Stochastic dynamical systems in neuroscience

Nils Berglund
MAPMO, Université d'Orléans
CNRS, UMR 6628 & Fédération Denis Poisson
www.univ-orleans.fr/mapmo/membres/berglund

ANR project MANDy, Mathematical Analysis of Neuronal Dynamics
Coworkers: Barbara Gentz (Bielefeld), Christian Kuehn (Dresden)
Stéphane Cordier, Damien Landon, Simona Mancini (Orléans)

Dynamics of Stochastic Systems and their Approximation,
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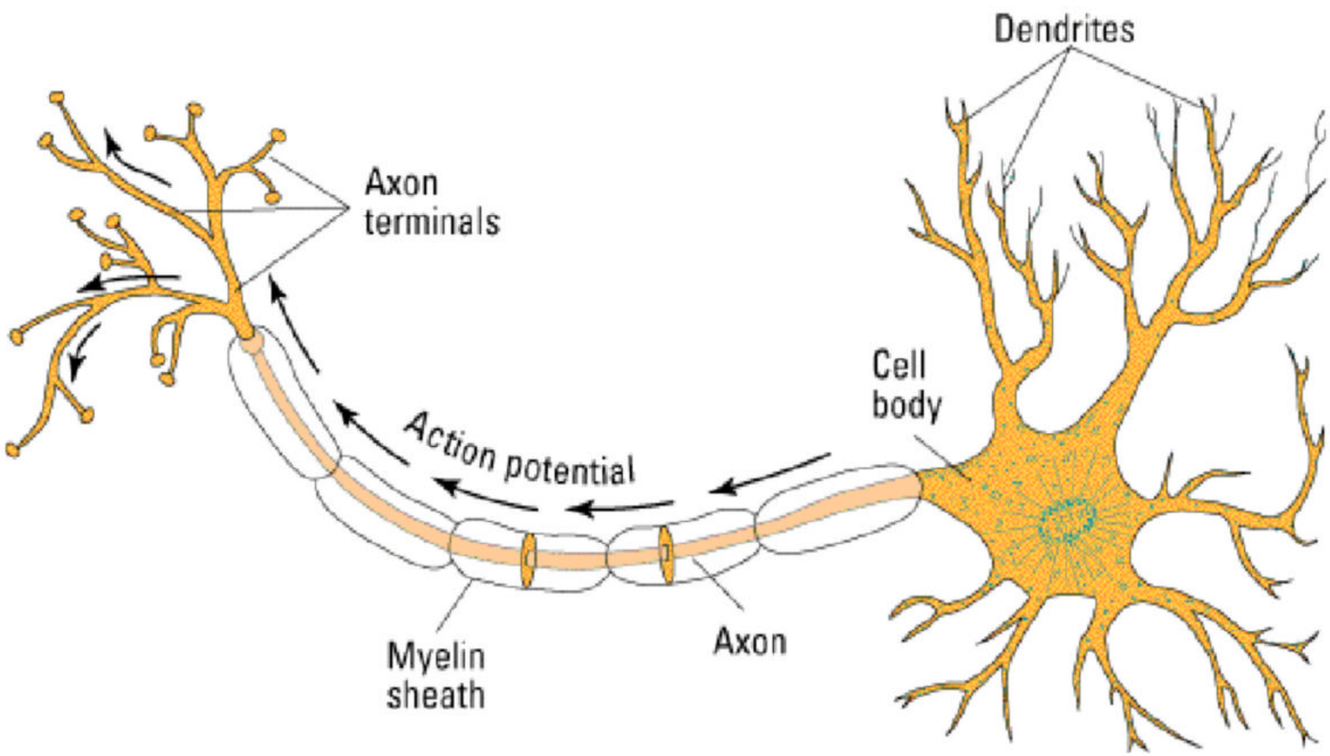
Plan

1. What kind of stochastic systems arise in neuroscience?
2. Which questions are relevant?
3. Which mathematical techniques are used?
4. Example: FitzHugh–Nagumo equations with noise



1. A hierarchy of problems

Single neuron	S(P)DEs for membrane potential Hodgkin–Huxley, Morris–Lecar, FitzHugh-Nagumo model, . . .

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Molecular dynamics	SDEs, Monte Carlo, . . .

1.1 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

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

1.2 Origins of noise

▷ External noise: input from other neurons (one level above)

▷ Internal noise: fluctuations in ion channels (one level below)

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Models for noise:

- ▷ Gaussian white noise $\mathrm{d}W_t$
- ▷ Time-correlated noise (Ornstein–Uhlenbeck)
- ▷ More general Lévy processes
- ▷ Point processes (Poisson or more general renewal processes)

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In the simplest case we have to study:

$$\begin{aligned}\mathrm{d}x_t &= \frac{1}{\varepsilon} f(x_t, y_t)\,\mathrm{d}t + \frac{\sigma}{\sqrt{\varepsilon}}\,\mathrm{d}W_t \\ \mathrm{d}y_t &= g(x_t, y_t)\,\mathrm{d}t + \sigma'\,\mathrm{d}W_t'\end{aligned}$$

2. What are the relevant questions?

Modelling (choice of noise)

Asymptotic behaviour

- ▷ Existence and uniqueness of invariant state (measure)
- ▷ Convergence to the invariant state

