Stochastic neuronal models

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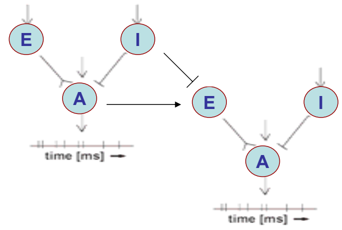

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Summary

- Basic Introduction to Neurosciences
  - Structure and function of the nervous system
  - Elements of Neuroanatomy
  - Neuronal signals
- Mathematical models for single units
  - Aims of models
    - First models
    - Hodgkin and Huxley type models
    - Stochastic models
    - Diffusion type models
- Mathematical methods and related problems
- Usefullness of the single neuron models
- Models for assemblies of neurons
  - Aims of the models
    - Models of jump diffusion type
  - Mathematical methods and related problems
  - Alternative approaches and new researches topics

Usefullness of the models?

- Diffusion models oversimplify the neuronal structure, to what aims can we use them?
  - To make light on the effect of particular external stimula (i.e. periodic stimula: next lessons by K.Pakdaman)
  - To investigate relationships between input and output signal
    - Methods: information measures (entropy, Fisher information)
    - To investigate the role of noise in neural coding (unexpected features can be related to the noise)

Optimal signal detection 1/3

- Interpret μ in the OU model as the input signal and the occurrence of a spike as the output signal. Our sample is then $(T_1, T_2, \ldots, T_n)$

$$\begin{cases} dX_t = (-\frac{X_t}{\tau} + \mu)dt + \sigma dW_t \\ X_{t_0} = x_0 \end{cases}$$

Recall the Cramer Rao inequality for an unbiased estimator of μ :

$$Var\widehat{\mu} \geq \frac{1}{J(\mu)}$$

where $J(\mu)$ is the Fisher information

$$J(\mu) = \int_0^\infty \frac{1}{g(\tau)} \left(\frac{dg(\tau)}{d\mu} \right)^2 d\tau$$

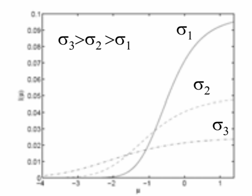
Larger values of the Fisher Information imply a better detection of the signal

Optimal signal detection 2/3

Introduce the normalized Fisher Information

$$I(\mu) = \frac{J(\mu)}{E(T)}.$$

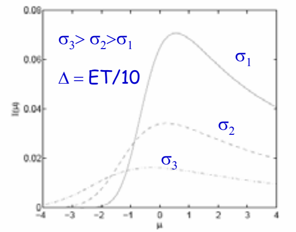
Ornstein-Uhlenbeck model



Weak signals are better determined with higher noise (Lansky et al. 2006)

Optimal signal detection 3/3

A signal at time t is recognized as happening at time Δ = t+δ



- All the shapes of $I(\mu)$ present a maximum that is located in the underthreshold region (where no detection is possible in absence of noise)
- Best estimation with the lowest noise

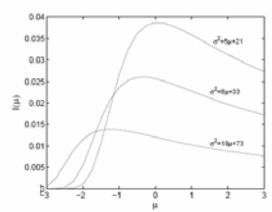
Optimal signal detection in the presence of input dependent noise

To get the diffusion limit we set:

$$\begin{aligned} \mu &= e(\lambda_E - \lambda_I) \\ \sigma^2 &= e^2(\lambda_E + \lambda_I) \end{aligned}$$

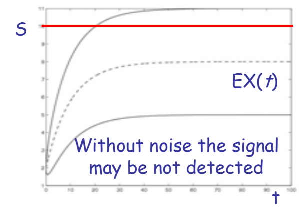
λ_E, λ_I and e appear both in μ and σ^2

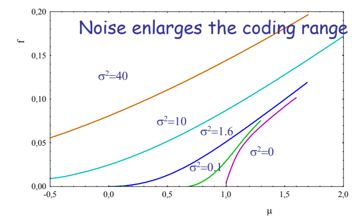
$$\sigma = \sigma(\mu)$$

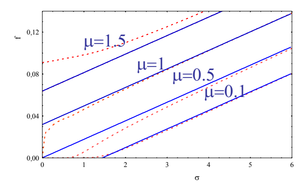


There is an optimum level of signal that can be detected in correspondence to the assigned threshold (Lansky et al.2007)

