# Various aspects of reaction-diffusion problems

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# Outline

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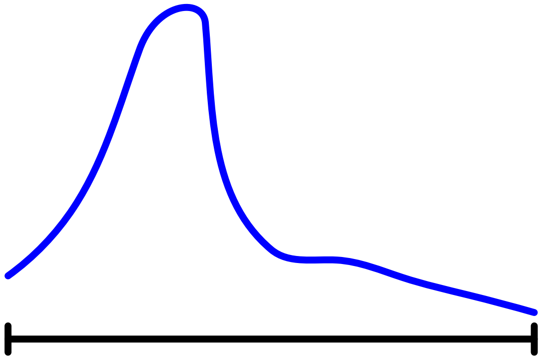
## Numerical analysis – Finite Element Method

- Mesh adaptivity
- A posteriori error estimates
- Discrete maximum principles

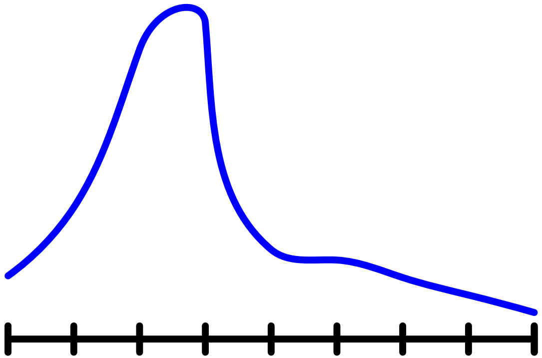
## Mathematical biology

- Circadian rhythms
- Skin patterns formation

# Mesh adaptivity



# Mesh adaptivity



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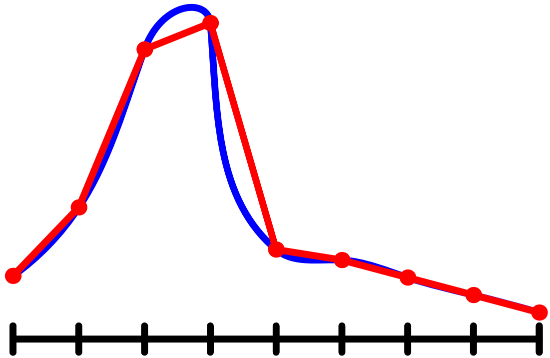

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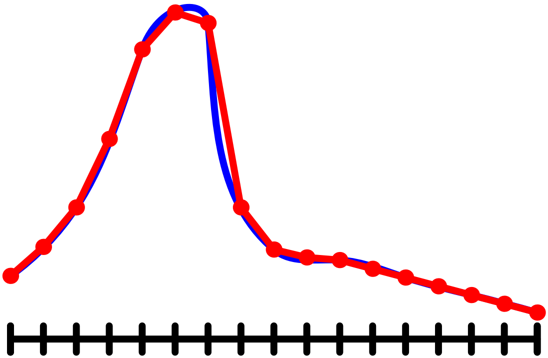

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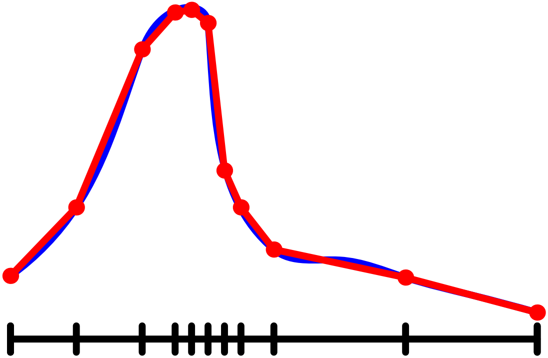
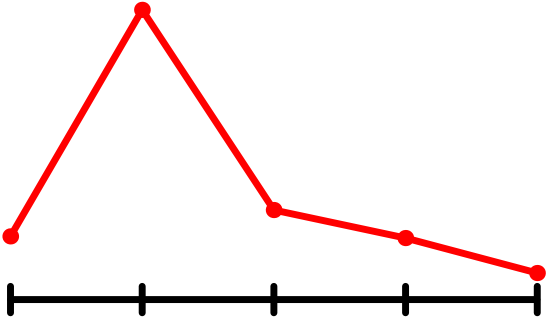


# Mesh adaptivity

?

