Deterministic and stochastic models of dynamics of chemical systems

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PANM 14, June 1–6 2008, Dolní Maxov

Outline

- Chemical system with SNIPER bifurcation
- Stationary distribution
- Period of oscillations

Chemical system with SINIPER bifurcation

$$\emptyset \xrightarrow{k_{1d}} Y \xrightarrow{k_{2d}} X \xrightarrow{k_{3d}} \emptyset \qquad 2X \underset{k_{5d}}{\overset{k_{4d}}{\rightleftarrows}} 3X$$

$$X + Y \xrightarrow{k_{6d}} X + 2Y \qquad 2X + Y \xrightarrow{k_{7d}} 2X$$

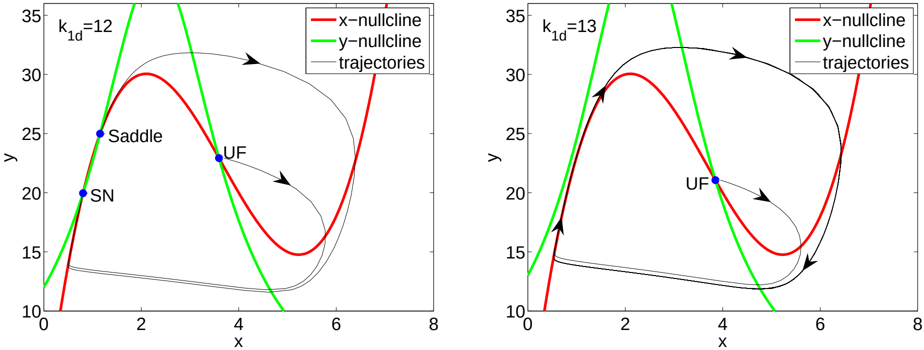
Mean-field ODE:

$$\begin{aligned} \frac{\mathrm{d}\widetilde{x}}{\mathrm{d}t} &= k_{2d}\,\widetilde{y} - k_{5d}\,\widetilde{x}^3 + k_{4d}\,\widetilde{x}^2 - k_{3d}\,\widetilde{x} \\ \frac{\mathrm{d}\widetilde{y}}{\mathrm{d}t} &= -k_{7d}\,\widetilde{x}^2\,\widetilde{y} + k_{6d}\,\widetilde{x}\,\widetilde{y} - k_{2d}\,\widetilde{y} + k_{1d} \end{aligned}$$

$X = X(t)$, $Y = Y(t)$ ... number of molecules

$\widetilde{x} = X/V$, $\widetilde{y} = Y/V$ ... concentrations $\qquad$ V ... volume

SNIPER bifurcation



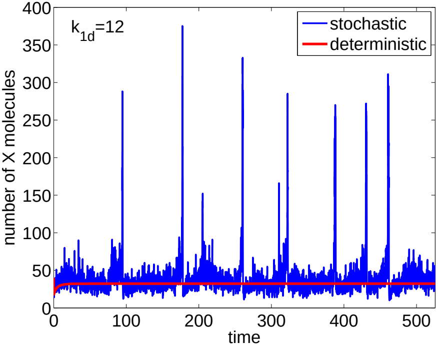
$k_{1d} = 12$ $[\mathrm{sec}^{-1}\,\mathrm{mm}^{-3}]$ $k_{1d} = 13$ $[\mathrm{sec}^{-1}\,\mathrm{mm}^{-3}]$

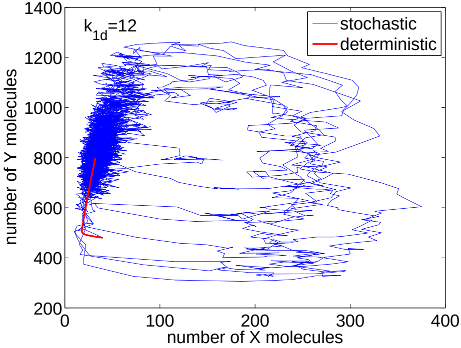
$k_{2d} = 1$ $k_{3d} = 33$ $[\mathrm{sec}^{-1}]$

