A Positivity Preserving Centrul-Upwind Scheme for Chemotaxis and Haptotaxis Models

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joint work with Alexander Kurganov

Outline

- Chemotaxis model: The Keller-Segel Model
- Numerical methods
- Derivation of a new positivity-preserving numerical scheme
- Numerical examples
- Related models:
  - Chemotactic Bacteria Patterns in Semi-Solid Medium
  - Chemotactic Bacteria Patterns in Liquid Medium
  - Haptotaxis

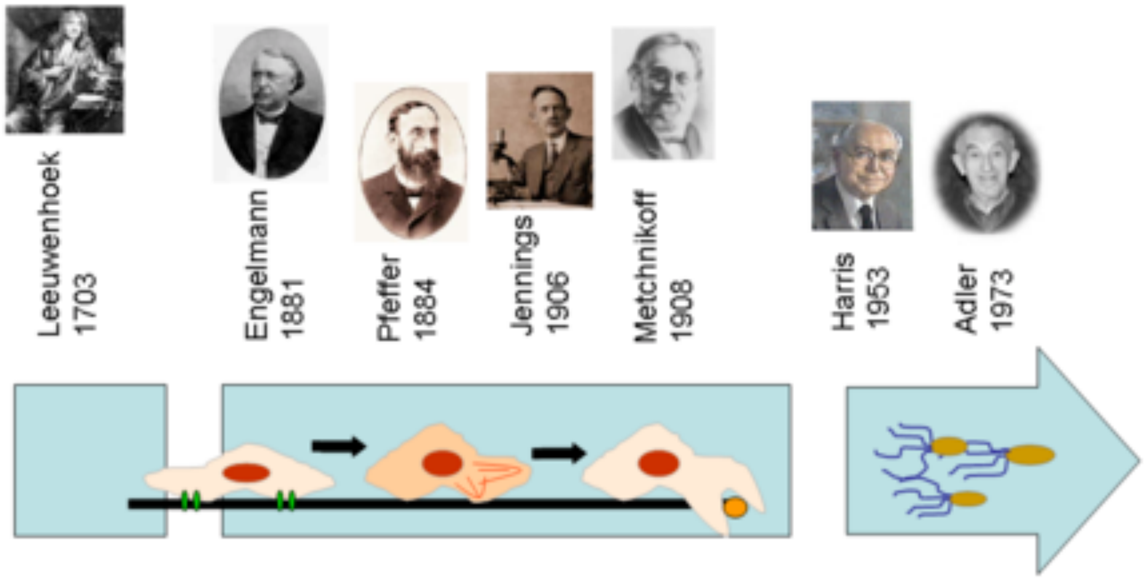
Chemotaxis

active orientation of cells and organisms along chemical gradients

- Numerous examples in animal and insect ecology, biological and biomedical sciences:
  - animals and insects rely on an acute sense of smell for conveying information between members of the species;
  - bacterial infection: invades the body and may be attacked by movement of cells towards the source as a result of chemotaxis;
  - development of cancer: very much related to the ability of cancerous cells to move, and thus spread faster that healthy cells.

- There are typically two kinds of patterns:
  - traveling waves (e.g., periodic swarm rings or band dynamics);
  - aggregate formation.

Milestones in chemotaxis research



PDE Based Chemotaxis Models

- typically two- or three-dimensional;
- highly nonlinear;
- described by time-dependent systems of PDEs, consisting of three distinct sets of terms:
  - reaction terms – model the interaction of different components (e.g., growth of cells, release of chemoattractant, etc.);
  - diffusion terms – model the random motion of each component;
  - chemotaxis terms – model the directed motion of one or more components in response to concentration gradient of another component (the chemoattractant).

Chemotaxis: the Keller-Segel Model

[Patlak (1953) and Keller & Segel (1970,71)]

$$\begin{cases} \rho_t + \nabla\cdot(\chi\rho\nabla c) = \Delta\rho \\ \alpha c_t = \Delta c - c + \rho \end{cases} \qquad \mathbf{x} = (x,y)^T \in \Omega,\ t > 0$$

$\alpha = 1$: parabolic case, $\quad \alpha = 0$: parabolic-elliptic case

Initial conditions: $\rho(x,y,t=0) = \rho_0(x,y), \quad c(x,y,t=0) = c_0(x,y)$

Flux boundary conditions: $\nabla\rho\cdot\mathbf{n} = \nabla c\cdot\mathbf{n} = 0, \quad \mathbf{x}\in\partial\Omega,\ t>0$

- $\rho(x,y,t)$ — cell density,
- $c(x,y,t)$ — chemoattractant concentration,
- χ — chemotactic sensitivity constant.

Analytical Results

[Herrero, Medina and Velázquez (1997), Horstmann (2003, 2004), Perthame (2007), ...]:

Recent review: [D. Horstmann; 2003, 2004]

Recent book: [B. Perthame; 2007]

- 1-D case – there are global smooth and unique solutions;
- 2-D case – global existence depends on a threshold:
  - initial mass lies below the threshold $\longrightarrow$ solutions exist globally;
  - initial mass lies above the threshold $\longrightarrow$ solutions blow up in finite time;
- Various regularizations.

Numerical Methods

finite-difference [Tyson, Stern & LeVeque (2000)], finite element [Marocco (2003), Saito (2007)], finite volume [Filbet (2006)] methods, ...

Difficulties:

- highly nonlinear chemotaxis and reaction terms;
- diffusion terms, which have infinite speed of propagation in the context of the solution;
- patterns are sought on large domains across which a disturbance must propagate for some time without hitting the boundary;
- local linear instability.

Approaches:

- to treat all terms simultaneously – typically need to be an implicit method due to diffusion and reaction terms;
- to apply fractional step methods to treat each term separately;

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- to apply fractional step methods to treat each term separately;

Goal: to develop a computationally efficient and stable method which can capture sharp gradients – difficult!

Keller-Segel Model – Numerical Example

$$\begin{cases} \rho_t + \nabla\cdot(\chi\rho\nabla c) = \Delta\rho \\ c_t = \Delta c - c + \rho \end{cases}$$

- Square domain $\Omega = [-\frac{1}{2}, \frac{1}{2}] \times [-\frac{1}{2}, \frac{1}{2}]$.

- Initial conditions:

$$\rho(x, y, 0) = 1000\, e^{-100(x^2+y^2)}, \qquad c(x, y, 0) = 500\, e^{-50(x^2+y^2)}.$$

- Nuemann boundary cinditions.

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According to theoretical results [Harrero, Velázquez (1997)], both ρ- and c-components of the solution are expected to blow up at the origin in finite time.

Naïve Finite-Difference Scheme

$$\begin{cases} \rho_t + (\chi\rho c_x)_x + (\chi\rho c_y)_y = \rho_{xx} + \rho_{yy} \\ c_t = c_{xx} + c_{yy} - c + \rho \end{cases}$$

$$\begin{cases} \dfrac{d\rho_{j,k}}{dt} = -\dfrac{H^x_{j+\frac{1}{2},k} - H^x_{j-\frac{1}{2},k}}{\Delta x} - \dfrac{H^y_{j,k+\frac{1}{2}} - H^y_{j,k-\frac{1}{2}}}{\Delta y} + D_0^2\rho_{j,k} \\ \dfrac{dc_{j,k}}{dt} = D_0^2 c_{j,k} - c_{j,k} + \rho_{j,k} \end{cases}$$