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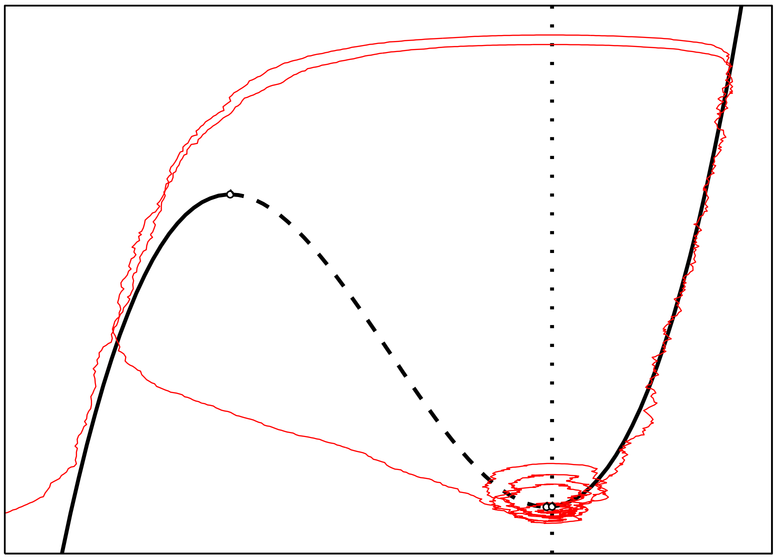
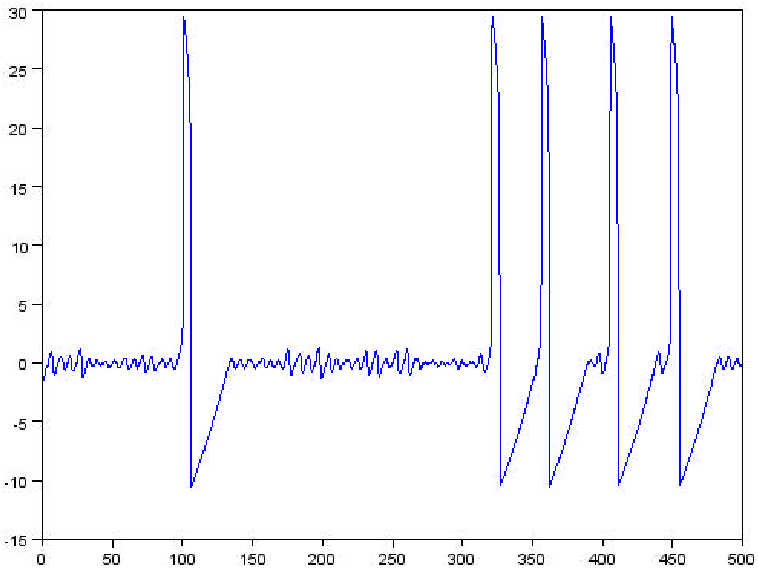
However, transients are important!

- ▷ Time-dependent forcing
- ▷ Metastability
- ▷ Excitability
- ▷ Stochastic resonance
- ▷ . . .

2.1 Example: FitzHugh–Nagumo with noise





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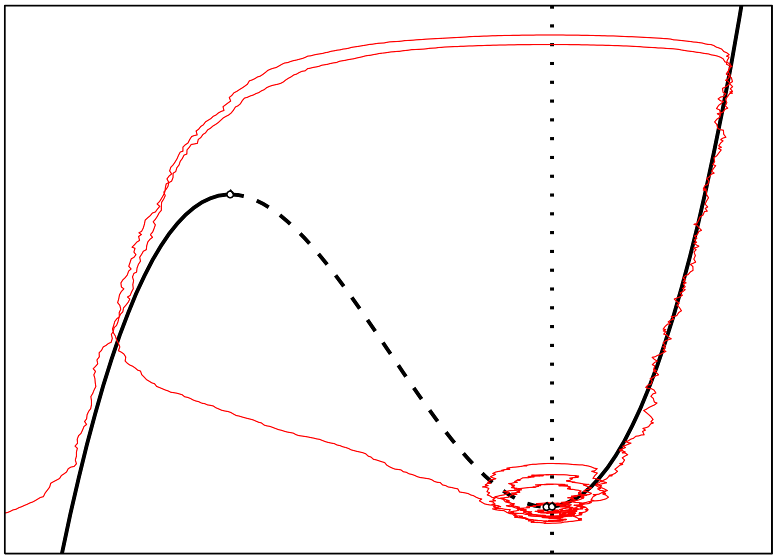
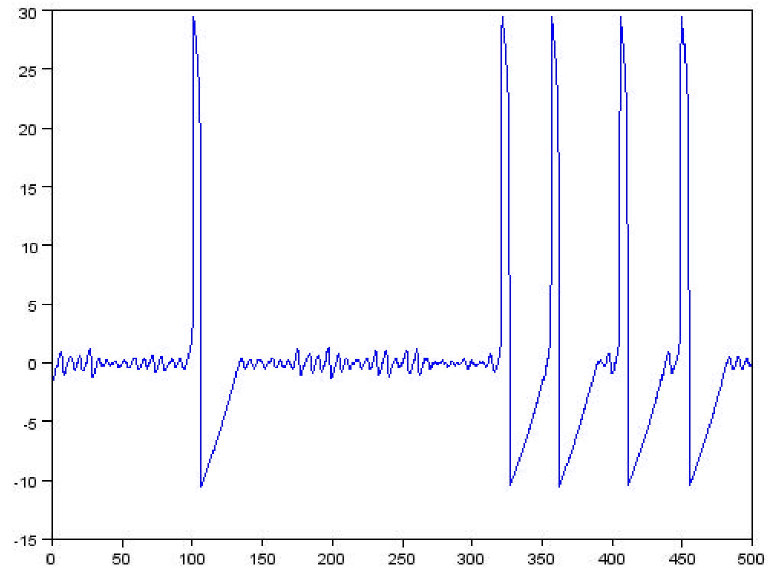




