

On the choice of limiters in a numerical approximation of a chemotaxis system with non-homogeneous boundary conditions

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Outline

Motivation

Model of HSCs' migration

FEM with COMSOL

FV approximation

Concluding remarks

- Motivation
- Model of HSCs' migration
- FEM based simulation with COMSOL Multiphysics
- Finite volume approximation
- Concluding remarks

Motivation

- Haematopoiesis
- HSCs after BMT ...
- Previous work

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Motivation

Blood cells production and regulation

Haematopoietic pluripotent stem cells (HSCs) in bone marrow give birth to 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

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:

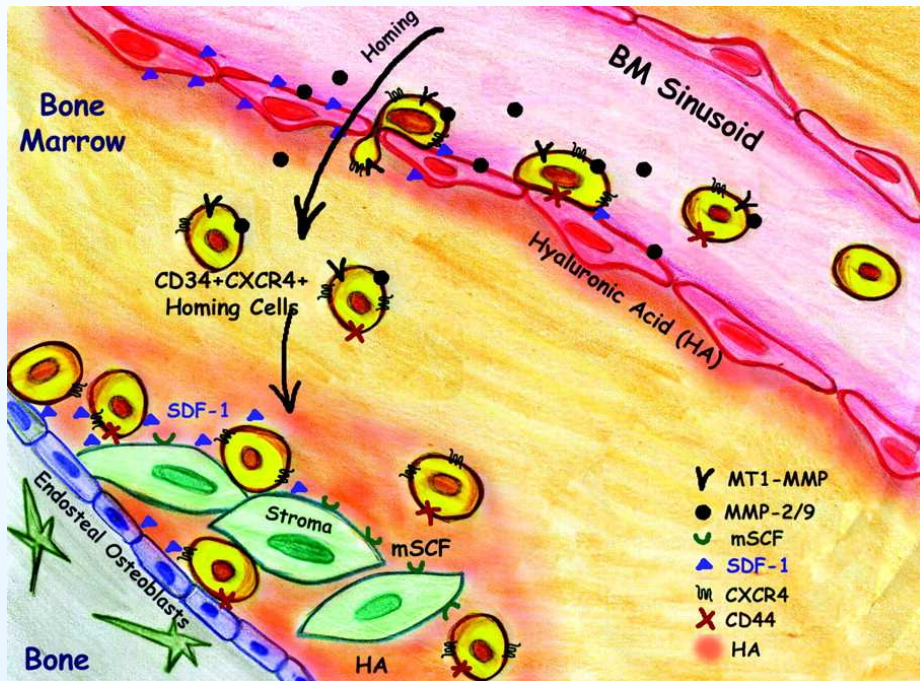
TBI: Total Body Irradiation – kill the "tumour" cells, but also the healthy ones.

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

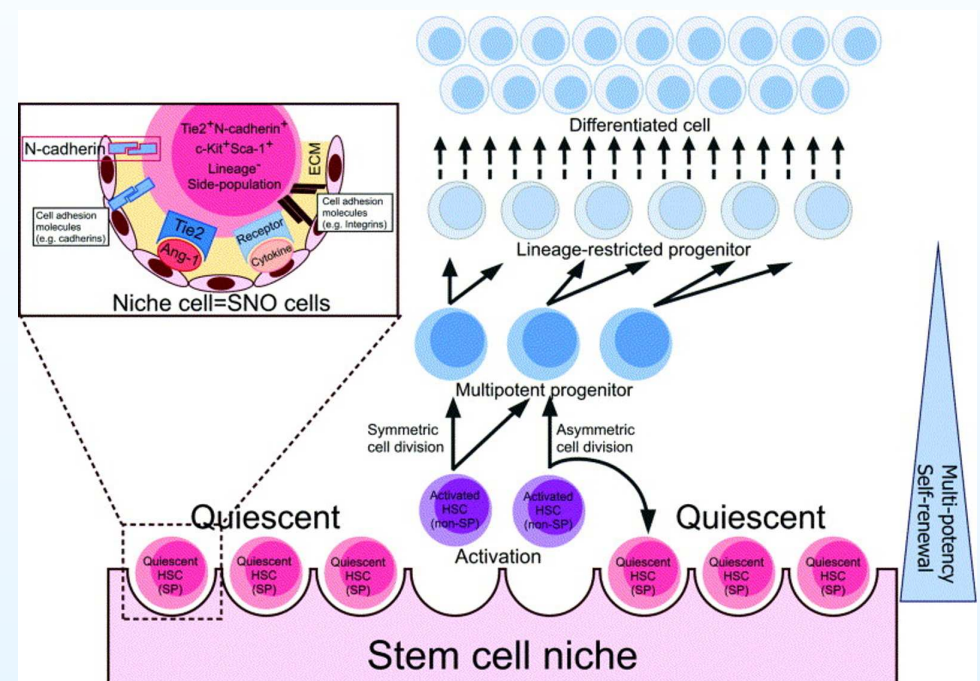
HSCs after BMT ...

1. find their way to the stem cell niche in the bone marrow; and ...

2. self-renew and differentiate to regenerate the patient's blood system



T. Lapidot, A. Dar, O. Kollet, 2005



T. Suda, F. Arai, A. Hirao, 2005

G.B. et.al., 2012

Adequate computer models would help medical doctors to shorten the period in which the patient is missing their effective immune system.

Previous work

Motivation

- Haematopoiesis
- HSCs after BMT ...
- **Previous work**

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Concluding remarks

- A. Kettemann, M. Neuss-Radu, J. Math. Biol. vol. 56 (2008)
 - Chemotaxis model with **nonlinear** flux BCs
 - Conditions for existence of unique positive solution of the model
- A. Gerisch, M. Chaplain, Math. Comp. Mod. vol. 43 (2006),
A. Chertock, A. Kurganov, Numer. Math. vol. 111 (2008),
Y. Epshteyn, JCAM vol. 224 (2009)
 - (Extended) chemotaxis model with **zero** flux BCs
 - Spatial discretization: Finite Volume Method / DG FEM
 - Time integration: Euler scheme, IMEX scheme, SSP RK methods
- G. Bencheva, Comp. Math. Appl. (2012)
 - (Extended) chemotaxis model with **nonlinear** flux BCs
 - FEM based simulation with COMSOL Multiphysics
 - Second-order finite volume based space discretization

Motivation

Model of HSCs' migration

- Involved data
- The model
- Types of CSF $\chi(a)$

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Model of HSCs' migration

Involved data

Unknowns:

$s(t, \mathbf{x})$ – concentration of HSCs 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

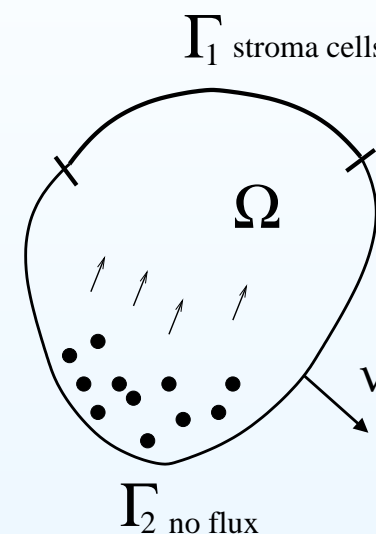
$\chi(a)$ – chemotactic sensitivity function

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



$$\mathbf{x} = (x, y) \in \Omega$$

$$\partial\Omega = \Gamma_1 \cup \Gamma_2$$

$$\Gamma_1 \cap \Gamma_2 = \emptyset$$

The model (A. Kettemann, M. Neuss-Radu, 2008)

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

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

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

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

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

Existence of unique solution is ensured by certain conditions for the involved functions.

Types of chemotactic sensitivity function $\chi(a)$

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Linear case of $\chi(a)$:

$$\chi(a) = \chi a, \quad \frac{\partial \chi}{\partial a} = \chi$$

Nonlinear forms of $\chi(a)$ (Post, 1999):

$$\chi(a) = \frac{\chi a}{1 + c a}, \quad \chi(a) = \frac{\chi a^2}{1 + c a^2}, \quad \chi(a) = \chi \log(a + c)$$

with constants $\chi > 0$ and $c \geq 1$.

$$\frac{\partial \chi}{\partial a} = \frac{\chi}{(1 + c a)^2}, \quad \frac{\partial \chi}{\partial a} = \frac{2 \chi a}{(1 + c a^2)^2}, \quad \frac{\partial \chi}{\partial a} = \frac{\chi}{(a + c) \ln 10}.$$

Motivation

Model of HSCs' migration

FEM with COMSOL

- Test data
- Numerical Results

FV approximation

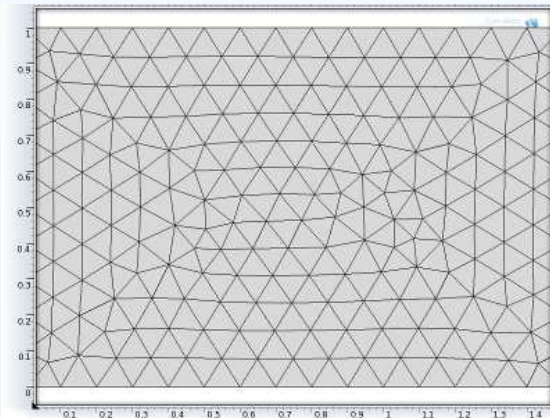
Concluding remarks

FEM based simulation with COMSOL Multiphysics

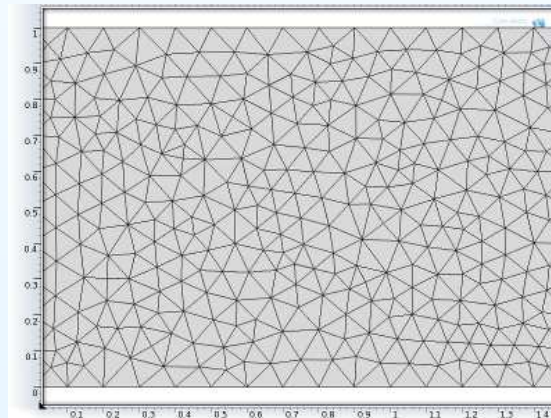
Numerical simulation with COMSOL Multiphysics (G.B., 2012)

- Linear finite elements for space discretization (nonuniform mesh);
- Implicit time integration;
- Direct or Iterative solution of linearized system.

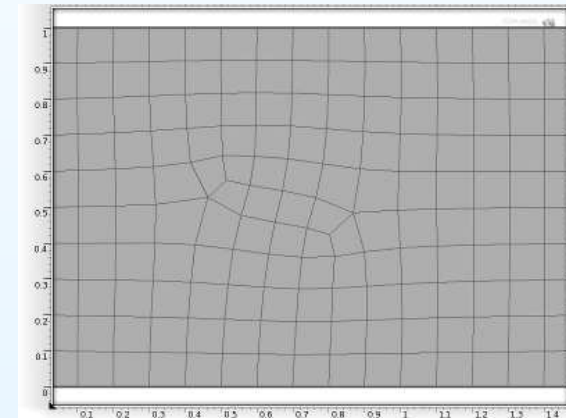
Mesh types



M1: Triangular
(Advancing front)



M2: Triangular
(Delaunay)



