Séminaire probabilités, statistique et applications, LMA Poitiers

Distribution de spikes pour des modèles stochastiques de neurones et chaînes de Markov à espace continu

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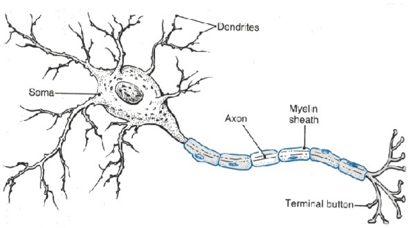
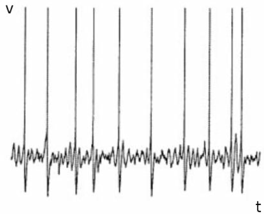
Poitiers, 12 mars 2015

Avec Barbara Gentz (Bielefeld), Christian Kuehn (Vienne) and Damien Landon (Dijon)

Neurons and action potentials

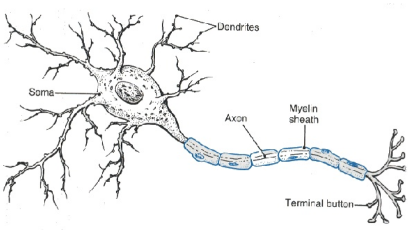


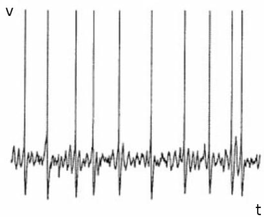


Action potential [Dickson 00]

- Neurons communicate via patterns of spikes in action potentials

Neurons and action potentials





Action potential [Dickson 00]

- Neurons communicate via patterns of spikes in action potentials
- Question: effect of noise on interspike interval statistics?
- Poisson hypothesis: Exponential distribution
  $\Rightarrow$ Markov property

Conduction-based models for action potential

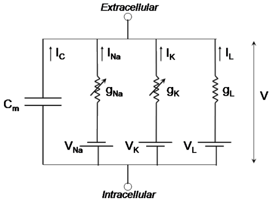
- Hodgkin–Huxley model (1952)

$$C\frac{\mathrm{d}V}{\mathrm{d}t} = -g_{\mathrm{K}}n^4(V - V_{\mathrm{K}}) - g_{\mathrm{Na}}m^3h(V - V_{\mathrm{Na}}) - g_{\mathrm{L}}(V - V_{\mathrm{L}}) + I$$

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \alpha_n(V)(1-n) - \beta_n(V)n$$

$$\frac{\mathrm{d}m}{\mathrm{d}t} = \alpha_m(V)(1-m) - \beta_m(V)m$$

$$\frac{\mathrm{d}h}{\mathrm{d}t} = \alpha_h(V)(1-h) - \beta_h(V)h$$



Conduction-based models for action potential

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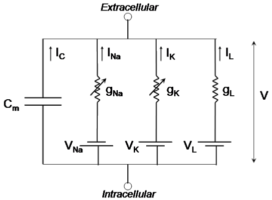

- FitzHugh–Nagumo model (1962)

$$\frac{C}{g}\frac{\mathrm{d}V}{\mathrm{d}t} = V - V^3 + w$$

$$\tau\frac{\mathrm{d}w}{\mathrm{d}t} = \alpha - \beta V - \gamma w$$

- Morris–Lecar model (1982) $2d$, more realistic eq for $\frac{\mathrm{d}V}{\mathrm{d}t}$
- Koper model (1995) $3d$, generalizes FitzHugh–Nagumo

Deterministic FitzHugh–Nagumo (FHN) model

Consider the FHN equations in the form

$$
\begin{aligned}
\varepsilon\dot{x} &= x - x^3 + y \\
\dot{y} &= a - x - by
\end{aligned}
$$

- $x \propto$ membrane potential of neuron
- $y \propto$ proportion of open ion channels (recovery variable)
- $\varepsilon \ll 1 \Rightarrow$ fast–slow system
- $b = 0$ in the following for simplicity (but results more general)

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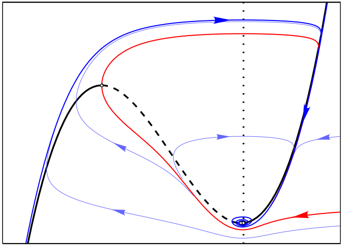
Stationary point $P = (a, a^3 - a)$
Linearisation has eigenvalues $\frac{-\delta \pm \sqrt{\delta^2 - \varepsilon}}{\varepsilon}$ where $\delta = \frac{3a^2 - 1}{2}$

- $\delta > 0$: stable node ($\delta > \sqrt{\varepsilon}$) or focus ($0 < \delta < \sqrt{\varepsilon}$)
- $\delta = 0$: singular Hopf bifurcation [Erneux & Mandel '86]
- $\delta < 0$: unstable focus ($-\sqrt{\varepsilon} < \delta < 0$) or node ($\delta < -\sqrt{\varepsilon}$)

Deterministic FitzHugh–Nagumo (FHN) model

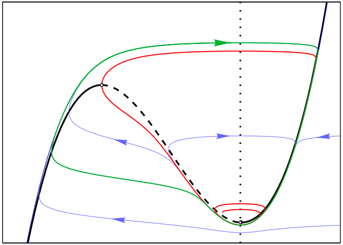
$\delta > 0$:

- P is asymptotically stable
- the system is excitable
- one can define a separatrix



$\delta < 0$:

P is unstable
$\exists$ asympt. stable periodic orbit
sensitive dependence on δ:
canard (duck) phenomenon
[Callot, Diener, Diener '78,
Benoît '81, . . .]



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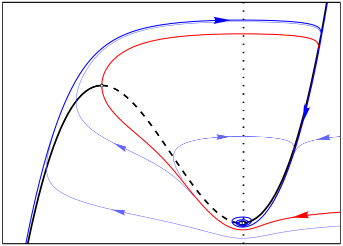

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(Link to simulation)

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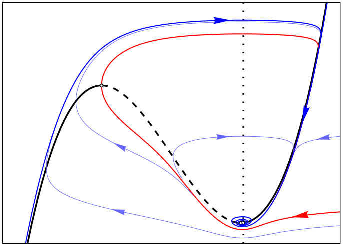

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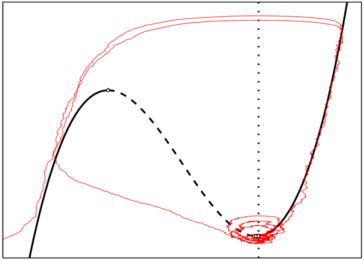
Stochastic FHN equation

$$\mathrm{d}x_t = \frac{1}{\varepsilon}[x_t - x_t^3 + y_t]\,\mathrm{d}t + \frac{\sigma_1}{\sqrt{\varepsilon}}\,\mathrm{d}W_t^{(1)}$$

