CFD Letters

Journal homepage:
https://semarakilmu.com.my/journals/index.php/CFD_Letters/index
ISSN: 2180-1363

Investigation of Digestion Processes in the Stomach and Duodenum using Computational Fluid Dynamics Model

Marat Reshidovich Kamaltdinov[1,2,*], Peter Valentinovich Trusov[1,2], Nina Vladimirovna Zaitseva[1]

[1] Federal Budget Scientific Institution “Federal Scientific Center for Medical and Preventive Health Risk Management Technologies”, 614045Perm, Russia
[2] Department of Mathematical Simulation of Systems and Processes, Perm National Research Polytechnic University, 614990 Perm, Russia

ARTICLE INFO

Article history:
Received 9 June 2023
Received in revised form 12 July 2023
Accepted 9 August 2023
Available online 12 December 2023

Keywords:
Numerical simulation; Multiphase flow; Food; Enzymes; Acidity

ABSTRACT

The stomach and intestines play an important role in homogenizing the contents of the tract, mixing food with enzymes. The study of digestion processes in a fed state remains difficult by experimental methods. Using computational fluid dynamics models it is possible to obtain flow characteristics at any point in the computational domain. At the previous stages of research, we developed a model to describe the flow of a multiphase multicomponent mixture in the antroduodenum, taking into account the processes of mass transfer between phases, biochemical reactions, mass sources and effluents. In this article, we propose an improvement of the model for describing the multiphase flow in the whole stomach and duodenum, taking into account the gas phase. The mathematical formulation of the problem includes the balance equations of mass and momentum for a multiphase medium with mass sources. Boundary conditions take into account the peristalsis of the tract. In numerical experiments we studied the influence of the density of food particles on the distribution of volume fractions of phases, mass fractions of food components and enzymes, pH level in the digestive tract. In the future, it is necessary to continue working with the rheological properties of the flow.

1. Introduction

The stomach is a sophisticated organ with unique physiology and biochemistry [1]. The four key components of gastric digestive function are food storage, acid secretion, enzyme secretion and motility [2]. The normal rate of gastric emptying of chyme into the duodenum is very important for further digestion and absorption [3]. The duodenum mixes gastric chyme with pancreatico-biliary secretions, reduces food particles to simple nutrients that can diffuse into the blood [4], and increases *pH* value of the chyme [5]. The diseases of the stomach and duodenum are often associated with helicobacter infection [6, 7], high acidity in the tract lumen [8], alcohol consumption [9], smoking [10], unhealthy diet [11, 12], stress [13] and other reasons [14]. However, many pathophysiologic mechanisms associated with environmental factors and individual features remain unclear.

* *Corresponding author.*
E-mail address: kmr@fcrisk.ru (Marat Reshidovich Kamaltdinov)

https://doi.org/10.37934/cfdl.16.3.8295

The existing experimental equipment is mainly aimed at medical purposes for diagnosing the state and functions of the organs of the digestive system and the gastrointestinal tract [15]. At the same time, it is still very difficult to obtain the characteristics of the digestive process in the human body in a fed state [16]. Therefore, it is very important to develop non-invasive approaches for research tasks [17]. Computational fluid dynamics (CFD) models have a number of advantages: saving time and resources for research, the ability to control input parameters, evaluate and predict process characteristics at any point in the computational domain [18-23]. One of the first models of the stomach created on the basis of magnetic resonance imaging (MRI) data to study the role of peristaltic waves in the antrum [24, 25]. Recent studies use three-dimensional models to describe gastric motility, drug dissolution, food mixing and transport (from stomach to intestine) with different rheological characteristics [26-29]. Chyme in the stomach is considered as a Newtonian fluid [30, 31], shear thinning fluid [32], or multiphase medium [33, 34], and in the intestine as a Newtonian fluid [35-37], non-Newtonian fluid with a kinematic viscosity described by the power-law model [38], Bird–Carreau fluid [39], suspension of rigid particulates in a viscous Newtonian fluid [40].

The presence of a gas phase in the stomach is not often considered using CFD models. A small amount of air enters the stomach when food is swallowed, so in the next phase of digestion, a bubble forms in the upper part of the stomach [4]. Also, gas can be contained in the food taken or formed as a result of biochemical reactions in the gastrointestinal tract [41]. At the same time, experiments have shown that most of the gas passes from the stomach to subsequent sections of the tract [42]. In this regard, taking into account the gas phase in the model seems to be important for a more correct description of gastric processes. Hao *et al.,* [33] developed a 2-D model of multiple-phase flows for the simulation of gastric emptying. At the entrance to the stomach atmospheric pressure is set, at the exit from the stomach a constant speed (0.3 mm/s) is set. Because of such boundary conditions, the stomach is emptied. Ishida *et al.,* [43] determined vertical position of the air-liquid interface using the outflow flux at the pylorus assuming that the interface remained flat during the process. Imai *et al.,* [44] considered the effects of posture on mixing in the closed stomach using free-surface modeling, assuming that viscous traction of gastric gas is negligible. The presented works do not consider the change in the density and viscosity of the medium during the action of digestive juices on food. It is reasonable to continue work in this field, paying particular attention to the mixture rheological properties, the individual shape features and parameters of the stomach and duodenum in normal conditions and disease.

This study is performed within the general multilevel model of functional disorders accumulation in a human body, developed by a team of authors [45]. For more detailed description we considers “meso-level” models of the cardiovascular, respiratory [46], digestive, neuro-endocrine [47], and other systems. At the previous stages of research, the developed “meso-level” model was used to describe the flow of a multiphase multicomponent mixture in the antroduodenum, taking into account the processes of mass transfer between phases as a result of the dissolution of food particles, biochemical reactions that contribute to the transformation of more complex food components of the mixture into easily digestible elements, mass sources and effluents component due to the processes of secretion of digestive enzymes and absorption of nutrients [48]. The model also describes the peristaltic movement of the walls of the tract. At the previous stages, we did not consider the gas phase in the stomach. Also, the digestive processes were considered only in the lower part of the stomach (antrum). Therefore, we eliminated these shortcomings and introduced some new features into the model. This article is devoted to the study of digestion processes in the whole stomach and duodenum, taking into account the gas phase.

2. Methodology

2.1 Conceptual and Mathematical Statement of the Problem

The stomach and duodenum are considered as a complex-shaped biochannel with moving boundaries. A mixture of food particles and digestive juices in the cavity of the tract is considered as a multiphase medium. The first phase is a multicomponent liquid with components dissolved at the molecular level. It is assumed that food particles are liquid phases and have different viscosities, exceeding the viscosity of the first phase. The gas is considered as a separate phase with a low density and viscosity compared to the other phases. The mathematical formulation of the problem is based on the use of the laws of conservation of mass and momentum for the phases and components of the medium. When writing Eq. (1) – (3), we use the Eulerian approach, where the liquids phases are treated as interpenetrating continua. It is assumed that each phase occupies a certain proportion of the total volume of the mixture. The exchange of momentum between phases due to friction forces depends on the difference in the velocities of the interacting phases. Therefore, we do not work with particles directly and no not consider surface tension. We apply the assumption of sphericity of particles of secondary phases only to use the ratio for the coefficient of interfacial interaction. Interfacial interaction coefficients also depend on the viscosity and density of the medium and change in the process of digestion. The main conservation equations for the first phase and food particles are given in a previous publication [45]. Later we expanded the list of components of the first phase and at the current time it describes 21 components: water, hydrochloric acid (HCl), sodium bicarbonate ($NaHCO_3$), the reaction product with hydrochloric acid and sodium bicarbonate (carbon dioxide and sodium chloride), dissolved proteins, fats, carbohydrates, chemicals, polypeptides, pepsin, peptidases, amino acids, trypsin, bile salts, emulsified lipids, lipase, monoglycerides, amylase, polysaccharides, monosaccharides, glycosidases [48].