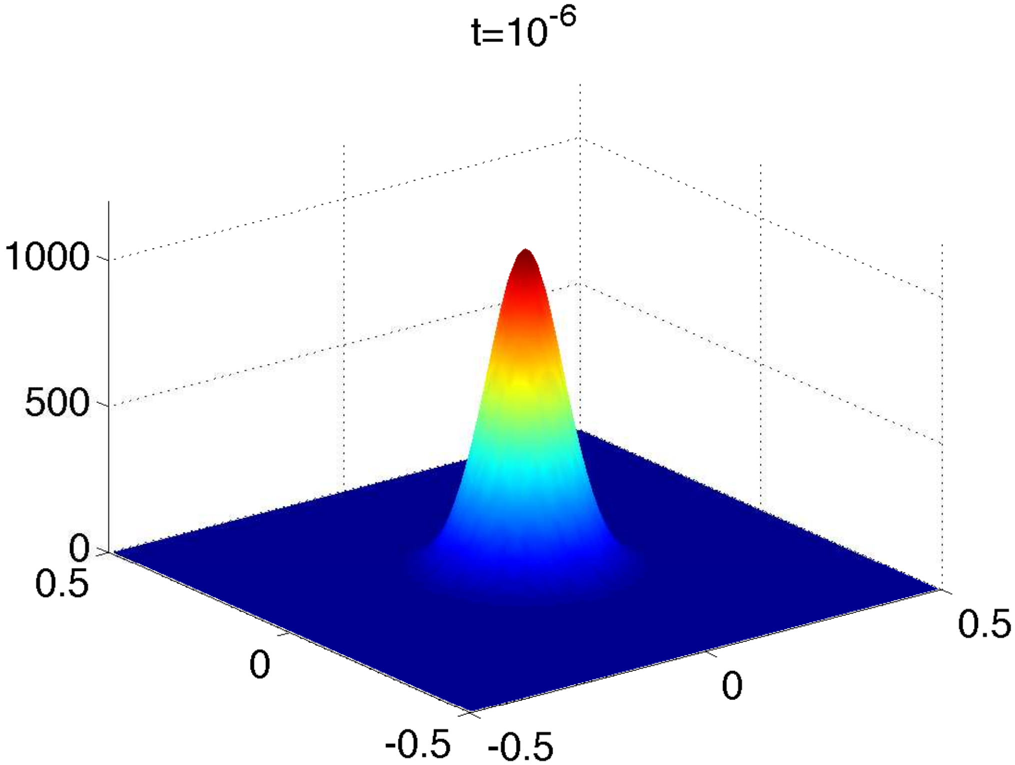
where

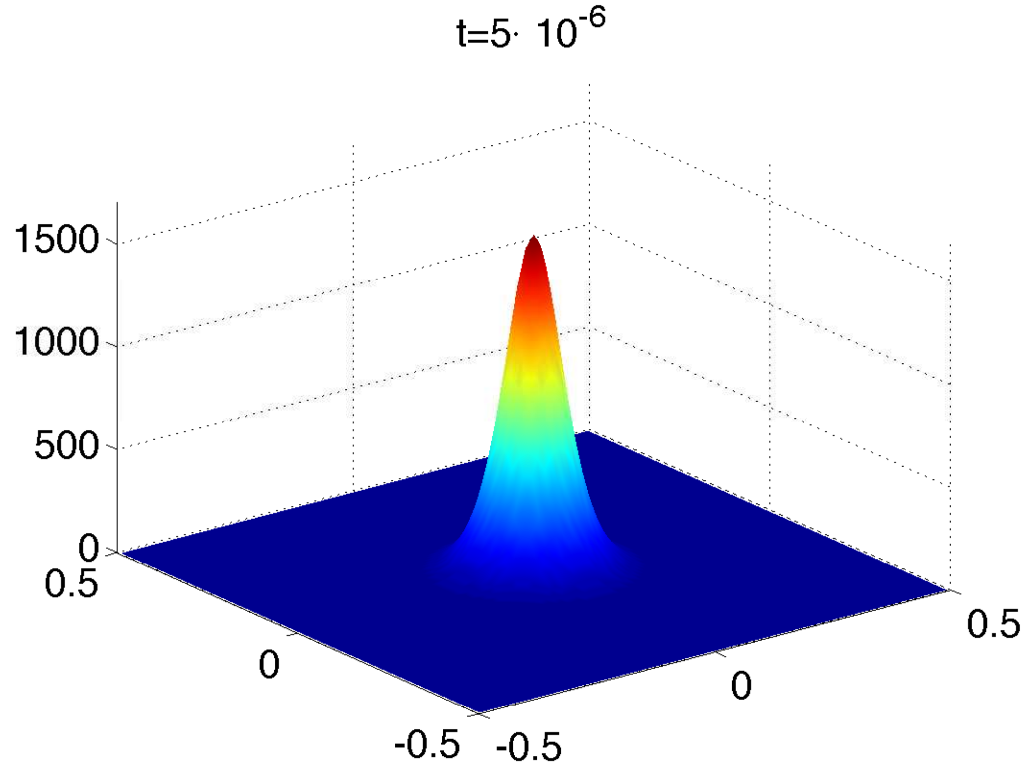
$$H^x_{j+\frac{1}{2},k} = \chi\frac{\rho_{j+1,k} + \rho_{j,k}}{2} \cdot \frac{c_{j+1,k} - c_{j,k}}{\Delta x}$$

$$H^y_{j,k+\frac{1}{2}} = \chi\frac{\rho_{j,k+1} + \rho_{j,k}}{2} \cdot \frac{c_{j,k+1} - c_{j,k}}{\Delta y}$$

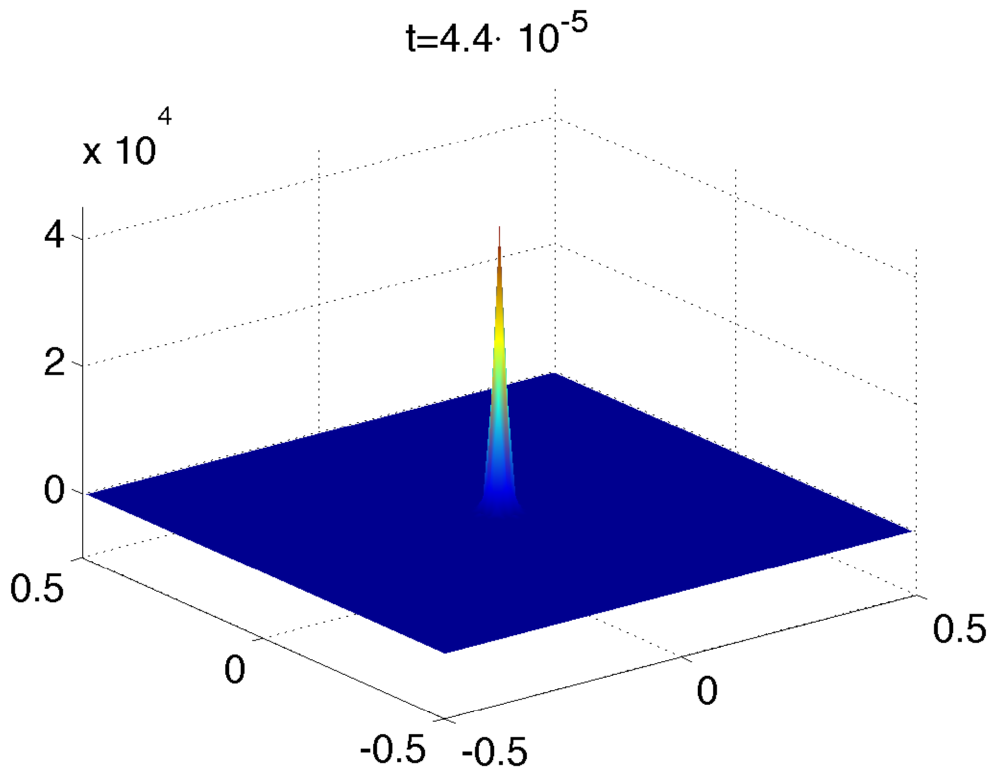
$$D_0^2\rho_{j,k} = \frac{\rho_{j+1,k} - 2\rho_{j,k} + \rho_{j-1,k}}{(\Delta x)^2} + \frac{\rho_{j,k+1} - 2\rho_{j,k} + \rho_{j,k-1}}{(\Delta y)^2}$$

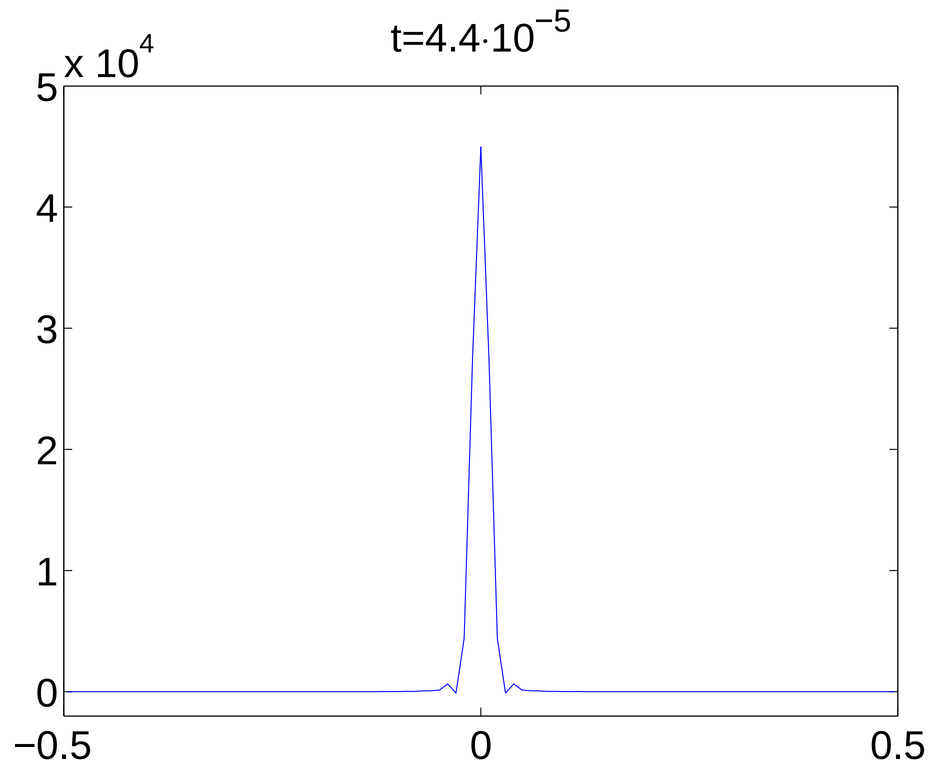
Small Times





Later Times





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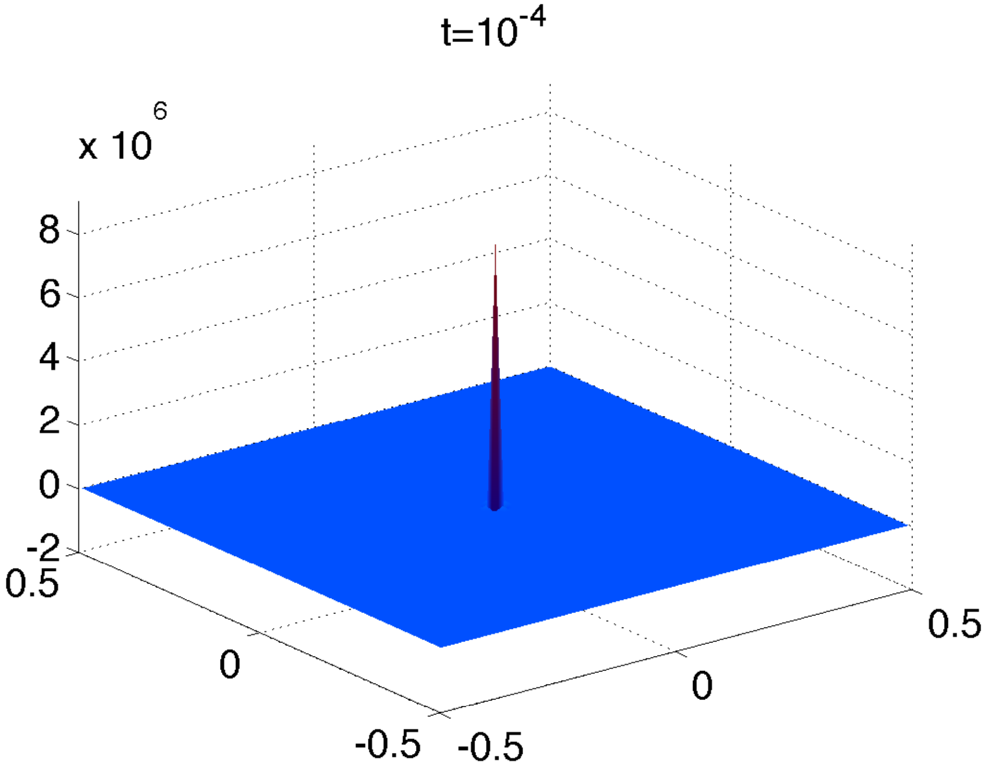

