Periodic Ergodicity of Hodgkin-Huxley with random periodic dendritic input.

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Model

Our model is made of 3 parts :

- a deterministic Hodgkin-Huxley system (V_t, n_t, m_t, h_t) which receives
- a stochastic dendritic input $\xi(t)$,
- and a deterministic periodic signal S encoded in the drift of ξ.

Our model

We consider $X_t = (V_t, n_t, m_t, h_t, \xi_t)$ solution of the 5-dim. SDE where V_t, n_t, m_t, h_t satisfy

$$\begin{array}{rcl} dV_t & = & F(V_t, n_t, m_t, h_t)dt + d\xi_t \\ dm_t & = & \alpha_m(V_t)(1 - m_t) - \beta_m(V_t)m_t \\ dh_t & = & \alpha_h(V_t)(1 - h_t) - \beta_h(V_t)h_t \\ dn_t & = & \alpha_n(V_t)(1 - n_t) - \beta_n(V_t)n_t \end{array}$$

with

$$F(V, n, m, h) = -g_{\mathrm{Na}}\, m^3 h\,(V - V_{\mathrm{Na}}) - g_{\mathrm{K}}\, n^4\,(V - V_K) - g_{\mathrm{L}}\,(V - V_L),$$

Stochastic Dendritic Input ξ

and the dendritic input (ξ_t) is either an Ornstein-Uhlenbeck type process :

$$d\xi_t = (S(t) - \xi_t)\tau dt + \gamma\sqrt{\tau} dW_t, \tag{1}$$

or a CIR (Cox Ingersoll Ross) type process :

$$d\xi_t = (a + S(t) - \xi_t)\tau dt + \gamma\sqrt{\tau}\sqrt{\xi_t}\, dW_t. \tag{2}$$

S is a given deterministic smooth T-periodic signal $S(t)$ with $S(t) \geq 0$ in (2).

τ (resp. γ) is a speed (resp. spread) parameter. In this talk we take $\tau = \gamma = 1$.

About ξ

- Biological relevance of OU or CIR : Höpfner' s statistical study (2007)
- when $2a \geq 1$ and $\xi_0 > 0$, process ξ of (2) never attains 0 a.s.
- SDE (2) can be modified to get $\xi_t \in]-K, +\infty[$ for some $K > 0$.
- If (ξ_t) is ergodic, the following identity holds :

$$E_\pi(\xi_t) = \int_0^\infty S(\, t - r \,)\, e^{-r} dr$$

where π is the invariant law of the chain (ξ_{kT}) (cf. Höpfner and Kutoyants).

Periodic Ergodicity

- Periodicity in the semi-group : for all $k \in \mathbb{N}$,

$$p_{\,s,\,t}\ (x,y) = p_{\,s+kT,\,t+kT}\ (x,y).$$

- The Markov chain $(X_{kT})_{k\in\mathbb{N}}$ is time homogeneous.
- The process $\overline{X}_t := (\ i_T(t)\ ,\ X_t\ )$ is time-homogeneous where $i_T(t) = t \mod T$.
- Periodic ergodicity corresponds to $(X_{kT})_{k\in\mathbb{N}}$, or equivalently $(\overline{X}_t)$, being positive Harris-recurrent.

Ergodicity of OU-HH and CIR-HH

Theorem ([HLT 2015]) : CIR-HH with $2a > 1$ and OU-HH are ergodic.

Key arguments of the proof : existence of an *attainable* point where some weak Hörmander condition is satisfied $+$ existence of a Lyapounov function.

In this talk we focus on existence of an *attainable* point.

Attainable Point : definition

Below take $U = \mathbb{R}$ for OU-HH or $U =]0, +\infty[$ for CIR-HH.

A point x^* is *attainable* if for arbitrary $x \in \mathbb{R} \times [0,1]^3 \times U$ we can find a deterministic φ s.t. $\dot{\varphi} \in L^2_{loc}$ such that the solution of the ode

$$\dot{x}(t) = \tilde{b}(t, x(t))dt + \sigma(x(t))\dot{\varphi}(t)dt, \quad x(0) = x,$$

satisfies

$$x^* = \lim_{t \to +\infty} x(t).$$

Here $\tilde{b}$ is the Stratonovich drift of (X_t) :

- for OU-HH, $\sigma \equiv 1$, $\tilde{b}(t,x) \equiv b(t,x)$,
- for CIR-HH, $\sigma(x) = \sqrt{x}$, $\tilde{b}^i(t,x) \equiv b^i(t,x)$ if $i = 2,3,4$ and $\tilde{b}^i(t,x) = b^i(t,x) - \frac{1}{4}$ for $i = 1,5$.

Attainable Point for CIR-HH (I)

Consider $(v^0, m_\infty(v^0), h_\infty(v^0), n_\infty(v^0))$, the (stable) equilibrium point of deterministic 4d-HH with zero input ($v^0 \sim 0.0462\mathrm{mV}$).

We show that

$$x^* := (v^0, m_\infty(v^0), h_\infty(v^0), n_\infty(v^0), 1)$$

is attainable for CIR-HH.

