A Review of In Vitro and In Silico Swallowing Simulators: Design and Applications

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***Abstract*—Swallowing is a primary and complex behaviour that transports food and drink from the oral cavity, through the pharynx and oesophagus, into the stomach at an appropriate rate and speed. To understand this sophisticated behaviour, a tremendous amount of research has been carried out by utilising the in vivo approach, which is often challenging to perform, poses a risk to the subjects if interventions are undertaken and are seldom able to control for confounding factors. In contrast, in silico (computational) and in vitro (instrumental) methods offer an alternate insight into the process of the human swallowing system. However, the appropriateness of the design and application of these methods have not been formally evaluated. The purpose of this review is to investigate and evaluate the state of the art of in vitro and in silico swallowing simulators, focusing on the evaluation of their mechanical or computational designs in comparison to the corresponding swallowing mechanisms during various phases of swallowing (oral phase, pharyngeal phase and esophageal phase). Additionally, the potential of the simulators is also discussed in various areas of applications, including the study of swallowing impairments, swallowing medications, food process design and dysphagia management. We also address current limitations and recommendations for the future development of existing simulators.**

***Index Terms*—Simulation, swallowing, biomedical engineering, instrumental method, computational method.**

I. Introduction

SWALLOWING is defined, by the ICF-CY (International Classification of Functioning, Disability and Health for Children and Youth), as an essential and complex function to clear food and drink from the oral cavity into the stomach, via the pharynx and oesophagus [1], [2]. Dysphagia, defined as difficulty swallowing [3], [4], impacts the enjoyment of eating a variety of foods and may potentially increase mortality rates when found in a post-acute care facility [5], [6], [7]. For a better understanding of the impairments, the main interest of medical professionals lies in the study of the physiological mechanisms of human swallowing. There are generally three types of studies of the GI tract: In vivo, in vitro and in silico studies [8].

The most common method is by in vivo approach, which utilises various imaging techniques to characterise the flow of the material through the GI tract to gain insight into the mechanisms of swallowing. The common techniques are: Videofluoroscopic Swallowing Study (VFSS) [9], [10], [11], [12], [13], Fiberoptic endoscopic evaluation of swallowing (FEES) [14], High-resolution manometry (HRM) [10], [15], [16] and Functional lumen imaging probe (FLIP) [17], [18], [19], [20], [21]. However, this type of investigations involves human or animal subjects, presenting several concerns, such as exposure to radiation, implant surgery required for sensors and health and ethical issues related to human participants and animal subjects. Therefore, methods have been developed to assist in vivo studies by exploring swallow function and dysfunction through in vitro (instrumental methods) and in silico (computational methods) models. The word “in vitro” generally refers to the study of deglutition externally of the human body, while the word “in silico” indicates the swallowing processes are simulated by using numerical and computational approaches [8]. Compared to in vivo studies, in vitro and in silico approaches are suited for testing multiple scenarios whilst maintaining the testing environment in the same condition throughout the experiments.

The in vitro and in silico types of approaches (simulators) can be commonly categorised according to the three phases of swallowing, such as the oral phase, the pharyngeal phase and the esophageal phase [27], [28], [29]. During the oral-propulsive stage in the oral phase, the tongue tip rises, contacting the hard palate, and starts to generate a series of wave motions progressively from anterior to posterior, forcing the bolus to travel backward along the palate and finally into the oropharynx [30]. Once the bolus enters the pharynx, the soft palate starts to elevate and touch the lateral and posterior walls of the pharynx, which prevents bolus regurgitation into the nasal cavity [31]. Meanwhile, the root of the tongue is activated, along with other muscles (anterior digastric, geniohyoid, stylohyoid, styloglossus, palatoglossus and palatopharyngeus) to produce a series of contractions driving bolus transport caudally [4], [30]. The length of the pharynx is also shortened simultaneously to

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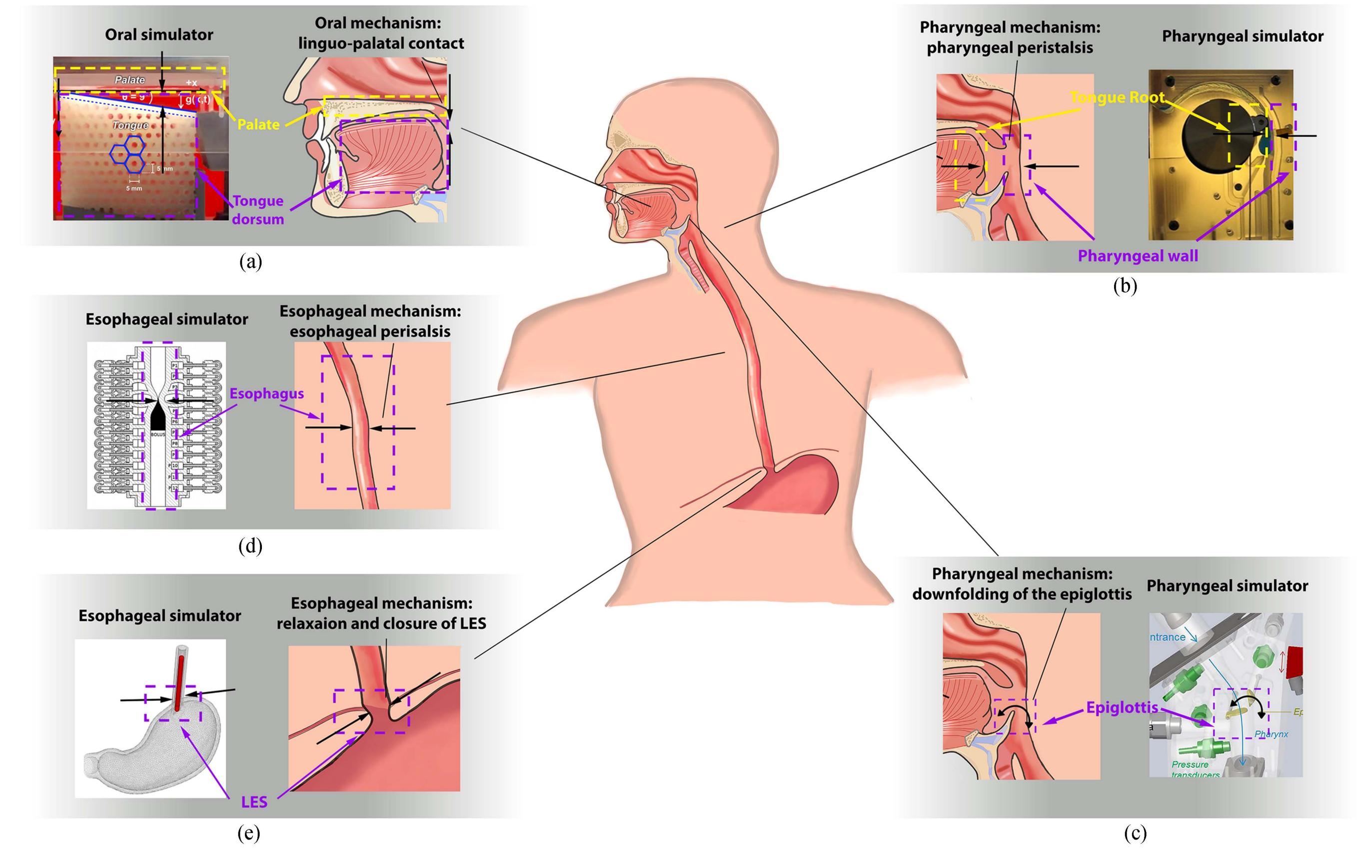

Fig. 1. Swallowing mechanisms presented in this review include the linguo-palatal contact, the pharyngeal peristalsis, the downfolding of the epiglottis, the esophageal peristalsis and the relaxation and the closure of lower esophageal sphincter (LES). Each mechanism is presented along with an example of simulators in the figure. (a) An in vitro simulator mimicked the tongue and the palate to simulate the linguo-palatal contact [22]. (b) In vitro simulator Cambridge Throat simulated the pharyngeal peristalsis by using a roller system [23]. (c) The adjustable valve was adapted in an in vitro simulator to mimic the epiglottis [24]. (d) The esophageal peristalsis was imitated in a soft esophageal simulator called RoSE [25]. (e) The LES to prevent the retrograde flow from the stomach was simulated in an in silico simulator [26].

decrease the volume of the pharyngeal cavity [32]. Once the bolus passes the upper esophageal sphincter (UES), transport occurs through peristaltic waves generated over the length of the oesophagus and extending to the lower esophageal sphincter and into the stomach [33], [34], [35].