Mass conservation equations for the gas phase:

$$\frac{\partial}{\partial t}(\rho_{(J)}\alpha_{(J)}) + \nabla\cdot(\rho_{(J)}\alpha_{(J)}\mathbf{v}_{(J)}) = S_{(J)}, \mathbf{r}\in\overline{\Omega}, t\in[0;T) \tag{1}$$

where $\rho_{(J)}$ is the density of the gas phase, kg/m^3, (J) is an index of gas phase, $\alpha_{(J)}$ is a volume fraction of the gas phase, $\mathbf{v}_{(J)}$ is a velocity vector of the gas phase, m/s, $S_{(J)}$ is an intensity of the mass source of the gas phase, kg/(m^3·s), $\mathbf{r}$ is a radius vector of spatial points, $\overline{\Omega}$ is a closed area (the interior of the area and its border), t is the time.

The momentum conservation equations for the phases are written taking into account the hypotheses about the equality of the phase pressures, the proportionality of the interfacial interaction forces to the difference in the velocities of the interacting phases:

$$\begin{aligned}\frac{\partial}{\partial t}(\alpha_{(1)}\rho_{(1)}\mathbf{v}_{(1)}) + \nabla\cdot(\alpha_{(1)}\rho_{(1)}\mathbf{v}_{(1)}\mathbf{v}_{(1)}) = -\alpha_{(1)}\nabla p + \nabla\cdot\tau_{(1)} + \\ +\alpha_{(1)}\rho_{(1)}\mathbf{g} + \sum_j K_{(j)(1)}(\mathbf{v}_{(j)} - \mathbf{v}_{(1)}) + \sum_j(\sum_{i=3,4,5,6,9} m'_{(j)(i)}\mathbf{v}_{(j)}),\end{aligned} \tag{2}$$

$$\frac{\partial}{\partial t}(\alpha_{(j)}\rho_{(j)}\mathbf{v}_{(j)})+\nabla\cdot(\alpha_{(j)}\rho_{(j)}\mathbf{v}_{(j)}\mathbf{v}_{(j)})=-\alpha_{(j)}\nabla p+\nabla\cdot\tau_{(j)}+\alpha_{(j)}\rho_{(j)}\mathbf{g}+$$
$$+\sum_{q}K_{(q)(j)}(\mathbf{v}_{(q)}-\mathbf{v}_{(j)})-(\sum_{i=3,4,5,6,9}m'_{(j)(i)})\mathbf{v}_{(j)}+m''_{(j-1)(j)}\mathbf{v}_{(j-1)}-m''_{(j)(j+1)}\mathbf{v}_{(j)}, \tag{3}$$
$$\mathbf{r}\in\Omega,\quad t\in[0;T),\quad j=\overline{2,J},\quad q=\overline{1,J},\quad m''_{(1)(2)}=m''_{(J-1)(J)}=0,$$

Where p is a pressure, Pa, j, q are indices of phases, when the index is equal to one, it denotes the first phase (multicomponent liquid), **τ** is a deviatoric part of the Cauchy stress tensor for a viscous incompressible fluid, **g** is a vector characterizing the action of mass forces, m/s^2, $K_{(q)(j)}$ is a coefficient of interfacial interaction of the q-th and j-th phase, kg/(m^3·s), $m'_{(j)(i)}$ is a term determining the intensity of mass transition from the j-th phase to the i-th component of the first phase, $m''_{(j-1)(j)}$ is the term of the intensity of the mass transition from phase of particles of larger size to the phase of particles of smaller size. The rate of mass transition into the components of the first phase is proportional to the fraction of the components in the phases of food particles. Particles of the smallest size do not dissolve.

The viscosity of the first phase is assumed to be variable and depends on the concentration of food components [49]:

$$\frac{\eta_{(1)}}{\eta_{(fc)}}=\left(1+\frac{1.25a}{1-a/a_{\max}}\right)^2 \tag{4}$$
$$\eta_{(fc)}=\eta_{(w)}(1+(\sum_{i}C_{(i)})\exp(\ln\eta_0+(\sum_{i}C_{(i)})K\eta_0)), \tag{5}$$

Where $\eta_{(fc)}$ is a viscosity of fat and carbohydrate solution, Pa·s, a is a volume fraction of micellar particles, and $a_{\max}$ – hypothetical maximum volume fraction of micellar particles at "tight arrangement", $\eta_{(w)}$ is the viscosity of water (equals $0.7\cdot10^{-3}$ at a temperature of 37˚C), Pa·s, $C_{(i)}$ is a volume concentration of the i-component (fats and carbohydrates) of the first phase, kg/m^3; $\eta_{(0)}$ is the parameter of intrinsic viscosity, m^3/kg, which represents the volume occupied per unit mass for infinite dilution conditions, K is a dimensionless parameter.

The density of the first phase is also variable and is calculated by averaging over the components. Kinematic boundary conditions are set on the walls of the stomach and duodenum. The wall boundary condition is set at the inlet. So, the gastroesophageal sphincter is assumed to be closed. In the outlet section the pressure values and the conditions of equality to zero of the tangential components of the stress vector are set.

2.2 Description of the Method for Constructing the Geometry of the Computational Domain and the Numerical Method

Previously, we developed an algorithm for constructing a computational domain based on the results of an ultrasound study [50]. Peristalsis parameters also are given in our previous publications [45, 50]. Images of the stomach were obtained in planes parallel to two main anatomical planes: horizontal (parallel to the ground level) and middle (dividing the human body into two symmetrical halves). A 2D shape of the stomach is obtained from the images and a "center line" is drawn. The 3D domain construction is based on the approximation of a real geometric shape by a finite number of ellipses. Ellipses are located in the normal plane to the "central line" of the stomach. The duodenum is supposed to be a round C-shaped tube. The resulting computational domain is shown in Figure 1.