Examples on the role of noise







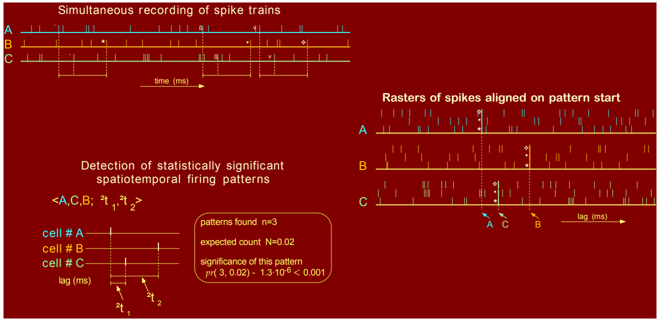
Transfer function: $f(\mu)=1/ET$.

$$f(\mu) \overset{\text{large } \sigma}{=} \frac{1}{\pi\theta S}\left(\sigma\sqrt{\pi\theta} + 2\theta - S\right)$$

Increasing s linearizes the transfer function

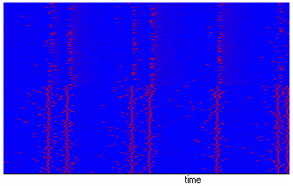
From single neuron activity models to small network models

Observed features: spatio-temporal patterns



Spatio temporal patterns in the brain

EXPERIMENTS



- Self organizing networks
- Rhythmic activities
- Synchrony behavior

Involved features
•Coding the information transmission
•Improvement of signal reliability
•Relationship with various diseases

MATHEMATICS

?

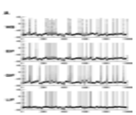
Mathematical Models

Purpose:
• Detecting of different mechanisms, biologically compatible with pattern formation, rythmic activities
• Understanding their interaction to produce the wealth of rythms and synchronicity

Spatio-temporal patterns

Experimental evidence
1. Frequency of specific pattern cannot be casual
2. Periodic spiking activity may be observed in different instances:
   - In the presence of external periodic inputs
   - In absence of any external periodicity

Mathematical representation
1. Multimodality of ISI distribution
   - With or without periodic inputs
2. Signal to noise ratio
3. Crosscorrelograms, autocorrelograms



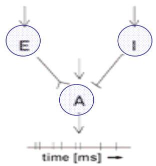
A multimodal ISI distribution is an indicator of synchronicity between different neurons?
Is it related to spatio or to temporal patterns?
How to measure a temporal synchronicity

Models for assemblies of neurons

Different approaches
- Small networks
  - constituted HH model neurons interconnected
  - Jump diffusion models
- Large networks
  - Object oriented simulation
    - Training networks (weights determined through Hebbian rule: an increase in synaptic efficacy arises from the presynaptic cell's *repeated* and *persistent* stimulation of the postsynaptic cell).
  - Macroscopic description not related with microscopic one (nonlinear systems exhibiting multitude of different behaviours)

LIF models for small networks

E: excitatory neuron
I: inhibitory neuron
A: reference neuron



Contributions small and highly frequent: approximated with **a diffusion process**

Strong contributions : modeled with **counting processes** characterized by constant amplitude jump sizes a>0 and i<0

Underthreshold membrane potential evolution:

$$dX(t) = -\frac{X(t)}{\theta}dt + \delta dN_1^+(t) + \rho dN_2^-(t) + a dN^+(t) + i dN^-(t)$$

Neuron A fires when $X_{(t)}>S$ ⇒ FPT problem for a jump diffusion process

Renewal process

- Alternative analysis of the model:
  - Renewal process (the impinging neurons and the reference one are restarted after each spike):
    - jumps event are Poisson distributed (Markov process)
    - jumps are Inverse Gaussian distributed but after each spike of the observed neuron the whole network is started again.
  - We can
    - simulate the ISI distribution
    - Estimate synchronization probabilities between the reference neuron and the others
    - analyse the crosscorrelation between spike trains of different neurons

....versus time series

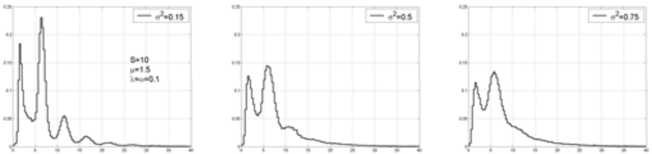
- Time series process:
  - If jumps event are Poisson distributed and the reference neuron is restarted after each spike the time series coincides with a renewal process
  - If jumps are Inverse Gaussian distributed successive spikes time of the reference neuron are **not independent**
- We can
  - simulate the **normalized count process** but it is no more the estimation of a probability.
  - estimate synchronization probabilities between the reference neuron and the others
  - Analyze crosscorrelograms

