

Computer Modelling of Haematopoietic Stem Cells Migration

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Contents

Motivation

Model of HSCs' movement

Numerical solution

Concluding remarks

- Motivation
- Model of HSCs' chemotactic movement
- Numerical solution
- Concluding remarks

Motivation

- Haematopoiesis
- Blood pathologies
- HSCs after transplantation ...

Model of HSCs' movement

Numerical solution

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Motivation

Blood cells production and regulation

Motivation

● Haematopoiesis

● Blood pathologies

● HSCs after transplantation ...

Model of HSCs' movement

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Concluding remarks

Haematopoietic pluripotent stem cells (HSCs) in bone marrow give birth to the three blood cell types, because of their

- *rapid migratory activity* and ability to "home" to their niche in the bone marrow;
- *high self-renewal and differentiation capacity*, responsible for the production and regulation of the three blood cell types.

Growth factors or **Colony Stimulating Factors** (CSF) – specific proteins that stimulate the production and maturation of each blood cell type.

Blast cells – blood cells that have not yet matured.

Blood cell type	Function	Growth factors
Erythrocyte	Transport oxygen to tissues	Erythropoietin
Leukocyte	Fight infections	G-CSF, M-CSF, GM-CSF, Interleukins
Thrombocyte	Control bleeding	Thrombopoietin

Blood pathologies

Various **hematological diseases** (including leukaemia) are characterized by **abnormal production** of particular blood cells (matured or blast).

Main stages in the therapy of blood diseases:

TBI: Total body irradiation (TBI) and chemotherapy – kill the "tumour" cells, but also the healthy ones.

BMT: Bone marrow transplantation (BMT) – stem cells of a donor (collected under special conditions) are put in the peripheral blood.

After BMT, HSCs have to:

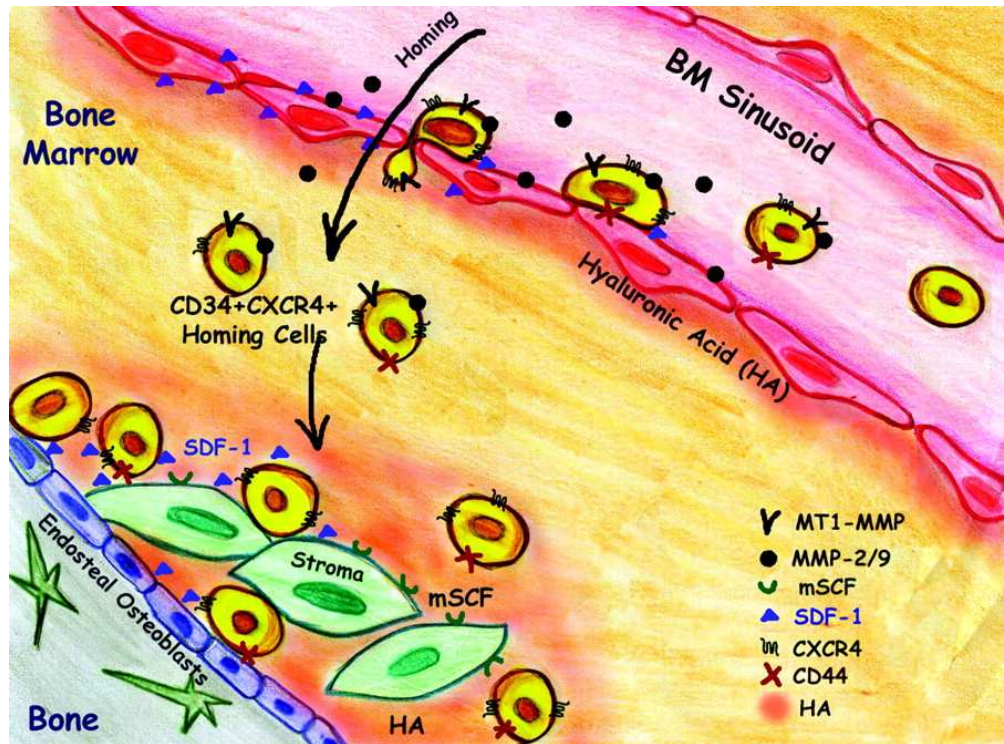
1. find their way to the stem cell niche in the bone marrow; and
2. selfrenew and differentiate to regenerate the patient's blood system.

Adequate computer models would help medical doctors to

- understand better the HSCs migration and differentiation processes;
- design nature experiments for validation of hypotheses;
- predict the effect of various treatment options for specific blood diseases;
- shorten the period in which the patient is missing their effective immune system.

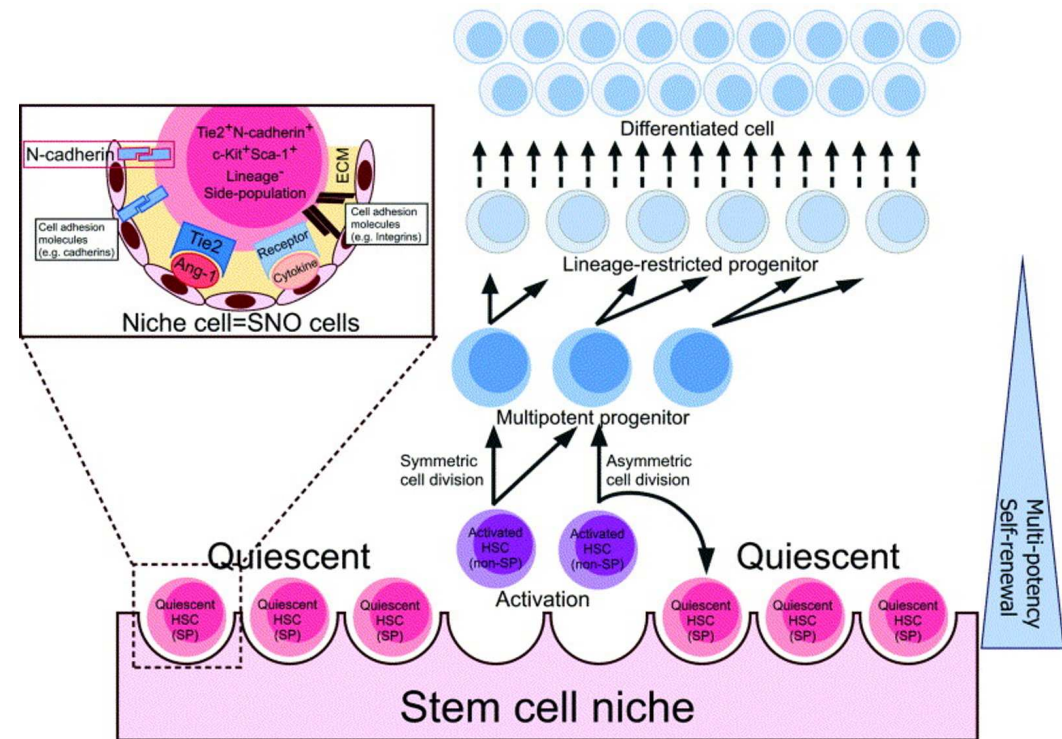
HSCs after transplantation ...

