Single Neuron Models: some ideas on the role of noise

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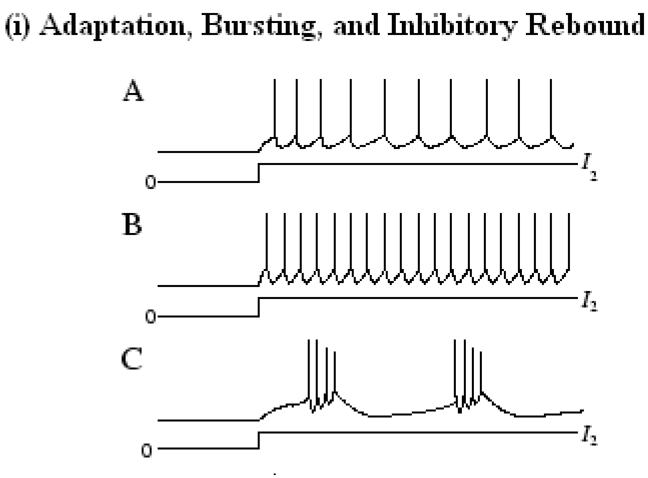
Summary

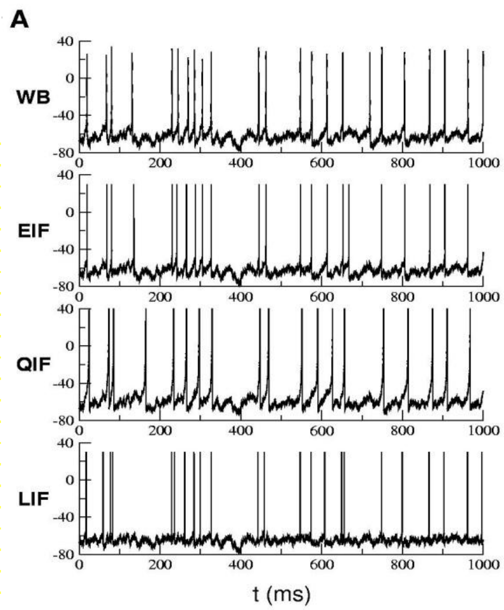
State of Art:

Single Neuron models : with and without noise

- Lapique model
- Cable Model
- Hodgkin and Huxley, Fitzhugh Nagumo, Moris Lecar Models
- Leaky Integrate and Fire Models

Spike trains

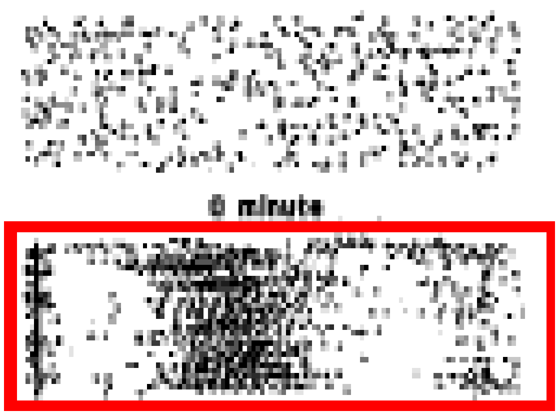




4 recordings

- Use of different scales disclose different properties.
- Using the raster displays one can observe <u>spatio-temporal patterns</u>
- Simultaneos recording show <u>synchronization periods, delays</u>,…

Synchronization in the presence of noise??



Raster display

Models: should work at different scales

Noise

The ISI time series measured in experiments contain a high level of noise. Although research work shows that noise may play

- a **positive role** in detection of a weak signal for sensory neurons,
- it is a **nuisance** for analysis of irregular ISI data using traditional chaotic time series methods

Noise can both hide deterministic dynamics underlying the ISI signals and help the arising of "deterministic" dynamics

Role of Noise

Noise is unavoidable in any living system

- **experimental results**, supported by theoretical investigations, show the prominent role of noise in the transfer of information in neural systems (Moss et al., 1993; Wiesenfeld and Moss, 1995; Cecchi et al., 2000)
- **enhancement** of the signal by noise for subthreshold stimulation (Segundo et al., 1994;),
- **resonant behavior in phase-locking periodic signal** (Hangi, Bulsara et al., 1996; ; Plesser and Tanaka, 1997; Shimokawa et al., 1999) and linearization of the signal transfer function by noise (Yu and Lewis, 1989).

