New Developments in Dynamical Systems Arising from the Biosciences

Mathematical Biosciences Institute, 22–26 March 2011

The Effect of Noise on Mixed-Mode Oscillations

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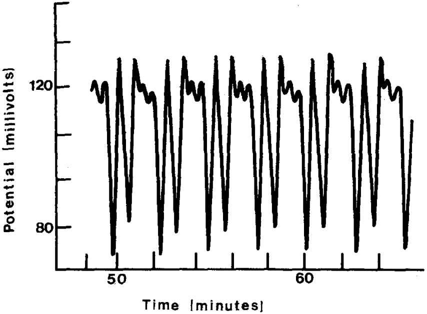
Mixed-Mode Oscillations (MMOs)

Belousov–Zhabotinsky reaction

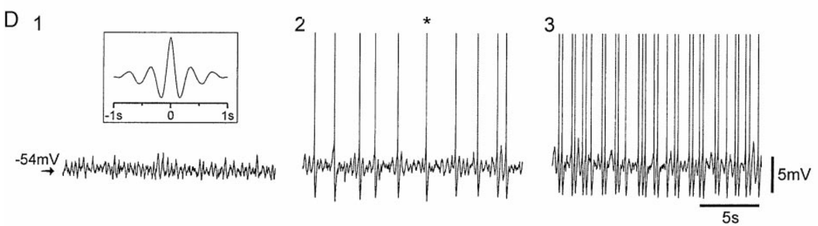


Recording from bromide ion electrode; T=25° C; flow rate = 3.99 ml/min; Ce^{+3} catalyst [Hudson, Hart, Marinko '79]

Notation: $\dots L_{j-1}^{s_{j-1}} L_j^{s_j} L_{j+1}^{s_{j+1}} \dots$ (here $L^s = 2^2$)

MMOs in Biology

Layer II Stellate Cells



D: subthreshold membrane potential oscillations (1 and 2) and spike clustering (3) develop at increasingly depolarized membrane potential levels positive to about –55 mV. Autocorrelation function (*inset* in 1) demonstrates the rhythmicity of the subthreshold oscillations [Dickson *et al* '00]

Questions: Origin of small-amplitude oscillations?
Source of irregularity in pattern?

MMOs & Slow–Fast Systems

MMOs can be observed in slow–fast systems undergoing a folded-node bifurcation (1 fast, 2 slow variables)

Normal form of folded-node [Benoît, Lobry '82; Szmolyan, Wechselberger '01]

$$\begin{aligned} \epsilon\dot{x} &= y - x^2 \\ \dot{y} &= -(\mu+1)x - z \\ \dot{z} &= \frac{\mu}{2} \end{aligned}$$

Questions: Dynamics for small $\varepsilon > 0$?
Effect of noise?

First step: General results for slow–fast systems (deterministic / subject to noise)

General Slow–Fast Systems: Singular Limits

In slow time t

$$\varepsilon\dot{x} = f(x,y)$$
$$\dot{y} = g(x,y)$$

$$\overset{t\mapsto s}{\Longleftrightarrow}$$

In fast time $s = t/\varepsilon$

$$x' = f(x,y)$$
$$y' = \varepsilon g(x,y)$$

$$\Big\downarrow \varepsilon\to 0$$

Slow subsystem

$$0 = f(x,y)$$
$$\dot{y} = g(x,y)$$

$$\not\Longleftrightarrow$$

Fast subsystem

$$x' = f(x,y)$$
$$y' = 0$$

Study slow variable y on *slow* or *critical* manifold $f(x,y) = 0$

Study fast variable x for frozen slow variable y

Slow (or Critical) Manifolds

$$\mathcal{C}_0 = \{(x, y) \in \mathbb{R}^n \times \mathbb{R}^m \colon f(x, y) = 0\}$$

Definition

- $\mathcal{C}_0$ is *normally hyperbolic* at $(x, y) \in \mathcal{C}_0$ if

$$\frac{\partial}{\partial x} f(x, y) \text{ has only eigenvalues } \lambda_j = \lambda_j(x, y) \text{ with } \operatorname{Re} \lambda_j \neq 0$$

