Biological Modeling of Neural Networks

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

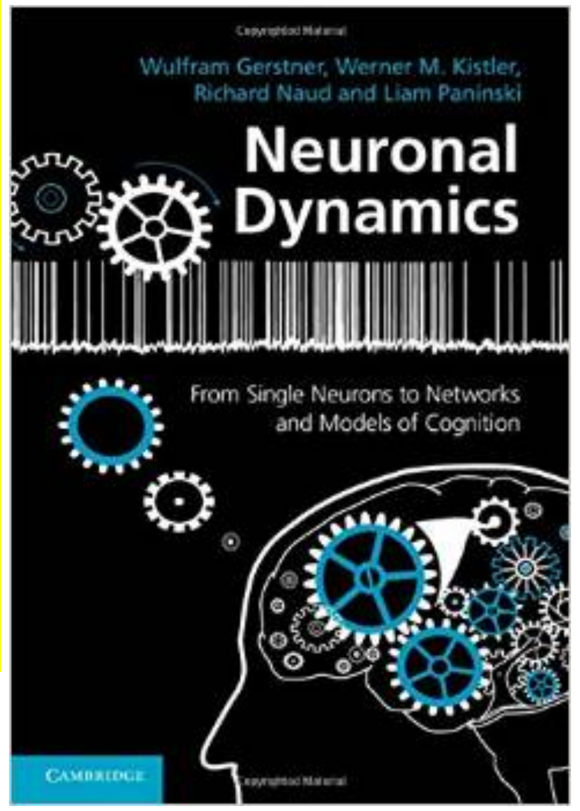
Week 10 – Variability and Noise:
The question of the neural code

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

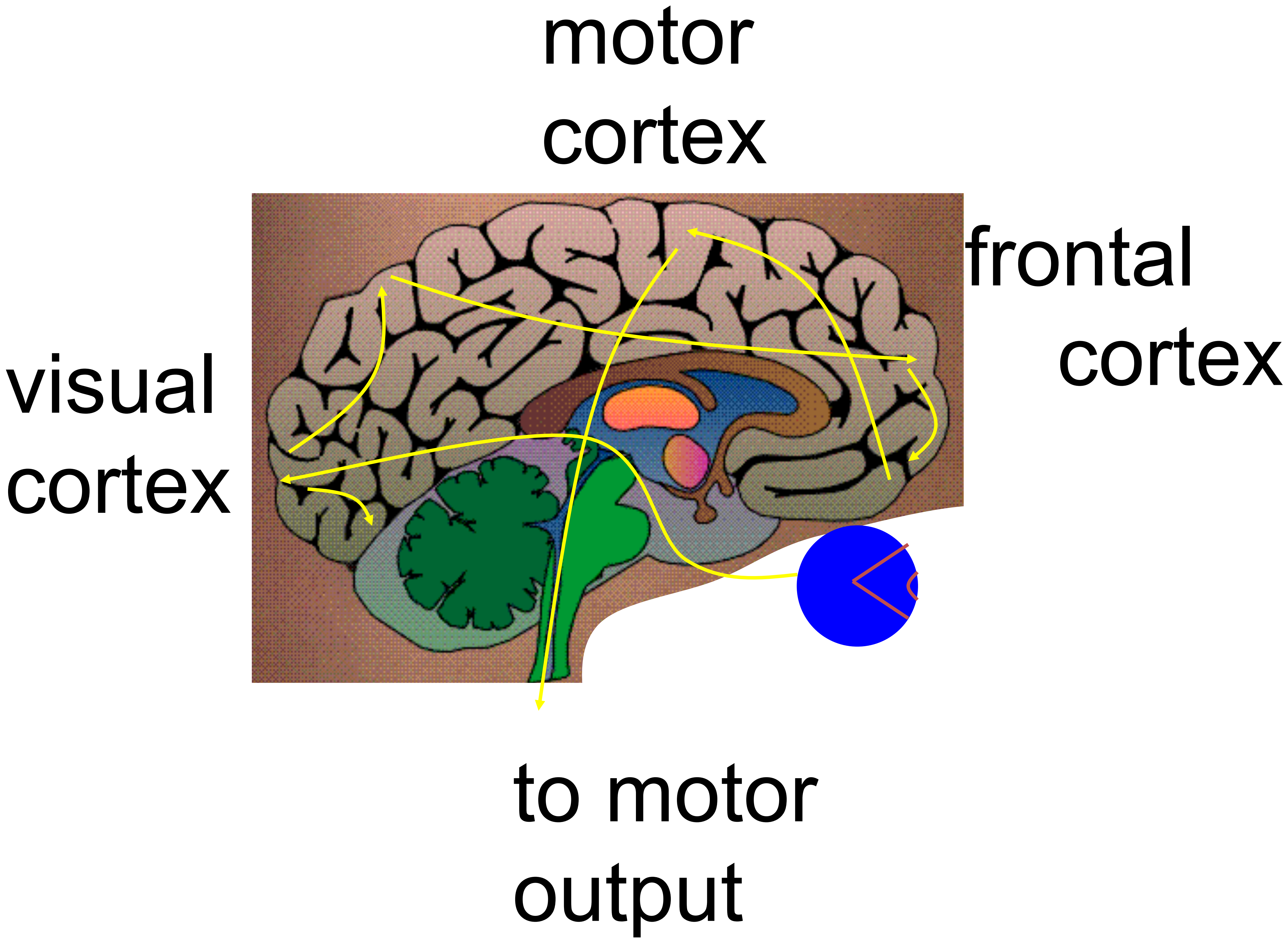
10.2 Sources of Variability?
- Is variability equal to noise?

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

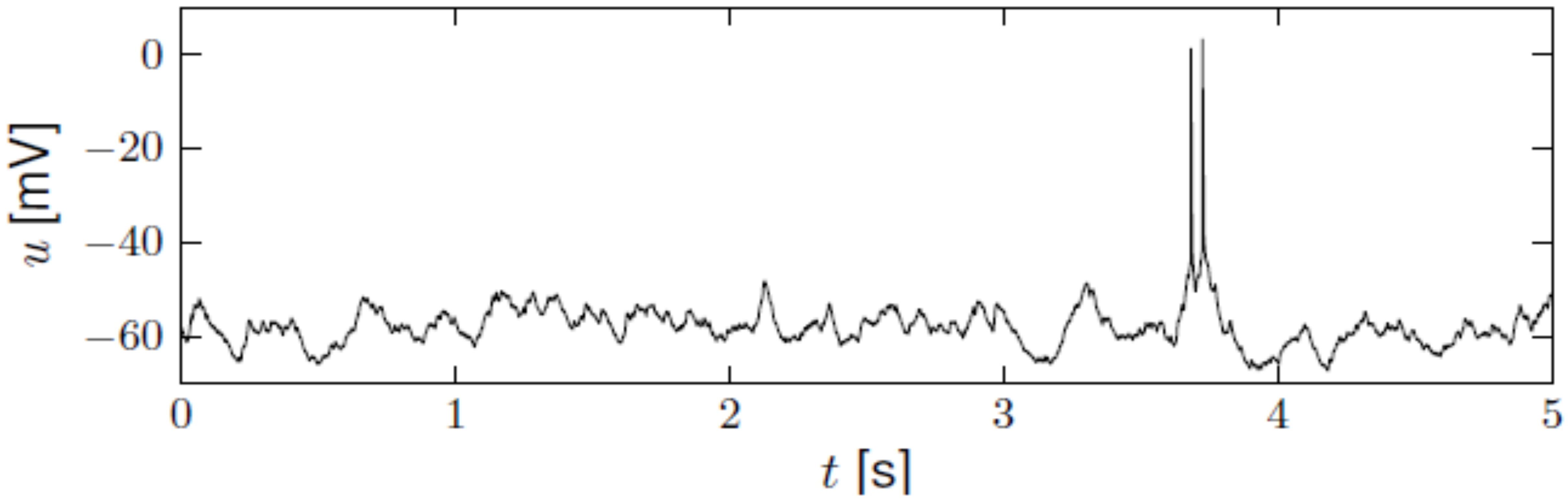


10.1 Variability in vivo – review from week 1

Spontaneous activity *in vivo*

Variability
- of membrane potential?
- of spike timing?

awake mouse, cortex, freely whisking,

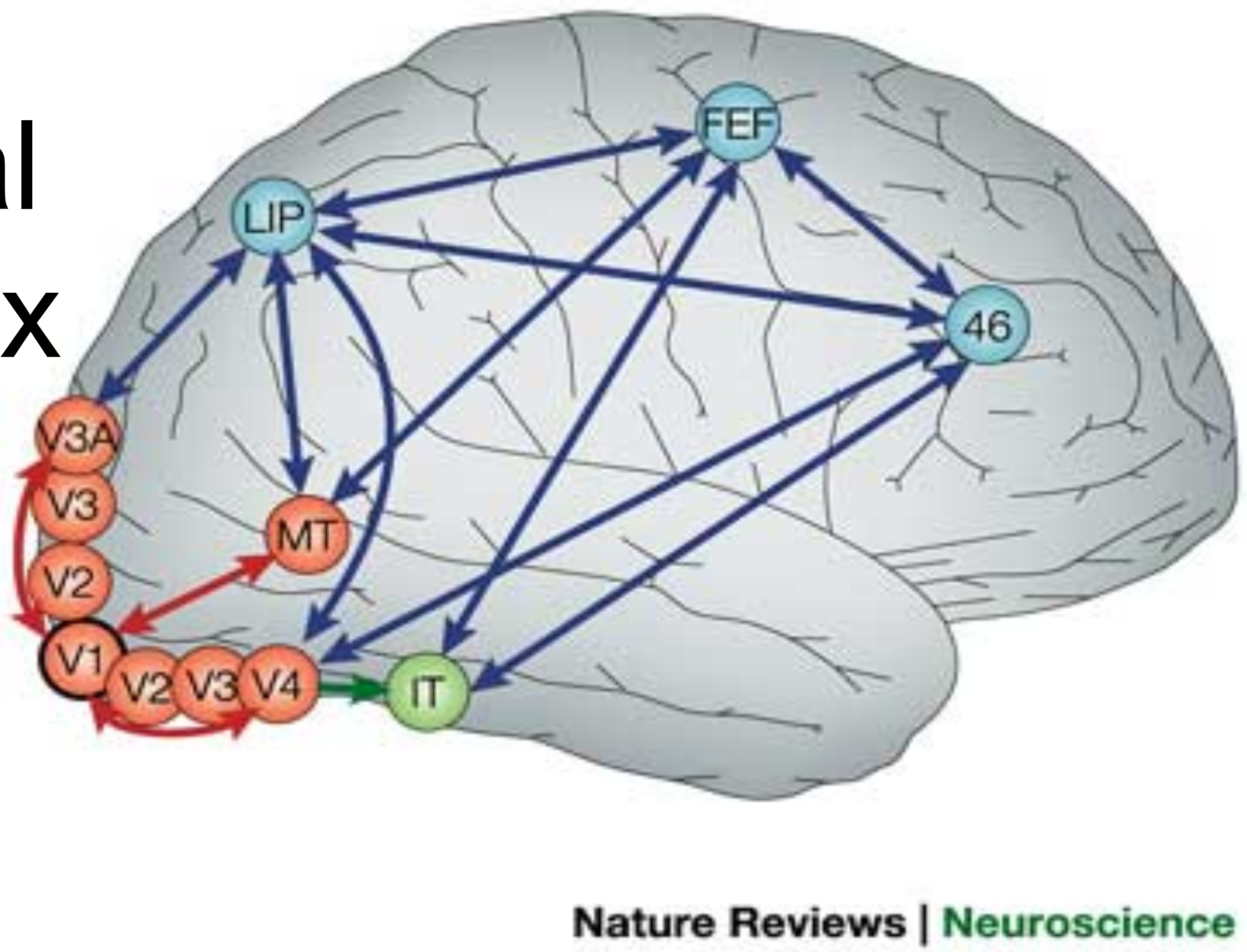


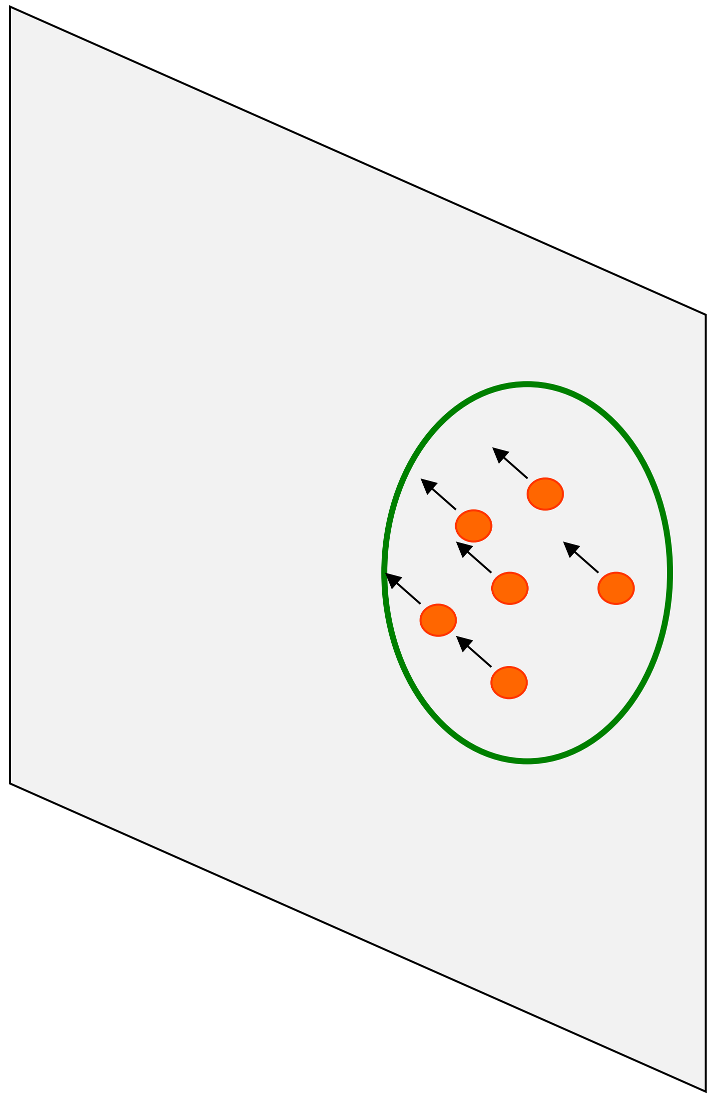
Crochet et al., 2011

10.1 Variability in vivo – Detour: Motion Sensitive Neurons

Detour: Receptive fields in V5/MT

visual
cortex

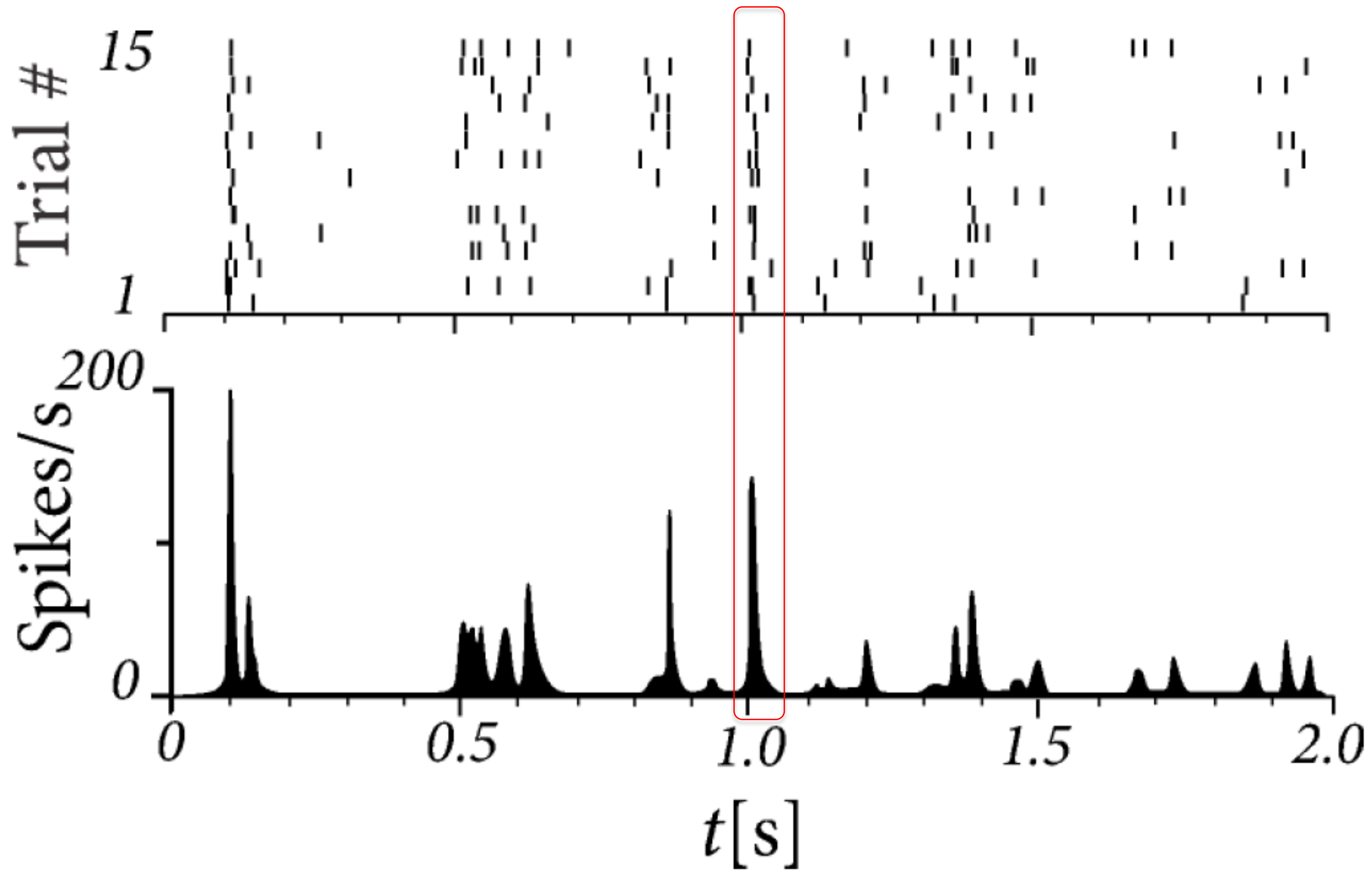


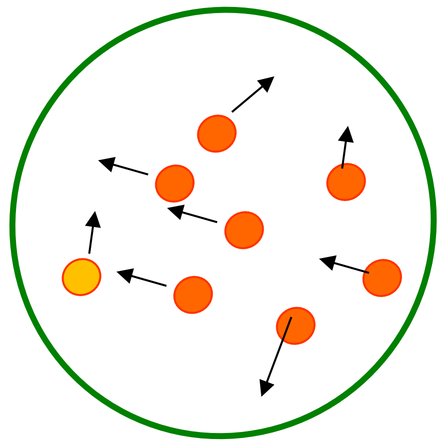


cells in visual cortex MT/V5
respond to motion stimuli

10.1 Variability in vivo – Neurons in MT/V5

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



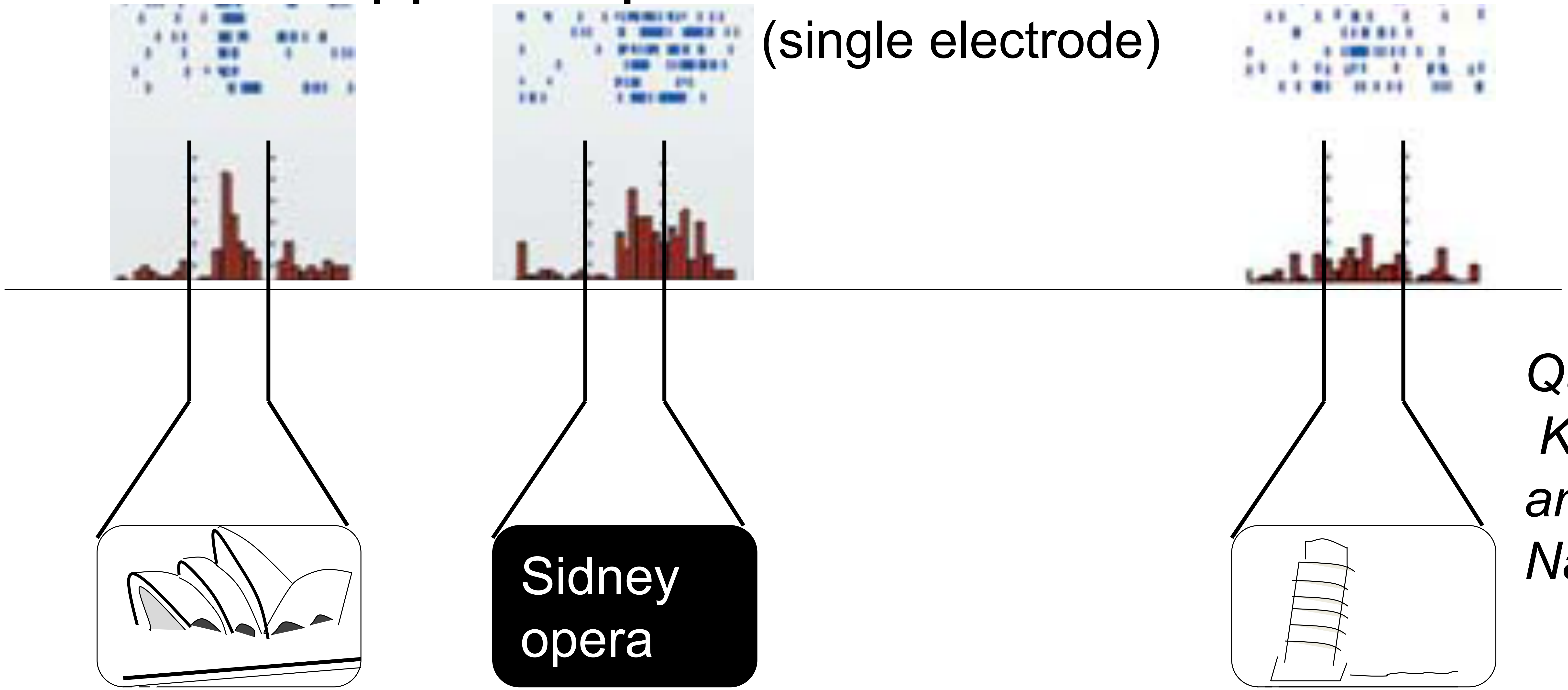


adapted from Bair and Koch 1996;
data from Newsome 1989

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,

brain slice

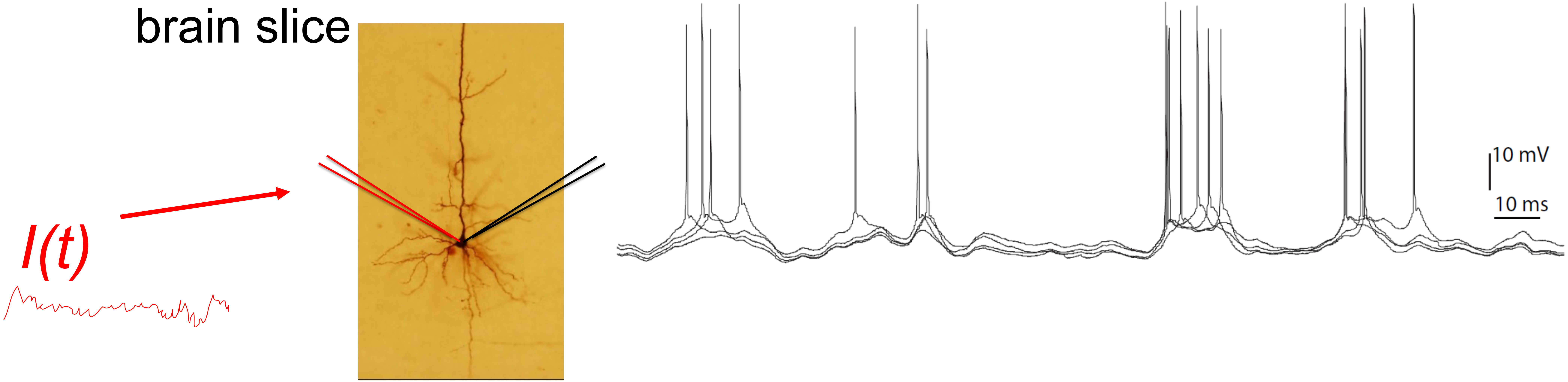


Image: Gerstner et al.
Neuronal Dynamics (2014)
Adapted from
Naud and Gerstner (2012)

10.1 Variability

In vivo data

→ looks 'noisy'

In vitro data

→ fluctuations

Fluctuations

-of membrane potential

-of spike times

fluctuations=noise?

relevance for coding?

source of fluctuations?

model of fluctuations?

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Week 10 – Variability and Noise:

The question of the neural code

Wulfram Gerstner

EPFL, Lausanne, Switzerland

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- Is variability equal to noise?