M3: Quadrilateral

Test data

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

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

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

$$\chi(a) = 10a \quad \chi(a) = \log(a + 1)$$

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

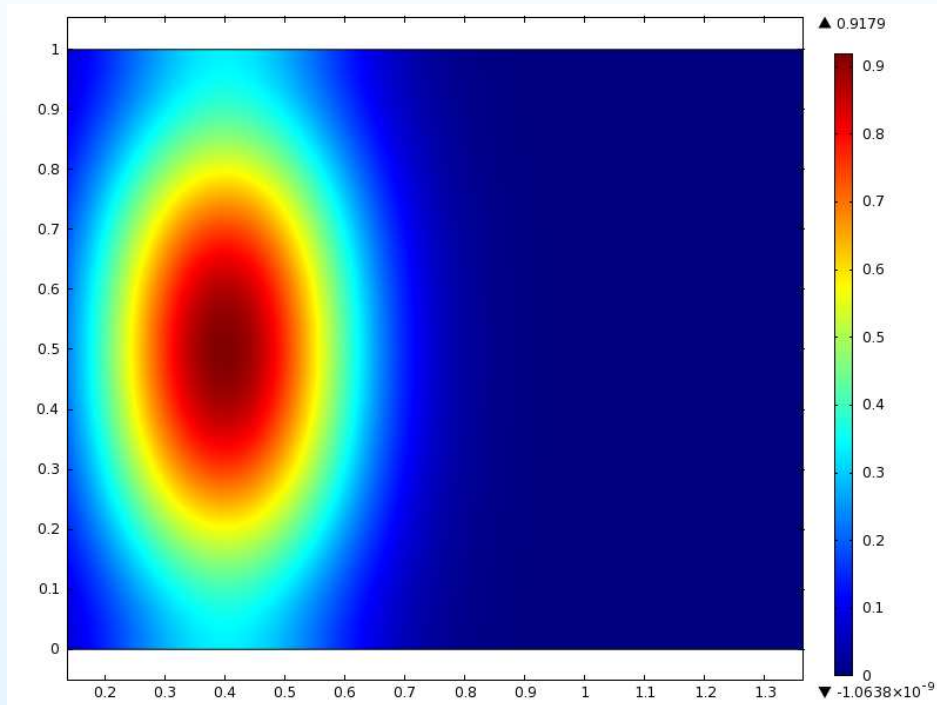
$$a_0 = 0, b_0 = 0 \text{ and}$$

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

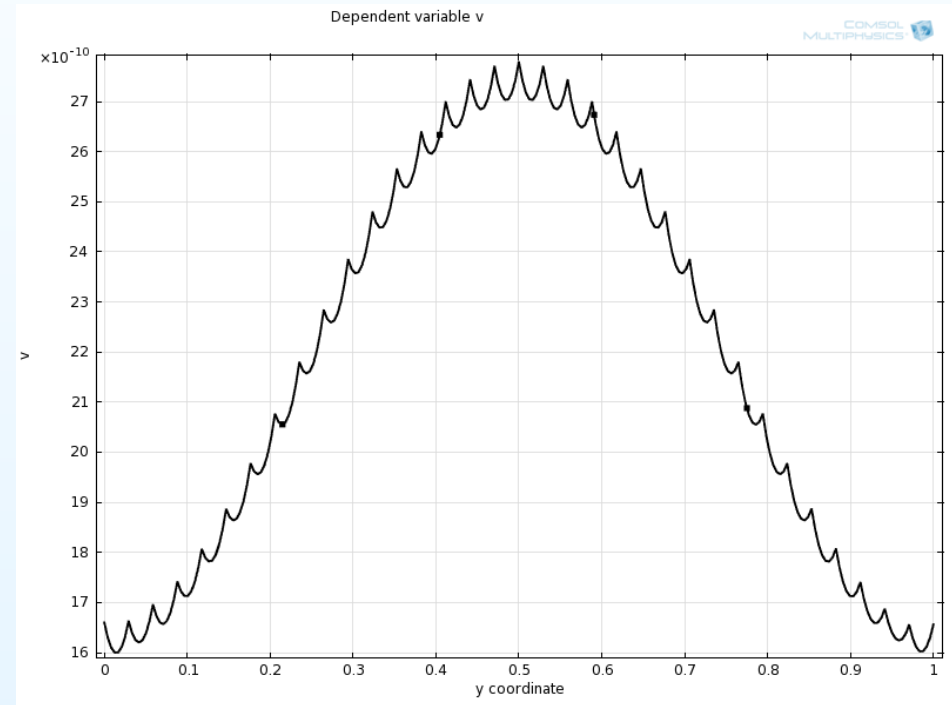
Solution $s(t, x)$ and $b(t, x)$ with for M1ef

Solution time: 21 s, 30 iterations, $T = 6.3$.

