Modern Numerical Continuation Methods for Biological Systems

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`www.multiscale.systems`

VolkswagenStiftung
DFG Deutsche Forschungsgemeinschaft
IAS TUM Institute for Advanced Study
Mathematisches Forschungsinstitut Oberwolfach
SEVENTH FRAMEWORK PROGRAMME
ÖAW Österreichische Akademie der Wissenschaften

Research Area(s)

Multiscale Methods

Stochastic Systems

Nonlinear Dynamical Systems

Nonlocality & Patterns

Network Dynamics

Research Area(s)

Multiscale Methods

- fast-slow systems
- perturbation methods
- geometric desingularization
- complex oscillations
- ...

Stochastic Systems

- path-based methods
- early-warning signs
- stochastic PDEs
- (rigorous) computation
- ...

Nonlocality & Patterns

- fractional & nonlocal PDEs
- numerical continuation
- travelling waves
- bifurcation theory
- ...

Network Dynamics

- adaptive networks
- graph limits
- data analysis
- moment closure
- ...

Motivation & Problem Formulation

Consider the general differential equation

$$\frac{\partial u}{\partial t} = a(u; p),$$

$p \in \mathbb{R}^n$ are parameters.

$\rightarrow$ $a(u; p)$ could be ODE, DDE, PDE, SDE, SPDE, etc.

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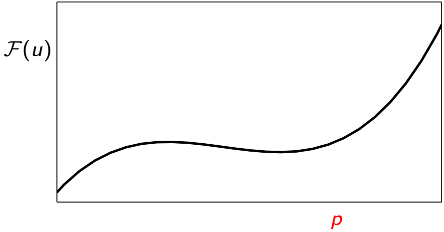
Problem: Simulation only the first step, expensive if we have to:

1. Simulate over initial values $u_0 \in \mathbb{R}^m$.
2. Simulate over parameter space $p \in \mathbb{R}^n$.
3. Simulate over noise realizations $\omega \in \Omega$.

Do you really understand the nonlinear dynamics from averages?

Motivation & Problem Formulation



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Typical goal: "parameter vs. quantity of interest"-diagram.

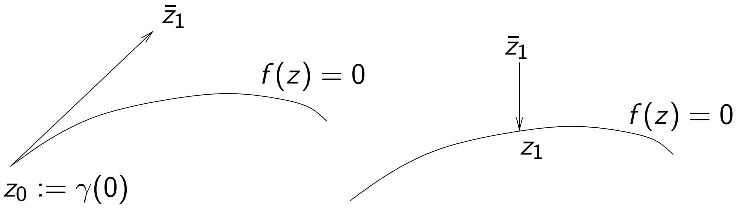
Deterministic DEs Standard Method: Continuation

Consider the ODE

$$x' = f(x; p), \qquad f : \mathbb{R}^m \times \mathbb{R} \to \mathbb{R}^m.$$

Let $(x; p) =: z$. A curve $z = \gamma(s)$ of equilibria satisfies

$$f(\gamma(s)) = 0. \qquad (\text{note: } \mathrm{D}f(\gamma(0))\gamma'(0) = 0)$$



(a) Prediction Step (b) Correction Step

Important: Excellent guess from (a) for Newton's Method in (b).

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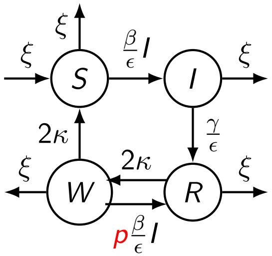
Remarks on Software:

- AUTO-07p: Doedel, Champneys, Sandstede, et al
- XPP-Aut: Ermentrout
- MatCont: Meijer, Govaerts, Kuznetsov, et al
- pde2path: Uecker, Rademacher, Dohnal, et al
- ...

