# Stochastic differential equations in neuroscience

Nils Berglund
MAPMO, Orléans (CNRS, UMR 6628)
http://www.univ-orleans.fr/mapmo/membres/berglund/

Barbara Gentz, Universität Bielefeld
Damien Landon, MAPMO-Orléans
Simona Mancini, MAPMO-Orléans

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## Plan

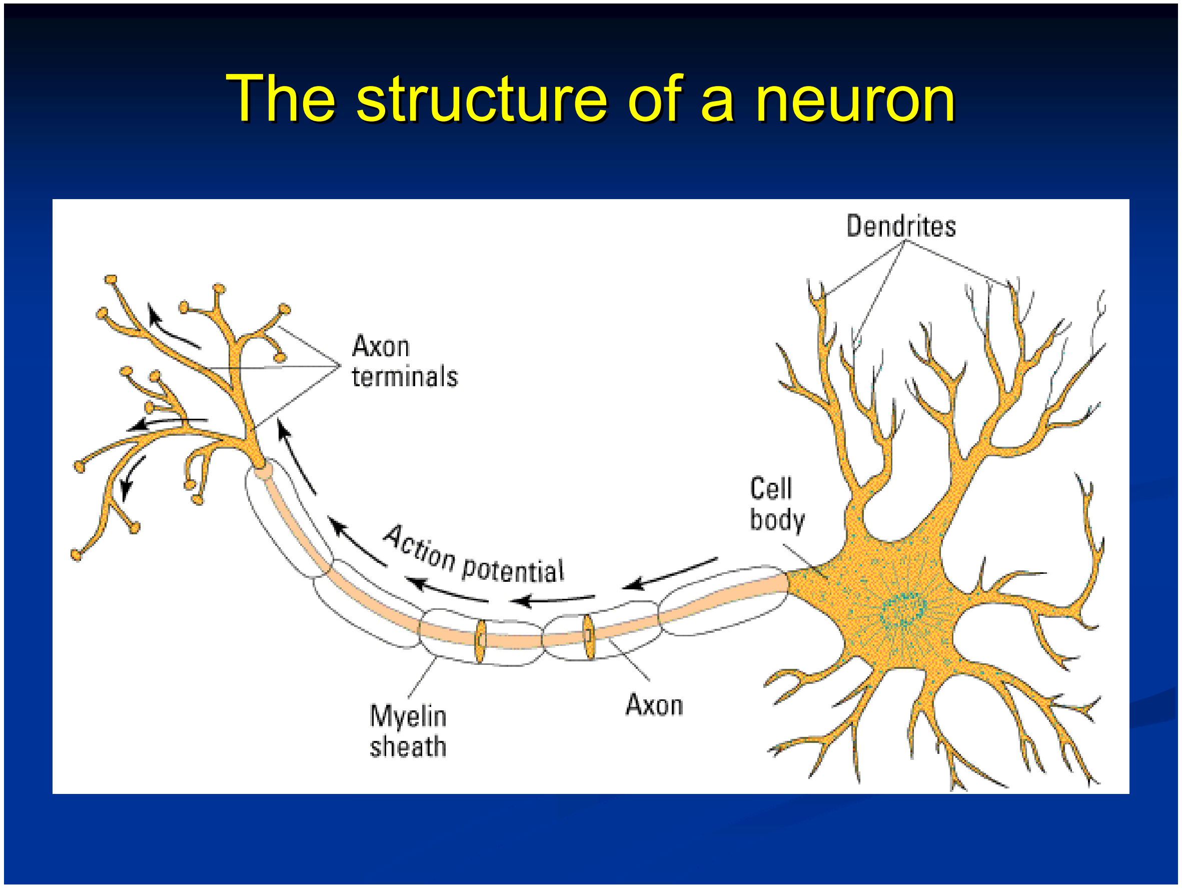
1. Deterministic

- ▷ Modeling neurons
- ▷ Slow–fast dynamical systems
- ▷ Excitability : Types I and II

2. Stochastic

- ▷ Mathematical tools
- ▷ Sample-path approach
- ▷ Application to excitable systems

## Excitable systems




▷ Single neuron communicates by generating action potential
▷ Excitable: small change in parameters yields spike generation

## ODE models for action potential generation

- Hodgkin–Huxley model (1952)
- Morris–Lecar model (1982)

$$C\dot{v} = -g_{\mathrm{Ca}} m^*(v)(v - v_{\mathrm{Ca}}) - g_{\mathrm{K}} w(v - v_{\mathrm{K}}) - g_{\mathrm{L}}(v - v_{\mathrm{L}}) + I(t)$$
$$\tau_w(v)\dot{w} = -(w - w^*(v))$$

$$m^*(v) = \frac{1+\tanh((v-v_1)/v_2)}{2}, \quad \tau_w(v) = \frac{\tau}{\cosh((v-v_3)/v_4)},$$
$$w^*(v) = \frac{1+\tanh((v-v_3)/v_4)}{2}$$

- Fitzhugh–Nagumo model (1962)

$$\frac{C}{g}\dot{v} = v - v^3 + w + I(t)$$
$$\tau\dot{w} = \alpha - \beta v - \gamma w$$