- $\mathcal{C}_0$ is *asymptotically stable* or *attracting* at $(x, y) \in \mathcal{C}_0$ if

$$\operatorname{Re} \lambda_j(x, y) < 0 \quad \text{for all } j$$

- $\mathcal{C}_0$ is *unstable* at $(x, y) \in \mathcal{C}_0$ if

$$\operatorname{Re} \lambda_j(x, y) > 0 \quad \text{for at least one } j$$

Fenichel's Theorem: Adiabatic Manifolds

Theorem [Tihonov '52; Fenichel '79]

Assume $\mathcal{C}_0$ is normally hyperbolic.

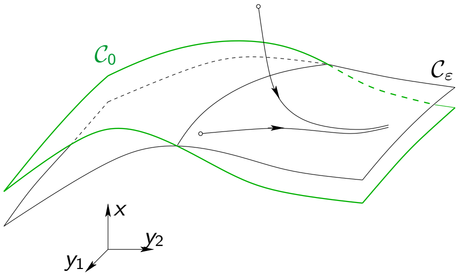
$\exists$ *adiabatic manifold* $\mathcal{C}_\varepsilon$ s.t.

- $\mathcal{C}_\varepsilon$ is locally invariant
- $\mathcal{C}_\varepsilon = \mathcal{C}_0 + \mathcal{O}(\varepsilon)$

If $\mathcal{C}_0$ is *uniformly attracting*, i.e.,

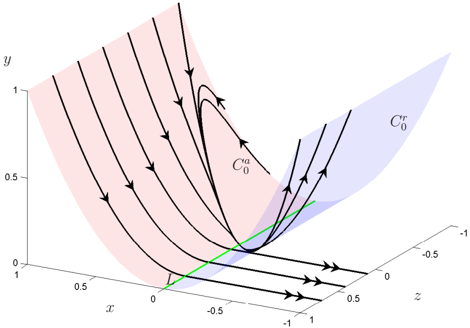
$$\mathrm{Re}(\lambda_j(x,y)) \leqslant -\delta < 0 \quad \forall (x,y)$$

then $\mathcal{C}_\varepsilon$ attracts nearby solutions exponentially fast



Folded-Node Bifurcation: Slow Manifold

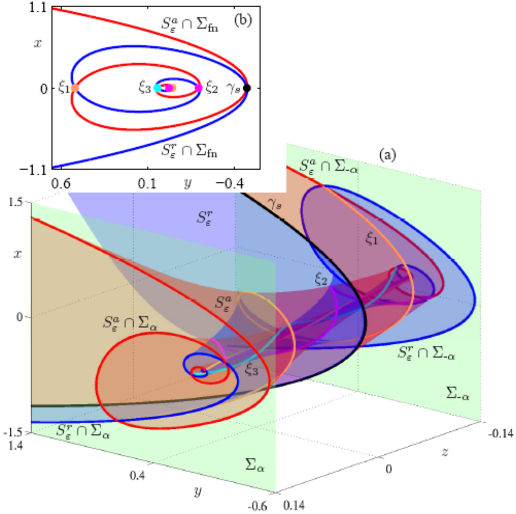
$$\epsilon \dot{x} = y - x^2$$
$$\dot{y} = -(\mu + 1)x - z$$
$$\dot{z} = \frac{\mu}{2}$$



Slow manifold has a decomposition

$$\mathcal{C}_0 = \{(x, y, z) \in \mathbb{R}^3 \colon y = x^2\} = \mathcal{C}_0^{\mathsf{a}} \cup L \cup \mathcal{C}_0^{\mathsf{r}}$$

Folded-Node: Adiabatic Manifolds and Canard Solutions



[Desroches *et al* '11 (to appear)]

