Response of single neuronal models to uncorrelated and correlated stochastic inputs

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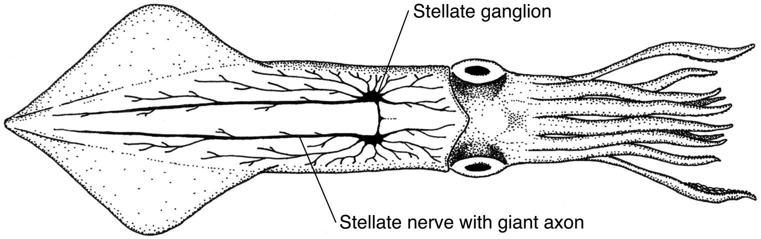

Main motivations

- A neuron in the brain cortex is subject to a continuous synaptic bombardament of inputs, resembling a background noise
  (A. Destexhe, M. Rudolph, D. Paré - Nature Reviews - Neuroscience - 2003)
- Inputs are mainly originating from the cortex itself, the statistical properties of the neural response (input) can be (roughly) summarized as
  - Frequency range $0 - 200$ Hz;
  - Distribution of interspike interval : approximately Poissonian;
  - Spike rate modulations ($5 - 10$ msec)

  (M.N. Shadlen & W.T. Newsome, J. Neuroscience - 1998)
- Neurons in the cortex, due to the high connectivity, can receive inputs from the same axon: correlation via common drive; correlations are important for information processing. (E. Salinas & T.J. Sejnowski, J. Neuroscience - 2000)

How do noise and correlated inputs influence the response of single neurons ?

Summary

- Brief introduction of the HH model
- Characterization of the stochastic stimulation protocol
- Analysis of the neuronal responses for different noise levels
- Looking for coherence in the neuronal response
- Influence of correlations on the coherent response
- Conclusions

The Hodgkin-Huxley model

Hodgkin

The HH model reproduces the time evolution of the membrane potential and of the ionic currents measured experimentally for a giant squid axon.

Huxley

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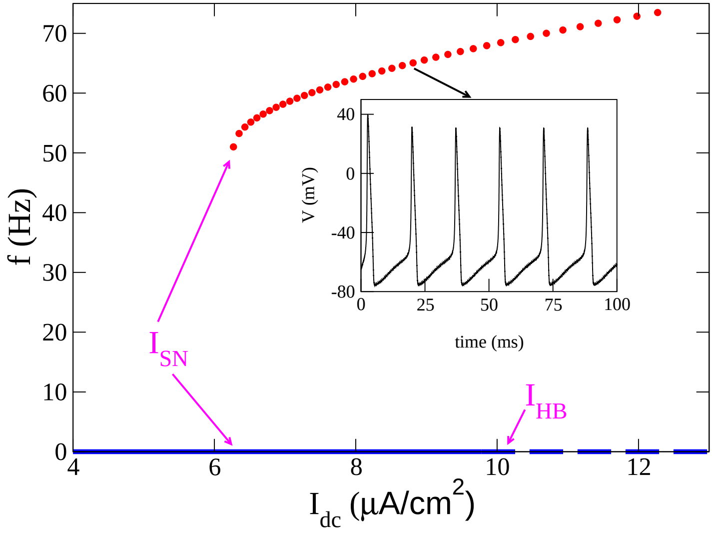

$C = 1\mu F/cm^2$ - Membrane capacitance

V - Membrane Potential (mV)

I_j - Ionic channel currents ($\mu A/cm^2$)

g_j - Maximal ionic conductances (mS/cm^2)

V_j - Ionic reversal potentials (mV)

$$C\dot{V} = \sum_j I_j + I_{syn} = -g_{Na}m^3h(V - V_{Na}) - g_K n^4(V - V_K) - g_L(V - V_L) + I_{syn}$$

$$\dot{x} = \alpha_x - x(\alpha_x + \beta_x) \qquad x = n, m, h \qquad \text{gating} \quad \text{variables}$$

$\alpha_x = \alpha_x(V)$ and $\beta_x = \beta_x(V)$ are highly nonlinear functions.

High-input regime

- Instead of a constant current I_{dc}, we consider N_E excitatory (EPSP) and N_I inhibitory postsynaptic inputs (IPSP), each corresponding to a voltage kick $\Delta V = 0.5$ mV.

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- This amounts to one excitatory (resp. inhibitory) Poissonian spike train with frequency $\nu_E = N_e \times \nu \sim 10^4 - 10^5$ Hz (resp. $\nu_I = N_I \times \nu$) for $N_e \sim N_I \sim 100 - 1,000$.

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For these frequencies the net input spike count within a temporal window ΔT (≥ 1 msec) is essentially Gaussian distributed and it can be characterized by