M1ef (triangular): Number of elements 4 268, Degrees of freedom 17 479



$s(t, \mathbf{x})$

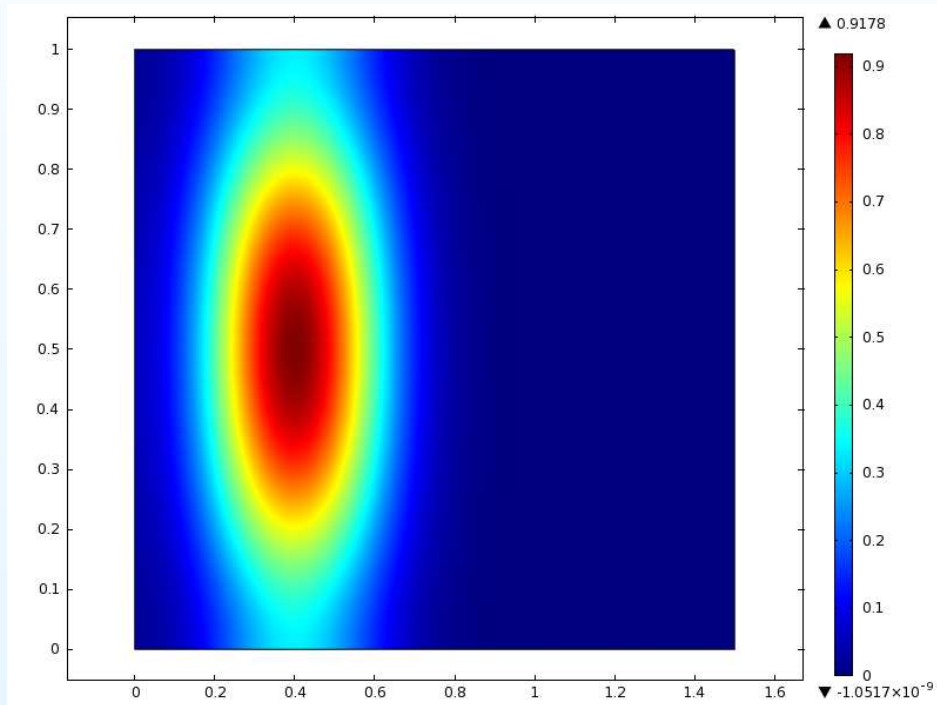


$b(t, \mathbf{x})$

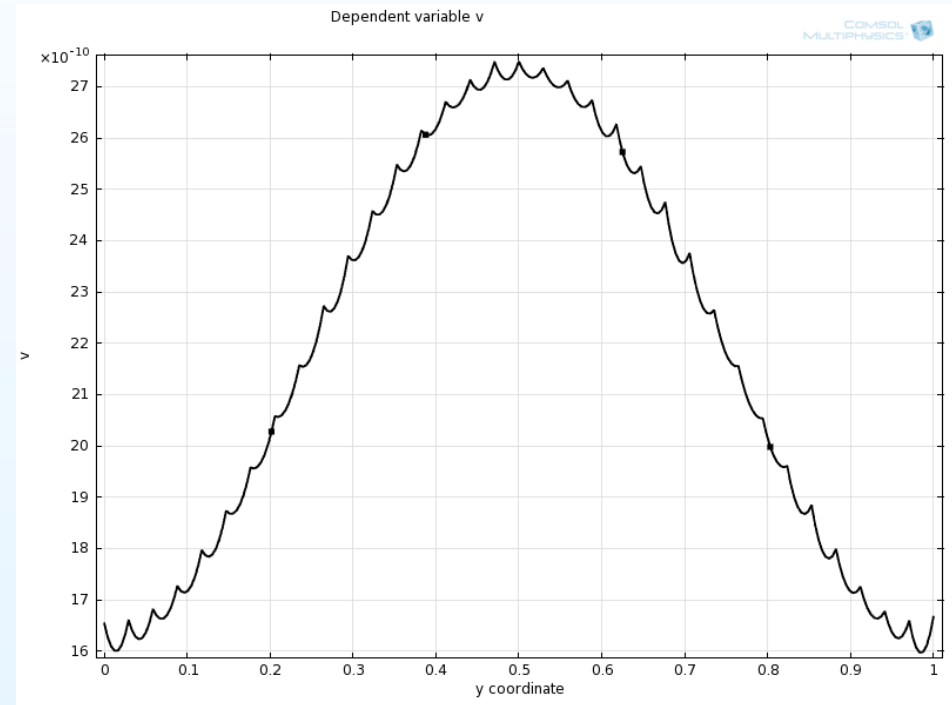
Solution $s(t, x)$ and $b(t, x)$ with for M2ef

Solution time: 34 s, 30 iterations, $T = 6.3$.

M2ef (triangular, Delaunay): Number of elements 7 160, Degrees of freedom 29 047



$s(t, \mathbf{x})$

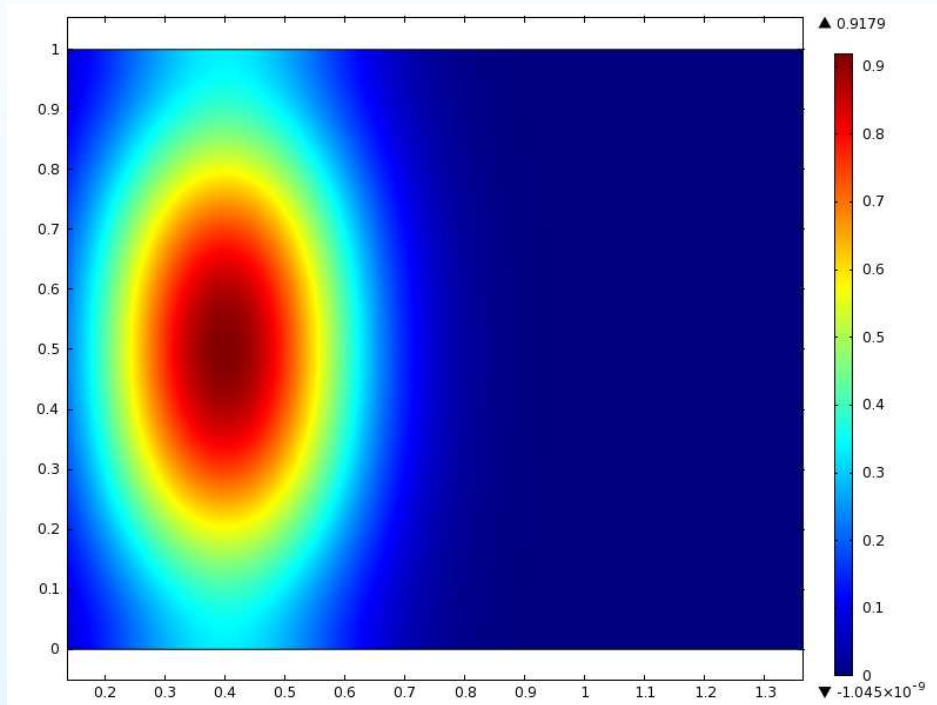


$b(t, \mathbf{x})$

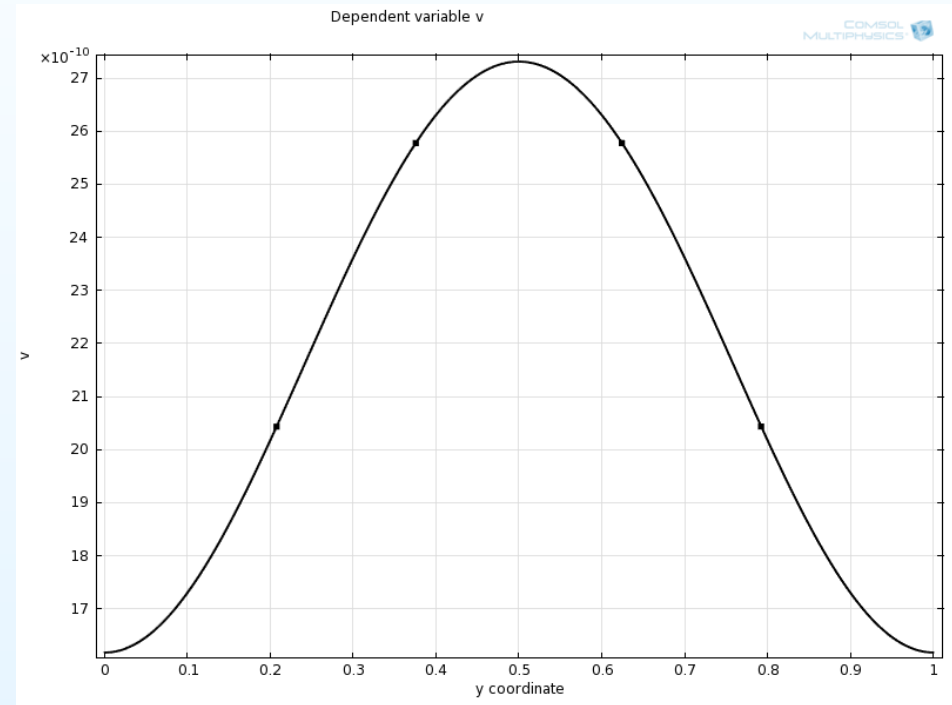
Solution $s(t, x)$ and $b(t, x)$ with for M3ef

Solution time: 18 s, 30 iterations, $T = 6.3$.

