mathematics

MDPI

Article

Invadopodia Formation in Cancer Cell: The Mathematical and Computational Modelling Based on Free Boundary Problem

Muhammad Akmal Ramlee [1,*], Nuha Loling Othman [1,*] and Takashi Suzuki [2]

[1] Faculty of Computer Science and Information Technology, Universiti Malaysia Sarawak, Jalan Datuk Mohd Musa, 94300 Kota Samarahan, Sarawak, Malaysia
[2] Center for Mathematical Modeling and Data Science, Osaka University, 1-3 Machikaneyama-cho, Toyonaka City 560-8531, Osaka, Japan; suzuki@sigmath.es.osaka-u.ac.jp
* Correspondence: muhdakmal.lee@gmail.com (M.A.R.); zzt230c@gmail.com (N.L.O.)

Abstract: We present a mathematical model of an individual cell to expand the simulation of invadopodia formation to a three-dimensional (3D) domain for a more realistic complexity. Simulating invadopodia replication in order for it to be biologically relevant is important since it helps us to understand cancer invasion and metastasis better as well as giving some insight into investigating ways to stop the spread of this fatal disease. Invadopodia formation is formulated using the Stefan problem approach, where the free boundary is characterised by the Stefan free boundary condition, in which the boundary membrane is not known in advance. Level set method is proposed to indicate the behaviour of the cell interface and the motion of the plasma membrane. An enthalpy method (phase-transition problem) is used to describe the cell membrane diffusion. In addition to this, we were able to improve the simulation outcome, giving it a more realistic complexity by using a different simulation technique and domain as well as a different data set. Singularities and instabilities were eliminated. The results that were achieved have the potential to be helpful for novel approaches or to be extended to other methods in the development of a more accurate numerical simulation.

Keywords: invadopodia; individual cell model; free boundary problem; finite element method; Stefan problem; level set method; phase transition; enthalpy

MSC: 92-08; 92-10

check for updates

Citation: Ramlee, M.A.; Loling Othman, N.; Suzuki, T. Invadopodia Formation in Cancer Cell: The Mathematical and Computational Modelling Based on Free Boundary Problem. *Mathematics* **2023**, *11*, 3044. https://doi.org/10.3390/math11143044

Academic Editor: Hongbin Fang

Received: 10 June 2023
Revised: 29 June 2023
Accepted: 30 June 2023
Published: 9 July 2023

Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

The term cancer encompasses a variety of diseases that are broadly categorised by abnormal cell behaviour which act differently from normal cells due to the gene mutations that alter the normal cellular instructions [1]. Tissue invasion and metastasis are one of the "hallmarks of cancer" [2,3] and the leading cause of death among cancer patients [4]. Invasion of cancer cells is the capacity of the cells to disrupt the basement membrane (BM) and secondary tumours arise when it penetrates the surrounding tissue or extracellular matrix (ECM), also referred to as metastasis.

The key factor in tumour invasion and metastasis is proteolytic deterioration of the ECM [5,6] which are propelled by actin-rich protrusions of the plasma membrane, also called invadopodia [7]. Invadopodia is also called 'invasive feet' as it is most commonly detected on the basal surfaces of invasive cancer cells; invadopodia have the ability to invade through the ECM [8]. The morphology of invadopodia is a small punctuated finger-like protrusion or elongated shapes [9]. According to Saitou et al. [10], cancer cells can form one to ten invadopodia with a lifespan of several tens of minutes to 60 min and a size ranging from 0.05 to 2 μm [11]. Numerous cell biological processes must be coordinated for the formation of invadopodia and the degradation of ECM. The formation of invadopodia