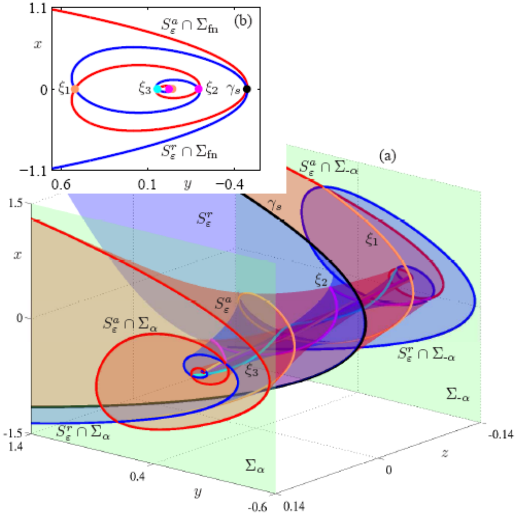
Assume

- ε sufficiently small
- $\mu \in (0,1)$, $\mu^{-1} \notin \mathbb{N}$

Theorem

[Benoît, Lobry '82;
Szmolyan, Wechselberger '01;
Wechselberger '05;
Brøns, Krupa, Wechselberger '06]

Folded-Node: Adiabatic Manifolds and Canard Solutions



[Desroches *et al* '11 (to appear)]

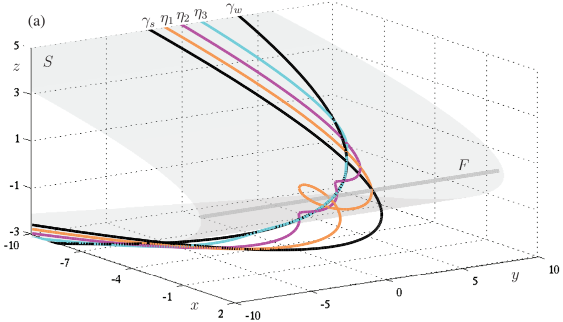
Assume

- ε sufficiently small
- $\mu \in (0, 1)$, $\mu^{-1} \notin \mathbb{N}$

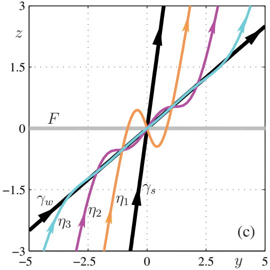
Theorem

- Existence of *strong* and *weak* (maximal) canard $\gamma_\varepsilon^{\mathrm{s,w}}$
- $2k + 1 < \mu^{-1} < 2k + 3$: $\exists$ k *secondary* canards γ_ε^j
- γ_ε^j makes $(2j + 1)/2$ oscillations around $\gamma_\varepsilon^{\mathrm{w}}$

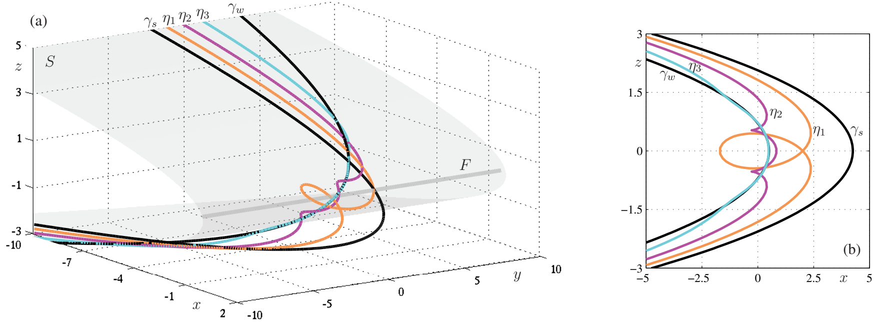
Folded-Node: Canard Spacing



[Desroches, Krauskopf, Osinga '08]



Folded-Node: Canard Spacing



[Desroches, Krauskopf, Osinga '08]

Lemma

For $z = 0$: Distance between canards γ_ε^k and γ_ε^{k+1} is $\mathcal{O}(\mathrm{e}^{-c_0(2k+1)^2\mu})$

