Corso di dottorato:
Modelli semplici di interesse biologico -
Dalle proteine ai neuroni

Neuroni:
Effetti di coerenza indotti dal rumore (Noise induced coherence resonance)

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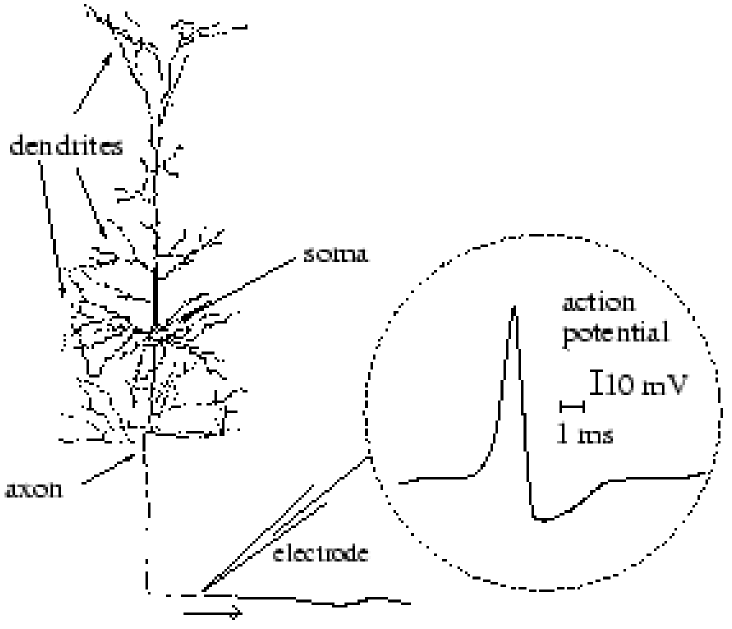
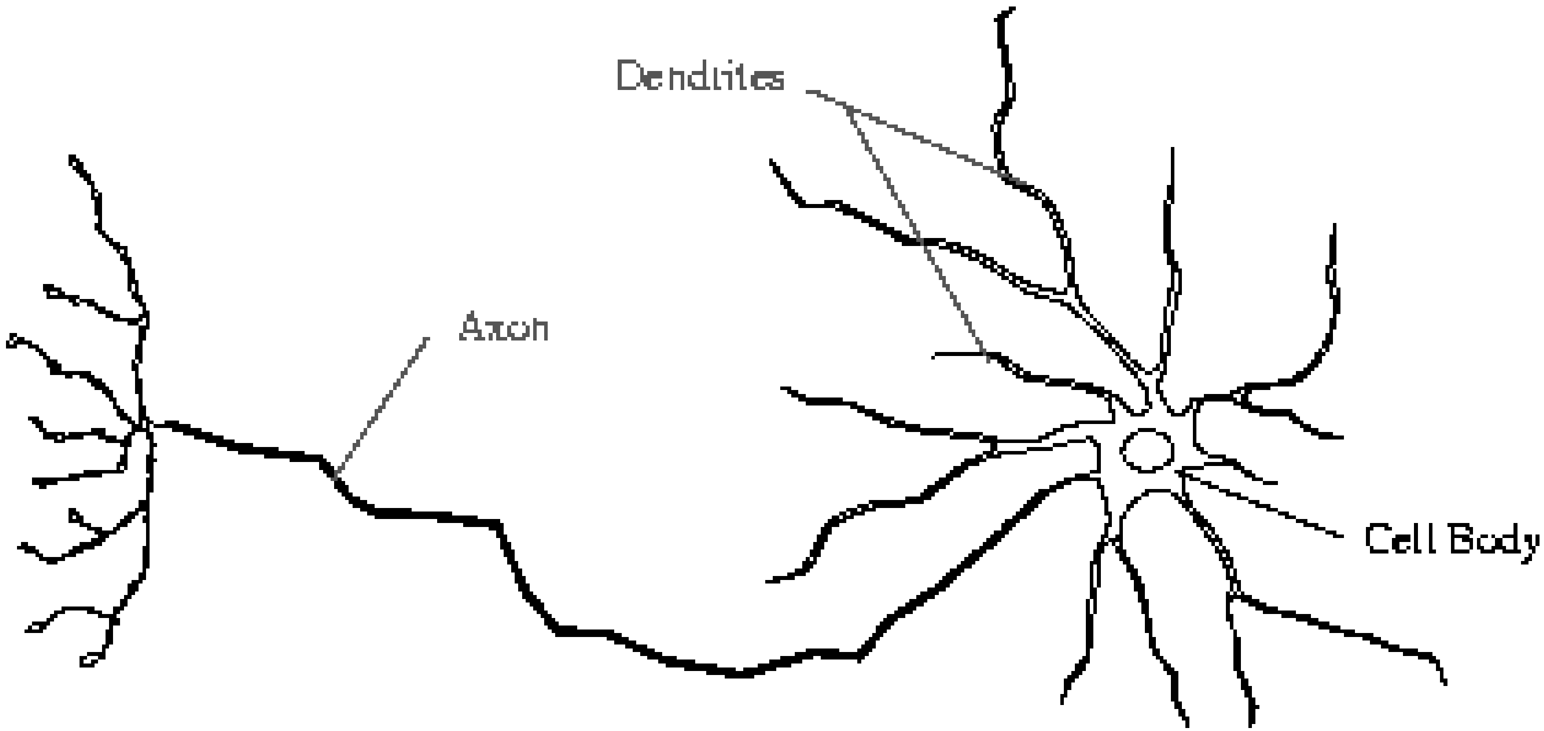
Content

- Repetition: **Information transfer** between neurons
- Simple models of **neuronal spiking**
  - Integrate and fire (IF)
  - Leaky integrate and fire (LIF)
- Characterization of **spike trains**
- **Coherence Resonance (CR)**
- CR with **correlated synaptic input**
  - FitzHugh-Nagumo (FHN)

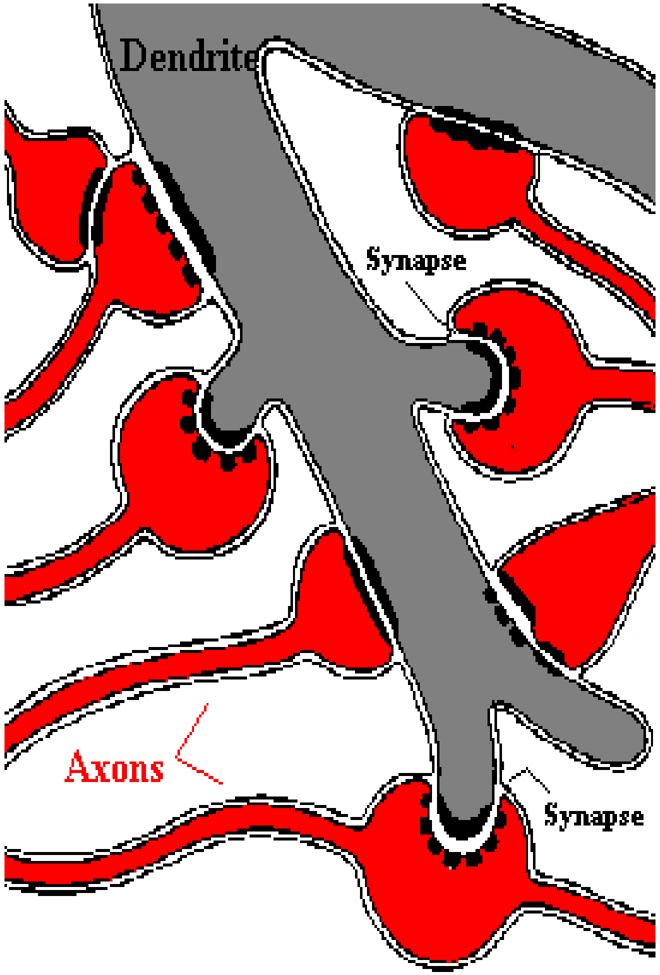


Morphology of neurons



- **Cell Body:** A globular compartment with a variety of organelles including the nucleus
- **Axon:** A cellular extension that projects to the dendrites of other neurons **(OUT)**
- **Dendrites:** Extend from the cell body and receive input from other neurons **(IN)**

Communication between neurons



Neurons communicate through **action potentials.** These are waves of electrical discharge that travel along the membrane of a cell.

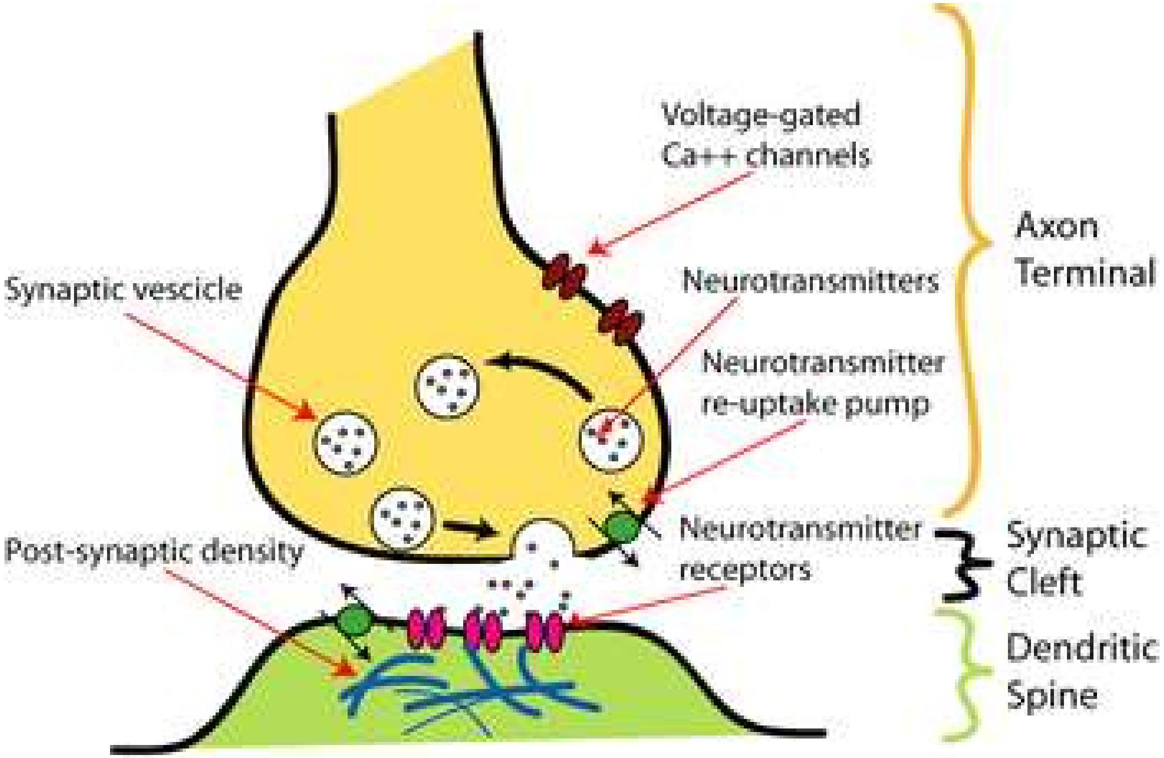
This signal is transferred from one neuron to the other via a **synapse**, where the axon terminal of one cell impinges upon a dendrite (typically).

Two types of synapses:

1. Electrical synapses
(direct conductive junctions between cells)

2. **Chemical synapses**
(communicate via neurotransmitters)

Chemical synapses



Three basic parts:

1. **Presynaptic ending**
   Contains neurotransmitters, mitochondria and other cell organelles
2. **Synaptic cleft**
   Space between the presynaptic and postsynaptic endings, ~20 nm
3. **Postsynaptic ending**
   Contains receptor sites for neurotransmitters.

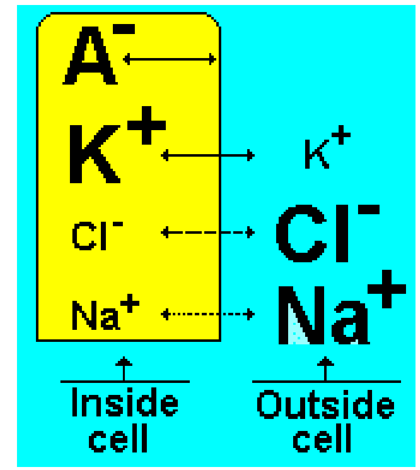
Action potential travel down the axon to the **presynaptic ending** where an electrical impulse (Ca++) triggers the migration of vesicles toward the presynaptic membrane. The vesicle fuses with the presynaptic membrane releasing neurotransmitters into the **synaptic cleft**. On the **postsynaptic ending** the neurotransmitter molecules bind with receptor sites to influence the membrane potential of the postsynaptic neuron.

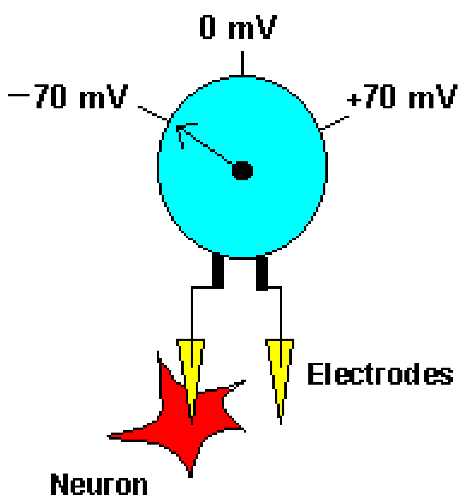
The membrane potential at rest

Semi-permeable membrane with selective **ion channels**

Important **ions**:

Sodium **Na +**, potassium **K+**, chloride **Cl -**, proteins **A-**





At rest (equilibrium) the inside is negative relative to the outside: The neuron is **polarized**.

More sodium ions outside and more potassium ions inside the neuron

The **resting membrane potential** of a neuron is about **-70 mV**.

The postsynaptic potential

Beyond the synaptic gap receptors respond by opening ion channels causing a change of the local membrane potential.

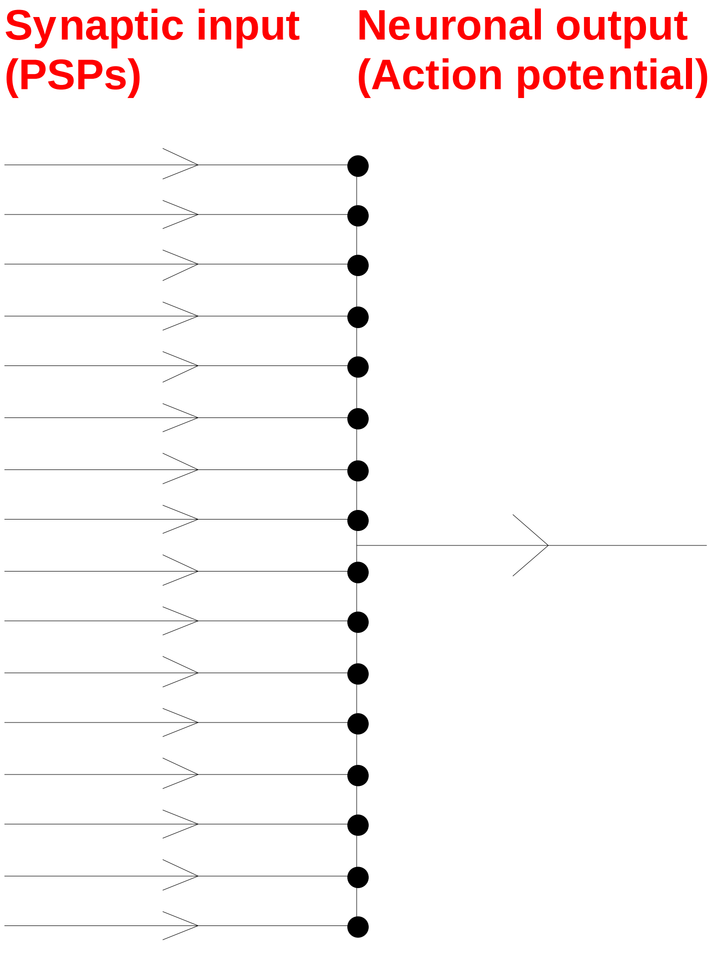
This is called a **postsynaptic potential (PSP)**.

PSPs change the postsynaptic cell's excitability:
It makes the postsynaptic cell either more or less likely to fire.

The result is **excitatory (EPSP)**, in the case of depolarizing currents, or **inhibitory (IPSP)** in the case of hyperpolarizing currents.

If the number of EPSPs is sufficient, an **action potential** is fired.

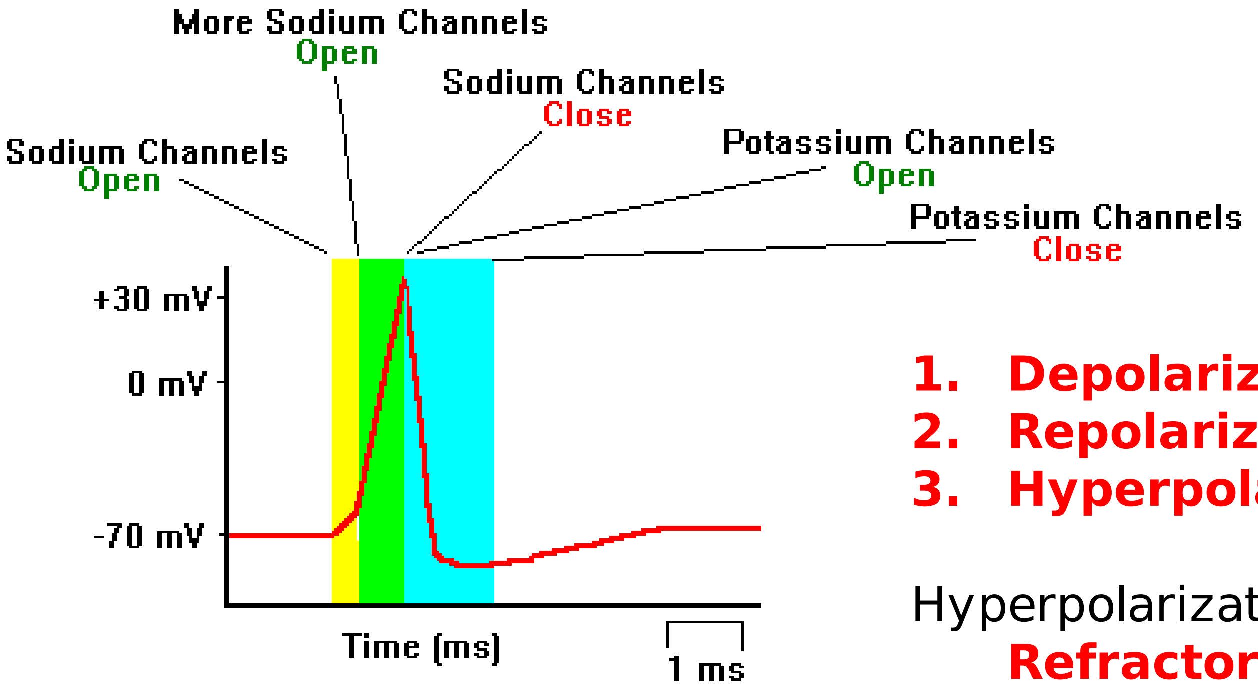
Neuronal integration:



The action potential

A sufficient depolarization (**Threshold-voltage** V_{thr}~ -55 mV) caused by EPSPs leads to an action potential (spike).

"**All or None**"-principle: The size of the action potential is always the same. Either the neuron does not reach the threshold or a full action potential is fired.

