Mathematical Models for Tumour Angiogenesis: Numerical Simulations and Nonlinear Wave Solutions

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To ensure its sustained growth, a tumour may secrete chemical compounds (TAF) which cause neighbouring capillaries to form sprouts which then migrate towards it.

1 Mathematical Model

1.1 Variables

t := time.
n := sprout tip density
ρ := vessel density
c := chemoattractant (TAF) concentration

1.2 The Model

\[ \frac{\partial \rho}{\partial t} = -nv - d \quad , \quad v=velocity \ of \ tips; \ d=death \ rate \quad (1) \]

\[ \frac{\partial n}{\partial t} = \frac{\partial J}{\partial x} + \sigma \quad , \quad J=tip-density-flux; \ \sigma = tip \ creation \ rate \quad (2) \]

\[ \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} - \lambda c - \alpha_1 H(c - \hat{c})nc \quad , \quad D=diffusion \ coefficient; \ \lambda=nature \ decay \ rate \quad (4) \]

\[ \rho(L,t) = \rho_{min} + (\rho_L - \rho_{min})e^{-kt}, \rho(x,0) = 0 \ for \ 0 \leq x < L, \ \rho(L,0) = \rho_L \]

\[ n(0,t) = 0, n(L,t) = n_L e^{-kt}, n(x,0) = 0 \ for \ 0 \leq x < L, \ n(L,0) = n_L \]

\[ c(x,0) = c_0, c(L,t) = 0, c(x,0) = c_0(x) \ for \ 0 < x \leq L \]

1.3 Nondimensionalization

\[ \frac{\partial \rho}{\partial \tau} = \mu \frac{\partial n}{\partial \xi} - \lambda n \frac{\partial c}{\partial \xi} - \gamma \rho \quad (8) \]

\[ \frac{\partial n}{\partial \tau} = \mu \frac{\partial^2 n}{\partial \xi^2} - \chi \frac{\partial}{\partial \xi} (n \frac{\partial c}{\partial \xi}) + \alpha_0 \rho c + \alpha_1 H(c - \hat{c})nc - \beta n \rho \quad (9) \]

\[ \frac{\partial c}{\partial \tau} = \frac{\partial^2 c}{\partial \xi^2} - \lambda c - \alpha_1 H(c - \hat{c})nc \quad (10) \]
\[ \rho(1, t) = \rho_{\text{min}} + (1 - \rho_{\text{min}})e^{-kt}, \quad \rho(x, 0) = 0 \text{ for } 0 \leq x < 1, \quad \rho(1, 0) = 1 \]
\[ n(0, t) = 0, n(1, t) = n_L e^{-kt}, \quad n(x, 0) = 0 \text{ for } 0 \leq x < 1, \quad n(1, 0) = n_L \]
\[ c(0, t) = 1, c(1, t) = 0, c(x, 0) = 0 \text{ for } 0 < x \leq 1 \]

2 Numerical Results

3 Model Simplification and Mathematical Analysis

- with \( \alpha_1 = 0 \) in (10) we obtain the steady-state TAF profile: 
  \[ c(x) = \frac{\sinh \sqrt{\lambda}(1-x)}{\sinh \sqrt{\lambda}} \]
- neglect tip motility and fix \( \mu = 0 \):
  \[ \frac{\partial \rho}{\partial t} = -\chi n \frac{dc}{dx} - y \rho \quad (15) \]
- \[ \frac{\partial n}{\partial t} = -\chi \frac{\partial}{\partial x} (n \frac{dc}{dx}) + \alpha_0 \rho c + \alpha_1 n c H(c - \hat{c}) - \beta n \rho \quad (16) \]
- \( \rho(x, 0) = 0 \text{ for } x \in [0, 1], \rho(1, 0) = 1, \quad (17) \]
- \( n(0, t) = 0, n(x, 0) = n_0(x) \text{ for } x \in [0, 1], n(1, t) = n_L \quad (18) \]
- \( \rightarrow \) nonlinear wave equation (19): 
  \[ \frac{\partial n}{\partial t} + \chi \frac{dc}{dx} \frac{\partial c}{\partial x} = (\alpha_1 H(c - \hat{c}) - \chi \lambda - \frac{\alpha_0 \chi}{\lambda} \frac{dc}{dx})cn + \frac{\beta x}{y} \frac{dc}{dx} n^2 \equiv F(n, c) \rightarrow \text{wave speed: } \frac{dc}{dt} \]
  \[ \frac{dc}{dx} = -\chi \sqrt{\lambda} \coth \sqrt{\lambda}(1-x) \quad (19) \]
- by solving (19) we get that angiogenesis fails if: 
  \[ e^{\frac{\alpha_1 \lambda}{2}} (1-\epsilon^2) \leq 1 + \frac{\beta x}{y} \]
- In conclusion, the success or failure of angiogenesis is essentially governed by the 
  balance between the proliferation parameter and the death parameters.