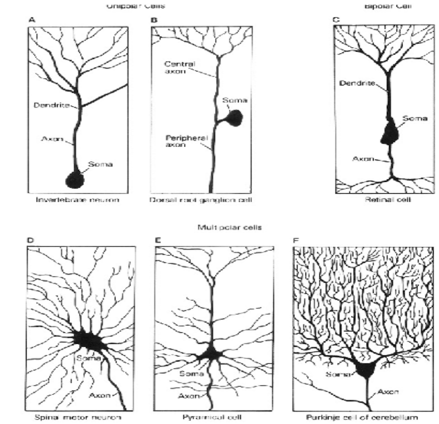
Mathematical models: milestones

- Lapique Model (1907)
- Biophysical models: Hodgkin and Huxley (1952) and its variants
- Till seventies: a golden period. **Illusion to be proximal to "understand" the laws of the brain and the mind.**
- Till Eighties: main focus on single neuron activity models
- Ninties: a crisis period. **Lack of mathematical results to support further improvements and slow entrance of computer science methods** (simulations numerics). Only specific results
- ...new millenium: a new golden age? High speed computers and new techniques for simultaneous recording from groups of neurons open new challenges: powerful simulation... **but also good mathematics .**

Single neuron and their models

Focus on the role of noise

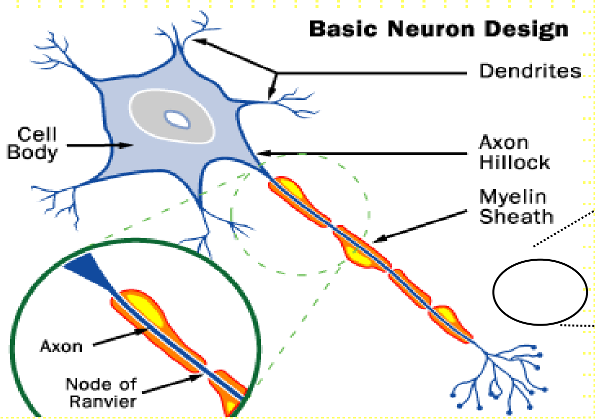
Single Neuron and noise

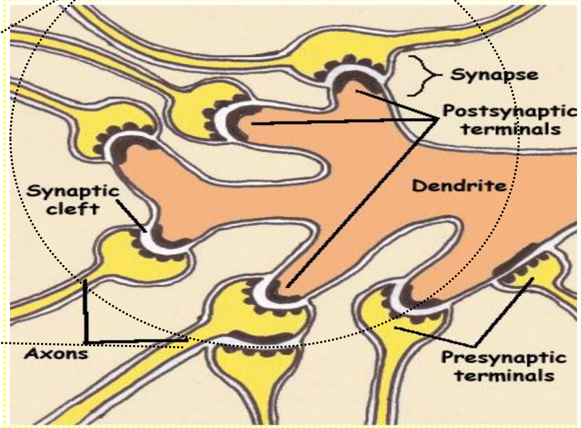


Three functionally distinct parts: dendrites, soma and axon

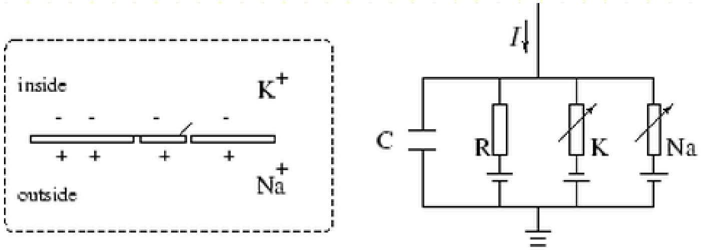
- dendrites: input device collecting signals
- soma: central processing unit (nonlinear)
- axon: output device

Junction between two neurons: synapses (presynaptic, postsynaptic): **chemical** neurotransmitter (receptors in postsynaptic membrane; electrical)





Single neuron: Biophysical nonlinear models



Schematic diagram for the Hodgkin-Huxley model

2b. **Hodgkin and Huxley type models**

4 coupled deterministic non linear

differential equations : the voltage varies as a function of the openings and closing of voltage-dependent channels of sodium and potassium and the conductances change with the voltage

$$I(t) = I_C(t) + \sum_k I_k(t)$$

$$C \frac{du}{dt} = -\sum_k I_k(t) + I(t)$$

$C = Q/u$ where Q is a charge and u the voltage across the capacitor.