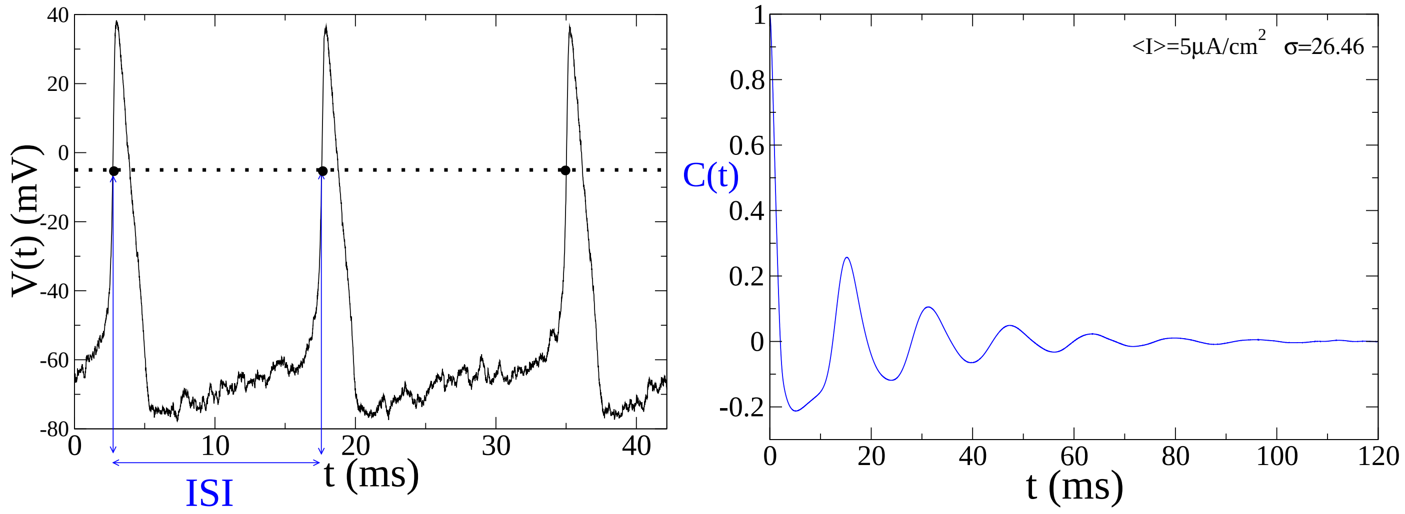
$$\text{average} \qquad \mu = \nu(N_E - N_I)\Delta T \qquad ; \quad \text{variance} \qquad V = \nu(N_E + N_I)\Delta T = \nu\sigma^2\Delta T$$

The response of the neuron is examined for fixed average input current

$$\bar{I} = C\Delta V \nu(N_E - N_I)$$

by varying only the standard deviation of the noise σ

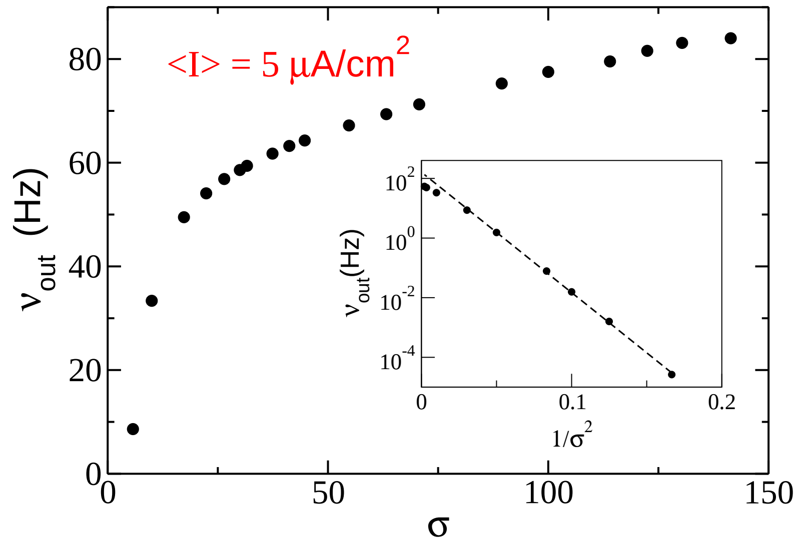
Statistical and dynamical indicators

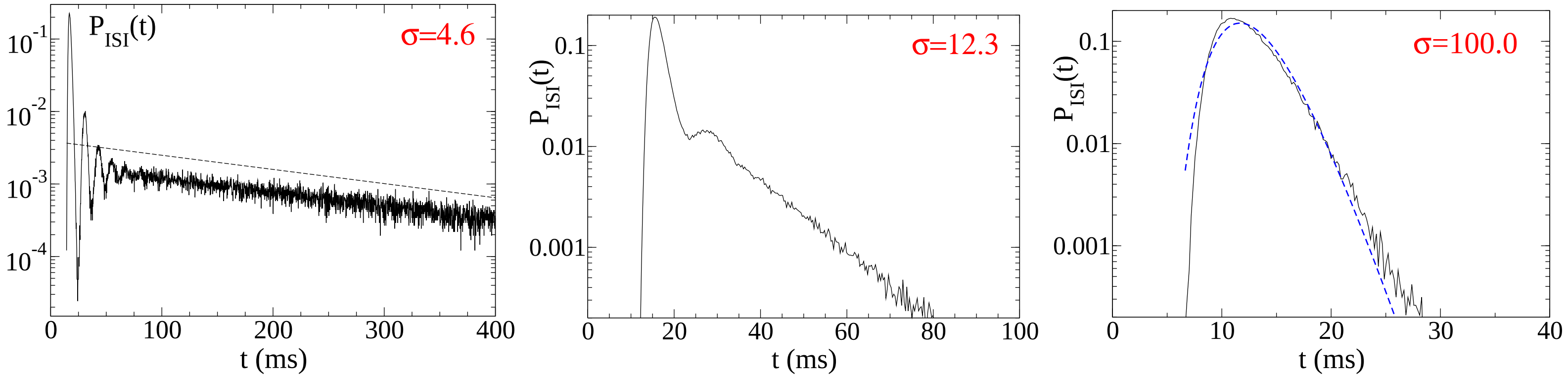


- ISI distribution → $P_{ISI}(t)$;
- $CV = \frac{Std(ISI)}{\langle ISI \rangle}$ → coefficient of variation of the ISIs:
  Poissonian distribution → $CV = 1$
  regular sequence → $CV = 0$;
- $\tau_c = \int_0^\infty C^2(t)dt$ → correlation time,
  $C(\tau) = \frac{\langle V(t+\tau)V(t)\rangle - \langle V \rangle^2}{\langle V^2 \rangle - \langle V \rangle^2}$