For $C/g \ll \tau$: slow–fast systems of the form

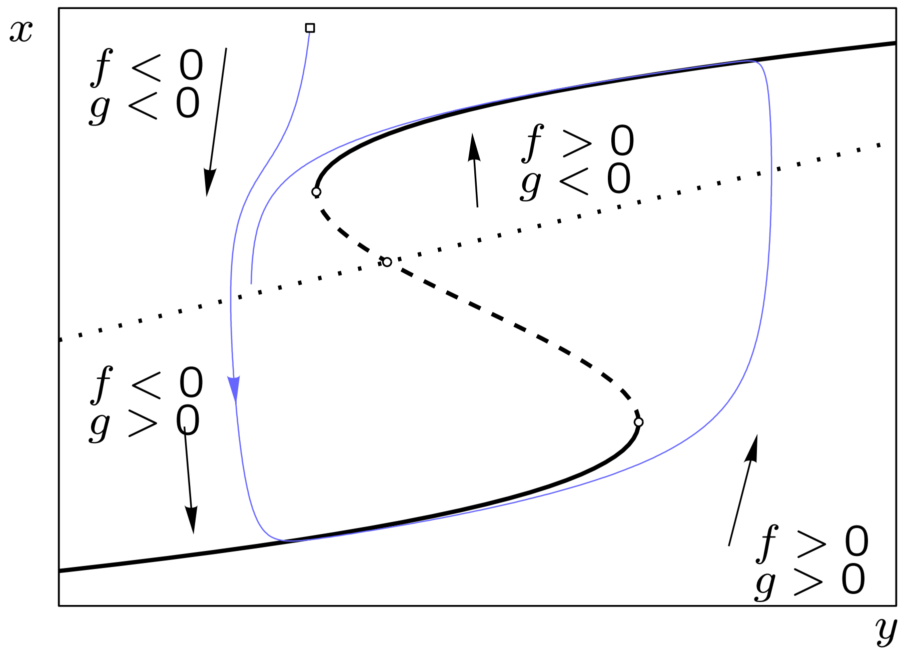
$$\varepsilon\dot{v} = f(v,w)$$
$$\dot{w} = g(v,w)$$

## Deterministic slow–fast systems

$$\varepsilon \dot{x} = f(x,y) \qquad x : \text{fast variable}$$
$$\dot{y} = g(x,y) \qquad y : \text{slow variable}$$

$\varepsilon \ll 1$: Singular perturbation theory

Qualitative analysis: nullclines $f = 0$ and $g = 0$

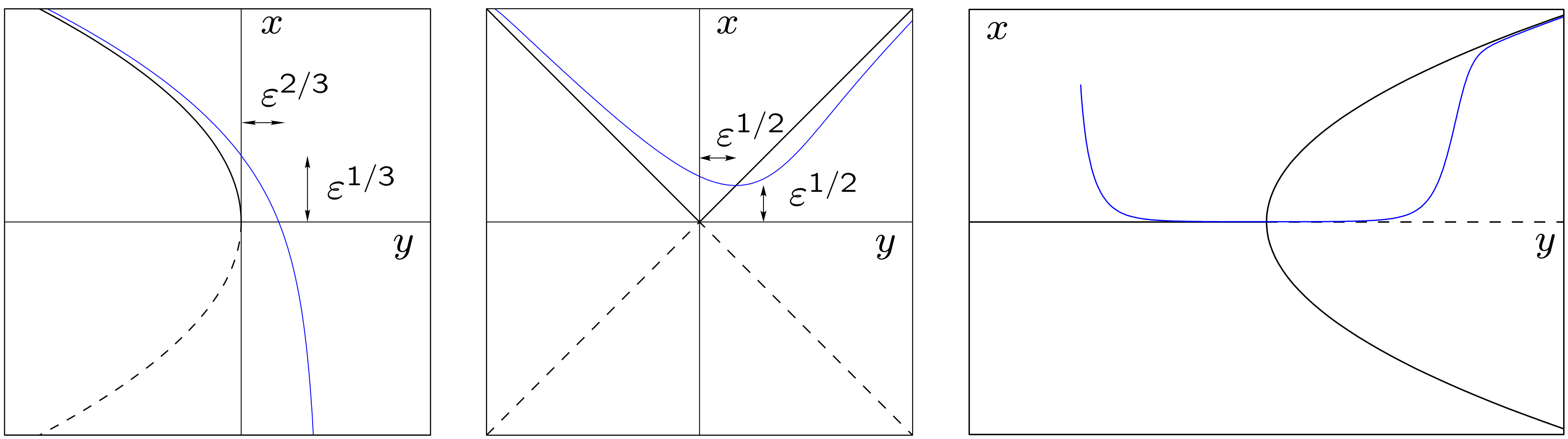


## Quantitative results

**Stable slow manifold**: $f = 0$, $\partial_x f < 0$

Tikhonov (1952) / Fenichel (1979):
Orbits converge to $\varepsilon$-neighbourhood of stable slow manifold

