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During the vascular phase of growth, angiogenesis (i.e. the formation of blood vessels from a pre-existing vasculature) is induced by the tumour. The tumour is highly regulated by the resulting capillary network around it. It is also through this network that chemotherapeutic drugs will be delivered to the tumour. The aim of the presented paper is to model and examine fluid flow through these tumour-induced capillary networks.

1 Modelling of network growth

1.1 the continuum model

The model focusses on three key variables involved in tumour-induced angiogenesis: endothelial cells (n: endothelial cell density per uni area), Tumour Angiogenic Factors (c) and fibronectin (f).

The (nondimensional) equations are taken to hold on a 2D domain (the unit square).

\[ \frac{\partial n}{\partial t} = D \nabla \cdot (d(c) \nabla n) - \chi \nabla \cdot (g(n)c \nabla c) - \rho \nabla \cdot (n \nabla f) \]

\[ \frac{\partial c}{\partial t} = -\eta nc \]

\[ \frac{\partial f}{\partial t} = \beta n - \gamma nf \]

1.2 the discrete model

To capture processes on a smaller scale it is better to use a discrete model. It involves a discretized form of the partial differential equations from the continuum model.

The continuous 2D domain is approximated by a grid of discrete points and time by discrete increments.(Anderson and Chaplain, 1998)

The discrete endothelial cell equation:

\[ n_{i,m}^{q+1} = n_{i,m}^{q}P_0 + n_{i+1,m}^{q}P_1 + n_{i-1,m}^{q}P_2 + n_{i,m+1}^{q}P_3 + n_{i,m-1}^{q}P_4 \]

(superscripts: specify time step, subscripts: specify the location on the grid)
A biased random walk is then generated which governs the movement of individual endothelial cells at the capillary sprout tips by using the five coefficients $P_0$ to $P_4$. These coefficients can be thought of being proportional to the probabilities of the endothelial cell being stationary or moving left, right, up or down on the grid.

2 Modelling of flow through vascular networks

In order to be consistent with the theoretical networks generated by the discrete model, simulations are restricted to 2D lattice networks of bond elements (where bonds correspond to capillaries and nodes correspond to junctions between capillaries).

Construction of the vascular network: The vascular pattern generated by the discrete mathematical model is mapped onto the lattice template.

A radius $R$ is assigned to each capillary element.

- the elemental flow rate for a capillary element is assumed to follow Poiseuille’s law:
  \[ Q_{ij} = \frac{\pi R^4_{ij} \Delta P_{ij}}{8 \mu L_{ij}} \]

- assuming incompressible flow, mass conservation means:
  \[ \sum_{j=1}^{4} Q_{ij} = 0 \]

The application of this last equation to the whole network of nodes leads to a sparse set of linear pressure equations. The simultaneous solution of these can then be used to calculate elemental flows.

3 Simulations and results

We consider 4 suites of flow simulations: two network structures differing in connectedness and for each two different drug delivery regimes.

The results of the simulation show that the vascular structure and the mode of delivery are important in determining how much drug reaches the tumour. Although the total mass of drug within each vasculature is similar under all delivery regimes, the vasculature induced by a large solid tumour permits a greater drug supply than the vasculature induced by a small circular tumour. The key result is that highly interconnected vascular structures around a tumour cause relatively low rates of drug delivery to the tumour itself, the majority of drug is by-passing the tumour and returning to the parent vessel. This can have important implications for Chemotherapy strategies, for example suggesting that the structure of the vasculature around the tumour should be considered when planning chemotherapy.

Literature