Parallel Algorithms for Solution of a Chemotaxis System in Haematology

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Contents

Motivation

Blood cells production and regulation

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.

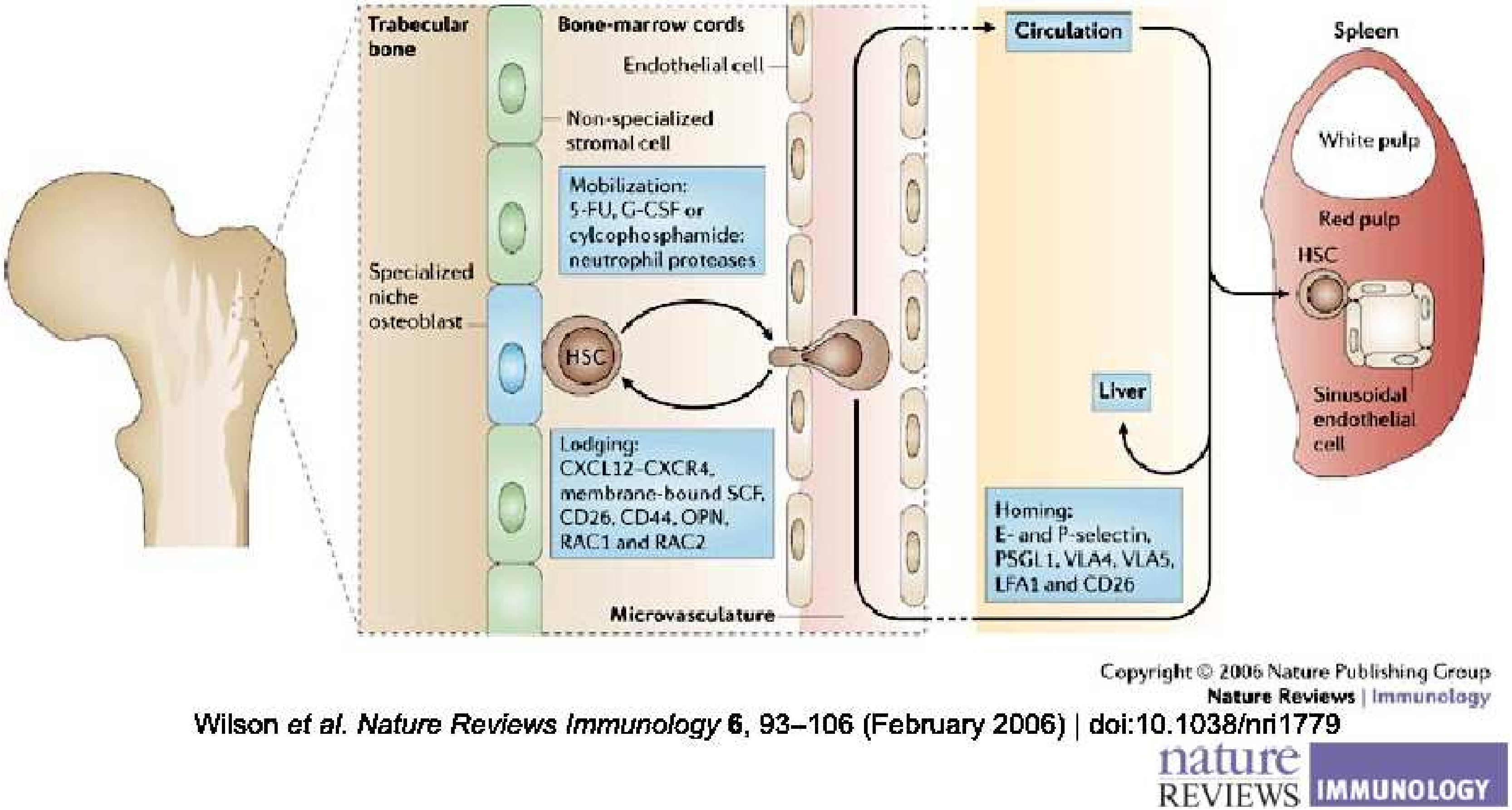
After BMT, HSCs have to:

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 mobilization, homing and lodging



A. Wilson, A. Trumpp, Bone-marrow haematopoietic-stem-cell niches, Nature Reviews Immunology, Vol.6, (2006), 93–106.

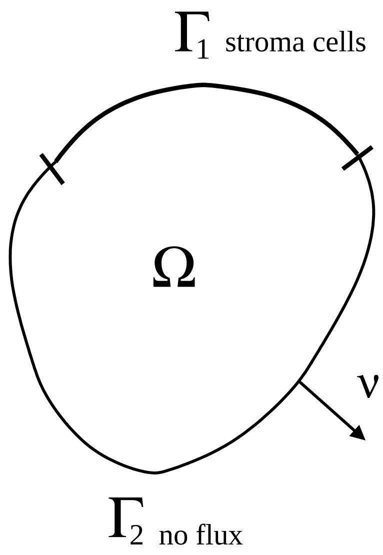
Model of HSCs' chemotactic movement

Involved data

Unknowns:

$s(t,x)$ – concentration of stem cells in Ω
$a(t,x)$ – concentration of chemoattractant
$b(t,x)$ – concentration of stem cells bound to stroma cells at the boundary part Γ_1

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



$$\Omega \in R^2$$
$$\partial\Omega = \Gamma_1 \cup \Gamma_2$$
$$\Gamma_1 \cap \Gamma_2 = \emptyset$$

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
$c(x)$ – concentration of stroma cells on Γ_1
$\beta(t,b)$ – proportionality function in the production rate of chemoattractant

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.

The model

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

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

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

$$\partial_t b = c_1 s - c_2 b \,, \ \text{on } (0,T) \times \Gamma_1 \text{ and } b = 0, \ \text{on } (0,T) \times \Gamma_2$$

$$s(0) = s_0,\ a(0) = a_0 \text{ in } \Omega, \text{ and } b(0) = b_0 \text{ on } \Gamma_1$$

Existence of unique solution is ensured by

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

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

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

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

Numerical solution

Finite volume method

$$\mathbf{U}_t + \mathbf{f}(\mathbf{U})_x + \mathbf{g}(\mathbf{U})_y = \Lambda(\mathbf{U}_{xx} + \mathbf{U}_{yy}) + \mathbf{R}(\mathbf{U})$$

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

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

$\lambda_i^{\mathbf{f}}, \lambda_i^{\mathbf{g}}$ – eigenvalues of $\dfrac{\partial \mathbf{f}}{\partial \mathbf{U}}$ and $\dfrac{\partial \mathbf{g}}{\partial \mathbf{U}}$

$$x_\alpha = \alpha \Delta x, \; y_\beta = \beta \Delta y, \quad C_{j,k} := [x_{j-\frac{1}{2}}, x_{j+\frac{1}{2}}] \times [y_{k-\frac{1}{2}}, y_{k+\frac{1}{2}}]$$

$\bar{\mathbf{U}}_{j,k}(t) = \dfrac{1}{\Delta x \Delta y} \iint\limits_{C_{j,k}} U(x,y,t)\,dxdy$ – unknowns of the discrete system

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

$$\tilde{\mathbf{U}}(x,y) := \bar{\mathbf{U}}_{j,k} + (\mathbf{U}_x)_{j,k}(x - x_j) + (\mathbf{U}_y)_{j,k}(y - y_k), \;\; (x,y) \in C_{j,k}$$

should be conservative, nonoscilatory and positivity preserving.