Recently, a few researchers attempted to review the state of the arts of the swallowing simulators with a branching frame of approach. Marconati et al. [33] outlined both in vitro and in silico models to predict the ease of swallowing. Chen et al. [30] and Qazi et al. [36] abridged the physical swallowing simulators since 2004, whereas Almeida et al. [37] summarised the models in the computational domain. However, these works primarily focus on the rheological study of food bolus during swallowing simulation with less evaluation of the design of the simulators. Discussion of the application of these simulators was also lacking.

To the best of our knowledge, this is the first attempt to comprehensively review the current state of swallowing simulators and their correspondence with the mechanisms of swallowing, as well as to summarise the various applications of these simulators. The aims of this review are the following: 1) To evaluate the simulator designs compared with their physiological counterparts in their functionality (Fig. 1); 2) To explore how swallowing simulators can be applied to study swallowing impairments, assess swallowing medications, optimise food processing techniques, and facilitate effective dysphagia management. Throughout this review, we pay particular attention to the swallowing mechanisms targeted by the simulators. The abnormal conditions simulated in the presented simulators are also discussed, to explore alternative explanations of impaired swallowing. Studies focusing on other applications of simulators are also reviewed, such as investigating food texture for safe swallowing, evaluating the performance of dysphagia treatments and mimicking swallowing medications. In addition, the scope of the review is limited to 1) the general overview of the normal deglutition process excluding mastication; 2) causes of dysphagia excluding neurological disorders. The reasons are mainly due to the focus on the process of moving the food bolus from the mouth to the stomach and the interest in the pathologies related to mechanical aspects.

The review is structured in eight sections. Section II describes the strategy we applied to search and select relevant studies. Sections III–V focus on presenting the computational and physical simulators with the design evaluation and Section VI summarises the available and potential areas of the applications. In Section VII, a discussion is presented to outline the state of swallowing simulators, along with their limitations and suggestions for future application. Finally, a conclusion is drawn in the Section VIII.

II. Review Methodology

A. Search Strategy

Four electronic databases, Scopus, PubMed, Web of Science, and IEEEXplore, were selected for the comprehensive search. These databases were chosen for their broad coverage of interdisciplinary literature relevant to simulation models for in vitro or in silico studies of the human swallowing process. The search encompassed articles published from the inception of each database, spanning the years 2010 to 2022. The search terms were carefully identified based on the primary focus of this review paper, and they are: "*Swallowing*", "*Deglutition*", "*Simulation*", "In Vitro" and "In Silico". The search terms were combined using the Boolean operators "AND" and "OR", finding articles that contain any combination of the terms within each category. Specifically, the query utilized was: "("*Swallowing*" OR "*Deglutition*") AND ("*Simulation*" OR "In Vitro" OR "In Silico")."

B. Selection Criteria

Specific selection criteria were established to ensure the relevance and appropriateness of the studies included in this review. The research fields were refined and limited to the domains of robotics, engineering, computer science, mathematics, food science, medicine and mechanical design. Furthermore, we confined our examination to peer-reviewed English language research articles. Notably, specific article types, such as expert opinions, letters to the editor, commentaries, editorials, and textbooks, were intentionally omitted to maintain a sharp focus on our predefined criteria. These restrictions were applied to narrow down the results and focus on the primary objectives of the review.

Inclusion criteria applied for screening results include: 1) Swallowing devices: studies focusing on the design and development of instrumental simulators and they should be related to the mechanics of human swallowing; 2) Computational Models: Studies involving computational models or simulations relevant to human swallowing mechanics; 3) Swallowing Phases: The studies should relate to one or more phases of the swallowing process, including oral, pharyngeal, and esophageal phases; 4) Applications of Swallowing: Studies discussing the practical applications of swallowing simulators were considered for inclusion.

Exclusion criteria applied included: 1) Irrelevant to the scope: Studies that did not align with the main objectives of the review, such as those in unrelated research domains; 2) Studies narrowly focusing on the physiology of swallowing, pharmacology, pharmaceutics, medical or clinical practice were excluded.

To ensure the accuracy of study selection, two authors independently applied the inclusion/exclusion criteria to the titles and abstracts of potential studies. Any discrepancies were resolved through discussion and, if necessary, a third author provided additional review and arbitration.

C. Data Extraction and Analysis

Data extraction was carried out by the two independent reviewers to identify the most pertinent studies. Our primary focus during this process revolved around harvesting data associated with several key aspects. These aspects encompassed the phases of the swallowing process, intricacies of the mechanical design underpinning the simulators, methodologies employed for constructing computational models, and the performance metrics used to benchmark these models against in vivo outcomes. Furthermore, we extracted information pertaining to the limitations of the studies, shedding light on their constraints and challenges. Finally, we delved into the applications of these swallowing simulators within defined domains, which included but were not limited to the study of swallowing impairments, investigation of food texture, drug swallowing dynamics, and the management and treatment of dysphagia.

D. Outcomes

The electronic database search initially yielded 1,917 articles, with an additional 31 articles discovered through suggestions, references in other review articles, and collaborative research efforts. After removing duplicates, 1,075 unique articles remained. A two-round screening process was then employed, applying inclusion/exclusion criteria to titles and abstracts, resulting in 186 articles passing the primary screening.

Subsequently, the 186 articles underwent a full-text assessment with inclusion/exclusion criteria. Of these, 19 articles fell outside the scope of our review's domains, 6 focused solely on pharmacology, 16 on pharmaceutics, 15 on clinical procedures, 31 on the physiology of swallowing, 1 on medical aspects, and 17 provided insufficient results. After this rigorous screening, a total of 81 articles met the inclusion criteria and were included in our review. For a detailed overview of the entire screening process, please refer to Fig. 2.

III. Oral Simulators

The primary mechanism of swallowing during the oral phase is that the food material is mixed with saliva and is manipulated onto and across the surface of the tongue until a bolus is formed [38]. If there is impairment of the tongue and or facial muscles, difficulty forming and retaining bolus in the oral cavity can be identified. Loss of material from the oral cavity, either externally via the lips (oral incompetence) or prematurely into the pharynx (premature spillage), may occur and can result in secondary consequences such as laryngeal penetration or (if the airway remains open) aspiration.

A. Linguo-Palatal Contact

Linguo-palatal contact occurs in the oral cavity, bringing the tongue to the roof of the mouth to provide masticatory benefit and propulsion to the bolus, directing this toward the oropharynx [39]. The design of simulators, therefore, focuses on capturing and simulating the behaviours of these organs. Studies focused on the design of the flexibility and the geometry to match the anatomical structure of the human tongue [40], [41], [42],

