2nd-semester report

Tahreem Zaheer (tahreem@student.elte.hu)

Doctoral School of Physics

Department of Biological Physics

Supervisor: Vicsek Tamás

Title: Modelling the migration and shape changes of immune cells during inflammatory episodes

1. Introduction

My study aims to model the distribution of immune cells, particularly neutrophils, using advanced molecular modelling and simulation approaches. Neutrophils, the first line of defence, originate from bone marrow. Around ~10^{11} neutrophils are produced in bone marrow making them one of the most abundant cell types in blood. Neutrophil homeostasis maintains a balance between the production and elimination of neutrophils, hence the number of neutrophils in the blood remains constant (von Vietinghoff & Ley, 2009).

Infiltration of neutrophils in the tissues.

Neutrophils and monocytes are recruited from the blood to the sites of infection by binding to adhesion molecules on endothelial cells and by chemoattractant produced in response to the infection. In the absence of infection, these leukocytes circulate in the blood and do not migrate into the tissues. Their recruitment to sites of infection is a multistep process involving adherence of the circulating leukocytes to endothelial cells and migration through the vessel wall. This type of recruitment of leukocytes is called forward migration (Lämmermann, 2016). However, after achieving a threshold, the migration of neutrophils can change and they travel back to blood vessels, this phenomenon is called reverse migration (Nourshargh et al., 2016).

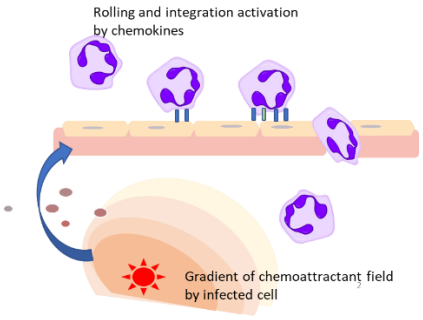

Figure 1 Mechanism of neutrophil infiltration to tissues and development of a chemoattractant gradient

The neutrophil swarming comprises 5 stages, namely, swarm initiation, swarm amplification, additional swarm amplification through intercellular signalling, swarm aggregation and tissue remodelling, and recruitment of myeloid cells and swarm resolution. My project aims to model the neutrophils swarming and

2. Description of computer simulation studies carried out in the current semester:

In order to get more insight into statistical physics and modelling, we started with modelling elementary-level phenomena in biological physics. The start of which was to model percolation.

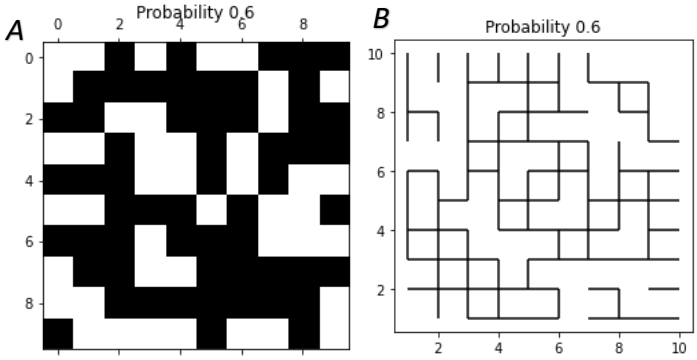

Figure 2 Percolation. A) Site Percolation. B) Bond Percolation.

The next phase was to implement the Hoshen-Kopelman algorithm and determine the cluster sizes for larger systems (like, e.g., 50 x50). The results of which can be seen in Figure 3 The largest cluster size of the percolating cluster was found to be 1035.

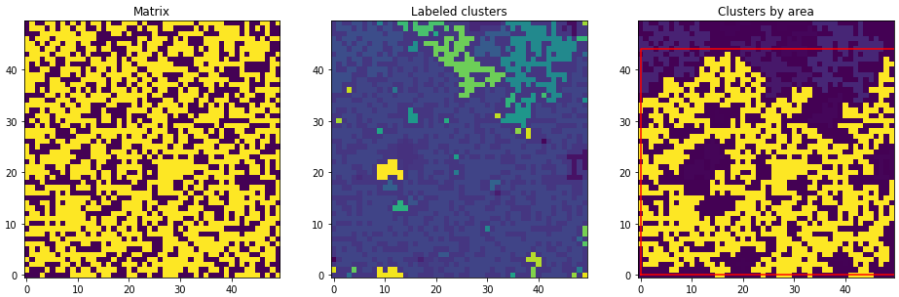

Figure 3 The red square/rectangle shows the size of the percolated cluster. These are the results of running the simulation on a probability of 0.6. No percolation from top to bottom but there was a percolation from left to right. The matrix shows the overall matrix, yellow being the regions having value 1 while the purple are regions having value 0. Labelled clusters mean when the numbers start getting assigned to clusters. All clusters were numbered as per the algorithm and then the cluster size having the largest area was highlighted in the figure under the title Clusters by area

The same simulation was repeated and in the next round at a probability of 0.6, top to bottom percolating cluster appeared in the results of the simulation which can be seen in Figure 4. The largest cluster size was found to be 931.