Example 1: SIRWS Epidemics



$$\dot{S} = -\frac{\beta}{\epsilon}SI + 2\kappa W + \xi(1 - S),$$
$$\dot{I} = \frac{\beta}{\epsilon}SI - \frac{\gamma}{\epsilon}I - \xi I,$$
$$\dot{R} = \frac{\gamma}{\epsilon}I - 2\kappa R + p\frac{\beta}{\epsilon}IW - \xi R,$$
$$\dot{W} = 2\kappa R - 2\kappa W - p\frac{\beta}{\epsilon}IW - \xi W,$$

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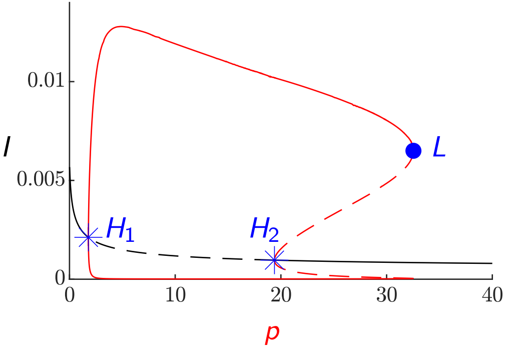

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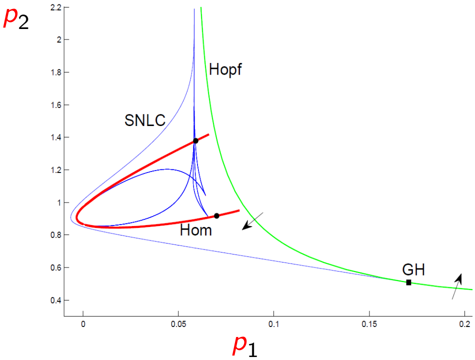
Example 2: The 3D FitzHugh-Nagumo Equation

$$\begin{aligned} x_1' &= x_2, \\ x_2' &= \tfrac{1}{5} p_2 x_2 - x_1(1 - x_1)(x_1 - 0.1) - y + p_1, \\ y' &= \varepsilon(x_1 - \gamma y) \end{aligned}$$



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Example 3: Shigesada-Kawasaki-Teramoto (SKT)

$$
\begin{aligned}
\partial_t u &= \Delta((p_1 + d_{11} u + d_{12} v) u) + (r_1 - a_1 u - b_1 v) u, \\
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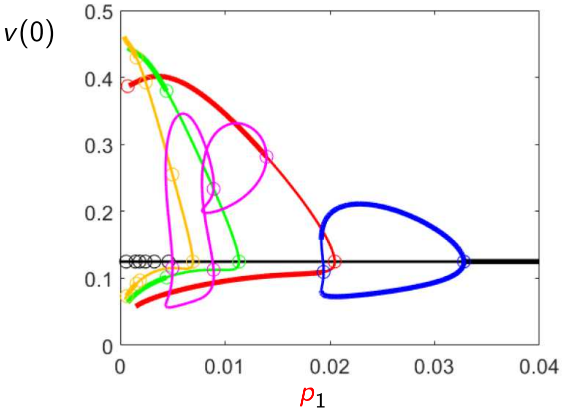

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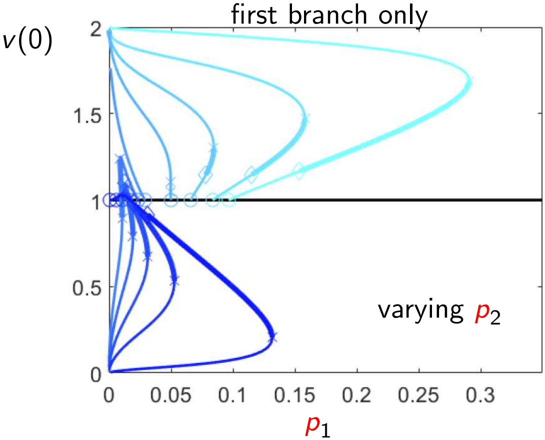