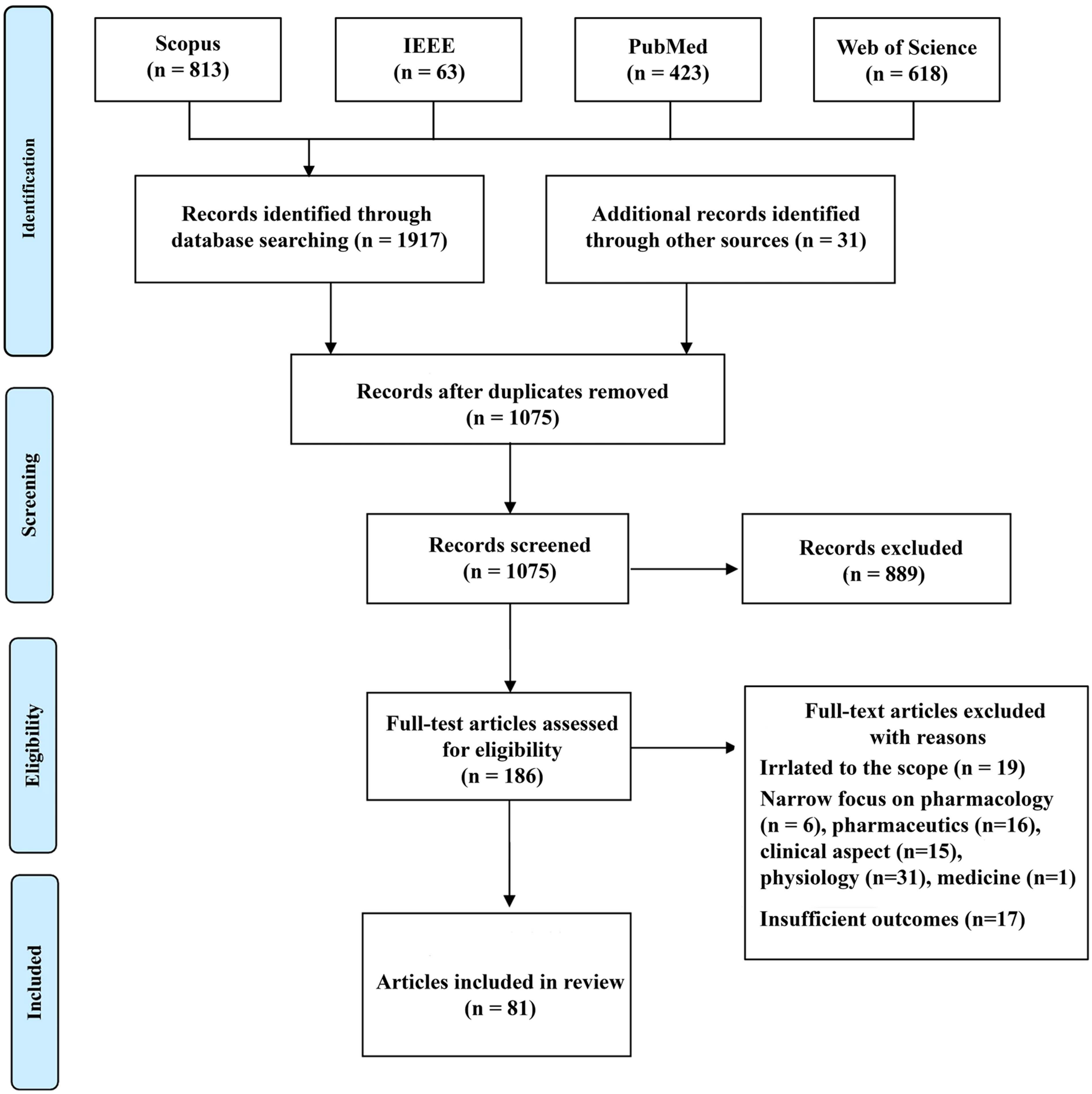

Fig. 2. Outcomes of the search and the flow of information during the process of selecting studies.

[43], [44], but are lacking evidence of their functionality to manipulate and interact with bolus during swallowing. Meanwhile, others focused on its strength to move food by compressing against the palate, [45], [46], [47], [48], [49], [50] to relate this to bolus propulsion in normal swallowing.

A method to imitate bolus propulsion is to incline the posture of the tongue to transport the bolus passively by gravitational force. In an in vitro study, tongue and palate were designed in the Video Fluorographic Swallowing Study dynamic simulation system (VFSS-DSS, shown in Fig. 3(a)) to mimic human oral swallowing. A 16-wiring mechanism system was applied to control the motions of the robot, with one on the tongue tip, three on the center of the tongue, six on the hyoid bone and the other six on the mandible. By controlling wires, linguo-palatal contact is simulated with the lifting of the tongue to allow the bolus to fall into the pharynx with the help of gravity. The impact of the roughness of oral mucosa was not considered in this study but illustrated in the model presented by Ershad et al. [51]. The in vitro model (Fig. 3(b)) provided a framework to investigate the influence of the friction between bolus and mucosa surface, by using artificial saliva as lubrication transport the bolus on an inclined ramp freely. However, the above simulators only transport the bolus by applying gravitational force without indicating the compressing force between the tongue and the palate, which takes an important role during oral swallowing.

An approach to simulating compression is employing a two-parallel-plate system to squeeze the bolus. Nicosia et al. (Fig. 3(c)) [52] focused on estimating the shear rate of bolus in a simple theoretical model that simulates the oral cavity by using two parallel rigid plates to mimic the tongue (upper plate)

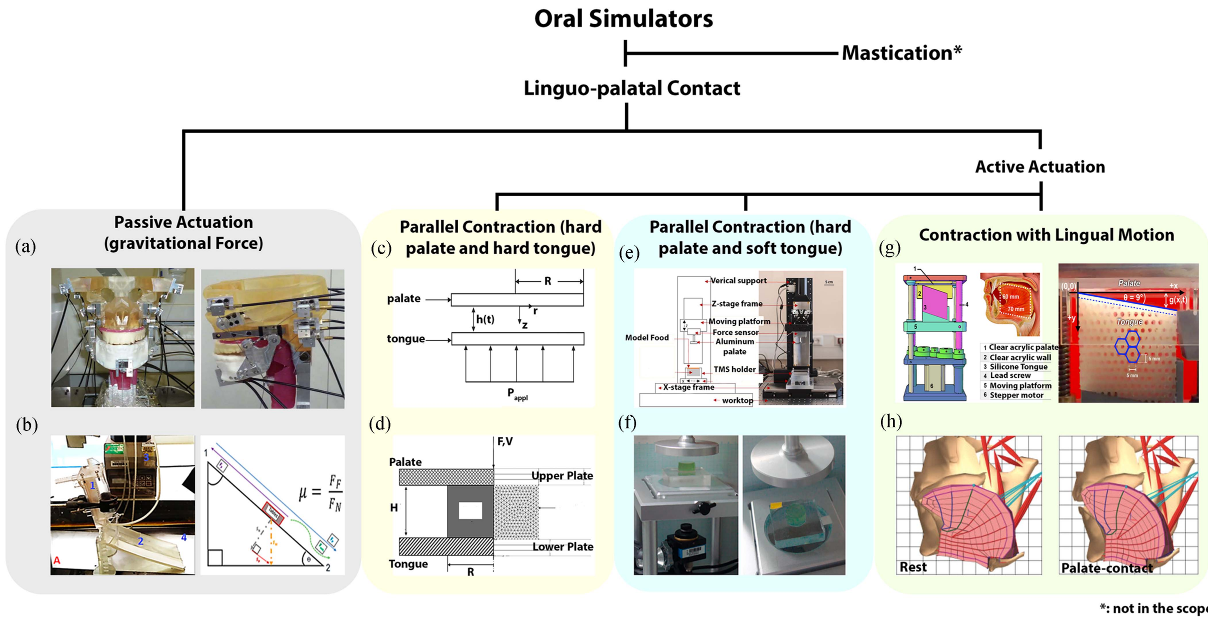

Fig. 3. This figure shows examples of the oral simulators. Only linguo-palatal contact mechanism is shown in the picture, as mastication mechanism is not in the scope of this review. The simulators can be grouped based on the actuation type (active or passive) and the bolus transport method, either by the gravitational force, parallel contraction or a contraction following the lingual motion. (a) The VFSS-DSS robotic model introduced by Noh et al. contains the structure of the oral cavity, the larynx and the pharynx [47]. (b) Bolus is transported by sliding down on a slope with salivary lubrication and artificial oral mucosa [51]. (c), (d) Two parallel plates were used to simulate the palate (upper) and the tongue (lower) to squeeze the food [46], [52]. (e), (f) The parallel contraction is imitated by a rigid upper plate (hard palate) and a silicone (tongue) [55], [56]. (g) A soft tongue was developed by Redfearn et al. to mimic the tongue compressing against the palate [48]. (h) A computational method performs the motion of human tongue to mimic palate-contact [65].

and the palate (low plate). The compression is simulated by shortening the distance between two plates until they are fully in contact with each other. This conceptual design was later realised by Mossaz et al. (Fig. 3(d)) [46] to construct a physical two-parallel-plate system. This in vitro model aims to investigate the influence parameters on the spreading area on the tongue based on this system. The swallowing experiments consist of three steps, with a constant speed (2–35 mm/s) generated by a motor in step 1, a constant force (0.8–30 N) provided by the weight of the upper plate in step 2, and a relaxation state in step 3. This follows the swallowing process reported in the literature [53], [54]. Additionally, the roughness of the plate surfaces could be adjusted to evaluate the effects of wall resistance on bolus transport. The parallel-plate system was later adapted and improved by Srivastava et al. [55](Fig. 3(e)) and Kohyama et al. [56], [57](Fig. 3(f)) by replacing the tongue (lower plate) with various hardness soft material. Although the bolus in the two-plate system illustrates the compression behaviours compared to in vitro VFSS-DSS dynamic system, due to the parallel motion restriction, the bolus is only compressed and lacks the peristaltic wave of the tongue.

More biomimetic simulators that are able to mimic linguo-palatal contract instead of only compression were presented by Nicosia et al. [45] and Redfearn et al. [48]. The in silico model developed by Nicosia et al. [45] was based on the Arbitrary Lagrangian and Eulerian (ALE) methods, with a defined working space between the tongue and palate. A time-variant equation, based on the bi-plane videofluoroscopic study [58], was adapted to describe the lingual gesture of the tongue. Meanwhile, Redfearn et al. (Fig. 3(g)) [48] developed an in vitro model for simulating the behaviours of the tongue compressing against the palate. Compared to the previous simulators, the highlighted design is: 1) Considering the softness of the tongue according to the physiological values of the human tongue reported in clinical studies [59], [60], [61]; 2) A space left between the top surface of the tongue and the palate, with an inclination angle to perform a sweeping pattern that matches the findings of human swallowing. However, these two models focused on linguo-palatal contact by isolating the tongue from the oral cavity. Studies have discovered that the movements of the tongue are associated with the jaw and hyoid, especially during talking and eating [62], [63], [64]. A significant contribution from the work of Stavness et al. (Fig. 3(h)) was to simulate and investigate the lingual contact when the movement of the jaw and hyoid was involved [65]. The work was based on in silico model that contained two parts: The deformable FEM model for the tongue and the rigid parts for the jaw and hyoid. All the parts were based on the geometry of the CT data obtained from a subject. In the later study of the same group, facial muscles were considered to investigate the biomechanics of the orofacial movements during speech [66].