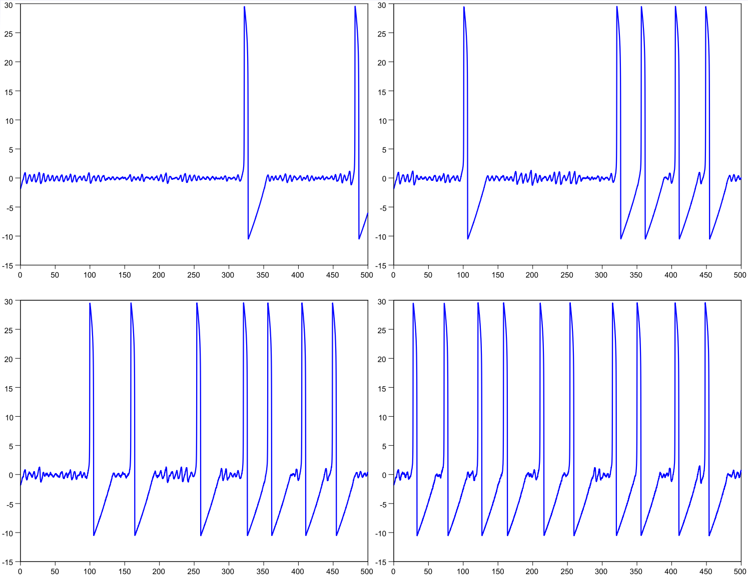
$$\mathrm{d}y_t = [a - x_t - by_t]\,\mathrm{d}t + \sigma_2\,\mathrm{d}W_t^{(2)}$$

- Again $b = 0$ for simplicity in this talk
- $W_t^{(1)}, W_t^{(2)}$: independent Wiener processes (white noise)
- $0 < \sigma_1, \sigma_2 \ll 1$, $\sigma = \sqrt{\sigma_1^2 + \sigma_2^2}$

$\varepsilon = 0.1$
$\delta = 0.02$
$\sigma_1 = \sigma_2 = 0.03$

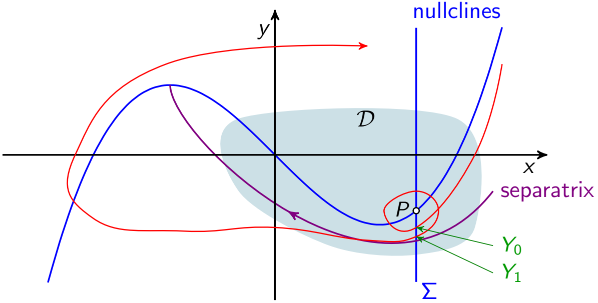


Mixed-mode oscillations (MMOs)



Time series $t \mapsto -x_t$ for $\varepsilon = 0.01$, $\delta = 3 \cdot 10^{-3}$, $\sigma = 1.46 \cdot 10^{-4}, \dots, 3.65 \cdot 10^{-4}$

Random Poincaré map



$Y_0, Y_1, \dots$ substochastic Markov chain describing process killed on $\partial\mathcal{D}$
Number of small oscillations:

$$N = \inf\{n \geqslant 1 \colon Y_n \notin \Sigma\}$$

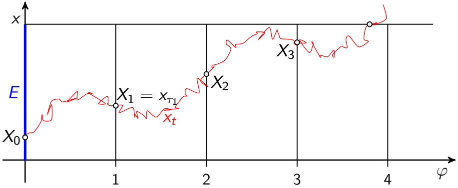
Law of N?

Random Poincaré maps

In appropriate coordinates

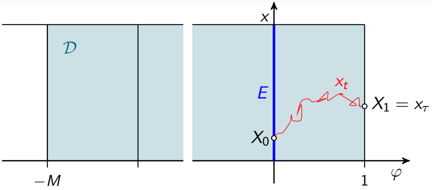
$$\mathrm{d}\varphi_t = f(\varphi_t, x_t)\,\mathrm{d}t + \sigma F(\varphi_t, x_t)\,\mathrm{d}W_t \qquad \varphi \in \mathbb{R} \quad (\text{or } \mathbb{R}/\mathbb{Z})$$
$$\mathrm{d}x_t = g(\varphi_t, x_t)\,\mathrm{d}t + \sigma G(\varphi_t, x_t)\,\mathrm{d}W_t \qquad x \in E \subset \Sigma$$

- all functions periodic in φ (say period 1)
- $f \geqslant c > 0$ and σ small $\Rightarrow$ φ_t likely to increase
- process may be killed when x leaves E



$X_0, X_1, \dots$ form (substochastic) Markov chain

Harmonic measure



- τ: first-exit time of $z_t = (\varphi_t, x_t)$ from $\mathcal{D} = (-M, 1) \times E$
- $A \subset \partial\mathcal{D}$: $\mu_z(A) = \mathbb{P}^z\{z_\tau \in A\}$ harmonic measure (wrt generator $\mathcal{L}$)
- [Ben Arous, Kusuoka, Stroock '84]: under hypoellipticity cond, μ_z admits (smooth) density $h(z, y)$ wrt arclength on $\partial\mathcal{D}$
- Remark: $\mathcal{L}_z h(z, y) = 0$ (kernel is harmonic)
- For $B \subset E$ Borel set

$$\mathbb{P}^{X_0}\{X_1 \in B\} = K(X_0, B) := \int_B K(X_0, \mathrm{d}y)$$

where $K(x, \mathrm{d}y) = h((0, x), (1, y))\,\mathrm{d}y =: k(x, y)\,\mathrm{d}y$

Fredholm theory

Consider integral operator K acting

- on L^∞ via $f \mapsto (Kf)(x) = \displaystyle\int_E k(x,y) f(y)\,\mathrm{d}y = \mathbb{E}^x[f(X_1)]$
- on L^1 via $m \mapsto (mK)(y) = \displaystyle\int_E m(x) k(x,y)\,\mathrm{d}x = \mathbb{P}^\mu\{X_1 \in \mathrm{d}y\}$

Thm [Fredholm 1903]:
If $k \in L^2$, then K has eigenvalues λ_n of finite multiplicity
Right/left eigenfunctions: $Kh_n = \lambda_n h_n$, $h_n^* K = \lambda_n h_n^*$, form complete ON basis

Thm [Perron, Frobenius, Jentzsch 1912, Krein–Rutman '50, Birkhoff '57]:
Principal eigenvalue λ_0 is real, simple, $|\lambda_n| < \lambda_0 \ \forall n \geqslant 1$, $h_0, h_0^* > 0$

Spectral decomp: $k\ (x,y) = \lambda_0 h_0(x) h_0^*(y) + \lambda_1 h_1(x) h_1^*(y) + \dots$

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$$\Rightarrow \mathbb{P}^x\{X_n \in \mathrm{d}y | X_n \in E\} = \pi_0(\mathrm{d}x) + \mathcal{O}((|\lambda_1|/\lambda_0)^n)$$

where $\pi_0 = h_0^* / \int_E h_0^*$ is quasistationary distribution (QSD)
[Yaglom '47, Bartlett '57, Vere-Jones '62, …]

Consequence for FitzHugh–Nagumo model

Theorem 1 [B & Landon, Nonlinearity 2012]

N is asymptotically geometric: $\lim_{n\to\infty} \mathbb{P}\{N = n+1 | N > n\} = 1 - \lambda_0$

where $\lambda_0 \in (0,1)$ if $\sigma > 0$ is principal eigenvalue of the chain

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Proof:

- $x^* = \operatorname{argmax} h_0 \quad \Rightarrow \quad \lambda_0 = \displaystyle\int_E k(x^*,y)\frac{h_0(y)}{h_0(x^*)}\,\mathrm{d}y \leqslant K(x^*,E) < 1$

  by ellipticity (k bounded below)

- $$\begin{aligned}\mathbb{P}^{\mu_0}\{N > n\} = \mathbb{P}^{\mu_0}\{X_n \in E\} &= \textstyle\int_E \mu_0(\mathrm{d}x)K^n(x,E) \\ &= \textstyle\int_E \mu_0(\mathrm{d}x)\lambda_0^n h_0(x)\|h_0^*\|_1[1+\mathcal{O}((|\lambda_1|/\lambda_0)^n)] \\ &= \lambda_0^n\langle\mu_0,h_0\rangle\|h_0^*\|_1[1+\mathcal{O}((|\lambda_1|/\lambda_0)^n)]\end{aligned}$$

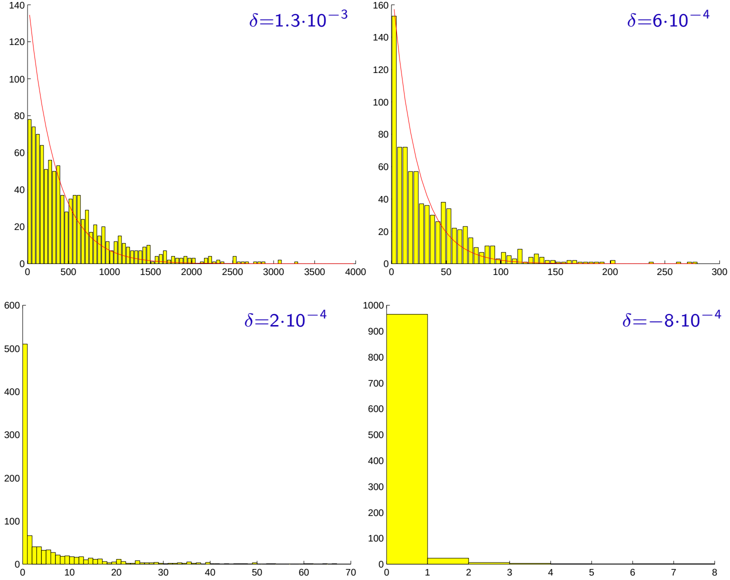
- $$\begin{aligned}\mathbb{P}^{\mu_0}\{N = n+1\} &= \textstyle\int_E\int_E \mu_0(\mathrm{d}x)K^n(x,\mathrm{d}y)[1-K(y,E)] \\ &= \lambda_0^n(1-\lambda_0)\langle\mu_0,h_0\rangle\|h_0^*\|_1[1+\mathcal{O}((|\lambda_1|/\lambda_0)^n)]\end{aligned}$$

- Existence of spectral gap follows from positivity condition [Birkhoff '57]

  ▸▸ More

Histograms of distribution of N (1000 spikes)

$\sigma = \varepsilon = 10^{-4}$



Weak-noise regime

Theorem B & Landon , Nonlinearity 2012

Assume ε and $\delta/\sqrt{\varepsilon}$ sufficiently small
There exists $\kappa > 0$ s.t. for $\sigma^2 \leqslant (\varepsilon^{1/4}\delta)^2/\log(\sqrt{\varepsilon}/\delta)$

- Principal eigenvalue:

$$1 - \lambda_0 \leqslant \exp\Big\{-\kappa\frac{(\varepsilon^{1/4}\delta)^2}{\sigma^2}\Big\}$$

- Expected number of small oscillations:

$$\mathbb{E}^{\mu_0}[N] \geqslant C(\mu_0)\exp\Big\{\kappa\frac{(\varepsilon^{1/4}\delta)^2}{\sigma^2}\Big\}$$

where $C(\mu_0)$ = probability of starting on Σ above separatrix

Proof:

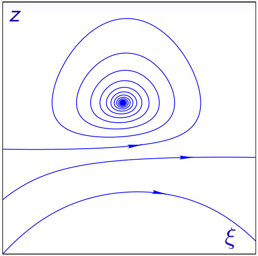
- Construct $A \subset \Sigma$ such that $K(x,A)$ exponentially close to 1 for all $x \in A$
- $\lambda_0 \int_A h_0^*(y)\,dy = \int_E h_0^*(x)K(x,A)\,dx \geqslant \inf_{x\in A} K(x,A) \int_A h_0^*(y)\,dy$

Dynamics near the separatrix

Change of variables:

- Translate to Hopf bif. point
- Scale space and time
- Straighten nullcline $\dot{x} = 0$

$\Rightarrow$ variables (ξ, z) where nullcline: $\{z = \frac{1}{2}\}$



$$d\xi_t = \left(\frac{1}{2} - z_t - \frac{\sqrt{\varepsilon}}{3}\xi_t^3\right) dt$$

$$dz_t = \left(\tilde{\mu} + 2\xi_t z_t + \frac{2\sqrt{\varepsilon}}{3}\xi_t^4\right) dt$$

where

$$\tilde{\mu} = \frac{\delta}{\sqrt{\varepsilon}}$$

Dynamics near the separatrix

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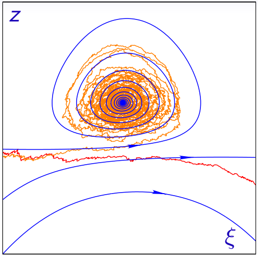
- ▹ Scale space and time
- ▹ Straighten nullcline $\dot{x} = 0$



$\Rightarrow$ variables (ξ, z) where nullcline: $\{z = \frac{1}{2}\}$

$$\mathrm{d}\xi_t = \left(\frac{1}{2} - z_t - \frac{\sqrt{\varepsilon}}{3}\xi_t^3\right)\mathrm{d}t + \tilde{\sigma}_1\,\mathrm{d}W_t^{(1)}$$

$$\mathrm{d}z_t = \left(\tilde{\mu} + 2\xi_t z_t + \frac{2\sqrt{\varepsilon}}{3}\xi_t^4\right)\mathrm{d}t - 2\tilde{\sigma}_1\xi_t\,\mathrm{d}W_t^{(1)} + \tilde{\sigma}_2\,\mathrm{d}W_t^{(2)}$$

where

$$\tilde{\mu} = \frac{\delta}{\sqrt{\varepsilon}} - \tilde{\sigma}_1^2 \qquad \tilde{\sigma}_1 = -\sqrt{3}\frac{\sigma_1}{\varepsilon^{3/4}} \qquad \tilde{\sigma}_2 = \sqrt{3}\frac{\sigma_2}{\varepsilon^{3/4}}$$

Upward drift dominates if $\tilde{\mu}^2 \gg \tilde{\sigma}_1^2 + \tilde{\sigma}_2^2 \Rightarrow (\varepsilon^{1/4}\delta)^2 \gg \sigma_1^2 + \sigma_2^2$

Rotation around P: use that $2z\,\mathrm{e}^{-2z-2\xi^2+1}$ is constant for $\tilde{\mu} = \varepsilon = 0$