# Mesh adaptivity



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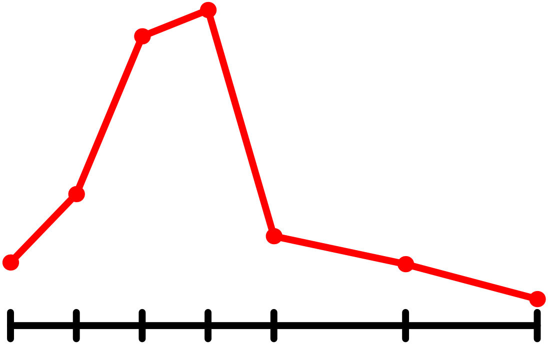

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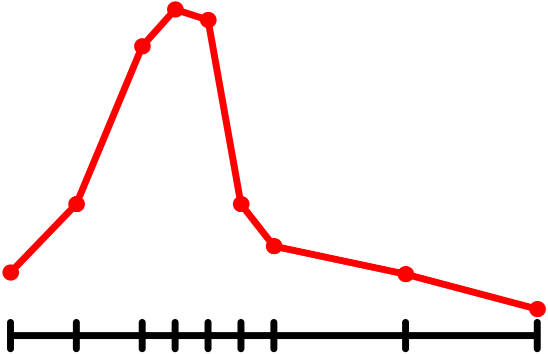
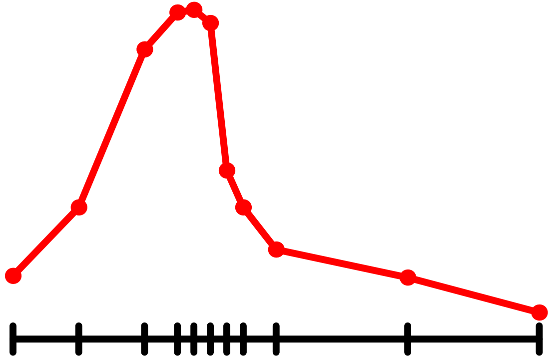
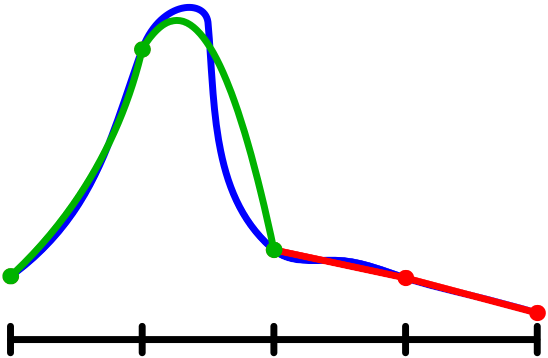


# Mesh adaptivity



# Mesh adaptivity – *hp* version





# A posteriori error estimates

Error indicators $\times$ Error estimators

Properties

- Efficiency and reliability
- Guaranteed upper bound
- Guaranteed lower bound
- Asymptotic exactness
- Robustness
- Locality

Approaches

- Explicit residual
- Implicit residual – Dirichlet
- Implicit residual – Neumann
- Hierarchical
- Postprocessing
- Complementarity
- Quantity of interest

# Discrete maximum principles

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$$-\Delta u = f \text{ in } \Omega = (0,4)\times(0,2), \quad u = 0 \text{ on } \partial\Omega$$

Conservation of nonnegativity: $f \geq 0 \quad \Rightarrow \quad u \geq 0$

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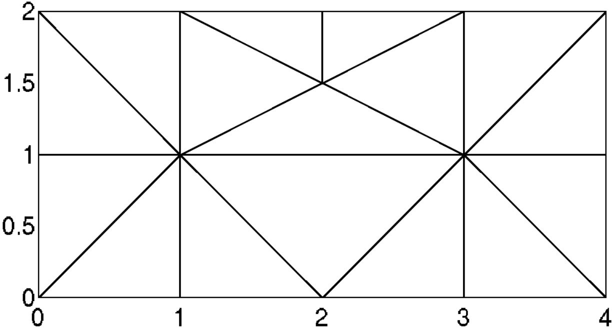
Conservation of nonnegativity: $f \geq 0 \quad \Rightarrow \quad u \geq 0$

$$f(x_1,x_2) = \begin{cases} 1 & \text{for } x_1 < 1 \\ 0 & \text{for } x_1 \geq 1 \end{cases}$$

