Week 7 – part 1 :Variability

ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

Biological Modeling of Neural Networks

Week 7 – Variability and Noise:
The question of the neural code

Wulfram Gerstner

EPFL, Lausanne, Switzerland

7.1 Variability of spike trains
- experiments

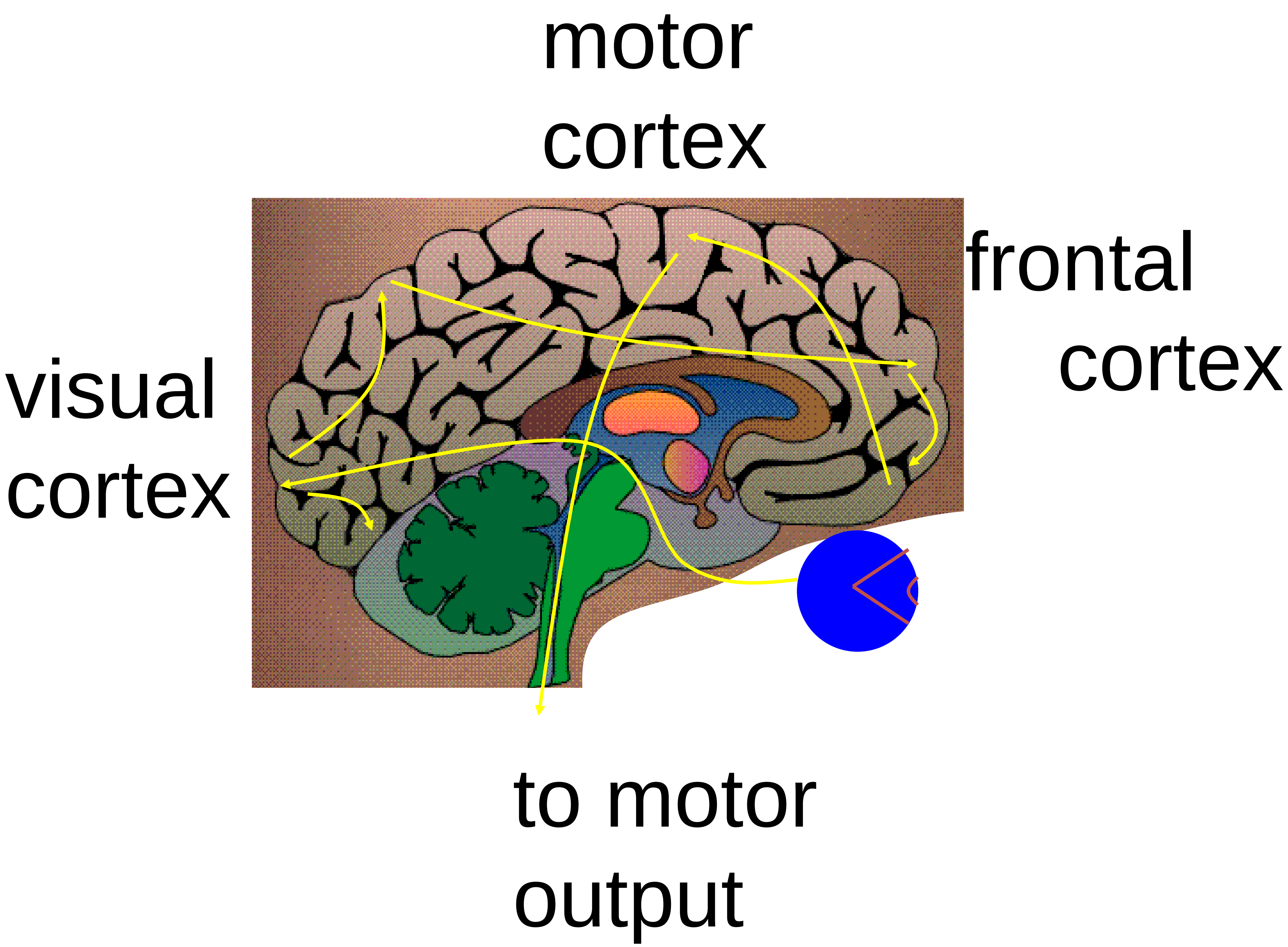
7.2 Sources of Variability?
- Is variability equal to noise?

7.3 Poisson Model
-Three definitions of Rate code

7.4 Stochastic spike arrival
- Membrane potential fluctuations

7.5. Stochastic spike firing
- stochastic integrate-and-fire

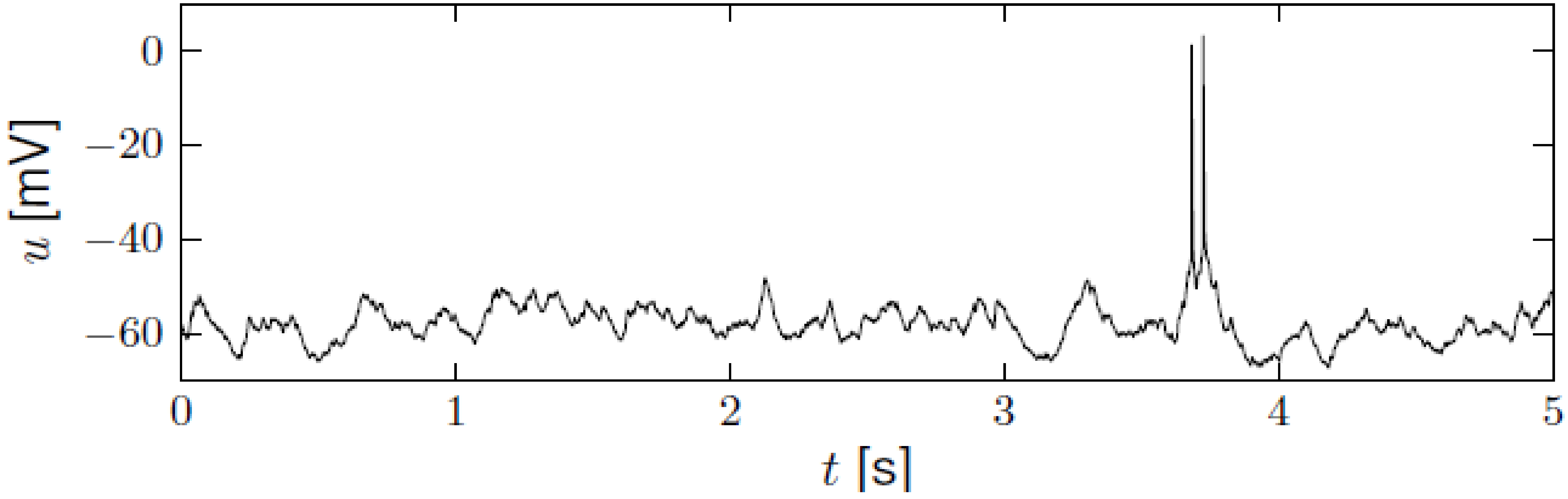
Neuronal Dynamics – 7.1. Variability



Spontaneous activity *in vivo*

Variability
- of membrane potential?
- of spike timing?

