# Biological Modeling of Neural Networks

ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

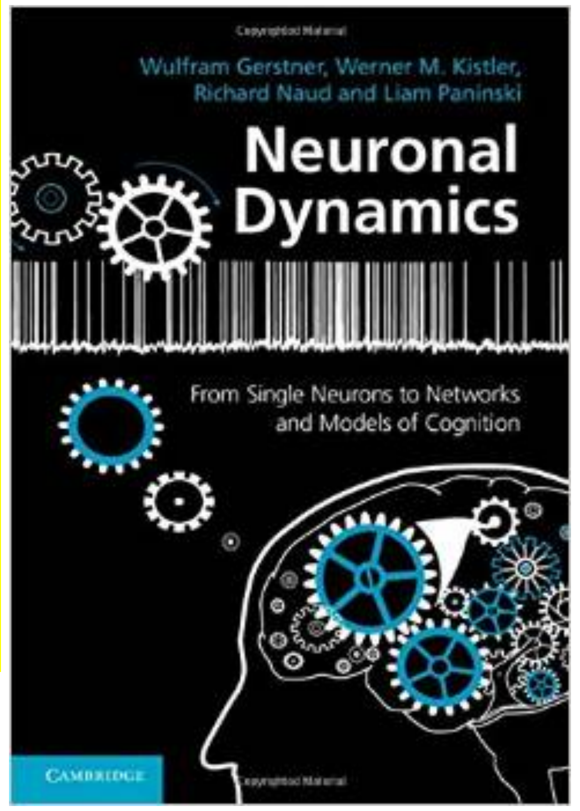
## Week 10 – Variability and Noise: The question of the neural code


Wulfram Gerstner

EPFL, Lausanne, Switzerland


*Reading for week 10*:
NEURONAL DYNAMICS
Ch. 7.1-7.3

Cambridge Univ. Press




**10.1 Variability of spike trains**
- experiments

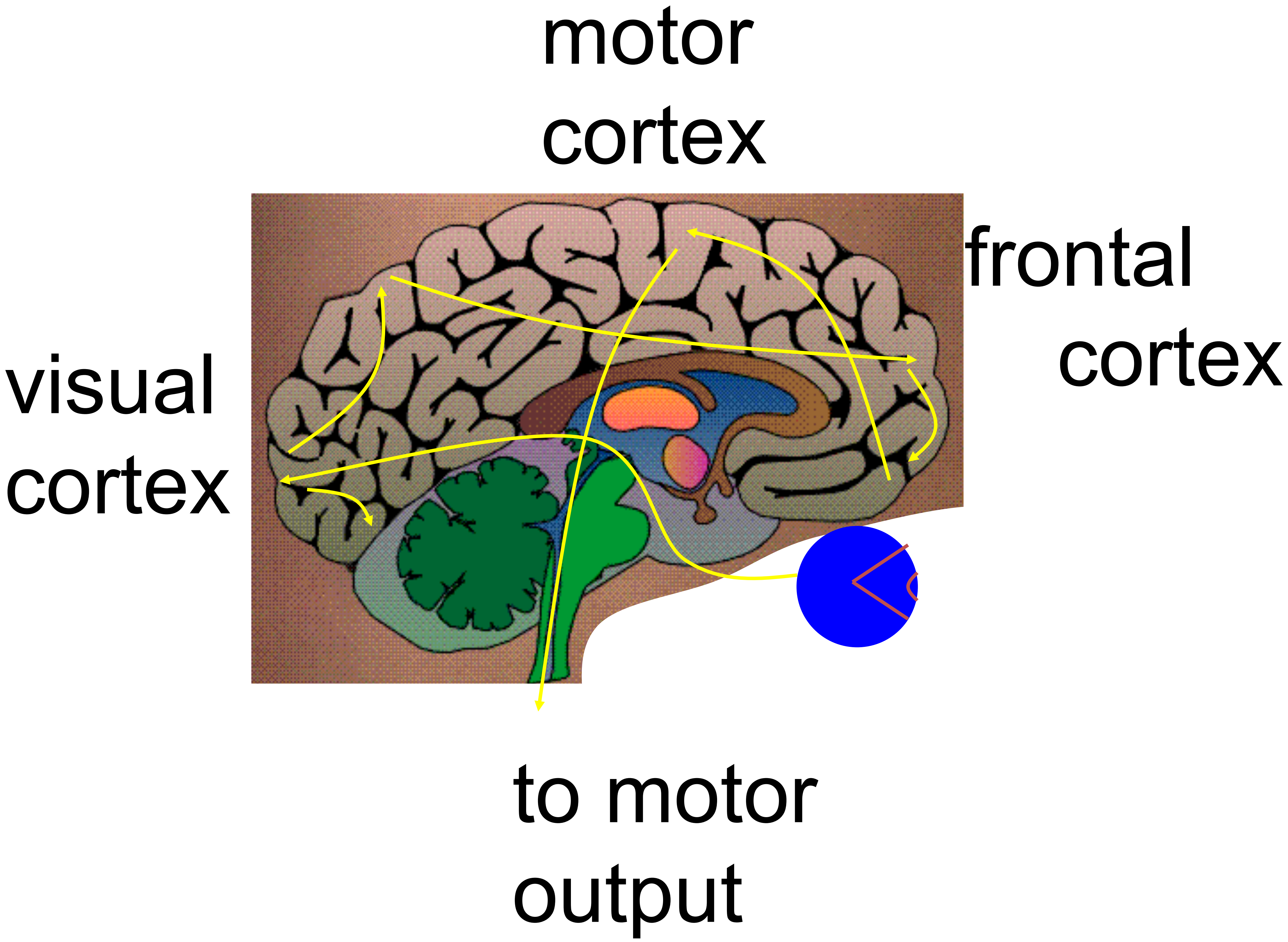
**10.2 Sources of Variability?**
- Is variability equal to noise?

**10.3 Poisson Model**
- homogeneous/inhomogeneous

**10.4 Three definitions of Rate Code**

**10.5 Stochastic spike arrival**
- Membrane potential fluctuations

# 10.1 Variability in vivo – review from week 1

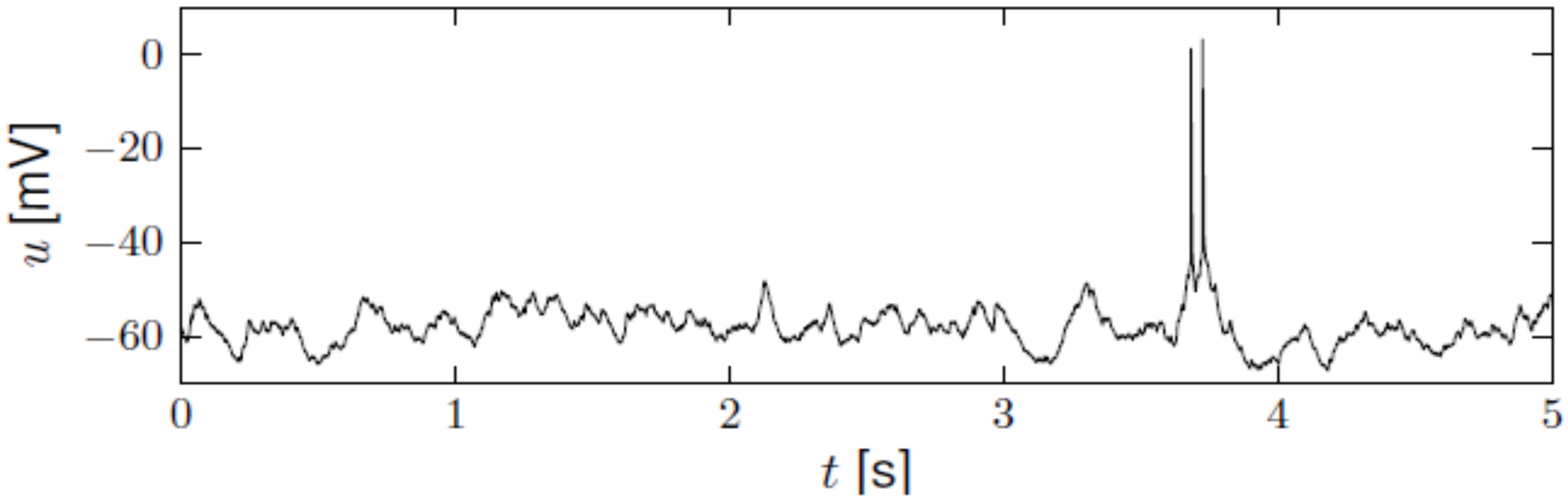


# 10.1 Variability in vivo – review from week 1

Spontaneous activity *in vivo*

Variability
- of membrane potential?
- of spike timing?

awake mouse, cortex, freely whisking,

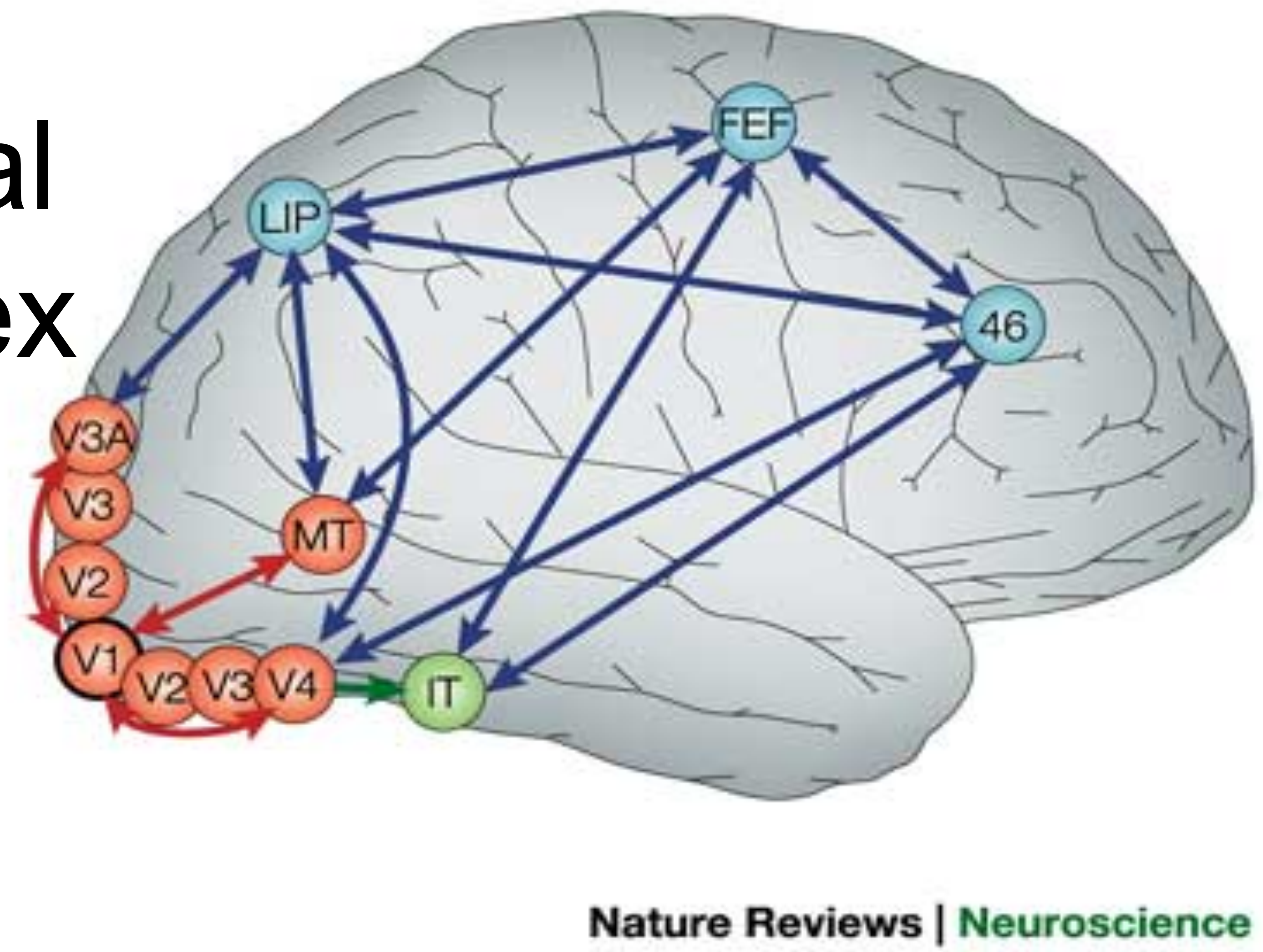


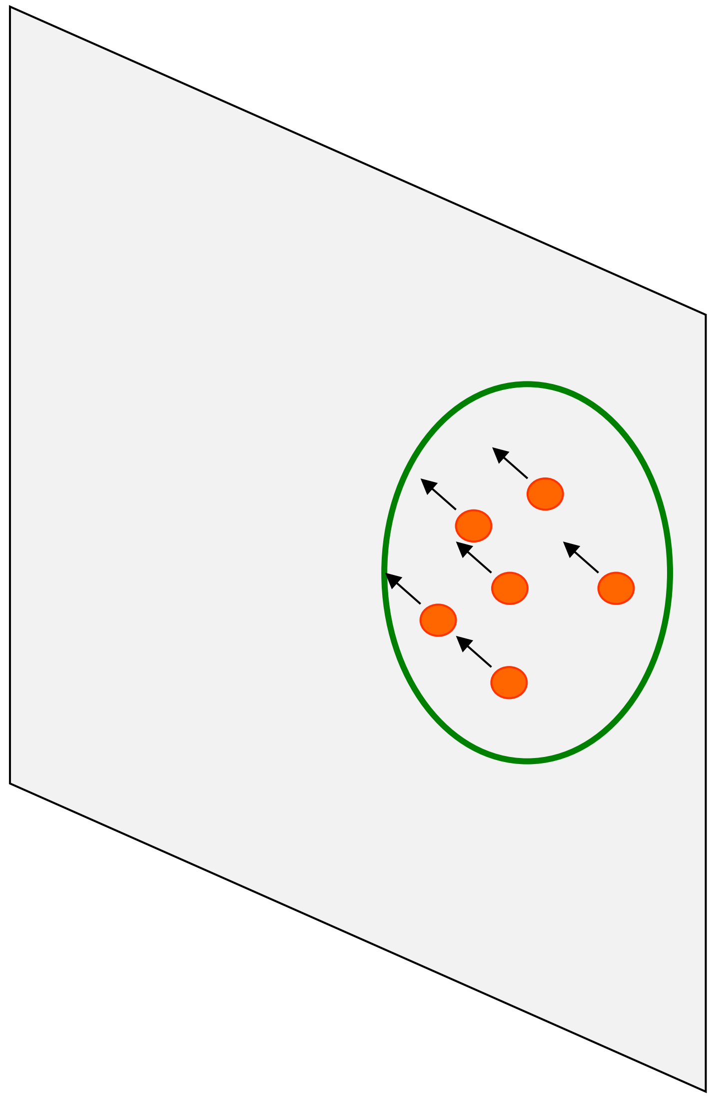

*Crochet et al., 2011*

# 10.1 Variability in vivo – Detour: Motion Sensitive Neurons

Detour: Receptive fields in V5/MT

visual cortex

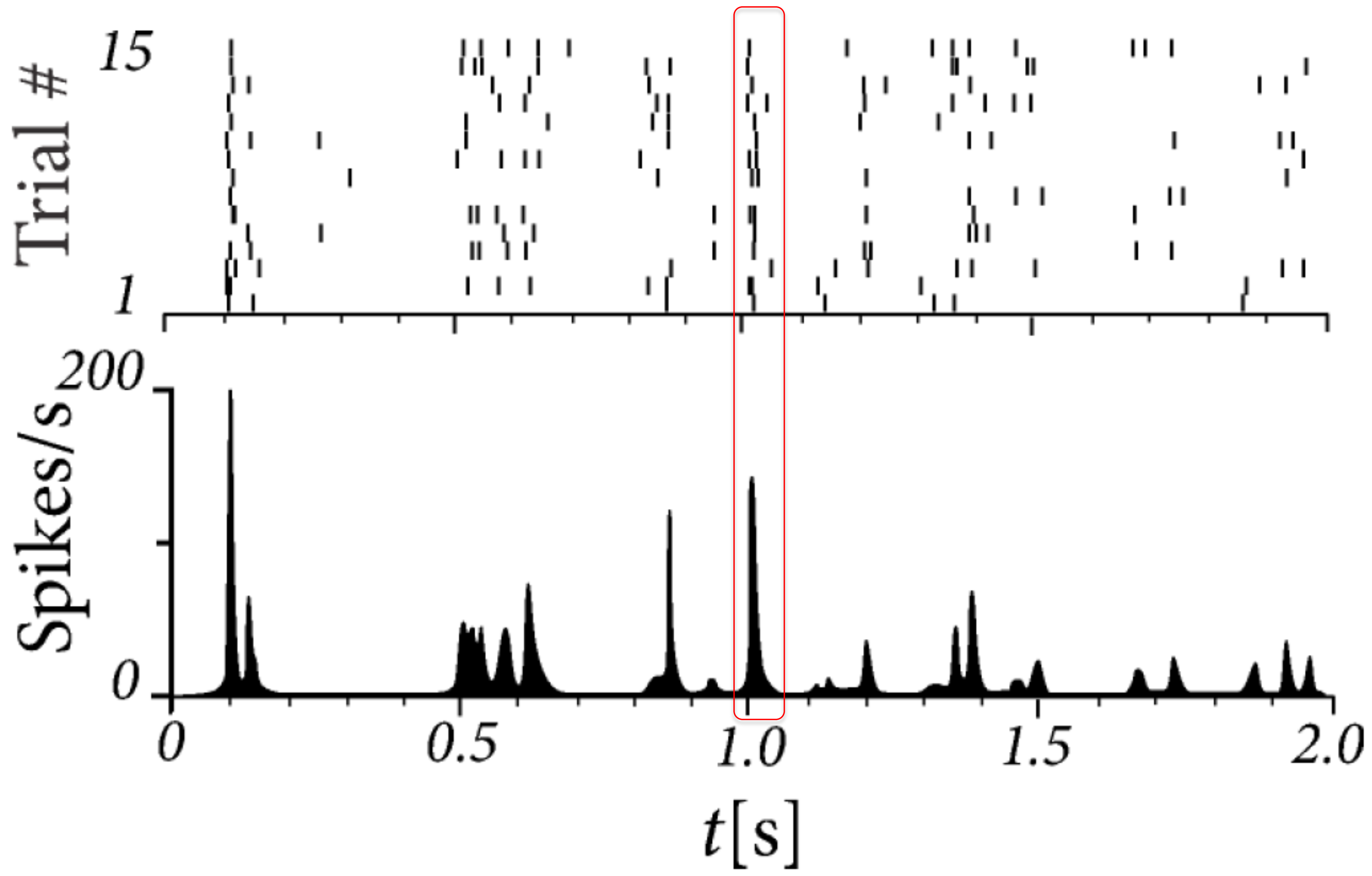


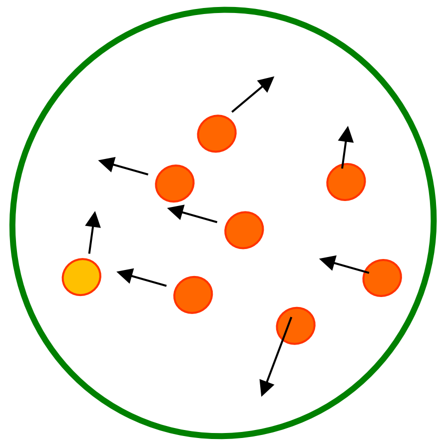



cells in visual cortex MT/V5 respond to motion stimuli

# 10.1 Variability in vivo – Neurons in MT/V5

15 repetitions of the **same** random dot motion pattern



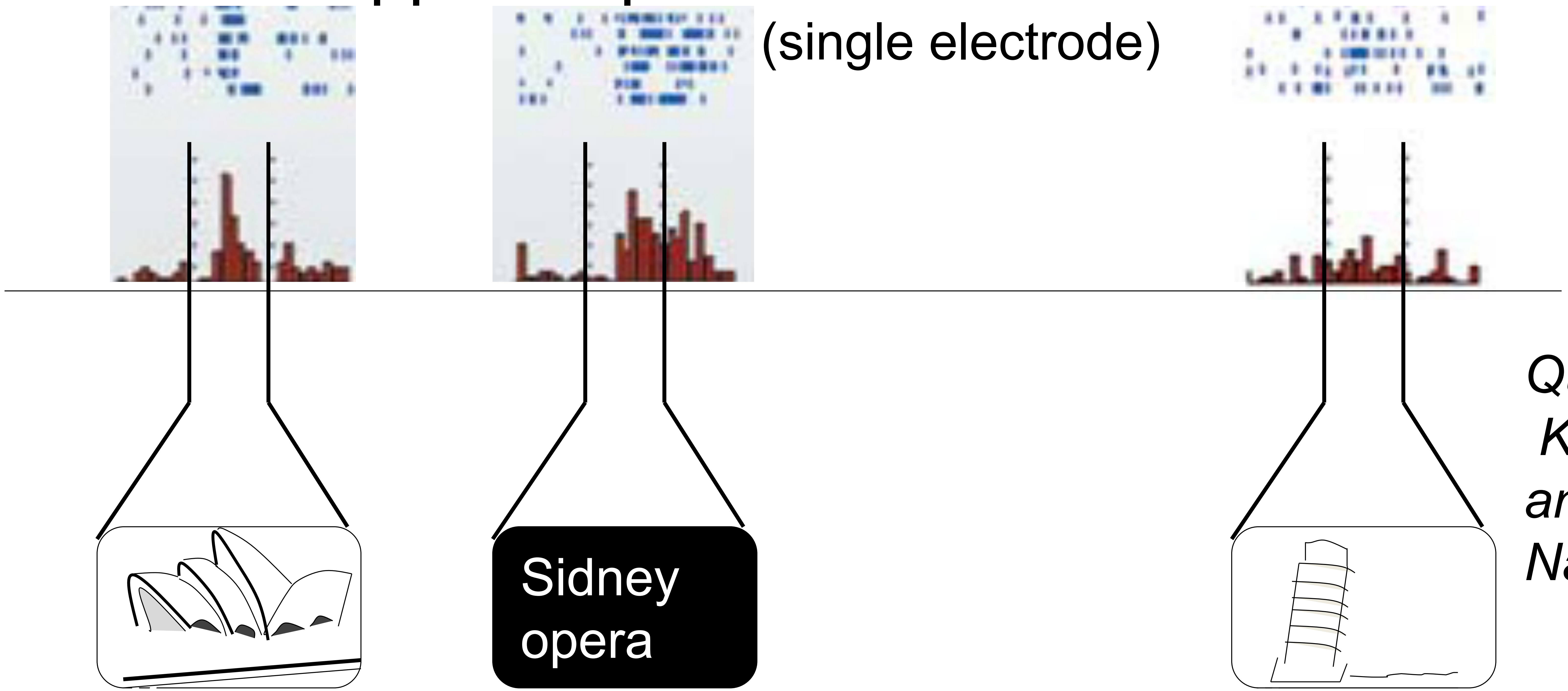



*adapted from Bair and Koch 1996;*
*data from Newsome 1989*

# 10.1 Variability in vivo

Human Hippocampus

(single electrode)




*Quiroga, Reddy, Kreiman, Koch, and Fried (2005). Nature, 435:1102-1107.*

# 10.1 Variability in vitro

4 repetitions of the same time-dependent stimulus,

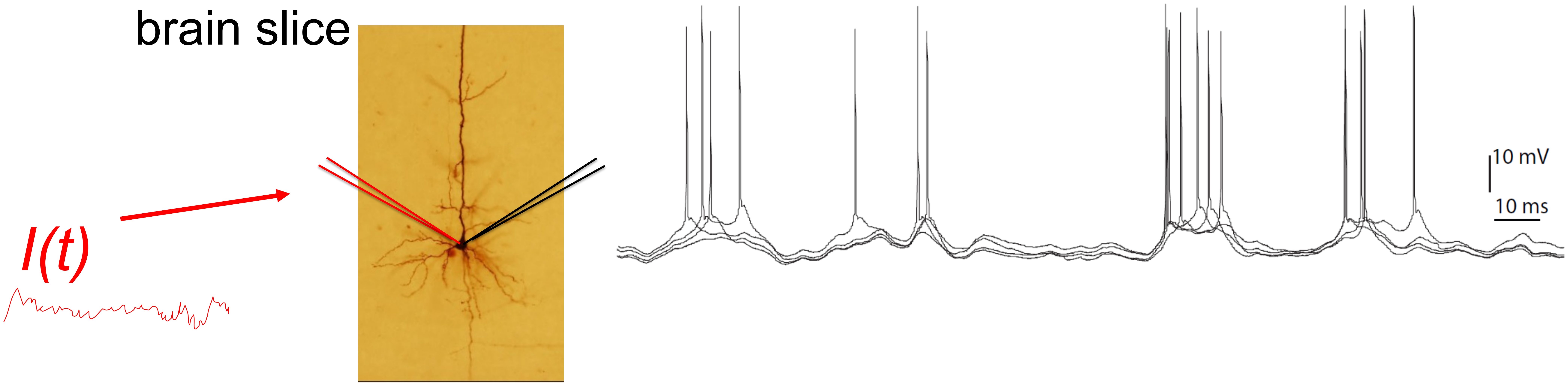



*Image: Gerstner et al.*
*Neuronal Dynamics (2014)*
*Adapted from*
*Naud and Gerstner (2012)*

# 10.1 Summary and Questions: Variability

In vivo data

→ looks ‘noisy’

→ differences between trials

→ fluctuations of membrane potential

In vitro data

→ fluctuations of membrane potential

→ spikes at slightly different times in each trail

**Observed Fluctuations**

-of membrane potential

-of spike times

fluctuations=noise?

relevance for coding?

source of fluctuations?

model of fluctuations?