Response of the silent neuron

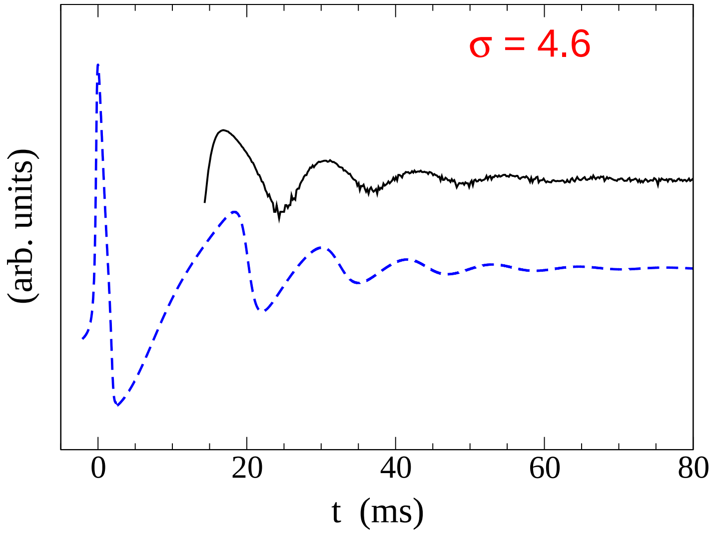
The HH neuron is in the silent state, i.e. the average input current $\bar{I}$ is smaller than I_{SN}.

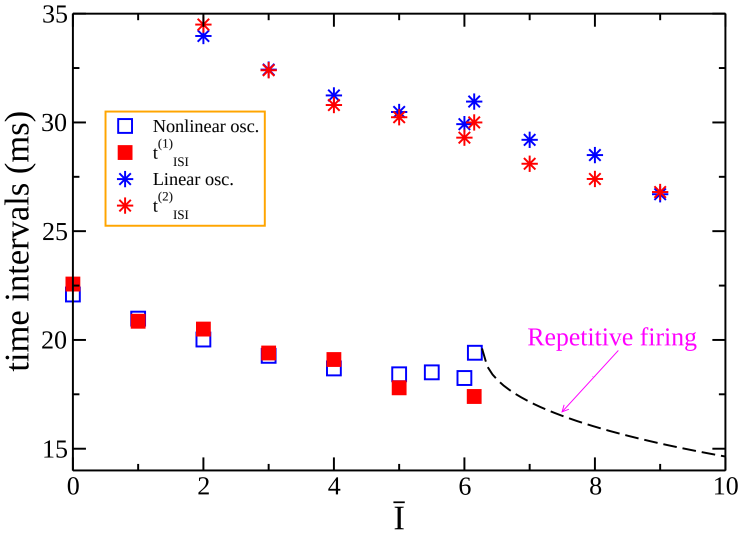




Response of the silent neuron

Spikes triggered by relaxation oscillations





The neuronal spiking is enhanced in correspondence of the maxima of the relaxation oscillations following a spike emission.

The first oscillation has a nonlinear origin, while the period of the subsequent ones can be obtained via a linear analysis around the stable fixed point solution (focus).

Response of the silent neuron

Firing activated by noise

Two mechanisms compete:

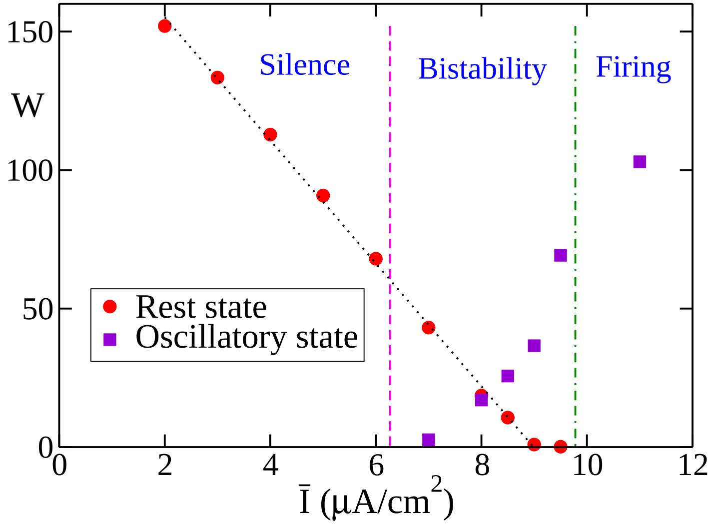
- the HH dynamics tends to relax towards the rest state;
- noise fluctuations lead the system towards an excitation threshold.

The dynamics of $V(t)$ resembles the overdamped dynamics of a particle in a potential well under the influence of thermal fluctuations, and the firing times can be expressed in terms of the Kramers expression (for sufficiently small noise)

$$t_a \propto \mathrm{e}^{W_S/\sigma^2}$$

the time distribution is Poissonian ($CV = 1$).