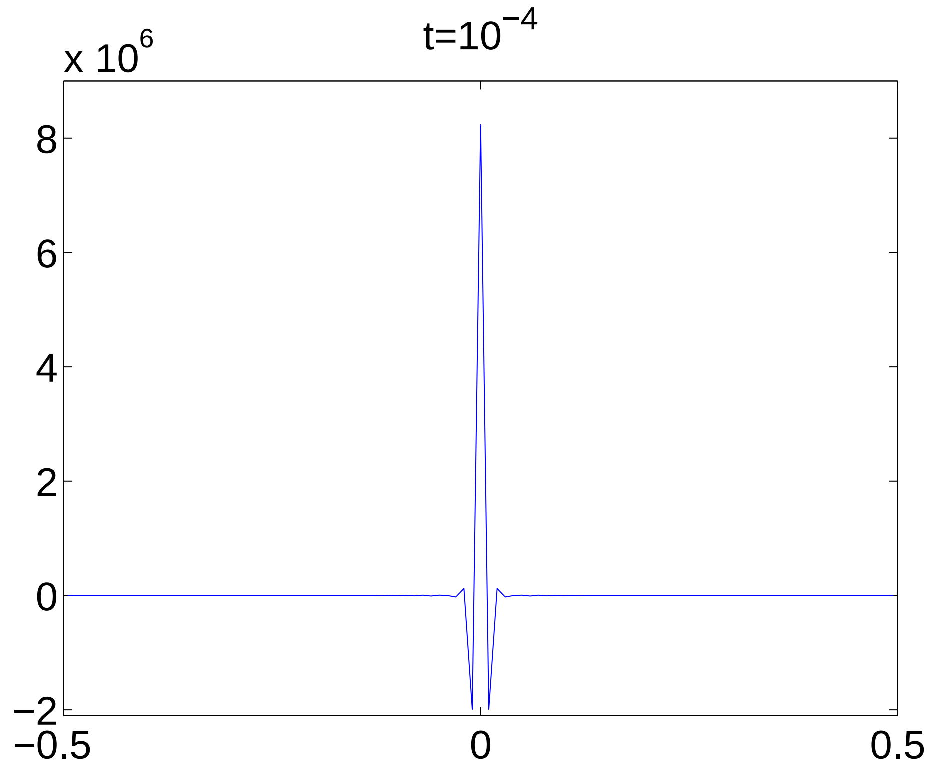

Keller-Segel Model – Properties

$$\begin{cases} \rho_t + (\chi\rho\, c_x)_x + (\chi\rho\, c_y)_y = \rho_{xx} + \rho_{yy} \\ c_t = c_{xx} + c_{yy} - c + \rho \end{cases}$$

Denote $u := c_x$ and $v := c_y$ and rewrite the Keller-Segel system

$$\begin{cases} \rho_t + (\chi\rho\, u)_x + (\chi\rho\, v)_y = \rho_{xx} + \rho_{yy} \\ u_t - \rho_x = u_{xx} + u_{yy} - u \\ v_t - \rho_y = v_{xx} + v_{yy} - v \end{cases}$$

This is a system of convection-diffusion-reaction equations:

$$\mathbf{U}_t + \mathbf{f}(\mathbf{U})_x + \mathbf{g}(\mathbf{U})_y = \Delta\mathbf{U} + \mathbf{R}(\mathbf{U})$$

$\mathbf{U} := (\rho, u, v)^T$, $\mathbf{f}(\mathbf{U}) := (\chi\rho u, -\rho, 0)^T$, $\mathbf{g}(\mathbf{U}) := (\chi\rho v, 0, -\rho)^T$, $\mathbf{R}(\mathbf{U}) := (0, -u, -v)^T$.

Keller-Segel Model – Properties

$$\mathbf{U}_t + \mathbf{f}(\mathbf{U})_x + \mathbf{g}(\mathbf{U})_y = \Delta\mathbf{U} + \mathbf{R}(\mathbf{U})$$

$$\begin{pmatrix} \rho \\ u \\ v \end{pmatrix}_t + \begin{pmatrix} \chi\rho u \\ -\rho \\ 0 \end{pmatrix}_x + \begin{pmatrix} \chi\rho v \\ 0 \\ -\rho \end{pmatrix}_y = \begin{pmatrix} \Delta\rho \\ \Delta u \\ \Delta v \end{pmatrix} - \begin{pmatrix} 0 \\ u \\ v \end{pmatrix}$$

The Jacobians of $\mathbf{f}$ and $\mathbf{g}$ are:

$$\frac{\partial \mathbf{f}}{\partial \mathbf{U}} = \begin{pmatrix} \chi u & \chi\rho & 0 \\ -1 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \qquad \frac{\partial \mathbf{g}}{\partial \mathbf{U}} = \begin{pmatrix} \chi v & 0 & \chi\rho \\ 0 & 0 & 0 \\ -1 & 0 & 0 \end{pmatrix}$$

Their eigenvalues are:

$$\lambda^{\mathbf{f}}_{1,2} = \frac{\chi}{2}\left(u \pm \sqrt{u^2 - \frac{4\rho}{\chi}}\right), \quad \lambda^{\mathbf{f}}_3 = 0$$

$$\lambda^{\mathbf{g}}_{1,2} = \frac{\chi}{2}\left(v \pm \sqrt{v^2 - \frac{4\rho}{\chi}}\right), \quad \lambda^{\mathbf{g}}_3 = 0$$

Keller-Segel Model – Properties

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The key (new) observation: the "purely" convective system

$$\mathbf{U}_t + \mathbf{f}(\mathbf{U})_x + \mathbf{g}(\mathbf{U})_y = \mathbf{0}$$

is

- hyperbolic (real e-values) if both $\chi u^2 \geq 4\rho$ and $\chi v^2 \geq 4\rho$
- elliptic (complex e-values) if $\chi \min(u^2, v^2) < 4\rho$

  Notice that the ellipticity condition is satisfied in generic cases, for example, when $u = c_x = 0$ and $\rho > 0$.

The operator splitting approach may not be applicable!

Semi-Discrete Central-Upwind Scheme

Central-upwind schemes were developed for multidimensional hyperbolic systems of conservation laws in 2000–2007 by Kurganov, Lin, Noelle, Petrova, Tadmor, ...

Central-upwind schemes are Godunov-type finite-volume projection-evolution methods:

- at each time level a solution is globally approximated by a piecewise polynomial function,
- which is then evolved to the new time level using the integral form of the conservation law system.

Semi-Discrete Central-Upwind Scheme

[Kurganov, Tadmor, Levy, Petrova, Noelle, Lin, Balbas, ...]

$$\mathbf{U}_t + \mathbf{f}(\mathbf{U})_x + \mathbf{g}(\mathbf{U})_y = \Delta \mathbf{U} + \mathbf{R}(\mathbf{U})$$

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

Denote: $\overline{\mathbf{U}}_{j,k}(t) := \dfrac{1}{\Delta x \Delta y} \displaystyle\iint\limits_{C_{j,k}} \mathbf{U}(x,y,t)\,dxdy$

Evolve in time:

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

$$\Lambda^h_{j,k} = \frac{\overline{\mathbf{U}}_{j+1,k} - 2\overline{\mathbf{U}}_{j,k} + \overline{\mathbf{U}}_{j-1,k}}{(\Delta x)^2} + \frac{\overline{\mathbf{U}}_{j,k+1} - 2\overline{\mathbf{U}}_{j,k} + \overline{\mathbf{U}}_{j,k-1}}{(\Delta y)^2}$$

$$\overline{R}_{j,k} = (0, -\overline{u}_{j,k}, -\overline{v}_{j,k})^T.$$

Godunov-Type Schemes for Conservation Laws: projection-evolution methods

$$\{\overline{\mathbf{U}}_j(t)\} \to \widetilde{\mathbf{U}}(\cdot,t) \to \left\{\begin{array}{c} \mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t) \\ a^{\pm}_{j+\frac{1}{2},k}(t) \\ b^{\pm}_{j,k+\frac{1}{2}}(t) \end{array}\right\} \to \left\{\begin{array}{c} \mathbf{H}^x_{j+\frac{1}{2},k}(t) \\ \mathbf{H}^y_{j,k+\frac{1}{2}}(t) \end{array}\right\} \to \{\overline{\mathbf{U}}_{j,k}(t{+}\Delta t)\}$$

via either a fully-discrete scheme

$$\overline{\mathbf{U}}^{n+1}_{j,k} = \overline{\mathbf{U}}^{n}_{j,k} - \frac{\Delta t}{\Delta x}\left[\mathbf{H}^x_{j+\frac{1}{2},k} - \mathbf{H}^x_{j-\frac{1}{2},k}\right] - \frac{\Delta t}{\Delta y}\left[\mathbf{H}^x_{j,k+\frac{1}{2}} - \mathbf{H}^x_{j,k-\frac{1}{2}}\right] + \Lambda^h_{j,k} + \overline{\mathbf{R}}_{j,k}$$

or a semi-discrete scheme

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

$$\{\overline{\mathbf{U}}_j(t)\} \to \widetilde{\mathbf{U}}(\cdot,t) \to \left\{\begin{array}{c} \mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t) \\ a^{\pm}_{j+\frac{1}{2},k}(t) \\ b^{\pm}_{j,k+\frac{1}{2}}(t) \end{array}\right\} \to \left\{\begin{array}{c} \mathbf{H}^{x}_{j+\frac{1}{2},k}(t) \\ \mathbf{H}^{y}_{j,k+\frac{1}{2}}(t) \end{array}\right\} \to \{\overline{\mathbf{U}}_{j,k}(t+\Delta t)\}$$

(Discontinuous) piecewise-linear reconstruction:

$$\widetilde{\mathbf{U}}(x,y,t) := \overline{\mathbf{U}}_{j,k} + (\mathbf{U}_x)_{j,k}(x-x_j) + (\mathbf{U}_y)_{j,k}(y-y_k), \quad (x,y) \in C_{j,k},$$

It is conservative, second-order accurate, and non-oscillatory provided the slopes are computed by a nonlinear limiter

Example — the Generalized Minmod Limiter

$$\widetilde{\mathbf{U}}(x,y,t) := \overline{\mathbf{U}}_{j,k} + (\mathbf{U}_x)_{j,k}(x - x_j) + (\mathbf{U}_y)_{j,k}(y - y_k), \quad (x,y) \in C_{j,k}$$

