Bio-materials and chemotaxis

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Bio-materials

Biomaterial is a substance that interacts with biological systems.

Alone or as part of a complex system, is used to direct by controlling of interactions with components of the living system, the course of a phenomenon or (therapeutic or diagnostic) procedure.

Biomaterials in connection with chemotaxis

Chemotaxis is a biological phenomenon describing the change of motion when a population of individuals (b) reacts in response to an external stimulus spread in the environment by another population or substance (chemoattractant c). As a consequence, the population b directs its movement towards (positive chemotaxis) a higher concentration of the chemical substance.

Lecture Notes in Biomathematics, 89, Eds:Alt & Hoffmann, 1990

T. Hillen, K. J. Painter (2009). A user's guide to PDE models for chemotaxis. J. Math. Biol. 58:183–217.

Chemotaxis: Examples

Chemoattractant c:	$\longleftarrow\!\!\longleftarrow$	Attracted population b:
chemotactic agent possessing	$\longleftarrow\!\!\longleftarrow$	individuals searching for food
chemotaxis-inducer	$\longleftarrow\!\!\longleftarrow$	leukocytes moving toward inviding microorganisms
effect in motile cells		endothelial cells attracted by solid tumours chemical signals
bioremediation of polluted media		
a pollutant (oil)	$\longleftarrow\!\!\longleftarrow$	bacteria

Chemotaxis: Examples

Biomaterial ←−←− allow cell colonization of biomaterials, prevent bacterial adhesion and in regenerative medicine and tissue engineering

monocytes ———> tissue ————> tissue/biomaterial ————> biomaterial

monocytes	———>	tissue	————>	tissue/biomaterial	————>	biomaterial
	chemotaxis		chemotaxis migration-adhesion		differentiation	

Chemotaxis: mathematical model

$$\frac{\partial b}{\partial t} - \nabla \cdot \left(D\left(t,x,b,c\right) \nabla b \right) + \nabla \cdot \left(K\left(t,x,b,c\right) b \nabla c \right) = f_1\left(t,x,b,c\right) - f_2\left(t,x,b,c\right),$$

$$\frac{\partial c}{\partial t} - \nabla \cdot \left(\delta\left(t,x,b,c\right) \nabla c \right) = \varphi_1\left(t,x,b,c\right) - \varphi_2(t,x,b,c)$$

$$\textit{initial and boundary conditions}$$

$D(t,x,b,c)$ diffusion coefficient of the attracted population b
$\delta(t,x,b,c)$ diffusion coefficient of the chemoattractant c
$K(t,x,b,c)$ chemotactic sensitivity
$f_1\left(t,x,b,c\right)$, $f_2\left(t,x,b,c\right)$ rates of growth and death of b
$\varphi_1(t,x,b,c)$, $\varphi_2(t,x,b,c)$ rates of production and degradation of c

$$f(t,x,b,c) = f_1(t,x,b,c) - f_2(t,x,b,c), \quad \varphi(t,x,b,c) = \varphi_1\left(t,x,b,c\right) - \varphi_2(t,x,b,c) = \text{kinetic term}$$

Chemotaxis: references

- A. Blanchet, J.A. Carrillo, P. Laurençot, Critical mass for a Patlak–Keller–Segel model with degenerate diffusion in higher dimensions, Calculus of Variations and Partial Differential Equations, 35, 2, 133-168, 2009.
- Adrien Blanchet, J.A. Carrillo, N. Masmoudi, Infinite time aggregation for the critical Patlak-Keller-Segel model in R^2, Comm. Pure Appl. Math. 61, 1449–1481, 2008.
- J. Dyson, R. Villella-Bressan, G. F. Webb, Global Existence and Boundedness of Solutions to a Model of Chemotaxis, Math. Model. Nat. Phenom. 3, 7, 17-35, 2008
- J. Dyson, R. Villella-Bressan, G.F. Webb, An age and spatially structured model of tumor invasion with haptotaxis II, Mathematical Population Studies, 15, 73–95, 2008

$$\frac{\partial b}{\partial t} - D\Delta b + \nabla \cdot (K(x,b,c)\, b\nabla c) = \omega_p b + \mu(x,c,b)b, \quad \frac{\partial c}{\partial t} - \delta\Delta c = \omega_c c + \gamma(x,c,b)$$

- A. Fasano and D. Giorni, On a one- dimensional problem related to bioremediation of polluted soils, Advances in Mathematical Sciences and Applications 14, 443-455, 2004

$$\frac{\partial c}{\partial t} = -\frac{\beta_1 c}{1+\beta_2 c} b,$$

- I.Borsi, A.Farina, A.Fasano, M.Primicerio, Applications of Mathematics, Modelling bioremediation of polluted soils in unsaturated condition and its effect on the soil hydraulic properties, Appl. Math. 53, 5, 409–432, 2008
- B. Perthame, Transport equations in Biology, Birkhäuser, Basel, 2007

$$\frac{\partial b}{\partial t} - \Delta b + \nabla \cdot (Kb\nabla c) = 0, \quad -\Delta c = b.$$

