Macroscale modelling of tumour growth

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Abstract

Various modelling frameworks exist for the description of tissue growth processes. These can be divided into (i) individual-based approaches, which seek to capture the behaviour of individual cells within the tissue, (ii) spatio-temporal continuum models (typically in the form of partial differential equations) that in effect average out the behaviour of individual cells and (iii) compartmentalised models (usually ordinary differential equations) that cannot capture spatial heterogeneity in detail but may describe the overall growth dynamics. We shall focus on (ii), but will illustrate how simpler models of the form (iii) arise from these as instructive limit cases.

Partial-differential-equation formulations can in turn be divided into reaction-diffusion systems (applicable at low cell densities) and continuum-mechanics-based approaches that are more appropriate at high cell densities, whereby cell division (for example) necessarily leads to the deformation of the surrounding tissue (cell growth requiring neighbouring cells to be pushed away). The simplest representatives of these two classes of model are, respectively,

$$\frac{\partial n}{\partial t} = D_n \nabla^2 n + kn \tag{1}$$

where n is the volume fraction of tumour cells (with $0 \leq n \ll 1$ being required for (1) to be applicable) and the constants D_n and k represent the cellular diffusivity and division rate, and

$$\frac{\partial n}{\partial t} + \nabla^2 \cdot (\mathbf{v}n) = kn, \quad \frac{\partial n}{\partial t} + \nabla^2 \cdot (\mathbf{v}m) = 0, \quad n + m = 1 \tag{2}$$

where m is the volume fraction of non-tumour material and v is the velocity field within the growing continuum. The assumption of radial symmetry is needed for the system (2) to lead to a closed model; more generally, momentum equations and constitutive assumptions must also be invoked - viscoelastic descriptions are often adopted for the latter, but we shall pursue the simplest (viscous-Newtonian-fluid) choices.

The applicability of models such as (1) and (2) requires in particular that the entire tumour be well supplied with nutrients - otherwise the mitotic rate k should not be taken to be constant. Numerous other refinements are also needed if the models are to

provide viable descriptions of the actual growth processes: worth noting here is the role of multiphase models in bridging between the distinct mathematical approaches represented by (1) and (2).