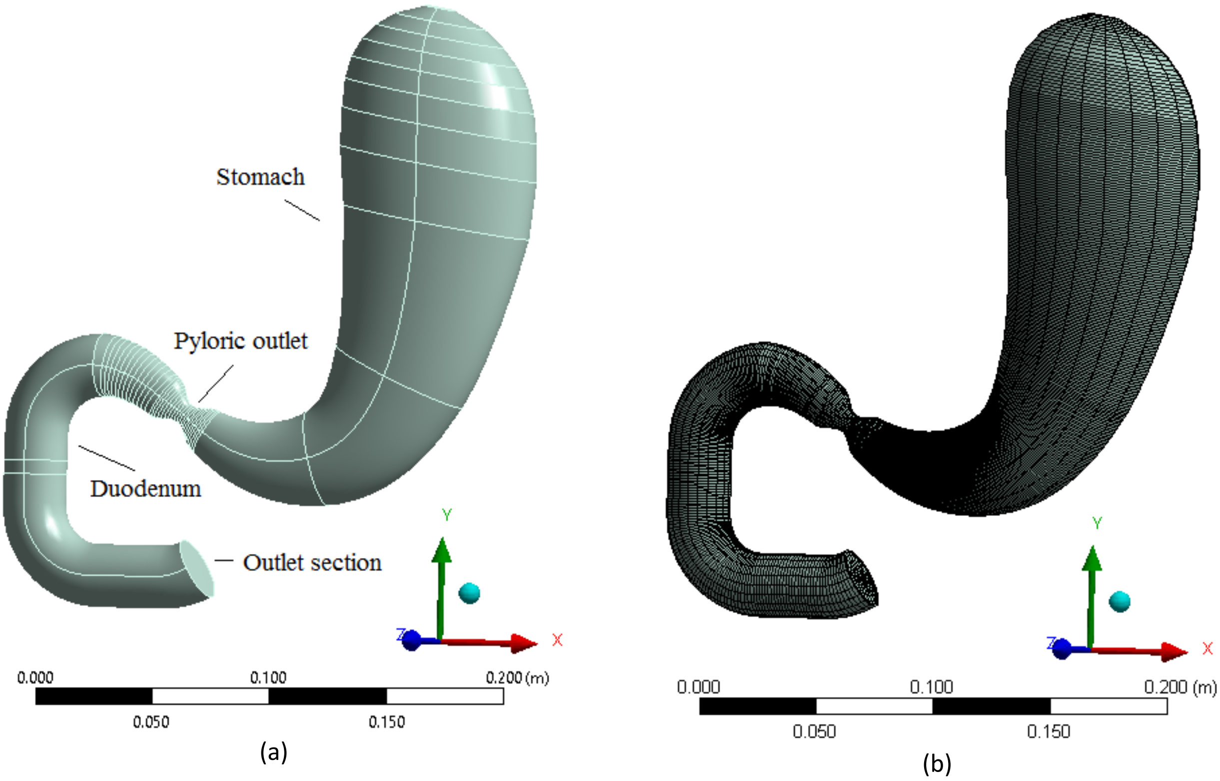


Fig. 1. (a) The computational domain (b) The computational mesh

When using numerical approaches to solve the systems of equations included in the mathematical formulation of the problem, questions inevitably arise related to the reliability of the results obtained. It should be noted that the use of numerical methods in itself introduces some error into the results obtained. In addition, the use of a coarse mesh can lead to errors at large deformations due to the propagation of peristaltic waves. Due to the impossibility of obtaining an analytical solution, it is necessary to check the computational stability of the numerical solution, as well as to analyze the differences in the obtained flow characteristics at different grid sizes and time steps. The question of the rational choice of the calculation parameters is also important due to the significant computational complexity of the problem (solution of the conservation equations for many phases and mixture components), it is necessary to obtain a stable solution with a small error in the minimum possible calculation time.

From the point of view of the physiology of the process, special attention should be paid to the characteristics showing the mass of various food components and enzymes located in the stomach and intestines. We used the total mass of sodium bicarbonate in the domain as a measure of comparison, which is calculated during one cycle of peristaltic activity after the start of the simulation (18 s). Table 1 shows the study results of the solution sensitivity depending on the grid size and time step. Relative error indicates the error of the solution relative to a fine grid with a fine time step. In numerical experiments, it is rational to use a grid with 59920 elements and time step equal to 0.01 s.

The phase of digestion in which food begins to pass into the intestines is considered. The peristalsis of the tract is supposed to be periodical. The shape of the peristaltic waves in the antrum and duodenum is given by the sinusoidal law. The main parameters of the waves (periodicity, width, amplitude, speed) are given in the previous publication [45]. The displacements of the boundary nodes of the mesh occur only in the corresponding elliptical cross-section imitating circular muscle contractions.

Table 1
Study of the sensitivity of the solution depending on the grid size and time step

Mesh element	No of elements	Time scale	Time step, s	Relative error, %
coarse	27467	coarse	0.02	3.87
coarse	27467	normal	0.01	1.61
coarse	27467	fine	0.0025	0.74
normal	59920	coarse	0.02	0.69
normal	59920	normal	0.01	0.13
normal	59920	fine	0.0025	0.08
fine	273567	coarse	0.02	0.07
fine	273567	normal	0.01	0.03
fine	273567	fine	0.0025	-

The CFD analysis is carried out in Ansys Fluent. 32 cores with frequency of 2.4 GHz (AMD Opteron processors) are used in numerical experiments, which takes about 324 h for calculating a 30-minute digestion with a standard mesh element and time step. For calculations, the pressure-based solver is used; for time discretization, implicit schemes of the first order of accuracy are used, which are stable with respect to the size of the time step. User defined functions (UDF) are applied for setting mass sources, interphase interactions, dynamic mesh.

At the initial moment of time, the first phase contains only the water component, therefore its density is 1000 kg/m^3, viscosity is $7 \cdot 10^{-4}$ Pa·s. The density of the gas phase is 1.14 kg/m^3, the viscosity is $1.86 \cdot 10^{-5}$ Pa·s.

3. Results

Two scenarios are considered in numerical experiments. In the first scenario, the density of food particles is assumed to be higher (equal to 1046 kg/m^3) than the density of the first phase (multicomponent liquid). The density of food particles is 950 kg/m^3 in the second scenario. The viscosity of the food phases is $2 \cdot 10^{-3}$ Pa·s in both scenarios. At the initial moment of time, the gas phase is located in the upper part of the stomach with a volume fraction of 0.5. This value is set to avoid the instability of the solution at the beginning of the calculations. Food particles of different sizes are considered as separate phases. The total volume fraction of food phases is 0.9 in the lower part of the stomach and the initial part of the intestine. Medium sizes and initial volume fractions for each food phase are given as in the previous paper [45].

3.1 Volume Fraction of Phases

The calculation results show that already 2 minutes after the start of the simulation, phase separation occurs due to the difference in densities. The gas phase is concentrated in the upper part of the stomach. In the first scenario, the food phases are concentrated in the lower part of the stomach, and a small amount of food particles are contained in the lower part of the duodenum (Figure 2 (a)). Liquid solution (first phase) forms a layer in the stomach between gas and food. The rest of the first phase is observed in the upper and middle parts of the duodenum. In the second scenario, a liquid solution is observed in the antrum and the descending part of the duodenum (Figure 2 (b)). Food particles are located in the middle part of the stomach and in the ascending part of the duodenum. After 30 minutes, the volume of food particles in the stomach decreased by about 1.5 times due to dissolution with hydrochloric acid, the transition of food components into solution (multicomponent liquid) and transport to the intestine (Figure 3). The volume of the liquid phase in the stomach increased due to the secretion of gastric juice, the volume of the gas phase also increased due to the term on the right side of Eq. (1).

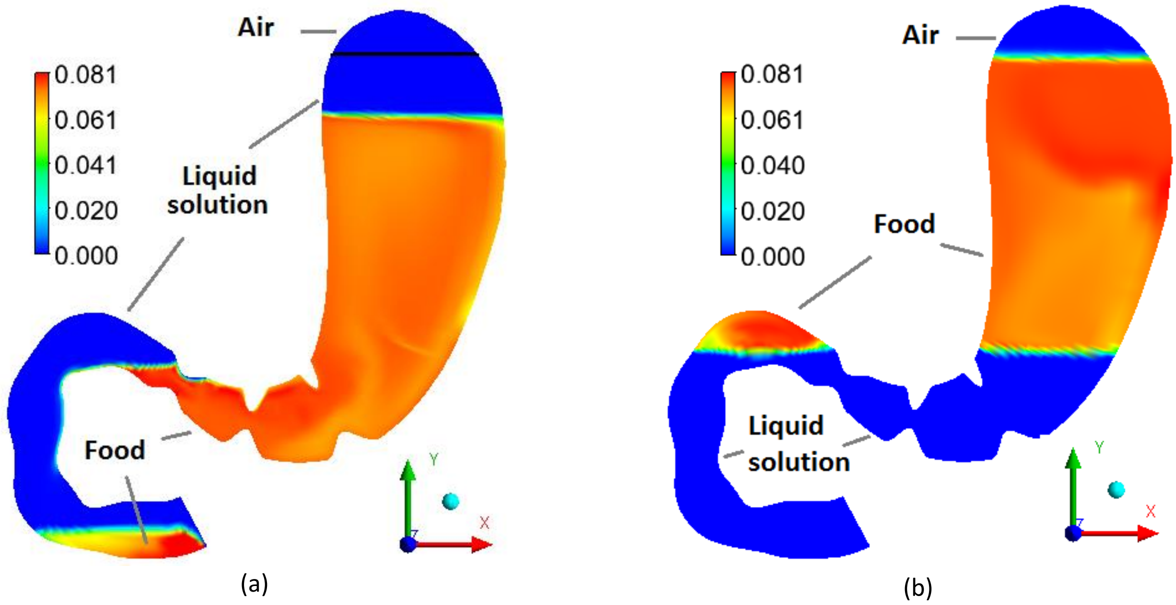


Fig. 2. Volume fraction of the second phase (food particles with the largest size), *t*=2 min (a) Scenario 1 (b) Scenario 2

