On the Hamiltonian structure of large deviations in stochastic hybrid systems

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Motivations

The example of SDEs (Freidlin and Wentzel 1984, 1998, 2012)

The PDMP model

LDP and action

Ion channels example

Concluding remarks

PDMPs (Davis 1984)

- The coupling of a piecewise deterministic dynamical system

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- with a time-homogeneous Markov chain on some discrete space Γ

PDMPs (Davis 1984)

- The coupling of a piecewise deterministic dynamical system
- with a time-homogeneous Markov chain on some discrete space Γ
- produces a hybrid stochastic system or piecewise deterministic Markov process (PDMP)

PDMP example

Membrane voltage fluctuations due to the stochastic opening and closing of ion channels.

- $\#$ ion channels $\to \infty$, one recovers, e.g., the H.-H. model (e.g. Pakdaman, Thieullen, Wainrib, 2010, 2012)
- Finite size effects can result in Spontaneous Action Potentials (SAPs)

Two time scales

- Transition rates between discrete states in Γ are faster than the relaxation rate of the piecewise deterministic dynamics (ratio of the time constants is ε).
- Assuming the Markov chain is ergodic, there is a unique stationary measure.
- In the limit $\varepsilon \to 0$ the system converges toward a deterministic dynamical system in which one averages the piecewise dynamics w.r.t. this stationary measure.

The question

Characterize how, for $\varepsilon << 1$, the law of the underlying stochastic process approaches the deterministic limit.

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Action functional, Lagrangian and Hamiltonian

Consider the 1D SDE

$$dx_t = b(x_t)dt + \varepsilon\sigma(x_t)dw_t$$

- b, σ are bounded and uniformly continuous. σ is non-degenerate.
- There exists an LDP for the random path of the SDE over $[0, T]$:

$$P_\varepsilon[x] \sim e^{-J_T(x)/\varepsilon^2}$$

- J_T is the rate function or the normalized action functional:

$$J_T(x) = \int_0^T L(x, \dot{x})\, dt$$

Action functional, Lagrangian and Hamiltonian

- L is the Lagrangian:

$$L(x, \beta) = \frac{(b(x) - \beta)^2}{2\sigma^2(x)}$$

- The corresponding Hamiltonian is given by the Legendre transform:

$$H(x, \alpha) = \sup_{\beta}\{\alpha\beta - L(x, \beta)\} = b(x)\alpha + \frac{1}{2}\sigma^2(x)\alpha^2$$

Action functional, Lagrangian and Hamiltonian

Amenable to explicit calculations:

- Asymptotics for the mean exit time for the neighborhood D of an equilibrium x_0
- Most probable paths of escape from D

Action functional, Lagrangian and Hamiltonian

Involves a quasi-potential $\Phi(x)$ solution to a Hamilton-Jacobi equation

$$H(x, \Phi'(x)) = 0$$

- If there is a unique point $y_0 \in \partial D$ minimizing $\Phi(y)$, $y \in \partial D$, then with probability 1, x_t will exit D near y_0 when $\varepsilon \to 0$.
- If τ^ε is the first exit time from D

$$\lim_{\varepsilon \to 0} \varepsilon^2 \log \mathbb{E}\tau^\varepsilon = \min_{y \in \partial D} \Phi(y)$$

where $\tau^\varepsilon = \inf\{t : x_t \in \partial D\}$

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The continuous dynamics

- State $(x, n) \in \Omega \times \Gamma$, $\Gamma = \{1, \cdots, K\}$ discrete set of internal states, Ω open bounded set of $\mathbb{R}^d$.
- When the internal state is n the dynamics of x obeys

$$\dot{x} = F_n(x)$$

Some technical conditions:

- F_n is locally Lipschitz continuous,
- the vector field $F(x) = (F_1(x), \cdots, F_K(x))$ does not have identical components for all $x \in \Omega$,
- $\partial\Omega$

The discrete dynamics

Given the K^2 functions $W_{mn}(x)$, $\Gamma \times \Gamma \times \Omega \to \mathbb{R}$ such that

- $\forall m,\ n,\ W_{mn}(\cdot)$ is $C^1(\Omega)$
- $\forall x,\ m,\ W_{m\cdot}(x)$ is a probability measure on Γ, $W_{nn}(x) = 0$.