IV. Pharyngeal Simulators

Three main activities occur during this phase, which are pharyngeal peristalsis, downfolding of the epiglottis and the opening of the UES. However, to the best of our knowledge, the availability of simulators that accurately replicate the dynamic

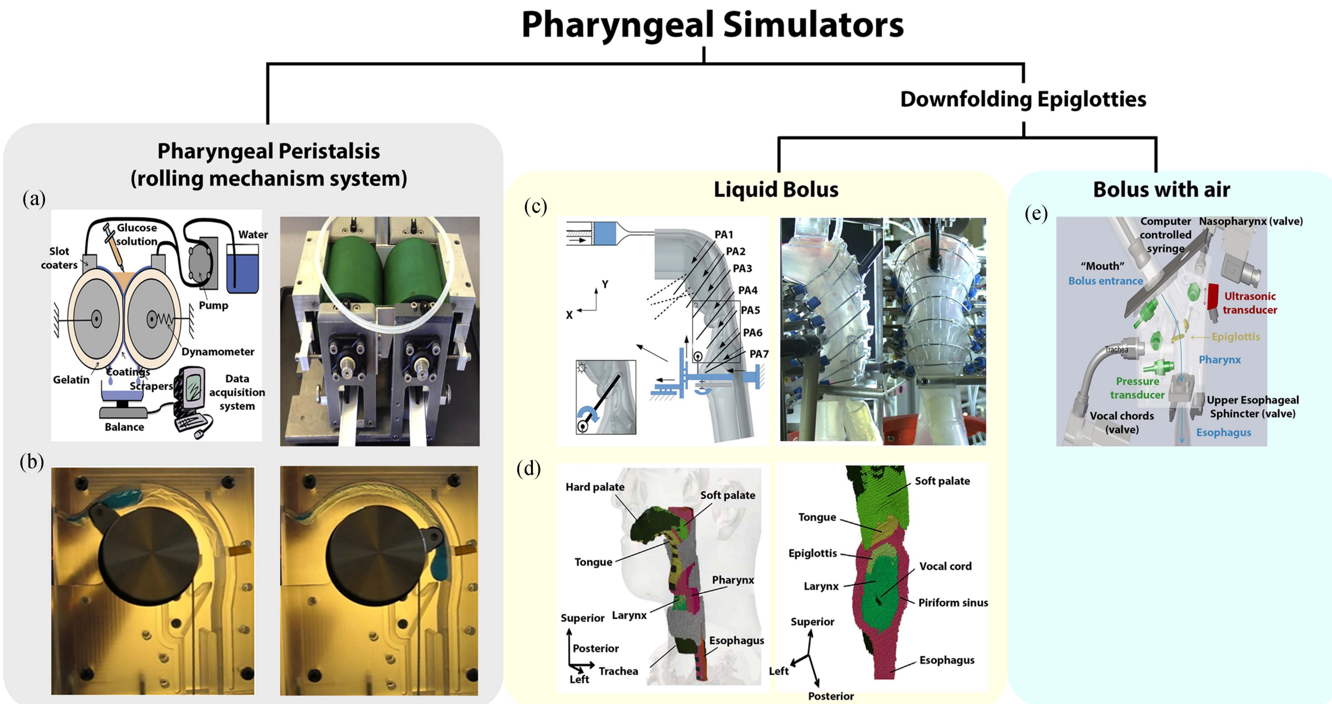

Fig. 4. This figure shows examples of the pharyngeal simulators. The simulators can be grouped based on the mechanisms (pharyngeal peristalsis and downfolding epiglottis). Examples under the pharyngeal peristalsis category are fixed or without epiglottis design, whilst the examples under the other category focus on simulation involved with the movable epiglottis and can be categorised based on the bolus type, whether air influence is considered or not. (a) A double-roller rolling mechanism is to imitate pharyngeal peristalsis. (b) Cambridge throat is presented by Mowlavi et al. to perform swallowing during the pharyngeal phase [75]. (c) The pharyngeal simulator is actuated by 16 wires with movable epiglottis design [67]. (d) A computational approach simulates pharyngeal swallowing with adjustable epiglottis [78]. (e) The Gothern throat considers both air flow and liquid flow during pharyngeal swallowing [36].

behaviour of the UES is relatively limited. While a handful of studies do incorporate UES functionality into their designs, the UES's specific performance is not always the central focus of these investigations [24], [67], [68], [69], [70]. Furthermore, it is worth noting that the design characteristics of the UES simulators frequently share similarities with those designed for modelling other mechanisms, such as circular contractions within either pharyngeal or esophageal peristalsis [67], [69], [70]. Thus, the studies included in this review evaluate simulators that only focus on the other two mechanisms through various approaches. Although some models were capable of simulating both mechanisms, they were classified by the mechanism that was predominantly the focus of the studies.

A. Pharyngeal Peristalsis

Mathieu et al. [71](Fig. 4(a)) proposed an in vitro model by applying a rolling mechanism (two rollers system) to mimic the swallowing procedure in the oropharynx. The rolling mechanism consists of two rollers (radius = 35 mm, length = 80 mm) that were attached to spring dynamometers and actuated by electric motors. When a force was applied to the spring dynamometers, two rollers would contact each other generating pharyngeal contractions. This design followed the in silico model [72], [73] that assumed the function of the pharyngeal walls during the peristalsis acting as being in rotation to each other. A soft layer of gelatin with a thickness of 5 mm was covered on the surface of the rollers to mimic the pharyngeal mucosa. The saliva was simulated by thin films of water at a controllable thickness. In the study, the flow rate of the water coating decided the velocity of the peristaltic waves as well as the thickness of the coating. During swallowing, a food bolus (5 ml) was slowly injected into the middle of the two rotating rotors with a contacting force at 2 N. This design mimicked pharyngeal peristalsis with the consideration of lubrication, which is barely simulated in other pharyngeal simulators. However, only Newtonian fluid was tested in this model and other parts of swallowing organs were not considered in this design.

A more biomimetic design - the Cambridge Throat (Fig. 4(b)) presented by Mackley et al. [23], later improved by Hayoun et al. [74] and Mowlavi et al. [75], was based on a similar mechanism but only with a single roller. This simulated peristalsis is generated from the oral phase to the pharyngeal phase. The roller was attached to a rotating arm to simulate the tongue compressing the palate with an adjustable rotating range, while a polyethylene membrane containing the bolus was placed between the palate and the roller. Other organs were also presented but remained stationary, such as a fixed epiglottis, the larynx and the oesophagus. However, the primary purpose of this model focused on pharyngeal peristalsis rather than other mechanism; thus, the function of other organs was not studied. During swallowing, a bolus was injected into the membrane via a syringe and later pushed by the roller from the anterior part of the mouth to the oropharynx. The range of the rotating force was within 1–5 N of clinical experiments [76], [77]. Compared to the two rollers system presented by Mathieu et al. [71], the influence of lubrication was not considered in this design. Also, as the bolus was contained in the soft membrane, the flow of the bolus might be constrained and the impacts of its stiffness were not investigated in the study.

B. Downfolding of the Epiglottis

A recent standard method that obtains the geometry of the related organs from CT, videofluorography (VF), or magnetic resonance imaging (MRI) images, was applied among these studies [70], [78], [79], [80]. Kikuchi et.al [79] (Fig. 4(d)) constructed a 3D numerical model based on the VF and CT images from a healthy 25-year-old subject. Another in silico model, for understanding the pathology of the aspiration, was developed by Michiwaki et al. [70]. The geometry of this model was based on the VF and CT images of two subjects, a 25-year-old healthy subject and an 82-year-old subject with mild dysphagia. Later, Michiwaki et al. [80] established a simulation model that depended on the CT and VF images of a 9-year-old child, aiming to simulate the scenario when a child accidentally swallows a toy. Among these studies, the simulation models followed a five-step procedure to create the organs model, including extracting the boundaries of organs from CT images, improving the geometry with the help of the VF images in two directions (anterior-posterior and lateral projections), modelling the bolus, integrating the bolus with the organs and comparing the simulation models to the CT and VF images. The behaviours of the bolus were described by the moving particle simulation method and manipulated by multiple control regions over the organ models. These control regions allow the muscle of the organ models to move in desired directions with desired forces. The movements of the organ models would result in the changes in the shapes and these changes were validated with the VF images during the swallowing simulation. The swallowing simulation followed the physiologic swallowing process, with the squeezing motion of the tongue, the shortened pharyngeal wall, the downfolding mechanism of the epiglottis and the opening of the UES. The limitations of this in silico design stated by Michiwaki et al. [80] was the time assumption of building the model at about 2–3 months and the organs were defined as rigid bodies without consideration of muscle deformation.