M3ef (quadrangular): Number of elements 1 777, Degrees of freedom 14 623



$s(t, \mathbf{x})$



$b(t, \mathbf{x})$

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Remarks

- Observations:
 - Not always convergent
 - Negative values and oscillations for the solution
- Needed improvements in the direction of:
 - Extended model with appropriate space discretization
 - Robust discretization of nonlinear boundary conditions
 - Explicit efficient time integration

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- Conservation form
- Semi-discrete scheme
- Interior cells
- Second order limiters
- Neighbour to b. cells
- Boundary cells
- Case Γ^W
- Evaluation of $\bar{U}_{0,k}$
- Time integration

Concluding remarks

Second-order finite volume approximation

Initial system in conservation form (Chertock, Kurganov, 2008)

Extended system of PDEs:

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

Boundary conditions:

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

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

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

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

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

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

$$b = 0, \text{ on } (0, T) \times \Gamma_2$$

$$b(0, \mathbf{x}) = b_0(\mathbf{x}), \text{ on } \Gamma_1$$

Initial system in conservation form – cont.

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

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

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

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

$$\frac{\partial \mathbf{f}}{\partial \mathbf{U}} : \quad \lambda_1^{\mathbf{f}}(\mathbf{U}) = \frac{1}{2} \left(\chi_a p - \sqrt{4\omega + (\chi_a p)^2} \right), \quad \lambda_2^{\mathbf{f}}(\mathbf{U}) = \frac{1}{2} \left(\chi_a p + \sqrt{4\omega + (\chi_a p)^2} \right), \quad \lambda_{3,4}^{\mathbf{f}}(\mathbf{U}) = 0,$$

$$\frac{\partial \mathbf{g}}{\partial \mathbf{U}} : \quad \lambda_1^{\mathbf{g}}(\mathbf{U}) = \frac{1}{2} \left(\chi_a q - \sqrt{4\omega + (\chi_a q)^2} \right), \quad \lambda_2^{\mathbf{g}}(\mathbf{U}) = \frac{1}{2} \left(\chi_a q + \sqrt{4\omega + (\chi_a q)^2} \right), \quad \lambda_{3,4}^{\mathbf{g}}(\mathbf{U}) = 0.$$

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FV approximation

• Conservation form

- Semi-discrete scheme
- Interior cells
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Concluding remarks

Finite volume method

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

$$\Omega = \cup C_{j,k}, \quad j = 1, \dots, N_x, \quad k = 1, \dots, N_y,$$

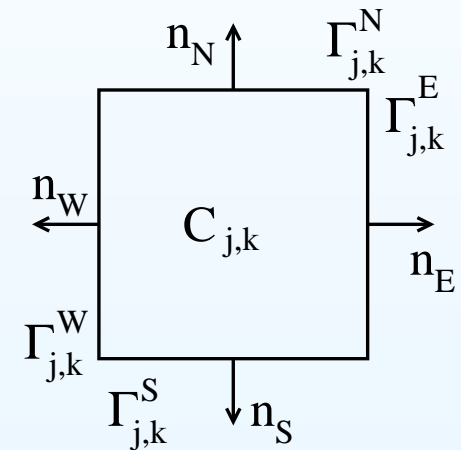
$$\partial\Omega = \Gamma^E \cup \Gamma^W \cup \Gamma^N \cup \Gamma^S$$

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

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

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

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



$$\bar{U}_{j,k}(t) = \frac{1}{\Delta x \Delta y} \iint_{C_{j,k}} U(x, y, t) dx dy$$
 – 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.

Semi-discrete scheme

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

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

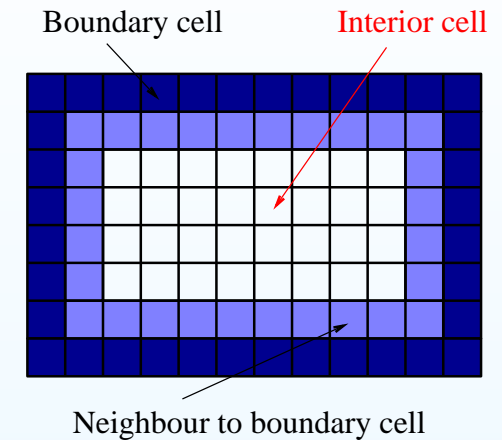
$$I_{j,k}^c = \int_{\partial C_{j,k}} \mathbf{F}_c \cdot \mathbf{n} \, d\gamma \quad \text{and} \quad I_{j,k}^d = \int_{\partial C_{j,k}} \mathbf{F}_d \cdot \mathbf{n} \, d\gamma$$

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

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.

Semi-discrete scheme – interior cells $j = 3, \dots, N_x - 2, k = 3, \dots, N_y - 2$

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



$$Q_{j+\frac{1}{2},k}^x = \frac{\Lambda}{\Delta x} (\bar{U}_{j+1,k} - \bar{U}_{j,k}), \quad Q_{j-\frac{1}{2},k}^x = \frac{\Lambda}{\Delta x} (\bar{U}_{j,k} - \bar{U}_{j-1,k})$$

$$Q_{j,k+\frac{1}{2}}^y = \frac{\Lambda}{\Delta y} (\bar{U}_{j,k+1} - \bar{U}_{j,k}), \quad Q_{j,k-\frac{1}{2}}^y = \frac{\Lambda}{\Delta y} (\bar{U}_{j,k} - \bar{U}_{j,k-1})$$

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

Semi-discrete scheme – interior cells (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 $\mathbf{U}_{j,k}^E, \mathbf{U}_{j+1,k}^W, \mathbf{U}_{j,k}^N, \mathbf{U}_{j,k+1}^S$

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

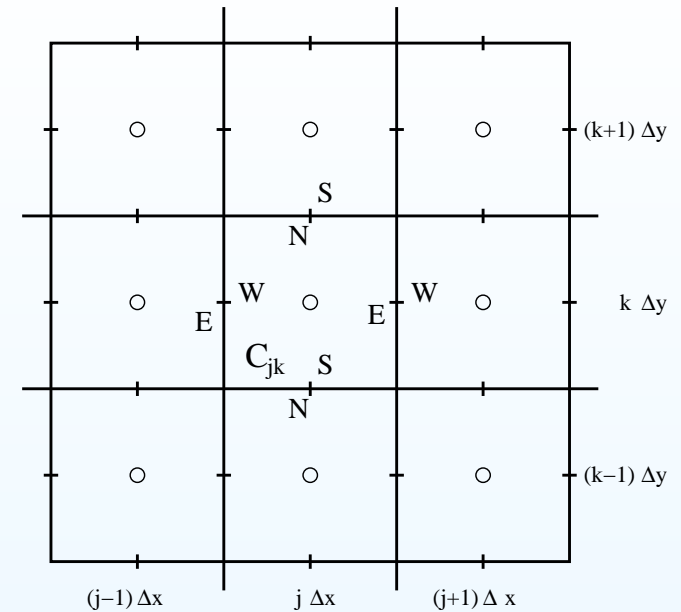
Semi-discrete scheme – interior cells (cont.)