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Fast reaction SKT model ($u = u_1 + u_2$):

$$
\begin{aligned}
\partial_t u_1 &= p_1 \Delta u_1 + (p_2 - a_1 u - b_1 v) u_1 + \frac{1}{\varepsilon}\left(u_2\left(1 - \frac{v}{M}\right) - u_1 \frac{v}{M}\right), \\
\partial_t u_2 &= (p_1 + d_{12} M)\Delta u_2 + (p_2 - a_1 u - b_1 v) u_2 \\
&\qquad - \frac{1}{\varepsilon}\left(u_2\left(1 - \frac{v}{M}\right) - u_1 \frac{v}{M}\right), \\
\partial_t v &= d_2 \Delta v + (r_2 - b_2(u_1 + u_2) - a_2 v) v.
\end{aligned}
$$

Cross-diffusion ($\varepsilon \to 0$ limit) SKT model:

$$
\begin{aligned}
\partial_t u &= \Delta((p_1 + d_{12} v) u) + (p_2 - a_1 u - b_1 v) u, \\
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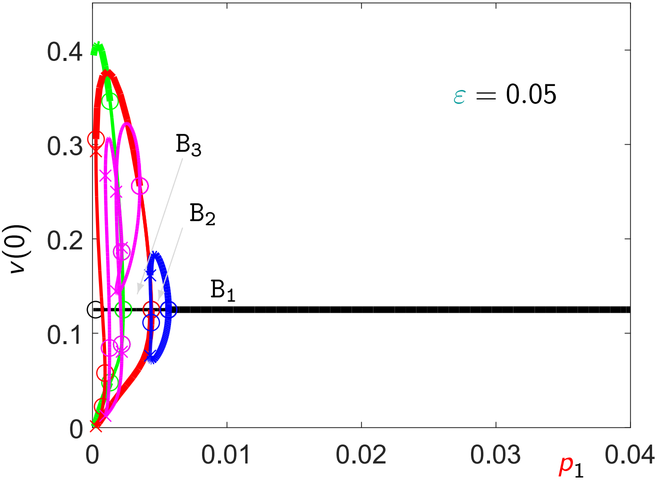
Fast reaction SKT model bifurcation diagram:



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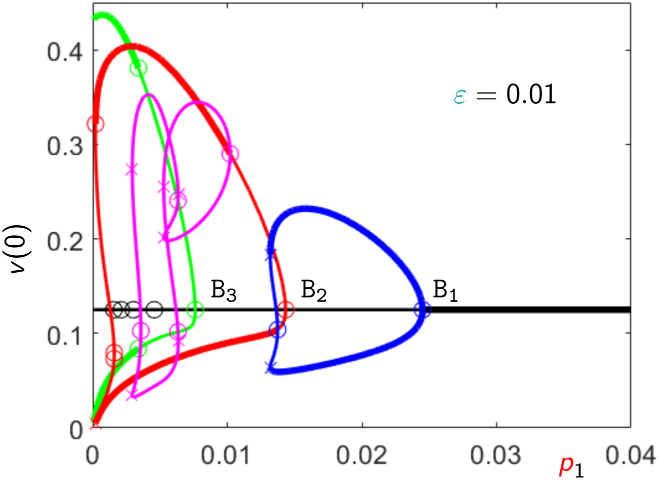

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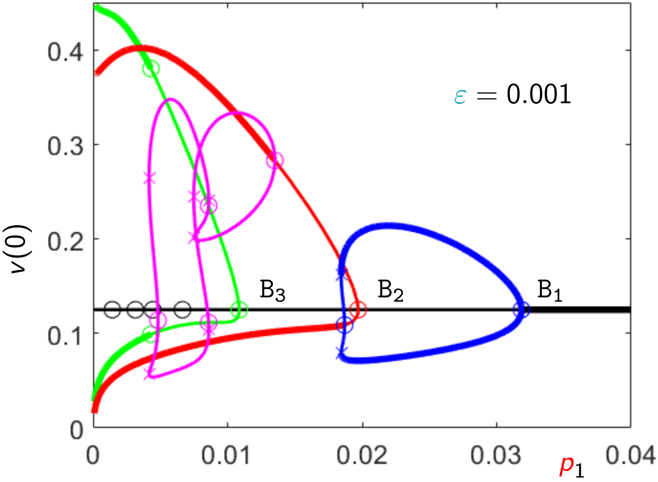