From below to above threshold

Linear approximation:

$$\mathrm{d}z_t^0 = \left(\tilde{\mu} + tz_t^0\right)\mathrm{d}t - \tilde{\sigma}_1 t\,\mathrm{d}W_t^{(1)} + \tilde{\sigma}_2\,\mathrm{d}W_t^{(2)}$$

$$\Rightarrow \quad \mathbb{P}\{\text{no small osc}\} \simeq \Phi\left(-\pi^{1/4}\frac{\tilde{\mu}}{\sqrt{\tilde{\sigma}_1^2+\tilde{\sigma}_2^2}}\right) \qquad \Phi(x) = \int_{-\infty}^{x} \frac{\mathrm{e}^{-y^2/2}}{\sqrt{2\pi}}\,\mathrm{d}y$$

From below to above threshold

Linear approximation:

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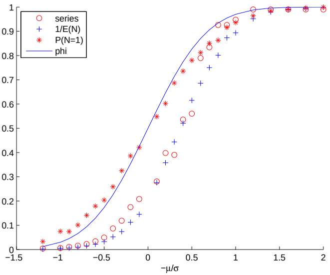
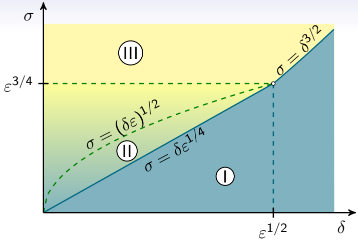


$*$: $\mathbb{P}\{\text{no small osc}\}$
$+$: $1/\mathbb{E}[N]$
$\circ$: $1-\lambda_0$
curve: $x \mapsto \Phi(\pi^{1/4}x)$

$$x = -\frac{\tilde{\mu}}{\sqrt{\tilde{\sigma}_1^2+\tilde{\sigma}_2^2}} = -\frac{\varepsilon^{1/4}(\delta-\sigma_1^2/\varepsilon)}{\sqrt{\sigma_1^2+\sigma_2^2}}$$

Summary: Parameter regimes

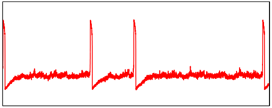


$\sigma_1 = \sigma_2$:
$\mathbb{P}\{N = 1\} \simeq \Phi\Big(-\frac{(\pi\varepsilon)^{1/4}(\delta-\sigma^2/\varepsilon)}{\sigma}\Big)$

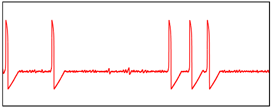
see also

[Muratov & Vanden Eijnden '08]

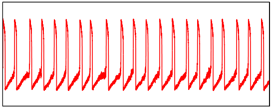
Regime I: rare isolated spikes
Theorem 2 applies ($\delta \ll \varepsilon^{1/2}$)
Interspike interval $\simeq$ exponential



Regime II: clusters of spikes
interspike osc asympt geometric
$\sigma = (\delta\varepsilon)^{1/2}$: geom(1/2)

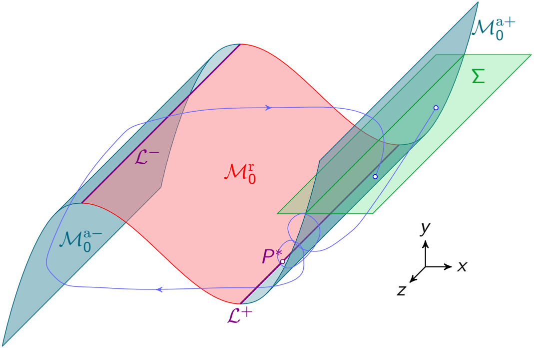


Regime III: repeated spikes
$\mathbb{P}\{N = 1\} \simeq 1$
Interspike interval $\simeq$ constant



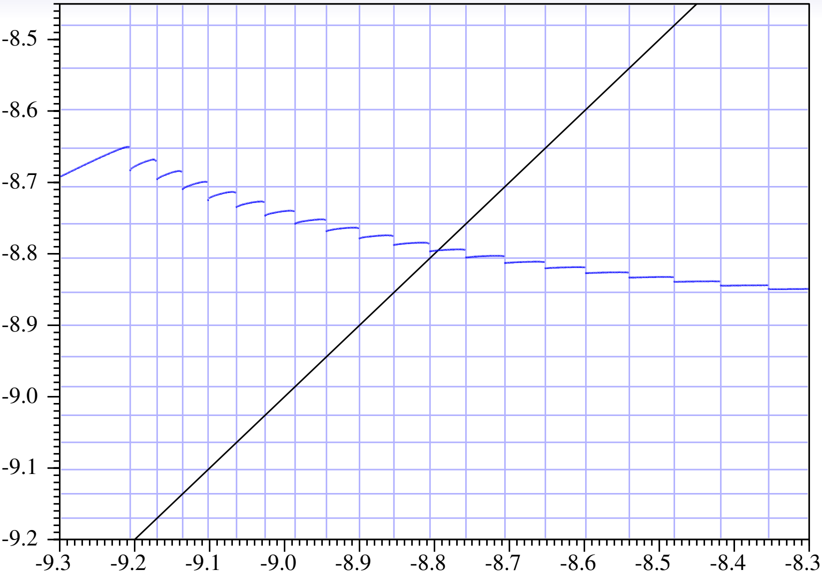
The Koper model

$$\begin{aligned}
\varepsilon\, dx_t &= [y_t - x_t^3 + 3x_t]\, dt && + \sqrt{\varepsilon}\sigma F(x_t, y_t, z_t)\, dW_t \\
dy_t &= [kx_t - 2(y_t + \lambda) + z_t]\, dt && + \sigma' G_1(x_t, y_t, z_t)\, dW_t \\
dz_t &= [\rho(\lambda + y_t - z_t)]\, dt && + \sigma' G_2(x_t, y_t, z_t)\, dW_t
\end{aligned}$$



Folded-node singularity at P^* induces mixed-mode oscillations
[Benoît, Lobry '82, Szmolyan, Wechselberger '01, ...]
Poincaré map $\Pi : \Sigma \to \Sigma$ is almost $1d$ due to contraction in x-direction

Poincaré map $z_n \mapsto z_{n+1}$



$k = -10, \lambda = -7.6, \rho = 0.7, \varepsilon = 0.01, \sigma = \sigma' = 0$ – c.f. [Guckenheimer, Chaos, 2008]

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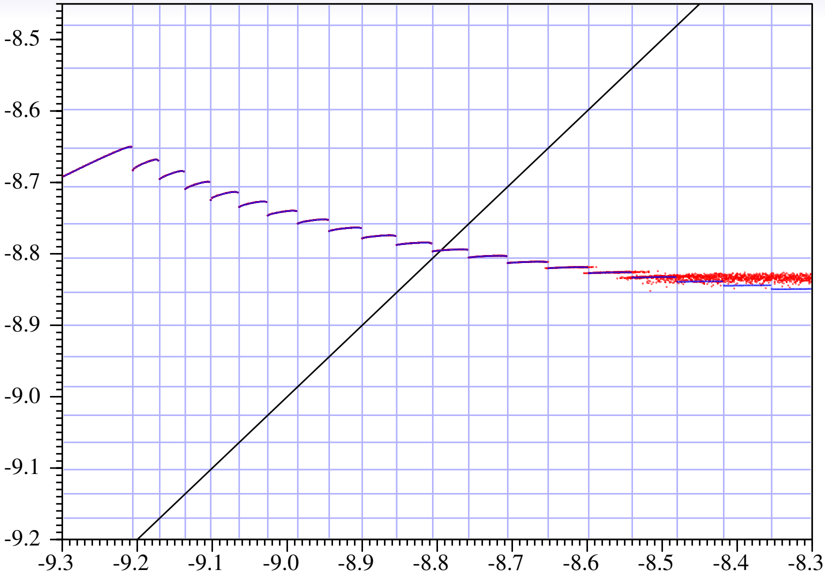

