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SCIENCE & TECHNOLOGY CENTER IN UKRAINE

Project report

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ID# 3036
Project title **Computational Intelligence in Predictive Modelling of Mechanical Responses of Human Blood Vessels Affected by Atherosclerotic Plaque**
Project start date **01/05/2024**
Reporting period: **Q1 (MAY-AGST)**

Content of the quarterly progress report for quarter Q1 PAGE

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Project report

1. Summary of progress

According to the Project time plan, it is stand that the 1st stage (3 months) deals with the parallel development of the work package 1 (WP1), WP2, and WP3 and assumes the development of the basic algorithms and some simplified benchmark solutions.

A symbolic regression (SR) method was used to model the viscoelastic nonlinear behavior of materials within WP1. A Python code using the DSO open library was developed for findings the direct symbolic formulation of the material model within a benchmark problem. The team explored the application of SR using synthetic data from the Mooney-Rivlin model in combination with linear viscosity term. A novel error metric based on implicit derivatives is used here for additional accuracy improvement and fitting robustness. It was compared with the standard normalized root mean squared error. The findings highlight the need for refining error metrics in SR applications that are used for complex cases with parametric data sets, especially within indirect parametric representations. The first obtained results were presented and discussed with EU partners from the Continuum Mechanics Department of RWTH Aachen in June 2024 and are scheduled for presentation at the IEEE 5th KhPI Week on Advanced Technology (October 2024), and a related paper has received positive reviews and is generally accepted for publication.

Parametric computational modelling plaques is provided within a WP2 using finite element methods (FEM) to simulate human blood vessels with atherosclerotic affection. At the beginning here is the schematic 2D model that includes two arterial wall layers and geometry of a plague is developed. It incorporates viscoelastic effects using the Prony series and simplified linear isotropic elasticity following many other literature data. It allows analysis of strain and stress distribution, showing significant stress concentrations. The model allowed us to study the influence of the size of the plague on the deformed state of the blood vessel that could be used for prognosis problems and statistical inference analysis. The first obtained results were presented and discussed with EU partners of the project as well as with practical medical professionals. The last allowed to organise cooperation with the Department of Interventional Cardiology of the Institute of General and Emergency Surgery named after V.T. Zaytseva of the National Academy of Sciences of Ukraine in the scope of the project 1st stage.

Several critical consultations from medical practice have facilitated the development of patient-specific models from Optical Coherent Tomography (OCT) images, highlighting the practical implications for identifying high-risk plaques. This cooperation is now actively being further developed to enhance the project's impact. A research paper detailing these initial findings has been submitted to a scientific journal, with additional results published in a regional journal.

As a background of WP3 task a comprehensive literature review is underway, analyzing current approaches and mathematical methods for estimating atherosclerotic plaque variations and models of prediction of its stochastic growth. The results are being accumulated, critically analysed and discussed inside the team for next-stage tasks.

The project also benefits from international collaboration in the 1st stage as well, particularly through personal contacts with EU partners at RWTH Aachen, which has been instrumental in advancing the research. Project Principal Investigator (Prof. oleksiy Larin) had an in-person visit to the RWTH Aachen in June 2024 for several consultations, workshop discussions and some renovations of the problem statements.

Dissemination of results is also ongoing, with 2 papers submitted to journals and 1 conference-accepted presentation, ensuring broad visibility and early-stage scientific community feedback.

2. Current status of the project

The following specific task statements based on the Project Methodology are set for the current stage and within the scope of the following Work Packages (WP) :

WP1. Development of a symbolic regression method for the identification of the mathematical model of the complex visco-elastic behavior based on synthetic data

WP2. Development of a parametric computational model (based on FEM) for human blood vessels with an atherosclerotic plaque for mechanical response of vessels under blood pressure pulsations

WP3. Development of a model and analysis for the prediction of the stochastic growth of atherosclerotic plaque

For **WP1** Prof. Larin and Ms. N. Fomenko is set as a responsible group. For this WP it was investigated the application of symbolic regression (SR) for modeling hyperelastic material behavior.

The following tasks were solved:

+ synthetic data based on the hyperelastic Mooney-Rivlin model with linear viscosity term have been generated in a way that can be typically obtained from experiments. The dataset has: time, deformations and stresses for the case of uniaxial loading;

+ compared the calculations for: different methods of error estimation, for one and two loops, for cases with and without constant search.