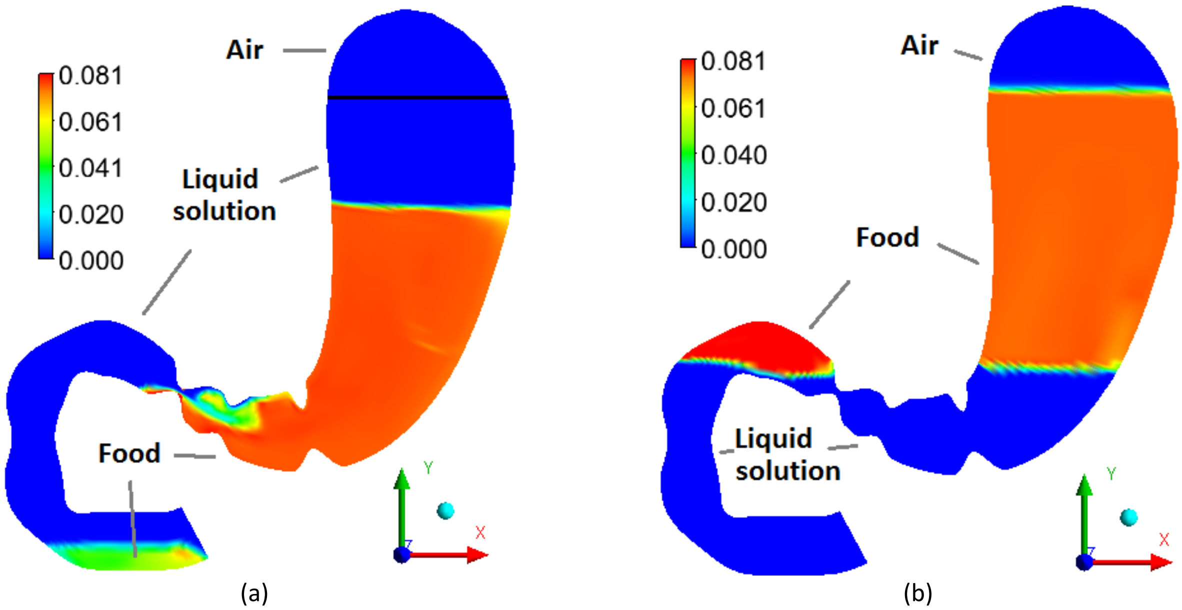
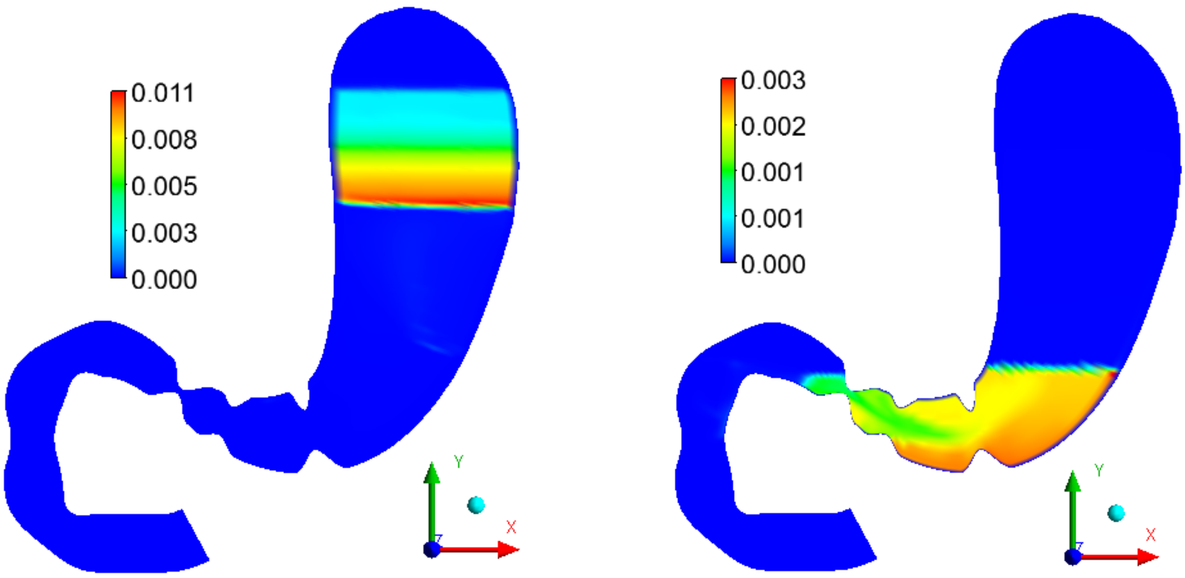


Fig. 3. Volume fraction of the second phase (food particles with the largest size), t=30 min (a) Scenario 1 (b) Scenario 2

3.2 Dissolved Proteins

Figure 4 shows the distribution of the mass fraction of dissolved complex proteins. After 30 minutes, food components dissolved in the liquid phase are found in the upper part of the stomach (Figure 4 (a)) as a result of the mass transfer from the food phases due to the dissolution of particles. The mass fraction of dissolved proteins reaches 0.01 in the first scenario, while the maximum values of the mass fraction of proteins are found at the boundary between the food phases and the liquid phase. Near the gas-liquid interface, the mass fraction of dissolved complex proteins is about 0.003. In the second scenario, dissolved complex proteins are observed only in the antrum, their mass fraction reaches 0.003 (Figure 4 (b)). The field of volume fractions of dissolved complex fats and carbohydrates visually coincides with the field of volume fractions of dissolved complex proteins. Differences are observed only in absolute values due to the different component composition of food particles. A similar picture is observed for pepsin, an enzyme secreted in the stomach.