- for $\sigma < \sqrt{W_S} \rightarrow$ Activation Process
- for $\sigma > \sqrt{W_S} \rightarrow$ Diffusive Dynamics



Response of the silent neuron

High noise limit

The effect of noise fluctuations on the neuron dynamics is twofold:

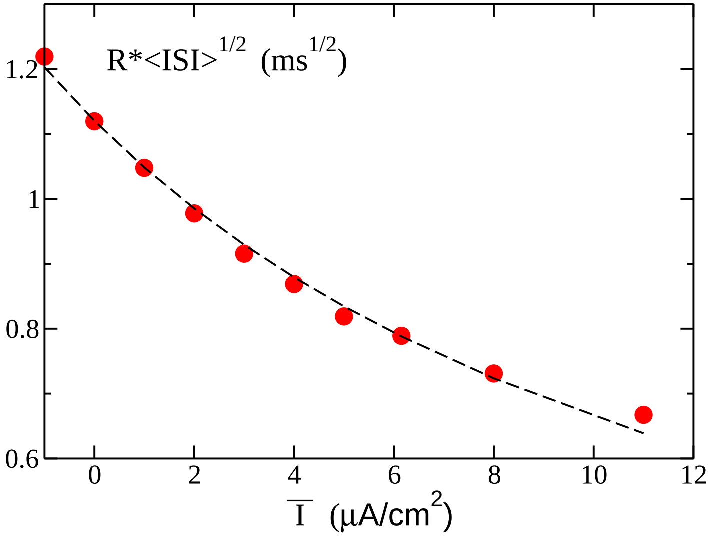
- a constant current $\bar{I}$ driving the system;
- a stochastic term with zero average.

The dynamics of $V(t)$ can therefore be described in terms of a Langevin process with a drift and the distribution of the first passage times is given by the inverse Gaussian distribution:

$$f(t) = \frac{\alpha}{\sqrt{2\pi\beta t^3}} \mathrm{e}^{-\frac{(t-\alpha)^2}{2\beta t}}$$

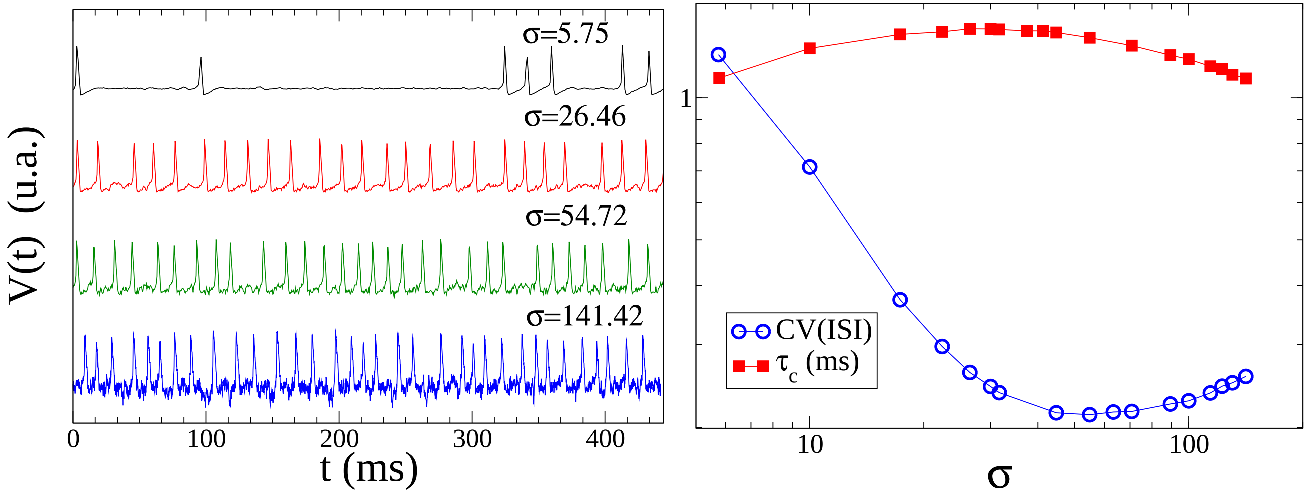
In this case the coefficient of variation should be given by

