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Review report on PhD thesis
Discipline Council for Biomedical Engineering
Silesian University of Technology

Name and surname of the candidate: .....Maria Gracka.....

Title of the PhD thesis: ...Modeling and analysis of the blood flow using multiphase approach..

Supervisor: .....PhD, DSc, Assoc. Prof. Ziemowit Ostrowski.....

Co-supervisor:.....PhD, Prof. Alain Kassab.....

Reviewer: .....PhD, DSc, dr hab. prof. Nataliya Kizilova.....

1. Basic information on the PhD candidate **Maria Gracka**
a) the date when the MS degree was awarded and the name of the department which awarded it
Date of graduation 20.09.2016, Silesian University of Technology, Faculty of Energy and Environmental Engineering

b) information on whether the candidate has previously applied for the award of the PhD degree, including, if appropriate, information on the time duration and term of previous PhD application
The candidate has not previously applied for PhD degree.

c) scientific and professional background (workplace, positions held)
Place of work - Silesian University of Technology
1) Contractor in the project: Numerical modeling and analysis of systolic vessel compression on atherosclerotic plaque deposition in coronary arteries, Nov. 2019 – Aug. 2021
2) Contractor in the project: Design and implementation of technology for the production of innovative microfluidic chips for 3D observation of human cell cultures in conditions reflecting the *in vivo* conditions, Sep. 2017 - Sep. 2018
3) Contractor in the project: Modeling and analysis of multiphase blood flow, Jun. 2017 - Dec. 2017
4) Contractor in the project: Transient multiphase model of the blood flow in elastic blood vessels, Nov. 2015 - May 2016

2. The PhD thesis untitled "Modeling and analysis of the blood flow using multiphase approach" submitted to the Discipline Council for Biomedical Engineering of Silesian University of Technology is published on 150 pages. The PhD thesis is written in English. It consists of 7 chapters, Bibliography, three Appendixes (A, B and C) and Abstract of the thesis in English and Polish languages.

The study is **aimed** at development, comparative analysis and testing the models used for numerical simulations of blood flow. As a result of the study, detailed propositions for the multiphase model parameters and CFD settings are formulated for practical application of the proposed approach.

In the **first chapter** motivation, short background and current state of the research on the topic are presented. Special attention is paid to the multiphase properties of the blood as suspensions of the blood cells in the blood plasma. The differences in the main blood properties in the larger, smaller vessels and the microchannels like the blood capillaries or the tubes of different microfluidic units are described. Importance of numerical methods and CFD simulations on realistic blood vessel geometries is substantiated. The problems which are connected with non-Newtonian properties of blood is the dependence of its viscosity on the blood cell concentration, shear rate and other parameters are observed. It is shown, a detailed multiphase model of blood that can be used for CFD studies in the 3D models of the large, small and microvessels is of great interest for biomedical engineering. In the chapter 1.2 the current state of the research including the Euler-Euler and hybrid Euler-Lagrangian approaches to the microfluids and blood as a suspension of microparticles are presented. Possible particle-particle and particle-fluid interactions in the blood are observed. Importance of the blood vessel wall elasticity in fluid-structure interaction problems in the fluid-filled distensible tubes is shown. The implementation of the Windkessel elements as boundary conditions for larger blood vessels is discussed.

In the **second chapter** the objectives and outline of the thesis are given. The main goals of the thesis are pointed out as (1) comparison and testing the models used for numerical simulations of blood flow and (2) elaboration of an appropriate methodology for the blood flow simulations in the blood vessel of different scales. The blood is modeled as a non-heterogeneous mixture of solid (blood cells) and fluid (blood plasma) components. Three scales of the blood vessel types are considered: aorta as a large artery, coronary vessels as small arteries, and a microvessel as a capillary. AnSys Fluent 17.2 is pointed out as a CFD software that was used to develop a numerical model of blood flow in the blood vessels and microchannels.

In the **third chapter** the mathematical problem formulation including the Carreau rheological model for blood, standard Euler-Euler approach for the continuous multiphase media, and hybrid Euler-Lagrange approach for the suspensions are presented. The dependence of the viscosity of the solid phase on the temperature, diameters of the particles, and energy dissipation due to elastic and inelastic collisions f the particles is accounted for the Euler-Euler approach.