The discrete dynamics

- System starts in state (x_0, n_0), $x_0(t)$ the solution.
- Draw the time τ_1 with values in $[0, \infty)$ from the law

$$\frac{1}{\varepsilon} \exp\left(-\frac{t}{\varepsilon}\right)$$

- In the interval $[0, \tau_1)$ the state is $(x_0(t), n_0)$
- Draw n_1 from the law $W_{n_0 \cdot}(x_0(\tau_1))$
- $x_1(t)$ is the solution to the Cauchy problem

$$\left\{ \begin{array}{lcl} \dot{x}_1(t) & = & F_{n_1}(t), \;\; t \geq \tau_1 \\ x_1(\tau_1) & = & x_0(\tau_1) \end{array} \right.$$

The discrete dynamics

The stochastic process $\{x(t), n(t)\}$ is called a piecewise deterministic stochastic process (PDMP).

Theorem (Harris 1984)

The stochastic process $\{x(t), n(t)\}$ has the strong Markov property.

- Natural path space is $C([0, T], \Omega) \times D([0, T], \Gamma)$
- Given (x_0, n_0) in $\Omega \times \Gamma$ we note $\mathbb{P}^{\varepsilon}_{x_0,n_0}$ the law of the process $(x(t), n(t))$ starting at (x_0, n_0).

The generator

Its generator is given by

$$L\,g(x,n) = F_n(x)\cdot\nabla_x g(x,n) + \frac{1}{\varepsilon}\sum_{m\in\Gamma} W_{nm}(x)(g(x,m)-g(x,n))$$

for regular functions $g:\Omega\times\Gamma\to\mathbb{R}$.

The generator

We rewrite it as

$$L\,g(x,n) = F_n(x)\cdot\nabla_x g(x,n) + \frac{1}{\varepsilon}\sum_{m\in\Gamma} A_{nm}(x)g(x,m)$$

where

$$A_{nm} = W_{nm} - \delta_{nm}$$

Note that

$$\sum_{m\in\Gamma} A_{nm} = 0$$

The averaged dynamics

- Assume that for every $x \in \Omega$ the matrix $\mathbf{A}(x) = A_{nm}(x)$ is irreducible.
- There is a unique invariant measure $\rho(x, \cdot)$ satisfying

$$\sum_{m \in \Gamma} A_{nm}(x)\rho(x, m) = 0 \quad \forall n \in \Gamma$$

Define the averaged vector field

$$\bar{F}(x) = \sum_{n \in \Gamma} F_n(x)\rho(x, n)$$

The averaged dynamics

$\bar{F}(x)$ is locally Lipschitz because the $\rho(\cdot, n)$ are C^1.
The Cauchy problem

$$\begin{cases} \dot{x} & = & \bar{F}(x) \\ x(0) & = & x_0 \end{cases}$$

has a unique solution for all $x_0 \in \Omega$

The averaged dynamics

Theorem (Faggionato et al. 2009)

Given (x_0, n_0) in $\Omega \times \Gamma$, call $x_*(t)$ the unique solution of the Cauchy problem

$$\begin{cases} \dot{x}_* & = & \bar{F}(x_*) \\ x_*(0) & = & x_0 \end{cases}$$

Then for every $\delta > 0$, $n \in \Gamma$ and for any continuous function $f : [0, T] \to \mathbb{R}$ it holds

$$\lim_{\varepsilon \to 0} \mathbb{P}^{\varepsilon}_{x_0, n_0} \left(\left| \int_0^T f(t) \chi(n(t) = n)\, dt - \int_0^T f(t) \rho(x_*(t), n)\, dt \right| > \delta \right) = 0$$

and

$$\lim_{\varepsilon \to 0} \mathbb{P}^{\varepsilon}_{x_0, n_0} \left(\sup_{t \in [0, T]} |x(t) - x_*(t)| > \delta \right) = 0$$

