Morphodynamic modelling of hematopoietic stem cells

Internship Position
Biological Image Analysis Unit, Institut Pasteur, Paris, France

Biological context. In vertebrates, hematopoietic stem cells are generated during the embryonic period. This occurs in arterial vascular tissue, particularly in the dorsal aorta, where specific (endothelial) cells undergo a morphological evolution that accompanies their extrusion from the aortic wall.

This emergence process, known as endothelial-hematopoietic transition (EHT), is characterized by a highly unusual curvature of the cell membrane towards the subaortic space. The cells are then released into the bloodstream and become hematopoietic stem cells, the origin of embryonic and adult blood and immune cells.

This type of cell emergence process has been studied qualitatively in zebrafish embryos in recent work [1, 2] using time-lapse confocal imaging. A recent algorithm [3], developed by our team, reconstructs confocal volumes to visualize membrane shape in 3D over time. The next step is to establish a model of membrane evolution to explain its morphological changes and quantify the associated biophysical parameters.

Project. The internship's objective is to define a shape regression model [4] for the evolution related to EHT. The first approach is to study regression models based on the Helfrich energy, which is widely used to study membrane equilibrium. This functional, which depends on membrane curvatures, models the elastic deformation of the membrane under mechanical stress and enables its geometric deformation to be described.

Subsequently, quantitative methods need to be developed to estimate the physical parameters involved in the EHT process (e.g. tissue forces, blood flow pressure). Their estimation can be achieved via an inverse problem approach based on analytical models [5] or using a machine learning approach [6].

Beyond EHT modeling, this project aims to explore new frameworks for shape evolution, which is a vast field of study for several biomedical applications [7].

Expected work. A good knowledge of mathematics and machine learning theory is needed for this topic. After a review of the literature on shape regression models and Helfrich energy, a novel method for EHT analysis will be developed. The results will be validated on confocal time-lapse sequences in collaboration with biologists.

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