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

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

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

$$\{\overline{\mathbf{U}}_j(t)\} \to \widetilde{\mathbf{U}}(\cdot,t) \to \left\{ \begin{array}{c} \mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t) \\ a^{\pm}_{j+\frac{1}{2},k}(t) \\ b^{\pm}_{j,k+\frac{1}{2}}(t) \end{array} \right\} \to \left\{ \begin{array}{c} \mathbf{H}^{x}_{j+\frac{1}{2},k}(t) \\ \mathbf{H}^{y}_{j,k+\frac{1}{2}}(t) \end{array} \right\} \to \{\overline{\mathbf{U}}_{j,k}(t+\Delta t)\}$$

$\mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t)$ are the point values of

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

at $(x_{j+\frac{1}{2}},y_k)$, $(x_{j-\frac{1}{2}},y_k)$, $(x_j,y_{k+\frac{1}{2}})$, and $(x_j,y_{k-\frac{1}{2}})$, respectively:

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

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

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

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

$$\{\overline{\mathbf{U}}_j(t)\} \to \widetilde{\mathbf{U}}(\cdot,t) \to \left\{\begin{array}{c} \mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t) \\ a^{\pm}_{j+\frac{1}{2},k}(t) \\ b^{\pm}_{j,k+\frac{1}{2}}(t) \end{array}\right\} \to \left\{\begin{array}{c} \mathbf{H}^x_{j+\frac{1}{2},k}(t) \\ \mathbf{H}^y_{j,k+\frac{1}{2}}(t) \end{array}\right\} \to \{\overline{\mathbf{U}}_{j,k}(t+\Delta t)\}$$

One-sided local speeds

- in the x-direction – $a^{\pm}_{j+\frac{1}{2},k}(t)$ – obtained from the largest and the smallest eigenvalues of the Jacobian $\dfrac{\partial\mathbf{f}}{\partial\mathbf{U}}$;
- in the y-direction – $b^{\pm}_{j,k+\frac{1}{2}}(t)$ – obtained from the largest and the smallest eigenvalues of the Jacobian $\dfrac{\partial\mathbf{g}}{\partial\mathbf{U}}$.

$$\lambda^{\mathbf{f}}_{1,2} = \frac{\chi}{2}\left(u \pm \sqrt{u^2 - \frac{4\rho}{\chi}}\right), \quad \lambda^{\mathbf{g}}_{1,2} = \frac{\chi}{2}\left(v \pm \sqrt{v^2 - \frac{4\rho}{\chi}}\right),$$
$$\lambda^{\mathbf{f}}_3 = 0, \qquad \lambda^{\mathbf{g}}_3 = 0.$$

$$\{\overline{\mathbf{U}}_j(t)\} \to \widetilde{\mathbf{U}}(\cdot,t) \to \left\{ \begin{array}{c} \mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t) \\ a^{\pm}_{j+\frac{1}{2},k}(t) \\ b^{\pm}_{j,k+\frac{1}{2}}(t) \end{array} \right\} \to \left\{ \begin{array}{c} \mathbf{H}^x_{j+\frac{1}{2},k}(t) \\ \mathbf{H}^y_{j,k+\frac{1}{2}}(t) \end{array} \right\} \to \{\overline{\mathbf{U}}_{j,k}(t+\Delta t)\}$$

If all λ^{f} are real, then

$$a^+_{j+\frac{1}{2},k} = \max\left(\lambda^{\mathbf{f}}(\mathbf{U}^{\mathrm{E}}_{j,k}), \lambda^{\mathbf{f}}(\mathbf{U}^{\mathrm{W}}_{j+1,k}), 0\right)$$

$$a^-_{j+\frac{1}{2},k} = \min\left(\lambda^{\mathbf{f}}(\mathbf{U}^{\mathrm{E}}_{j,k}), \lambda^{\mathbf{f}}(\mathbf{U}^{\mathrm{W}}_{j+1,k}), 0\right)$$

otherwise

$$a^+_{j+\frac{1}{2},k} = \chi \max\left(u^{\mathrm{E}}_{j,k},\ u^{\mathrm{W}}_{j+1,k},\ 0\right),$$

$$a^-_{j+\frac{1}{2},k} = \chi \min\left(u^{\mathrm{E}}_{j,k},\ u^{\mathrm{W}}_{j+1,k},\ 0\right).$$

If all λ^{g} are real, then,

$$b^+_{j,k+\frac{1}{2}} = \max\left(\lambda^{\mathbf{g}}(\mathbf{U}^{\mathrm{N}}_{j,k}), \lambda^{\mathbf{g}}(\mathbf{U}^{\mathrm{S}}_{j,k+1}), 0\right)$$

$$b^-_{j,k+\frac{1}{2}} = \min\left(\lambda^{\mathbf{g}}(\mathbf{U}^{\mathrm{N}}_{j,k}), \lambda^{\mathbf{g}}(\mathbf{U}^{\mathrm{S}}_{j,k+1}), 0\right)$$

otherwise

$$b^+_{j,k+\frac{1}{2}} = \chi \max\left(v^{\mathrm{N}}_{j,k},\ v^{\mathrm{S}}_{j,k+1},\ 0\right),$$

$$b^-_{j,k+\frac{1}{2}} = \chi \min\left(v^{\mathrm{N}}_{j,k},\ v^{\mathrm{S}}_{j,k+1},\ 0\right).$$

$$\{\overline{\mathbf{U}}_j(t)\} \longrightarrow \widetilde{\mathbf{U}}(\cdot,t) \longrightarrow \left\{ \begin{array}{c} \mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t) \\ a^{\pm}_{j+\frac{1}{2},k}(t) \\ b^{\pm}_{j,k+\frac{1}{2}}(t) \end{array} \right\} \longrightarrow \left\{ \begin{array}{c} \mathbf{H}^x_{j+\frac{1}{2},k}(t) \\ \mathbf{H}^y_{j,k+\frac{1}{2}}(t) \end{array} \right\} \longrightarrow \{\overline{\mathbf{U}}_{j,k}(t+\Delta t)\}$$

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

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

$$\{\overline{\mathbf{U}}_j(t)\} \longrightarrow \widetilde{\mathbf{U}}(\cdot,t) \longrightarrow \left\{ \begin{array}{c} \mathbf{U}^{\mathrm{E,W,N,S}}_{j,k}(t) \\ a^{\pm}_{j+\frac{1}{2},k}(t) \\ b^{\pm}_{j,k+\frac{1}{2}}(t) \end{array} \right\} \longrightarrow \left\{ \begin{array}{c} \mathbf{H}^x_{j+\frac{1}{2},k}(t) \\ \mathbf{H}^y_{j,k+\frac{1}{2}}(t) \end{array} \right\} \longrightarrow \{\overline{\mathbf{U}}_{j,k}(t+\Delta t)\}$$

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

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

Positivity Preserving Property

Theorem (A.C. & A. Kurganov): *The cell densities* $\{\overline{u}_{j,k}(t)\}$, *computed by the described semi-discrete central-upwind scheme with a positivity preserving piecewise linear reconstruction for* u, *remain nonnegative provided the initial cell densities are nonnegative, the system of ODEs is discretized by the forward Euler method and the following CFL condition is satisfied:*

$$\Delta t \le \min\left\{\frac{\Delta x}{8a},\ \frac{\Delta y}{8b},\ \frac{(\Delta x)^2(\Delta y)^2}{4((\Delta x)^2+(\Delta y)^2)}\right\},$$

$$a := \max_{j,k}\left\{\max\{a^+_{j+\frac{1}{2},k}, -a^-_{j+\frac{1}{2},k}\}\right\}, \quad b := \max_{j,k}\left\{\max\{b^+_{j,k+\frac{1}{2}}, -b^-_{j,k+\frac{1}{2}}\}\right\}.$$

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Remark. The theorem is also valid if the forward Euler method is replaced by a higher-order SSP ODE solver, because a time step in such solvers can be written as a convex combination of several forward Euler steps.

Example 1 – Blowup at the Center of a Square Domain

$$\begin{cases} \rho_t + \nabla\cdot(\chi\rho\nabla c) = \Delta\rho, \\ c_t = \Delta c - c + \rho. \end{cases}$$

- Square domain $\Omega = [-\frac{1}{2}, \frac{1}{2}] \times [-\frac{1}{2}, \frac{1}{2}]$.

- Initial conditions:

$$\rho(x,y,0) = 1000\, e^{-100(x^2+y^2)}, \quad c(x,y,0) = 500\, e^{-50(x^2+y^2)}.$$

- Neumann boundary conditions.