A numerical simulation model that mimicked the deformation of the organs was presented by Mizunuma et al. [81] to study the flow of the thickened liquid bolus. The simulation model contained several swallowing organs, such as the tongue dorsum, palate, pharynx, epiglottis, and oesophagus. The finite element method was adapted to build the simulation model, with organ parts assumed to display linear elastic behaviours. Also, the bolus was based on a power law model having non-Newtonian behaviours. Later studies, conducted by Sonomura et al. [82] and Mizunuma et al. [83], updated this model with some improvements on the shell elements to increase the simulation accuracy. The overall swallowing process in this simulation model was that a bolus was first fed into the oral cavity. The gravitational force was applied to the bolus to move it into the posterior tongue. Pharyngeal peristalsis was generated with the help of a squeezing movement between the root of the tongue and the retropharyngeal wall, to transport the bolus into the oesophagus. The epiglottis was movable and could be utilised to simulate both normal and abnormal swallowing conditions. The study of Sonomura et al. [82] focused on investigating these conditions, while Mizunuma et al. [83] modified the resistance of the organs (the tongue and the retropharyngeal wall) to study the impact of the lubrication during the pharyngeal swallowing.

The designs of the above simulators only considered liquid swallowing, except a simulation of swallowing toys was conducted by Michiwaki et al. [80]. The influence of air involved in swallowing had not been addressed in these designs. An in vitro model (Fig. 4(e)), presented by Qazi and Stading [36] called the Gothenburg throat, aims to understand the breathing-swallowing relationship and the rheological parameters of the bolus [24]. The model contains aspects of both the pharynx and airway, which are intimately connected to pharyngeal structures and in some cases, structures are shared in function. This includes the airway path through the nasopharynx, around the epiglottis and into the larynx, with two valves attached to mimic control at the nasopharyngeal region, and a moveable epiglottis that helps direct bolus flow. A sensory system that includes four pressure sensors and an ultrasound sensor was combined with the Ultrasound Velocimetry Profiling (UVP) technique to capture the information of bolus flow, for example, velocity, pressure, movement and location. To have an environment close to in vivo study, temperature-controlled water was circulating in the system to maintain the desired temperature [24]. The bolus (20 ml) was fed into the oral part at a fixed speed via a syringe and driven by gravity passing through the pharyngeal part and flowing into the oesophagus. One of the limitations of this design was that the device was built with hard materials as its main body. Due to the properties of the materials, the simulator was not compliant enough to generate the pharyngeal peristalsis to drive the bolus. Instead, it only relied on the gravitational force and pressure difference to transport the bolus. Meanwhile, another in vitro model presented by Fujiso et al. [67] (Fig. 4(c)) also considered the air impact; however, there was no sensory system designed in this model and the swallowing experiments conducted in the study were not validated by clinical reports.

V. Esophageal Simulators

Common esophageal disorders, including gastroesophageal reflux disease (GERD), motility disorders including achalasia and esophageal spasms [86], can impede the flow of a food bolus through the oesophagus into the stomach. In addition, failure of the upper or lower esophageal sphincter to close or open at the correct time will also alter bolus kinematics. Meanwhile, most available in vitro and in silico studies focus on investigating esophageal peristalsis and the closure of the LES. Only a few studies target on anatomical structure; however, they neglect the swallowing mechanism, which is beneficial for the surgical training [87]. Failure of closure of the LES will lead to

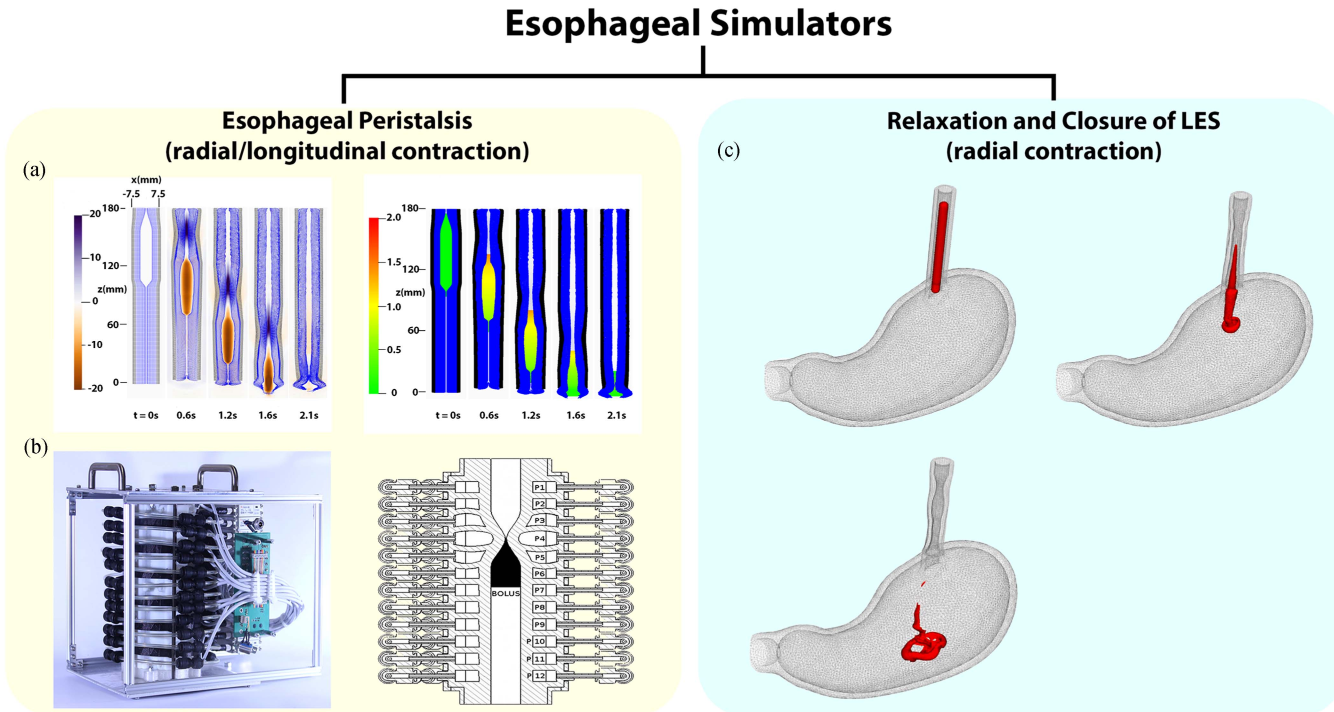

Fig. 5. This figure shows the examples of esophageal simulators. The simulators can be categorised based on the swallowing mechanisms, such as esophageal peristalsis and the relaxation and closure of LES. (a) A numerical approach to simulate the esophageal swallowing is based on finite element method [84]. (b) RoSE - the soft robotic esophageal to perform the peristaltic waves during the esophageal phase swallowing [85]. (c) The simulation model simulates the gastroesophageal reflux conditions [26].

a retrograde flow along the oesophagus. Several studies related to retrograde flows were discussed in this section.

A. Esophageal Peristalsis

A simulated oesophagus was presented by Kou et al. [69], [84], [88]. The oesophagus model (Fig. 5(a)) had a length of 180 mm, with multi-layers such as mucosa, interfascial layer, circular muscle (CM) and longitudinal muscle (LM) to match the in vivo data of the human oesophagus. Two actuation systems were designed to mimic the peristaltic contractions from two layers, CM contraction and LM shortening. Peristalsis was achieved by dynamically changing the rest lengths of these two layers along the esophageal wall.

To mimic esophageal peristalsis, esophageal simulator RoSE [89], [90] (Fig. 5(b)) was proposed. RoSE is a soft robot comprising compliant materials [91] and a pneumatic actuation system. The actuation system was applied on a hollow silicone tube that was fabricated by Ecoflex 00–30 with an inner diameter of 18 mm, a thickness of 8 mm and a length of 185 mm. Four chambers were placed in a circular arrangement around the tube to form a single ring layer and with a total of 12 layers uniformly distributed along the length of the conduit resulting in 48 chambers in total. The chambers on each layer were inflated with air pressure in sequence to generate a peristaltic wave that provided a maximum intrabolus pressure of 120 mmHg (16 kPa) and various wave velocities from 2 to 4 cm/s. A stretchable sensory system developed by Din et al. [92] was embedded in RoSE to measure the pressure, shear stress and strain during bolus swallowing. The accuracy of the stretchable sensors was validated by manometric data and a root-mean-square error was discovered at 5.67% by comparing pressure from both measurements. Based on the previous work conducted by Dirven et al. [93], Zhu et al. [94] developed a controller relying on a central pattern generator (CPG) model to accordingly control the pressure input of each chamber, by considering the feedback information from the stretchable sensors [92]. The outcomes of this study indicated that the sinusoidal peristaltic waves could be achieved with errors ranging from 0% to 12%, with errors in the range of 2% when the chambers were actuated with higher pressures more reflective of food swallowing. However, due to the design of the sinusoidal waves, the bolus was only propelled by contraction at the tail without another contraction at its head, which is different from swallowing physiology.