$$\dot{m} = \alpha_m(u)\,(1-m) - \beta_m(u)\,m$$

$$\dot{n} = \alpha_n(u)\,(1-n) - \beta_n(u)\,n$$

$$\dot{h} = \alpha_h(u)\,(1-h) - \beta_h(u)\,h$$

$$\sum_k I_k = g_{Na}\, m^3 h\,(u - E_{Na}) + g_K\, n^4\,(u - E_K) + g_L\,(u - E_L).$$

Contain a set of parameters that should be estimated

Features of nonlinear models: bifurcations, stable cycles,….

NON LINEAR ITY DOMINATE POSSIBLE DYNAMICS

Single neuron: Biophysical nonlinear models

2c. **Fitzhugh Nagumo Models** (FHN):

$$dv = \frac{1}{\varepsilon}\left(v - v^3 + w\right)dt,$$
$$dw = (a - v)dt.$$

ν: voltage
ω: conductance
a: fixed point

- Mathematical study: using methods of non linear analysis
- FHN spatial models with noise have been studied

(H. C. Tuckwell. Random perturbations of the reduced FitzHugh-Nagumo equation. *Physica Scripta*, 46(6):481–484, 1992. H. C. Tuckwell. Analytical and simulation results for the stochastic spatial FitzHugh-Nagumo model neuron. *Neural Computation*, 20(12):3003–3033, 2008).

2d. **Moris Lecar Model** (ML) Like the FHN, the ML has two differential equations, which tell how the interrelated voltage and conductance evolve.

- The FHN structure: directly from a stable limit point to a limit cycle via a singular Hopf bifurcation (with unstable limit point), the ML has an intermediate range: there are both a stable fixed point and a stable limit cycle
- Moris Lecar models can be related with LIF models

(S. Ditlevsen and P. E. Greenwood, "The Morris-Lecar neuron model embeds a leaky integrate-and-fire model," arXiv 1108.0073, 2011; P.E. Greenwood A Stochastic Dynamics Viewpoint of Some Neuron Models, preprint)

Model with noise

Causes of noise:

- Synaptic noise
- fluctuations of the mean number of open ion channels around the corresponding mean values

Collective properties of ion channel are affected by internal noise stemming from the stochastic dynamics of individual ion channels

There exists an optimal size of the membrane patch for which the internal noise alone causes a regular spontaneous generation of action potentials

Living organisms may adapt the densities of ion channels in order to optimally regulate the spontaneous spiking activity

MODELS WITH NOISE:

HH with noise: **study through simulation technique**

FN with noise: analytical and simulation methods

ML with noise: analytical and simulation methods

G. Schmid, I. Goychuk and P. Hanggi Effect of channel block on the spiking activity of excitable membranes in a stochastic Hodgkin-Huxley model *Physical Biology 2007*

Non linear models

Common feature of HH, FN, ML models: involve systems of partial differential equations involving spatial diffusion

FN with noise:

$$u_t = D_1 u_{xx} + \kappa u(u-a)(1-u) - \lambda v + I(x,t)$$
$$v_t = D_2 v_{xx} + \epsilon'[u - pv + b],$$

$$\mathrm{Cov}[w(x,s), w(y,t)] = \delta(x-y)\delta(s-t).$$

I(x,t)=σ(x)W(x,t): two parameter Wiener process

H. Tuckwell Analytical and Simulation Results for the Stochastic Spatial Fitzhugh-Nagumo Model Neuron *Neural Computation* **20, 3003–3033** (2008)

Uniform noise of even a small amplitude may **interfere with propagation**

- disturbing wave passage
- by instigating secondary waves or other nonlocal responses
- In the trigger zone the transmission process is less easily disrupted