# 10.1 Summary and Questions: Variability

We observe fluctuations in data  recorded in vivo or in vitro.

Today and in the next weeks we ask the question:

- Are this fluctuations really noise?
- Or do they reflect a coding scheme?
- What is the physical or biological source of the observed variability?
- Can we write down a good model to describe the membrane potential fluctuations or variability of spike times between trials?

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## Week 10 – Variability and Noise: The question of the neural code

Wulfram Gerstner

EPFL, Lausanne, Switzerland

√ **10.1 Variability of spike trains**
- experiments

**10.2 Sources of Variability?**
- Is variability equal to noise?

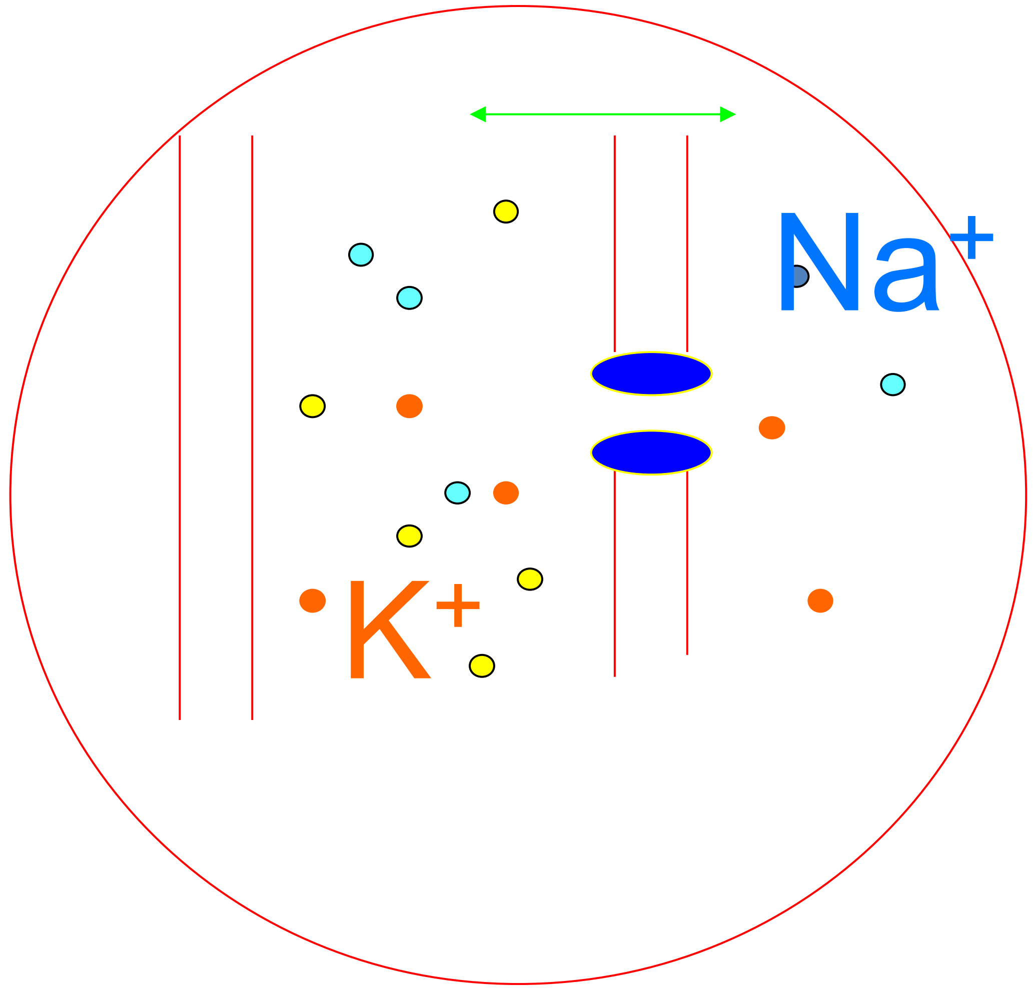
**10.3 Poisson Model**
- homogeneous/inhomogeneous

**10.4 Three definitions of Rate Code**

**10.5 Stochastic spike arrival**
- Membrane potential fluctuations

# 10.2. Sources of Variability

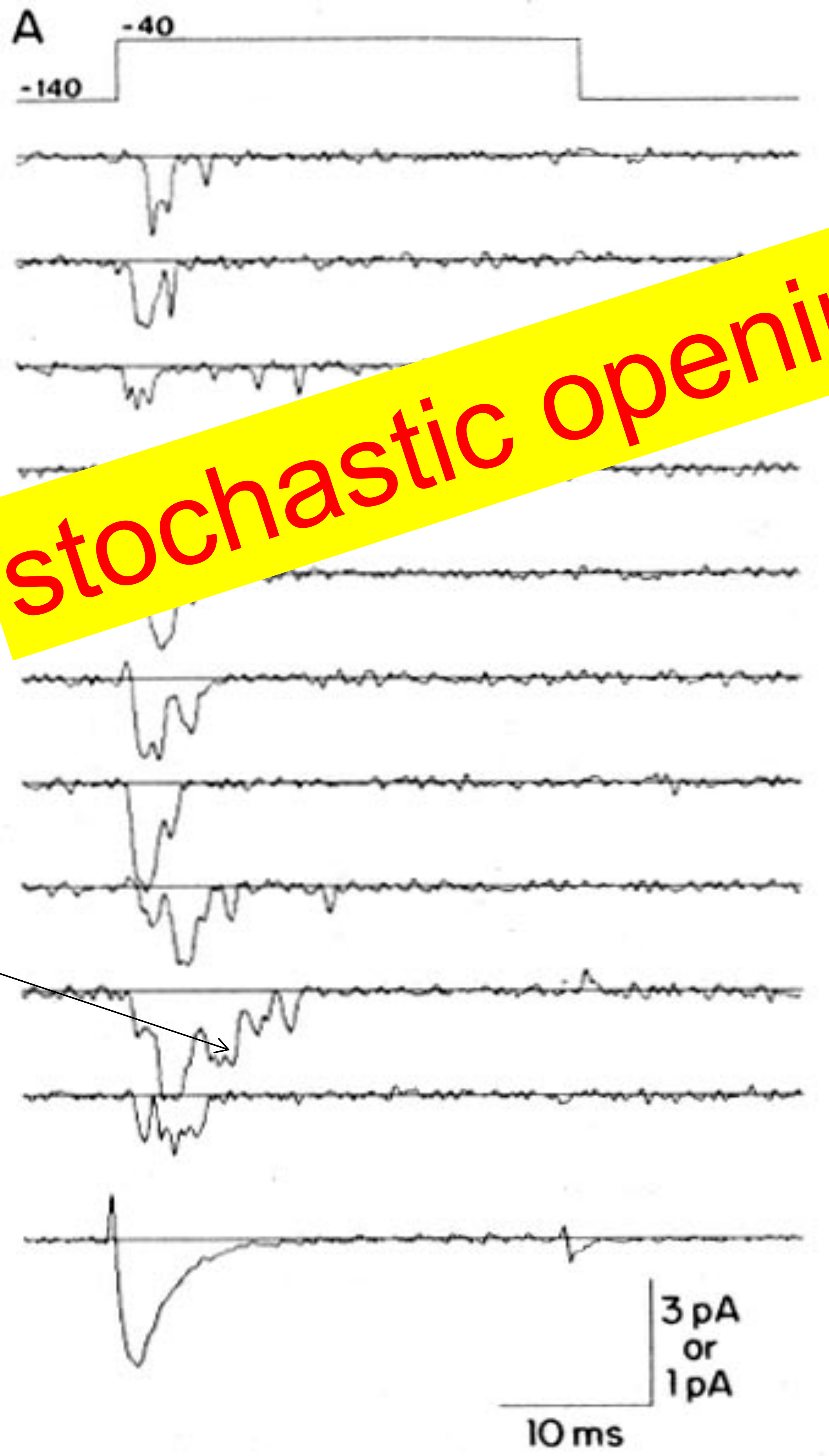
- Intrinsic noise (ion channels)



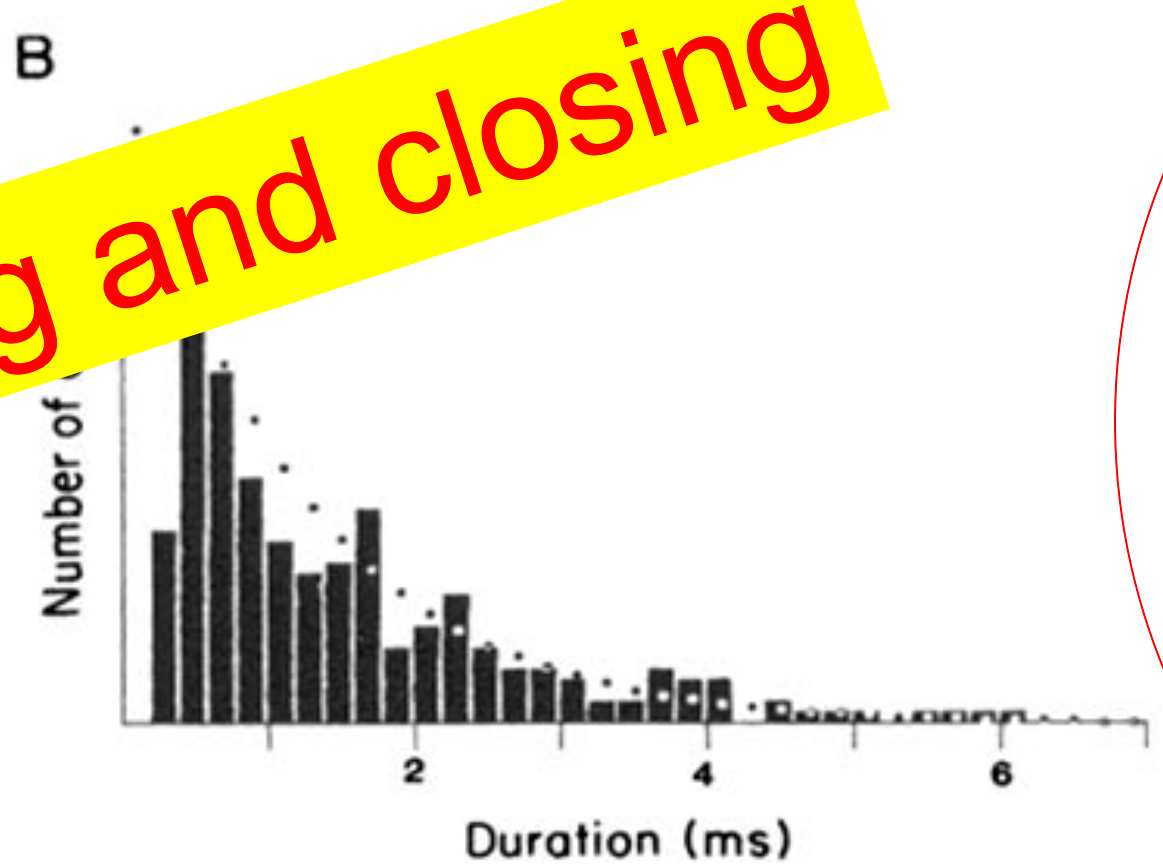

-Finite number of channels
-Finite temperature

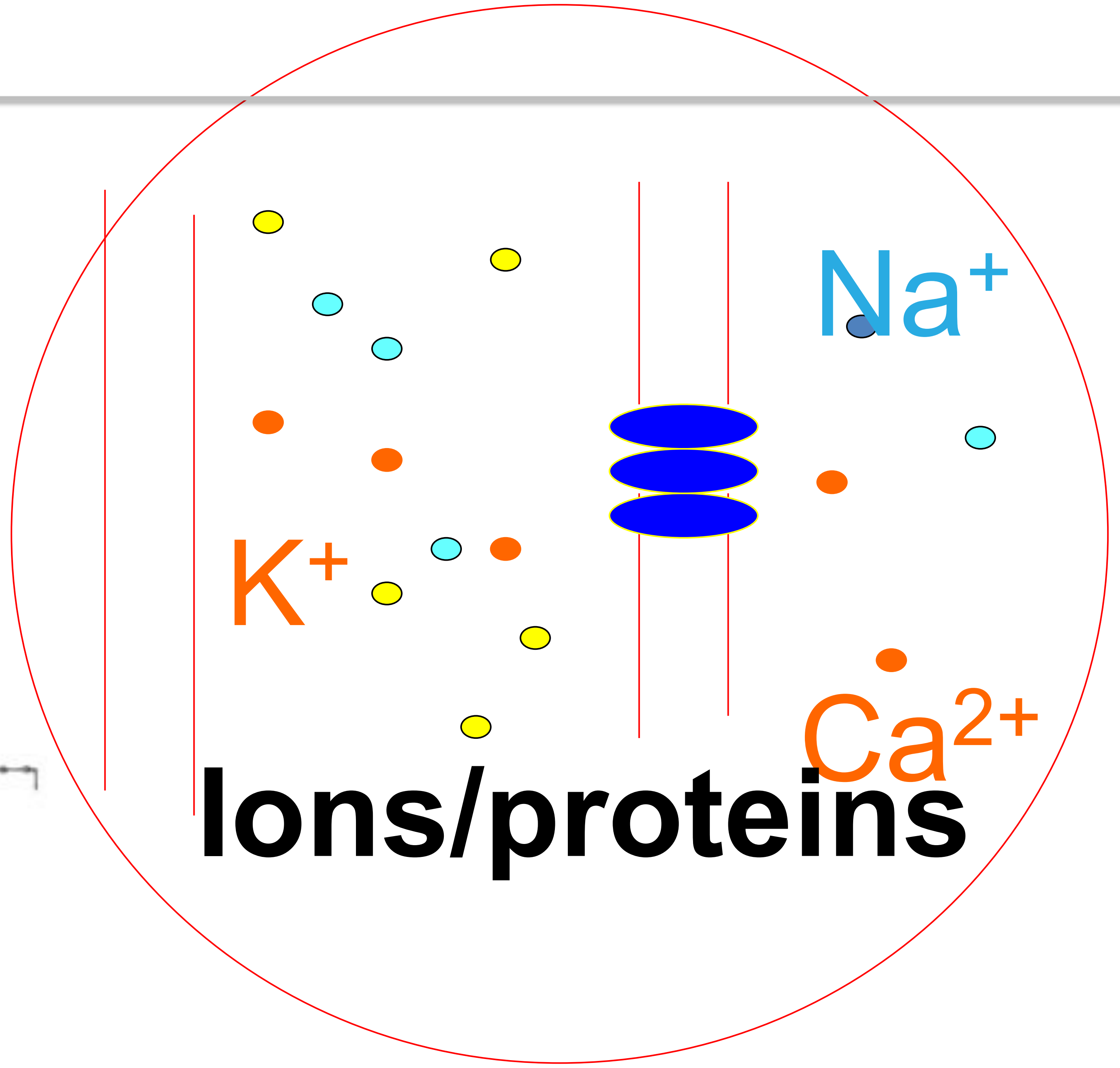
# Review from week 2 Ion channels

Steps: Different number of open channels




stochastic opening and closing

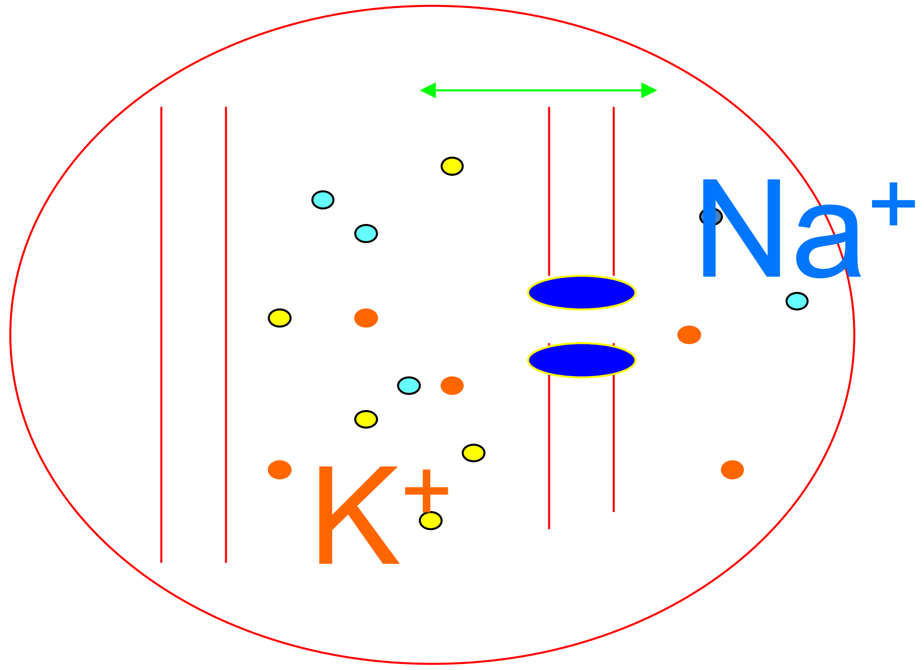



Na+ channel from rat heart *(Patlak and Ortiz 1985)*
**A** traces from a patch containing several channels.
Bottom: average gives current time course.
**B.** Opening times of single channel events

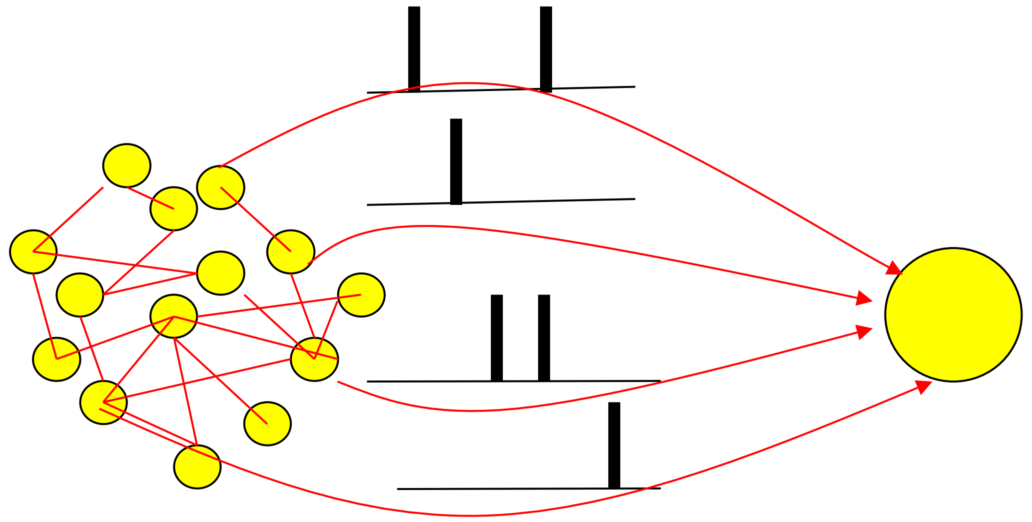
# 10.2. Sources of Variability

- Intrinsic noise (ion channels)




-Finite number of channels
-Finite temperature

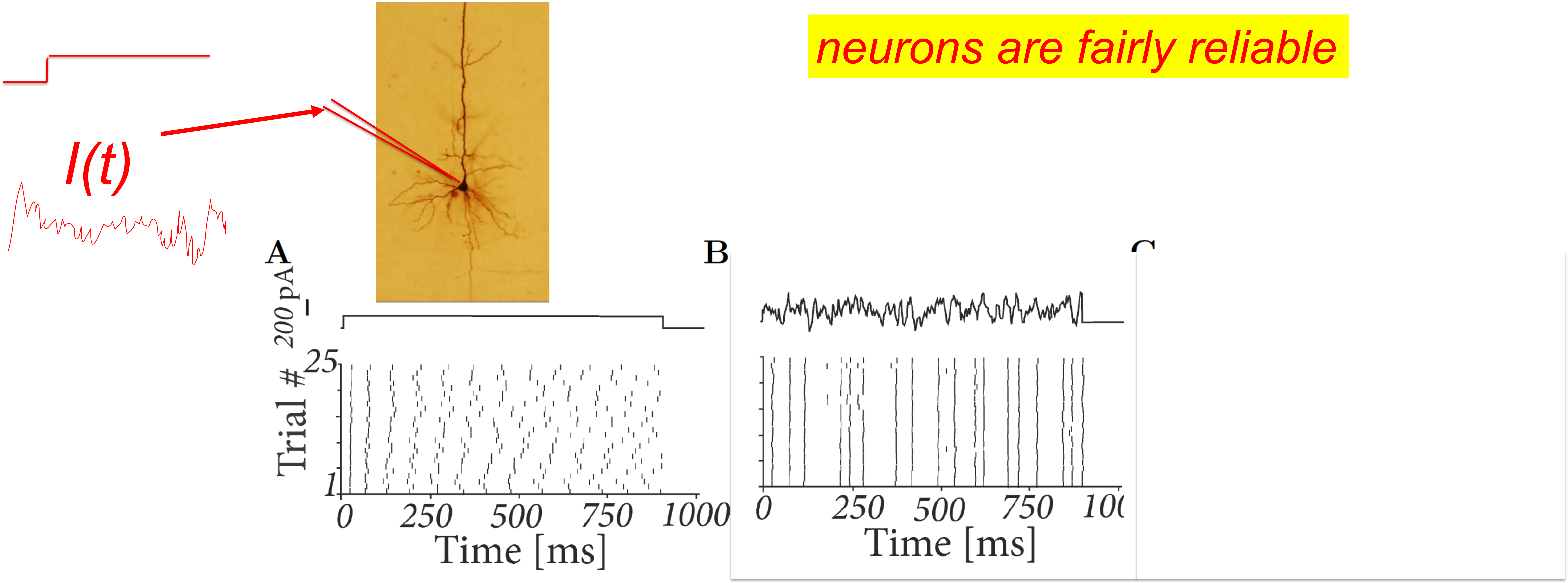
-Network noise (background activity)