To interpret intra-fluid behaviours on an artificial oesophagus, Ruiz-Huerta et al. [95] presented an alternative artificial esophageal simulator (AES) by altering RoSE to swallow barium sulfate paste mixed with baby food. There were three main differences between this study and the previous studies with RoSE: 1) The number of pneumatic chambers in this study was 24 instead of 48 in RoSE; 2) The maximum pressure generated from chambers was up to 190 mmHg instead of 120 mmHg in RoSE; 3) The sequence of activating the chambers was dissimilar. The sequence utilised in the AES was able to inflate the chambers to form a closed space to carry the bolus, while a sinusoidal wave was applied in RoSE to perform a wave of contractions to transport the bolus from its tail. The swallowing experiments were recorded in X-Ray images, which were later analysed to find the flow and velocity vector of the bolus. Although this study investigated the fluid dynamic inside the esophageal simulator, however, due to the pressure (190 mmHg) difference stated before, it may generate abnormal intrabolus pressure.

B. Relaxation and Closure of the LES

Acharya et al. [26] presented a simulation of a transient LES relaxation event with a flow returning from the stomach to the oesophagus. The simulation model (Fig. 5(c)) combined an esophageal model based on the study of Kou et al. [69], [84], [88] and a 3D model for the stomach. The 3D model for the stomach followed the physical geometry of the human stomach and contained both circular and longitudinal muscle layers to produce the gastric peristaltic waves along the organ [26]. However, the design of the esophagogastric junction (EGJ) was simplified, missing some physiologic features. The control of LES at the EGJ was only simulated by the circular muscle layer with symmetric pressure, but neglecting the participation of the extrinsic sphincter that consisted of sling fibers from the crural diaphragm [96].

Except for simulating the retrograde flow returning from the stomach, two additional studies simulating reflux during esophageal peristalsis were discovered, with one focusing on the fluid dynamics of the bolus transport through the oesophagus [97], and the other studying the heat transfer of peristalsis by introducing an additional parameter, thermal conductivity, to that of the bolus transport [98]. Compared to the study of Acharya et al. [26], the main differences were only mathematical models applied in [97], [98] to simulate an oesophagus instead of the visualised 3D model in [26] and the driving forces were generated from the pressure gradients among the conduit [97], [98] instead of the difference of density between confined liquids and ambient liquids [26].

VI. Applications of Swallowing Simulators

Swallowing simulators are generally known for the ability to perform swallowing simulations in normal conditions. Recently, studies have been invested in other areas of applications to discover the potential of these simulators in different settings, such as in the study of swallowing impairments, food process design, and dysphagia management and treatments. The following sections reviewed related studies for these aspects of applications (summarised in Table I).

A. Study of Swallowing Impairments

1) Spillage of Food (Difficulty Containing Bolus in the Oral Cavity): During drinking liquid, a sealed space is created by the lips, the tongue and the palate to prevent spillage of the liquid [34]. Dysfunction in this mechanism can be inappropriately leaked from the closed space [38]. Bolus material may spill into the pharynx from the oral cavity whilst the airway is open, which may result in material entering the laryngeal vestibule (penetration) or below the vocal folds (aspiration). Strong reflexes exist to prevent this from occurring; however, disease, mistiming, or iatrogenic damage (e.g., Post-surgical) may result in an inability to protect the airway [99]. Investigations suggest that the vital force to hold bolus relies primarily on bolus viscosity rather than size [100]. However, it is important to note that oversized bolus can also lead to spillage. In practice, experiments conducted on the in vitro tongue simulator typically applied boluses that generated a pressing pressure of up to 40 kPa, consistent with findings from in vivo studies [101], [102].

Meanwhile, an investigation of the properties of the bolus affecting the tongue's holding ability was conducted by Nicosia et al. [45] based on a computational model. The results indicated that if the lingual motion generated from the tongue is at the same amplitude, it requires less effort to hold the bolus with a larger viscosity. Thus, if a patient has weak tongue muscle (low amplitude of lingual motion), the simulation showed that the bolus could be contained if the viscosity is high enough. However, high viscosity may result in other issues, such as negatively impacting propelling force [100]. Nonetheless, the mentioned simulators solely focused on the oral phase of swallowing, incorporating tongue muscles and the palate. The intricate process of human swallowing, particularly the movement of tongue retraction, engages additional muscles and structures like the hyoglossus, palatoglossus, styoglossus muscles and hydraulic linkage [103]. Incorporating these muscles' contributions could yield even more insightful simulation outcomes, offering medical professionals valuable insights to uncover therapeutic solutions.

2) Xerostomia: Xerostomia, also called dry mouth, can cause several issues, especially on bolus transport from the oral cavity into the pharynx, increasing swallowing difficulties. Some patients with low saliva production rates require water assistance to improve food swallowing. However, the relationship between saliva and bolus transport in human swallowing is still under investigation. Some in vitro and in silico studies provide alternative insights into the role of salivary lubrication. In vitro studies presented by Mathieu et al. [71] and De Loubens et al. [72], [73] investigated the influence of the food bolus on the pharyngeal mucosa coating. The water acted as the salivary lubrication layer and the outcomes indicated that the thickness of the coatings is largely affected by the viscosity of the food bolus, the layer of the salivary lubrication and the pharyngeal peristaltic wave. This information holds significant practical implications for developing interventions to improve swallowing function for xerostomia patients. Furthermore, another computational model proposed by Ho et al. [104] provided an opposite perspective that saliva has no influence on the lubrication of the aerodigestive tract during liquid swallowing. Understanding such contrasting findings is beneficial for guiding medical professionals in devising suitable treatment strategies for patients with swallowing difficulties caused by xerostomia.

3) Aspiration: Laryngeal penetration is material entering the laryngeal vestibule and then usually ejected during the swallow or by a cough response. Aspiration is material passing below the level of the vocal folds and may either be ejected by a cough response, partially ejected, or no attempt made to eject material (silent aspiration). To avoid aspiration, the epiglottis deflects bolus away from the airway, whilst the vestibular and true vocal

TABLE I
SUMMARY OF THE APPLICATIONS OF SWALLOWING SIMULATORS

Application	Simulation Study	Bolus Type/ Swallowing Object	Outcomes	Ref.
Study of swallowing impairments	Spillage of food	Thickened liquid bolus	• Higher viscosity bolus is easier contained in the oral cavity. • Weak tongue muscle affects the ability to contain the bolus.	[52]
	Aspiration	Thickened liquid bolus/Toys/air	• 5 ml thickened bolus could be swallowed properly, if a patient has issue with throat lifting and retroflexion of the epiglottis. • The bolus was spread wider and flowed faster in the dysphagia model than in healthy model. • The air was involved during swallowing may cause a larger flow rate of the non- Newtonian fluid.	[10], [78], [79], [82], [102]
	Xerostomia	Thickened liquid bolus	• The thickness of the coatings on the pharyngeal mucosa is largely affected by the viscosity of the food bolus, the layer of the salivary lubrication and the pharyngeal peristaltic wave. • Salivahas no influence on the lubrication of the aerodigestive tract during the liquid swallowing	[69]–[71], [104]
	Esophageal reflux	Thickened liquid bolus	• The length of the oesophagus affects the retrograde flow behaviours. • The reflux region of the flow increases with a larger thermal conductivity of the liquid, and because of other parameters.	[12], [87], [88], [95], [98], [99]
Enhancement of food design/Food texture study	Food destruction under the tongue-palatal contact	Jelly/cheese/soft solid gel	• The consistency of the food has a large impact on the area of spread. • The strength of the tongue affects the deformation of both food gel and tongue itself. • The fracture deformation ratio influences on the destruction process largely.	[53], [62]–[64]
Drug swallowing	Solid drug dosage swallowing	Tablets/capsules/solid particles/ thickened liquid bolus	• An increasing size of multiparticulates will increase the post-swallow residues. • Low-viscosity Newtonian liquid carrier will reduce the residue but slow down the velocity of bolus transport. • Thin elastic liquid was suggested as an alternative carrier to assist drug swallowing.	[58], [120], [121]
Dysphagia management and treatments	Texture-modified food swallowing	Thickened liquid bolus	• Liquids with thin viscoelastic properties resulted in a fast and low residue swallow. • With higher concentration of xanthan gum or starch, the bolus produces higher transit time and more residues.	[124], [125]
	Endoprosthetic stent performance testing	Endoprosthetic stent	• With a stiffer stent, stent migration could be minimised under contractions. • However, the IBPS dramatically decreased, as well as the efficacy of the stent, resulting in recurrent swallow dysfunction.	[96]
Surgery training platform	Esophagogastric anastomosis	-	• The feedback from the reported study participants (both faculty and residents) gave an average of ratings at 3.33 out of 4.	[85]
Mealtime assistant training platform	Meal assistance	-	• The food should be placed at the centre of patient's tongue with a weight less than 200 grams.	[126]