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

Semi-discrete scheme

$$\frac{d}{dt}\bar{\mathbf{U}}_{j,k} = -\frac{\mathbf{H}^x_{j+\frac{1}{2},k} - \mathbf{H}^x_{j-\frac{1}{2},k}}{\Delta x} - \frac{\mathbf{H}^y_{j,k+\frac{1}{2}} - \mathbf{H}^y_{j,k-\frac{1}{2}}}{\Delta y}$$

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

$$\mathbf{H}^x_{j+\frac{1}{2},k} = \frac{a^+_{j+\frac{1}{2},k}\mathbf{f}(\mathbf{U}^E_{j,k}) - a^-_{j+\frac{1}{2},k}\mathbf{f}(\mathbf{U}^W_{j+1,k})}{a^+_{j+\frac{1}{2},k} - a^-_{j+\frac{1}{2},k}} + \frac{a^+_{j+\frac{1}{2},k}\, a^-_{j+\frac{1}{2},k}}{a^+_{j+\frac{1}{2},k} - a^-_{j+\frac{1}{2},k}} \left[\mathbf{U}^W_{j+1,k} - \mathbf{U}^E_{j,k}\right]$$

$$\mathbf{H}^y_{j,k+\frac{1}{2}} = \frac{b^+_{j,k+\frac{1}{2}}\mathbf{g}(\mathbf{U}^N_{j,k}) - b^-_{j,k+\frac{1}{2}}\mathbf{g}(\mathbf{U}^S_{j,k+1})}{b^+_{j,k+\frac{1}{2}} - b^-_{j,k+\frac{1}{2}}} + \frac{b^+_{j,k+\frac{1}{2}}\, b^-_{j,k+\frac{1}{2}}}{b^+_{j,k+\frac{1}{2}} - b^-_{j,k+\frac{1}{2}}} \left[\mathbf{U}^S_{j,k+1} - \mathbf{U}^N_{j,k}\right]$$

$a^\pm_{j+\frac{1}{2},k}, b^\pm_{j,k+\frac{1}{2}}$ – computed from $\lambda^{\mathbf{f}}_i, \lambda^{\mathbf{g}}_i$ for $\mathbf{U}^E_{j,k}$, $\mathbf{U}^W_{j+1,k}$, $\mathbf{U}^N_{j,k}$, $\mathbf{U}^S_{j,k+1}$

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

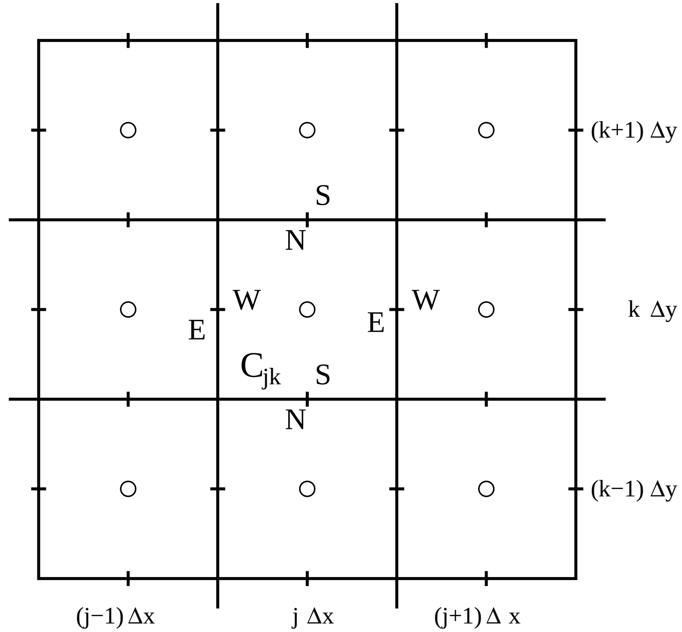
Semi-discrete scheme – cont.