... find the way to the niche, and ...



T. Lapidot, A. Dar, O. Kollet, How do stem cells find their way home?, Blood, Vol. 106(6), (2005), 1901–1910.

... self-renew and differentiate



T. Suda, F. Arai, A. Hirao, Hematopoietic stem cells and their niche, Trends in Immunology, Vol. 26(8), (2005), 426–433.

Motivation

Model of HSCs' movement

- Involved data
- The model

Numerical solution

Concluding remarks

Model of HSCs' chemotactic movement

Involved data

Unknowns:

$s(t, \mathbf{x})$ – concentration of stem cells in $\Omega \in R^2$

$a(t, \mathbf{x})$ – concentration of chemoattractant

$b(t, \mathbf{x})$ – concentration of stem cells bound to stroma cells at the boundary part Γ_1

$$s(t, \mathbf{x}) \geq 0, a(t, \mathbf{x}) \geq 0, b(t, \mathbf{x}) \geq 0$$

Parameters:

ε – random motility coefficient of HSCs

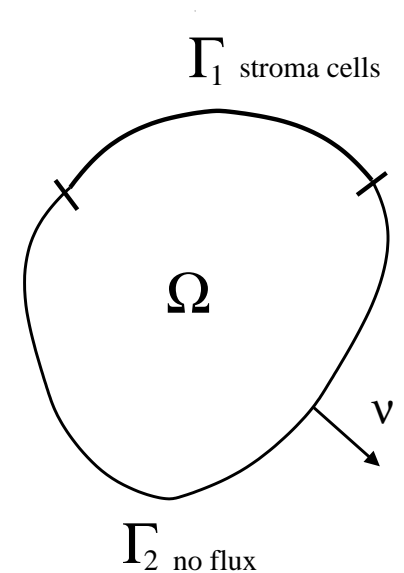
$\chi(a)$ – chemotactic sensitivity function

D_a – diffusion coefficient of chemoattractant

γ – consumption rate-constant for SDF-1

$c(\mathbf{x})$ – concentration of stroma cells on Γ_1

$\beta(t, b)$ – proportionality function in the production rate of chemoattractant



$$\begin{aligned} \mathbf{x} &= (x, y) \in \Omega \\ \partial\Omega &= \Gamma_1 \cup \Gamma_2 \\ \Gamma_1 \cap \Gamma_2 &= \emptyset \end{aligned}$$

A. Kettemann, M. Neuss-Radu, Derivation and analysis of a system modeling the chemotactic movement of hematopoietic stem cells, Journal of Mathematical Biology, 56, (2008), 579-610.

Motivation

Model of HSCs' movement

● Involved data

● The model

Numerical solution

Concluding remarks

The model

Motivation

Model of HSCs' movement

● Involved data

● The model

Numerical solution

Concluding remarks

$$\begin{cases} \partial_t s &= \nabla \cdot (\varepsilon \nabla s - s \nabla \chi(a)), & \text{in } (0, T) \times \Omega \\ \partial_t a &= D_a \Delta a - \gamma a s, & \text{in } (0, T) \times \Omega \end{cases}$$

$$-(\varepsilon \partial_\nu s - s \chi'(a) \partial_\nu a) = \begin{cases} c_1 s - c_2 b, & \text{on } (0, T) \times \Gamma_1 \\ 0, & \text{on } (0, T) \times \Gamma_2 \end{cases}$$

$$D_a \partial_\nu a = \begin{cases} \beta(t, b) c(\mathbf{x}), & \text{on } (0, T) \times \Gamma_1 \\ 0, & \text{on } (0, T) \times \Gamma_2 \end{cases}$$

$$\begin{aligned} \partial_t b &= c_1 s - c_2 b, \quad \text{on } (0, T) \times \Gamma_1 \quad \text{and} \quad b = 0, \quad \text{on } (0, T) \times \Gamma_2 \\ s(0) &= s_0, \quad a(0) = a_0 \quad \text{in } \Omega, \quad \text{and} \quad b(0) = b_0 \quad \text{on } \Gamma_1 \end{aligned}$$

Existence of unique solution is ensured by

$$c \in H^{\frac{1}{2}}(\partial\Omega), \quad \beta \in C^1(R \times R, R), \quad \chi \in C^2(R)$$

$$0 \leq c(\mathbf{x}) \leq \bar{c}, \quad \mathbf{x} \in \Gamma_1 \quad \text{and} \quad c \equiv 0, \quad \mathbf{x} \in \Gamma_2$$

$$\beta(0, b_0) = 0, \quad 0 \leq \beta(t, b) \leq M, \quad \left| \frac{\partial \beta}{\partial b}(t, b) \right| \leq M_s, \quad \left| \frac{\partial \beta}{\partial t}(t, b) \right| \leq M_t$$

$$\chi \in \{ \chi \in C^2(R) \mid 0 \leq \chi(a), 0 \leq \chi'(a) \leq C_\chi, |\chi''(a)| \leq C'_\chi, a \in R \}$$

Motivation

Model of HSCs' movement

Numerical solution

- Conservation form
- Semi-discrete scheme
- Time integration
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Concluding remarks