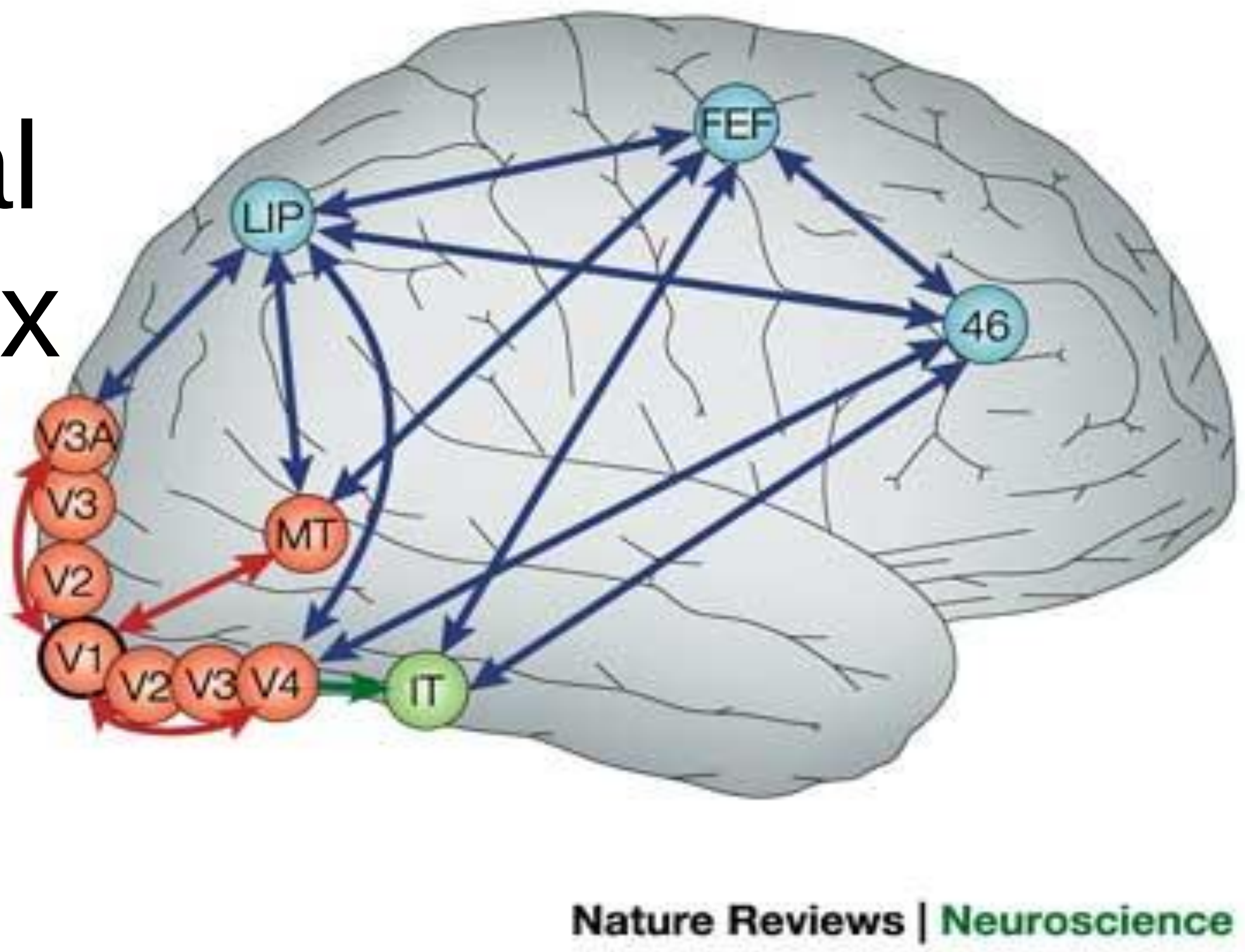
awake mouse, cortex, freely whisking,

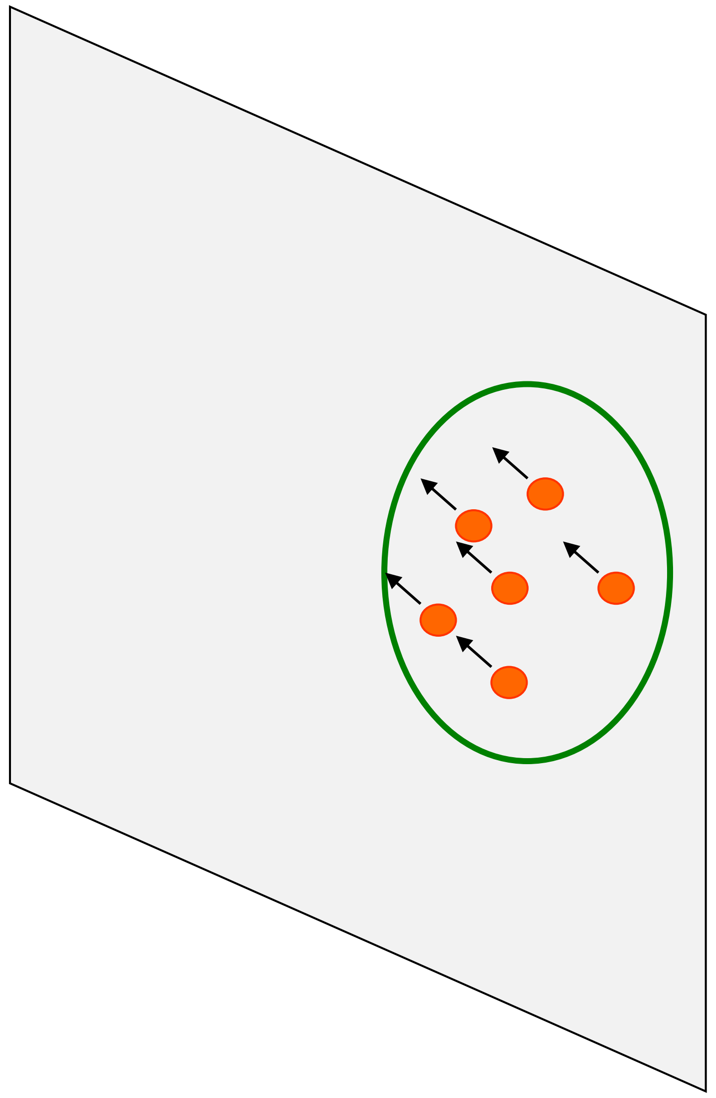


Crochet et al., 2011

Detour: Receptive fields in V5/MT

visual
cortex

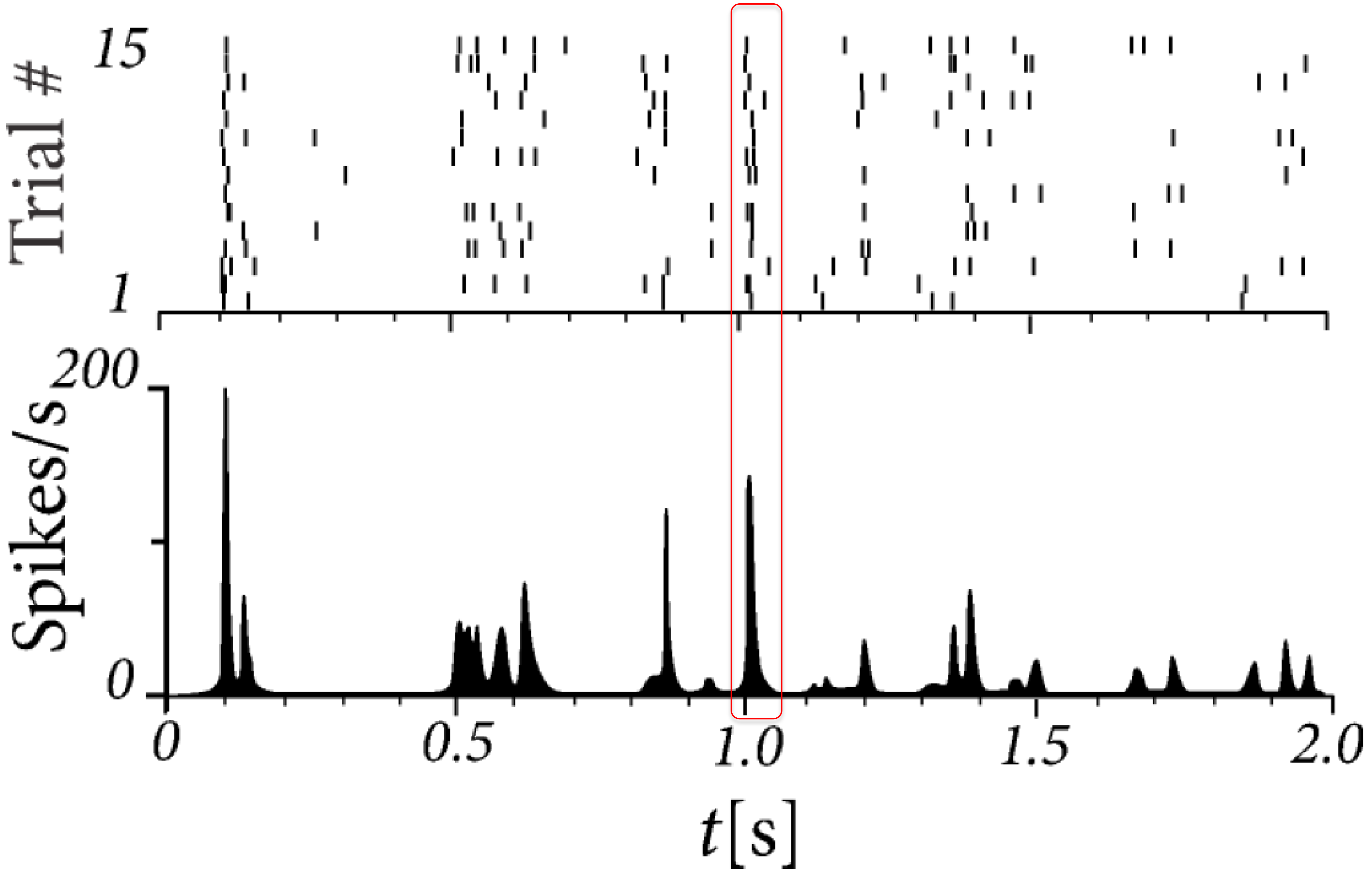




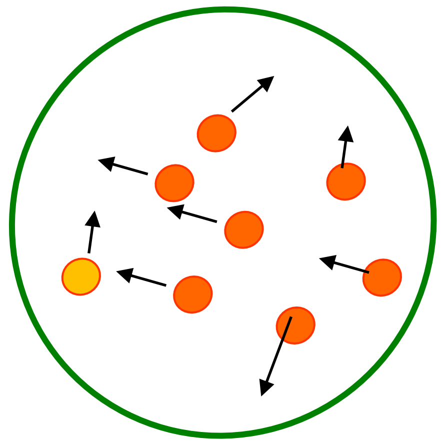
cells in visual cortex MT/V5
respond to motion stimuli

Neuronal Dynamics – 7.1 Variability in vivo

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

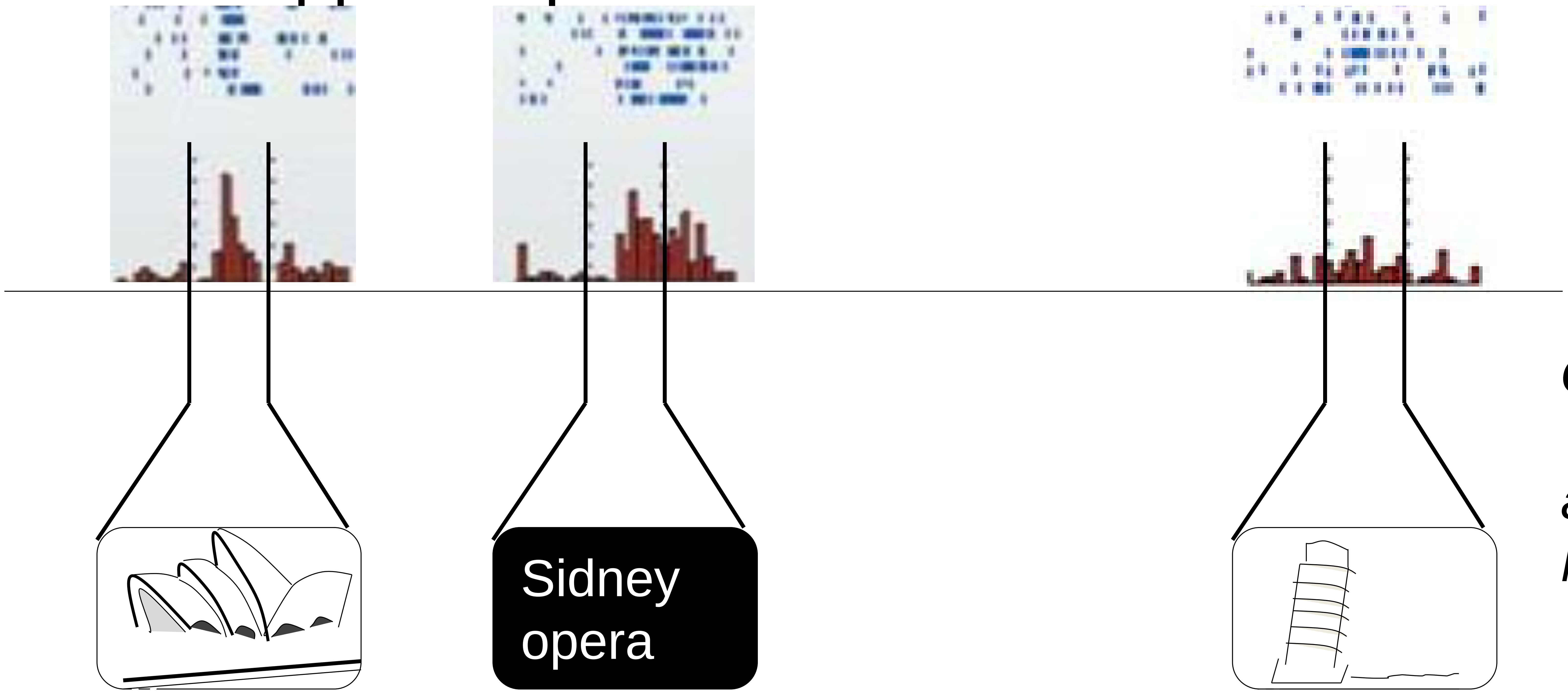


adapted from Bair and Koch 1996;
data from Newsome 1989



Neuronal Dynamics – 7.1 Variability in vivo

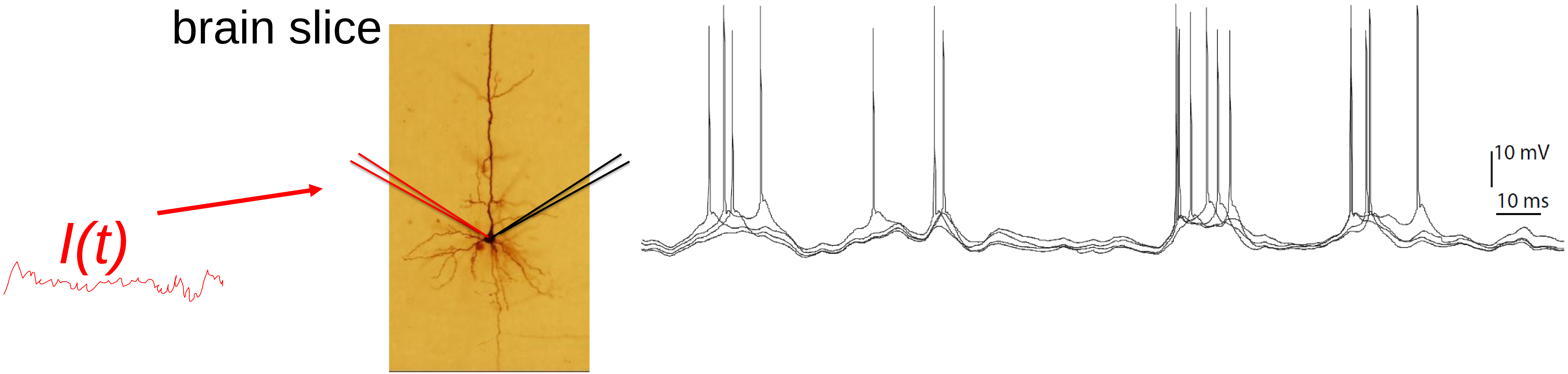
Human Hippocampus



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

Neuronal Dynamics – 7.1 Variability in vitro

4 repetitions of the same time-dependent stimulus,



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?

Week 7 – part 2 : Sources of Variability

ÉCOLE POLYTECHNIQUE
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Biological Modeling of Neural Networks

Week 7 – Variability and Noise:
The question of the neural code

Wulfram Gerstner
EPFL, Lausanne, Switzerland

√ **7.1 Variability of spike trains**
- experiments

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

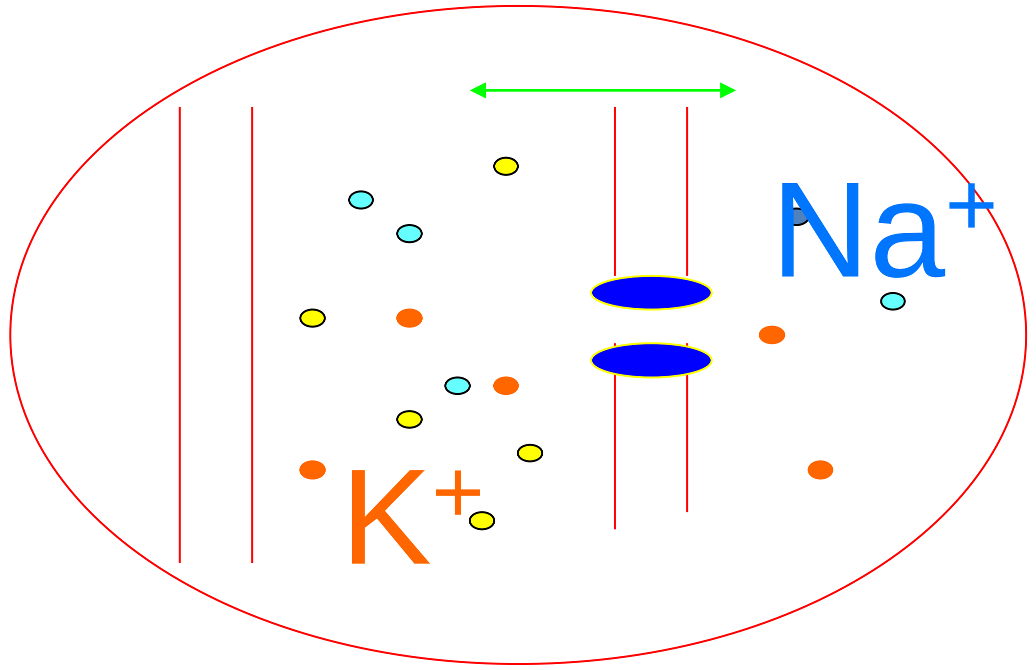
7.3 Three definitions of Rate code
- Poisson Model