-Spike arrival from other neurons
-Beyond control of experimentalist

→ Check intrinisic noise by removing the network

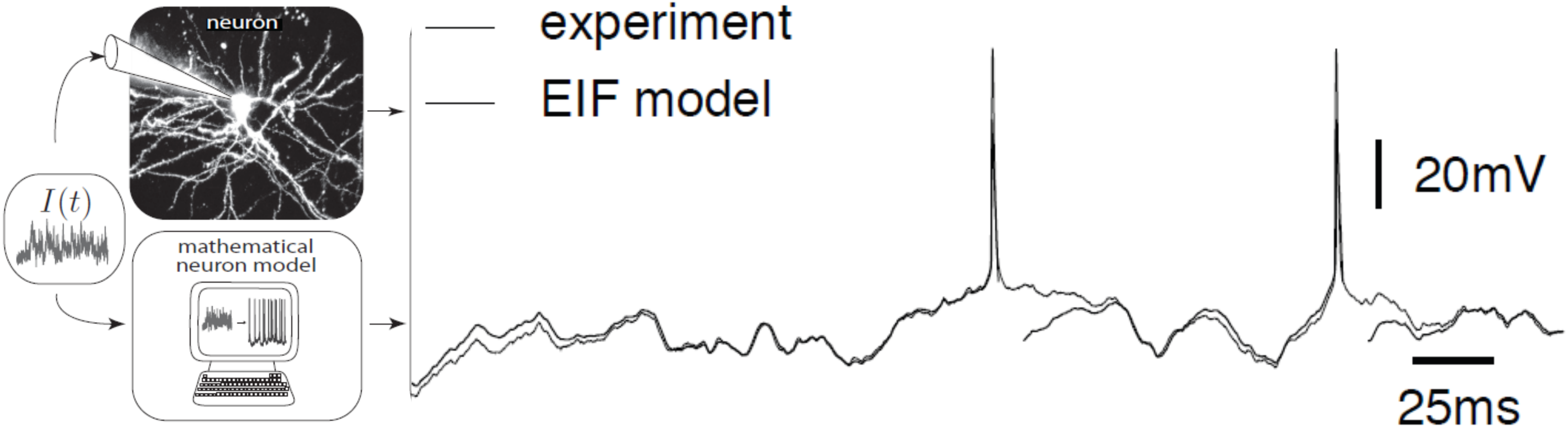
# 10.2 Variability in vitro is low




*neurons are fairly reliable*

*Image adapted from Mainen&Sejnowski 1995*

# REVIEW from week1: How good are integrate-and-fire models?



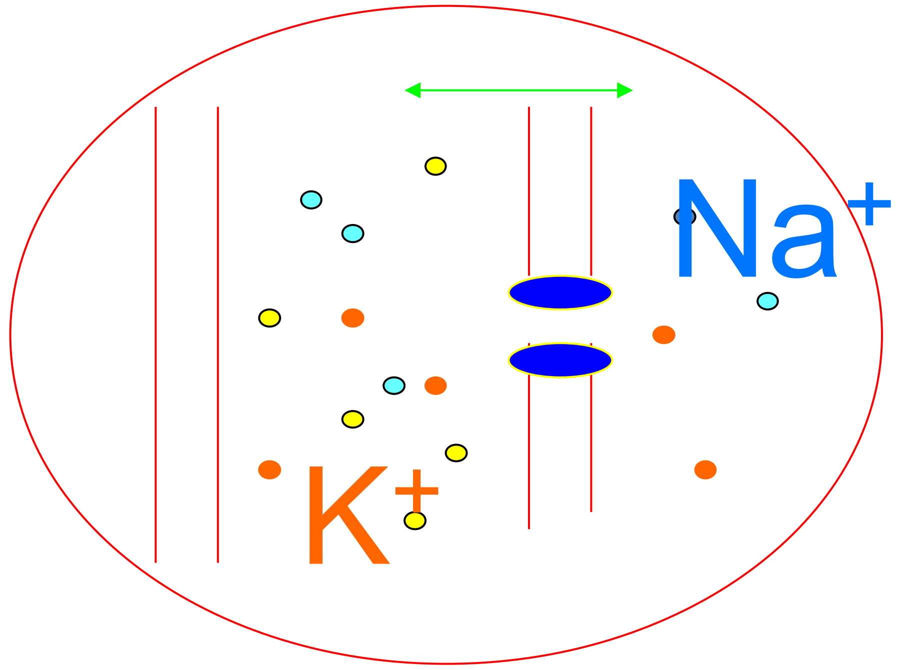

Badel et al., 2008

Aims: - predict spike initiation times
- predict subthreshold voltage

*only possible, because neurons are fairly reliable*

# 10.2. Sources of Variability

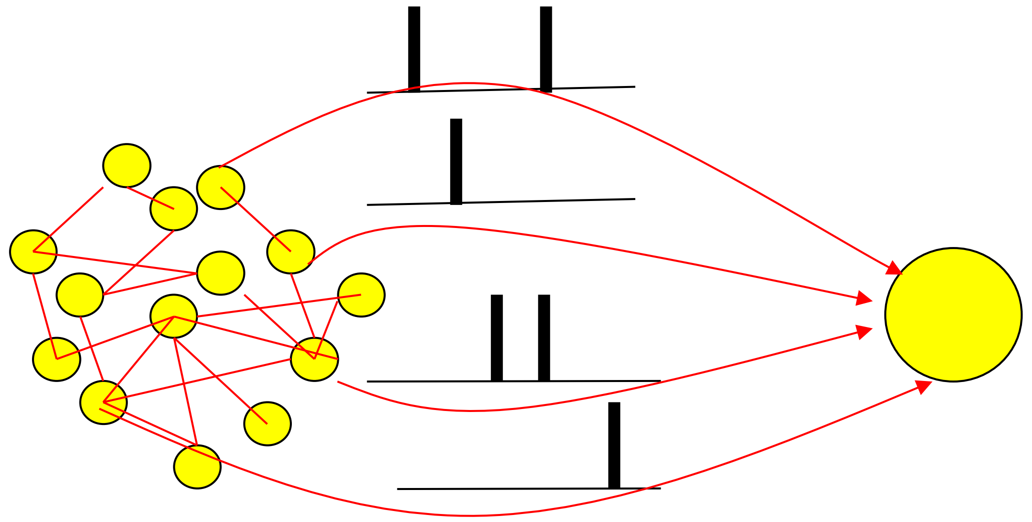
- Intrinsic noise (ion channels)




-Finite number of channels
-Finite temperature

small contribution!

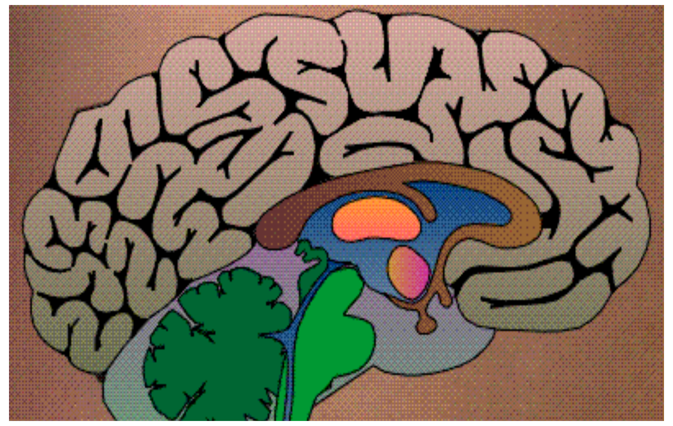
-Network noise (background activity)



-Spike arrival from other neurons
-Beyond control of experimentalist

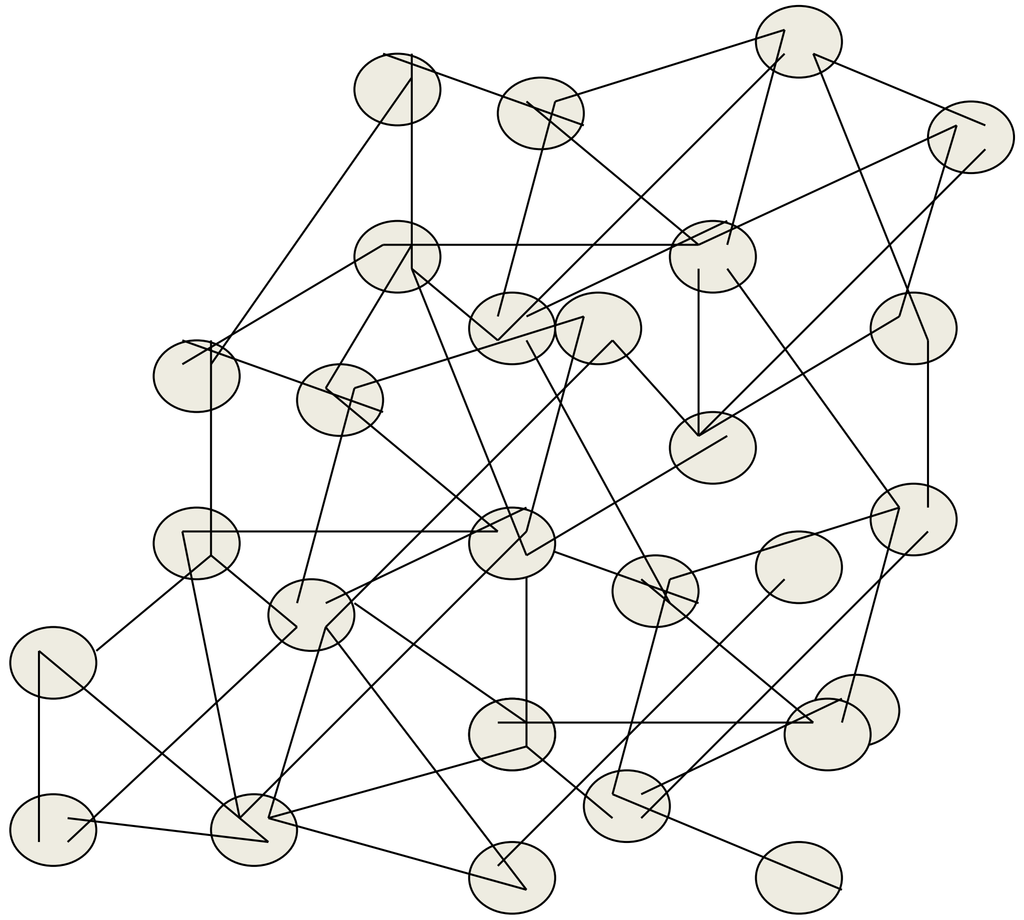
→ Check network noise by simulation!

# 10.2 Sources of Variability



Brain

The Brain: a highly connected system



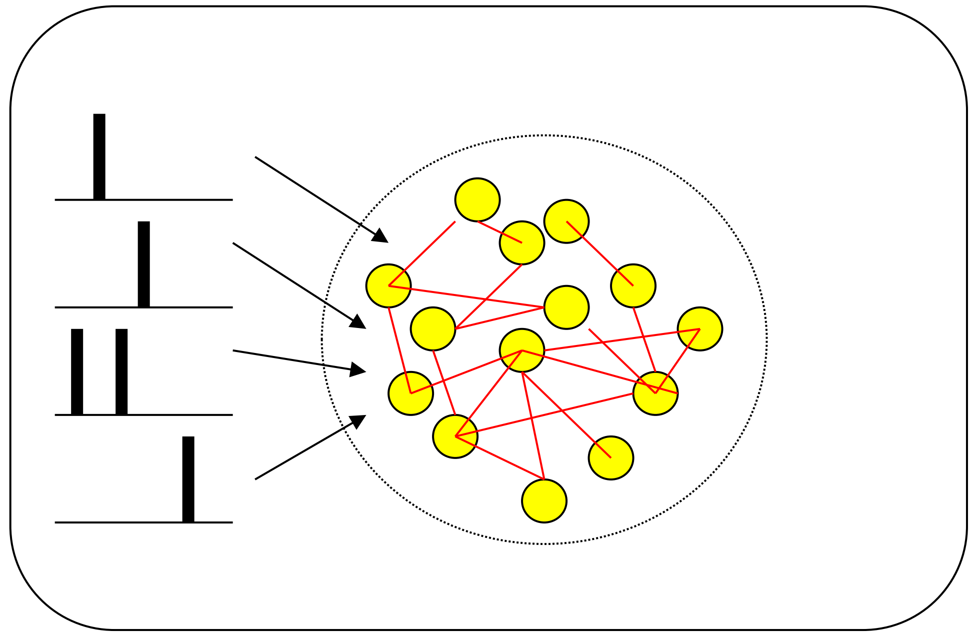
High connectivity:
systematic, organized in local populations
but **seemingly random**

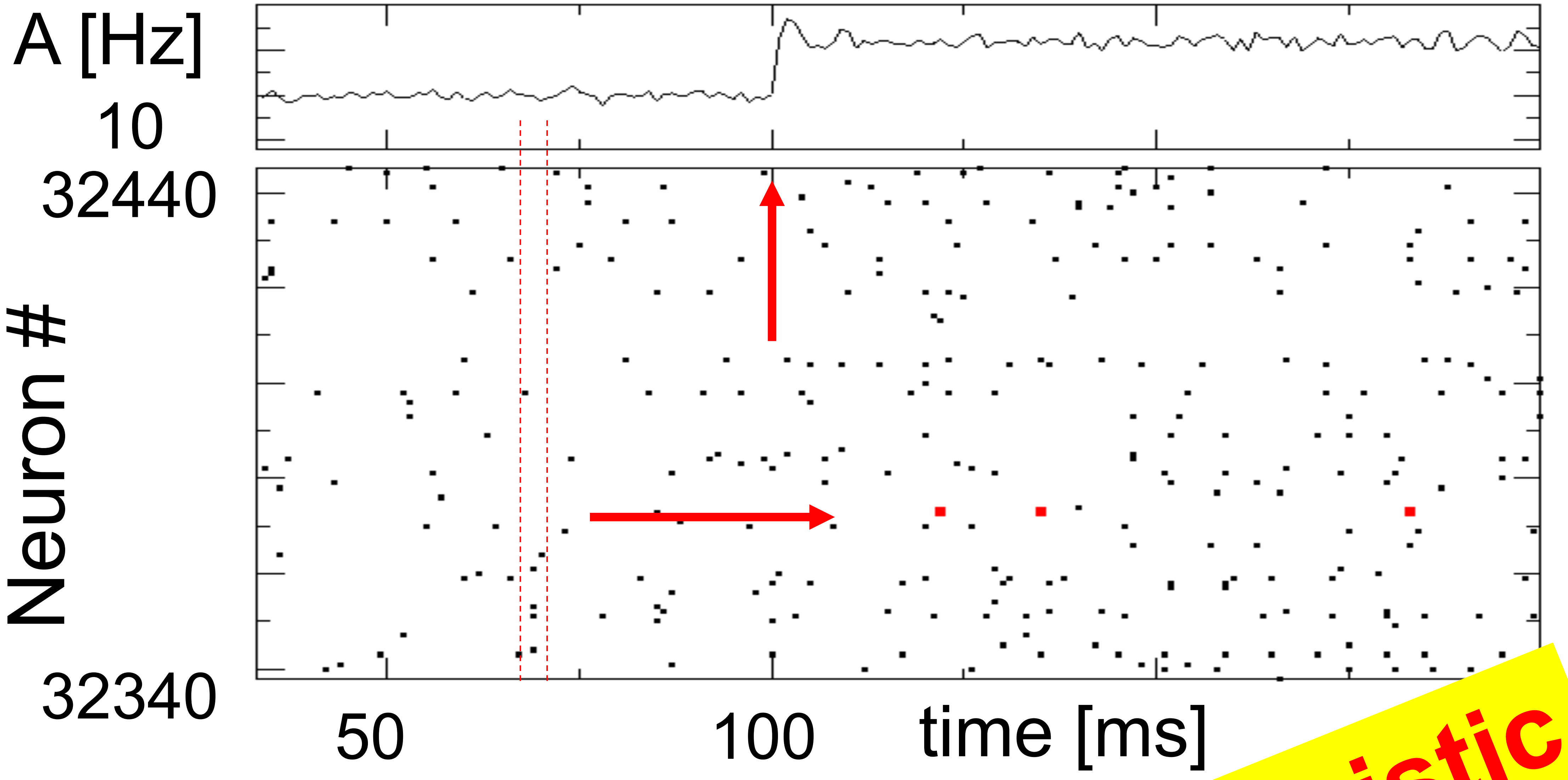
Distributed architecture

$10^{10}$ neurons

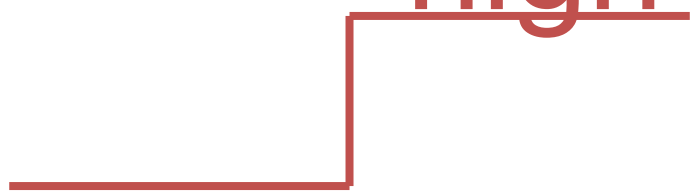
$10^{4}$ connections/neurons

# 10.2 Random firing in a population of LIF neurons






**input** {low rate, high rate}

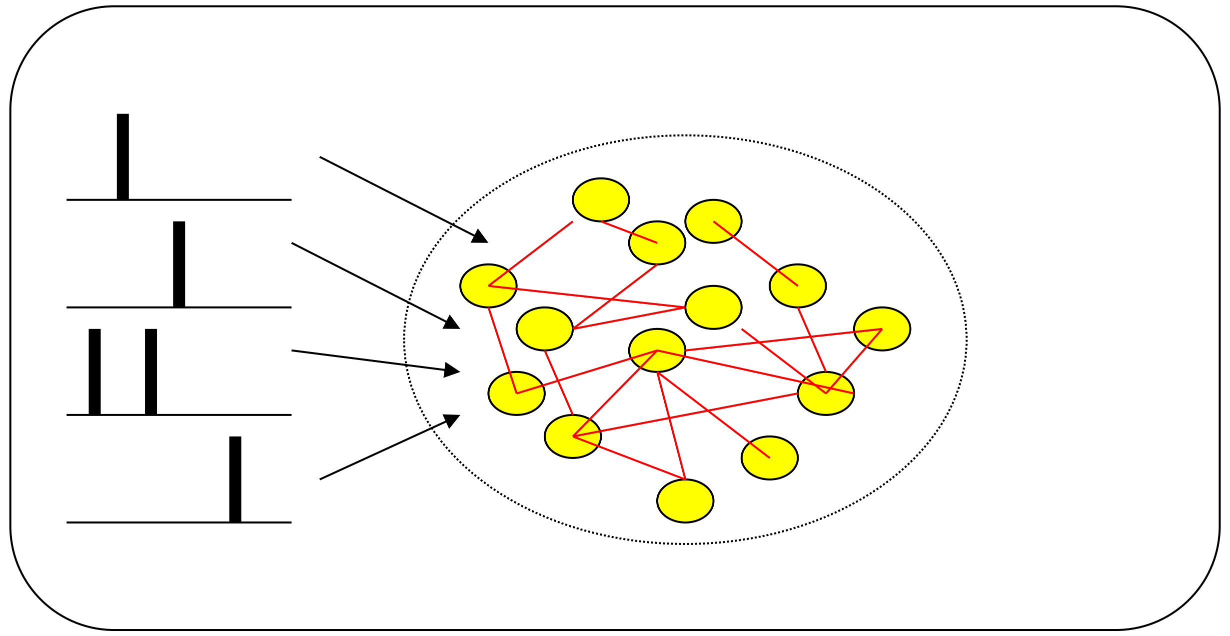


*Brunel, J. Comput. Neurosc. 2000*
*Mayor and Gerstner, Phys. Rev E. 200*
*Vogels et al., 2005*

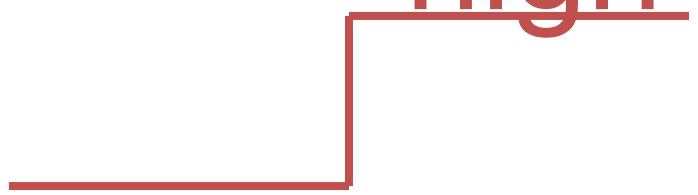
Network of **deterministic** leaky integrate-and-fire: 'fluctuations'

Population
- 50 000 neurons
- 20 percent inhibitory
- **randomly connected**

# 10.2 Random firing in a population of LIF neurons



input {low rate, high rate}



Population
- 50 000 neurons
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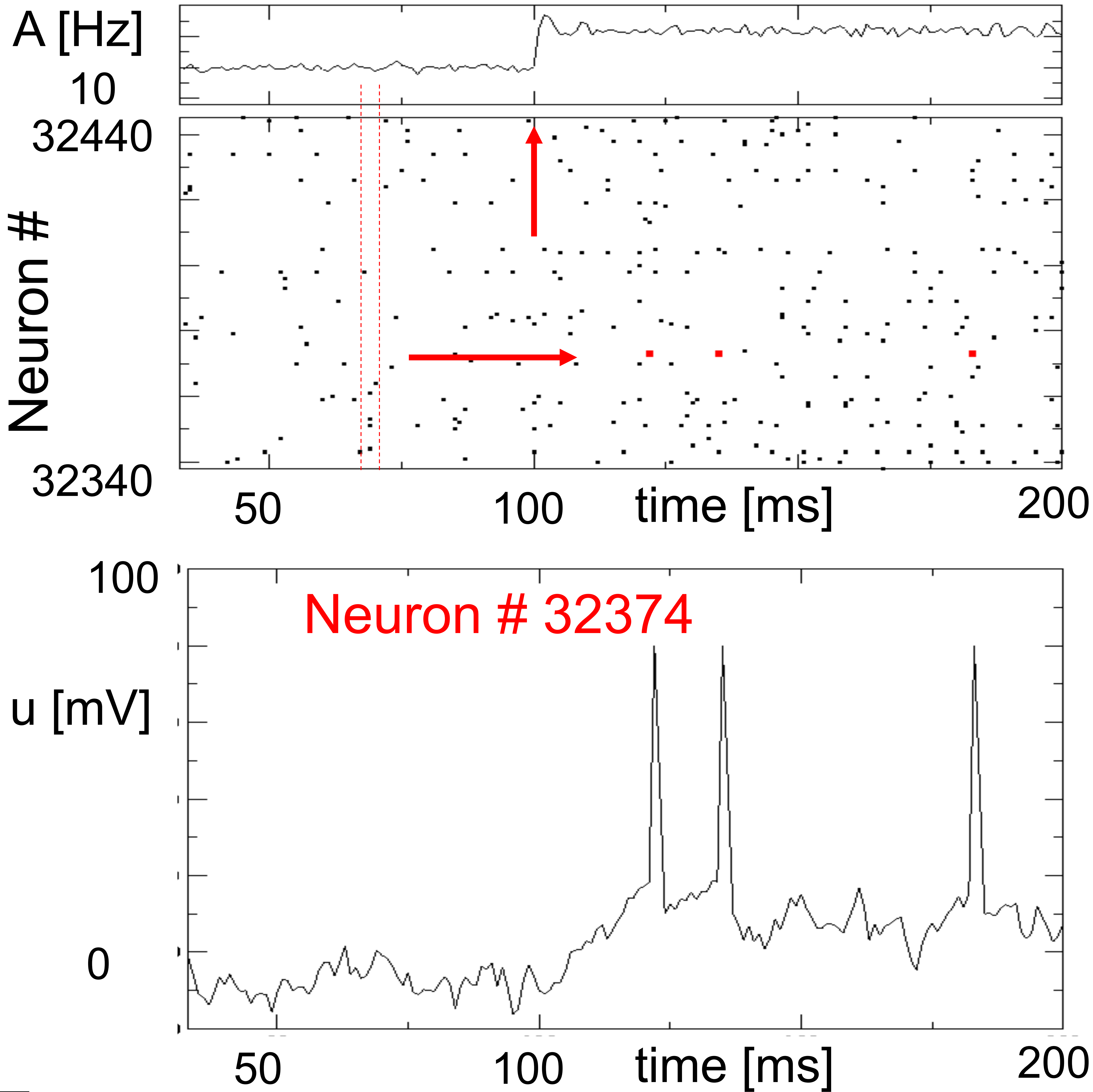
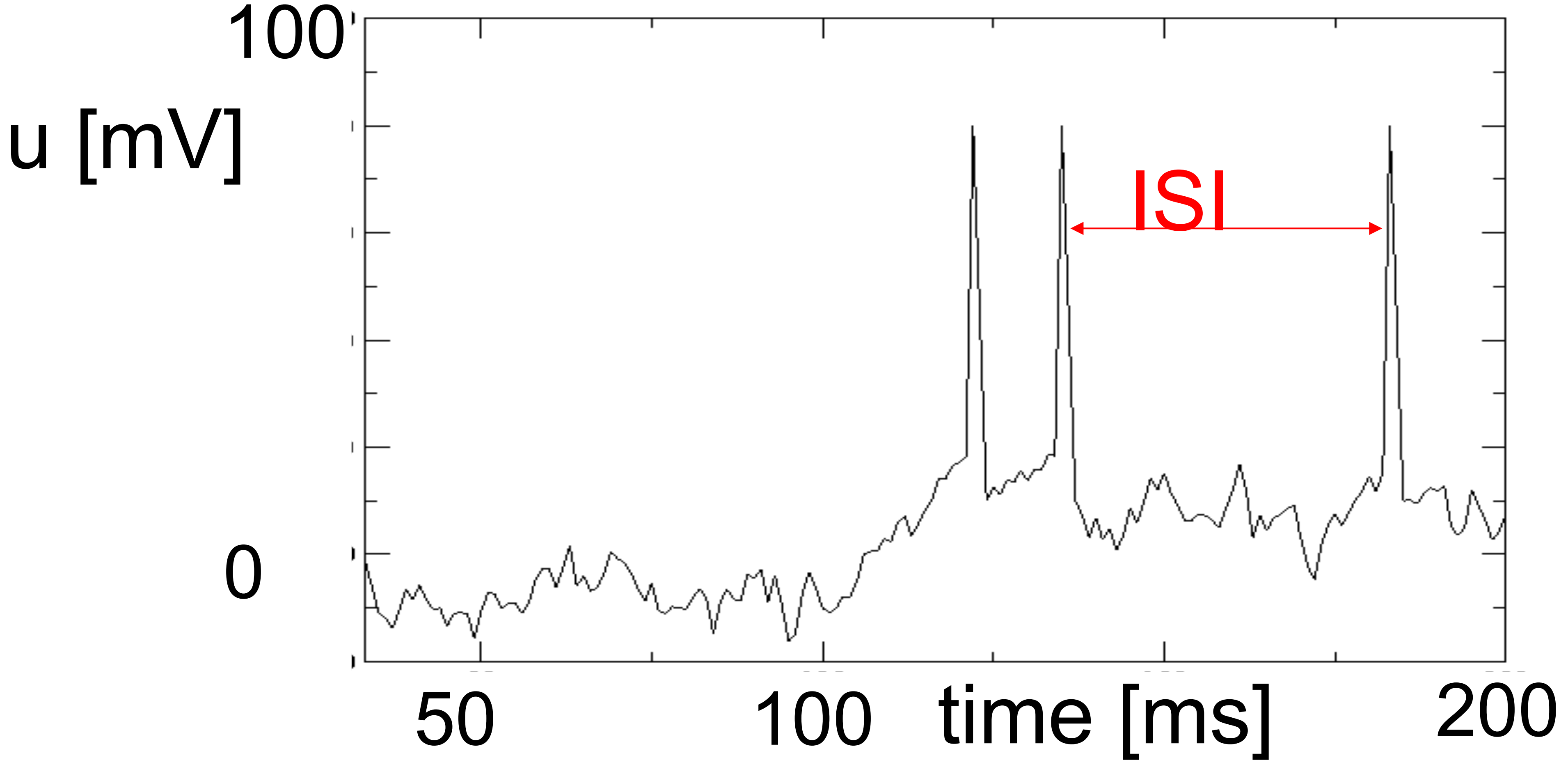
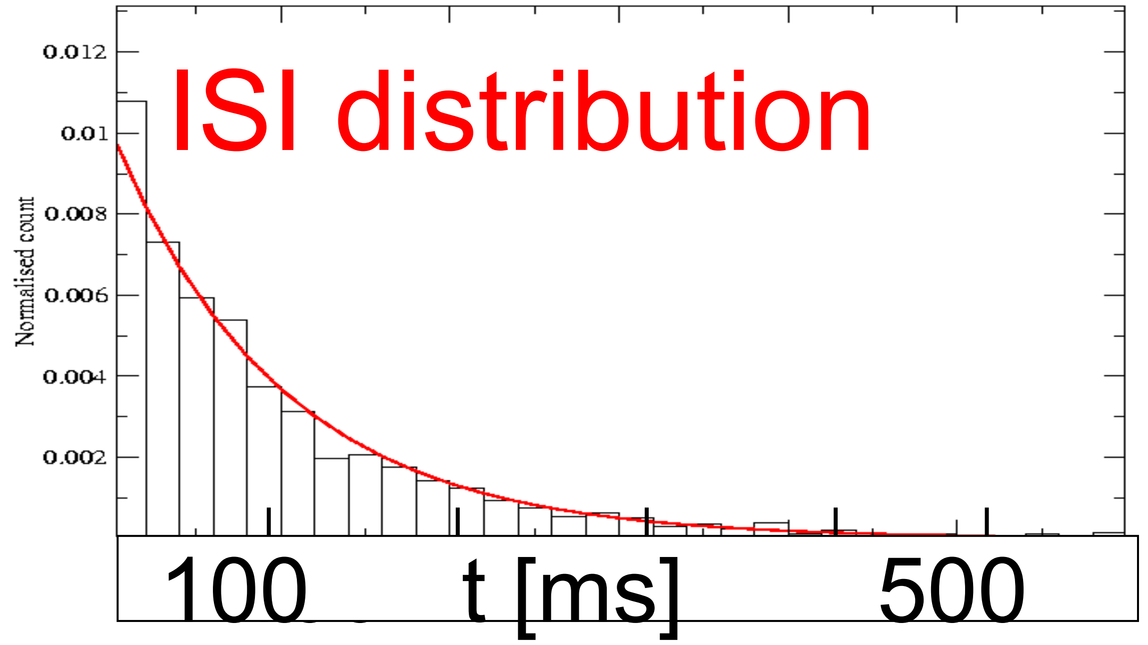