The **chapter 4** is dedicated to the numerical model of the blood flow in the large vessels like aorta and its main branches. The geometry of the system at consideration, boundary conditions applied, materials and model parameters used for the numerical computations are discussed. The first analyzed case is related to human aorta including the aortic root and arch with right and left subclavian and common carotid arteries, thoracic and partially the abdominal aorta. A typical periodic function for the inlet velocity taken from MRI data has been used as UDF in Fluent. Three-element Womersley models have been used as the outlet boundary conditions for the aortic model. Model parameters have been taken from the literature. The standard k-ε turbulent model has been used for the blood flow modeling in the aortic model.

The mesh generated for the computational domain is presented and its quality has been estimated by the standard Y^+ function in Fluent software. The main results of the numerical simulations are presented.

In the **chapter 5** the numerical model of the blood flow in the smaller blood vessels like coronary arteries is described. The corresponding geometrical model of the RCA, material parameters of the blood properties, and velocity inlet and granular temperature boundary conditions are discussed. The details of mesh generation are given. The results of CFD computations using the AnSys Fluent are presented.

In the **chapter 6** the numerical model of the flow of RBC suspension in dextran through the microchannels is described. Geometric model of the microchannel and its mesh are presented. The details of the boundary conditions are given. The detailed numerical results as contour plots, particle plots and x0y profiles are presented. The model validation is carried out on the microofluidic experimental data.

In the **chapter 7** a detailed discussion of the results presented in the chapters 4-6 is presented. The main conclusions important for practical implementation of the developed model are summarized. Several open topic for further studies are described.

The **Bibliography** contains 98 refrences on different theoretical and experimental aspects of the blood rheology and blood flow modeling at different scales.

In the **Appendix A** the source code for the inlet velocity profile and the pressure outlet profiles for the aortic model (AnSys Fluent) is presented.

In the **Appendix B** the code for the granular temperature source term and the inlet velocity profile (AnSys Fluent) is presented.

In the **Appendix C** the source code for the viscosity term (AnSys Fluent) is presented.

3. Estimation of the research methods used in the work.

Numerical methods implemented in the software AnSys Fluent, namely, the standard k-ε turbulent model have been used for the blood flow modeling in the large arteries like aorta. The geometry modeling, mesh generation, boundary conditions and materials parameters have been correctly assigned.

The Euler-Euler approach for the blood flows in the smaller arteries (RCA) has been implemented in the UDF functions and used in the viscous laminar flow model simulations with AnSys Fluent at Re=150. The chosen model and UDF are applicable to the RCA geometry and flow regime.

Material parameters for the numerical modeling in different scales have been taken from the published literature and open-source datasets that have been thoroughly examined.

A detailed literature review and usage of the available experimental data for the boundary conditions for the models and the model validations are confirmed by vast bibliography.

4. Results of the study.

The results of the CFD simulations of the turbulent blood flow in the aortic model (chapter 4) are presented as distributions of the blood cell volume fraction (Fig.4.8-4.12), pressure contour plots (Fig.4.15), and velocity vector plots (Fig. 4.16-17) during the systole and diastole. The computed blood pressure variations with time at different outlets of the model are plotted in Fig.4.13. The time variations of the mass flow at the inlet and the outlets are presented in Fig.4.14. The gradual pressure decrease along the aorta from its root towards the outlet of the model corresponds to the measured *in vivo* data. The pressure and flow variations along the coarctation of aorta are close to experimental Doppler ultrasound observations. The computed blood pressure (Fig.4.13) and blood mass flow rate (Fig.4.14) profiles are correct.

The results of the numerical simulations based on the Euler-Euler approach (chapter 5) are presented as distributions of the RBC volume fraction (Figures 5.6, 5.7, 5.8) and granular temperatures (Fig.5.9). The displacement of the RBC towards the outer surfaces of the elbows along the RCA (planes 4-7 and 10-12) due to the centrifugal forces (Fig.5.8) is correct. The velocity profiles in the entrance region of the RCA are presented in Figures 5.10, 5.11. The contour plots of the RBC volume fraction and granular temperature along the whole RCA model are given in Figures 5.12, 5.13. The velocity profiles at the outflow of the entrance part of the RCA (Fig.5.14) have been validated on the literature data (REF [37]).