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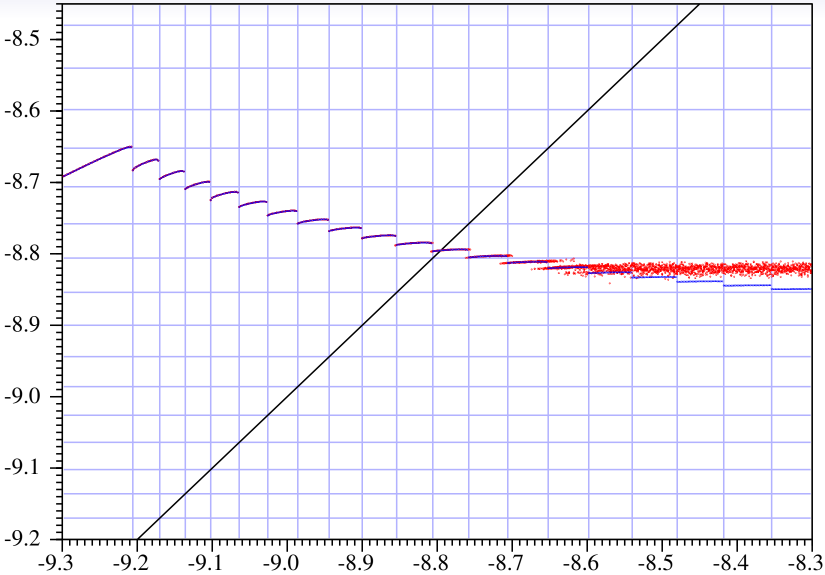

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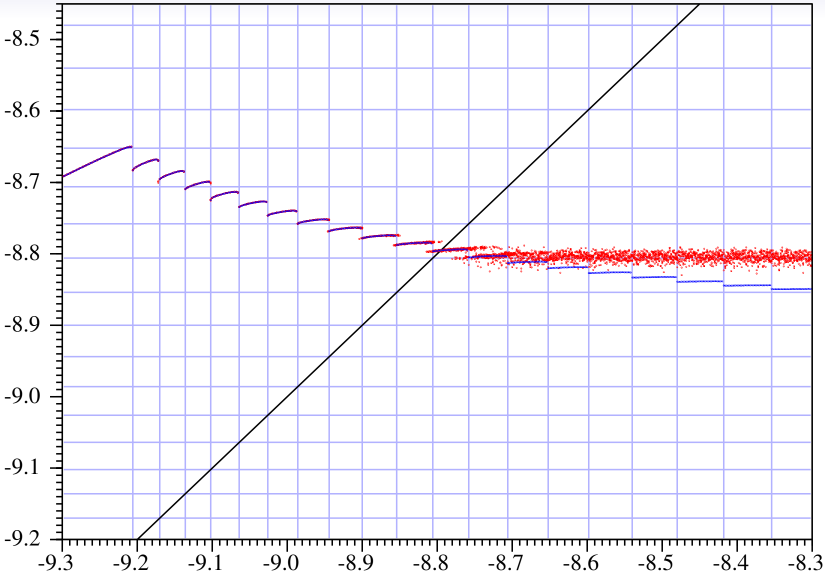

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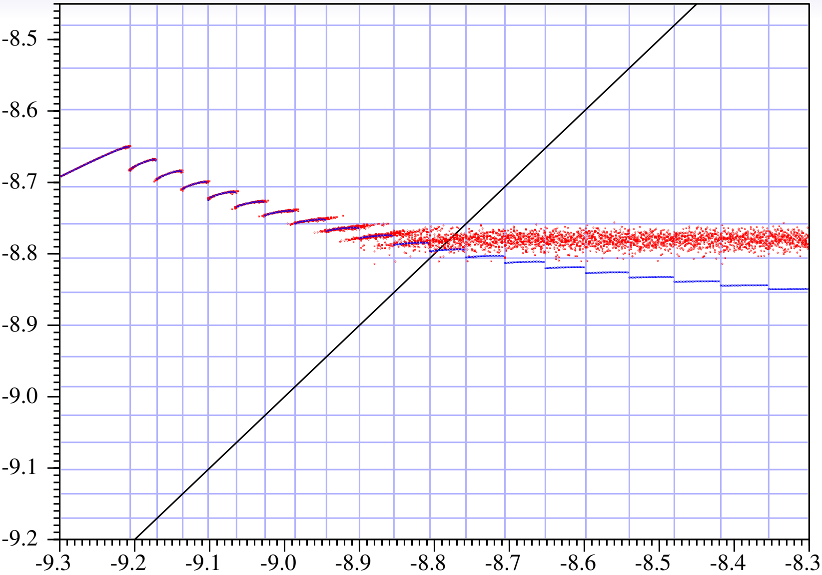

$k = -10, \lambda = -7.6, \rho = 0.7, \varepsilon = 0.01,$ $\sigma = \sigma' = 2 \cdot 10^{-4}$

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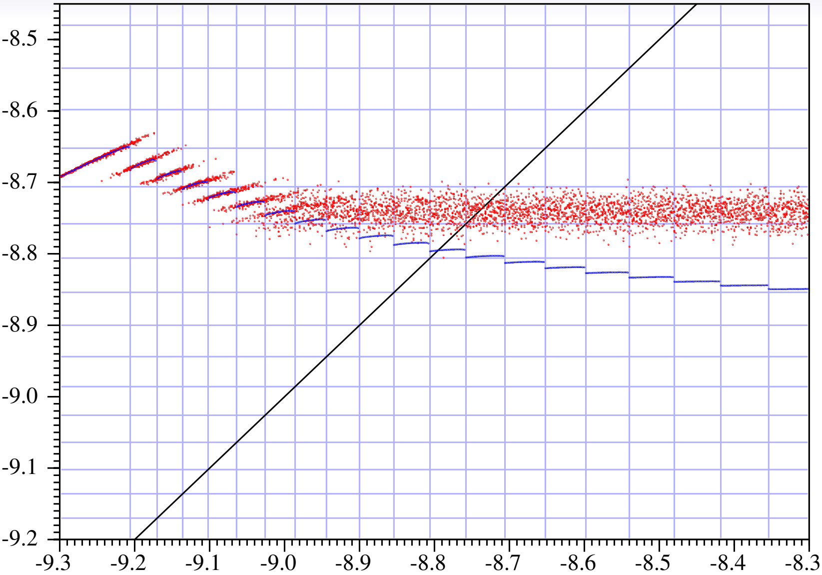