**Dynamic bifurcations**: $f = 0$, $\partial_x f = 0$ $\Rightarrow$ local analysis



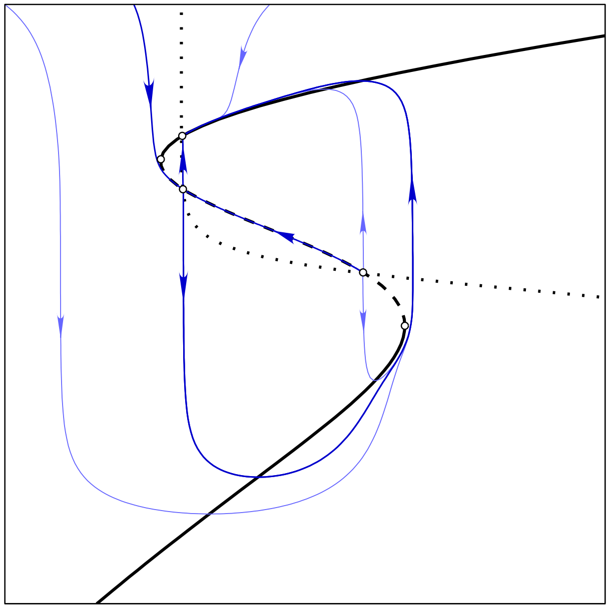

Saddle–node $f(x,y) = -x^2 - y + \dots$

Transcritical $f(x,y) = -x^2 + y^2 + \dots$

Pitchfork $f(x,y) = yx - x^3 + \dots$

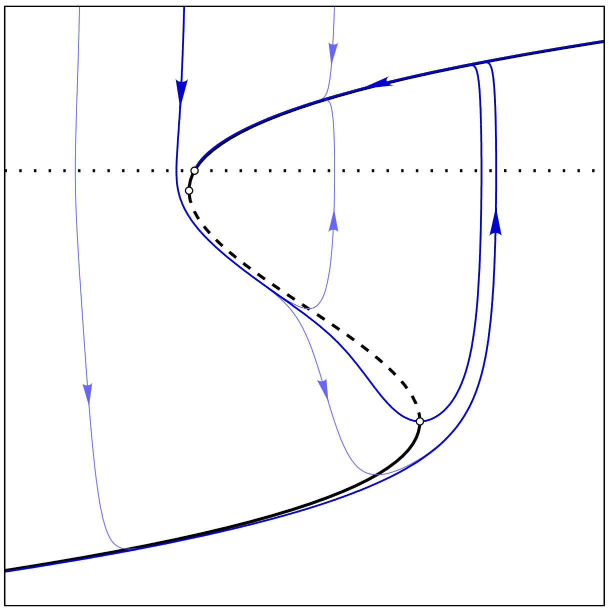
## Excitability of type I

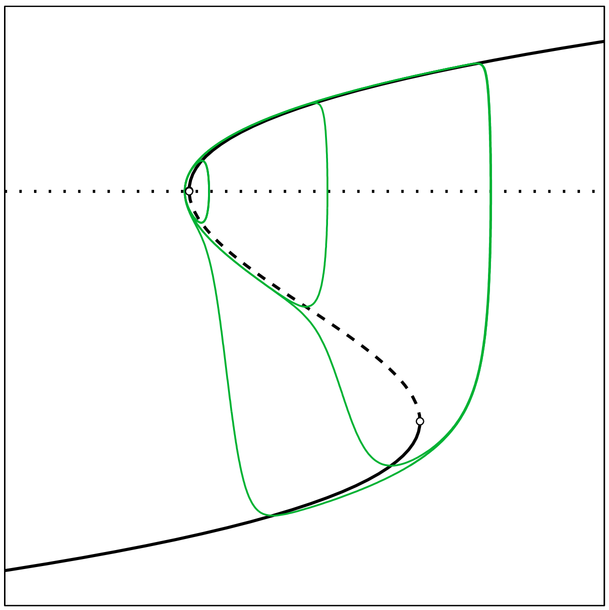
- ▷ Stable equilibrium point at intersection of $f = 0$ and $g = 0$
- ▷ Close to a saddle–node-on-invariant-circle (SNIC) bifurcation
- ▷ At bifurcation, periodic solutions appear
- ▷ Period diverges at bifurcation point
- ▷ Example: Morris–Lecar model



## Excitability of type II

- ▷ Stable equilibrium point at intersection of $f = 0$ and $g = 0$
- ▷ Close to a Hopf bifurcation
- ▷ At bifurcation, periodic solutions appear
- ▷ Period converges at bifurcation point
- ▷ Canard (french duck) phenomenon
- ▷ Example: Fitzhugh–Nagumo model





## Adding noise

$$\mathrm{d}x_t = \frac{1}{\varepsilon} f(x_t, y_t)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t$$
$$\mathrm{d}y_t = g(x_t, y_t)\,\mathrm{d}t + \sigma'\,\mathrm{d}W'_t$$

$W_t, W'_t$: Brownian motions (independent) $\Rightarrow$ $\dot{W}_t, \dot{W}'_t$: white noises

**Different mathematical methods :**

- ▷ PDEs $\Rightarrow$ evolution of probability density, exit from domain
- ▷ Large deviations $\Rightarrow$ rare events, exit from domain
- ▷ Stochastic analysis $\Rightarrow$ sample-path properties
- ▷ ...

## Noise and partial differential equations

$$\mathrm{d}x_t = f(x_t)\,\mathrm{d}t + \sigma\,\mathrm{d}W_t \qquad x \in \mathbb{R}^n$$

**Generator:** $L\varphi = f \cdot \nabla\varphi + \frac{1}{2}\sigma^2\Delta\varphi$

Adjoint: $L^*\varphi = \nabla \cdot (f\varphi) + \frac{1}{2}\sigma^2\Delta\varphi$

