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Review

A survey of small bowel modelling and its applications for capsule endoscopy☆

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ABSTRACT

The small intestine, an anatomical site previously considered inaccessible to clinicians due to its small diameter and length, is the part of the gastrointestinal tract between the stomach and the colon. Since its introduction into clinical practice two decades ago, capsule endoscopy has become established as the primary modality for examining the surface lining of the small intestine. Today, researchers continue to develop ground-breaking technologies for novel miniature devices aiming for tissue biopsy, drug delivery and therapy. The purpose of this paper is to provide researchers and engineers in this area a comprehensive review of the progress in understanding the anatomy and physiology of the small intestine and how this understanding was translated to virtual and physical test platforms for assessing the performance of these intestinal devices. This review will cover both theoretical and practical studies on intestinal motor activities and the work on mathematical modelling and experimental investigation of capsule endoscope in the small intestine. In the end, the requirements for improving the current work are drawn, and the expectations on future research in this field are provided.

1. Introduction

1.1. Background

The gastrointestinal (GI) tract (or alimentary canal) consists of the mouth, larynx, oesophagus, stomach, small intestine and large intestine (colon). Whereas the oesophagus, stomach and colon are easily accessed via the mouth (oesophagus and stomach) or anus (colon), the majority of the small intestine defied straightforward examination until recently due to its formidable length (typically 3–5 m) and narrow diameter (typically 1.5–2.5 cm) [1]. The fact for developing diagnostic techniques is that the vast majority of GI tract pathology affects the oesophagus, stomach, proximal small intestine and colon, which can be readily assessed through the use of radiological imaging techniques [2] (to assess anatomical changes), inserted probe studies (to assess functions, such as motility and acid–base status) and endoscopy [3] (video examination of the surface lining of these structures). From its invention in 1932 by Rudolf Schindler [4] to the present day, the use of flexible endoscopy has expanded until it has become one of the most widely used techniques in the modern diagnostic procedures. However, despite major advances in image acquisition and processing over recent decades, the basic design and ergonomics of endoscopes have barely changed in more than four decades. Endoscopy remains

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challenging for both clinicians and patients. Some patients experience significant pain during procedures, which require a team of clinicians both to sedate and monitor patients and to maintain and decontaminate increasingly complex and expensive devices. For clinicians to acquire the required expertise and practice safely, lengthy training periods and highly developed professional regulatory frameworks are required. Because of these considerations, the demand for accurate simulators of the oesophagus, stomach and colon for initial training has grown to the point that increasingly sophisticated devices are now available, incorporating, for example, virtual reality live feedback and patient variation [5–7].

As stated above, diseases of the surface lining of the small intestine are highly challenging to diagnose and treat. The vast majority of these disorders can be divided into three pathological entities: bleeding lesions (such as angioectasias or aberrant surface vessels), mass lesions (such as benign, pre-malignant and malignant tumours) and inflammatory diseases (such as coeliac disease and Crohn's disease) [8]. Historically, such disorders were often presumed to occur on the basis of radiological imaging and/or the absence of pathology at other, more accessible sites. Only the extreme proximal and distal segments of the small intestine (duodenum and terminal ileum) were accessible via standard flexible endoscopy. The remainder and vast majority of the small intestine (jejunum and ileum) was considered largely impenetrable until the simultaneous development of two techniques approximately twenty years ago: device-assisted enteroscopy (small bowel endoscopy) [9,10] and video capsule endoscopy (CE) [11–13]. Device-assisted enteroscopy is a complex and challenging technique [14] that allows clinicians to use sleeves around flexible endoscopes to pleat and shorten segments of small bowel so that the endoscope can be passed deeper into the small intestine. Whilst this has allowed clinicians to examine, biopsy and even treat newly accessible regions of the small intestine, the technique is not suitable for widespread use due to the duration and discomfort to patients involved.

1.2. Capsule endoscopy

Video CE [15,16] involves the ingestion of a device, typically 26×11 mm, which captures upwards of 100,000 photographic images over a number of hours, either storing them internally or transmitting them to an externally worn receiver. Software combines these images into video footage for clinicians to view. In the twenty years since it was invented, the only significant improvements in CE have been in image quality (typically 512×512 pixels), frame rate (2–6 per second) and angle of view [17]. All the available CE systems continue to rely on peristalsis for passage through the GI tract, and this leads to significant limitations, in particular due to the unpredictable and variable locomotion velocity. Significant abnormalities may be missed, due to intermittent high transit speeds that lead to incomplete visualisation of the intestinal surface [17]. CE retention can occur in about 1% of the examinations [18]. This can be related to Crohn's disease or suspected tumour and can create serious complications [19]. On the other hand, the often lengthy small bowel transit times and resulting videos (typically 2–8 h) make the procedure time-consuming for both patients and clinicians. Very recently, attempts have been made to incorporate artificial intelligence algorithms into the interpretation of the videos in an attempt to reduce viewing times [20–22], such as GI Genius [23] and ENDOANGEL [24].

CE is a diagnostic procedure and cannot offer therapeutic benefit, then, they still cannot replace optical inspection. In particular, passive peristalsis locomotion and the time required to travel along the intestines affect negatively the performance of these devices. These limitations have required to develop new devices with an active locomotion and on-board instrumentations [25]. This design has several challenges due to the limited space, the length and tortuous shape of the digestive tract. Off-the-shelf components are limited and this requires the design of new electronic and mechanical parts. This needs the use of new actuators [26–28] and sensors together with an effective locomotion solution [29–31] with many challenges ahead due to the biomechanics of the wall and low friction of the mucosa of the GI tract. In theory, an active and controllable locomotive mechanism for CE could dramatically reduce the duration of the procedure, whilst at the same time allowing clinicians to focus visualisation onto potential areas of interest. The ability to fix the capsule at a specific position within the small intestine opens up the possibility of introducing new modalities, such as biopsy and targeted drug delivery. In practice, such developments are extremely challenging to deliver without a much deeper understanding of the mechanical function and motility of the small intestine. This deeper understanding could then inform attempts to develop more accurate and representative laboratory models of the structure and function of the small intestine.

1.3. Structure of this survey

The rest of the paper is organised as follows. In the next section, modelling of the small intestine is studied. Our review will focus on the motor activities of the small intestine from both mathematical modelling and experimental investigation points of view. In Section 3, mathematical and experimental modelling of capsule endoscope in the small intestine with the consideration of intestinal motor activities is reviewed. Finally, conclusions and future works are drawn in Section 4.

2. Modelling of the small intestine

A large part of the early literature on the small intestine has focused on mathematical modelling and experimental investigation of intestinal motor activity, e.g., the contraction of the intestinal wall, to evaluate diagnostic and therapeutic procedures related to motility disorders. The movements of the small intestine can be divided into peristaltic and segmental contractions as illustrated in Fig. 1. For the peristaltic contraction, chyme is propelled through the small intestine by peristaltic waves, which can occur in any part of the intestine and move toward the anus at a speed of 5 to 20 mm/s that is faster in the proximal intestine and slower in the terminal intestine. When a portion of the small intestine becomes distended with chyme, stretching of the intestinal wall elicits localised concentric contractions spaced at intervals along the intestine and lasting a fraction of a minute [32]. Such a contraction divides the intestine into spaced segments and can "chop" the chyme at two to three times per minute promoting progressive mixing of the food with secretions of the small intestine.

2.1. Mathematical modelling of intestinal motor activities

2.1.1. Early works

Very early investigations on the small intestine can trace back to 1960s which aimed to analyse the control mechanisms of the intestine and the transport phenomena in the intraluminal content [33]. The work done by Parkes and Burns [34,35] and Fung and Yih [36,37] which studied the fluid motion associated with peristalsis has become a cornerstone for the later research work on the intestinal motor activity. By following this pioneering work, Li [38] analysed the problem of peristaltic pumping in a circular cylindrical tube by adopting a long wave approximation. Zien and Ostrach [39] studied analytically the problem of motion of a viscous incompressible fluid induced by travelling wave motions of the confining walls for the two-dimensional geometry by employing a long wave approximation. The analysis was proposed to the possible application for urine flow in human ureters, but later was used for developing a mathematical model of small bowel peristalsis with the consideration of peristaltic carrying and mixing of chyme in the bowel [40].

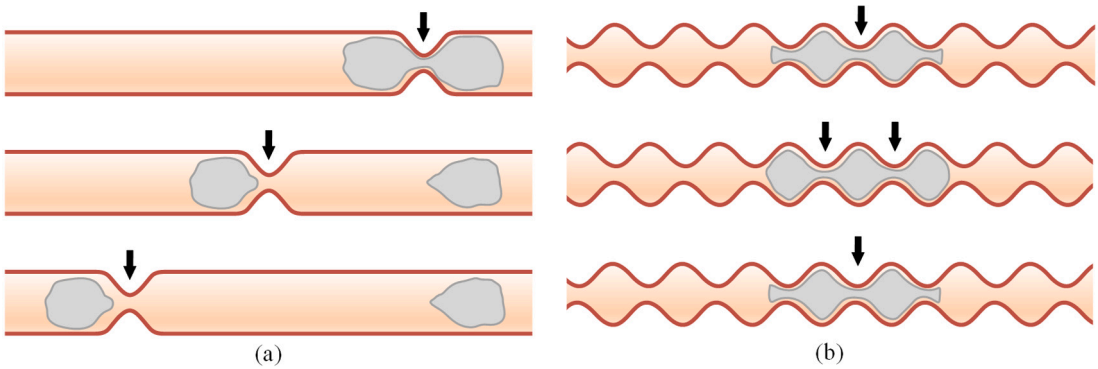

Fig. 1. Movements of the small intestine: (a) peristaltic and (b) segmental contractions.

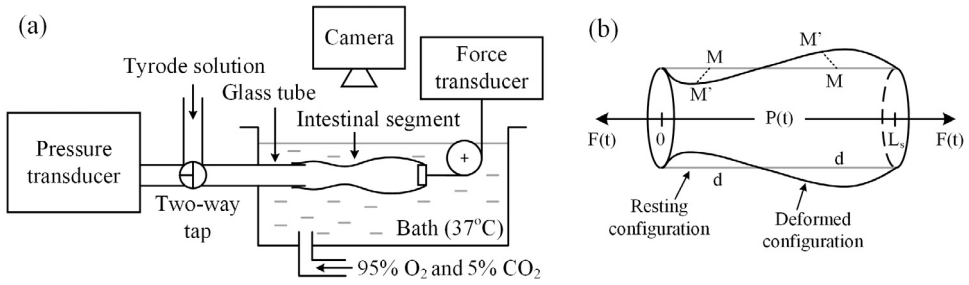

Fig. 2. [41] (a) Experimental schematic of the modified Trendelenburg preparation. (b) Resting and deformed configuration of the intestinal segment in the preparation considered, where L_s is the segment length, r_o is the undeformed segment radius, d is the undeformed length, $P(t)$ is the action due to longitudinal fibres, $F(t)$ is the action due to circular fibres, and MM' is the deformation vector.