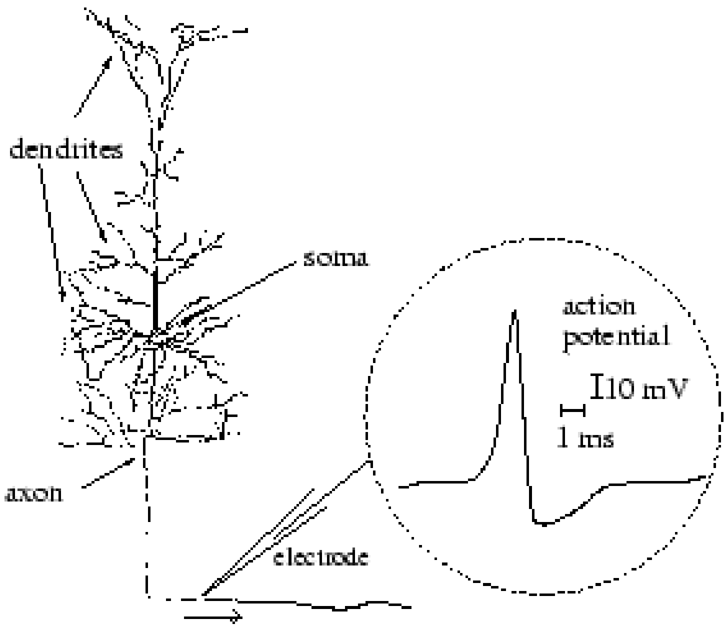


1. **Depolarization** (Na+ in)
2. **Repolarization** (K+ out)
3. **Hyperpolarization** (stillK+out)

Hyperpolarization, Exhaustion:
Refractoriness
(All sodium channels inactivated)

Single neuron models: Basic ingredients

- Variable of interest: **Membrane potential V_m** of postsynaptic neuron **(State)**
- Neuron receives excitatory and inhibitory **postsynaptic potentials** **(Input)**
- Neuron emits **action potentials** **(Output)**



- **"All or none"** behavior
  (Action potentials stereotyped)
- **Threshold** behavior (V_{Thr})
- **Resting potential** (V_R)
- **Refractoriness**

Single neuron models: Simplifications

- Neuron without spatial extension **(Point neuron)**
  (Multi-compartment models)

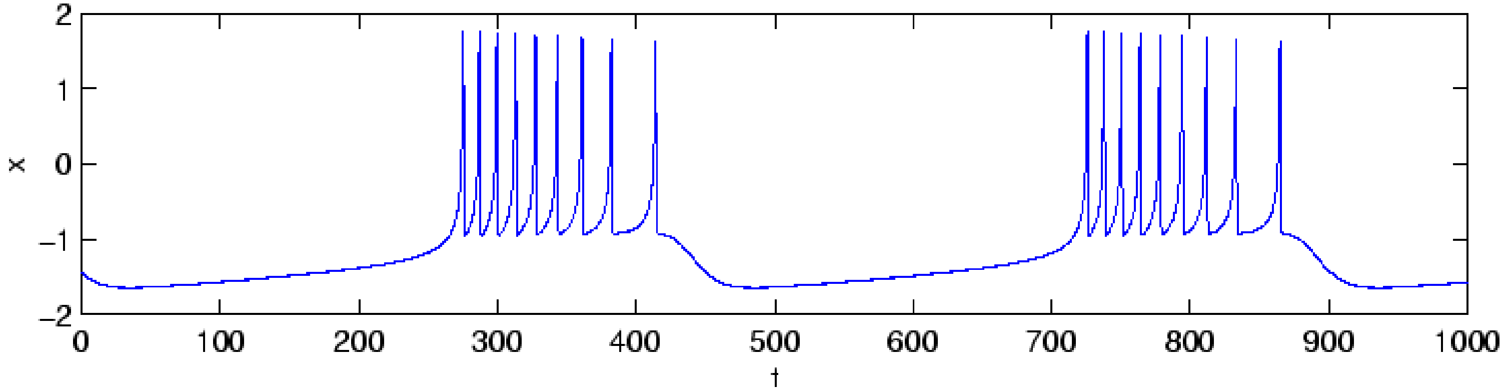
  Real neurons:
  - Temporal delays due to propagation of PSPs from dendrites to cell body.

- PSPs have **constant amplitude**

  Real neurons:
  - Amplitude of PSP depends on voltage and on position of synapse

- Neurons without memory (**Reset mechanism**: All spikes are independent)

  Real neurons:
  - Bursting
  - Adaptation
  - ...



Simple neuronal model: Integrate & Fire

Basic assumptions:

Input: Excitatory and inhibitory post-synaptic potentials (**Kicks**)

Output: Action potentials (**Spikes**)

Neuron acts as **integrator** (Electrical equivalent: **Membrane Capacity C_m**)

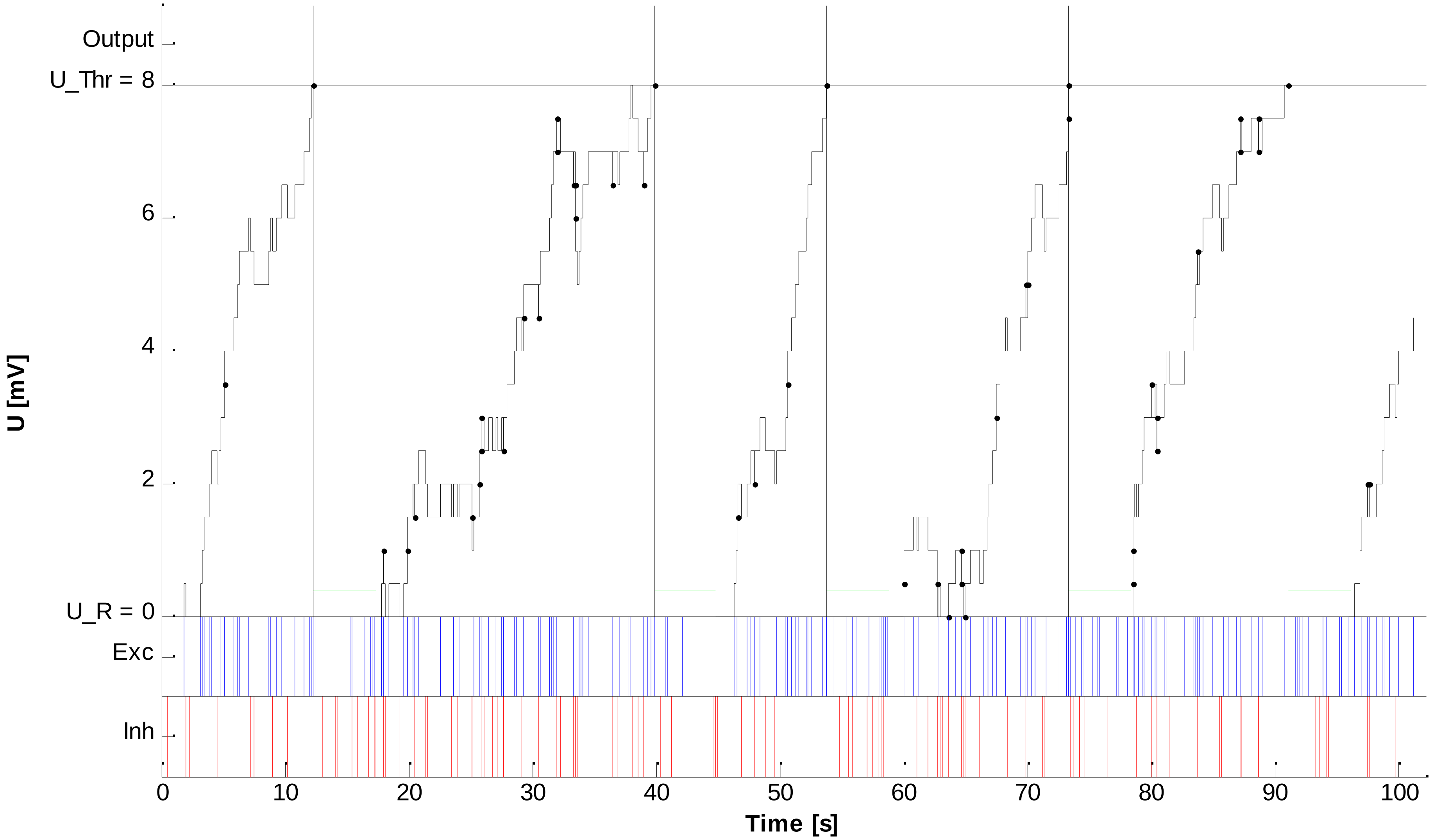
PSPs as instantaneous jumps in the voltage

$$I(t) = C_m \frac{d V_m(t)}{dt}$$

Spike times: $\int_{t_i}^{t_{i+1}} I(t)\, dt = C_m V_{thr}$

Here: Threshold V_{Thr}=8mV, Reset potential V_R=0 mV (absorbing)

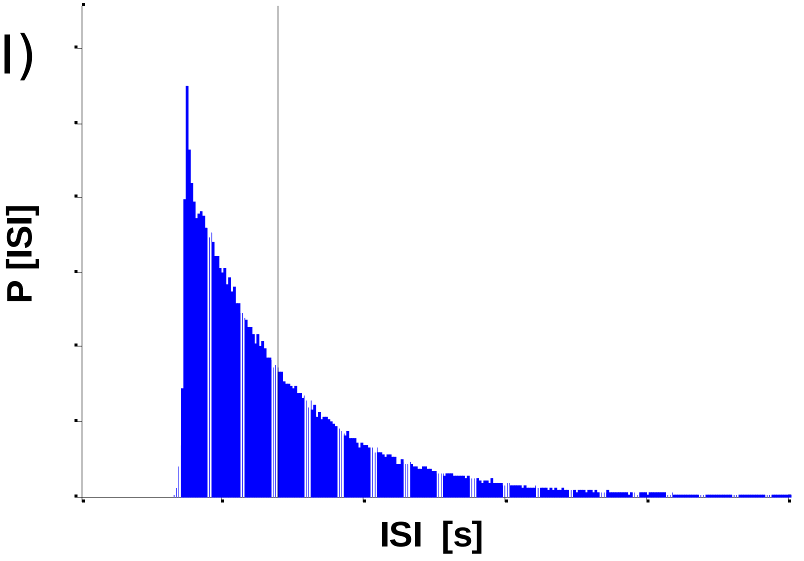
Integrate & Fire



Characterization of spike trains I

Spike train: Series of Delta-Functions $x(t) = \sum_k \delta(t - t_k)$

- Distribution of Inter-Spike-Intervals (ISI)
- Average ISI: $< ISI >$
- **Firing rate:** $r = \frac{1}{< ISI >}$

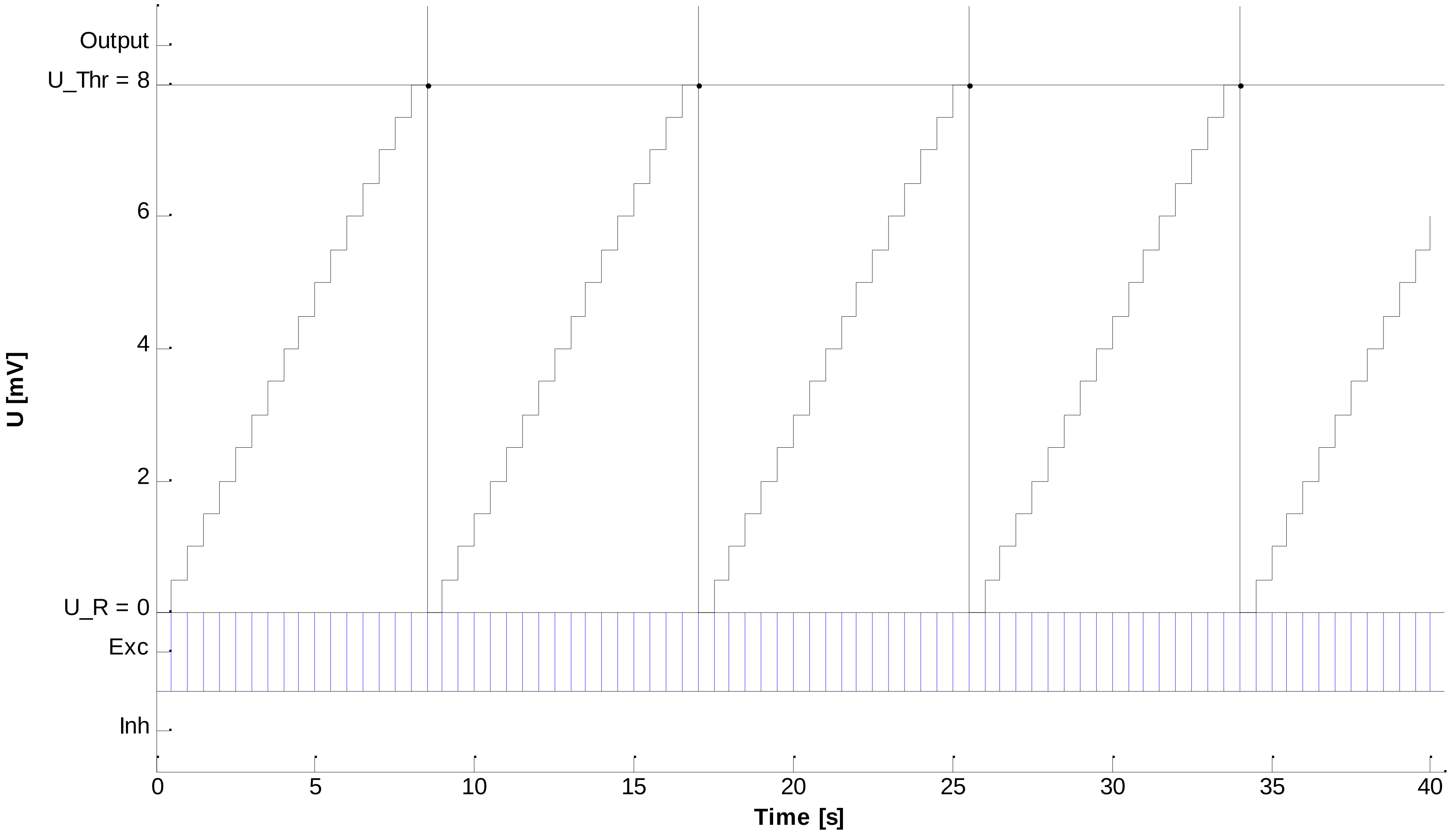


Aim: Characterization of output in dependence on input

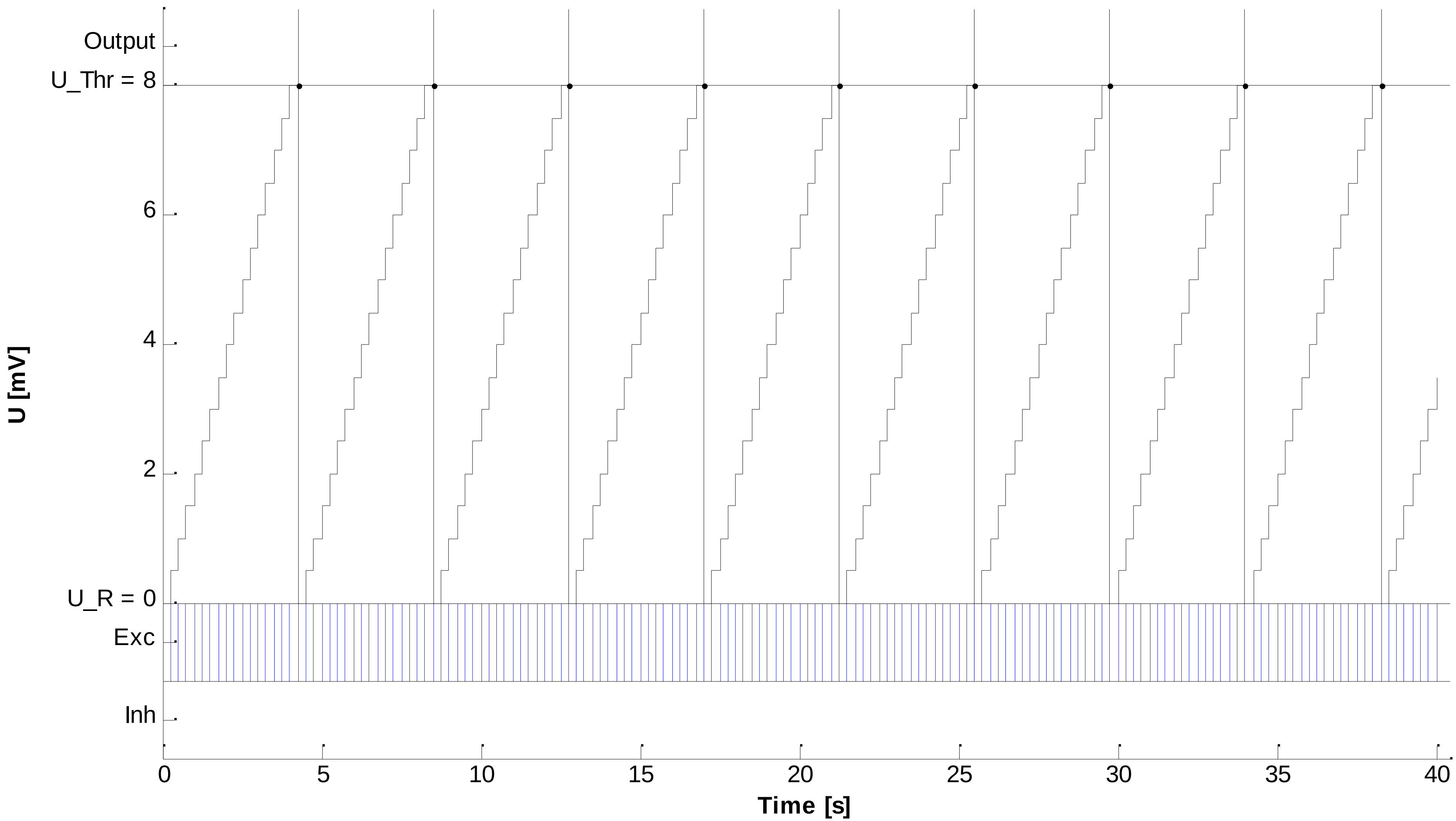
Further simplifications:

No inhibition, no refractoriness, periodic excitatory kicks (~ constant positive current)