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A Large deviation principle

- $\mathcal{M}_{0+}([0,T])$ the set of non-negative finite measures on $[0,T]$ absolutely continuous w.r.t. to Lebesgue.
  Given the internal state trajectory $\{n(t)\}_{t\in[0,T]}$ associate the K-dimensional vector $\{\psi(t)\}_{t\in[0,T]}$

$$\psi_n(t) = \chi(n(t) = n)$$

A Large deviation principle

Topology:

$$d(\{x(t),\psi(t)\}_{t\in[0,T]}, \left\{\tilde{x}(t),\tilde{\psi}(t)\right\}_{t\in[0,T]} = \sup_{t\in[0,T]} |x(t)-\tilde{x}(t)| + \sum_{n\in\Gamma} \sup_{t\in[0,T]} \left| \int_0^t |\psi_n(s)-\tilde{\psi}_n(s)|\, ds \right|$$

$\mathcal{Y}$ is compact.

A Large deviation principle

Theorem (Faggionato et al.)

Given (x_0, n_0) in $\Omega \times \Gamma$, the family of laws $\mathbb{P}^{\varepsilon}_{x_0,n_0}$ on $\mathcal{Y}$ satisfies an LDP with rate function $J : \mathcal{Y} \to [0, \infty)$ defined by

$$J(x, \psi) = \int_0^T j(x(t), \psi(t))\, dt$$

and

$$j(x, \psi) = \sup_{z \in (0,\infty)^\Gamma} \sum_{m,\, n \in \Gamma} \psi_m W_{nm}(x) \left[1 - \frac{z_m}{z_n}\right]$$

A Large deviation principle

$$\limsup_{\varepsilon \to 0} \varepsilon \log \mathbb{P}^{\varepsilon}_{x_0, n_0}(C) \leq -J(C) \ \forall C \text{ closed } \subset \mathcal{Y}$$

$$\liminf_{\varepsilon \to 0} \varepsilon \log \mathbb{P}^{\varepsilon}_{x_0, n_0}(O) \geq -J(O) \ \forall O \text{ open } \subset \mathcal{Y}$$

A Large deviation principle

By the contraction principle

Theorem (Faggionato et al.)

Given (x_0) in Ω, the family of laws $\mathbb{P}^{\varepsilon}_{x_0}$ on $C([0,T],\Omega)$ satisfies an LDP with rate function $J_T : C([0,T],\Omega) \to [0,\infty)$ defined by

$$J_T(x) = \inf_{\{\psi(t)\}_{t\in[0,T]} : \{x(t),\psi(t)\}_{t\in[0,T]} \in \mathcal{Y}} J(x,\psi)$$

A Large deviation principle

Rephrased:

$$\mathbb{P}^{\varepsilon}_{x_0}\left(\{x(t)\}_{t\in[0,T]} : \{x(t)\}_{t\in[0,T]} \approx \{\hat{x}(t)\}_{t\in[0,T]}\right) \sim e^{-\frac{1}{\varepsilon}J_T(\hat{x})}$$

Our result in 1D (Bressloff and F. 2015)

- The rate function J_T can be written in the form

$$J_T(\{x(t)\}_{t\in[0,T]}) = \int_0^T L(x,\dot{x})\,dt$$

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- The Lagrangian

$$L(x,\dot{x}) = \mu(x,\dot{x})\dot{x} - \lambda(x,\mu(x,\dot{x}))$$

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- $\lambda(x, \mu)$ is the Perron eigenvalue of

$$\mathbf{A}(x) + \mu \mathrm{diag}(F_1(x), \cdots, F_K(x))$$

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- $\lambda(x, \mu)$ is the Perron eigenvalue of
$$\mathbf{A}(x) + \mu \mathrm{diag}(F_1(x), \cdots, F_K(x))$$
- $R(x, \mu)$ one corresponding eigenvector.
$\mu = \mu(x, \dot{x})$ is the solution to
$$\dot{x} = \sum_{m \in \Gamma} \psi_m(x, \mu) F_m(x)$$
with
$$\psi(x, \mu) = z(x, \mu) \cdot R(x, \mu)$$

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  with

$$\psi(x,\mu) = z(x,\mu)\cdot R(x,\mu)$$

- z is a Perron eigenvector of

$$\mathbf{A}'(x) + \mu\mathrm{diag}(F_1(x), \cdots, F_K(x))$$

  with the normalization

$$\langle z, R\rangle = 1$$

Our result in 1D (Bressloff and F. 2015)