Kolmogorov forward or Fokker–Planck equation: $\partial_t\mu = L^*\mu$

where $\mu(x,t) =$ probability density of $x_t$

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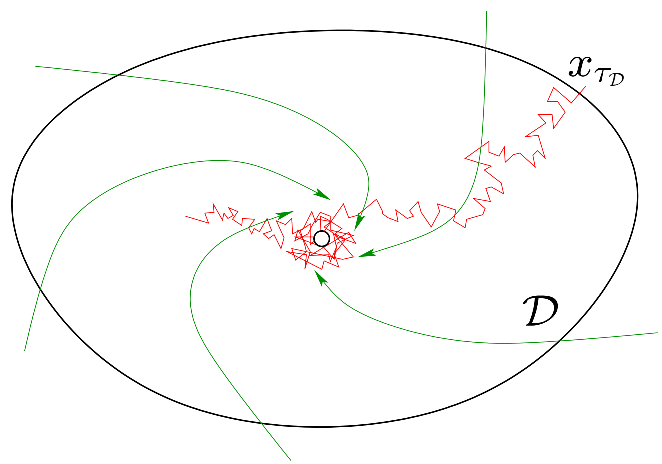
**Exit problem:**

Given $\mathcal{D} \subset \mathbb{R}^n$, characterise

$$\tau_{\mathcal{D}} = \inf\{t > 0 \colon x_t \notin \mathcal{D}\}$$

Fact: $u(x) = \mathbb{E}^x\{\tau_{\mathcal{D}}\}$ satisfies

$$\begin{cases} Lu(x) = -1 & x \in \mathcal{D} \\ u(x) = 0 & x \in \partial\mathcal{D} \end{cases}$$




Similar boundary value problems give distribution of exit time and exit location

## Noise and large deviations

$$\mathrm{d}x_t = f(x_t)\,\mathrm{d}t + \sigma\,\mathrm{d}W_t \qquad x \in \mathbb{R}^n$$

**Large deviation principle:** Probability of sample path $x_t$ being close to given curve $\varphi : [0,T] \to \mathbb{R}^n$ behaves like $\mathrm{e}^{-I(\varphi)/\sigma^2}$

**Rate function:** (or action functional or cost functional)

$$I_{[0,T]}(\varphi) = \frac{1}{2}\int_0^T \|\dot{\varphi}_t - f(\varphi_t)\|^2\,\mathrm{d}t$$

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**Application to exit problem:** (Wentzell, Freidlin 1969)
Assume $\mathcal{D}$ contains unique equilibrium point $x^\star$

- ▷ Cost to reach $y \in \partial\mathcal{D}$: $\overline{V}(y) = \inf\limits_{T>0} \inf\{I_{[0,T]}(\varphi) \colon \varphi_0 = x^\star, \varphi_T = y\}$
- ▷ Gradient case: $f(x) = -\nabla V(x) \Rightarrow \overline{V}(y) = 2(V(y) - V(x^\star))$
- ▷ Mean first-exit time: $\mathbb{E}[\tau_{\mathcal{D}}] \sim \exp\Bigl\{\dfrac{1}{\sigma^2} \inf\limits_{y\in\partial\mathcal{D}} \overline{V}(y)\Bigr\}$

## Noise and stochastic analysis

$$\mathrm{d}x_t = f(x_t)\,\mathrm{d}t + \sigma(x)\,\mathrm{d}W_t \qquad x \in \mathbb{R}^n$$

Integral form for solution:

$$x_t = x_0 + \int_0^t f(x_s)\,\mathrm{d}s + \int_0^t \sigma(x_s)\,\mathrm{d}W_s$$

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**Application to the exit problem:**

The Itô integral is a martingale $\Rightarrow$ its maximum can be controlled in terms of variance at endpoint (Doob) :

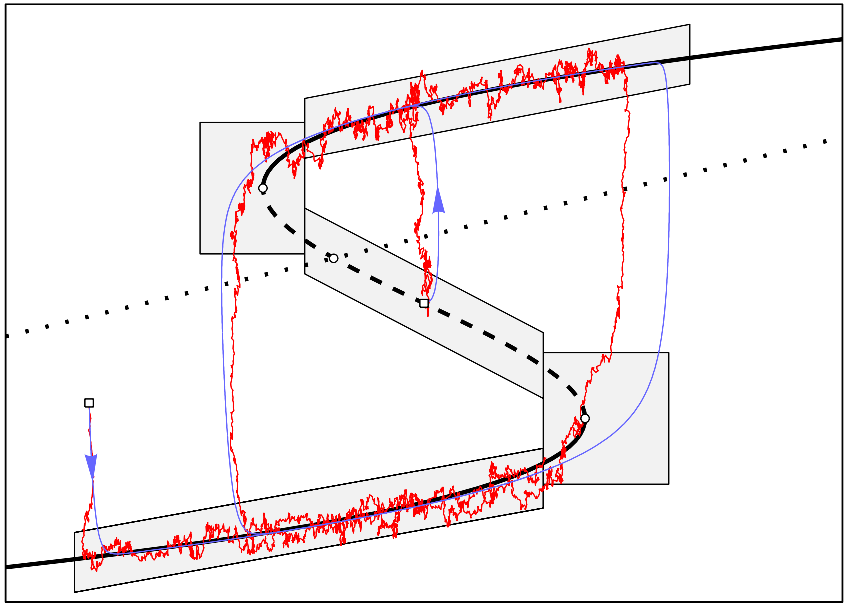
$$\mathbb{P}\left\{\sup_{t\in[0,T]}\left|\int_0^t \sigma(x_s)\,\mathrm{d}W_s\right| \geqslant \delta\right\} \leqslant \frac{1}{\delta^2}\mathbb{E}\left[\left(\int_0^T \sigma(x_s)\,\mathrm{d}W_s\right)^2\right]$$

Itô isometry:

$$\mathbb{E}\left[\left(\int_0^T \sigma(x_s)\,\mathrm{d}W_s\right)^2\right] = \int_0^T \mathbb{E}[\sigma(x_s)^2]\,\mathrm{d}s$$