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- homogeneous/inhomogeneous

10.4 Three definitions of Rate Code

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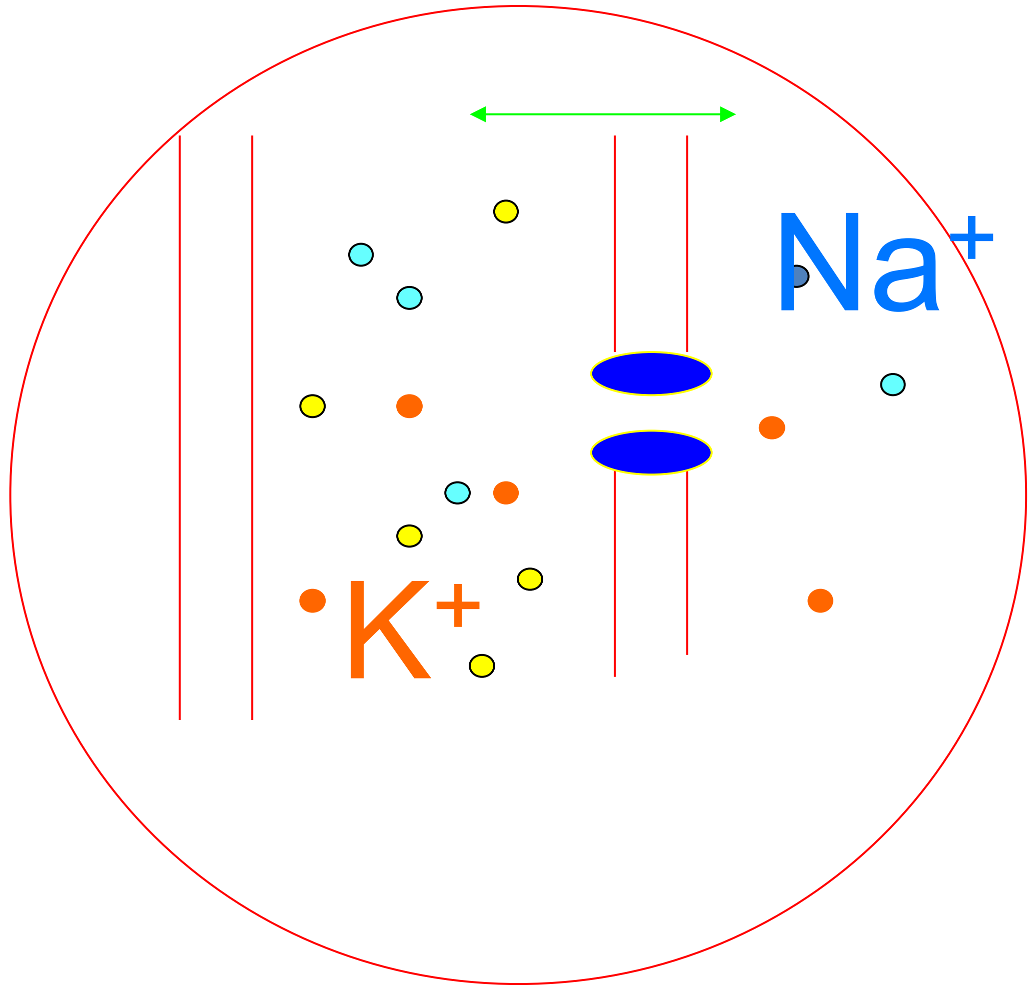
- Membrane potential fluctuations

10.2. Sources of Variability

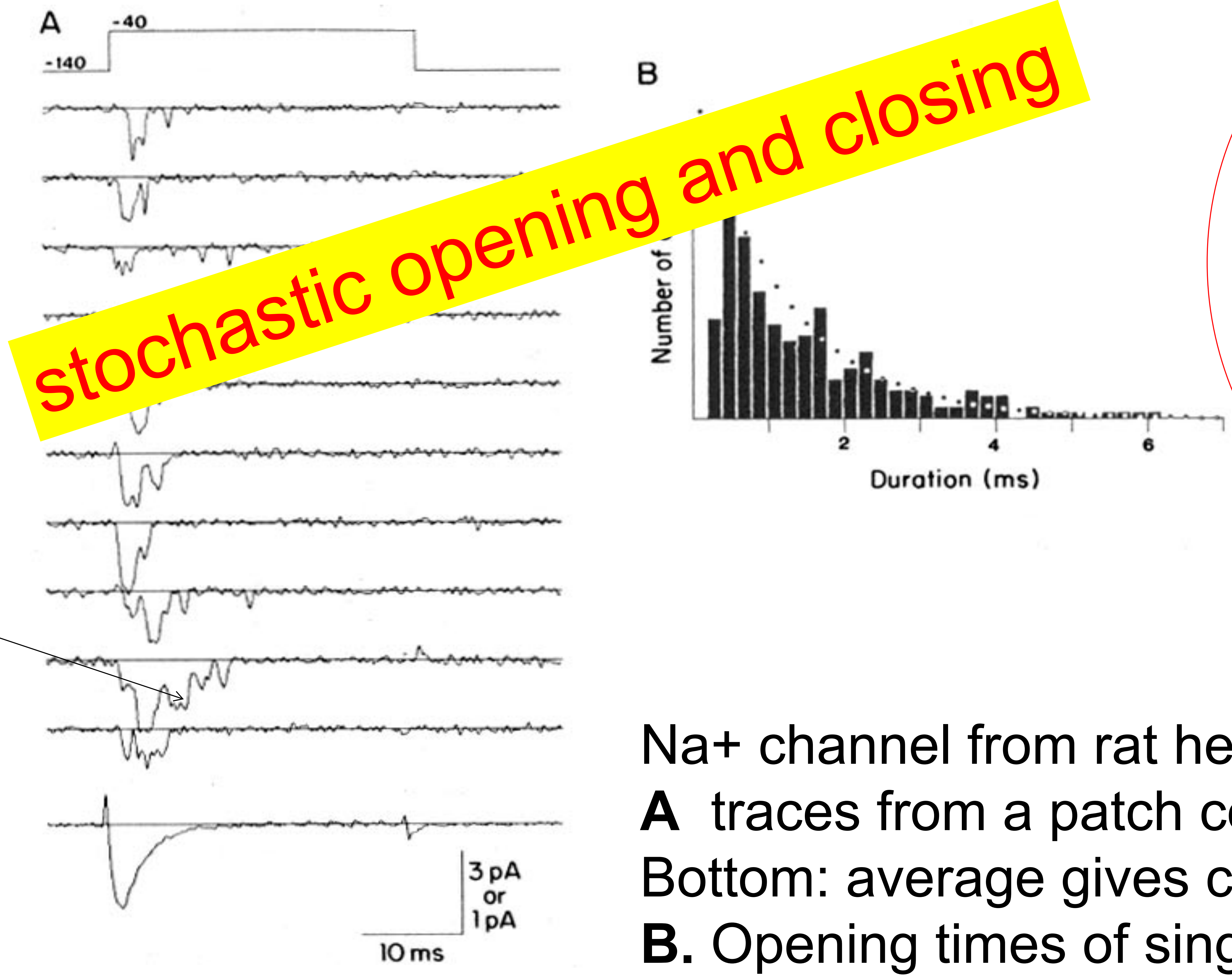
- Intrinsic noise (ion channels)

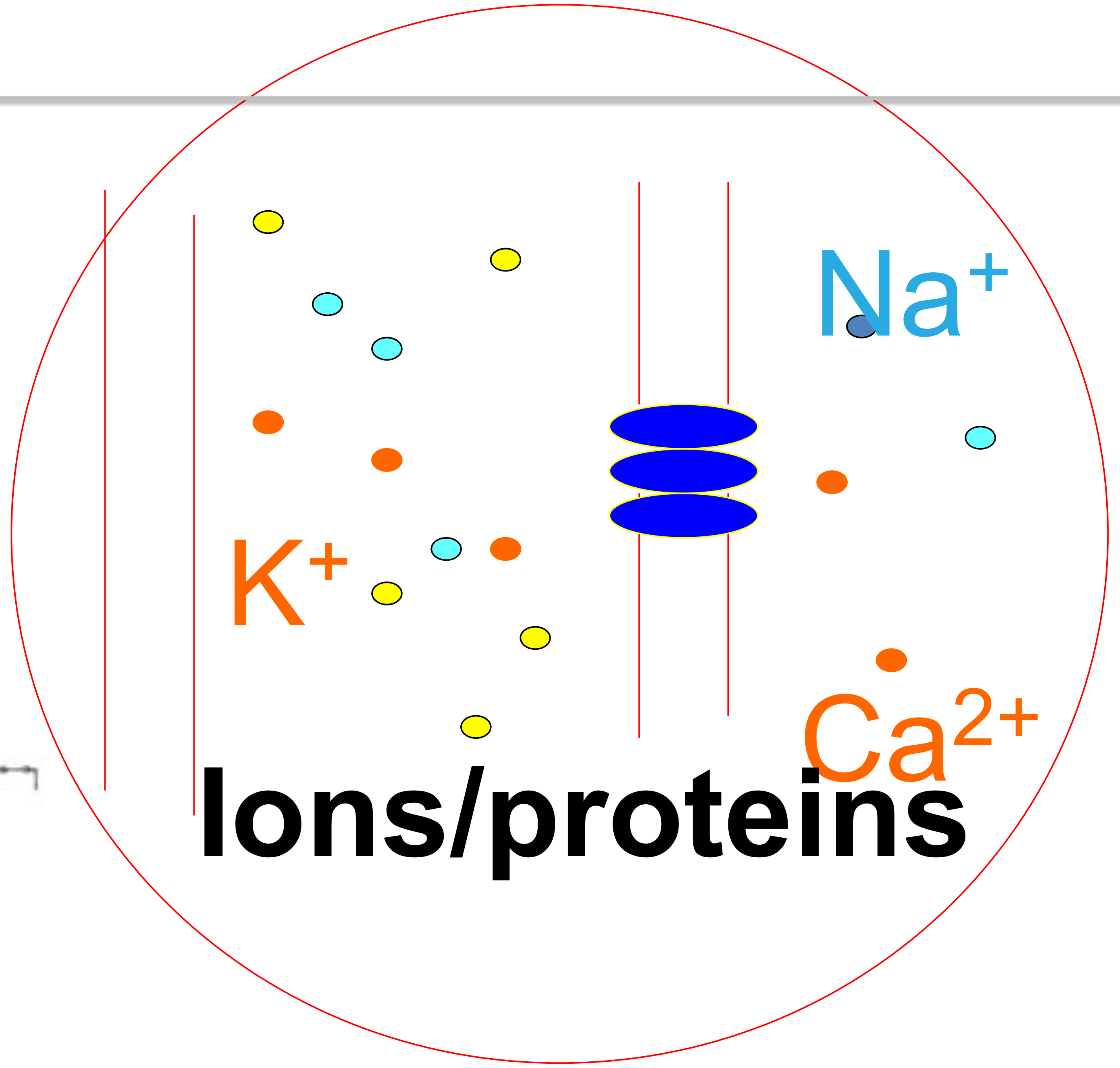


-Finite number of channels
-Finite temperature

Review from week 2 Ion channels

Steps: Different number of open channels

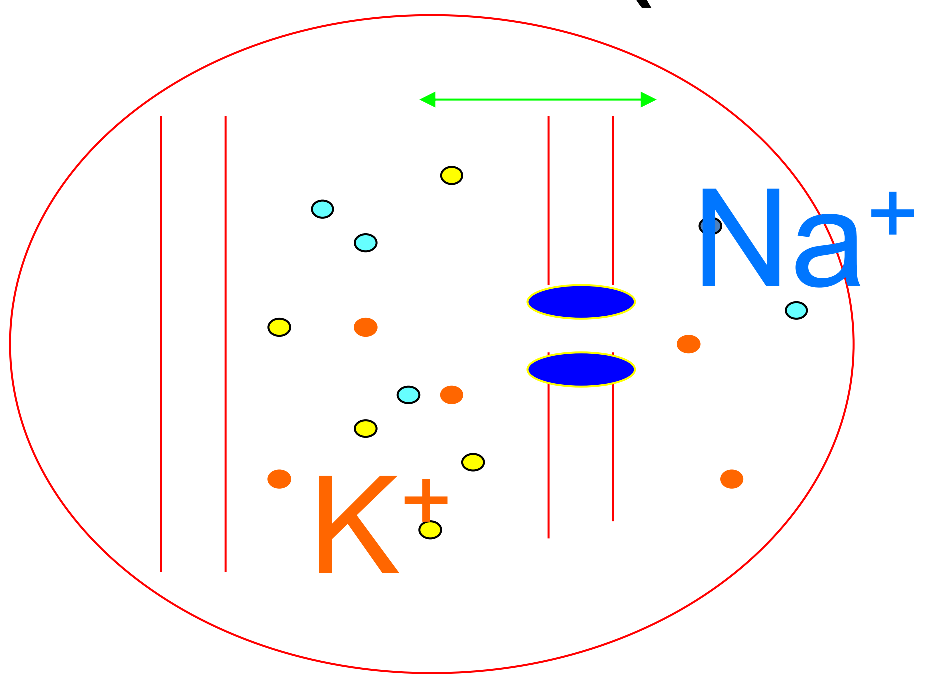




Na+ channel from rat heart *(Patlak and Ortiz 1985)*
A traces from a patch containing several channels.
Bottom: average gives current time course.
B. Opening times of single channel events

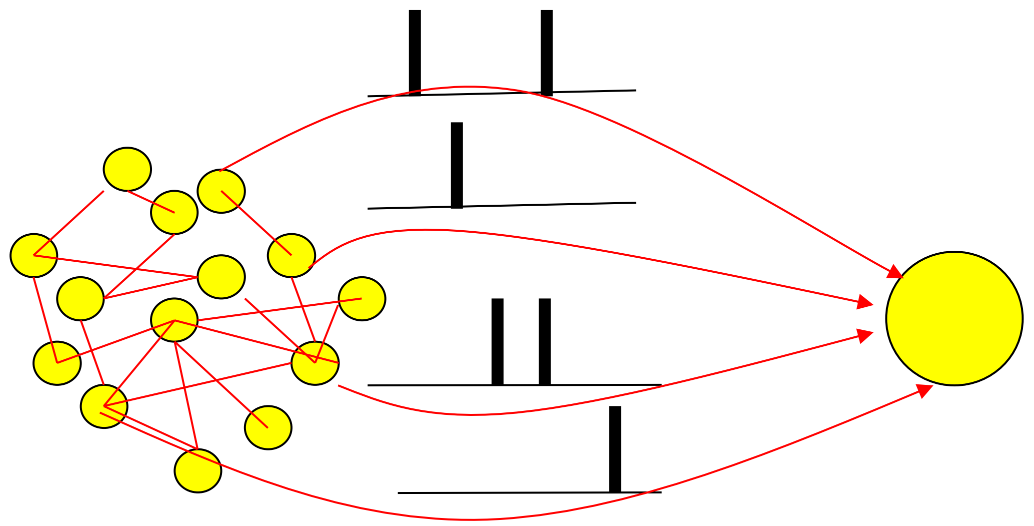
10.2. Sources of Variability

- Intrinsic noise (ion channels)



-Finite number of channels
-Finite temperature

-Network noise (background activity)

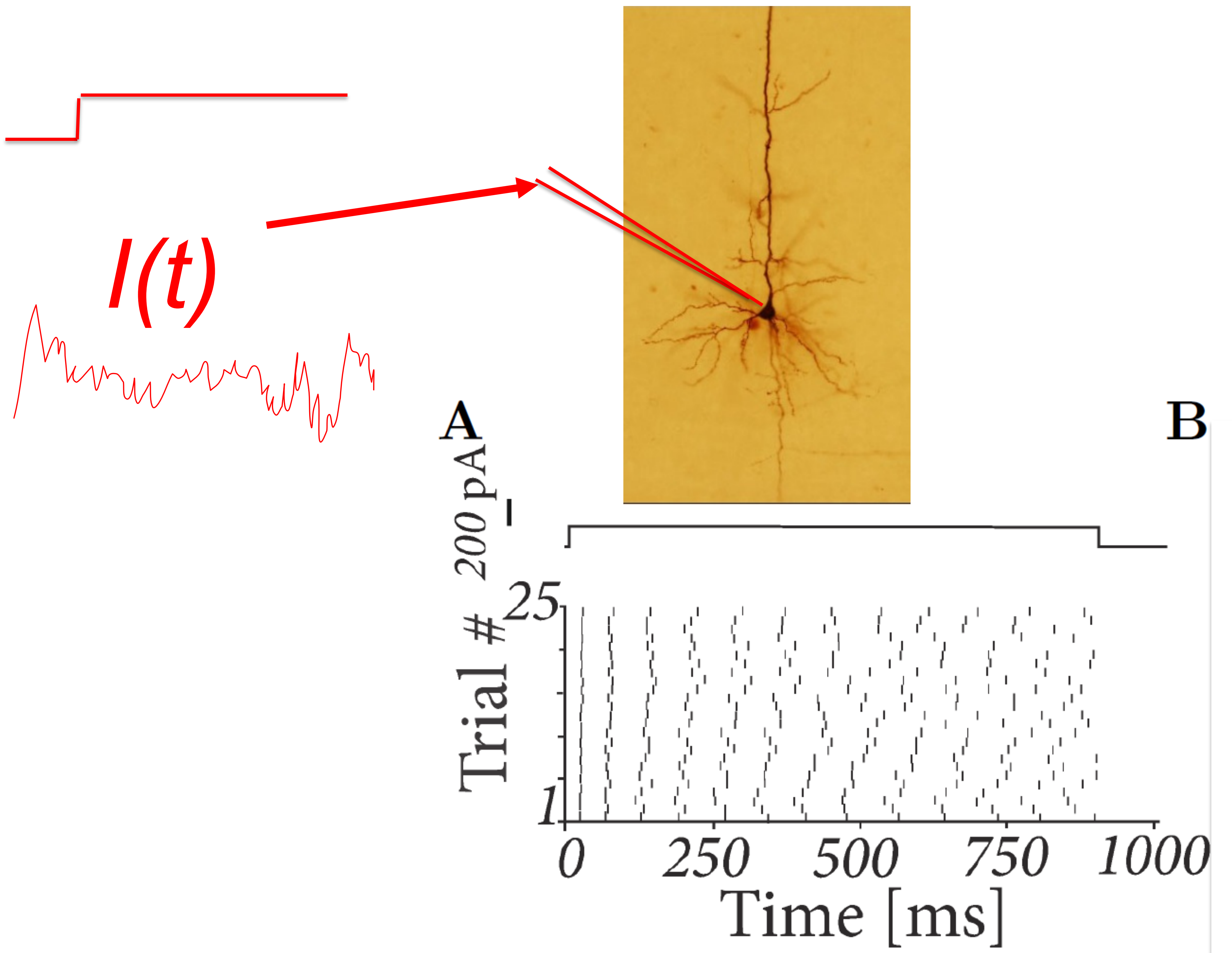


-Spike arrival from other neurons
-Beyond control of experimentalist

→ Check intrinisic noise by removing the network

10.2 Variability in vitro is low

neurons are fairly reliable



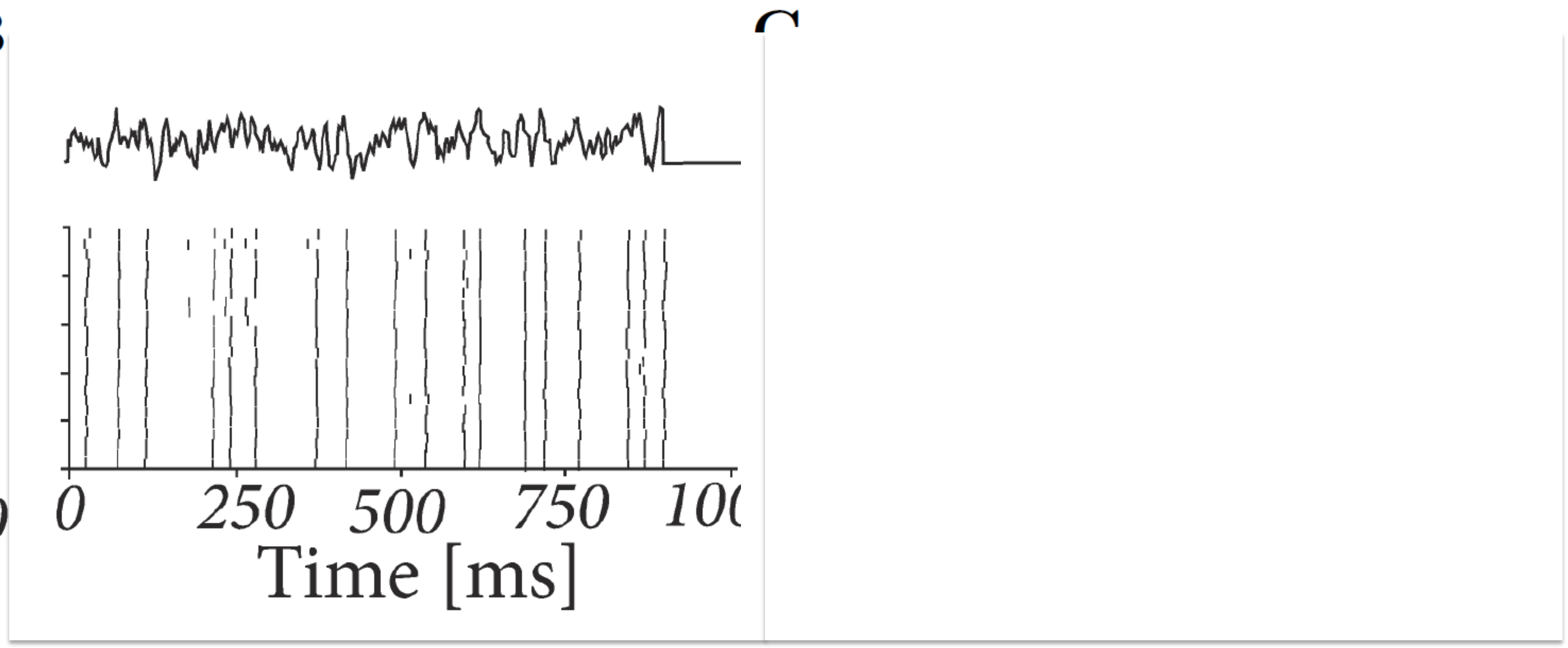
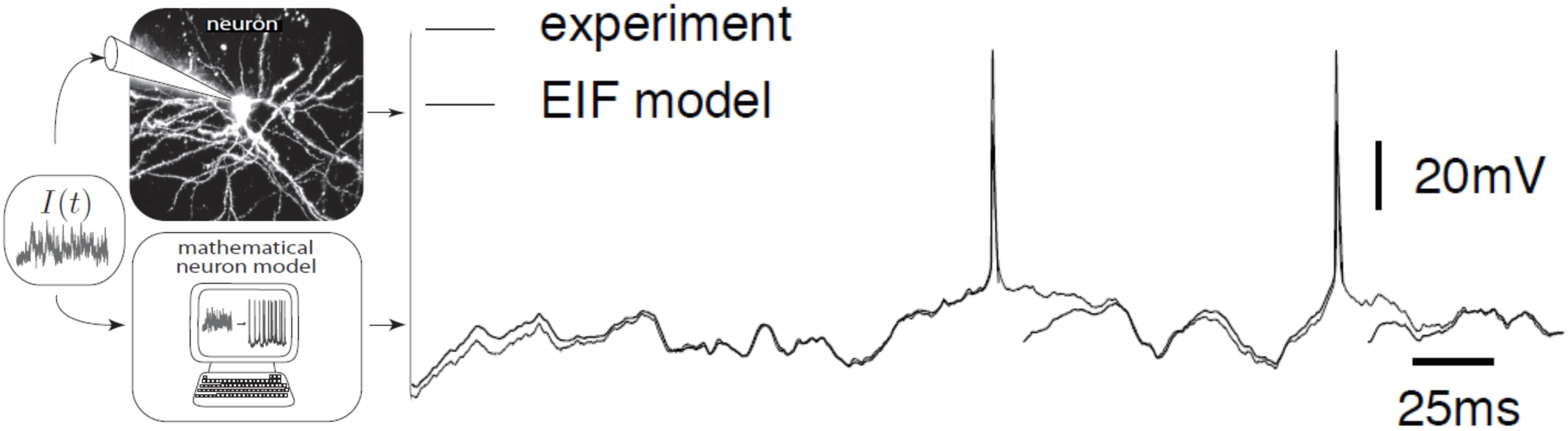


Image adapted from
Mainen&Sejnowski 1995

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



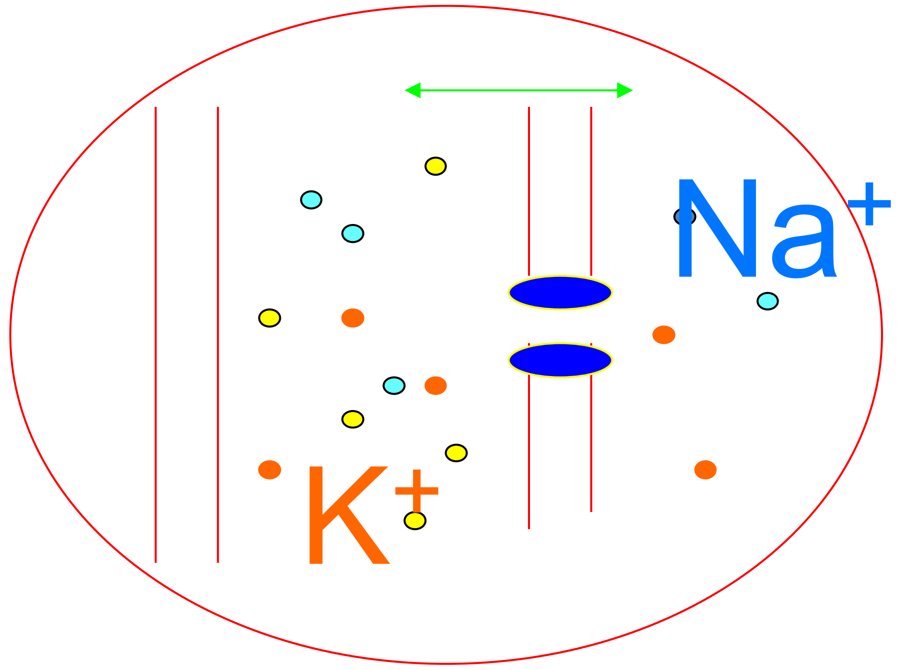
Badel et al., 2008

Aims: - predict spike initiation times
- predict subthreshold voltage

only possible, because neurons are fairly reliable

10.2. Sources of Variability

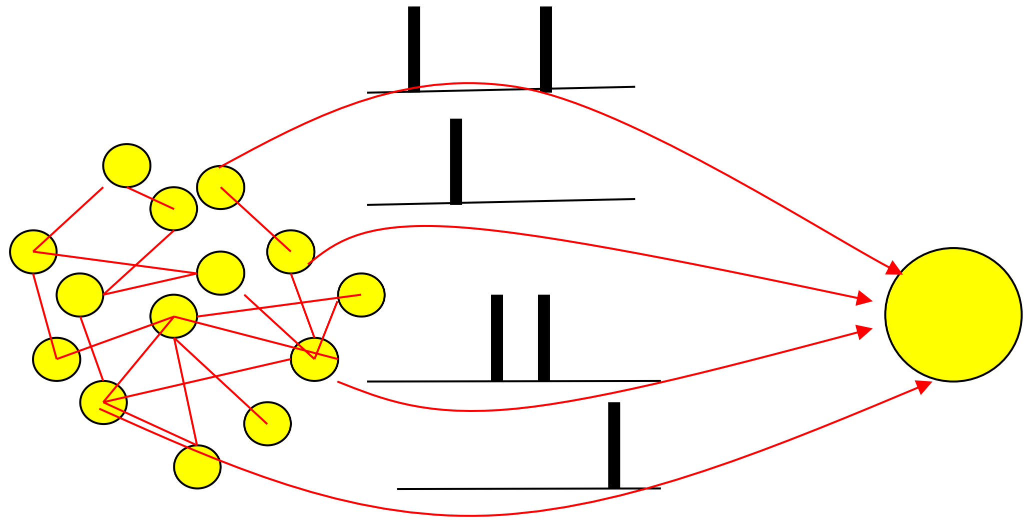
- Intrinsic noise (ion channels)



-Finite number of channels
-Finite temperature

small contribution!