For that, the deep learning framework for Python – Deep Symbolic Optimization (DSO) was used, which is a deep learning framework for symbolic optimization tasks.

The new metric was added to the source code of the package locally on the computer and tested first on cases where the result was known exactly. Two variants of model training with and without constant search were used. At that stage it was explored the potential of symbolic regression for modeling hyperelastic material behavior. We investigated an error metric based on implicit derivatives (E2) alongside the standard inverse normalized root mean squared error (NRMSE, E1).

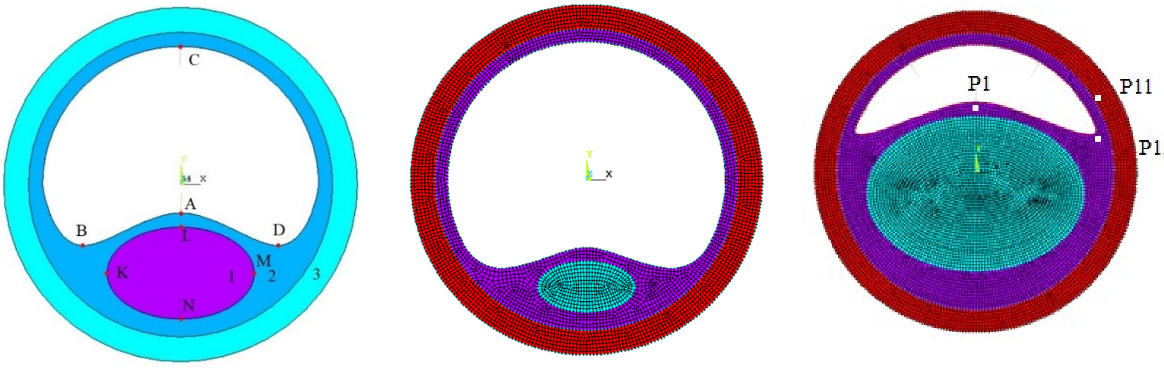
While SR successfully captured the qualitative trends of the material behavior (R-squared up to 0.86), the novel E2 metric did not consistently outperform the established E1 metric. However, E2 offered a visually better fit in specific scenarios (single hysteresis loop without constant search).

These findings highlight the ongoing challenge of defining appropriate error metrics for SR in material behavior modeling. Future research should focus on refining the E2 metric and exploring alternative approaches to enhance the accuracy and generalizability of SR for this application. Additionally, incorporating uncertainty quantification and multiscale modeling capabilities would strengthen the practical applicability of SR in material design and analysis.

The results of the WP1 obtained in the 1st stage will be presented in October 2024 in the conference IEEE 5th KhPI week on advanced technology with conference paper that is submitted in June and currently received Positive review status.

For **WP2** Prof. Larin and Dr. K. Potopalska Mr. I. Hovoruha and Mr. M. Mironenko are set as a responsible group. For this WP a methodology for assessing the stress state of human lipid-core arteries, which have different types of development were created. The first part of that study focuses on analyzing the deformation of human blood arteries affected by atherosclerotic plaque, dependent on plaque size, through direct computer simulations.

Finite element analysis was employed to understand strain and stress distribution over time. The initial model was a 2D schematic and considered 2 arterial wall layers, with specific mechanical properties on each, and explicitly models the atherosclerotic plaque. Viscoelastic effects were incorporated using Proni series, accounting for arterial tissue deformation over time. Geometric modeling (Fig 1) allows for varying plaque sizes, influencing stress patterns akin to pulse waves. In this study, we introduce an internal hyperparameter: degree of overlap D, which is defined as the ratio of plaque area to the primary luminal area of the vessel. Fig. 1b and Fig. 1c shows finite element models with different sizes of atherosclerotic plaques.



a) b) c)

Fig.1 The model of human vessel with plaque: a) Geometric model of an artery, b) FE model with degree of overlap parameter equals 0.1, c) FE model with degree of overlap parameter equals 0.8

The implemented code allows us to change the geometric dimensions of the artery and vary the dimensions of the atherosclerotic plaque. Based on the models comprehensive set of simulations has been done and allow us to underscore the impact of plaque size on arterial wall stress distribution, and deformation hysteresis cycle behaviour depending on the D parameter that represents the state of atherosclerotic vessel affection (Fig 2).