The results of the numerical computations for the microfluidic flows along a microchannel of complex geometry are presented in the chapter 6. The contour plots of the velocity magnitude (Fig.6.3) and particle distributions (Fig.6.4) in the microchannel correspond to physical principles. The RBC volume fractions (Fig.6.5), particle distributions (Fig.6.6), velocity field (Fig.6.7, 6.9), particle distribution colored by velocity magnitude (Fig.6.8,6.10) also refer to the microfluidic numerical simulations. The model validation has been carried out on the experimental results on the particle distributions (Figures 6.11 – 6.16) and velocity tracking (Figures 6.21-6.23).

Discussions of the computed results are collected in chapter 7. The advantages of the multiphase approach to the blood flows in the larger arteries (aortic model), smaller arteries (RCA model) and microcirculation (microchannel flow) are listed. The propositions for the more detailed modeling of blood and RBC suspensions based on the numerical results computed at each of three scales are summarized. The open topics for future research are formulated in the subchapter 7.2.

The list of reverences contains 98 items; 18 of them was published during the last five tears (2017-2021). All the REFs relate to the topic of the PhD thesis.

5. Practical applications of the approach developed and results obtained

The developed approaches based on the multiphysical modeling of blood properties, Windkessel-type of the boundary conditions for the larger blood vessels, the Euler-Euler approach to the blood flow modeling in the smaller vessels, the Euler-Euler and Euler-Lagrangian approaches to the flow modeling at the miscoscales are very useful for direct implementation in medicine. Digital human subject aimed at the detailed 3D modeling of human circulatory system modeling, and the appropriate models accounted for the realistic blood rheology as a suspension of microparticles (blood cells) are of great interest as a fluid model for the blood circulation at different scales from the largest (aorta, vena cava) to the smallest (capillaries) vessels with significant influence of the blood (shear-thinning) rheology. The obtained results can be used for more detailed diagnostics of the physiological dysfunctions connected with anomalous blood rheology (RBC shape, size, rigidity, aggregate ability, etc.). The obtained results on the blood cell volume fraction distribution in different geometries can be used together with medical image analysis. Novel diagnostic indexes could be further developed based on the presented results of the PhD study.

6. Remarks and corrections.

Information presented in the **chapters 1 and 2** is not well structured. The microfluidic systems as perfect ones for the individual blood rheology estimation and model validation are partially discussed in both chapters 1&2. Abbreviation for RBC was introduced several times in different subchapters. For typical RBC concentrations different values are repeatedly presented in the chapters1&2. Rheological properties of blood including the shear-thinning behavior, Fahraeus-Lindqvist effect, cell-free layer formation and the rheological models for blood viscosity are split between the subchapters of the chapters 1 and 2.

A brief review of the existing models of the blood flow (lumped parameter, 1D plane pulse wave, 2D cylindrical pulse wave, 3D turbulent models for the rigid and soft boundaries, particle dynamics simulations, Lattice-Boltzmann approach, etc. with their subdivision into the discrete and continuous ones) had to be presented before the subchapter dedicated to the boundary conditions.

As it is correctly stated in the thesis (pages 14, 17) "a numerical model capable of reproducing the actual behavior of the blood, including its components ... will be precious for many biomedical applications". Therefore, the shortcomings of the already developed models must be shown based on the appropriate literature review.

In the **chapter 2** dextran is called as one of two major blood components together with RBC which is wrong. It had to be mentioned that blood model was used in the numerical simulations in the larger (aorta) and smaller (RCA) models while a suspension of RBCs in dextran has been used in the microcirculatory flow simulations in order to have experimental data for the model validation.

In the **chapter 3** the Yasuda rheological model for the blood viscosity is used while in the chapters 1&2 the Carreau-Yasuda rheological model was discussed. In the chapter 3 (page 31) the extension of the Carreau-Yasuda is mentioned, while the simplified model was used in (3.1). Actually Carreau-Yasuda model produce Carreau model by substitution a=2.

The blood plasma viscosity μ_f in (3.1) is supposed to be constant as for the Newtonian liquids, while in the subchapter 4.2 the Carreau model for the plasma is mentioned.

Eq. (3.11): the Ref [J. Ding and D. Gidaspow. A Bubbling Fluidization Model Using Kinetic Theory of Granular Flow. AIChE J., 36(4):523-538, 1990] is more relevant than [76].