Numerical solution

Initial system in conservation form

$$\begin{aligned}
 s_t + \left(s \frac{\partial \chi}{\partial a} p \right)_x + \left(s \frac{\partial \chi}{\partial a} q \right)_y &= \nabla \cdot (\varepsilon \nabla s) & \mathbf{x} = (x, y) \in \Omega \\
 a_t &= D_a \Delta a - \gamma a s & p(t, \mathbf{x}) := \left(a(t, \mathbf{x}) \right)_x \\
 p_t + (\gamma a s)_x &= D_a \Delta p & q(t, \mathbf{x}) := \left(a(t, \mathbf{x}) \right)_y \\
 q_t + (\gamma a s)_y &= D_a \Delta q
 \end{aligned}$$

Boundary conditions:

$$-(\varepsilon \partial_\nu s - s \chi'(a) \partial_\nu a) = \begin{cases} c_1 s - c_2 b, & \text{on } (0, T) \times \Gamma_1 \\ 0, & \text{on } (0, T) \times \Gamma_2 \end{cases}$$

$$D_a \partial_\nu a = \begin{cases} \beta(t, b) c(\mathbf{x}), & \text{on } (0, T) \times \Gamma_1 \\ 0, & \text{on } (0, T) \times \Gamma_2 \end{cases}$$

$$D_a \partial_\nu p = \begin{cases} \left(\beta(t, b) c(\mathbf{x}) \right)_x, & \text{on } (0, T) \times \Gamma_1 \\ 0, & \text{on } (0, T) \times \Gamma_2 \end{cases}$$

$$D_a \partial_\nu q = \begin{cases} \left(\beta(t, b) c(\mathbf{x}) \right)_y, & \text{on } (0, T) \times \Gamma_1 \\ 0, & \text{on } (0, T) \times \Gamma_2 \end{cases}$$

Initial conditions:

$$\begin{aligned}
 s(0, \mathbf{x}) &= s_0(\mathbf{x}), \\
 a(0, \mathbf{x}) &= a_0(\mathbf{x}),
 \end{aligned}$$

$$\begin{aligned}
 p(0, \mathbf{x}) &= p_0(\mathbf{x}) \equiv \left(a_0(\mathbf{x}) \right)_x \\
 q(0, \mathbf{x}) &= q_0(\mathbf{x}) \equiv \left(a_0(\mathbf{x}) \right)_y
 \end{aligned}$$

Evolution of $b(t, \mathbf{x})$:

$$\begin{aligned}
 \partial_t b &= c_1 s - c_2 b, & \text{on } (0, T) \times \Gamma_1 \\
 b &= 0, & \text{on } (0, T) \times \Gamma_2 \\
 b(0, \mathbf{x}) &= b_0(\mathbf{x}), & \text{on } \Gamma_1
 \end{aligned}$$

Initial system in conservation form – cont.

	PDE	ODE
	$\frac{d\mathbf{U}}{dt} + \operatorname{div}\mathbf{F}(\mathbf{U}) = \mathbf{R}(\mathbf{U}), \quad t \in (0, T), \mathbf{x} \in \Omega$	$\frac{db}{dt} = B(U, b), \quad t \in (0, T), \mathbf{x} \in \Gamma_1$
	$\frac{\partial \mathbf{F}}{\partial \mathbf{n}} = h(U, b, \mathbf{x}, t), \quad t \in (0, T), \mathbf{x} \in \partial\Omega$	$b(0, \mathbf{x}) = b_0(\mathbf{x}), \quad \mathbf{x} \in \Gamma_1$
	$\mathbf{U}(\mathbf{x}, 0) = \mathbf{U}_0, \quad \mathbf{x} \in \Omega$	$b = 0, \quad t \in (0, T), \mathbf{x} \in \Gamma_2$

$$\mathbf{F}(\mathbf{U}) = \mathbf{F}_c(\mathbf{U}) + F_d(\mathbf{U}), \text{ where } \mathbf{F}_c(\mathbf{U}) = (\mathbf{f}, \mathbf{g}), \mathbf{F}_d(\mathbf{U}) = -\Lambda \nabla \mathbf{U}$$

$$\mathbf{U} = (s, a, p, q)^T, \quad \mathbf{f}(\mathbf{U}) = (s\chi_a p, 0, \gamma a s, 0)^T, \quad \mathbf{g}(\mathbf{U}) = (s\chi_a q, 0, 0, \gamma a s)^T$$

$$p = a_x, \quad q = a_y, \quad \Lambda = \operatorname{diag}(\varepsilon, D_a, D_a, D_a), \quad \mathbf{R}(\mathbf{U}) = (0, -\gamma a s, 0, 0)^T$$

$$\lambda_i^{\mathbf{f}}(U), \lambda_i^{\mathbf{g}}(U) - \text{eigenvalues of } \frac{\partial \mathbf{f}}{\partial \mathbf{U}} \text{ and } \frac{\partial \mathbf{g}}{\partial \mathbf{U}}$$

A. Chertock, A. Kurganov, A second-order positivity preserving central-upwind scheme for chemotaxis and haptotaxis models, Numer. Math. (2008) 111: 169-205.

Finite volume method

$$\bar{\Omega} = [0, A] \times [0, B], \quad A, B > 0, \quad \Delta x = \frac{A}{N_x}, \quad \Delta y = \frac{B}{N_y}$$