1 A chemotaxis model in a stratified medium

$$\frac{\partial b}{\partial t} - \nabla \cdot (D(x) \nabla b) + \nabla \cdot (K(b,c)\, b \nabla c) = f(b,c)$$

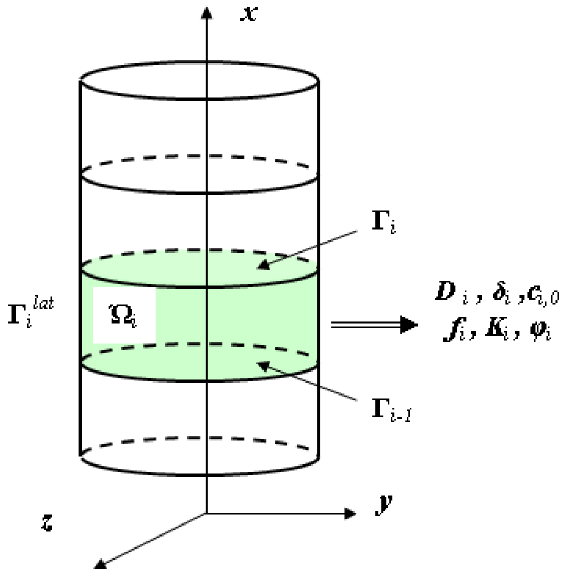
$$\frac{\partial c}{\partial t} - \varepsilon \nabla \cdot (\delta(x) \nabla c) = \varepsilon \varphi(b,c)$$

$$initial\ and\ boundary\ conditions$$

$$in\ a\ stratified\ medium$$

E.R. Ardeleanu, G.M., An asymptotic solution to a nonlinear reaction-diffusion system with chemotaxis, Num. Funct. Anal. Optim., in press

A chemotaxis model in a stratified medium



$$\Omega = \{\xi = (x,y,z) \in \mathbb{R}^3;\ x \in (x_0, x_n),\ \xi' = (y,z) \in \Omega_2\}$$

Parameters do not depend on the layer depth

$D_i,\ \delta_i,\ c_{i,0}$ = constant

A chemotaxis model in a stratified medium

$$\frac{\partial b_i}{\partial t} - \overline{D} D_i \Delta b_i + \overline{K} \nabla \cdot [b_i K_i (b_i, c_i) \nabla c_i] = \overline{f} f_i (b_i, c_i) \text{ in } Q_i = (0,T) \times \Omega_i,$$

$$\frac{\partial c_i}{\partial t} - \varepsilon \overline{\delta} \delta_i \triangle c_i = \varepsilon \overline{\varphi} \varphi_i (b_i, c_i) \text{ in } Q_i,$$

$$c_i(0,\xi) = c_{i,0}(\xi) \text{ in } \Omega_i,$$

$$b_i(0,\xi) = b_{i,0}(\xi) \text{ in } \Omega_i,$$

interface boundary conditions

$$-\overline{D} D_i \frac{\partial b_i}{\partial x} + \overline{K} b_i K_i (b_i, c_i) \frac{\partial c_i}{\partial x} = -\overline{D} D_{i+1} \frac{\partial b_{i+1}}{\partial x} + \overline{K} b_{i+1} K_{i+1} (b_{i+1}, c_{i+1}) \frac{\partial c_{i+1}}{\partial x} \text{ on } \Sigma_i = (0,T) \times \Gamma_i,$$

$$b_i = b_{i+1} \text{ on } \Sigma_i,$$

$\overline{D}, \overline{K}, \overline{f}, \overline{\delta}, \overline{\varphi}$ are dimensionless parameters

A chemotaxis model in a stratified medium

$$\frac{\partial b_i}{\partial t} - \overline{D} D_i \Delta b_i + \overline{K} \nabla \cdot [b_i K_i (b_i, c_i) \nabla c_i] = \overline{f} f_i (b_i, c_i) \text{ in } Q_i = (0,T) \times \Omega_i,$$

$$\frac{\partial c_i}{\partial t} - \varepsilon \overline{\delta} \delta_i \triangle c_i = \varepsilon \overline{\varphi} \varphi_i (b_i, c_i) \text{ in } Q_i,$$

$$c_i(0,\xi) = c_{i,0} \text{ in } \Omega_i,$$

$$b_i(0,\xi) = b_{i,0}(\xi) \text{ in } \Omega_i,$$

boundary conditions on the exterior boundaries

$$-\overline{D} D_1 \frac{\partial b_1}{\partial x} + \overline{K} b_1 K_1 (b_1, c_1) \frac{\partial c_1}{\partial x} = 0 \text{ on } \Sigma_0 = (0,T) \times \Gamma_0,$$

$$-\overline{D} D_n \frac{\partial b_n}{\partial x} + \overline{K} b_n K_n (b_n, c_n) \frac{\partial c_n}{\partial x} = 0 \text{ on } \Sigma_n = (0,T) \times \Gamma_n,$$

$$\nabla b_i \cdot \nu = 0 \text{ on } \Sigma_i^{lat} = (0,T) \times \Gamma_i^{lat}.$$