▷ System is excitable (sensitive to small random perturbations)

▷ Invariant measure: gives probability to be spiking/quiescent

▷ We are interested in distribution of interspike time interval

2.2 Paradigm: the stochastic exit problem

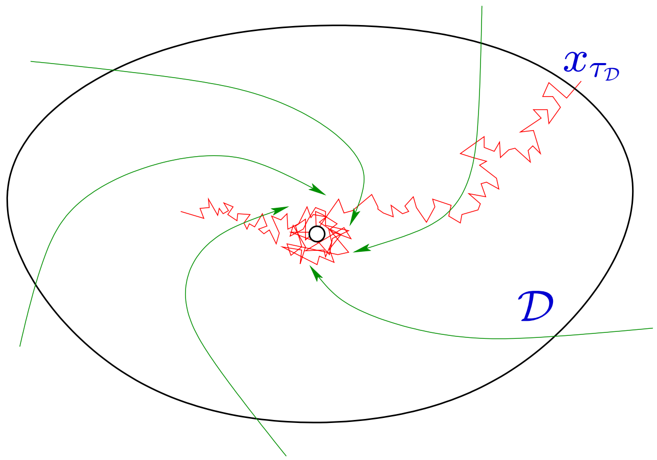
$$\mathrm{d}x_t = f(x_t)\,\mathrm{d}t + \sigma\,\mathrm{d}W_t \qquad x \in \mathbb{R}^n$$

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

▷ Law of first-exit time

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

▷ Law of first-exit location x_τ (harmonic measure)



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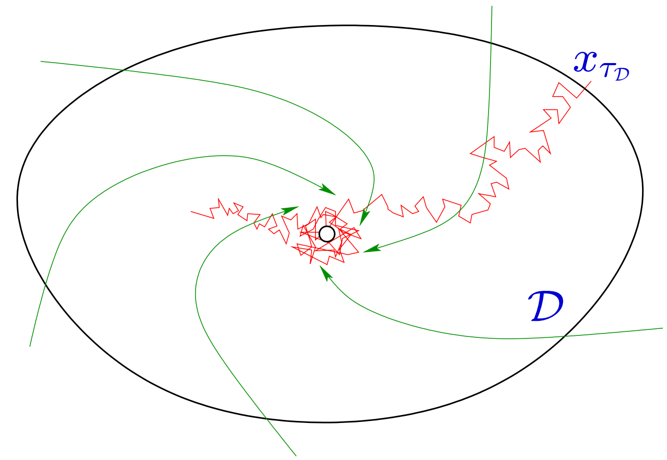

▷ Dynamics within $\mathcal{D}$ may be described by quasistationary state

▷ May be able to use coarse-grained description of motion between attractors (e.g. Markovian jump process)

3. What mathematical techniques are available?

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

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

3.1 Large deviations

Advantages

- ▷ Works for very general class of equations (including SPDEs)
- ▷ Problem is reduced to deterministic variational problem
  (can be expressed in Euler–Lagrange or Hamilton form)
- ▷ Can be extended to situations with multiple attractors
- ▷ Can be extended to (very) slowly time-dependent systems

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Limitations

▷ Only applicable in the limit $\sigma \to 0$

▷ $\overline{V}$ difficult to compute, except in gradient (reversible) case

▷ Leads little information on distribution of τ

3.2 PDEs

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

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: $\partial_t\mu = L^*\mu$

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Exit problem: Dirichlet–Poisson problems via Dynkin's formula and Feynman–Kac type equations, e.g.

▷ $u(x) = \mathbb{E}^x[\tau_{\mathcal{D}}]$ satisfies $\begin{cases} Lu(x) = -1 & x \in \mathcal{D} \\ u(x) = 0 & x \in \partial\mathcal{D} \end{cases}$

▷ $v(x) = \mathbb{E}^x[\phi(x_{\tau_{\mathcal{D}}})]$ satisfies $\begin{cases} Lv(x) = 0 & x \in \mathcal{D} \\ v(x) = \phi(x) & x \in \partial\mathcal{D} \end{cases}$

▷ Similar formulas for Laplace transform $\mathbb{E}^x[\mathrm{e}^{\lambda\tau_{\mathcal{D}}}]$, etc

3.2 PDEs

Advantages

- ▷ Yields precise information on laws of $\tau_{\mathcal{D}}$ and $x_{\tau_{\mathcal{D}}}$ if Dirichlet–Poisson problems can be solved
- ▷ Exactly solvable in one-dimensional and some linear cases
- ▷ In gradient case, precise results can be obtained in combination with potential theory [Bovier, Eckhoff, Gayrard, Klein]
- ▷ Accessible to perturbation (WKB) theory
- ▷ Accessible to numerical simulation
- ▷ Conversely, yields Monte–Carlo algorithms for solving PDEs

