On some PDE models related to tumor angiogenesis

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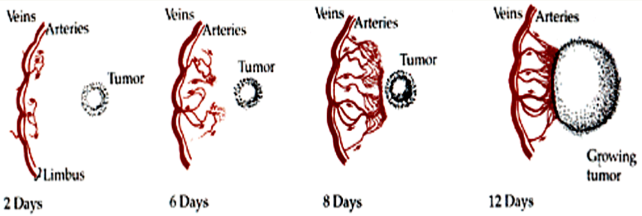
Veins
Arteries
Tumor
Limbus
2 Days
Veins
Arteries
Tumor
6 Days
Veins
Arteries
Tumor
8 Days
Veins
Arteries
Growing tumor
12 Days

- u: Endothelial cells (living organism)
- v: TAF (chemical agent)

$$u_t = \underbrace{\Delta u}_{Diffusion} - \underbrace{\nabla \cdot (\alpha(v) u \nabla v)}_{Chemotaxis} + \underbrace{f(u,v)}_{Reaction} \quad in \;\; \Omega \times (0,T),$$

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2. Drift dominant (Blow-up)
3. Equilibrium

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A.R.A Anderson and M.A.J. Chaplain, Bull. Math. Biol. (1998)

- u: Endothelial Cells.
- v: TAF.
- f: Fibronectin.

$$u_t = \underbrace{\Delta u}_{Diffusion} - \underbrace{\nabla \cdot (\alpha(v) u \nabla v)}_{Chemotaxis} - \underbrace{\nabla \cdot (\rho u \nabla f)}_{Haptotaxis} \;\; in \;\; \Omega \times (0,T),$$

$$v_t = \underbrace{-\mu u v}_{Consumption} \quad in \;\; \Omega \times (0,T),$$

$$f_t = \beta u - \gamma u f \;\; in \;\; \Omega \times (0,T),$$

+Neumann Boundary Conditions

- u: Endothelial Cells.
- v: TAF.

$$u_t = \underbrace{\Delta u}_{Diffusion} - \underbrace{\nabla \cdot \left(\frac{u}{v} \nabla v \right)}_{Chemotaxis} \quad in \ \ \Omega \times (0, T),$$

$$v_t = \underbrace{-\mu u v}_{Consumption} \quad in \ \ \Omega \times (0, T),$$

+Neumann Boundary Conditions

Theorem (with M. Winkler)

Let $(u_0, v_0) \in C(\overline{\Omega}) \times W^{1,p}(\Omega)$ *with* $p > n$ *then for* $n \leq 3$ *there exists a global weak solution.*

Theorem (with M. Winkler)

Let (u, v) *a global weak solution then*

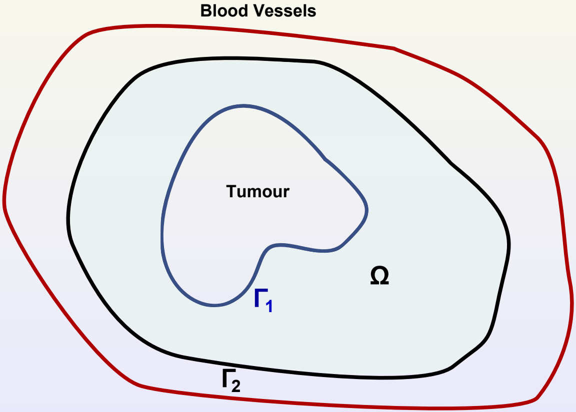
$$\lim_{t \to +\infty} \|u(t) - \overline{u}\|_{L^1(\Omega)} = 0, \quad \lim_{t \to +\infty} \|v(t)\|_{L^\infty(\Omega)} = 0,$$

where $\overline{u} = \frac{1}{|\Omega|} \int_\Omega u$.

v: TAF z: Anti-TAF

$$v + z \rightharpoonup c \text{ binding of } v \text{ and } z$$

$$c \rightharpoonup v + z \text{ unbinding of } v \text{ and } z$$


Blood Vessels
Tumour
Ω
Γ_1
Γ_2

Equation and boundary conditions for EC

- u: Endothelial Cells, v:TAF
- c: TAF-Anti complex, z: Anti-TAF

$$u_t = \underbrace{d_1 \Delta u}_{Diffusion} - \underbrace{\nabla \cdot (\alpha(v) u \nabla v)}_{Chemotaxis} + \underbrace{\lambda \beta(v) u - u^2}_{Reaction} \quad in \quad \Omega \times (0,T),$$

$$\frac{\partial u}{\partial n} = \underbrace{\gamma_2 u}_{ECs\, enter} \quad on \quad \Gamma_2 \times (0,T),$$

$$\frac{\partial u}{\partial n} = \underbrace{-\gamma_1 u}_{ECs\, out} \quad on \quad \Gamma_1 \times (0,T),$$

