Research Diary

Computational Engineering at the Cardiovascular Mechanics Laboratory

Dr Anand Mohan,
Associate Professor,
Department of Chemical Engineering

KID: 20210409

Cardiovascular diseases (CVDs) are the leading cause of death in India and accounted for 24.8% of mortality in the year 2010 [1]. Pathologies of the cardiovascular system are greatly influenced in their progression by the flow behavior of blood in blood vessels, by the biochemistry of the reactions involved in clot formation (or coagulation) and dissolution (fibrinolysis), and by the mechanics of vascular tissue [2]. The thrust of our research is to generate an understanding of these pathologies by characterizing the mechanical and biochemical variables in flow situations that present in the human vasculature, and by identifying conditions that precipitate potentially life-threatening events (like thrombo-embolisms and strokes). Towards this end, we integrate various tools like mathematical modeling of coagulation and fibrinolysis, constitutive modeling of blood, and computational fluid dynamics (CFD) simulation of blood flow in rigid and flexible-walled vessels.

Computational tests using mathematical models of coagulation have been accepted for the generation of hypotheses by an influential section of the hemostasis community [3]. They have been used to detect novel reaction mechanisms as well as to determine the efficacy and dosage of novel antithrombotic drugs. This has triggered the development of models that are increasingly comprehensive and incorporate the latest understanding of coagulation pathways and active constituents. One such model was developed by our lab in collaboration with senior researchers from a constituent center of the Russian Academy of Sciences (see [4]). The schematic of the model pathway is shown in Fig. 1 and its predictions are shown in Fig. 2.

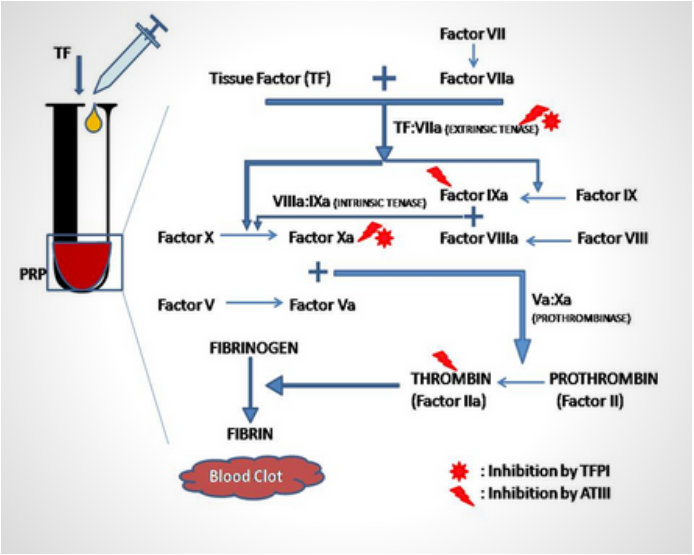


Fig. 1: Schematic of reactions used in a mathematical model of coagulation

The predictions for thrombin concentration (the precursor enzyme to clot formation) show clearly that incorporating the latest experimental hypothesis of thrombin dose-dependent procoagulant platelets as a fraction, as well as competitive binding of enzymes to those platelets, is essential to get accurate results for clot formation time; clot formation time is a key diagnostic parameter for blood diseases.