FN spatial model

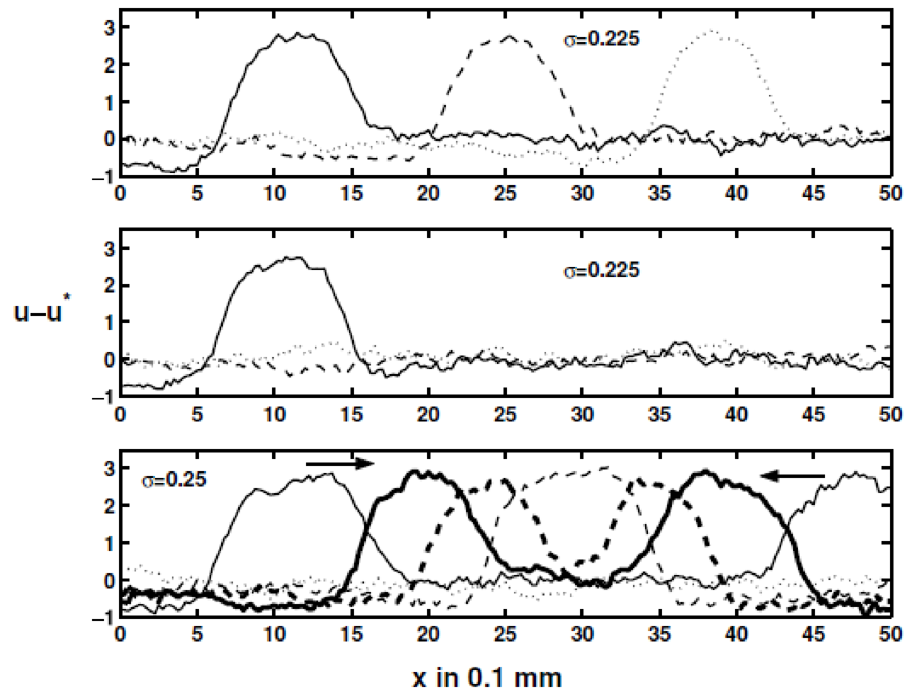


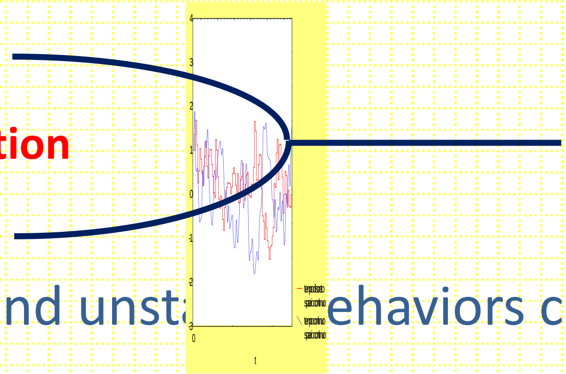
Figure 2: Simulated solutions of the FN system with original parameters as in equations 2.3 and 2.4 for larger (uniform) noise amplitudes. $u - u^*$ is plotted versus distance at 0.75 msec (solid line), 1.5 msec (dashed line), and 2.25 msec (dotted line). In the top two examples, $\sigma = 0.225$, whereas in the bottom figure, $\sigma = 0.25$. For $\sigma = 0.25$, $u - u^*$ is also shown for 1.1 msec (thick solid line) and 1.3 msec (thick dashed line) illustrating the annihilation of the original wave by a left-going noise-induced wave.

Noise in non-linear biophysical models

- Non-linear systems- no noise : fixed point, limit cycle, bifurcations,….
- Non-linear systems- with noise:
  - fixed point may become limit cycles;
  - The system exhibits limit cycles even when the deterministic system does not

Example: pitchfork bifurcation can be destroyed by noise

A small noise destroys a pitchfork bifurcation



Relationships between stable and unst[illegible]ehaviors change

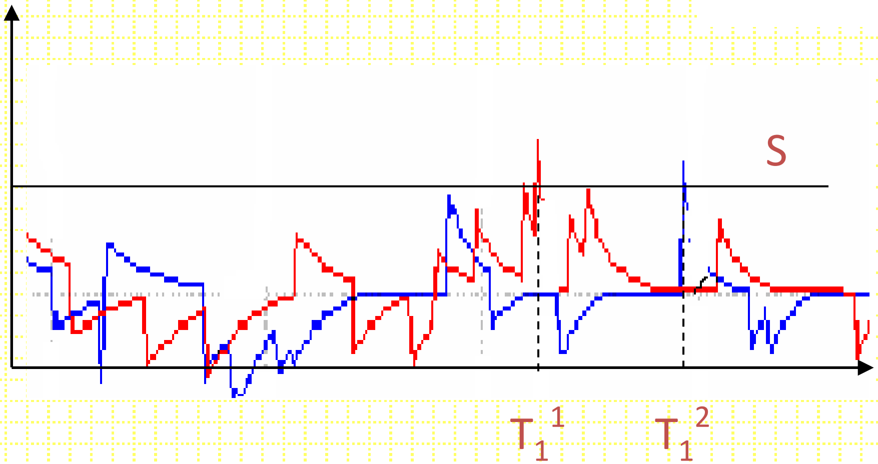
HH , FN, ML models with noise are too complex for an analytical study