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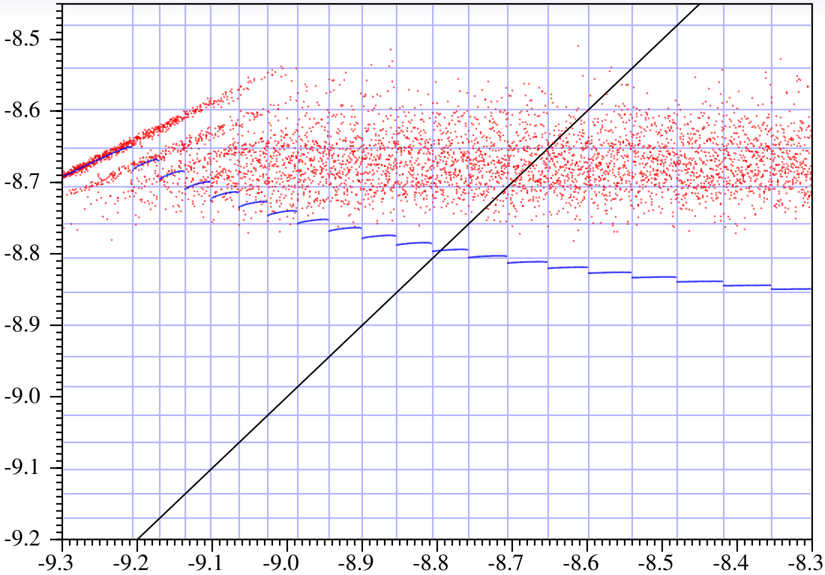
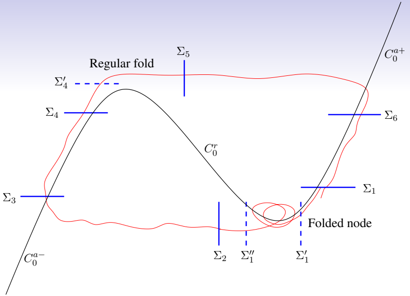


$k = -10, \lambda = -7.6, \rho = 0.7, \varepsilon = 0.01,$ $\sigma = \sigma' = 10^{-2}$

Size of fluctuations

$\mu \ll 1$: eigenvalue ratio
at folded node



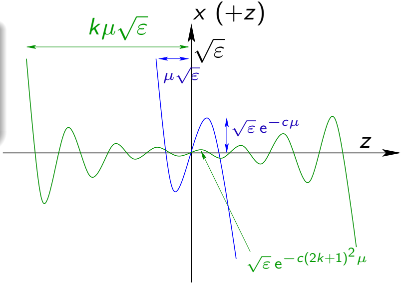
Transition	Δx	Δy	Δz
$\Sigma_2 \to \Sigma_3$	$\sigma + \sigma'$		$\sigma\sqrt{\varepsilon} + \sigma'$
$\Sigma_3 \to \Sigma_4$	$\sigma + \sigma'$		$\sigma\sqrt{\varepsilon} + \sigma'$
$\Sigma_4 \to \Sigma_4'$	$\dfrac{\sigma}{\varepsilon^{1/6}} + \dfrac{\sigma'}{\varepsilon^{1/3}}$		$\sigma\sqrt{\varepsilon\lvert\log\varepsilon\rvert} + \sigma'$
$\Sigma_4' \to \Sigma_5$		$\sigma\sqrt{\varepsilon} + \sigma'\varepsilon^{1/6}$	$\sigma\sqrt{\varepsilon} + \sigma'\varepsilon^{1/6}$
$\Sigma_5 \to \Sigma_6$	$\sigma + \sigma'$		$\sigma\sqrt{\varepsilon} + \sigma'$
$\Sigma_6 \to \Sigma_1$	$\sigma + \sigma'$		$\sigma\sqrt{\varepsilon} + \sigma'$
$\Sigma_1 \to \Sigma_1'$		$(\sigma + \sigma')\varepsilon^{1/4}$	σ'
$\Sigma_1' \to \Sigma_1''$ if $z = \mathcal{O}(\sqrt{\mu})$		$(\sigma + \sigma')(\varepsilon/\mu)^{1/4}$	$\sigma'(\varepsilon/\mu)^{1/4}$
$\Sigma_1'' \to \Sigma_2$		$(\sigma + \sigma')\varepsilon^{1/4}$	$\sigma'\varepsilon^{1/4}$

Main results

[B, Gentz, Kuehn, JDE 2012 & JDDE 2015]

Theorem 1: canard spacing

At $z = 0$, k^{th} canard lies at distance $\sqrt{\varepsilon}\,\mathrm{e}^{-c(2k+1)^2\mu}$ from primary canard



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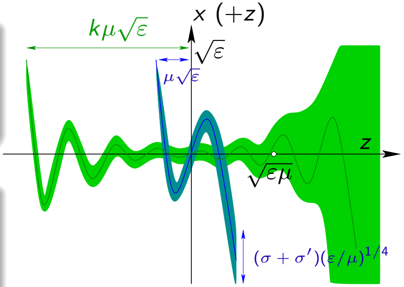

Theorem 1: canard spacing

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Theorem 2: size of fluctuations ▸▸ More

$(\sigma+\sigma')(\varepsilon/\mu)^{1/4}$ up to $z = \sqrt{\varepsilon\mu}$

$(\sigma+\sigma')(\varepsilon/\mu)^{1/4}\,\mathrm{e}^{z^2/(\varepsilon\mu)}$ for $z \geqslant \sqrt{\varepsilon\mu}$

Theorem 3: early escape

$P_0 \in \Sigma_1$ in sector with $k > 1/\sqrt{\mu} \Rightarrow$ first hitting of Σ_2 at P_2 s.t.

$\mathbb{P}^{P_0}\{z_2 \geqslant z\} \leqslant C|\log(\sigma+\sigma')|^{\gamma}\,\mathrm{e}^{-\kappa z^2/(\varepsilon\mu|\log(\sigma+\sigma')|)}$

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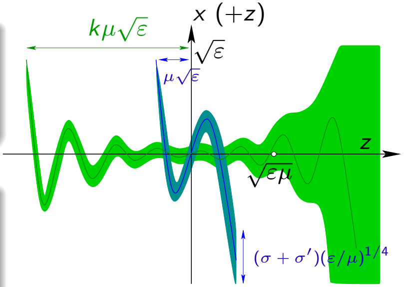

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- Saturation effect occurs at $k_c \simeq \sqrt{|\log(\sigma + \sigma')|/\mu}$
- For $k > k_c$, behaviour indep. of k and $\Delta z \leqslant \mathcal{O}(\sqrt{\varepsilon\mu|\log(\sigma + \sigma')|}\,)$

Concluding remarks

- Noise can induce spikes that may have non-Poisson interval statistics
- Noise can increase the number of small-amplitude oscillations
- Important tools: random Poincaré maps and quasistationary distrib.
- Future work: more quantitative analysis of oscillation patterns, using singularly perturbed Markov chains and spectral theory ⏩ More

References

- N. B., Damien Landon, *Mixed-mode oscillations and interspike interval statistics in the stochastic FitzHugh-Nagumo model*, Nonlinearity **25**, 2303–2335 (2012)
- N. B., Barbara Gentz and Christian Kuehn, *Hunting French Ducks in a Noisy Environment*, J. Differential Equations **252**, 4786–4841 (2012)
- ______, *From random Poincaré maps to stochastic mixed-mode-oscillation patterns*, J. Dynam. Differential Equations **27**, 83–136 (2015)
- N. B. and Barbara Gentz, *Stochastic dynamic bifurcations and excitability* in C. Laing and G. Lord (Eds.), *Stochastic methods in Neuroscience*, p. 65-93, Oxford University Press (2009)
- ______, *On the noise-induced passage through an unstable periodic orbit II: General case*, SIAM J Math Anal **46**, 310–352 (2014)

How to estimate the spectral gap

Various approaches: coupling, Poincaré/log-Sobolev inequalities, Lyapunov functions, Laplace transform + Donsker–Varadhan, ...

