Polytech network form for PhD Research Grants from the China Scholarship Council

This document describes the PhD subject and supervisor proposed by the French Polytech network of 14 university engineering schools. Please contact the PhD supervisor by email or Skype for further information regarding your application.

Supervisor information	
Family name	Nicoud
First name	Franck
Email	franck.nicoud@umontpellier.fr
Web reference	http://imag.umontpellier.fr/~nicoud/
Lab name	Institut Montpelliérain Alexander Grothendieck
Lab web site	http://imag.edu.umontpellier.fr/
Polytech name	Montpellier
University name	University of Montpellier
Country	France

PhD information	
Title	Modeling and computation of thrombus formation in blood flows.
Main topics regards to CSC list (3 topics at maximum)	Biomedical engineering ; Large scale computation
Required skills in science and engineering	Fluid or solid Mechanics, Scientific computing, High Performance Computing (optional), Biomechanics

	(optional), chemistry (optional)

Subject description (two pages maximum)

Computational Fluid Dynamics (CFD) is now a key ingredient in the design chain of many industrial systems in the aerospace, aeronautic and automotive industries, to cite a few. The use of CFD for optimizing blood-wetted devices (e.g.: total artificial hearts, ventricular assist devices, extra-corporeal circulation systems, flow diverters, artificial aortic or mitral valves,…) is not as mature as in other fields, due to many challenges specific to blood flows. The main one is that blood is a living tissue with a complex rheological behavior (including shear-thinning, viscoelasticity and thixotropy) and the capability to generate clots or thrombus.

The Biomechanics group at the Institute of Montpellier Alexander Grothendieck (IMAG) has been developing a numerical solver dedicated to the computation of blood flows since 2010. The so-called YALES2BIO solver (http://imag.umontpellier.fr/~yales2bio/) gathers some unique properties in terms of High Performance Computing, turbulence modeling and fluid-structure interaction methods for both micro and macro scales blood flows [1]–[3]. The solver was already successfully used to compute the intracardiac blood flow in a realistic left heart [4], [5] as well as a variety of micro-circulation situations [6]–[8]. After a five-year period of intense development/validation, its use to support the design and optimization of biomedical devices [9], [10] and medical imaging techniques [11], [12] has now started.
A major phenomenon which is yet not properly accounted for in virtually all the simulations reported in the literature dealing with blood flows is the generation of thrombus in the presence of an artificial material, as it is the case when any blood-wetted biomedical device is used within a therapeutic treatment (artificial heart, ventricular assist device, cardiac valves, flow diverter, extra corporeal circulation). Actually, thrombus formation is the major issue preventing the wide spreading of biomechanical devices in the treatment of cardio-vascular diseases.
A new mechanism of thrombin formation due to the contact system and which was not properly accounted for in the literature was successfully implemented with the PhD work of R. Mendez at IMAG [13]. This is the first study which properly indicates how and where the presence of an artificial surface can initiate the generation of an undesired thrombus (see also http://imag.umontpellier.fr/~yales2bio/recent-thrombus.html); it also raises many questions which are still to be addressed. The general objective of this research proposal is thus to continue the work initiated for the computation of thrombus formation. The following issues will notably be considered during the PhD work:

1. Uncertainty quantification: the description of the hemostasis in blood usually requires several tens of chemical species appearing in as many chemical reactions. The experimental data necessary to characterize these reactions are sparse so that the many input parameters required in a proper thrombus formation model are very uncertain, to say the least. The natural question is then: what is the uncertainty of the computation outcomes (thrombus location, growth rate

and shape) given the uncertainties in the input parameters ? We thus have on-going collaborations with experts in Uncertainty Quantification at University Pierre and Marie Curie in Paris (Dr. Lucor) and Federal School of Zurich (Prof. Koumoutsakos). One of the main tasks of the PhD student will be to interact with these groups to device how their strategies can be adapted to the YALES2BIO/thrombus formation framework.

2. Reduced-order modeling: Another task will be to propose reduced-order models of thrombus formation. This will require performing proper sensitivity analysis of the current models (which of the many input parameters have more impact on the outcomes of the simulations ?) in order to gain knowledge about the chemical reactions which could be removed or merged in order to obtained a lower-complexity description of the phenomenon. The advantage of developing such reduced-order model is two-fold: reduce the computational load of each state evaluation on the one hand, reduce the number of uncertain input parameters on the other hand. This will require a thorough analysis of the literature to gain the necessary physical understanding of the different mechanisms at play and propose physically meaningful model simplifications.

The PhD candidate will be part of the YALES2BIO research group; as such, he will participate to the development of the flow solver and be invited to the regular group meetings where the different research activities are presented/discussed by the members. He will have full access to local and national super-computing facilities and benefit from the stimulating scientific environment offered by the institute. F. Nicoud, Prof. at IMAG and leader of the YALES2BIO group will act as thesis advisor. Support from the HPC support group at IMAG will also be provided as well as access to Master/doctoral complementary courses if required.

Selected bibliography from the YALES2BIO Group:

[1] S. Mendez, E. Gibaud, and F. Nicoud, *J. Comput. Phys.*, vol. 256, 2014.
[2] J. Sigüenza, S. Mendez, D. Ambard, F. Dubois, F. Jourdan, R. Mozul, and F. Nicoud, *J. Comput. Phys.*, vol. 322, 2016.
[3] F. Nicoud, C. Chnafa, J. Siguenza, V. Zmijanovic, and S. Mendez, in *Biomedical Technology Modeling, Experiments and Simulation*, Peter Wriggers & Thomas Lenarz, Ed. Springer, 2017, pp. 147–167.
[4] C. Chnafa, S. Mendez, and F. Nicoud, *Comput. Fluids*, vol. 94, 2014.
[5] C. Chnafa, S. Mendez, and F. Nicoud, *Ann. Biomed. Eng.*, vol. 44, no. 11, pp. 3346–3358, 2016.
[6] L. Lanotte, J. Mauer, S. Mendez, D. A. Fedosov, J.-M. Fromental, V. Claveria, F. Nicoud, G. Gompper, and M. Abkarian, *Proc. Natl. Acad. Sci. U. S. A.*, vol. 113, no. 47, 2016.
[7] J. Sigüenza, S. Mendez, and F. Nicoud, *Biomech. Model. Mechanobiol.*, vol. 16, no. 5, pp. 1645–1657, 2017.
[8] M. Martins Afonso, S. Mendez, and F. Nicoud, *J. Fluid Mech.*, vol. 746, pp. 300–331, 2014.
[9] V. Zmijanovic, S. Mendez, V. Moureau, and F. Nicoud, *Int. j. numer. method. biomed. eng.*, vol. 33, no. 1, 2017.
[10] J. Sigüenza, D. Pott, S. Mendez, S. J. Sonntag, T. A. Kaufmann, U. Steinseifer, and F. Nicoud, *Int. j. numer. method. biomed. eng.*, 2018.
[11] T. Puiseux, R. Moreno, S. Mendez and F. Nicoud, Assessing phase-contrast Magnetic Resonance Imaging-based hemodynamics using Computational Fluid Dynamics, 12th ERCOFTAC ETTM Symposium, 2018
[12] K. Assi, E. Gay, C. Chnafa, S. Mendez, F. Nicoud, J. Abascal, P. Lantelme, F. Tournoux, and D. Garcia, *Phys. Med. Biol.*, vol. 62, no. 17, pp. 7131–7147, Aug. 2017.
[13] R. Mendez, S. Mendez, and F. Nicoud, *Biomech. Model. Mechanobiol.*, pp. 1–12, 2018