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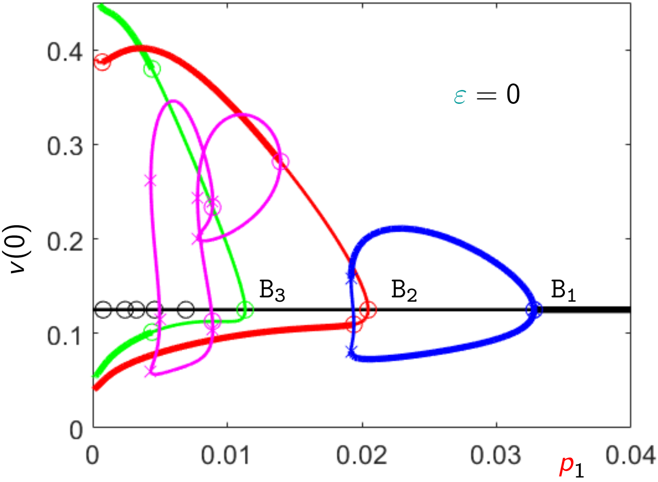

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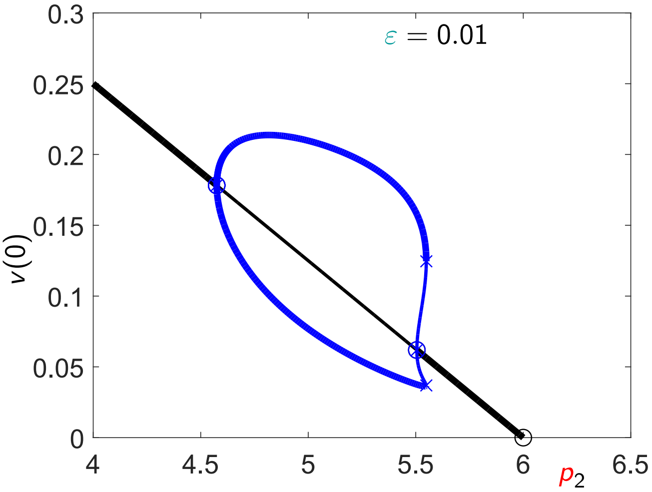

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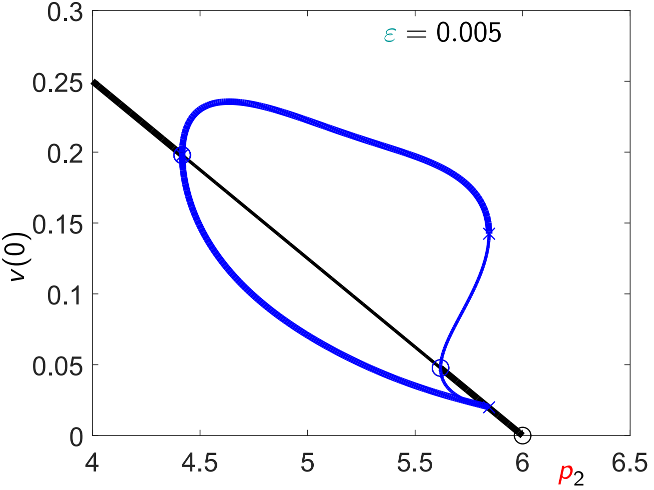