7.4 Stochastic spike arrival
- Membrane potential fluctuations

7.5. Stochastic spike firing
- stochastic integrate-and-fire

Neuronal Dynamics – 7.2. Sources of Variability

- Intrinsic noise (ion channels)

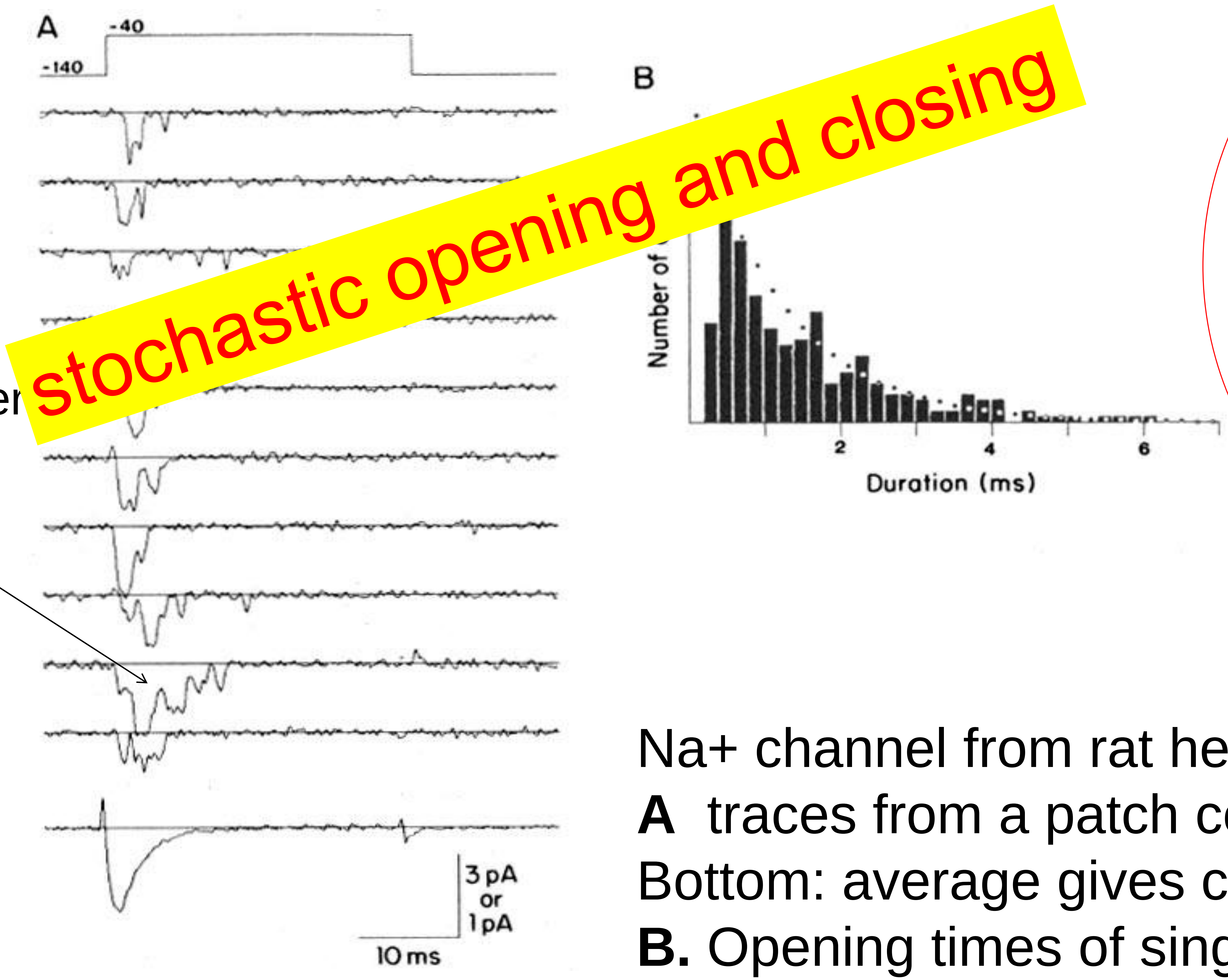


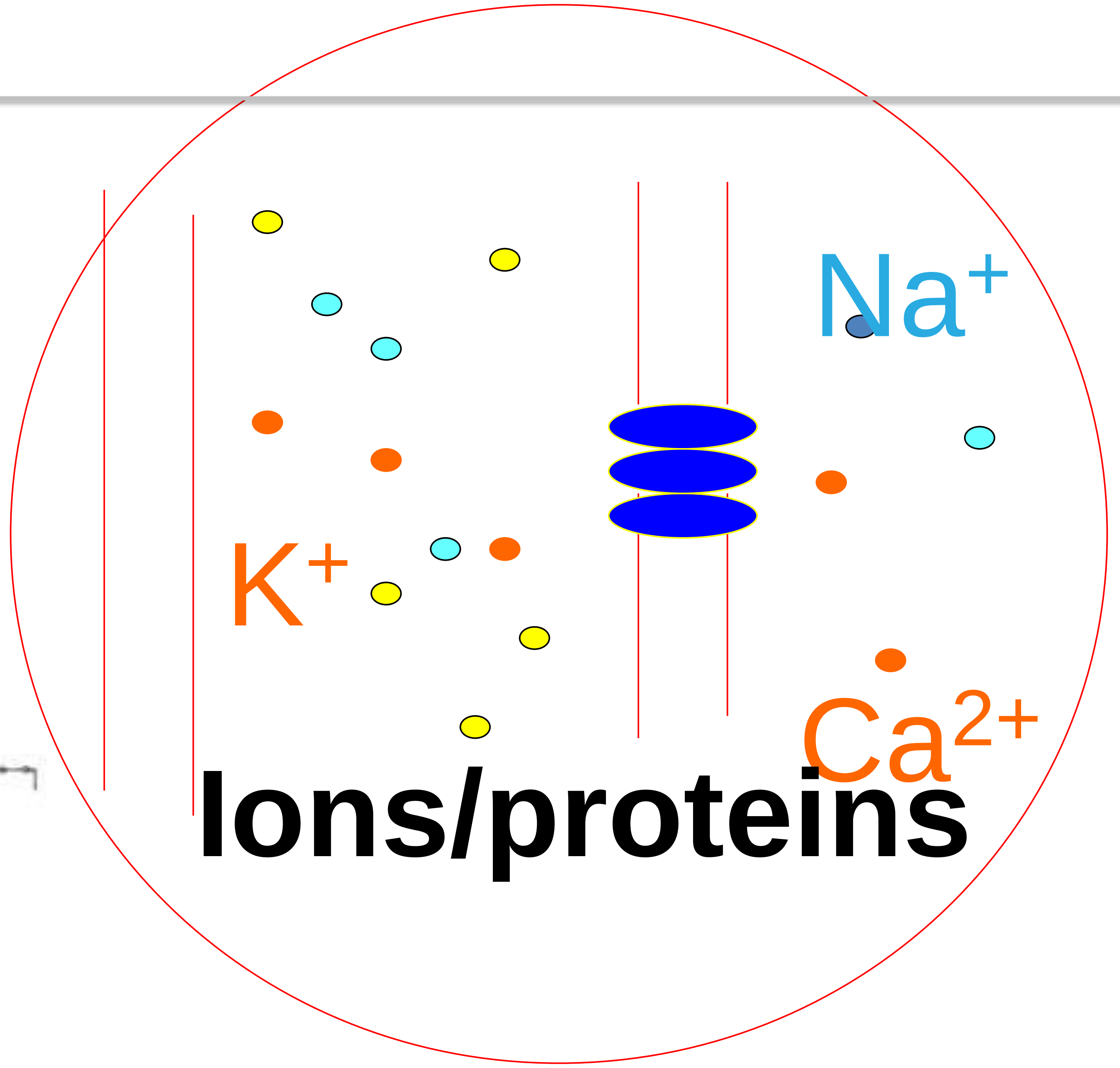
-Finite number of channels

-Finite temperature

Review from 2.5 Ion channels

Steps:
Different number
of channels

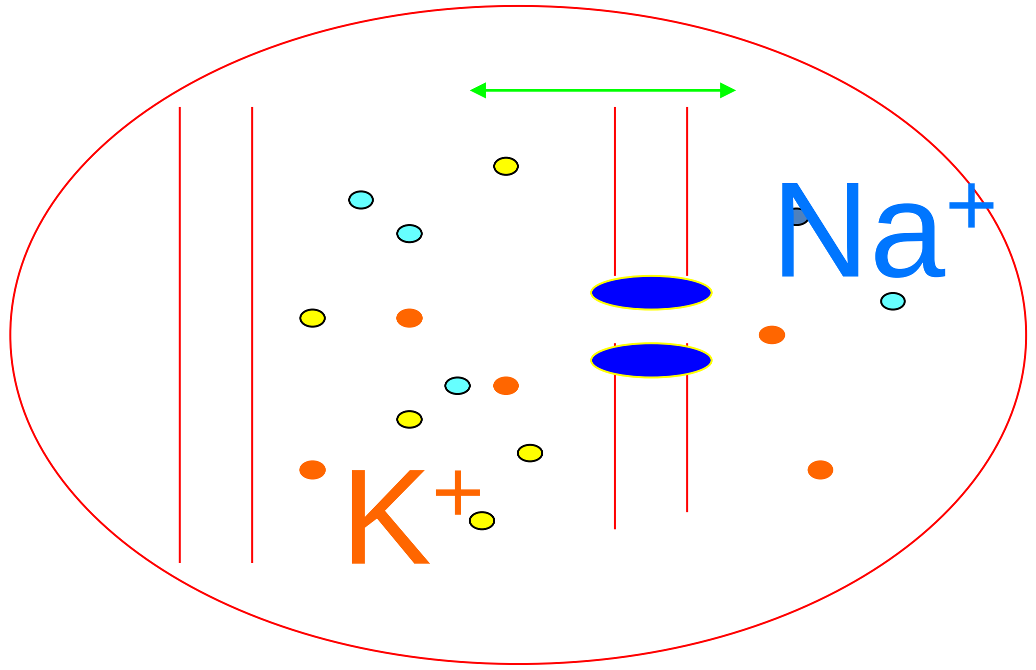




Na+ channel from rat heart *(Patlak and Ortiz 1985)*
A traces from a patch containing several channels.
Bottom: average gives current time course.
B. Opening times of single channel events

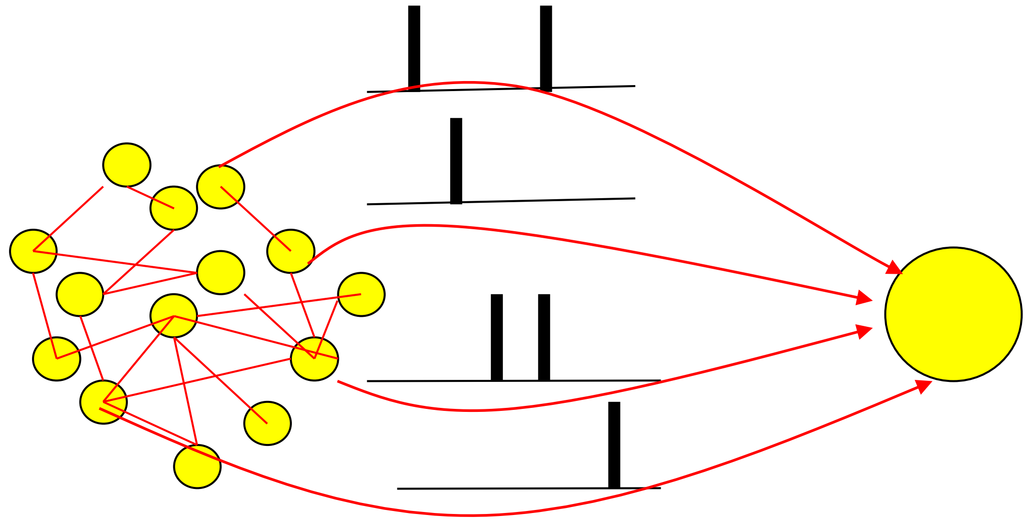
Neuronal Dynamics – 7.2. Sources of Variability

- Intrinsic noise (ion channels)