2.1.2. The modified Trendelenburg preparation

Bertuzzi et al. [41] developed a mathematical model describing the dynamics of intestinal wall with large deformations. The physical system to be considered for model construction is an intestinal segment 3–7 cm long in the so-called modified Trendelenburg or isometric isovolumic preparation [42] as presented in Fig. 2(a). The intestinal segment was put horizontally in a bath of oxygenated Tyrode solution at a constant temperature.

The mathematical model to be considered for the intestinal segment is illustrated in Fig. 2(b), where the wall configuration of the tubular segment of constant length L_s is given at time t in the indicated reference system by the vector MM' function of x, where $x \in [0, L_s]$. The intestinal wall was anatomically arranged in two muscle layers, the external layer for longitudinal fibres and the internal layer for circular fibres, which contract independently but in a coordinated way. Assuming that the external pressure equals to zero, both of the undeformed length d are displaced and deformed by the contraction of longitudinal and circular fibres, $P(t)$ and $F(t)$, respectively. Deformation and forces were considered in the model as a consequence of the evolution of two simulation functions that play in the segment for circular and longitudinal fibres as the inputs of the model [41].

In [43], Bertuzzi et al. studied the peristaltic propulsion of a solid spherical bolus enclosed in a contractile membrane by using the mathematical model based on *in vitro* preparations of intestinal segment in [41]. The sequence of deformed configurations of the membrane and the displacement of the bolus obtained by the model could also be used for other studies in biomechanics, e.g., uterine contraction and the motion of red blood cells in narrow capillaries.

2.1.3. Miftakhov's work

Rustem Miftakhov and David Wingate are the pioneers in the field of modelling the motor activity of small bowel. In the early 90's, Miftakhov and Wingate [44] developed a biomechanical model for the motor activity of small bowel by considering the following equations of motion [45],

$$\begin{cases} r_o\left(\frac{\partial v_r}{\partial t} - \frac{v_s^2}{r}\right) = \frac{\partial}{\partial s_1}(T_1 e_{1r}\sqrt{g_{22}}) + \frac{\partial}{\partial s_2}(T_2 e_{2r}\sqrt{g_{11}}) + p\sqrt{g}n_r, \\ r_o\left(\frac{\partial v_s}{\partial t} + \frac{v_s v_r}{r}\right) = \frac{\partial}{\partial s_1}(T_1 e_{1s}\sqrt{g_{22}}) + \frac{\partial}{\partial s_2}(T_2 e_{2s}\sqrt{g_{11}}) + p\sqrt{g}n_s, \\ r_o\frac{\partial v_z}{\partial t} = \frac{\partial}{\partial s_1}(T_1 e_{1z}\sqrt{g_{22}}) + \frac{\partial}{\partial s_2}(T_2 e_{2z}\sqrt{g_{11}}) + p\sqrt{g}n_z, \\ C_m\frac{\partial \varphi_{(l,c)}}{\partial t} = I_{m1(l,c)}\left[\left(\frac{\partial}{\partial s_1}\left(\frac{g_{0s_1}}{\lambda_l}\frac{\partial \varphi_l}{\partial s_1}\right) + \frac{\partial}{\partial s_2}\left(\frac{g_{0s_1}}{\lambda_c}\frac{\partial \varphi_c}{\partial s_2}\right)\right)\right] + I_{m2(l)} - I^*_{ion}, \end{cases} \tag{1}$$

where T_1 is the total force per unit length in longitudinal direction, T_2 is the total force per unit length in orthogonal circumferential direction, λ is the rate of elongation, v is the velocity of contraction, e_{ij} is the direction cosines of the outward norma, n_j, with respect to the cylindrical j-axis, g_{11} and g_{22} are the components of the metric tensor of surface, g is the determinant of the metric tensor, v_j are the velocities of the wall displacement in circumferential, radial and longitudinal directions, γ_0 is the linear density of a biomaterial, s_i are the Lagrangian coordinates of the surface, C_m is the membrane capacitance of smooth muscle, φ is the electrical wave of depolarisation that is generated by the pacemaker located on the left boundary of the intestinal segment, $I_{m1(l,c)}$ and $I_{m2(l)}$ are the transmembrane ion currents, I^*_{ion} is the total ionic current defined in [46], g_{0s1} and g_{0s2} are the maximal conductances of smooth muscle in longitudinal and circumferential directions, and $t > 0$ is the time. Also, the subscripts l and c are related to the longitudinal and circular muscle layers, respectively. The subscripts $i = 1, 2$ and $j = s, r, z$, where $s \in (0, 2\pi r)$ and $z \in (0, l)$.

Eq. (1) considers a segment of small intestine as a soft orthotropic cylindrical shell reinforced by the smooth muscle elements of orthogonal type of weaving, embedded in a connective tissue network. The intestinal wall considered contains two muscle layers, where the muscle fibres in the outer and the inner layers are orientated in the longitudinal and the circular directions, respectively. To carry out numerical calculations, the initial conditions of Eq. (1) are

$$v_s = v_r = v_z = 0 \quad \text{and} \quad \varphi_{(l,c)} = 0,$$

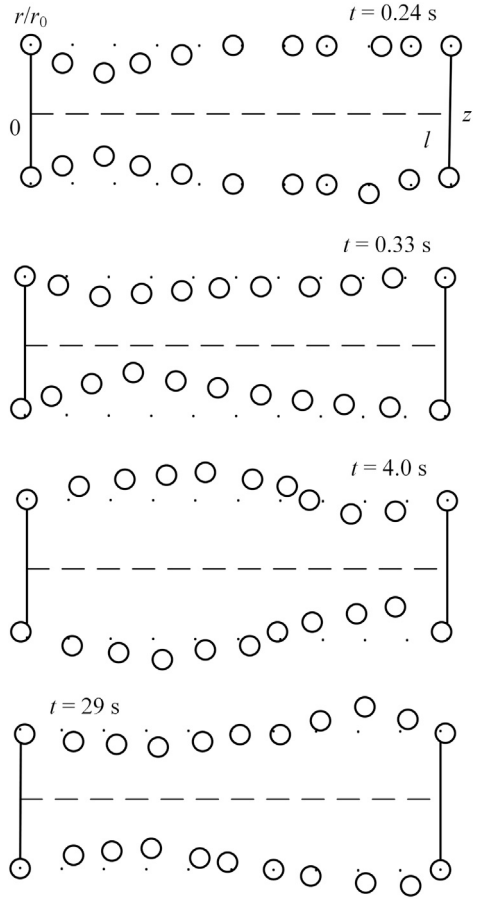

Fig. 3. [44] A representation of intestinal segment morphology at the times as indicated, where the open circles indicate the positions of the points of the wall with respect to the rest positions of the same points indicated by dots.

and its boundary conditions are

$$\varphi_l = \begin{cases} \varphi_0, & 0 \le t \le 0.002 \text{ sec} \\ 0, & t > 0.002 \text{ sec} \end{cases}$$

$$\varphi_c = \begin{cases} 0, & 0 \le t \le t_f \\ \varphi_0, & t_f < t \le t_f + 0.002 \text{ sec} \\ 0, & t > t_f + 0.002 \text{ sec} \end{cases}$$

and $\lambda_{1,2} = 0$ at $z = 0$; $\lambda_{1,2} = 0$ and $\varphi_{l,c} = 0$ at $z = l$, where t_f is the time when the contractile force T_l achieves its maximum, φ_0 is a known excitatory impulse. The first contraction (preliminary stage) starts in the outer muscle layer, and an activation of the inner muscle layer starts with simultaneous relaxation of the outer layer at t_f [47]. Then Eq. (1) can be solved numerically using an explicit finite-difference scheme of the second order approximation [48] over the spatial and time variables.

An example of numerical results calculated by using Eq. (1) is presented in Fig. 3, at where the configurations of the intestinal segment wall are depicted for the four indicated times. As can be observed from the results, there is no axial symmetry of the intestinal deformation for $t \in (0, 0.33]$ seconds, which corresponds to the preliminary stage of peristaltic motility due to the intensive contractions of the outer longitudinal muscle layer. Then these contractions propagate along the length of the intestinal segment with the velocity of the depolarisation wave, which do not change the shape and intraluminal pressure of the shell, but activate the mechanoreceptor of the inner muscle layer. After the second propulsive stage of the small bowel motility ($t > 0.45$ seconds), symmetric deformation is developed by the activations of the mechanoreceptor and circular muscle fibres as well as the ring contractions as demonstrated by the results at $t = 4$ and 29 seconds.

A further detailed analysis using model (1) was carried out in [51], indicating that the model can adequately explain the dynamics of electromechanical coupling in the small bowel. Miftakhov et al. [52] also used this model to study the peristaltic propulsion of a rigid bolus in the small intestine, which was subjected to dry and viscous friction. The contact forces between the bowel wall and the bolus were assumed to be orthogonal to the sphere surface, and the analysis mainly focused on the stress–strain distribution during the transportation. In order to use more general principles and remove excessive assumptions and speculative hypotheses, Davyd'an and Regirer [53] developed a modified model of intestinal motility, which can describe a wide range of situations, including the normal intestinal phenomena, physiological experiments [54], and the behaviour of surgically formed reservoirs [55].

2.1.4. Reflex reaction models

In fact, the peristalsis of the small bowel is a complex physiological reflex reaction between contraction and relaxation of the longitudinal and circular layers of intestinal muscle. In [56], Miftakhov attempted to develop a mathematical model capable of simultaneously recording the quantitative changes in the muscular components and in the intramural nervous system. The model included the specific features of intramural innervation of the intestinal wall, the chemistry of the synaptic transmission of excitation and inhibition, and electromechanical interaction. Later on, Miftakhov and Wingate [57] further developed the model of the small intestine which was under the control of a simple reflex represented by a single cholinergic neurone. In [58], Miftakhov and Abdusheva studied a mathematical model for the excitation–contraction coupling within a functional unit of the small bowel. The new model can describe electrical processes of the propagation of excitation along the neural circuit, chemical mechanisms of nerve-pulse transmission at the synaptic zones and the dynamics of active force generation. Numerical simulations in the paper have shown that the model is capable of presenting various electrical patterns and mechanical responses of the bowel segment. Furthermore, Miftakhov et al. [59] developed a complete mathematical model of the periodic myoelectrical activity of a functional unit of the small intestine, which was validated in [60] by comparing with the simulation results of pharmacological compounds to their effects in biological studies.