## Application to slow–fast systems

$$\mathrm{d}x_t = \frac{1}{\varepsilon} f(x_t, y_t)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t$$
$$\mathrm{d}y_t = g(x_t, y_t)\,\mathrm{d}t + \sigma'\,\mathrm{d}W'_t$$



Use different methods

- ▷ Near stable slow manifold ($f = 0, \partial_x f < 0$)
- ▷ Near bifurcation points ($f = 0, \partial_x f = 0$)
- ▷ Far from slow manifold ($f \neq 0$)

## Near stable slow manifold

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

Slow–fast system with $y_t = t$

If $\exists$ stable slow manif: $f(x^\star(t), t) = 0$,

$$a^\star(t) = \partial_x f(x^\star(t), t) \leqslant -a_0$$

then $\exists$ adiabatic solution: $\bar{x}(t, \varepsilon) = x^\star(t) + \mathcal{O}(\varepsilon)$ of $\varepsilon \dot{x} = f(x, t)$

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Observation: Let $\bar{a}(t,\varepsilon) = \partial_x f(\bar{x}(t,\varepsilon), t) = a^\star(t) + \mathcal{O}(\varepsilon)$

Consider linearised equation at $\bar{x}(t,\varepsilon)$:

$$\mathrm{d}\xi_t = \frac{1}{\varepsilon}\bar{a}(t,\varepsilon)\xi_t\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t$$

$\xi_t$: gaussian process with variance $\sigma^2 v(t)$, s.t. $\varepsilon\dot{v} = 2\bar{a}(t,\varepsilon)v + 1$

Asymptotically, $v(t) \simeq v^\star(t) = 1/2|\bar{a}(t,\varepsilon)|$

$\mathcal{B}(h)$: strip of width $\simeq h\sqrt{v^\star(t,\varepsilon)}$ around $\bar{x}(t,\varepsilon)$

## Near stable slow manifold

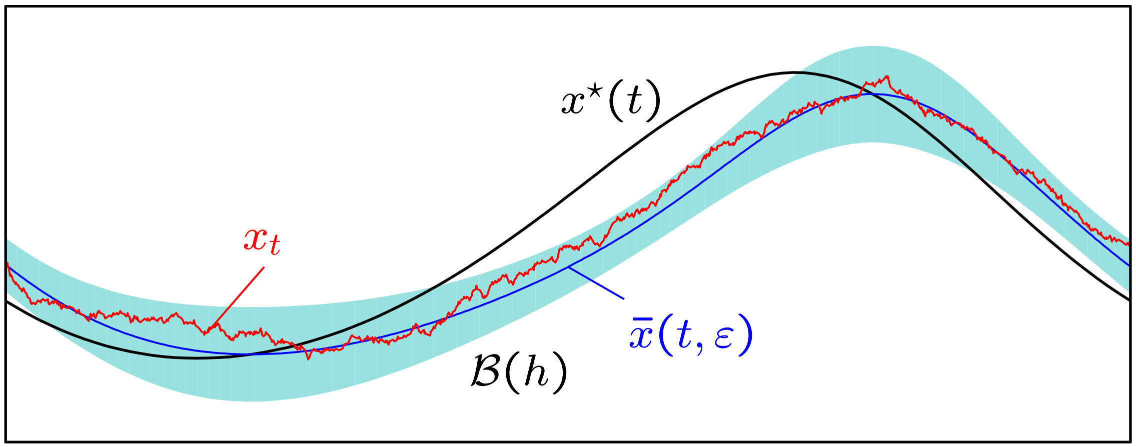
$$\mathrm{d}x_t = \frac{1}{\varepsilon} f(x_t, t)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t$$

**Theorem:** [B. & Gentz, PTRF 2002]

$$C(t,\varepsilon)\mathrm{e}^{-\kappa_- h^2/2\sigma^2} \leqslant \mathbb{P}\Big\{\text{leaving } \mathcal{B}(h) \text{ before time } t\Big\} \leqslant C(t,\varepsilon)\mathrm{e}^{-\kappa_+ h^2/2\sigma^2}$$

$$\kappa_\pm = 1 \mp \mathcal{O}(h)$$

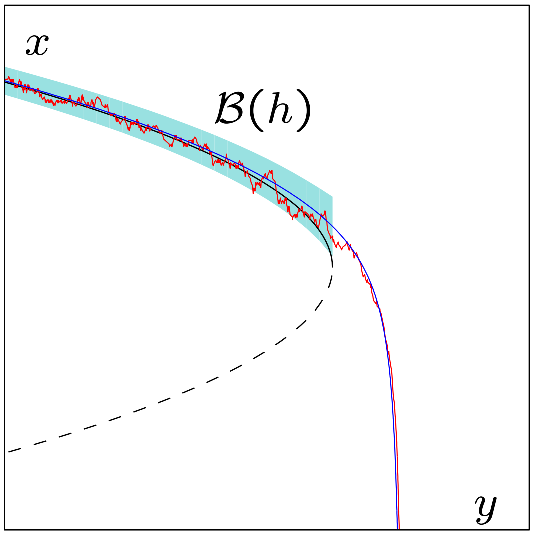
$$C(t,\varepsilon) = \sqrt{\frac{2}{\pi}\frac{1}{\varepsilon}}\bigg|\int_0^t \bar{a}(s,\varepsilon)\,\mathrm{d}s\bigg|\frac{h}{\sigma}\Big[1 + \text{error of order } \mathrm{e}^{-h^2/\sigma^2}\, t/\varepsilon\Big]$$