-Finite number of channels
-Finite temperature

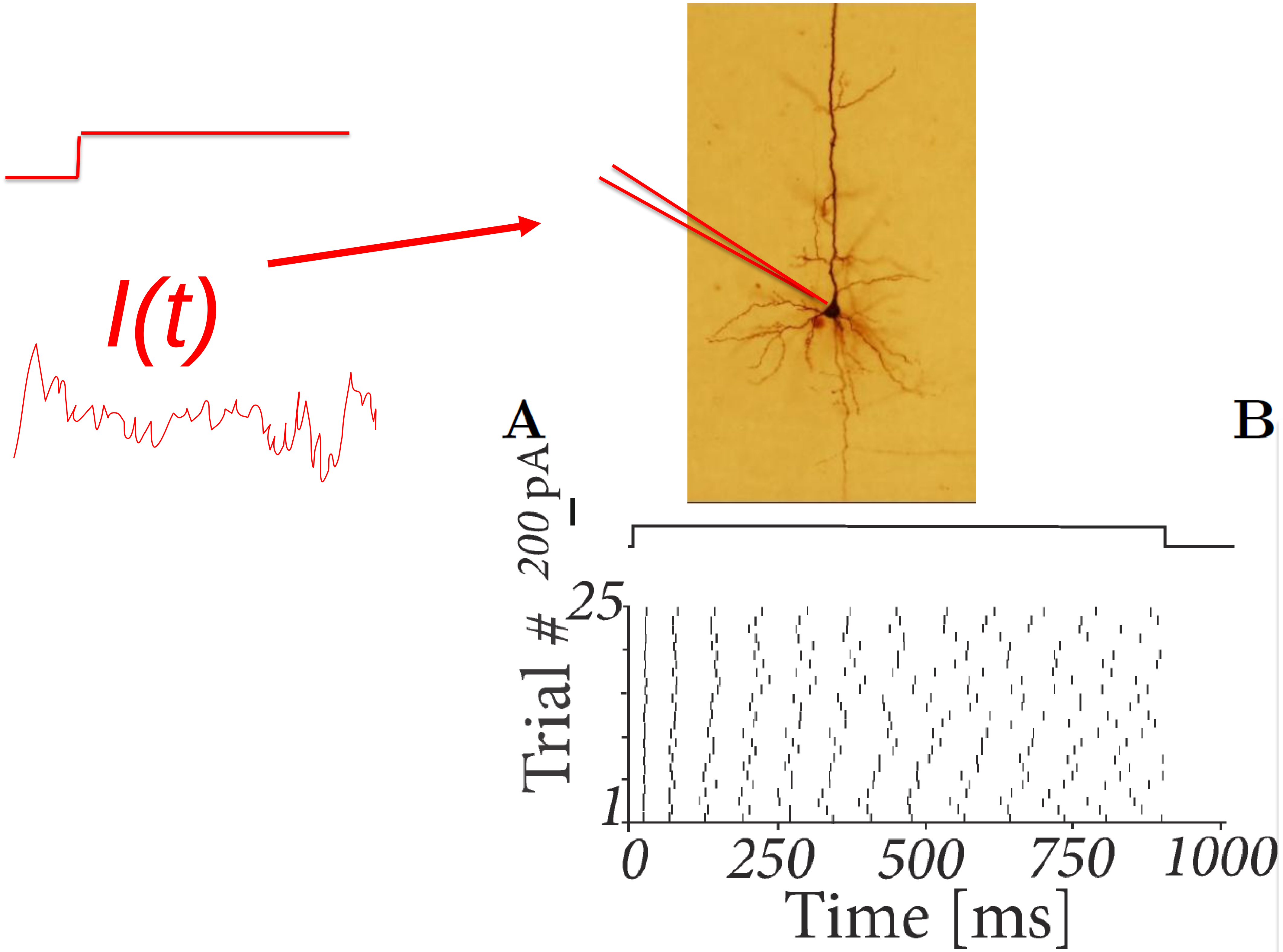
-Network noise (background activity)



-Spike arrival from other neurons
-Beyond control of experimentalist

→ Check intrinisic noise by removing the network

Neuronal Dynamics – 7.2 Variability in vitro



neurons are fairly reliable

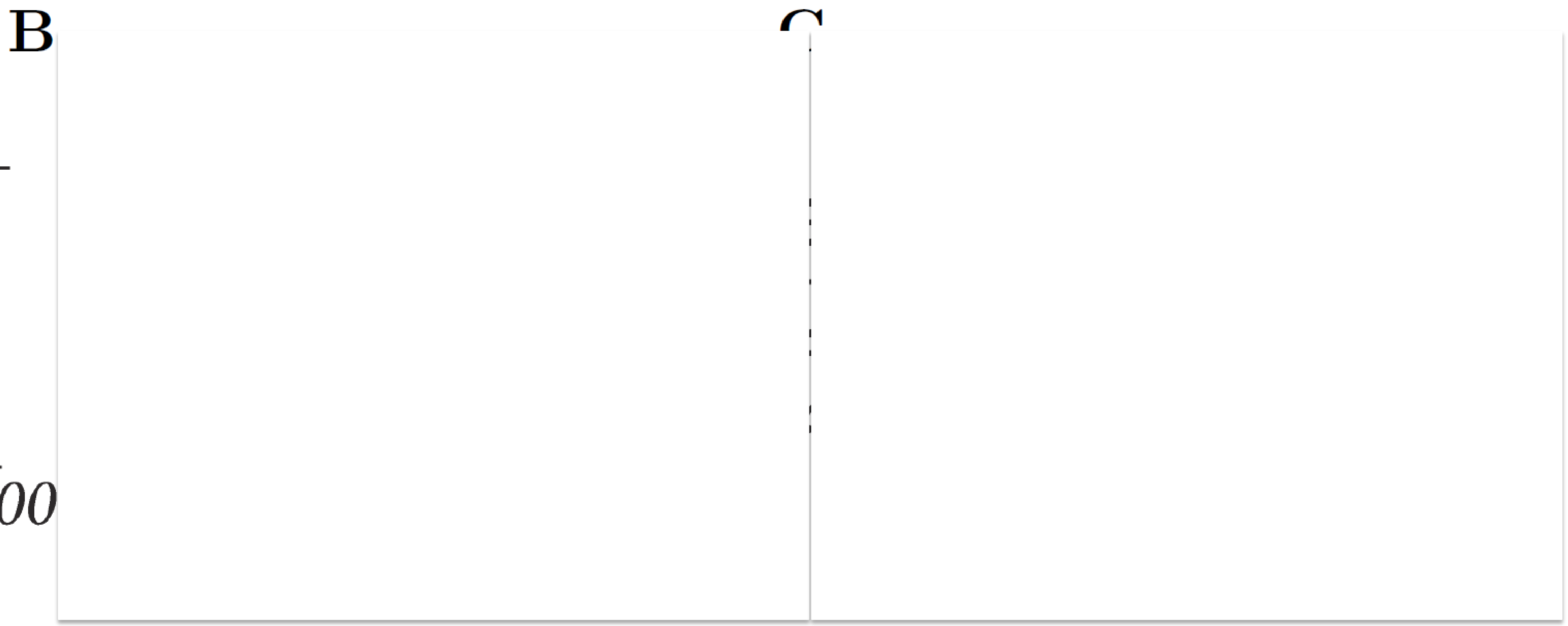
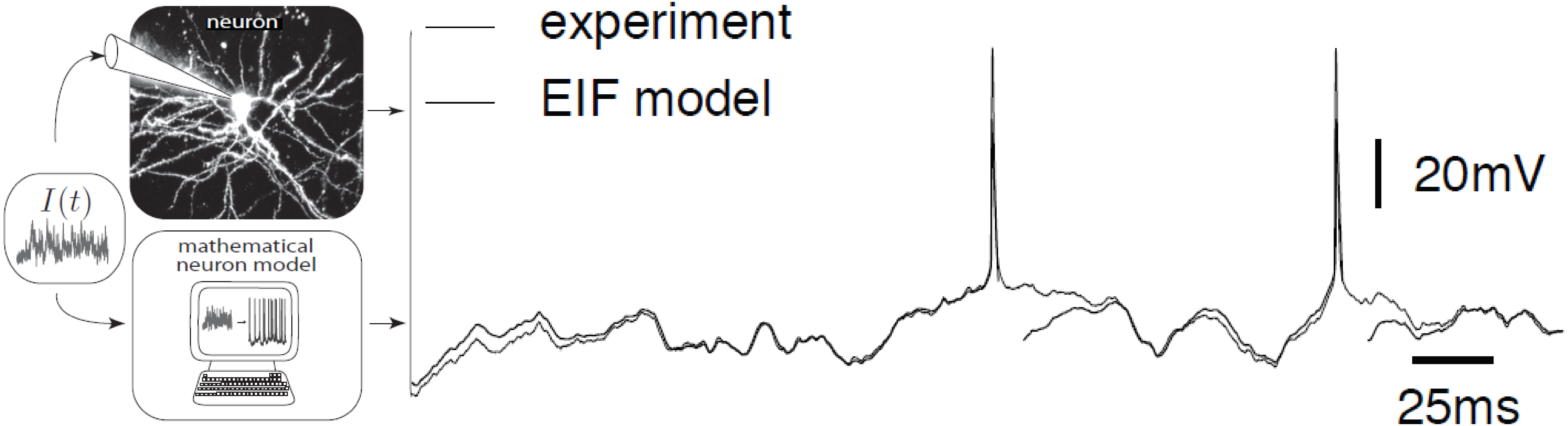


Image adapted from Mainen&Sejnowski 1995

REVIEW from 1.5: How good are integrate-and-fire models?



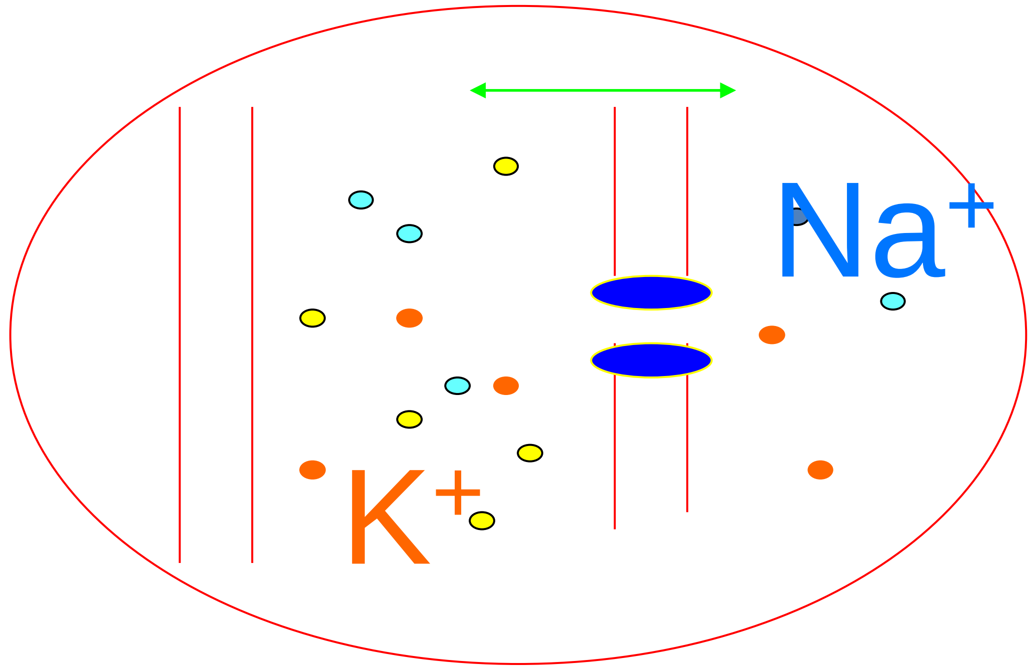
Badel et al., 2008

Aims: - predict spike initiation times
- predict subthreshold voltage

only possible, because neurons are fairly reliable

Neuronal Dynamics – 7.2. Sources of Variability

- Intrinsic noise (ion channels)

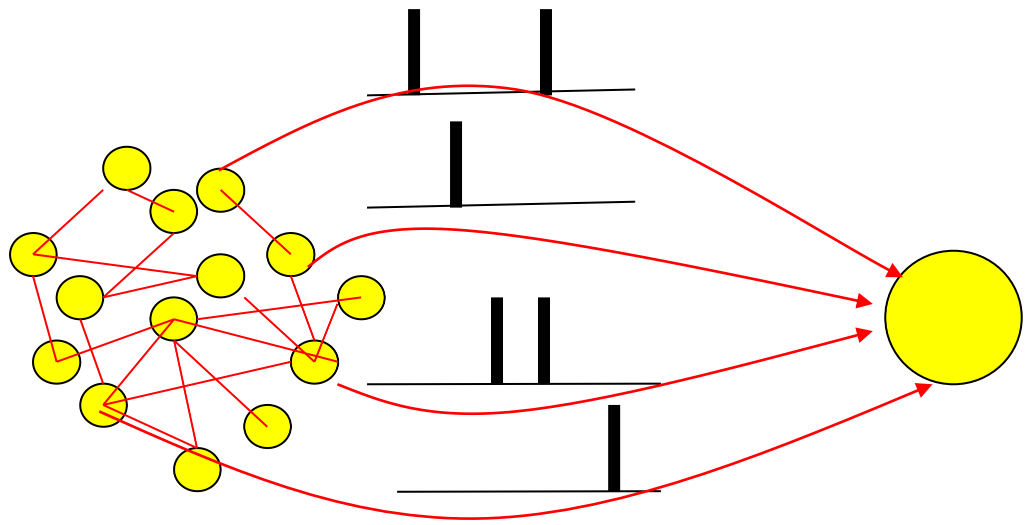


-Finite number of channels

-Finite temperature

small contribution!