A chemotaxis model in a stratified medium: hypotheses

$$c_{i,0} = \text{ constant, } \; c_{i,0} \geq 0, \;\; b_{i,0} \geq 0,$$

$$f_i \in C^1, \; K_i \in C^1, \; \varphi_i \in C^2, \text{ bounded with bounded derivatives}$$

$$f_i(r_1, r_2) r_1 \leq 0, \; \forall r_1, r_2 \in \mathbb{R},$$

$$f_i(0, r_2) = 0, \; \forall r_2 \in \mathbb{R},$$

$$\left| \frac{\partial f_i}{\partial r_1}(r_1, r_2) \right| \leq C_1^i (1 + |r_1|^p), \; \forall r_1, r_2 \in \mathbb{R}$$

$$\begin{aligned} 0 \; &\leq \; p < 2 \;\; \text{if } N = 3, \\ 0 \; &\leq \; p < \infty \text{ if } N = 1, 2. \end{aligned}$$

A chemotaxis model in a stratified medium: Perturbation technique

$$b_i(t,\xi) = b_i^0(t,\xi) + \varepsilon b_i^1(t,\xi) + ...,$$

$$c_i(t,\xi) = c_i^0(t,\xi) + \varepsilon c_i^1(t,\xi) + ...,$$

$$f_i(b_i,c_i) = f_i\left(b_i^0,c_i^0\right) + \varepsilon\left(f_i\right)_{b_i}\left(b_i^0,c_i^0\right) b_i^1 + \varepsilon\left(f_i\right)_{c_i}\left(b_i^0,c_i^0\right) c_i^1 + ...,$$

$$K_i(b_i,c_i) = K_i\left(b_i^0,c_i^0\right) + \varepsilon\left(K_i\right)_{b_i}\left(b_i^0,c_i^0\right) b_i^1 + \varepsilon\left(K_i\right)_{c_i}\left(b_i^0,c_i^0\right) c_i^1 + ...,$$

$$\varphi_i(b_i,c_i) = \varphi_i\left(b_i^0,c_i^0\right) + \varepsilon\left(\varphi_i\right)_{b_i}\left(b_i^0,c_i^0\right) b_i^1 + \varepsilon\left(\varphi_i\right)_{c_i}\left(b_i^0,c_i^0\right) c_i^1 + ...$$

J. Cole (1968). Perturbation Methods in Applied Mathematics. Blaisdell, Walthem, MA.

2 0-order approximation

$$\frac{\partial c_i^0}{\partial t} = 0$$
$$c_i^0(0,\xi) = c_{i,0}.$$

$c_i^0(t,\xi) = c_{i,0} =$ constant.

0-order approximation

$$
\begin{aligned}
&\frac{\partial b_i}{\partial t} - \overline{D} D_i \Delta b_i - \overline{f} f_i \left(b_i, c_{i,0}\right) = 0 \text{ in } Q_i, \\
&b_i(0,\xi) = b_{i,0}(\xi) \text{ in } \Omega_i, \\
&b_i = b_{i+1} \text{ on } \Sigma_i, \\
&D_i \frac{\partial b_i}{\partial x} = D_{i+1} \frac{\partial b_{i+1}}{\partial x} \text{ on } \Sigma_i, \\
&\frac{\partial b_1}{\partial x} = 0 \text{ on } \Sigma_0, \\
&\frac{\partial b_n}{\partial x} = 0 \text{ on } \Sigma_n, \\
&\nabla b_i \cdot \nu = 0 \text{ on } \Sigma_i^{lat}.
\end{aligned}
$$

0-order approximation

$$\frac{\partial b_i}{\partial t} - \overline{D} D_i \Delta b_i + \mu_i(b_i) = 0 \;\text{ in } Q_i,$$
$$b_i(0,\xi) = b_{i,0}(\xi) \;\text{ in } \Omega_i,$$
$$b_i = b_{i+1} \;\text{ on } \Sigma_i,$$
$$D_i \frac{\partial b_i}{\partial x} = D_{i+1} \frac{\partial b_{i+1}}{\partial x} \;\text{ on } \Sigma_i,$$
$$\frac{\partial b_1}{\partial x} = 0 \;\text{ on } \Sigma_0,$$
$$\frac{\partial b_n}{\partial x} = 0 \;\text{ on } \Sigma_n,$$
$$\nabla b_i \cdot \nu = 0 \;\text{ on } \Sigma_i^{lat}.$$

$$|\mu_i'(r)| \leq \overline{f} C_1^i (1 + |r|^p), \;\forall r \in \mathbb{R},$$

$$0 \;\leq\; p < 2 \text{ if } N = 3,$$
$$0 \;\leq\; p < \infty \text{ if } N = 1, 2.$$

