

A Monte-Carlo Simulation of Cancer Invasion Using The Extended Potts Model

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ABSTRACT

Invasive cancer cells are characterised by alterations in adhesiveness, enzyme secretion rate, motility and mitotic rate, and the processes underlying these changes are intimately linked. Our independent understanding of the microscopic phenomena involved is not matched, however, by a detailed understanding of their relative effects. Mathematical modelling provides a means by which we may quantify the various phenomena involved in the invasion process, and investigate their interdependence. By using experimental results for the various microscopic quantities involved, we may build up models which reveal the relationships between cellular and biochemical parameters and macroscopic phenomena.

The simulation of invasive cells as discrete entities is the most appropriate way of investigating the invasion process, as the successful implantation of even a single malignant cell at a site distant from the primary tumour can establish a secondary colony, with devastating consequences for the host and the likelihood of therapeutic intervention being successful. Monte-Carlo simulation allows us to develop a model of cancer invasion which accurately reflects the stochastic behaviour of a collection of discrete cells during this first step in the process of metastasis.

Our approach, therefore, is to develop a discrete model of cancer invasion using a thermodynamic argument which has an accurate treatment of the microscopic interactions between invading cells at its core. The Potts model, more commonly used in the study of spin networks in condensed matter theory, is used to model the interactions between neighbouring biological cells occupying regions of a square lattice. The cells experience both cell-cell and cell-medium interactions while also secreting proteolytic enzymes and both generating and experiencing a haptotactic gradient. In this way we model the effect of cell-cell interactions on the invasion process. We demonstrate that the macroscopic morphology of the advancing front of a tumour is dependent on the microscopic interactions between the cells, and in particular on the strength of their adhesion to their neighbours. We demonstrate also that the depth of invasion of the tumour after a given time can be related to adhesion. We show that cell-cell adhesion has less of an influence on invasiveness compared with cell-medium adhesion, and that increases in both the proteolytic enzyme secretion rate and

the coefficient of haptotaxis act in synergy to promote invasion.

We extend the simulation by including proliferation, and, closely following experimental evidence, develop an algorithm for cell division in which the mitotic rate is explicitly related to changes in the magnitude of cell-cell and cell-medium adhesiveness. We show that, although an increased proliferation rate usually results in an increased depth of invasion into the surrounding healthy tissue, it does not invariably do so, and may, indeed, cause invasiveness to be reduced.

The model of the invasion process which we develop not only allows the important stochastic aspect of individual cell behaviour to be taken into account; it also allows the close relationship between changes in cell adhesion and the aggressiveness of a tumour's invasive potential to be made explicit.

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