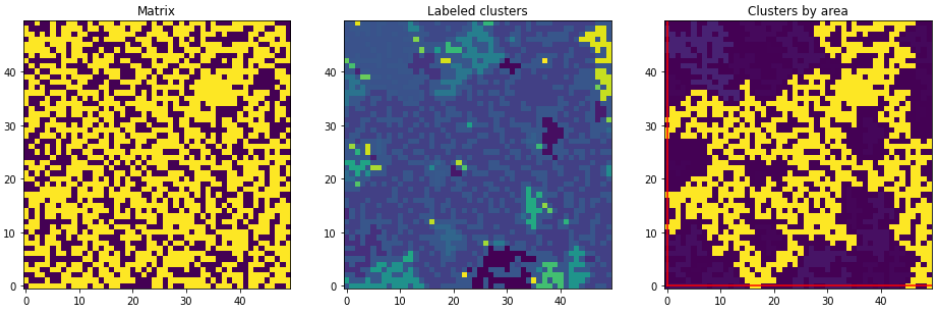

Figure 4 Percolating cluster at the probability of 0.6

The next task was to model Radial distribution for which the following equation was used to obtain the value of <g(r)>, which defines the probability of finding a particle at a distance r from another tagged particle.

$$volume = \frac{4}{3}\pi((r+dr)^3 - r^3$$

$$g(r) = \frac{number\ of\ valid\ particles}{volume \times \rho}$$

$$< g(r) > = \frac{1}{100}\sum_{i=1}^{100}(g(r)_i)$$

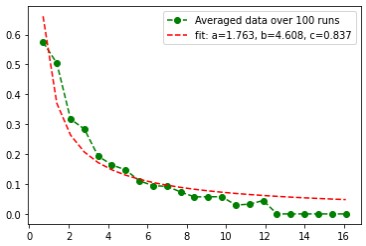

Figure 5 Radial distribution function of a particle exhibiting random walk

where a power law was fitted to the data. The formula of power-law was $a + b(x + c)^d$.

Moving particles

A total of 10 particles following a random walk were modelled in a lattice of 10x10. Boundary conditions ([-8,8] on the x-axis, [-8,8] on the y-axis) were implemented so that the moving particle does not leave the boundary. The full video is available at (https://drive.google.com/file/d/1SWVg7y4T-BnAlyNRVxKiObWbiNGuzFLz/view?resourcekey) This is an elementary-level model of neutrophils moving without a concentration gradient. Our next step is to model the neutrophils that move under a concentration gradient.

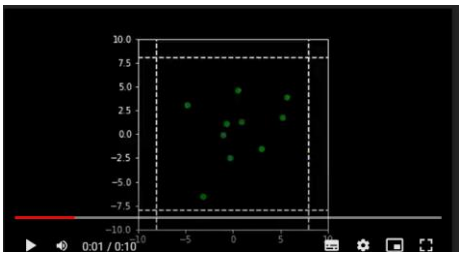

Figure 6 Motion of particles randomly moving in a lattice taking step size derived from a uniform distribution.

Conferences and Workshops

A conference was attended from 9th May 2022 to 13th May which was covered by Marie Skłodowska-Curie Actions. The following workshops were attended:

1. Zebrafish imaging and big data handling (1 day) 2. ImageJ (0,5 day) 3. Image analysis course (0,5 day) 4. Inflammation; Gene editing (0,5 day) 5. INFLANET review meeting & midterm check (1 day)

Studies in current semester:

Probability and Statistics – Lecture and Practical

This course helped me in learning the concepts of statistics and probability theory. The course was from the faculty of informatics.

Data Visualization and Exploration

This course helped me practice my python programming skills. This course was from the Department of Biological Physics.

Biophysics-1

The course was needed for my research to understand the physics behind biological principles. This course was from the Department of Biological Physics.

References

Lämmermann, T. (2016). In the eye of the neutrophil swarm-navigation signals that bring neutrophils together in inflamed and infected tissues. *Journal of Leukocyte Biology*, *100*(1), 55–63. https://doi.org/10.1189/jlb.1MR0915-403

Nourshargh, S., Renshaw, S. A., & Imhof, B. A. (2016). Reverse Migration of Neutrophils: Where, When, How, and Why? *Trends in Immunology*, *37*(5), 273–286. https://doi.org/10.1016/j.it.2016.03.006

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