folds act as a valvular closure mechanism, preventing airway entry. The simulation of epiglottic deflection, as demonstrated by Sonomura et al. [82], served as a bridge between simulation-based studies and clinical scenarios. Considering a dysfunction in lifting and retroflexion of the epiglottis, this model offered insights into the potential challenges individuals might face in swallowing thickened boluses. It was found that the thickened bolus could be swallowed properly only within a certain range of volumes (around 5 ml); otherwise, aspiration may occur. However, the volume range causing aspiration was not specified in this study. Another simulation scenario was also presented in the same in vitro model by disabling all the swallowing movements and only allowing the bolus to be driven by gravity. The results indicated that after swallowing the liquid bolus, a part of the thickened bolus remained on top of the epiglottis. When the epiglottis returned to a neutral position, the residues flowed into the larynx causing aspiration. This outcome provided a mechanistic understanding of how dysfunctional epiglottic movement could lead to clinical complications. A study on the VFSS-DSS also agreed that liquid bolus has more chance of causing aspiration [47]. Whilst these models offer insight as to mechanisms of aspiration in humans, the variability of human volume sizes and additional factors such as temperature and intrinsic moisturization by saliva are not accounted for in these models and may affect the outcomes.

An alternative in silico model for understanding aspiration was developed by Michiwaki et al. [70] and validated by Kamiya et al. [105]. Two models were built based on either a young healthy subject or an older patient with mild dysphagia in the study of pathology behind dysphagia [70]. The following outcomes were revealing: Firstly, due to aging, the dysphagia model has a descended larynx compared to the healthy model, which increased the risk of aspiration; Secondly, the bolus was spread wider and flowed faster in the dysphagia model than in the healthy model, which was considered as the reasons to cause the increased aspiration. These outcomes suggested that the altered bolus dynamics, both in spread and velocity, Following the same procedure of simulation model construction, could be the indication of the aspiration. Beyond the domain of dysphagia, these simulations extend to investigate pediatric choking incidents involving toy ingestion [80]. This simulation modelled the parts for soft-tissue organs (tongue, larynx and pharynx) as hyperelastic and the part for a toy as rigid components. This study investigated various sizes, friction and repulsive coefficients of toys. In most cases, the toy was not spotted entering the airway but instead was observed to compress the epiglottis retroverting it, leading to the closure of the larynx. While illustrating potential choking mechanisms, it is noteworthy that this study only mainly contributed dysphagic simulations without direct validation from the existing literature.

Airflow in the pharynx is also studied as it is also one of the impact factors of swallowing motility. Incoordination of swallowing and breathing can result in aspiration. The Gothenburg throat developed by Qazi and Stading [36] took into account the dynamic interplay between both air and bolus in the simulation model. The experiments conducted on the model contained two types of liquid solutions: Rapeseed oil as a Newtonian liquid and Fresubin Clear as a shear-thinning liquid [24]. The results were compared with the reference measurements (bucket and stopwatch) and the values obtained from other clinical studies. The flow rates for Newtonian fluid were close to the calculation from the reference measurements; however, the non-Newtonian fluid was mainly found to be different from the reference at a maximum value of 25%, which could be due to the excessive air involved in the flow suggested by the authors. Compared to the flow rate, the velocities (0.1444−0.22 m/s) detected in the experiments with both Newtonian and non-Newtonian liquids were found within the range of velocities (0.1−0.5 m/s) reported in clinical studies. This alignment underscored the simulator's potential to closely replicate physiological fluid dynamics during the pharyngeal phase of swallowing. Meanwhile, the measured pressure (21.84−23.38 kPa) along the in vitro system was close to the value in literature [106], where the reported value ranges from 13−20 kPa. Despite variations in the tested bolus volume, the results indicated the simulator's capability to approximately mirror clinical conditions.

4) Esophageal Reflux: GERD results from an incompetent LES, delayed gastric emptying, dysfunctional peristalsis and/or increased intraabdominal pressure [107], [108]. This results in intragastric contents overcoming the pressure at the LES, resulting in gastric contents escaping back into the oesophagus from the stomach [109].

To mimic retrograde flows from the stomach to the oesophagus, [26] a simulation model was designed and followed the strategy that the flow was driven by the buoyancy forces generated from the differences of density in the fluids contained in the stomach and in the ambient fluids. The process of reflux shown in Fig. 3(c) involves three main steps, the closure of LES after swallowing, the bolus raised by the buoyancy forces and the opening of LES leading to the retrograde flows. It is prudent to acknowledge that, while the simulation architecture successfully mimicked the reflux phenomenon, a gap arose when considering the direct comparisons with clinical data.

Apart from the previous studies of GERD, the roles of CM contraction and LM shortening in the oesophagus model were investigated, as well as the impacts of the delays of these muscle activations [84]. It was found that CM contraction aims to generate high luminal pressure to transport bolus, while LM shortening helps to maintain the contraction force and period. The delay of LM shortening can cause more significant influence, such as dysmotility, compared to the delay of CM contraction. Meanwhile, in another study [69], the same in silico model was utilised to understand the influence of the flexibility of mucosa in bolus transport. The results indicated that with compliant mucosa, accommodation and lubrication of the incoming bolus were improved. In contrast, with stiff mucosa, esophageal distensibility was decreased and the luminal pressure was increased, causing impairment of bolus transport. Furthermore, Misra et al. [97] indicated that the length of the oesophagus has an impact on the retrograde flow behaviours; while Tripathi et al. [98] suggested that the reflux region of the flow increases with the increase of the thermal conductivity. In addition, an in vitro study also observed a small reverse upwards flow in the simulator while bolus transport occurred from cephalad (head) to caudal (tail) [95].

B. Enhancement of Food Design/Food Texture Study

Food design is a wide topic that includes food space design, food product design, food process design and eating design [110]. The food process design is involved with the food texture, flavour and colour, and the food texture plays one of the most important roles in consumers' preferences [111]. The texture studies devote tremendous effort to the food processing during the oral phase (i.e., chewing and squeezing) [112], while the processing in the other phases of swallowing lacks investigation. As for the food ingested in the oral cavity, the attention is more drawn to the chewing behaviours rather than the squeezing behaviours, by using mastication simulators [113], [114], [115], [116]. However, if the food is soft enough or in a liquid state, chewing is unnecessary, and squeezing is the main mechanism involved in food destruction and transport [117], for example, as jelly and cheese. The perception of dairy gel texture was investigated in terms of spreading area in an oral cavity simulator [46], as the texture of the food may affect the release and perception of aroma compounds [118]. The consistency of the food was observed to have a large impact on the area of spread. Other studies indicated that another parameter influencing food destruction is the strength of the tongue [56], [57]. By testing various softness of the artificial tongue, the strength of the tongue was seen, affecting the deformation of the food gel and the tongue. Moreover, the fracture deformation ratio was suggested as having a marked influence on destroying the food bolus. Another property of the texture that has been investigated is the friction coefficient of the food bolus. It was also studied by in vitro simulation and results suggested that when higher compressing force was applied on the food bolus, less friction coefficient was observed during the experiments [55]. Overall, the previously mentioned range of swallowing simulators has intricately explored the elements that impact food breakdown by the tongue in the oral phase. These investigations spanned factors as diverse as food consistency and tongue strength and assessed the outcomes with the measurements that contained the area of food spread, the degree of deformation, and the friction coefficient characterizing food bolus degradation. Moreover, these outcomes assumed a pivotal role in shaping the design and formulation of food products, especially when viewed through the prism of safe swallowing.