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Limitations

- ▷ Few rigorous results in non-gradient case (L not self-adjoint)
- ▷ Moment methods: no rigorous control in nonlinear case
- ▷ Problems are stiff for small σ

3.3 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:

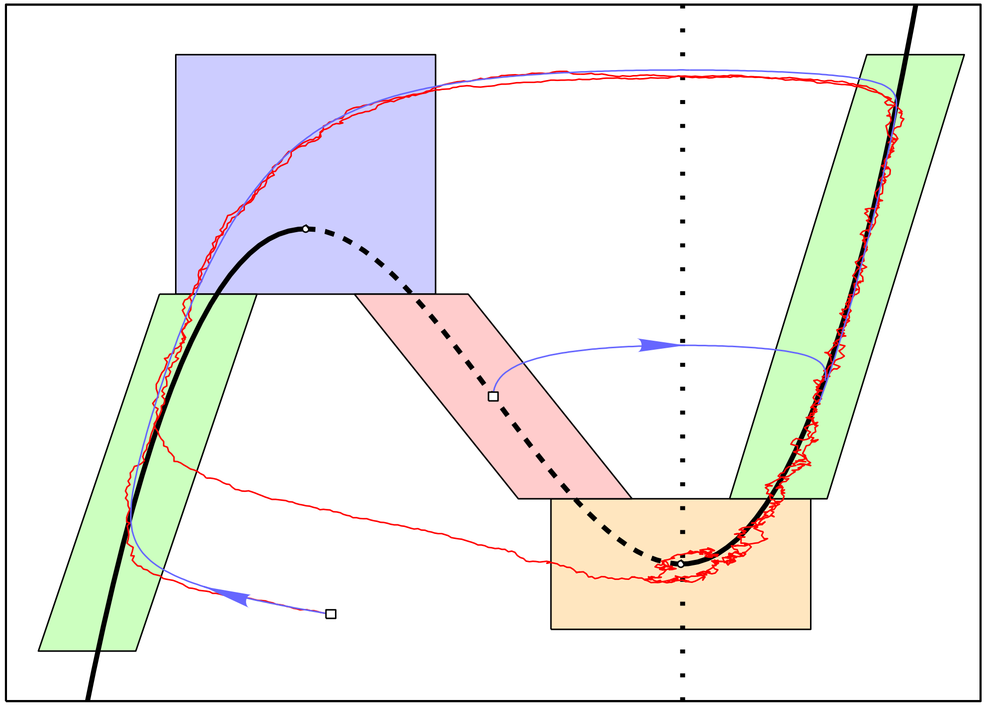
The Itô integral is a martingale $\Rightarrow$ its maximum can be controlled in terms of variance at endpoint (Doob) :

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

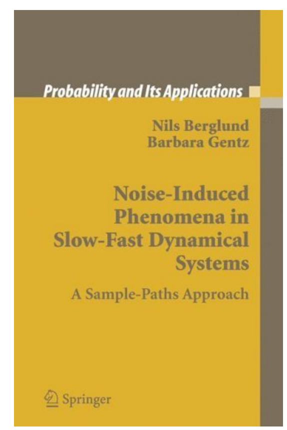
Itô isometry:

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

3.3 Stochastic analysis



▷ Local methods describe dynamics near stable branch, unstable branch, saddle–node bifurcation, etc



3.3 Stochastic analysis

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- ▷ Well adapted to fast–slow SDEs
- ▷ Rigorous control of nonlinear terms
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Limitations

- ▷ Bounds on nonlinear terms are not optimal
- ▷ Requires case-by-case studies of different bifurcations
- ▷ Control of higher-dimensional bifurcations is not (yet) sufficient

4. Example: Stochastic FitzHugh–Nagumo equations

$$\begin{aligned} \mathrm{d}x_t &= \frac{1}{\varepsilon}[x_t - x_t^3 + y_t]\,\mathrm{d}t + \frac{\sigma_1}{\sqrt{\varepsilon}}\,\mathrm{d}W_t^{(1)} \\ \mathrm{d}y_t &= [a - x_t]\,\mathrm{d}t + \sigma_2\,\mathrm{d}W_t^{(2)} \end{aligned}$$

- ▷ $W_t^{(1)}, W_t^{(2)}$: independent Wiener processes
- ▷ $0 < \sigma_1, \sigma_2 \ll 1$, $\sigma = \sqrt{\sigma_1^2 + \sigma_2^2}$