$$CV \propto \frac{\sigma}{(\bar{I}+I_0)\sqrt{<ISI>}}$$



Coherence resonance

Coherence of the emitted spike trains

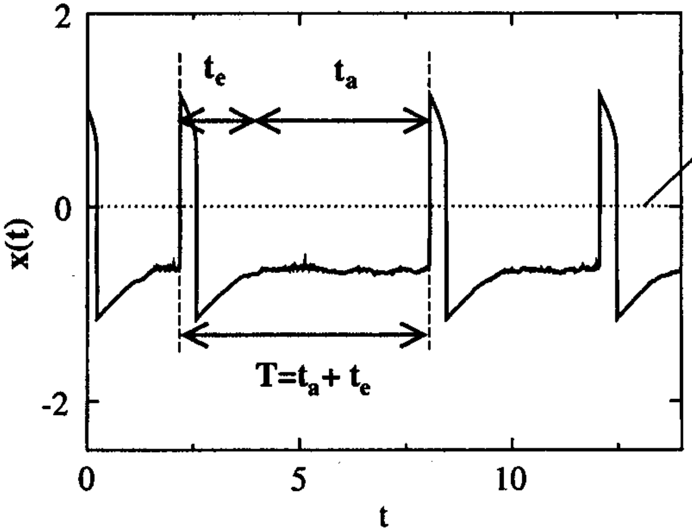


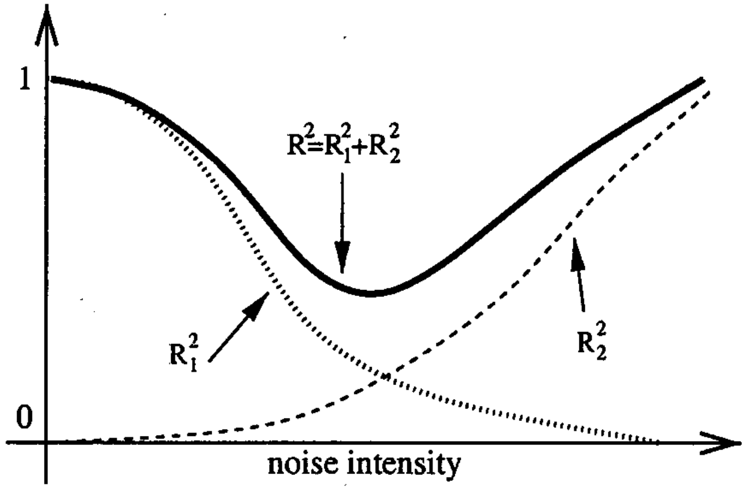
In the silent and bistable regime ($I < 8\mu$A/cm^2):

- by increasing σ the firing rate increases, the spike train becomes more regular (Activation Process);
- the maximal coherence is reached for a optimal σ-value;
- for higher noise amplitudes the noise influence even the duration of the single spike, the response becomes again more irregular (Brownian motion + drift).

A. Pikovsky & J. Kurths, PRL 78, 775 (1997)

Coherence resonance





- The system is characterized by two characteristic times → $ISI \equiv T = t_a + t_e$:
  - t_a=activation time → time needed to excite the system;
  - t_e=excursion time → duration of the spike (excited state).
- $CV(T)$ can be splitted in two contributions

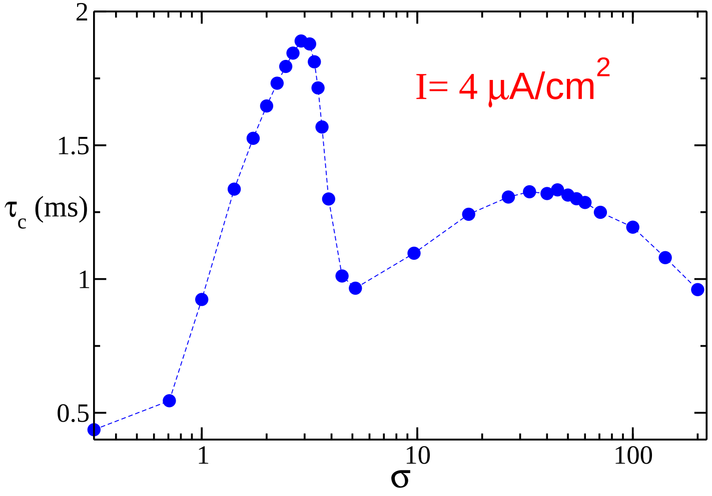
  $$CV(T)^2 = CV(t_a)^2 \frac{<t_a>^2}{<T>^2} + CV(t_e)^2 \frac{<t_e>^2}{<T>^2} = R_1^2(t_a) + R_2^2(t_e)$$

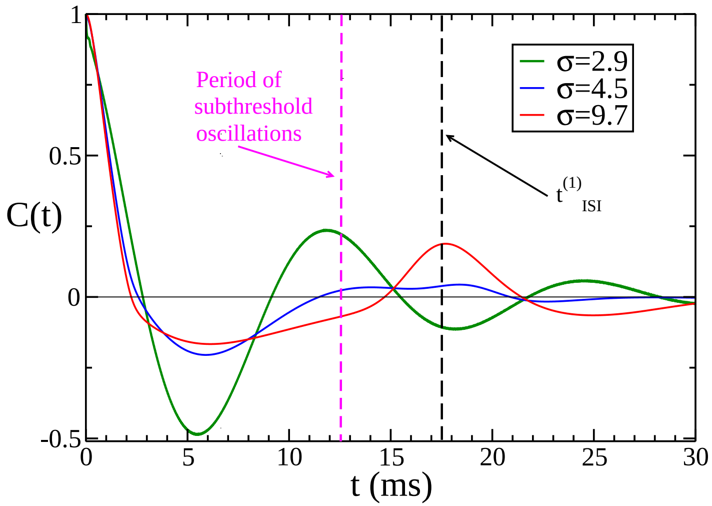
  $R_1^2(t_a)$ decreases with σ, while $R_2^2(t_e)$ increases → minimum in $CV(T)$

B. Lindner *et al.*, Phys Rep. 392 (2004) 321-424

Coherence resonance

Coherence of the subthreshold oscillations





A second coherence resonance is revealed by analyzing the correlations of the potential:

- for $\sigma < 3$ almost no spikes are emitted, but the increase of noise leads to more and more regular subthreshold oscillations;
- for $\sigma > 3$ the statistics of the emitted spikes is no more negligible and this decorrelates the signal;
- for $\sigma > 10$ the dynamics is dominated by sequences of spikes and a second peak occurs related to the regularization of the spike trains.

S. Luccioli. T. Kreuz, A.T. Phys. Rev. E (2006)

The FitzHugh-Nagumo Model

The FitzHugh-Nagumo (FHN) model is a two dimensional *"simplification"* of the HH model:

$$\dot{V} = \phi(V - \frac{V^3}{3} - W) \qquad ;$$

$$\dot{W} = V + a_0 - I(t)$$

where V is a voltage-like variable, W is a recovery variable and a is the bifurcation parameter.

