Inverse First Passage Time methods and their applications to neuronal modeling

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The problem

- The neuronal activity can be described using stochastic models: stochastic leaky integrate and fire (LIF) model with a time dependent boundary.
- The inverse first passage time algorithm (IFPT) allows to determine the boundary given the first passage time (FPT) distribution.
  - Classify simultaneously recorded neuronal activity. Differences in the dynamics of neurons are recognized in terms of the shape of the boundary of the LIF model fitting the data.
  - Detect the evolution of the dynamics of firing activity of experimentally recorded spike trains.
  - Is it possible to have a Gamma distribution as output for a neuronal model?

SUMMARY

- The model for the membrane potential evolution: Stochastic Leaky Integrate and Fire.
- The IFPT method:
  - Classification algorithm.
  - Moving window IFPT algorithm.
  - Boundary corresponding to a Gamma FPT probability density function.
- Discussion and conclusions.

The model: stochastic leaky integrate and fire (LIF)

The membrane potential of a neuron can be described with an Ornstein-Uhlenbeck process

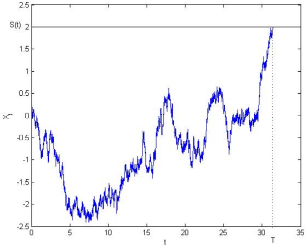
$$\begin{cases} dX_t = \left(-\frac{X_t}{\theta} + \mu\right) dt + \sigma dW_t \\ X_0 = 0 \end{cases}$$

where we know or we can estimate the parameters μ, σ^2 and θ. The process is characterized by its transition probability density function

$$f(x, t|y, s) = \frac{\partial}{\partial x} P(X(t) \leq x | X(s) = y)$$

The model: the interspike time intervals (ISI)

The OU process is constrained by a time dependent boundary S(t)



$$\begin{aligned} T &= \inf\{t > 0 | X_t \geq S(t)\} \\ g(t) &= \frac{\partial}{\partial t} P(T < t) \end{aligned}$$

The direct and inverse FPT problems

- The direct problem: the process and the boundary are known
  $\longrightarrow$ we look for the FPT distribution
- The inverse problem: the process and the FPT distribution are known
  $\longrightarrow$ we look for the boundary

Suppose that the FPT probability density function of an Ornstein Uhlenbeck process is known.
What can be said about the shape of the boundary?

The IFPT method

Fortet equation

$$f(x,t|0,0) = \int_0^t g(\tau) f(x,t|S(\tau),\tau) d\tau$$

where $x \geq S(t)$. We integrate with respect to x.
For an OU process

$$1 - \Phi\left(\frac{S(t) - \mu\theta + \mu\theta e^{-\frac{t}{\theta}}}{\sqrt{\frac{\theta\sigma^2}{2}\left(1 - e^{-\frac{2t}{\theta}}\right)}}\right) =$$

$$= \int_0^t g(\tau)\left\{1 - \Phi\left(\frac{S(t) - \mu\theta + (\mu\theta - S(\tau))\, e^{-\frac{t-\tau}{\theta}}}{\sqrt{\frac{\theta\sigma^2}{2}\left(1 - e^{-\frac{2(t-\tau)}{\theta}}\right)}}\right)\right\} d\tau,$$

where $\Phi(\cdot)$ is the standard normal distribution.

The IFPT algorithm

Introducing now a partition of $[0, \Theta]$

$$t_i = ih, \qquad i = 0, ..., \frac{\Theta}{h}, \tag{1}$$

with $h > 0$, for $i = 1, ..., n$ one obtains

$$1 - \Phi\left(\frac{S(t_i) - \mu\theta + \mu\theta e^{-\frac{t_i}{\theta}}}{\sqrt{\frac{\theta\sigma^2}{2}\left(1 - e^{-\frac{2t_i}{\theta}}\right)}}\right) =$$

$$= \sum_{j=1}^{i} g(t_j)\left\{1 - \Phi\left(\frac{S(t_i) - \mu\theta + (\mu\theta - S(t_j))\, e^{-\frac{t_i - t_j}{\theta}}}{\sqrt{\frac{\theta\sigma^2}{2}\left(1 - e^{-\frac{2(t_i - t_j)}{\theta}}\right)}}\right)\right\} h$$

triangular non linear system of n equations in the n unknowns $S(t_1), ..., S(t_n)$.

Classification algorithm

- Assume that the noise acts in the same way on each neuron.
- Assume that simultaneously recorded spike trains can be interpreted as generated from the same Ornstein-Uhlenbeck (OU) diffusion process.

