Consistent maximum likelihood estimates for the parameter of LIF neuronal models

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joint work with S. Ditlevsen (Copenhagen University)

Topic of the talk

Assuming a LIF model

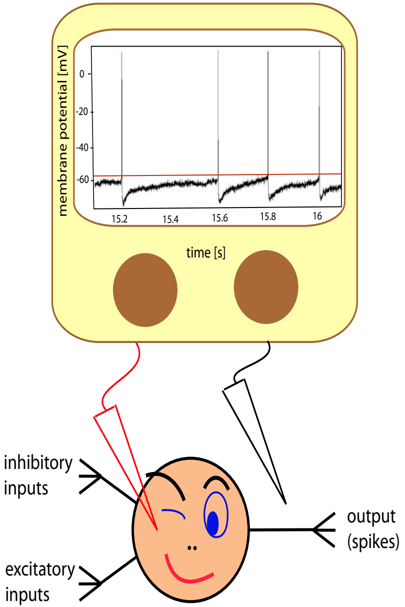
OU (or Feller) stochastic SDE

$$dX_t = (-\beta X_t + \mu)\ dt + \sigma dW_t$$
$$X_0 = x_0$$

we want to estimate the parameters

$$\theta = (\tau,\ \mu,\ \sigma^2)$$

from intracellular recordings from one (some) ISI. The resetting x_0 and the threshold b are assumed as known.



Isn't that easy?

We have Maximum Likelihood estimates!

To each trajectory $(x_1, \cdots, x_n)$ we associate the

Likelihood function

$$LK_\theta^W(x_1, \cdots, x_n) = f(x_1|x_0)\cdots f(x_n|x_{n-1})$$

and we maximize it!

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and we maximize it!

Let's test the method by this procedure

1. We generate 10.000 trajectories stopping them the first time the process crosses a constant threshold b
2. From each trajectory we estimate β, μ and σ parameters
3. We take the means

Results - 1

We try two settings. Fixed parameters which are common to both settings are

$$N = 10000,\ h = 0.2ms\ (h_s = 0.05),\ x_0 = 0mV, b = 10mV$$

Sub-threshold regimen ($\mu/\beta < b$)

The true parameters are

$$\mu = 0.5\ \text{mVms}^{-1}\ \beta = 0.0556\ \text{ms}^{-1}$$
$$\sigma = 0.6\ \text{mV}^1\text{ms}^{-1/2}$$

The estimates are

$$\hat{\mu} = 0.584 \qquad \hat{\beta} = 0.0604$$
$$\hat{\sigma} = 0.596$$

Supra-threshold reg. ($\mu/\beta > b$)

The true parameters are

$$\mu = 1.5 \qquad \beta = 0.0556$$
$$\sigma = 0.6$$

The estimates are

$$\hat{\mu} = 1.615 \qquad \hat{\beta} = 0.0681$$
$$\hat{\sigma} = 0.579.$$

cf. Bibbona, Lansky, Sacerdote, Sirovich, Phys Rev E, 2008

and R. Sirovich's talk this afternoon

What's wrong?

First problem: Model misspecification

The presence of the threshold is not accounted for into the model!

LK_θ^W is for a general OU process

Trajectories in our sample are not allowed to span the whole state space $(-\infty, \infty)$ of an OU process.
In the presence of the threshold the statistical properties of the process are changed and in particular a specific likelihood theory has to be specified.

Likelihood for the stopped process - 1/2

Given that you are in x_{n-1} at time t_{n-1}, at the next sampling time $t_n = t_{n-1} + h$ the process may:

- have crossed b with probability

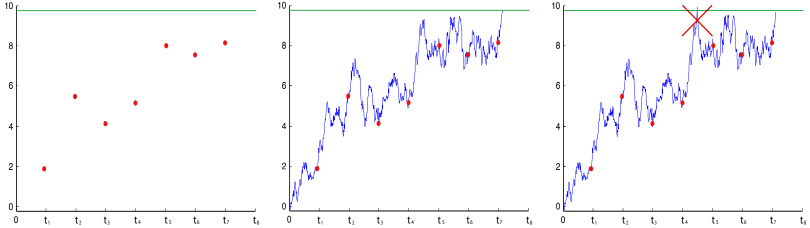
$$P_\theta(T \leq h|x_{n-1}) = \int_0^h g_b(r|x_s)\, dr$$

- alternatively it may have been below the threshold for all the time between t_{n-1} and t_n and it may go at t_n to a state x_n with a probability density

$$f_\theta^b(x_n|x_n - 1) = \frac{\partial}{\partial y} P_\theta(X_t \leq y \ \&\ T > h \mid x_{n-1})\Big|_{y=x_n}$$

Likelihood for the stopped process - 2/2

If we observe the trajectory $(x_1, \cdots, x_n)$ in the presence of the threshold



it means that the process has been below the threshold until t_n (also while it was not observed), but before t_{n+1} it has crossed somewhere

Given the trajectory $(x_1, \cdots, x_n)$ we associate to it the following

likelihood function in the presence of a threshold

$$LK_\theta^{b}(x_1, \cdots, x_n) = f_\theta^b(x_1|x_0) \cdots f_\theta^b(x_n|x_{n-1}) P_\theta(T \leq h|x_n)$$

How to calculate $f_\theta^b(x_i|x_{i-1})$?