Random Perturbations of General Slow–Fast Systems

$$\mathrm{d}x_t = \frac{1}{\varepsilon} f(x_t, y_t)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}} F(x_t, y_t)\,\mathrm{d}W_t$$

$$\mathrm{d}y_t = g(x_t, y_t)\,\mathrm{d}t + \sigma' \, G(x_t, y_t)\,\mathrm{d}W_t$$

- $\{W_t\}_{t \geqslant 0}$ k-dimensional (standard) Brownian motion
- adiabatic parameter $\varepsilon > 0$ (*no quasistatic* approach)
- noise intensities $\sigma = \sigma(\varepsilon) > 0$, $\sigma' = \sigma'(\varepsilon) \geqslant 0$ with $\sigma'(\varepsilon)/\sigma(\varepsilon) = \varrho(\varepsilon) \leqslant 1$

Timescales: We are interested in the regime

$$T_{\mathrm{relax}} = \mathcal{O}(\varepsilon) \ll T_{\mathrm{driving}} = 1 \ll T_{\mathrm{Kramers}} = \varepsilon\, \mathrm{e}^{\overline{V}/\sigma^2} \qquad \text{(in slow time)}$$

Assumption: $\mathcal{C}_0$ is uniformly attracting (for the deterministic system)

Deviation from the Adiabatic Manifold due to Noise

Main idea

- Consider deterministic process $(x_t^{\text{det}}, y_t^{\text{det}}) \in \mathcal{C}_\varepsilon$ (using invariance of $\mathcal{C}_\varepsilon$)
- Linearize SDE for deviation $\xi_t := x_t - x_t^{\text{det}}$ from adiabatic manifold

$$\mathrm{d}\xi_t^0 = \frac{1}{\varepsilon} A(y_t^{\text{det}})\xi_t^0 \, \mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}} F_0(y_t^{\text{det}}) \, \mathrm{d}W_t$$

where $A(y_t^{\text{det}}) = \partial_x f(x_t^{\text{det}}, y_t^{\text{det}})$ and F_0 is $0th$-order approximation to F

Key observation

- Resulting process ξ_t^0 is Gaussian
- $\dfrac{1}{\sigma^2} \operatorname{Cov} \xi_t^0$ is a particular solution of the deterministic slow–fast system

$$\varepsilon \dot{X}(t) = A(y_t^{\text{det}})X(t) + X(t)A(y_t^{\text{det}})^{\mathrm{T}} + F_0(y_t^{\text{det}})F_0(y_t^{\text{det}})^{\mathrm{T}}$$
$$\dot{y}_t^{\text{det}} = g(x_t^{\text{det}}, y_t^{\text{det}})$$

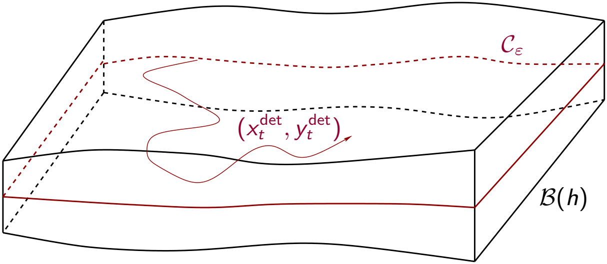
- System admits an adiabatic manifold $\{(\bar{X}(y,\varepsilon), y) \colon y \in \mathcal{D}_0\}$

Defining Typical Neighbourhoods of Adiabatic Manifolds

Typical neighbourhoods

$$\mathcal{B}(h) = \left\{ (x, y) \colon \left\langle \left[x - \bar{x}(y, \varepsilon) \right], \bar{X}(y, \varepsilon)^{-1} \left[x - \bar{x}(y, \varepsilon) \right] \right\rangle < h^2 \right\}$$

where $\mathcal{C}_\varepsilon = \{ (\bar{x}(y, \varepsilon), y) \colon y \in \mathcal{D}_0 \}$



First-exit times

$$\tau_{\mathcal{D}_0} = \inf\{ s > 0 \colon y_s \notin \mathcal{D}_0 \}$$
$$\tau_{\mathcal{B}(h)} = \inf\{ s > 0 \colon (x_s, y_s) \notin \mathcal{B}(h) \}$$