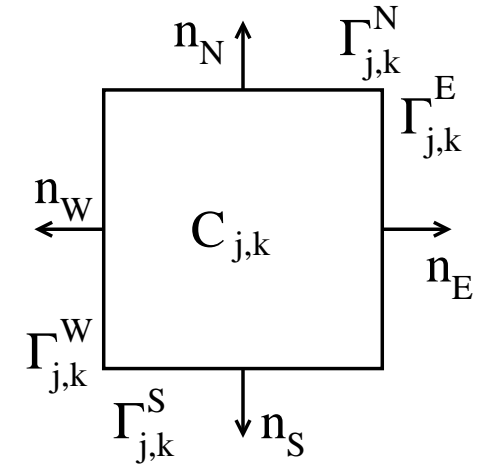
$$\Omega = \cup C_{j,k}, \quad j = 1, \dots, N_x, \quad k = 1, \dots, N_y, \quad \partial\Omega = \Gamma^E \cup \Gamma^W \cup \Gamma^N \cup \Gamma^S$$

$$C_{j,k} := [x_{j-\frac{1}{2}}, x_{j+\frac{1}{2}}] \times [y_{k-\frac{1}{2}}, y_{k+\frac{1}{2}}]$$

$$x_{\frac{1}{2}} = 0, \quad x_{N_x+\frac{1}{2}} = A, \quad x_{j+\frac{1}{2}} = x_{j-\frac{1}{2}} + \Delta x$$

$$y_{\frac{1}{2}} = 0, \quad y_{N_y+\frac{1}{2}} = B, \quad y_{k+\frac{1}{2}} = y_{k-\frac{1}{2}} + \Delta y$$

$$\partial C_{j,k} = \Gamma_{j,k}^E \cup \Gamma_{j,k}^W \cup \Gamma_{j,k}^N \cup \Gamma_{j,k}^S$$



$$\bar{U}_{j,k}(t) = \frac{1}{\Delta x \Delta y} \iint_{C_{j,k}} U(x, y, t) dx dy - \text{unknowns of the discrete system}$$

Piecewise linear reconstruction \tilde{U} for U obtained at each time step:

$$\tilde{U}(x, y) := \bar{U}_{j,k} + (U_x)_{j,k}(x - x_j) + (U_y)_{j,k}(y - y_k), \quad (x, y) \in C_{j,k}$$

should be conservative, nonoscillatory and positivity preserving.

Motivation

Model of HSCs' movement

Numerical solution

● Conservation form

● Semi-discrete scheme

● Time integration

● Numerical tests

Concluding remarks

Semi-discrete scheme

$$\iint_{C_{j,k}} \mathbf{U}_t \, dx dy + \iint_{C_{j,k}} \operatorname{div}(\mathbf{F}_c + \mathbf{F}_d) \, dx dy = \iint_{C_{j,k}} \mathbf{R} \, dx dy ,$$

$$\frac{d}{dt} \bar{\mathbf{U}}_{j,k}(t) + \frac{1}{\Delta x \Delta y} \int_{\partial C_{j,k}} (\mathbf{F}_c + \mathbf{F}_d) \cdot \mathbf{n} \, d\gamma = \bar{\mathbf{R}}_{j,k} ,$$

$$I_{j,k}^c = \int_{\partial C_{j,k}} \mathbf{F}_c \cdot \mathbf{n} \, d\gamma \quad \text{and} \quad I_{j,k}^d = \int_{\partial C_{j,k}} \mathbf{F}_d \cdot \mathbf{n} \, d\gamma$$

$$\begin{aligned} I_{j,k}^c + I_{j,k}^d &= \int_{\Gamma_{j,k}^E} (\mathbf{F}_c + \mathbf{F}_d) \cdot \mathbf{n}_E \, d\gamma + \int_{\Gamma_{j,k}^W} (\mathbf{F}_c + \mathbf{F}_d) \cdot \mathbf{n}_W \, d\gamma \\ &+ \int_{\Gamma_{j,k}^N} (\mathbf{F}_c + \mathbf{F}_d) \cdot \mathbf{n}_N \, d\gamma + \int_{\Gamma_{j,k}^S} (\mathbf{F}_c + \mathbf{F}_d) \cdot \mathbf{n}_S \, d\gamma , \end{aligned}$$

Integrals on $\Gamma_{1,k}^W$, $\Gamma_{N_x,k}^E$, $\Gamma_{j,1}^S$ and Γ_{j,N_y}^N are computed from b.c.

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- Conservation form
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Concluding remarks

Semi-discrete scheme – cont.

$$\begin{aligned} \frac{d}{dt} \bar{U}_{j,k} = & -\frac{\mathbf{H}_{j+\frac{1}{2},k}^x - \mathbf{H}_{j-\frac{1}{2},k}^x}{\Delta x} - \frac{\mathbf{H}_{j,k+\frac{1}{2}}^y - \mathbf{H}_{j,k-\frac{1}{2}}^y}{\Delta y} \\ & + \frac{\mathbf{Q}_{j+\frac{1}{2},k}^x - \mathbf{Q}_{j-\frac{1}{2},k}^x}{\Delta x} + \frac{\mathbf{Q}_{j,k+\frac{1}{2}}^y - \mathbf{Q}_{j,k-\frac{1}{2}}^y}{\Delta y} + \bar{\mathbf{R}}_{j,k} \end{aligned}$$

Terms with $\mathbf{H}^{x,y}$ come from approximation of $I_{j,k}^c$
 Terms with $\mathbf{Q}^{x,y}$ come from approximation of $I_{j,k}^d$

$$\begin{aligned} \mathbf{Q}_{j+\frac{1}{2},k}^x &= \frac{\Lambda}{\Delta x} (\bar{U}_{j+1,k} - \bar{U}_{j,k}), & \mathbf{Q}_{j-\frac{1}{2},k}^x &= \frac{\Lambda}{\Delta x} (\bar{U}_{j,k} - \bar{U}_{j-1,k}) \\ \mathbf{Q}_{j,k+\frac{1}{2}}^y &= \frac{\Lambda}{\Delta y} (\bar{U}_{j,k+1} - \bar{U}_{j,k}), & \mathbf{Q}_{j,k-\frac{1}{2}}^y &= \frac{\Lambda}{\Delta y} (\bar{U}_{j,k} - \bar{U}_{j,k-1}) \\ \bar{h}_k^E &= \frac{1}{\Delta x} (\mathbf{Q}_{j+\frac{1}{2},k}^x - \mathbf{H}_{j+\frac{1}{2},k}^x), & \bar{h}_k^W &= -\frac{1}{\Delta x} (\mathbf{Q}_{j-\frac{1}{2},k}^x - \mathbf{H}_{j-\frac{1}{2},k}^x) \\ \bar{h}_j^N &= \frac{1}{\Delta y} (\mathbf{Q}_{j,k+\frac{1}{2}}^y - \mathbf{H}_{j,k+\frac{1}{2}}^y), & \bar{h}_j^S &= -\frac{1}{\Delta y} (\mathbf{Q}_{j,k-\frac{1}{2}}^y - \mathbf{H}_{j,k-\frac{1}{2}}^y) \end{aligned}$$