$k_{4d} = 11$ $k_{6d} = 0.6$ $[\mathrm{sec}^{-1}\,\mathrm{mm}^{3}]$

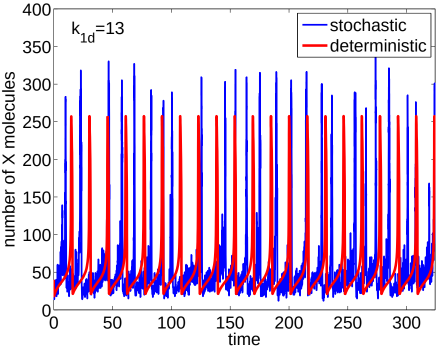
$k_{5d} = 1$ $k_{7d} = 0.13$ $[\mathrm{sec}^{-1}\,\mathrm{mm}^{6}]$

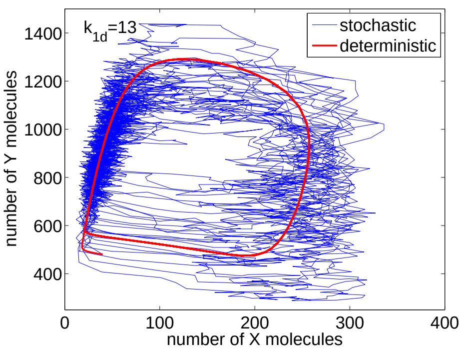
Stochastic simulations $k_{1d} = 12$





Stochastic simulations $k_{1d} = 13$





Propensities and rate constants

$$\begin{aligned}
\alpha_1(x,y) &= k_1 & k_1 &= k_{1d}V \\
\alpha_2(x,y) &= k_2 y & k_2 &= k_{2d} \\
\alpha_3(x,y) &= k_3 x & k_3 &= k_{3d} \\
\alpha_4(x,y) &= k_4 x(x-1) & k_4 &= k_{4d}/V \\
\alpha_5(x,y) &= k_5 x(x-1)(x-2) & k_5 &= k_{5d}/V^2 \\
\alpha_6(x,y) &= k_6 xy & k_6 &= k_{6d}/V \\
\alpha_7(x,y) &= k_7 x(x-1)y & k_7 &= k_{7d}/V^2
\end{aligned}$$

$\alpha_i(X(t), Y(t))dt =$ probability that i-th reaction occures in $(t, t+dt)$

"Naive" stochastic simulations

1. for $i = 1, 2, \ldots, 7$ do
   - r_i ... random number uniformly distributed in $(0, 1)$
   - $p_i = \alpha_i \Delta t$
   - if $0 < r_i < p_i \quad \Rightarrow \quad$ Reaction $i \Rightarrow$ update numbers of reactants and products

   end
2. $t := t + \Delta t$, go to 1.

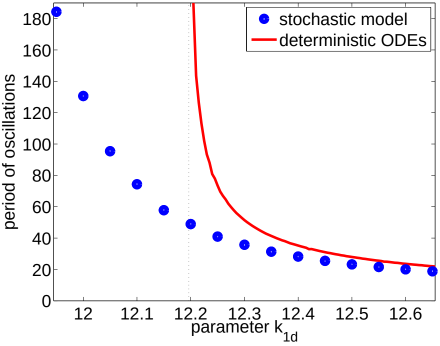
Reaction 1 :		$Y(t + \Delta t) = Y(t) + 1$
Reaction 2 :	$X(t + \Delta t) = X(t) + 1$	$Y(t + \Delta t) = Y(t) - 1$
Reaction 3 :	$X(t + \Delta t) = X(t) - 1$	
Reaction 4 :	$X(t + \Delta t) = X(t) + 1$	
Reaction 5 :	$X(t + \Delta t) = X(t) - 1$	
Reaction 6 :		$Y(t + \Delta t) = Y(t) + 1$
Reaction 7 :		$Y(t + \Delta t) = Y(t) - 1$

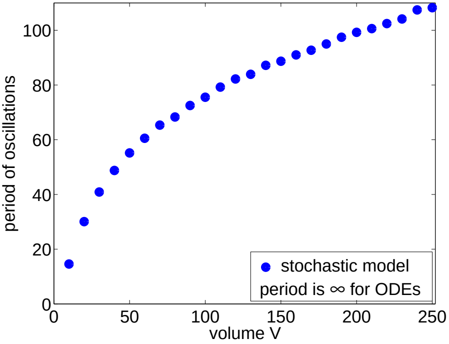
Gillespie SSA

1. r_1, r_2 ... two random numbers uniformly distributed in $(0,1)$
2. $\alpha_0 = \sum_{i=1}^{7} \alpha_i(t)$ ... where $\alpha_i(t)$ propensities of all reactions
3. $\tau = \frac{1}{\alpha_0} \ln \left(\frac{1}{r_1} \right)$ ... next reaction takes place at $t + \tau$
4. Find j such that $\frac{1}{\alpha_0} \sum_{i=1}^{j-1} \alpha_i(t) \leq r_2 < \frac{1}{\alpha_0} \sum_{i=1}^{j} \alpha_i(t)$.