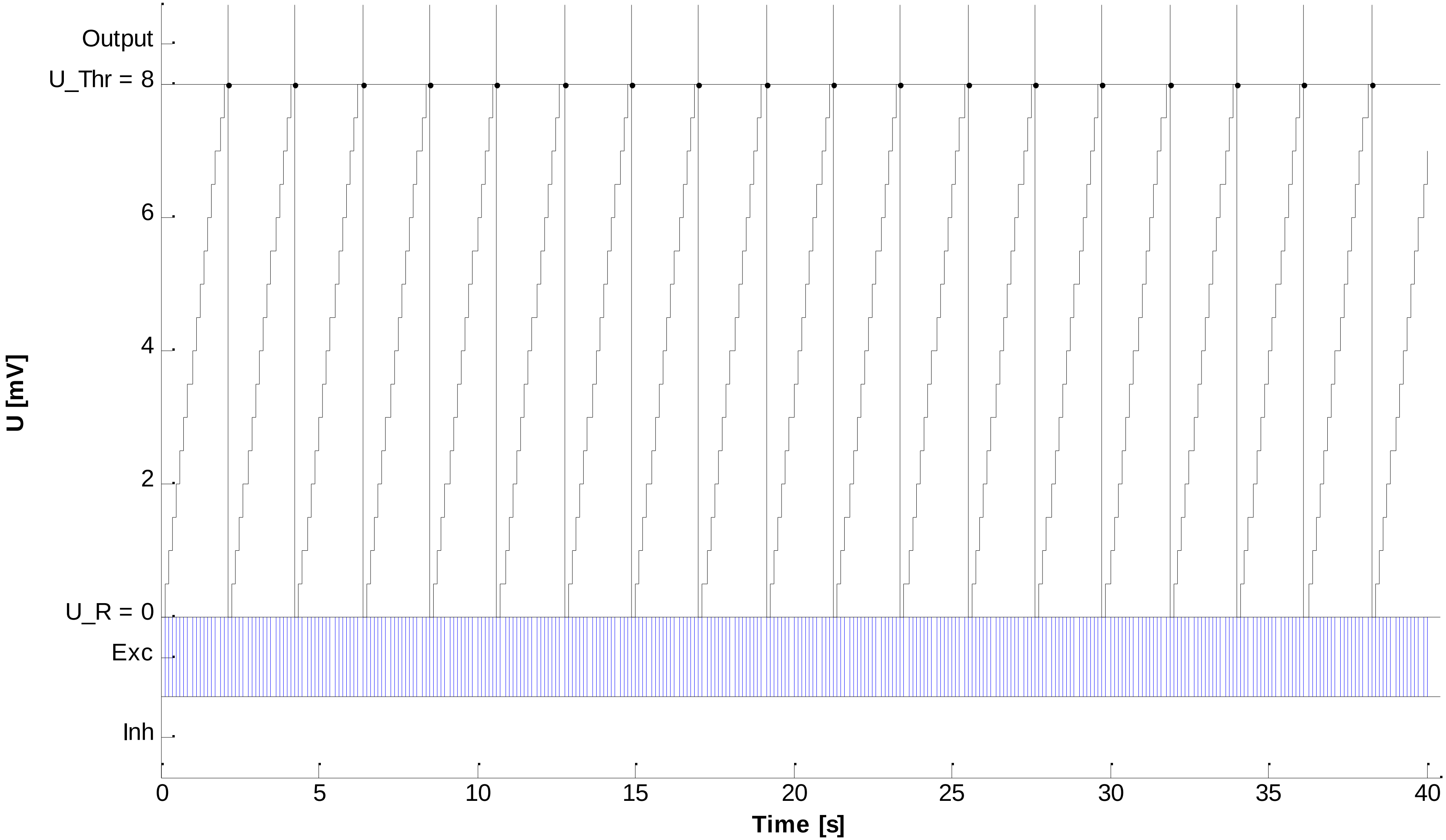
Integrate & Fire: Periodic excitation



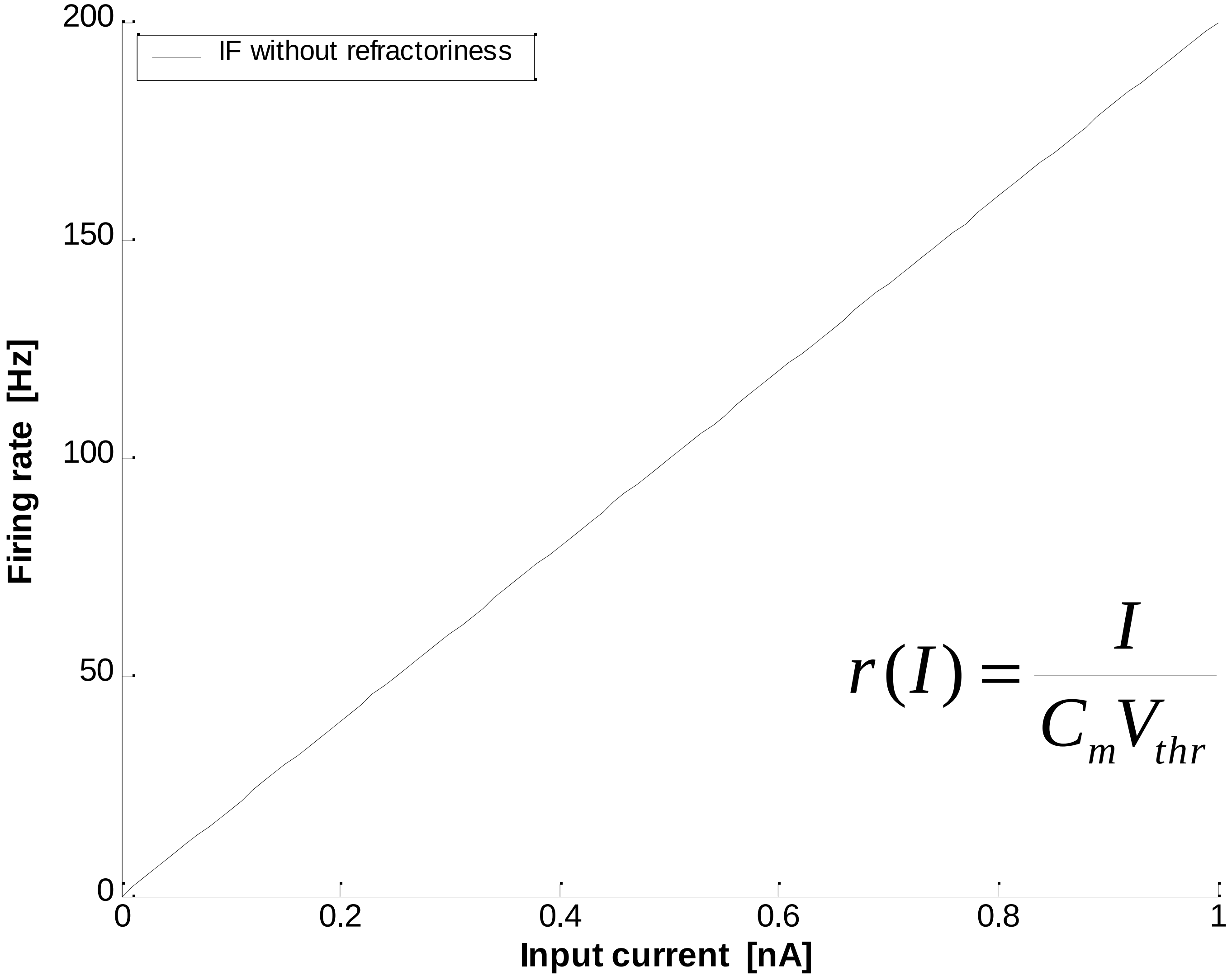
Integrate & Fire: Increasing rate (current)



Integrate & Fire: And so on

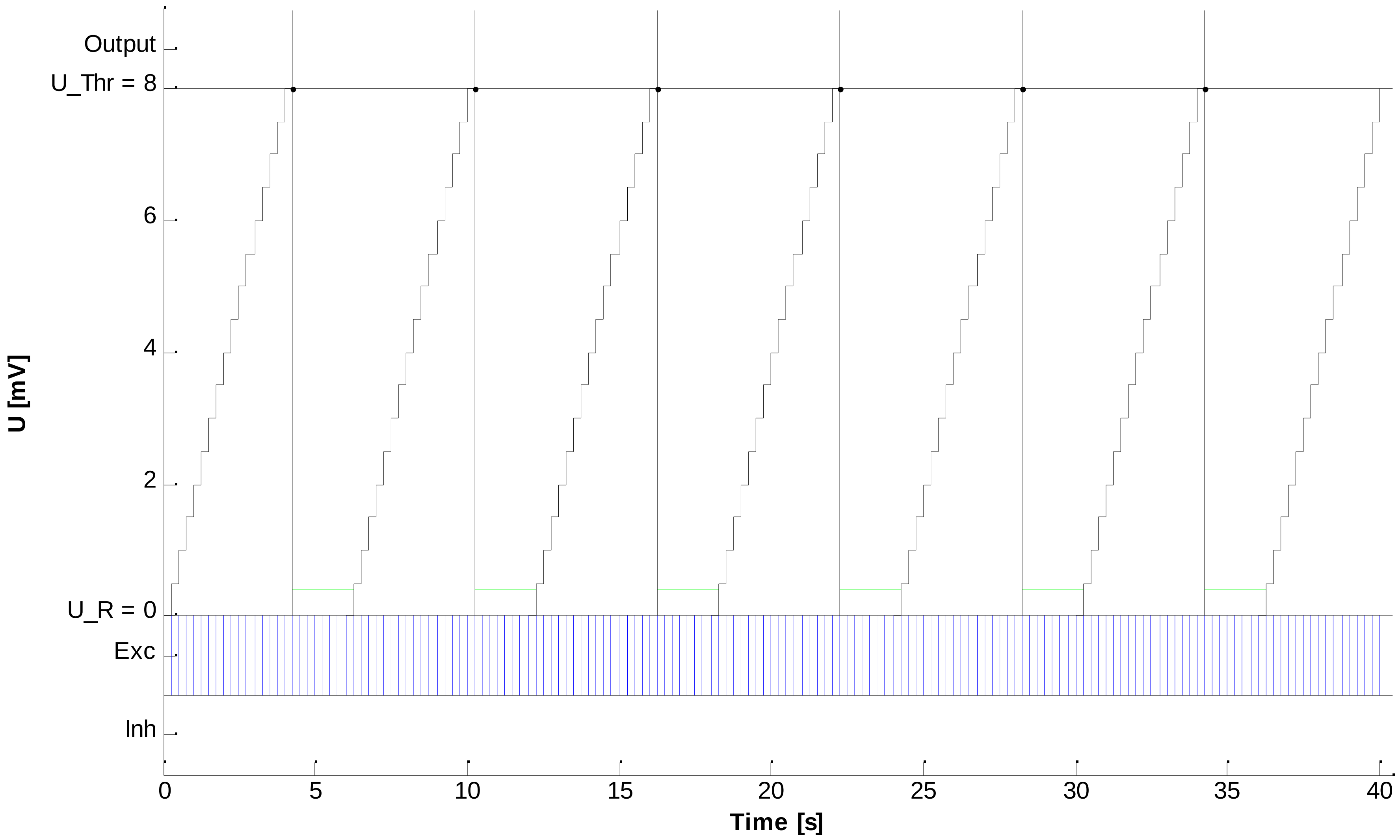


Gain function

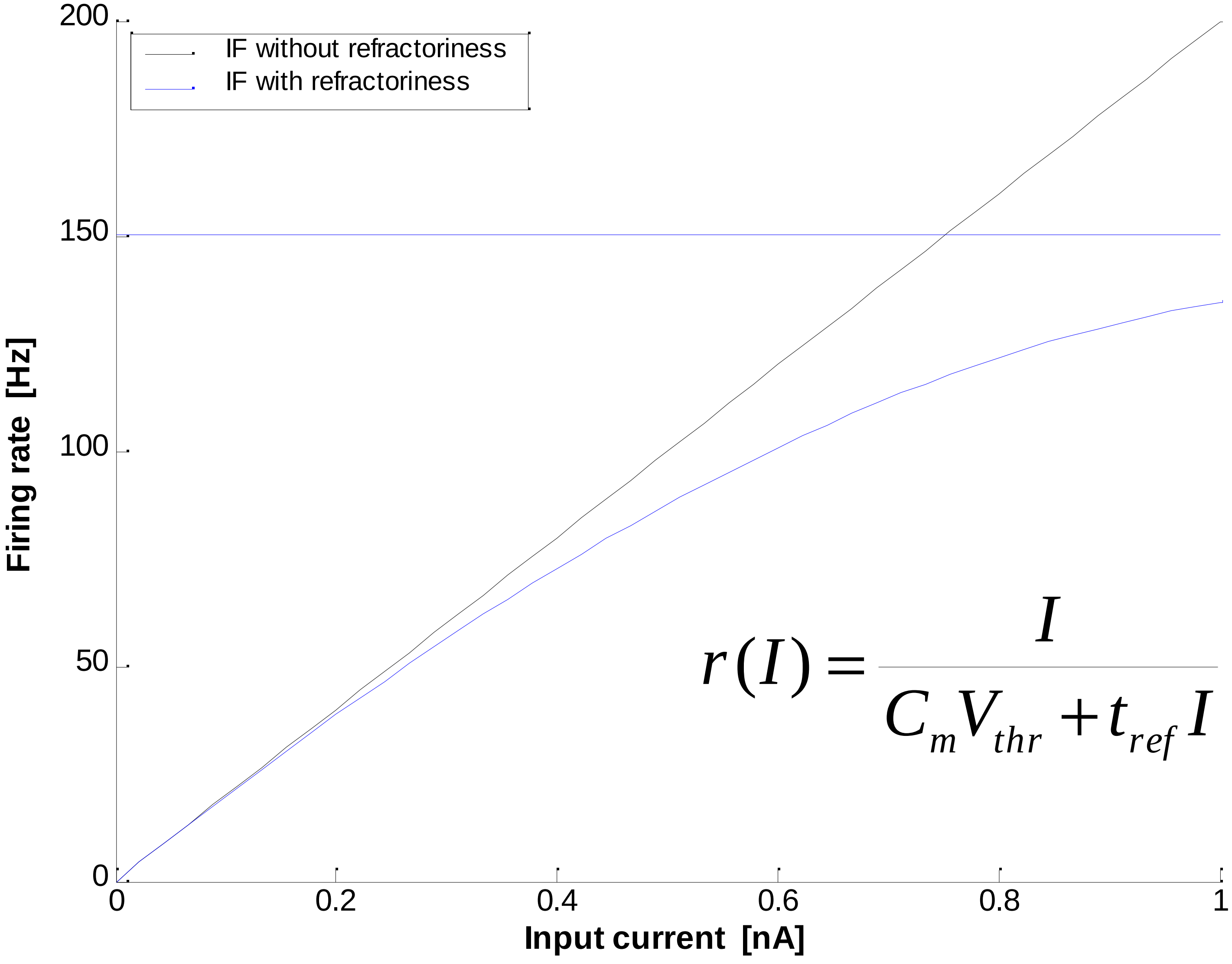


$$r(I) = \frac{I}{C_m V_{thr}}$$

Integrate & Fire: Refractory time



Gain function II



Maximum frequency:

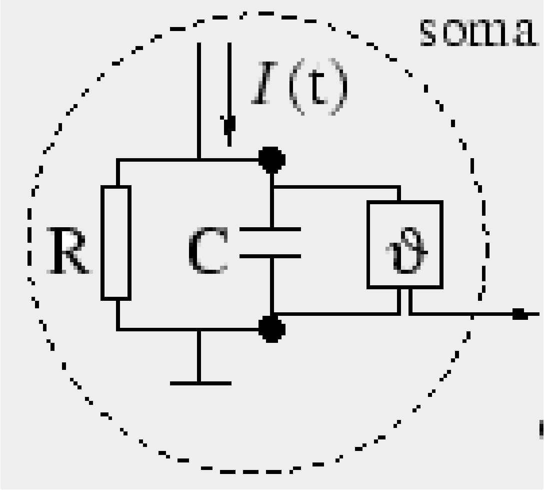
$$\frac{1}{t_{ref}}$$

$$r(I) = \frac{I}{C_m V_{thr} + t_{ref} I}$$

Leaky Integrate & Fire (LIF)

Real neurons: Existence of leakage channels which remain always open (no gating)

K+ out, N+ and Cl- in (**Leak current**); Net efflux of positive charge (**Hyperpolarization**)



$$I = I_R + I_C$$

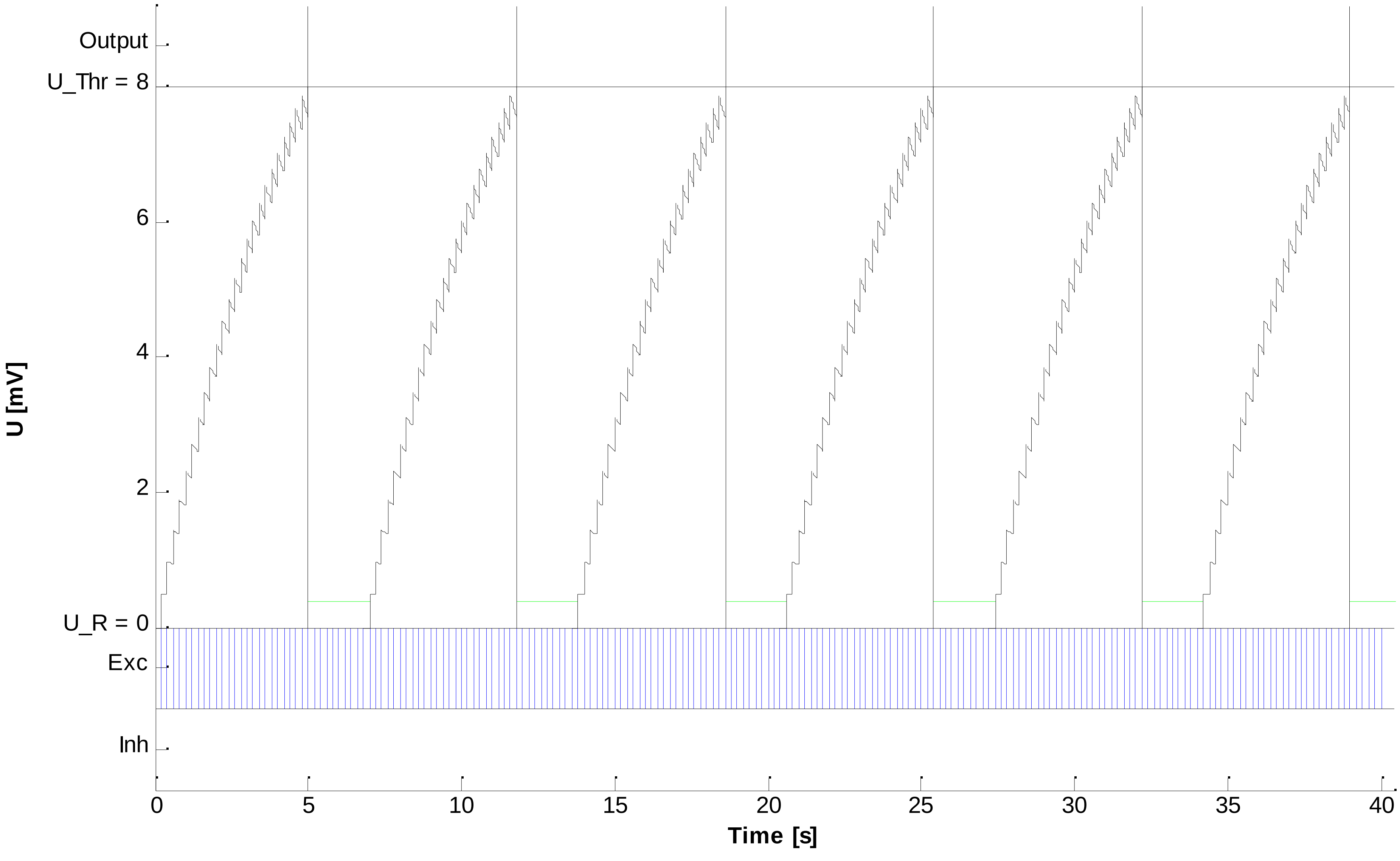
Electrical equivalent: **Resistance R**

$$I(t) = \frac{u(t)}{R} + C\frac{d\,u(t)}{dt}$$

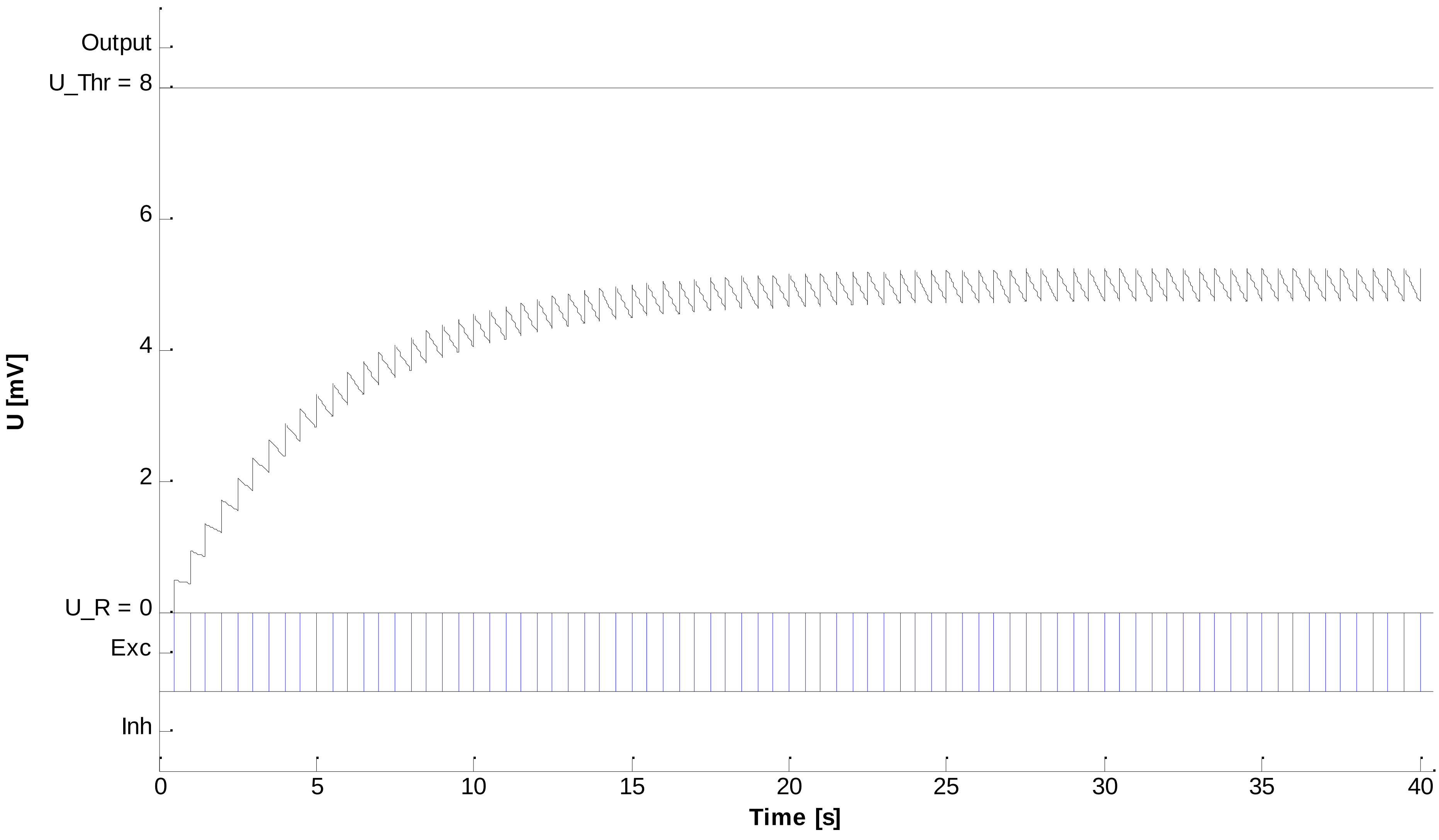
New variable: **Time constant** of membrane