# 10.2. Interspike interval distribution

- Variability of interspike intervals (ISI)

here in simulations, but also *in vivo*




Variability of spike trains: broad ISI distribution

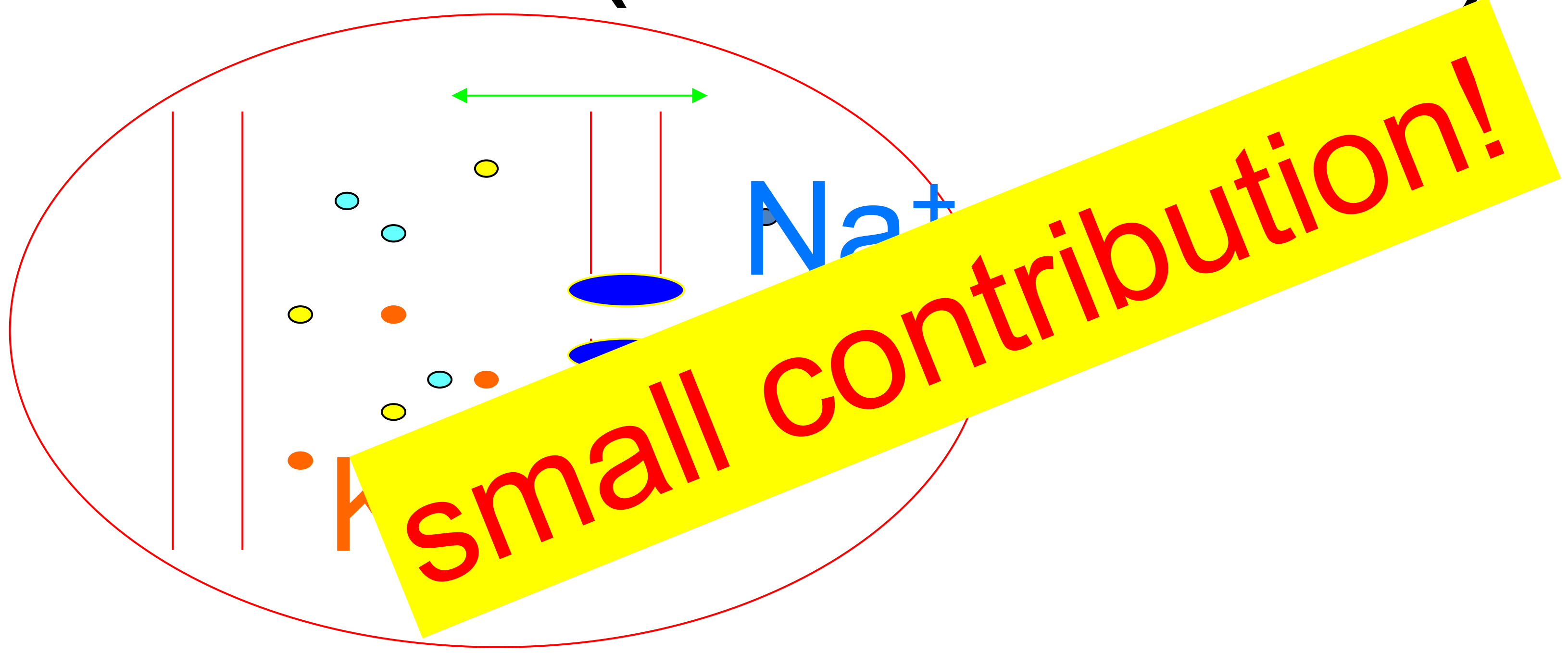
*Brunel, J. Comput. Neurosc. 2000*
*Mayor and Gerstner, Phys. Rev E. 2005*
*Vogels and Abbott, J. Neuroscience, 2005*

# 10.2. Sources of Variability

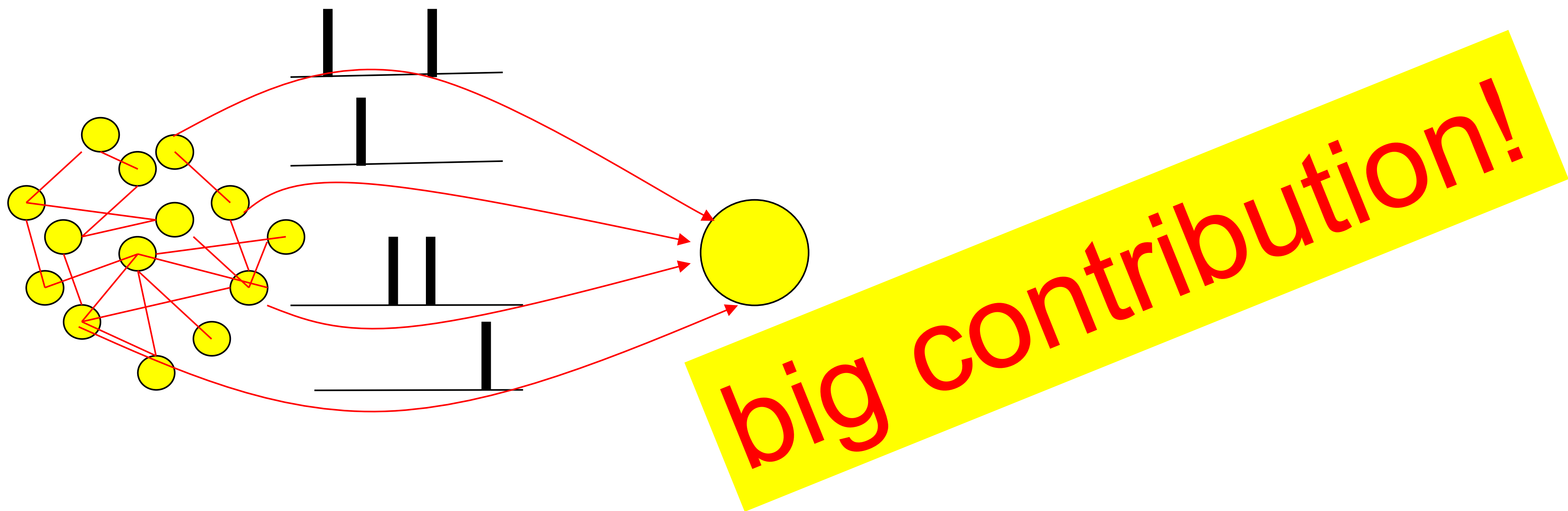
In vivo data
→ looks 'noisy'

In vitro data
→small fluctuations
→nearly deterministic

- Intrinsic noise (ion channels)




-Network noise



# Quiz 10.1.

**A- Spike timing in vitro and in vivo**

[ ] Reliability of spike timing can be assessed by repeating several times the same stimulus

[ ] Spike timing in vitro is more reliable under injection of constant current than with fluctuating current

[ ] Spike timing in vitro is more reliable than spike timing in vivo

**B – Interspike Interval Distribution (ISI)**

[ ] An isolated deterministic leaky integrate-and-fire neuron driven by a constant current can have a broad ISI

[ ] A deterministic leaky integrate-and-fire neuron embedded into a randomly connected network of integrate-and-fire neurons can have a broad ISI

[ ] A deterministic Hodgkin-Huxley model as in week 2 embedded into a randomly connected network of Hodgkin-Huxley neurons can have a broad ISI

# 10.2 Summary: Sources of variability

There are two important sources of fluctuations observed in data recorded in vivo or in vitro:

1. Intrinsically generated fluctuations caused by a finite temperature together with a finite number of ion channels. Individual Ion channels open and close stochastically. We refer to these intrinsically generated fluctuations as 'intrinsic noise'. Given that for current injection into the soma a neuron behaves rather reliably, we conclude that the importance of intrinsic noise is relatively low.
2. A single neuron j embedded in the network receives spikes from many other neurons. Since an external observer cannot control the spike times of all neurons, the spike arrival times to neuron j the spike arrival times are often considered as 'random'. In fact, even in a simulation of a deterministic network of spiking neurons, spike arrival looks 'random'. We refer to these effects as 'network noise'.

As a first measure of the variability of spike trains, we have used the interspike interval distribution (ISI). A deterministic network of spiking neurons with fixed (but random) connectivity often exhibits stationary activity with a broad ISI.

# Biological Modeling of Neural Networks

## Week 10 – Variability and Noise:

## The question of the neural code

Wulfram Gerstner

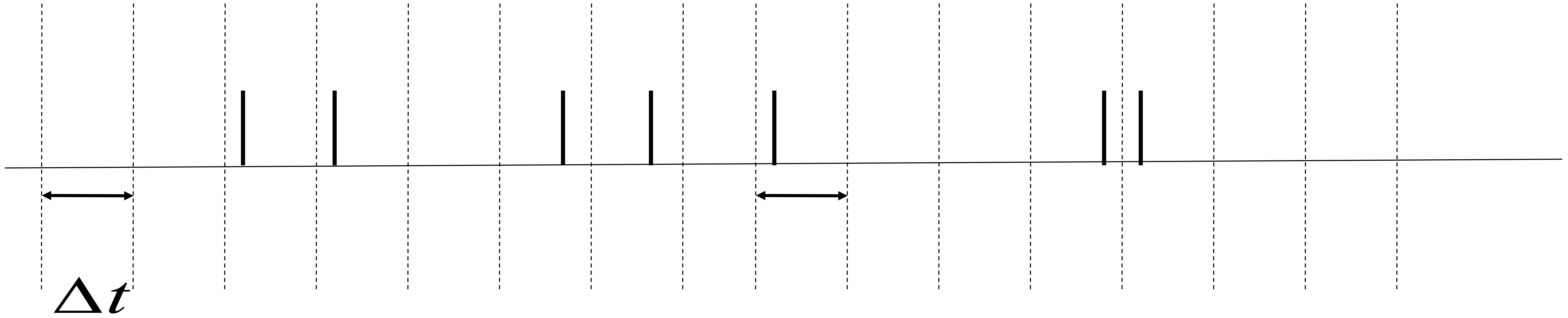
EPFL, Lausanne, Switzerland

- √ **10.1 Variability of spike trains**
  - experiments
- √ **10.2 Sources of Variability?**
  - Is variability equal to noise?
- **10.3 Poisson Model**
  - homogeneous/inhomogeneous
- **10.4 Three definitions of Rate Code**
- **10.5 Stochastic spike arrival**
  - Membrane potential fluctuations

# 10.3 Poisson Model

Homogeneous Poisson model: constant rate

*Blackboard1: Poisson model*



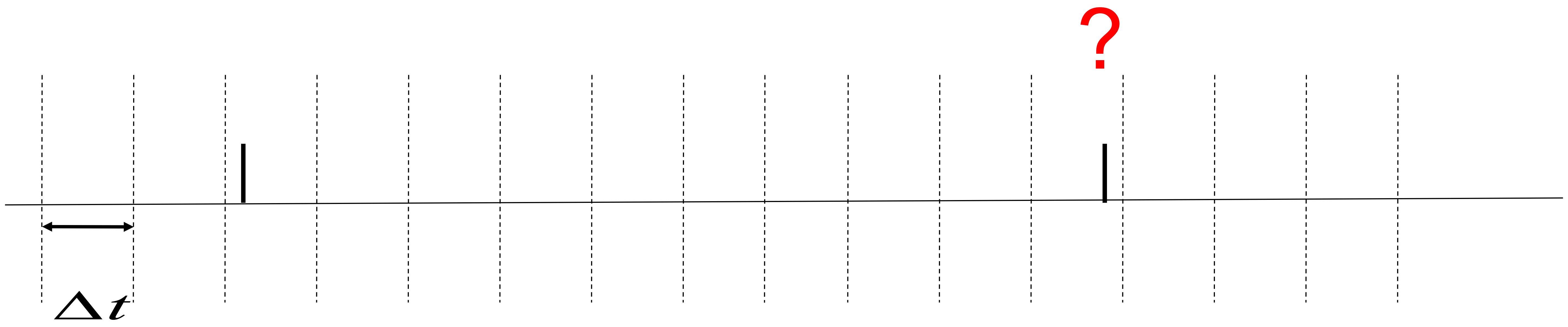

Probability of finding a spike $P_F = \rho_0 \, \Delta t$

stochastic spiking → Poisson model

# 10.3 Interval distribution of Poisson Process

Probability of firing:

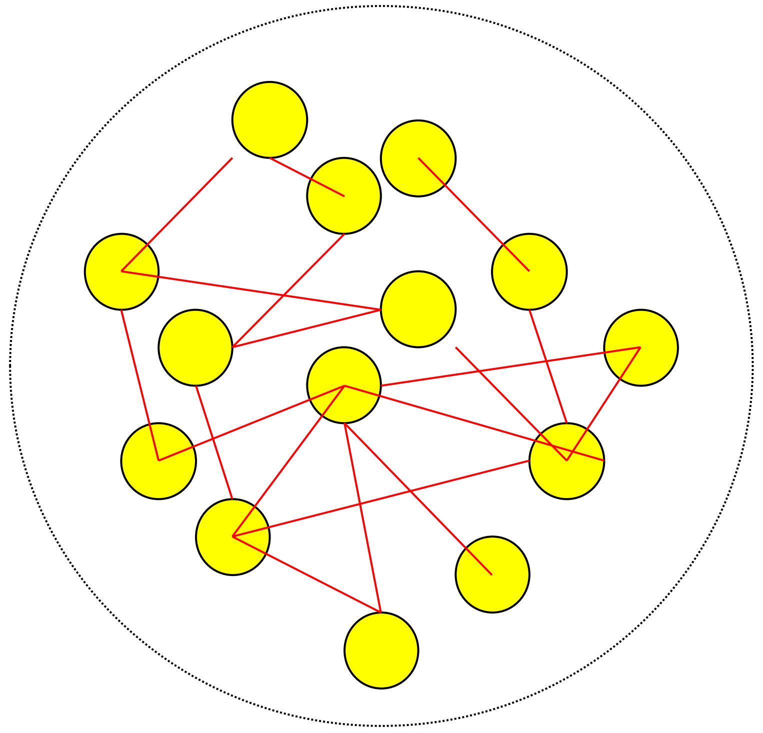
$$P_F = \rho_0 \, \Delta t$$




(i) Continuous time

*prob to 'survive'*

$$\Delta t \to 0$$



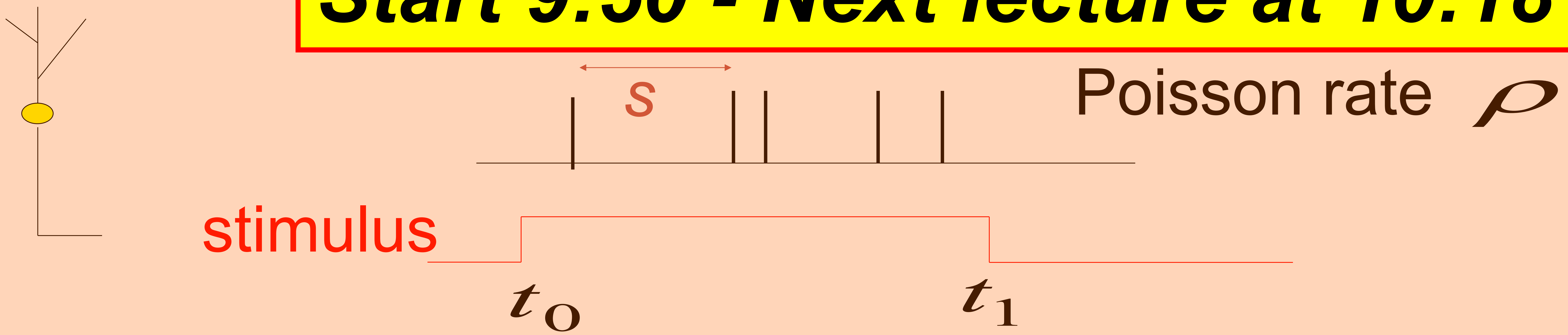
(ii) Discrete time steps

***Blackboard2: Poisson model***

$$\frac{d}{dt} S(t_1 \,|\, t_0) = -\rho_0 \; S(t_1 \,|\, t_0)$$

# Exercise 1.1, 1.2, and 1.3: Poisson neuron

**Start 9:50 - Next lecture at 10:18**




1.1. - Probability of NOT firing during time t?

1.2. - Interval distribution *p(s)?*

1.3.- How can we detect if rate switches from

$$\rho_0 \longrightarrow \rho_1$$

(1.4 at home:)

-2 neurons fire stochastically (Poisson) at 20Hz.

*Percentage of spikes that coincide within +/-2 ms?)*

# Week 10 – Two short quizzes (derivatives)

Quiz 1: define

$$x(t) = \exp(-\rho_0 \cdot (t - \hat{t}))$$

What is

$$\frac{d}{dt} x(t) = ?$$

Quiz 2: define

$$x(t) = \exp(-\int_{\hat{t}}^{t} \rho(t')\, dt')$$

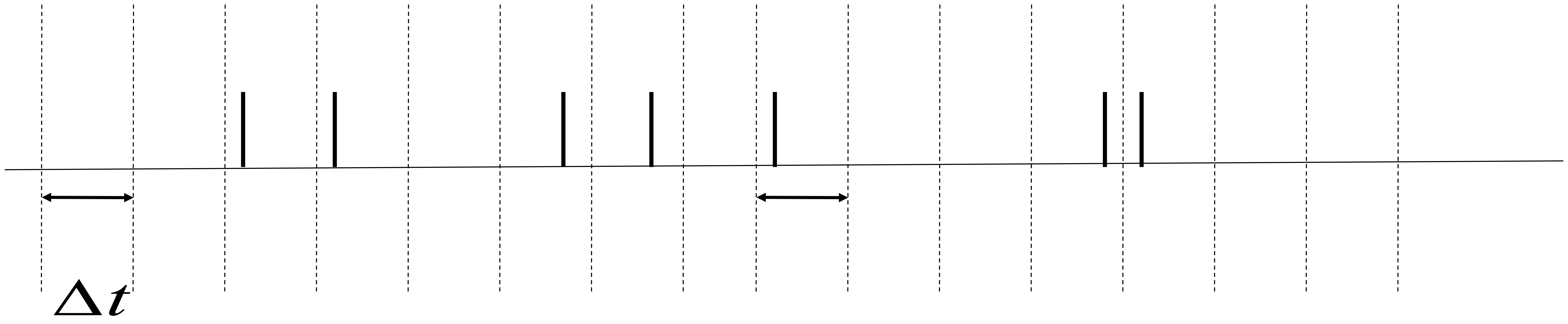
What is

$$\frac{d}{dt} x(t) = ?$$

# 10.3 Inhomogeneous Poisson Process

rate changes

$\rho(t)$




Probability of firing $P_F = \rho(t)\,\Delta t$

Survivor function $S(t\,|\,\hat{t}) = \exp(-\int_{\hat{t}}^{t} \rho(t')\,dt')$

Interval distribution $P(t\,|\,\hat{t}) = \rho(t)\exp(-\int_{\hat{t}}^{t} \rho(t')\,dt')$

# Week 10 Quiz 3 Poisson Process

**A Homogeneous Poisson Process**:

A spike train is generated by a homogeneous Poisson process with rate 25Hz with time steps of 0.1ms.

[ ] The most likely interspike interval is 25ms.
[ ] The most likely interspike interval is 40 ms.
[ ] The most likely interspike interval is 0.1ms
[ ] We can't say.

**B Inhomogeneous Poisson Process**

A spike train is generated by an inhomogeneous Poisson process with a rate that oscillates periodically (sine wave) between 0 and 50Hz (mean 25Hz). The period is 40ms. A first spike has been fired at a time when the rate was at its maximum. Time steps are 0.1ms.

[ ] The most likely interval before the next spike is 20ms.
[ ] The most likely interval before the next spike is 40 ms.
[ ] The most likely interval before the next spike is 0.1ms.
[ ] We can't say.

# 10.3 Summary: Poisson model

In a Poisson model, spike times are independent from each other. Knowledge of the last firing time does not help to predict the present firing time.
The Poisson model is formulated in continuous time with a 'stochastic intensity' or 'firing intensity' $\rho$, sometimes also called the 'rate' of the Poisson process.

In the homogeneous (or stationary) Poisson process, the stochastic intensity is constant.
In the inhomogeneous Poisson process, the stochastic intensity is time dependent.

Two important concepts are the interval distribution and the survivor function.
The interval distribution of the inhomogeneous Poisson Process is:

$$P(t\,|\,\hat{t}) = \rho(t)\exp\left(-\int_{\hat{t}}^{t} \rho(t')\,dt'\right)$$

And the survivor function is: $S(t\,|\,\hat{t}) = \exp\left(-\int_{\hat{t}}^{t} \rho(t')\,dt'\right)$

For the homogeneous Poisson process both functions simplify to a standard exponential decay as a function of the time difference $t - \hat{t}$ where $\hat{t}$ is the previous spike time.

