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Multiscale modelling of vascular tumour growth and angiogenesis

A three-dimensional multiscale model of vascular tumour growth is presented. In our model, cells are modelled as individual entities (agent-based approach) each with their own cell cycle and subcellular-signalling machinery. Nutrients are supplied by a dynamic vascular network, which is subject to remodelling and angiogenesis.

The model is formulated on a regular grid that subdivides the simulation domain into lattice sites. Each lattice site can be occupied by several biological cells whose movement on the lattice is governed by reinforced random walks, and whose proliferation is controlled by a subcellular cell cycle model. The vascular network consists of vessel segments connecting adjacent nodes on the lattice, with defined inflow and outflow nodes with prescribed pressures. We also specify the amount of haematocrit entering the system through the inlets. The vessel network evolves via sprouting of tip cells with a probability that increases with the local VEGF concentration, tip cell movement is described by a reinforced random walk, and new connections forming via anastomosis. In addition, vessel segments with low wall shear stress may be pruned away. Elliptic reaction-diffusion equations for the distributions of oxygen and VEGF are implemented on the same spatial lattice

using finite difference approximations, and include source and sink terms based on the location of vessels (which act as sources of oxygen and sinks of VEGF) and the different cell types (e.g. cells act as sinks for oxygen and hypoxic cells as sources of VEGF).

In our simulations we demonstrate how our model may be combined with experimental data, to predict the spatio-temporal evolution of a vascular tumour together with angiogenesis.