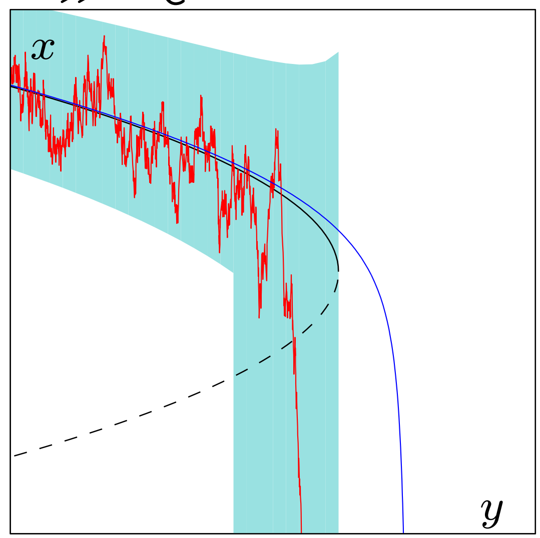
## Saddle–node bifurcation

e.g. $f(x,y) = -y - x^2$

$\sigma \ll \sigma_{\mathrm{c}} = \varepsilon^{1/2}$




$\sigma \gg \sigma_{\mathrm{c}} = \varepsilon^{1/2}$




Deterministic case $\sigma = 0$: Solutions stay at distance $\varepsilon^{1/3}$ above bifurcation point until time $\varepsilon^{2/3}$ after bifurcation.

**Theorem:** [B. & Gentz, Nonlinearity 2002]

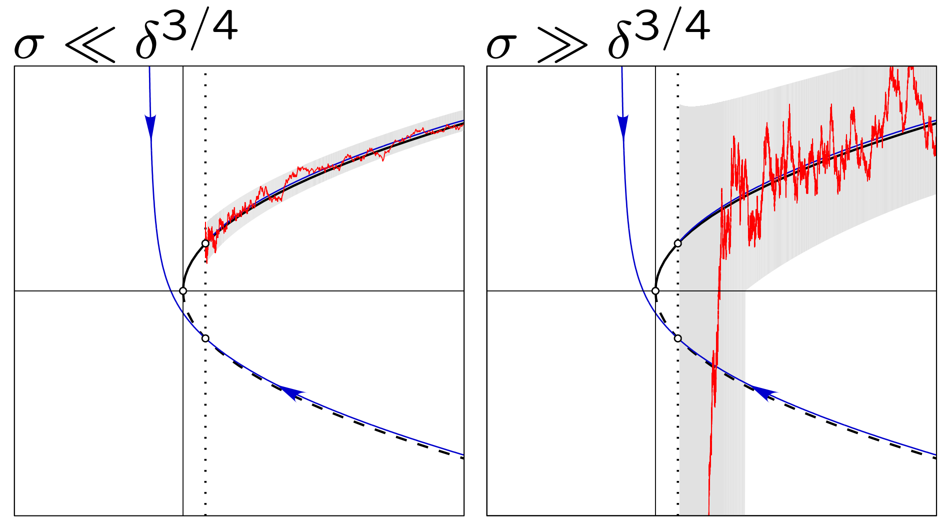
1. If $\sigma \ll \sigma_{\mathrm{c}}$: Paths likely to stay in $\mathcal{B}(h)$ until time $\varepsilon^{2/3}$ after bifurcation, maximal spreading $\sigma/\varepsilon^{1/6}$.
2. If $\sigma \gg \sigma_{\mathrm{c}}$: Transition typically for $t \asymp -\sigma^{4/3}$ transition probability $\geqslant 1 - \mathrm{e}^{-c\sigma^2/\varepsilon|\log\sigma|}$

# Excitability of type I

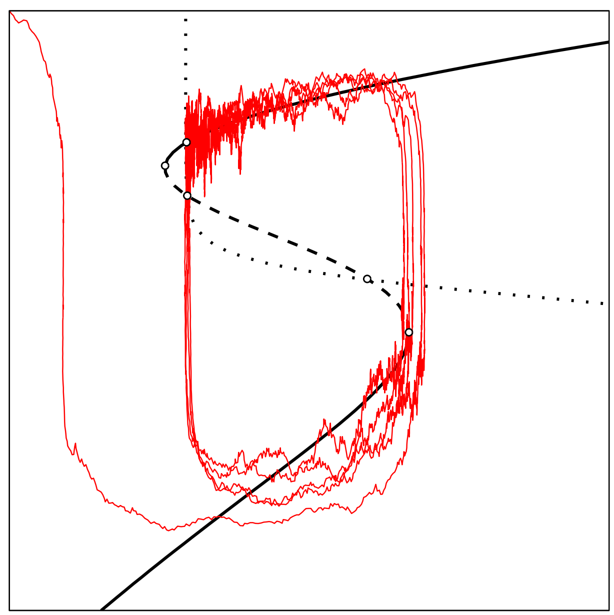
Near bifurcation point:

$$\mathrm{d}x_t = \frac{1}{\varepsilon}(y_t - x_t^2)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t$$