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Concluding remarks

Semi-discrete scheme – cont.

$$\frac{d}{dt} \bar{U}_{j,k} = - \frac{\mathbf{H}_{j+\frac{1}{2},k}^x - \mathbf{H}_{j-\frac{1}{2},k}^x}{\Delta x} - \frac{\mathbf{H}_{j,k+\frac{1}{2}}^y - \mathbf{H}_{j,k-\frac{1}{2}}^y}{\Delta y} + \Lambda \left[\frac{\bar{U}_{j+1,k} - 2\bar{U}_{j,k} + \bar{U}_{j-1,k}}{(\Delta x)^2} + \frac{\bar{U}_{j,k+1} - 2\bar{U}_{j,k} + \bar{U}_{j,k-1}}{(\Delta y)^2} \right] + \bar{\mathbf{R}}_{j,k}$$

$$\mathbf{H}_{j+\frac{1}{2},k}^x = \frac{a_{j+\frac{1}{2},k}^+ \mathbf{f}(\mathbf{U}_{j,k}^E) - a_{j+\frac{1}{2},k}^- \mathbf{f}(\mathbf{U}_{j+1,k}^W)}{a_{j+\frac{1}{2},k}^+ - a_{j+\frac{1}{2},k}^-} + \frac{a_{j+\frac{1}{2},k}^+ a_{j+\frac{1}{2},k}^-}{a_{j+\frac{1}{2},k}^+ - a_{j+\frac{1}{2},k}^-} [\mathbf{U}_{j+1,k}^W - \mathbf{U}_{j,k}^E]$$

$$\mathbf{H}_{j,k+\frac{1}{2}}^y = \frac{b_{j,k+\frac{1}{2}}^+ \mathbf{g}(\mathbf{U}_{j,k}^N) - b_{j,k+\frac{1}{2}}^- \mathbf{g}(\mathbf{U}_{j,k+1}^S)}{b_{j,k+\frac{1}{2}}^+ - b_{j,k+\frac{1}{2}}^-} + \frac{b_{j,k+\frac{1}{2}}^+ b_{j,k+\frac{1}{2}}^-}{b_{j,k+\frac{1}{2}}^+ - b_{j,k+\frac{1}{2}}^-} [\mathbf{U}_{j,k+1}^S - \mathbf{U}_{j,k}^N]$$

$a_{j+\frac{1}{2},k}^\pm, b_{j,k+\frac{1}{2}}^\pm$ – computed from $\lambda_i^{\mathbf{f}}, \lambda_i^{\mathbf{g}}$ for $\mathbf{U}_{j,k}^E, \mathbf{U}_{j+1,k}^W, \mathbf{U}_{j,k}^N, \mathbf{U}_{j,k+1}^S$

$\bar{\mathbf{R}}_{j,k} = \frac{1}{\Delta x \Delta y} \iint_{C_{j,k}} R(U(x, y, t)) dx dy$ – computed using midpoint rule

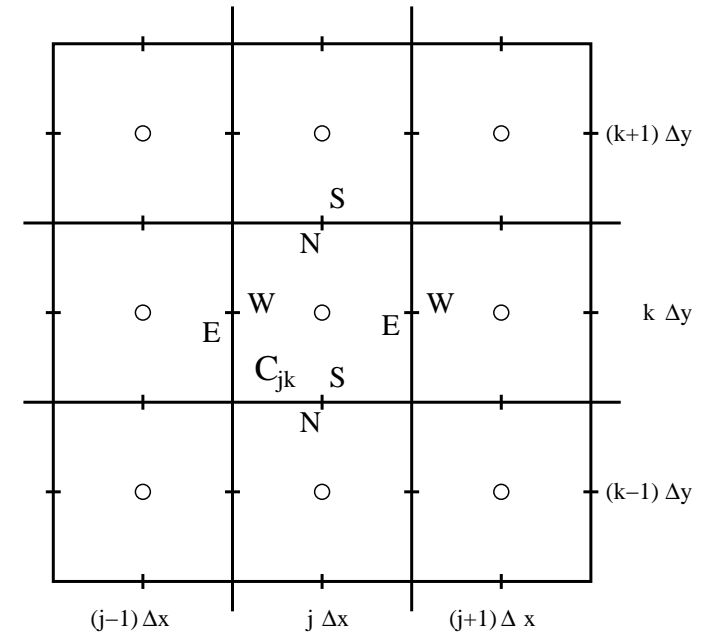
Semi-discrete scheme – cont.

$$\mathbf{U}_{j,k}^E := \tilde{\mathbf{U}}(x_{j+\frac{1}{2}} - 0, y_k) = \bar{\mathbf{U}}_{j,k} + \frac{\Delta x}{2} (\mathbf{U}_x)_{j,k}$$

$$\mathbf{U}_{j,k}^W := \tilde{\mathbf{U}}(x_{j-\frac{1}{2}} + 0, y_k) = \bar{\mathbf{U}}_{j,k} - \frac{\Delta x}{2} (\mathbf{U}_x)_{j,k}$$

$$\mathbf{U}_{j,k}^N := \tilde{\mathbf{U}}(x_j, y_{k+\frac{1}{2}} - 0) = \bar{\mathbf{U}}_{j,k} + \frac{\Delta y}{2} (\mathbf{U}_y)_{j,k}$$

$$\mathbf{U}_{j,k}^S := \tilde{\mathbf{U}}(x_j, y_{k-\frac{1}{2}} + 0) = \bar{\mathbf{U}}_{j,k} - \frac{\Delta y}{2} (\mathbf{U}_y)_{j,k}$$