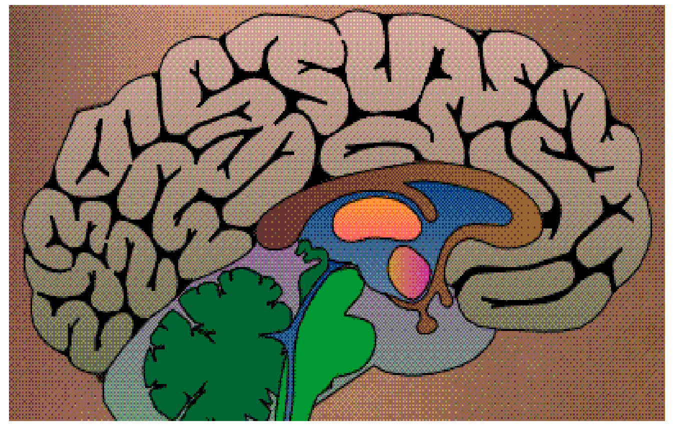
-Network noise (background activity)



-Spike arrival from other neurons

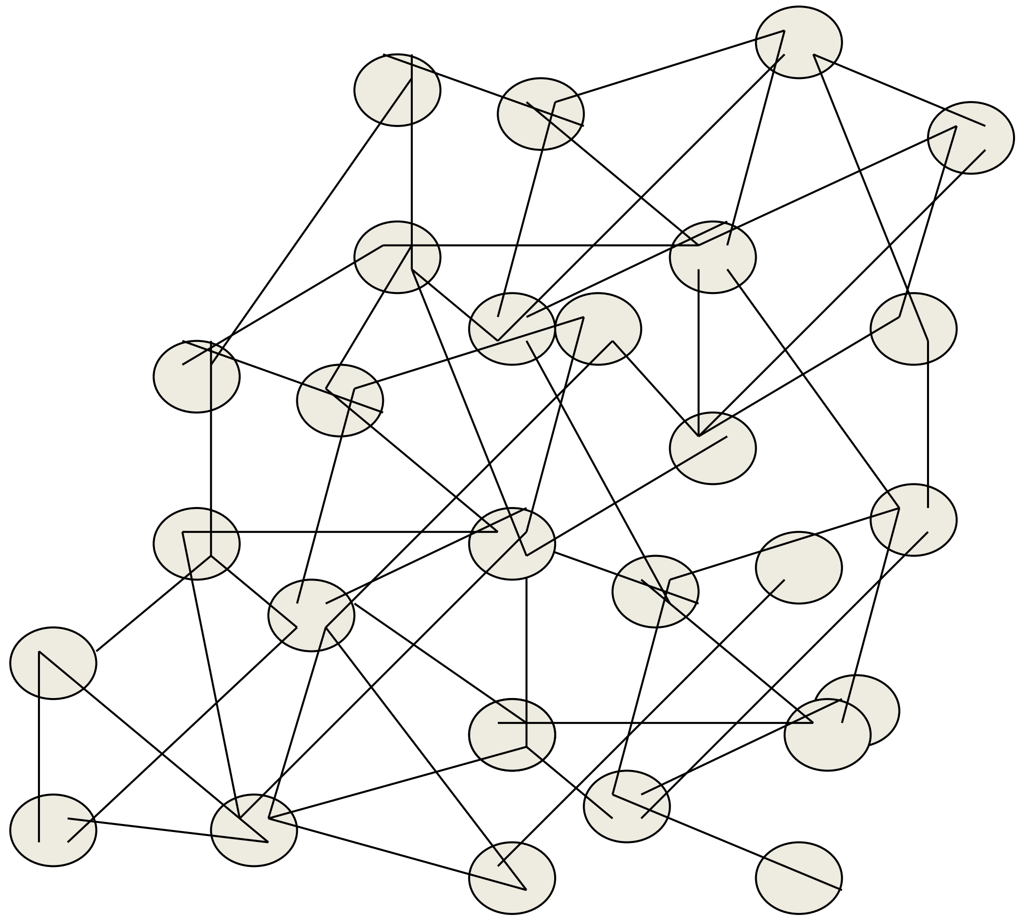
-Beyond control of experimentalist

→ Check network noise by simulation!



Brain

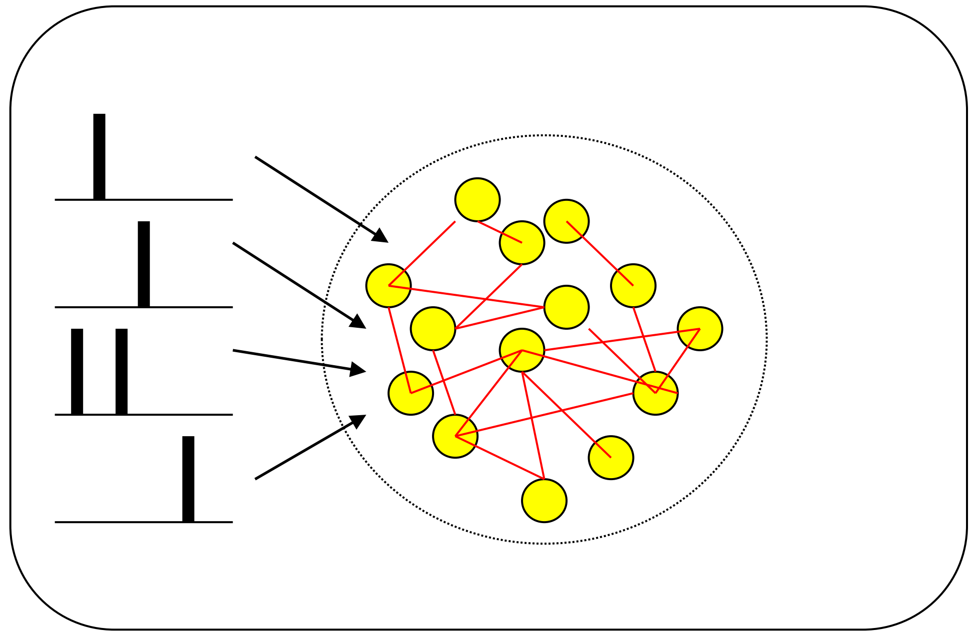
The Brain: a highly connected system

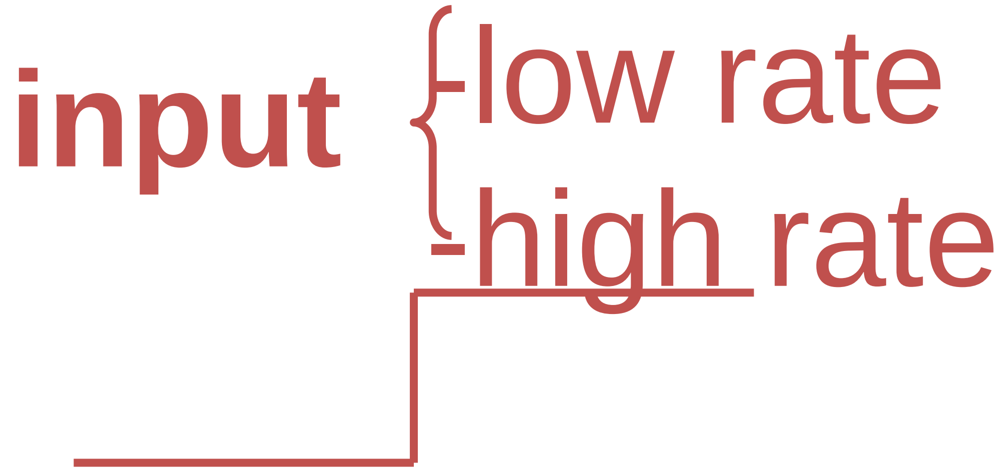


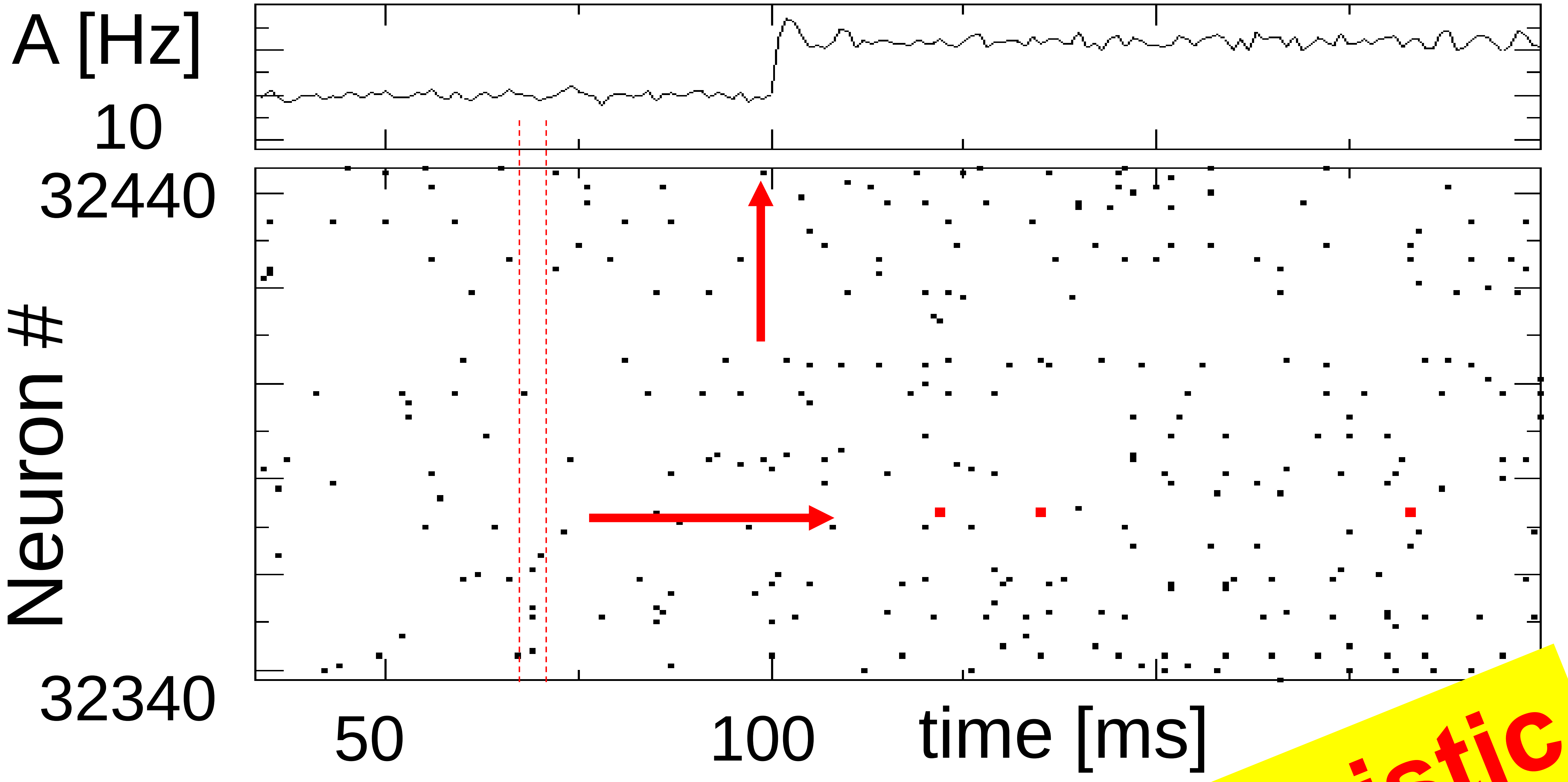
High connectivity:
systematic, organized in local populations
but **seemingly random**