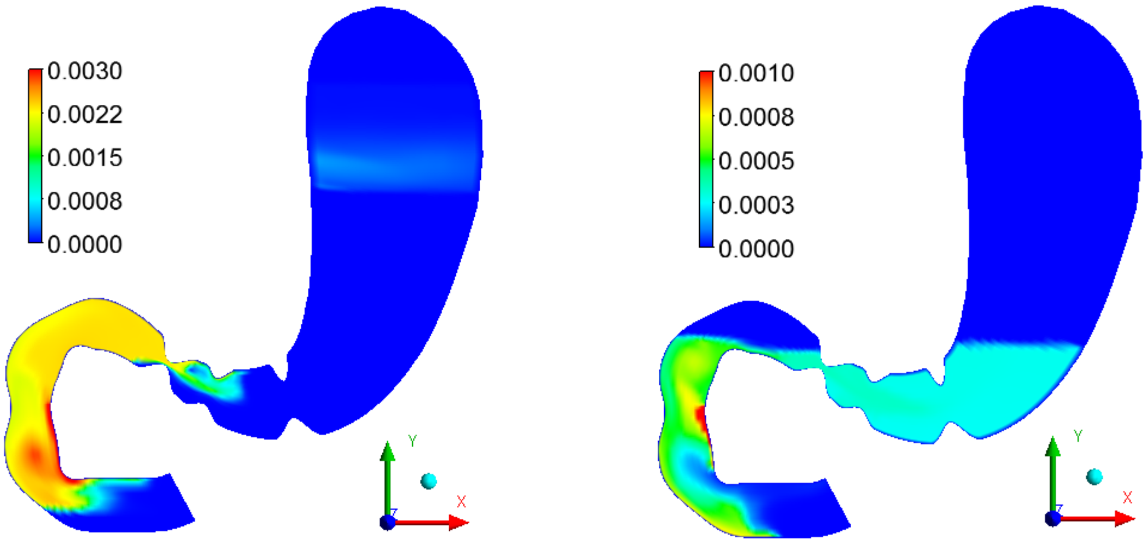


(a) (b)

Fig. 4. Mass fraction of dissolved complex proteins, t=30 min (a) Scenario 1 (b) Scenario 2

3.3 Trypsin

Figure 5 shows the distribution of the mass fraction of trypsin, which transforms complex proteins to polypeptides. Trypsin is produced by the pancreas and enters the intestine through the biliary system. In the first scenario, the mass fractions of trypsin in the duodenum reach $3 \cdot 10^{-3}$ at the time t=30 minutes (Figure 5 (a)). The concentrations are lower in the second scenario, the maximum values of the mass fractions are $1 \cdot 10^{-3}$ (Figure 5 (b)). Higher concentrations in the first scenario are explained by the presence of a regulatory effect. Since the concentrations of dissolved proteins in the stomach in the first scenario are higher, the mass source of trypsin is more intense.

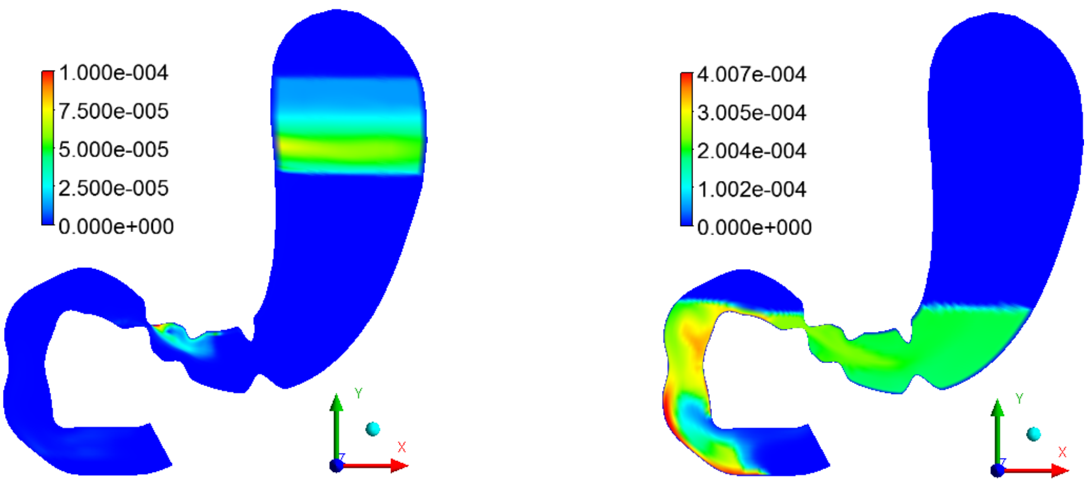


(a) (b)

Fig. 5. Mass fraction of trypsin, *t*=30 min (a) Scenario 1 (b) Scenario 2

3.4 Polypeptides

Figure 6 (a) shows the distribution of the mass fraction of polypeptides in the first scenario. The polypeptides are predominantly found in the stomach due to the action of pepsin on complex proteins. Due to the lower density of polypeptides compared to complex food components, high concentrations are observed not at the boundary separating the food and the liquid phase, but in higher layers. In the intestine, there is a relatively small amount of polypeptides formed under the influence of trypsin. Figure 6 (b) shows the distribution of the mass fraction of polypeptides in the second scenario. Polypeptides are found in the duodenum and antrum, where they are formed from complex proteins under the influence of trypsin. At the same time, the concentrations of polypeptides in the second scenario are higher, the volume fractions reach $4 \cdot 10^{-4}$. Therefore, the rate of enzymatic reaction is higher under the influence of trypsin in the intestine. The higher reaction rate partially explains the lower concentrations of complex proteins in scenario 2 (Figure 4 (b)).



(a) (b)

Fig. 6. Mass fraction of polypeptides, *t*=30 min (a) Scenario 1 (b) Scenario 2

3.5 Amino Acids

In the first scenario, the maximum concentrations of amino acids are observed in the region of the upper intestine (Figure 7 (a)). Here is a small amount of polypeptides, which under the influence of intestinal enzymes (peptidases) are transformed into amino acids. In the second scenario, amino acids are found in the descending part of the duodenum and in the antrum (Figure 7 (b)). The maximum concentrations of amino acids are lower than in the first scenario, mass fractions reach $1.7 \cdot 10^{-5}$. Thus, in the first scenario, the conversion of polypeptides into amino acids under the action of intestinal enzymes (peptidases) is carried out at a faster pace. It should be noted that intestinal digestive enzymes (including peptidases) within a few minutes after food intake are distributed throughout the duodenum and have an active effect on food components. In the future, their concentration increases much more slowly.