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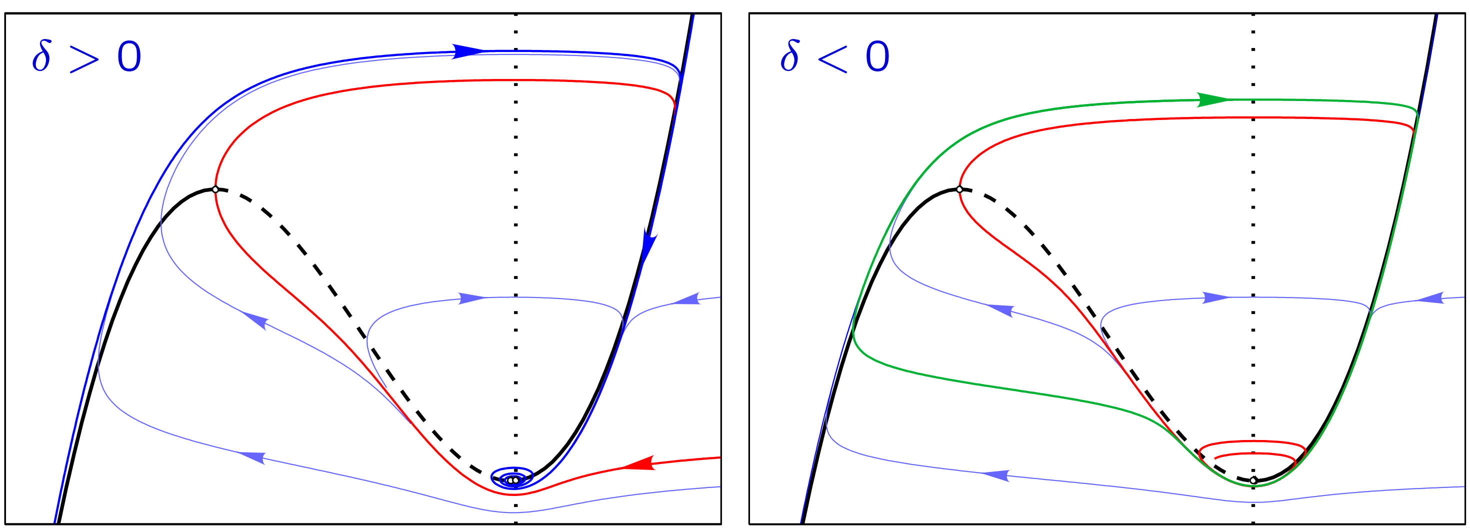
- ▷ $0 < \sigma_1, \sigma_2 \ll 1$, $\sigma = \sqrt{\sigma_1^2 + \sigma_2^2}$