$$\mathrm{d}y_t = (\delta - y_t)\,\mathrm{d}t$$

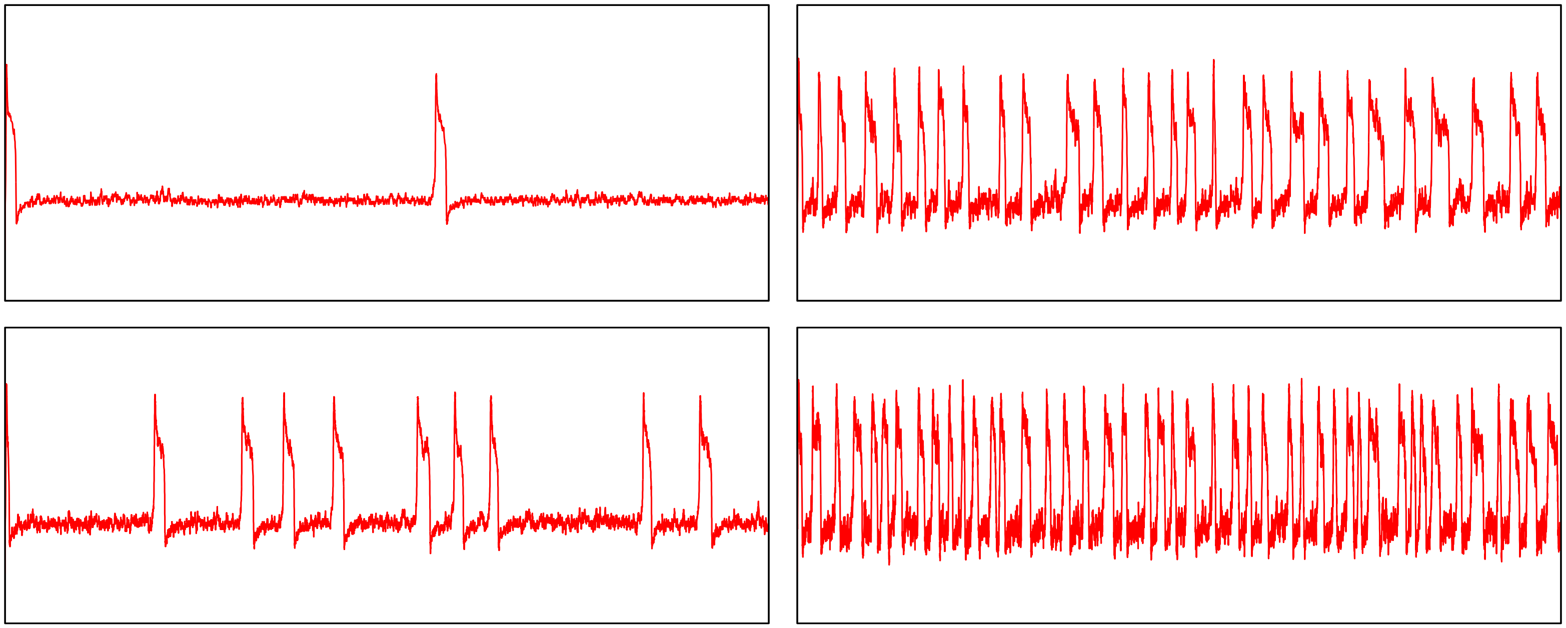



Global behaviour:



## Excitability of type I

Time series of $-x_t$:



- $\triangleright$ $\sigma \ll \delta^{3/4}$: rare spikes, times between spikes $\sim$ exponentially distributed, mean waiting time of order $e^{\delta^{3/2}/\sigma^2}$

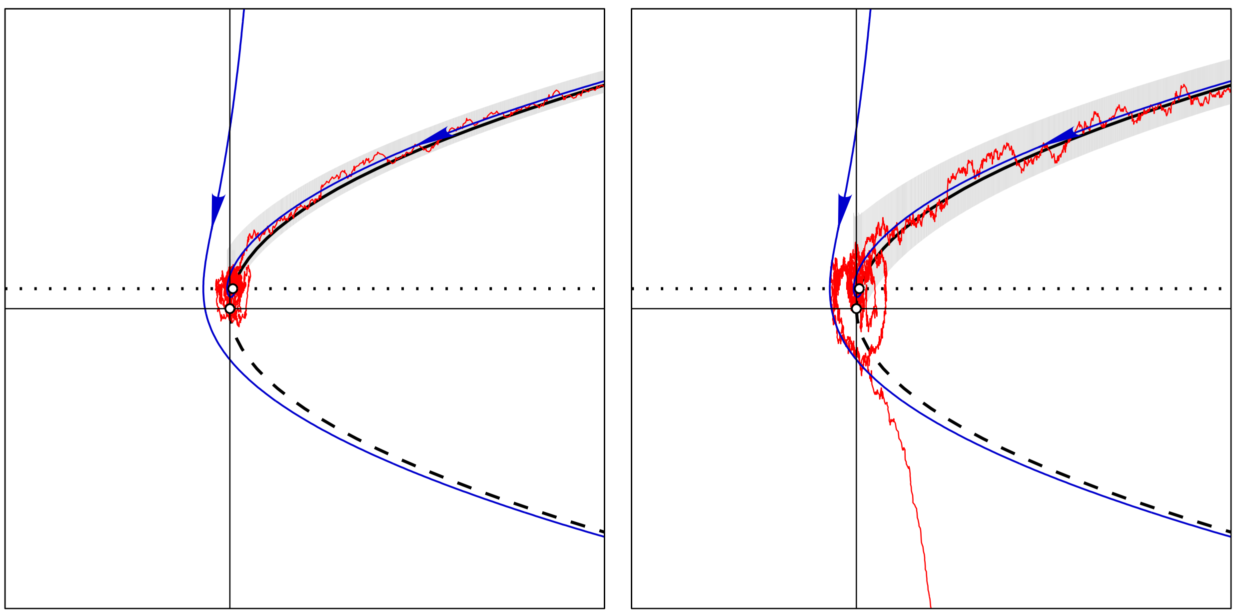
  $\Rightarrow$ Poisson point process
- $\triangleright$ $\sigma \gg \delta^{3/4}$: frequent spikes, more regularly spaced, waiting time of order $|\log \sigma|$