To simulate the shape of excitations with better accuracy, the models developed in [58,59,61] will be required. However, the difficulty to implement these models is the large number of equations involved with hundreds or thousands of cells linked together. To address this issue, Aliev et al. [49] proposed a simple nonlinear model for the electrical activity in the intestine, which contained the coupled layers of longitudinal muscle and interstitial cells of Cajal as shown in Fig. 4. The model suggests that pacemaker activity is caused by the longitudinal muscle, while the pulse propagation involves the longitudinal muscle layer that is in the excitatory state. As the pacemaker activity of interstitial cells of Cajal is the key to initiate the propagation of slow waves along the small intestine, Youm et al. [62] studied the mechanism of the pacemaker activity of interstitial cells of Cajal in a mouse small intestine and tested it using a mathematical model.

2.1.5. Intestinal propulsion models

In the meantime, Miftahof and Fedotov further developed their two-layer model of small bowel motility by considering the intestinal propulsion of a solid non-deformable bolus [63]. The results have led to a new quantitative insight into the complex spatio-temporal patterns of GI transit. They suggested that the reciprocal relationship in contraction of the longitudinal and circular smooth muscle syncytia is necessary to provide the "mixing" type of movements during the preparatory phase of propulsion. Strong simultaneous contractions of the both smooth muscle layers are required to expel the

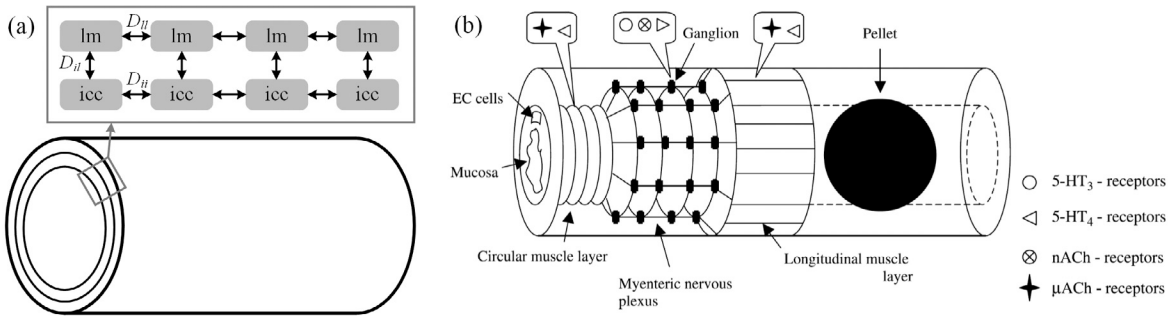

Fig. 4. (a) A schematic presentation of the simplified nonlinear model [49]. Two layers of intestine were simulated: longitudinal muscle (lm) and interstitial cells of Cajal (icc). The quantities D_{ll}, D_{ii} and D_{il} simulate the connectivity inside and between layers. (b) Schematic diagrams of the spatio-temporal model used in numerical simulations in [50], where the distribution of serotonergic and cholinergic receptors is as indicated.

"mixed" bolus from the segment. In particular, Miftahof studied the role of co-transmission by acetylcholine and serotonin on intestinal motility in [64]. Miftahof and Akhmadeev investigated the dynamics of intestinal propulsion for a bolus in [65], and concluded that the pendular movements alone provide an aboral transit, without mixing though, of the bolus. Non-propagating segmental contractions show small amplitude librations of the bolus without its visible propulsion. Only the coordinated activity of both smooth muscle layers in a form of the peristaltic reflex provides physiologically significant simultaneous propulsion and mixing of the intraluminal content. Then they studied the electrophysiological mechanisms of co-transmission on the intestinal propulsion of a solid non-deformable bolus [50] which was subject to the physiological effects of various drugs. The proposed model allows us to study phenomenologically the effects of different classes of pharmacological compounds on intestinal propulsion and to predict the general trend of their action on the system. Srivastava [66] carried out a theoretical study to discuss the effects of an inserted endoscope on chyme movement in the small intestine. It was found that the chyme movement can be significantly influenced due to the presence of the endoscope. For the endoscope with a large radius and a small flow rate, its pressure drop is low, while it becomes high when the flow rate increases. The frictional forces on the intestinal wall and the endoscope possess the same character as the pressure drops, and the frictional force on the intestinal wall is much larger than the one on the endoscope. In 2008, Tharakan studied the modelling of physical and chemical processes in the small intestine [67] by using the computational fluid dynamics (CFD) method. He created a model of the segmentation motion which allowed the theoretical fluid flow for the complex fluids to be simulated and compared with the experimental fluids work.

In the early 2010s, Dudchenko and Guria [69] studied a simple mathematical model of a shear-stress sensitive vessel which was used for securing peristaltic motility coordination. This coordination was interpreted as the ability to ensure sustained propagation of deformation waves in many transporting systems in human body, e.g., gastrointestinal, cardiovascular, lymphatic, urinary, and so on. Then they proposed a much simpler, analytically tractable model of peristaltic pumping in [70], which aimed to derive explicit albeit approximate solutions that would allow one to make qualitative predictions concerning peristaltic motility. Hari et al. [71] developed a computational model of the human duodenum by using CFD. The model coupled peristaltic motions of the duodenum wall together with the flow of chyme, known as a fluid, described using the Navier–Stokes equations, while the intestinal contractions were approximated by the smoothed Heaviside step function. Kano et al. [68] developed an autonomous decentralised control scheme for a multi-functional intestine-like robot that exhibited both peristaltic and segmental motions. As shown in Fig. 5, the two-dimensional model consisted of an intestinal wall and the contents, and coupled oscillators with local sensory feedback were used to design the control scheme. Later on, Akbar and Nadeem [72] considered the

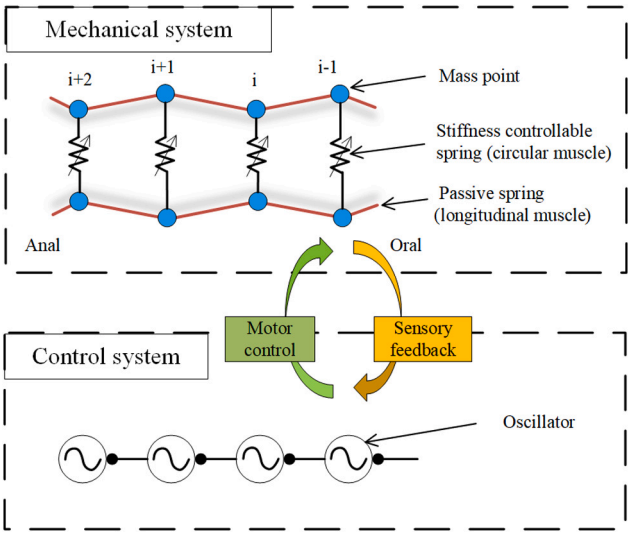

Fig. 5. Schematic representation of the mechanical and control systems of the multi-functional intestine-like robot [68].

couple stress fluid for the peristaltic flow of chyme in the small intestine under the assumption that two non-periodic sinusoidal waves of different wavelength propagate with the same speed along the outer wall of the intestine. It was observed that the frictional forces have an opposite behaviour as compared to the pressure rise for both inner and outer intestine. Sinnott et al. [73] studied a numerical model for peristalsis in the duodenum using a suspension of rigid particulates in a viscous Newtonian fluid to represent simple digesta. The model consisted of a thin viscoelastic membrane representing the gut wall coupled to the particle-based methods, smoothed particle hydrodynamics and discrete element methods which were used to predict the motion of liquid and solids content, respectively. They found that the propulsive events caused significant non-homogeneity of the solids distribution along the length of the duodenum. The inclusion of solids mildly modified the overall propulsive flow behaviour and the retrograde jet in the wake of the contraction. In addition, a transverse wobbling instability in the fluid filled viscoelastic tube was also observed in the absence of solids and connective tissue constraints.

2.2. Experimental investigation of intestinal motor activities

Experimental investigation of intestinal motor activity can trace back to Bayliss and Starling's work [75] at the Physiological Laboratory of Guy's Hospital in 1899. In order to record the contractions of the muscular wall without the introduction of any foreign material

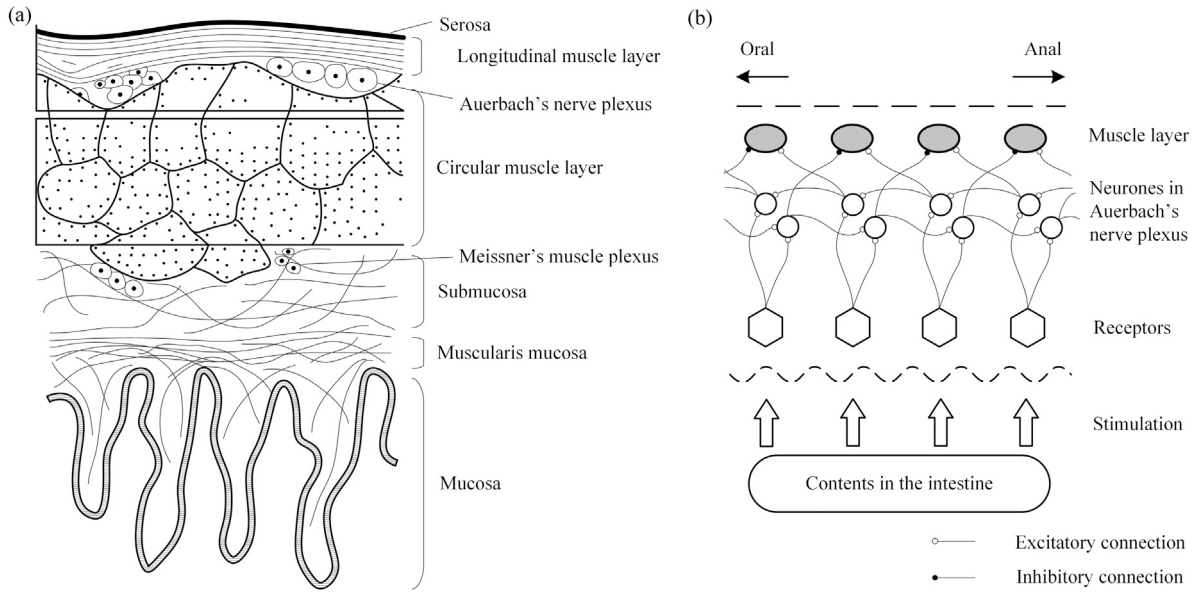

Fig. 6. [74] (a) Longitudinal section of small intestine and (b) neural network causing a peristaltic transporting motion.

into the gut, they developed an instrument known as an "enterograph" by means of which one may record the contractions of either the longitudinal or circular coat, or of both coats simultaneously. In 1917, Trendelenburg [76] introduced an experimental apparatus, the so-called Trendelenburg preparation, which can study the propulsive activity in an isolated intestinal segment avoiding the complexity of *in vivo* behaviour, and was used to measure the electrical and mechanical variables in the given experimental conditions. Mackenna and McKirdy [42] investigated the peristalsis in the rabbit distal colon *in vitro* by using a modified Trendelenburg's apparatus, which was then adopted by Bertuzzi et al. [41] later for studying the dynamics of small-bowel wall as presented schematically in Fig. 2(a).