$$\tau = RC \rightarrow \tau\frac{du}{dt} = -u(t) + R\,I(t)$$

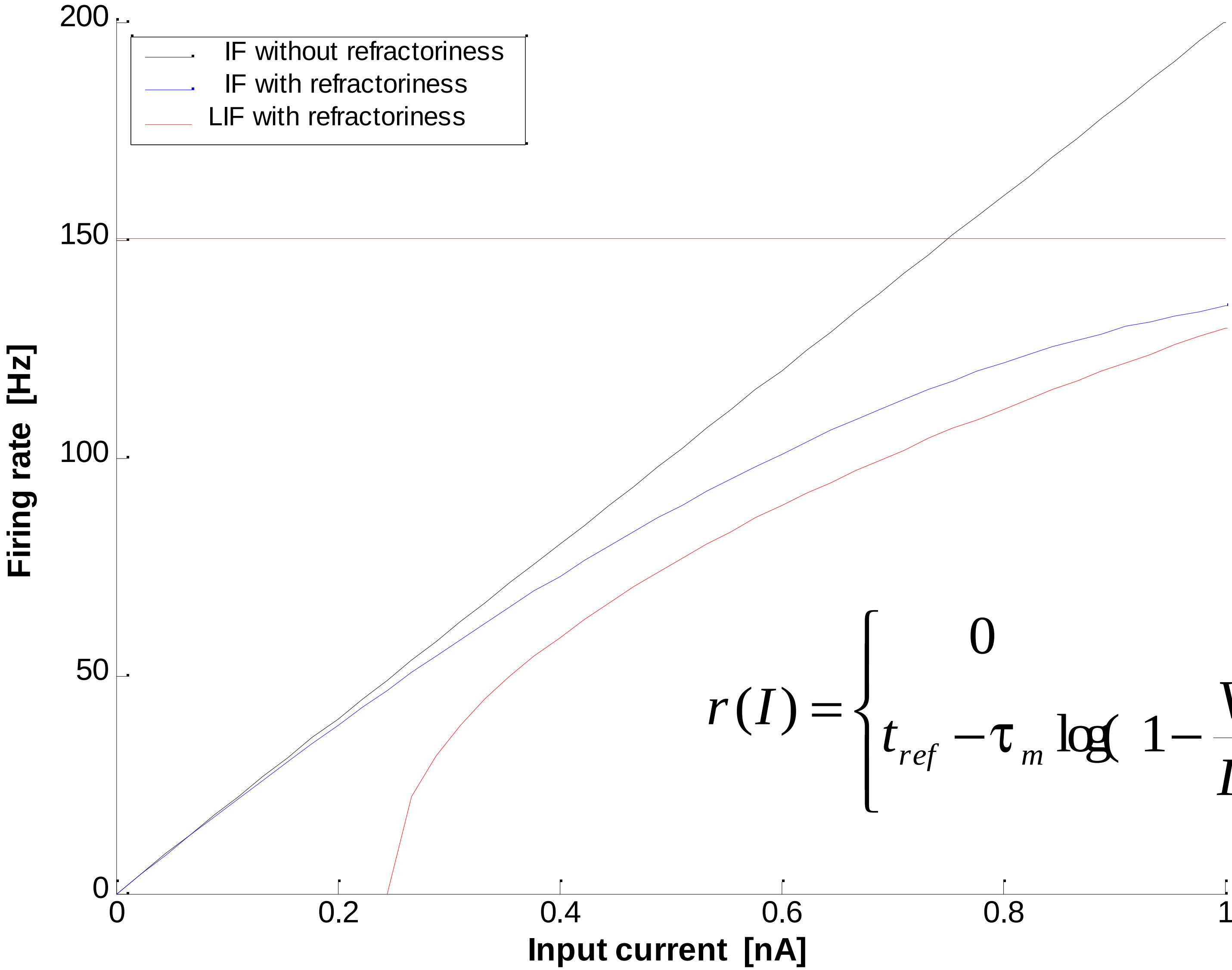
Leaky Integrate & Fire



Leaky Integrate & Fire

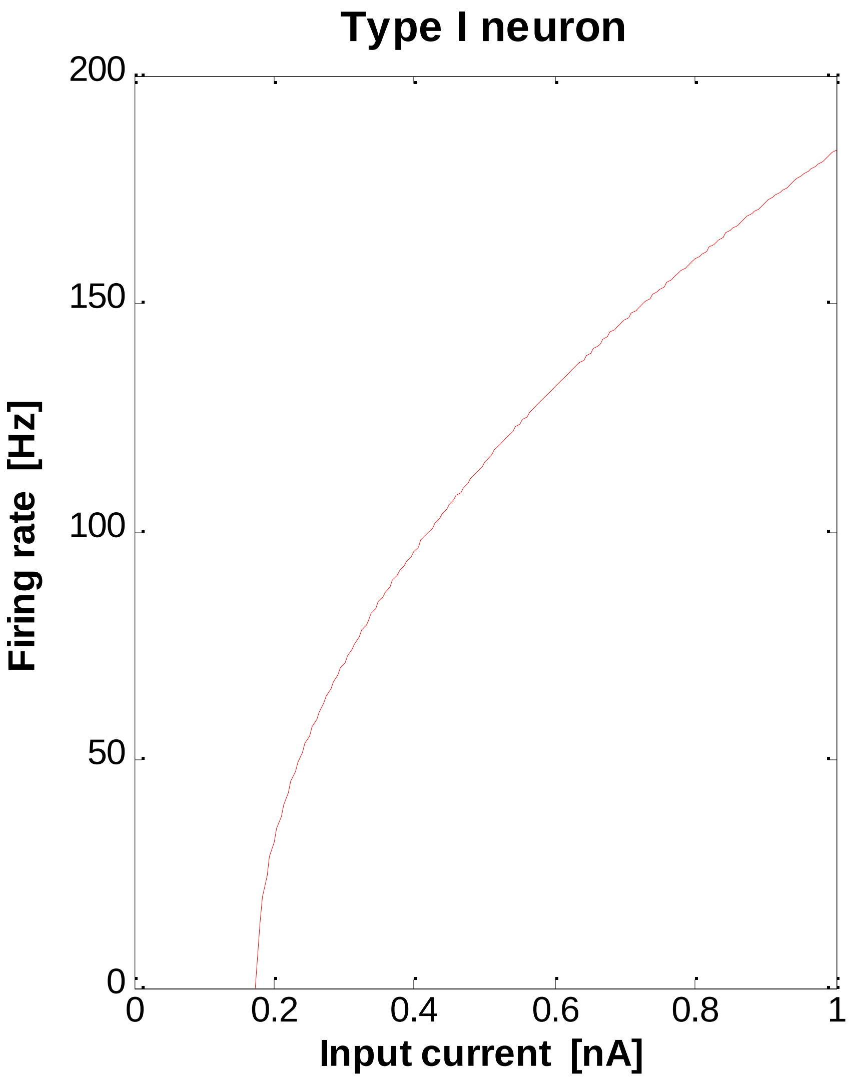


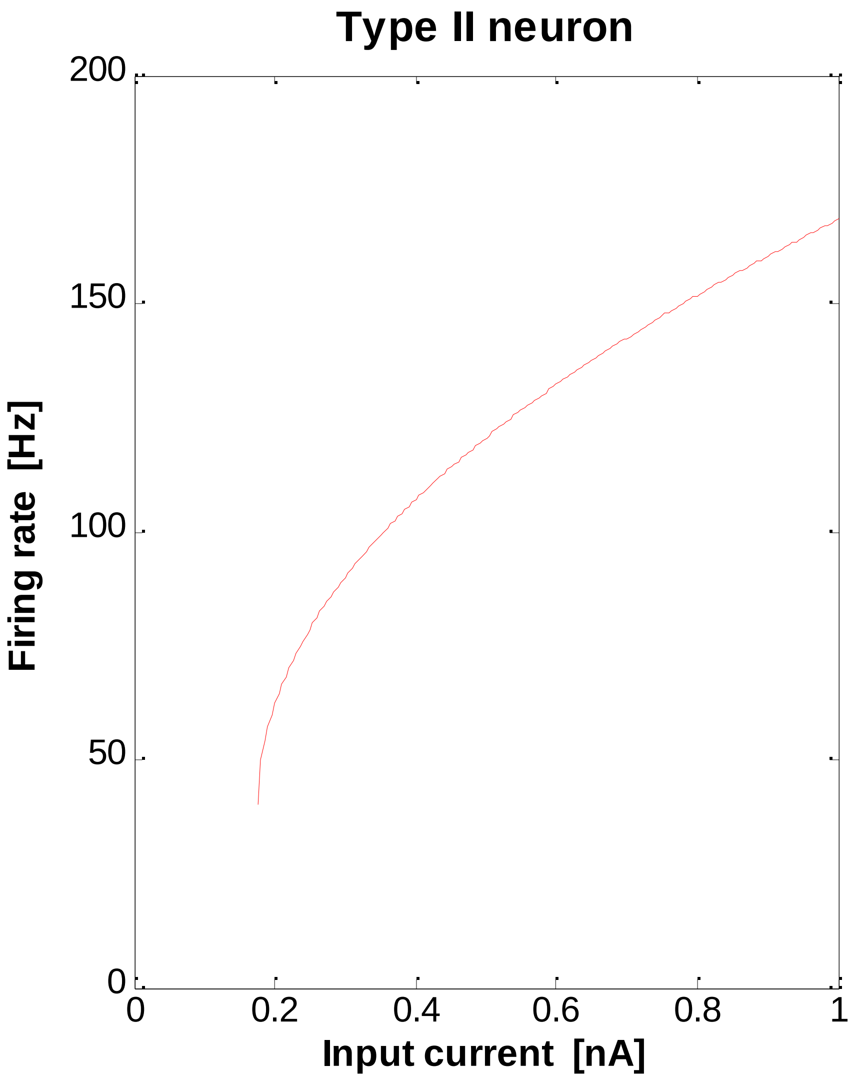
Gain function III



$$r(I) = \begin{cases} 0 & , I \leq I_{Thr} \\ t_{ref} - \tau_m \log\left(1 - \frac{V_{thr}}{IR_m}\right)^{-1} & , I > I_{Thr} \end{cases}$$

Two types of neuronal models



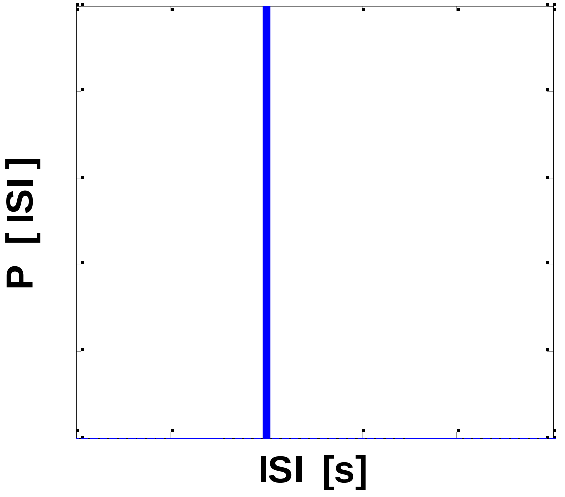


Random input (Noise)

So far:

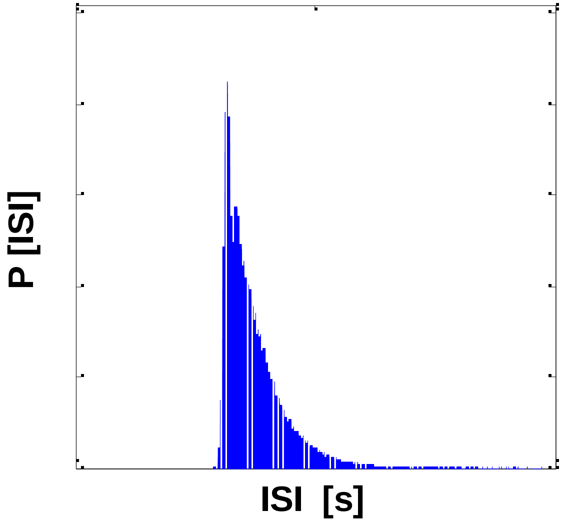
- **Periodic input** (Constant current)
- Characterization in terms of **firing rate**

  Periodic output (completely regular)



Now:

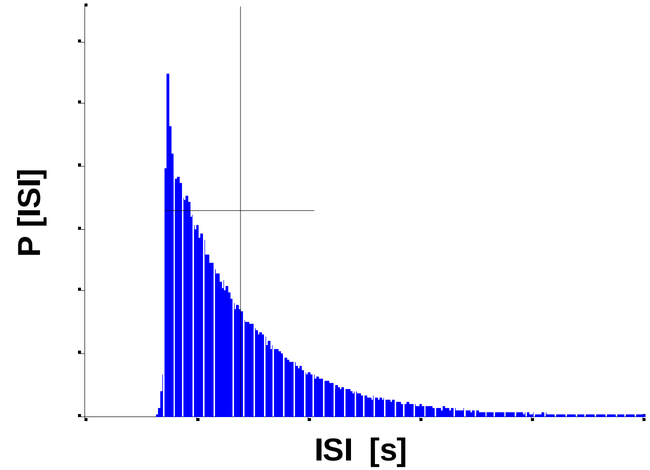
- **Random input** (Noise)
- Characterization in terms of **regularity**



Question: What makes a neuron spike regular/irregular???

Characterization of spike trains II

Firing rate: $r = \dfrac{1}{< ISI >}$

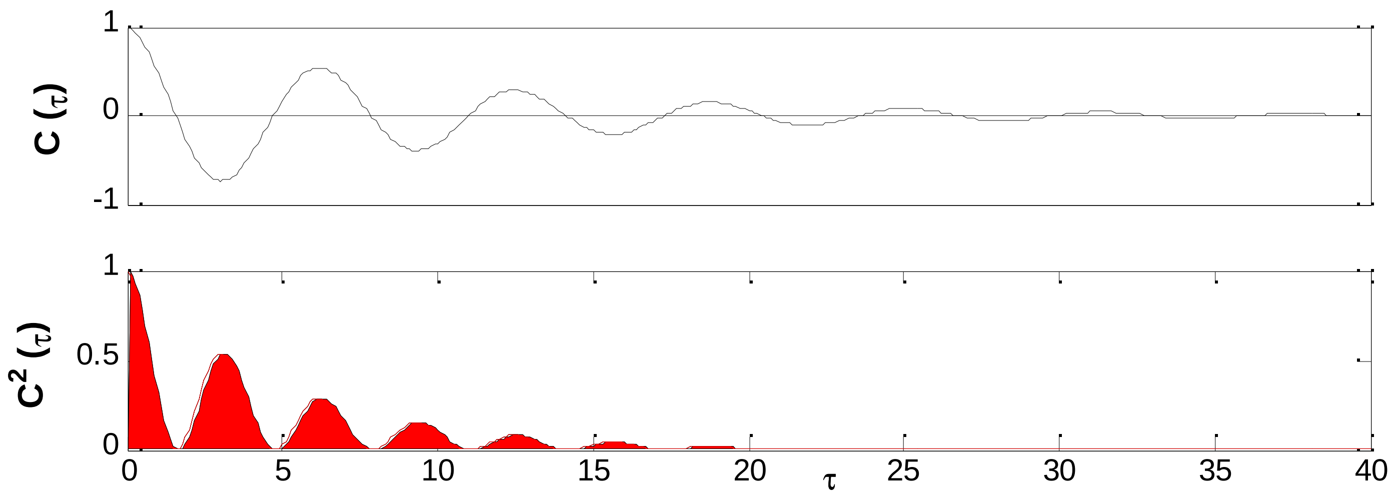


- **Coefficient of variation:** $C_V = \dfrac{std(ISI)}{< ISI >}$

- Autocorrelation function: $C(\tau) = < x(t)x(t+\tau) > - < x(t) >^2$

  - **Correlation time:**

$$\tau_c = \int_0^\infty C^2(t)\, dt$$



Input: Poisson distribution

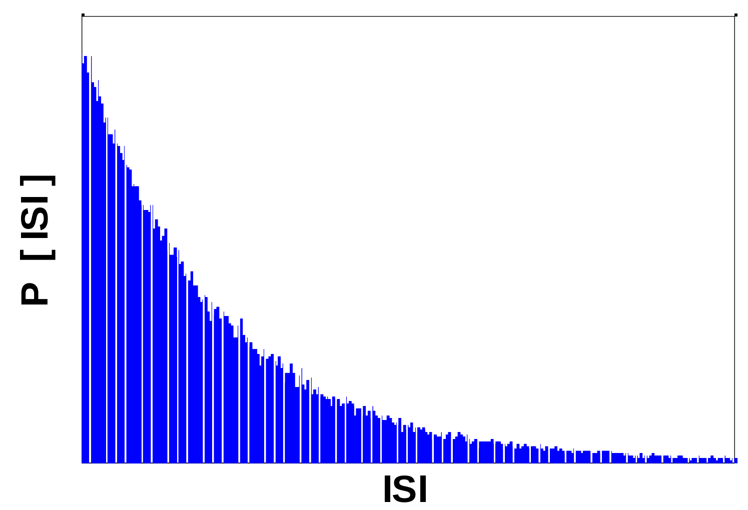
Three conditions:

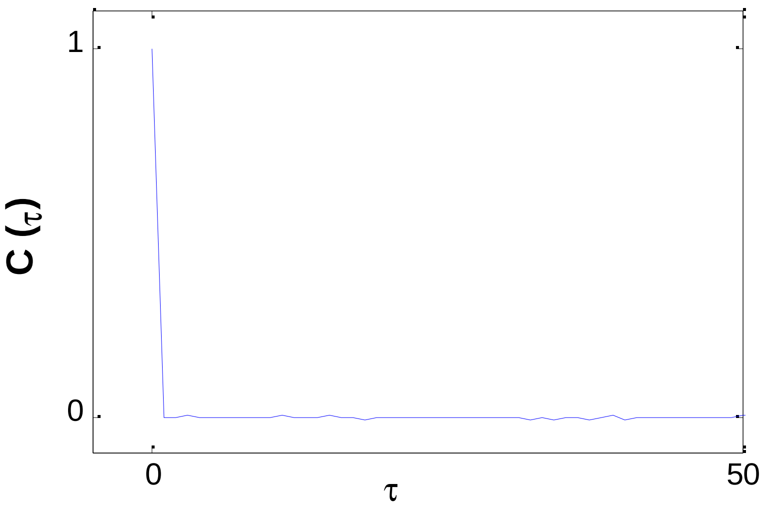
Every kick is generated

- randomly
- independently of other kicks
- with a uniform probability of occurrence in time

Properties:

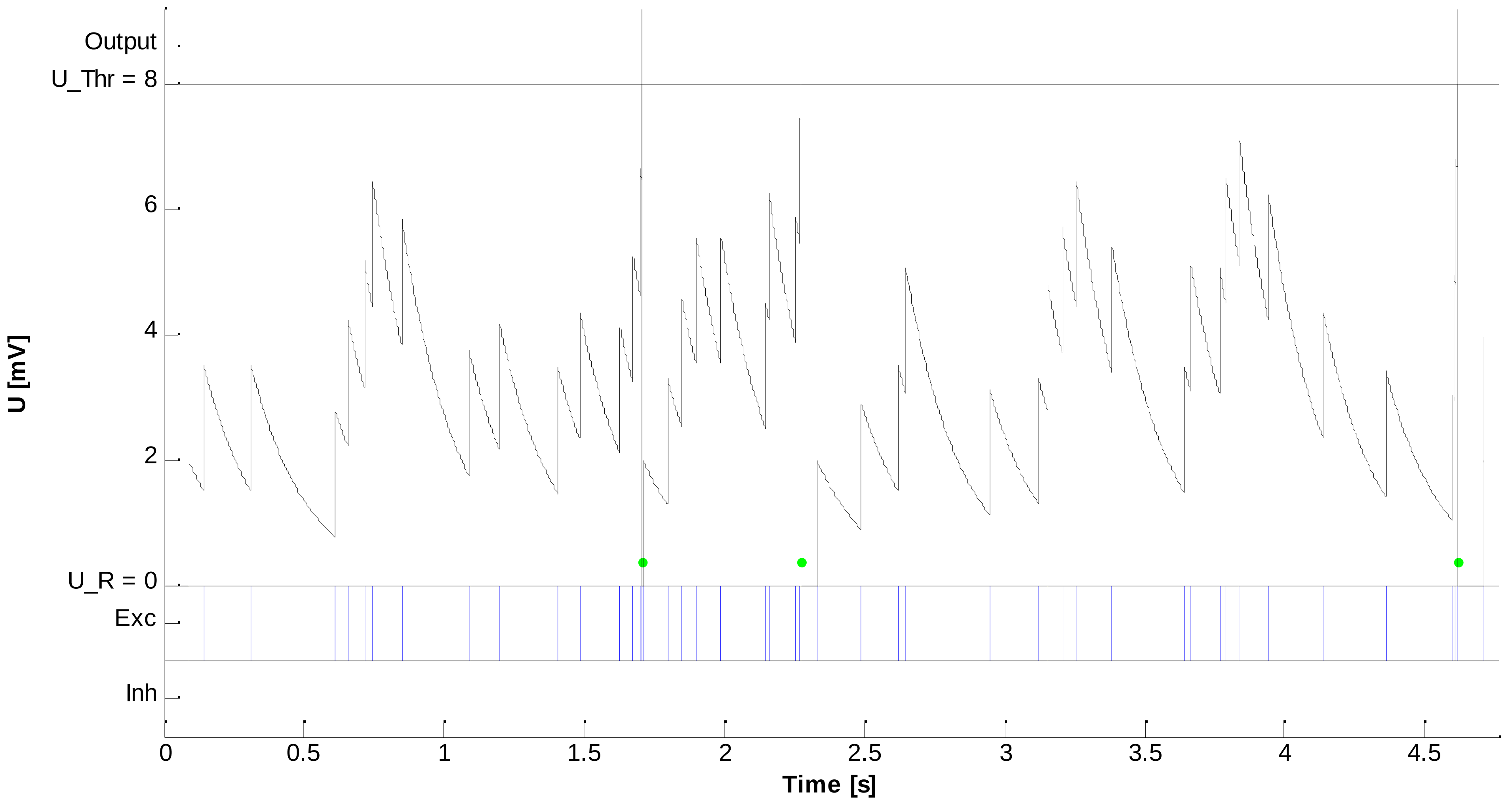
- Exponential distribution
- Autocorrelation function flat: $C(\tau) = \delta(0)$
- **Coefficient of variation:** $C_V = 1 - \frac{t_{ref}}{< ISI >}$





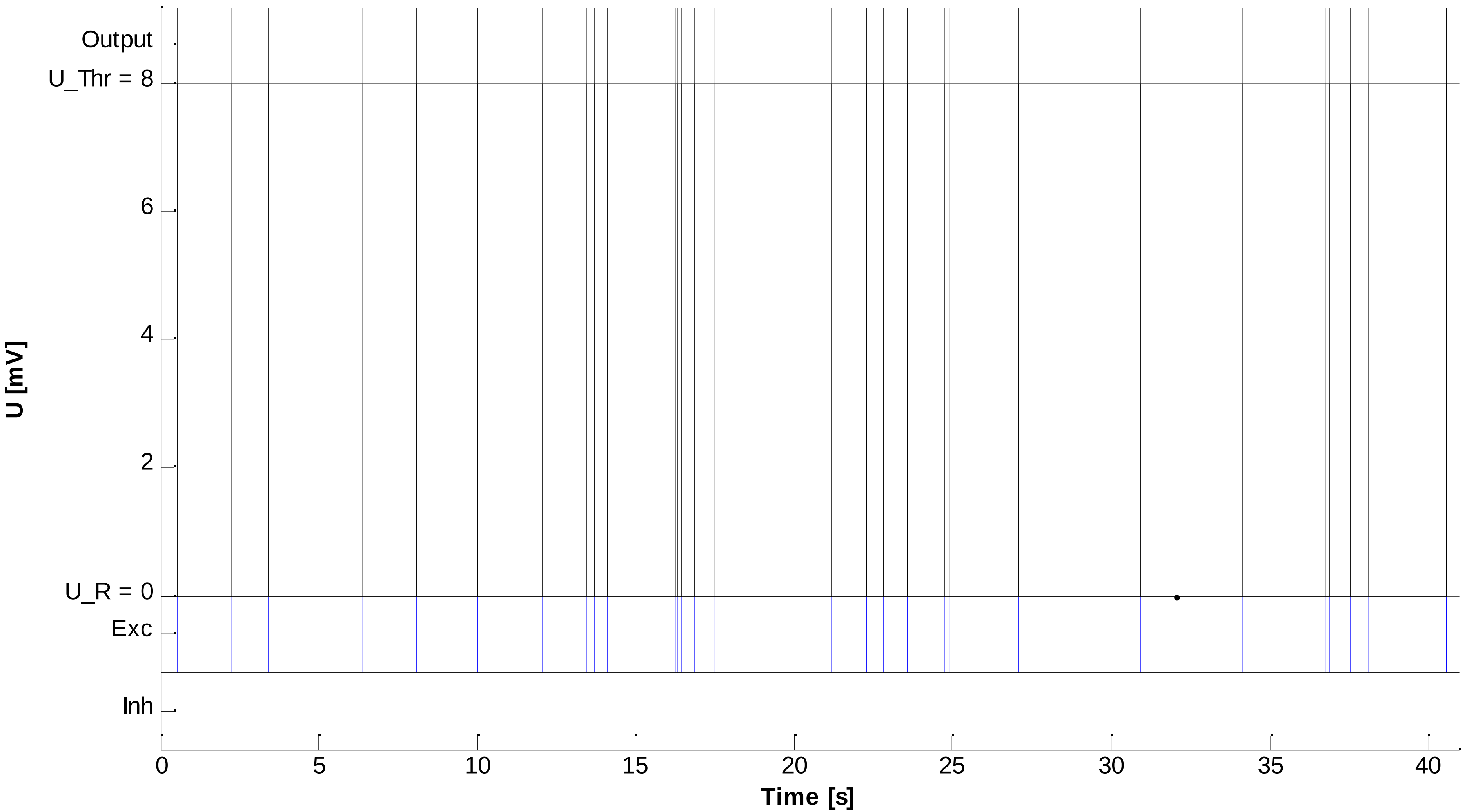
Leaky Integrate & Fire (LIF)

Low time constant: **Coincidence detection** (rather irregular)



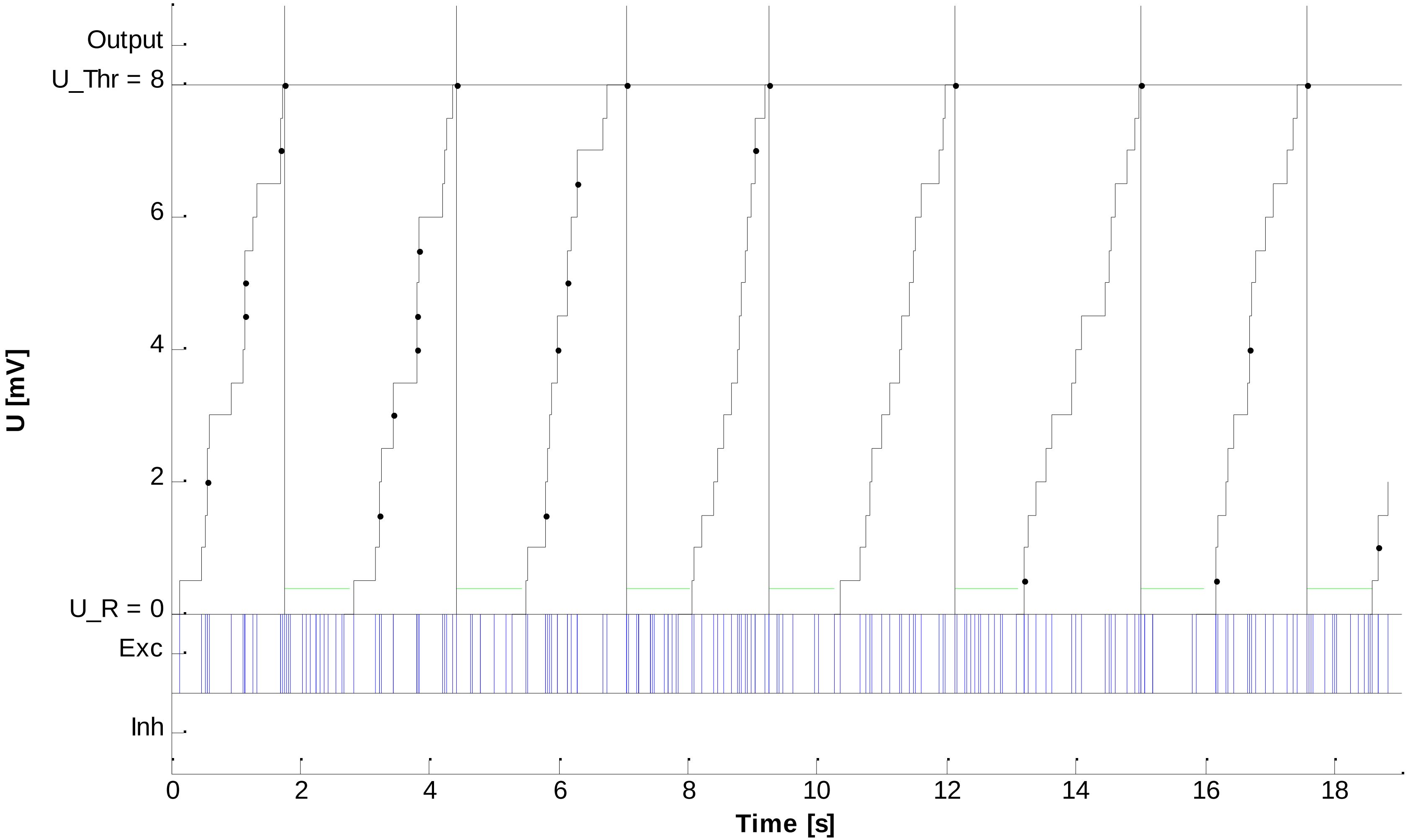
Integrate & Fire

High amplitudes: **1:1 synchronization** (Output follows input)



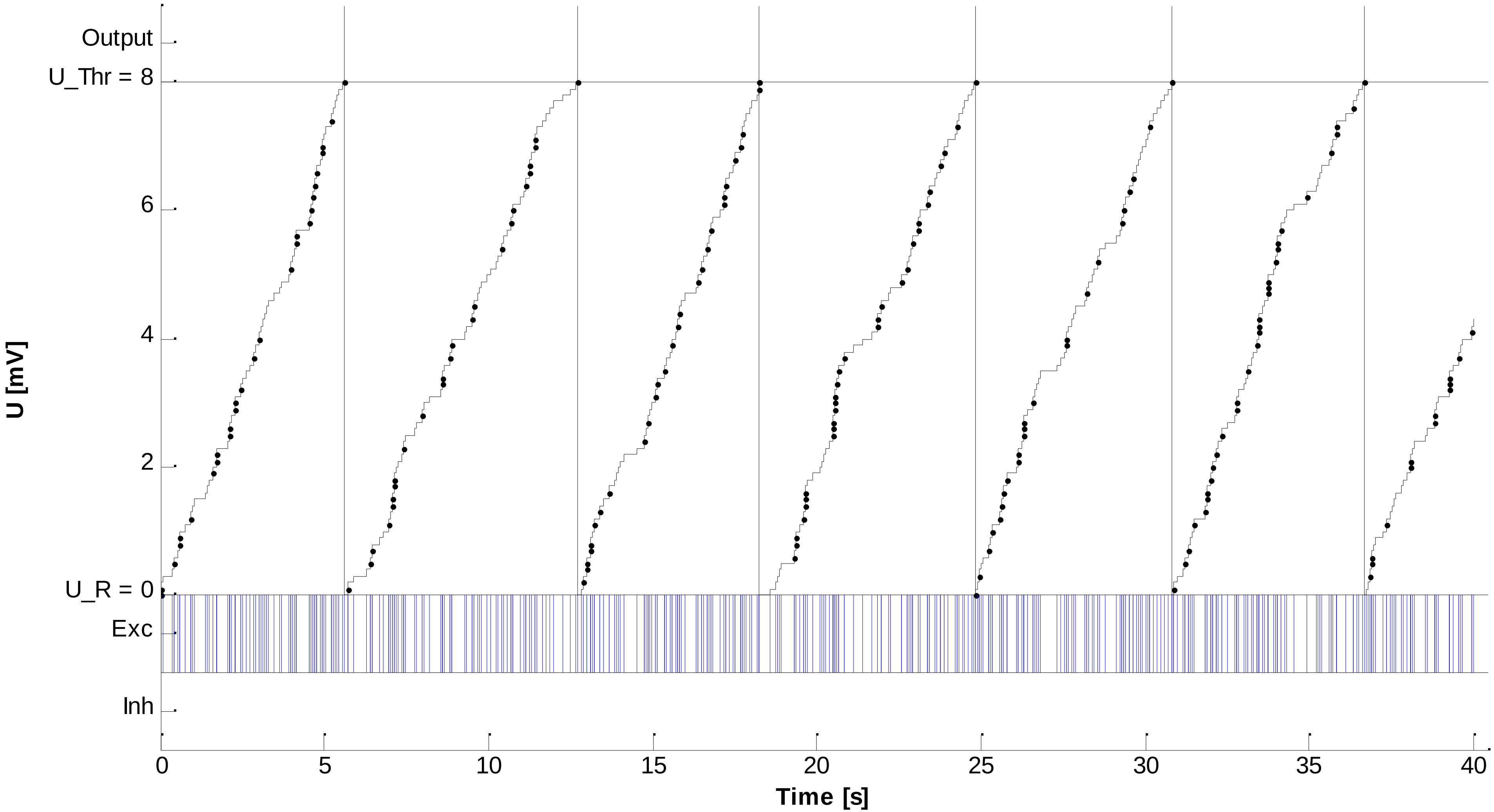
Integrate & Fire

Refractoriness: **Higher regularity**

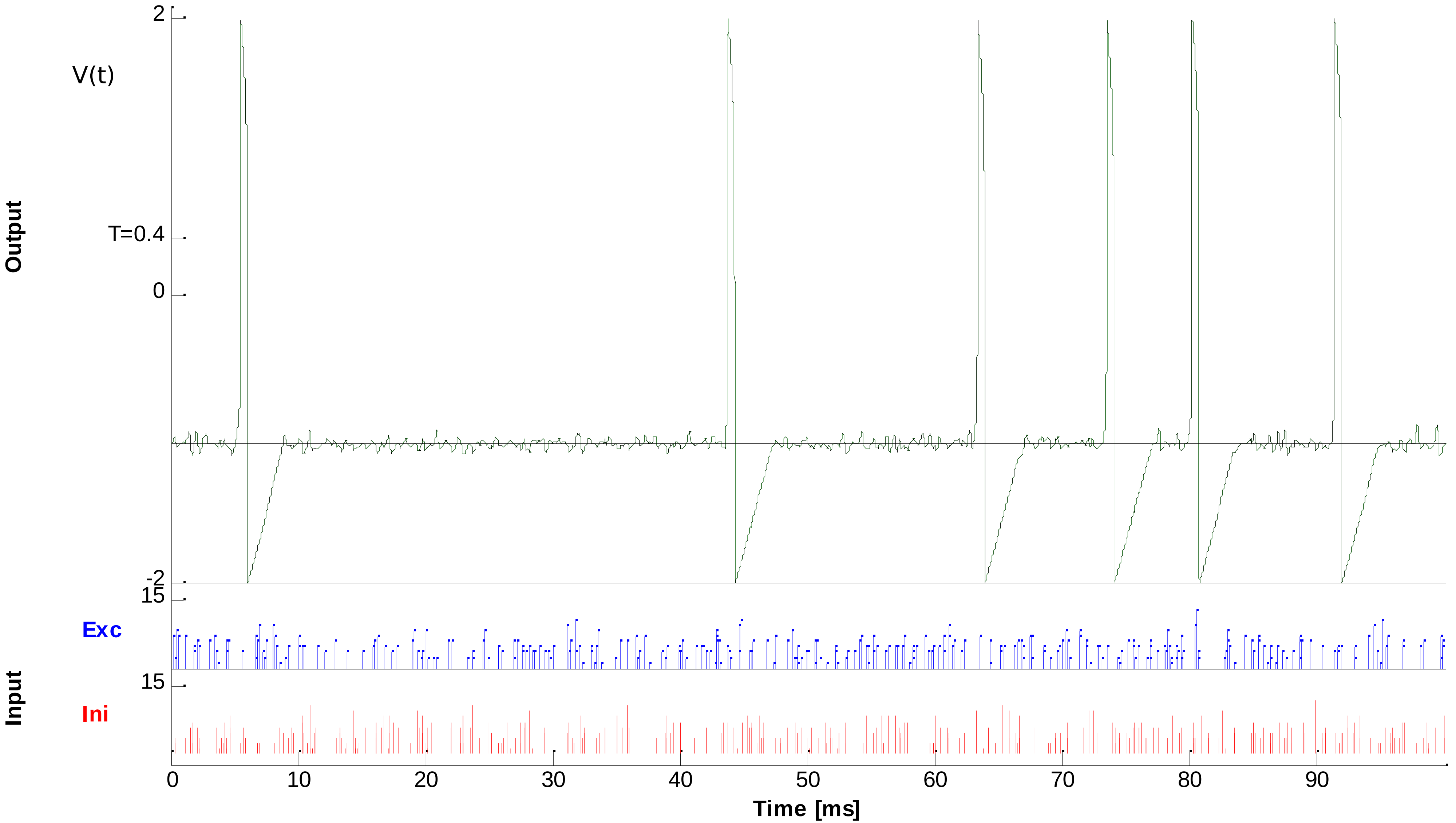


Integrate & Fire

Averaging over many kicks: **Higher regularity**



What causes regularity under more general conditions?