Concentration of Sample Paths near Adiabatic Manifolds

Theorem [Berglund & G '03]

- Assume *non-degeneracy of noise term*:

$$\|\bar{X}(y,\varepsilon)\| \text{ and } \|\bar{X}(y,\varepsilon)^{-1}\| \text{ uniformly bounded in } \mathcal{D}_0$$

- Then $\exists\, \varepsilon_0 > 0 \;\exists\, h_0 > 0 \;\forall\, \varepsilon \leqslant \varepsilon_0 \;\forall\, h \leqslant h_0$

$$\mathbb{P}\Big\{\tau_{\mathcal{B}(h)} < \min(t, \tau_{\mathcal{D}_0})\Big\} \leqslant C_{n,m}(t) \exp\biggl\{-\frac{h^2}{2\sigma^2}\bigl[1 - \mathcal{O}(h) - \mathcal{O}(\varepsilon)\bigr]\biggr\}$$

where $C_{n,m}(t) = \bigl[C^m + h^{-n}\bigr]\biggl(1 + \dfrac{t}{\varepsilon^2}\biggr)$

Remarks

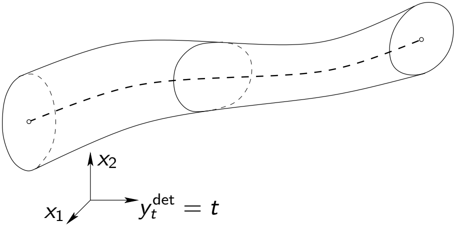
- Bound is sharp: Similar lower bound
- If initial condition not on $\mathcal{C}_\varepsilon$: additional transitional phase
- On longer time scales: Behaviour of slow variables becomes crucial ($\rightarrow$ Assumptions on g)

Special Case: Slowly Driven Systems

$$\mathrm{d}x_t = \frac{1}{\varepsilon} f(x_t, t)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}} F(x_t, t)\,\mathrm{d}W_t$$

Typical neighbourhood

$$\mathcal{B}(h) = \Big\{(x,t) \colon \Big\langle \big[x - x_t^{\det})\big], \bar{X}(t,\varepsilon)^{-1}\big[x - x_t^{\det}\big]\Big\rangle < h^2\Big\}$$



Estimate for all admissible t

$$\mathbb{P}\Big\{\tau_{\mathcal{B}(h)} < t\Big\} \leqslant C_{n,m}(t)\,\exp\bigg\{-\frac{h^2}{2\sigma^2}\big[1 - \mathcal{O}(h) - \mathcal{O}(\varepsilon)\big]\bigg\}$$

Stochastic Folded Nodes: Rescaling

$$
\begin{aligned}
\mathrm{d}x_t &= \frac{1}{\varepsilon}(y_t - x_t^2)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t^{(1)} \\
\mathrm{d}y_t &= [-(\mu+1)x_t - z_t]\,\mathrm{d}t + \sigma'\,\mathrm{d}W_t^{(2)} \\
\mathrm{d}z_t &= \frac{\mu}{2}\,\mathrm{d}t
\end{aligned}
$$

Rescaling (blow-up transformation): $(x, y, z, t) = (\sqrt{\varepsilon}\bar{x}, \varepsilon\bar{y}, \sqrt{\varepsilon}\bar{z}, \sqrt{\varepsilon}\,\bar{t})$

$$
\begin{aligned}
\mathrm{d}x_t &= (y_t - x_t^2)\,\mathrm{d}t + \frac{\sigma}{\varepsilon^{3/4}}\,\mathrm{d}W_t^{(1)} \\
\mathrm{d}y_t &= [-(\mu+1)x_t - z_t]\,\mathrm{d}t + \frac{\sigma'}{\varepsilon^{3/4}}\,\mathrm{d}W_t^{(2)} \\
\mathrm{d}z_t &= \frac{\mu}{2}\,\mathrm{d}t
\end{aligned}
$$