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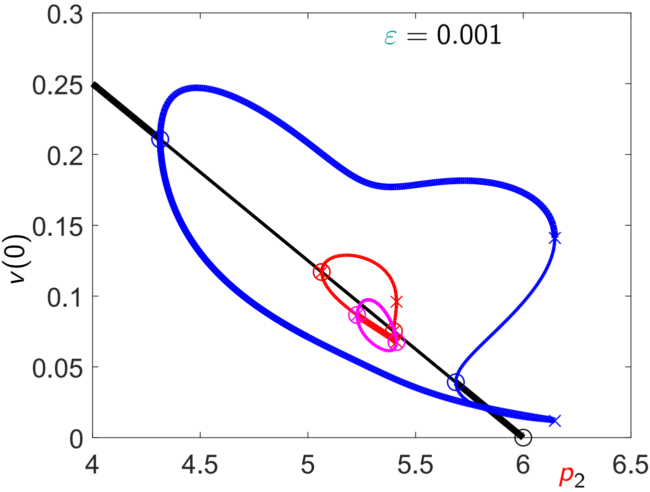

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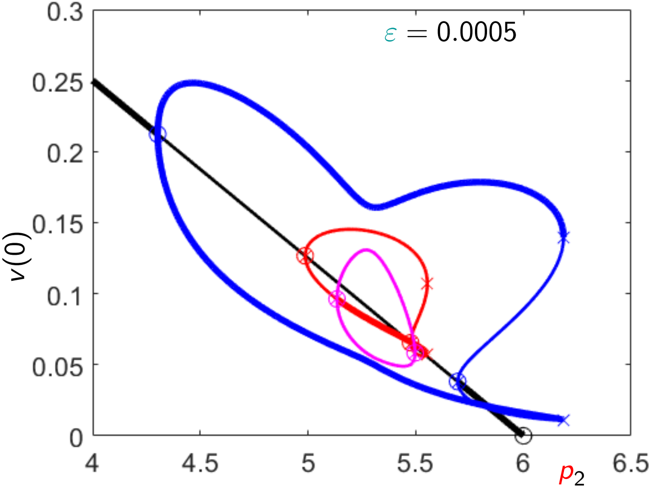

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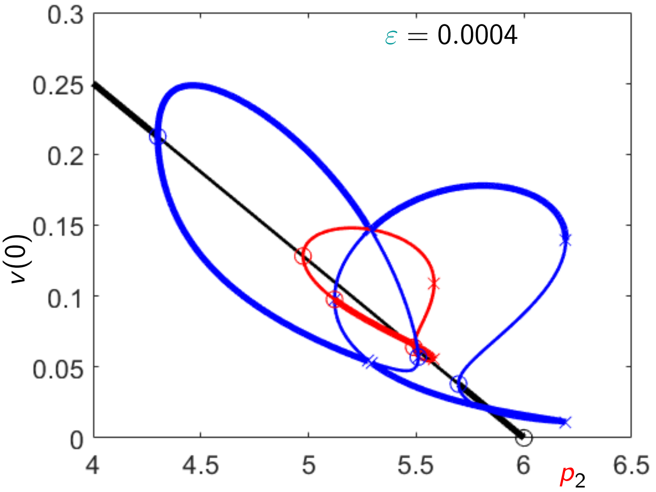

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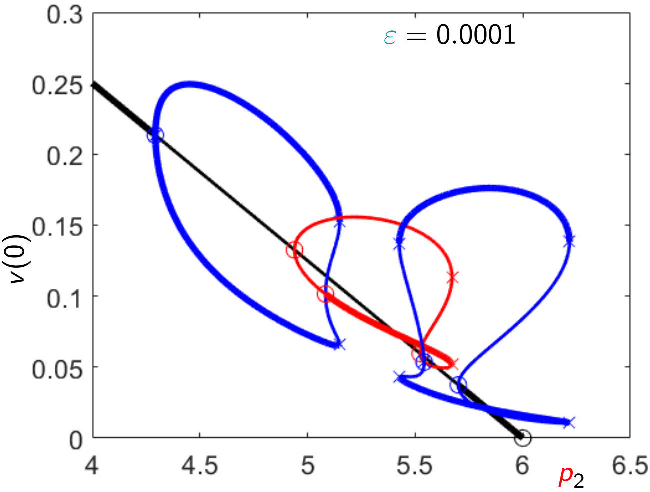

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Numerical Bifurcation Analysis for Stochastic Systems?