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**10.4 Three definitions of Rate Code**

**10.5 Stochastic spike arrival**
- Membrane potential fluctuations

# 10.4. Three definitions of Rate Codes

**3 definitions**

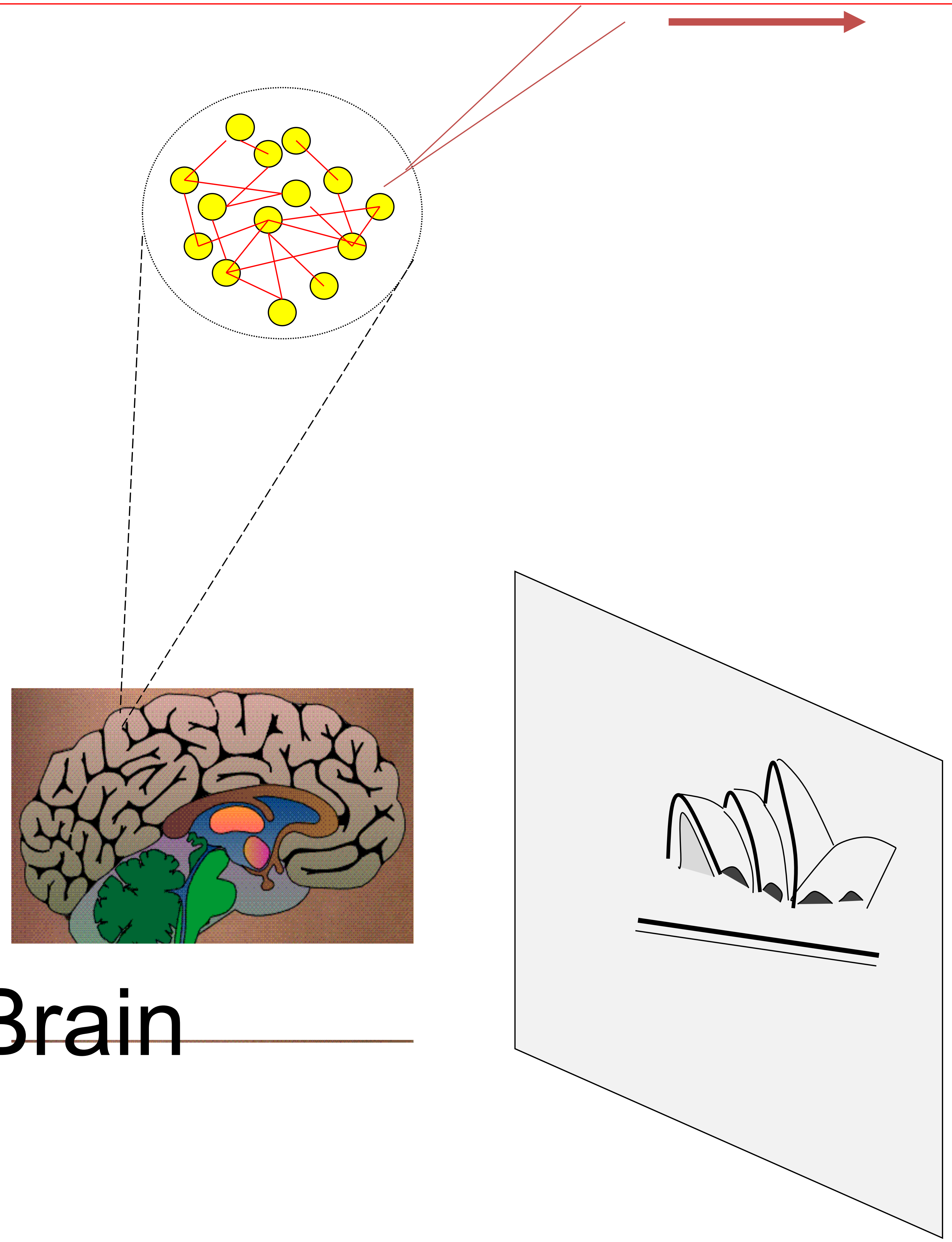
-Temporal averaging

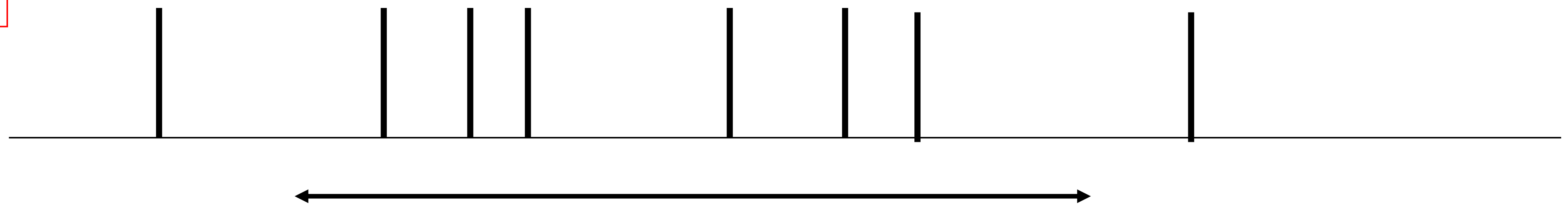
- Averaging across repetitions

- Population averaging ('spatial' averaging)

# 10.4. Rate codes: spike count

Variability of spike timing





trial 1

rate as a (normalized) spike count:

$$\nu(t) = \frac{n^{sp}}{T}$$

single neuron/single trial:
temporal average

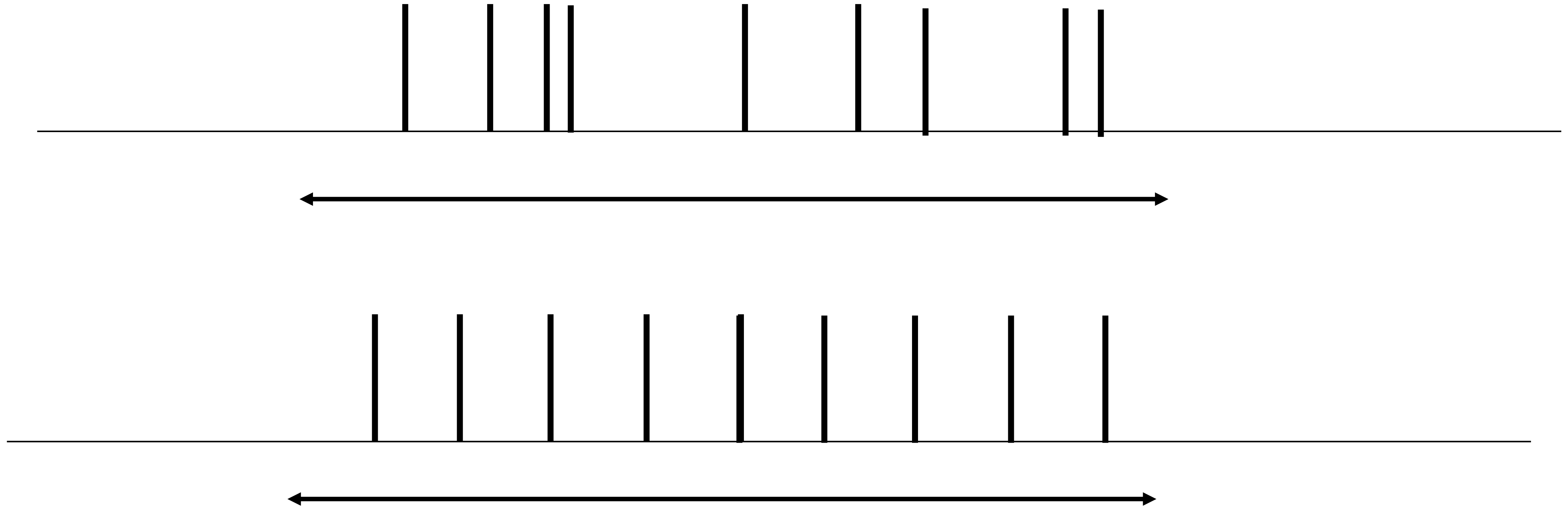
T=1s

Brain

stim

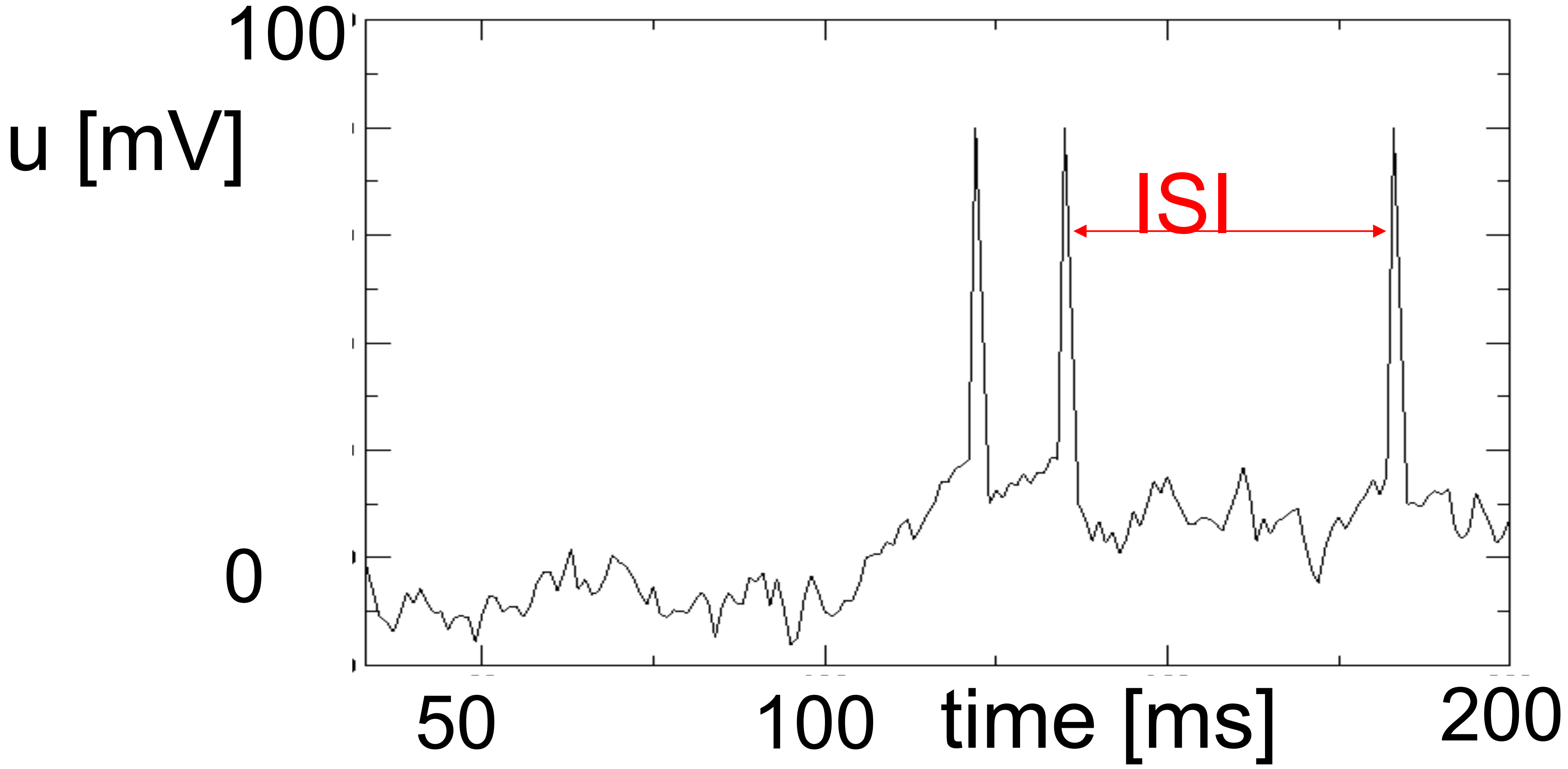
# 10.4. Rate codes: spike count

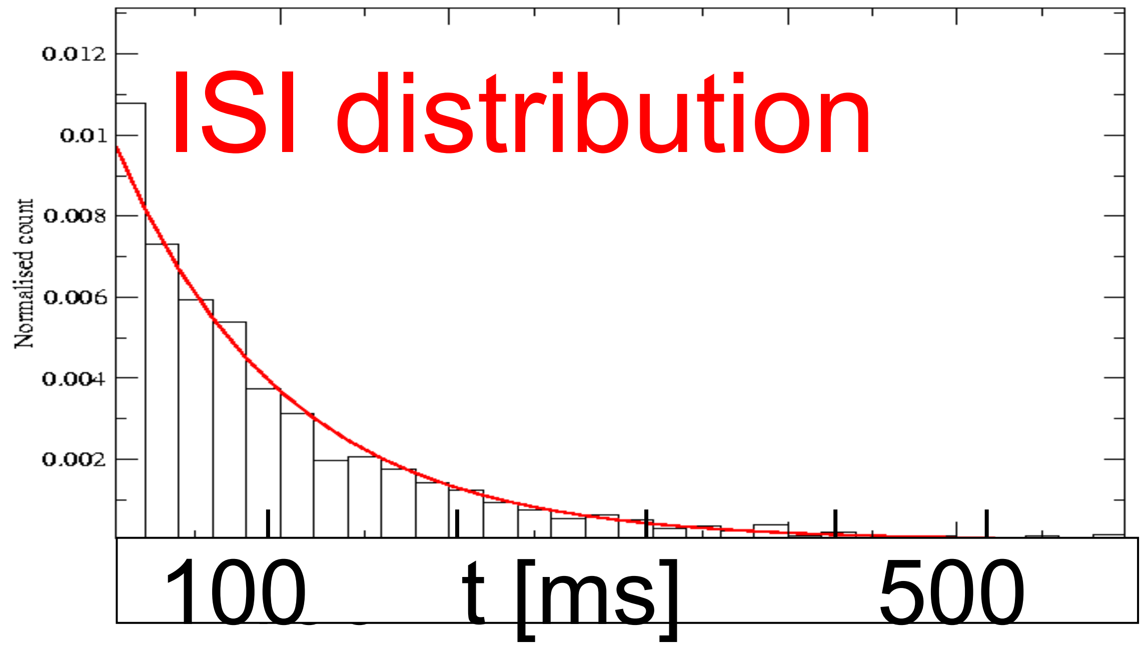
single neuron/single trial:
temporal average



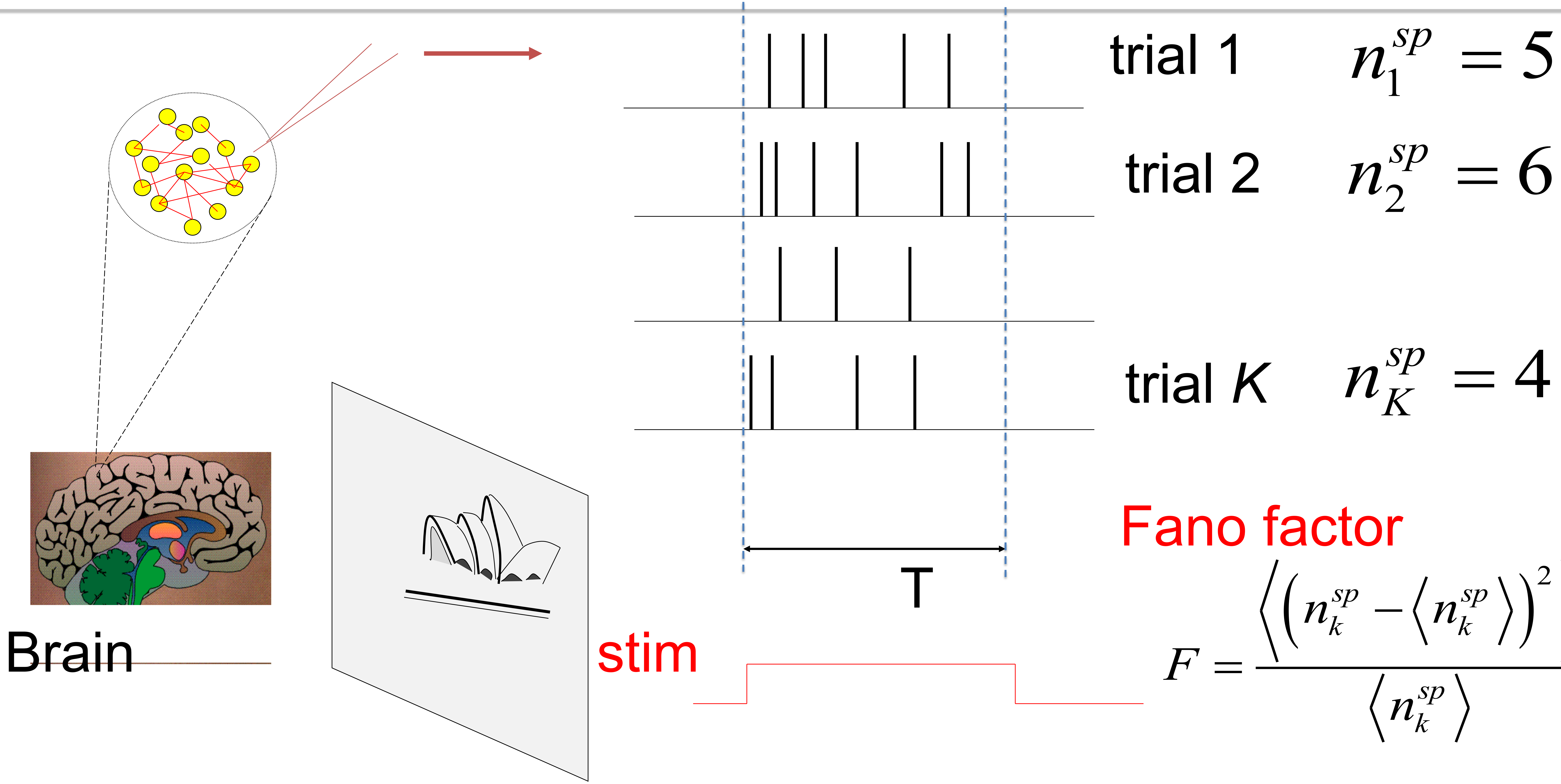
$$\nu(t) = \frac{n^{sp}}{T}$$

Variability of interspike intervals (ISI) measure regularity



# 10.4. Spike count: FANO factor




Fano factor

$$F = \frac{\left\langle \left( n_k^{sp} - \left\langle n_k^{sp} \right\rangle \right)^2 \right\rangle}{\left\langle n_k^{sp} \right\rangle}$$

# 10.4. Three definitions of Rate Codes

## 3 definitions

√ -Temporal averaging (spike count)

Problem: slow!!!

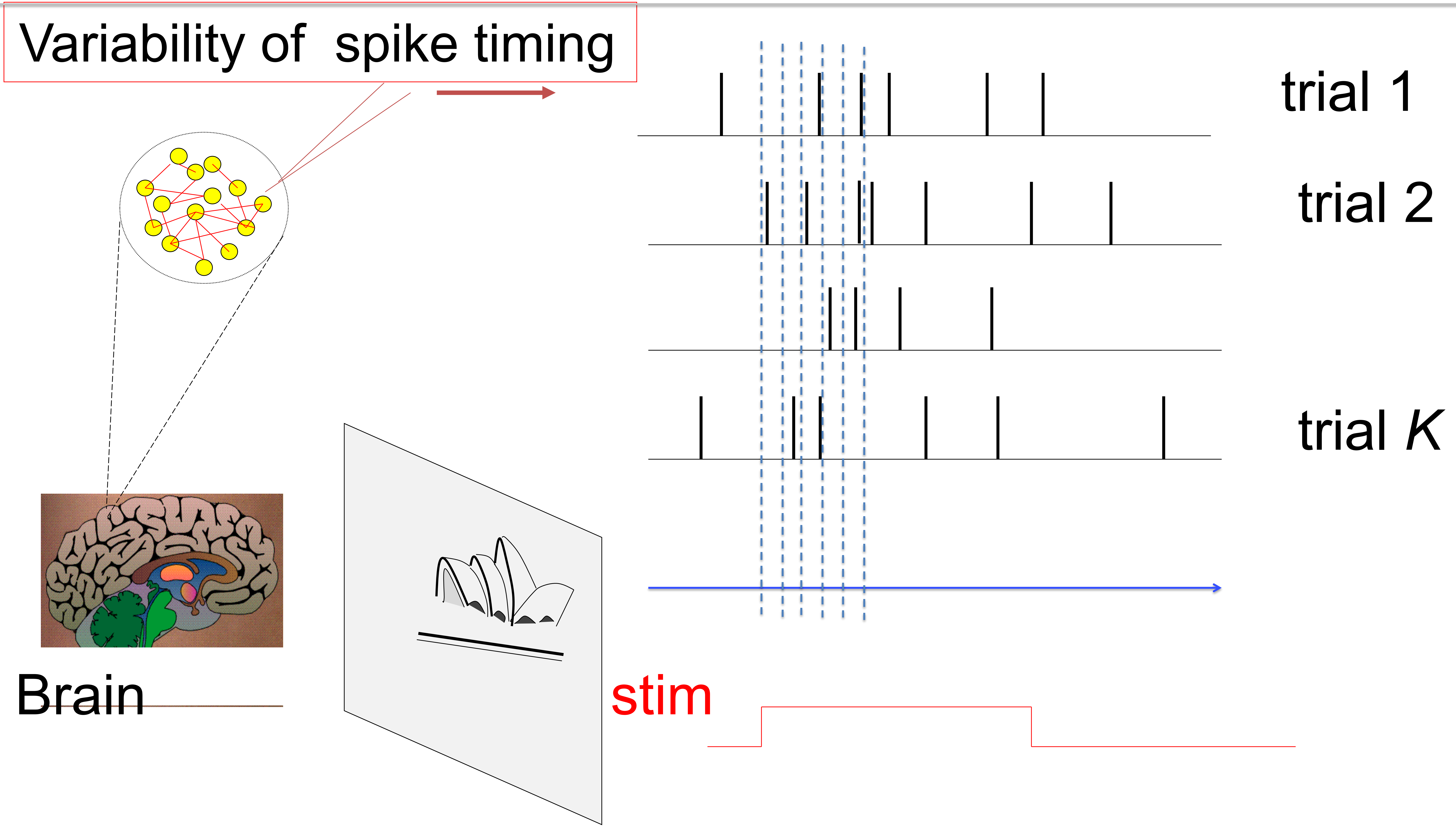
*ISI distribution (regularity of spike train)*

*Fano factor (repeatability across repetitions)*

- Averaging across repetitions

- Population averaging ('spatial' averaging)