   Reaction $j \Rightarrow$ update numbers of reactants and products
5. $t := t + \tau$, go to 1.

Period of oscillations





Chemical Fokker-Planck equation

$$\frac{\partial P}{\partial t} = \frac{\partial^2}{\partial x^2}\left[d_x\, P\right] + \frac{\partial^2}{\partial x \partial y}\left[d_{xy}\, P\right] + \frac{\partial^2}{\partial y^2}\left[d_y\, P\right] - \frac{\partial}{\partial x}\left[v_x\, P\right] - \frac{\partial}{\partial y}\left[v_y\, P\right]$$

$P = P(x, y, t) \ldots$ probability that $X(t) = x$ and $Y(t) = y$

$$\begin{aligned}
v_x(x,y) &= \alpha_2(x,y) - \alpha_3(x,y) + \alpha_4(x,y) - \alpha_5(x,y) \\
v_y(x,y) &= \alpha_1(x,y) - \alpha_2(x,y) + \alpha_6(x,y) - \alpha_7(x,y) \\
d_x(x,y) &= [\alpha_2(x,y) + \alpha_3(x,y) + \alpha_4(x,y) + \alpha_5(x,y)]/2 \\
d_y(x,y) &= [\alpha_1(x,y) + \alpha_2(x,y) + \alpha_6(x,y) + \alpha_7(x,y)]/2 \\
d_{xy}(x,y) &= -\alpha_2(x,y)
\end{aligned}$$

Stationary distribution

$$0 = \frac{\partial^2}{\partial x^2}\left[d_x\, P_s\right] + \frac{\partial^2}{\partial x \partial y}\left[d_{xy}\, P_s\right] + \frac{\partial^2}{\partial y^2}\left[d_y\, P_s\right] - \frac{\partial}{\partial x}\left[v_x\, P_s\right] - \frac{\partial}{\partial y}\left[v_y\, P_s\right]$$

$$\int_0^\infty \int_0^\infty P_s(x,y)\,\mathrm{d}x\mathrm{d}y = 1 \qquad P_s(x,y) \geq 0 \qquad (x,y) \in [0,\infty) \times [0,\infty)$$

$$P_s = P_s(x,y) = \lim_{t\to\infty} P(x,y,t) \ \ldots \ \text{stationary distribution}$$

$$\begin{aligned} -\operatorname{div}(\mathcal{A}\nabla P_s + P_s \mathbf{b}) &= 0 \quad \text{in } S = (0,500) \times (0,2000) \\ (\mathcal{A}\nabla P_s + P_s \mathbf{b}) \cdot \mathbf{n} &= 0 \quad \text{on } \partial S \end{aligned}$$

$$\mathcal{A} = -\begin{pmatrix} d_x & d_{xy}/2 \\ d_{xy}/2 & d_y \end{pmatrix} \quad \mathbf{b} = \left(v_x - \frac{\partial d_x}{\partial x} - \frac{1}{2}\frac{\partial d_{xy}}{\partial y}, v_y - \frac{\partial d_y}{\partial y} - \frac{1}{2}\frac{\partial d_{xy}}{\partial x} \right)$$

Stationary distribution

$$0 = \frac{\partial^2}{\partial x^2}\left[d_x\, P_s\right] + \frac{\partial^2}{\partial x \partial y}\left[d_{xy}\, P_s\right] + \frac{\partial^2}{\partial y^2}\left[d_y\, P_s\right] - \frac{\partial}{\partial x}\left[v_x\, P_s\right] - \frac{\partial}{\partial y}\left[v_y\, P_s\right]$$

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Remark:

$$\begin{aligned} -\operatorname{div}(\mathcal{A}\nabla P_s) - \mathbf{b} \cdot \nabla P_s - \operatorname{div}(\mathbf{b})\, P_s &= 0 \quad \text{in } S \\ (\mathcal{A}\nabla P_s) \cdot \mathbf{n} &= 0 \quad \text{on } \partial S \end{aligned}$$

Finite Element Method

Classical form

$$
\begin{aligned}
-\operatorname{div}(\mathcal{A}\nabla P_s + P_s\mathbf{b}) &= 0 \quad \text{in } S = (0,500)\times(0,2000)\\
(\mathcal{A}\nabla P_s + P_s\mathbf{b})\cdot\mathbf{n} &= 0 \quad \text{on } \partial S
\end{aligned}
$$