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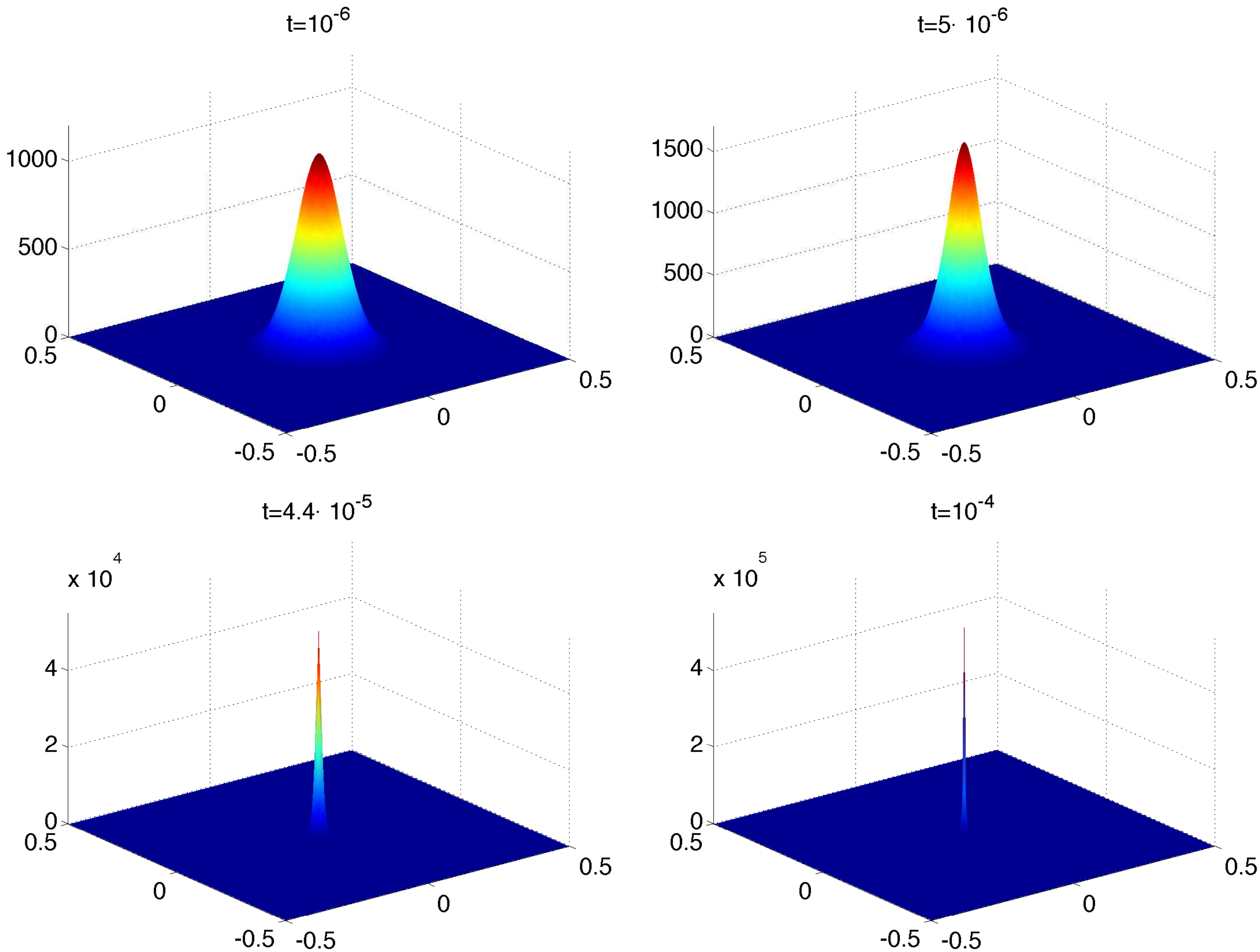
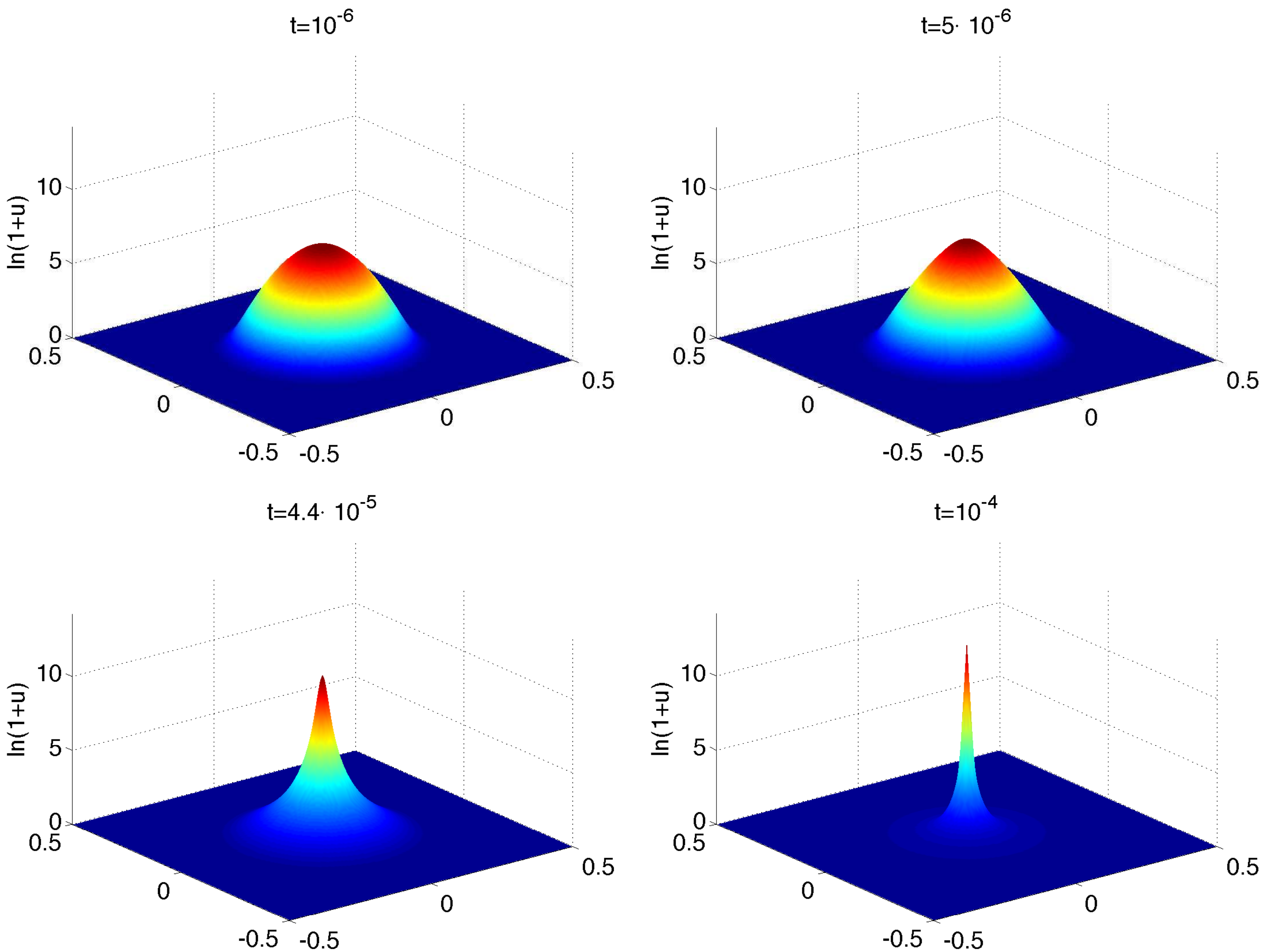
According to theoretical results [Harrero, Velázquez (1997)], both ρ- and c-components of the solution are expected to blow up at the origin in finite time.


t=10^-6
1000
500
0
0.5
0
-0.5
-0.5
0
0.5
t=5· 10^-6
1500
1000
500
0
t=4.4· 10^-5
x 10^4
4
2
0
t=10^-4
x 10^5
4
2
0

Logarithmic Vertical Scale



Example 2 – Blowup at the Center of a Square Domain

$$\begin{cases} \rho_t + \nabla\cdot(\chi\rho\nabla c) = \Delta\rho, \\ c_t = \Delta c - c + \rho. \end{cases}$$

- Square domain $\Omega = [-\frac{1}{2}, \frac{1}{2}] \times [-\frac{1}{2}, \frac{1}{2}]$.
- Initial conditions: $\rho(x, y, 0) = 1000\, e^{-100(x^2+y^2)}, \quad c(x, y, 0) \equiv 0.$
- Neumann boundary conditions.

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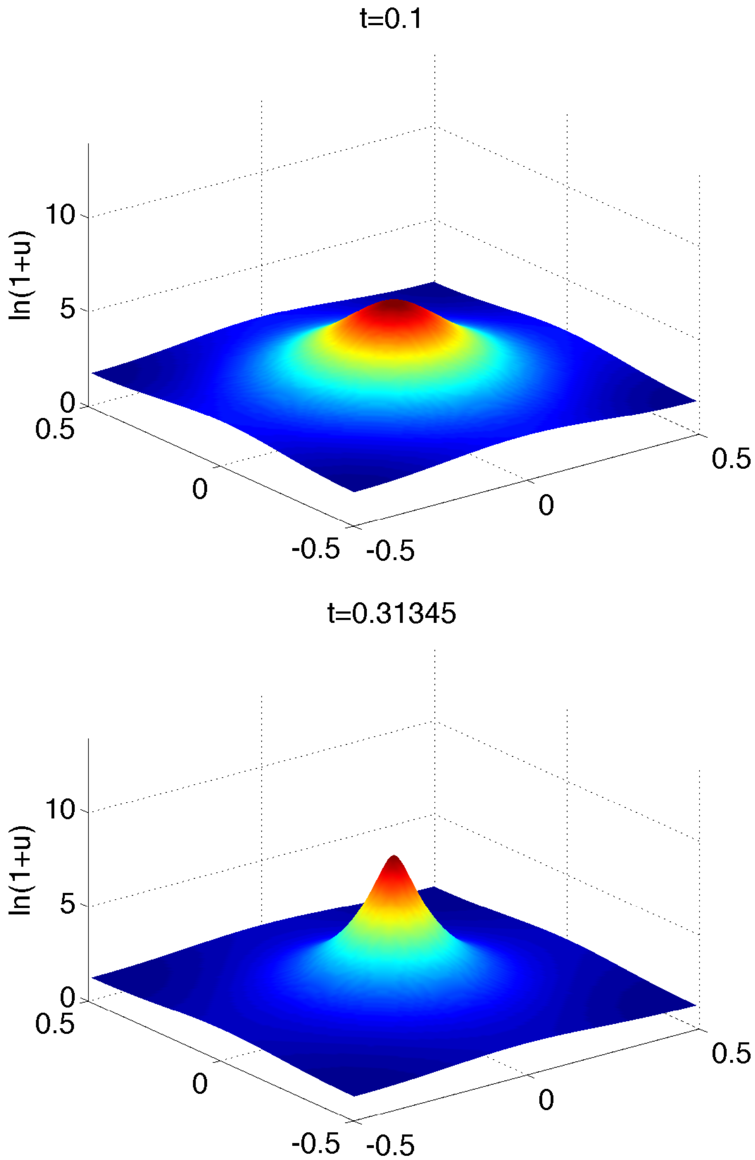
- Neumann boundary conditions.

Properties:

- both ρ- and c-components of the solution are expected to blow up at the origin in finite time;
- the blowup is expected to occur much later than in Example 1;
- the diffusion initially dominates the concentration mechanism and hence, the cell density spreads out and its maximum decreases at small times.

Logarithmic Vertical Scale



Examples 3 – Blowup at the Corner of a Square Domain

$$\begin{cases} \rho_t + \nabla\cdot(\chi\rho\nabla c) = \Delta\rho, \\ c_t = \Delta c - c + \rho. \end{cases}$$

- Square domain $\Omega = [-\frac{1}{2}, \frac{1}{2}] \times [-\frac{1}{2}, \frac{1}{2}]$.