Rescale noise intensities: $(\sigma, \sigma') = (\varepsilon^{3/4}\bar{\sigma}, \varepsilon^{3/4}\bar{\sigma}')$ and consider z as "time"

Stochastic Folded Nodes: Final Reduction Step

Deviation $(\xi_z, \eta_z) = (x_z - x_z^{\det}, y_z - y_z^{\det})$ satisfies

$$
\begin{aligned}
d\xi_z &= \frac{2}{\mu}(\eta_z - \xi_z^2 - 2x_z^{\det}\xi_z)\,dz + \frac{\sqrt{2}\sigma}{\sqrt{\mu}}\,dW_z^{(1)} \\
d\eta_z &= -\frac{2}{\mu}(\mu+1)\xi_z\,dz + \frac{\sqrt{2}\sigma'}{\sqrt{\mu}}\,dW_z^{(2)}
\end{aligned}
$$

We're in business . . . (almost)

- For small μ: Slowly driven system with two fast variables
- Calculate asymptotic covariance matrix
- Use Neishtadt's theorem on delayed Hopf bifurcations to obtain the correct asymptotic behaviour of the size of the covariance tube
- Use general result on concentration of sample paths

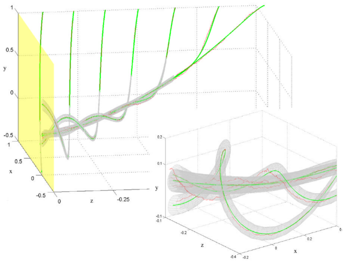
Stochastic Folded Nodes: Concentration of Sample Paths

Theorem [Berglund, G & Kuehn '10 (submitted)]

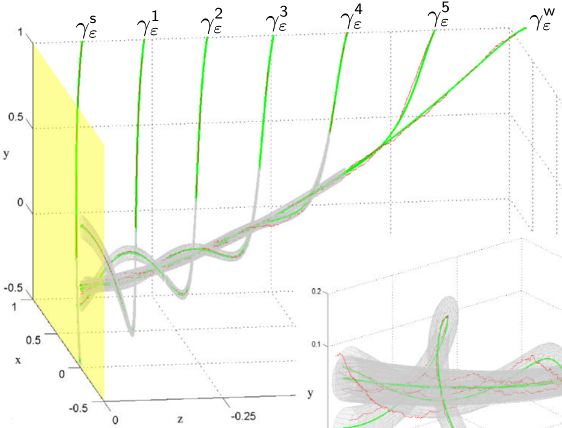
$$\mathbb{P}\left\{\tau_{\mathcal{B}(h)} < z\right\} \leqslant C(z_0, z) \exp\left\{-\kappa \frac{h^2}{2\sigma^2}\right\} \qquad \forall z \in [z_0, \sqrt{\mu}]$$

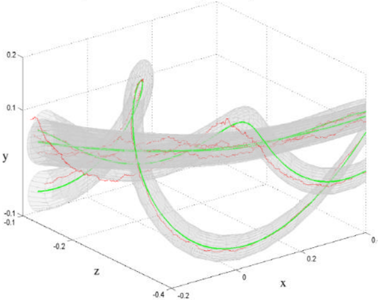
Recall: For $z = 0$

- Distance between canards γ_ε^k and γ_ε^{k+1} is $\mathcal{O}(\mathrm{e}^{-c_0(2k+1)^2\mu})$
- Section of $\mathcal{B}(h)$ is close to circular with radius $\mu^{-1/4}h$
- Noisy canards become indistinguishable when typical radius $\mu^{-1/4}\sigma \approx$ distance



Canards or Pasta . . . ?