1. $f_\theta^b(x_i|x_{i-1})$ is know in closed form for brownian motion and a few more cases, it is a joint "probability density" of being in $x_i < b$ and not passing, it may be calculated conditioning:

$$f_\theta^b(x_i|x_{i-1}) = f_\theta(x_i|x_{i-1})(1-p_i)$$

   where $p_i = P(t_{i-1} < T \leq t_i|x_{i-1}, x_i)$ is the crossing probability for a Bridge process (pinned diffusion)
2. for the probability p_i Caramellino and Baldi (Ann. Appl. Prob., 2005) proposed a large deviation estimate when $h = t_i - t_{i-1} \to 0$ in a very general context
3. for the OU process its expression is compact and looks like the following

$$p_i \approx \exp\left[-\frac{2}{h}(b-x_{i-1})(b-x_i)\right]\Big(1 - h\,\phi(x_{i-1}, x_i, b)\Big)$$

   where ϕ is a rational function.

How to calculate $P_\theta(T \leq h|x_{n-1})$?

$$P_\theta(T \leq h|x_{n-1}) = \int_0^h g_b(r|x_{n-})\, dr$$

The density $g_b(r|x_s)$ of the first passage time satisfies (cf. Sacerdote Tomassetti, Adv. Appl. Prob., 1996) the following integral equation

$$g_b(r|x_{n-1}) = -2\Psi_b(r|x_{n-1}) + 2\int_0^r d\tau\; g_b(\tau|x_{n-1})\,\Psi_b(r-\tau|b)$$

for a known function $\Psi_b(r|x_{n-1})$.
For $h \longrightarrow 0$, a not too rude approximation is

$$g_b(r|x_{n-1}) \approx -2\Psi_b(r \mid x_{n-1})$$

and

$$P_\theta(T \leq h|x_{n-1}) = \int_0^h \Psi_b(r \mid x_{n-1})\, dr$$

Did we solve? Results - 2

Again same two settings. Fixed parameters which are common to both settings are

$$N = 10000,\ h = 0.2ms\ (h_s = 0.05),\ x_0 = 0mV, b = 10mV$$

Sub-threshold regimen ($\mu/\beta < b$)

The true parameters are

$$\mu = 0.5\ \text{mVms}^{-1}\ \beta = 0.0556\ \text{ms}^{-1}$$
$$\sigma = 0.6\ \text{mV}^{1}\text{ms}^{-1/2}$$

The estimates are

$$\hat{\mu} = 0.568 \qquad \hat{\beta} = 0.0565$$
$$\hat{\sigma} = 0.597$$

Supra-threshold reg. ($\mu/\beta > b$)

The true parameters are

$$\mu = 1.5 \qquad \beta = 0.0556$$
$$\sigma = 0.6$$

The estimates are

$$\hat{\mu} = 1.570 \qquad \hat{\beta} = 0.0553$$
$$\hat{\sigma} = 0.579.$$

What's wrong now?

Second problem: short trajectories

- Likelihood estimates for discretized diffusions have very good properties for $n \to \infty$ (n is the length). In our setting we don't have any freedom to increase the length of the trajectories further as they stop at the hitting time
- To increase the number of observations by taking have $h \to 0$ but keeping the last time fixed helps just for the diffusion parameters and not for the drift.

How can I increase my sample, then?
Estimating from more than one trajectory at a time! Trajectories are independent and the global likelihood of a group of them is just the product of the individual ones.

In this setting however it is needed the assumption that the values of the parameters is stationary along the different trajectories

Did we solve now? Results - 2

Again same two settings. Common fixed parameters are

$$N = 10000,\ h = 0.2ms\ (h_s = 0.05),\ x_0 = 0mV, b = 10mV$$

we group the trajectories into groups of size 100 and we take a global estimate for each group. Then we take the mean of the 100 results.

Sub-threshold regimen ($\mu/\beta < b$)

The true parameters are

$$\mu = 0.5 \text{ mVms}^{-1} \quad \beta = 0.0556 \text{ ms}^{-1}$$
$$\sigma = 0.6 \text{ mV}^{1}\text{ms}^{-1/2}$$

The estimates are

$$\hat{\mu} = 0.501 \qquad \hat{\beta} = 0.0556$$
$$\hat{\sigma} = 0.599$$

Supra-threshold reg. ($\mu/\beta > b$)

The true parameters are

$$\mu = 1.5 \qquad \beta = 0.0556$$
$$\sigma = 0.6$$

The estimates are

$$\hat{\mu} = 1.506 \qquad \hat{\beta} = 0.0562$$
$$\hat{\sigma} = 0.597.$$

Conclusions

- the presence of the threshold brings a systematic error into the estimate of parameters for LIF models (more generally on stochastic process in the presence of a barrier)
- the bias can be eliminated if we correctly specify the likelihood function and if we take global estimates from groups of trajectories.

Thanks are due to L. Sacerdote and M. Jacobsen for some enlightening discussions on this topic.