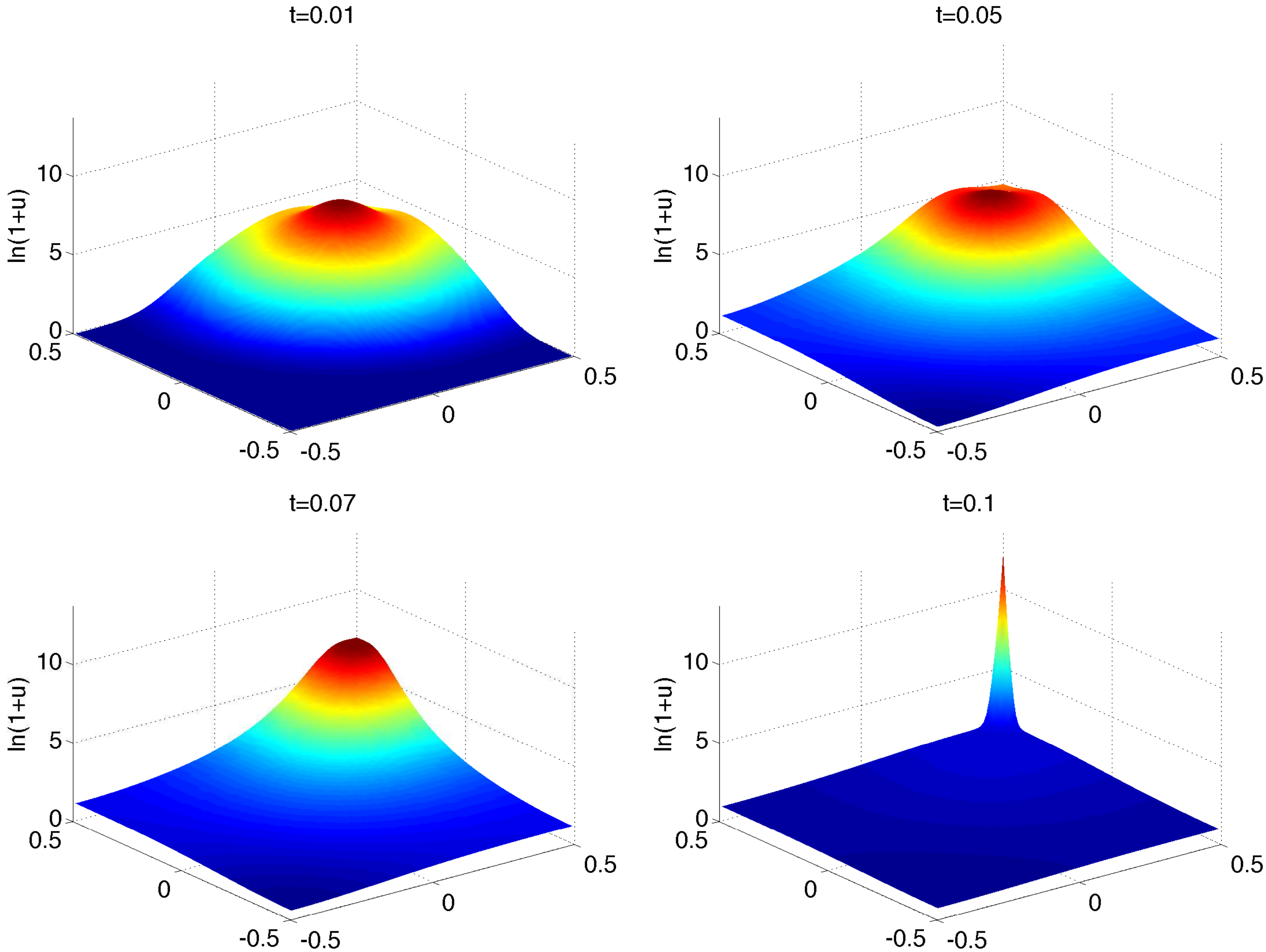
- Different initial conditions:
  - $\rho(x,y,0) = 1000\, e^{-100\left((x-0.25)^2+(y-0.25)^2\right)}, \quad c(x,y,0) = 0$

    The solution is expected to blow up at the corner $(\frac{1}{2}, \frac{1}{2})$.

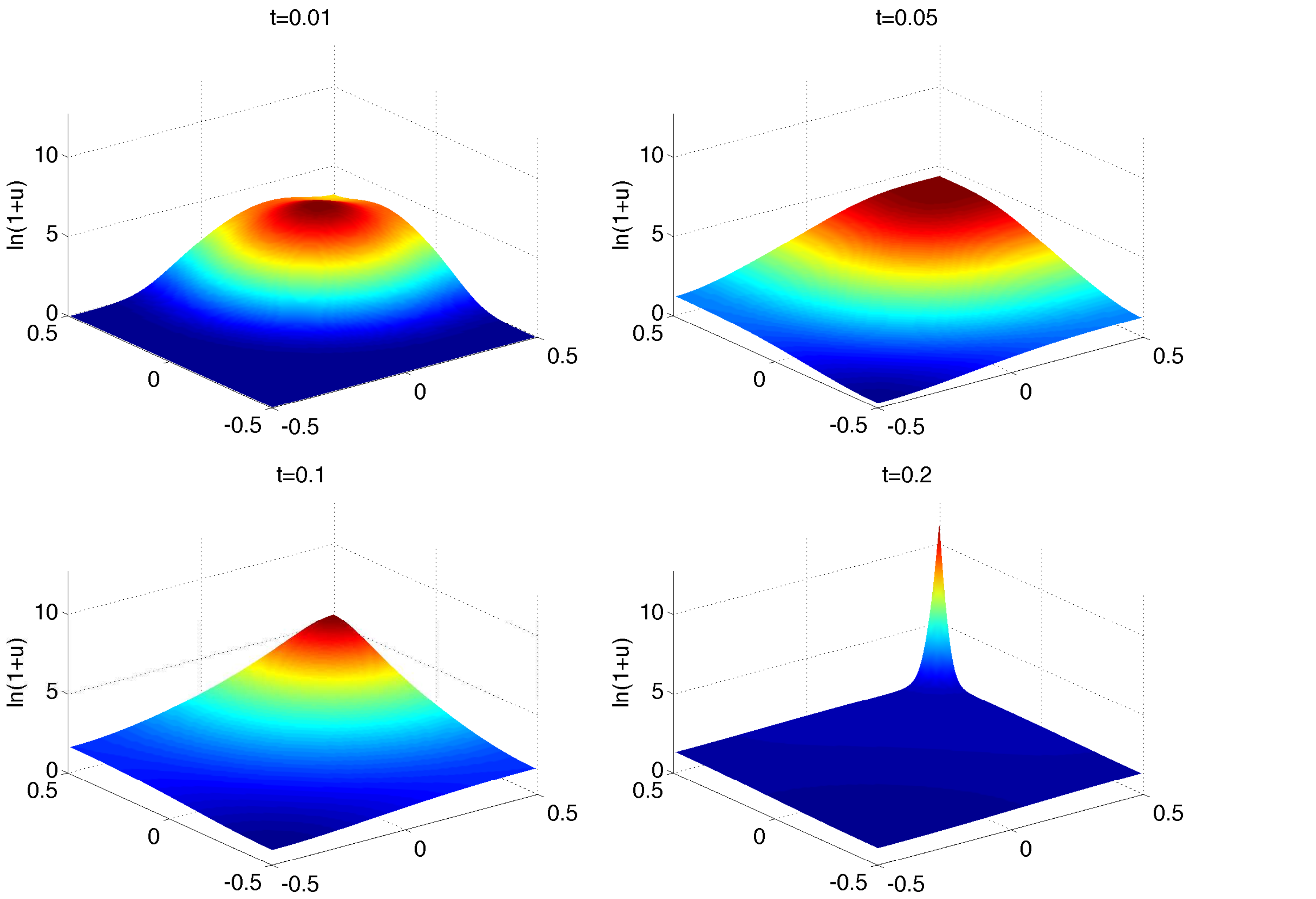
  - $\rho(x,y,0) = 500e^{-100((x-0.25)^2+((y-0.25)^2)}, \qquad c(x,y,0) = 0$

    The initial total mass is now below the critical value, and thus the solution may or may not blow up, and if it does, it has to concentrate at the same corner $(\frac{1}{2}, \frac{1}{2})$.

Critical ID – Logarithmic Vertical Scale



Subcritical ID – Logarithmic Vertical Scale



Related Models

Model of Chemotactic Bacteria Patterns in Semi-Solid Medium

[Tyson, Lubkin and Murray (1999)]

$$\rho_t + \alpha \nabla \cdot \left[\frac{\rho}{(1+c)^2} \nabla c \right] = d_\rho \Delta \rho + r\rho \left(\delta \frac{w^2}{1+w^2} - \rho \right)$$
$$c_t = d_c \Delta c + \beta \frac{w\rho^2}{\mu + \rho^2} - \gamma \rho c$$
$$w_t = d_w \Delta w - \kappa \rho \frac{w^2}{1+w^2}$$

- $\rho(x, y, t)$ – the cell density
- $c(x, y, t)$ – a chemoattractant concentration
- new variable: $w(x, y, t)$ – the nutrient concentration
- $\alpha, d_u, \rho, \delta, d_v, \beta, \mu, \gamma, d_w$, and κ – positive constants

Model of Chemotactic Bacteria Patterns in Semi-Solid Medium

1. $$\rho_t + \alpha \nabla \cdot \left[\frac{\rho}{(1+c)^2} \nabla c \right] = d_\rho \Delta \rho + r\rho \left(\delta \frac{w^2}{1+w^2} - \rho \right)$$

   rate of change of cell density = chemotaxis of cells to chemoattractant + diffusion cells + growth and death of cells

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   rate of change of cell density = chemotaxis of cells to chemoattractant + diffusion cells + growth and death of cells

2. $c_t = d_c \Delta c + \beta \frac{w\rho^2}{\mu + \rho^2} - \gamma \rho c$

   rate of change of chemoattractant = diffusion of chemoattractant + production of chemoattractant by cells + uptake of chemoattractant by cells

