Multiscale model to recapitulate breast cancer invasion phenotypes

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Understanding tumour invasion mechanisms is crucial to improve prognosis and develop new cancer treatment strategies, but this is hindered by the lack of understanding of detailed molecular determinants of this process and their interactions leading to different ways cancer cells invade the surrounding tissues. Tumour invasion varies from individual to collective cell movement or if proteases facilitate their migration.

We devised a multi-scale mathematical model that incorporates information of a series of traits, cellular and environmental, that output in a set of invasion modes. For this, the model incorporates different intracellular and signalling pathways and the resulting influence network has been translated into a mathematical model using discrete logical modelling. We have taken advantage of continuous time Boolean modelling based on Markovian stochastic process defined on the model state transition graph to simulate intracellular molecular processes determining individual cellular properties. We have embedded this Boolean model in a lattice-free individual cell population model to cope with interaction between cells and microenvironment affecting cell properties, leading to various patterns of collective cell behaviour.

The model is now tuned to recapitulate major breast cancer invasion phenotypes such as mesenchymal single cell invasion, solid strand multicellular invasion and bulk growth tumour. Present work is part of a collaborative effort to model tumour invasion in order to identify treatment strategies and to understand underlying properties of metastasis.