$$(\mathbf{U}_x)_{j,k} = \text{minmod} \left(\ominus \frac{\bar{\mathbf{U}}_{j,k} - \bar{\mathbf{U}}_{j-1,k}}{\Delta x}, \frac{\bar{\mathbf{U}}_{j+1,k} - \bar{\mathbf{U}}_{j-1,k}}{2\Delta x}, \ominus \frac{\bar{\mathbf{U}}_{j+1,k} - \bar{\mathbf{U}}_{j,k}}{\Delta x} \right)$$

$$(\mathbf{U}_y)_{j,k} = \text{minmod} \left(\ominus \frac{\bar{\mathbf{U}}_{j,k} - \bar{\mathbf{U}}_{j,k-1}}{\Delta y}, \frac{\bar{\mathbf{U}}_{j,k+1} - \bar{\mathbf{U}}_{j,k-1}}{2\Delta y}, \ominus \frac{\bar{\mathbf{U}}_{j,k+1} - \bar{\mathbf{U}}_{j,k}}{\Delta y} \right)$$

$$\text{minmod}(z_1, z_2, \dots) := \begin{cases} \min_j \{z_j\}, & \text{if } z_j > 0 \quad \forall j, \\ \max_j \{z_j\}, & \text{if } z_j < 0 \quad \forall j, \\ 0, & \text{otherwise} \end{cases}$$

Time integration

$$\lambda := \frac{\Delta t}{\Delta x}, \quad \mu := \frac{\Delta t}{\Delta y}, \quad a := \max_{j,k} \{ \max \{ a_{j+\frac{1}{2},k}^+, -a_{j+\frac{1}{2},k}^- \} \}, \quad b := \max_{j,k} \{ \max \{ b_{j,k+\frac{1}{2}}^+, -b_{j,k+\frac{1}{2}}^- \} \}$$

■ Explicit Euler $\Delta t \leq \min\left(\frac{\Delta x}{8a}, \frac{\Delta y}{8b}, c\right)$, $c := \frac{(\Delta x)^2(\Delta y)^2}{4((\Delta x)^2 + (\Delta y)^2)}$

$$\begin{aligned} \bar{U}_{j,k}(t + \Delta t) = & \bar{U}_{j,k}(t) - \lambda \left(H_{j+\frac{1}{2},k}^x(t) - H_{j-\frac{1}{2},k}^x(t) \right) - \mu \left(H_{j,k+\frac{1}{2}}^y(t) - H_{j,k-\frac{1}{2}}^y(t) \right) \\ & + \Delta t \Lambda \frac{\bar{U}_{j+1,k}(t) - 2\bar{U}_{j,k}(t) + \bar{U}_{j-1,k}(t)}{(\Delta x)^2} \\ & + \Delta t \Lambda \frac{\bar{U}_{j,k+1}(t) - 2\bar{U}_{j,k}(t) + \bar{U}_{j,k-1}(t)}{(\Delta y)^2} + \Delta t \bar{\mathbf{R}}_{j,k}(t) \end{aligned}$$

■ IMEX Scheme $\Delta t \leq \min\left(\frac{\Delta x}{4a}, \frac{\Delta y}{4b}\right)$

$$\begin{aligned} \bar{U}_{j,k}(t + \Delta t) = & \bar{U}_{j,k}(t) - \lambda \left(H_{j+\frac{1}{2},k}^x(t) - H_{j-\frac{1}{2},k}^x(t) \right) - \mu \left(H_{j,k+\frac{1}{2}}^y(t) - H_{j,k-\frac{1}{2}}^y(t) \right) \\ & + \Delta t \Lambda \frac{\bar{U}_{j+1,k}(t + \Delta t) - 2\bar{U}_{j,k}(t + \Delta t) + \bar{U}_{j-1,k}(t + \Delta t)}{(\Delta x)^2} \\ & + \Delta t \Lambda \frac{\bar{U}_{j,k+1}(t + \Delta t) - 2\bar{U}_{j,k}(t + \Delta t) + \bar{U}_{j,k-1}(t + \Delta t)}{(\Delta y)^2} + \Delta t \bar{\mathbf{R}}_{j,k}(t + \Delta t) \end{aligned}$$

Numerical tests

Motivation

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- Conservation form
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Concluding remarks

Test data: $\Omega = (0, 1.5) \times (0, 1)$, $\Gamma_1 = \{x_1 = 1.5\}$, $\Delta t = 0.1$

$c(x_2) = 0.01(1 + 0.2 \sin(5\pi x_2))$, $\beta(t, b) = V(t)\beta^*(b)$ with

$$V(t) = \left\{ \begin{array}{ll} 4t^2(3 - 4t) & \text{for } t \leq 0.5 \\ 1 & \text{for } t > 0.5 \end{array} \right\} \text{ and } \beta^*(b) = \frac{0.005}{0.005 + b^2}$$

$$\chi(a) = 10a \quad \chi(a) = \log(a)$$

$$\varepsilon = 0.0015, D_a = 2, \gamma = 0.1, c_1 = 0.3, c_2 = 0.5$$

$$a_0 = 0, b_0 = 0 \text{ and}$$

$$s_0(x_1, x_2) = \left\{ \begin{array}{ll} (1 + \cos(5\pi(x_1 - 0.4)))\sin(\pi x_2), & \text{for } 0.2 \leq x_1 \leq 0.6 \\ 0 & \text{otherwise} \end{array} \right.$$