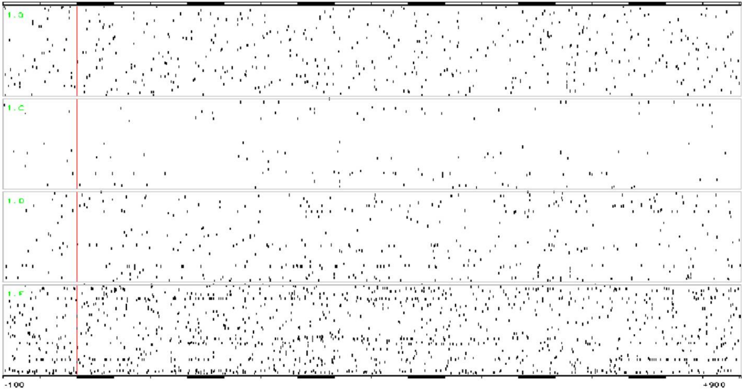
Is it possible to discriminate each single neuron by means of its deterministic properties?

$\Downarrow$

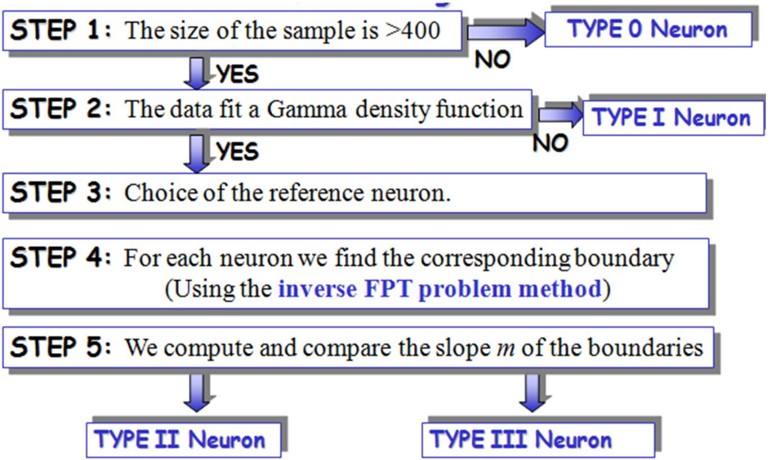
We look for different features in the shape of the boundary.

Biological data

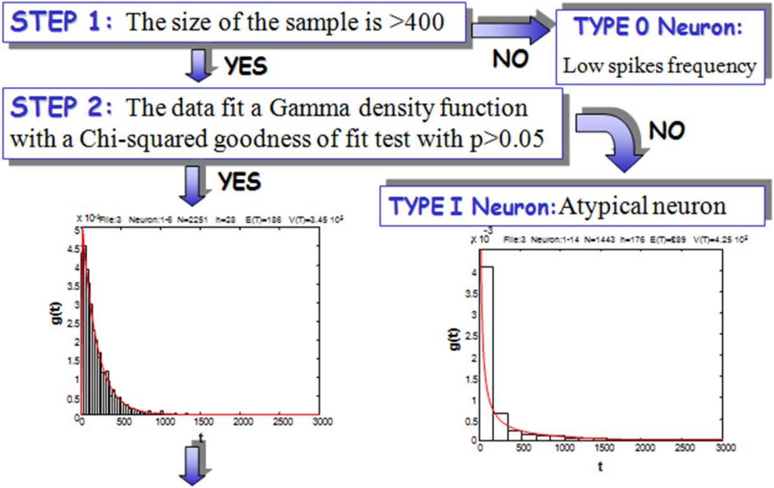
Spontaneous activity of mice. Raster display of four neurons.



Classification Algorithm



Classification Algorithm: Step 1 and 2



Classification Algorithm: Step 3

STEP 3: Choice of the reference neuron
⇒ we obtain the reference σ for the OU underlying process.

We assume that $\mu = 0$ mV, $\theta = 10$ ms^{-1}; values suggested by biologists.
Choice of the reference neuron (Step 3).

- We compute the CV_i of each neuron i.
- We estimate σ_i by means of moment method for an OU process with $\mu = 0$ mV, $\theta = 10$ ms^{-1}.
- We compute the variance of the FPT of the OU_i process and the CV_{OU_i}.
- We choose as a reference neuron the neuron that minimizes $|CV_i - CV_{OUi}|$ between all the feasible neurons.
- The reference σ is obtained by the reference neuron.