# 10.4. Rate codes: PSTH

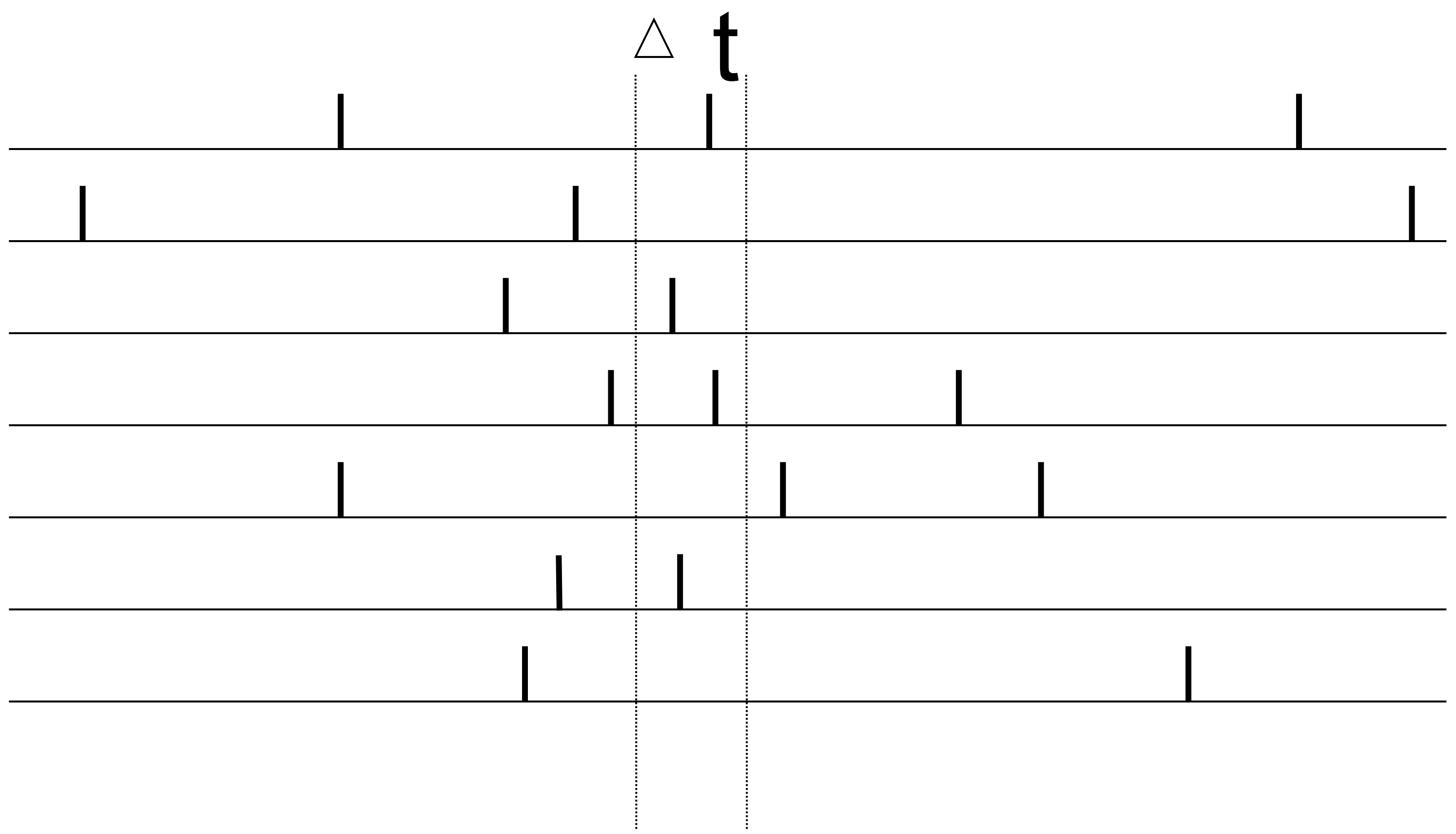


# 10.4. Rate codes: PSTH

Averaging across repetitions

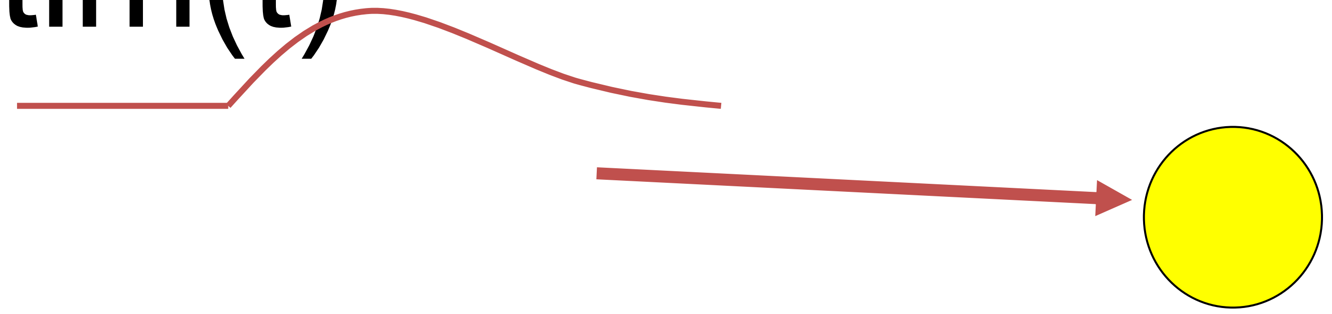
**single neuron/many trials:**
**average across trials**

*K* repetitions



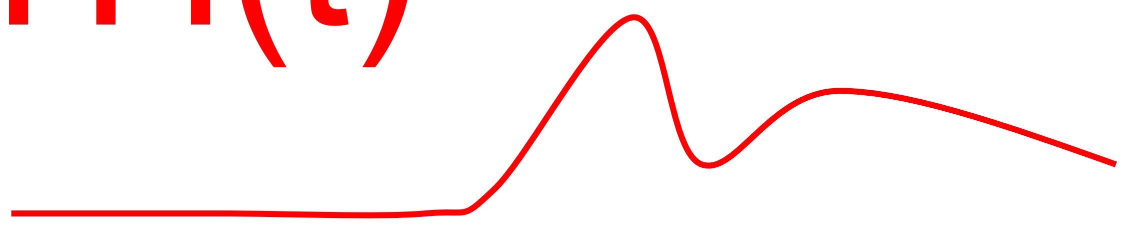

$$PSTH(t) = \frac{n(t;t+\Delta t)}{K\,\Delta t}$$

Stim(t)



*K*=50 trials

PSTH(t)



# 10.4. Three definitions of Rate Codes

**3 definitions**

√ -Temporal averaging

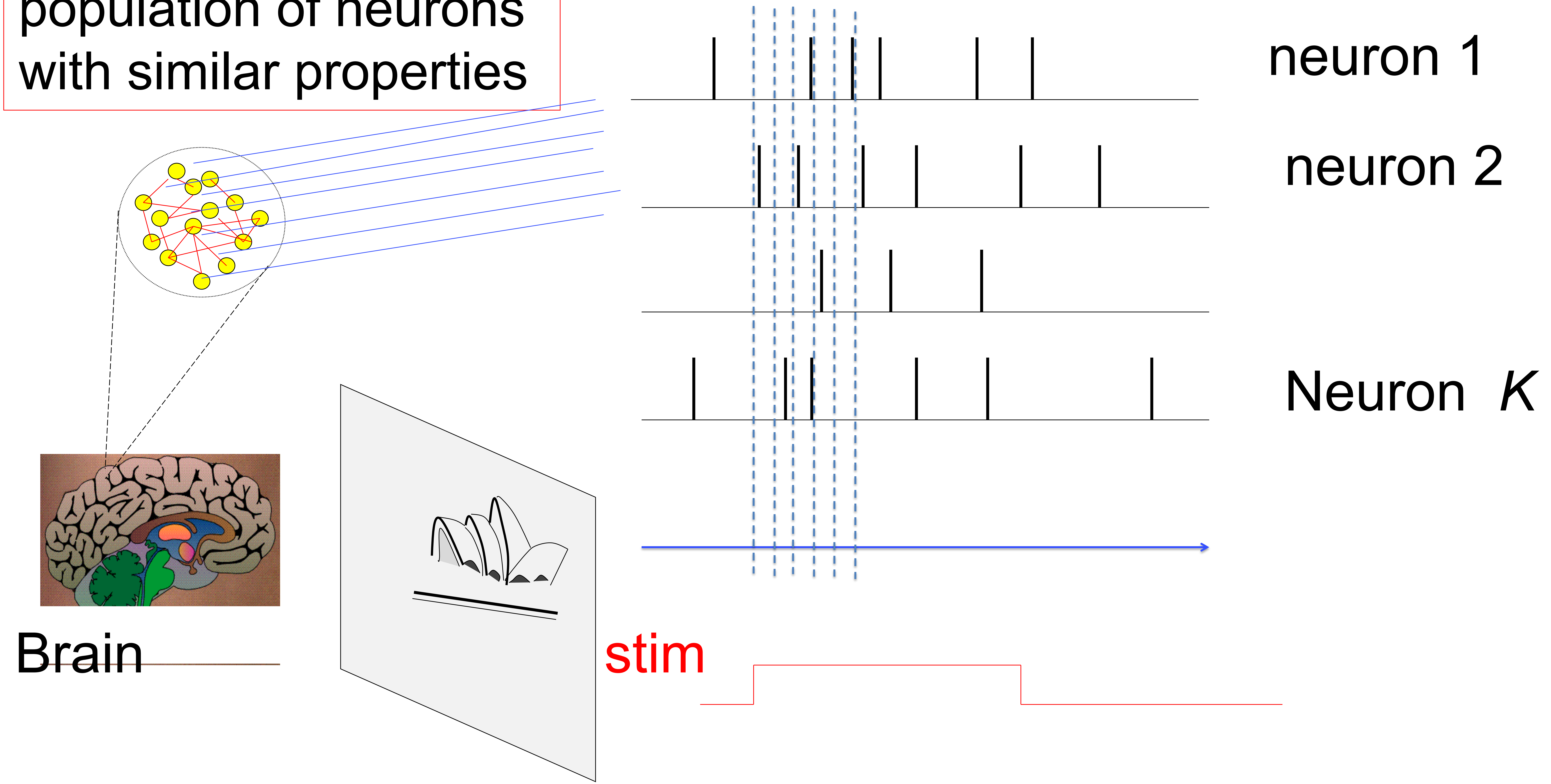
√ - Averaging across repetitions

Problem: not useful for animal!!!

- Population averaging

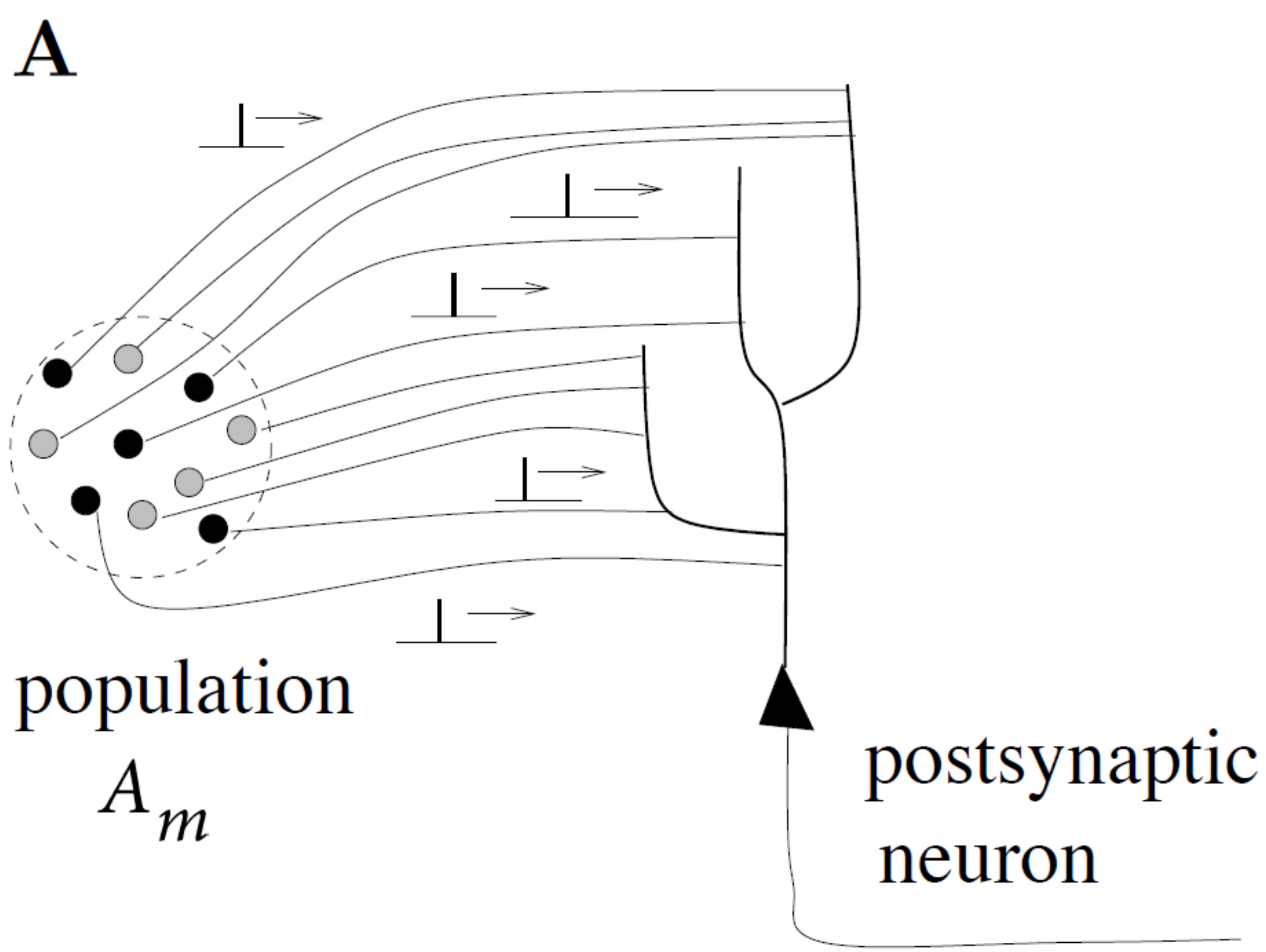
# 10.4. Rate codes: population activity

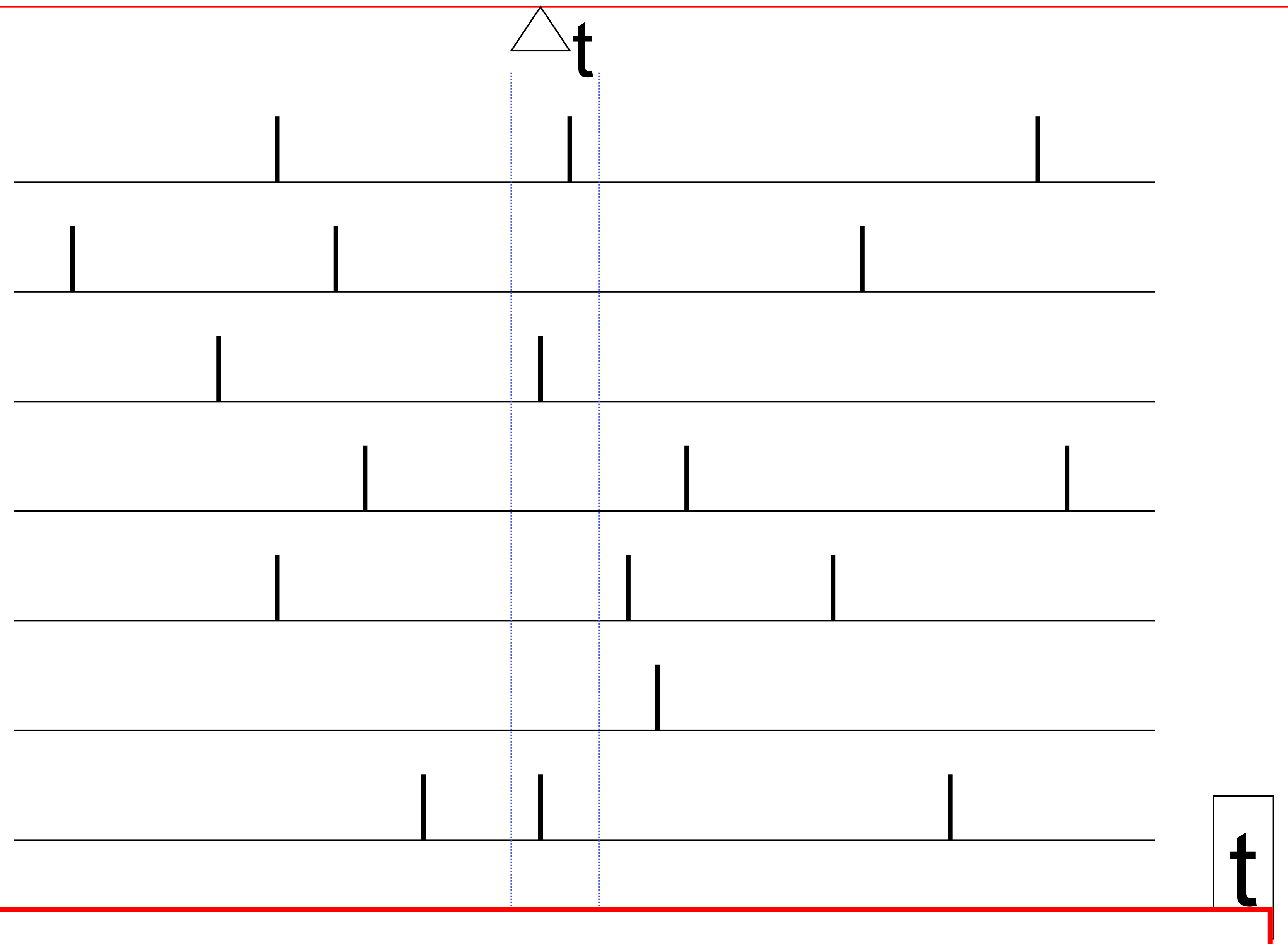
population of neurons
with similar properties



# 10.4. Rate codes: population activity (review from week 7)

population activity - rate defined by population average



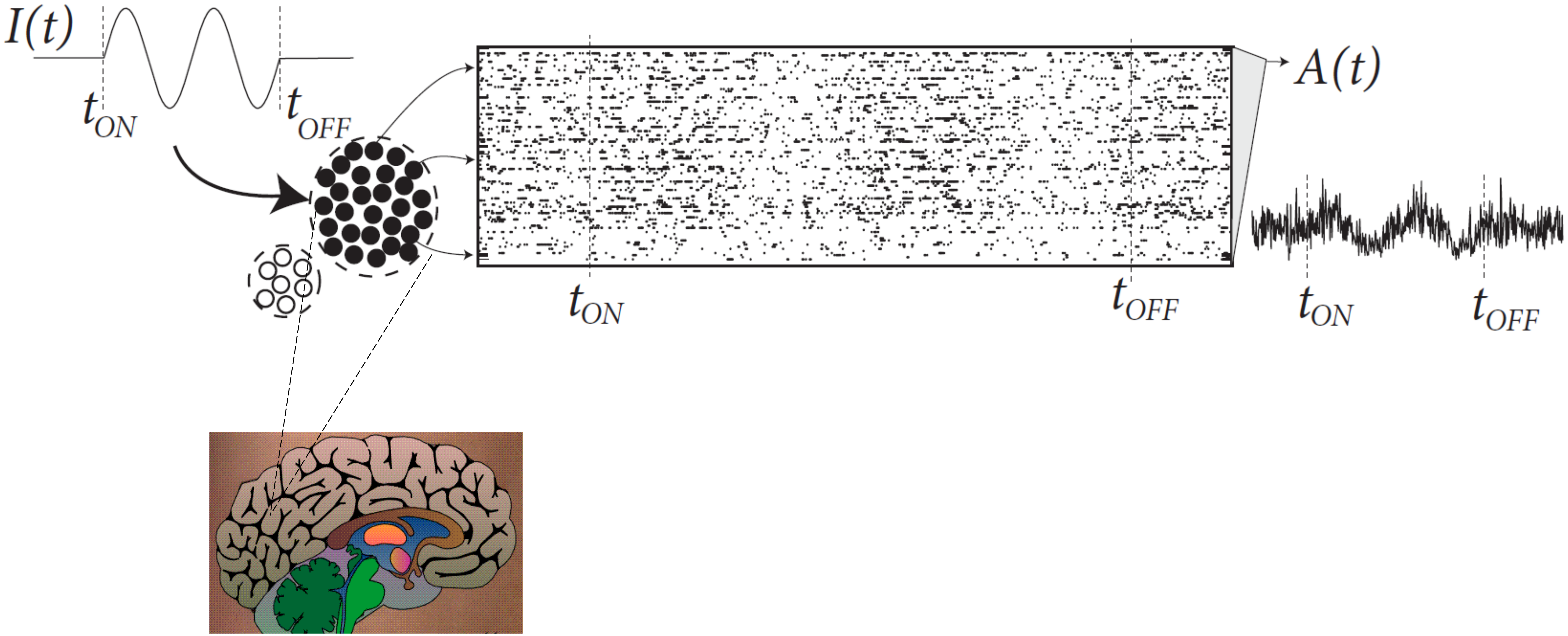

'natural readout'

population activity

$$A(t) = \frac{n(t;t+\Delta t)}{N\Delta t}$$

# 10.4. Rate codes: population activity (review from week 7)

population of neurons
with similar properties

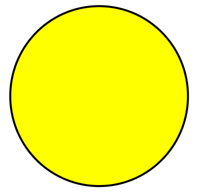



Brain

# 10.4. Three definitions of Rate codes: summary

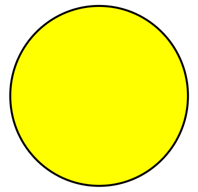
**Three averaging methods**

-over time

*single neuron* 

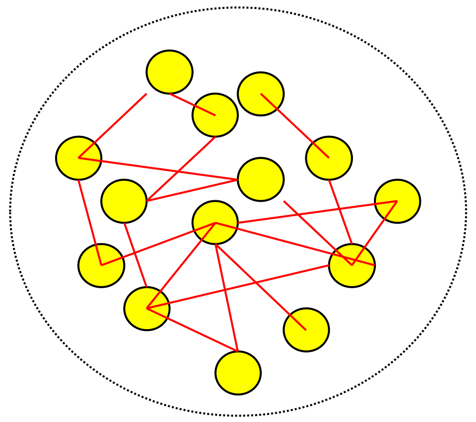
Too slow
for animal!!!

- over repetitions

*single neuron* 

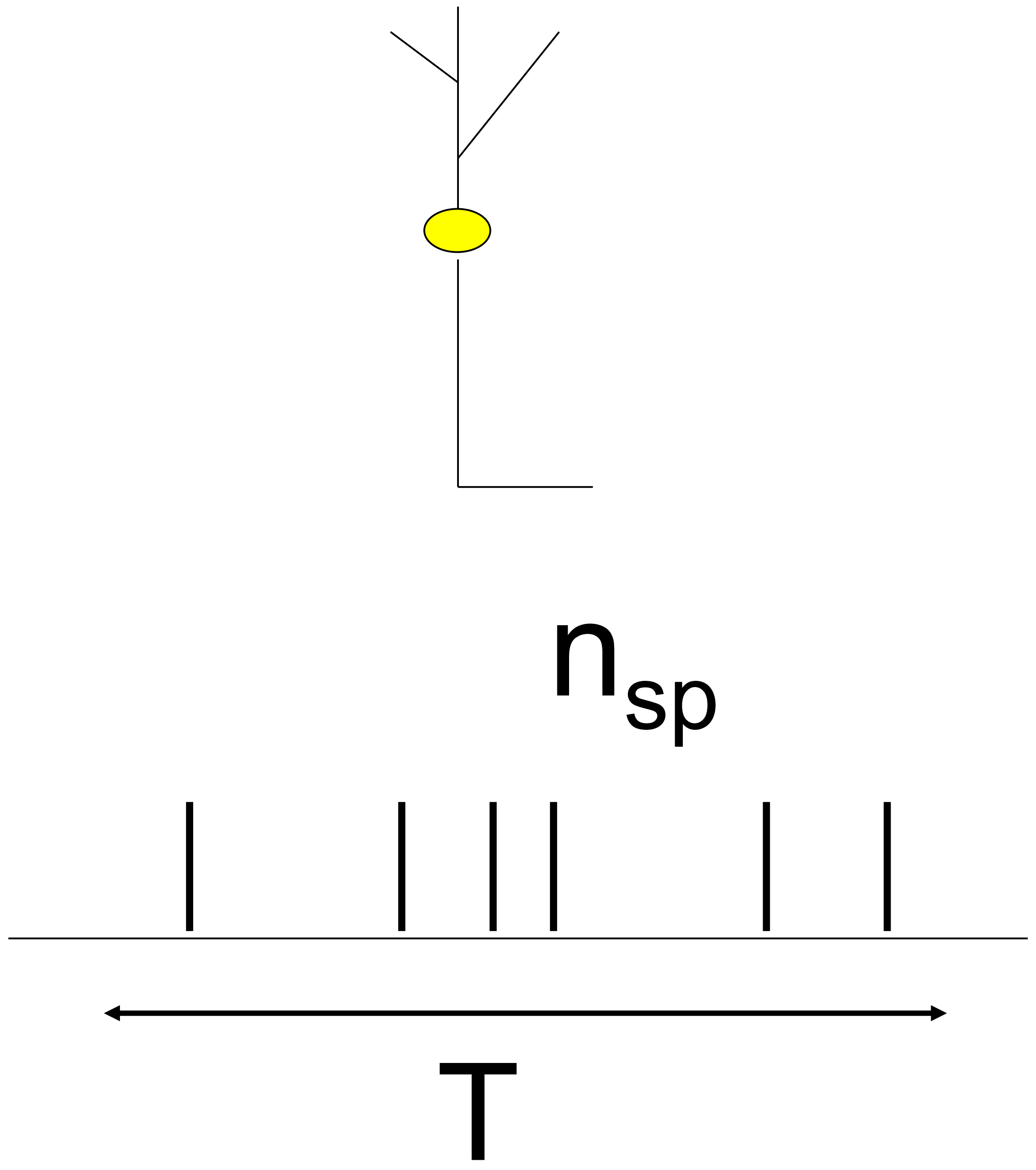
Not possible
for animal!!!