For $\phi = 100$ the silent regime is observed for $a_0 < 1$, while at $a_0 > 1$ one has periodic firing.

$$I(t) = \Delta W_0 \left[\sum_{k=1}^{N_e} \sum_{l} \delta(t - t_k^l) - \sum_{m=1}^{N_i} \sum_{n} \delta(t - t_m^n) \right]$$

We examine the FHN model subject to N_E (resp. N_I) trains of excitatory (resp. inhibitory) post-synaptic potentials, in the balanced case (i.e. for $N_E = N_I \equiv N$) where $< I > \equiv 0$ for $a_0 = 1.05$ and $\Delta W_0 = 0.0014$.

Correlations via shared inputs

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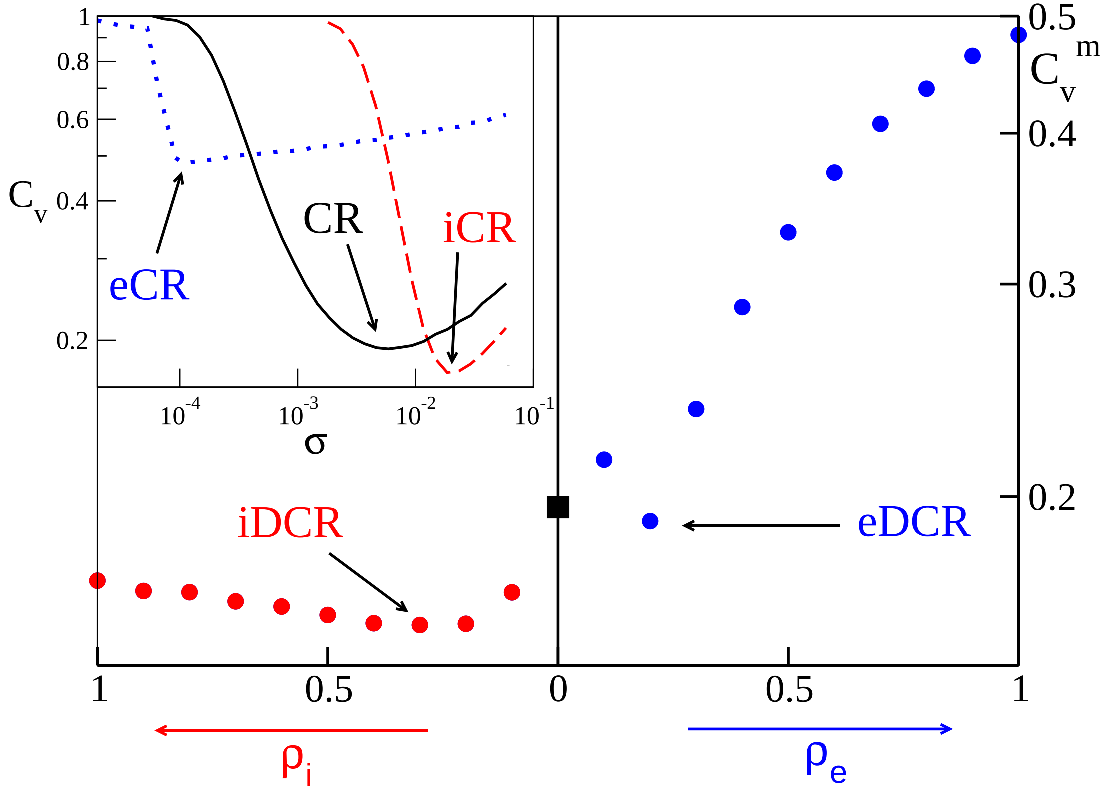
- The correlated inhibitory (resp. excitatory) inputs are large amplitude events delivered at a much lower rate $\nu_x << \nu_U$;
- The effect of the uncorrelated inputs lead to a renormalization of the bifurcation parameter: $\bar{a} = a_0 \pm (N\nu_0 \Delta W_0)$;
- The influence of correlated kicks is embodied in noise variance $\sigma^2 \simeq \rho_x \nu_0 N^2 \delta W_0^2$;

M.N. Shadlen & W.T. Newsome (1998) – E. Salinas & J. Sejnowski (2000)

Response to correlated inputs

We have studied the response of the (balanced $N_E = N_I$) Fitz-Hugh Nagumo model in the silent regime for excitatory (resp. inhibitory) correlated inputs by varying INDEPENDENTLY correlation ρ and noise variance σ^2.

- Coherence Resonance (CR) is observed for any excitatory (resp. inhibitory) level of correlation at finite noise amplitude.
- Double Coherence Resonance (DCR) : an absolute CR with respect to noise and correlation can be identified for excitatory (resp. inhibitory) correlated inputs.