Distributed architecture
10^{10} neurons
10^{4} connections/neurons

Random firing in a population of LIF neurons





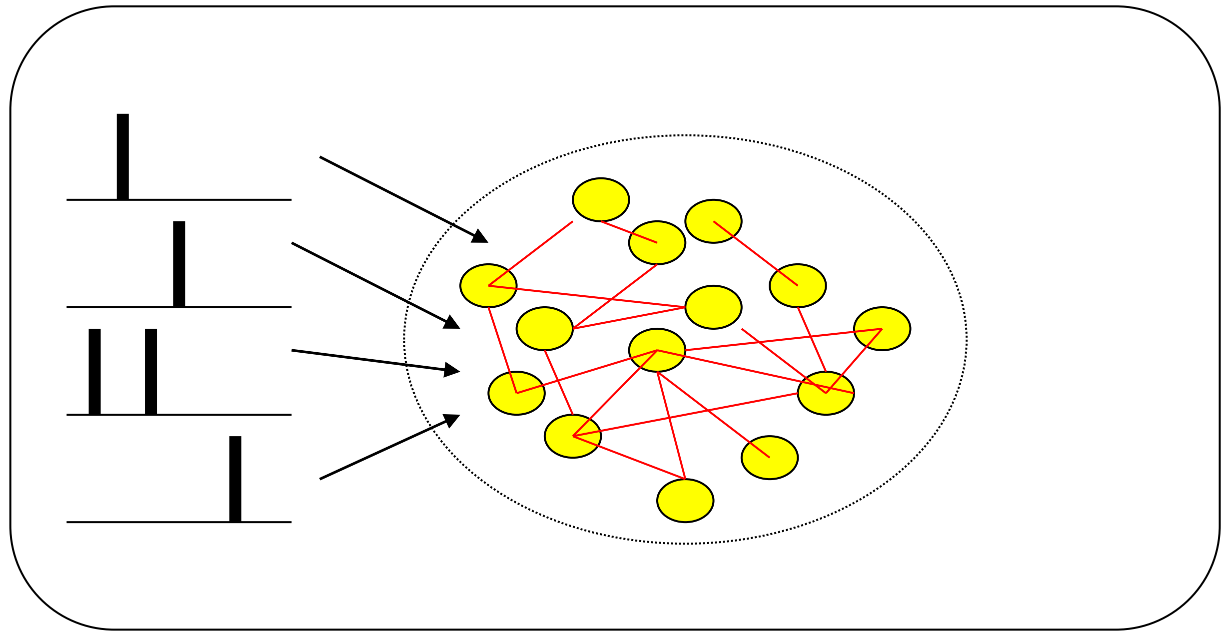


Brunel, J. Comput. Neurosc. 2000
Mayor and Gerstner, Phys. Rev E. 200
Vogels et al., 2005

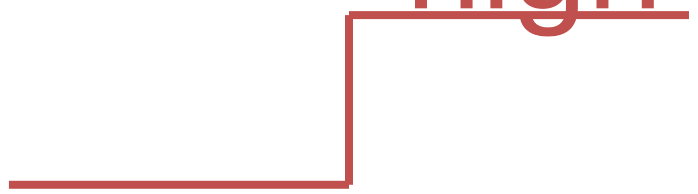
Population
- 50 000 neurons
- 20 percent inhibitory
- **randomly connected**

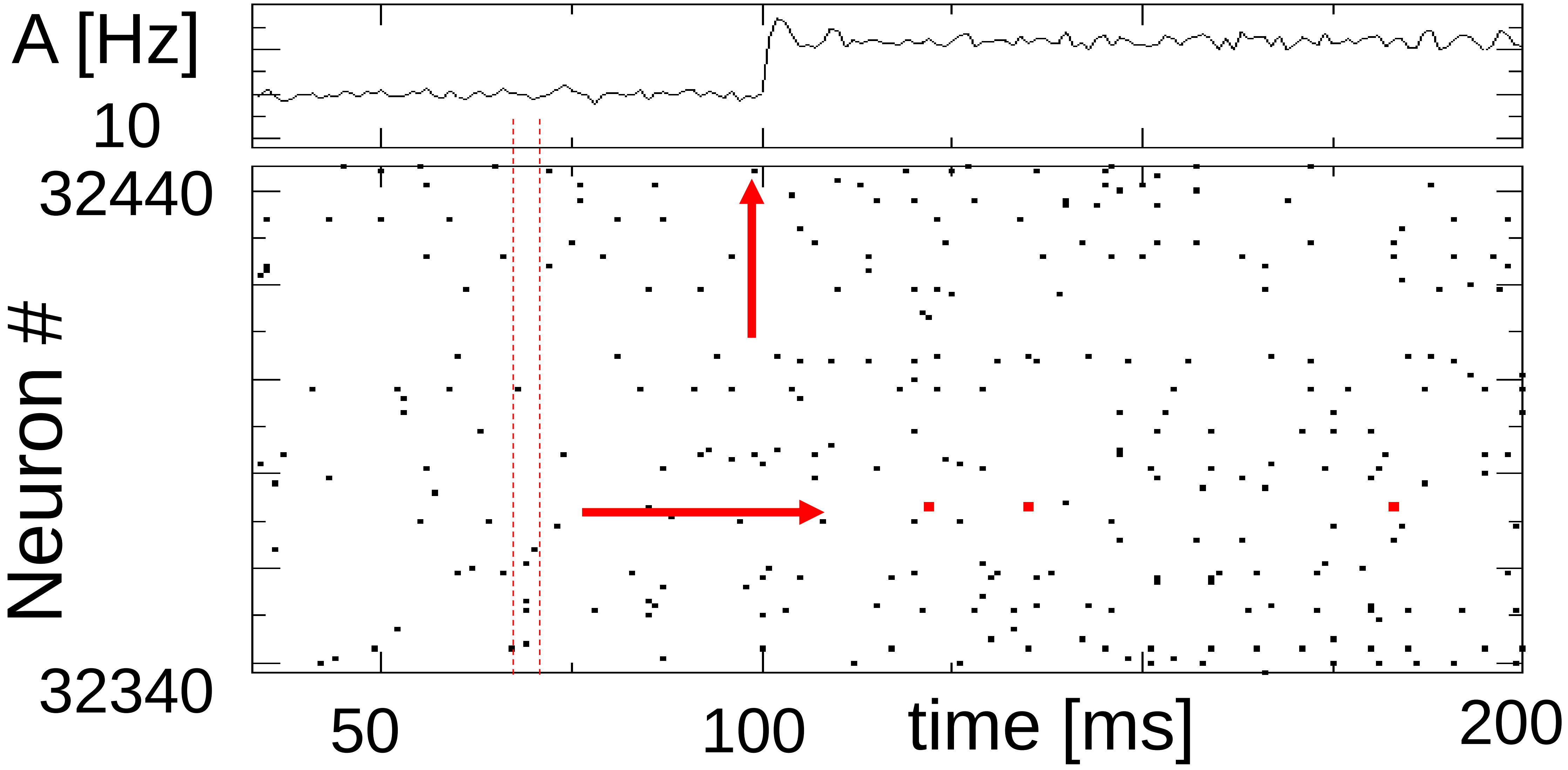
Network of **deterministic** leaky integrate-and-fire: 'fluctuations'

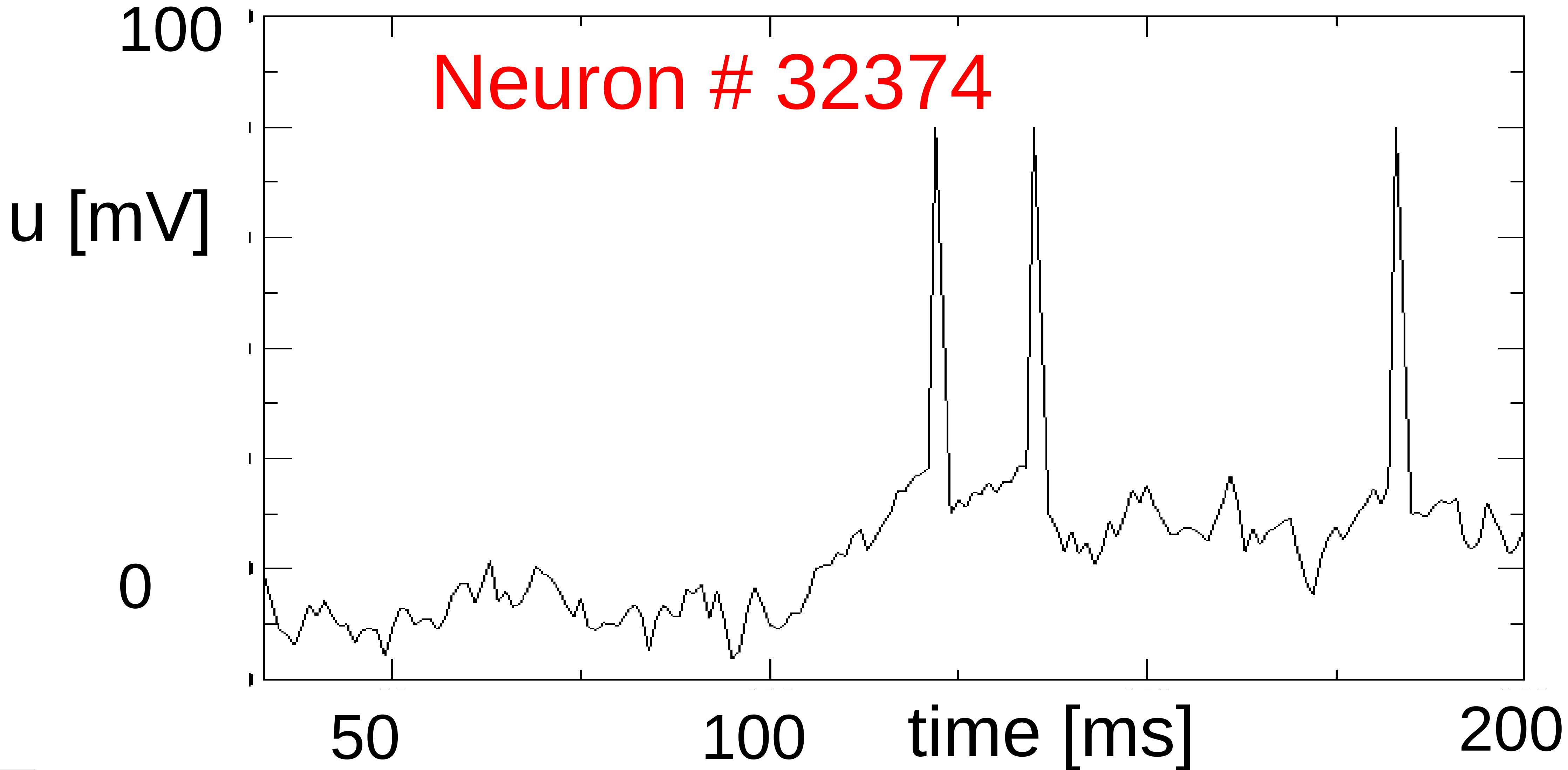
Random firing in a population of LIF neurons