$u_h$ by linear FEM




Brandts, Korotov, Křížek, Šolc, SIAM Review 51 (2009), 317–335

# Discrete maximum principles

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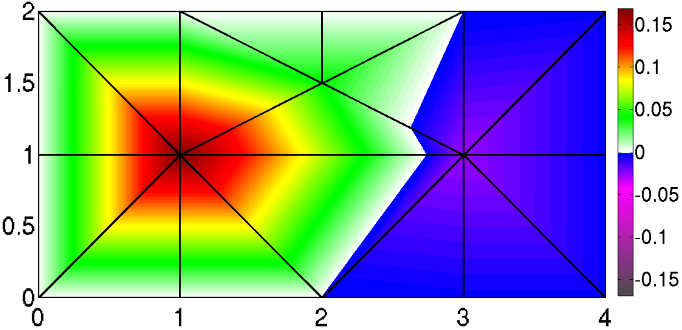



Negative values $10\times$ magnified.

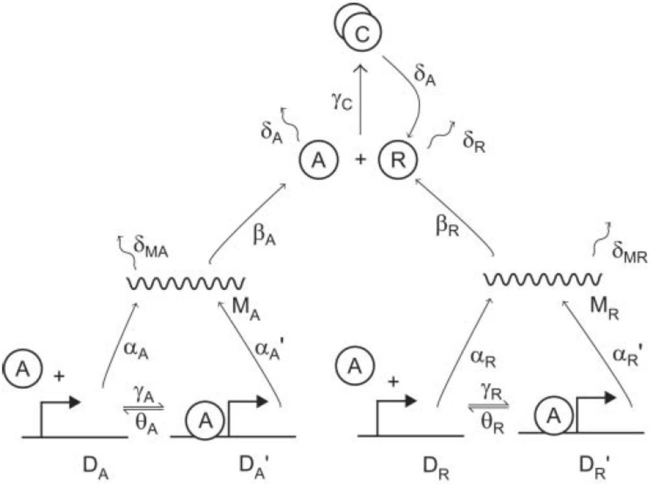
# Project StochDetBioModel

Marie Curie Intra-European Fellowship for Career Development

Scope:

- Analytical and computational methods for reaction-diffusion systems [Cotter, Vejchodsky, Erban, 2013]
- Models with and without stochastic effects [Erban, Chapman, Kevrekidis, Vejchodsky, 2009]
- Circadian rhythms – spatial aspects
- Skin pattern formation – unilateral regulation

# Circadian rhythms – chemical reactions




[Vilar et al, 2002]

$\alpha_A = 50\,\mathrm{h}^{-1}$
$\alpha'_A = 500\,\mathrm{h}^{-1}$
$\alpha_R = 0.01\,\mathrm{h}^{-1}$
$\alpha'_R = 50\,\mathrm{h}^{-1}$
$\beta_A = 50\,\mathrm{h}^{-1}$
$\beta_R = 5\,\mathrm{h}^{-1}$
$\gamma_A = 1\,\mathrm{mol}^{-1}\ \mathrm{h}^{-1}$
$\gamma_R = 1\,\mathrm{mol}^{-1}\ \mathrm{h}^{-1}$
$\gamma_C = 2\,\mathrm{mol}^{-1}\ \mathrm{h}^{-1}$
$\delta_A = 1\,\mathrm{h}^{-1}$
$\delta_R = 0.2\,\mathrm{h}^{-1}$
$\delta_{M_A} = 10\,\mathrm{h}^{-1}$
$\delta_{M_R} = 0.5\,\mathrm{h}^{-1}$
$\theta_A = 50\,\mathrm{h}^{-1}$
$\theta_R = 100\,\mathrm{h}^{-1}$

# Circadian rhythms – equations



Law of mass action:

$$\mathrm{d}\overline{D}_A/\mathrm{dt} = \theta_A \overline{D}'_A - \gamma_A \overline{D}_A \overline{A}$$

$$\mathrm{d}\overline{D}'_A/\mathrm{dt} = -\theta_A \overline{D}'_A + \gamma_A \overline{D}_A \overline{A}$$

$$\mathrm{d}\overline{D}_R/\mathrm{dt} = \theta_R \overline{D}'_R - \gamma_R \overline{D}_R \overline{A}$$

$$\mathrm{d}\overline{D}'_R/\mathrm{dt} = -\theta_R \overline{D}'_R + \gamma_R \overline{D}_R \overline{A}$$