Coherence resonance

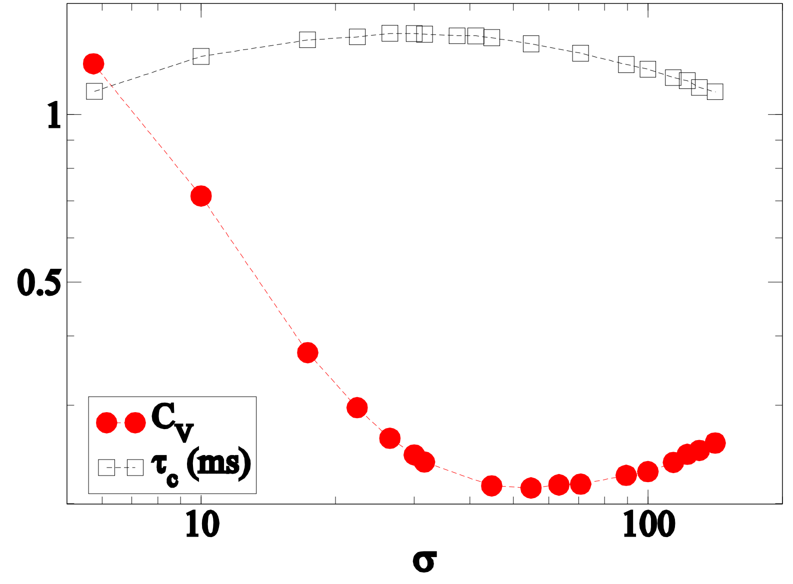
Maximum regularity of neuronal response for an intermediate noise strength σ

Low noise: Activation process (Poissonian ISI-Distribution)

High noise: Diffusion with threshold (Inverse Gaussian ISI-Distribution)

In between: Spiking most regular

Hodgkin-Huxley:



Indications:

- **Minimum of coefficient of variation C_V**
- Maximum of correlation time τ_c

Correlated input

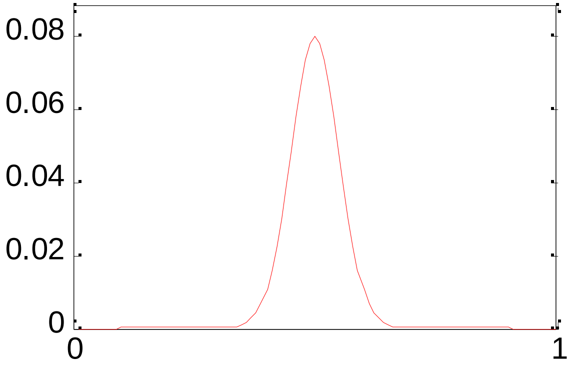
Shared input: Different neurons fire together

Correlation coefficient C_{xx}: Average fraction of shared neurons $(0 \le C_{xx} \le 1)$

Intervals between kicks: **Poissonian distribution**

Kick amplitudes: **Binomial distribution:**

$$p_w^{N_x} = \frac{N_x!}{w!(N_x - w)!} C_{xx}^w (1 - C_{xx}^w)^{N_x - w}$$

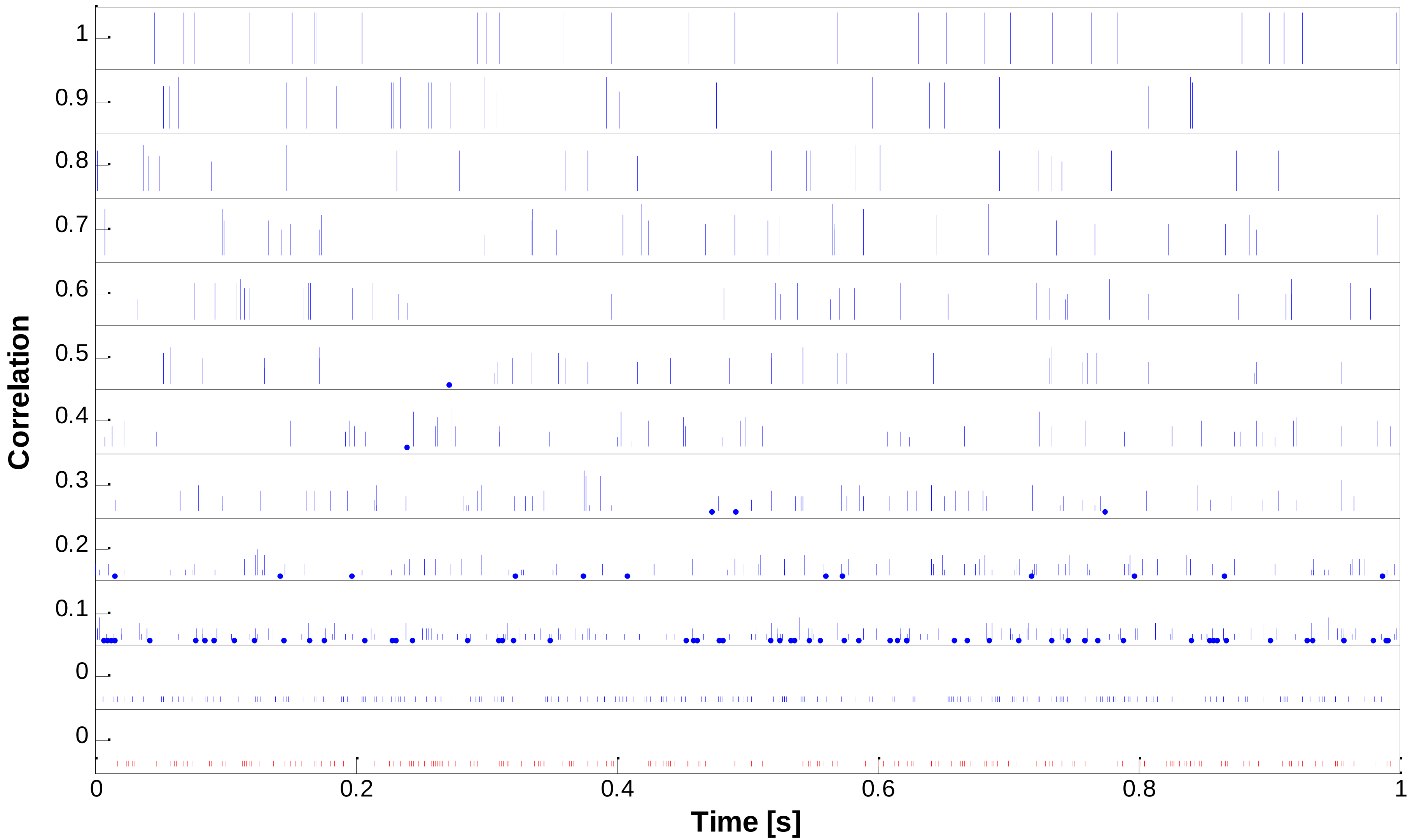


Correlated kicks: **Increase of variance σ :**

- Low frequency
- High amplitude

Correlated kicks:	↔	Uncorrelated kicks:
Increase in amplitude		Increase in frequency

Correlated input (Different correlations)



FitzHugh-Nagumo (FHN)

Two-dimensional single neuron model:

$$\frac{dV(t)}{dt} = \Phi\left(V - \frac{V^3}{3} - W\right)$$

$$\frac{dW(t)}{dt} = V + a + I(t)$$

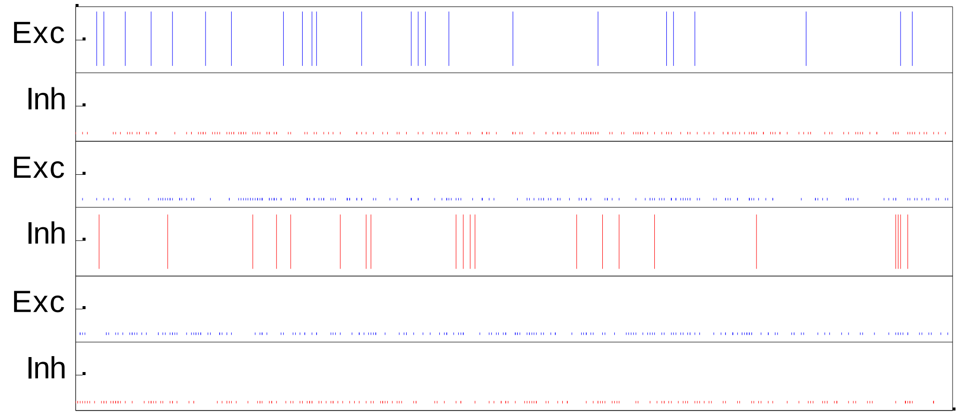
- **Balanced neuron:** Total amount of excitation = Total amount of inhibition

- Three different cases:

- Only correlation in the excitation

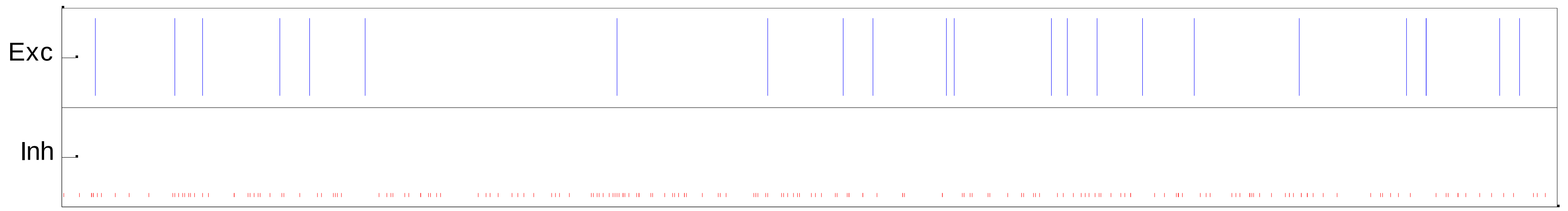
- Only correlation in the inhibition

- [No correlation]



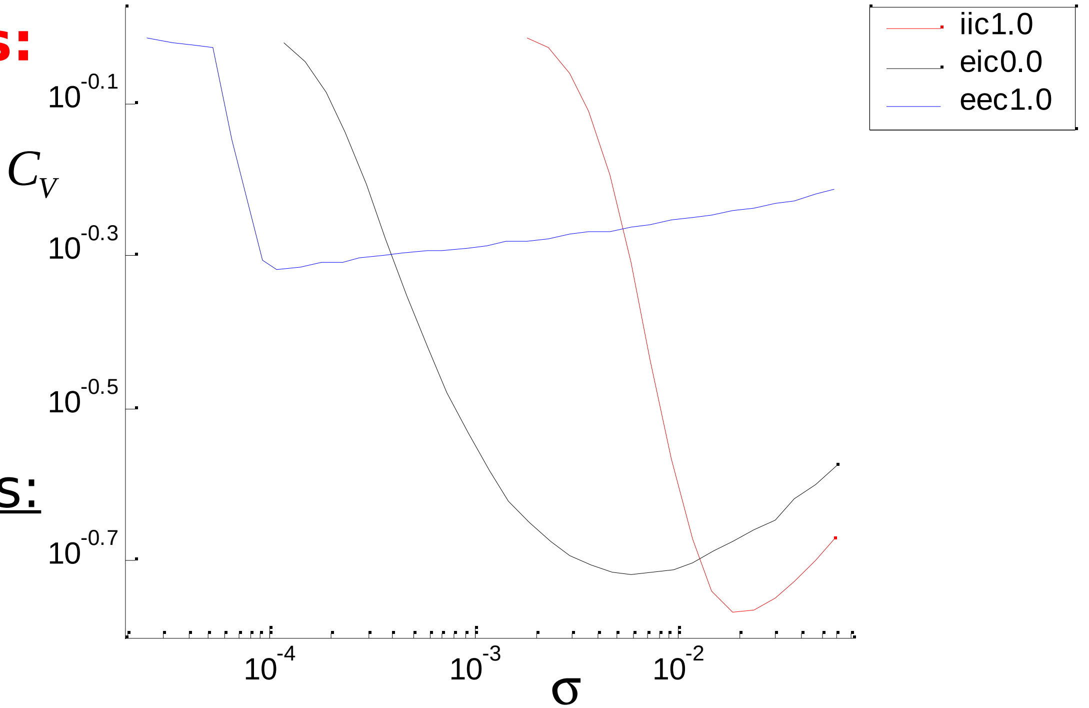
- For each correlation: Dependence of C_V on the noise strength σ

Full excitatory correlation

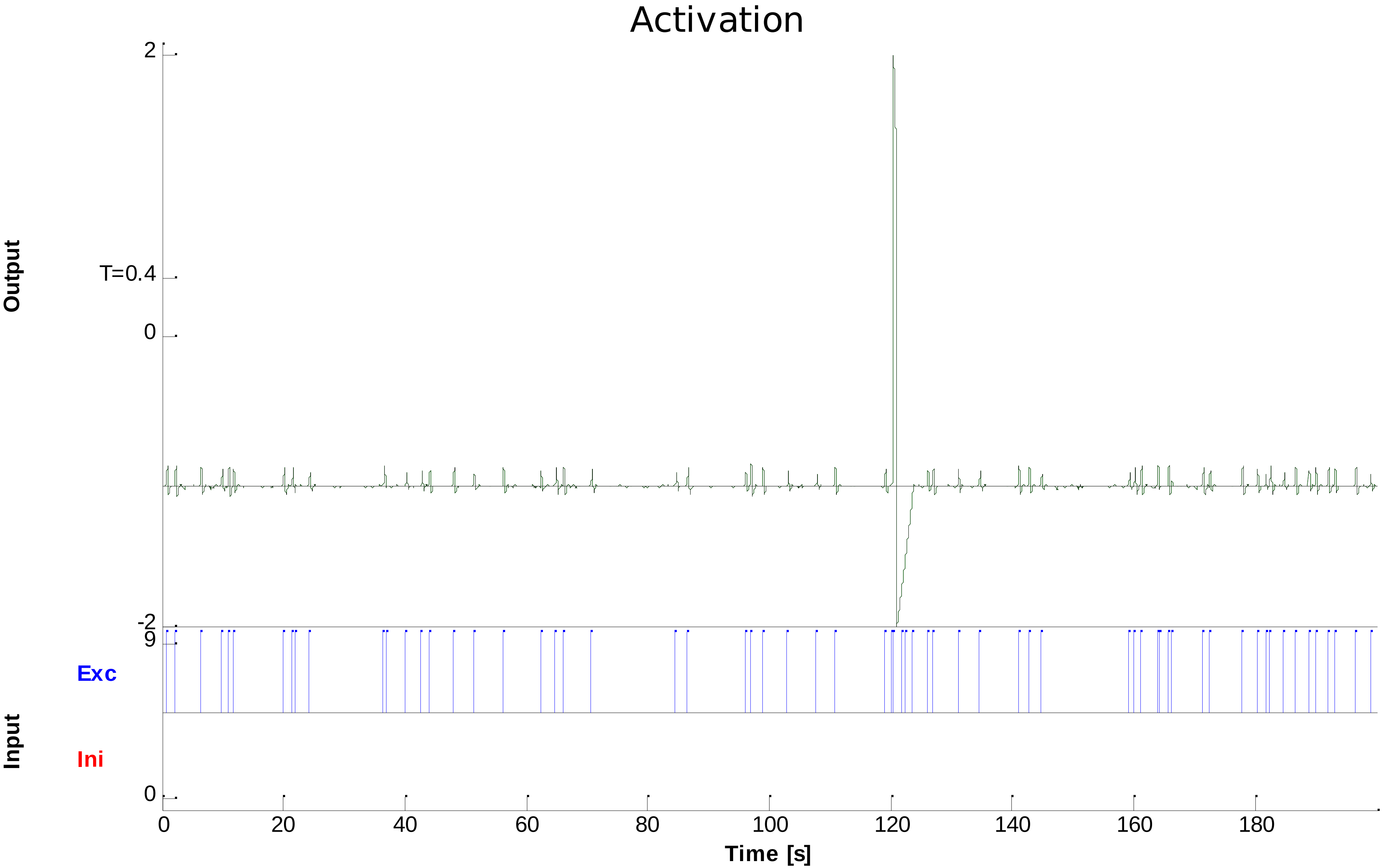


Correlated excitatory kicks:
- Low frequency
- High amplitude

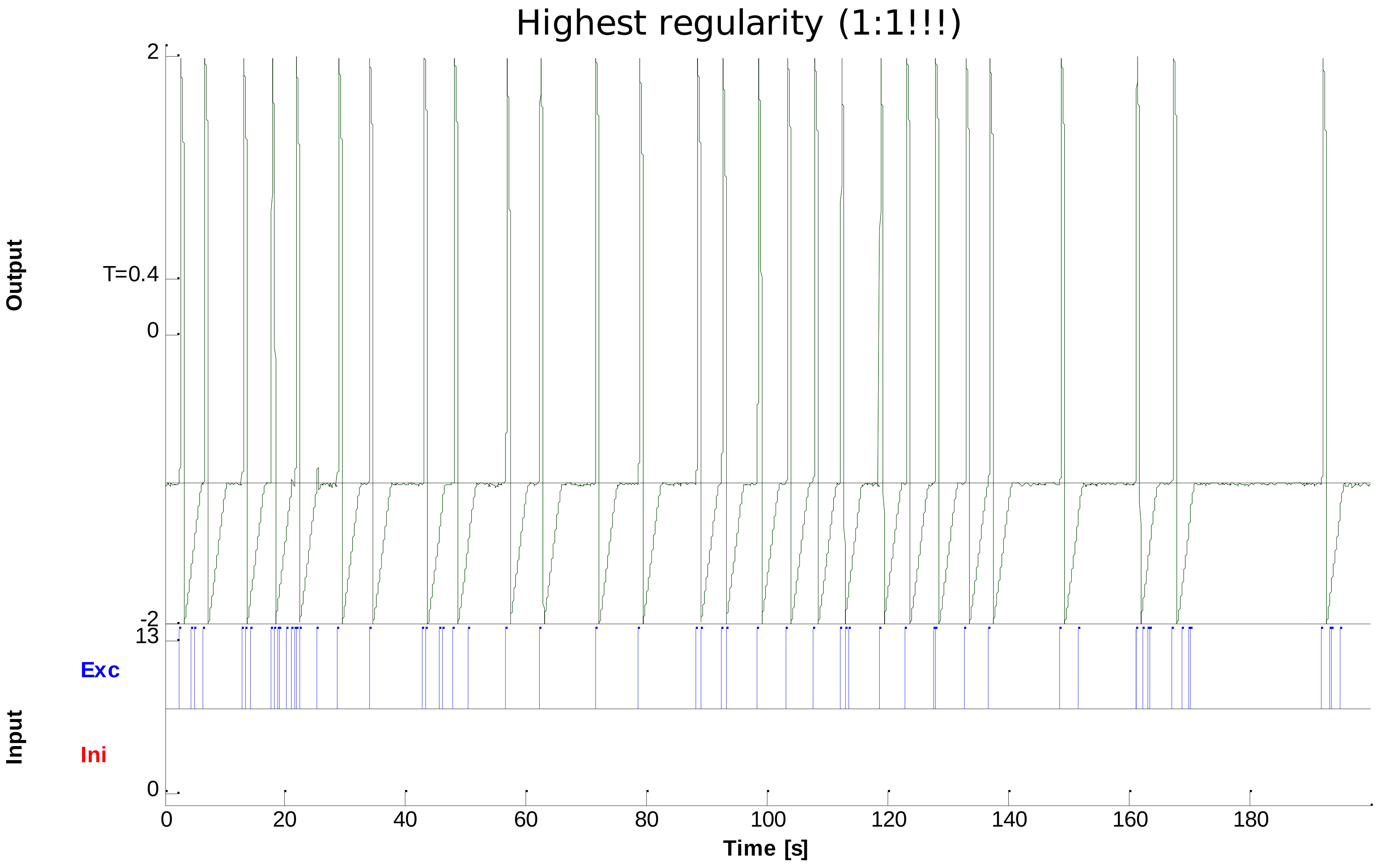
Increase of variance σ :
- Correlated excitatory kicks:
  Increase in amplitude
- Uncorrelated inhibitory kicks:
  Increase in frequency