TAF

- u: Endothelial Cells, v:TAF
- c: TAF-Anti complex, z: Anti-TAF

$$v_t = \underbrace{d_2 \Delta v}_{Diffusion} \underbrace{-v}_{Decay} + \underbrace{k_b c}_{Dissociation} \underbrace{-k_f v z}_{Association} \quad in \;\; \Omega \times (0,T),$$

$$\frac{\partial v}{\partial n} = \underbrace{-\tau_2 v}_{TAF\,out} \quad on \;\; \Gamma_2 \times (0,T),$$

$$\frac{\partial v}{\partial n} = \underbrace{\widetilde{\gamma}(oxygen)}_{TAF\,enter} \quad on \;\; \Gamma_1 \times (0,T),$$

$\widetilde{\gamma}$ is a positive decreasing function.

TAF

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$$\frac{\partial v}{\partial n} = \underbrace{-\tau_2 v}_{TAF\,out} \quad on \ \ \Gamma_2 \times (0,T),$$

$$\frac{\partial v}{\partial n} = \underbrace{\widetilde{\gamma}(oxygen) = \widetilde{\gamma}(s(u))}_{TAF\,enter} \quad on \ \ \Gamma_1 \times (0,T),$$

$\widetilde{\gamma}$ is a positive decreasing function. $oxygen = s(u)$ with s a positive increasing function. Therefore $\widetilde{\gamma} \cdot s = \gamma$ is decreasing.

TAF-Anti complex

- u: Endothelial Cells, v:TAF
- c: TAF-Anti complex, z: Anti-TAF

$$c_t = \underbrace{d_3 \Delta c}_{Diffusion} \underbrace{-c}_{Decay} \underbrace{-k_b c}_{Dissociation} + \underbrace{k_f v z}_{Association} \quad in \;\; \Omega \times (0,T),$$

$$\frac{\partial c}{\partial n} = \underbrace{-\rho_2 c}_{TAF-Anti\,out} \quad on \;\; \Gamma_2 \times (0,T),$$

$$\frac{\partial c}{\partial n} = \underbrace{-\rho_1 c}_{TAF-Anti\,out} \quad on \;\; \Gamma_1 \times (0,T),$$

Anti-TAF

- u: Endothelial Cells, v:TAF
- c: TAF-Anti complex, z: Anti-TAF

$$z_t = \underbrace{d_4 \Delta z}_{Diffusion} \underbrace{-z}_{Decay} + \underbrace{k_b c}_{Dissociation} \underbrace{-k_f v z}_{Association} + \underbrace{I_0}_{Input} \quad in \;\; \Omega \times (0,T),$$

$$\frac{\partial z}{\partial n} = \underbrace{-\theta_2 z}_{Anti-TAF\, out} \qquad on \;\; \Gamma_2 \times (0,T),$$

$$\frac{\partial z}{\partial n} = \underbrace{-\theta_1 z}_{Anti-TAF\, out} \qquad on \;\; \Gamma_1 \times (0,T),$$

$$u_t = \underbrace{d_1 \Delta u}_{Diffusion} - \underbrace{\nabla \cdot (\alpha(v) u \nabla v)}_{Chemotaxis} + \underbrace{\lambda \beta(v) u - u^2}_{Reaction} \quad in \;\; \Omega \times (0,T),$$

$$v_t = \underbrace{d_2 \Delta v}_{Diffusion} \underbrace{-v}_{Decay} + \underbrace{k_b c}_{Dissociation} \underbrace{-k_f v z}_{Association} \quad in \;\; \Omega \times (0,T),$$

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$$\frac{\partial v}{\partial n} = \underbrace{\gamma(u)}_{TAF\, enter} \quad on \;\; \Gamma_1 \times (0,T),$$

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$$\frac{\partial v}{\partial n} = \underbrace{\gamma(u)}_{TAF\,enter} \quad on \;\; \Gamma_1 \times (0,T),$$

Long time behavior and interpretation

From the biological point of view we should know the conditions to assure that

$$\lim_{t\to+\infty} \|u(t)\|_{C^0(\overline{\Omega})} = 0$$

because then we can avoid angiogenesis.

Long time behavior

Theorem (with M. Delgado, I. Gayte and A. Suárez)

For $\lambda < 0$ sufficiently large we have that

$$\lim_{t \to +\infty} \|u(t)\|_{C(\overline{\Omega})} = 0$$

Stationary solutions with $u = 0$

$$0 = \underbrace{d_2 \Delta v}_{Diffusion} \underbrace{-v}_{Decay} + \underbrace{k_b c}_{Dissociation} \underbrace{-k_f v z}_{Association} \quad in \ \ \Omega,$$

$$\frac{\partial v}{\partial n} = \underbrace{\gamma(0)}_{TAF\,enter} \quad on \ \ \Gamma_1,$$

$$0 = \underbrace{d_3 \Delta c}_{Diffusion} \underbrace{-c}_{Decay} \underbrace{-k_b c}_{Dissociation} + \underbrace{k_f v z}_{Association} \quad in \ \ \Omega,$$

$$0 = \underbrace{d_4 \Delta z}_{Diffusion} \underbrace{-z}_{Decay} + \underbrace{I_0}_{Input} \quad in \ \ \Omega,$$

