A model for cell migration in non-isotropic fibrin networks with an application to pancreatic tumor islets

Jiao Chen[1], Daphne Weihs[2], and F.J.Vermolen[1]

[1]Delft Institute of Applied Mathematics, Delft University of Technology, Mekelweg 4, 2628 CD, Delft, The Netherlands
[2]Faculty of Biomedical Engineering, TechnionIsrael Institute of Technology, 3200003 Haifa, Israel

Cell migration, known as an orchestrated movement of cells, is crucially important for wound healing, tumor growth, immune response as well as other biomedical processes. This work presents a cell-based model to describe micro-scale T-lymphocytes migration in non-isotropic fibrin networks around the vicinity of the T-islet in pancreatic cancer [1]. This migration is determined by the mechanical strain energy density as well as cytokines-driven chemotaxis. Cell displacement is modelled by solving a large system of ordinary stochastic differential equations where the stochastic parts result from random walk, and in which chemotaxis is taken into account through the use of superpositions of Green's Functions as a result of modelling the cellular secretion of chemicals by point sources. The stochastic differential equations are solved by the use of the classical Euler-Maruyama method. In this work, the influence of anisotropic stromal extracellular matrix in pancreatic tumor islets on T-lymphocytes migration in different immune systems is investigated [2].

As far as we know, this is the first mathematical modelling study devoted to the simulation of pancreatic cancer that takes into account orientation of the surrounding collagen. As we expected, tumor peripheral stromal extracellular matrix impedes the immune response of T-lymphocytes through changing direction of the migration of immune cells such that the cancer cells cannot be engulfed by the immune cells. Its obstruction effect increases with the increase of the degree of anisotropy, which inhibits T-lymphocytes migration towards the cancer cells. Moreover, the model is able to predict unlimited proliferation of carcinoma cells if the immune system is weak, and a state of equilibrium where cancer cells are eliminated if the immune system is sufficiently strong.

Reference

[1] Hélène Salmon and Emmanuel Donnadieu. Within tumors, interactions between t cells and tumor cells are impeded by the extracellular matrix. *OncoImmunology*, 1(6):992–994, 2012.

[2] FJ Vermolen, RP Van der Meijden, M Van Es, A Gefen, and D Weihs. Towards a mathematical formalism for semi-stochastic cell-level computational modeling of tumor initiation. *Annals of biomedical engineering*, 43(7):1680–1694, 2015.