Semi-annual report

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Doctoral School of Physics

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

1. Introduction

My project aims to model the process of motion of immune cells in inflammation using partial differential equation (PDE) and modelling approaches. Inflammation is a physiological response of the immune system that can be triggered by a variety of factors, including toxins, damaged cells, and pathogens. These factors alter the homeostasis and bring the body into a state of stress. As a result, a defence mechanism is triggered which is called inflammation. Inflammatory responses upon activation start a signalling cascade that impedes the stimulus to restore homeostasis. In the case of pathogens, Pathogen Associated Molecular Patterns are recognized by immune cells that release various chemokines and cytokines that in turn trigger chemotaxis of leucocytes to the site of infection causing acute inflammation. As a further important variant, chronic inflammation is reported to be one of the most common causes of death. The analysis of each inflammation stage shows a different cell size and shape and can help in the identification of the associated stage of inflammation. Immune cells are programmed in a way to recognize a pattern and trigger a signalling cascade which helps in the recruitment of immune cells to the site of infections. Although the collective behaviour of immune cells has been widely studied, understanding the shape morphology and behaviour of the immune cells in case of inflammation is yet to be studied. To model the inflammation, collective motion of immune cells towards the site of infection, a basic understanding of phenomena of physics are required. Hence, to start our research, we planned to develop simple algorithms in python language to develop basic models of Random walk. This exercise also introduced me to the concepts of statistical physics.

2. Description of research work carried out in the current semester:

We started with participation in Hackathon project where a toy model on inflammation in cancer was designed. This was a basic model that was designed in collaboration with students from the University of Duisburg-Essen, University of Colorado, Harvard University, and Indian Institute of Science Education and Research. It was a simple and generalized model to show the pro-inflammatory and regulatory response of the immune system in case of cancer. The model incorporated PDE and an Agent-based modelling approach using CompuCell 3D. Initially, the size of tumour decreased upon infiltration of immune cells/leucocytes because of the high concentration of damage-associated molecular patterns (DAMP) secreting from the cancer cells, but, after a while, the inflammatory response of immune cells was suppressed. The cancer cells start releasing TGF-Beta that is an anti-inflammatory cytokine causing inhibition of the activation of Interleukin 2 ((IL-2), a pro-inflammatory cytokine) resulting in reduced infiltration of immune cells.

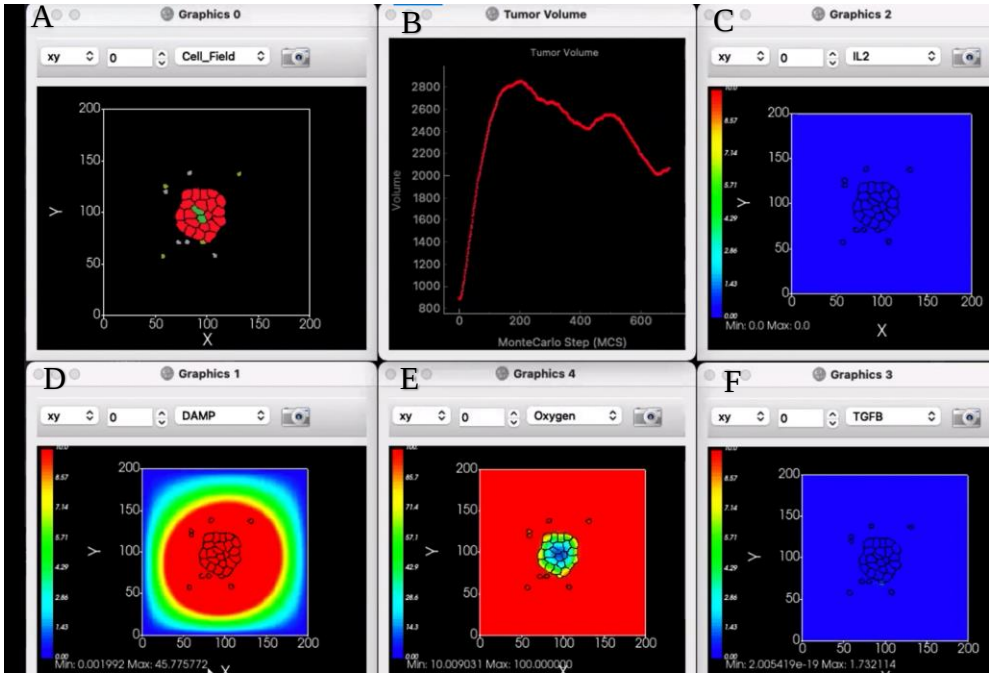

Figure 1 The simulation of immune cells infiltrating the cancer cells. A) Red region depicts the cancer cells, the green region shows the cancer cells undergoing apoptosis, while the surrounding cells are immune cells infiltrating the cancer cells because of diffusion. B) The volume/size of the tumour started decreasing as the Monte-Carlo steps increased. C) IL-2 secretion has not started D) DAMP signal increased; higher secretion of DAMP causes the recruitment of immune cells towards the cancer cells. E) The concentration of oxygen inside the cancer cell is low, and the apoptosis begins inside the cancer cell triggering the release of DAMP signals. F) The TGF-Beta signal is low so, the anti-inflammatory response has not started yet.