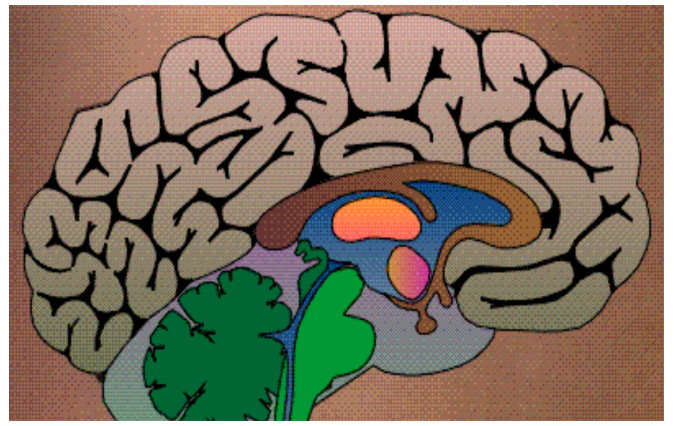
-Network noise (background activity)



-Spike arrival from other neurons
-Beyond control of experimentalist

→ Check network noise by simulation!

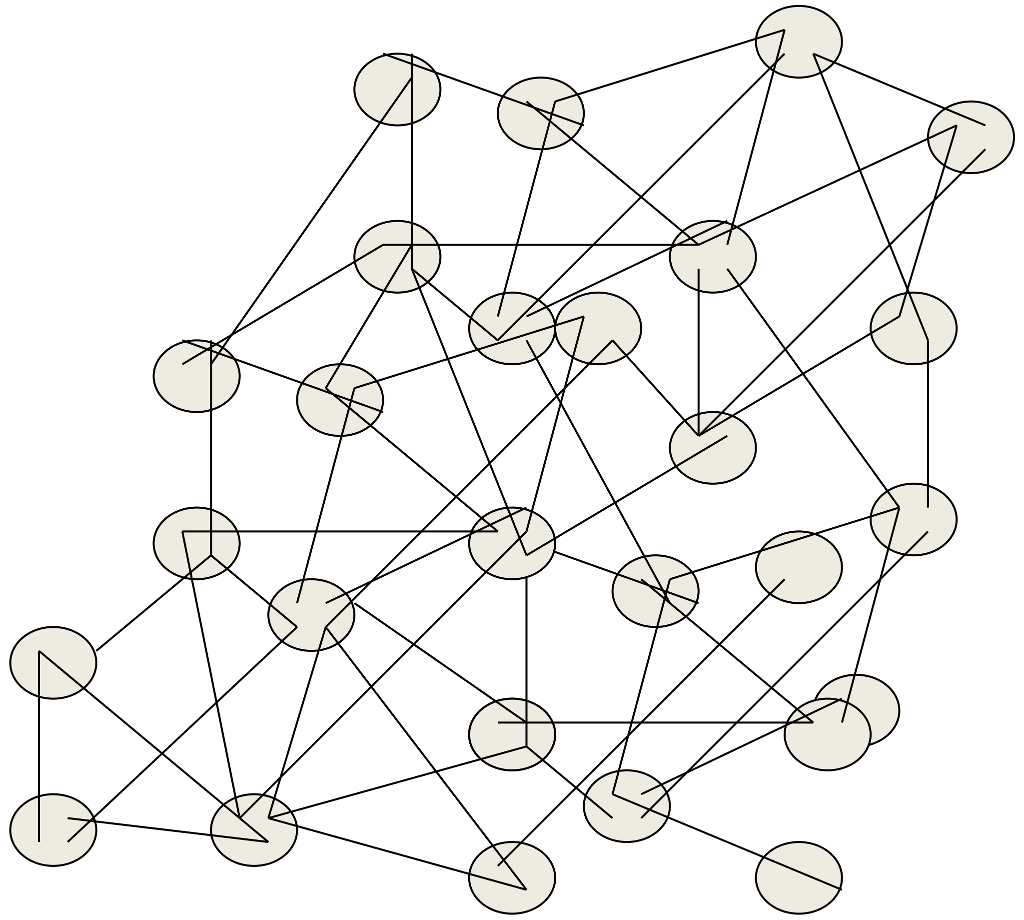
10.2 Sources of Variability



Brain

The Brain: a highly connected system

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

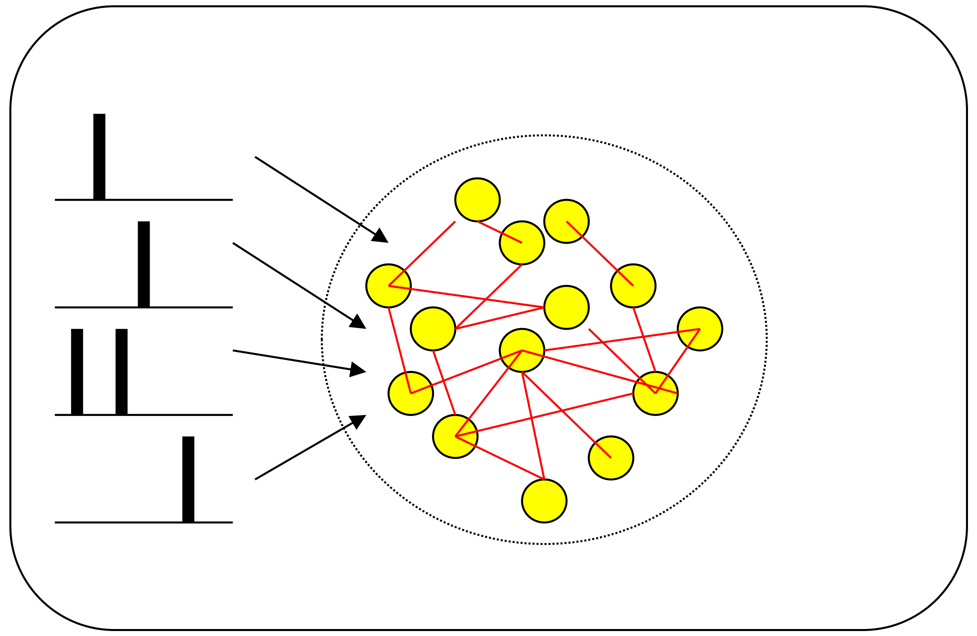


Distributed architecture

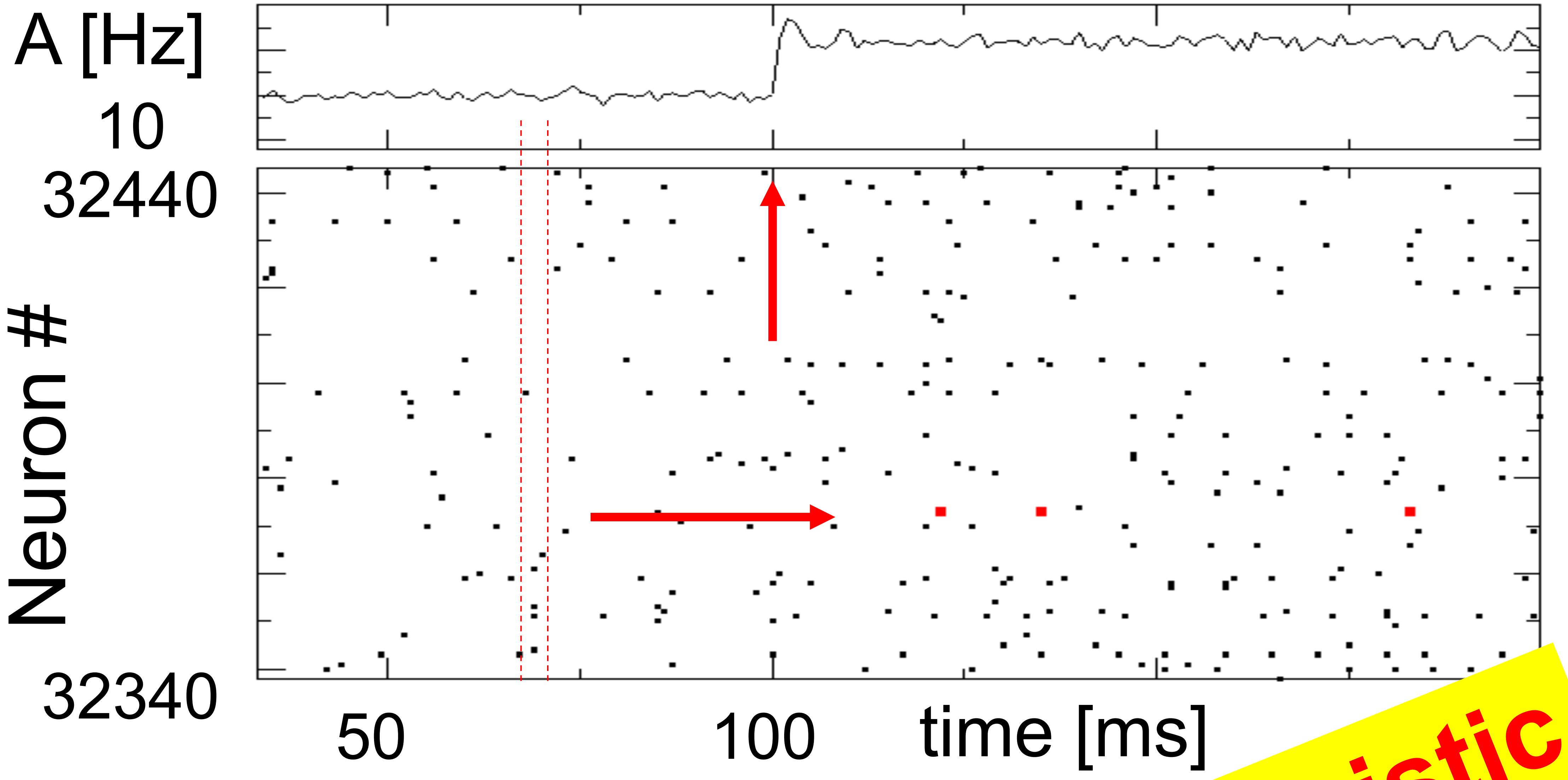
10^{10} neurons

10^{4} connections/neurons

10.2 Random firing in a population of LIF neurons



input {low rate, high rate}

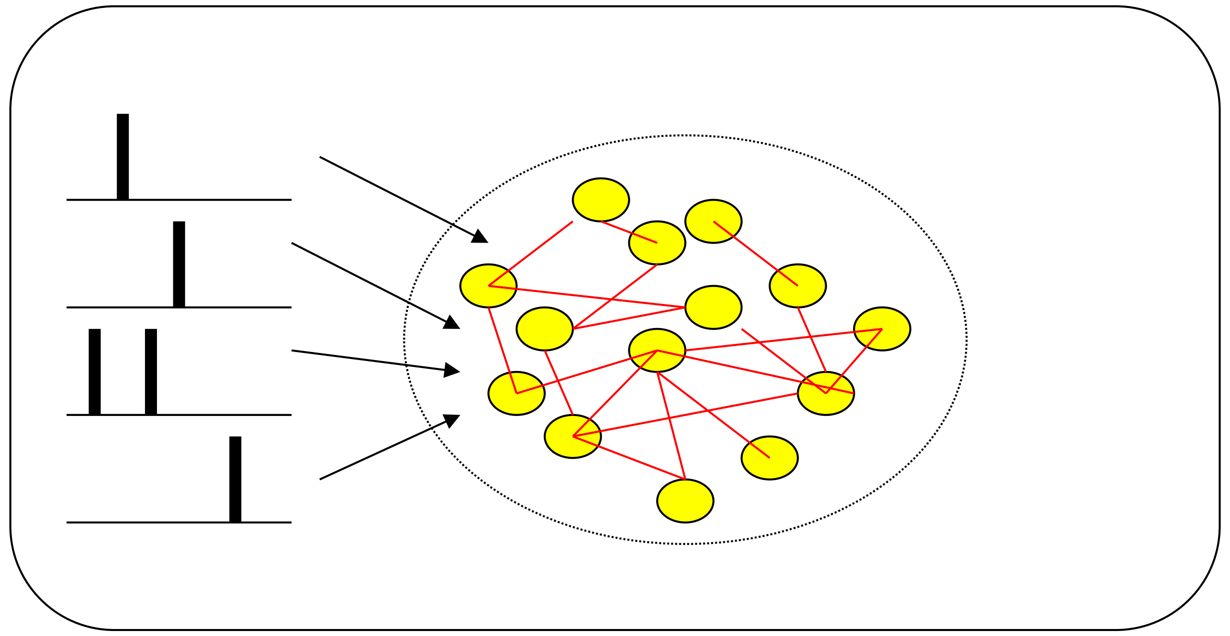


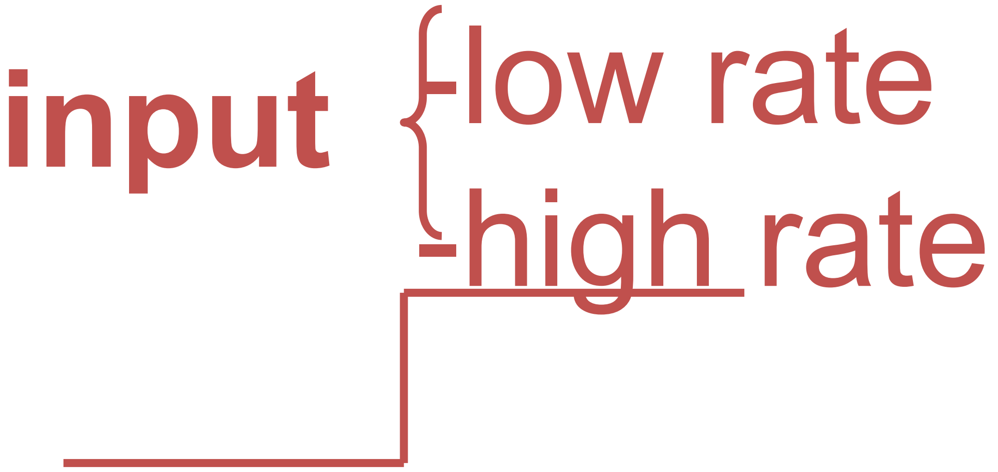
Brunel, J. Comput. Neurosc. 2000
Mayor and Gerstner, Phys. Rev E. 200
Vogels et al., 2005

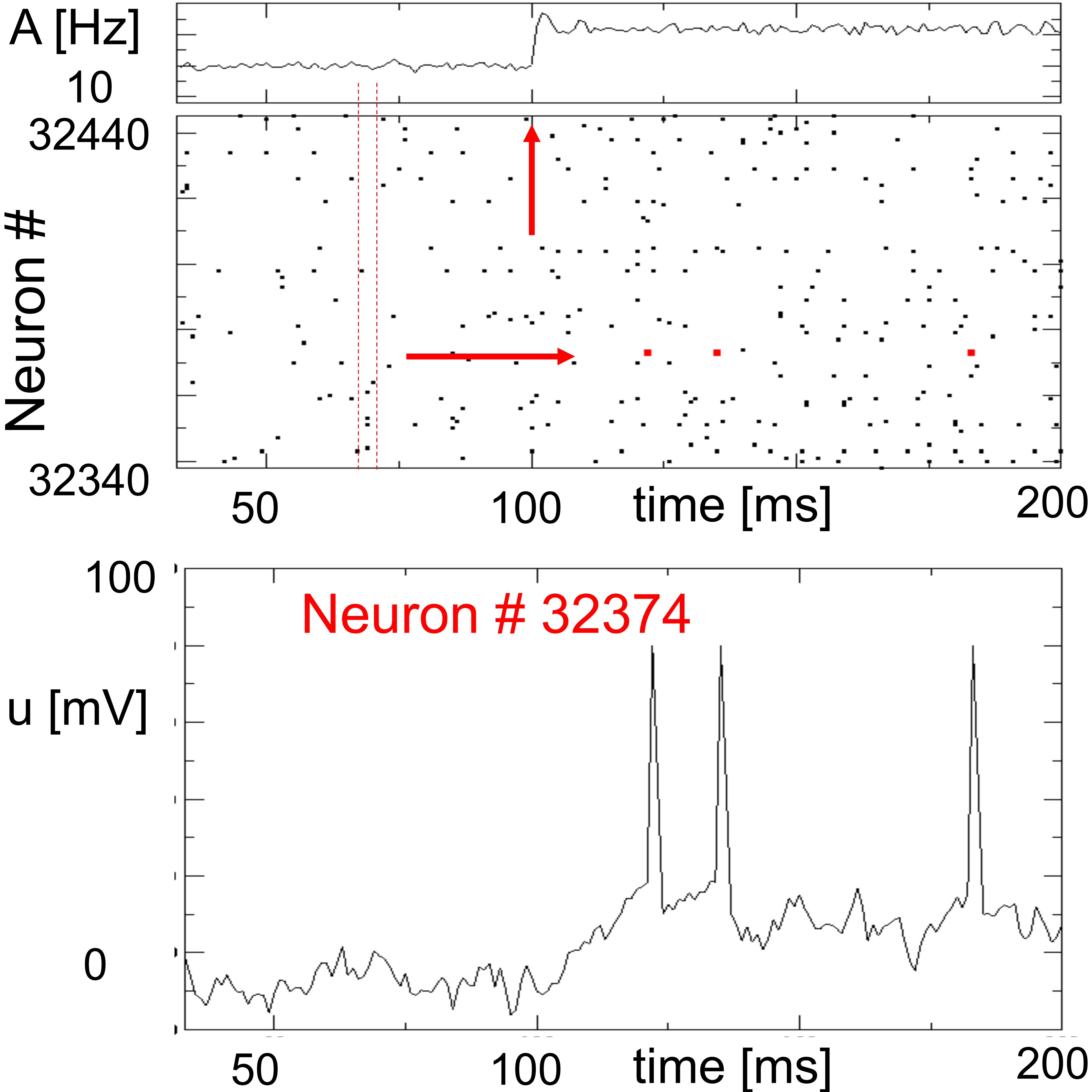
Network of **deterministic** leaky integrate-and-fire: 'fluctuations'

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

10.2 Random firing in a population of LIF neurons





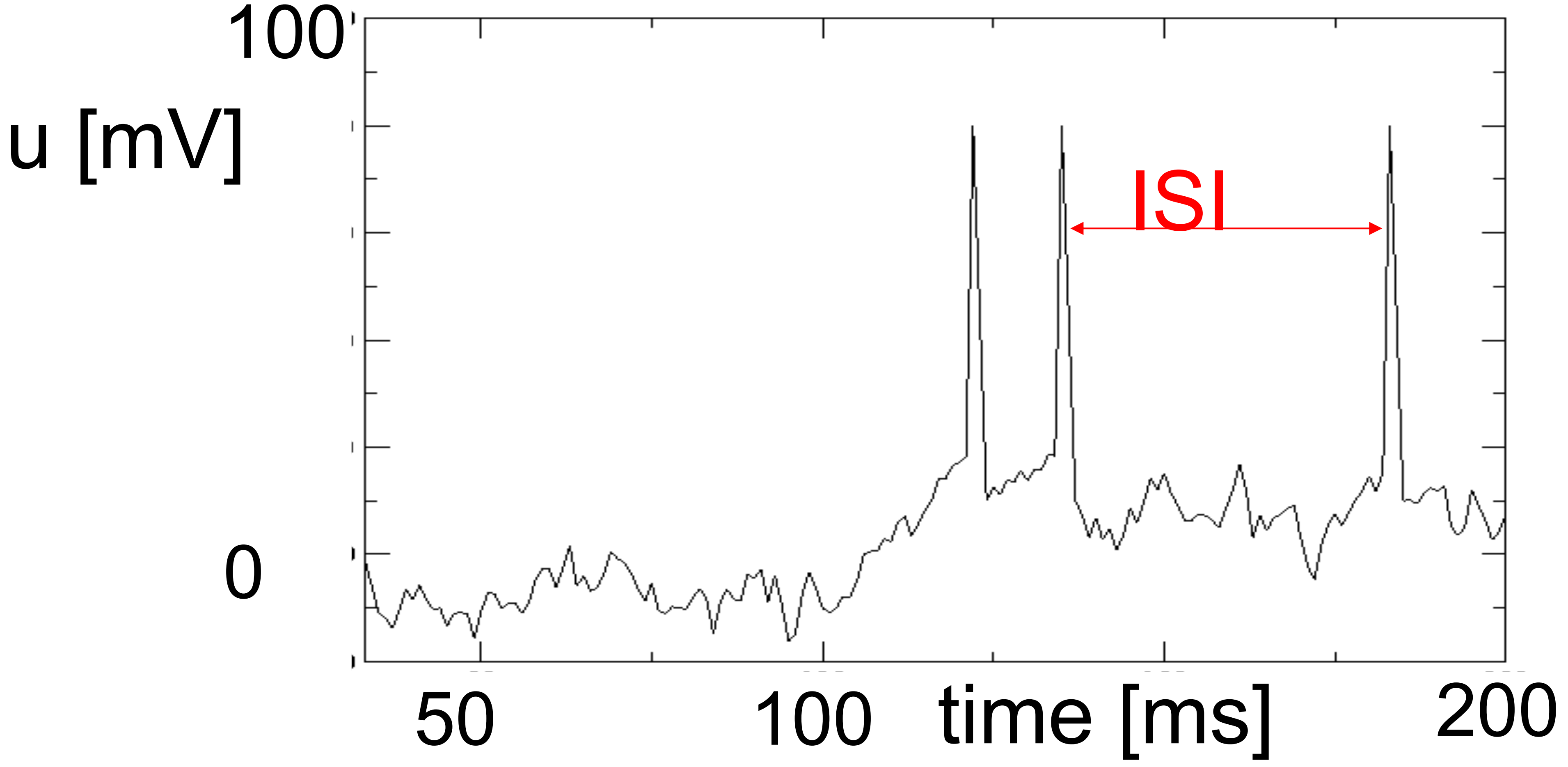


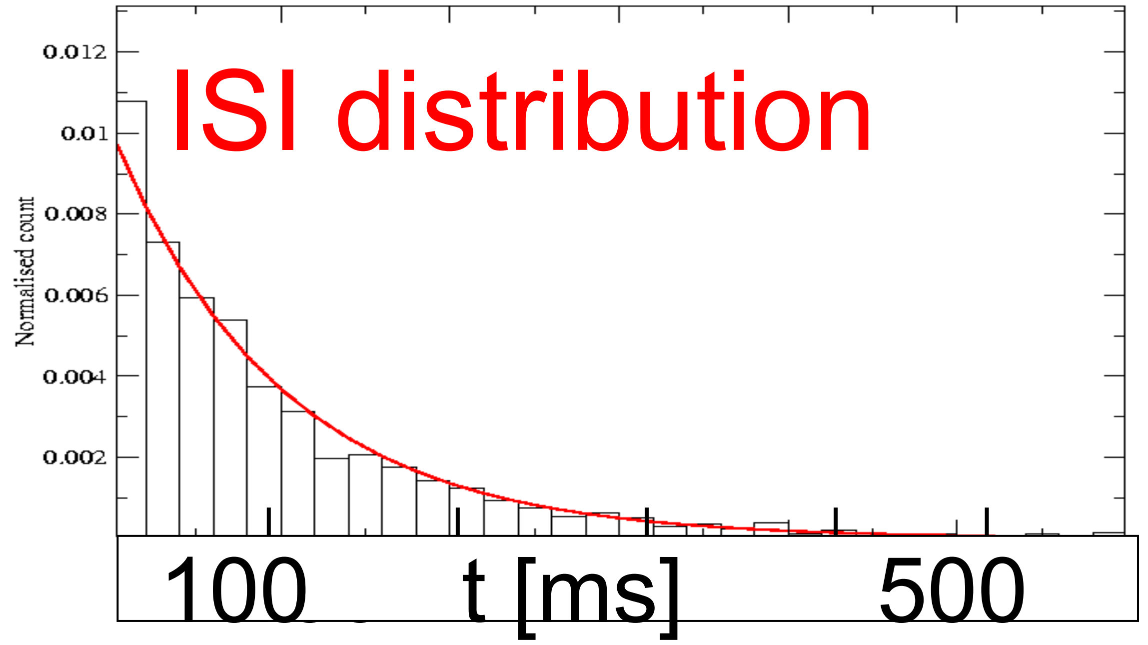
Population
- 50 000 neurons
- 20 percent inhibitory
- **randomly connected**

