Angiogenesis Equations

Start with general mass conservation with a flux and source/sink term.

$$\frac{\partial \rho_{\mathrm{v}}}{\partial t} = -\nabla \cdot \mathbf{J} + \mathrm{S} \tag{1}$$

In our case -

$$\mathbf{J} = \mu_{\mathrm{v}} \rho_{\mathrm{v}} \frac{\nabla \mathbf{a}}{\parallel \nabla \mathbf{a} \parallel} \mathrm{v_m} \tag{2}$$

where μ_{v} is the maximum vascular migration rate, ρ_{v} is the vascular density, $\nabla \mathbf{a}$ is the gradient of the angiogenic factor a, and $\mathrm{v_m}$ the vascular migration rate as a function of the local concentration of the angiogenic factor.

And for the source and sink term:

$$\mathrm{S} = \overbrace{\beta_{\mathrm{v}}(1 - \frac{\rho_{\mathrm{v}}}{\overline{\rho}_{\mathrm{v}}})\rho_{\mathrm{v}} \mathrm{b_v}}^{\text{Vascular Birth}} - \overbrace{\mathrm{d_v} \frac{\rho_{\mathrm{t}}}{\overline{\rho}_{\mathrm{t}}} \rho_{\mathrm{v}}}^{\text{Vas. Death}} \tag{3}$$

where β is the maximum vascular birth rate, ρ_{v} is the vascular density growing with logistic growth, a birth rate $\mathrm{b_v}$ determined by concentration of the angiogenic factor (see below) and a vascular death term determined by a constant death rate $\mathrm{d_v}$, the presence of tumor tissue, and the presence of vasculature.

Combining them all together ...

$$\frac{\partial \rho_{\mathrm{v}}}{\partial \mathrm{t}} = \overbrace{-\nabla \cdot \left(\mu_{\mathrm{v}} \rho_{\mathrm{v}} \frac{\nabla \mathbf{a}}{\parallel \nabla \mathbf{a} \parallel} \mathrm{v_m} \right)}^{\text{Advection}} + \overbrace{\beta(1 - \frac{\rho_{\mathrm{v}}}{\overline{\rho}_{\mathrm{v}}})\rho_{\mathrm{v}} \mathrm{b_v}}^{\text{Vascular Birth}} - \overbrace{\mathrm{d_v} \frac{\rho_{\mathrm{t}}}{\overline{\rho}_{\mathrm{t}}} \rho_{\mathrm{v}}}^{\text{Vas. Death}} \tag{4}$$

With the following "sub-functions" for environmentally controlled vascular chemotaxis and growth.

Chemotaxis modification:

$$v_{\mathrm{m}} = \begin{cases} 1 & \text{if } a > a_{\text{saturation,chem}} \\ \frac{a - a_{\text{threshold,chem}}}{a_{\text{saturation,chem}} - a_{\text{threshold,chem}}} & \text{if } a_{\text{threshold,chem}} \leq a \leq a_{\text{saturation,chem}} \\ 0 & \text{if } a < a_{\text{threshold,chem}} \end{cases} \tag{5}$$

Growth rate modification:

$$b_{\text{rate}} = \begin{cases} 1 & \text{if } a > a_{\text{saturation,prol}} \\ \frac{a - a_{\text{threshold,prol}}}{a_{\text{saturation,prol}} - a_{\text{threshold,prol}}} & \text{if } a_{\text{threshold,prol}} \leq a \leq a_{\text{saturation,prol}} \\ 0 & \text{if } a < a_{\text{threshold,prol}} \end{cases} \tag{6}$$

Where the there are various angiogenic concentration parameters that can be set to make a "ramp" or sigmoidal function to modify the rates movement and growth rates between 0 (a threshold) and 1 (saturation/max).

Finally, in the prototype model, we used a threshold to remove vascular density completely from a voxel. This is a condition such that if the vascular density goes below a threshold, the value at that point is set to 0. This is due to the numerics allowing a point in space to carry a non-biological amount of vasculature, which under the right conditions, could regrow instead of having new vasculature chemotax there.