A series of important biomechanical studies of peristalsis in the small intestine were carried out by Umetani and Inou in 1980s. In [74], they made an assumption about the structure of a neural network which existed in the intestine to control the peristaltic motion as illustrated in Fig. 6. Simulations were run using computer to examine the functional property of receptors, and the results indicated that the receptors did respond to the inside pressure caused by the contents to be transported. Then a mechanical model for expressing the physiological phenomena in the small intestine was made, and its performance transporting solids in various shapes was examined in simulation.

In [77], Umetani and Inou developed a practical strain gauge shown in Fig. 7(a) for measuring the displacement of animal intestinal constriction, and evaluated the influence of stiffness to the movement by using a mechanical transducer-intestinal muscle model. Then they used the strain gauge in experiment to investigate the relation between intestinal movements and the contents in the small intestine [78]. They found that for the contents with high consistency, such as minced meat, the intestine showed neither periodic nor propagative movement of muscle contraction as if mixing the contents. In case of the contents with low consistency, such as soup, it shows either periodic or propagative movement as if transporting the contents. From these results, they concluded that the small intestine had an adaptive capability varying its modes of movements according to the intraluminal contents.

Umetani and Inou [79] carried out a study of the neural mechanism by using a mechanical simulator as shown in Fig. 7(b) which can handle actual fluid contents. The simulator consisted of a thin plastic tube mimicking the intestinal wall and 16 actuators spaced evenly on the tube, which can contract vertically and deform the tube. The simulator was controlled by a microcomputer which performed neurodynamical simulation in real time while sensing fluid contents in the tube through the mechanical sensors of the simulator. Finally, a neural network model was obtained which can transport various viscid fluids, and the simulation showed that this model had a function of modifying the movement according to the fluidity of the contents.

In [80], Umetani and Inou studied the mechanism of rhythmic segmentation in the small intestine. They firstly performed an animal experiment using an abdominal window method which can enable *in vivo* observation of the intestinal movement. Experimental data was analysed by presenting the rhythmic segmentation as a contraction pattern on a plane, and a neural network model was proposed on a computer to generate similar contraction pattern. Thereafter, they further developed the model which consisted of a train of cylindrical short segments with consideration to the mechanical properties of the wall in [81]. The proposed model of the small intestine can be described by a simple matrix representation that could give proper mechanical events of various types of movement, such as peristalsis and rhythmic segmentation. A summary of Umetani and Inou's series work was presented in [82].

3. Modelling of capsule endoscope in the small intestine

Since its introduction into clinical practice two decades ago, CE has become established as the primary modality for examining the surface lining of the small intestine, an anatomical site previously considered to be inaccessible to clinicians. With the emergence of new computational methods, new modelling tools, such as ANSYS Workbench and Fluent, have been employed by researchers to analyse CE in the small intestine. Recent numerical and experimental studies have concentrated on investigating the mechanical properties of the small bowel, e.g., the contact pressure, the intestinal friction and the peristaltic propulsion, for the purposes of understanding capsule's locomotion under intestinal peristalsis and developing controllable capsule robots for live examinations.

Early work on biomechanical modelling of the small intestine for the design and operation of a robotic endoscope has been done by Høeg et al. [83]. The goal of their work was to develop quantitative analytical models and their experimentally determined parameters that can be used to predict the mechanical response of small bowel tissue to applied stresses and to predict the onset of ischaemia. These quantitative models can then provide them with a means to design an endoscope that operates safely and reliably.

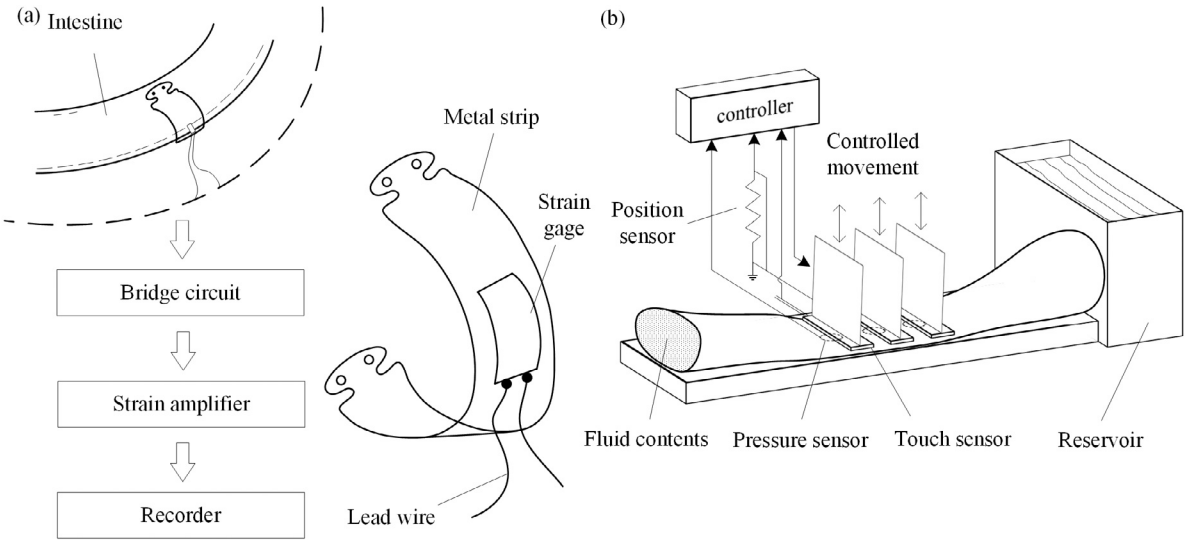

Fig. 7. (a) Strain gauge method and the transducer [77] and (b) schematic diagram of the peristaltic simulator [79].

Pullan et al. [84] reported their work on modelling GI bioelectric activity in 2004. They developed an anatomically realistic biophysically based model of the human GI tract by using the finite element (FE) method. It was done by fitting derivative continuous meshes to digitised data taken from images of the visible man. Structural information, such as fibre distributions of the smooth muscle layers and the arrangement of the networks of interstitial cells of Cajal, were also incorporated using published information. This extensible modelling framework and their initial simulation results have shown great promise, which allow us to address many of the open questions associated with normal and abnormal GI activities.

To develop pill-sized swallowable capsule endoscopes for examining the small intestine, the mechanical characteristics of the intestine and the interaction between the intestinal wall and the capsule need to be investigated to optimise capsule design while preventing tissue damage. Baek et al. [85] investigated the effect of capsule shape on its frictional resistance in the small intestine through an experimental testing using porcine intestines. Experimental results indicated that a smooth cylindrical capsule can cause the least frictional resistance due to its relative small contact area with the intestine. The variation of frictional resistance of the capsule was closely related to the local change in the viscoelastic property of the intestine due to the heterogeneity of the internal structure of the intestine.

Wang et al. [86] studied the features, motility and frictional force of the small intestine for determining the design strategy of an active capsule endoscope through *in vitro* experiments. They also found that the resistant force from the intestine was related to the size and moving speed of the capsule. The capsule with a large diameter that exceeds the intestinal diameter may increase the intestinal drag force. *In vitro* experimental results showed that the required forcing magnitude for driving the capsule could be up to 300 mN. In [87], Wang and Meng carried out *in vitro* experiments to investigate the resistant force of the small intestine using 15 specially designed capsule prototypes, and analysed the effect of capsule's dimension and moving speed. It was found that a resistant force of 20 to 100 mN was measured for the capsule diameter in the range of 8 to 13 mm when moving at a speed of 0.5 mm/s. More importantly, this investigation shows that the viscoelastic properties of the tissue play an important role in the resistant characteristics of the small intestine.

Kim et al. [90] carried out a similar work to investigate the fundamental frictional characteristics and the viscoelastic behaviours of the small intestine experimentally using porcine intestines. Experimental results showed that the average frictional force on the capsule was 10–50 mN, the frictional coefficient varied between 0.08 and 0.2, and a higher moving speed of the capsule can lead to a larger frictional resistance. In [91], an analytical model that can predict the frictional resistance of the capsule moving in the intestine was developed to optimise the design of locomotion mechanism of a self-propelled capsule endoscope. The proposed model can provide quantitative estimation of frictional resistance of the capsule under various moving speeds. In addition, FE analysis of the capsule moving in the intestine was also carried out. FE results of various stress components revealed the stress relaxation of the intestine and concluded that such a stress relaxation characteristics can lead to a lower frictional force as the speed of the capsule decreases.

In 2011, Bellini et al. [92] developed a phenomenological constitutive model of porcine small intestine to predict the mechanical response of the intestinal tissue under complex mechanical loading. Parameters characterising the mechanical behaviour of the material were estimated from planar biaxial test data, where intestinal tissue specimens were simultaneously loaded along the circumferential and longitudinal directions. It was found that specimen-specific Fung constitutive model was able to accurately predict the planar stress–strain behaviour of the tested samples under a wide range of loading conditions. Woo et al. [93] proposed a small intestine model by considering the intestinal drag and friction using a thin walled model and Stokes' drag equation for electrically propelled CE. The electrical stimulus can cause contraction of the small intestine and propel the capsule along the lumen. According to the proposed model, two exterior shapes of the capsule were proposed, and one of the proposed capsule showed an average speed in forward direction of 2.91 mm/s and 2.23 mm/s in backward direction.