Consider the stochastic (ordinary) differential equation (SDE)

$$\mathrm{d}x_t = f(x_t; p)\,\mathrm{d}t + \sigma F(x_t; p)\,\mathrm{d}W_t, \quad x_t \in \mathbb{R}^n,$$

$W_t = (W_{1,t}, W_{2,t}, \dots, W_{k,t})^\top$ iid Brownian motions,
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- **Problem:** Sampling often prohibitive ($\rightarrow$ **gsMC**).

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  * = graduate-student Monte-Carlo method: *Efficient gluing of numerical continuation and a multiple solution method for elliptic PDEs*", **CK**, Appl. Math. Comput., Vol. 266, pp. 656-674, 2015

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- **Approach 1:** Forward Monte-Carlo simulation.
- **Problem:** Sampling often prohibitive ($\rightarrow$ **gsMC**).
- **Approach 2:** Use probability density $p = p(x, t)$:

$$\frac{\partial p}{\partial t} = -\sum_{i=1}^{n} \frac{\partial}{\partial x_i}(f(x; p)p) + \frac{\sigma^2}{2} \sum_{i,j=1}^{n} \frac{\partial}{\partial x_i \partial x_j}(\mathfrak{D}_{ij}(x; p)p).$$

- **Problem:** High-dimensional PDE; not even $\sigma = 0$ is easy!

Strategy - Generalization of Continuation to SDEs

Step 1: Recall

$$\mathrm{d}x_t = f(x_t; p)\, \mathrm{d}t + \sigma F(x_t; p)\, \mathrm{d}W_t.$$

Step 2: Expand near (locally stable) deterministic equilibrium x^*

$$\mathrm{d}X_t = A(x^*; p) X_t\, \mathrm{d}t + \sigma F(x^*; p)\, \mathrm{d}W_t$$

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Step 4: Define the covariance ellipsoid ("Mahalanobis distance")

$$\mathcal{B}(h) := \left\{x \in \mathbb{R}^n : (x - x^*)^\top C^{-1}(x - x^*) \le h^2\right\}.$$

Covariance Ellipsoids via Continuation

Important observations:

- Continue the equilibrium $x^* = x^*(p)$ as usual.
- For covariance ellipsoid one has to solve a Lyapunov equation

$$AC + CA^\top + BB^\top = 0$$

- During continuation the matrix

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  is available as a submatrix of $\mathrm{D}f(x^*; p)$.
- Efficient iterative methods for Lyapunov equations exist.
- A simple initial guess for $C(p_{(j+1)})$ at $(x^*(p_{(j+1)}), p_{(j+1)})$ is

$$C(x^*(p_{(j)}); p_{(j)}).$$

Ellipsoids and Distance

Question: What is the distance between ellipsoids?

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Let Q be positive semi-definite then

$$\mathcal{E} := \left\{ x \in \mathbb{R}^n : v^\top x \leq v^\top x^* + (v^\top Q v)^{1/2} \quad \forall v \in \mathbb{R}^n \right\}.$$

defines an ellipsoid centered at x^*.

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Fact: May solve an optimization problem

$$\begin{aligned} \delta &= \delta(\mathcal{E}(x_1^*, Q_1), \mathcal{E}(x_2^*, Q_2)) \\ &= \max_{\|v\|=1} \left(v^\top x_1^* - (v^\top Q_1 v)^{1/2} - v^\top x_2^* + (v^\top Q_2 v)^{1/2} \right). \end{aligned}$$

Idea: Use iterative method (e.g. SQP) & initial guess from continuation to compute δ.

