Semester report

By **Venceslas Ngounou** (vngounou@staff.elte.hu)

PhD program: *Statistical Physics, Biological Physics and Physics of Quantum Systems*

Supervisors: *Prof. Tamas Vicsek, Dr Elod Mehes*

Title: *Computer simulations of neutrophil swarming and phagocytosis at various stages of inflammatory events*

1. Introduction

Inflammation is an essential mechanism of our immune system for our body healing after an exposure to injury or undesired bodies. It consists on the recruitment of immune cells to the site of infection or injury. Immune cells have the ability to change their shape in many circumstances. Those changes in their morphology help them to extravasate, migrate and perform their effector functions. The primary effector function of phagocytes (neutrophils, macrophages) is to phagocytose pathogens or cellular debris. Elucidating such mechanisms is fundamental to understanding their behaviour. In this work, we are interested in two of them: neutrophil migration and phagocytosis.

Video recordings – [2] for instance – show neutrophils migration to the site of injury and previous works make hypothesis, conjectures and endeavour to explain the causes of (or the parameters that influence) these observations. However, quantitative elements to assess the veracity of and/or complement those claims are missing.

Regarding phagocytosis, mechanistic analyses of single-live-cell encounters with microbes are scarce in the biomedical literature. This shortage can be attributed, among others, to methodological limitations of traditional single-cell experiments. Nevertheless, previous studies made it clear that localised forces strongly alter the shape of cell membranes from inside [1]. However, it remains challenging to design a minimal system of those forces which explains the morphological dynamics observed during phagocytosis.

2. Description of research work carried out in current semester

2.1.Neutrophil swarming

The first aspect of the topic is the modelling and simulation of neutrophil swarming during an inflammatory episode. I have started by implementing an early version of a 2D model consisting on solving numerically a diffusion equation with sources and sinks on a lattice grid using the finite difference methods.

I have also immersed myself in literature review which had two main goals:

- Understand the physiological processes happening within immune cells of the innate immunity realms (in general and neutrophils in particular) which lead to their recruitment to the site of infection or injury.
- Find relevant physical principles which can describe the motion of neutrophils during their recruitment observed by biologists.

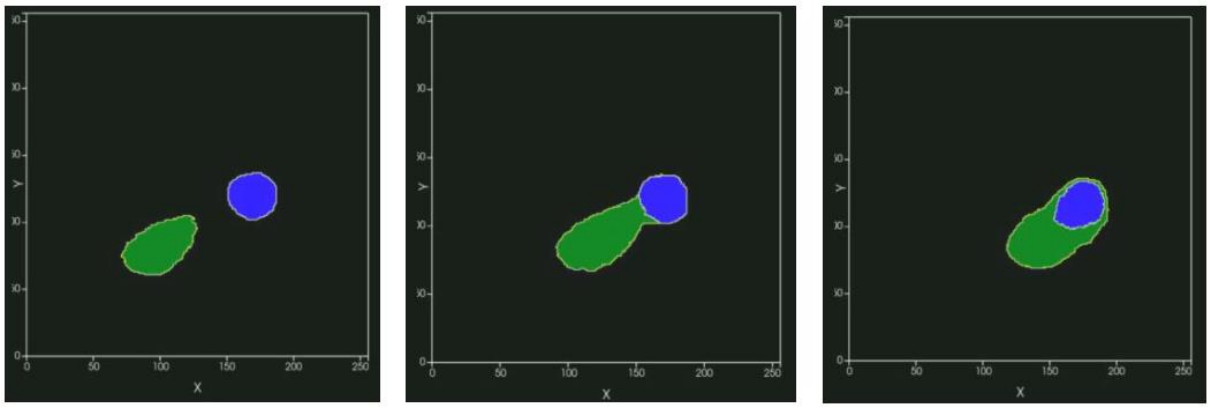
That lead to another implementation of a model considering the secretion of diffusive chemo-attractants and non-diffusive intracellular inhibitor [3]. That was done essentially in 3D, using finite volume methods which generally provide more precise solutions in physical phenomena.

Besides the modelling/simulation aspect, I have studied several multi-particles tracking software in 2D which will be used to analyse the videos from biologists in order to extract quantitative data necessary to validate our model. Some of those software are CellProfiler, Cell Tracker GNN and TrackMate7+Cellpose.

2.2.Cell shape dynamics during phagocytosis

The simulation of phagocytosis taking into account a minimal system of local forces exerted on the phagocyte's cell membrane has lead us to consider first the adhesion forces only.

That was done on CompuCell3D [4]. The macrophage (in green) moves as random walk biased by chemotaxis due to secretion and diffusion of a chemoattractant from the pathogen (in blue). After contact, we could simulate a simplistic phagocytosis in 2D, visualised by output images considering only the adhesion energy.



3. Studies in current semester

During this semester, I enrolled to three courses: Statistical physics of biological systems (FIZ/3/003) and Statistical physics of polymers and membranes (FIZ/3/021) from the Doctoral School of Physics and Immunology of infections (BIO/3/6) from the Doctoral School of Biology.

The first two courses were important to have general knowledge on the use of statistical physics in the various fields of biology among inflammation of which my topic aims at modelling two major processes namely neutrophil swarming and phagocytosis.

The last course was needed to provide solid foundational knowledge in immunology.

4. Conferences in current semester

In November 2023, I attended the conference MIFOBIO in Presqu'iles de Giens, France. It was mainly about acquisition and processing of biological images.

I have submitted an abstract – authored by Venceslas Ngounou, Elod Mehes and Tamas Vicsek – which has been accepted, on the topic cell shape dynamics of phagocytes during phagocytosis for a poster presentation at the European Phagocyte Workshop set to take place in Visegrad, Hungary in March 2024.

References

1. Vutukuri, H.R., Hoore, M., Abaurrea-Velasco, C. et al. Active particles induce large shape deformations in giant lipid vesicles. Nature 586, 52–56 (2020)
2. Hannah M Isles, Catherine A Loynes, Sultan Alasmari, Fu Chuen Kon, Katherine M Henry, Anastasia Kadochnikova, Jack Hales, Clare F Muir, Maria-Cristina Keightley, Visakan Kadirkamanathan, Noémie Hamilton, Graham J Lieschke, Stephen A Renshaw, Philip M Elks. Pioneer neutrophils release chromatin within in vivo swarms. eLife 10:e68755 (2021)
3. Strickland J, Pan D, Godfrey C, Kim JS, Hopke A, Degrange M, Villavicencio B, Mansour MK, Zerbe CS, Irimia D, Amir A, Weiner OD. Self-extinguishing relay waves enable homeostatic control of human neutrophil swarming. bioRxiv [Preprint]. 2023 Jun 28:2023.06.27.546744.
4. M. Swat, Gilberto L. Thomas, Julio M. Belmonte, A. Shirinifard, D.Hmeljak, J. A. Glazier. Multi-Scale Modeling of Tissues Using CompuCell3D. Computational Methods in Cell Biology, Methods in Cell Biology 110: 325-366 (2012).