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

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

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

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



Generalized minmod limiter (GML), second order:

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

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

$$\text{minmod}(z_1, z_2, \dots) := \begin{cases} \min_j \{z_j\}, & \text{if } z_j > 0 \quad \forall j, \\ \max_j \{z_j\}, & \text{if } z_j < 0 \quad \forall j, \\ 0, & \text{otherwise} \end{cases} \quad \ominus = 2$$

Second order limiters

Motivation

Model of HSCs' migration

FEM with COMSOL

FV approximation

- Conservation form
- Semi-discrete scheme
- Interior cells
- **Second order limiters**
- Neighbour to b. cells
- Boundary cells
- Case Γ^W
- Evaluation of $\bar{\mathbf{U}}_{0,k}$
- Time integration

Concluding remarks

$$r_{j,k}^x = \frac{\bar{\mathbf{U}}_{j+1,k} - \bar{\mathbf{U}}_{j,k} + \bar{\varepsilon}}{\bar{\mathbf{U}}_{j,k} - \bar{\mathbf{U}}_{j-1,k} + \bar{\varepsilon}}, \quad r_{j,k}^y = \frac{\bar{\mathbf{U}}_{j,k+1} - \bar{\mathbf{U}}_{j,k} + \bar{\varepsilon}}{\bar{\mathbf{U}}_{j,k} - \bar{\mathbf{U}}_{j,k-1} + \bar{\varepsilon}}$$

$\bar{\varepsilon} = 10^{-10}$ to avoid division by zero

- Koren limiter (KL), $\delta = 2$

$$(\mathbf{U}_x)_{j,k} = \phi_{KL}(r_{j,k}^x) = \max \left\{ 0, \min \left\{ 2r_{j,k}^x, \delta, \frac{1}{3} + \frac{2}{3}r_{j,k}^x \right\} \right\},$$

$$(\mathbf{U}_y)_{j,k} = \phi_{KL}(r_{j,k}^y) = \max \left\{ 0, \min \left\{ 2r_{j,k}^y, \delta, \frac{1}{3} + \frac{2}{3}r_{j,k}^y \right\} \right\},$$

- van Leer limiter (VLL), symmetric $\frac{\phi_{VLL}(r)}{r} = \phi_{VLL} \left(\frac{1}{r} \right)$

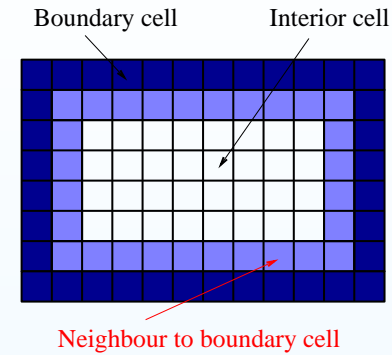
$$(\mathbf{U}_x)_{j,k} = \phi_{VLL}(r_{j,k}^x) = \frac{r_{j,k}^x + |r_{j,k}^x|}{1 + |r_{j,k}^x|},$$

$$(\mathbf{U}_y)_{j,k} = \phi_{VLL}(r_{j,k}^y) = \frac{r_{j,k}^y + |r_{j,k}^y|}{1 + |r_{j,k}^y|}.$$

Semi-discrete scheme – neighbour to boundary cells

$$j = 2, j = N_x - 1, \quad k = 2, \dots, N_y - 1$$

$$j = 2, \dots, N_x - 1, \quad k = 2, k = N_y - 1$$



$$(\bar{U}_{2,k})_t = -\frac{\mathbf{H}_{\frac{5}{2},k}^x - \mathbf{H}_{\frac{3}{2},k}^x}{\Delta x} - \frac{\mathbf{H}_{2,k+\frac{1}{2}}^y - \mathbf{H}_{2,k-\frac{1}{2}}^y}{\Delta y} + \frac{Q_{\frac{5}{2},k}^x - Q_{\frac{3}{2},k}^x}{\Delta x} + \frac{Q_{2,k+\frac{1}{2}}^y - Q_{2,k-\frac{1}{2}}^y}{\Delta y} + \bar{\mathbf{R}}_{2,k}$$

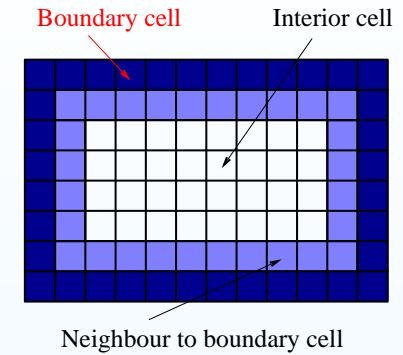
$$(\bar{U}_{N_x-1,k})_t = -\frac{\mathbf{H}_{N_x-\frac{1}{2},k}^x - \mathbf{H}_{N_x-\frac{3}{2},k}^x}{\Delta x} - \frac{\mathbf{H}_{N_x-1,k+\frac{1}{2}}^y - \mathbf{H}_{N_x-1,k-\frac{1}{2}}^y}{\Delta y} + \frac{Q_{N_x-1+\frac{1}{2},k}^x - Q_{N_x-1-\frac{1}{2},k}^x}{\Delta x} + \frac{Q_{N_x-1,k+\frac{1}{2}}^y - Q_{N_x-1,k-\frac{1}{2}}^y}{\Delta y} + \bar{\mathbf{R}}_{N_x-1,k}$$

$$(\bar{U}_{j,2})_t = -\frac{\mathbf{H}_{j+\frac{1}{2},2}^x - \mathbf{H}_{j-\frac{1}{2},2}^x}{\Delta x} - \frac{\mathbf{H}_{j,\frac{5}{2}}^y - \mathbf{H}_{j,\frac{3}{2}}^y}{\Delta y} + \frac{Q_{j+\frac{1}{2},2}^x - Q_{j-\frac{1}{2},2}^x}{\Delta x} + \frac{Q_{j,\frac{5}{2}}^y - Q_{j,\frac{3}{2}}^y}{\Delta y} + \bar{\mathbf{R}}_{j,2}$$

$$(\bar{U}_{j,N_y-1})_t = -\frac{\mathbf{H}_{j+\frac{1}{2},N_y-1}^x - \mathbf{H}_{j-\frac{1}{2},N_y-1}^x}{\Delta x} - \frac{\mathbf{H}_{j,N_y-\frac{1}{2}}^y - \mathbf{H}_{j,N_y-\frac{3}{2}}^y}{\Delta y} + \frac{Q_{j+\frac{1}{2},N_y-1}^x - Q_{j-\frac{1}{2},N_y-1}^x}{\Delta x} + \frac{Q_{j,N_y-\frac{1}{2}}^y - Q_{j,N_y-1\frac{3}{2}}^y}{\Delta y} + \bar{\mathbf{R}}_{j,N_y-1}$$