Weak form

$$
P_s \in H^1(S): \quad a(P_s,\varphi) = 0 \quad \forall\varphi\in H^1(S)
$$

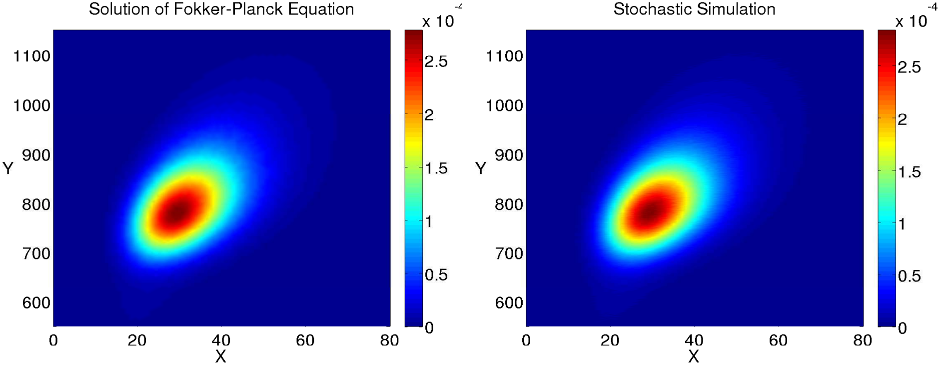
$$
a(P_s,\varphi) = \int_S (\mathcal{A}\nabla P_s + P_s\mathbf{b})\cdot\nabla\varphi \,\mathrm{d}x\mathrm{d}y
$$

FEM

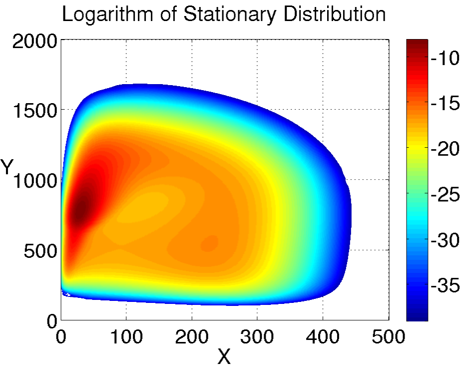
$$
P_{s,h}\in W_h: \quad a(P_{s,h},\varphi_h) = 0 \quad \forall\varphi_h\in W_h
$$

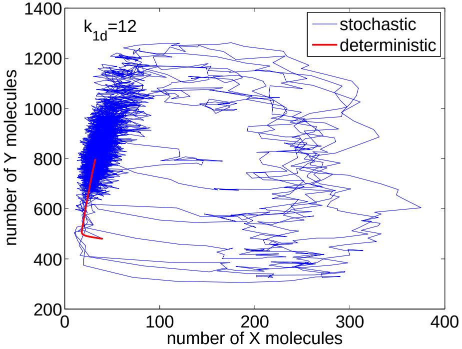
$$
W_h = \{\varphi_h\in H^1(S) : \varphi_h|_K \in P^1(K),\ K\in\mathcal{T}_h\}
$$

Stationary distribution – results



Stationary distribution – results





Period of oscillations

$$d_x \frac{\partial^2 \tau}{\partial x^2} + d_{xy} \frac{\partial^2 \tau}{\partial x \partial y} + d_y \frac{\partial^2 \tau}{\partial y^2} + v_x \frac{\partial \tau}{\partial x} + v_y \frac{\partial \tau}{\partial y} = -1 \quad \text{for } (x, y) \in \Omega$$

$\tau = \tau(x, y) \ \ldots$ average time to leave $\Omega = \{(x, y) \mid x < 200\}$

Classical form

$$\begin{aligned} -\operatorname{div}(\mathcal{A}\nabla\tau) + \mathbf{b} \cdot \nabla\tau &= -1 \quad \text{in } \widetilde{S} = (0, 200) \times (0, 2000) \\ \tau &= 0 \quad \text{on line } x = 200 \\ (\mathcal{A}\nabla\tau) \cdot \mathbf{n} &= 0 \quad \text{on lines } y = 0,\ y = 2000,\ x = 0 \end{aligned}$$