Zhang et al. [94] studied the modelling of velocity-dependent frictional resistance for a capsule robot moving in the small intestine. The model consists of three essential parts, an environmental resistance, a viscous friction and a Coulomb friction. Experimental results indicated that the model can predict the friction between the capsule and the intestinal wall efficiently when the moving speed of the capsule was less than 20 mm/s. The biomechanical and biotribological properties of a real small intestine, including the stress relaxation and the stress–strain relations, were studied by Zhou et al. [95] for the optimal design of a spiral-type robotic capsule endoscope. In [96], Zhang et al. further investigated the frictional resistance of the capsule robot moving in the small intestine at a constant speed. Experimental results were obtained from porcine intestine to validate the effectiveness of the proposed frictional model. They also investigated the intestinal frictional resistance at the start-up of capsule's moving experimentally in [97]. Later on, Zhang and Liu [98] developed an analytical friction model

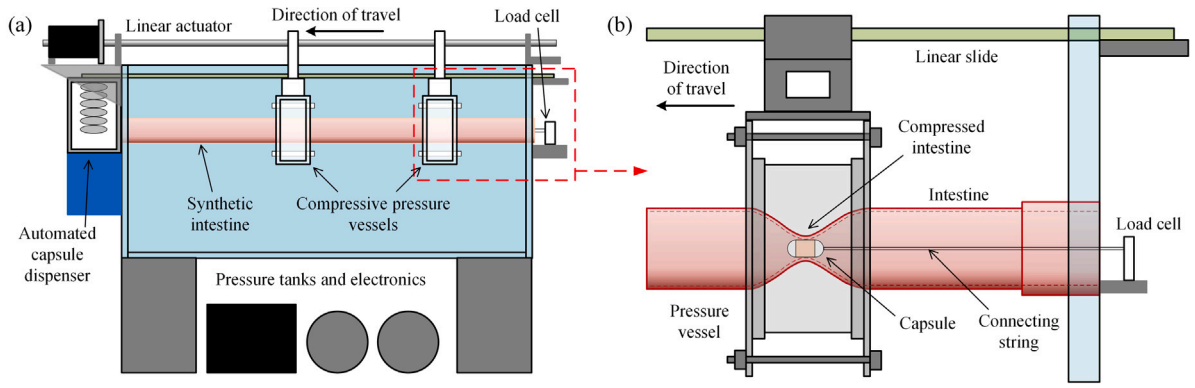

Fig. 8. (a) Schematic of the small-bowel simulator [88] and (b) the experimental set-up for traction force measurement [89].

of the capsule robot moving in the small intestine by considering the hyperelastic constitutive model of small-bowel material's properties.

More interestingly, Li et al. [99] studied the friction trauma mechanism of small intestine caused by surgeon's fingers in the process of surgery *in vivo* by means of reciprocal sliding friction tests. Rabbit's small intestine was used for testing which showed that with the normal force and friction time increasing, the total frictional energy dissipation on the intestine increased, leading to the aggravation of damage degree. Similarly, they studied the friction behaviour between the front-tip of gastroscopy and esophageal wall tissue during endoscopy by using a UMT-II Micro-Tribometer in [100]. Fresh porcine oesophagus of different anatomical sites (thoracic, abdominal and cervical oesophagus) and layers were tested *in vitro*. The normal force applied was from 0.2 to 1.0 N, the sliding speed was from 0.1 to 0.9 mm/s, and the unidirectional sliding displacement was 22 mm to simulate the endoscopy manipulation. Stick–slip phenomenon appeared in the process of the front-tip sliding on the esophageal internal surface, which was related to the alternating deformation, recovery as well as the energy dissipation, was observed in experiments.

Slawinski et al. [88,89] developed an automated device shown in Fig. 8 that can simulate the biomechanical behaviour and environment of the small intestine to expedite the development of robotic capsule endoscopes. The device can support two independently controlled compressive pressure vessels that mimic peristaltic waves and traverse at the speed of 0.08–2 cm/s, the traction force of 0.039–0.392 N, and the contact force of 0.785–4.90 N. Mounted synthetic intestines were kept moist by humidifying the device, creating an environmental chamber. The device can be used as an *in vitro* method for testing the robotic capsule endoscopes without the need of repetitive expensive animal experimentation. Li et al. [101] used the same device to test the capsule that can measure the contraction pressure of the small intestine. Then the capsule was tested at a single location in a live pig model to perform a preliminary evaluation of its pressure measuring capability. The error of the contraction rate measurement from the device was 2.7%, but allows for differentiating between average contraction rates in human that correspond to the location within the GI tract.

In 2016, Sliker et al. [102] developed a frictional resistance model shown in Fig. 9 for tissue-capsule sliding contact in the GI tract. Experimental validation was carried out by performing drag force experiments using various design parameters of the cylindrical capsule and tissue properties. According to their results, the edge radius of the capsule influences frictional resistance the most, and the average normalised root-mean-square error between the proposed model and experimental results was 6.25%.

Rotman et al. [103] developed a mechanical simulator of the small intestine as presented in Fig. 10 which allows effective testing of new capsule endoscopic devices and offline practice with endoscopic devices. The simulator, loaded with *ex vivo* porcine small intestine, was functionally validated using two ingestible commercialised capsule

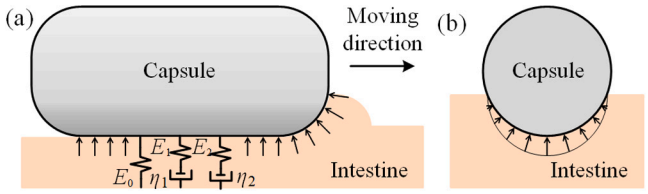

Fig. 9. (a) A side-view and (b) end-view of a capsule endoscope in contact with a viscoelastic tissue substrate (represented as a five-element Double Maxwell-arm Wiechert model) [102].

products. Fracczak et al. [104] presented their experimental results of examination of frictional factor between the small intestine and a cube with silicone coat. The tests were done with vaseline, saline, feminum and lignocainum, indicating that adding of selected substances between intestine and silicone may reduce the friction coefficient between the intestine and the medical device.

In 2019, Yan et al. [105] studied the modelling of a vibro-impact self-propelled capsule system moving in a contracted small intestine. Their study has focused on understanding the dynamic characteristics of the capsule and its performance in terms of the average speed and energy efficiency under various system and control parameters, such as capsule's radius and length, and the frequency and magnitude of external excitation. They found that the resistance from the small bowel becomes larger once the capsule's size or instantaneous speed increases.

Guo et al. [106] studied the modelling of capsule-intestine contact through experimental and numerical investigation for designing a self-propelled capsule robot (26 mm in length and 11 mm in diameter) for small-bowel examination. According to the natural peristalsis of the intestinal tract, three typical contacts between a synthetic small intestine and the capsule, as shown in Fig. 11, were considered. Extensive experimental testing and FE analysis were conducted to compare the contact pressure on the capsule, and analytical, experimental and numerical results showed a good agreement.

The schematic diagram of the experimental rig used in [106] for measuring capsule-intestine contact pressure is presented in Fig. 12. This investigation suggested that the contact pressure could vary from 0.5 to 16 kPa according to different contact conditions using a synthetic small intestine. Guo et al. [107] further investigate the frictional resistance in the small intestine by using an experimental rig shown in Fig. 13. According to the experimental results, intestinal frictions varied from 7 mN to 4.5 N which can be used as a guidance for designing the propelling mechanism of the controllable capsule robots. It was also found that the friction coefficient is a function of capsule's progression speed, and the hoop-induced friction is very sensitive to the radius of the intestine.

A summary of all the above studies on modelling of capsule endoscope in the small intestine has been tabulated in Table 1.

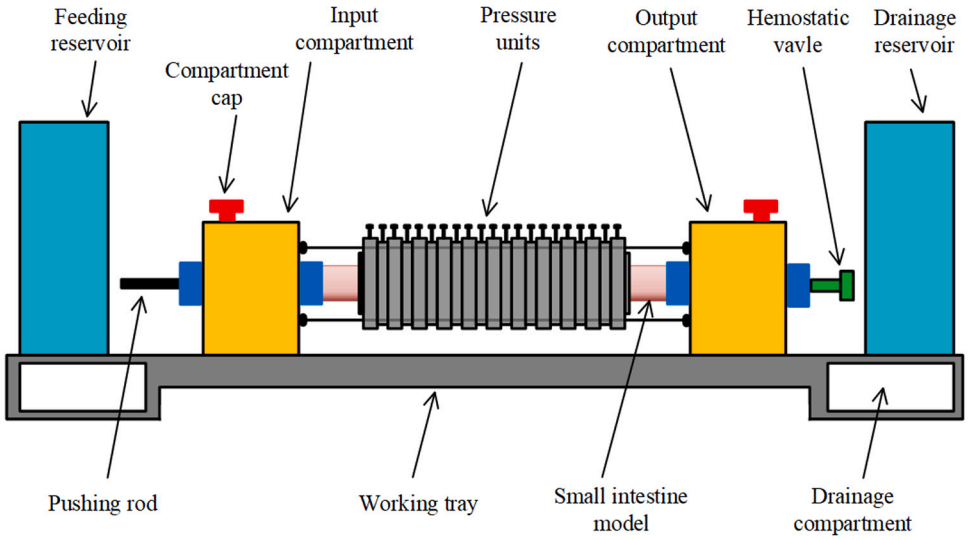

Fig. 10. Schematic diagram of the small intestine mechanical simulator [103].

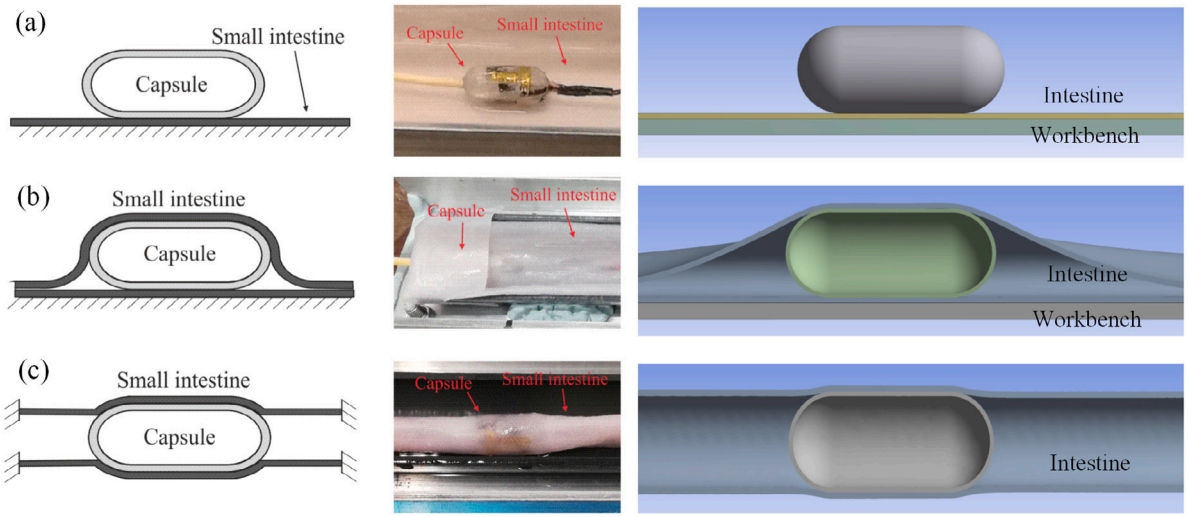

Fig. 11. [106] Three contact cases, where the small intestine and the capsule are marked by dark and light grey, respectively. (a) Case 1: the capsule moves on a cut-open small intestinal surface; (b) Case 2: the capsule slides inside a collapsed intestine; (c) Case 3: the capsule is surrounded by the small intestine. Photographs on the middle panels show the experimental set-ups, and pictures on the right panels present the FE set-ups for these contact cases.