Functional framework

$$\Phi(x) = \begin{cases} \Phi_1, \ \ x \in (x_0, x_1) \\ \ldots \\ \Phi_n, \, x \in (x_{n-1}, x_n) \end{cases}$$

$b_0, c_0, D, \ldots$

$$D(x) = \begin{cases} D_1, \ \ x \in (x_0, x_1) \\ \ldots \\ D_n, \, x \in (x_{n-1}, x_n) \end{cases}$$

0-order approximation: Functional framework

$$V = H^1(\Omega),\ V' = (H^1(\Omega))'$$

Introduce $A_0 : V \to V'$

$$\begin{aligned}\langle A_0 b, \psi\rangle_{V',V} &= \sum_{i=1}^{n} \int_{\Omega_i} \left[\overline{D} D_i \nabla b_i \cdot \nabla\psi + \mu_i\left(b_i\right)\psi\right] d\xi \\ &= \int_{\Omega} \left[D(x)\nabla b \cdot \nabla\psi + \mu\left(b, x\right)\psi\right] d\xi,\ \ \forall\psi \in V\end{aligned}$$

Introduce $A : D\left(A\right) \subset L^2\left(\Omega\right) \to L^2\left(\Omega\right)$

$$Ab = A_0 b,\ \forall b \in D\left(A\right)$$

where $D(A) = \left\{b \in V,\ Ab \in L^2\left(\Omega\right)\right\}$.

0-order of approximation

$$\frac{db}{dt}(t) + Ab(t) = 0 \text{ a.e. } t \in (0,T)\,,$$
$$b(0) = b_0.$$

0-order of approximation

$$\frac{db}{dt}(t) + Ab(t) = 0 \text{ a.e. } t \in (0,T)\,,$$
$$b(0) = b_0.$$

Theorem. *Let*

$$b_0 \in H^1(\Omega),\ Ab_0 \in L^2(\Omega),\ b_0 \geq 0\ a.e.\ in\ \Omega.$$

Then the Cauchy problem has a unique solution

$$b \in W^{1,\infty}([0,T];L^2(\Omega)) \cap L^\infty\left(0,T;H^1(\Omega)\right)$$

which is positive and satisfies the estimate

$$\|b(t)\|_{H^1(\Omega)} \leq C_V, \text{ for any } t \in [0,T],$$

where C_V depends on the problem data.

0-order of approximation

Sketch of the proof

I. Prove

$$b \longrightarrow \mu(b, x) \text{ is locally Lipschitz from } H^1(\Omega) \text{ to } L^2(\Omega) \text{ uniformly in } x$$

0-order of approximation

Sketch of the proof

I. Prove

$$b \longrightarrow \mu(b,x) \text{ is locally Lipschitz from } H^1(\Omega) \text{ to } L^2(\Omega) \text{ uniformly in } x$$

II. Operator truncation: A (corresponding to μ) is replaced by A_N corresponding to

$$\mu_N(b,x) = \begin{cases} \mu(b,x), & \|b\|_{H^1(\Omega)} \leq N \\ \mu\left(\dfrac{Nb}{\|b\|_V}, x\right), & \|b\|_{H^1(\Omega)} > N \end{cases}$$

which is Lipschitz from $H^1(\Omega)$ to $L^2(\Omega)$.

0-order of approximation

III. Prove existence for the problem

$$\frac{db_N}{dt}(t) + A_N b_N(t) = 0 \text{ a.e. } t \in (0,T)\,,$$
$$b_N(0) = b_0.$$

$$b_N \in W^{1,\infty}([0,T]; L^2(\Omega)) \cap L^\infty\left(0,T; H^1(\Omega)\right),$$

$$\|b_N(t)\|_{H^1(\Omega)} \le C_0 \|b_0\|_{H^1(\Omega)} := C_V, \text{ for any } t \in [0,T].$$

0-order of approximation

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IV. Take $N > C_V \Longrightarrow$

$$A_N b_N(t) = A b_N(t)$$

$\Longrightarrow b_N(t)$ is the solution to the problem.