Results show significant stress concentration above the plaque's lateral edges, with the layer adjacent to the lipid core experiencing compression. Maximum stresses increase nonlinearly with plaque size, indicating a critical point. Strain analysis reveals oscillatory behavior, lagging behind stresses due to viscoelasticity. Gradual plaque size increases leads to rising stresses and strains, highlighting potential complications.

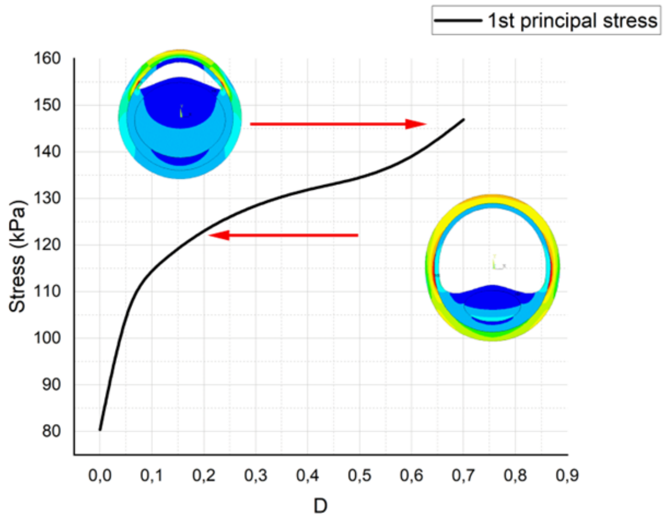


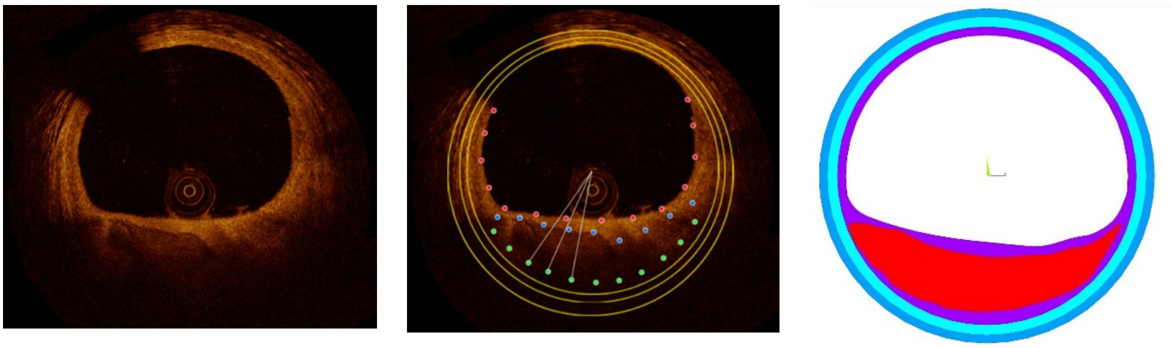
Fig. 2 Changes in maximum stresses depending on the degree of overlap of the vessel lumen

The basic results of the parametric schematic modelling of the human artery and deformed state analysis are disseminated as a research paper that is submitted to the Journal Strength of Materials.

Potentially such results allow one to identify patients who are at high risk of plaque rupture, which prediction is paramount for preventing catastrophic cardiovascular events. The mentioned results were presented to practical medical vessel surgeons for model justification and updating.

During the 1st stage, we also initiated close partnerships with the Department of Interventional Cardiology of the Institute of General and Emergency Surgery named after V.T. Zaytseva of the National Academy of Sciences of Ukraine and organized several working meetings to discuss the results and to modify the problem statement for mathematical modelling moving it to reasonable practical cases. The set-up cooperation (in particular close discussions with Dr. Med., PhD in Med Sc. Ihor Polivenok, Head of the Department of Interventional Cardiology) allowed the team to move from schematic models to patient-specific models and to obtain anonymized data of the real medical cases of the atherosclerotic plague defected human coronary vessels obtained from the Optical Coherent Tomography (OCT) images. Based on that data, the project team proposed an updated algorithm for the modelling and switched the focus on specific cases of vulnerable plaques identification and analysis.