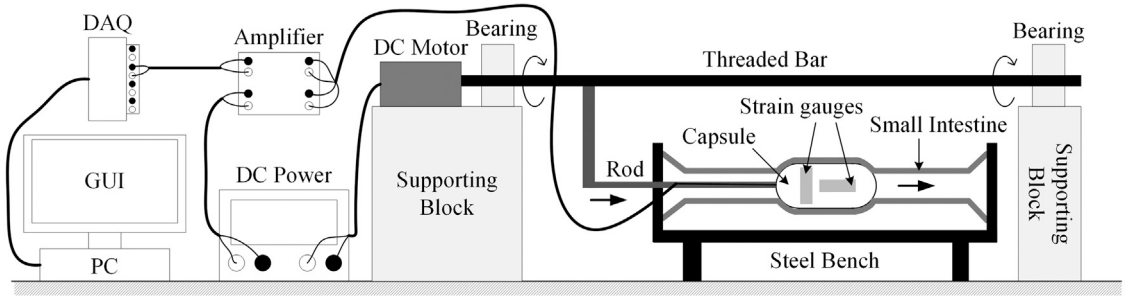

Fig. 12. [106] Schematic diagram of the experimental set-up. A DC motor was used to drive the capsule to move inside a synthetic small intestine at a constant speed. The speed was varied by adjusting the DC power supply for each experimental trial. Two pairs of strain gauges were attached to the external surface of the capsule, and their signals were amplified and then collected by a National Instrument data acquisition (DAQ) card via a graphic user interface (GUI) in LabVIEW.

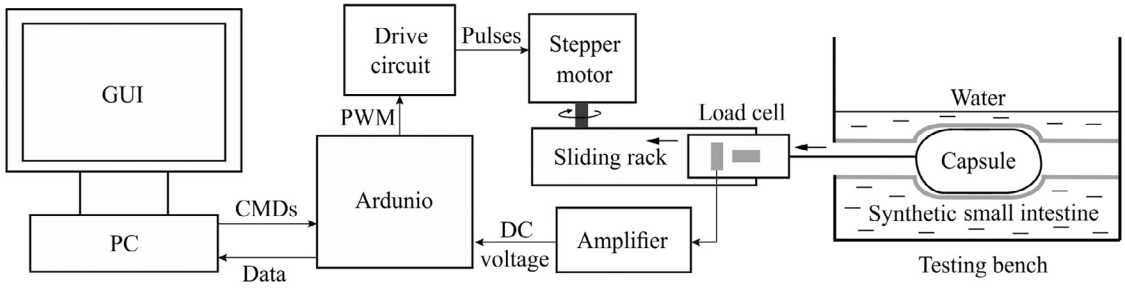

Fig. 13. [107] Schematic diagram of the experimental rig for measuring the frictional resistance acting on the capsule. An Arduino microcontroller unit was used to control a DC stepper motor by sending pulse width modulation (PWM) signals to a drive circuit. The DC stepper motor drove the sliding rack at a constant speed through gearing, and the rack pulled the capsule moving inside a synthetic small intestine using a nylon rope. A load cell was mounted on the sliding rack, and its output was amplified and then collected by the Arduino unit connecting to a personnel computer (PC). The PC sent commands (CMDs) to control the Arduino unit through a graphic user interface (GUI), while receiving the measured data from the Arduino unit for data logging.

Table 1
Summary of studies on capsule-intestine modelling.

Name (year)	Research	Approach	Remark
Høeg et al. (2000) [83]	To develop quantitative analytical model to predict the mechanical response of the small intestine.	Analytical and experimental	The authors sought to find a relationship between blood flow rate in the intestinal vessels and the pressure applied by the endoscope to predict the onset of ischaemia.
Pullan et al. (2004) [84]	To develop an anatomically realistic biophysically based model of the human GI tract.	FE	An extensible modelling framework that can be used to integrate the physiological, anatomical and medical knowledge of the GI system.
Baek et al. (2004) [85]	To study the effect of capsule's shape on the frictional resistance of the capsule in the small intestine.	Experimental	A smooth cylindrical capsule has the least resistance, and its variation depends on the local change in the viscoelastic property of the intestine.
Wang et al. (2005) [86]	To study the features, motility and frictional force of the small intestine to find the design strategy of an active CE.	Experimental	*In vitro* experimental results indicated that the required forcing for driving the capsule can go up to 300 mN.
Wang and Meng (2009) [87]	To investigate the effect of capsule's dimension and moving speed on the resistant force of the small intestine.	Experimental	*In vitro* experiments showed that the resistant force was 20–100 mN for the capsules with the diameter in the range of 8–13 mm when moving at a speed of 0.5 mm/s.
Kim et al. [90]	To investigate the frictional characteristics and the viscoelastic behaviours of the small intestine.	Experimental	The average frictional force on the capsule was 10–50 mN, and the frictional coefficient varied between 0.08 and 0.2.
Kim et al. [91]	To study an analytical model to predict the frictional resistance of capsule's moving in the intestine.	Analytical and FE	Stress relaxation of the intestine may lead to lower friction as the capsule's speed decreases.
Bellini et al. [92]	To develop a phenomenological constitutive model to predict the mechanical response of the intestinal tissue under complex mechanical loading.	Experimental and FE	The Fung constitutive model was able to accurately predict the planar stress–strain behaviour of the tested intestine samples under a wide range of loading conditions.
Woo et al. (2011) [93]	To develop a small intestine model for electrically propelled CE.	Analytical, FE and experimental	Two exterior shapes of the capsule were proposed, and one showed the average speeds of 2.91 and 2.23 mm/s in forward and backward directions, respectively.
Zhang et al. (2012) [94]	To model the velocity-dependent frictional resistance for a capsule robot moving in the small intestine.	Analytical and experimental	The model can predict efficiently for a low speed (< 20 mm/s), but for a high speed, the viscoelasticity of the intestine does not fit well with the model.
Zhou et al. (2013) [95]	To study the biomechanical and biotribological properties of a real small intestine.	Experimental	The small intestine shows the typical behaviour of a viscoelastic material, but within some certain ranges of strains, the tissue appears to have a quasi-linear viscoelasticity.
Zhang et al. (2014) [96]	To model the frictional resistance of a capsule robot moving in the small intestine at a constant speed.	Analytical and experimental	The model can induce the stick–slip phenomenon for the capsule robot and is only effective at a low speed.
Zhang et al. (2014) [97]	To study the intestinal resistance at the start-up of capsule's moving.	Experimental	The capsule's original state, velocity and acceleration can affect the intestinal resistance at the start-up of capsule's moving.
Zhang and Liu (2016) [98]	To develop an analytical friction model of a capsule robot moving in the small intestine.	Analytical and experimental	The model is based on the size of the capsule robot, the hyperelastic constitutive model of the intestine's material and the capsule-intestine interactions. The constitutive model should be further improved.

(*continued on next page*)

Table 1 (*continued*).

Name (year)	Research	Approach	Remark
Li et al. (2014) [99]	To study the friction trauma mechanism of small intestine caused by surgeon's fingers in the process of surgery.	Experimental	With the normal force and friction time increased, the total frictional energy dissipation on the intestine increased, leading to the aggravation of damage degree.
Lin et al. (2017) [100]	To investigate the friction behaviour between the front-tip of gastroscopy and esophageal wall tissue during endoscopy.	Experimental	Stick–slip phenomena were observed in the process of the front-tip sliding on the esophageal internal surface. The friction coefficient decreased with the increasing normal load and sliding speed.
Slawinski et al. (2014/5) [88,89,101]	To develop an automated device to simulate the biomechanical behaviour and environment of the small intestine.	Experimental	The device can be used as an *in vitro* method for testing the robotic capsule endoscopes without the need of repetitive expensive animal experimentation.
Sliker et al. (2016) [102]	To develop a frictional resistance model for tissue-capsule sliding contact in the GI tract.	Analytical and experimental	The edge radius of the capsule affected the resistance the most, and the model fitted with the experimental results well.
Rotman et al. (2016) [103]	To design a mechanical simulator of the small intestine.	Experimental	The simulator, loaded with *ex vivo* porcine small intestine, was functionally validated using two ingestible commercialised capsule products.
Fracczak et al. (2022) [104]	To test the friction between the intestine and a cube with silicone coat.	Experimental	The adding of selected substances between the intestine and the silicone may reduce the friction between the intestine and the medical device.
Yan et al. (2019) [105]	To model a vibro-impact self-propelled capsule moving in a contracted small intestine.	Analytical	The intestinal resistance may become larger once the capsule's size or instantaneous speed increases.
Guo et al. (2019) [106]	To study the modelling of capsule-intestine contact.	Analytical, FE and experimental	According to the natural peristalsis of the small intestine, three typical capsule-intestine contacts were considered, and their contact pressures varied from 0.5 to 16 kPa.
Guo et al. (2020) [107]	To investigate the frictional resistance on a moving capsule endoscope in the small intestine.	Analytical, FE and experimental	The intestinal friction varied from 7 mN to 4.5 N. The friction coefficient is a function of capsule's speed, and the hoop-induced friction is very sensitive to the diameter of the intestine.

4. Conclusions and future work

CE is a procedure used predominantly to examine the surface lining of the small intestine. However, its reliance on peristalsis for passage through the intestine leads to intermittent high and low transit speeds, with the result that the intestinal surface may be incompletely visualised and abnormalities may be missed. The purpose of modelling small intestine is to develop controllable, reliable and efficient diagnostic tools for future endoscopic procedures. A controllable capsule-based device that provides the means to examine areas of interest by clinicians both carefully and reliably in real time, represents a major advance in endoscopic practice. Being independent of small-bowel peristalsis, the controllable capsule endoscope can significantly reduce examination time, and clinicians will be able to control the speed of the examination. The expensive, extensive and rigorous periods of training in endoscope passage can be reduced from years to days. In addition, the introduction of controllable capsule-based diagnostic devices affords the possibility of providing a new modality to meet future demands for diagnostic imaging and drug delivery. This can provide direct improvements in patient care, thanks to the enhanced safety, comfort, accuracy and reliability of such devices. The need for patients to be sedated can be minimised, allowing them to undergo examinations with minimal disruption to their lives and own workplaces.