First passage time problems for jump-diffusion processes

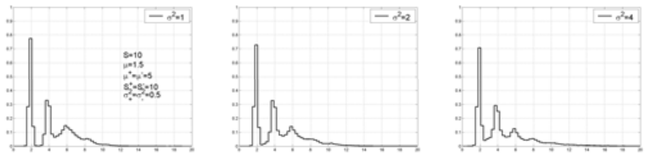
- Numerical methods: only in special instances (approximate formula for perfect integrate model with jumps)
- Reliable simulation method: generalizes existing ones for diffusion processes
  - One first generates the jump time
  - The process between two jump times is a diffusion and can be simulated with standard techniques

Analysis of the small network features via simulations

Perfect integrator 1/2



Wiener with Poisson time distributed jumps



Wiener with Inverse Gaussian time distributed jumps

Perfect integrator 2/2

Poisson

σ^2	I peak (%)	II peak (%)	III peak (%)
0.15	29.43	45.94	14.45
0.50	26.79	48.89	/
0.75	24.68	50.85	/
1.00	24.98	50.65	/

IG

σ^2	I peak (%)	II peak (%)	III peak (%)
0.50	38.43	21.92	34.04
1.00	36.29	25.88	30.31
2.00	35.40	28.00	26.82
4.00	37.23	27.52	23.13

Common feautures:

1. the percentage of samples that builds the first peak decreases as σ^2 increases
2. the percentage of samples that builds the second peak increases as σ^2 increases

Different feautures:

Poisson distributed jumps:
multimodality is determined by the composition of the randomness of the jumps with the Wiener process whose behavior is **higly dominated by the drift term** (the abscissae of the peaks correspond to the modes of the ISI distribution of a Wiener model with threshold *S+ka, k*=-1,0,1....)

Inverse Gaussian distributed jumps:
multimodality is **dominated by the jumps distribution** (the abscissae of the peaks are determined by the mode *m* of the IG distribution leading the jump process and occur at values *km, k*=1,2,..)

Multimodal ISI distribution

Diffusion models with deterministic periodic stimulation.

Shimokawa, T., Pakdaman, K. And Sato, S.,1999.

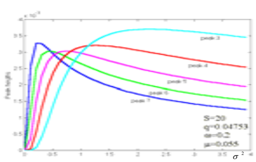
Longtin A., Bulsara A. and Moss F (1991)

In the case of **Wiener** underlying diffusion →

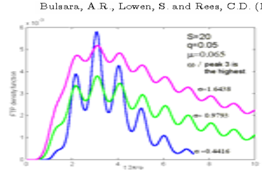
$$dX_t = (\mu + q\cos(\omega t))dt + \sigma\, dW_t$$

Main features:

Bulsara, A.R., Lowen, S. and Rees, C.D. (1994)

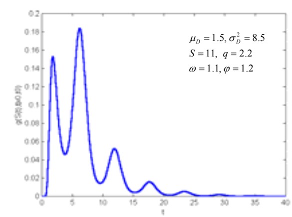


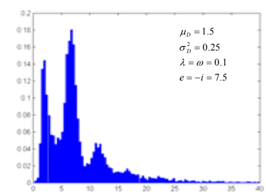
Peak heights go through maxima as function of the noise



Anti-resonant behavior: the height at the mode of the density function goes through a minimum as a function of noise

Periodic versus Strong excitatory-inhibitory stimula





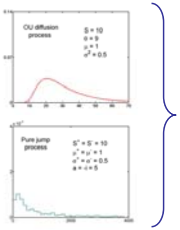
Jump diffusion model explains observed multimodal ISI distributions in absence of external periodic stimula

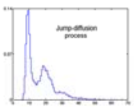
FPT for jump diffusions processes

The merging of two causes of randomness determine the arising of multimodal FPT distributions

The regularity of the Wiener process seems to be one of the causes of the multimodality of the ISI distribution in the case of Wiener process with jumps
Can the modulation appear also when we consider more complex models?