Neural Competition

Consider two neural populations

$$\begin{aligned}
x_1' &= -x_1 + S(p - \beta x_2 - g y_1), \\
x_2' &= -x_2 + S(p - \beta x_1 - g y_2), \\
y_1' &= \varepsilon(x_1 - y_1), \\
y_2' &= \varepsilon(x_2 - y_2),
\end{aligned}$$

where

- $x_{1,2}$ = averaged firing rates,
- $y_{1,2}$ = fatigue/reset variables,
- $S(u) := \frac{1}{1+\exp(-r(u-\theta))}$.

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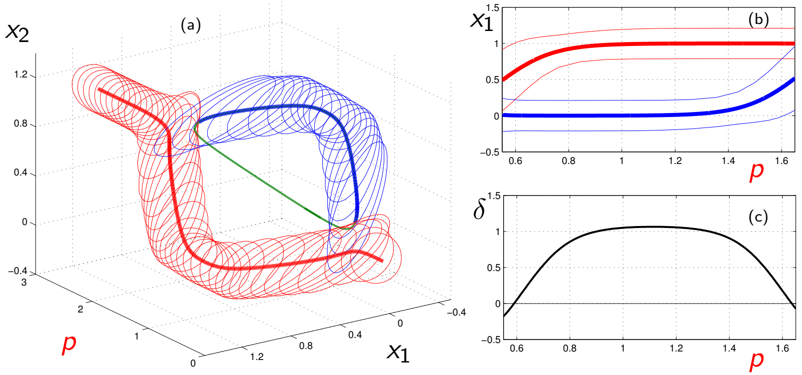
Look at noisy fast subsystem $\varepsilon = 0$

$$\begin{pmatrix} \mathrm{d}x_1 \\ \mathrm{d}x_2 \end{pmatrix} = \begin{pmatrix} -x_1 + S(p - \beta x_2 - g y_1) \\ -x_2 + S(p - \beta x_1 - g y_2) \end{pmatrix} \mathrm{d}t + \sigma^2 F(x)\, \mathrm{d}W_t$$

Numerical Continuation...



For parameter values

$$y_1 = 0.7, \quad y_2 = 0.75, \quad \beta = 1.1, \quad g = 0.5, \quad r = 10, \quad \theta = 0.2.$$

and

$$\sigma^2 F(x^*)F(x^*)^\top = \sigma^2 \begin{pmatrix} 1 & 0.4 \\ 0.4 & 1 \end{pmatrix} \qquad \text{for } \sigma^2 = 0.3.$$

Extension to SPDEs

Starting point: (cubic-quintic) Allen-Cahn PDE

$$\frac{\partial u}{\partial t} = \Delta u + 4(pu + u^3 - u^5).$$

$u = u(x, t)$, $x \in \Omega \subset \mathbb{R}^2$, given boundary conditions.

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Main Steps:

1. Compute bifurcation for PDE (e.g. $\rightarrow$ `pde2path`).

Extension to SPDEs

Starting point: (cubic-quintic) Allen-Cahn PDE

$$\frac{\partial u}{\partial t} = \Delta u + 4(pu + u^3 - u^5) + g(u)\xi.$$

$u = u(x, t)$, $x \in \Omega \subset \mathbb{R}^2$, given boundary conditions.

Main Steps:

1. Compute bifurcation for PDE (e.g. $\rightarrow$ `pde2path`).
2. Consider the SPDE version (e.g. $\rightarrow$ trace-class noise).
3. Discretize in space (e.g. $\rightarrow$ FDM, FEM, Galerkin).