Given $x \in \mathbb{R} \times [0,1]^3 \times]0,+\infty[$ we have to build φ such that the following system of odes

Attainable Point for CIR-HH (II)

$$
\begin{aligned}
\frac{d}{ds}x^1(s) &= \frac{d}{ds}x^5(s) \; - F(x^1(s), x^2(s), x^3(s), x^4(s)) \\
\frac{d}{ds}x^2(s) &= \alpha_m(x^1(s))\,(1 - x^2(s)) \; - \; \beta_m(x^1(s))\, x^2(s) \\
\frac{d}{ds}x^3(s) &= \alpha_h(x^1(s))\,(1 - x^3(s)) \; - \; \beta_h(x^1(s))\, x^3(s) \\
\frac{d}{ds}x^4(s) &= \alpha_n(x^1(s))\,(1 - x^4(s)) \; - \; \beta_n(x^1(s))\, x^4(s) \\
\frac{d}{ds}x^5(s) &= [\, a - \frac{1}{4} + S(s) - x^5(s)\,] \; + \; \sqrt{x^5(t)}\; \dot{\varphi}(s).
\end{aligned}
$$

with $x(0) = x$, satisfies $x^* = \lim_{t \to +\infty} x(t)$.

Role of x^*

For arbitrarily small neighborhoods U^* of the attainable point x^* in $\mathrm{int}(E)$ and for arbitrary starting points $x \in E$, we have :

$$Q_x \left(X_{jT} \in U^* \right) \quad > \quad 0 \quad \text{for large enough} \quad j.$$

This is due to a kind of support theorem that we prove.

Going on we use x^* to build **the** invariant measure and together with our Lyapounov assumption to ensure that this measure is a probability measure.

ISI : Def. of spiking/non spiking

- During a spike we observe $m >> h$ (actually m close to 1 and h small).
- At the end of a spike and during an interspike $m < h$.

Accordingly we consider

- two regions $D = \{(v, m, h, n, \xi);\ m > h\}$, $B = \{(v, m, h, n, \xi);\ m < h\}$

and we define

- two sequences (γ_ℓ), (τ_ℓ)

$$\begin{aligned}
\gamma_0 &:= 0 \\
\tau_\ell &:= \inf\{t > \gamma_{\ell-1} : X_t \in D\} \\
\gamma_\ell &:= \inf\{t > \tau_\ell + \delta : X_t \in B\}\,.
\end{aligned}$$

Application 1 :
time spent spiking

Proportion of time spent spiking (or in D).

We prove that

$$\begin{aligned}\lim_{n\to+\infty}\frac{1}{\tau_n}\sum_{j=1}^{n}(\sigma_j-\tau_j) &= \lim_{t\to+\infty}\frac{1}{t}\int_0^t 1_D(X_s)\,ds\\ &= \frac{1}{T}\int_0^T ds\,[\mu P_{0,s}](D)\quad \text{a.s.}\end{aligned}$$

as an application of the following limit theorems :

Limit Theorems

limit theorems are of LLN type :

- for the chain (X_{kT}) :

$$\frac{1}{n}\sum_{k=1}^{n}\phi\,(X_{kT}) \to \int_{\mathbb{R}^d}\mu(dy)\,\phi(y),$$

- for the process (X_t) :

$$\frac{1}{t}\int_0^t \phi\,(i_T(s), X_s)\,ds \to \frac{1}{T}\int_0^T ds\int_{\mathbb{R}^d}\mu P_{0,s}(dy)\,\phi(s,y),$$

where μ denotes the invariant probability of the chain (X_{kT}).

Application 2 :
Empirical distribution for the length of ISI

Define

$$F_n(t) := \frac{1}{n}\sum_{j=1}^{n} 1_{[0,t]}(\tau_{j+1} - \tau_j) \quad \text{and} \quad F(t) := Q_{\overline{\mu}}\left(\tau_2 - \tau_1 \leq t\right),$$

where $\overline{\mu}$ is the invariant measure of $\overline{X}_t = (i_T(t), X_t)$.

Then $Q_{(0,x)}$-almost surely,

$$\sup_{t\geq 0} \left| F_n(t) \; - \; F(t) \right| \to 0 \quad \text{as } n \to \infty,$$

for every choice of a starting point $x \in E$.

Role of x^* (II)

- in these empirical means appear non independent r.v.
- existence of x^* enables us to build regeneration times and split the trajectory in independent pieces and to go back to classical LLN.
- uniform convergence follows by the Glivenko-Cantelli lemma for i.i.d. random variables.

Conclusion. Perspective

In this talk we addressed ergodicity properties of a stochastic Hodgkin-Huxley model with a dendritic input which encodes a periodic deterministic signal.

We have used (cf. [HLT 2015]) our ergodicity result to prove limit theorems (LLN).

In future work we want to address the question of estimation of the unknown signal S or of its period T.

Bibliography

[HLT 2015] Höpfner, R., Löcherbach, E., Thieullen, M., *A general scheme for ergodicity in degenerate diffusions with time periodic drift, and an application to limit theorems in a stochastic Hodgkin-Huxley model.* arXiv :1503.01648v1 [math.PR] 5 Mar 2015