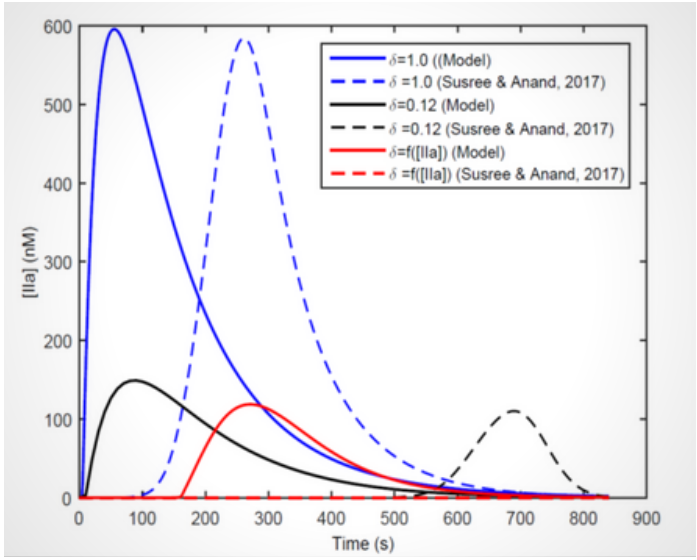


Fig. 2: Predictions of model with latest experimental hypotheses [4] versus an older model

Atherosclerosis is a major sub-class of CVDs characterized by the formation of fatty deposits in the artery wall which reduces and, sometimes, blocks flow. The phenomenon underlying atherosclerosis is blood flow in complex-shaped, flexible-walled tubes with soft blockages. CFD simulation of blood flow is a useful non-invasive tool for doctors to predict the locations of atherosclerosis in geometries of the human vasculature [5]. CFD simulations based on images derived from patients yield variables like wall shear stress (WSS) which cannot be measured in vivo, but which play a crucial role in the growth of atherosclerotic plaque. Our group developed a new two-phase mixture theory model of plasma and cell matter for blood. We then used CFD in locally available software to predict the locations of atherosclerosis using WSS-based indicators and low-density lipoprotein (LDL) in a 3D patient-derived geometry of the abdominal aorta (see [6]). Results in Fig. 3 show that the inclusion of LDL transport enhances the accuracy of predictions.

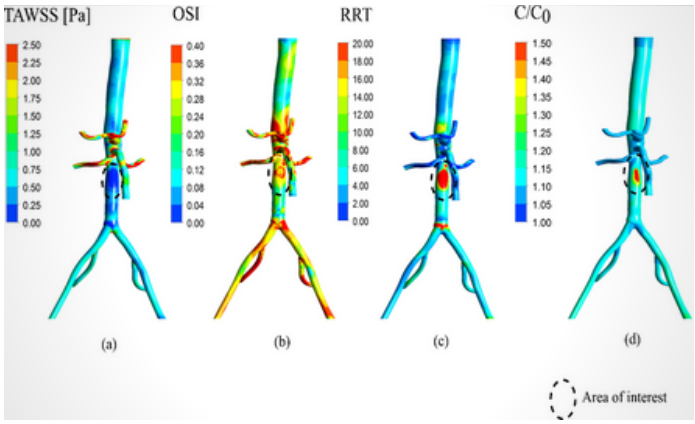


Fig. 3: CFD predictions of locations of atherosclerosis using WSS-based indicators and LDL concentration. Refer (d) vs (c) for the improvement in accuracy due to LDL transport

References:

1) Prabhakaran D., Jeemon P., and Roy A., 2016, "Cardiovascular diseases in India. Current epidemiology and future directions," Circulation, 133(16):1605–1620.

2) Anand M., Rajagopal K., and Rajagopal K. R., 2003, "A model incorporating some of the mechanical and biochemical factors underlying clot formation and dissolution in flowing blood," J. Theor. Med. 5(3–4): 183–218.

3)Mann K. G., 2012, "Is there value in kinetic modeling of thrombin generation? Yes," J. Thromb. Haemost. 10(8): 1463–1469.

4)Susree M., Panteleev M. A., and Anand M., 2018, "Coated platelets introduce a significant delay in onset of peak thrombin production: Theoretical predictions," J. Theor. Biol. 453: 108-116.

5)Morris P. D., Narracott A., von Tengg-Kobligk H., Silva Soto D. A., Hsiao S., Lungu A., Evans P., Bresslof N.W., Lawford P.V., Hose D.R., and Gunn J.P., 2016, "Computational fluid dynamics modeling in cardiovascular medicine," Heart, 102(1):18-28.