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

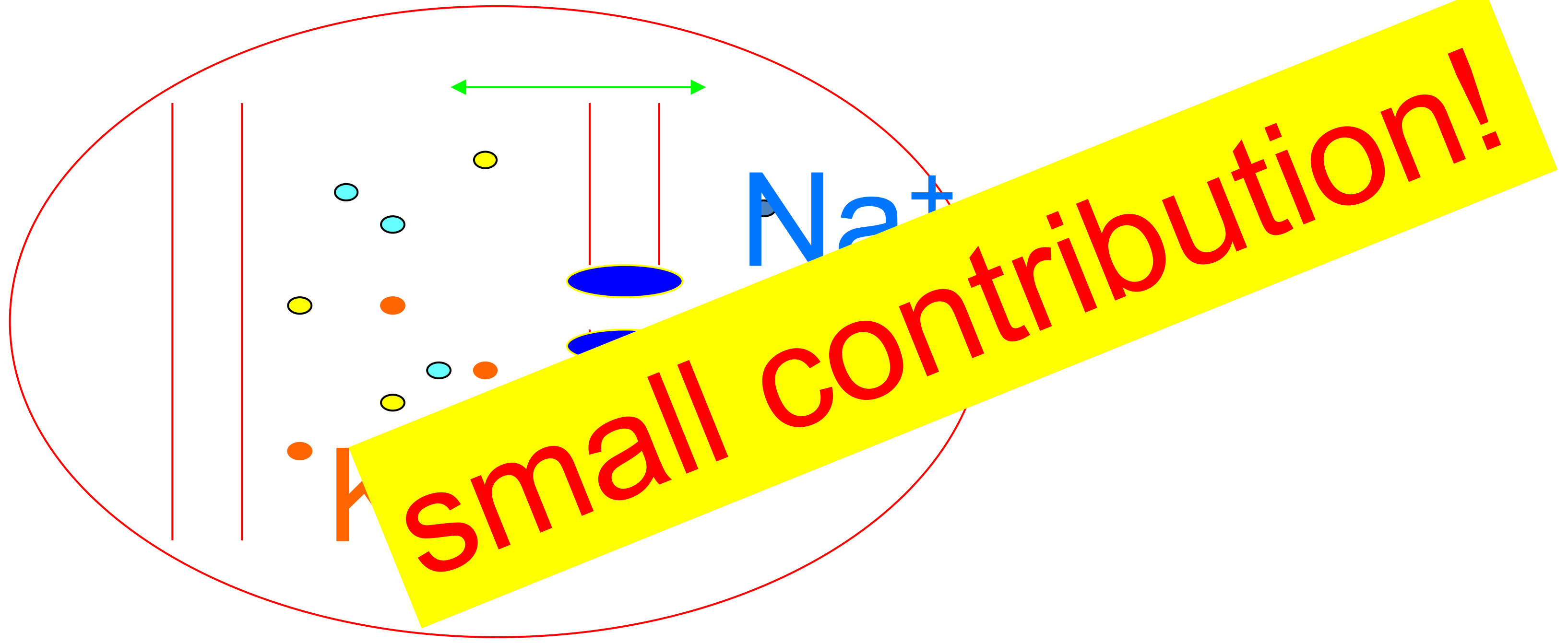
→ looks 'noisy'

In vitro data

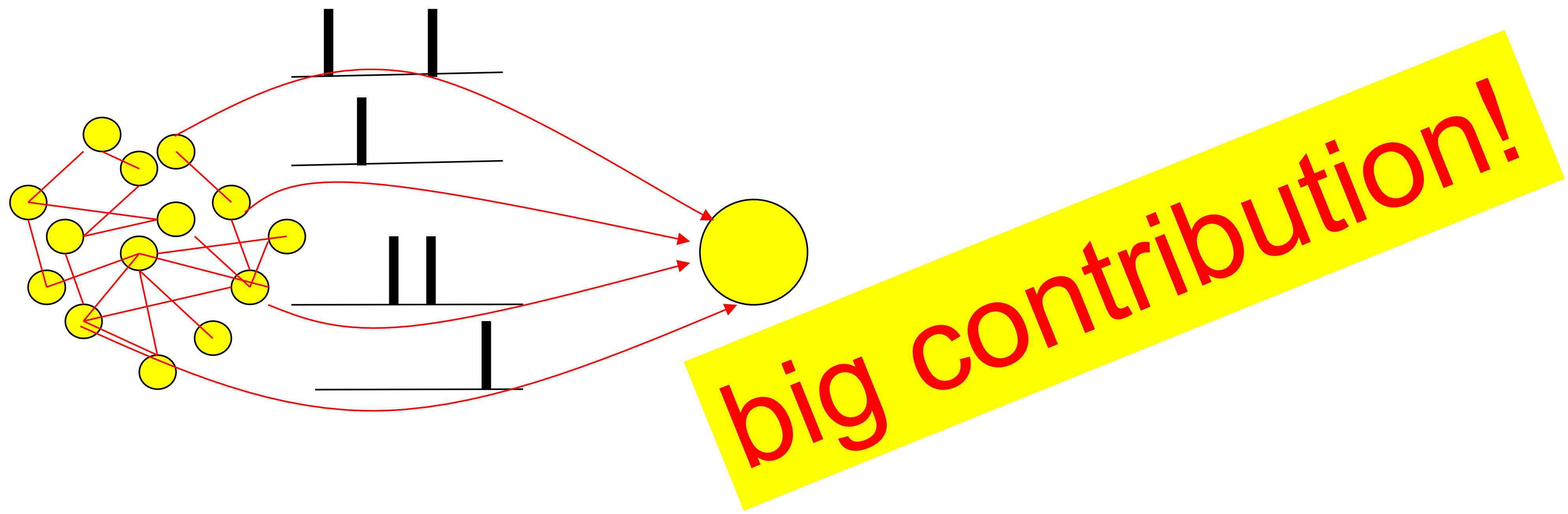
→small fluctuations

→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

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- homogeneous/inhomogeneous

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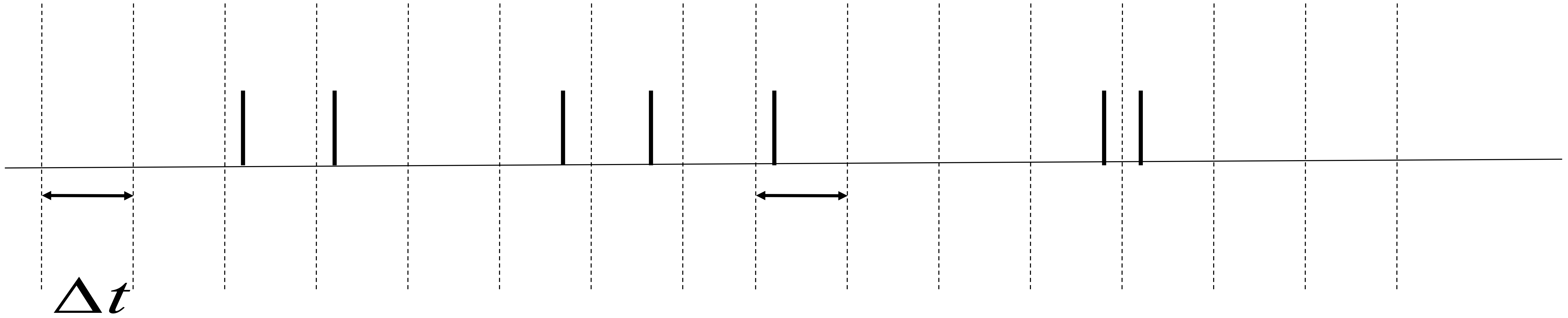
10.3 Poisson Model

Homogeneous Poisson model: constant rate

Blackboard: Poisson model



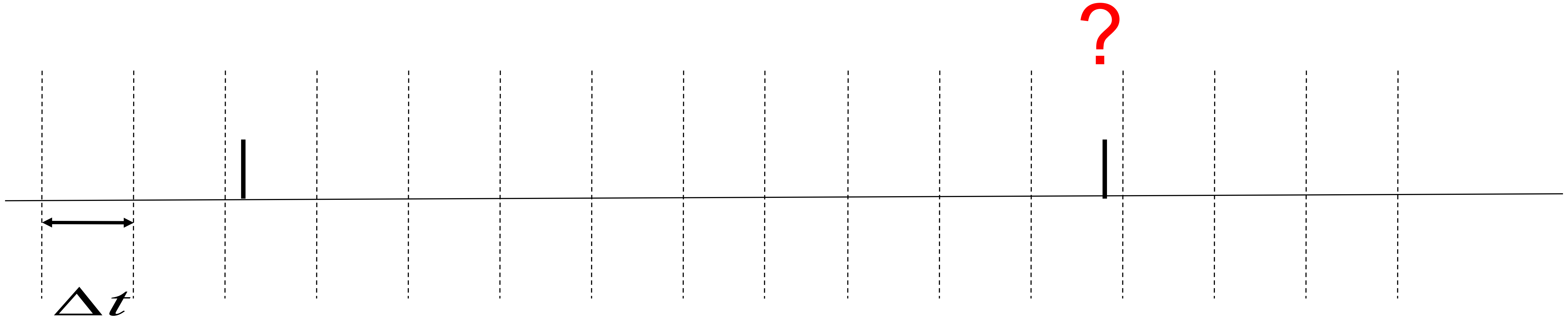
Probability of finding a spike $P_F = \rho_0 \Delta t$

stochastic spiking → Poisson model

10.3 Interval distribution of Poisson Process

Probability of firing:

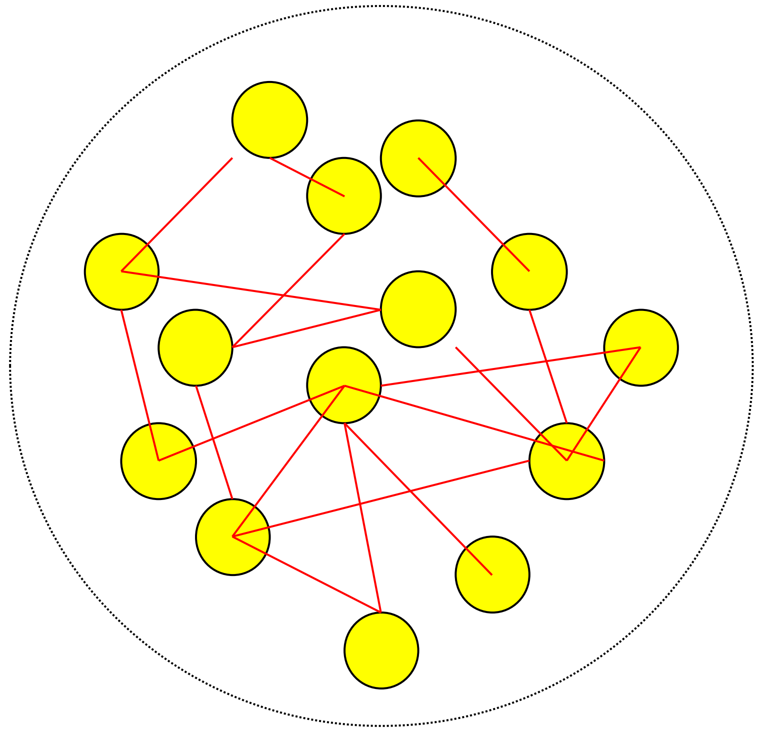
$$P_F = \rho_0 \, \Delta t$$



(i) Continuous time

prob to 'survive'

$$\Delta t \to 0$$



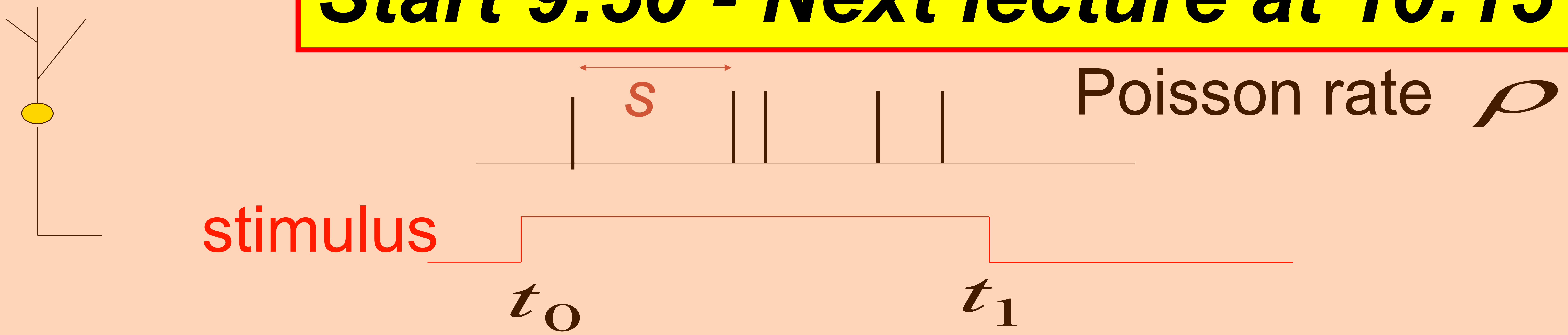
(ii) Discrete time steps

Blackboard: Poisson model

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

Exercise 1.1 and 1.2: Poisson neuron

Start 9:50 - Next lecture at 10:15



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

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

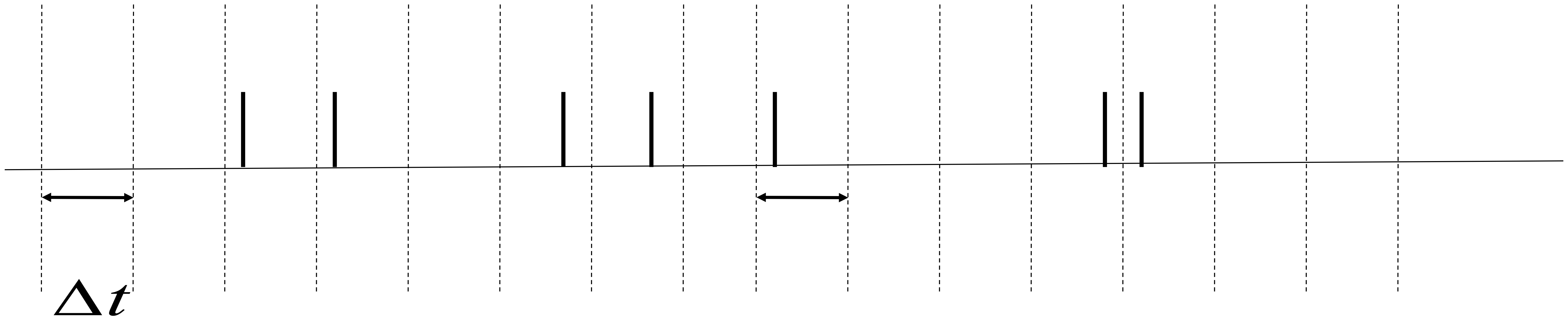
What is

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

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

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). 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.

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- homogeneous/inhomogeneous

$\boxed{\text{10.4 Three definitions of Rate Code}}$

10.5 Stochastic spike arrival
- Membrane potential fluctuations

10.4. Three definitions of Rate Codes

3 definitions

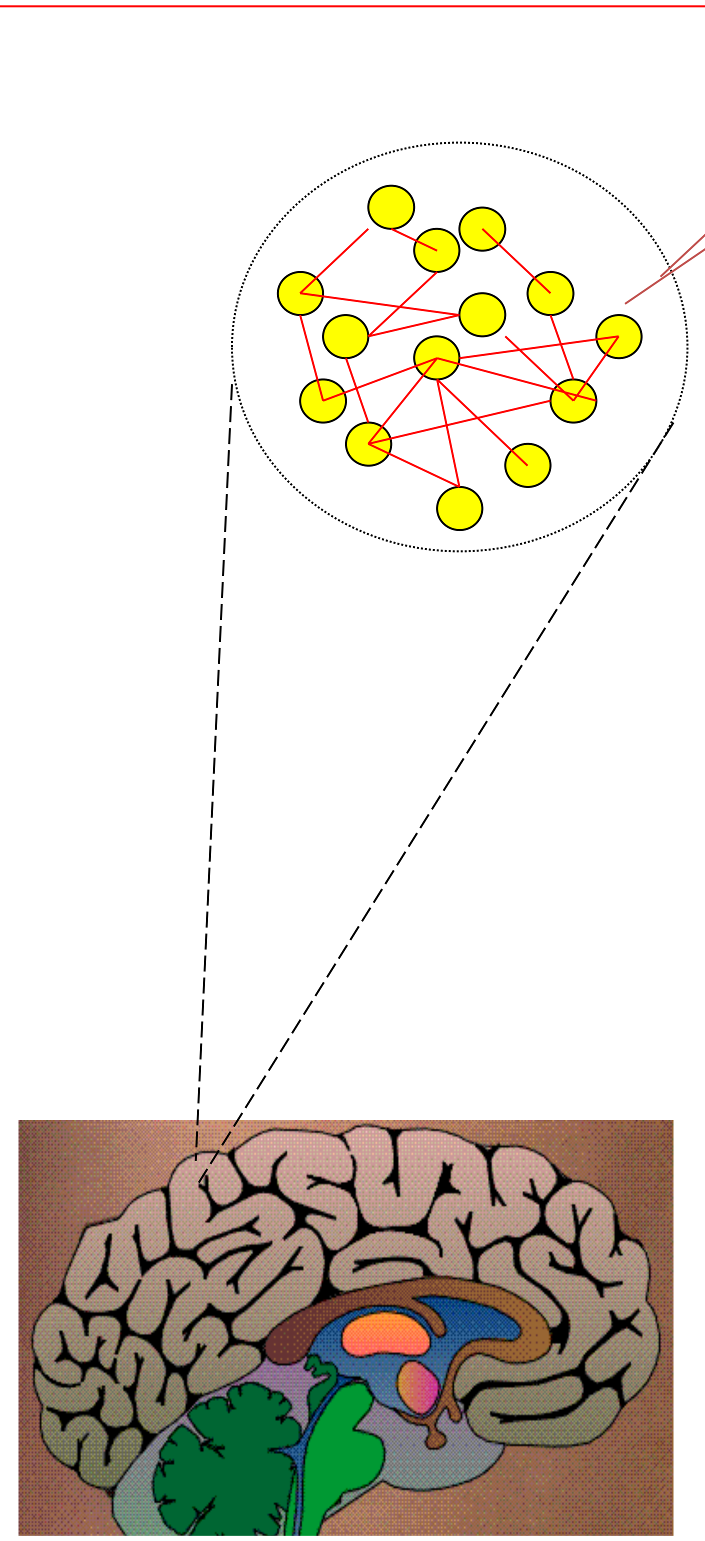
-Temporal averaging

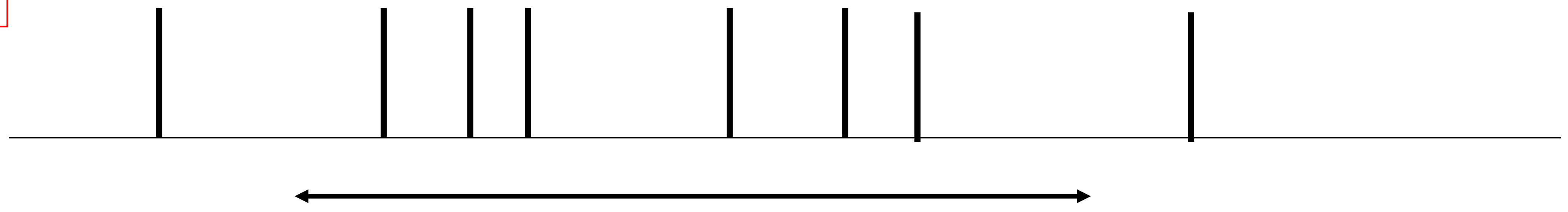
- Averaging across repetitions

- Population averaging (‘spatial’ averaging)

10.4. Rate codes: spike count

Variability of spike timing





trial 1

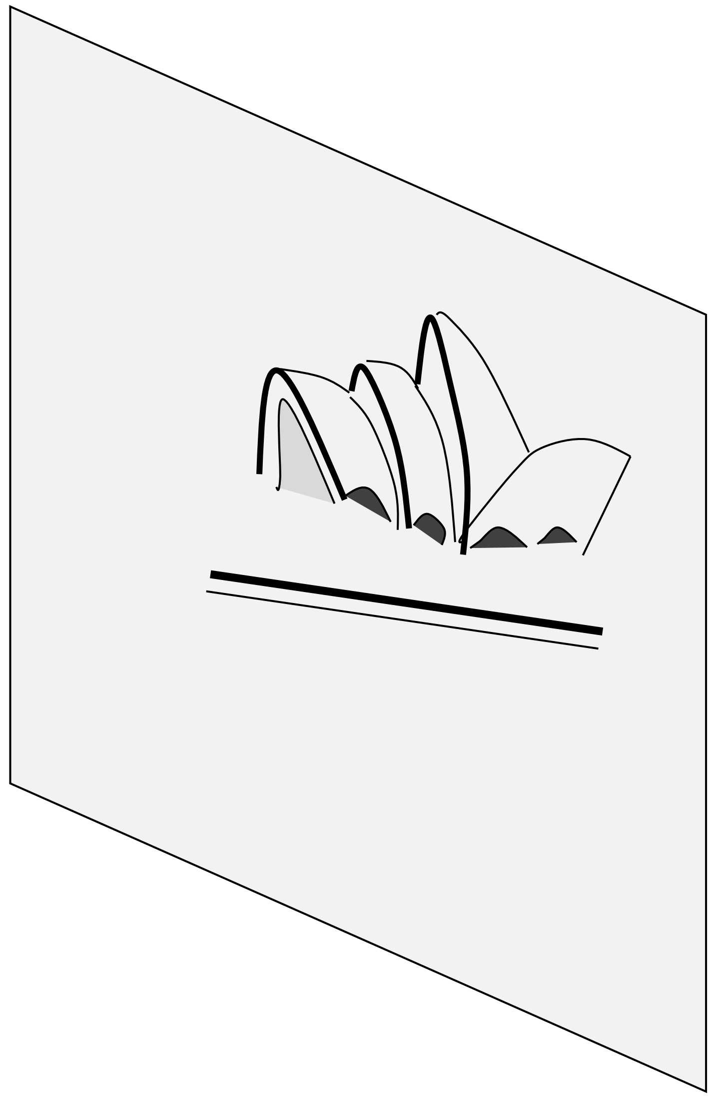
rate as a (normalized) spike count:

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

single neuron/single trial:
temporal average

T=1s

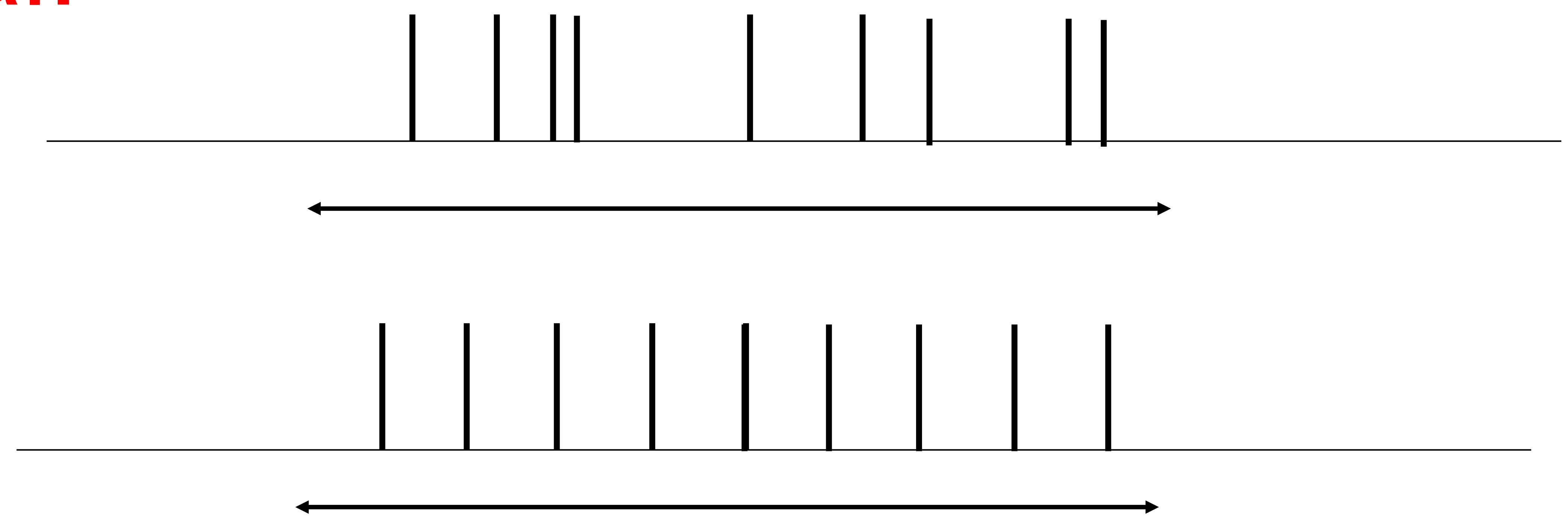
Brain



stim

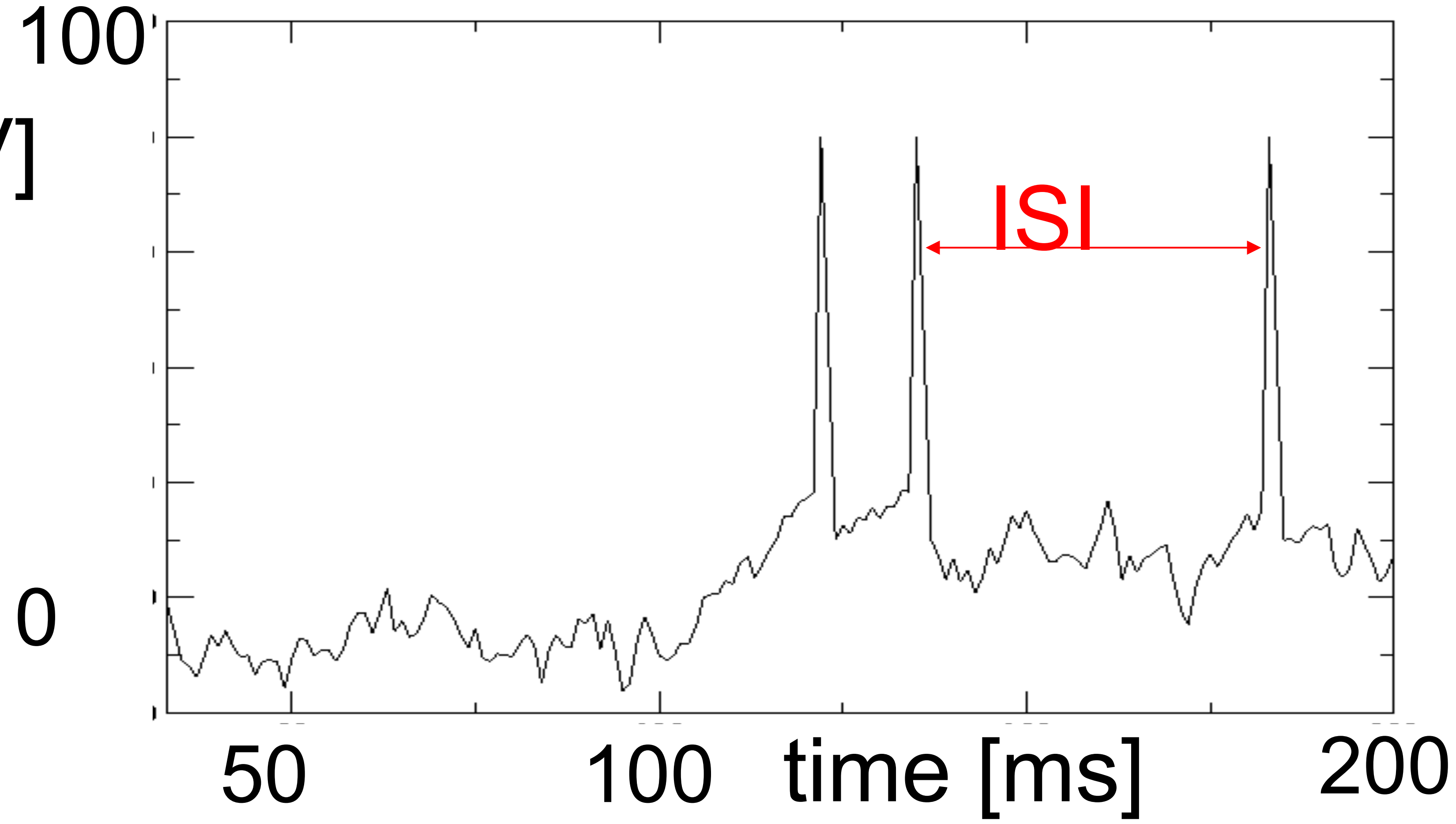
10.4. Rate codes: spike count

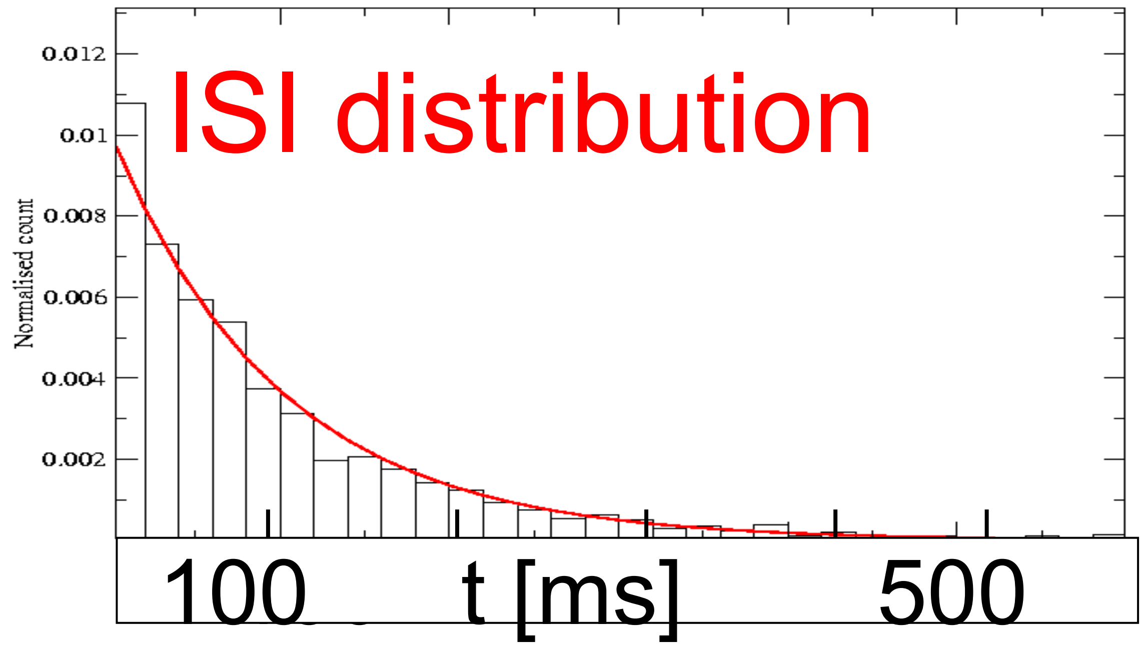
single neuron/single trial:
temporal average



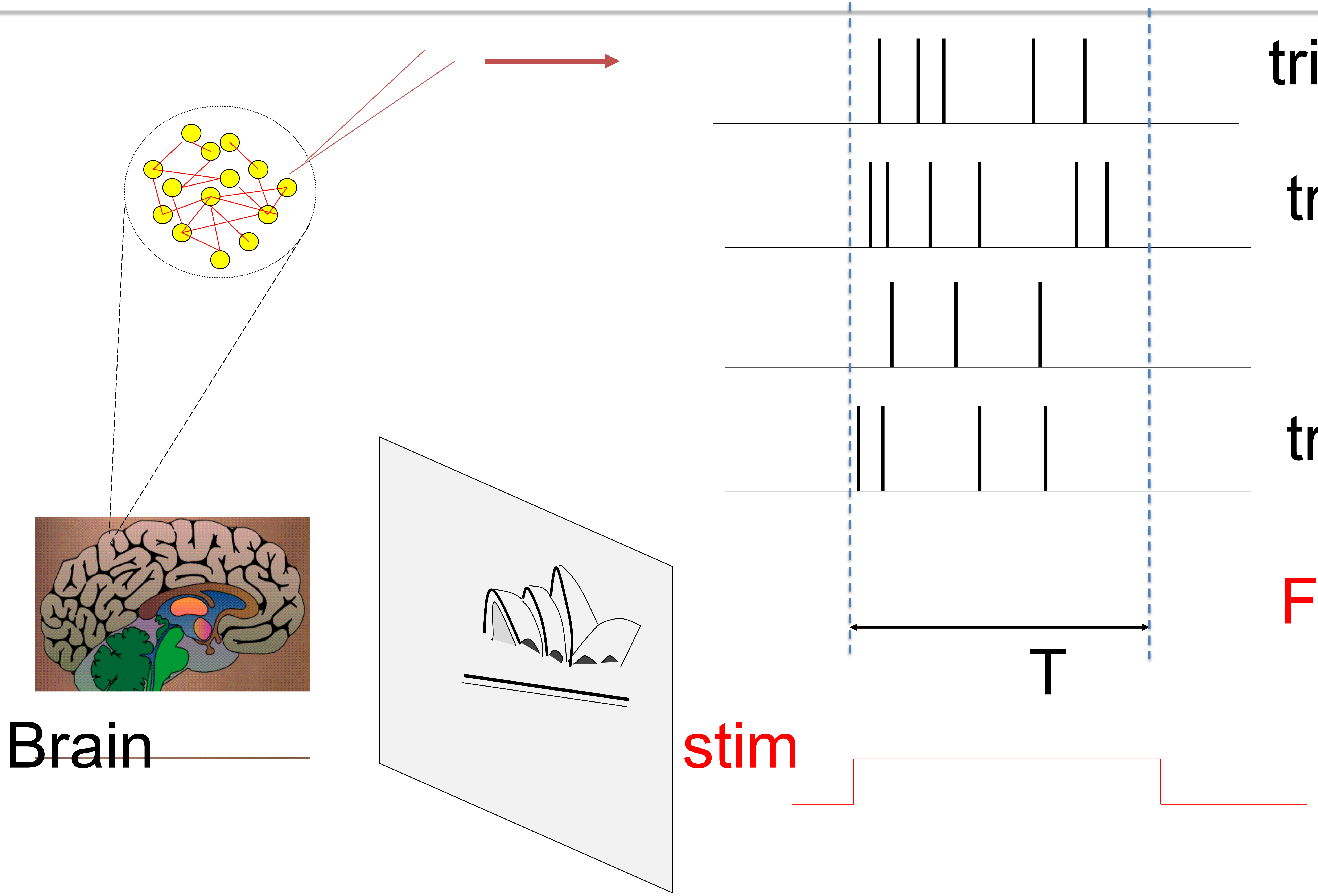
$$\nu(t) = \frac{n^{sp}}{T}$$

Variability of interspike intervals (ISI) measure regularity





10.4. Spike count: FANO factor



trial 1 $n_1^{sp} = 5$

trial 2 $n_2^{sp} = 6$

trial K $n_K^{sp} = 4$

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)

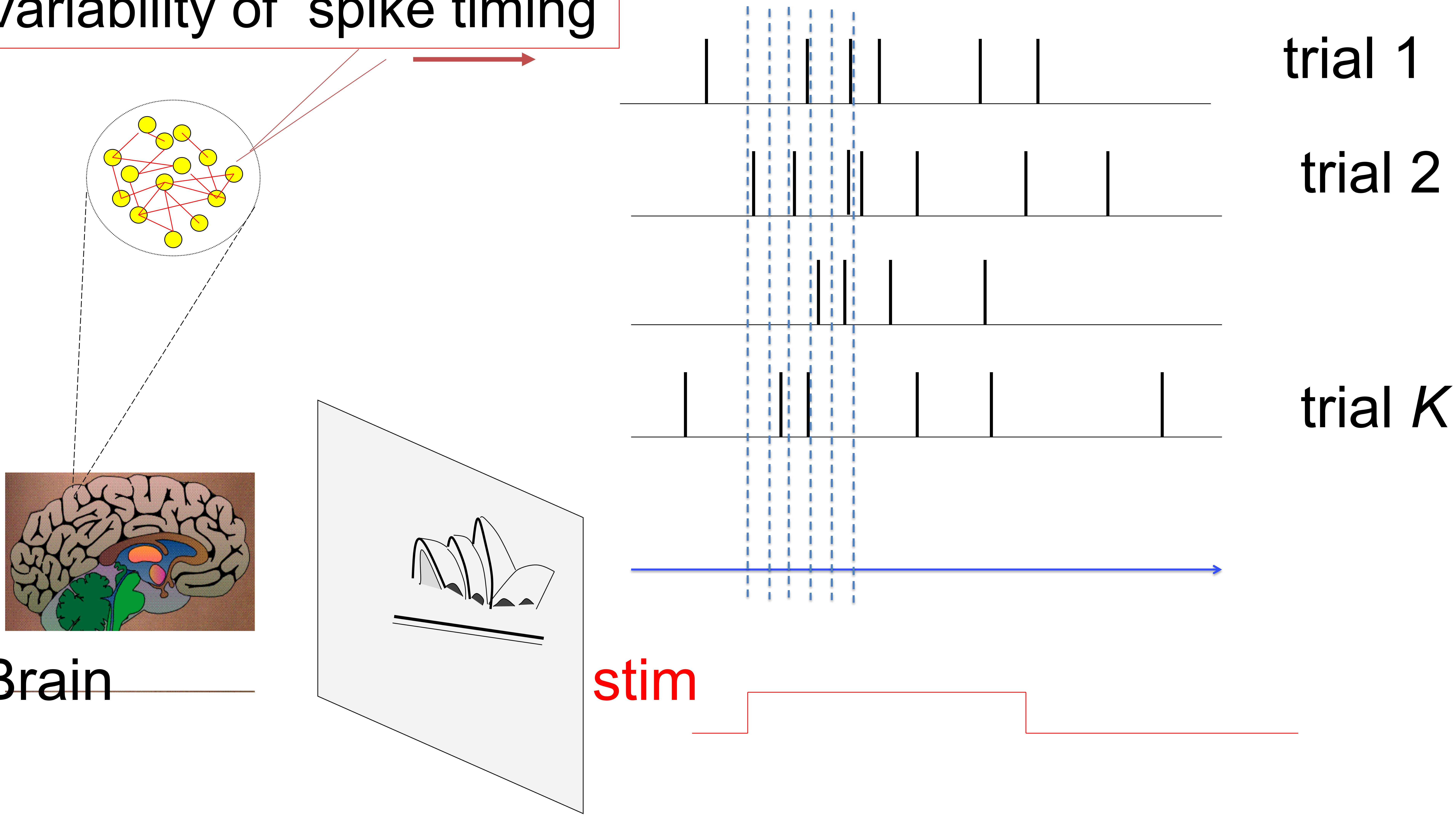
Fano factor (repeatability across repetitions)

- Averaging across repetitions

- Population averaging ('spatial' averaging)

10.4. Rate codes: PSTH

Variability of spike timing

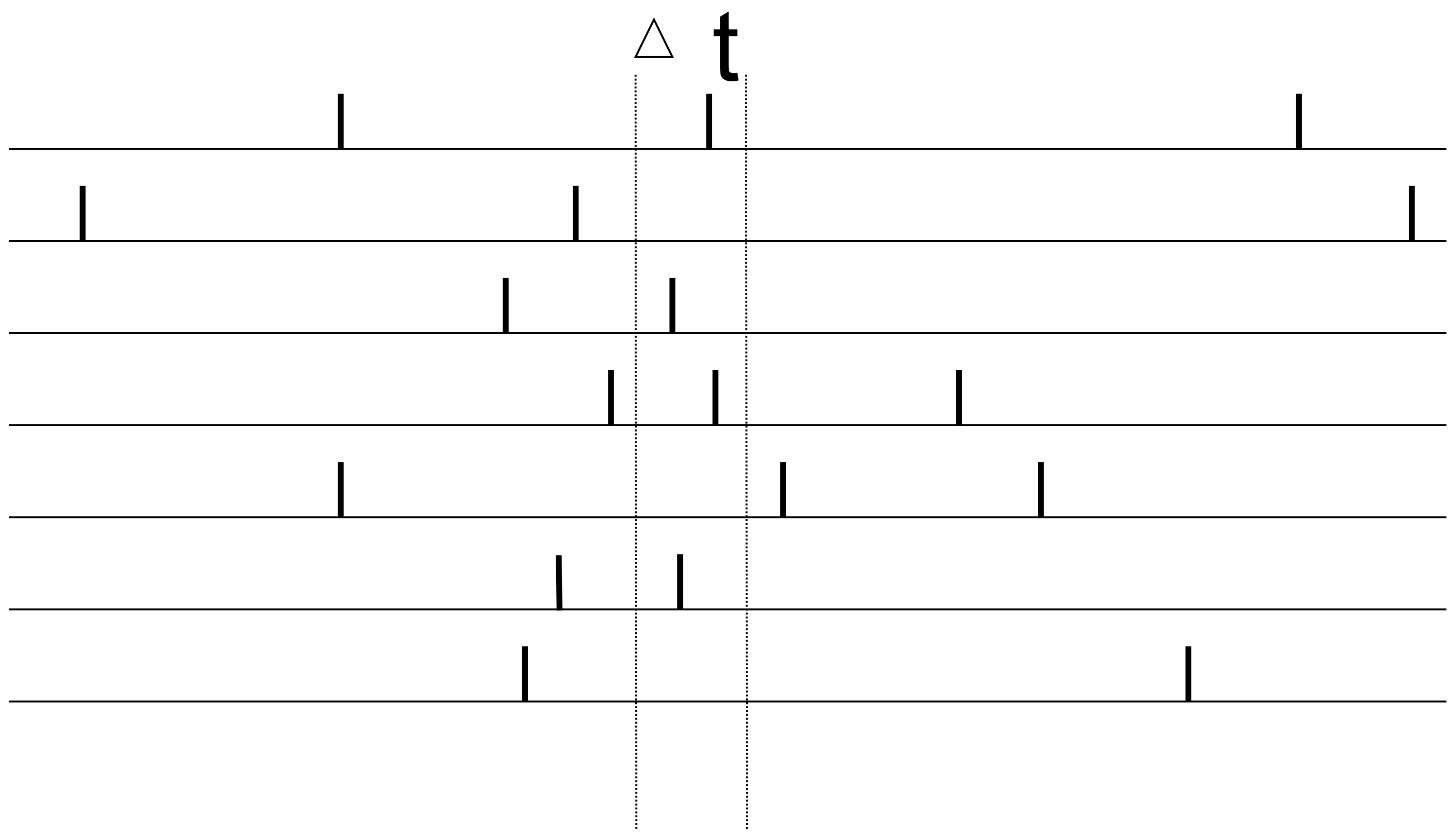


10.4. Rate codes: PSTH

Averaging across repetitions

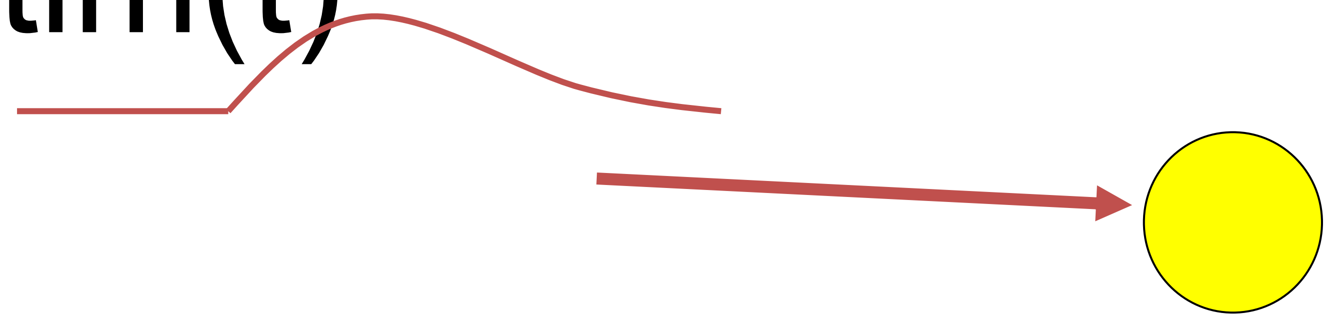
single neuron/many trials:
average across trials

K repetitions



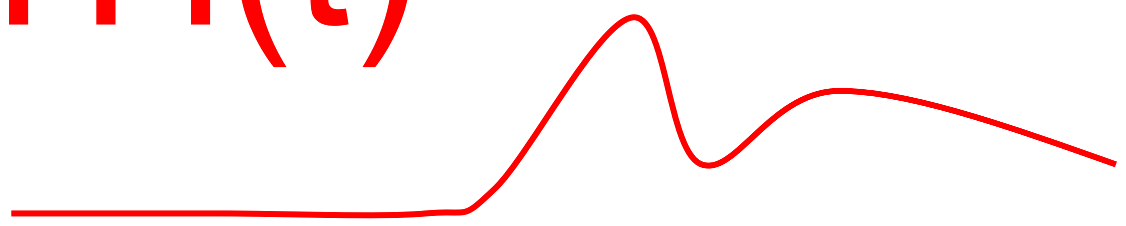
$$PSTH(t) = \frac{n(t;t+\Delta t)}{K\,\Delta t}$$

Stim(t)



K=50 trials

PSTH(t)



10.4. Three definitions of Rate Codes

3 definitions

√ -Temporal averaging

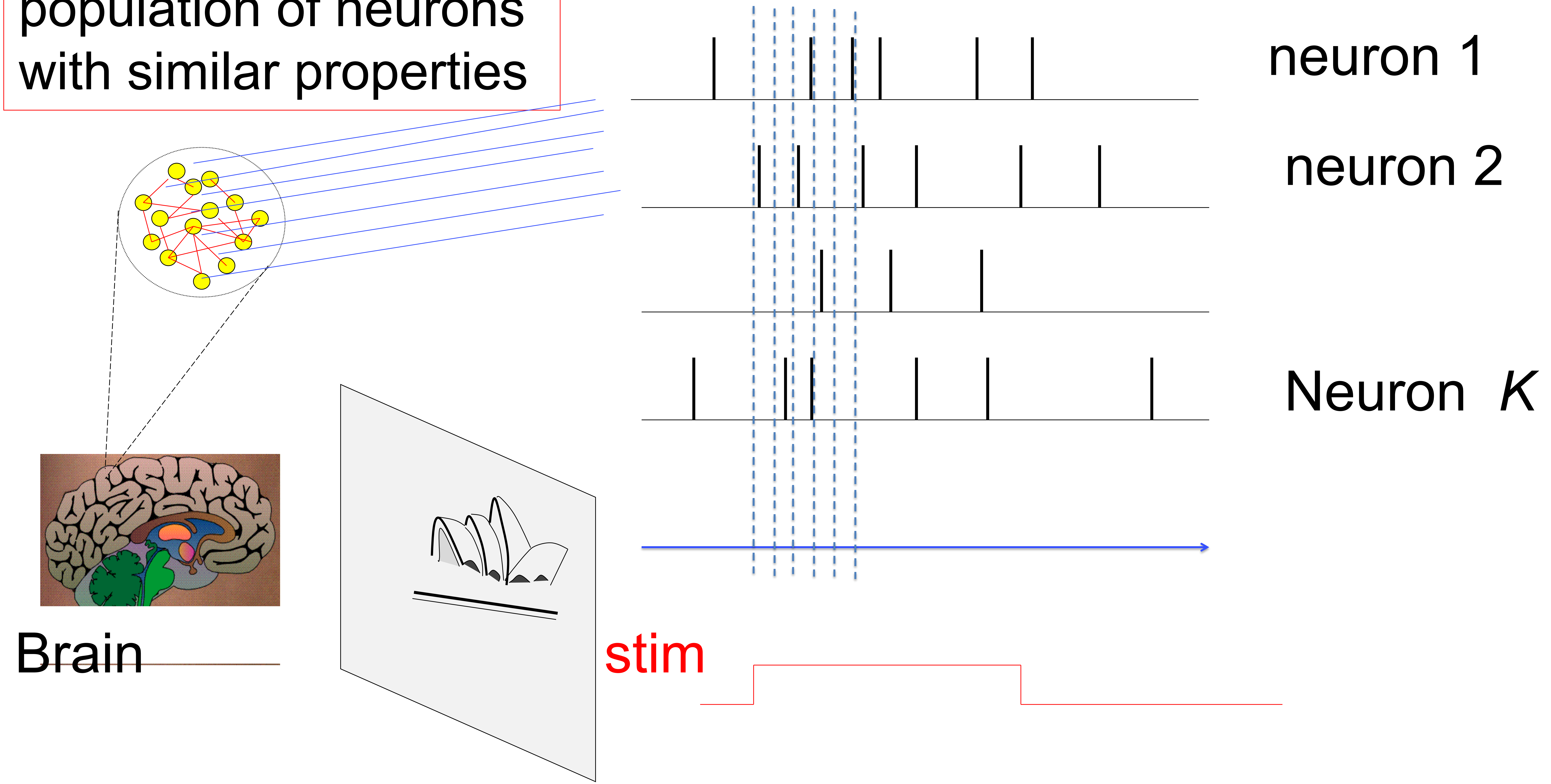
√ - Averaging across repetitions

Problem: not useful for animal!!!