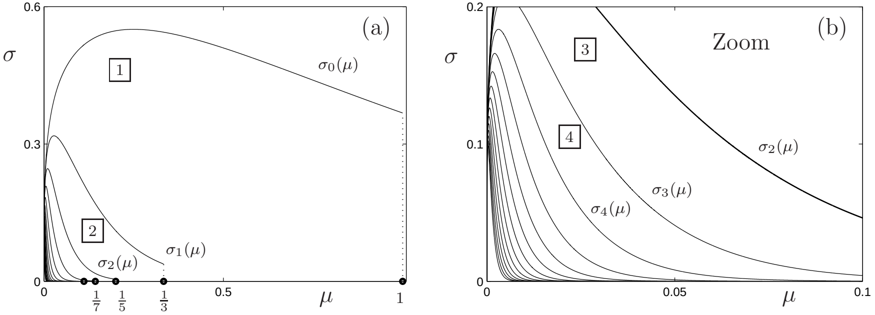


Noisy Small-Amplitude Oscillations

Theorem [Berglund, G & Kuehn '10 (submitted)]

Canards with $\frac{2k+1}{2}$ oscillations become indistinguishable from noisy fluctuations for

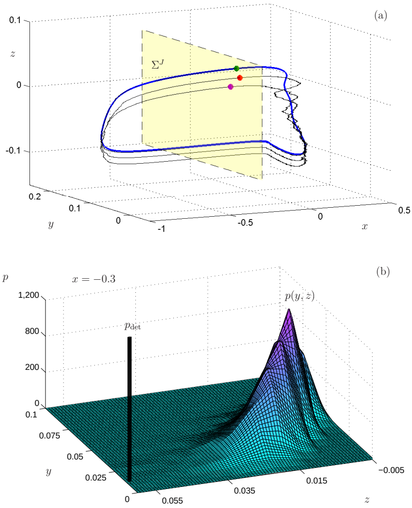
$$\sigma > \sigma_k(\mu) = \mu^{1/4}\, \mathrm{e}^{-(2k+1)^2\mu}$$



Early Escape

Model allowing for global returns

- Consider $z > \sqrt{\mu}$
- $\mathcal{S}_0 =$ neighbourhood of γ^{w}, growing like $\sqrt{z}$



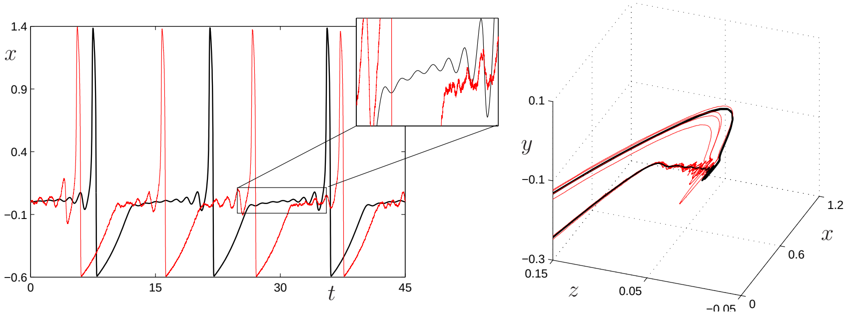
Theorem [Berglund, G & Kuehn '10]

$\exists \kappa, \kappa_1, \kappa_2, C > 0$
s.t.
for $\sigma |\log \sigma|^{\kappa_1} \leqslant \mu^{3/4}$

$$\mathbb{P}\{\tau_{\mathcal{S}_0} > z\} \leqslant C |\log \sigma|^{\kappa_2} \,\mathrm{e}^{-\kappa(z^2-\mu)/(\mu|\log \sigma|)}$$

Remark
r.h.s. small for $z \gg \sqrt{\mu |\log \sigma| / \kappa}$

Mixed-Mode Oscillations in the Presence of Noise



Observations

- ▷ Noise smears out small-amplitude oscillations
- ▷ Early transitions modify the mixed-mode pattern

References

MMOs with Noise

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Slow–Fast Systems with Noise

- Nils Berglund, Barbara Gentz, *Geometric singular perturbation theory for stochastic differential equations*, J. Differential Equations 191, 1–54 (2003)
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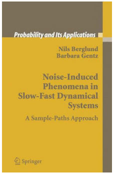

Introduction to Noise in Slowly-Driven Systems

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- ______, *Metastability in simple climate models: Pathwise analysis of slowly driven Langevin equations*, Stoch. Dyn. 2, 327–356 (2002)