$$\mathrm{d}\overline{M}_A/\mathrm{dt} = \alpha'_A \overline{D}'_A + \alpha_A \overline{D}_A - \delta_{M_A} \overline{M}_A$$

$$\mathrm{d}\overline{M}_R/\mathrm{dt} = \alpha'_R \overline{D}'_R + \alpha_R \overline{D}_R - \delta_{M_R} \overline{M}_R$$

$$\mathrm{d}\overline{A}/\mathrm{dt} = \beta_A \overline{M}_A + \theta_A \overline{D}'_A + \theta_R \overline{D}'_R - \overline{A}(\gamma_A \overline{D}_A + \gamma_R \overline{D}_R + \gamma_C \overline{R} + \delta_A)$$

$$\mathrm{d}\overline{R}/\mathrm{dt} = \beta_R \overline{M}_R - \gamma_C \overline{AR} + \delta_A \overline{C} - \delta_R \overline{R}$$

$$\mathrm{d}\overline{C}/\mathrm{dt} = \gamma_C \overline{AR} - \delta_A \overline{C}$$

Initial conditions:

$\overline{D}_A = \overline{D}_R = 1$ mol

$\overline{D}'_A = \overline{D}'_R = \overline{M}_A = \overline{M}_R = \overline{A} = \overline{R} = \overline{C} = 0$ mol

# Circadian rhythms – equations

Law of mass action:

$$
\begin{aligned}
\mathrm{d}\overline{D}_A/\mathrm{d}t &= \theta_A - (\theta_A + \gamma_A \overline{A})\overline{D}_A \\
\overline{D}'_A &= 1 - \overline{D}_A \\
\mathrm{d}\overline{D}_R/\mathrm{d}t &= \theta_R - (\theta_R + \gamma_R \overline{A})\overline{D}_R \\
\overline{D}'_R &= 1 - \overline{D}_R \\
\mathrm{d}\overline{M}_A/\mathrm{d}t &= \alpha'_A + (\alpha_A - \alpha'_A)\overline{D}_A - \delta_{M_A}\overline{M}_A \\
\mathrm{d}\overline{M}_R/\mathrm{d}t &= \alpha'_R + (\alpha_R - \alpha'_R)\overline{D}_R - \delta_{M_R}\overline{M}_R \\
\mathrm{d}\overline{A}/\mathrm{d}t &= \beta_A \overline{M}_A + \theta_A(1 - \overline{D}_A) + \theta_R(1 - \overline{D}_R) \\
&\quad - \overline{A}(\gamma_A \overline{D}_A + \gamma_R \overline{D}_R + \gamma_C \overline{R} + \delta_A) \\
\mathrm{d}\overline{R}/\mathrm{d}t &= \beta_R \overline{M}_R - \gamma_C \overline{AR} + \delta_A \overline{C} - \delta_R \overline{R} \\
\mathrm{d}\overline{C}/\mathrm{d}t &= \gamma_C \overline{AR} - \delta_A \overline{C}
\end{aligned}
$$

# Circadian rhythms – equations

Law of mass action:

$$\mathrm{d}D_A/\mathrm{d}t = \theta_A - (\theta_A + \gamma_A A)D_A$$

$$D'_A = 1 - D_A$$

$$\mathrm{d}D_R/\mathrm{d}t = \theta_R - (\theta_R + \gamma_R A)D_R$$

$$D'_R = 1 - D_R$$

$$\partial M_A/\partial t = \alpha'_A + (\alpha_A - \alpha'_A)D_A - \delta_{M_A} M_A + d_{M_A}\partial^2 M_A/\partial x^2$$

$$\partial M_R/\partial t = \alpha'_R + (\alpha_R - \alpha'_R)D_R - \delta_{M_R} M_R + d_{M_R}\partial^2 M_R/\partial x^2$$

$$\partial A/\partial t = \beta_A M_A + \theta_A(1 - D_A) + \theta_R(1 - D_R) - A(\gamma_A D_A + \gamma_R D_R + \gamma_C R + \delta_A) + d_A\partial^2 A/\partial x^2$$

$$\partial R/\partial t = \beta_R M_R - \gamma_C AR + \delta_A C - \delta_R R + d_R\partial^2 R/\partial x^2$$

$$\partial C/\partial t = \gamma_C AR - \delta_A C + d_C\partial^2 C/\partial x^2$$