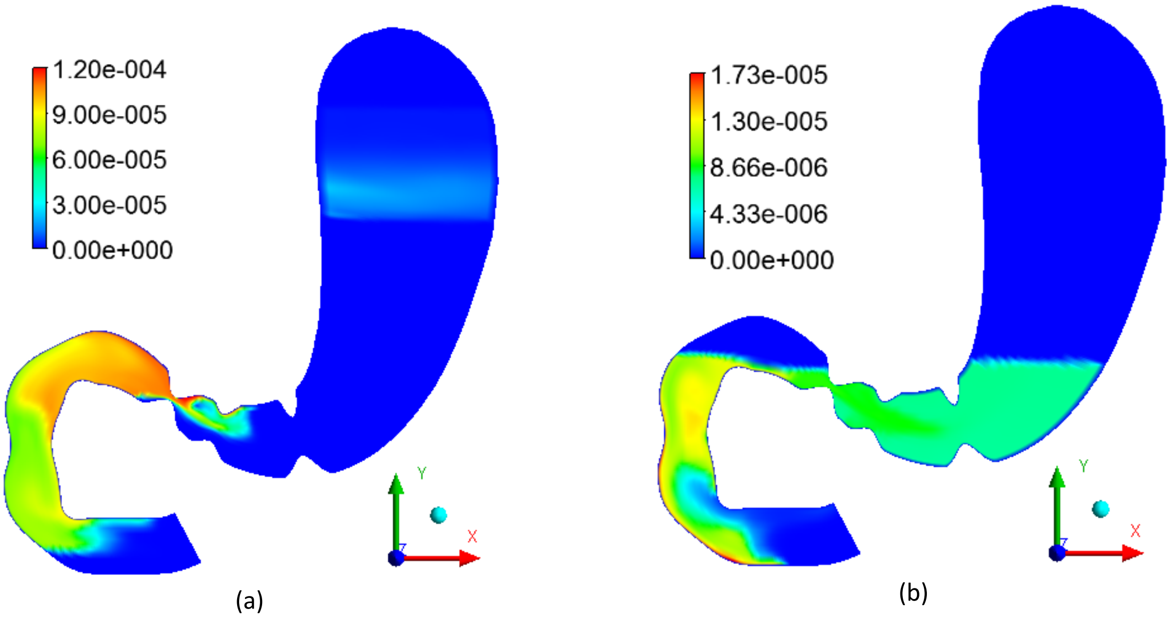
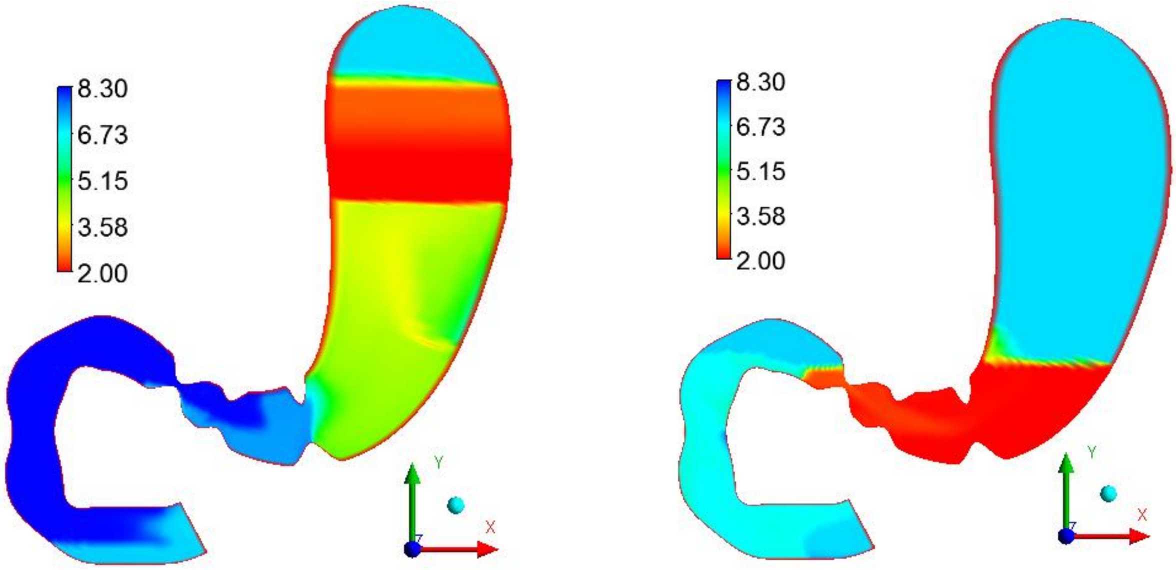


Fig. 7. Mass fraction of amino acids, *t*=30 min (a) Scenario 1 (b) Scenario 2

3.6 pH Level

Figure 8 shows the distribution of the *pH* level in the digestive tract, as one of the main factors of mucosal damage. In the first scenario, an increased level of acidity is observed in the upper part of the stomach due to the release of hydrochloric acid. The presence of food particles helps to reduce the concentration of acid and decreases the *pH* to 4-5 in the middle part of the stomach. In the lower part of the stomach, under the influence of sodium bicarbonate secreted in the antrum, the acidity decreases and the *pH* level is about 7.5. In the duodenum, an alkaline environment is observed with a *pH* level of up to 8.3.This distribution of acidity satisfactorily correlates with the available experimental data in the stomach and duodenum [51]. In the second scenario, the upper and middle part of the stomach has a neutral level of acidity due to filling with gas and food particles (*pH* is about 7). In the antrum and in the region of the pyloric opening, an abnormally high level of acidity (*pH*=2) is observed, which can lead to damage to the mucous membrane. In the area of the descending part of the duodenum, the acidity is also slightly increased (*pH*=6).



(a) (b)

Fig. 8. pH level, t=30 min (a) Scenario 1 (b) Scenario 2

Thus, the results of numerical simulation show significant differences in the level of acidity with previous calculations, for example, for a single-phase medium [45, 48]. In the first scenario, protein digestion is more pronounced in the upper part of the stomach and in the upper part of the duodenum. In the second scenario, active transformation of food is observed in the antrum and the descending part of the intestine.

4. Conclusions

This study examined the digestive processes in the entire stomach and duodenum, taking into account the gas phase. We studied the influence of the density of food particles on the distribution of volume fractions of phases, mass fractions of food components and enzymes, *pH* level in the digestive tract. It should be noted that 30 minutes after the start of digestion, phase separation is observed, since the model does not take into account the transfer of mass from the liquid phase to food particles (water absorption). Also, other mechanisms for removing excess fluid are not taken into account. For the same reason, a high level of acidity is observed, since the acid is not absorbed by food particles. In reality, the content in the tract should become more homogeneous over time. In the future, more careful work with dynamically changing rheological properties of the contents of the tract is necessary. It seems appropriate to take into account the influence of food properties on the parameters of tract motility. It is also necessary to take into account the decrease in the volume of the stomach as it empties [52]. For these purposes, we are planning to conduct experimental studies to obtain individual parameters of stomach geometry and motility in response to food intake of various compositions.

Acknowledgement
This research was funded by Ministry of science and higher education of the Russian Federation (Project № FSNM-2023-0003)

References

[1] Hunt, R. H., Micheal Camilleri, S. E. Crowe, E. M. El-Omar, J. G. Fox, E. J. Kuipers, Peter Malfertheiner et al. "The stomach in health and disease." *Gut* 64, no. 10 (2015): 1650-1668. https://doi.org/10.1136/gutjnl-2014-307595