Alternative stochastic models

Single Neuron: stochastic threshold models

3. **Stein model** (Stein 1965)

$$dV(t) = -\frac{V(t)}{\theta} + e\,dN_E(t) + i\,dN_I(t)$$



T= inf {t: X_t>S}

After each spike the membrane potential is reset to V_0:
Renewal process

4. **Diffusion approximation**

$e_n \to 0 \quad i_n \to 0 \quad \lambda_n^E \to \infty \quad \lambda_n^I \to \infty$

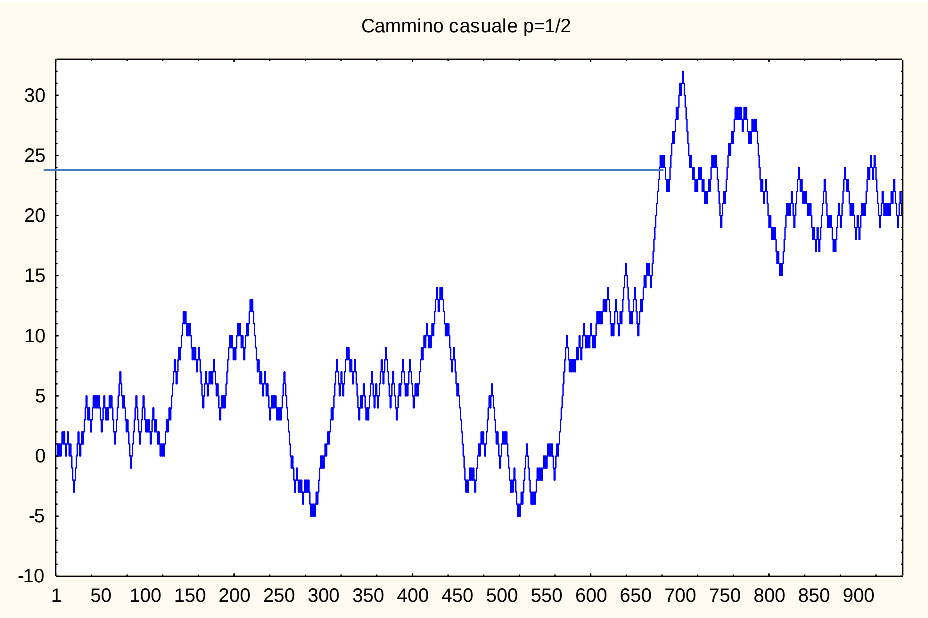
in such a way to get:

$\mu_n = e_n \lambda_n^E + i_n \lambda_n^I \to \mu < +\infty$
$\sigma_n^2 = e_n^2 \lambda_n^E + i_n^2 \lambda_n^I \to \sigma^2 < +\infty$

Single neuron: LIF models

LIF: Leaky Integrate and Fire

$$dV(t) = -\frac{V(t)}{\theta} + e\,dN_E(t) + i\,dN_I(t)$$



Diffusion limit

- Convergence Kolmogorov eq.
  - Roy Smith, 1969
  - Capocelli Ricciardi, 1971
  - Tuckwell Cope, 1980
- Weak convergence
  - Lansky 1984
  - Lansky Lanska 1987
  - Kallianpur Wolpert, 1987

$$\begin{aligned} dV_t &= \left(-\frac{V_t}{\theta} + \mu\right) dt + \sigma dW_t \\ V_0 &= 0 \end{aligned}$$