Ornstein-Uhlenbeck with jumps

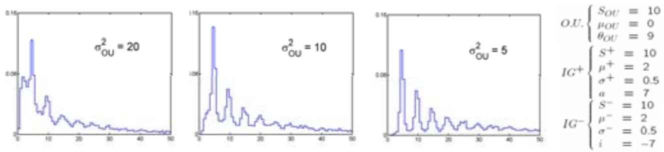




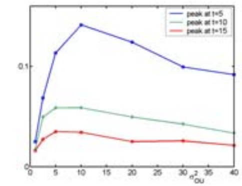
multimodality

- characteristic times for a single neuron
- possible cause of sinchronization

OU with IG jumps (renewal process)



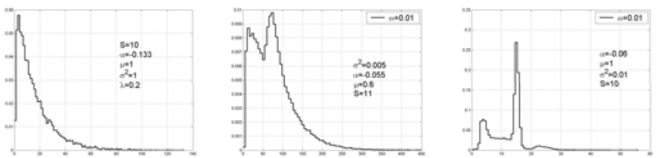
Resonant-like behavior:
the height of the ISI distribution at the modes goes through a maximum with increasing σ



OU with Poisson jumps (renewal process)

Inverse Gaussian distribution is sufficiently regular to allow multimodality also with the Ornstein-Uhlenbeck process.

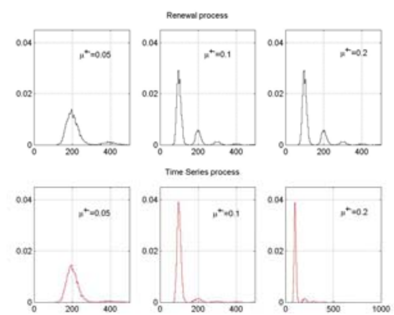
What happens when jumps are Poisson distributed?



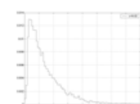
Very often

For suitable tuning of the parameters

IG jumps: histograms versus normalized counts



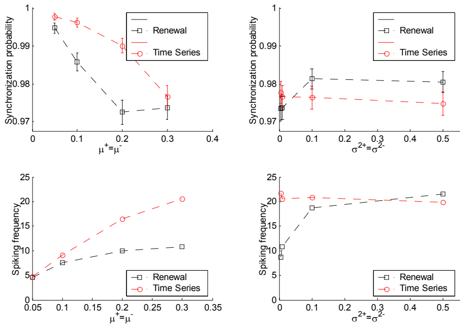
Poisson jumps



Poisson jumps: multimodal histograms arise in a different range of the parameters

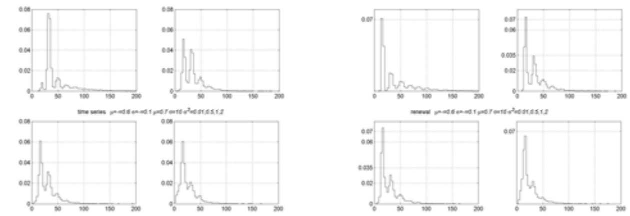
$\mu=0.7$ $\sigma^2=0.1$ $\theta=10$ $\sigma^{\pm}=0.01$

IG jumps: syncronization estimates



Sinchronization probability decreases when $\mu^{\pm}$ increases while multimodality increases when $\mu^{\pm}$ increases: **multimodality and sinchronicity are two different features**

Renewal versus time series: resonance like phenomena



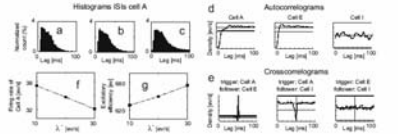
Time series | Renewal

Ranges of "resonance like phenomena" are different in the two models (renewal/time series)

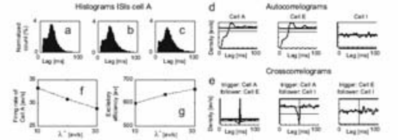
Small network features

As the frequency of inhibitory strong inputs λ_I increases the efficiency of the excitatory unit E (i.e. the number of spikes in the spike train of cell E that excite cell A) increases too.