Semi-discrete scheme – boundary cells

$$\bar{h}_{j,k}^l := \frac{1}{|\Gamma_{j,k}^l|} \int_{\Gamma_{j,k}^l} \mathbf{h}^l d\bar{\gamma}, \quad \begin{array}{l} l \in \{E, W, N, S\} \\ j = 1, j = N_x, k = 1, \dots, N_y \\ j = 1, \dots, N_x, k = 1, k = N_y \end{array}$$



$$(\bar{U}_{1,k})_t = \frac{Q_{\frac{3}{2},k}^x - \mathbf{H}_{\frac{3}{2},k}^x - \bar{h}_{1,k}^W}{\Delta x} - \frac{H_{1,k+\frac{1}{2}}^y - H_{1,k-\frac{1}{2}}^y}{\Delta y} + \frac{Q_{1,k+\frac{1}{2}}^y - Q_{1,k-\frac{1}{2}}^y}{\Delta y} + \bar{R}_{1,k},$$

$$(\bar{U}_{N_x,k})_t = \frac{\mathbf{H}_{N_x-\frac{1}{2},k}^x - Q_{N_x-\frac{1}{2},k}^x - \bar{h}_{N_x,k}^E}{\Delta x} - \frac{H_{N_x,k+\frac{1}{2}}^y - H_{N_x,k-\frac{1}{2}}^y}{\Delta y} + \frac{Q_{N_x,k+\frac{1}{2}}^y - Q_{N_x,k-\frac{1}{2}}^y}{\Delta y} + \bar{R}_{N_x,k},$$

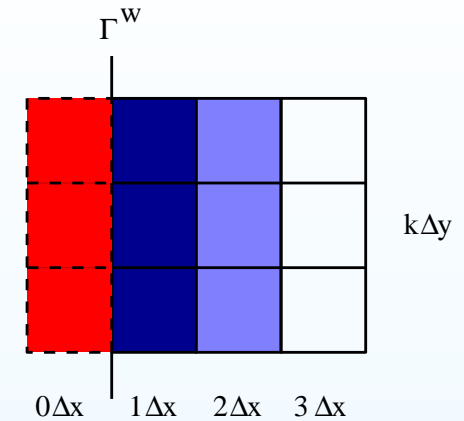
$$(\bar{U}_{j,1})_t = -\frac{H_{j+\frac{1}{2},1}^x - H_{j-\frac{1}{2},1}^x}{\Delta x} + \frac{Q_{j,\frac{3}{2}}^y - \mathbf{H}_{j,\frac{3}{2}}^y - \bar{h}_{j,1}^S}{\Delta y} + \frac{Q_{j+\frac{1}{2},1}^x - Q_{j-\frac{1}{2},1}^x}{\Delta x} + \bar{R}_{j,1},$$

$$(\bar{U}_{j,N_y})_t = -\frac{H_{j+\frac{1}{2},N_y}^x - H_{j-\frac{1}{2},N_y}^x}{\Delta x} + \frac{\mathbf{H}_{j,N_y-\frac{1}{2}}^y - Q_{j,N_y-\frac{1}{2}}^y - \bar{h}_{j,N_y}^N}{\Delta y} + \frac{Q_{j+\frac{1}{2},N_y}^x - Q_{j-\frac{1}{2},N_y}^x}{\Delta x} + \bar{R}_{j,N_y}.$$

Boundary cells and neighbours – case Γ^W

$$\bar{\mathbf{h}}_{1,k}^W := \frac{1}{|\Gamma_{1,k}^W|} \int_{\Gamma_{1,k}^W} \mathbf{h}^W d\bar{\gamma} = \mathbf{h}^W(\bar{\mathbf{U}}_{\frac{1}{2},k}, b_{\frac{1}{2},k}, x_{\frac{1}{2}}, y_k, t)$$

$$k = 1, \dots, N_y$$



$$\mathbf{H}_{\frac{3}{2},k}^x = \frac{a_{\frac{3}{2},k}^+ \mathbf{f}(\mathbf{U}_{1,k}^E) - a_{\frac{3}{2},k}^- \mathbf{f}(\mathbf{U}_{2,k}^W)}{a_{\frac{3}{2},k}^+ - a_{\frac{3}{2},k}^-} + \frac{a_{\frac{3}{2},k}^+ a_{\frac{3}{2},k}^-}{a_{\frac{3}{2},k}^+ - a_{\frac{3}{2},k}^-} [\mathbf{U}_{2,k}^W - \mathbf{U}_{1,k}^E]$$

$$a_{\frac{3}{2},k}^+ = \max(\lambda_2^{\mathbf{f}}(\mathbf{U}_{1,k}^E), \lambda_2^{\mathbf{f}}(\mathbf{U}_{2,k}^W), 0), \quad a_{\frac{3}{2},k}^- = \min(\lambda_1^{\mathbf{f}}(\mathbf{U}_{1,k}^E), \lambda_1^{\mathbf{f}}(\mathbf{U}_{2,k}^W), 0)$$

$$\mathbf{U}_{1,k}^E = \bar{\mathbf{U}}_{1,k} + \frac{\Delta x}{2} (\mathbf{U}_x)_{1,k}, \quad \mathbf{U}_{2,k}^W = \bar{\mathbf{U}}_{2,k} - \frac{\Delta x}{2} (\mathbf{U}_x)_{2,k}$$

Boundary cells and neighbours – case Γ^W (cont.)