As seen in this survey, there has been much progress in understanding the anatomy and physiology of the small bowel and translating this understanding to virtual and physical test platforms for assessing the performance of intestinal devices. There is, however, much work to be done to improve these test systems. For example, there is currently no accurate synthetic tissue analogue. Synthetic analogues, such as silicone-based tubing, are poor approximations of intestinal tissue. Because of this, excised (and therefore dead) tissue is usually used to test and validate devices. Excised tissue degrades within hours and does not fully recover from initial stress, so the tissue is often preconditioned to be stable for experiments. Excised tissue in its preconditioned state is much thinner and poorly represents live intact tissue. More importantly, the enteric nervous system is deactivated in excised tissue, and there is no active response of the tissue to stress like the one *in vivo*. Attempts have been made to animate the tissue, so it mimics physiological levels of muscular contraction in bench-top settings, but these systems do not cause muscle contraction and the resulting thickening and hardening of the intestinal wall. Overall, fully contracted intestine behaves quite differently mechanically from excised tissue. Another example is the variation in anatomy and physiology of the small intestine that occurs across multiple domains is not well understood. For example, it is generally understood that the intestine changes in thickness, diameter, and vascularisation along its length within a single animal, but specific details of this variation are not known. Likewise, it also varies between animals and between genders. Age also impacts the intestine. Each of these variations is not well understood. Furthermore, the disease state of the intestine presumably impacts its mechanical and physiological properties, but research in this area is lacking. Despite that devices will more frequently be used on patients experiencing intestinal disease, most devices were tested and validated using healthy tissue, thus a disease model of Crohn's, coeliac, or other common diseases would be helpful for device testing.

Fully understanding of device-intestine interaction is a prerequisite for the development of innovative biopsy and therapeutic devices. In addition to the development of new test platforms and synthetic tissue analogues, the refined modelling of device-intestine interaction will be an important complement to the *in vitro* experiments at the early stage of research. Mathematical modelling based on the geometry of the device and the anatomy of the small intestine will still be an important means to study the device-intestine interaction and optimise the device's movement in the small intestine. In particular, FE modelling could be a handy approach to simulate new devices in such a complicated environment. Future work along this direction can be the development of a complete small-intestine FE model with the consideration of its dynamic peristalsis and food residues in both solid and liquid forms. This model could inform researchers the required propulsion force for their newly designed devices in the presence

of intestinal resistance. By using the model, researchers are able to optimise and test their devices under different parameter variations. However, FE modelling requires excessive computational efforts and is time-consuming. Therefore, a trade-off between the complexity of the FE model and its computational cost should be compromised for future modelling works.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Drake R, Vogl AW, Mitchell A. Gray's anatomy for students. 4th ed.. Amsterdam: Elsevier; 2019.
[2] Gore RM, Levine MS. Textbook of gastrointestinal radiology. 4th ed.. Philadelphia: Saunders; 2014.
[3] Early DS, Ben-Menachem T, Decker GA, Evans JA, Fanelli RD, Fisher DA, et al. Appropriate use of GI endoscopy. Gastrointest Endosc 2012;75:1127–31.
[4] Haubrich WS. Schindler who pioneered gastroscopy. Gastroenterology 1999;117:326.
[5] Ekkelenkamp VE, Koch AD, de Man RA, Kuipers EJ. Training and competence assessment in GI endoscopy: a systematic review. Gut 2016;65:607–15.
[6] Khan R, Plahouras J, Johnston BC, Scaffidi MA, Grover SC, Walsh CM. Virtual reality simulation training for health professions trainees in gastrointest endosc. Cochrane Database Syst Rev 2018;17:CD008237.
[7] ASGE Technology Committee. Endoscopic simulators. Gastrointest Endosc 2019;90:1–12.
[8] Feldman M, Friedman LS, Brandt LJ, Chung RT, Rubin DT, Wilcox CM. Sleisenger and fordtran's gastrointestinal and liver disease. 11th ed.. Philadelphia: Elsevier; 2020.
[9] Yamamoto H, Sekine Y, Sato Y, Higashizawa T, Miyata T, Iino S, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. Gastrointest Endosc 2001;53:216–20.
[10] Anvari S, Lee Y, Patro N, Soon MS, Doumouras AG, Hong D. Double-balloon enteroscopy for diagnostic and therapeutic ERCP in patients with surgically altered gastrointestinal anatomy: a systematic review and meta-analysis. Surg Endosc 2021;35:18–36.
[11] Iddan G, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. Nature 2000;405:417.
[12] Koulaouzidis A, Iakovidis DK, Karargyris A, Rondonotti E. Wireless endoscopy in 2020: Will it still be a capsule? World J Gastroenterol 2015;21(17):5119.
[13] Slawinski PR, Obstein KL, Valdastri P. Capsule endoscopy of the future: What's on the horizon? World J Gastroenterol 2015;21(37):10528.
[14] Takabayashi K, Hosoe N, Kato M, Hayashi Y, Nanki K, Fukuhara K, et al. Significance of endoscopic deep small bowel evaluation using balloon-assisted enteroscopy for crohn's disease in clinical remission. J Gastroenterol 2021;56:25–33.
[15] McCaffrey C, Chevalerias O, O'Mathuna C, Twomey K. Swallowable-capsule technology. IEEE Pervasive Comput 2008;7(1):23–9.
[16] Bouchard S, Ibrahim M, Van Gossum A. Video capsule endoscopy: perspectives of a revolutionary technique. World J Gastroenterol 2014;20(46):17330–44.
[17] Vasilakakis M, Koulaouzidis A, Yung DE, Plevris JN, Toth E, Iakovidis DK. Follow-up on: optimizing lesion detection in small bowel capsule endoscopy and beyond: from present problems to future solutions. Expert Rev Gastroenterol Hepatol 2019;13:129–41.
[18] Höög CM, Bark L, Arkani J, Gorsetman J, Broström O, Sjöqvist U. Capsule retentions and incomplete capsule endoscopy examinations: An analysis of 2300 examinations. Gastroenterol Res Pract 2012;2012:1–7.
[19] Ormeci AC, Akyuz F, Baran B, Gokturk S, Ormeci T, Pinarbasi B, et al. Retention during capsule endoscopy: Is it a real problem in routine practice? J Int Med Res 2016;44:968–75.
[20] Yang YJ. The future of capsule endoscopy: The role of artificial intelligence and other technical advancements. Clin Endosc 2020;53:387–94.
[21] Soffer S, Klang E, Shimon O, Nachmias N, Eliakim R, Ben-Horin S, et al. Deep learning for wireless capsule endoscopy: a systematic review and meta-analysis. Gastrointest Endosc 2020;92:831–9.
[22] Koulaouzidis A, Toth E. Image database, AI and capsule endoscopy; the bets are on. Endosc Int Open 2020;08:E421–2.
[23] GI genius™ intelligent endoscopy module, https://www.medtronic.com/covidien/en-gb/products/gastrointestinal-artificial-intelligence/gi-genius-intelligent-endoscopy.html [Accessed: 20 Nov 2021].
[24] Gong D, Wu L, Zhang J, Mu G, Shen L, Liu J, et al. Detection of colorectal adenomas with a real-time computer-aided system (ENDOANGEL): a randomised controlled study. Lancet Gastroenterol Hepatol 2020;5(4):352–61.
[25] Singeap A-M, Stanciu C, Trifan A. Capsule endoscopy: the road ahead. World J Gastroenterol 2016;22(1):369.
[26] Gao J, Yan G. Locomotion analysis of an inchworm-like capsule robot in the intestinal tract. IEEE Trans Biomed Eng 2015;63(2):300–10.
[27] Manfredi L, Huan Y, Cuschieri A. Low power consumption mini rotary actuator with SMA wires. Smart Mater Struct 2017;26(11):115003.
[28] Manfredi L, Cuschieri A. Design of a 2 DOFs mini hollow joint actuated with SMA wires. Materials 2018;11:2014.
[29] Kim HM, Yang S, Kim J, Park S, Cho JH, Park JY, et al. Active locomotion of a paddling-based capsule endoscope in an in vitro and in vivo experiment (with videos). Gastrointest Endosc 2010;72(2):381–7.
[30] Sun Z-J, Ye B, Qiu Y, Cheng X-G, Zhang H-H, Liu S. Preliminary study of a legged capsule robot actuated wirelessly by magnetic torque. IEEE Trans Magn 2014;50(8):1–6.
[31] Manfredi L, Capoccia E, Ciuti G, Cuschieri A. A soft pneumatic inchworm double balloon (SPID) for colonoscopy. 2019, p. 11109, 9.
[32] Guyton AC, Hall JE. Textbook of medical physiology. 11th Ed.. Philadelphia: Saunders; 2006.
[33] Daniel EE, Chapman KM. Electrical activity of the gastrointestinal tract as an indication of mechanical activity. Am J Digest Dis 1963;8:54–102.
[34] Parkes T. Peristaltic motion. Australian National University; 1967.
[35] Burns JC, Parkes T. Peristaltic motion. J Fluid Mech 1967;29:731–43.
[36] Fung YC, Yih CS. Peristaltic transport. Trans ASME: J Appl Mech 1968;35:669–75.
[37] Yin F, Fung YC. Peristaltic waves in circular cylindrical tubes. Trans ASME: J Appl Mech 1969;36:579–87.
[38] Li CH. Peristaltic transport in circular cylindrical tubes. J Biomech 1970;3:513–23.
[39] Zien TF, Ostrach S. A long wave approximation to peristaltic motion. J Biomech 1970;3:63–75.
[40] Lew HS, Fung YC, Lowenstein CB. Peristaltic carrying and mixing of chyme in the small intestine. J Biomech 1971;4:297–315.
[41] Bertuzzi A, Mancinelli R, Ronzoni G, Salinari S. A mathematical model of intestinal motor activity. J Biomech 1978;11:41–7.
[42] Mackenna BR, McKirdy HC. Peristalsis in the rabbit distal colon. J Physiol 1972;220:33–54.
[43] Bertuzzi A, Salinari S, Mancinelli R, Pescatori M. Peristaltic transport of a solid bolus. J Biomech 1983;16:459–64.
[44] Miftakhov R, Wingate D. A biomechanical model of small bowel motility. In: Proceedings of the 14th annual international conference of the IEEE engineering in medicine and biology society. Paris, France; 1992, p. 1637–9.
[45] Miftakhov R. Nonlinear electromechanical waves in cylindrical shells. Biomech Soft Tissues (In Russian) 1986;40–72.
[46] Plonsey R, Barr RG. Current flow patterns in two-dimensional anisotropic bisyncytia with normal and extreme conductivities. Biophys J 1984;43:557–71.
[47] Kottegoda S. An analysis of possible nervous mechanisms involved in the peristaltic reflex. J Physiol 1969;200:687–712.
[48] LeVeque RJ. Finite difference methods for ordinary and partial differential equations: steady state and time dependent problems. Philadelphia: Society for Industrial and Applied Mathematics (SIAM); 2007.
[49] Aliev R, Richards W, Wikswo J. A simple nonlinear model of electrical activity in the intestine. J Theoret Biol 2000;204:21–8.
[50] Miftakhov R, Akhmadeev N. Numerical simulations of effects of multiple neurotransmission on intestinal propulsion of a non-deformable bolus. Comput Math Methods Med 2007;8:11–36.
[51] Miftakhov R, Wingate D. Biomechanics of small bowel motility. Med Eng Phys 1994;16:406–15.
[52] Miftakhov R, Wingate D, Abdusheva G. Transport of a solid sphere in the peristaltic tube. WIT Trans Eng Sci 1993;1:425–32.
[53] Davyd'an G, Regirer S. On the modeling of intestinal segment motion. Fluid Dyn 1994;29:28–32.
[54] Kendall G, Thompson D, Day S. Motor responses of the small intestine to intraluminal distension in normal volunteers and patients with visceral neuropathy. Gut 1987;28:714.
[55] O'Connell P, Pemberton J, Kelly K. Motor function of the ileal J-pouch and its relation to clinical outcome after ileal pouch-anal anastomosis. World J Surg 1987;11:735.
[56] Miftakhov R. Mathematical modeling of the peristaltic reflex: a numerical experiment. J Math Sci 1994;71:2775–89.
[57] Miftakhov R, Wingate D. Numerical simulation of the peristaltic reflex of the small bowel. Biorheology 1994;31:309–25.