Full excitatory correlation: Low noise

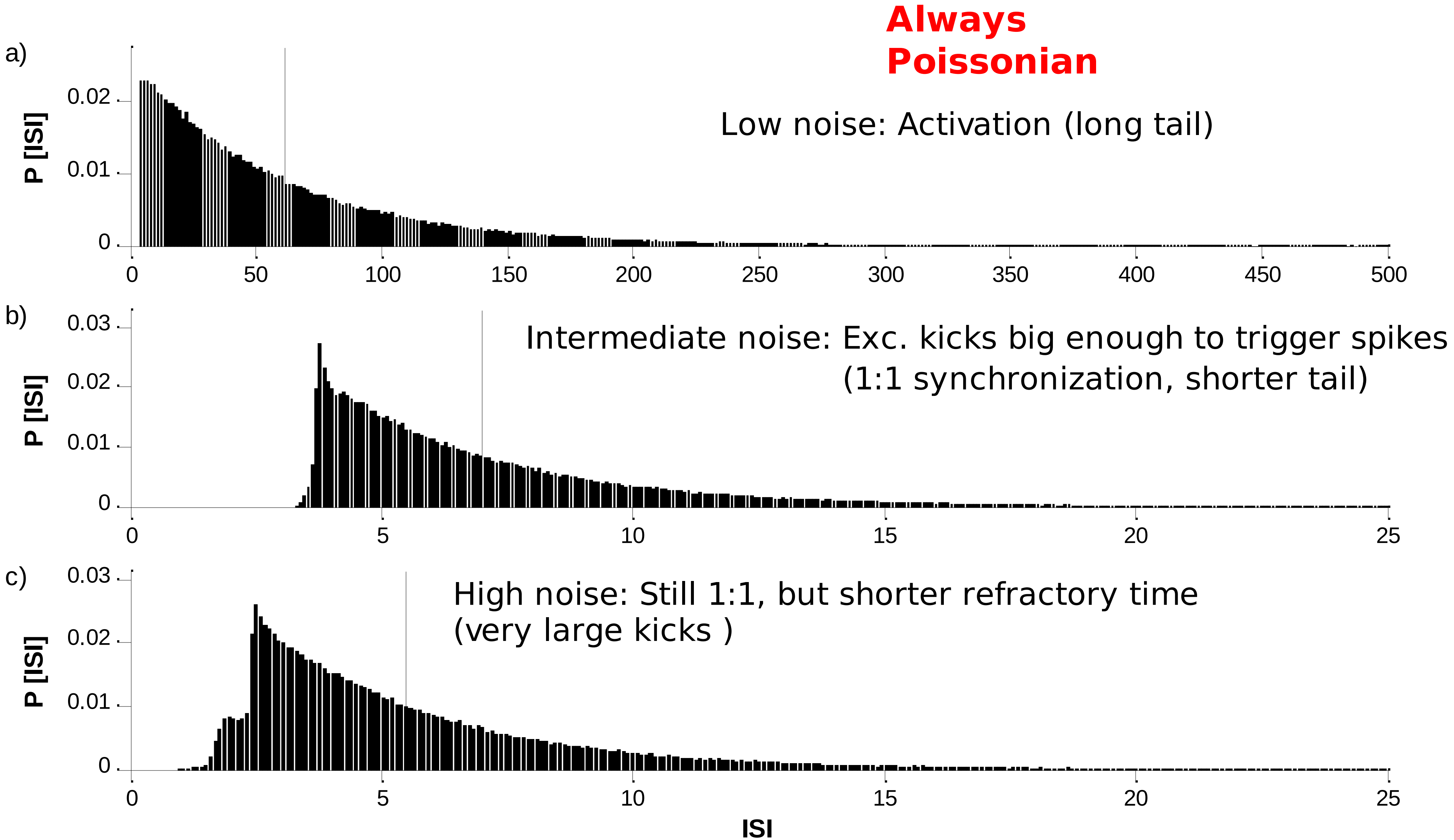


Full excitatory correlation: Medium noise

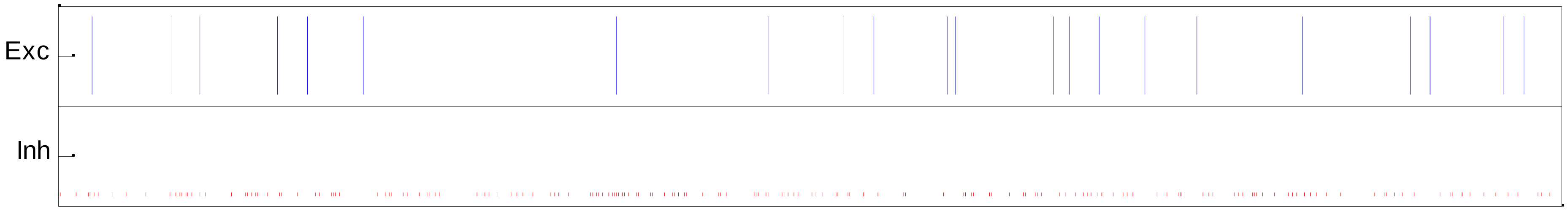


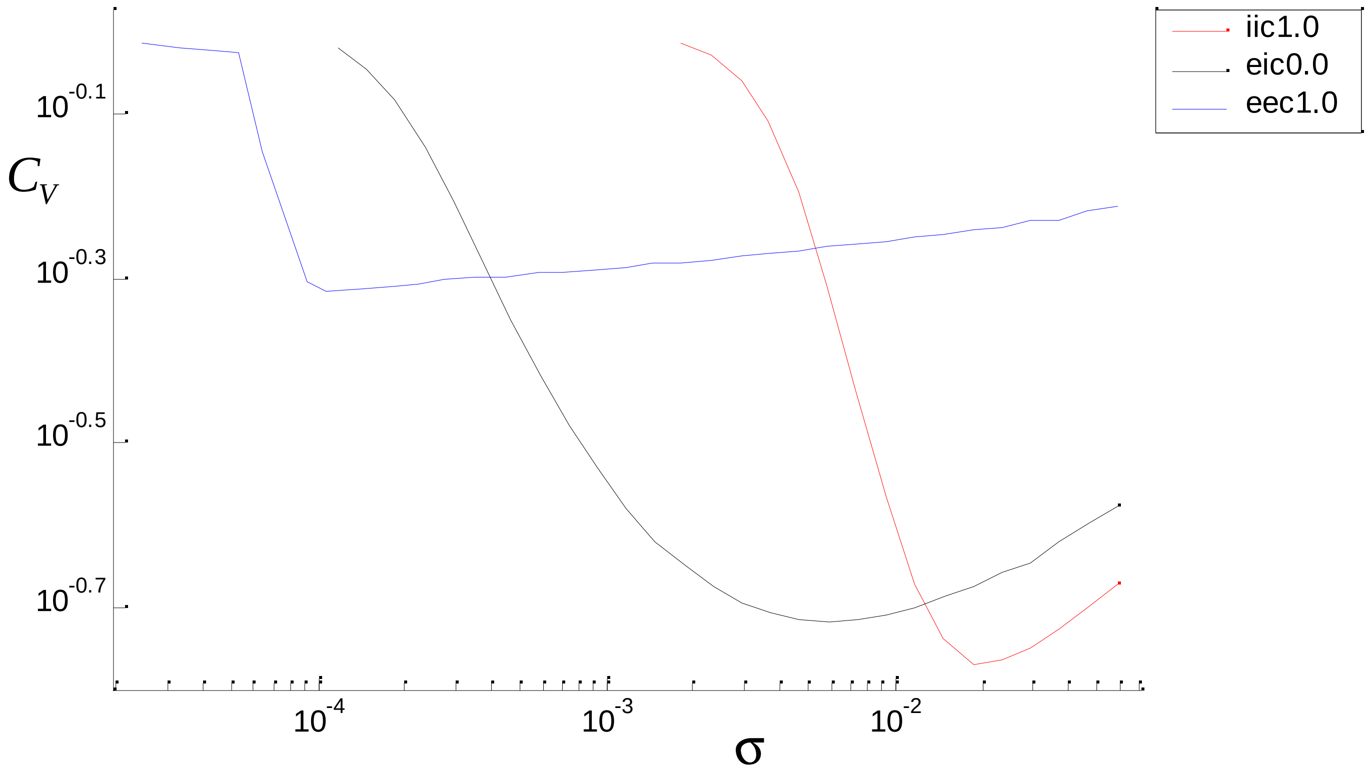
Full excitatory correlation: High noise

Full excitatory correlations: ISI-Distributions

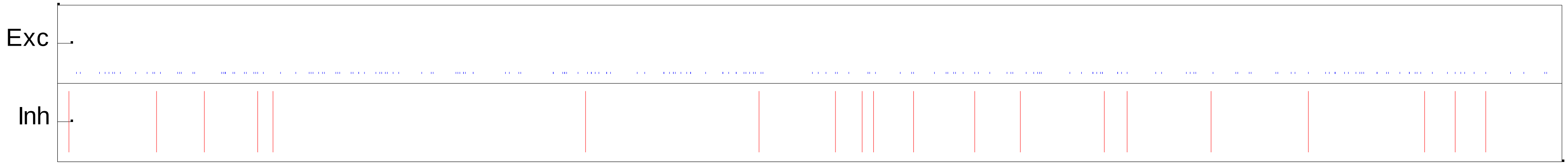


Full excitatory correlation



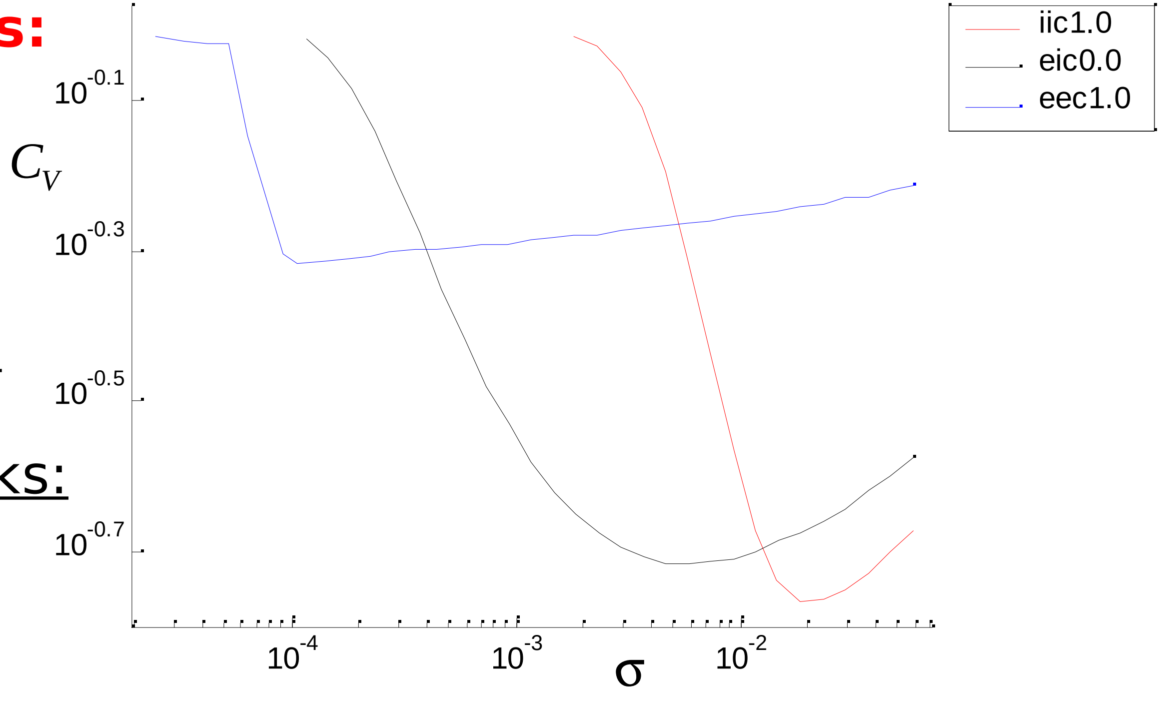


Full inhibitory correlation

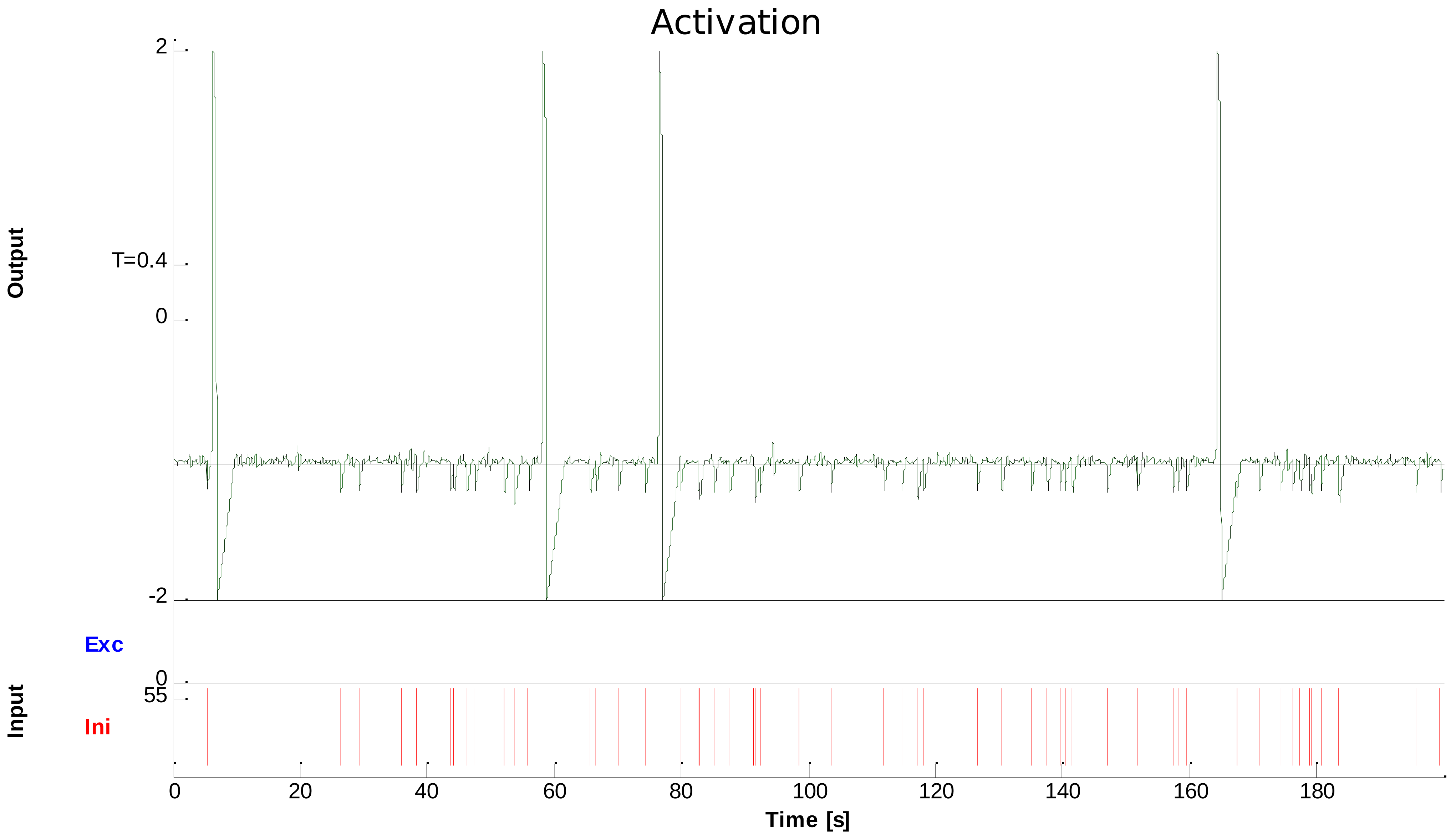


Correlated inhibitory kicks:
- Low frequency
- High amplitude

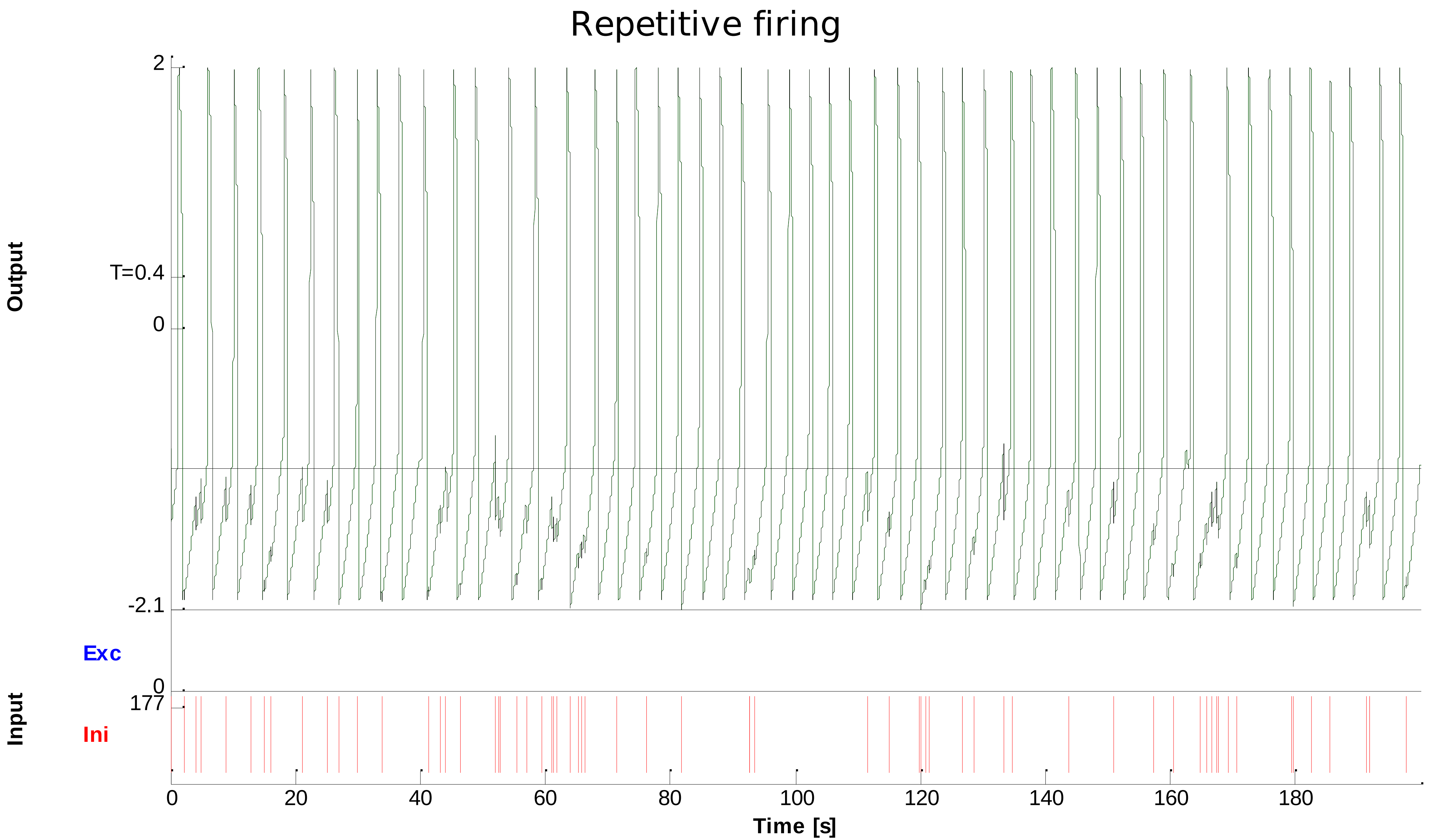
Increase of variance σ :
- Correlated inhibitory kicks:
  Increase in amplitude
- Uncorrelated excitatory kicks:
  Increase in frequency