The improved methodology includes an algorithm of semi-manual image processing for the medical cases of atherosclerotic plague-defected human coronary vessels obtained from the Optical Coherent Tomography (OCT) images (Fig. 3a). The geometric models of affected blood vessels were built using a specific macro that implements parametric description. The internal structure geometry were defined by a developed algorithm that was realized within Python code and then automatically transferred into APDL macros for further FE analysis (Fig. 3c).



a) b) c)

Fig.3 The process of creating the geometrical model of human vessel with plaque: a) initial image from OCT, b) schematic view of definition the geometrical parameters of internal structure, c) the geometrical model, which was build based on parameters from b)

At that stage three different cases were considered: non-calcified, calcified and low-density non-calcified plaques. The team succeded in several computations for the mentioned patient-specific cases that allowed us to study the stress and deformed states of the affected vessels. The material models are also modified here to switch into the 3-layer wall structure and to orthotopic behaviour.

*The results of implementation of methodology of definition the deformed state analysis of human artery based on the Optical Coherent Tomography (OCT) images are also submitted in regional UA Journal: Herald of Khmelnytskyi National University. Technical science*s

For currently **WP3** progress Dr. Potopalska is engaged within the advanced literature review. The analysis of current used approaches and investigations of stochastic development of plaque in human vessel in time and mathematical method of estimation of possible variation plaque dimension were carried out.

3. Summary of personnel commitment

Oleksiy LARIN - **WP1**: Integration of machine learning methods into the modeling the nonlinear behavior of soft biological tissues, for which, in particular, hyperelastic models, **WP2**: Creating an algorithm for image processing of vessel with an atherosclerotic plaque based on real patient diagnostic.
Preparing a conference paper *for IEEE 5th KhPI week*.
Preparing paper for publication in *Journal Strength of Materials*.
Preparing a paper for publication in regional Journal: *Herald of Khmelnytskyi National University. Technical sciences .*

Nataliia FOMENKO – **WP1**: Investigation of the application of symbolic regression (SR) for modeling hyperplastic material behavior. Performing the calculation for the different metrics. **WP2**: Computer modeling of the process involves the development of a geometric model of a vessel with an atherosclerotic plaque. Development of APDL macros of parametric geometrical model. Taken part of algorithm development for image processing of vessel with an atherosclerotic plaque based on real patient diagnostic.
Preparing a conference paper for IEEE 5th KhPI week.
Preparing paper for publication in *Journal Strength of Materials*.

Kseniia POTOPOLSKA – **WP2**: Investigate the materials definition for internal vessel with an atherosclerotic plaque, literature overview. Taken part of algorithm development for image processing of vessel with an atherosclerotic plaque based on real patient diagnostic. **WP3:** Deep literature overview of modeling the growth rate of atherosclerotic plaque in human vessel, defining appreciable mathematical model of prognosis of the stochastic growth of the atherosclerotic plaque.
Preparing a paper for publication in regional Journal: *Herald of Khmelnytskyi National University. Technical sciences*

Ilia HOVORUKHA – **WP2**: The development and implementation of the algorithm in Python code for determining geometrical parameters of vessel with plaque. Create an APDL macros for parametric model of vessel with plaque. Providing calculation for definition of human artery with atherosclerotic plaque deformed state.

Mikhail MIRONENKO – **WP2**: The development and implementation of the algorithm in Python code for determining geometrical parameters of vessel with plaque. Create an APDL macros for parametric model of vessel with plaque. Providing calculation for definition of human artery with atherosclerotic plaque deformed state.

4. Description of travels

Prof. Oleksiy Larin visited RWTH Aachen on 04-21, June 2024.

5. Dissemination

Dr. K. Potopalska and Ms. N. Fomenko are Executors of scientific project “Algorithms, models and artificial intelligence tools for two-level modeling of the behavior of complex materials for dual-purpose technology” 2023-2026 supported by Ministry of education and science of Ukraine.