Stationary solutions with $u = 0$

For each non-trivial $I_0 \geq 0$ there is a unique positive solution $z(I_0)$ to

$$
\begin{aligned}
\underbrace{-d_4 \Delta z}_{Diffusion} \underbrace{+z}_{Decay} &= \underbrace{I_0}_{Input} \quad in \quad \Omega, \\
\frac{\partial z}{\partial n} &= \underbrace{-\theta_2 z}_{Anti-TAF\, out} \quad on \quad \Gamma_2, \\
\frac{\partial z}{\partial n} &= \underbrace{-\theta_1 z}_{Anti-TAF\, out} \quad on \quad \Gamma_1.
\end{aligned}
$$

Stationary solutions with $u = 0$

$$0 = \underbrace{d_2 \Delta v}_{Diffusion} \underbrace{-v}_{Decay} + \underbrace{k_b c}_{Dissociation} \underbrace{-k_f v z(I_0)}_{Association} \quad in \quad \Omega,$$

$$\frac{\partial v}{\partial n} = \underbrace{\gamma(0)}_{TAF\, enter} \quad on \quad \Gamma_1,$$

$$0 = \underbrace{d_3 \Delta c}_{Diffusion} \underbrace{-c}_{Decay} \underbrace{-k_b c}_{Dissociation} + \underbrace{k_f v z(I_0)}_{Association} \quad in \quad \Omega,$$

Stationary solutions with $u = 0$

The previous linear system has a unique positive solution $V^0(I_0) = (v^0(I_0), c^0(I_0))$ for each $I_0 \geq 0$. Moreover, none of the components is trivial. Therefore in order to assure whether

$$\lim_{t \to +\infty} \|u(I_0)(t)\|_{C^0(\overline{\Omega})} = 0$$

or not (for initial data close to $(0, V^0(I_0))$) we should know the local stability of $(0, V^0(I_0))$.

Stationary solutions with $u = 0$

Let $\lambda_1(v^0(I_0))$ the principal eigenvalue of

$$-d_1\Delta\varphi = -\nabla\cdot(\alpha(v^0(I_0))\nabla v^0(I_0)\varphi) + \lambda\beta(v^0(I_0))\varphi \;\; in \;\; \Omega,$$

$$\frac{\partial\varphi}{\partial n} = \gamma_2\varphi \;\; on \;\; \Gamma_2,$$

$$\frac{\partial\varphi}{\partial n} = -\gamma_1\varphi \;\; on \;\; \Gamma_1.$$

Theorem (with M. Delgado, I. Gayte and A. Suárez)

If $\lambda < \lambda_1(v^0(I_0))$ (resp. $\lambda > \lambda_1(v^0(I_0))$) then the semi-trivial solution is locally stable (resp. unstable)

Coexistence state

By bifurcation we can show that

Theorem (with M. Delgado, I. Gayte and A. Suárez)

For $\lambda > \lambda_1(v^0(I_0))$ there exists at least a coexistence state.

Behavior of $\lambda_1(v^0(I_0))$ when I_0 large

For a given λ can I pick I_0 sufficiently to assure that $(0, V^0(I_0))$ is locally stable ? (if this is true then we can avoid angiogenesis).

Behavior of $\lambda_1(v^0(I_0))$ when I_0 large

For a given λ can I pick I_0 sufficiently to assure that $(0, V^0(I_0))$ is locally stable ? (if this is true then we can avoid angiogenesis). In other words can we prove that

$$\lim_{I_0 \to +\infty} \lambda_1(v^0(I_0)) = +\infty$$

Let λ^* be the principal eigenvalue of

$$-d_1\Delta\varphi = \lambda\varphi \;\; in \;\; \Omega,$$

$$\frac{\partial\varphi}{\partial n} - \gamma_2\varphi = 0 \;\; on \;\; \Gamma_2,$$

$$\frac{\partial\varphi}{\partial n} + (\gamma_1 + \alpha(0)\gamma(0))\varphi = 0 \;\; on \;\; \Gamma_1.$$

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$$\frac{\partial \varphi}{\partial n} + (\gamma_1 + \alpha(0)\gamma(0))\varphi = 0 \;\; on \;\; \Gamma_1.$$

Theorem (with M. Delgado, I. Gayte and A. Suárez)

If $\lambda^* > 0$ *then* $\lim_{I_0 \to +\infty} \lambda_1(v^0(I_0)) = +\infty$. *However if* $\lambda^* < 0$ *then* $\lim_{I_0 \to +\infty} \lambda_1(v^0(I_0)) = -\infty$.