[2] O'Connor, Anthony, and Colm O'Moráin. "Digestive function of the stomach." *Digestive diseases* 32, no. 3 (2014): 186-191. https://doi.org/10.1159/000357848
[3] Goyal, Raj K., Yanmei Guo, and Hiroshi Mashimo. "Advances in the physiology of gastric emptying." *Neurogastroenterology & Motility* 31, no. 4 (2019): e13546. https://doi.org/10.1111/nmo.13546
[4] Schulze, K. "Imaging and modelling of digestion in the stomach and the duodenum." *Neurogastroenterology & Motility* 18, no. 3 (2006): 172-183. https://doi.org/10.1111/j.1365-2982.2006.00759.x
[5] Clarysse, Sarah, Jan Tack, F. Lammert, G. Duchateau, C. Reppas, and Patrick Augustijns. "Postprandial evolution in composition and characteristics of human duodenal fluids in different nutritional states." *Journal of pharmaceutical sciences* 98, no. 3 (2009): 1177-1192. https://doi.org/10.1002/jps.21502
[6] Makola, Diklar, David A. Peura, and Sheila E. Crowe. "Helicobacter pylori infection and related gastrointestinal diseases." *Journal of clinical gastroenterology* 41, no. 6 (2007): 548-558. https://doi.org/10.1097/MCG.0b013e318030e3c3
[7] Lacy, Brian E., and Justin Rosemore. "Helicobacter pylori: ulcers and more: the beginning of an era." *The Journal of nutrition* 131, no. 10 (2001): 2789S-2793S. https://doi.org/10.1093/jn/131.10.2789S
[8] Lu, Pei-Jung, Ping-I. Hsu, Chung-Hsuan Chen, Michael Hsiao, Wei-Chao Chang, Hui-Hwa Tseng, Kung-Hung Lin, Seng-Kee Chuah, and Hui-Chun Chen. "Gastric juice acidity in upper gastrointestinal diseases." *World journal of gastroenterology: WJG* 16, no. 43 (2010): 5496. https://doi.org/10.3748/wjg.v16.i43.5496
[9] Franke, Andreas, Stephan Teyssen, and Manfred V. Singer. "Alcohol-related diseases of the esophagus and stomach." *Digestive diseases* 23, no. 3-4 (2006): 204-213. https://doi.org/10.1159/000090167
[10] Li, L. F., R. L. Y. Chan, L. Lu, J. Shen, L. Zhang, W. K. K. Wu, L. Wang, T. Hu, M. X. Li, and C. H. Cho. "Cigarette smoking and gastrointestinal diseases: the causal relationship and underlying molecular mechanisms." *International journal of molecular medicine* 34, no. 2 (2014): 372-380. https://doi.org/10.3892/ijmm.2014.1786
[11] D'Elia, Lanfranco, Giovanni Rossi, Renato Ippolito, Francesco P. Cappuccio, and Pasquale Strazzullo. "Habitual salt intake and risk of gastric cancer: a meta-analysis of prospective studies." *Clinical nutrition* 31, no. 4 (2012): 489-498. https://doi.org/10.1016/j.clnu.2012.01.003
[12] Morrison, Maia EW, Janine M. Joseph, Susan E. McCann, Li Tang, Hani M. Almohanna, and Kirsten B. Moysich. "Cruciferous vegetable consumption and stomach cancer: a case-control study." *Nutrition and cancer* 72, no. 1 (2020): 52-61. https://doi.org/10.1080/01635581.2019.1615100
[13] Huerta-Franco, María-Raquel, Miguel Vargas-Luna, Paola Tienda, Isabel Delgadillo-Holtfort, Marco Balleza-Ordaz, and Corina Flores-Hernandez. "Effects of occupational stress on the gastrointestinal tract." *World journal of gastrointestinal pathophysiology* 4, no. 4 (2013): 108. https://doi.org/10.4291/wjgp.v4.i4.108
[14] Greenwald, David A. "Aging, the gastrointestinal tract, and risk of acid-related disease." *The American Journal of Medicine Supplements* 117, no. 5 (2004): 8-13. https://doi.org/10.1016/j.amjmed.2004.07.019
[15] Beardslee, Luke A., George E. Banis, Sangwook Chu, Sanwei Liu, Ashley A. Chapin, Justin M. Stine, Pankaj Jay Pasricha, and Reza Ghodssi. "Ingestible sensors and sensing systems for minimally invasive diagnosis and monitoring: the next frontier in minimally invasive screening." *ACS sensors* 5, no. 4 (2020): 891-910. https://doi.org/10.1021/acssensors.9b02263
[16] Lex, Timothy R., Jason D. Rodriguez, Lei Zhang, Wenlei Jiang, and Zongming Gao. "Development of in vitro dissolution testing methods to simulate fed conditions for immediate release solid oral dosage forms." *The AAPS Journal* 24, no. 2 (2022): 40. https://doi.org/10.1208/s12248-022-00690-5
[17] Ghosh, Tilak, David Ian Lewis, A. T. R. Axon, and S. M. Everett. "methods of measuring gastric acid secretion." *Alimentary pharmacology & therapeutics* 33, no. 7 (2011): 768-781. https://doi.org/10.1111/j.1365-2036.2010.04573.x
[18] Fois, Chiara Anna Maria, Thi Yen Loan Le, Aaron Schindeler, Sina Naficy, Dale David McClure, Mark Norman Read, Peter Valtchev, Ali Khademhosseini, and Fariba Dehghani. "Models of the Gut for Analyzing the Impact of Food and Drugs." *Advanced Healthcare Materials* 8, no. 21 (2019): 1900968. https://doi.org/10.1002/adhm.201900968
[19] Kamaltdinov, M. R., and A. G. Kuchumov. "Application of a mathematical model of systemic circulation for determination of blood flow parameters after modified Blalock-Taussig shunt operation in newborns." *Russian Journal of Biomechanics* 25, no. 3 (2021): 268-284.
[20] Ningappa, Abhilash Hebbandi, Suraj Patil, Gowrava Shenoy Belur, Augustine Benjamin Valerian Barboza, Nitesh Kumar, Raghuvir Pai Ballambat, Adi Azriff Basri, Shah Mohammed Abdul Khader, and Masaaki Tamagawa. "Influence of altered pressures on flow dynamics in carotid bifurcation system using numerical methods." *Journal of Advanced Research in Fluid Mechanics and Thermal Sciences* 97, no. 1 (2022): 47-61. https://doi.org/10.37934/arfmts.97.1.4761
[21] Zin, Ahmad Faiz Mat, Ishkrizat Taib, Muhammad Hanafi Asril Rajo Mantari, Bukhari Manshoor, Ahmad Mubarak Tajul Arifin, Mahmod Abd Hakim Mohamad, Muhammad Sufi Roslan, and Muhammad Rafiuddin Azman. "Temperature Variation with Hemodynamic Effect Simulation on Wall Shear Stress in Fusiform Cerebral Aneurysm."

Journal of Advanced Research in Fluid Mechanics and Thermal Sciences 95, no. 2 (2022): 40-54. https://doi.org/10.37934/arfmts.95.2.4054

[22] Johari, Nasrul Hadi, M. Hamady, and Xiao Yun Xu. "Fluid-Structure Interaction Study of The Effect of Stent on Local Hemodynamics Parameters at The Stented Carotid Artery Bifurcation." *Journal of Advanced Research in Applied Sciences and Engineering Technology* 28, no. 2 (2022): 247-255. https://doi.org/10.37934/araset.28.2.247255

[23] Razhali, Nur Farahalya, Ishkrizat Taib, Nurul Fitriah Nasir, Ahmad Mubarak Tajul Arifin, Nor Adrian Nor Salim, Shahrul Azmir Osman, Nofrizal Idris Darlis, and A. K. Kareem. "Analysis of Hemodynamic Effect on Different Stent Strut Configuration in Femoral Popliteal Artery during the Physical and Physiological Conditions." *Journal of Advanced Research in Applied Sciences and Engineering Technology* 29, no. 1 (2022): 223-236. https://doi.org/10.37934/araset.29.1.223236

[24] Pal, Anupam, Keshavamurthy Indireshkumar, Werner Schwizer, Bertil Abrahamsson, Michael Fried, and James G. Brasseur. "Gastric flow and mixing studied using computer simulation." *Proceedings of the Royal Society of London. Series B: Biological Sciences* 271, no. 1557 (2004): 2587-2594. https://doi.org/10.1098/rspb.2004.2886

[25] Pal, Anupam, James G. Brasseur, and Bertil Abrahamsson. "A stomach road or "Magenstrasse" for gastric emptying." *Journal of biomechanics* 40, no. 6 (2007): 1202-1210. https://doi.org/10.1016/j.jbiomech.2006.06.006

[26] Kuhar, Sharun, Jae Ho Lee, Jung-Hee Seo, Pankaj J. Pasricha, and Rajat Mittal. "Effect of stomach motility on food hydrolysis and gastric emptying: Insight from computational models." *Physics of Fluids* 34, no. 11 (2022): 111909. https://doi.org/10.1063/5.0120933

[27] Li, Changyong, Jie Xiao, Xiao Dong Chen, and Yan Jin. "Mixing and emptying of gastric contents in human-stomach: A numerical study." *Journal of biomechanics* 118 (2021): 110293. https://doi.org/10.1016/j.jbiomech.2021.110293