- Population averaging

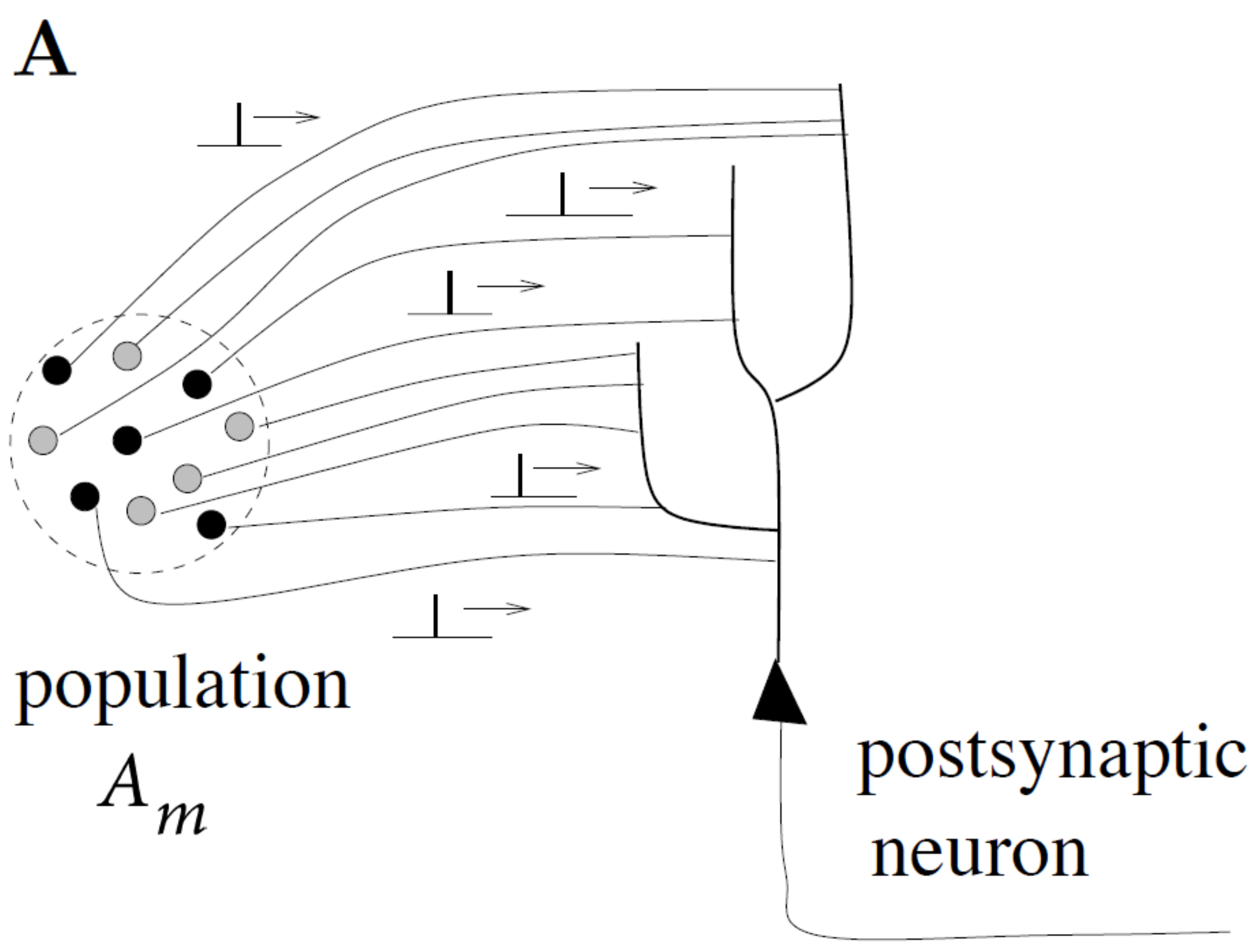
10.4. Rate codes: population activity

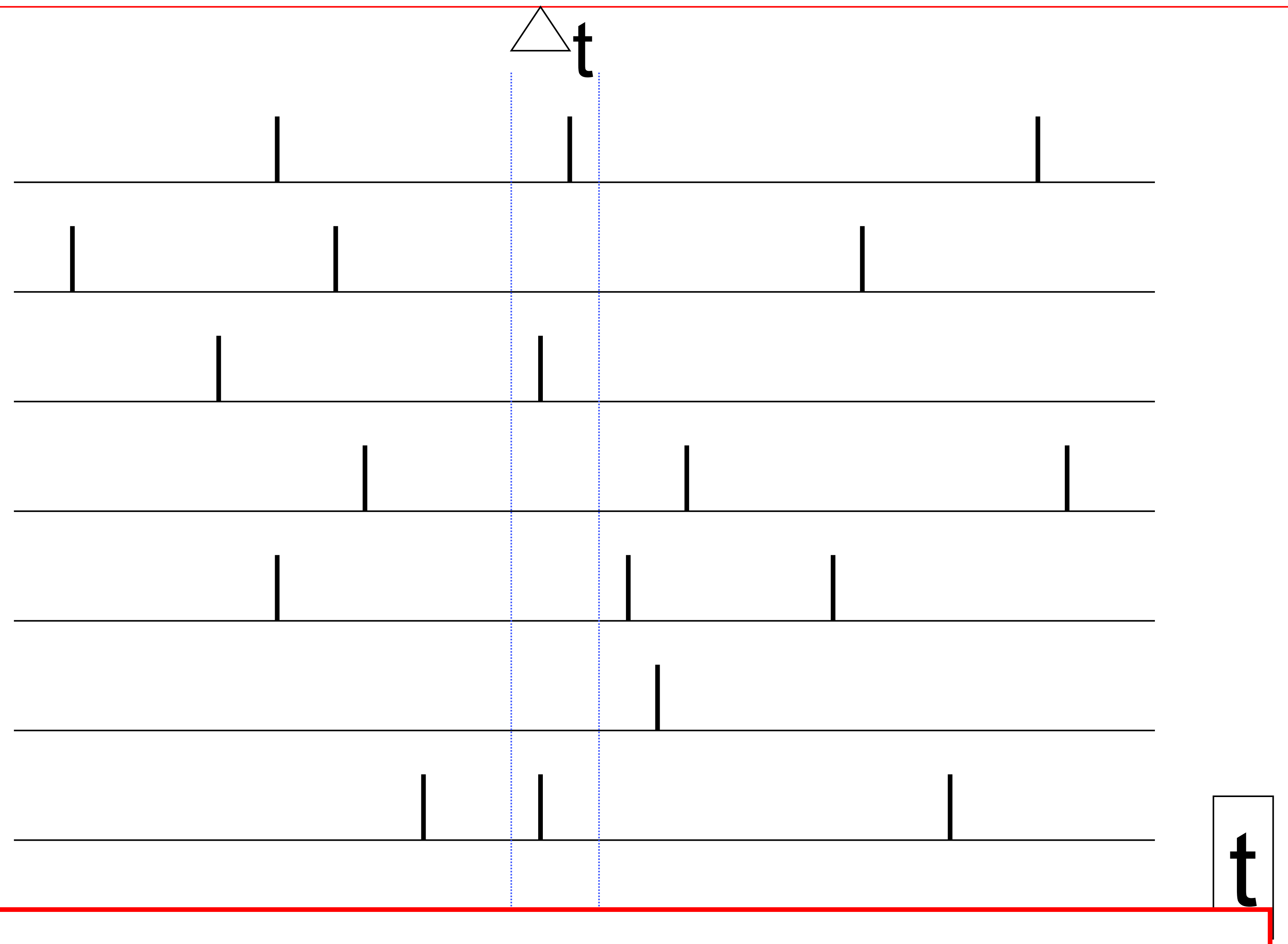
population of neurons
with similar properties



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

population activity - rate defined by population average





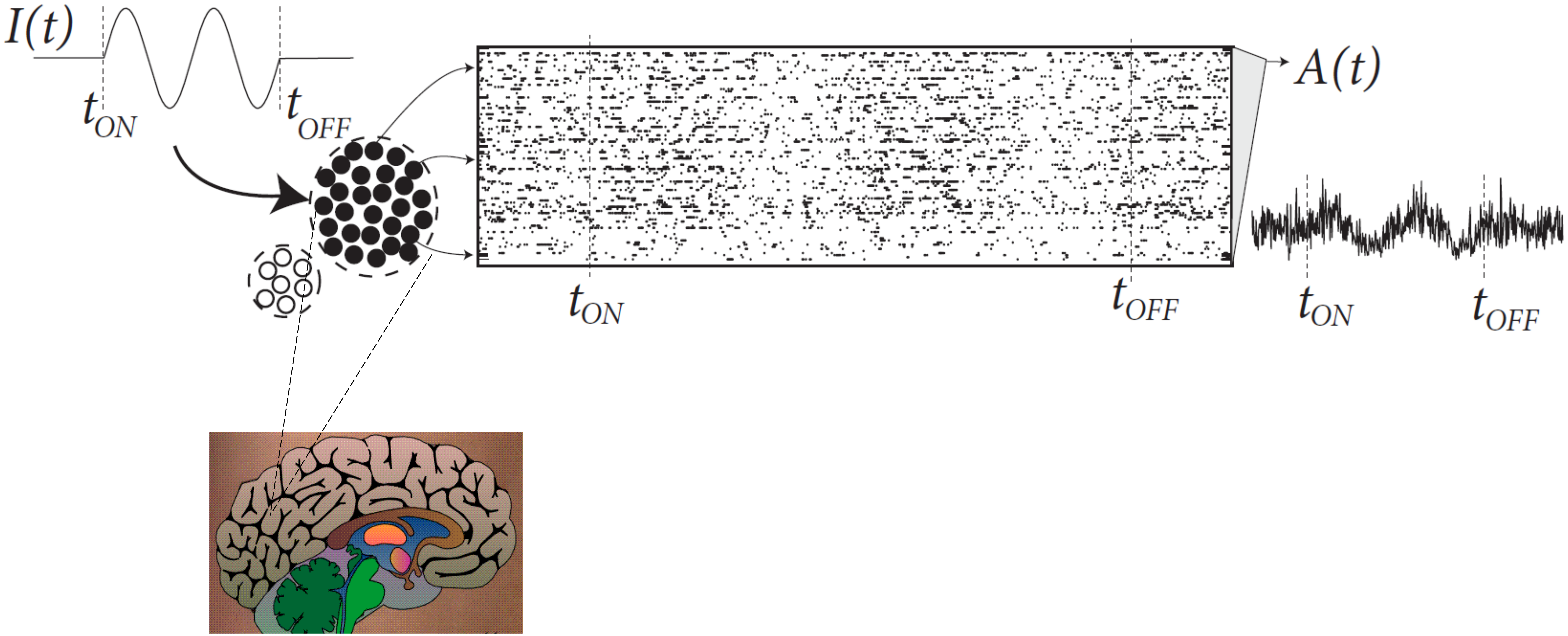
'natural readout'

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

single neuron

-over time

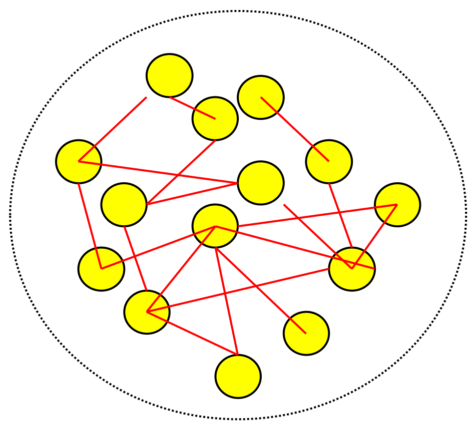
Too slow
for animal!!!

single neuron

- over repetitions

Not possible
for animal!!!

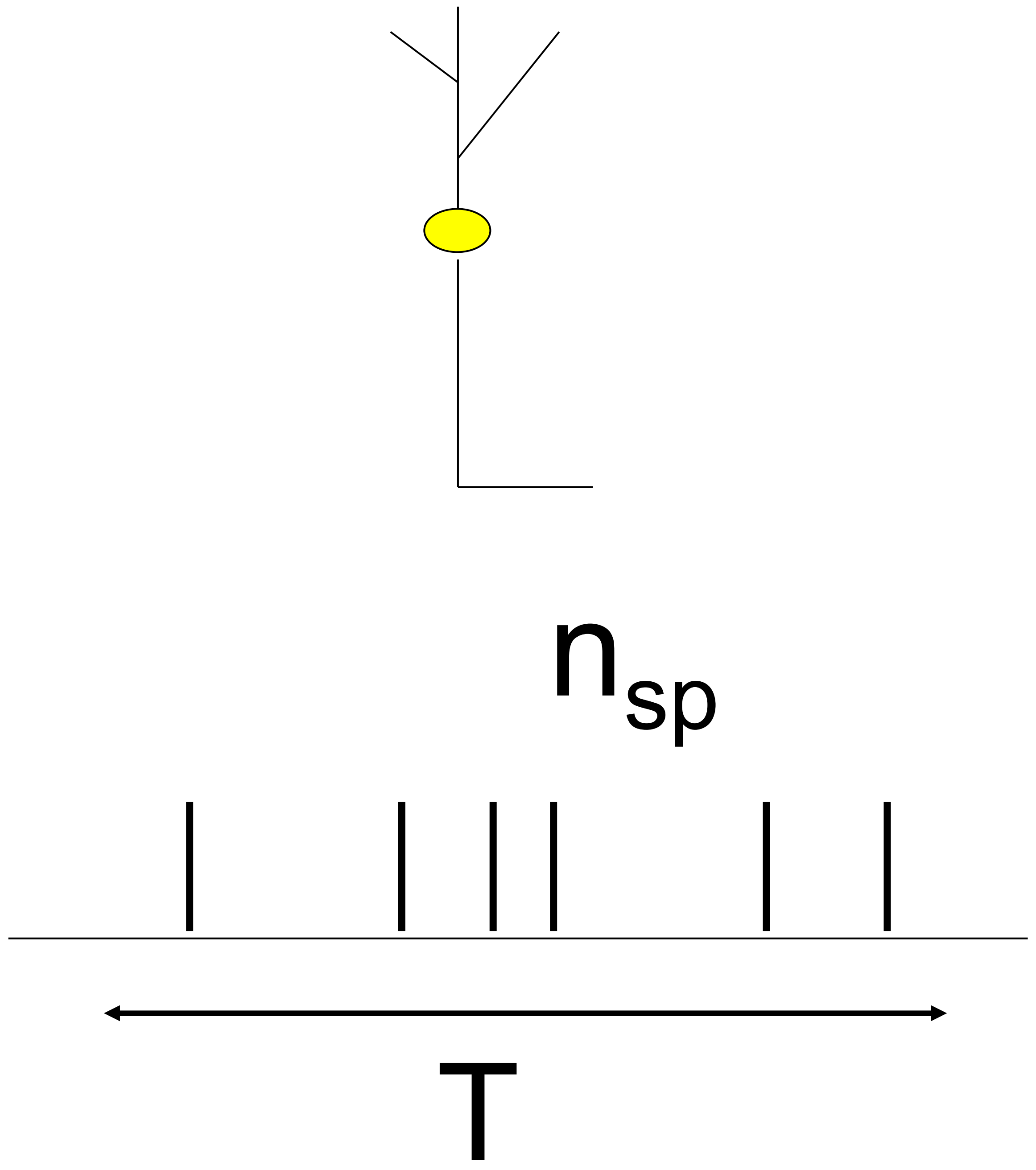
many neurons

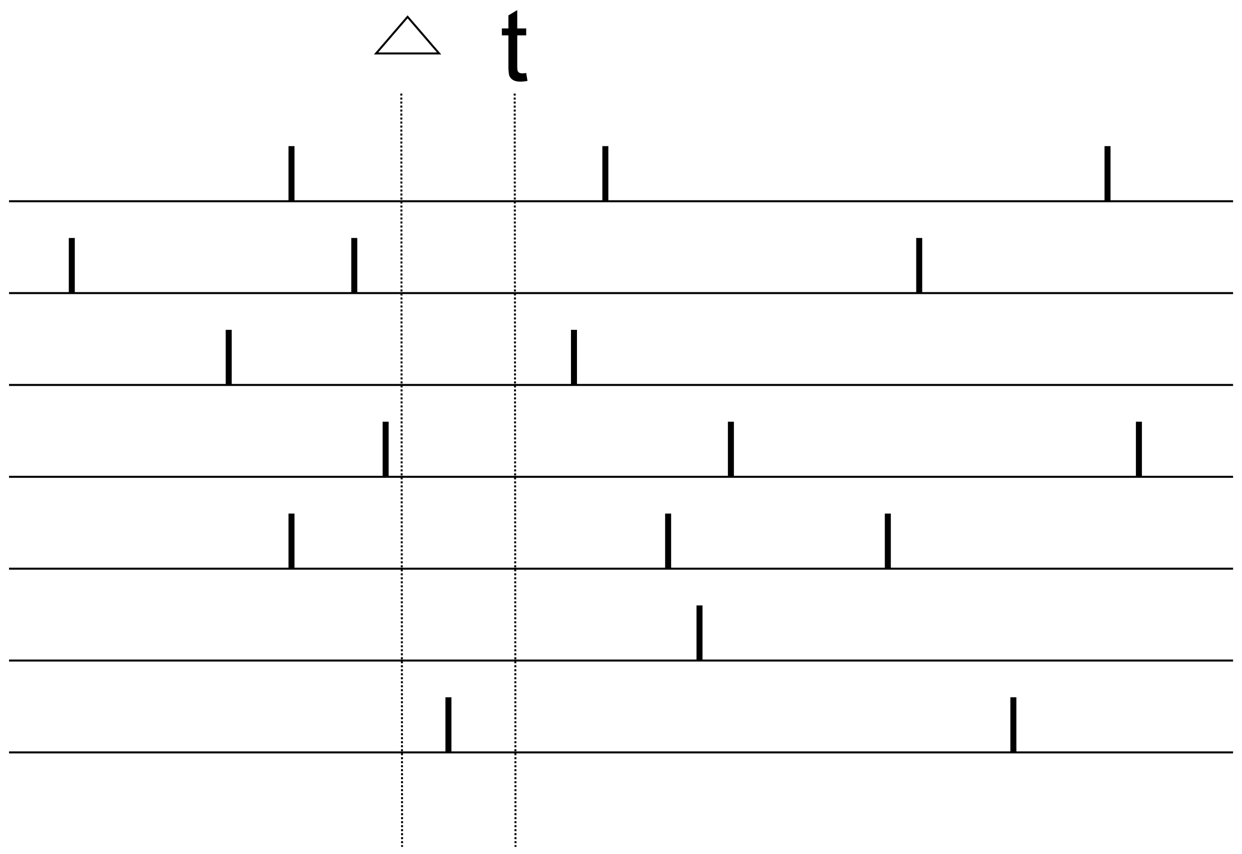


- over population (space)

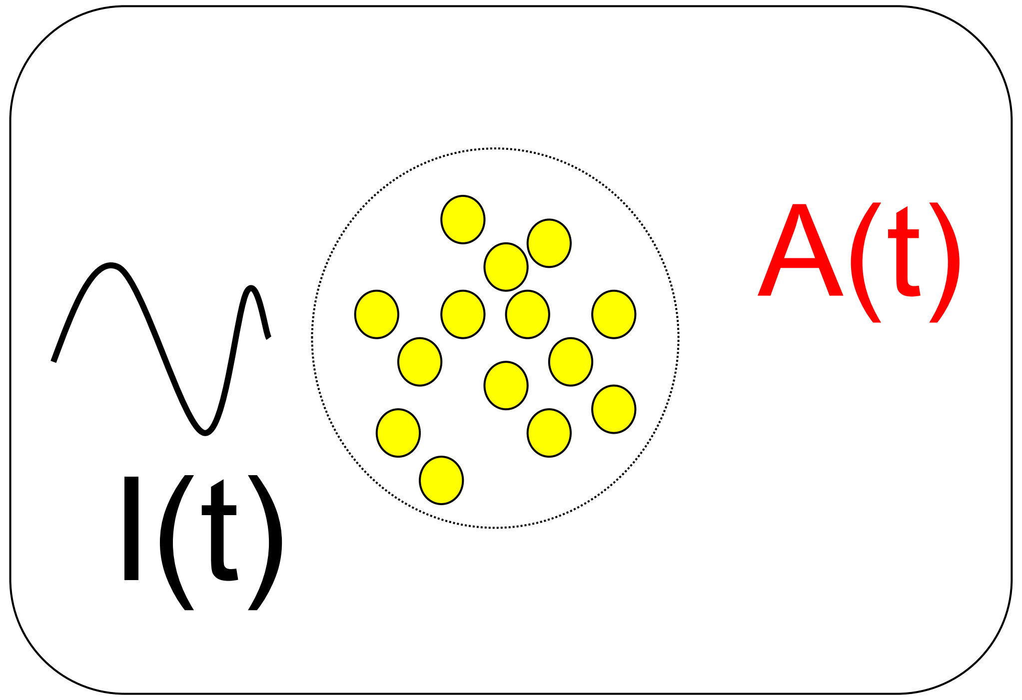
'natural'

