A Simple Mechanistic Model of Sprout Spacing in Tumour-Associated Angiogenesis

Physics of Biological Systems (PH 549)

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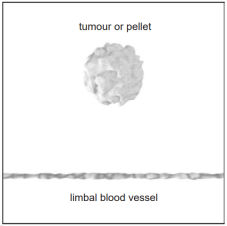
Contents

Introduction

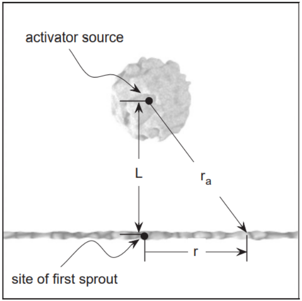
- The paper[1] being reviewed develops a simple mathematical model of sprout formation during the initiation of angiogenesis induced by tumours.
- We consider 2 quantities, **Activator** which is released by the tumour and **Inhibitor** which are released by the subsequent sprouts.



[1] Ref: B. Addison-Smith, D.L.S. McElwain and P.K. Maini. A simple mechanistic model of sprout spacing in tumour-associated angiogenesis. Journal of Theoretical Biology 250 (2008) 1–15.

Model Domain

- We assume a polar coordinate system in 2D with the axis passing perpendicular to the plane through the pellet.
- For sprouting, $A \geq A_{trig}$ and $I \leq I_{thresh}$.



1. Introduction
2. Mathematical Modeling
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Governing Equation for Activator

There is linear decay term for the activator for which the differential equation becomes

$$\frac{\partial A}{\partial t} = D_a \nabla^2 A - \lambda_a A \tag{1}$$

For a continuous point source:

$$A(r_a, t) = \frac{q}{4\pi D_a} \int_0^t \frac{1}{u} \exp\left(\frac{-r_a^2}{4 D_a u} - \lambda_a u \right) du \tag{2}$$

The steady state solution is given as a modified Bessel function of second kind.

$$A(r_a) = \frac{q}{2\pi D_a} K_0 \left(r_a \sqrt{\frac{\lambda_a}{D_a}} \right) \tag{3}$$

Governing Equation for Inhibitor

Decay term is not assumed for inhibitor and its differential equation is given by

$$\frac{\partial I}{\partial t} = D_i \nabla^2 I \tag{4}$$

For an instantaneous point source:

$$I(r,t) = \frac{p}{4\pi D_i t} \exp\left(\frac{-r^2}{4D_i t}\right) \tag{5}$$

For sprout n at r_n and t_n, the complete equation becomes

$$I(r,t) = \sum_{n=1}^{N_s} \frac{p}{4\pi D_i (t - t_n)} \exp\left(-\frac{(r - r_n)^2}{4D_i (t - t_n)}\right) H(t - t_n) \tag{6}$$

where H is the step function.

Non-Dimensionalization

We adopt re-scaling of all quantities:

$$
\begin{aligned}
r^* &= \frac{r}{L}, & t^* &= \frac{t}{\tau}, & \tau &= \frac{L^2}{4D_a}, \\
A^* &= \frac{A}{\hat{A}}, & \hat{A} &= \frac{q\tau}{\pi L^2}, & I^* &= \frac{I}{\hat{I}}, \\
\hat{I} &= \frac{p}{\pi L^2}, & \beta &= \frac{D_i}{D_a}, & \gamma &= \lambda\tau
\end{aligned}
\tag{7}
$$

The renormalisation gives

$$
\begin{aligned}
A^*(r^*, t^*) &= \int_0^{t^*} \frac{1}{u}\exp\left(\frac{-r_a^{*2}}{u} - \gamma u\right) du \\
I^*(r^*, t^*) &= \sum_{n=1}^{N_s} \frac{1}{(t^* - t_n^*)}\beta\exp\left(-\frac{(r^* - r_n^*)^2}{t^* - t_n^*}\beta\right) H(t^* - t_n^*)
\end{aligned}
\tag{8}
$$

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Simulation of Sprouts Positioning

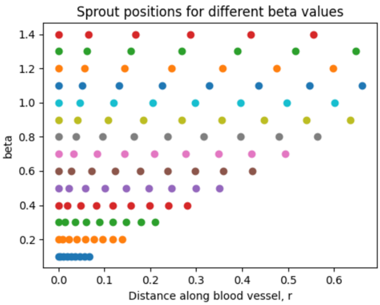

Fig 1. Variation of diffusion coefficient ratio (β)

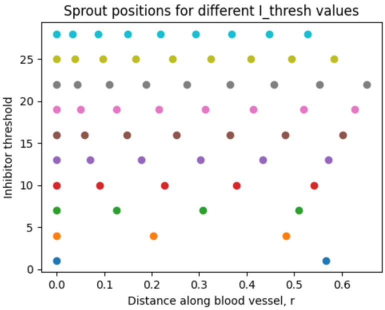

Fig 2. Variation of inhibitor threshold (I_{th})

Thank You!