[28] Seo, Jung Hee, and Rajat Mittal. "Computational modeling of drug dissolution in the human stomach." *Frontiers in Physiology* (2022): 2080. https://doi.org/10.3389/fphys.2021.755997

[29] Ebara, Rika, Shunichi Ishida, Taimei Miyagawa, and Yohsuke Imai. "Effects of peristaltic amplitude and frequency on gastric emptying and mixing: a simulation study." *Journal of the Royal Society Interface* 20, no. 198 (2023): 20220780. https://doi.org/10.1098/rsif.2022.0780

[30] Ferrua, M. J., and R. P. Singh. "Modeling the fluid dynamics in a human stomach to gain insight of food digestion." *Journal of food science* 75, no. 7 (2010): R151-R162. https://doi.org/10.1111/j.1750-3841.2010.01748.x

[31] Alokaily, Samer, Kathleen Feigl, and Franz X. Tanner. "Characterization of peristaltic flow during the mixing process in a model human stomach." *Physics of Fluids* 31, no. 10 (2019): 103105. https://doi.org/10.1063/1.5122665

[32] Ferrua, Maria J., Zhengjun Xue, and R. Paul Singh. "On the kinematics and efficiency of advective mixing during gastric digestion–A numerical analysis." *Journal of Biomechanics* 47, no. 15 (2014): 3664-3673. https://doi.org/10.1016/j.jbiomech.2014.09.033

[33] Hao, Shilei, Bochu Wang, and Yazhou Wang. "Density-dependent gastroretentive microparticles motion in human gastric emptying studied using computer simulation." *European Journal of Pharmaceutical Sciences* 70 (2015): 72-81. https://doi.org/10.1016/j.ejps.2015.01.009

[34] Xue, Zhengjun, Maria J. Ferrua, and Paul Singh. "Computational fluid dynamics modeling of granular flow in human stomach." *Alimentos hoy* 21, no. 27 (2012): 3-14.

[35] Ibitoye, S. E., I. K. Adegun, O. A. Olayemi, P. O. Omoniyi, and O. O. Alabi. "Experimental and numerical investigation of flow behaviors of some selected food supplements in modeled intestine." *Scientia Iranica* 30, no. 1 (2023): 39-51.

[36] Palmada, Nadun, John E. Cater, Leo K. Cheng, and Vinod Suresh. "Experimental and computational studies of peristaltic flow in a duodenal model." *Fluids* 7, no. 1 (2022): 40. https://doi.org/10.3390/fluids7010040

[37] Zha, Jinping, Siyu Zou, Jianyu Hao, Xinjuan Liu, Guillaume Delaplace, Romain Jeantet, Didier Dupont, Peng Wu, Xiao Dong Chen, and Jie Xiao. "The role of circular folds in mixing intensification in the small intestine: A numerical study." *Chemical Engineering Science* 229 (2021): 116079. https://doi.org/10.1016/j.ces.2020.116079

[38] Love, R. J., R. G. Lentle, P. Asvarujanon, Y. Hemar, and K. J. Stafford. "An expanded finite element model of the intestinal mixing of digesta." *Food Digestion* 4 (2013): 26-35. https://doi.org/10.1007/s13228-012-0017-x

[39] Fullard, Luke, Willem Lammers, Graeme C. Wake, and Maria J. Ferrua. "Propagating longitudinal contractions in the ileum of the rabbit–efficiency of advective mixing." *Food & function* 5, no. 11 (2014): 2731-2742. https://doi.org/10.1039/C4FO00487F

[40] Sinnott, Matthew D., Paul W. Cleary, and Simon M. Harrison. "Peristaltic transport of a particulate suspension in the small intestine." *Applied Mathematical Modelling* 44 (2017): 143-159. https://doi.org/10.1016/j.apm.2017.01.034

[41] Ploutz-Snyder, Lori, Jeanne Foley, Robert Ploutz-Snyder, Jill Kanaley, Kenneth Sagendorf, and Ronald Meyer. "Gastric gas and fluid emptying assessed by magnetic resonance imaging." *European journal of applied physiology and occupational physiology* 79 (1999): 212-220. https://doi.org/10.1007/s004210050498

[42] Caballero, N., I. Marin, and J. Serra. "Gastric gas dynamics in healthy humans." *Neurogastroenterology & Motility* 30, no. 11 (2018): e13408. https://doi.org/10.1111/nmo.13408
[43] Ishida, Shunichi, Taimei Miyagawa, Gregory O'Grady, Leo K. Cheng, and Yohsuke Imai. "Quantification of gastric emptying caused by impaired coordination of pyloric closure with antral contraction: a simulation study." *Journal of the Royal Society Interface* 16, no. 157 (2019): 20190266. https://doi.org/10.1098/rsif.2019.0266
[44] Imai, Yohsuke, Ikuma Kobayashi, Shunichi Ishida, Takuji Ishikawa, Martin Buist, and Takami Yamaguchi. "Antral recirculation in the stomach during gastric mixing." *American Journal of Physiology-Gastrointestinal and Liver Physiology* (2013). https://doi.org/10.1152/ajpgi.00350.2012
[45] Trusov, P. V., Nina V. Zaitseva, and M. R. Kamaltdinov. "A multiphase flow in the antroduodenal portion of the gastrointestinal tract: a mathematical model." *Computational and Mathematical Methods in Medicine* 2016 (2016). https://doi.org/10.1155/2016/5164029
[46] Trusov, P. V., N. V. Zaitseva, M. Yu Tsinker, and A. V. Babuskina. "Modelling dusty air flow in the human resperatory tract." *Russian Journal of Biomechanics* 22, no. 3 (2018): 262-274.
[47] Trusov, P. V., N. V. Zaitseva, V. M. Chigvintsev, and D. V. Lanin. "MATHEMATICAL MODEL FOR DESCRIBING ANTI-VIRUS IMMUNE RESPONSE REGULATION ALLOWING FOR FUNCTIONAL DISORDERS IN A BODY." *Health Risk Analysis* 4 (2017): 117-128. https://doi.org/10.21668/health.risk/2017.4.13.eng
[48] Kamaltdinov, M., P. Trusov, and N. Zaitseva. "A mathematical model of the multiphase flow in the antroduodenum: consideration of the digestive enzymes and regulation processes." *Series on biomechanics* (2018).
[49] Kamaltdinov, Marat R., Peter V. Trusov, and Nina V. Zaitseva. "Viscosity of a multicomponent mixture in the antroduodenum." In *AIP Conference Proceedings*, vol. 2627, no. 1. AIP Publishing, 2023. https://doi.org/10.1063/5.0117427
[50] Trusov, Petr Valentinovich, Nina Vladimirovna Zaitseva, and Marat Reshidovich Kamaltdinov. "Flow in antroduodenal part of digestive tract: mathematical model and some results." *Matematicheskaya Biologiya i Bioinformatika* 10, no. 1 (2015): 34-53. https://doi.org/10.17537/2015.10.34
[51] Haruma, Mihara, Okamoto, Kusunoki, Hananoki, Tanaka, Yoshihara, Sumii, and Kajiyama. "Eradication of Helicobacter pylori increases gastric acidity in patients with atrophic gastritis of the corpus—evaluation of 24-h pH monitoring." *Alimentary pharmacology & therapeutics* 13, no. 2 (1999): 155-162. https://doi.org/10.1046/j.1365-2036.1999.00459.x
[52] Li, Changyong, and Yan Jin. "Digestion of meat proteins in a human-stomach: A CFD simulation study." *Innovative Food Science & Emerging Technologies* 83 (2023): 103252. https://doi.org/10.1016/j.ifset.2022.103252