0-order of approximation

III. Prove existence for the problem

$$\frac{db_N}{dt}(t) + Ab_N(t) = 0 \text{ a.e. } t \in (0,T)\,,$$
$$b_N(0) = b_0.$$

$$b_N \in W^{1,\infty}([0,T]; L^2(\Omega)) \cap L^\infty\left(0,T; H^1(\Omega)\right),$$

$$\|b_N(t)\|_{H^1(\Omega)} \leq C_0 \|b_0\|_{H^1(\Omega)} := C_V, \text{ for any } t \in [0,T].$$

IV. Take $N > C_V \Longrightarrow$

$$A_N b_N(t) = Ab_N(t)$$

$\Longrightarrow b_N(t)$ is the solution to the problem.

Proposition. *Under the assumptions of* Theorem *it follows that*

$$b_i \in L^2(0, T; H^2(\Omega_i)),\ i = 1, ..., n.$$

3 1-order approximation

1-order approximation

$$\frac{\partial c_i^1}{\partial t} = \varphi_i(b_i^0(\tau,\xi), c_{i,0}),$$

$$c_i^1(0,x) = 0.$$

$\Longrightarrow$

$$c_i^1\,(t,\xi) = \int_0^t \varphi_i(b_i^0(\tau,\xi), c_{i,0})d\tau.$$

$$\frac{\partial b_i}{\partial t} - \overline{D}D_i \Delta b_i + a_i\left(t,\xi\right) b_i = F_i(t,\xi) \text{ in } Q_i,$$
$$b_i\left(0,\xi\right) = 0, \text{ in } \Omega_i,$$
$$b_i\left(t,x_i,\xi'\right) = b_{i+1}\left(t,x_i,\xi'\right) \text{ on } \Sigma_i,$$
$$\left(-\overline{D}D_i \frac{\partial b_i}{\partial x} + \overline{D}D_{i+1}\frac{\partial b_{i+1}}{\partial x}\right)\Bigg|_{x=x_i} = G_i\left(t,x_i,\xi'\right) \text{ on } \Sigma_i,$$
$$-\overline{D}D_1 \frac{\partial b_1}{\partial x}\Bigg|_{x=x_0} = G_0\left(t,x_0,\xi'\right) \text{ on } \Sigma_0,$$
$$\overline{D}D_n \frac{\partial b_n}{\partial x}\Bigg|_{x=x_n} = G_n\left(t,x_n,\xi'\right) \text{ on } \Sigma_n,$$
$$\nabla b_i \cdot \nu = 0 \text{ on } \Sigma_i^{lat}.$$

1-order approximation

The Cauchy problem:

$$\frac{db}{dt}(t) + B(t)b(t) = L\,(t) \text{ a.e. } t \in (0,T)\,,$$
$$b(0) = 0.$$

where $B(t) : H^1(\Omega) \to (H^1(\Omega))'$

$$\langle B\,(t)\,b, \psi\rangle_{(H^1(\Omega))', H^1(\Omega)} = \int\limits_\Omega D(x)\nabla b \cdot \nabla \psi d\xi + \int\limits_\Omega a\,(t,\xi)\,b\psi d\xi.$$

$$a_i\,(t,\xi) = -\overline{f}\,(f_i)_{b_i}\left(b_i^0\,(t,\xi)\,, c_{i,0}\right),$$

and $L\,(t) : H^1(\Omega) \longrightarrow (H^1(\Omega))'$

$$\begin{aligned}
&\langle L\,(t)\,, \psi\rangle_{(H^1(\Omega))', H^1(\Omega)} \\
&= \sum_{i=1}^n \int_{\Omega_i} \left(\overline{f}(f_i)_{c_i}(b_i^0(t,\xi), c_{i,0})\psi + \overline{K} b_i^0(t,\xi) K_i(b_i^0(t,\xi), c_{i,0}) \nabla c_i^1 \cdot \nabla \psi\right) d\xi \\
&+ \overline{K} \sum_{i=1}^n \int_{\Gamma_i} \left(-b_i^0(t,\xi)K_i(b_i^0, c_{i,0})\frac{\partial c_i^1}{\partial x} + b_{i+1}^0(t,\xi)K_{i+1}(b_{i+1}^0, c_{i+1,0})\frac{\partial c_{i+1}^1}{\partial x}\right)\psi\Big|_{x=x_i} d\sigma.
\end{aligned}$$

1-order approximation

Theorem. *The Cauchy problem for the ε^1-order approximation has a unique solution*

$$b^1 \in W^{1,2}\left([0,T];(H^1(\Omega))'\right) \cap L^2\left(0,T;H^1(\Omega)\right) \cap C\left([0,T];L^2(\Omega)\right).$$