No flux boundary conditions

Concentration: $D_A = \overline{D}_A/\nu,\ D_R = \overline{D}_R/\nu,\ \ldots \quad \nu = 1$ cell

# Spatial setting

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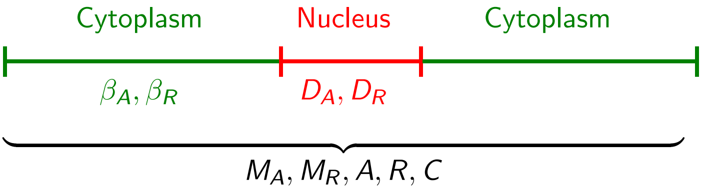



## Cell size:

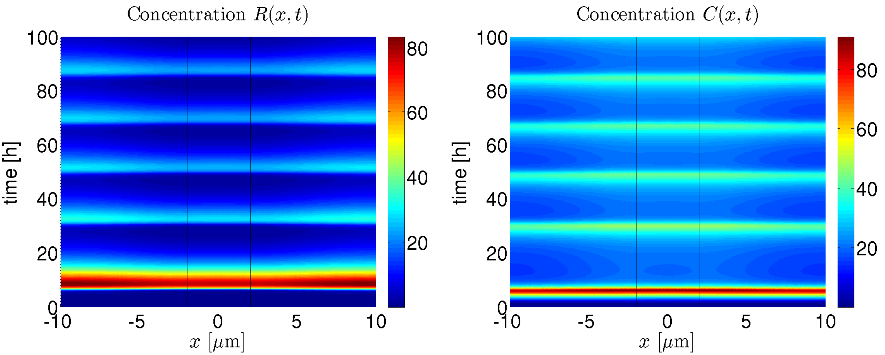
- $L_{\text{cell}} = 10\text{–}100\,\mu\text{m}$

## Diffusivities:

- Proteins:
  $d_A = d_R = d_C = 20\,000\,\mu\text{m}^2\text{h}^{-1} = 20\,000/L_{\text{cell}}^2\,\text{cell}^2\text{h}^{-1}$
  (measurements [Nenninger 2010]: $\approx 14\,400\text{–}36\,000\,\mu\text{m}^2\text{h}^{-1}$)
- mRNA:
  $d_{M_A} = d_{M_R} = d_A/\sqrt[3]{10}$
  (mRNA is roughly $10\times$ bigger than protein)