Classification Algorithm: Steps 4 and 5

STEP 4: Using the inverse problem method we determine the boundary corresponding to each neuron when the underlying OU process is characterized by μ, θ, σ of step 3

STEP 5: We compute the slope *m* of the boundary

$m \sim 10^{-4}, 10^{-3}$

TYPE III Neuron:

Linear boundary

$m \sim 10^{-5}, 10^{-6}$

TYPE II Neuron:

Constant boundary

Classification Algorithm: Step 5

STEP 5: We compute the slope m of the boundary

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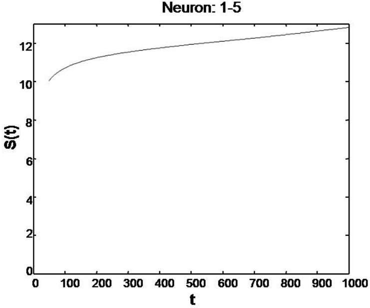
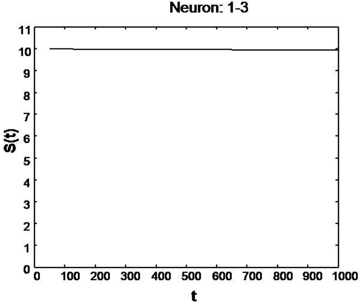
Constant boundary





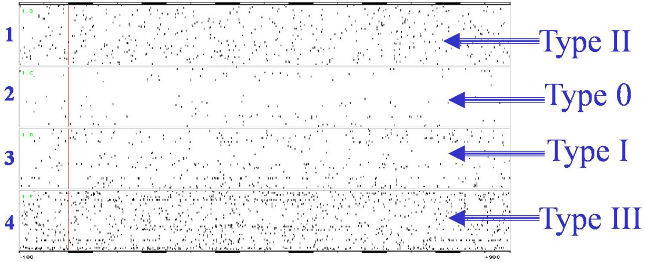
Example

Five multivarite records lasting 300-400 s have been analyzed.
Each record included 15 spike trains recorded simultaneously without external stimulations.

Neurons analyzed: 75

	File 1	File 2	File 3	File 4	File 5	TOT
Type 0	-	8	-	4	5	17
Type I	1	-	4	2	3	10
Type II	3	4	6	6	5	24
Type III	11	3	5	3	2	24

Example



Interpretation of the results

We get an OU model with linear boundary.
What is the corresponding process with constant boundary?

OU model with linear boundary

$$\Downarrow$$

$$dY_t = \left(-\frac{Y_t}{\theta} - b - \frac{b}{\theta}t\right)dt + \sigma dW_t$$

constrained by a constant boundary.

The deterministic component of the transformed process is no more time homogeneous since we have the dependence on the time t.

Problem

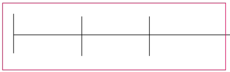
QUESTION: Considering the global sample for each neuron, do we loose the evolution of the dynamics?

$\Downarrow$

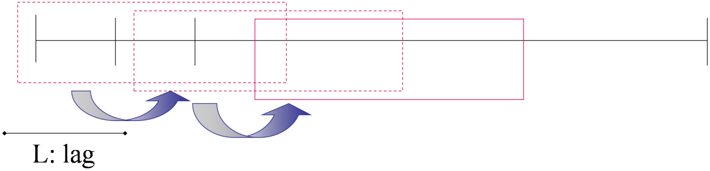
Is it possible to use the IFPT method to detect the evolution of the dynamics of firing activity of experimentally recorded spike trains?

Moving window IFPT method

We have a sample of size N and a window



We succcessively shift the window of a fixed lag

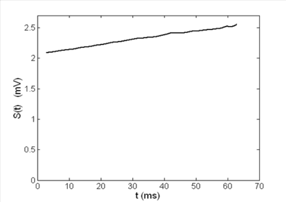


We apply the IFPT method successively to the selected windows in analogy with time-frequency analysis.

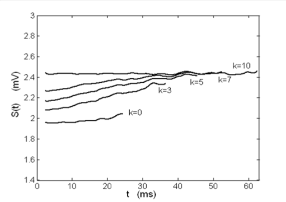
Simulations: example 1

We consider two samples of size $N = 10^6$ of FPT of an OU process through the constant boundaries $S = 2$, $S = 2.5$ respectively.

Boundary obtained when the IFPT method is applied to the global sample



Boundaries obtained with a window of size $n = 10^5$ and a lag $L = 10^4$.



Mixtures of FPT corresponding to constant boundaries give linear boundaries!!!

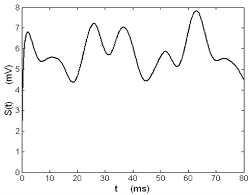
Simulations: example 2

We consider two samples of size $N = 10^6$ of FPT of an OU process through the oscillating boundary

$$S(t) = k + a\cos(\omega t)$$

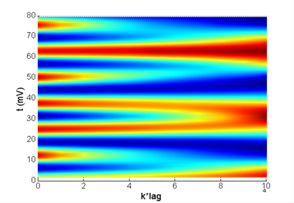
with $k = 3$, $\omega = 0.2$ and $\omega = 0.5$.

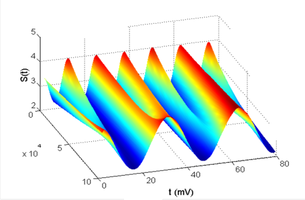
Boundary obtained when the IFPT method is applied to the global sample



Simulations: example2

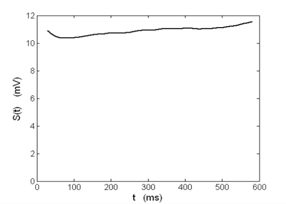
Boundaries obtained with a window of size $n = 10^5$ and a lag $L = 10^4$.