In the **chapter 4** the geometric model of the pathological aorta with significant (65%) coarctation (CoA) has been chosen. When a new detailed multiphase model is tested on different physiological geometries, a healthy case must be considered first because the main relationships between the pressures, flows, their mean and oscillating components, wall shear stress and mass flow rates at the outlets are very well studied for the healthy geometry [Milnor 1989, McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles 6th Edition, 2011].

Table 4.2: the parameters are not clearly explained. For instance, the relationships between the solid viscosity, solid bulk viscosity (page 43) and the RBC viscosity μ_f (page 32). Due to negligibly small WBC concentrations in comparison to the RBC concentrations (1% and 37-48%, accordingly), the needs in the term 'Interface exchange coefficient plasma-WBC' is unclear. The corresponding indications of the parameters in the Table 4.2 are absent. In (4.2) the fluid viscosity μ is used but its relation to the previously introduced relative mixture viscosity η, RBC μ_f, solid and solid bulk viscosities is not explained.

The statement about laminar flow in healthy aorta (page 47) is incorrect.

The Fluent solver settings are missed. If the standard k-ε model has been used, the pre-processing settings must be pointed out, namely, fluid and its thermomechanical parameters, cell zones (if any), numerical schemes, monitors chosen. How the multiphase approach has been applied to the fluid? Whether it was used as UDF functions in the boundary conditions only?

In the standard k-ε model thermodynamic temperature is used (eq.4.7-4.8) while in the boundary conditions (Womersley's elements) temperature is absent.

The contour plots in Figures 4.8-4.12 are non-uniform in the larger geometries while in the zoomed regions (in the rectangle areas) the cross-sectional distributions are non-uniform at the walls only (higher over the inner surface of the thoracic aorta and lower over

its outer surface while it is constant (and noticeably lower over the cross-section) that is looking as 'jumps' in the volume fractions of the blood cells in the lumen and at the walls.

Chapter 5. Strongly speaking, the Fahraeus-Lindqvist effect (page 63) is related to the steady laminar flows in straight tubes. The effect was confirmed in the experiments on circular transparent tubes and in the blood arterioles and capillaries (open brain tissue observation). In realistic complex geometries of the blood vessels the cell-free layer is influenced by the rotational flows, vortexes, and reverse flows.

REFs to (5.1)-(5.3) must be added. Most of the values in Table 5.2 are already presented in Table 4.2.

The blood flow in the RCA is not laminar (page 65) according to the common definition (fluid mechanics). In the non-uniform curved tapered tubes additional forces (like centrifugal) appear and make the flow much more complex (e.g. Dean vortexes in the curved tubes). When the 'laminar viscous' model is used in Fluent, it means 'laminar flow model'.

Detailed solver settings for AnSys Fluent (flow model, fluid, numerical schemes, etc.) are not given.

Chapter 6. Since the suspension of RBC in dextran has been used in the microfluidic simulations, this can not be named 'multifluid blood simulation' (page 75).

Since AnSys Fluent software has been used for numerical computations, the Fluent settings must be listed (see similar remarks to the chapters 4,5).

All the above-listed remarks and minor corrections do not influence the originality, correctness and importance of the results presented in the PhD thesis.

7. Final estimation of the PhD thesis.

The presented PhD thesis contains new original research methodology and results related to the blood flow modeling as a complex multiphase fluid in realistic 3D geometries at different scales from macro to meso and micro. The proposed approaches have been carefully tested and validated. The considered results are related to the discipline 'biomedical engineering' (Inżynieria biomedyczna).

The presented materials confirm very good theoretical knowledge of the candidate in mechanics, biomechanics and numerical methods, as well as good skills in CFD computations and ability to conduct independent scientific research.

I, the undersigned, certify that the reviewed doctoral dissertation, submitted by **Maria Gracka**, meets the conditions specified in Article 13.1 of the Act of 14 March 2003 on Scientific Degrees and Academic Title and Degrees and Title in Art (Journal of Laws No. 65, item 595, as amended) and apply to the Council of the Discipline Biomedical Engineering of the Silesian University of Technology in Gliwice to admit **Maria Gracka** to further stages of her doctoral dissertation.

TAK

25.11.2021

data sporządzenia recenzji
date of the review

Podpisała N. Kizilova (podpis całygazny)

podpis recenzenta
signature of the reviewer