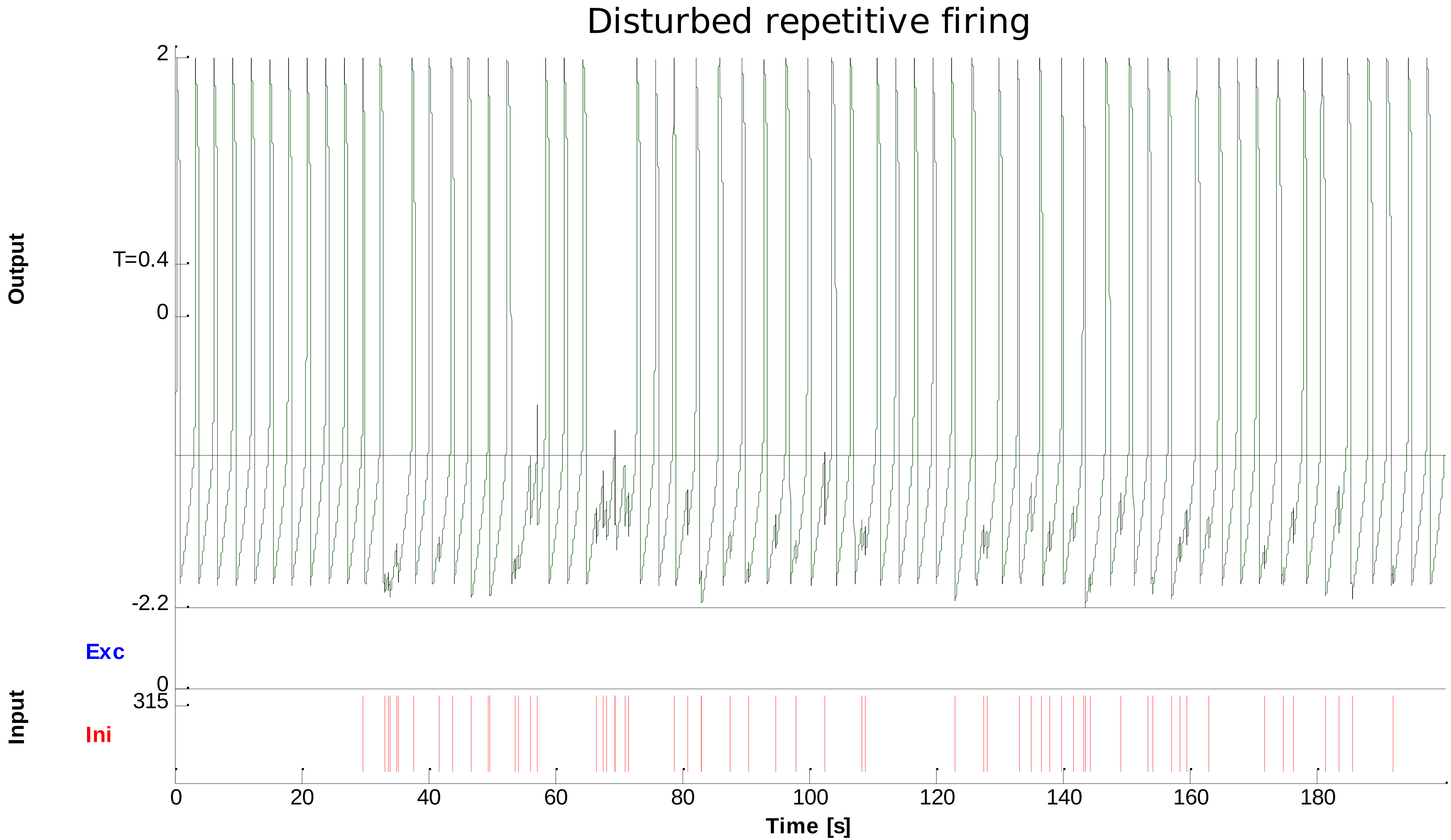
Full inhibitory correlation: Low noise



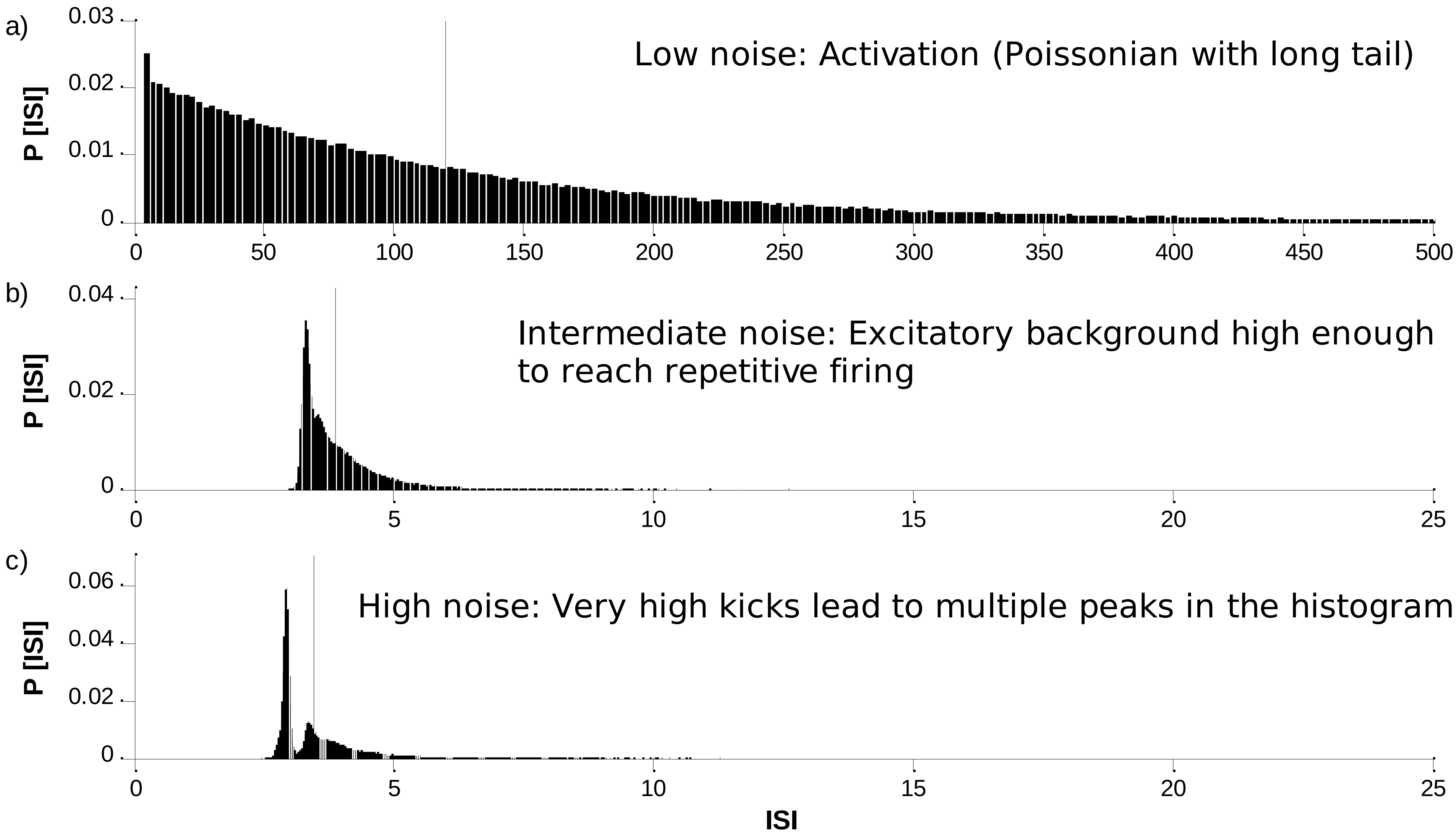
Full inhibitory correlation: Medium noise



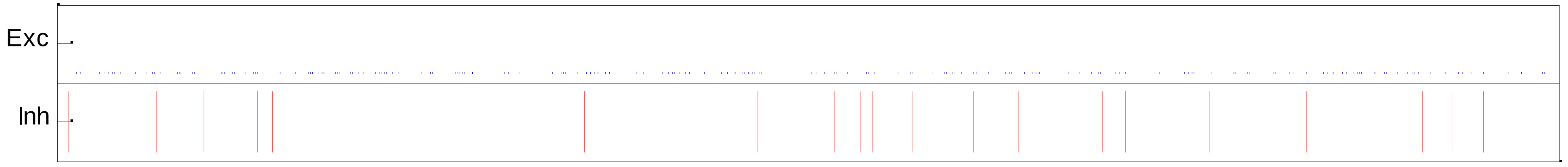
Full inhibitory correlation: High noise

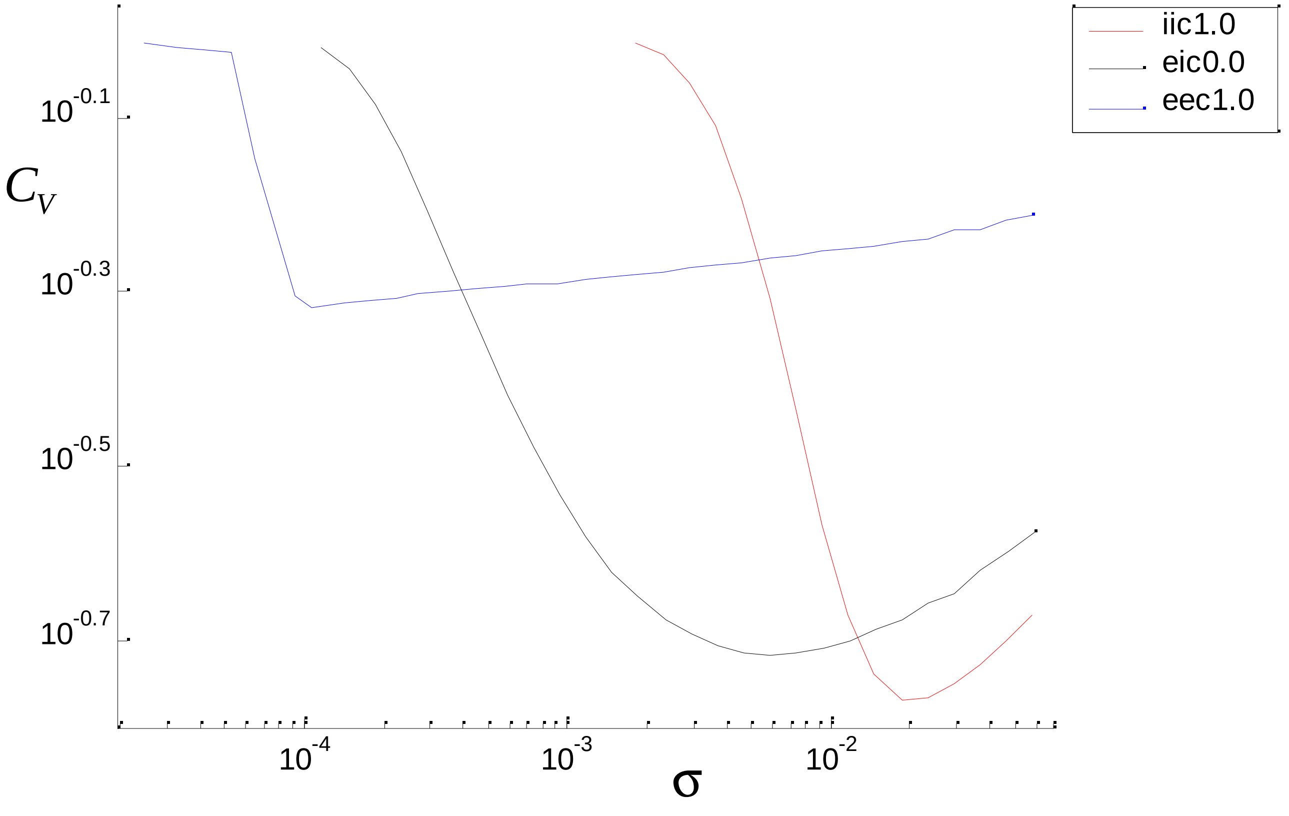


Full inhibitory correlations: ISI-Distributions

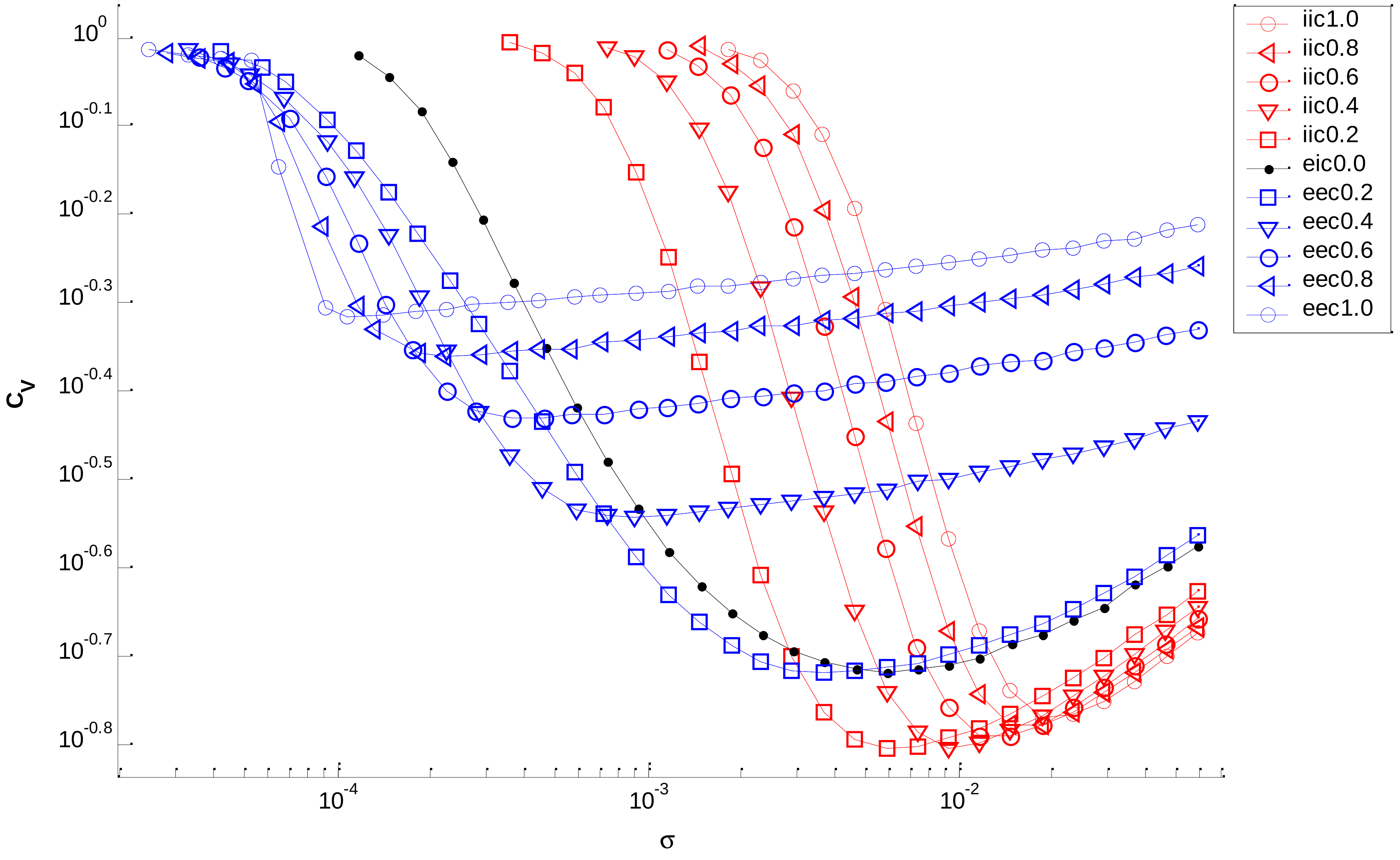


Full inhibitory correlation

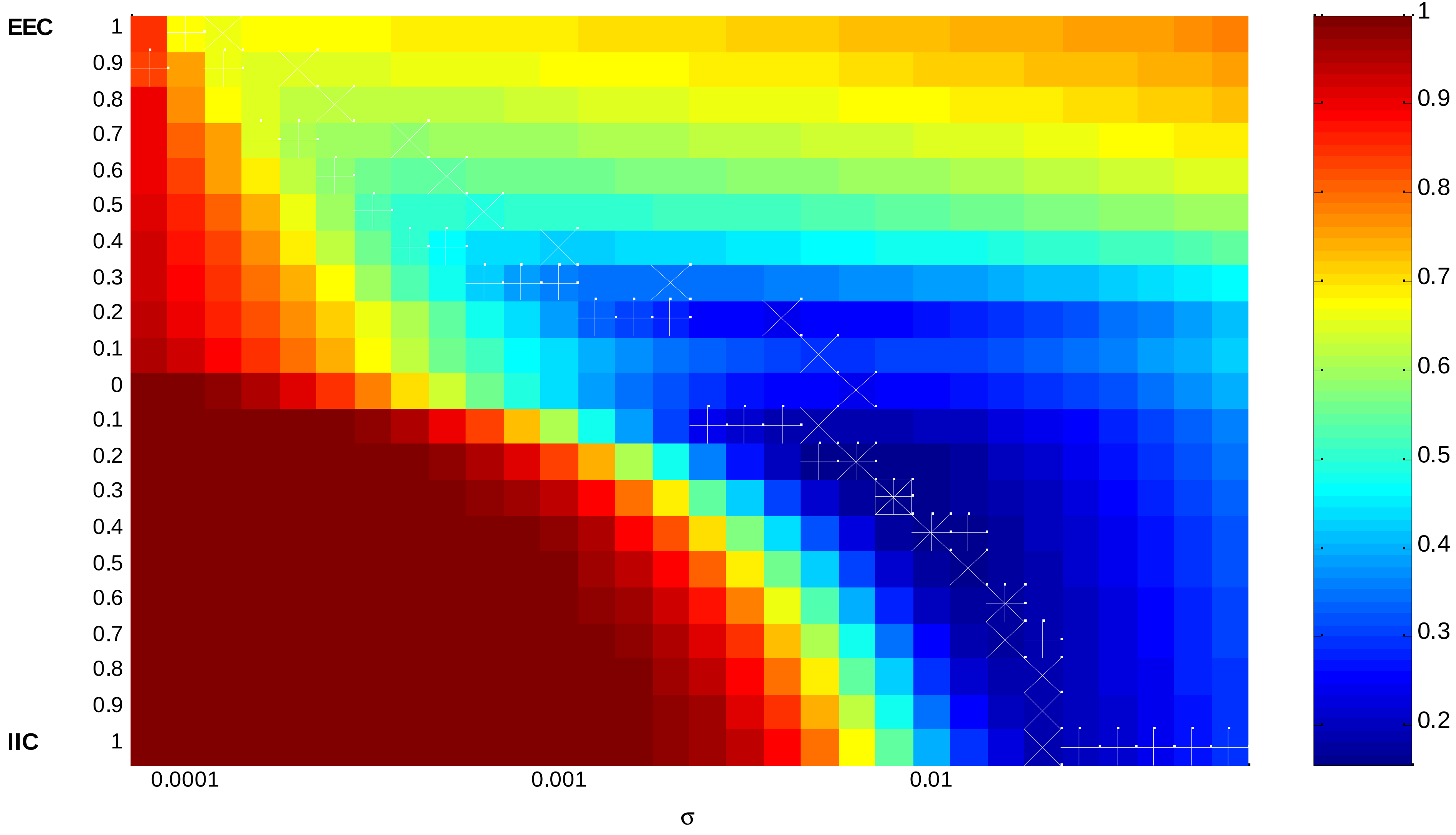




All correlations: Smooth transition



Double coherence resonance



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