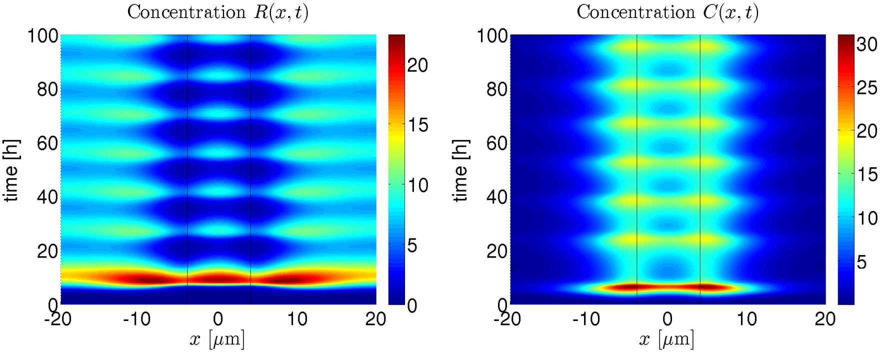
# Results

$L_{\mathrm{cell}} = 20\,\mu\mathrm{m}$



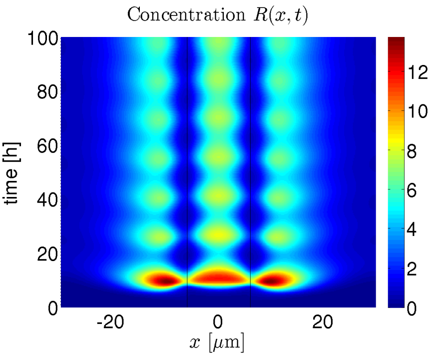
# Results

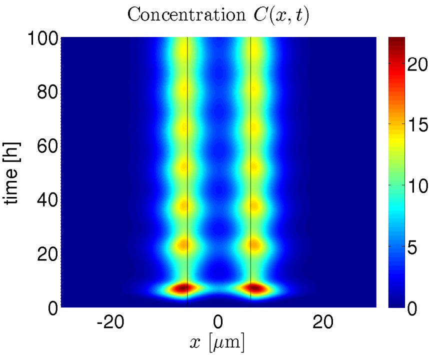
$L_{\text{cell}} = 40\ \mu\text{m}$



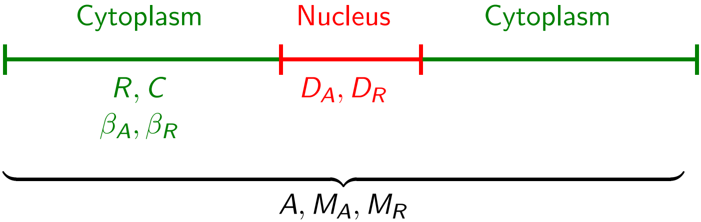
# Results

$L_{\text{cell}} = 60\,\mu\text{m}$



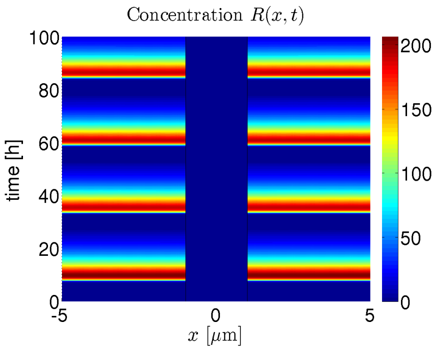
# $R$ and $C$ in cytoplasm only



# $R$ and $C$ in cytoplasm only – results

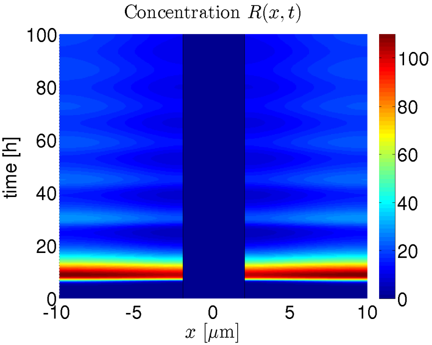


$L_{\text{cell}} = 10\,\mu\text{m}$



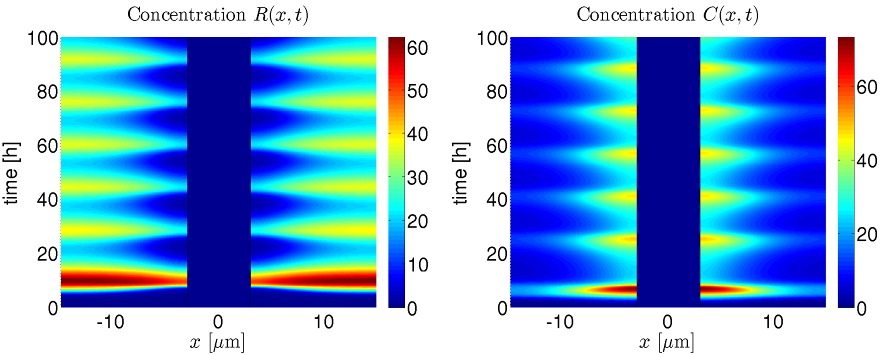
# $R$ and $C$ in cytoplasm only – results

$L_{\text{cell}} = 20\,\mu\text{m}$



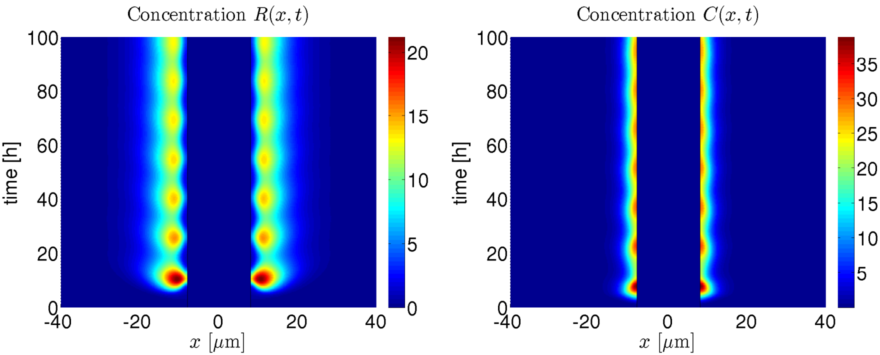
# $R$ and $C$ in cytoplasm only – results