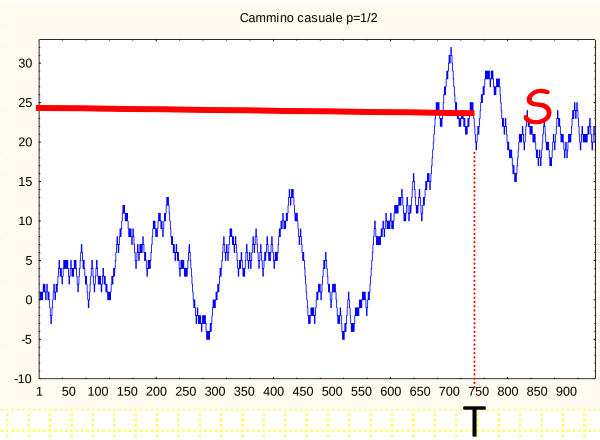
Ornstein-Uhlenbeck process

ISIs in LIF models

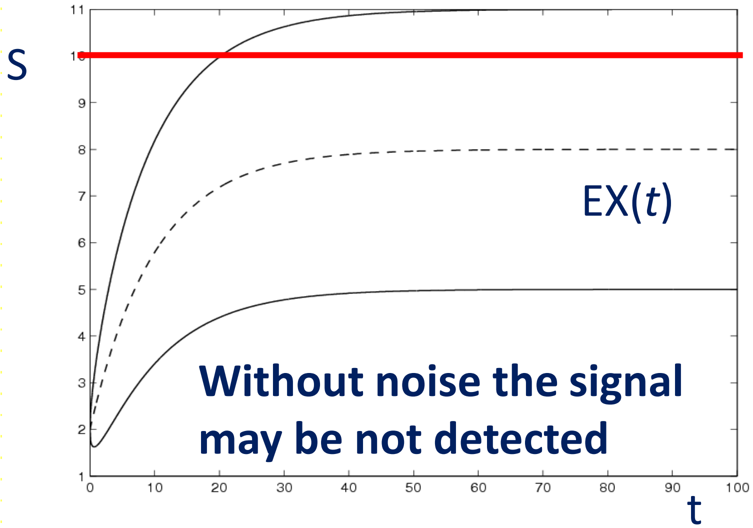
- Renewal hypothesis (relaxed in 2-compartment models)
- ISI are i.i.d random variables corresponding to first passage time through a boundary
- Distribution
  - Closed form expression: only for the perfect integrator
  - Numerical and simulation methods available

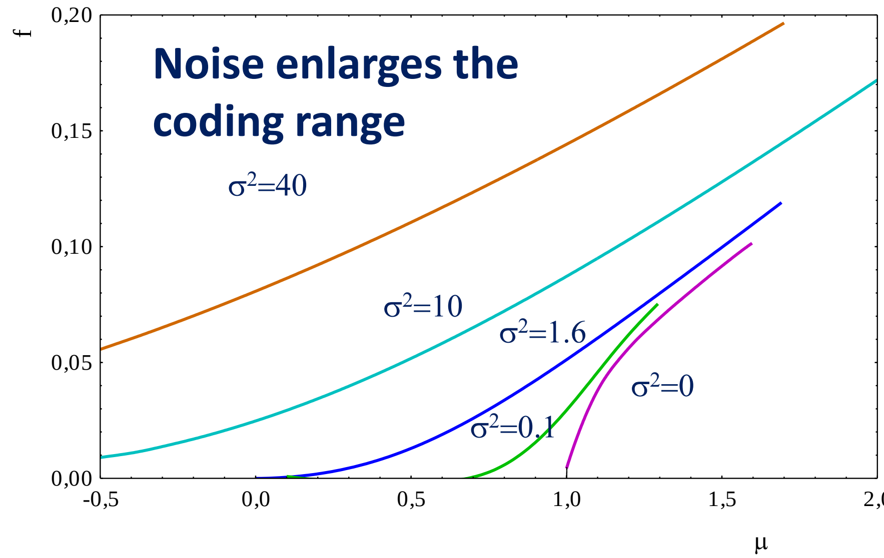
$$f(x,t\,|x_0,t_0) = \int g(S(\tau),\tau\,|x_0,t_0)\, f(x,t\,|S(\tau),\tau)\, d\tau \quad x > S(t)$$