The result is robust with respect to changes of excitatory distribution (Sacerdote et al. 2007)



Analysis of model (1) when the excitatory interspike intervals are T^{IG} distributed. ISIs histograms of cell A for $\lambda^- = 10$ (panel a), $\lambda^- = 20$ (panel b) and $\lambda^- = 30$ ev/s (panel c). Autocorrelation histograms of cells A, E and I (panel d) and crosscorrelation histograms of the cells (A,E), (A,I) and (E,I) for $\lambda^- = 20$ ev/s (panel e). Firing rate of cell A as a function of λ^- (panel f) and excitatory efficiency as a function of λ^- (panel g).



Analysis of model when the excitatory interspike intervals are T^{NET} distributed. ISIs histograms of cell A for $\lambda^- = 10$ (panel a), $\lambda^- = 20$ (panel b) and $\lambda^- = 30$ ev/s (panel c). Autocorrelation histograms of cells A, E and I (panel d) and crosscorrelation histograms of the cells (A,E), (A,I) and (E,I) for $\lambda^- = 20$ ev/s (panel e). Firing rate of cell A as a function of λ^- (panel f) and excitatory efficiency as a function of λ^- (panel g).

Jump-diffusion network

- Positive :
  - Allow to qualitatively recover (and hence "explain") some observed phenomena:
    - Multimodal behaviour in absence of periodic input
    - Role of inhibition that increases excitation efficiency
    - Synchronization
    - Stochastic like resonance (role of noise)
- Negative
  - No analytic or numeric approach (except for perfect integrator model)
  - Long simulation times
  - Large networks request too long computational times
  - Time series simulation request to follow the entire history of the involved neurons: one can deal network of more than 3 units but not larger ones
  - Statistical estimators request further studies

Further approaches toward large networks

- Use of Copulae should be investigated
- Mean field studies using LIF models
- Object oriented networks using LIF models

- ..... UP TO YOU!!!!

Integral equation for perfect integrate model

$$\tilde{g}(S,t\,|\,x_0) = e^{-\gamma t} g(S,t\,|\,x_0) + \lambda_E \int_0^t du\, e^{-\gamma u} \int_{-\infty}^{S-e} dz\, f_a(z,u\,|\,x_0)\, \tilde{g}(S,t\,|\,z+e,u)$$

$$+\lambda_I \int_0^t du\, e^{-\gamma u} \int_{-\infty}^{S} dz\, f_a(z,u\,|\,x_0)\, \tilde{g}(S,t\,|\,z-e,u) + \lambda e^{-\gamma t} \int_{S-e}^{S} dz\, f_a(z,t\,|\,x_0)$$

$\tilde{g}(S,t\,|\,x_0)$: $\frac{\partial}{\partial t}\mathbb{P}\{T \le t\}$

f_a: Wiener process transition PDF with absorbing boundary

$\gamma = \lambda_E + \lambda_I$

Holds if the parameters values avoid the occurrence of multiple jumps before the mean spike time of the diffusion

Diffusion parameters:
- Small $\sigma_D^2 (\cong 10^{-1} mV^2 ms^{-1})$*
- Large $\mu_D (\cong 1\, mV ms^{-1})$*

Jump process parameters:
- Small $\lambda, \omega (\cong 10^{-2} ms^{-1})$*
- Large $e (\cong 5 \div 9\, mV)$*

$*\ if\ S = 10$

Approximate formula for perfect integrate model

$$\tilde{g}_{app}(S,t\,|\,x_0) \approx \underbrace{e^{-\gamma t} g(S,t\,|\,x_0)} + \lambda_E \underbrace{e^{-\gamma t} g(S-e,t\,|\,x_0) \int_0^t du\, e^{-\gamma u} \int_{-\infty}^{S-e} dz\, f_a(z,u\,|\,x_0)}$$

$$+\lambda_I \underbrace{e^{-\gamma t} g(S+e,t\,|\,x_0) \int_0^t du\, e^{-\gamma u} \int_{-\infty}^{S} dz\, f_a(z,u\,|\,x_0)} + \lambda \underbrace{e^{-\gamma t} \int_{S-e}^{S} dz\, f_a(z,t\,|\,x_0)}$$

(Giraudo2008)

The single terms account for crossings happening:

1. Before the first jump
2. After the first excitatory jump
3. After the first inhibitory jump
4. In the instant when an excitatory jump occurs

(2 and 3: For diffusion)

The relative maxima correspond to the modes of the densities

$$g(S-e,t\,|\,x_0),\ g(S,t\,|\,x_0),\ g(S+e,t\,|\,x_0)$$