- For the case of GML:

$$(\mathbf{U}_x)_{1,k} = \text{minmod} \left(\ominus \frac{\bar{\mathbf{U}}_{1,k} - \bar{\mathbf{U}}_{0,k}}{\Delta x}, \frac{\bar{\mathbf{U}}_{2,k} - \bar{\mathbf{U}}_{0,k}}{2\Delta x}, \ominus \frac{\bar{\mathbf{U}}_{2,k} - \bar{\mathbf{U}}_{1,k}}{\Delta x} \right)$$

- For the case of KL:

$$(\mathbf{U}_x)_{1,k} = \max \left\{ 0, \min \left\{ 2 \frac{\bar{\mathbf{U}}_{2,k} - \bar{\mathbf{U}}_{1,k} + \bar{\varepsilon}}{\bar{\mathbf{U}}_{1,k} - \bar{\mathbf{U}}_{0,k} + \bar{\varepsilon}}, \delta, \frac{1}{3} + \frac{2}{3} \frac{\bar{\mathbf{U}}_{2,k} - \bar{\mathbf{U}}_{1,k} + \bar{\varepsilon}}{\bar{\mathbf{U}}_{1,k} - \bar{\mathbf{U}}_{0,k} + \bar{\varepsilon}} \right\} \right\}$$

- For the case of VLL:

$$(\mathbf{U}_x)_{1,k} = \frac{\frac{\bar{\mathbf{U}}_{2,k} - \bar{\mathbf{U}}_{1,k} + \bar{\varepsilon}}{\bar{\mathbf{U}}_{1,k} - \bar{\mathbf{U}}_{0,k} + \bar{\varepsilon}} + \left| \frac{\bar{\mathbf{U}}_{2,k} - \bar{\mathbf{U}}_{1,k} + \bar{\varepsilon}}{\bar{\mathbf{U}}_{1,k} - \bar{\mathbf{U}}_{0,k} + \bar{\varepsilon}} \right|}{1 + \left| \frac{\bar{\mathbf{U}}_{2,k} - \bar{\mathbf{U}}_{1,k} + \bar{\varepsilon}}{\bar{\mathbf{U}}_{1,k} - \bar{\mathbf{U}}_{0,k} + \bar{\varepsilon}} \right|}$$

Evaluation of $\bar{U}_{0,k}$ and $\bar{U}_{\frac{1}{2},k}$, $\mathbf{x} \in \Gamma^W \in \Gamma_1$, $\chi'(U^2) = \partial\chi/\partial U^2$

$$-(\varepsilon\partial_\nu U^1 - U^1\chi'(U^2)\partial_\nu U^2) = c_1U^1 - c_2b \Rightarrow \varepsilon\frac{\partial U^1}{\partial x} + U^1\chi'(U^2)\frac{-\partial U^2}{\partial x} = c_1U^1 - c_2b,$$

$$D_a\partial_\nu U^i = B_i(\beta(t,b)c(\mathbf{x})), i = 2, 3, 4 \Rightarrow -\frac{\partial U^i}{\partial x} = \frac{1}{D_a}B_i(\beta(t,b)c(\mathbf{x}))$$

$$\left.\frac{\partial U^1}{\partial x}\right|_{(\frac{1}{2},k)} + \mathbf{U}_{\frac{1}{2},k}^1 \frac{1}{\varepsilon} \left(\frac{\chi'(U^2)\beta(t,b)c(\mathbf{x})}{D_a} - c_1 \right) \Big|_{(\frac{1}{2},k)} = -\frac{c_2b}{\varepsilon} \Big|_{(\frac{1}{2},k)}$$

$$\left.\frac{\partial U^i}{\partial x}\right|_{(\frac{1}{2},k)} = -\frac{1}{D_a}B_i(\beta(t,b)c(\mathbf{x})) \Big|_{(\frac{1}{2},k)}, i = 2, 3, 4$$

$$\left.\frac{\partial U^i}{\partial x}\right|_{(\frac{1}{2},k)} = \frac{\mathbf{U}_{1,k}^i - \mathbf{U}_{0,k}^i}{\Delta x} + \mathcal{O}(\Delta x^2), \mathbf{U}_{\frac{1}{2},k}^i = \frac{3\mathbf{U}_{0,k}^i + 6\mathbf{U}_{1,k}^i - \mathbf{U}_{2,k}^i}{8} + \mathcal{O}(\Delta x^2)$$

$$\frac{\mathbf{U}_{1,k}^1 - \mathbf{U}_{0,k}^1}{\Delta x} + \frac{3\mathbf{U}_{0,k}^1 + 6\mathbf{U}_{1,k}^1 - \mathbf{U}_{2,k}^1}{8} \frac{1}{\varepsilon} \left(\frac{\chi'(U^2)\beta(t,b)c(\mathbf{x})}{D_a} - c_1 \right) \Big|_{(\frac{1}{2},k)} = -\frac{c_2b}{\varepsilon} \Big|_{(\frac{1}{2},k)}$$

$$\frac{\mathbf{U}_{1,k}^i - \mathbf{U}_{0,k}^i}{\Delta x} = -\frac{1}{D_a}B_i(\beta(t,b)c(\mathbf{x})) \Big|_{(\frac{1}{2},k)}, i = 2, 3, 4$$

Time integration

Motivation

Model of HSCs' migration

FEM with COMSOL

FV approximation

- Conservation form
- Semi-discrete scheme
- Interior cells
- Second order limiters
- Neighbour to b. cells
- Boundary cells
- Case Γ^W
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- Time integration

Concluding remarks

- Semi-discrete system: $\frac{d}{dt} \bar{U}(t) = F(\bar{U}, t)$
- Implicit schemes
 - high computational costs
 - in some cases require time step restrictions
- Explicit Euler/ IMEX scheme (A. Chertock, A. Kurganov, 2008)

- first order accuracy
- integration with the **smallest time-step**:

$$\Delta t_{EE} \leq \min \left(\frac{\Delta x}{8a}, \frac{\Delta y}{8b}, c \right), \quad \Delta t_{IMEX} \leq \min \left(\frac{\Delta x}{4a}, \frac{\Delta y}{4b} \right)$$

$$a := \max_{j,k} \{ \max \{ a_{j+\frac{1}{2},k}^+, -a_{j+\frac{1}{2},k}^- \} \}, \quad b := \max_{j,k} \{ \max \{ b_{j,k+\frac{1}{2}}^+, -b_{j,k+\frac{1}{2}}^- \} \}$$

$$c := \frac{(\Delta x)^2 (\Delta y)^2}{4((\Delta x)^2 + (\Delta y)^2)}$$

- Explicit **second order** Runge-Kutta based **local time-stepping**
(joint work with T. Mitkova)

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Concluding remarks

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Concluding remarks

Concluding remarks

- Ongoing work
 - Development of own simulation package
 - Robust discretization of the nonlinear boundary conditions
 - Second order local time-stepping time integration

- Further steps
 - Numerical study of the ranges for parameters where the model works or fails
 - Sensitivity analysis and parameter estimation
 - Parallel implementation of the numerical scheme

Thank you for your attention!