10.4 Inhomogeneous Poisson Process





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



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

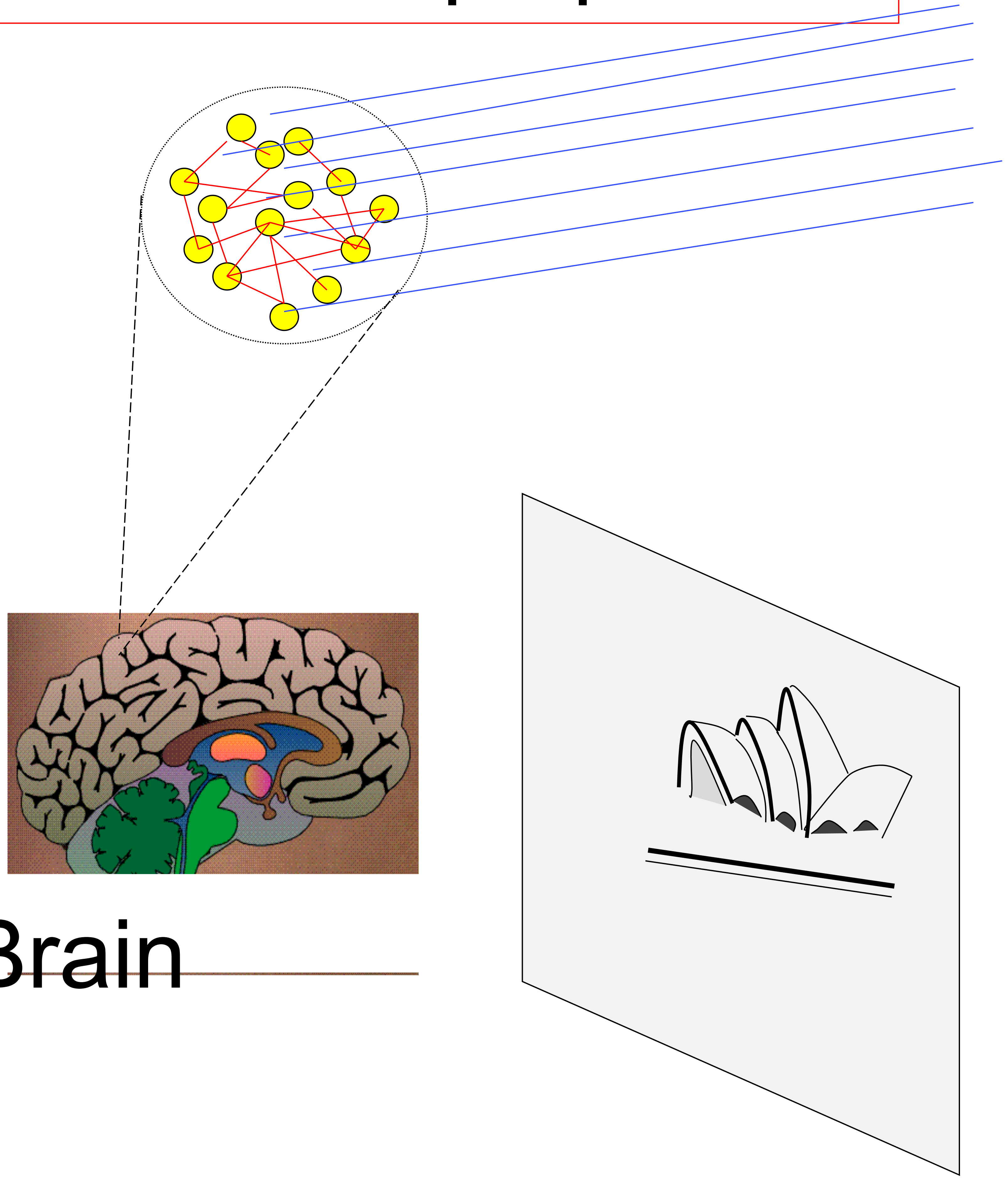
population activity

inhomogeneous Poisson model consistent with rate coding

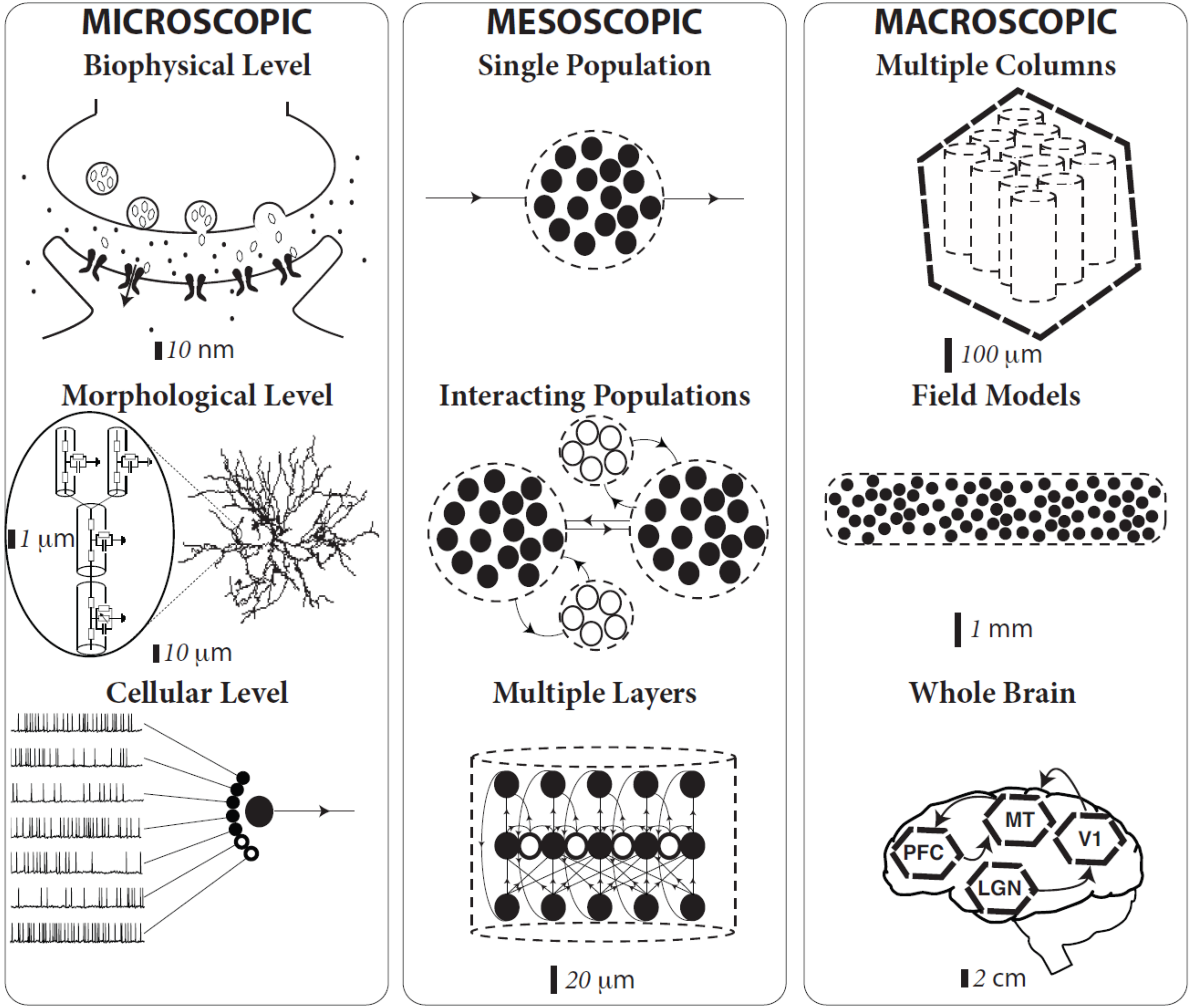
10.4: Scales of neuronal processes

Image: Gerstner et al. Neuronal Dynamics (2014)

population of neurons
with similar properties

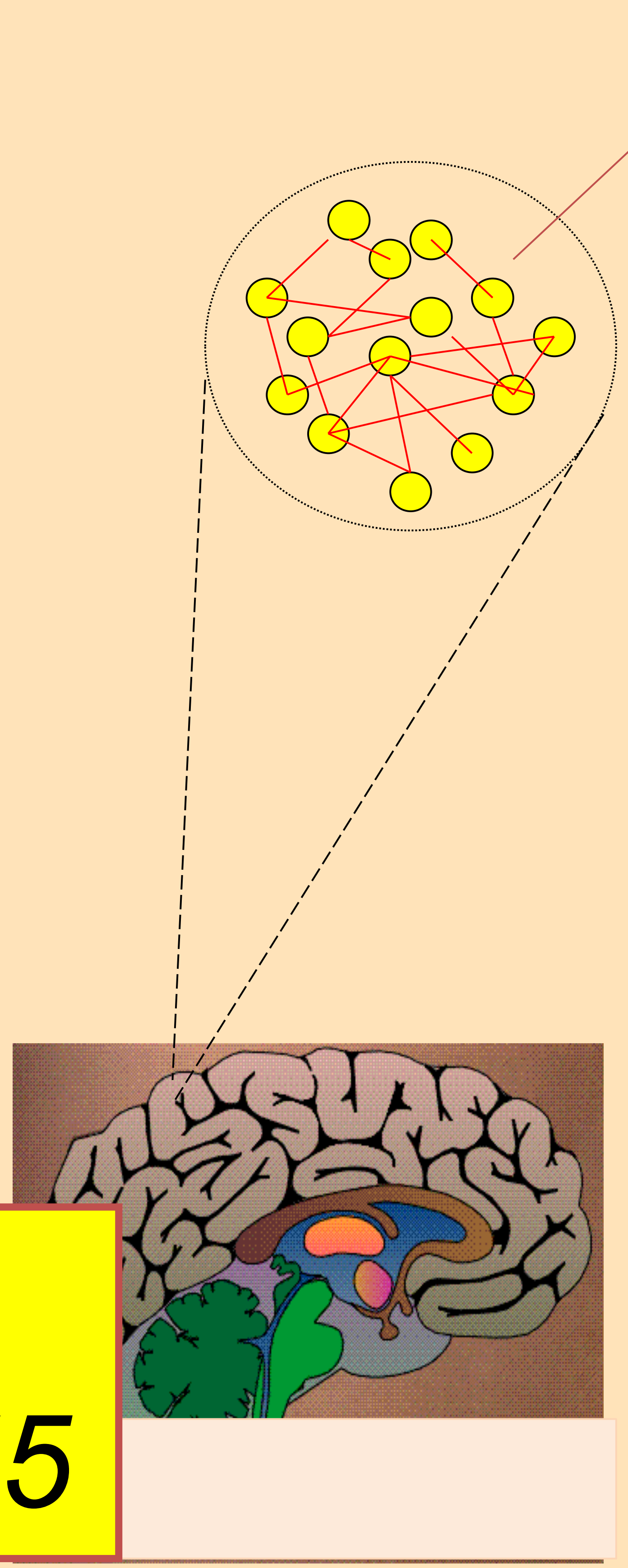


Brain



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 50
day he **picks a random neuron** (amongst the 500 neurons)

Start at 10:50,
Discussion at 10:55

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 different.

[ ] B and C are expected to find the same result, but that of A is expected to be different.

[ ] None of the above three options is correct.

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

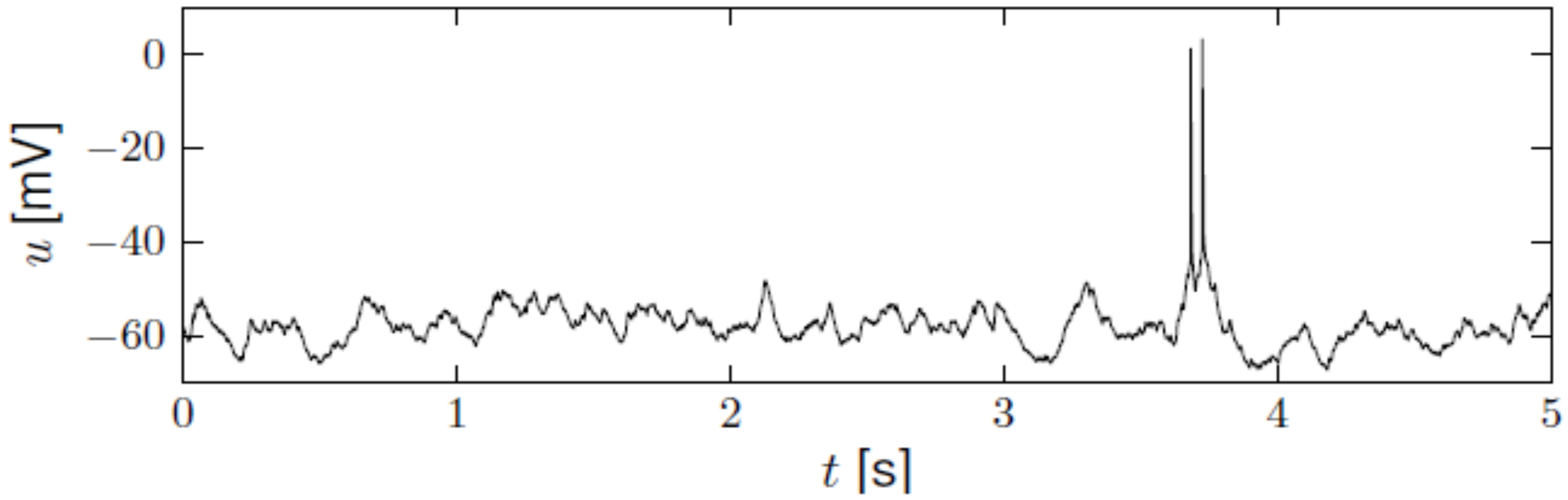
10.5 Stochastic spike arrival
- Membrane potential fluctuations

10.5 Variability in vivo – review from 10.1

Spontaneous activity *in vivo*

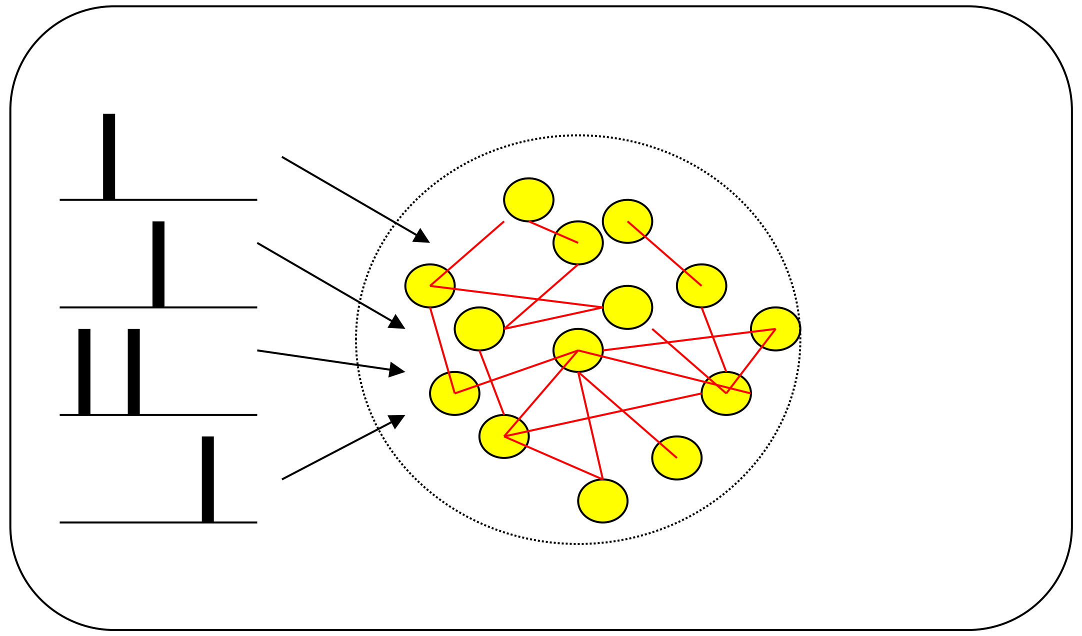
Variability
of membrane potential?

awake mouse, freely whisking,



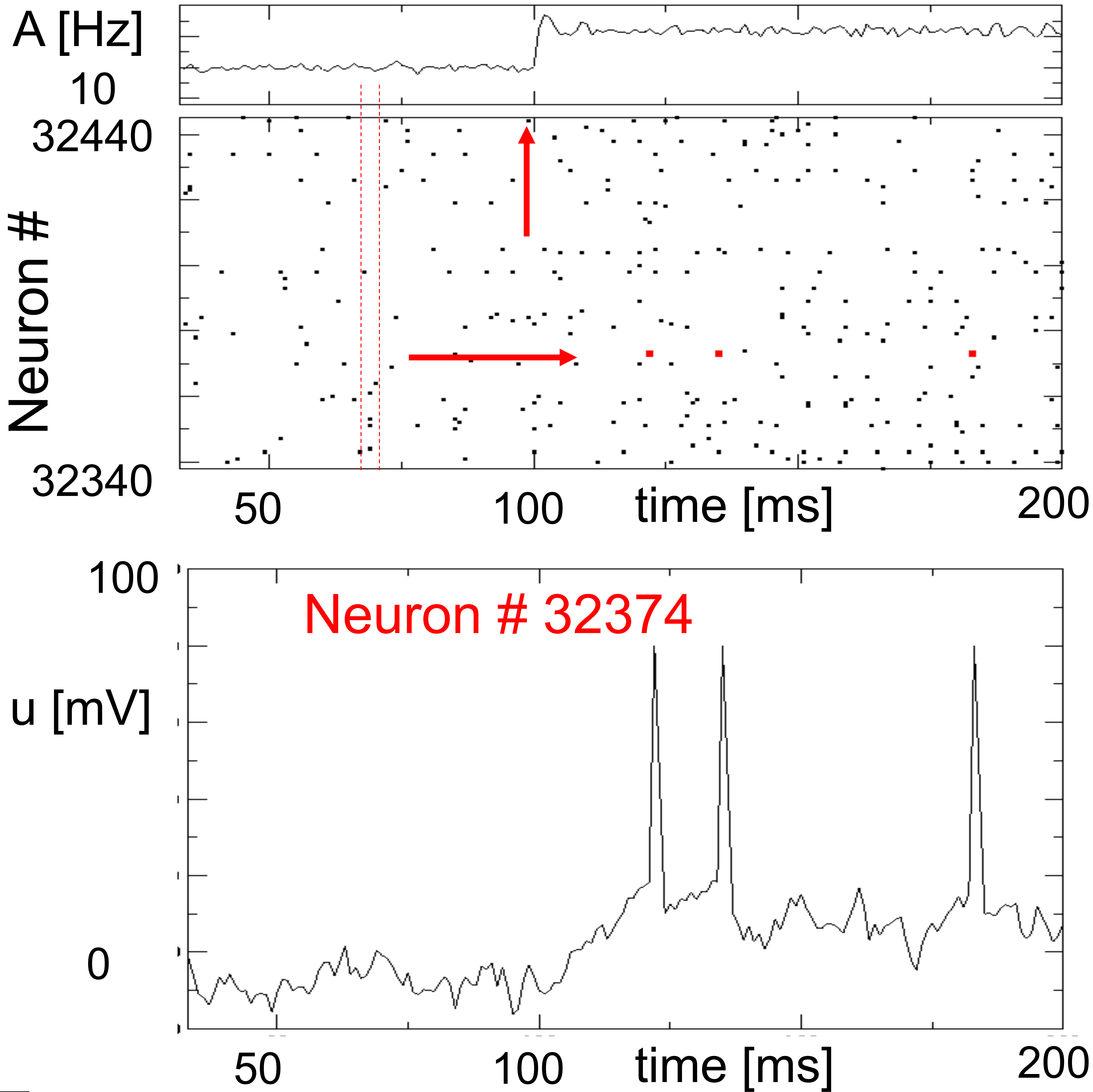
Crochet et al., 2011

10.5 Variability in networks – review from 10.2

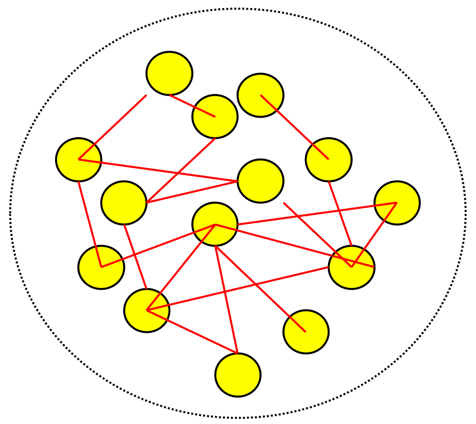


input {low rate
high rate

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



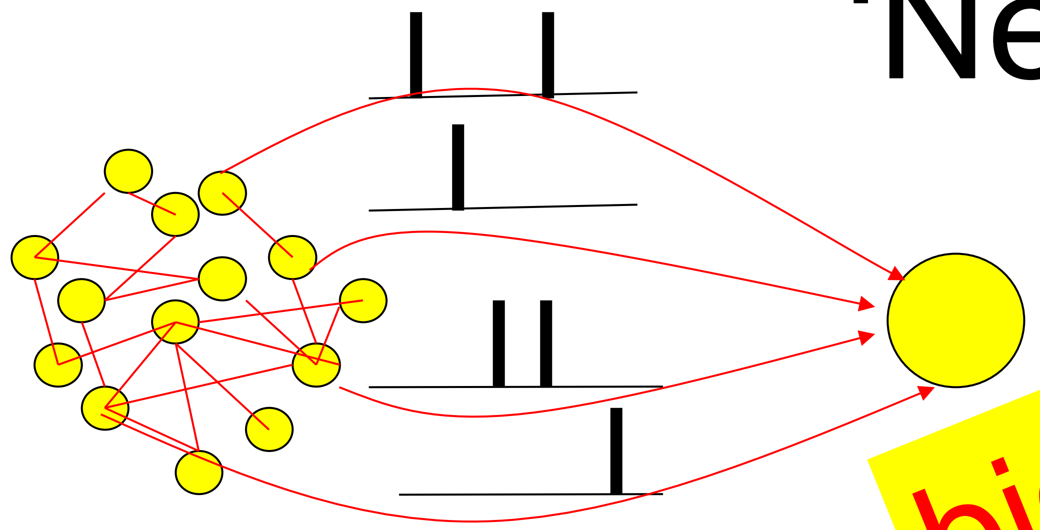
10.5 Membrane potential fluctuations



from neuron's point of view:

stochastic spike arrival

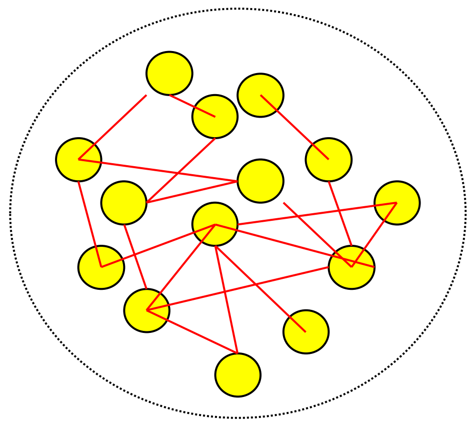
Pull out one neuron



'Network noise'

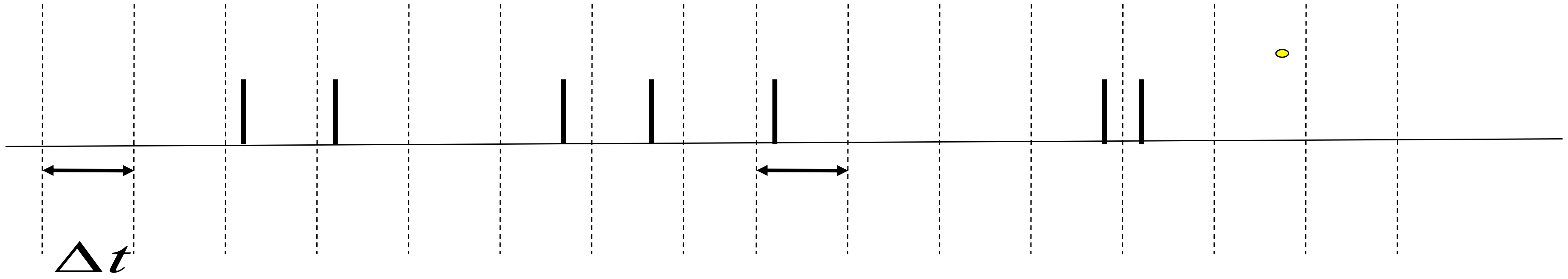
big contribution!

10.5. Stochastic Spike Arrival (Poisson model of input)



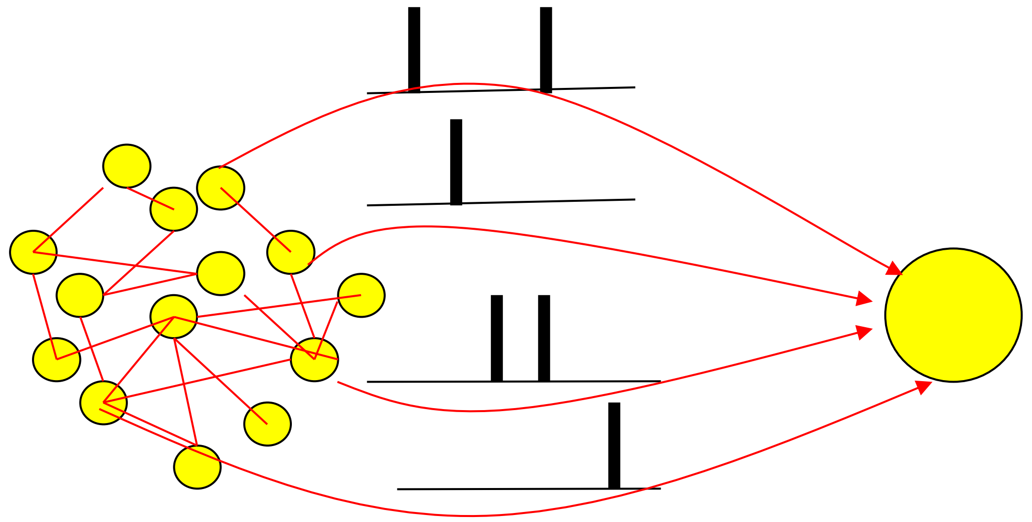
Blackboard now!