$L_{\text{cell}} = 30\,\mu\text{m}$



# $R$ and $C$ in cytoplasm only – results

$L_{\text{cell}} = 80\,\mu\text{m}$



# Skin pattern formation

Reaction–diffusion system:

$$\left.\begin{aligned}\frac{\partial u}{\partial t} &= \delta_1 \Delta u + f(u,v) \\ \frac{\partial v}{\partial t} &= \delta_2 \Delta v + g(u,v)\end{aligned}\right\} \text{in } \Omega \qquad \left.\begin{aligned}\frac{\partial u}{\partial n} &= 0 \\ \frac{\partial v}{\partial n} &= 0\end{aligned}\right\} \text{on } \partial\Omega$$

Patterns for $\dfrac{\delta_1}{\delta_2} < 1$

# Skin pattern formation

Idea: add a unilateral regulation to the Turing's mechanism

Reaction–diffusion system with Signorini b.c.:

$$\left.\begin{aligned} \frac{\partial u}{\partial t} &= \delta_1 \Delta u + f(u,v) \\ \frac{\partial v}{\partial t} &= \delta_2 \Delta v + g(u,v) \end{aligned}\right\} \text{in } \Omega \qquad \left.\begin{aligned} &\frac{\partial u}{\partial n} = 0 \\ &v \geq 0, \frac{\partial v}{\partial n} \geq 0, v\frac{\partial v}{\partial n} = 0 \end{aligned}\right\} \text{on } \partial\Omega$$

Patterns even for $\frac{\delta_1}{\delta_2} \approx 1$ [Kučera, Väth, 2012]

# Skin pattern formation

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Idea: add a unilateral regulation to the Turing's mechanism

Reaction–diffusion system with unilateral source:

$$\left.\begin{aligned}\frac{\partial u}{\partial t} &= \delta_1 \Delta u + f(u,v)\\ \frac{\partial v}{\partial t} &= \delta_2 \Delta v + g(u,v) + \gamma v^-\end{aligned}\right\}\text{ in }\Omega \qquad \left.\begin{aligned}\frac{\partial u}{\partial n} &= 0\\ \frac{\partial v}{\partial n} &= 0\end{aligned}\right\}\text{ on }\partial\Omega$$

# Skin pattern formation



Idea: add a unilateral regulation to the Turing's mechanism

Reaction–diffusion system with unilateral source:

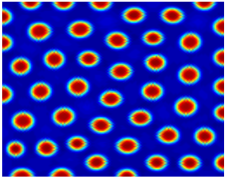
$$\left.\begin{aligned} \frac{\partial u}{\partial t} &= \delta_1 \Delta u + f(u,v) \\ \frac{\partial v}{\partial t} &= \delta_2 \Delta v + g(u,v) + \gamma v^- \end{aligned}\right\} \text{in } \Omega \qquad \left.\begin{aligned} \frac{\partial u}{\partial n} &= 0 \\ \frac{\partial v}{\partial n} &= 0 \end{aligned}\right\} \text{on } \partial\Omega$$

Numerical experiments

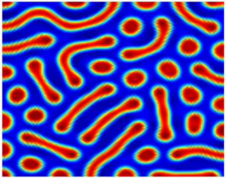
$$f(u,v) = \alpha u + v - r_2 uv - \alpha r_3 uv^2$$
$$g(u,v) = -\alpha u + \beta v + r_2 uv + \alpha r_3 uv^2$$

[Liu, Liaw, Maini, 2006]

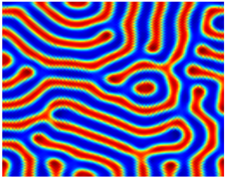
# Pattern formation – results



$\beta = -0.97$
$\gamma = 0.00$



$\beta = -0.89$
$\gamma = 0.08$



$\beta = -0.80$
$\gamma = 0.17$

# Collaborators

- Philip K. Maini
- Radek Erban
- Simon Cotter
- Shuohao Liao – Higher-dimensional Fokker-Planck equation

- Milan Kučera
- Filip Jaroš
- Martin Väth

# Outlook

## Circadian rhythms

- Analysis of the spatial model
- Stochastic spatial model

## Skin pattern formation

- Implementation of Signorini boundary conditions
- Another dynamics (Thomas system)

# Thank you for your attention

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CMB Group Meeting, Oxford, 10 June, 2013