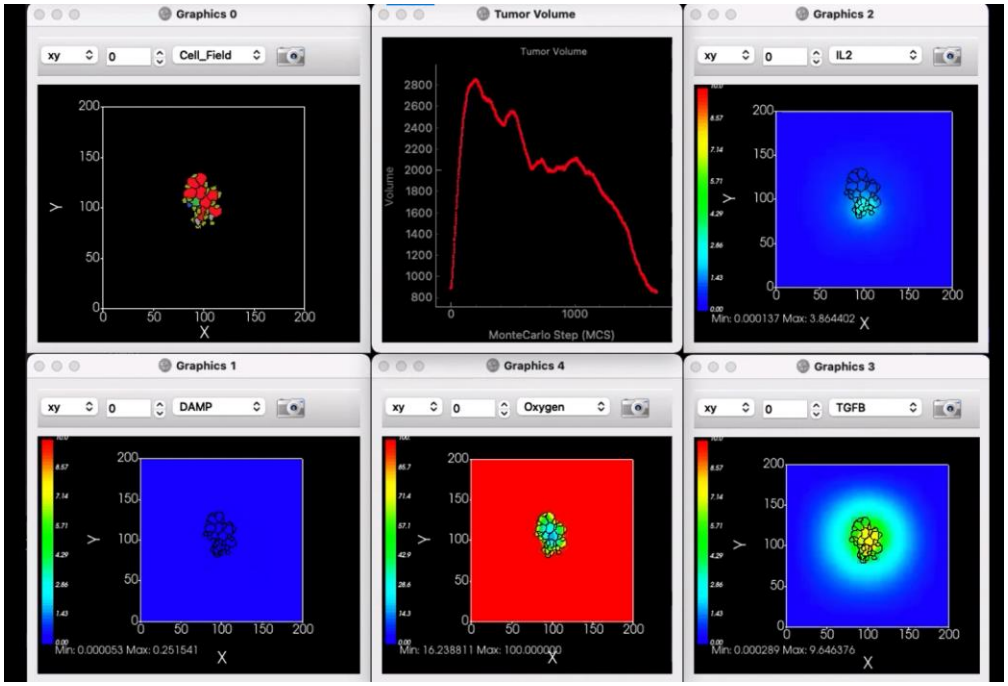

Figure 2 The size of the tumour decreased, IL-2 (pro-inflammatory cytokine) secretion by leucocytes further aids the recruitment of immune cells which reduce the volume of tumour, DAMP signalling is diminished as the cancer cell volume reduced and there is very less apoptosis, interestingly the immunosuppression will start soon as the concentration gradient of TGF-Beta field started to develop.