Corollary. *Problem in the stratified domain admits a unique asymptotic solution up the the order of approximation ε,*

$$\begin{aligned} \widetilde{b} &\in C\left([0,T];L^2(\Omega)\right) \cap W^{1,2}[0,T];(H^1(\Omega))' \cap L^2\left(0,T;H^1(\Omega)\right), \\ \widetilde{c} &\in L^\infty(Q), \end{aligned}$$

given by

$$\begin{aligned} \widetilde{b}(t,\xi) &= b^0(t,\xi) + \varepsilon b^1(t,\xi), \\ \widetilde{c}(t,\xi) &= c^0(t,\xi) + \varepsilon c^1(t,\xi). \end{aligned}$$

In particular, the restrictions of the solution to each layer have the properties

$$\begin{aligned} \widetilde{b_i} &\in W^{1,2}\left([0,T];(H^1(\Omega_i))' \cap L^2\left(0,T;H^1(\Omega_i)\right) \cap C\left([0,T];L^2(\Omega_i)\right)\right), \\ \widetilde{c_i} &\in W^{1,\infty}(Q_i) \cap W^{1,\infty}\left([0,T];H^1(\Omega_i)\right) \\ &\quad \cap C^1([0,T];L^2(\Omega_i)) \cap W^{1,2}(0,T;H^2(\Omega_i)). \end{aligned}$$

4 Numerical simulations

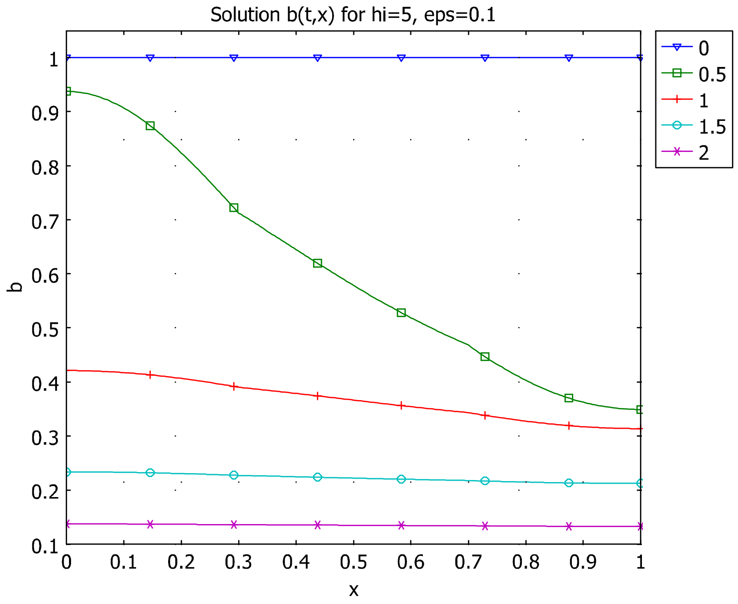
$$c_0 = \begin{cases} 2, & x \in [0, 0.3) \\ 1, & x \in [0.3, 0.7) \\ 0, & x \in [0, 7, 1]. \end{cases} , \quad \delta = \varepsilon \begin{cases} 1, & x \in [0, 0.3) \\ 2, & x \in [0.3, 0.7) \\ 1, & x \in [0, 7, 1]. \end{cases} , \quad D = 1$$