## Excitability of type II

Near bifurcation point:

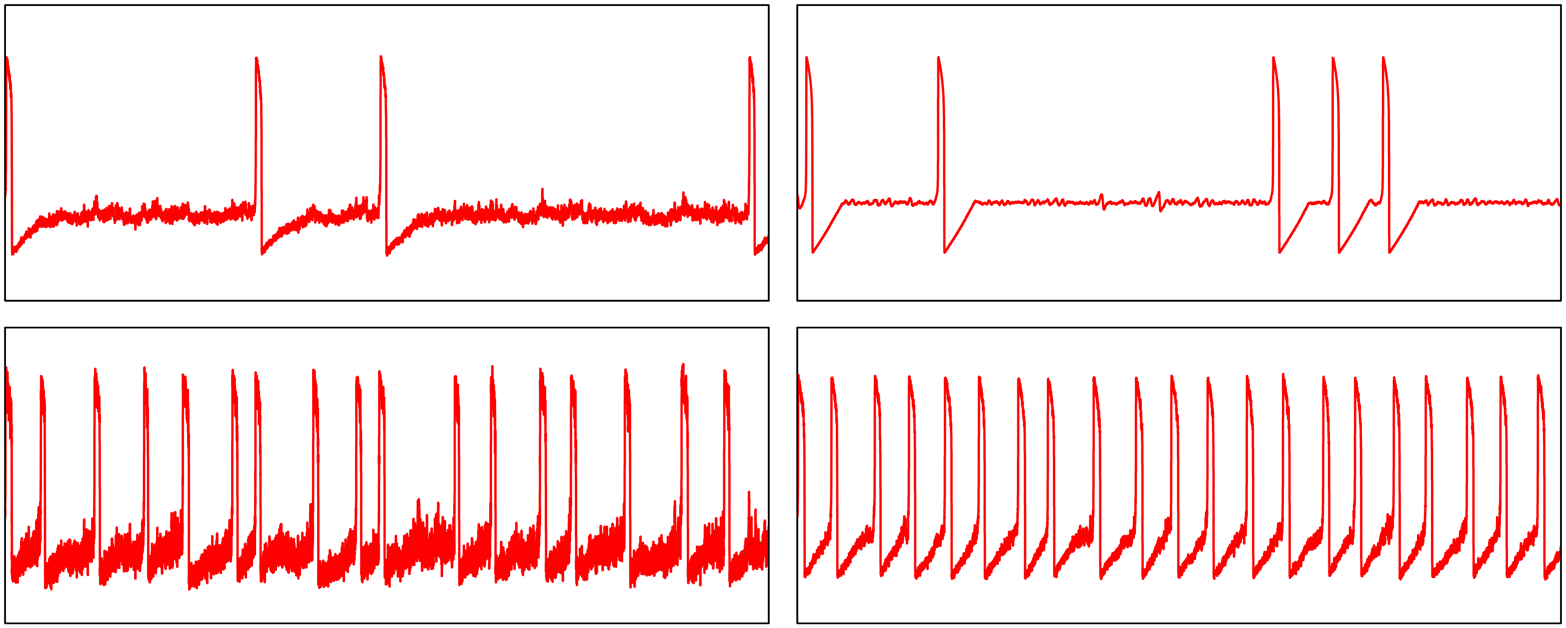
$$
\begin{aligned}
\mathrm{d}x_t &= \frac{1}{\varepsilon}(y_t - x_t^2)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t \\
\mathrm{d}y_t &= (\delta - x_t)\,\mathrm{d}t
\end{aligned}
$$

- ▷ $\delta > \sqrt{\varepsilon}$: equilibrium $(\delta, \delta^2)$ is a node
  Similar behaviour as before, crossover at $\sigma \sim \delta^{3/2}$
- ▷ $\delta < \sqrt{\varepsilon}$: equilibrium $(\delta, \delta^2)$ is a focus. Two-dimensional problem



## Excitability of type II

Time series of $-x_t$:



Muratov and Vanden Eijnden (2007):

- ▷ $\sigma \ll \delta\varepsilon^{1/4}$: rare spikes
- ▷ $\delta\varepsilon^{1/4} \ll \sigma \ll (\delta\varepsilon)^{1/2}$: rare sequences of spikes (MMOs)
- ▷ $\sigma \gg (\delta\varepsilon)^{1/2}$: more frequent and regularly spaced spikes

# References


- N. B. & B. Gentz, *Pathwise description of dynamic pitchfork bifurcations with additive noise*, Probab. Theory Related Fields **122**, 341–388 (2002)
- ______, *A sample-paths approach to noise-induced synchronization: Stochastic resonance in a double-well potential*, Ann. Appl. Probab. **12**, 1419-1470 (2002)
- ______, *The effect of additive noise on dynamical hysteresis*, Nonlinearity **15**, 605–632 (2002)
- ______, *Noise-Induced Phenomena in Slow-Fast Dynamical Systems. A Sample-Paths Approach.* Springer, Probability and its Applications, 276+xvi pages (2006)
- ______, *Stochastic dynamic bifurcations and excitability*, in C. Laing and G. Lord, (Eds.) *Stochastic Methods in Neuroscience*, Oxford University Press (2009)