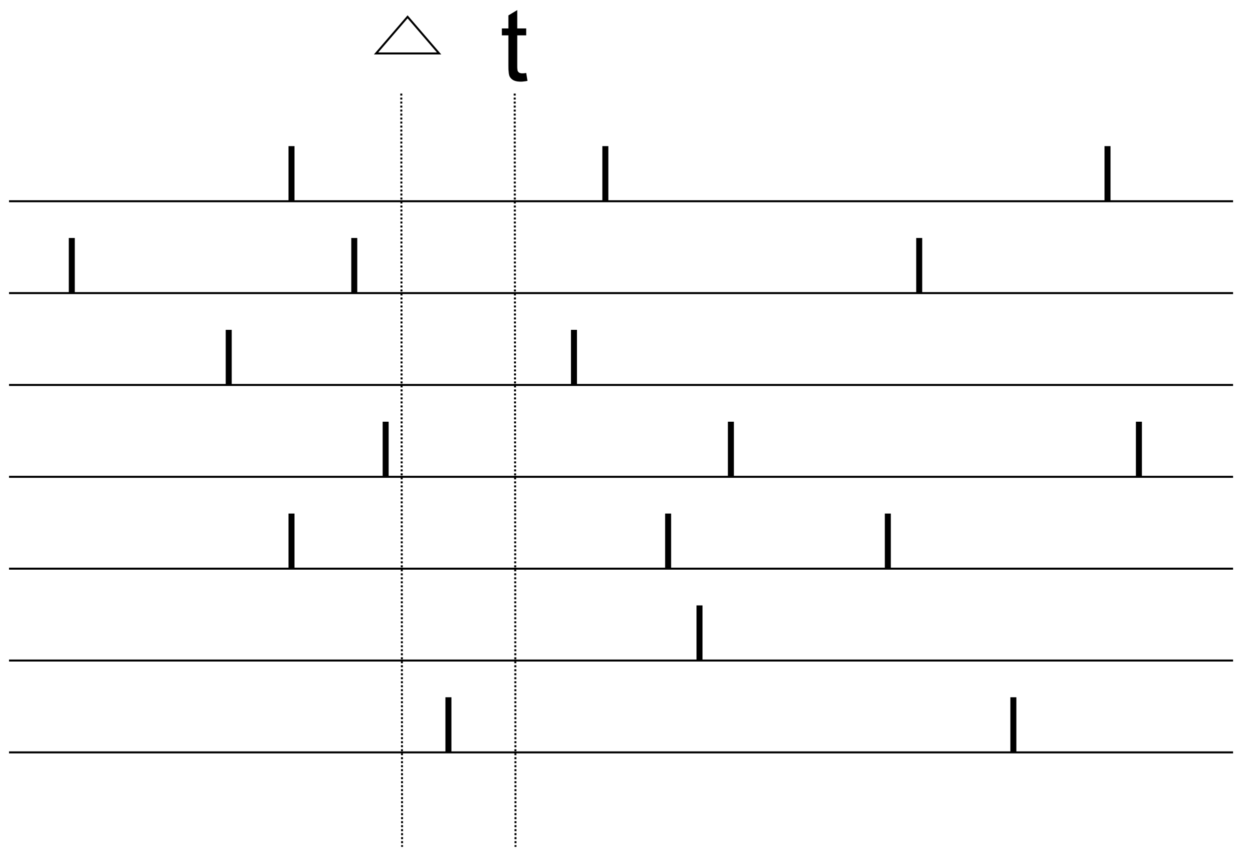
- over population (space)

*many neurons* 

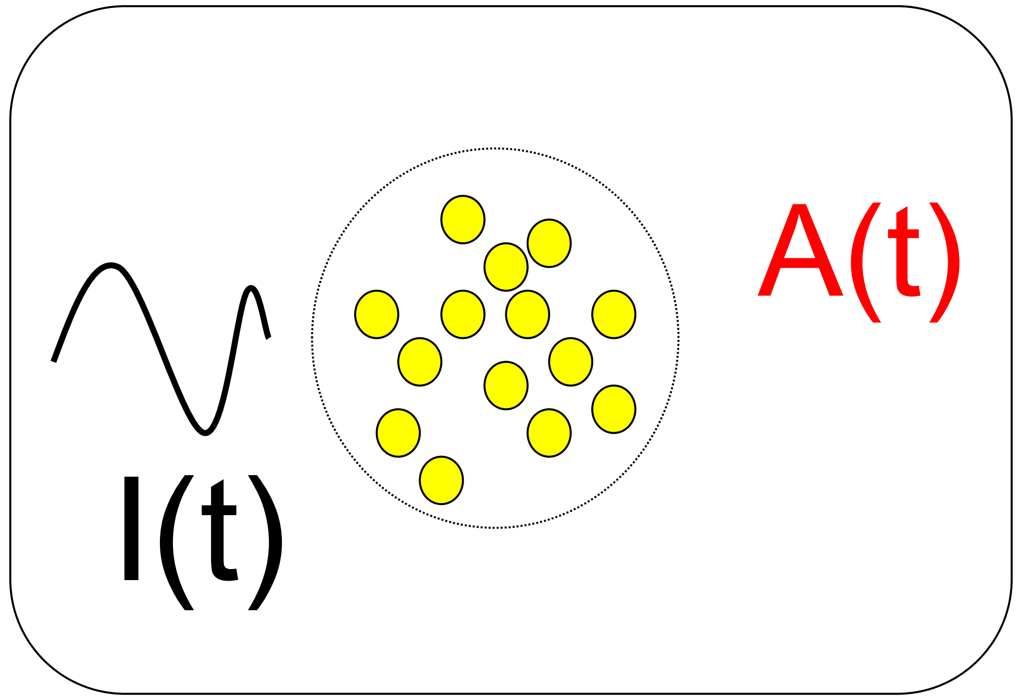
‘natural’

# 10.4 Inhomogeneous Poisson Process




$$PSTH(t) = \frac{n(t;t+\Delta t)}{K\,\Delta t}$$




$$A(t) = \frac{n(t;t+\Delta t)}{N\Delta t}$$

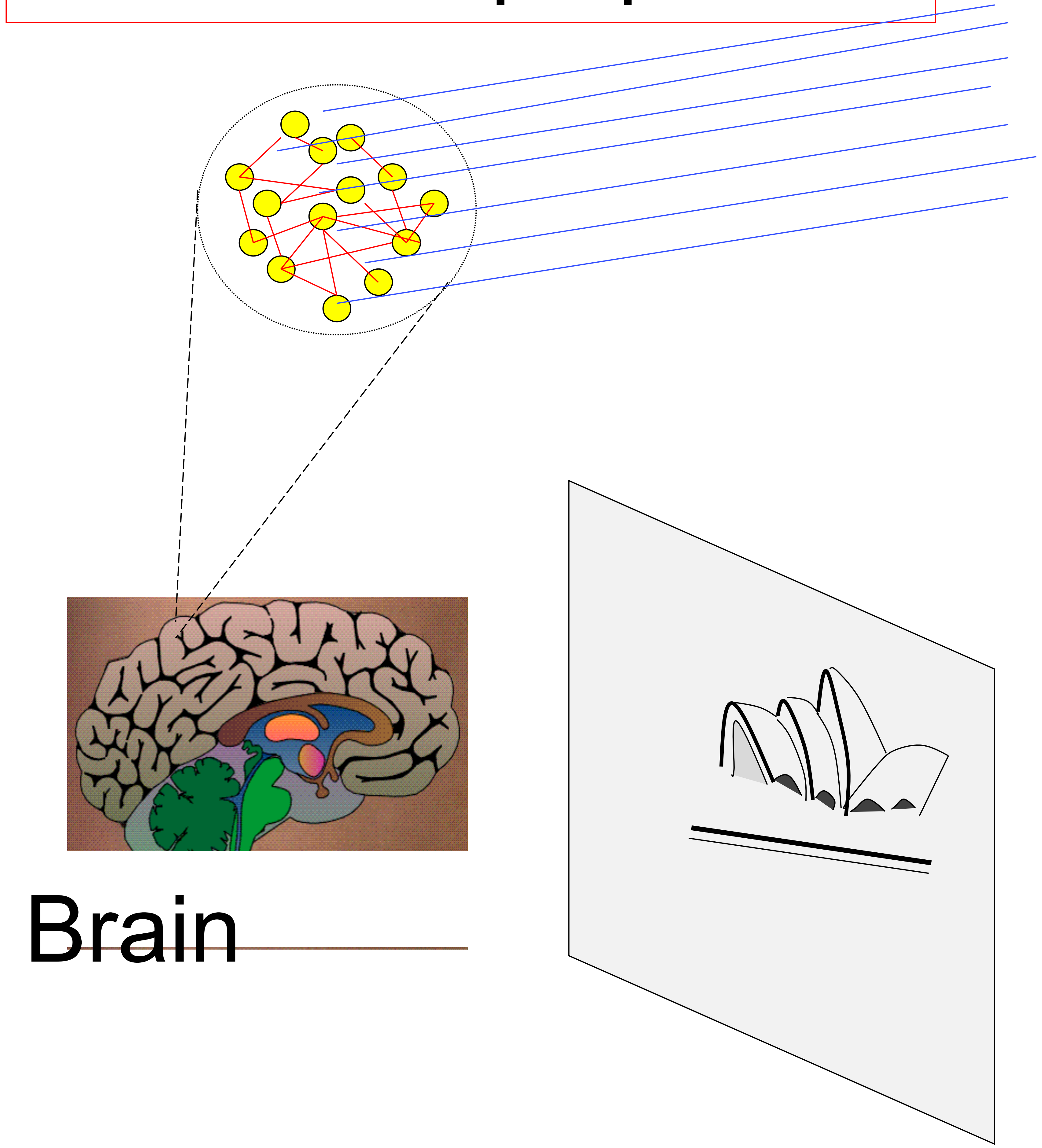
population activity

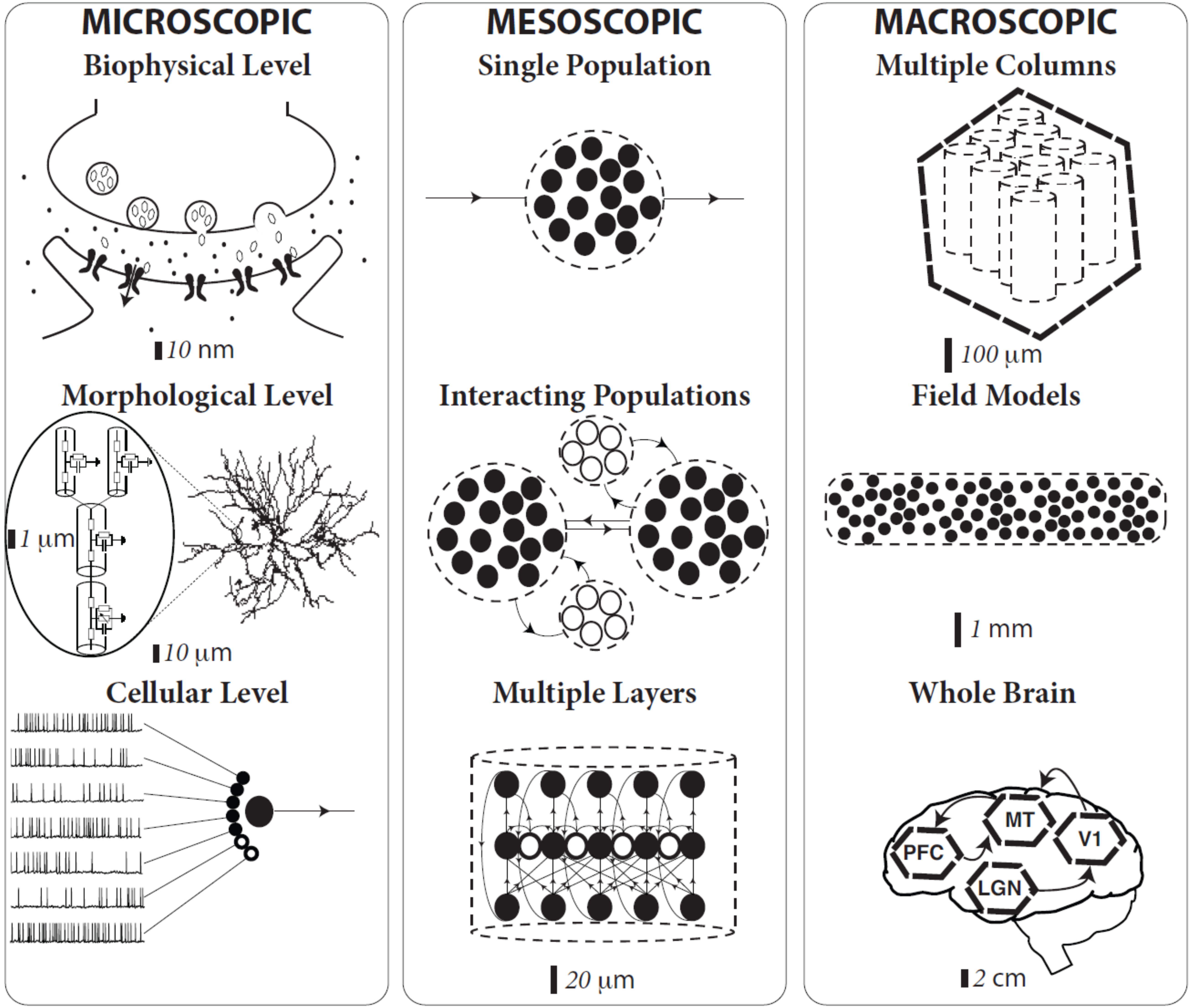
inhomogeneous Poisson model consistent with rate coding

# 10.4: Scales of neuronal processes

*Image: Gerstner et al. Neuronal Dynamics (2014)*

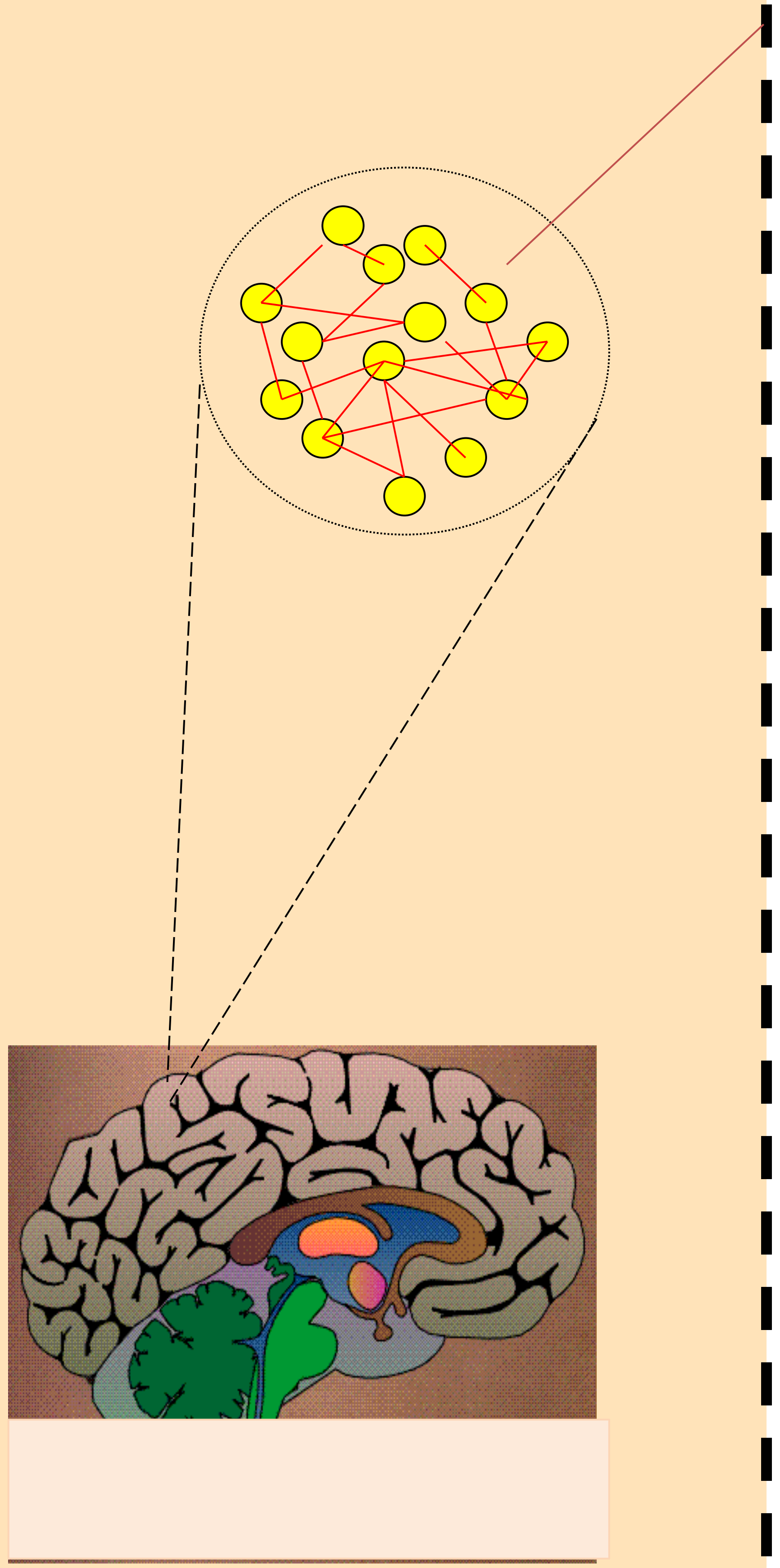
population of neurons
with similar properties



# Quiz 4.

**Rate codes.** Suppose that in some brain area we have a group of **500 neurons**. All neurons **have identical parameters** and they all receive **the same input (you decide what this means!)**. Input is given by sensory stimulation and passes through 2 preliminary neuronal processing steps before it arrives at our group of 500 neurons. Within the group, neurons are **not connected** to each other. The group is embedded in a brain model network containing 100 000 nonlinear integrate-and-fire neurons with some arbitrary connectivity, so that we know exactly how each neuron functions.



Experimentalist A makes a measurement in a **single trial on all 500 neurons** using a multi-electrode array, during a period of sensory stimulation.

Experimentalist B picks an arbitrary **single neuron and repeats** the same sensory stimulation 500 times (with long pauses in between, say one per day).

Experimentalist C **repeats** the same sensory stimulation 500 times (1 per day), but every day he **picks a random neuron** (amongst the 500 neurons).

All three determine the time-dependent firing rate.
[ ] A and B and C are expected to find the same result.
[ ] A and B are expected to find the same result, but that of C is expected to be differe
[ ] B and C are expected to find the same result, but that of A is expected to be differe
[ ] None of the above three options is correct.

*Start at 10:50,*
*Discussion at 10:55*

# 10.4 Summary: Rate models

There are three different definitions of rate.

1. Rate as a temporal average: spike count for a single neuron over a few hundred milliseconds are a few seconds, divided by the time. Disadvantage: it is too slow to be the biological code.

2. Rate as an average of several repetitions of the same experiment: spike count in a short time bin (a few milliseconds), summed over repetitions, divided by bin width and number of repetitions.

Disadvantage: it is too slow (we need repetitions!) to be the biological code, even though the temporal resolution is high

3. Rate as an average over a population: Populations activity A(t) defined earlier. several repetitions of the same experiment.

Disadvantage: works best for completely homogeneous populations, but should also work for 'similar' neurons such as those within one layer of a cortical column.

Advantages: it is a rapid code and averaging over group is natural since every postsynaptic neuron does this.

# Biological Modeling of Neural Networks

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

## Week 10 – Variability and Noise: The question of the neural code

Wulfram Gerstner

EPFL, Lausanne, Switzerland

√ 10.1 Variability of spike trains
- experiments

√ 10.2 Sources of Variability?
- Is variability equal to noise?

√ 10.3 Poisson Model
- homogeneous/inhomogeneous

√ 10.4 Three definitions of Rate Code

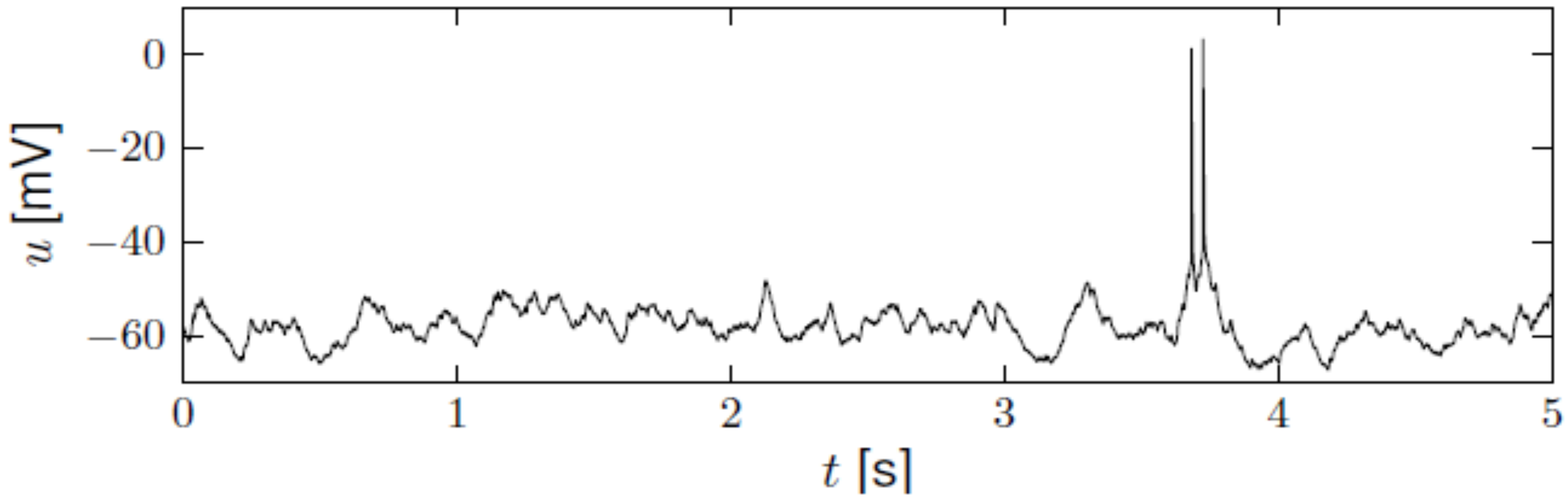
10.5 Stochastic spike arrival
- Membrane potential fluctuations

# 10.5 Variability in vivo – review from 10.1

Spontaneous activity *in vivo*

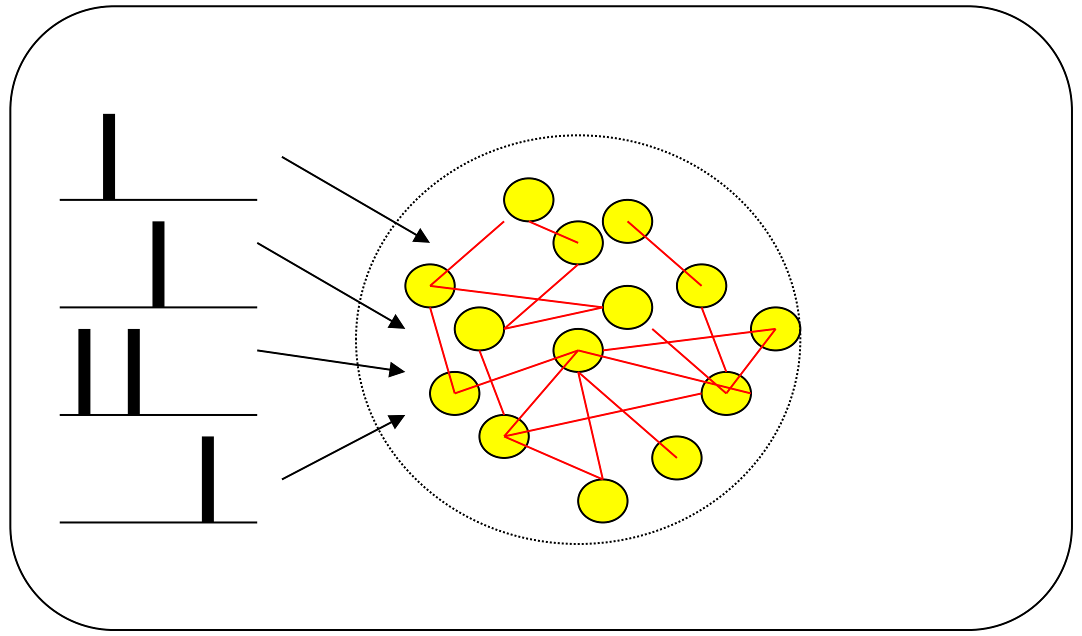
Variability
of membrane potential?