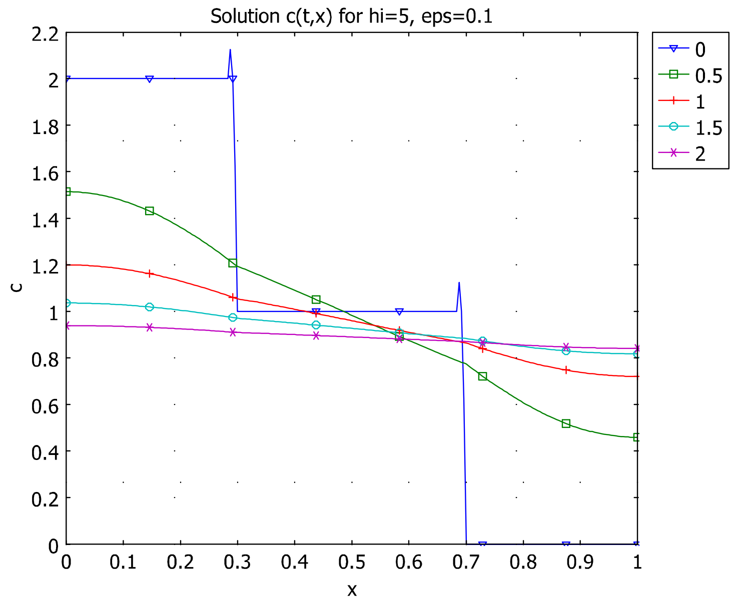
$$K(b, c) = \chi \frac{b}{(1 + c)^2}$$

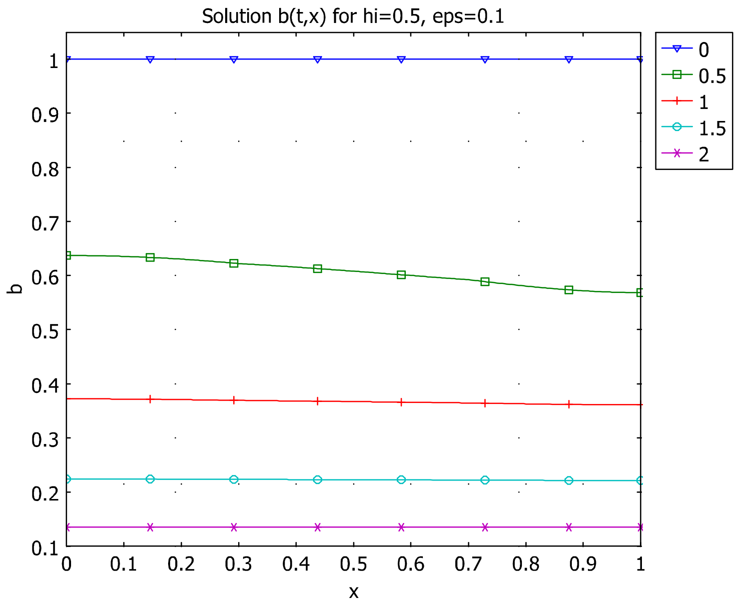
$$\varphi(b, c) = \varepsilon(b - c)$$

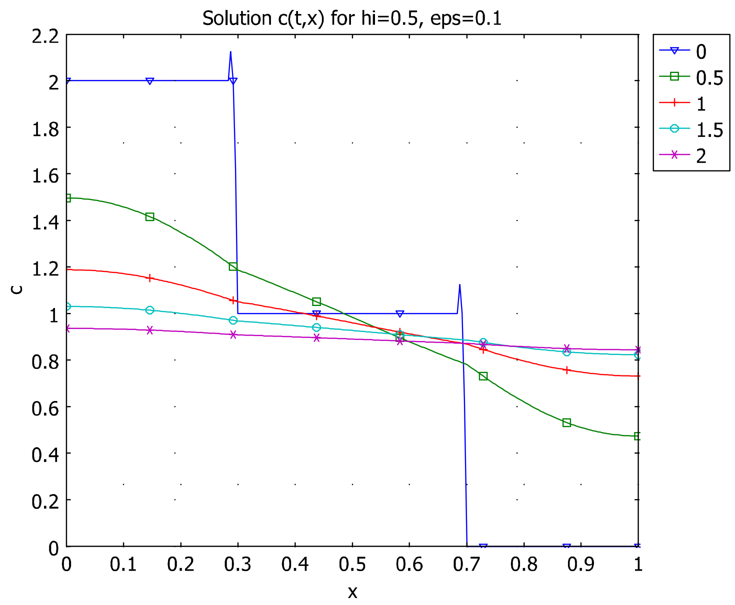
Comsol Multiphysics

A higher chemotactic sensitivity $\chi = 5$ versus a lower chemotactic sensitivity $\chi = 0.5$