[58] Miftakhov R, Abdusheva G. Numerical simulation of excitation-contraction coupling in a locus of the small bowel. Biol Cybernet 1996;74:455–67.
[59] Miftakhov R, Abdusheva G, Christensen J. Numerical simulation of motility patterns of the small bowel: I - formulation of a mathematical model. J Theoret Biol 1999;197:89–112.
[60] Miftakhov R, Abdusheva G, Christensen J. Numerical simulation of motility patterns of the small bowel: II - comparative pharmacological validation of a mathematical model. J Theoret Biol 1999;200:261–90.
[61] Vigmond E, Bardakjian B. Role of cellular orientation in electrical coupling between gastrointestinal smooth muscle. Ann Biomed Eng 1998;26:703–11.
[62] Youm J, Kim N, Han J, Kim E, Joo H, Leem C, et al. A mathematical model of pacemaker activity recorded from mouse small intestine. Phil Trans R Soc A 2006;364:1135–54.
[63] Miftakhof R, Fedotov E. Intestinal propulsion of a solid non-deformable bolus. J Theoret Biol 2005;235:57–70.
[64] Miftakhof R. Numerical simulation of the role of co-transmission by acetylcholine and serotonin on motility of the gut. J Mech Med Biol 2006;6:399–428.
[65] Miftakhov R, Akhmadeev N. Dynamics of intestinal propulsion. J Theoret Biol 2007;246:377–93.
[66] Srivastava V. Effects of an inserted endoscope on chyme movement in small intestine – a theoretical model. Appl Appl Math 2007;2:79–91.
[67] Tharakan A. Modelling of physical and chemical processes in the small intestine. (Ph.D. thesis), University of Birmingham: Department of Chemical Engineering; 2008.
[68] Kano T, Kawakatsu T, Ishiguro A. Generating situation-dependent behavior: decentralized control of multi-functional intestine-like robot that can transport and mix contents. J Robot Mechatron 2013;25:871–6.
[69] Dudchenko O, Guria G. Self-sustained peristaltic transport in biological systems: a theoretical study. In: Proceedings of the instabilities and control of excitable networks: from macro- to nano-systems. Dolgoprudny, Russia; 2012, p. 19–27.
[70] Dudchenko O, Guria G. Self-sustained peristaltic waves: explicit asymptotic solutions. Phys Rev E 2012;85:020902.
[71] Hari B, Bakalis S, Fryer P. Computational modelling and simulation of the human duodenum. In: Proceedings The 2012 COMSOL conference. Milan, Italy; 2012.
[72] Akbar N, Nadeem S. Simulation of peristaltic flow of chyme in small intestine for couple stress fluid. Meccanica 2014;49:325–34.
[73] Sinnott M, Cleary P, Harrison S. Peristaltic transport of a particulate suspension in the small intestine. Appl Math Model 2017;44:143–59.
[74] Umetani Y, Inou N. Biomechanical study of peristalsis - neural control mechanism of transport in gastrointestines. Trans Soc Instrum Control Eng 1981;17:133–8.
[75] Bayliss W, Starling E. The movements and innervation of the small intestine. J Physiol 1899;24:99–143.
[76] Trendelenburg P. Physiologische und pharmakologische Versuche über die Dünndarmperistaltik. Arch F Exp Path U Pharm 1917;81:55–129.
[77] Umetani Y, Inou N. Biomechanical study of peristalsis - strain gage transducer for measuring animal intestinal movement in vivo. Trans Soc Instrum Control Eng 1984;20:162–6.
[78] Umetani Y, Inou N. Biomechanical study of peristalsis - relation between intestinal movements and the contents. Trans Soc Instrum Control Eng 1984;20:548–53.
[79] Umetani Y, Inou N. Biomechanical study of peristalsis - simulation of peristalsis in case of fluid contents. Trans Soc Instrum Control Eng 1985;21:172–6.
[80] Umetani Y, Inou N. Biomechanical study of peristalsis - neural mechanism of rhythmic segmentation. Trans Soc Instrum Control Eng 1985;21:965–9.
[81] Umetani Y, Inou N. Biomechanical study of peristalsis - modeling and analysis of intestinal movements. Trans Soc Instrum Control Eng 1986;22:965–9.
[82] Inou N, Umetani Y. Small intestinal movements in vivo and the neuro-mechanical control mechanisms. In: Proceedings ISAD 93: international symposium on autonomous decentralized systems. Kawasaki, Japan; 1993, p. 407–13.
[83] Høeg H, Slatkin A, Burdick J, Grundfest W. Biomechanical modeling of the small intestine as required for the design and operation of a robotic endoscope. In: Proceedings of the 2000 IEEE international conference on robotics and automation. San Francisco, US; 2000, p. 1599–606.
[84] Pullan A, Cheng L, Yassi R, Buist M. Modelling gastrointestinal bioelectric activity. Prog Biophy Mole Biol 2004;85:523–50.
[85] Baek N, Sung I, Kim D. Frictional resistance characteristics of a capsule inside the intestine for microendoscope design. Proc Inst Mech Eng H 2004;218:193–201.
[86] Wang X, Meng M, Chan Y. Physiological factors of the small intestine in design of active capsule endoscopy. In: Proceedings of the 2005 IEEE engineering in medicine and biology. Shanghai, China; 2005, p. 2942–5.
[87] Wang X, Meng M. An experimental study of resistant properties of the small intestine for an active capsule endoscope. Proc Inst Mech Eng H 2009;224:107–18.
[88] Slawinski P, Terry B. An automated intestinal biomechanics simulator for expediting robotic capsule endoscope development. J Med Devices 2014;8:030901.
[89] Slawinski P, Oleynikov D, Terry B. Intestinal biomechanics simulator for robotic capsule endoscope validation. J Med Eng Technol 2015;39:54–9.
[90] Kim JS, Sung IH, Kim YT, Kwon EY, Kim DE, Jang YH. Experimental investigation of frictional and viscoelastic properties of intestine for microendoscope applicaton. Tribol Lett 2006;22:143–9.
[91] Kim JS, Sung IH, Kim YT, Kim DE, Jang YH. Analytical model development for the prediction of the frictional resistance of a capsule endoscope inside an intestine. Proc Inst Mech Eng H 2007;221:837–45.
[92] Bellini C, Glass P, Sitti M, Martino ED. Biaxial mechanical modeling of the small intestine. J Mech Behav Biomed 2011;4:1727–40.
[93] Woo S, Kim T, Mohy-Ud-Din Z, Park I, Cho J. Small intestinal model for electrically propelled capsule endoscopy. BioMed Eng Online 2011;10:108.
[94] Zhang C, Liu H, Tan R, Li H. Modeling of velocity-dependent frictional resistance of a capsule robot inside an intestine. Tribol Lett 2012;47:295–301.
[95] Zhou H, Alici G, Than T, Li W. An investigation into biomechanical and biotribological properties of a real intestine for design of a spiral-type robotic capsule. In: Proceedings of the 2013 IEEE/ASME international conference on advanced intelligent mechatronics. Wollongong, Australia; 2013, p. 71–6.
[96] Zhang C, Liu H, Li H. Modeling of frictional resistance of a capsule robot moving in the intestine at a constant velocity. Tribol Lett 2014;53:71–8.
[97] Zhang C, Liu H, Li H. Experimental investigation of intestinal frictional resistance in the starting process of the capsule robot. Tribol Int 2014;64:39.
[98] Zhang C, Liu H. Analytical friction model of the capsulr robot in the small intestine. Tribol Lett 2016;64:39.
[99] Li W, Shi L, Deng H, Zhou Z. Investigation on friction trauma of small intestine in vivo under reciprocal sliding conditions. Tribol Lett 2014;55:261–70.
[100] Lin C, Yu Q, Wang J, Ji W, Li W, Zhou Z. Friction behavior between endoscopy and esophageal internal surface. Wear 2017;376–377:272–80.
[101] Li P, Kothari V, Terry B. Design and preliminary experimental investigation of a capsule for measuring the small intestine contraction pressure. IEEE Trans Biomed Eng 2015;62:2702–8.
[102] Sliker LJ, Ciuti G, Rentschler ME, Menciassi A. Frictional resistance model for tissue-capsule endoscope sliding contact in the gastrointestinal tract. Tribol Int 2016;102:472–84.
[103] Rotman O, Zaretsky U, Birnhoim Y, Pascal A, Einav S. Mechanical simulator of the small intestine for in-vitro practice with endoscopic devices. J Biomed Eng Biosci 2016;3:1–3.
[104] Fracczak L, Zak P, Kolejwa M, Czkwianianc E. The influence of lubricants on friction coefficient between the intestines and a silicone. Int J Mech Eng Robot Res 2020;9:1–3.
[105] Yan Y, Liu Y, Manfredi L, Prasad S. Modelling of a vibro-impact self-propelled capsule in the small intestine. Nonlinear Dynam 2019;96:123–44.
[106] Guo B, Liu Y, Prasad S. Modelling of capsule-intestine contact for a self-propelled capsule robot via experimental and numerical investigation. Nonlinear Dynam 2019;98:3155–67.
[107] Guo B, Ley E, Tian J, Zhang J, Liu Y, Prasad S. Experimental and numerical studies of intestinal frictions for propulsive force optimisation of a vibro-impact capsule system. Nonlinear Dynam 2020;101:65–83.

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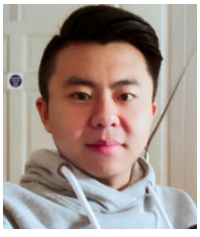

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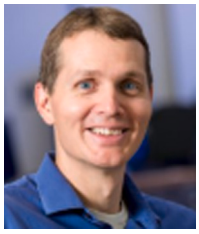

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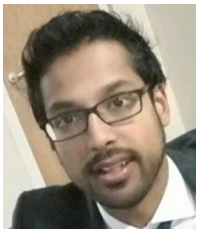

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