C. Drug Swallowing

Swallowing problems commonly affect patients when swallowing pills, especially among the elderly and pediatric generations. Three key attributes of medication intake behaviours are memorability, swallowability and palatability [119], [120]. The conventional approach to assess these attributes is by human sensory analysis, however, which is labour-intensive and expensive [121]. Swallowing simulators provide an alternative approach to conducting the primary stage of assessments. Currently, research efforts primarily target the study of solid oral dosage forms (SODFs) from three aspects, the size of drugs, the swallowing aids (liquid carriers) and the film coatings of drugs. By varying these three crucial elements in swallowing experiments on the simulators, the outcomes were assessed in terms of the post-swallow residues and the oral transit time (OTT) to predict ease of swallowing. Studies reported by the Cambridge Throat team identified that with increasing size of the multi-particulates, the post-swallow residues were also increased [122]. A liquid carrier for SODF, on the other hand, changes the amount of the post-swallow residues when the level of viscosity is varied [123]. Although fewer residues were observed with low-viscosity Newtonian liquids, the velocity of the bolus transport was also reduced. Thus, a trade-off is required to balance the amount of residues left over and the efficiency of the bolus transport. A statement provided by the author suggested that thin elastic liquids could be a superior choice to promote the safe swallowing of medicines; however, a further investigation of this option is required to be validated in a clinical study. As for the performance of the OTT, the lower velocity of the bolus increases the chance of drugs adhering to the surface mucosa because of the longer contact time. It will also result in abnormally large OTT. Proper film-coating techniques could prolong this period [51]. From the above simulation outcomes, it is concluded that the viscosity impacted the bolus behavious, as when it was low, the chance of the post-swallow residues was reduced. However, with low viscosity, the velocity was also reduced and the OTT increased, which increased the difficulty of swallowing. This intricate interplay of viscosity, bolus dynamics and oral transit time helps them understand the potential trade-offs, which could further impact the comfort of swallowing medicine.

D. Dysphagia Management and Treatments

Meanwhile, to assist eating, texture modification is a common practice in dysphagia management [110]. The food textures are classified by different standards, International Dysphagia Diet Standardisation Initiative (IDDSI) or National Dysphagia Diet (NDD) published by the American Dietetic Association, which provide recommended food diets for individuals with swallowing difficulties [124], [125]. Most studies focused on liquid food swallowing, investigating the influence of liquid food alternations in preventing dysphagia [126], [127]. Based on the results in terms of the oral transit time and the bolus length during the experiments, studies indicated that liquids with thin viscoelastic properties resulted in a fast and low residue swallow, while with a higher concentration of xanthan gum or starch, the bolus produces higher transit time and more residues. This finding offers medical practitioners a potential dietary solution for patients with dysphagia. However, investigations with clinical approaches are still required for validation purposes.

Investigating the current methods of dysphagia treatments or developing new methods is a potential application of the simulators. Bhattacharya et al. [85] investigated the effect of peristalsis on esophageal stent migration, a therapy for esophageal strictures. Two stents with different stiffness were utilised in the study. The outcomes showed that with a stiffer stent, stent migration could be minimised under contractions. However, the IBPS dramatically decreased, as well as the efficacy of the stent, resulting in recurrent swallow dysfunction. Although a notable distinction was discovered between the esophageal simulator's swallowing environment and the intricacies of the human oesophagus, the presence of a simulation itself is a remarkable advancement. It enables the testing of surgical techniques, such as esophageal stent migration, crucial for treating esophageal tumors. However, only a limited number of studies are available with similar implications, highlighting the importance of this avenue driven by simulations.

E. Other Applications

It is worth mentioning some other usages of the wallowing simulators, as they can enhance medical education, improve caregiver skills and offer valuable training opportunities for surgical procedures. As these simulators faithfully replicate anatomic structures with the functions of physiological mechanisms, medical students can study and improve their understanding of human swallowing by using simulators. Caregivers can be trained for proper feeding position when a sensory system is installed and enables a biomimetic tongue to feel the weight of the food [101]. It can improve a caregiver's meal assistance techniques, such as placing food on a patient's tongue with a specific weight (less than 200 grams) and position (the centre of the tongue's dorsal surface). This simulator can enhance caregiver skills in providing safe and effective feeding for patients. Another application of the swallowing simulators that have been reported is used for training surgical skills, in particular, esophagogastric anastomosis surgery [87]. In the reported study, participants (faculty and residents) gave an average rating of 3.33 out of 4 for simulator use. In conclusion, by incorporating the swallowing simulators for educational and training purposes, professionals in the medical field can gain valuable experience and knowledge without ethical concerns, which leads to better patient care and outcomes.

VII. Discussion

Swallowing simulators, inspired by biomimetic ideas, provide alternate views for understanding the swallowing process. As the designs of the simulated organs were based on the in vivo data from images (CT images, VFSS images or MRI images), the state of the art of the presented simulators show good promise in generating an approximated physiological environment. Especially, with the help of the recent innovation and development of soft materials and structures, the simulators could closely mimic the behaviours of organ tissue. Moreover, the studies of swallowing simulators have moved from a focus on biomimetic design to match physiological reality, such as the evaluation of texture-modified food and the training of esophageal surgery, which potentially reduces the need for human trials. Yet, various challenges and areas remain for discovering the full potential of swallowing simulators.

From the design perspective, it was discovered that most simulators concentrate on one specific mechanism having assumptions to simplify the complexity of the swallowing procedure, which could potentially lead to gaps between simulation results and in vivo findings. For oral simulators, the human tongue shows flexibility whilst having the strength to propel a food bolus into the pharynx; however, simulators targeting flexibility seem to lack compressing force, incompletely representing real life. For pharyngeal simulators, the challenge of mimicking human pharyngeal phase swallowing is related to the complexity of this phase which includes at least three crucial mechanisms, movement of the epiglottis, pharyngeal peristalsis and negative pressure from UES distraction. All current simulators fail to realise three mechanisms simultaneously while maintaining anatomical design, and only a small number of simulators included the air factor in the studies. As for esophageal simulators, the in silico studies followed the behaviours of a human oesophagus closely, while the in vitro simulator only mimicked the contractions of human radial muscle, neglecting the function of longitudinal muscle. Another challenge is temperature imitation. To our best knowledge, the existing simulators do not simulate human body temperature. Only in a few studies did researchers consider the thermal factor by testing with heated food. However, the lower ambient temperature will cool the food bolus and influence its physical properties, such as viscosity, rheology and consistency. This will lead to simulation outcomes differing from clinical data.

To enable better performance of simulators with convincing results, their mechanical designs should be further matured. Thus, a more advanced soft actuation system with sensory functions is also required. This actuation system should provide multiple mechanical functions at the same time. In this regard, a combination of soft and rigid approaches could be a reasonable solution. Soft actuators can imitate the tissue and muscles related to swallowing, while rigid actuators may provide strength. Rigid actuators may also provide a heating function and act as a skeleton or shell to provide firm support. In addition, there needs to be more sensory systems embedded in simulators to mimic human perception of food, such as flavor, size, heat and other properties.

Applications for swallowing simulators have drawn more attention recently. Researchers extended their interests in simulating swallowing in healthy conditions to other areas, such as dysphagia symptoms study, medical education and training, the study of swallowing medication and food process design. Some outcomes are valuable, as using simulators in the preliminary stage of evaluating new treatments could reduce the requirements of human trials. Yet, these applications are relatively new and more studies are necessary to enrich the functionalities of simulators. Therefore, future developments should pay attention to three areas: The study of swallowing disorders based on various swallowing scenarios, the evaluation of dysphagia treatments and the study of swallowing medications. For example, esophageal strictures caused by cancer can be simulated in RoSE with adjustments to balloon pressures at one actuation level or by making an artificial constriction, such as through a silicone 'tumour' placed inside the robot. Under this condition, studies can either focus on the performance of esophageal swallowing to discover a solution to ease patients' discomfort or as a training platform for resident doctors to practise surgical skills when esophageal peristalsis is involved.

Finally, as the presented swallowing simulators are unique and only available in the individual laboratory where they were fabricated, access to them is limited to a certain number of people. It is necessary to build up collaboration between the same type of simulators or among different fields, such as medical workers, food technology and medical device technology, to allow more widespread use of simulation. The benefits of such collaboration are facilitating improvements of the simulators, increasing recognition of this type of approach and standardising the requirements of the simulators. With the advantages of simulators that approximate realistic swallowing environments in either mechanical, physical and sensory perspectives isolated from the related complication in human swallowing, in the foreseeable future, swallowing simulators could be expected to take an essential role in the development of food and medicine design and the investigation of dysphagia management, for example, the simulators that mimic the swallowing mechanisms during pharyngeal phase can be utilised to investigate the empty time, the required strength of the pharyngeal peristalsis and the residue left in the pharynx with various theologies of the food content.

VIII. Conclusion

Various approaches to constructing a swallowing simulator were demonstrated in this review and grouped according to human swallowing mechanisms and swallowing phases - the oral, pharyngeal, and esophageal phases. We evaluated the limitations of current designs and potential improvements for the future. The areas of application of swallowing simulators were also reviewed to discover their potential in multiple areas of research, suggesting the importance of collaboration among different disciplines.

Declaration

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: This article does not contain any studies with human or animal subjects performed by any of the authors.

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