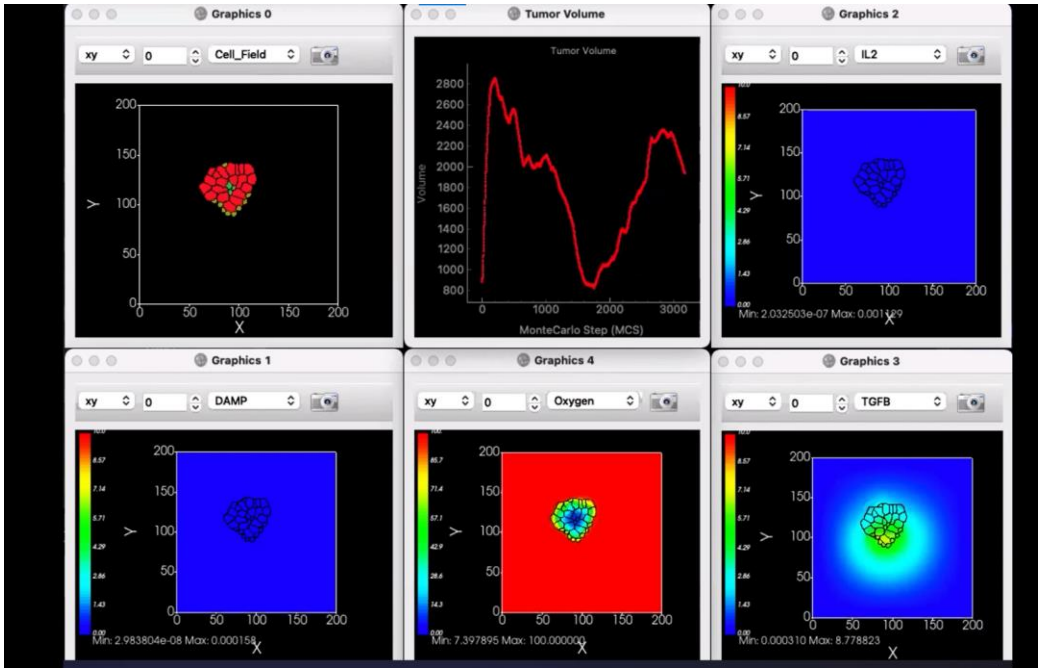

Figure 3 The relapse of cancer, where tumour size started increasing again because of concentration gradient developed as a result of increased TGF-Beta signalling. TGF-Beta suppressed the immune response by inhibiting the signalling of IL-2.

However, these results were generated using an existing tool, CompuCell3D, so to get a grasp of modelling physics phenomenon I started with modelling of Random Walks and the basic statistics.

Statistics from Random Walk

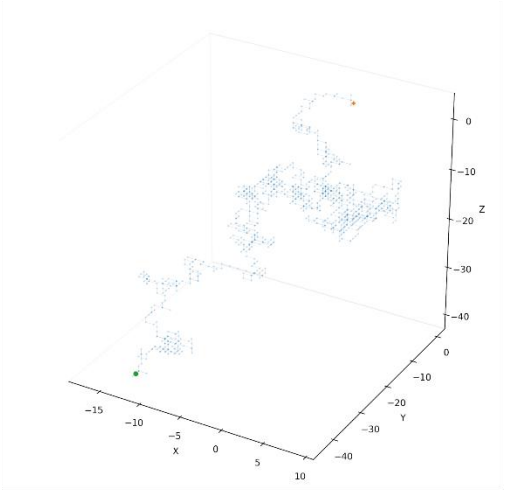

Figure 4 Random Walk of a particle taking 1000 steps in a 3D square lattice. The step of the walk means an increment taken in a direction forward or backwards in x, y or z-axis.

A B

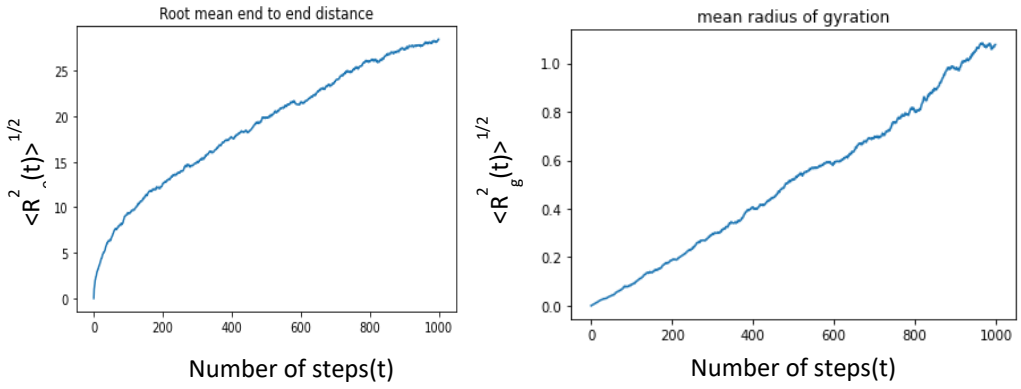

Figure 5 Statistics calculated from the trajectory of Random walk. A) Root-mean-square end to end distance: The distance between the walking particle and the initial position of the walking particle at time t. B) Average Radius of gyration of particle's trajectory taking 1000 steps calculated over 100 independent runs.

Publications:

Tool:

Farnoush Farahpour, Paulo Burke, Polly Y. Yu, Madheshvaran S, **Tahreem Zaheer** (2021), "A toy model of immune responses to immunogenic cancer," https://nanohub.org/resources/cc3dicdinpdac. (DOI: 10.21981/9J7M-V097).

Studies in the current semester:

Bioinformatics – Lecture (bioinfub17em) and Practical (bioinfub17gm)

This course helped me in revising the concepts of Bioinformatics, and the contents are also aligned with my complex exam. This course was from the Faculty of Science, TTK Department of Genetics.

Python Programming for Biologists (pytbioib19lm)

This course was needed to learn to program, I passed the subject with Excellent remarks from the instructor. This course was from the Faculty of Science, IK Department of Programming Languages and Compilers.

Pre-Clinical Models in Cancer Research (FIZ/3/082)

This course helped me in understanding the immune system in a better way. This was a doctoral course from the Biological physics department.

Imaging Techniques in Biology (FIZ/3/077E)

This course improved my understanding of Biological Physics by understanding the concepts behind imaging techniques such as MRI, CT scan and ultrasound. This was a doctoral course from the Biological physics department.