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3. $$w_t = d_w \Delta w - \kappa \rho \frac{w^2}{1+w^2}$$

   rate of change of nutrient = diffusion of nutrient + uptake of nutrient by cells

Model of Chemotactic Bacteria Patterns in Semi-Solid Medium

$$
\begin{cases}
\rho_t + \left(\dfrac{\alpha\rho u}{(1+c)^2}\right)_x + \left(\dfrac{\alpha\rho v}{(1+c)^2}\right)_y = d_\rho(\rho_{xx}+\rho_{yy}) + r\rho\left(\dfrac{\delta w^2}{1+w^2}-\rho\right) \\
c_t = d_c(c_{xx}+c_{yy}) + \dfrac{\beta w \rho^2}{\mu+\rho^2} - \gamma\rho c \\
u_t + \left(\gamma\rho c - \dfrac{\beta w\rho^2}{\mu+\rho^2}\right)_x = d_c(u_{xx}+u_{yy}) \\
v_t + \left(\gamma\rho c - \dfrac{\beta w\rho^2}{\mu+\rho^2}\right)_y = d_c(v_{xx}+v_{yy}) \\
w_t = d_w\Delta w - \dfrac{\kappa\rho w^2}{1+w^2}
\end{cases}
$$

where, as before, $u := c_x,\ u := v_y \quad \Longrightarrow \quad \mathbf{U} := (\rho, c, u, v, w)^T$

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

Numerical Example

- Initial Setup:

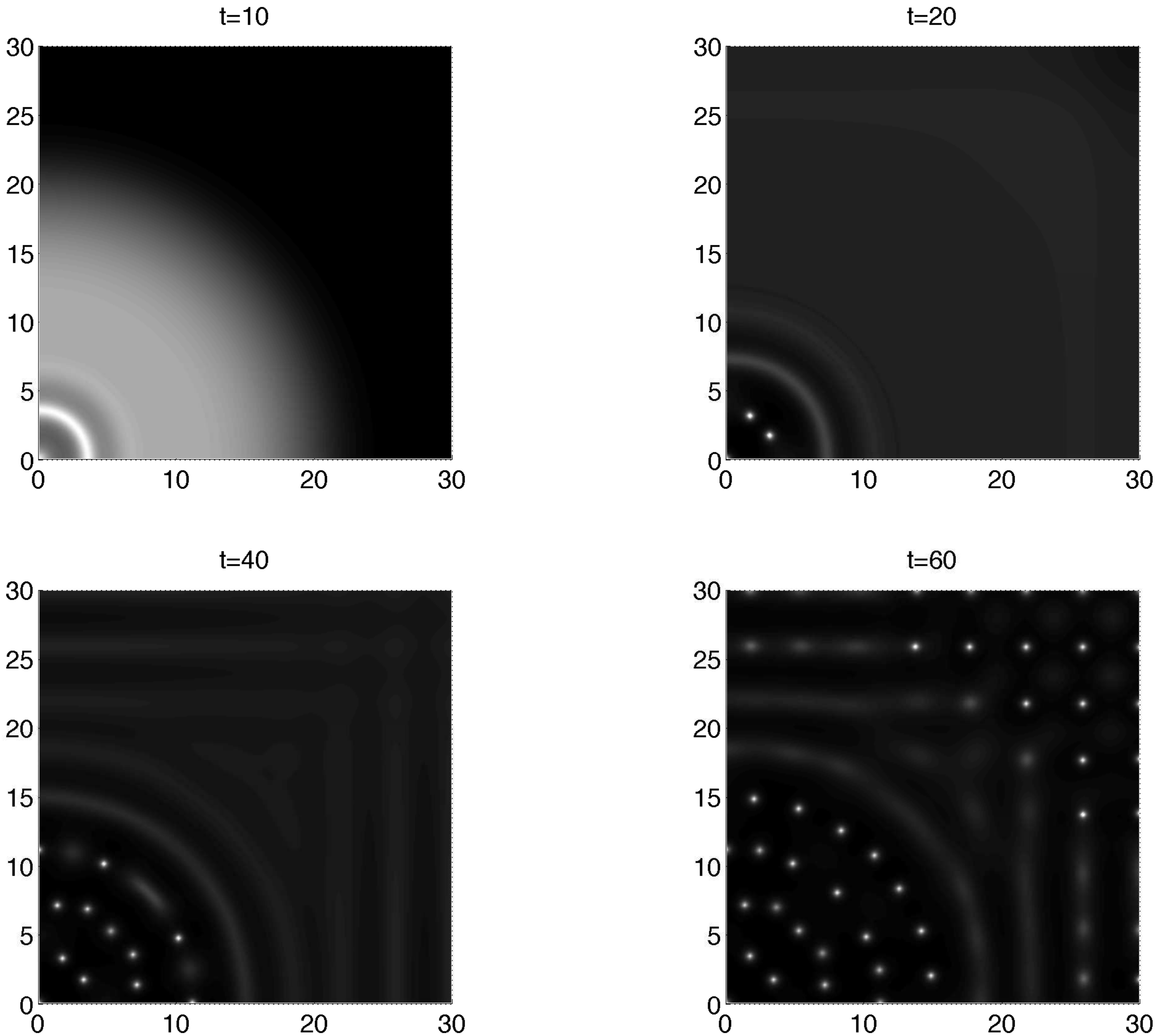
$$c(x,y,0) \equiv 0, \quad w(x,y,0) \equiv 1,$$

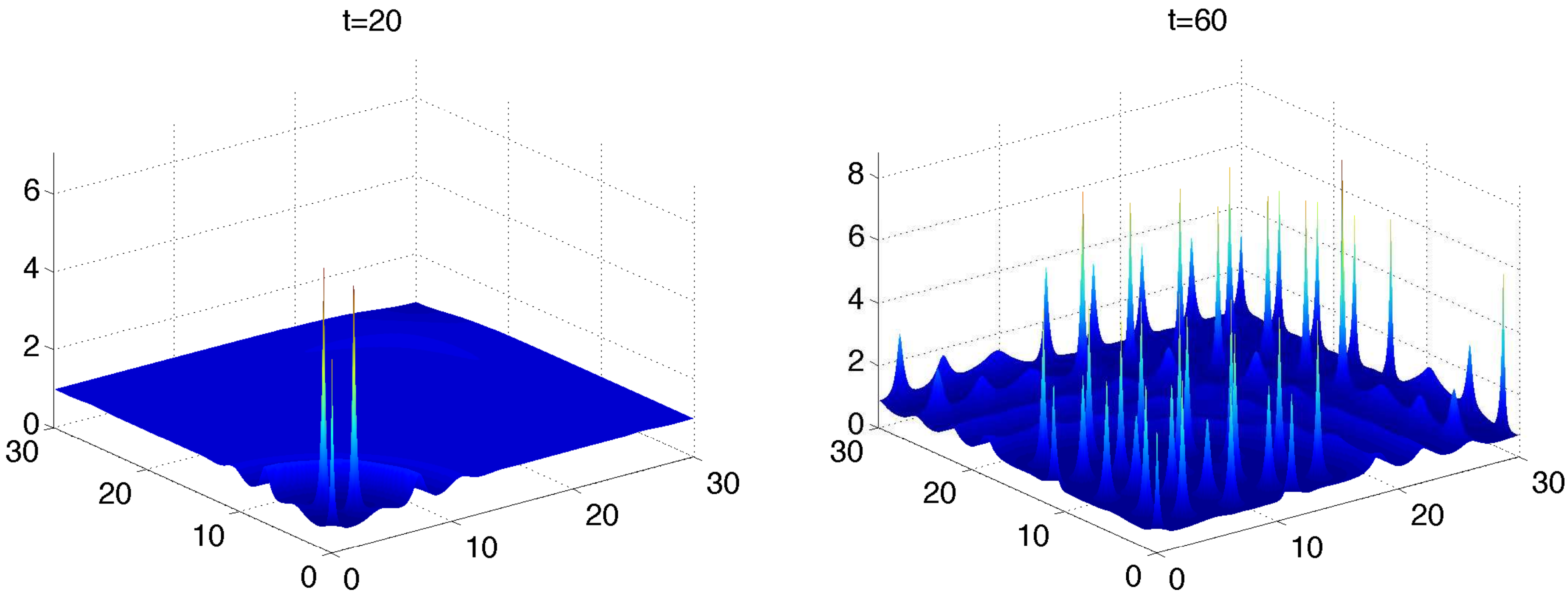
$$\rho(x,y,0) = \begin{cases} 5\cos^2\left(\dfrac{\pi\sqrt{x^2+y^2}}{4}\right), & \text{if} \quad x^2+y^2 \le 4, \\ 0, & \text{otherwise}, \end{cases}$$

- Parameters:

$$\alpha = 40, \quad d_\rho = 0.25, \quad r = 1.5, \quad \delta = 2, \quad d_c = 1,$$

$$\beta = 10, \quad \mu = 100, \quad \gamma = 1, \quad d_w = 0.8, \quad \kappa = 0.005$$


t=10
t=20
t=40
t=60
0
5
10
15
20
25
30



3-D plot of the solution at times $t = 20$ and $t = 60$.