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

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

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

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



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

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

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

Time integration

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

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

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

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

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

Algorithm – Explicit Euler case

$\Delta x = \frac{1}{N+1}$, $\Delta y = \frac{1}{M+1}$, $\Omega = (0,1)^2$

$K = \Lambda(\frac{1}{\Delta x^2}\Lambda_x \otimes I_M + \frac{1}{\Delta y^2}\Lambda_y \otimes I_N)$, $\Lambda_x = \Lambda_y = tridiag(1,-2,1)$

for each time step {

solve ODE on Γ_1

for each cell $C_{j,k}$ {

compute $\mathbf{U}^{E,W,N,S}_{j,k}(t)$ – require minmod evaluation with $\bar{\mathbf{U}}_{j,k}(t)$, $\bar{\mathbf{U}}_{j\pm1,k}(t)$, $\bar{\mathbf{U}}_{j,k\pm1}(t)$

$\lambda^{\mathbf{f}}_1$, $\lambda^{\mathbf{f}}_K$, $\lambda^{\mathbf{g}}_1$ $\lambda^{\mathbf{g}}_K$ – require $\mathbf{U}^{E,N}_{j,k}$, $\mathbf{U}^{W}_{j+1,k}$, $\mathbf{U}^{S}_{j,k+1}$

$a^{\pm}_{j\pm\frac{1}{2},k}(t)$, $b^{\pm}_{j,k\pm\frac{1}{2}}(t)$, $a(t)$, $b(t)$, c, Δt

$H^x_{j\pm\frac{1}{2},k}(t)$, $H^y_{j,k\pm\frac{1}{2}}(t)$ – including BC where needed

$\bar{\mathbf{R}}_{j,k}(t)$

}

$V(t) = \Delta t K \bar{\mathbf{U}}(t)$

$FR(t) = \bar{\mathbf{U}}(t) - \lambda H^x(t) - \mu H^y(t) + \Delta t \bar{\mathbf{R}}(t)$

update $\bar{\mathbf{U}}(t+\Delta t) = V(t) + FR(t)$

}

Algorithm – IMEX case

$\Delta x = \frac{1}{N+1}$, $\Delta y = \frac{1}{M+1}$, $\Omega = (0,1)^2$

$K = \Lambda(\frac{1}{\Delta x^2}\Lambda_x \otimes I_M + \frac{1}{\Delta y^2}\Lambda_y \otimes I_N)$, $\Lambda_x = \Lambda_y = tridiag(1,-2,1)$

for each time step {

solve ODE on Γ_1

for each cell $C_{j,k}$ {

compute $\mathbf{U}^{E,W,N,S}_{j,k}(t)$ – require minmod evaluation with $\bar{\mathbf{U}}_{j,k}(t)$, $\bar{\mathbf{U}}_{j\pm1,k}(t)$, $\bar{\mathbf{U}}_{j,k\pm1}(t)$

$\lambda^{\mathbf{f}}_1$, $\lambda^{\mathbf{f}}_K$, $\lambda^{\mathbf{g}}_1$ $\lambda^{\mathbf{g}}_K$ – require $\mathbf{U}^{E,N}_{j,k}$, $\mathbf{U}^{W}_{j+1,k}$, $\mathbf{U}^{S}_{j,k+1}$

$a^{\pm}_{j\pm\frac{1}{2},k}(t)$, $b^{\pm}_{j,k\pm\frac{1}{2}}(t)$, $a(t)$, $b(t)$, Δt

$H^x_{j\pm\frac{1}{2},k}(t)$, $H^y_{j,k\pm\frac{1}{2}}(t)$ – including BC where needed

$\bar{\mathbf{R}}_{j,k}(t)$

}

$FR(t) = \bar{\mathbf{U}}(t) - \lambda H^x(t) - \mu H^y(t) + \Delta t \bar{\mathbf{R}}(t)$

solve $(I - \Delta t K)\bar{\mathbf{U}}(t+\Delta t) = FR(t)$

}

Parallel algorithms

Data partitioning – possibilities

P processors; $N * M$ cells (unknowns)

How to distribute data among processors?