Thm [Garett Birkhoff '57] Under uniform positivity condition

$$s(x)\nu(A) \leqslant K(x,A) \leqslant Ls(x)\nu(A) \qquad \forall x \in E, \forall A \subset E$$

one has $|\lambda_1|/\lambda_0 \leqslant 1 - L^{-2}$

Back

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Localised version: assume $\exists\, A \subset E$ and $m : A \to \mathbb{R}_+^*$ such that

$$m(y) \leqslant k(x,y) \leqslant Lm(y) \qquad \forall x,y \in A \tag{1}$$

Then

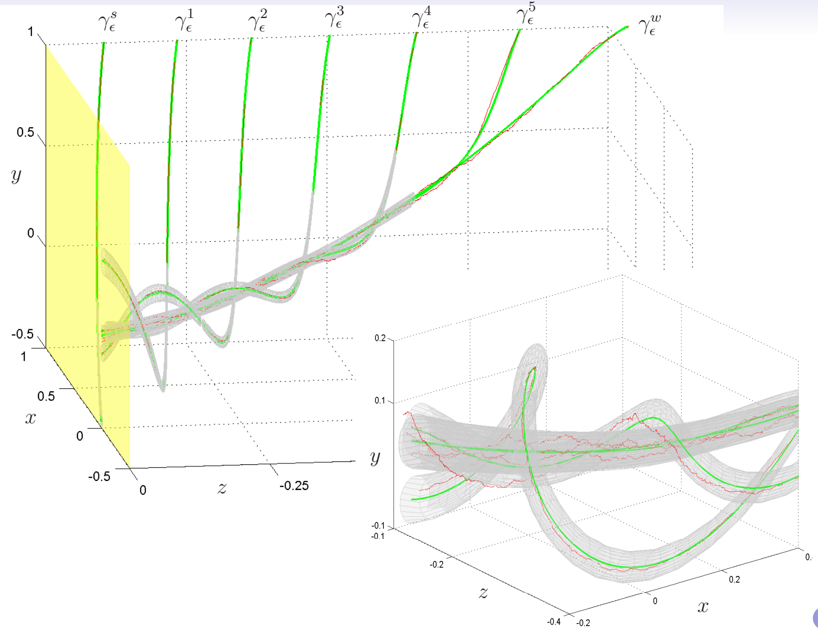
$$|\lambda_1| \leqslant L - 1 + \mathcal{O}\Big(\sup_{x\in E} K(x, E\setminus A)\Big) + \mathcal{O}\Big(\sup_{x\in A}[1 - K(x,E)]\Big)$$

To prove the restricted positivity condition (1):

- Show that $|Y_n - X_n|$ likely to decrease exp for $X_0, Y_0 \in A$
- Use Harnack inequalities once $|Y_n - X_n| = \mathcal{O}(\sigma^2)$

Back

Estimating noise-induced fluctuations



Back

Estimating noise-induced fluctuations

$\zeta_t = (x_t, y_t, z_t) - (x_t^{\text{det}}, y_t^{\text{det}}, z_t^{\text{det}})$

$$\mathrm{d}\zeta_t = \frac{1}{\varepsilon} A(t)\zeta_t \,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}} \mathcal{F}(\zeta_t, t) \,\mathrm{d}W_t + \frac{1}{\varepsilon} \underbrace{b(\zeta_t, t)}_{=\mathcal{O}(\|\zeta_t\|^2)} \,\mathrm{d}t$$

$$\zeta_t = \frac{\sigma}{\sqrt{\varepsilon}} \int_0^t U(t,s)\mathcal{F}(\zeta_s, s) \,\mathrm{d}W_s + \frac{1}{\varepsilon} \int_0^t U(t,s) b(\zeta_s, s) \,\mathrm{d}s$$

where $U(t,s)$ principal solution of $\varepsilon\dot{\zeta} = A(t)\zeta$.

Lemma (Bernstein-type estimate):

$$\mathbb{P}\biggl\{ \sup_{0 \leqslant s \leqslant t} \biggl\| \int_0^s \mathcal{G}(\zeta_u, u) \,\mathrm{d}W_u \biggr\| > h \biggr\} \leqslant 2n \exp\biggl\{ -\frac{h^2}{2V(t)} \biggr\}$$

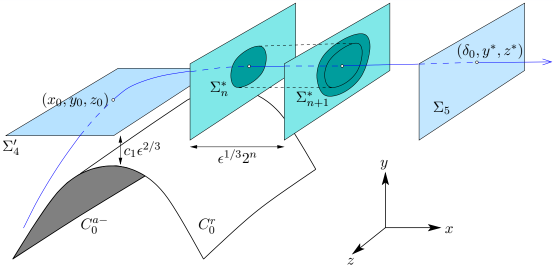
where $\int_0^s \mathcal{G}(\zeta_u, u)\mathcal{G}(\zeta_u, u)^T \,\mathrm{d}u \leqslant V(s)$ a.s. and $n = 3$ space dimension

Remark: more precise results using ODE for covariance matrix of

$$\zeta_t^0 = \frac{\sigma}{\sqrt{\varepsilon}} \int_0^t U(t,s)\mathcal{F}(0,s) \,\mathrm{d}W_s$$

Back

Example: analysis near the regular fold



Proposition: For $h_1 = \mathcal{O}(\varepsilon^{2/3})$

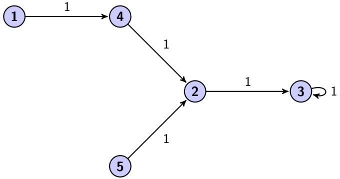
$$\mathbb{P}\Big\{ \|(y_{\tau_{\Sigma_5}}, z_{\tau_{\Sigma_5}}) - (y^*, z^*)\| > h_1 \Big\}$$
$$\leqslant C|\log\varepsilon| \bigg(\exp\bigg\{ -\frac{\kappa h_1^2}{\sigma^2\varepsilon + (\sigma')^2\varepsilon^{1/3}} \bigg\} + \exp\bigg\{ -\frac{\kappa\varepsilon}{\sigma^2 + (\sigma')^2\varepsilon} \bigg\} \bigg)$$

Useful if $\sigma, \sigma' \ll \sqrt{\varepsilon}$

Back

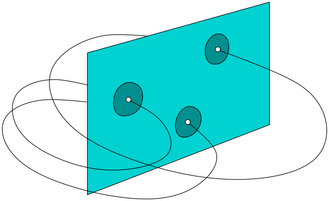
Further ways to anayse random Poincaré maps