Classical approach

Motivation

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- Numerical tests

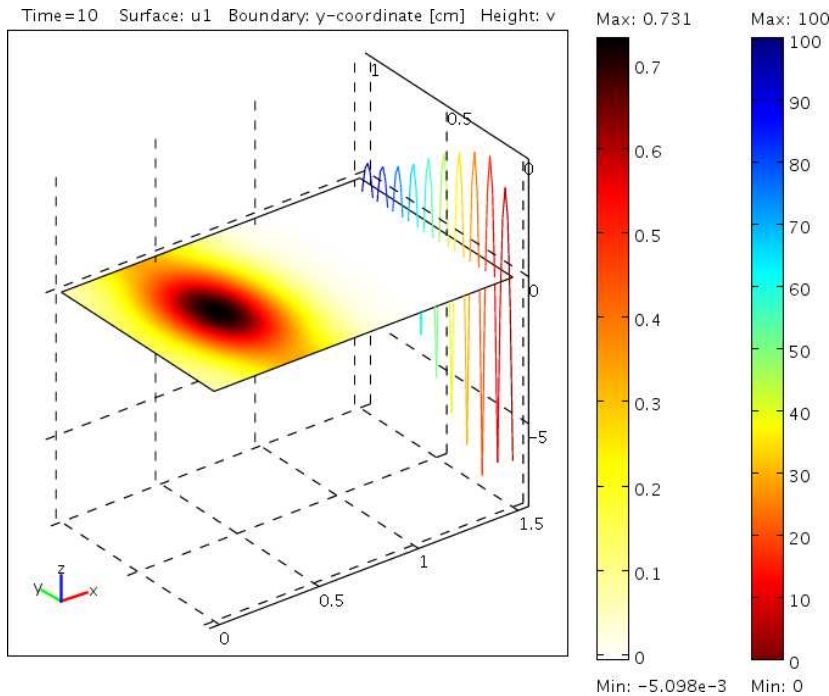
Concluding remarks

COMSOL Multiphysics (<http://www.comsol.com>)

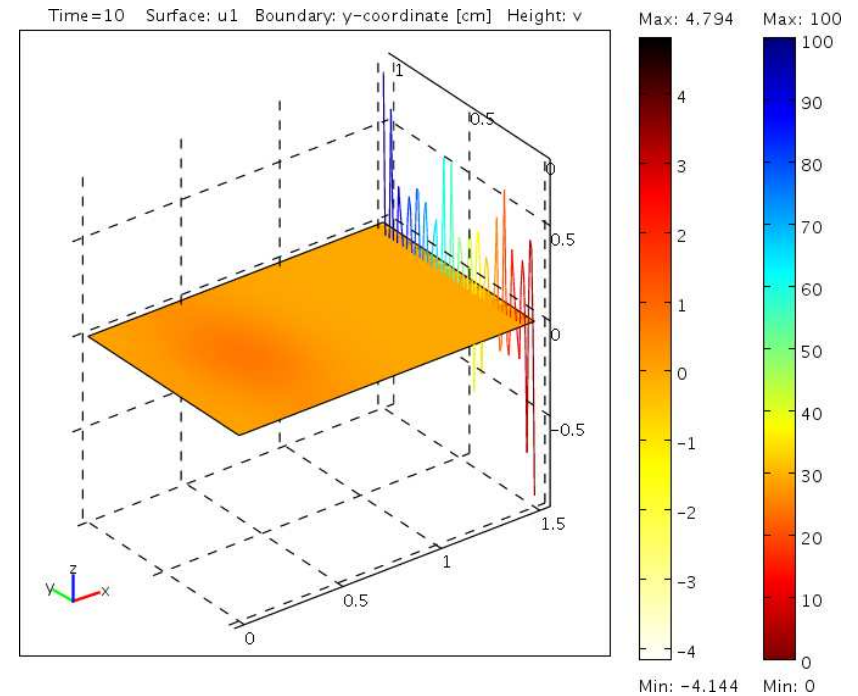
- PDE mode – system of 2 PDEs + ODE on the boundary;
- Finite Element Method – nonuniform mesh for space discretization;
- BDF for time integration;
- Automatic choice of nonlinear solver;
- Implicit Euler + PARDISO or GMRES/ILU for solution of linearized system.

Model data – solution $s(t, x)$ and $b(t, x)$, $T = 10$.