$\sigma = 0$: dynamics depends on $\delta = \frac{3a^2-1}{2}$



4.1 Some prior work

▷ Numerical: Kosmidis & Pakdaman '03, . . . , Borowski et al '11
▷ Moment methods: Tanabe & Pakdaman '01
▷ Approx. of Fokker–Planck equ: Lindner et al '99, Simpson & Kuske '11
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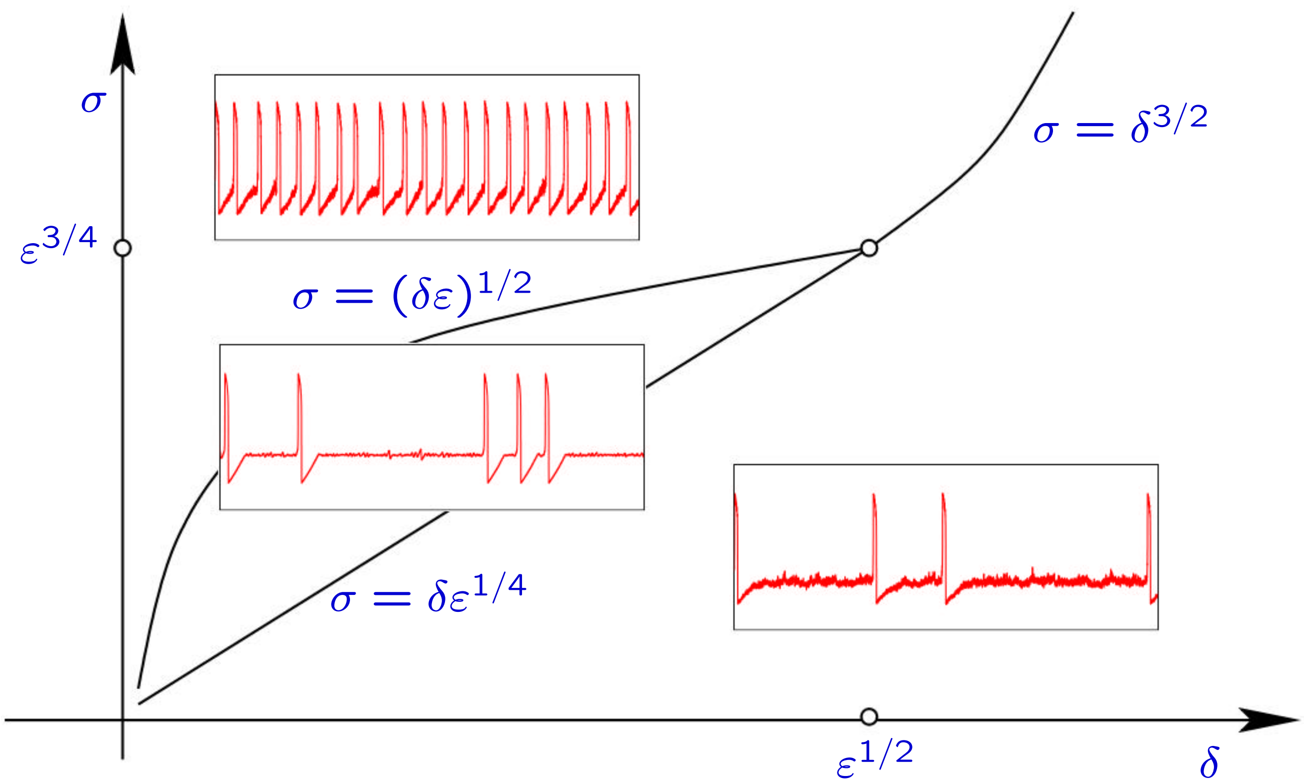
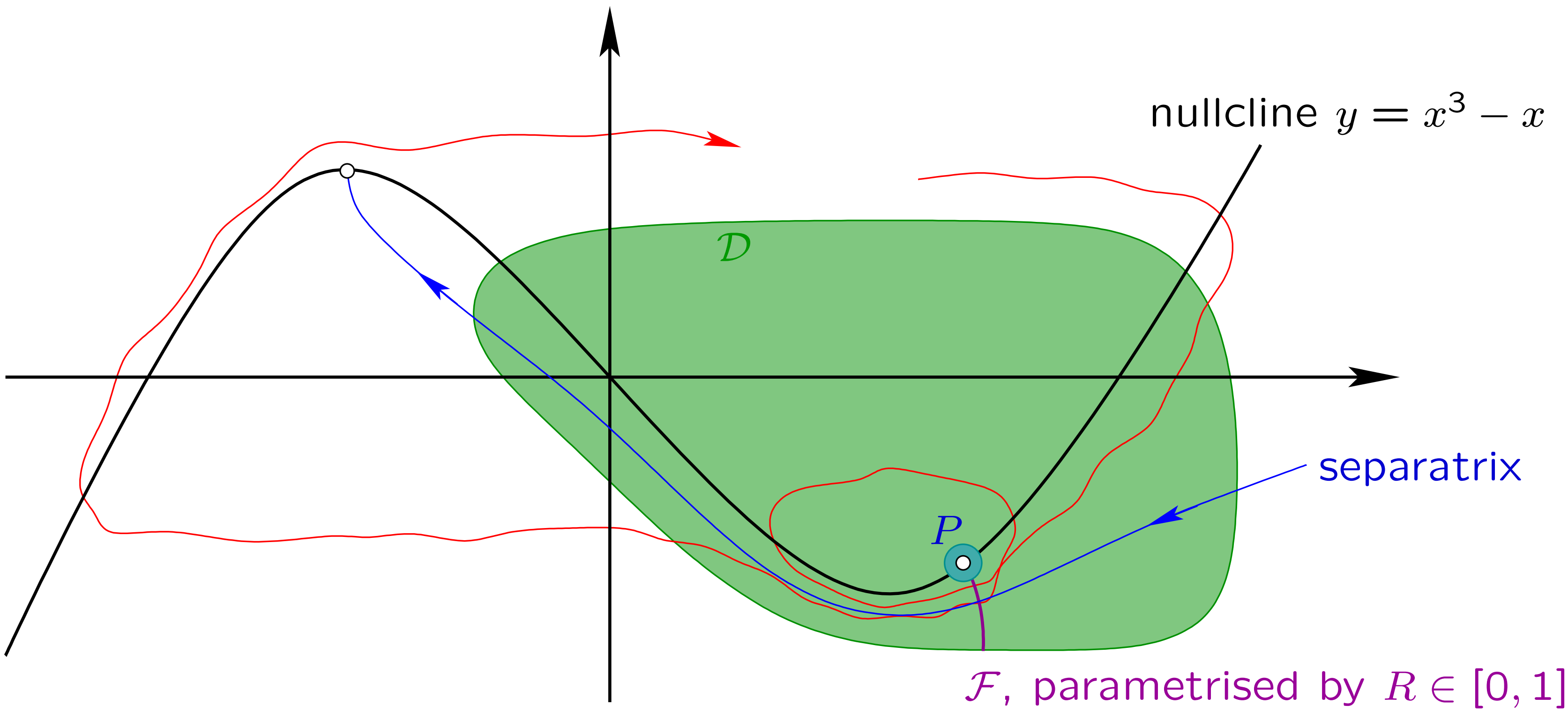
Proposed "phase diagram" [Muratov & Vanden Eijnden '08]



4.2 Small-amplitude oscillations (SAOs)

Definition of random number of SAOs N:



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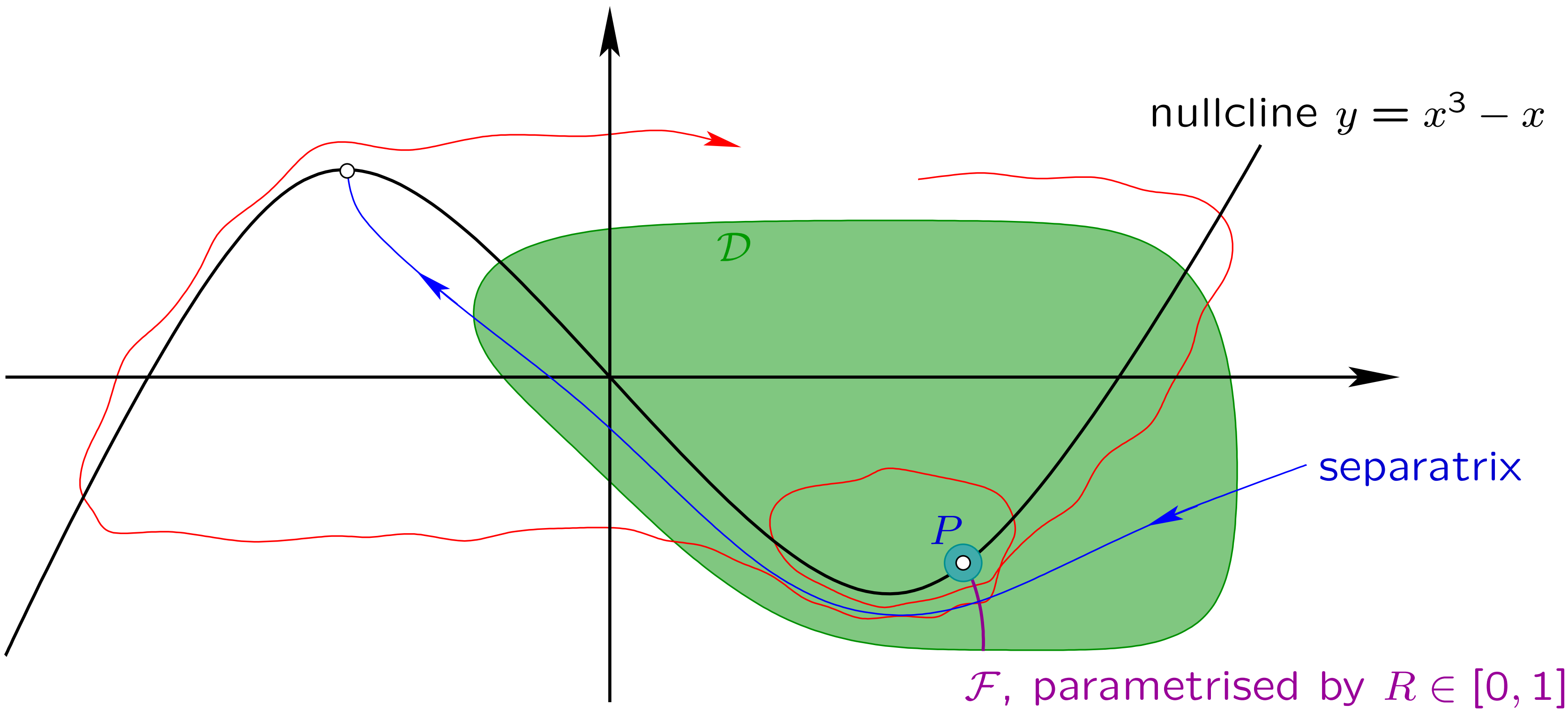

$(R_0, R_1, \dots, R_{N-1})$ substochastic Markov chain with kernel

$$K(R_0, A) = \mathbb{P}^{R_0}\{R_\tau \in A\}$$

$R \in \mathcal{F}$, $A \subset \mathcal{F}$, τ = first-hitting time of $\mathcal{F}$ (after turning around P)
N = number of turns around P until leaving $\mathcal{D}$

4.2 Small-amplitude oscillations (SAOs)

General theory of continuous-space Markov chains: [Orey '71, Nummelin '84]

Principal eigenvalue: eigenvalue λ_0 of K of largest module. $\lambda_0 \in \mathbb{R}$

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Theorem 1: [B & Landon, 2011] Assume $\sigma_1, \sigma_2 > 0$

- ▷ $\lambda_0 < 1$
- ▷ K admits quasistationary distribution π_0
- ▷ N is almost surely finite
- ▷ N is asymptotically geometric:

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

- ▷ $\mathbb{E}[r^N] < \infty$ for $r < 1/\lambda_0$, so all moments of N are finite

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Proof uses Frobenius–Perron–Jentzsch–Krein–Rutman–Birkhoff theorem and uniform positivity of K, which implies spectral gap

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Theorem 2: [B & Landon 2011]

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:

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

▷ Expected number of SAOs:

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

where $C(\mu_0)$ = probability of starting on $\mathcal{F}$ above separatrix

Proof:

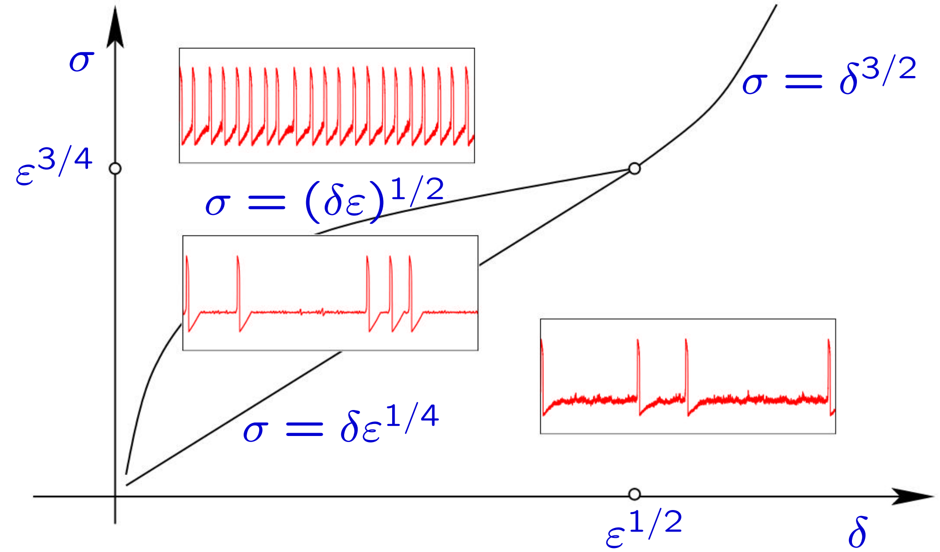
▷ Construct $A \subset \mathcal{F}$ such that $K(x, A)$ exponentially close to 1 for all $x \in A$