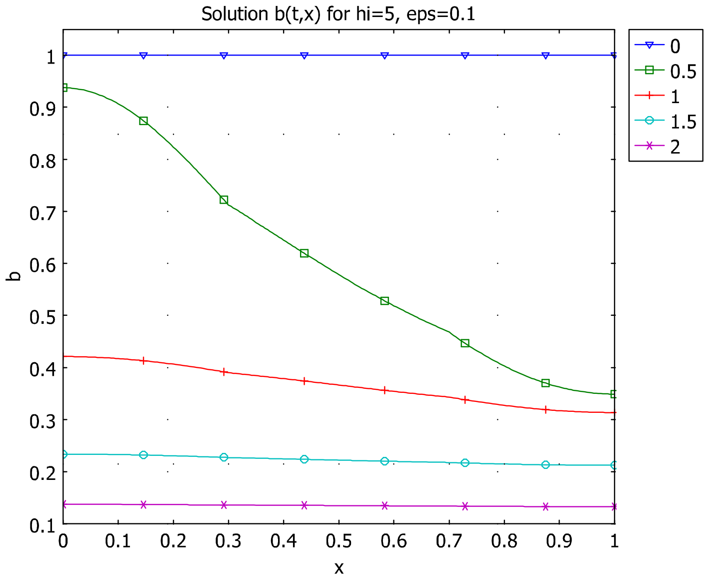

Solution b(t,x) for hi=5, eps=0.1
b
x
0
0.5
1
1.5
2

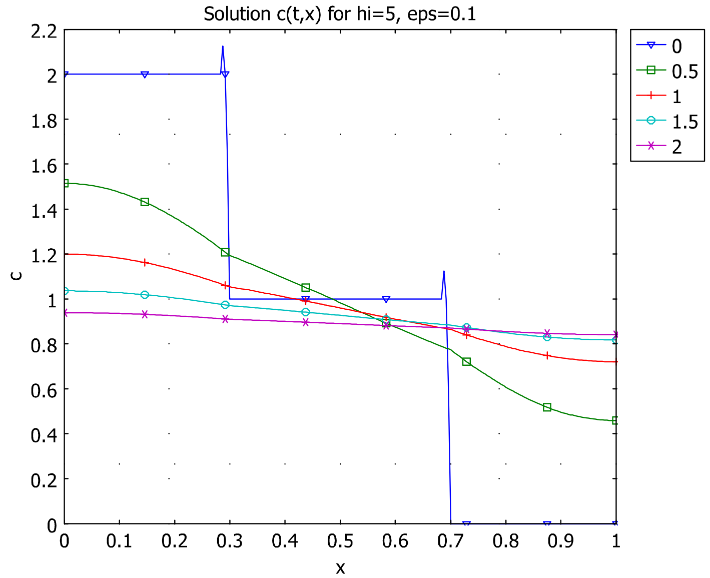

Solution c(t,x) for hi=5, eps=0.1
c
x
0
0.5
1
1.5
2

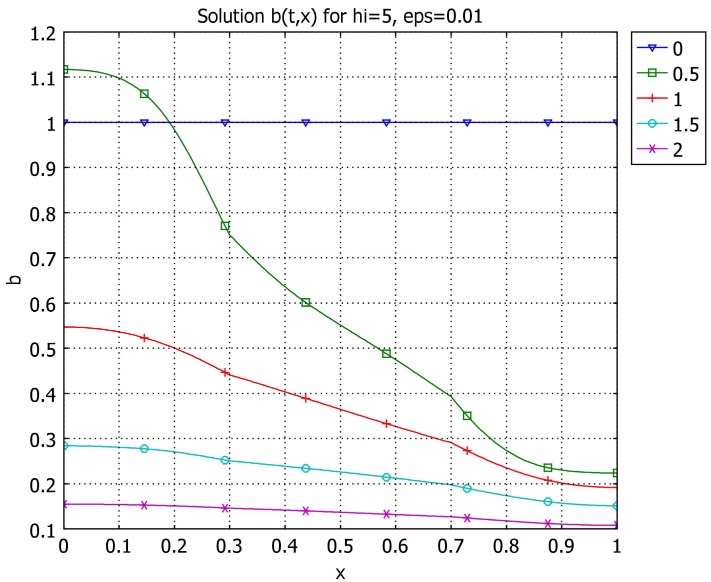

Solution b(t,x) for hi=0.5, eps=0.1
b
x
0
0.5
1
1.5
2

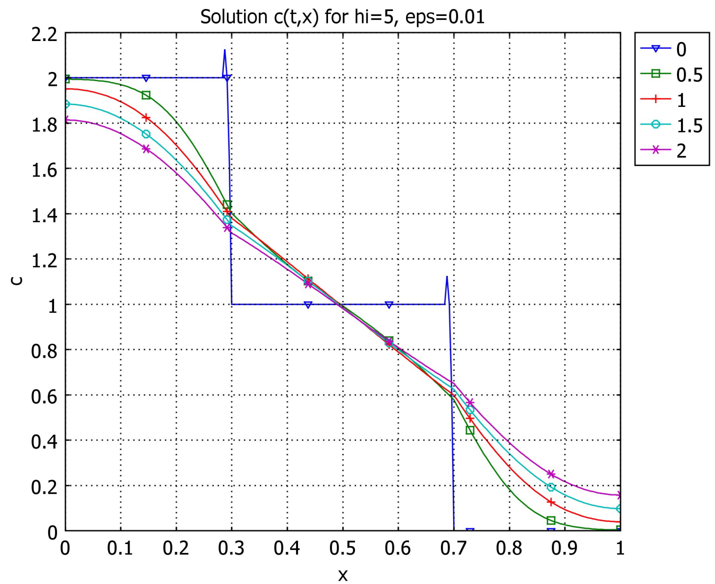

Solution c(t,x) for hi=0.5, eps=0.1
c
x
0
0.5
1
1.5
2

A higher rate of degradation and diffusion coefficient $\varepsilon = 0.1$ versus a lower rate of degradation and diffusion $\varepsilon = 0.01$


Solution b(t,x) for hi=5, eps=0.1
b
x
0
0.5
1
1.5
2


Solution c(t,x) for hi=5, eps=0.1
c
x
0
0.5
1
1.5
2


Solution b(t,x) for hi=5, eps=0.01
b
x
0
0.5
1
1.5
2


Solution c(t,x) for hi=5, eps=0.01
c
x
0
0.5
1
1.5
2

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Thank you for your attention !