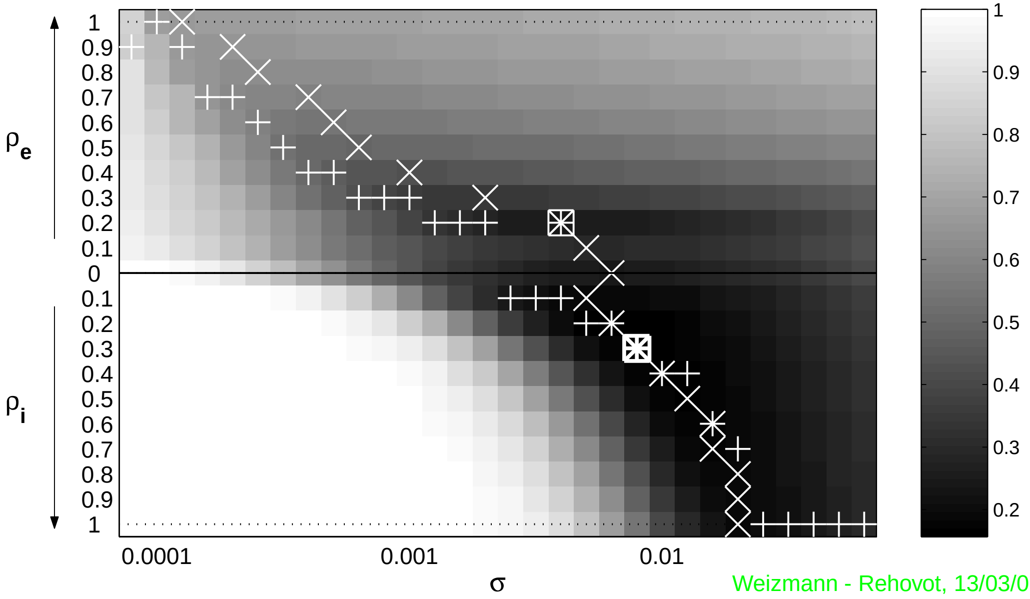


Response to correlated inputs

- CR has been usually observed for uncorrelated inputs with respect to noise intensity Hu Gang et al., PRL 71, 807 (1993) – A. Pikovsky & J. Kurths, PRL 78, 775 (1997)
- A second type of CR has been also observed with respect to the level of correlation :
  - lasers – Buldú et al, PRE (2001)
  - digital circuits – Brugioni et al., PRE (2005)
  - chemical reactions – Beato el al. PRE (2005)
  - neuronal models – Casado PLA (1997)
- The origin of the first CR has been fully explained, while for the the second CR this remains unclear.

A DCR with respect to correlation and noise intensity is a new phenomenon.

- X —> minima for fixed ρ
- $+$ —> minima for fixed σ

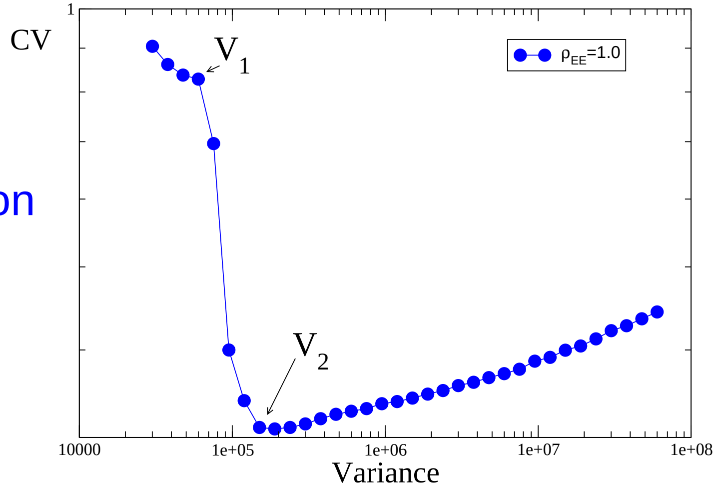


Response to correlated inputs

Strong excitatory correlation

The coherence phenomenon is now determined only by the kick amplitude and not by the properties of the asymptotic stochastic processes, since in the present case the output can be always described as a Poissonian process with a refractory time.

For increasing variance (N) the amplitude of the correlated kicks increases. and due to the uncorrelated (inhibitory) input the systems is more and more silent.



- for $Variance < V_1 \longrightarrow$ Activation Process
- for $V_1 < Variance < V_2$
  1 kick may be sufficient to induce a spike emission
- for $V_2 < Variance$
  One kick elicits always a spike - T_{ref} decreases

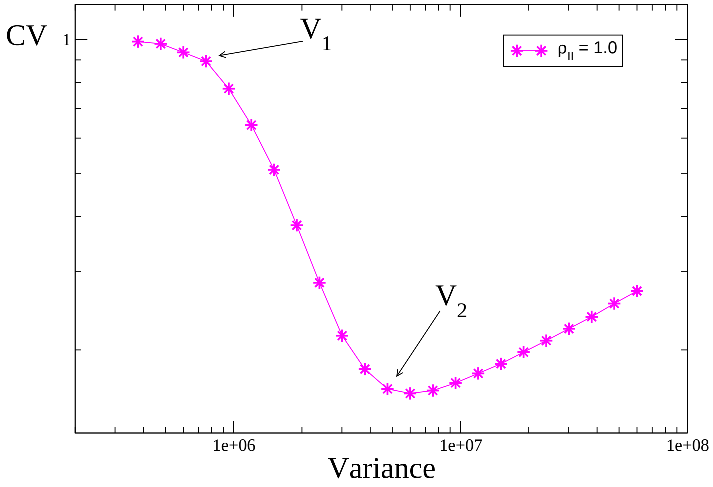
$$CV = \frac{T}{T + T_{ref}}$$

For $Variance > V_2 \rightarrow T = 1/\nu_0$, we have a $1:1$ synchronization between input and output (apart from the refractory period).

Response to correlated inputs

Strong inhibitory correlation

At large variances the dynamics is again ruled by the the amplitude of the correlated kicks, but at lower variances the inhibitory kicks are quite infrequent and their amplitude is not sufficient to influence the dynamics.