The corresponding Hamiltonian

$$H(x, \alpha) = \sup_{\beta} \{\alpha\beta - L(x, \beta)\}$$

is equal to

$$H(x, \alpha) = \lambda(x, \alpha)$$

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- Fast sodium channels, N of them

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The neuron model I

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- Piecewise deterministic equation

$$\dot{x}(t) = F_n(x) = \frac{n}{N} f(x) - g(x)$$

$$f(x) = g_{Na}(V_{Na} - x) \quad g(x) = -g_L(V_l - x) - I$$

The neuron model II

$\Gamma = \{0, 1, \cdots, N\}$
Markov chain obtained from the birth-death process

$$n \underset{\omega_+(n,x)/\varepsilon}{\rightarrow} n+1, \quad n \underset{\omega_-(n,x)/\varepsilon}{\rightarrow} n-1$$

with transition rates

$$\omega_+(x,n) = \alpha(x)(N-n), \quad \omega_-(x,n) = \beta(x)n.$$

The matrix **A** is tridiagonal

The neuron model III

The Markov chain is ergodic with unique invariant measure

$$\rho(x, n) = \frac{N!}{(N-n)!n!} a(x)^n b(x)^{N-n},$$

with

$$a(x) = \frac{\alpha(x)}{\alpha(x)+\beta(x)}, \quad b(x) = \frac{\beta(x)}{\alpha(x)+\beta(x)}.$$

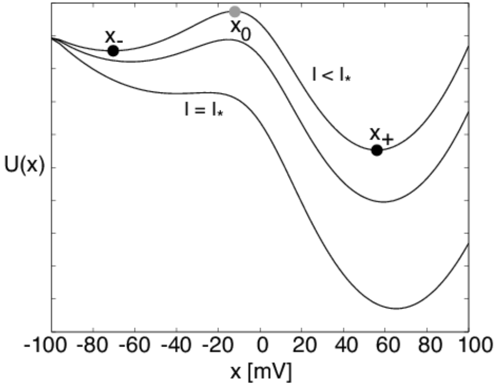
Deterministic kinetic equation

$$\dot{x} = a(x)f(x) - g(x)$$

$$a(x) = \langle n \rangle / N \quad \langle n \rangle = \sum_{n \in \Gamma} n\rho(x, n)$$

The neuron model IV

The averaged model can exhibit bistability:



x_- resting state

x_+ active state

The neuron model V

Transitions from x_- to x_+ can be interpreted as initiating spontaneous action potentials.
The Hamiltonian $H(x, \alpha)$ can be computed:

$$H(x, \alpha) = \alpha[-N\beta(x)g(x) + (N\alpha(x) + \alpha g(x))(f(x) - g(x))]$$

and so does the quasi-potential Φ solution of

$$H(x, \Phi'(x)) = 0$$

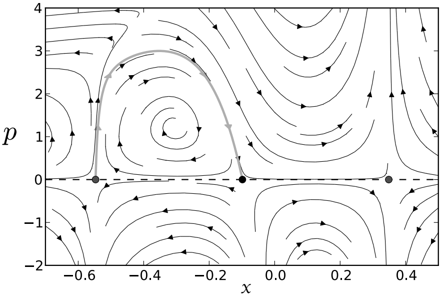
Two solutions are found:

$$\Phi'(x) = 0 \quad \Phi'(x) = -N\frac{\alpha(x)f(x) - (\alpha(x) + \beta)g(x)}{g(x)(f(x) - g(x))}$$

The neuron model VI

- $\Phi = \textit{constant}$ corresponds to deterministic trajectories converging to x_-.
- Non-trivial solution for Φ corresponds to the most likely escape trajectory.

Solutions to Hamilton's equations in the (x, α) plane:



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Some remarks

- Useful alternative to the Wentzel-Kramers-Brillouin (WKB) method, especially in dimensions larger than 1.
- "Easy" extension to the case where the slow process is a piecewise SDE.
- Use these ideas to model the pathologic gating induced by mutations of ion channels (found in epilepsy, migraine and neuropathic pain).