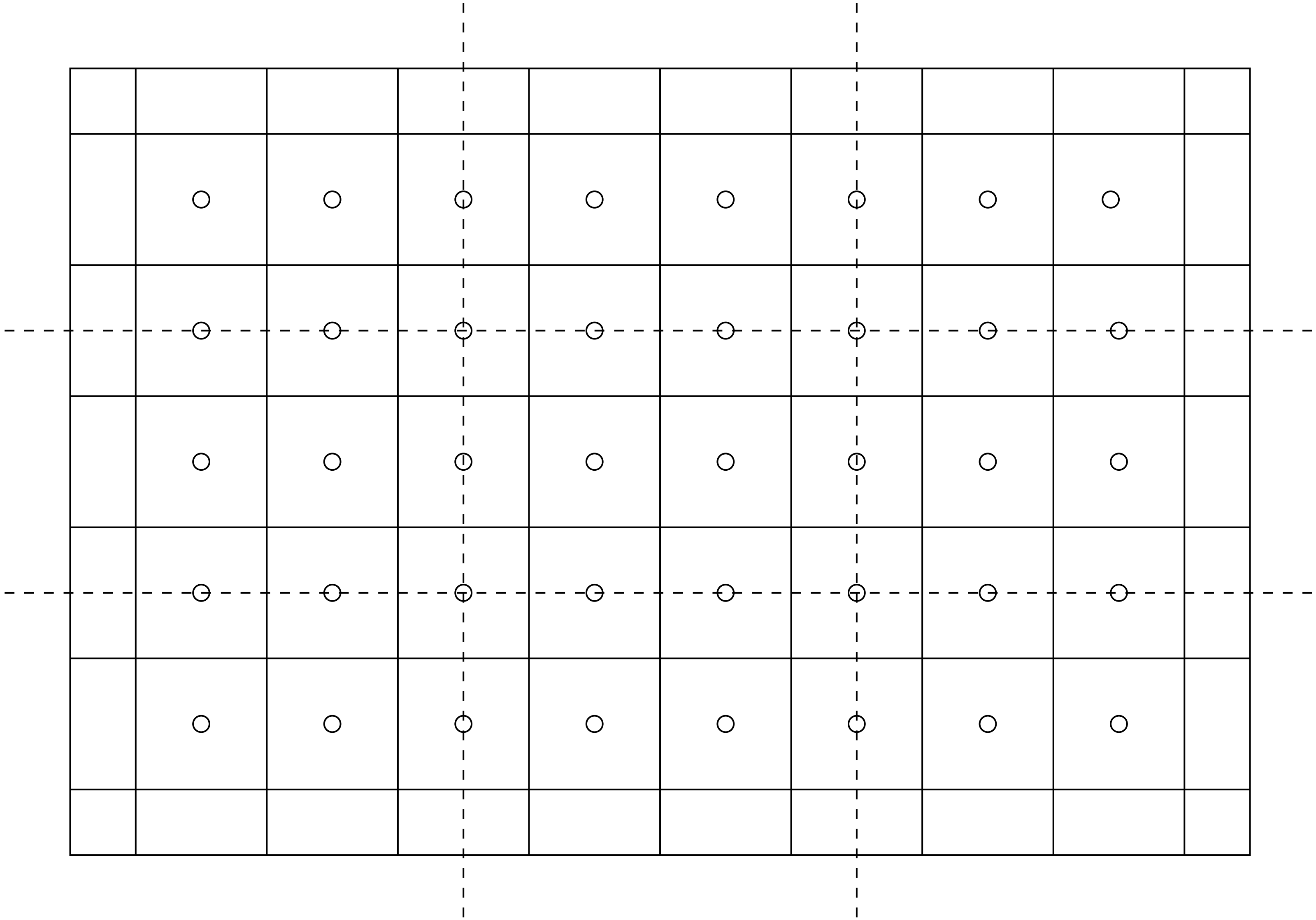
I way: Strips – horizontal or vertical; Γ_1 is either in a single processor or distributed among them.
II way: Rectangular blocks – Γ_1 is distributed among part of the processors.