- Theory of singularly perturbed Markov chains



- For coexisting stable periodic orbits:
  spectral-theoretic description of metastable transitions

More



Back

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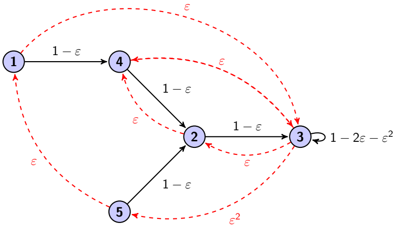

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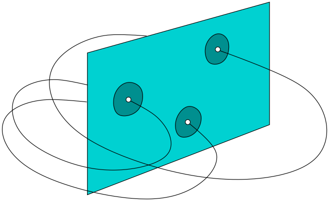

Back

Laplace transforms

$\{X_n\}_{n\geqslant 0}$: Markov chain on E, cemetery state Δ, kernel K

Given $A \subset E$, $B \subset E \cup \{\Delta\}$, $A \cap B = \emptyset$, $x \in E$ and $u \in \mathbb{C}$, define

$$\tau_A = \inf\{n \geqslant 1 \colon X_n \in A\} \qquad G^u_{A,B}(x) = \mathbb{E}^x[\mathrm{e}^{u\tau_A} 1_{\{\tau_A < \tau_B\}}]$$

$$\sigma_A = \inf\{n \geqslant 0 \colon X_n \in A\} \qquad H^u_{A,B}(x) = \mathbb{E}^x[\mathrm{e}^{u\sigma_A} 1_{\{\sigma_A < \sigma_B\}}]$$

- $G^u_{A,B}(x)$ is analytic for $|\mathrm{e}^u| < \left[\sup_{x\in(A\cup B)^c} K(x,(A\cup B)^c)\right]^{-1}$
- $G^u_{A,B} = H^u_{A,B}$ in $(A\cup B)^c$, $H^u_{A,B} = 1$ in A and $H^u_{A,B} = 0$ in B

Lemma: Feynman–Kac-type relation $\qquad KH^u_{A,B} = \mathrm{e}^{-u}\, G^u_{A,B}$

Back

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Lemma: Feynman–Kac-type relation $\qquad KH^u_{A,B} = \mathrm{e}^{-u}\, G^u_{A,B}$

Proof:

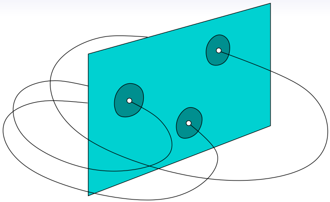
$$\begin{aligned}
(KH^u_{A,B})(x) &= \mathbb{E}^x\Big[\mathbb{E}^{X_1}\big[\mathrm{e}^{u\sigma_A} 1_{\{\sigma_A<\sigma_B\}}\big]\Big] \\
&= \mathbb{E}^x\Big[1_{\{X_1\in A\}}\mathbb{E}^{X_1}\big[\mathrm{e}^{u\sigma_A} 1_{\{\sigma_A<\sigma_B\}}\big]\Big] + \mathbb{E}^x\Big[1_{\{X_1\in A^c\}}\mathbb{E}^{X_1}\big[\mathrm{e}^{u\sigma_A} 1_{\{\sigma_A<\sigma_B\}}\big]\Big] \\
&= \mathbb{E}^x\big[1_{\{1=\tau_A<\tau_B\}}\big] + \mathbb{E}^x\big[\mathrm{e}^{u(\tau_A-1)} 1_{\{1<\tau_A<\tau_B\}}\big] \\
&= \mathbb{E}^x\big[\mathrm{e}^{u(\tau_A-1)} 1_{\{\tau_A<\tau_B\}}\big] = \mathrm{e}^{-u}\, G^u_{A,B}(x)
\end{aligned}$$

$\Rightarrow$ if $G^u_{A,B}$ varies little in $A\cup B$, it is close to an eigenfunction

Back

Small eigenvalues: Heuristics

(inspired by [Bovier, Eckhoff, Gayrard, Klein '04])



- Stable periodic orbits in $x_1, \dots, x_N$
- B_i small ball around x_i, $B = \bigcup_{i=1}^N B_i$
- Eigenvalue equation $(Kh)(x) = e^{-u} h(x)$
- Assume $h(x) \simeq h_i$ in B_i

Back

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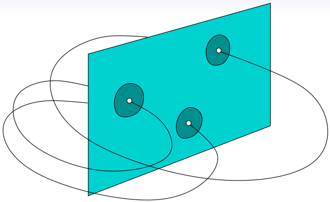

Ansatz: $h(x) = \displaystyle\sum_{j=1}^N h_j H^u_{B_j, B\setminus B_j}(x) + r(x)$

- $x \in B_i$: $h(x) = h_i + r(x)$
- $x \in B^c$: eigenvalue equation is satisfied by $h - r$ (Feynman–Kac)
- $x = x_i$: eigenvalue equation yields by Feynman–Kac

$$h_i = \sum_{j=1}^N h_j M_{ij}(u) \qquad M_{ij}(u) = G^u_{B_j, B\setminus B_j}(x_i) = \mathbb{E}^{x_i}\big[\mathrm{e}^{u\tau_B}\, 1_{\{\tau_B = \tau_{B_j}\}}\big]$$

$\Rightarrow$ condition $\det(M - 1\!\!1) = 0 \Rightarrow N$ eigenvalues exp close to 1

If $\mathbb{P}\{\tau_B > 1\} \ll 1$ then $M_{ij}(u) \simeq \mathrm{e}^u\, \mathbb{P}^{x_i}\{\tau_B = \tau_{B_j}\} =: \mathrm{e}^u\, P_{ij}$ and $Ph \simeq \mathrm{e}^{-u}\, h$

Back

Control of error term

The error term satisfies the boundary value problem

$$\begin{aligned} (Kr)(x) &= \mathrm{e}^{-u}\, r(x) & x \in B^c \\ r(x) &= h(x) - h_i & x \in B_i \end{aligned}$$

Lemma:

For u s.t. G^u_{B,E^c} exists, the unique solution of

$$\begin{aligned} (K\psi)(x) &= \mathrm{e}^{-u}\, \psi(x) & x \in B^c \\ \psi(x) &= \theta(x) & x \in B \end{aligned}$$

is given by $\psi(x) = \mathbb{E}^x[\mathrm{e}^{u\tau_B}\, \theta(X_{\tau_B})]$

$\Rightarrow$ $r(x) = \mathbb{E}^x[\mathrm{e}^{u\tau_B}\, \theta(X_{\tau_B})]$ where $\theta(x) = \sum_j [h(x) - h_j] 1_{\{x \in B_j\}}$
To show that $h(x) - h_j$ is small in B_j: use Harnack inequalities

Consequence: Reduction to an N-state process in the sense that

$$\mathbb{P}^x\{X_n \in B_i\} = \sum_{j=1}^{N} \lambda_j^n h_j(x) h_j^*(B_i) + \mathcal{O}(|\lambda_{N+1}|^n)$$

Back