Submitted papers:

1. N. Fomenko, O. Larin, "Investigating the Impact of Atherosclerotic Plaque Size on Arterial Wall stress-strain hysteresis loop and deformed state pattern", Strength Mater., 16 pages, 2024 (accepted by the journal's editorial board)

2. Larin O., Potopalska K., Fomenko N., Hovorukha I., Mironenko M., Polivenok I. FE simulations of the Static Deformed State of Atherosclerotic Vessels based on OCT Image data. Journal: *Herald of Khmelnytskyi National University. Technical sciences, p.12*

Submitted conference papers:

1. N. Fomenko, O. Larin, "Symbolic regression-based models for hyperelastic material", 2024 IEEE 5th KhPI Week on Advanced Technology (KhPIWeek), (5 pages), Oct. 2024 (accepted for presenting)

6. Delays and suggestions

According to the plan for the first stage of the project, it was planned to develop the ML-based model for the prognosis of the stochastic growth of the atherosclerotic plaque. That task was postponed to stage 2 after consultation with PhD in Medical Science, Dr. Med. I. Polivenok, because the algorithm of parametric modeling for arteries with atherosclerotic plaque needed to be improved, and that was done during this stage of the project. This issue does not have a negative impact on the project's process; instead, the review of results from practical surgery allowed us to improve the algorithm and, in the next stage, make the ML-based model more accurate.

7. Issues or Challenges

The project process is proceeding according to the plan outlined in the proposal. The external consultations contributed to the improvement of the proposed algorithm for parametric models.

8. Further elaborations, notes, etc.

In the upcoming stages of the project, significant advancements and some shifts in focus are planned.

WP1 will pivot from directly using the symbolic regression (SR) framework for stress-strain curve fitting to focusing on energy potentials. This shift of focus is based on fruitful discussions and collaborations with EU partners at RWTH Aachen that Prof. Larin had done in June. This adjustment aligns with the strategy of employing physically-informed machine learning (ML) by embedding core continuum mechanics nonlinear phenomena into the model before fitting. This approach has shown success in hyperelastic material modeling was successfully done by Prof. M. Itskov and Mr R. Abdulsalamov (Project partners from RWTH Aachen) and is now planned within our cooperation and the current Project next stage progress to be extended to nonlinear-viscoelasticity, crucial for bio-material modelling. The cooperation with RWTH Aachen's experts, who have achieved notable results with this method, will facilitate this transition.

Furthermore, the project's principal investigator has established a new collaboration with Dr. Kevin Linka, head of the Department of Structural Mechanics at RWTH Aachen. Dr. Linka recently introduced a novel data-driven approach for modeling the nonlinear viscoelasticity of human arteries. This collaboration opens up significant opportunities for benchmarking SR models against this new methodology, which will be vital for the continued development and validation of the project's approaches in the second stage. At the current moment, Prof.O. Larin and Ms N. Fomenko working on the Python code debugging and algorithm upgrading for the new approach within several cases of synthetic data of benchmark problems.

In the next phase of WP2, the focus will shift towards refining the algorithm for modeling atherosclerotic vessels from schematic representations to patient-specific cases, with an emphasis on vulnerable plaques. The team aims to develop a robust methodology for building parametric models that can support prognosis analysis. This will involve discussions with both practical medical professionals and the broader scientific community to validate and refine the finite element (FE) analysis results for vulnerable plaques.

The current approach to building patient-specific models based on Optical Coherent Tomography (OCT) data faces challenges due to image-based data biases. To address this, an updated algorithm will be developed to incorporate probabilistic modeling, which accounts for the potential geometrical identification uncertainties. This advancement will enable the creation of models that provide probabilistic risk analysis for vulnerable plaques, forming the basis for prediction of their stochastic growth and further reliability analysis.

Dr. Potopalska, Mr. Hovorukha and Mr. M. Myronenkowill lead the development of these new models and algorithms. Additionally, the analysis of the influence of the mechanical properties fuzziness of atherosclerotic vessel walls on the general mechanical response of the vessel with vulnerable plague will be a key focus.

Prof. O. Larin and Dr. Potopalska will also focus during the 2nd stage of the project on developing an approach for modeling the stochastic growth of vulnerable plaques (the main task of WP3). This approach will be used for probabilistic reliability and risk analysis of the affected vessels based on the developed and updated models and patient-specific data.

PUBLICATIONS AND ACKNOWLEDGMENT

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Acknowledgment of the EU funding

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Signed by: Oleksiy LARIN
2024.08.07
13:55:23 +03'00'