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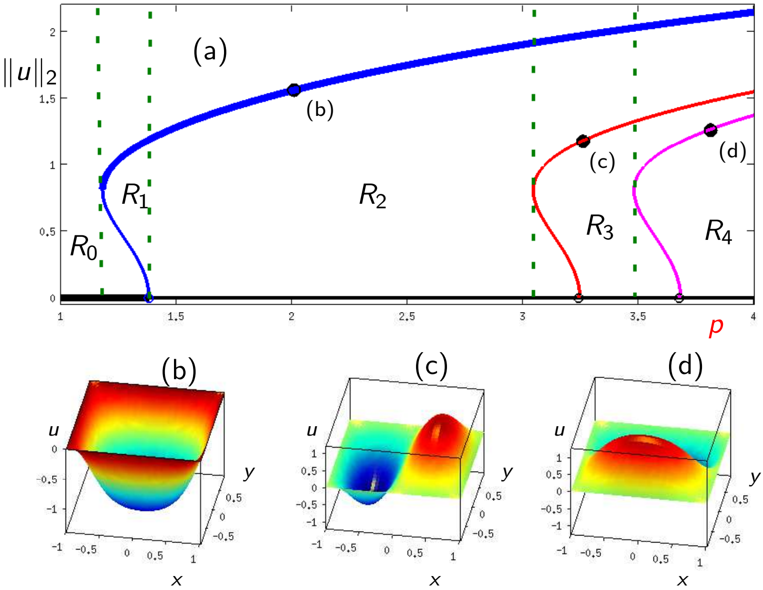
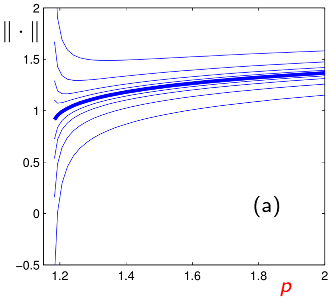
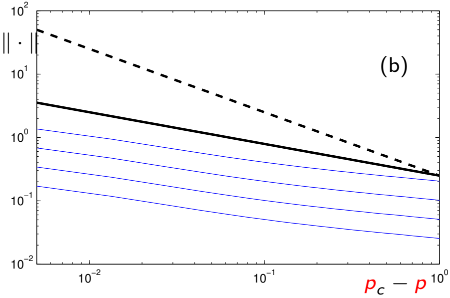
4. Apply numerical continuation for SDEs.

PDE: Deterministic Numerical Continuation



SPDE: Stochastic Numerical Continuation





- scaling law of the variance near bifurcation point
- link to early-warning signs
- Computation on standard desktop computer for SPDEs

Stochastic Continuation - Recent Developments

SODE/SPDE General Framework:

- "Deterministic continuation of stochastic metastable equilibria via Lyapunov equations and ellipsoids", **CK**, SIAM Journal on Scientific Computing, Vol. 34, No. 3, pp. A1635-A1658, 2012.
- "Numerical continuation and SPDE stability for the 2D cubic-quintic Allen-Cahn equation", **CK**, SIAM/ASA Journal on Uncertainty Quantification, Vol. 3, No. 1, pp. 762-789, 2015.

Climate Science Application:

- "Continuation of probability density functions using a generalized Lyapunov approach", S. Baars, J.P. Viebahn, T.E. Mulder, **CK**, F.W. Wubs and H.A. Dijkstra, Journal of Computational Physics, Vol. 336, No. 1, pp. 627643, 2017.

Full Error Analysis:

- "Combined error estimates for local fluctuations of SPDEs", **CK** and P. Kürschner, Advances in Computational Mathematics, accepted / to appear, 2020.

Link to Rigorous Proofs:

- "Rigorous validation of stochastic transition paths", M. Breden and **CK**, Journal de Mathmatiques Pures et Appliques, Vol. 131, pp. 88-129, 2019.

The Last Slide...

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- **www.multiscale.systems** and **arXiv**

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Thank you very much for your attention!!