▷ Use two different sets of coordinates to approximate K:
Near separatrix, and during SAO

4.3 Conclusions

Three regimes for $\delta < \sqrt{\varepsilon}$:

- ▷ $\sigma \ll \varepsilon^{1/4}\delta$: rare isolated spikes
  interval $\simeq \mathcal{E}xp(\sqrt{\varepsilon}\,\mathrm{e}^{-(\varepsilon^{1/4}\delta)^2/\sigma^2})$
- ▷ $\varepsilon^{1/4}\delta \ll \sigma \ll \varepsilon^{3/4}$: transition
  geometric number of SAOs
  $\sigma = (\delta\varepsilon)^{1/2}$: geometric($1/2$)
- ▷ $\sigma \gg \varepsilon^{3/4}$: repeated spikes



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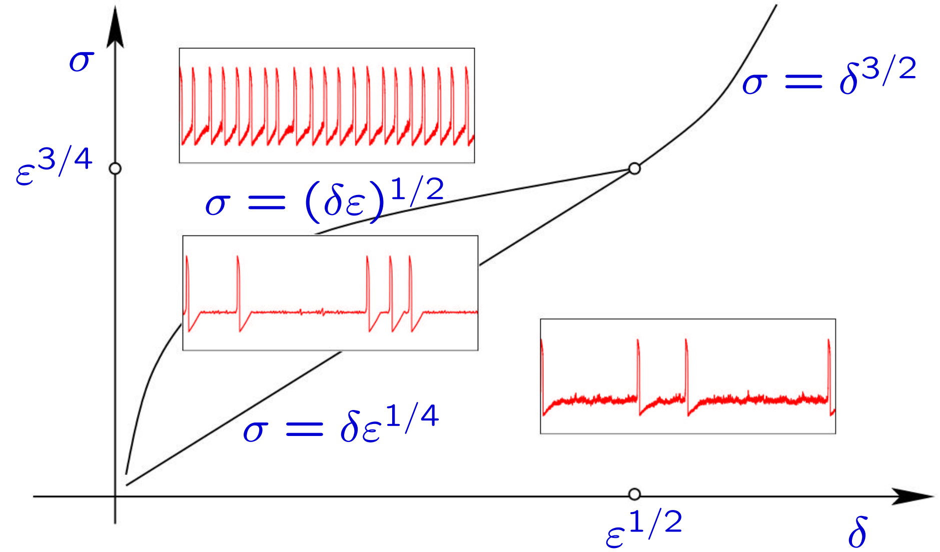


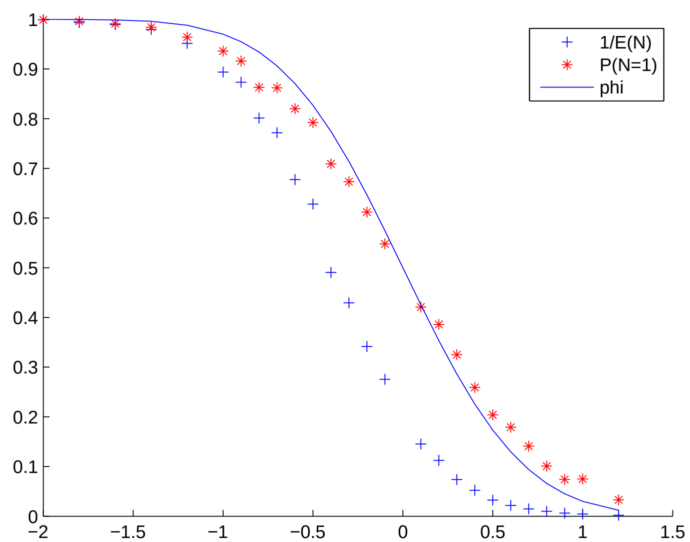
Warning:

If $\mu_0 = \pi_0$, we would have

$1 - \lambda_0 = \frac{1}{\mathbb{E}[N]} = \mathbb{P}\{N = 1\}$

However, except for weak noise,

$\mathbb{P}^{\mu_0}\{N = 1\} > \mathbb{P}^{\pi_0}\{N = 1\}$



Further reading

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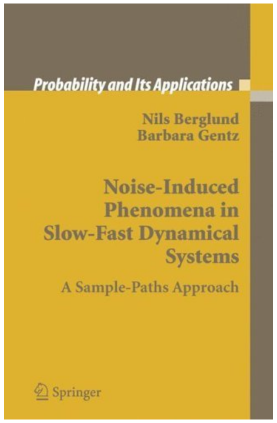

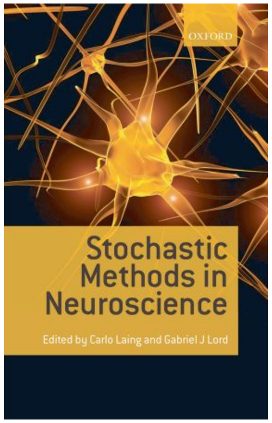

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