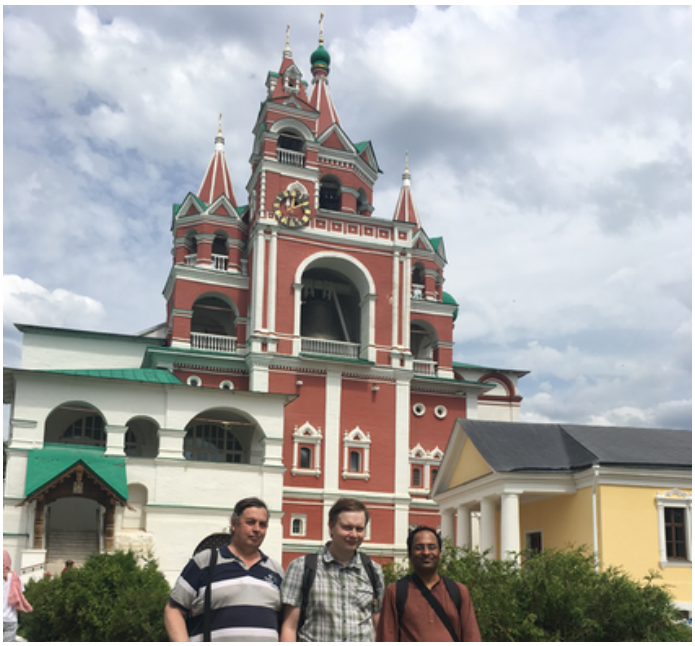
6) Ameenuddin M., and Anand M., 2020, "A mixture theory model for blood combined with low-density lipoprotein transport to predict early atherosclerosis regions in the idealized and patient-derived abdominal aorta," J. Biomech. Eng. 142(10):101008.r the 2022 year!

Experience with Dr Mohan & Group

Mikhail A Panteleev
Director, Center for Theoretical Problems of Physicochemical Pharmacology,
Russian Academy of Sciences

We have been collaborating with Professor Dr Anand Mohan from the Department of Chemical Engineering, IIT Hyderabad for many years on a number of subjects, ranging from joint research on blood coagulation to the establishment of new systems biology journal. I am particularly fond of the study that was pioneered by Dr Modepalli under Anand's guidance and published in J Theor Biol. It was focused on the mystery of the interaction between procoagulant platelets (which has been fascinating to me for more than a decade) and blood coagulation cascade.

It was great fun to be a part of this study, and I am very happy that this opportunity not only deepened our collaboration but also allowed Anand to travel to Russia so that we could meet even beyond the scope of just collaboration. My best wishes to the Anand lab and IITH for the 2022 year!



(L-R) Prof Alexey Lobanov, Mikhail A Panteleev & Dr Anand Mohan During Dr Anand Mohan visit to Moscow, Russia in June 2018

Integrated Computational Engineering

Dr Harikrishnan Narayanan Unni,,
Associate Professor,
Department of Biomedical Engineering
KID: 20210410

The need for multiscale understanding of materials and phenomena is well established recently and has applications ranging from aerospace design to DNA biology. Integrated computational engineering refers to the design of materials and understanding of scientific, engineering phenomena through multiscale computational techniques. This means virtual materials design, including virtual testing and virtual processing. Integration of modelling tools (coarse-grained/atomistic, computational thermodynamics, and phase-field) are normally employed to simulate the microstructural development of materials during processes. The relevant applications of such multiscale models are present in various fields and include evaluation of carbon nanotubes, the composition of superalloys, cancer metastasis, etc.

The computational biomechanics lab in the department of biomedical engineering is focused on the development of multiscale computational techniques for a detailed understanding of soft tissue mechanics in the human body. The evolution of tissue microstructure during physiological processes can be determined by computational models that integrate the features of macro and micro-nano scales. An effort on modeling neurodegeneration resulting from traumatic brain injury is underway, where brain strain data computed from a continuum-based finite element model is coupled to a neurobiological computational model in order to assess protein aggregation and death rate of neurons post-traumatic brain injury (TBI) **(Fig.1)**.