awake mouse, freely whisking,



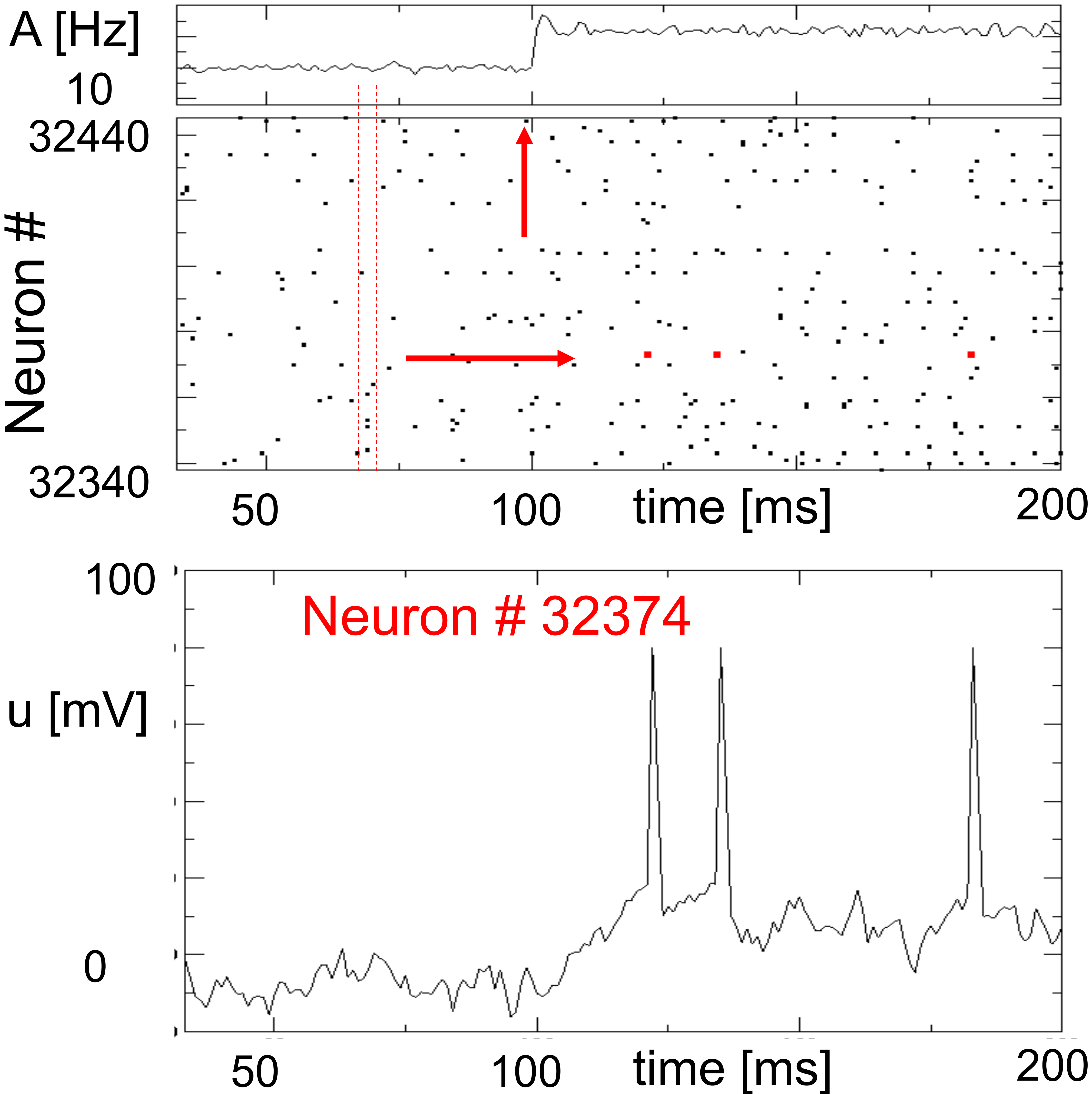

*Crochet et al., 2011*

# 10.5 Variability in networks – review from 10.2

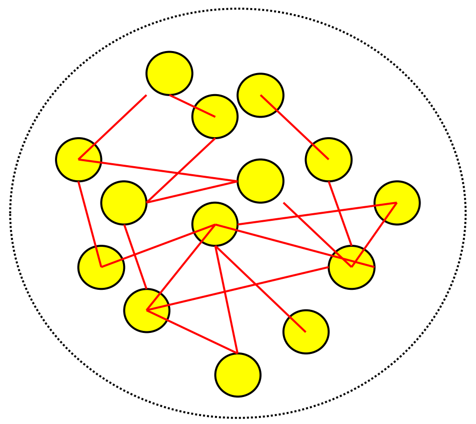


input {low rate / high rate

Population
- 50 000 neurons
- 20 percent inhibitory
- **randomly connected**



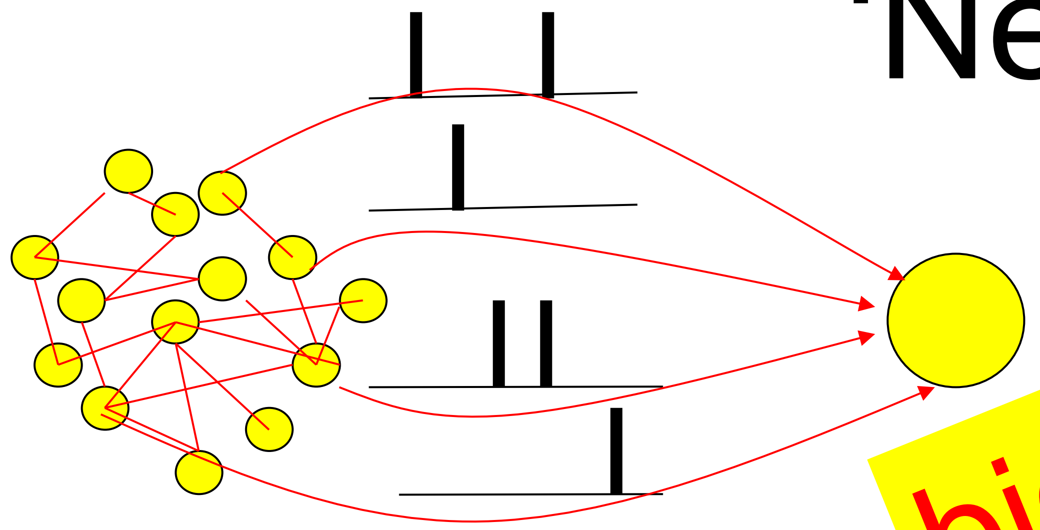
# 10.5 Membrane potential fluctuations



from neuron's point of view:

***stochastic spike arrival***

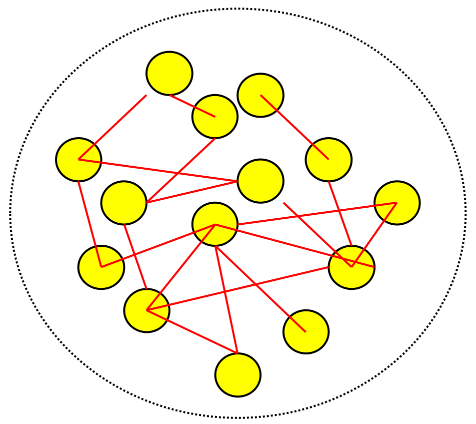
*Pull out one neuron*



'Network noise'

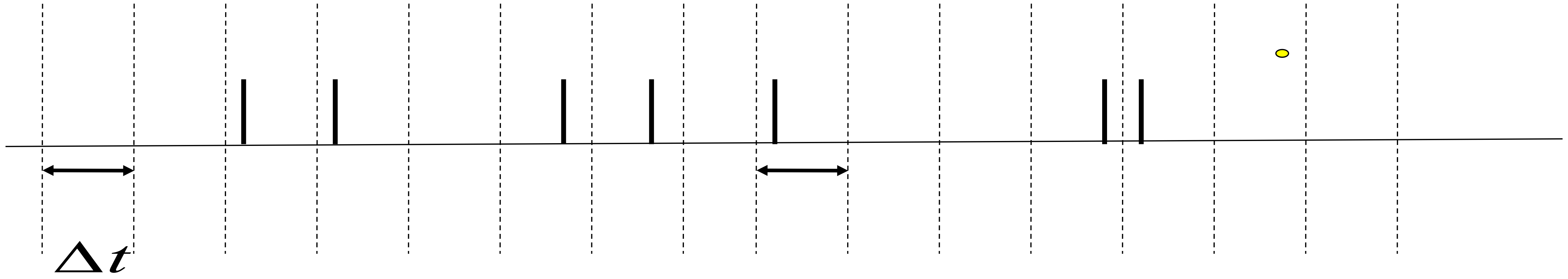
big contribution!

# 10.5. Stochastic Spike Arrival (Poisson model of input)



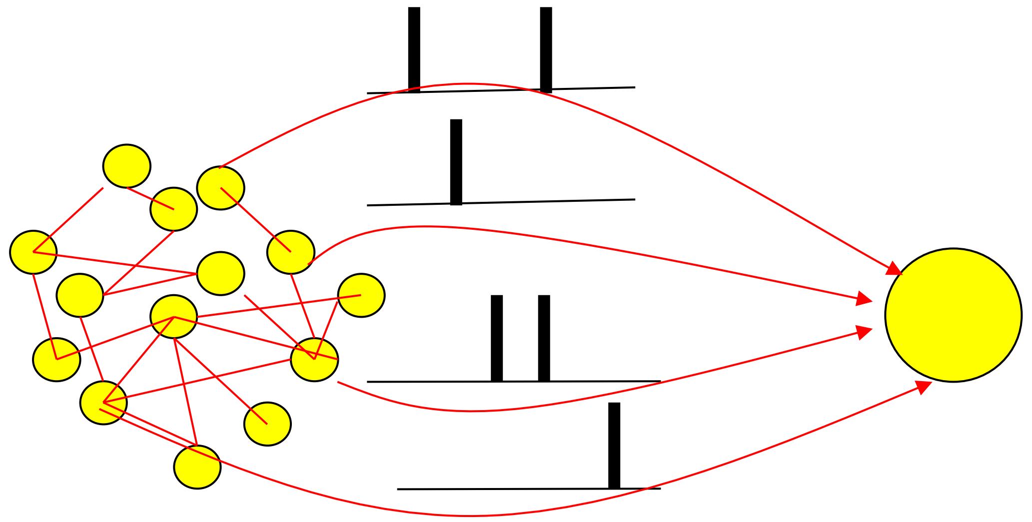
Blackboard now!

Total spike train of K presynaptic neurons




*spike train*

*Pull out one neuron*



Probability of spike arrival:

$$P_F = K\rho_0\,\Delta t$$

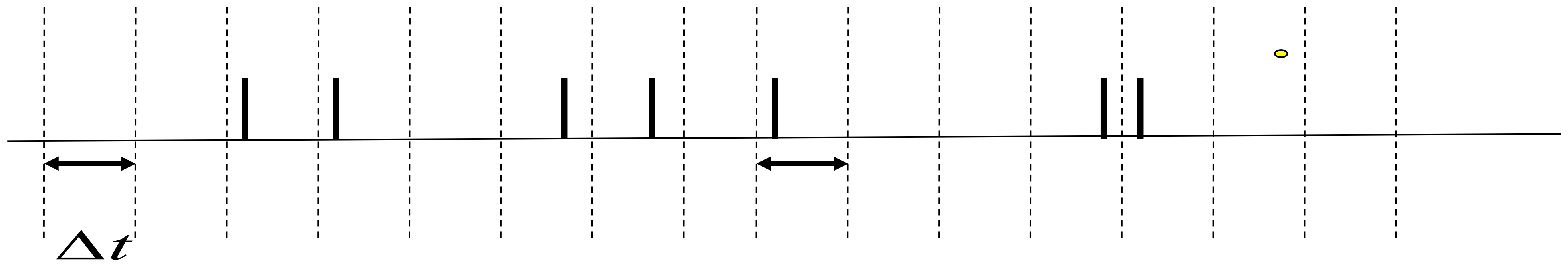
Take $\Delta t \to 0$

$$S(t) = \sum_{k=1}^{K}\sum_{f}\delta(t - t_k^f)$$

*expectation*

$$\langle S(t)\rangle = K\rho_0$$

# 10.5. Calculating the mean




$$x(t) = \sum_f \int dt' \, f(t-t') \, \delta(t'-t_k^f)$$

$$\langle x(t) \rangle = \int dt' \, f(t-t') \left\langle \sum_f \delta(t'-t_k^f) \right\rangle$$

use for exercise

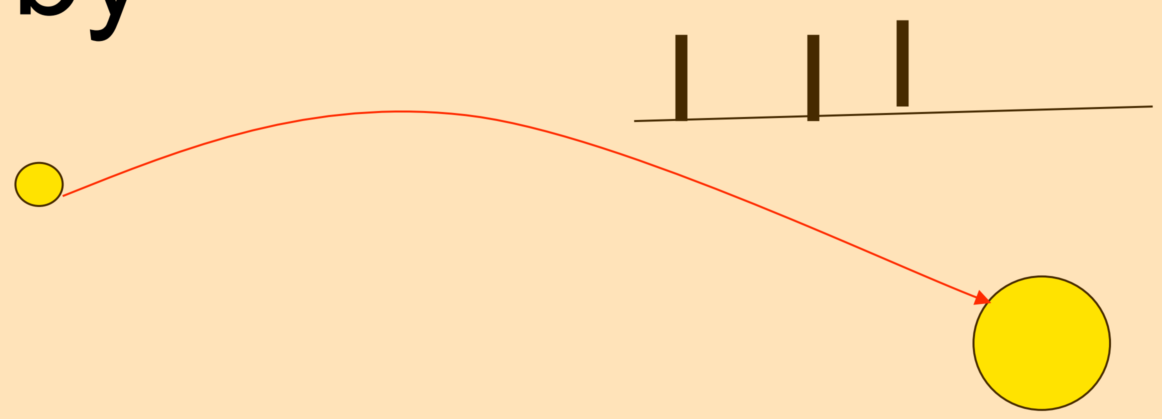
$$\langle x(t) \rangle = \int dt' \, f(t-t') \; \rho(t')$$

rate of inhomogeneous Poisson process

# week 10 – Quiz 5

A linear (=passive) membrane has a potential given by

$$u(t) = \sum_f \int dt' f(t-t')\,\delta(t'-t_k^f) + a$$



Suppose the neuronal dynamics are given by

$$\tau \frac{d}{dt}u = -(u-u_{rest}) \quad + q\sum_f \delta(t-t^f)$$

[ ] the filter *f* is exponential with time constant $\tau$

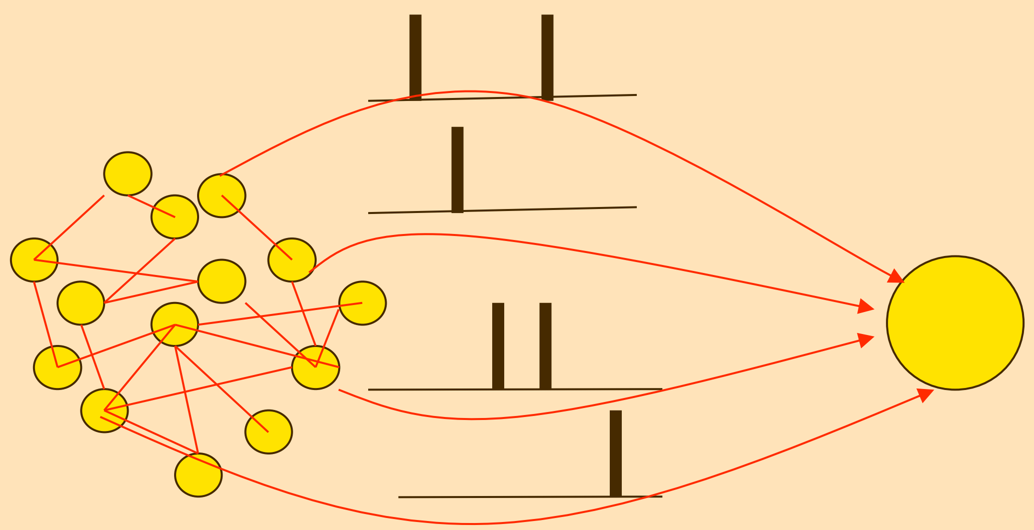
[ ] the constant *a* is equal to the time constant $\tau$

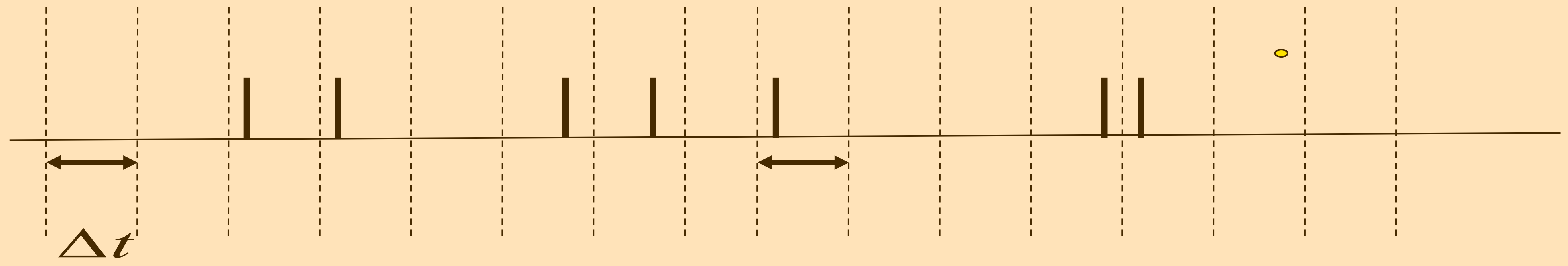
[ ] the constant *a* is equal to $u_{rest}$

[ ] the amplitude of the filter *f* is proportional to *q*

[ ] the amplitude of the filter *f* is q

# Week 10 - Exercise 2.1 NOW






**Passive membrane**

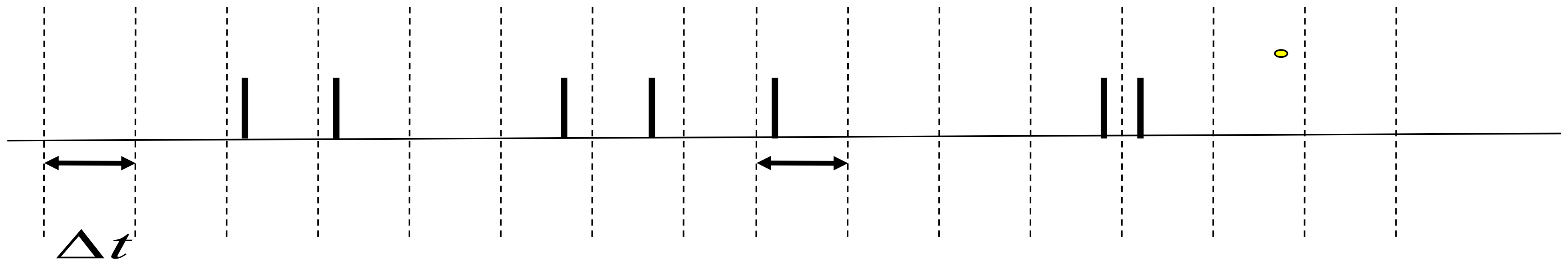
$$\tau \frac{d}{dt} u = -(u - u_{rest}) + R I^{syn}(t) \longrightarrow u(t) = \sum_f \int ds\, f(s)\, \delta(t - t_k^f - s)$$

A leaky integrate-and-fire neuron without threshold (=passive membrane) receives stochastic spike arrival, described as a homogeneous Poisson process. Calculate the **mean membrane potential**. To do so, use the above formula.

*Start at 11:40,*
*Discussion at 11:52*

# 10.5. Calculating the mean

$$RI^{syn}(t) = \sum_k w_k \sum_f \alpha(t - t_k^f)$$




$$I^{syn}(t) = \frac{1}{R} \sum_k w_k \sum_f \int dt' \alpha(t-t') \delta(t' - t_k^f)$$

$$x(t) = \sum_f \int dt' f(t-t') \delta(t' - t_k^f)$$

mean: assume Poisson process

$$\langle I^{syn}(t) \rangle = \frac{1}{R} \sum_k w_k \int dt' \alpha(t-t') \left\langle \sum_f \delta(t' - t_k^f) \right\rangle$$

use for exercise

$$\langle x(t) \rangle = \int dt' f(t-t') \left\langle \sum_f \delta(t' - t_k^f) \right\rangle$$

$$\langle x(t) \rangle = \int dt' f(t-t') \; \rho(t')$$

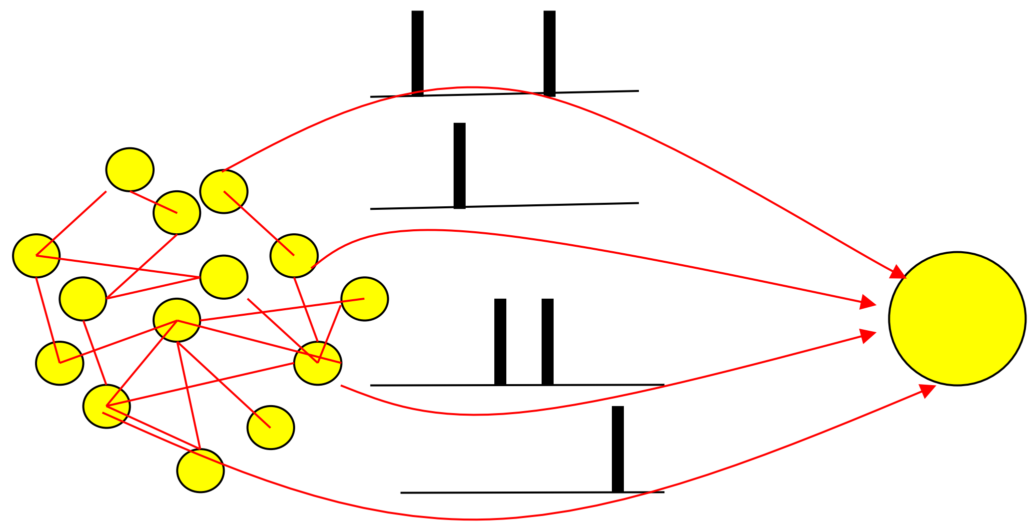
rate of inhomogeneous Poisson process

$$\langle I(t) \rangle = \frac{1}{R} \sum_k w_k \int_0^\infty \alpha(s) \rho(t-s) ds$$

# 10.5. Fluctuation of potential

for a passive membrane, we can analytically predict the mean of membrane potential fluctuations

*Passive membrane*
*=Leaky integrate-and-fire without threshold*



*Passive membrane*

$$\tau \frac{d}{dt} u = -(u - u_{rest}) \quad + R\, I^{syn}(t)$$

**Next week:**

**1) Calculate fluctuations**

**2) ADD THRESHOLD**

**→ Leaky Integrate-and-Fire**

# 10.5 Summary: Stochastic spike arrival

The network noise is often described as stochastic spike arrivals.
Suppose that spikes arrive stochastically (according to a Poisson Process) with time-dependent stochastic intensity $\rho$.

Since input currents sum up linearly, we can calculate the mean input current by 'averaging over the stochastic spike arrivals' which is equivalent to 'taking the expectation over stochasticity of the Poisson process'.

Similarly, if the voltage of the neuronal membrane is approximated by a linear model (see week 1, passive membrane, or week 8, input potential), then we can also calculate the mean membrane potential.

In both cases taking the expectation is easy since the average of the spike arrivals yields the stochastic intensity.

$$\langle \sum_f \delta(t - t^f) \rangle = \rho(t)$$

Next week we extend the calculation so as to also include fluctuations (not just the mean).

# week 10 – References and Suggested Reading

**Reading**: W. Gerstner, W.M. Kistler, R. Naud and L. Paninski,
*Neuronal Dynamics: from single neurons to networks and models of cognition.* Ch. 7: Cambridge, 201


-Rieke, F., Warland, D., de Ruyter van Steveninck, R., and Bialek, W. (1996). *Spikes - Exploring the neural code*. MIT Press.
-Faisal, A., Selen, L., and Wolpert, D. (2008). Noise in the nervous system. *Nat. Rev. Neurosci*., 9:202
-Gabbiani, F. and Koch, C. (1998). Principles of spike train analysis. In Koch, C. and Segev, I., editors,
Methods in Neuronal Modeling, chapter 9, pages 312-360. MIT press, 2nd edition.
-Softky, W. and Koch, C. (1993). The highly irregular firing pattern of cortical cells is inconsistent with temporal integration of random epsps. *J . Neurosci.*, 13:334-350.
-Stein, R. B. (1967). Some models of neuronal variability. *Biophys. J*., 7:37-68.
-Siegert, A. (1951). On the first passage time probability problem. Phys. Rev., 81:617{623.
-Konig, P., et al. (1996). Integrator or coincidence detector? the role of the cortical neuron revisited. *Trends Neurosci,* 19(4):130-137.


**THE END**