Period of oscillations

Weak form

$$\tau \in W: \quad \widetilde{a}(\tau, \varphi) = \int_{\widetilde{S}} -1 \cdot \varphi \, \mathrm{d}x\mathrm{d}y, \quad \forall \varphi \in W,$$

$$W = \left\{ v \in H^1(\widetilde{S}) : v = 0 \text{ on the line } x = 200 \right\}$$

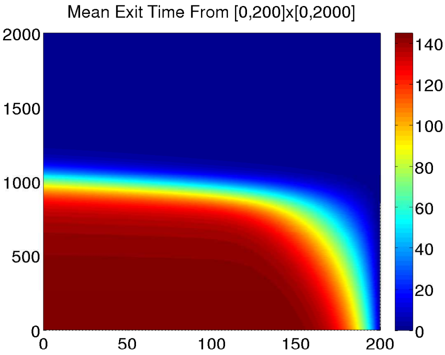
$$\widetilde{a}(\tau, \varphi) = \int_{\widetilde{S}} \mathcal{A} \nabla \tau \cdot \nabla \varphi \, \mathrm{d}x\mathrm{d}y + \int_{\widetilde{S}} \mathbf{b} \cdot \nabla \tau \varphi \, \mathrm{d}x\mathrm{d}y.$$

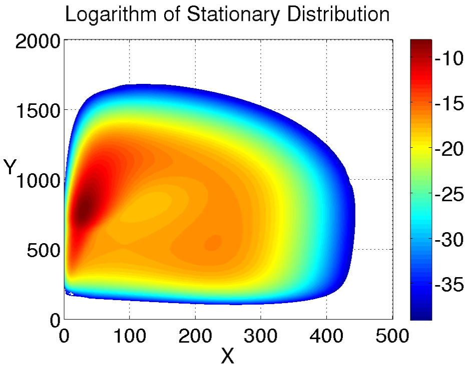
FEM

$$\tau_h \in \widetilde{W_h}: \quad \widetilde{a}(\tau_h, \varphi_h) = \int_{\widetilde{S}} -1 \cdot \varphi_h \, \mathrm{d}x\mathrm{d}y, \quad \forall \varphi_h \in \widetilde{W_h},$$

$$\widetilde{W_h} = \{ \varphi_h \in W : \varphi_h|_K \in P^1(K), \ K \in \mathcal{T}_h \}$$

Period of oscillations: $k_{1d} = 12$

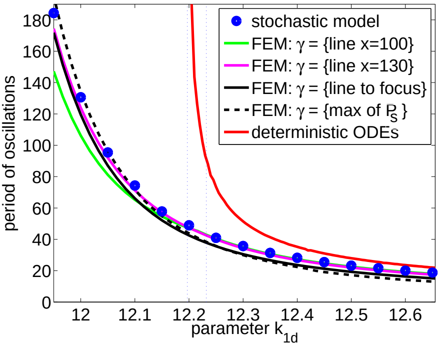


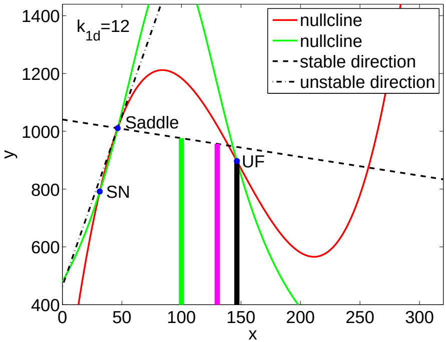


$$\tau_h(29.30, 781.25) \doteq 134.1$$
$$\tau_{stoch,10^5} \doteq 130.4$$

$$T(\gamma) = \frac{\int_\gamma \tau(x,y)\, P_s(x,y)\, \mathrm{d}\gamma}{\int_\gamma P_s(x,y)\, \mathrm{d}\gamma}$$

Period of oscillations: k_{1d} vary





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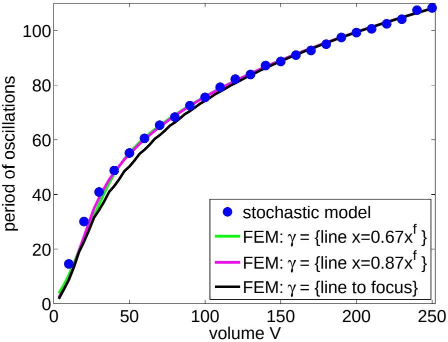
Period of oscillations: $k_{1d} \doteq 12.2$; volume vary



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Conclusions

- cell cycle modelling
- more chemical species $\Rightarrow$ higher dimension

Thank you for your attention

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