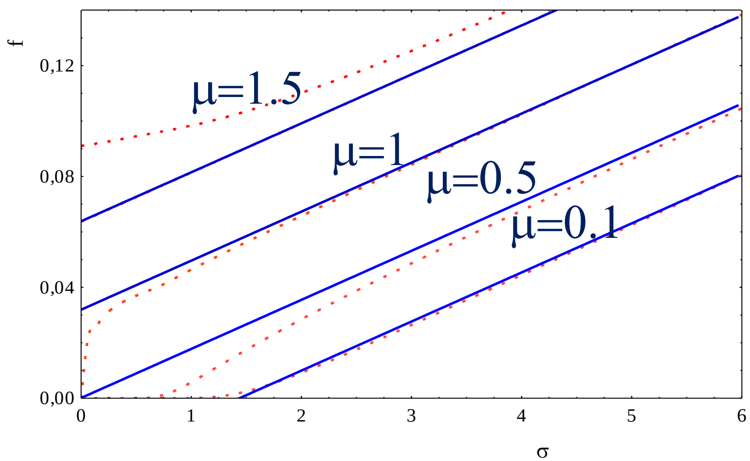
$$\begin{aligned} T &= \inf\{t>0 : V_t > S(t)\} \\ f(x,t\,|x_0,t_0) &= \frac{\partial}{\partial x} P(V_t < x\,|V_{t_0} = x_0) \\ g(S(t),t\,|x_0,t_0) &= \frac{d(T < t\,|V_{t_0} = x_0)}{dt} \end{aligned}$$



Noise and LIF models







Increasing σ linearizes the transfer function

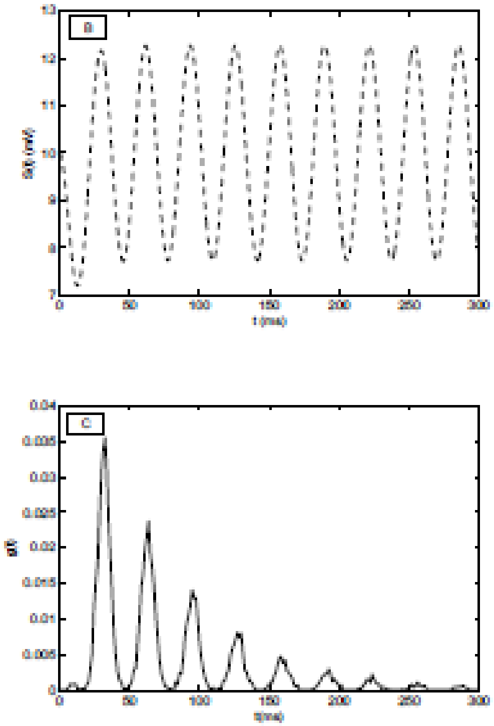
Transfer function: $f(\mu)=1/ET$.

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

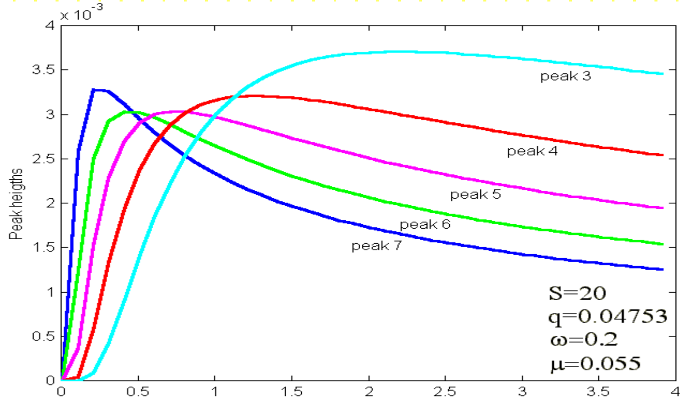
Stochastic resonance in LIF models

Diffusion models with deterministic periodic stimulation.

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



Phase locking



Peak heights go through maxima as function of the noise

LIF models: Questions

- **ISIs in a spike train can be assumed independent?**
- **How to test independence between ISIs?**
- **What information on the network geometry fron raster displays?**

    - Alternative models? **LIF Multicompartment models**

- **How to test the presence of dependencies between two spike trains?**

    – Parametric versus non-parametric tests

D. Brillinger (1976) Measuring the Association of Point Processes: A Case History. The American Mathematical Monthly, Vol. 83, No. 1 (Jan., 1976), pp. 16-22Published

M.S. Masud R. Borisyuk (2011) Statistical technique for analysing functional connectivity of multiple spike train Journal of Neurosciences Methods **196,** 201-219

L. Sacerdote, M. Tamborrino and C. Zucca (2011) Detecting dependencies between spike trains of pairs of neurons through copulas. Brain Research, Vol. 1434: 243-256.