Total spike train of K presynaptic neurons



spike train

Pull out one neuron



Probability of spike arrival:

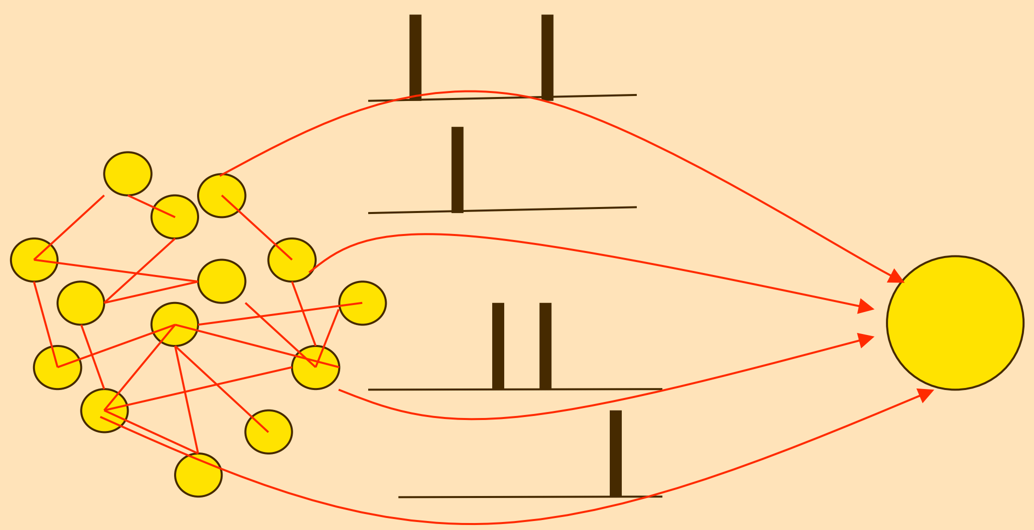
$$P_F = K\rho_0\,\Delta t$$

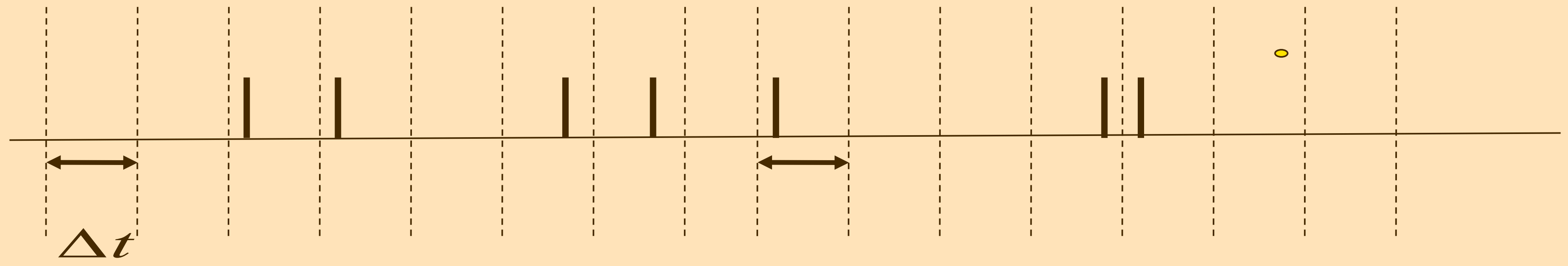
Take $\Delta t \rightarrow 0$

expectation

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

Week 10 - Exercise 2.1 NOW





Passive membrane

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

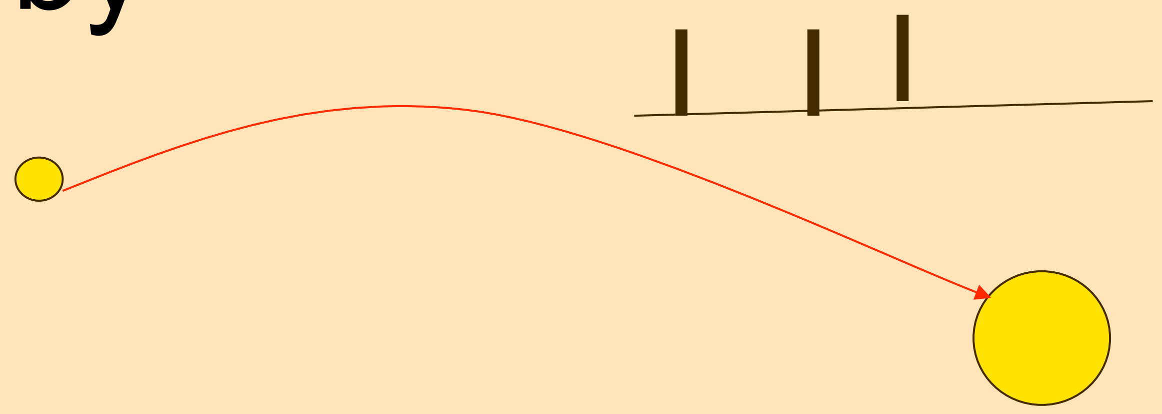
A leaky integrate-and-fire neuron without threshold (=passive membrane) receives stochastic spike arrival, described as a homogeneous Poisson process. Calculate the **mean membrane potential**. To do so, use the above formula.

Start at 11:35, Discussion at 11:48

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 τ

[ ] the constant *a* is equal to the time constant τ

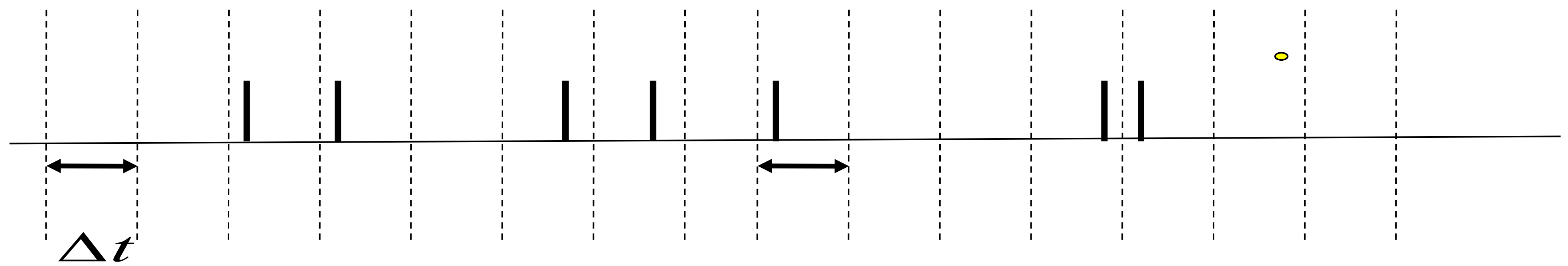
[ ] the constant *a* is equal to u_{rest}

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

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

10.5. Calculating the mean

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



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

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

mean: assume Poisson process

$$I_0 = \langle I^{syn}(t)\rangle = \tfrac{1}{R}\sum_k w_k \int dt' \alpha(t-t') \left\langle \sum_f \delta(t'-t_k^f) \right\rangle$$

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

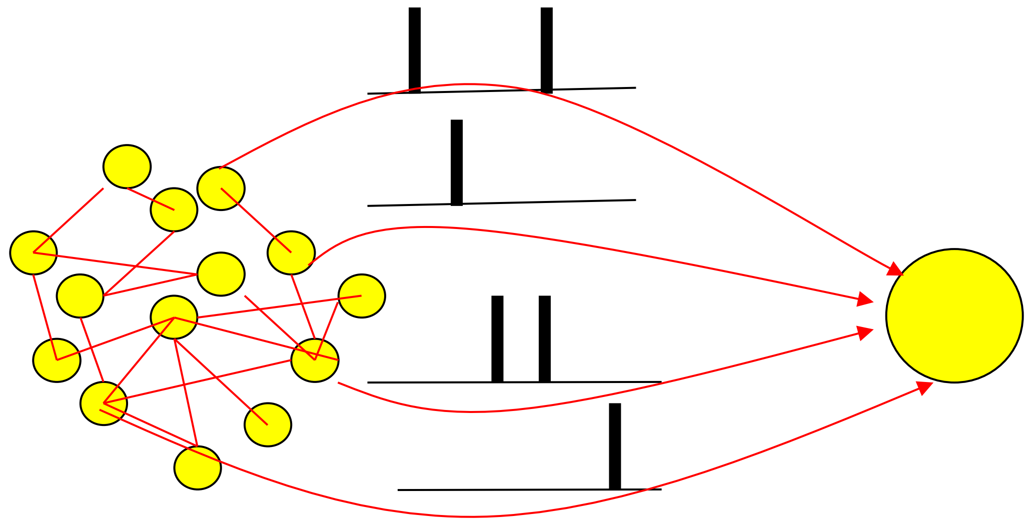
use for exercise

$$I_0 = \tfrac{1}{R}\sum_k w_k \int dt' \alpha(t-t')\ \nu_k$$

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

rate of inhomogeneous Poisson process

10.5. Fluctuation of current/potential



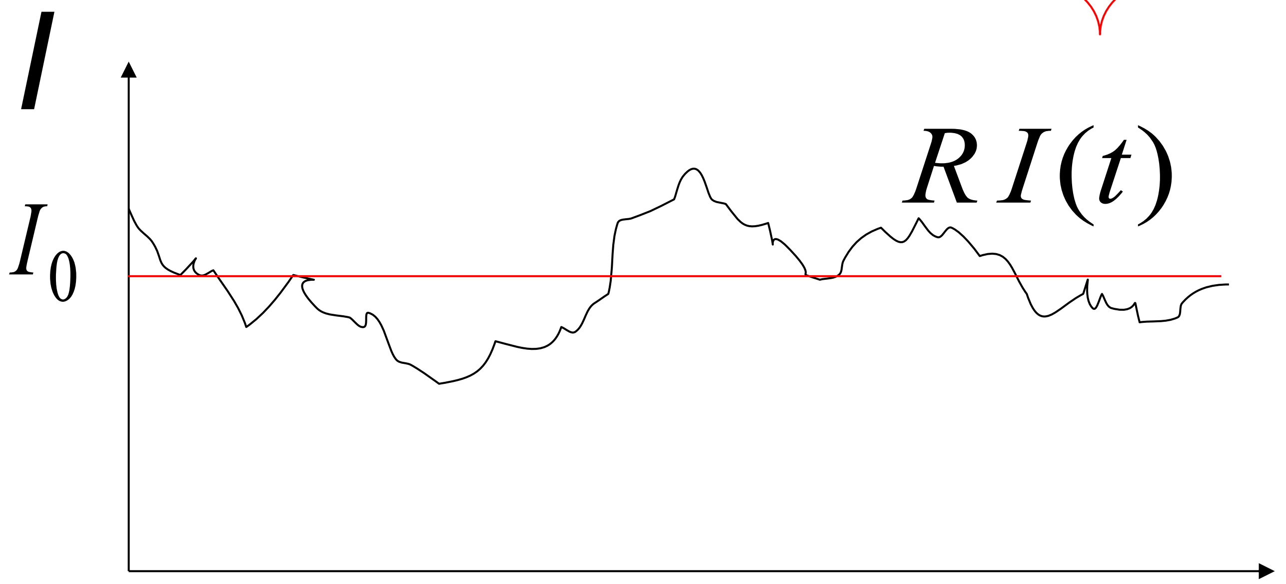
Synaptic current pulses of shape α

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

EPSC

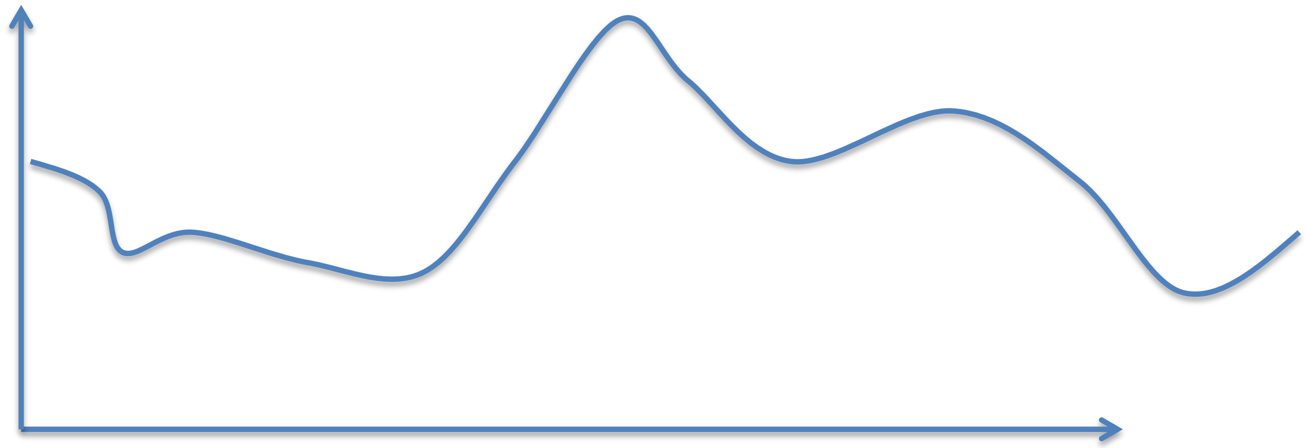
Passive membrane

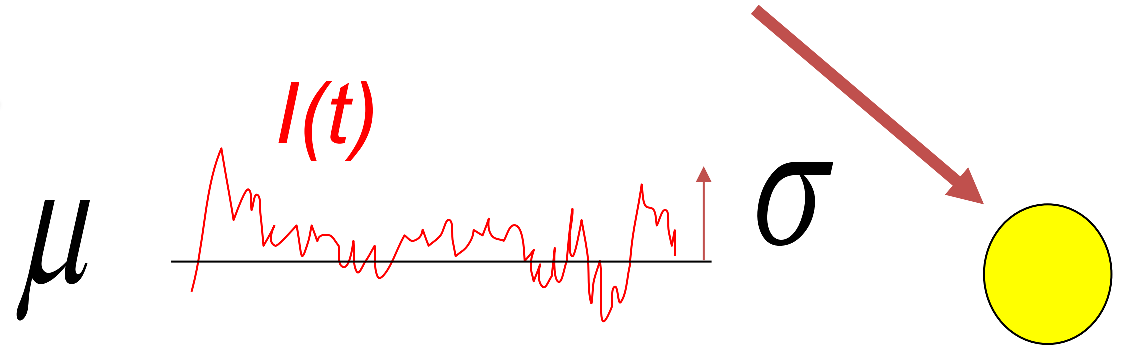
$$\tau \frac{d}{dt}u = -(u - u_{rest}) \quad + RI^{syn}(t)$$



$$I^{syn}(t) = I_0 + I^{fluct}(t)$$

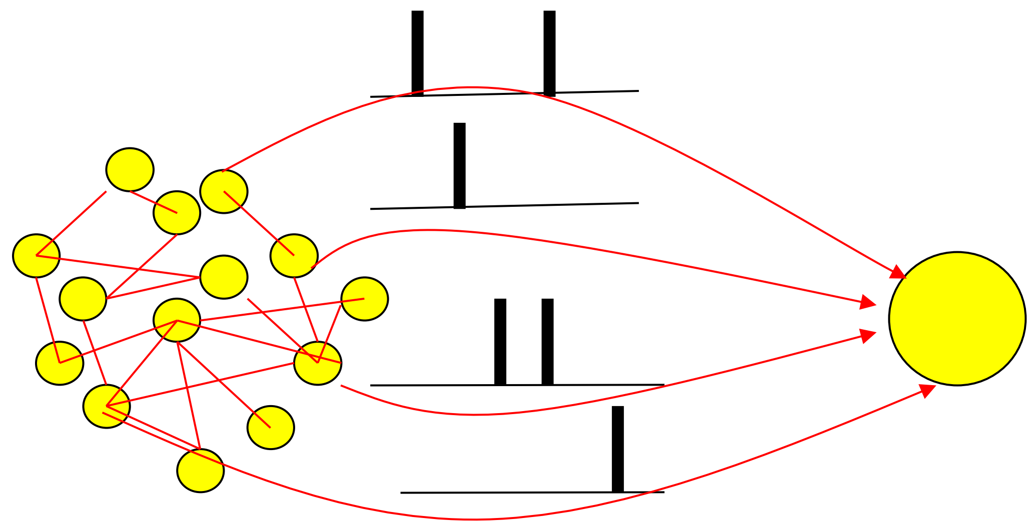
→ Fluctuating potential





Fluctuating input current

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

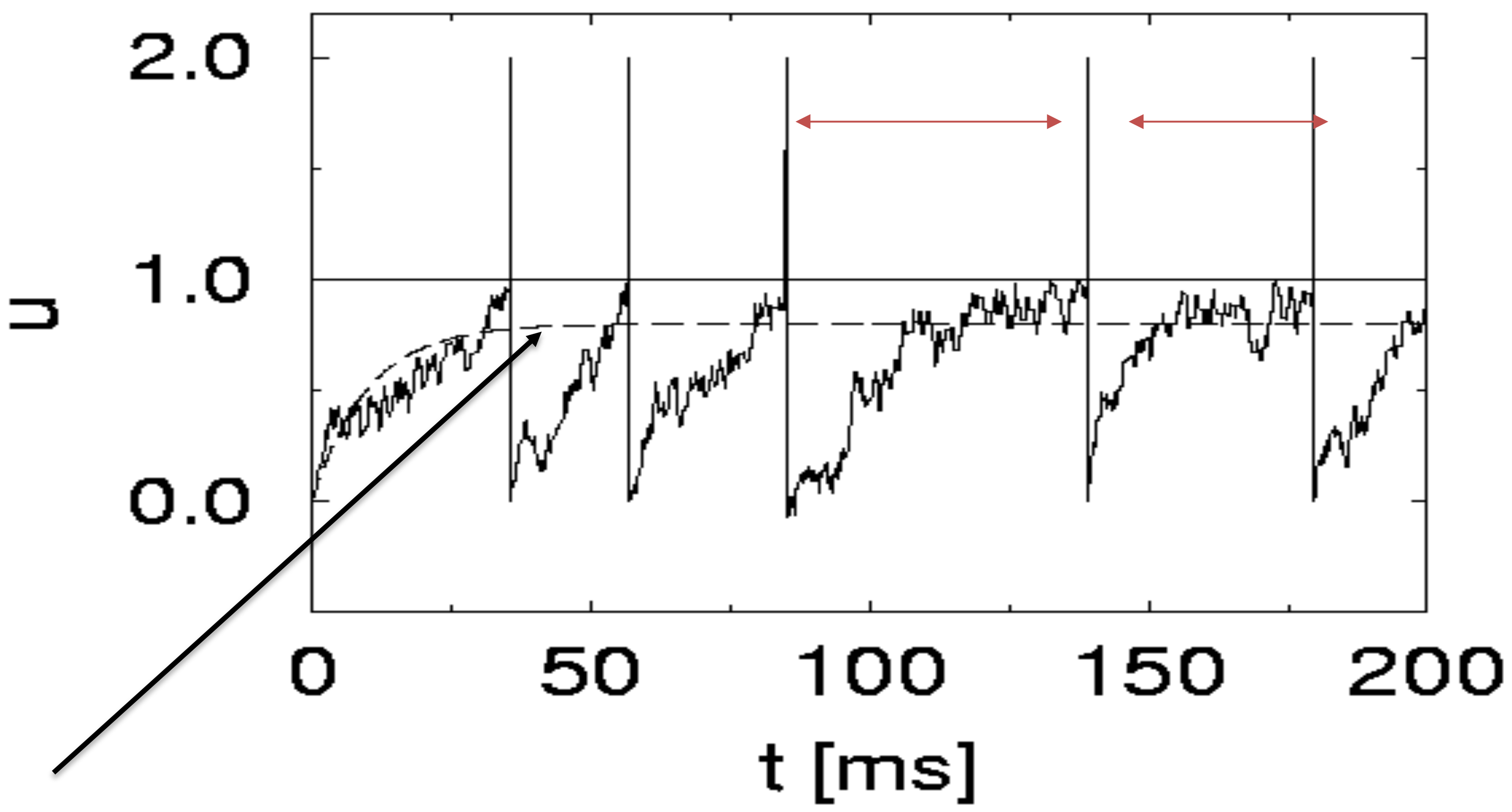
Passive membrane

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

Next week:

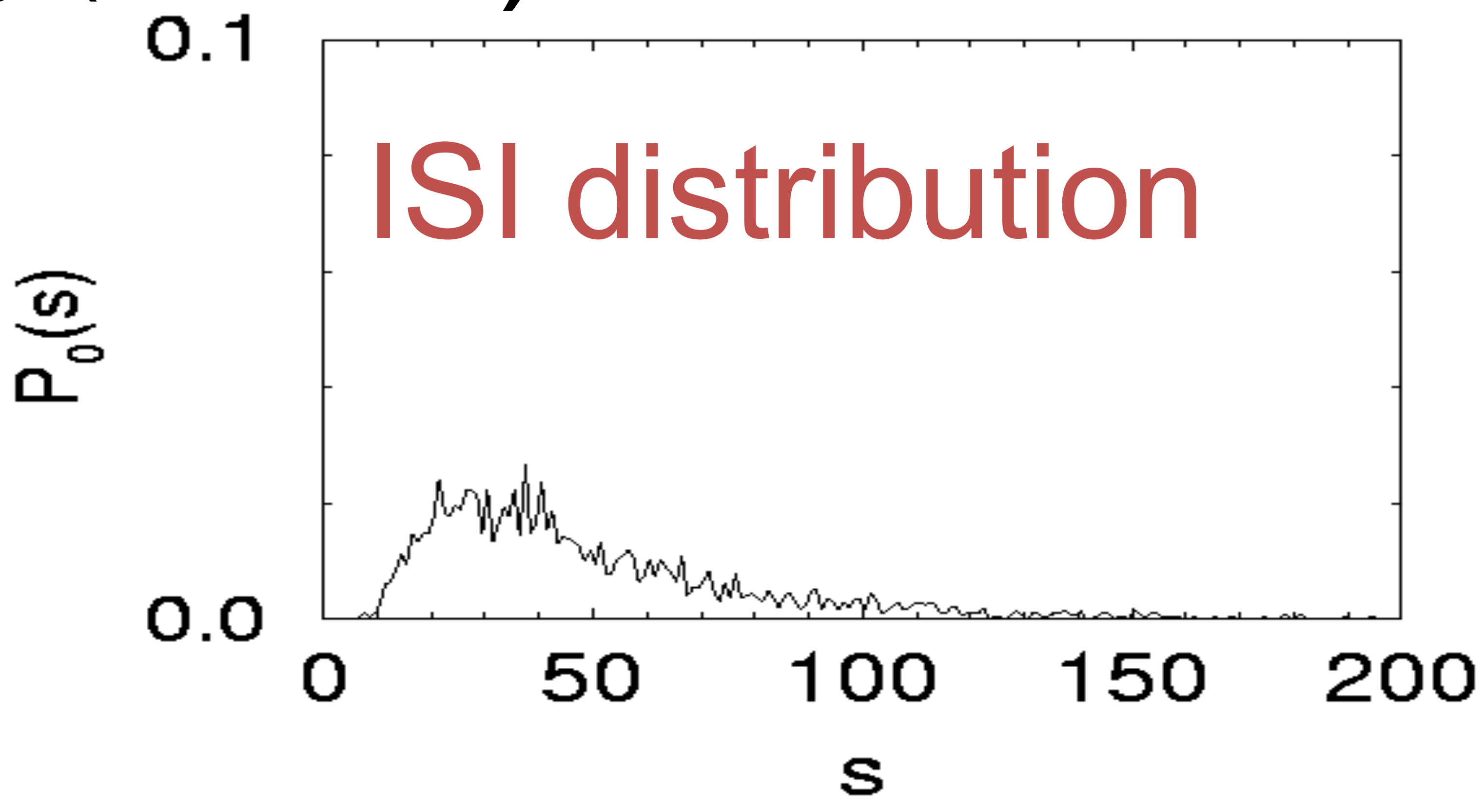
1) Calculate fluctuations
2) ADD THRESHOLD
   → Leaky Integrate-and-Fire

10.5. Fluctuations in Stochastic leaky integrate-and-fire

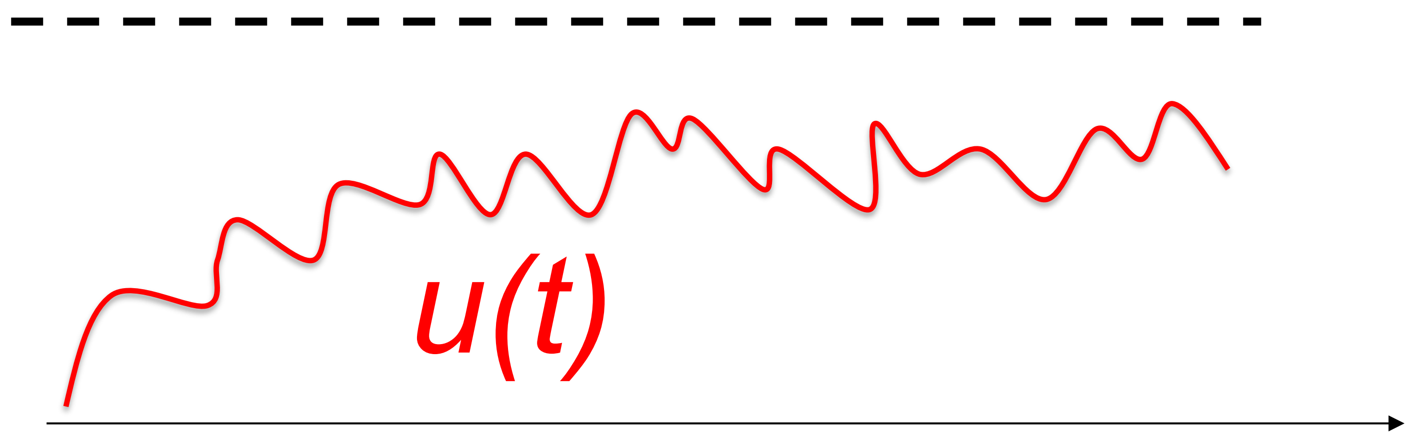


dashed:

expected trajectory (no noise)



noisy input/ diffusive noise/
stochastic spike arrival



subthreshold regime:
- firing driven by fluctuations
- **broad ISI distribution**
- *in vivo* like

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.
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-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