GMRES/ILU



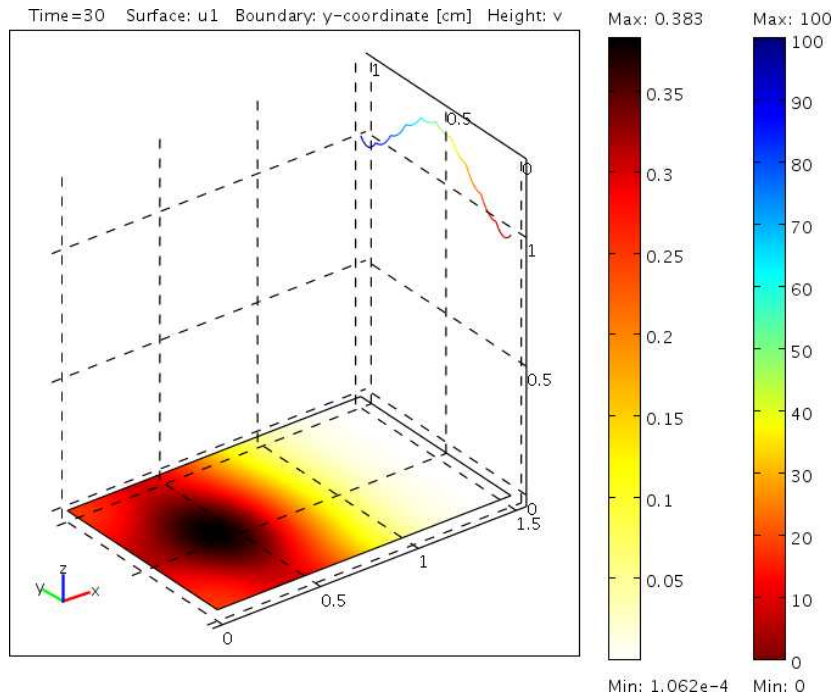
dof = 1723



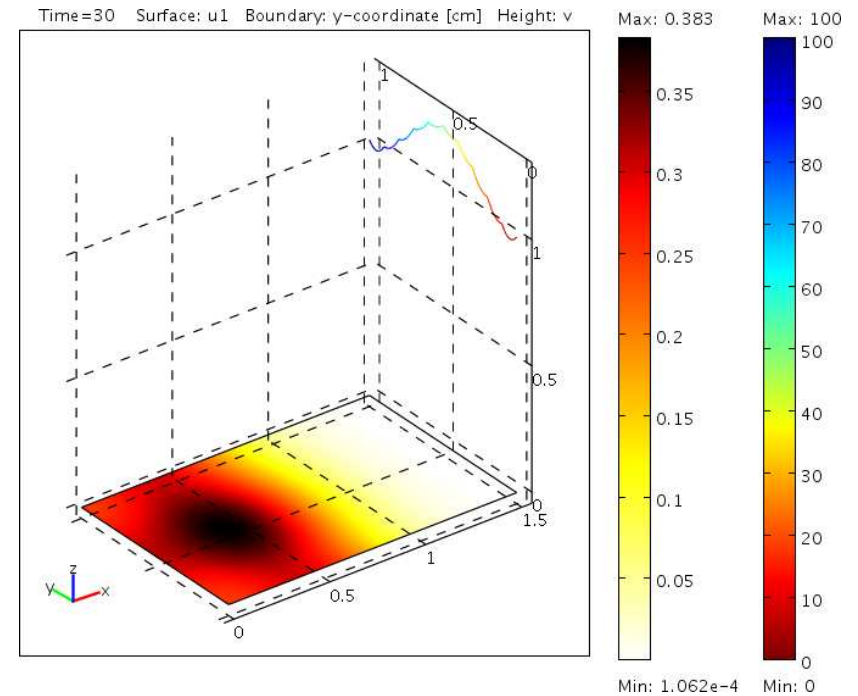
dof=6643

Model data – solution $s(t, x)$ and $b(t, x)$, $T = 30$.

GMRES/ILU

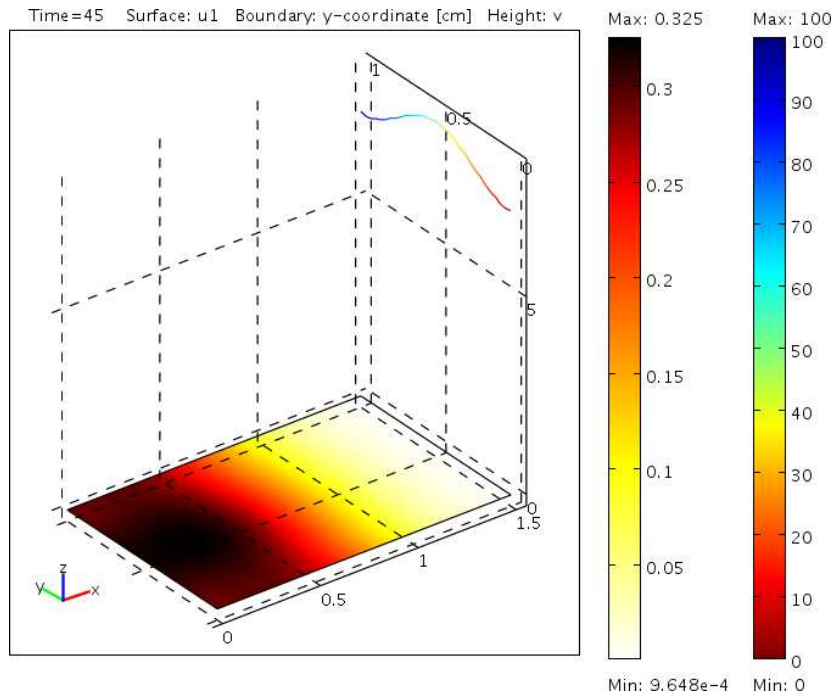


$$\chi = 10a$$

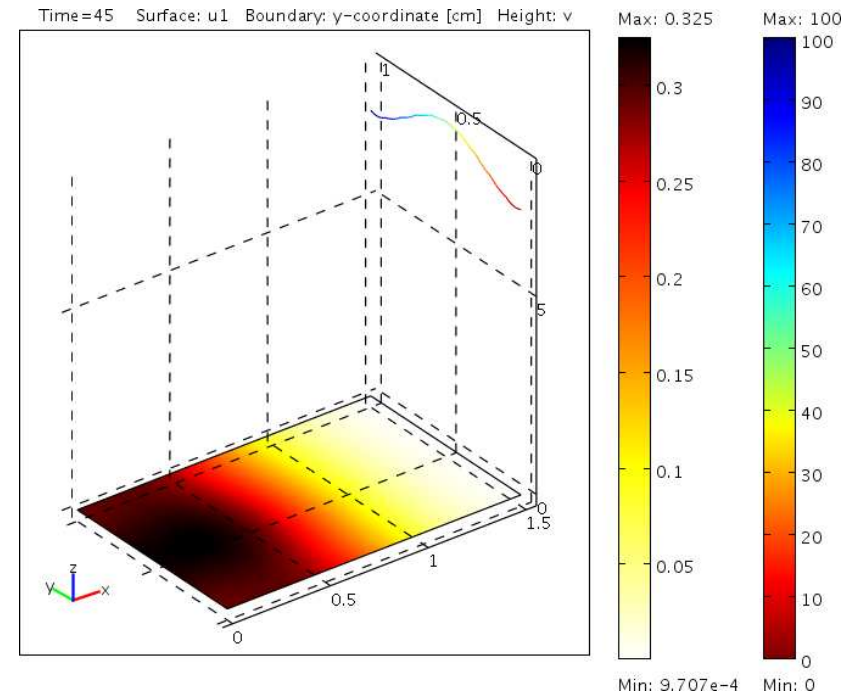


$$\chi = \log(a)$$

Model data – solution $s(t, x)$ and $b(t, x)$, $T = 45$.



GMRES/ILU



PARDISO

Motivation

Model of HSCs' movement

Numerical solution

Concluding remarks

Concluding remarks

Concluding remarks

- Ongoing work – development and debugging of own software
- Further steps
 - ◆ Chemotactic movement:
 - Ranges for parameters where the model works or fails?
 - Experimental/clinical data for calibration of the model?
 - Sensitivity analysis and parameter estimation.
 - ◆ Parallel algorithms
 - Comparative analysis of two approaches for parallel implementation;
 - Modifications for non-linear diffusion case.
- Acknowledgements
 - ◆ The study is motivated by recently initiated cooperation between DSC at IICT-BAS and the group of Dr. M. Guenova from Laboratory of Haematopathology and Immunology, National Specialized Hospital for Active Treatment of Haematological Diseases, Bulgaria.
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Thank you for your attention!