:2007037

563 Pocol, C. B., Marghitas, L. A., & Popa, A. A. (2012). Evaluation of sustainability of the beekeeping  
564 sector in the North West Region of Romania. *J Food Agric Environ*, 10, 1132–1138.

565 Potts, S. G., Biesmeijer, J. C., Kremen, C., Neumann, P., Schweiger, O., & Kunin, W. E. (2010). Global  
566 pollinator declines: trends, impacts and drivers. *Trends in Ecology & Evolution*, *25*(6), 345–  
567 353. doi:10.1016/j.tree.2010.01.007

568 Roberts, K. E., & Hughes, W. O. H. (2015). Horizontal transmission of a parasite is influenced by  
569 infected host phenotype and density. *Parasitology*, *142*(2), 395–405.

570 Roberts, Katherine E., & Hughes, W. O. H. (2014). Immunosenescence and resistance to parasite  
571 infection in the honey bee, *Apis mellifera*. *Journal of Invertebrate Pathology*, *121*, 1–6.  
572 doi:10.1016/j.jip.2014.06.004

573 Robinson, G. E., Page, R. E., Strambi, C., & Strambi, A. (1992). Colony Integration in Honey Bees:  
574 Mechanisms of Behavioral Reversion. *Ethology*, *90*(4), 336–348. doi:10.1111/j.1439-  
575 0310.1992.tb00844.x

576 Roetschi, A., Berthoud, H., Kuhn, R., & Imdorf, A. (2008). Infection rate based on quantitative real-  
577 time PCR of *Melissococcus plutonius*, the causal agent of European foulbrood, in honeybee  
578 colonies before and after apiary sanitation. *Apidologie*, *39*(3), 362–371.  
579 doi:10.1051/apido:200819

580 Rozins, C., & Day, T. (2016). Disease eradication on large industrial farms. *Journal of Mathematical*  
581 *Biology*, *73*(4), 885–902. doi:10.1007/s00285-016-0973-9

582 Seeley, T. D., & Smith, M. L. (2015). Crowding honeybee colonies in apiaries can increase their  
583 vulnerability to the deadly ectoparasite *Varroa destructor*. *Apidologie*, *46*(6), 716–727.  
584 doi:10.1007/s13592-015-0361-2

585 Stamets, P. E., Naeger, N. L., Evans, J. D., Han, J. O., Hopkins, B. K., Lopez, D., ... Sheppard, W. S.  
586 (2018). Extracts of Polypore Mushroom Mycelia Reduce Viruses in Honey Bees. *Scientific*  
587 *Reports*, *8*(1), 13936. doi:10.1038/s41598-018-32194-8

588 van den Driessche, P., & Watmough, J. (2002). Reproduction numbers and sub-threshold endemic  
589 equilibria for compartmental models of disease transmission. *Mathematical Biosciences*,  
590 *180*(1), 29–48. doi:10.1016/S0025-5564(02)00108-6

591 van Engelsdorp, D., Lengerich, E., Spleen, A., Dainat, B., Cresswell, J., Baylis, K., ... Saegerman, C.  
592 (2013). Standard epidemiological methods to understand and improve *Apis mellifera* health.  
593 *Journal of Apicultural Research*, 52(4), 1–16. doi:10.3896/IBRA.1.52.4.15

594 vanEngelsdorp, D., & Meixner, M. D. (2010). A historical review of managed honey bee populations  
595 in Europe and the United States and the factors that may affect them. *Journal of*  
596 *Invertebrate Pathology*, 103, S80–S95. doi:10.1016/j.jip.2009.06.011

597 Wilfert, L., Long, G., Leggett, H. C., Schmid-Hempel, P., Butlin, R., Martin, S. J. M., & Boots, M. (2016).  
598 Deformed wing virus is a recent global epidemic in honeybees driven by *Varroa* mites.  
599 *Science*, 351(6273), 594–597. doi:10.1126/science.aac9976

600