Each processor deals with part of the cells if $P \leq N * M$.
If $P > N * M$ additional distribution of the computations for each cell.

How to deal with the cells on the "interfaces" between processors?

- Duplicate data from a line with cells between the neighbours;
- Associate nodes (j,k) with one of the processors;
- Associate cells (j,k) with one of the processors.

Data partitioning – the domain



Computations and communications

Computations are distributed equally among processors;

Communications for each time step – local and global as follows (only steps with communications are listed):

for each time step {

for each cell $C_{j,k}$ {

for $\mathbf{U}^{E,W,N,S}_{j,k}(t)$ – local communications

$a^{\pm}_{j\pm\frac{1}{2},k}(t)$, $b^{\pm}_{j,k\pm\frac{1}{2}}(t)$ – local communications

$a(t)$, $b(t)$, Δt – global reduction communications

$H^{x}_{j\pm\frac{1}{2},k}(t)$, $H^{y}_{j,k\pm\frac{1}{2}}(t)$ – local communications

}

$V(t) = \Delta t K \bar{\mathbf{U}}(t)$ – local communications (EE)

$(I - \Delta t K)\bar{\mathbf{U}}(t + \Delta t) = FR(t)$ – depend on the solver (IMEX)

}

Some comments

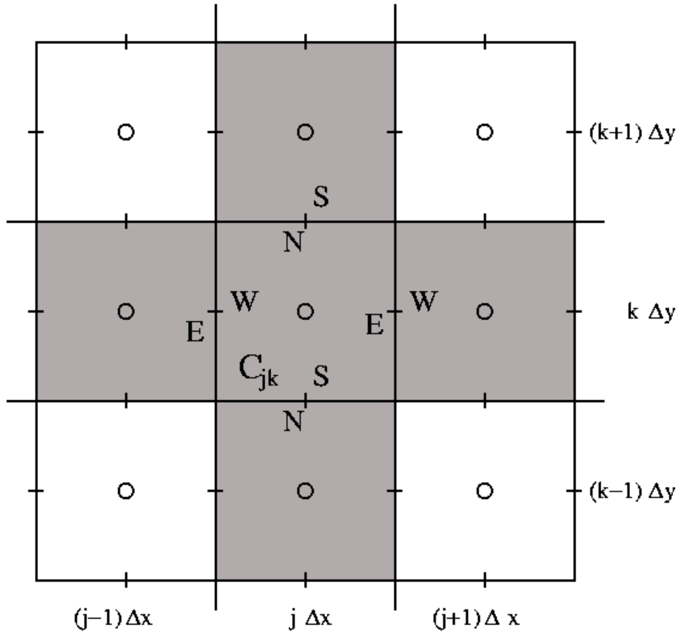
EE: Smaller time step, conditionally stable, but no need to solve a system

IMEX: Better for stiff problems, but for non-linear reaction and diffusion terms requires Newton iteration

Data distribution: processors which are neighbours in the algorithm, may not be physical neihbours.

Communications:

- Part of the data needed for V (EE) and solution of the system (IMEX) may already be transferred on the previous steps (for each cell)
- Order of processing of cells - crucial for the local communications (data from 4 neighbouring cells E,W,N,S)



Numerical tests

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

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

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

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

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

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

C/MPI implementation of the methods.

Tests to be performed on IBM Blue Gene P and GRID Sites.

Ongoing work:

- debugging of the computer programs (case of horizontal strip partitioning);
- implementation of EE, IMEX with the different data partitioning options.

Concluding remarks

Concluding remarks

- Further steps
  - Parallel algorithms
    - Runge Kutta schemes;
    - Detailed comparative analysis of the parallel algorithms;
    - Modifications for non-linear diffusion case.
  - Chemotactic movement:
    - Ranges for parameters where the model works or fails?
    - Experimental/clinical data for calibration of the model?
    - Sensitivity analysis and parameter estimation.

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Thank you for your attention!