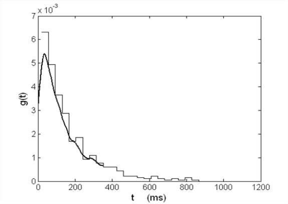
Experimental data

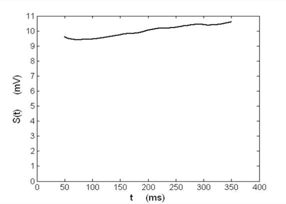
Biological data: spontaneous activity, activity recorded from the temporal cortex and thalamus of unanesthetized mice.
Boundary obtained when the IFPT method is applied to the global sample



Experimental data

Sample size =500
0-74 ms

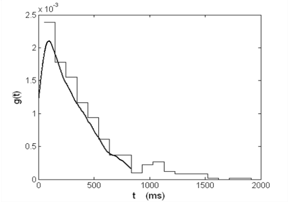


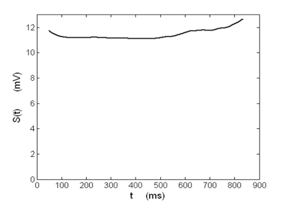


Linear boundary

Experimental data

Sample size =500
219 - 393 ms





Constant boundary

Problem

Assume that OU is a good model for the description of the membrane potential.
The Gamma distribution seems to be a good candidate for the FPT T.

$$\Downarrow$$

What can we say on the boundary shape?
Is it possible to have a Gamma distribution as output for a neuronal model?

The model

$$\begin{cases} dX_t = \left(-\frac{X_t}{\theta} + \mu\right) dt + \sigma dW_t \\ X_0 = x_0 \end{cases}$$

We choose:

- $\theta = 25$,
- $\sigma^2 = 0.16$,
- $x_0 = 0$.
- FPT: Gamma random variables with:
  - mean=10
  - CV=0.5, CV=1, CV=1.5.

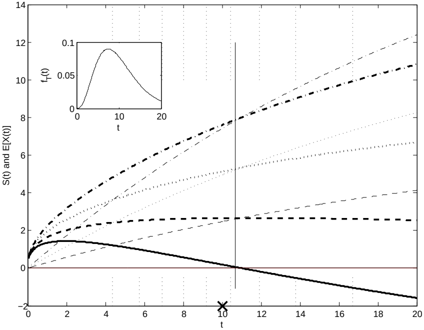
We look for the boundary.

Example 1: CV=0.5

FPT: Gamma random variables with:

- mean=10
- CV=0.5

$\mu = 0$ full line
$\mu = 0.3$ dashed line
$\mu = 0.6$ dotted line
$\mu = 0.9$ dash-dot line

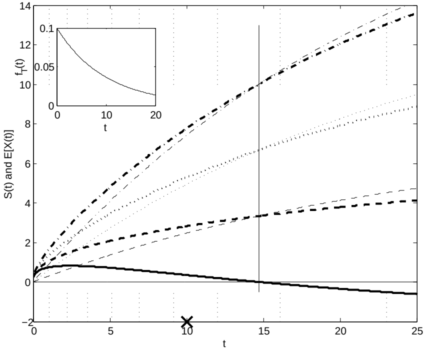


Example 2: CV=1

FPT: Gamma random variables with:

- mean=10
- CV=1

$\mu = 0$ full line
$\mu = 0.3$ dashed line
$\mu = 0.6$ dotted line
$\mu = 0.9$ dash-dot line

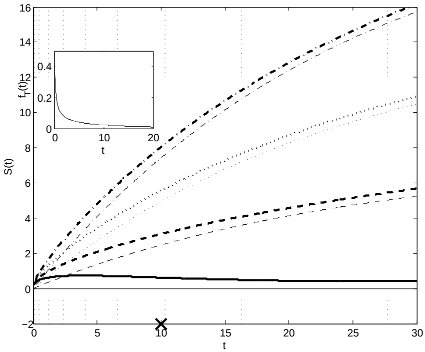


Example 3: CV=1.5

FPT: Gamma random variables with:

- mean=10
- CV=1.5

$\mu = 0$ full line
$\mu = 0.3$ dashed line
$\mu = 0.6$ dotted line
$\mu = 0.9$ dash-dot line



Conclusions and perspectives

The IFPT algorithm is a tool that allows to understand how the quantities of interest depend on each other.

Works in progress:

- Random initial condition: what is the distribution of the random initial condition that generates a Gamma FPT probability density function?
- IFPT with two boundaries.

Thank you for your attention

Bibliography

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