- for $Variance < V_1$
  Silent regime - Activation Process - $CV \simeq 1$
- for $V_1 < Variance < V_2$
  Dynamics dominated by uncorrelated excitatory input leading the system in the repetitive firing regime
- for $Variance > V_2$
  Each inhibitory kick induces a certain delay in the spike time of the neuron - A multimodal structure appears in the ISI distribution

Frequency of the correlated kicks (ν_0) $<<$ Frequency of the uncorrelated kicks ($N\nu_0$)

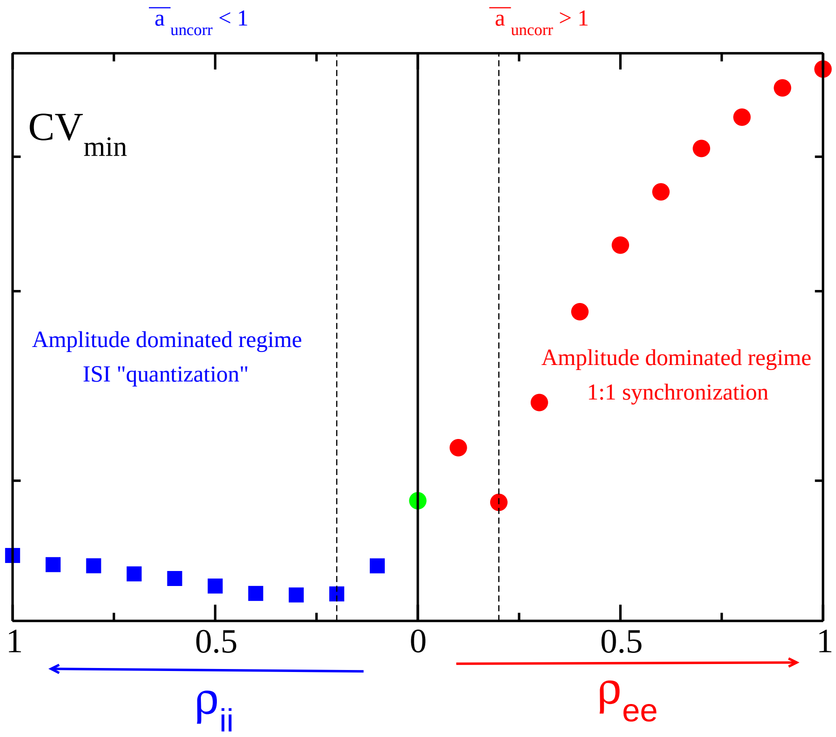
Response to correlated inputs

Maximal Coherence

Absolute minima of CV corresponding to maximal coherence are observed at finite noise and correlation for both inhibitory and excitatory case.

The extrema of CV_{min} indicate the change in the mechanisms inducing CR, from amplitude dominated to usual mechanisms related to the crossover from activated to (biased) diffusive processes.

The CV_{min} associated to inhibitory correlations are lower since the system is driven in the repetitive firing regime by the uncorrelated input.



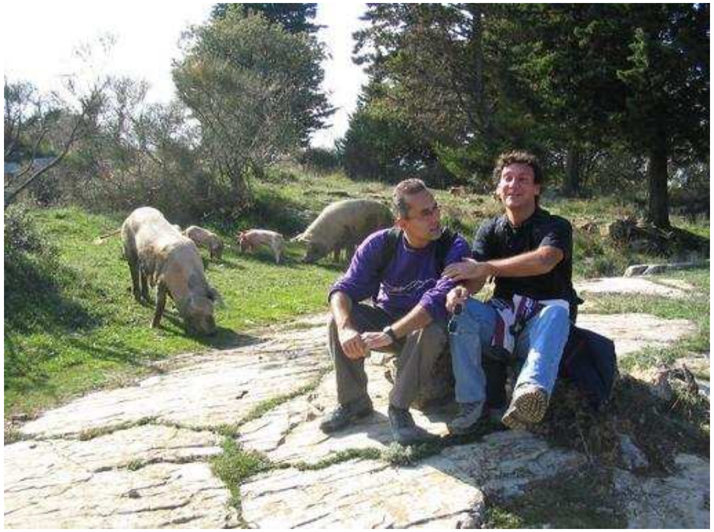
T. Kreuz, S. Luccioli & A.T. PRL (2006)

Conclusions

- Uncorrelated stochastic inputs
  - The response of a HH neuron depends only on the average and the variance of the input, at least in the high input regime;
  - at $I < I_{SN}$ the neuronal firing, induced by the stochastic inputs, can be expressed as an activation process at low variances (σ^2), while for large σ^2 this process becomes essentially diffusive;
  - at low noise, beside of the exponential tail, the ISI distributions reveal a multimodal structure due to spiking triggered by relaxation oscillations towards the rest state;
  - coherence resonance can be observed in a large interval of currents in the silent and bistable regime whenever $W_S > W_O$;
  - a second coherence resonance (associated to subthreshold oscillations) coexists with the usual one;
- Correlated stochastic inputs
  - new mechanisms for the coherence resonance have been reported at high excitatory and inhibitory correlations;
  - maximal coherence can be induced by an optimal combination of noise and correlation

Credits

- Stefano Luccioli - Msc in Physics (2004-2005)
- Dynamics of realistic single neuronal models



- Thomas Kreuz - Marie Curie Fellow (2005-2006)
- Dynamical Entropies in Assemblies of Neurons

http://www.fi.isc.cnr.it/users/alessandro.torcini/neurores.html