Model of Chemotactic Bacteria Patterns in Liquid Medium

[Tyson, Lubkin and Murray (1999)]

$$\rho_t + \alpha \nabla \cdot \left[\frac{\rho}{(1+c)^2} \nabla c \right] = d_\rho \Delta \rho$$
$$c_t = d_c \Delta c + \beta \frac{w \rho^2}{\mu + \rho^2}$$

- contains sufficient nutrients for the bacteria
- the coefficients $\rho = 0$ and $\gamma = 0$
- the nutritient concentration $w \equiv \mathrm{const}$
- α, d_u, d_v, β, and μ are positive constants

Numerical Example

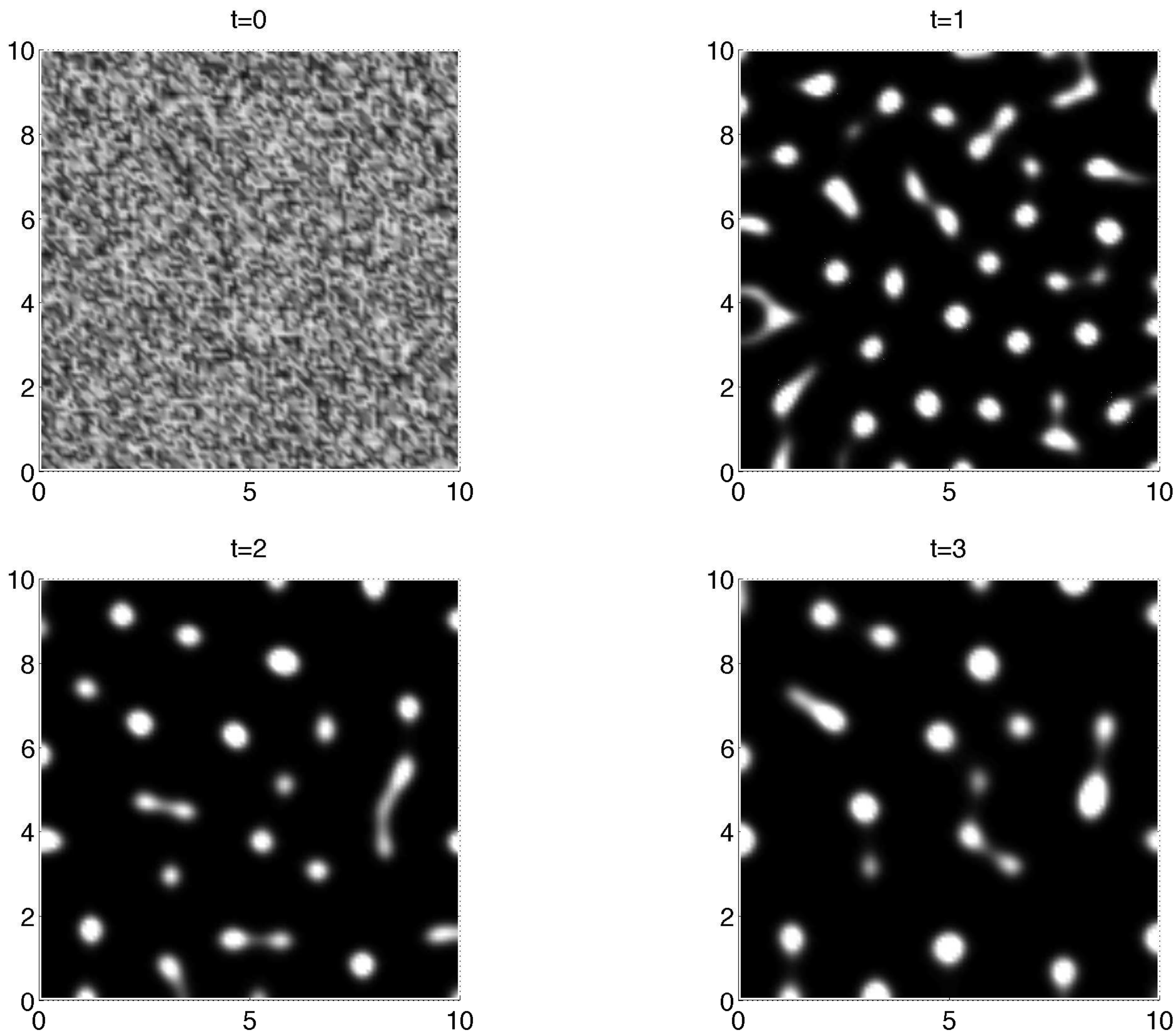
- Initial setup:

$$\rho(x,y,0) = 0.9 + 0.2\sigma(x,y), \qquad c(x,y,0) = 0,$$

σ is a random variable uniformly distributed on $[0,1]$.

- Parameters:

$$\alpha = 80, \quad d_u = 0.33, \quad d_v = \beta = \mu = w = 1.$$


t=0
t=1
t=2
t=3
10
8
6
4
2
0
0
5
10

A Haptotaxis Model

- The term haptotaxis originated with S. B. Carter in 1965:

  "*. . . the movement of a cell is controlled by the relative strengths of its peripheral adhesions, and that movements directed in this way, together with the influence of patterns of adhesion on cell shape are responsible for the arrangement of cells into complex and ordered tissues*".

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- Cell movement, e.g., in inflammation, wound healing, tumor invasion, are the result of haptotactic responses of cells to differential adhesion strengths.

- The mathematical formulation of haptotaxis: similar to chemotaxis processes.

- Unique features: the movement of tumor cells is directed to the nondiffusible extracellular environment, which supplies essential oxygen and available space, as it is degraded by the tumor-produced degradative enzyme.

A Haptotaxis Model

[Cartet (1965,67), Anderson (2005)]
[Ayati, Web, Anderson (2006), Walker, Web (2007)]

$$\rho_t + \underbrace{\nabla\cdot(\chi(c)\rho\nabla c)}_{haptotaxis} = \underbrace{d_\rho \Delta\rho}_{cell\ motility} - \underbrace{\psi(x,y,w)\rho}_{cell\ death} + \underbrace{r(x,y,w)\rho}_{cell\ division}$$

$$c_t = -\underbrace{\alpha(x,y)mc}_{degradation}$$

$$m_t = \underbrace{d_m \Delta m}_{diffusion} + \underbrace{\delta(x,y)\rho}_{production} - \underbrace{\beta(x,y)m}_{decay}$$

$$w_t = \underbrace{d_w \Delta w}_{diffusion} + \underbrace{\gamma(x,y)c}_{production} - \underbrace{e(x,y)w}_{decay} - \underbrace{\eta(x,y,\rho)w}_{uptake}$$

- $\rho(x,y,t)$ is the density of tumor cells,
- $c(x,y,t)$,the density of extracellular matrix macromolecules,
- $m(x,y,t)$ is the concentration of matrix degradative enzyme,
- $w(x,y,t)$ is the concentration of oxygen.

Numerical Example

- **Initial setup**:

$$\rho(x,y,0) = 5\max\{0.3-(x-3)^2-(y-3)^2, 0\},$$

$$c(x,y,0) = 0.05\cos\left(\frac{5\pi x^2}{18}\right)\sin\left(\frac{13\pi y^2}{72}\right) + 0.3$$

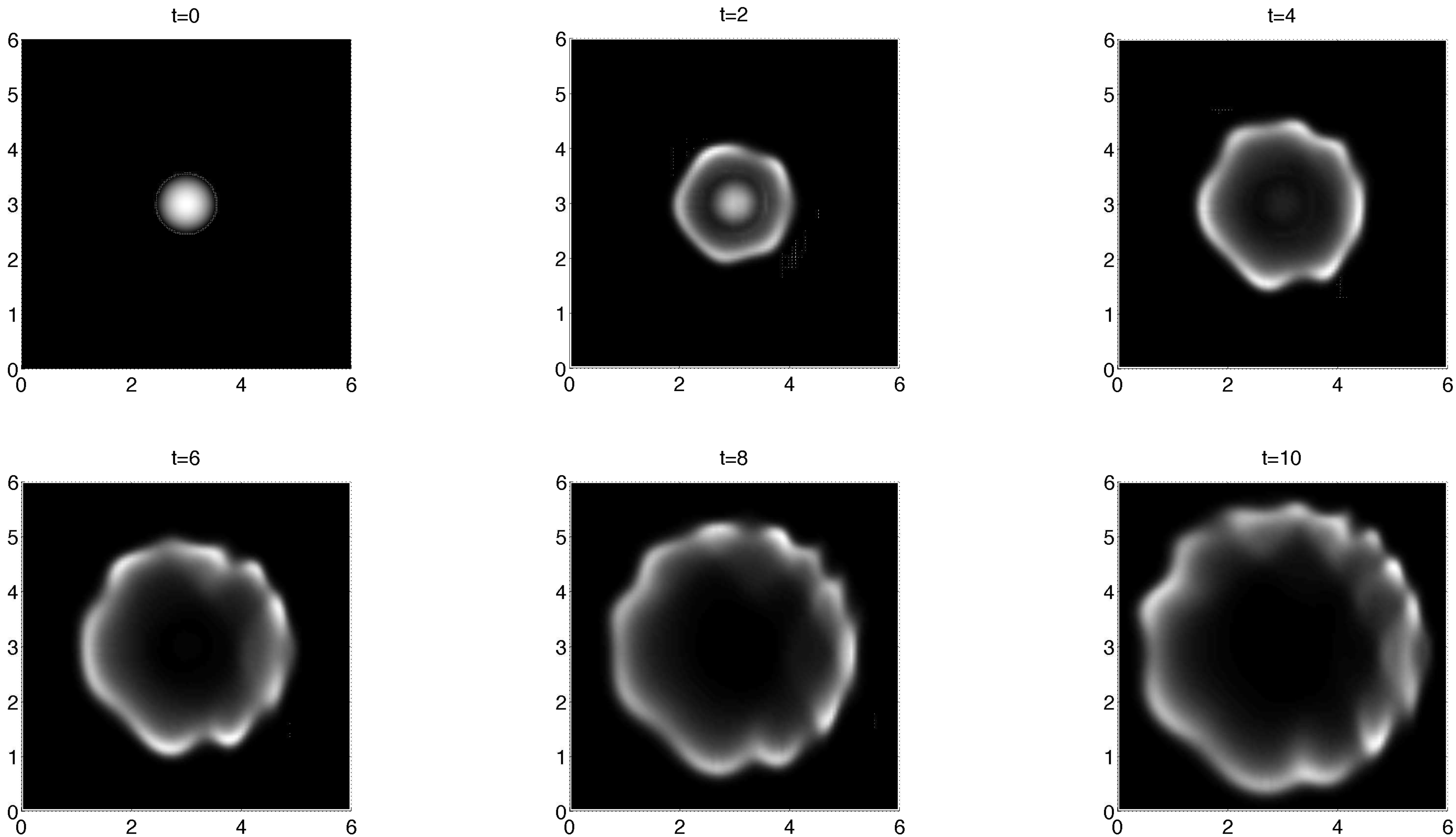
$$m(x,y,0) = \rho(x,y,0), \qquad w(x,y,0) = 4\,c(x,y,0),$$

- **Parameters**:

$$\chi(v) \equiv 0.4,\ d_u = 0.01,\ \psi(x,y,w) \equiv 1,\ \rho(x,y,w) = \frac{2w}{1+w},$$

$$\delta(x,y) \equiv 1,\ \beta(x,y) \equiv 0.01,\ d_w = 0.01,\ \gamma(x,y) \equiv 5,$$

$$\alpha(x,y) \equiv 5,\ d_m = 0.01,\ \eta(x,y,u) = \frac{2u}{1+u},\ e(x,y) \equiv 1.$$


t=0
t=2
t=4
t=6
t=8
t=10
0
1
2
3
4
5
6

THANK YOU!