input {low rate / high rate





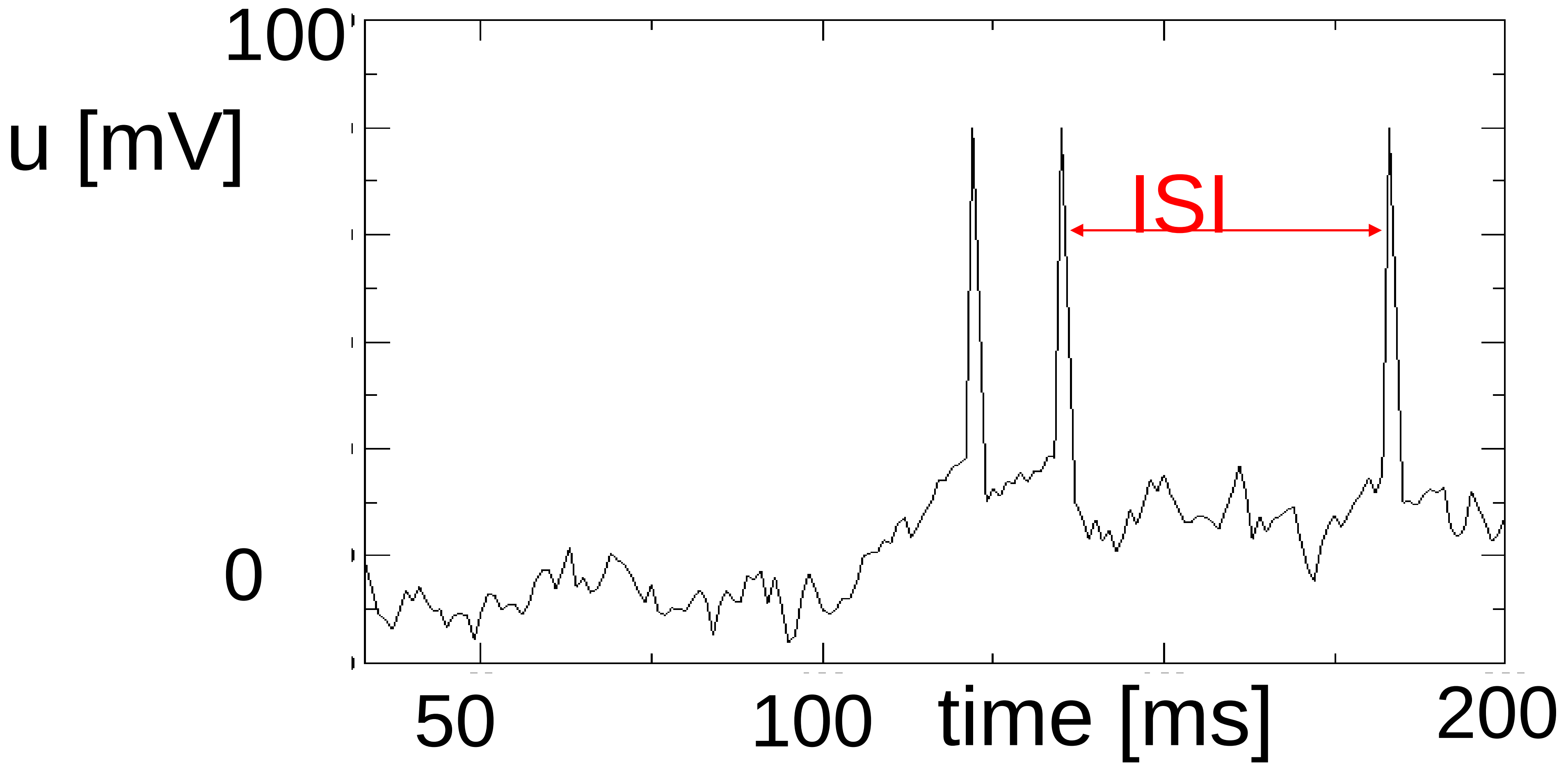


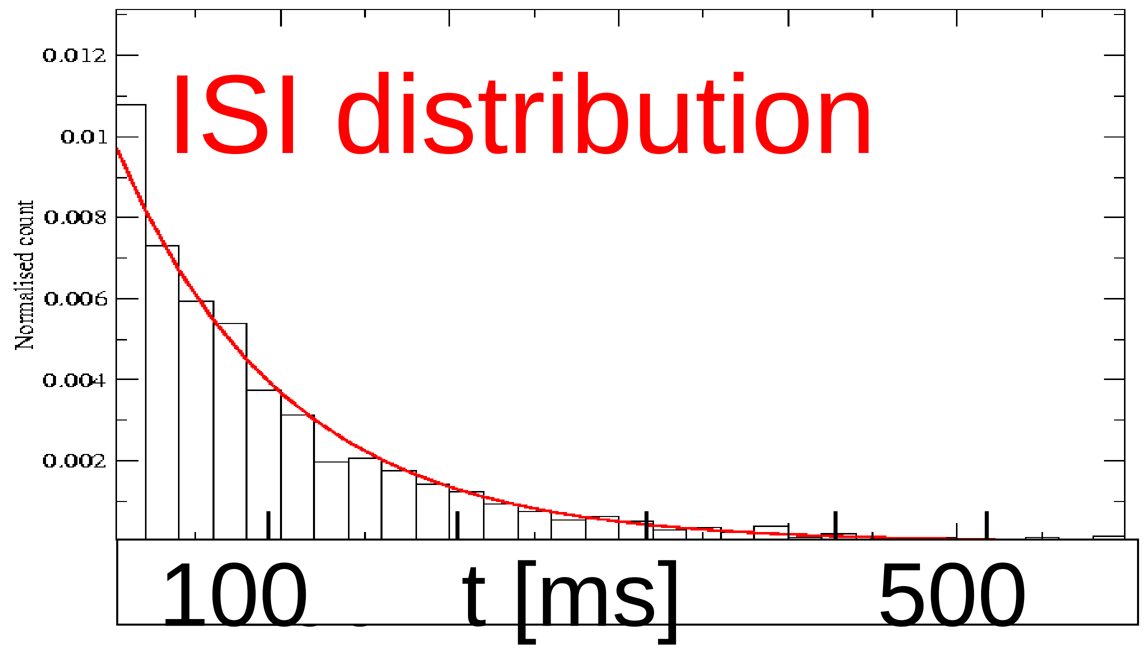
Population
- 50 000 neurons
- 20 percent inhibitory
- **randomly connected**

Neuronal Dynamics – 7.2. Interspike interval distribution

- Variability of interspike intervals (ISI)

here in simulations, but also *in vivo*

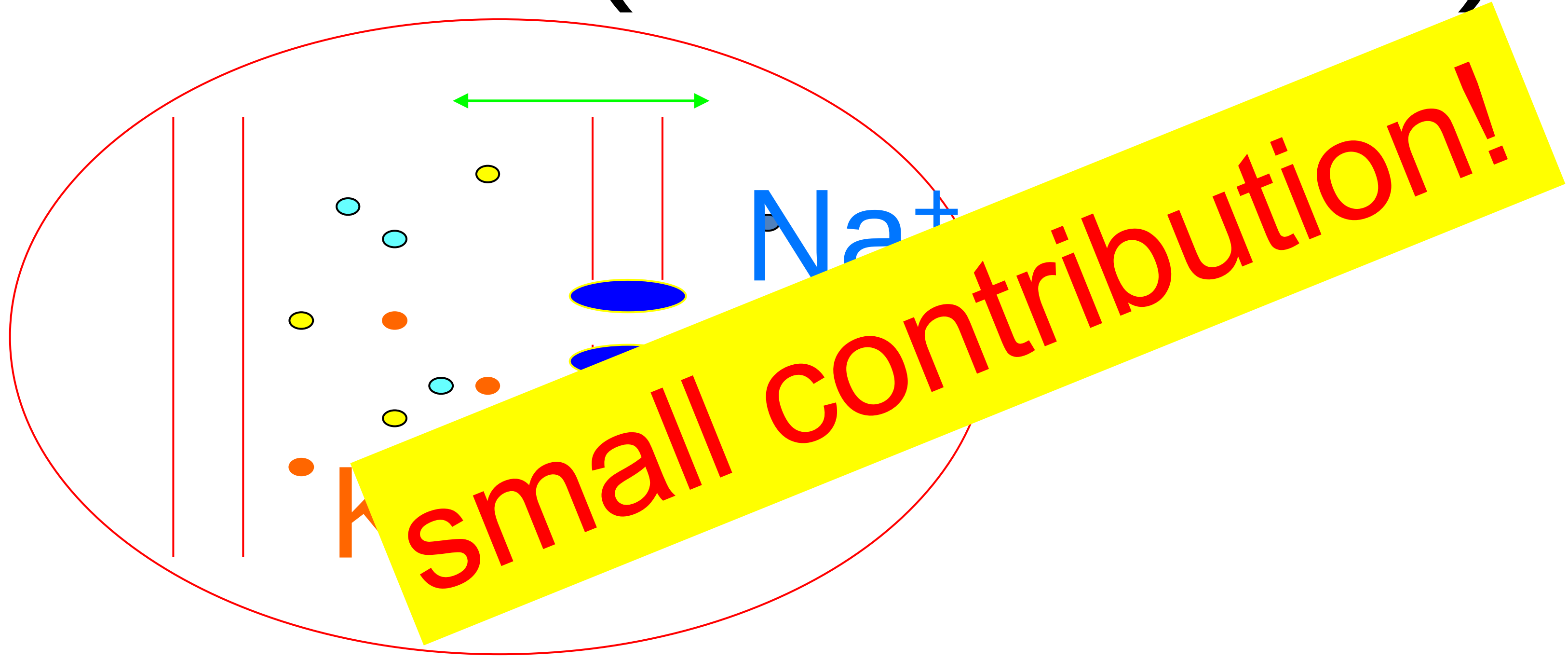




Variability of spike trains: broad ISI distribution

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

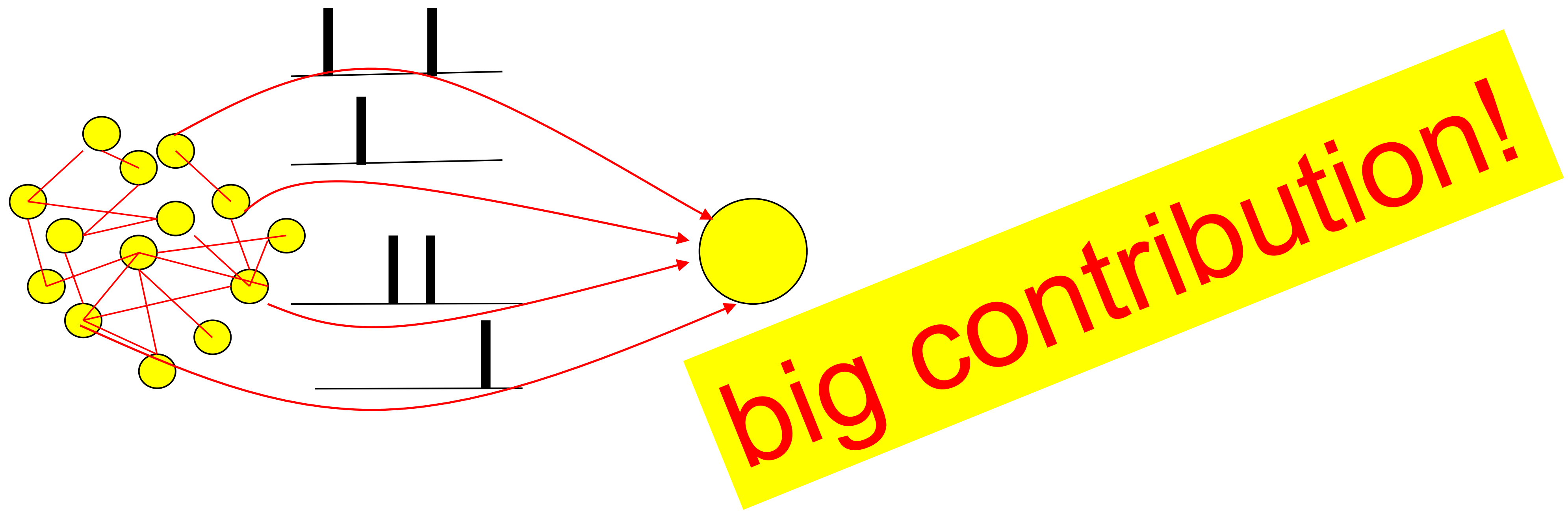
- Intrinsic noise (ion channels)



In vivo data
→ looks 'noisy'

In vitro data
→small fluctuations
→nearly deterministic

-Network noise



Neuronal Dynamics – Quiz 7.1.

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

Week 7 – part 3 : Poisson Model – rate coding

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Biological Modeling of Neural Networks

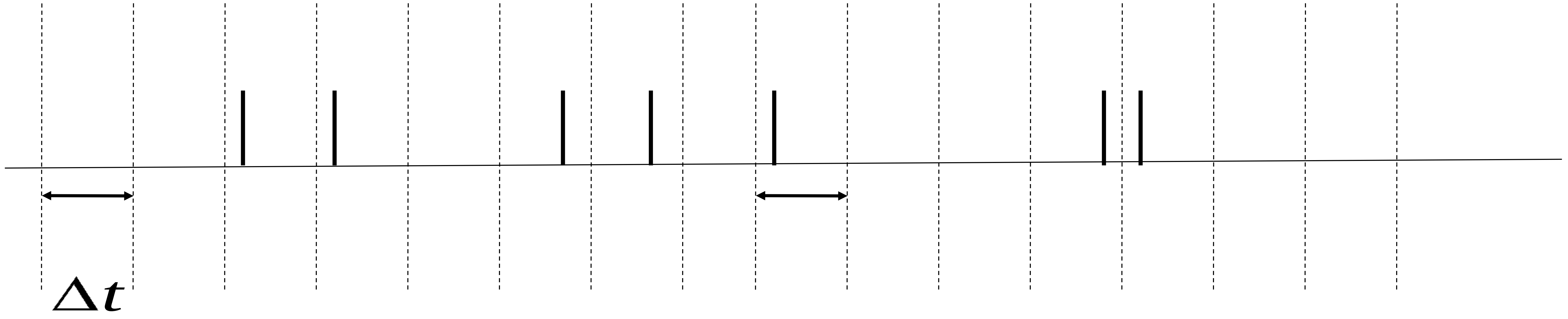
Week 7 – Variability and Noise: The question of the neural code

Wulfram Gerstner

EPFL, Lausanne, Switzerland

Homogeneous Poisson model: constant rate

Blackboard: Poisson model



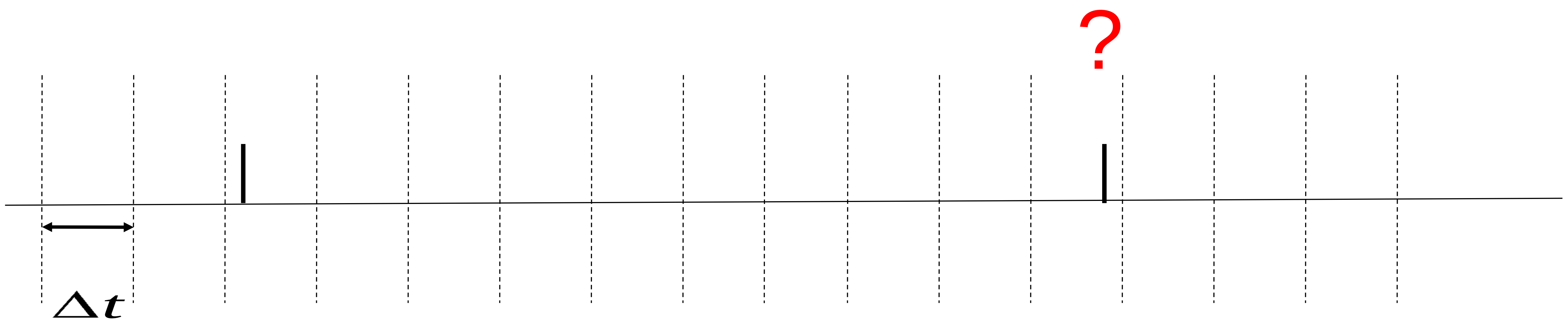
Probability of finding a spike $P_F = \rho_0 \, \Delta t$

stochastic spiking → Poisson model

Neuronal Dynamics – 7.3 Interval distribution

Probability of firing:

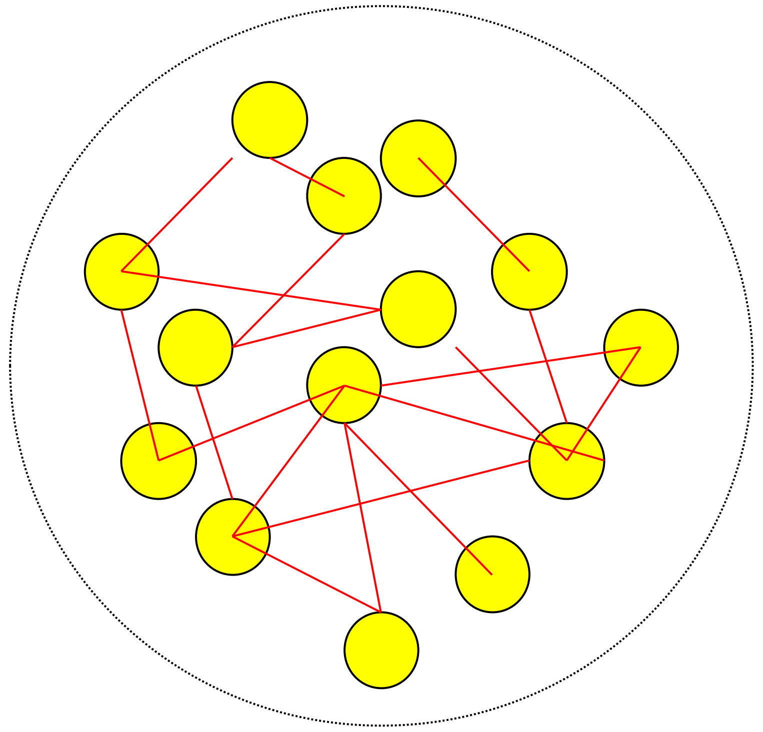
$$P_F = \rho_0 \, \Delta t$$



(i) Continuous time

prob to 'survive'

$$\Delta t \to 0$$



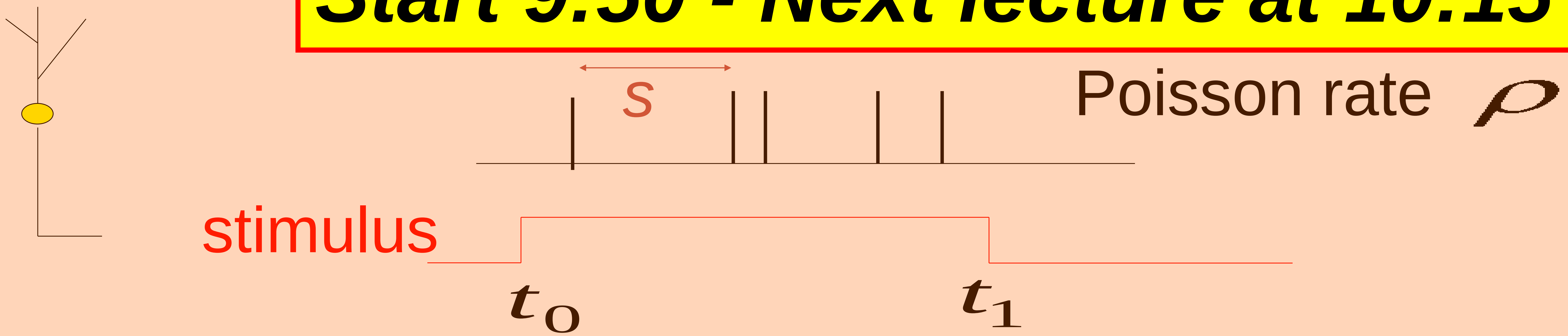
(ii) Discrete time steps

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 7 – part 3 : Poisson Model – rate coding

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Biological Modeling of Neural Networks

Week 7 – Variability and Noise: The question of the neural code

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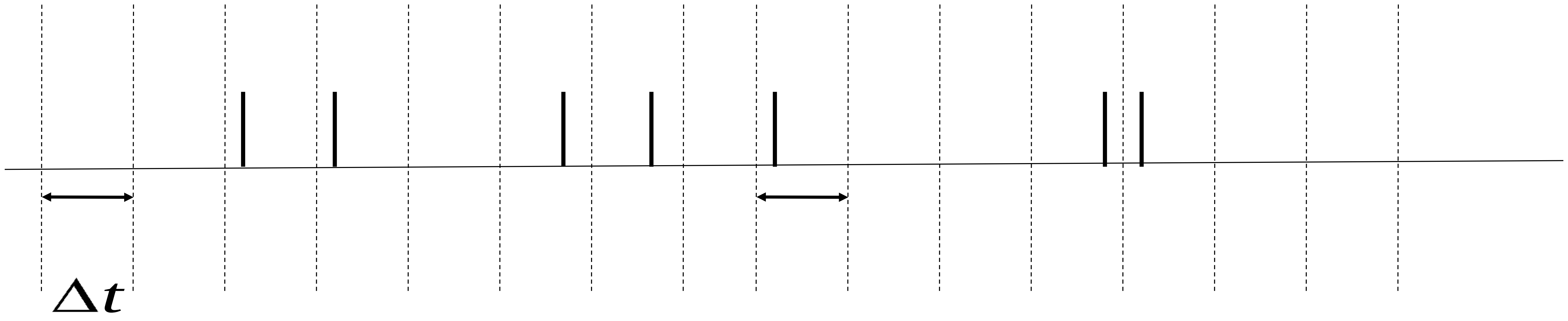
EPFL, Lausanne, Switzerland

rate changes



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

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

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

Neuronal Dynamics – Quiz 7.2.

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

3 definitions

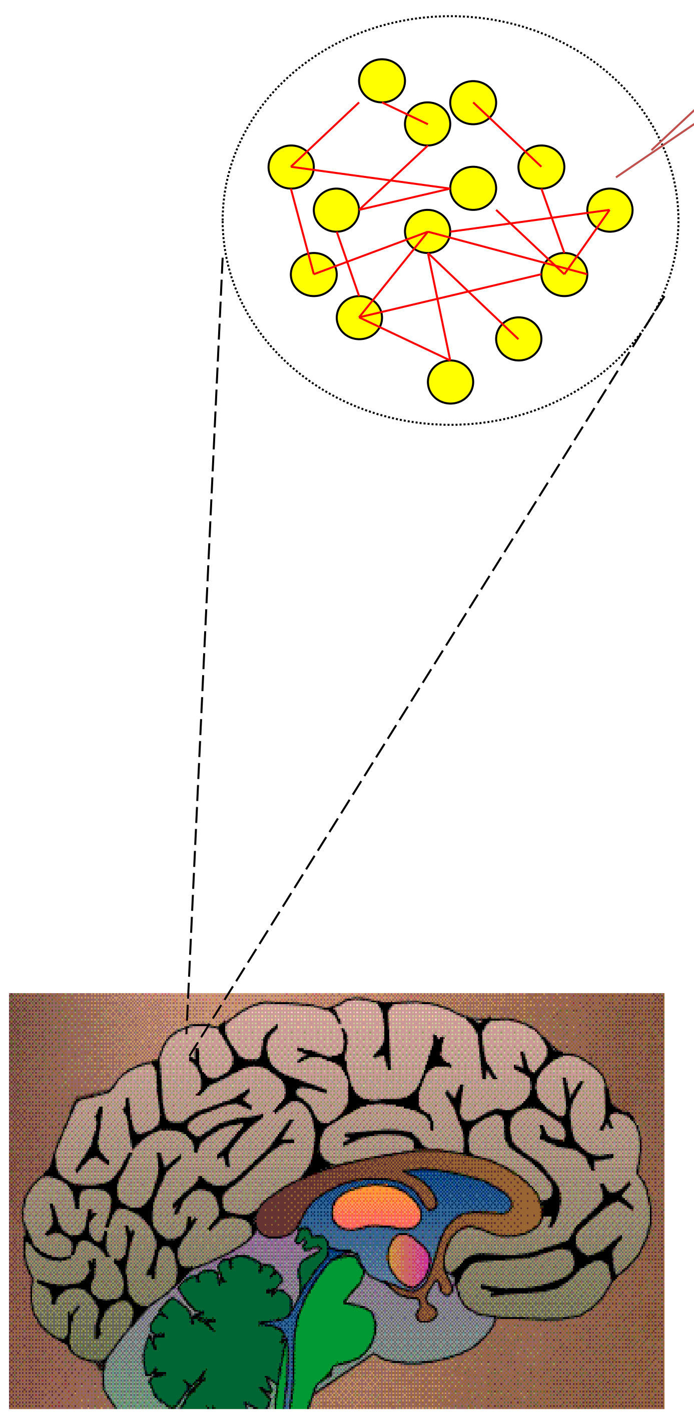
-Temporal averaging

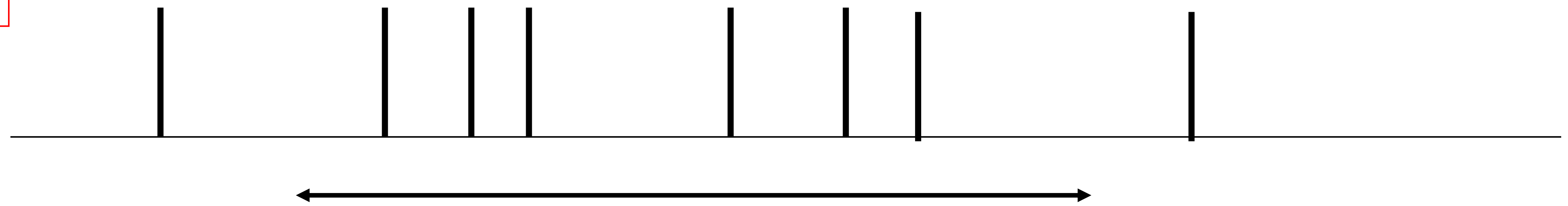
- Averaging across repetitions

- Population averaging (‘spatial’ averaging)

Neuronal Dynamics – 7.3. Rate codes: spike count

Variability of spike timing





trial 1

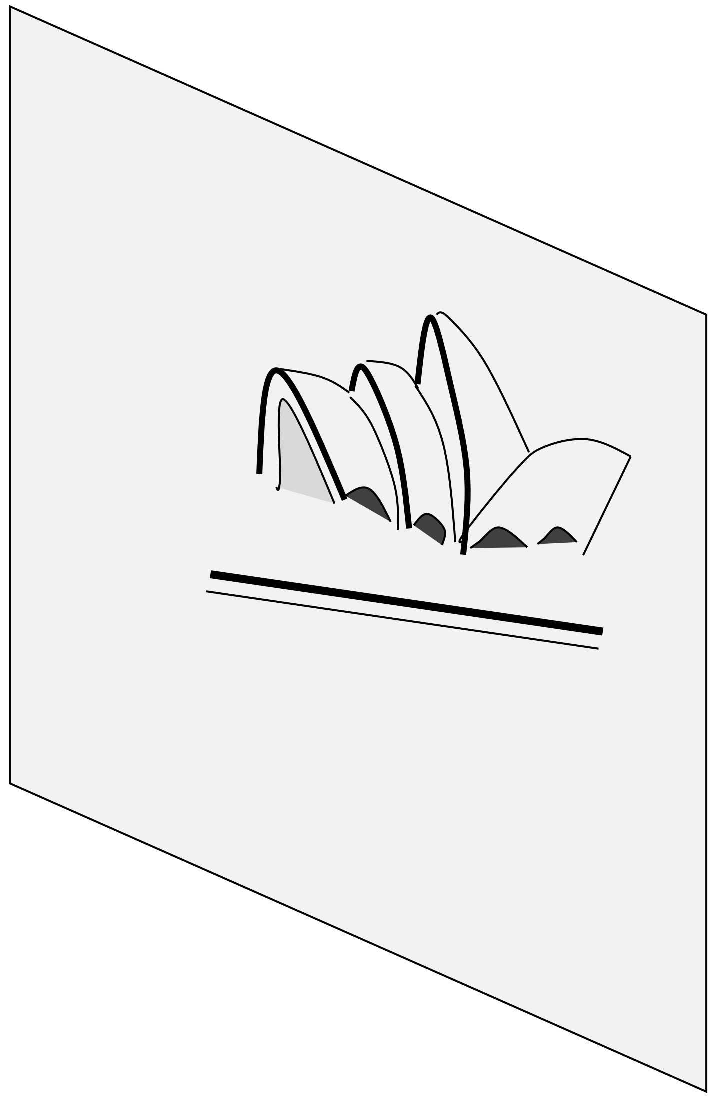
rate as a (normalized) spike count:

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

single neuron/single trial:
temporal average

T=1s

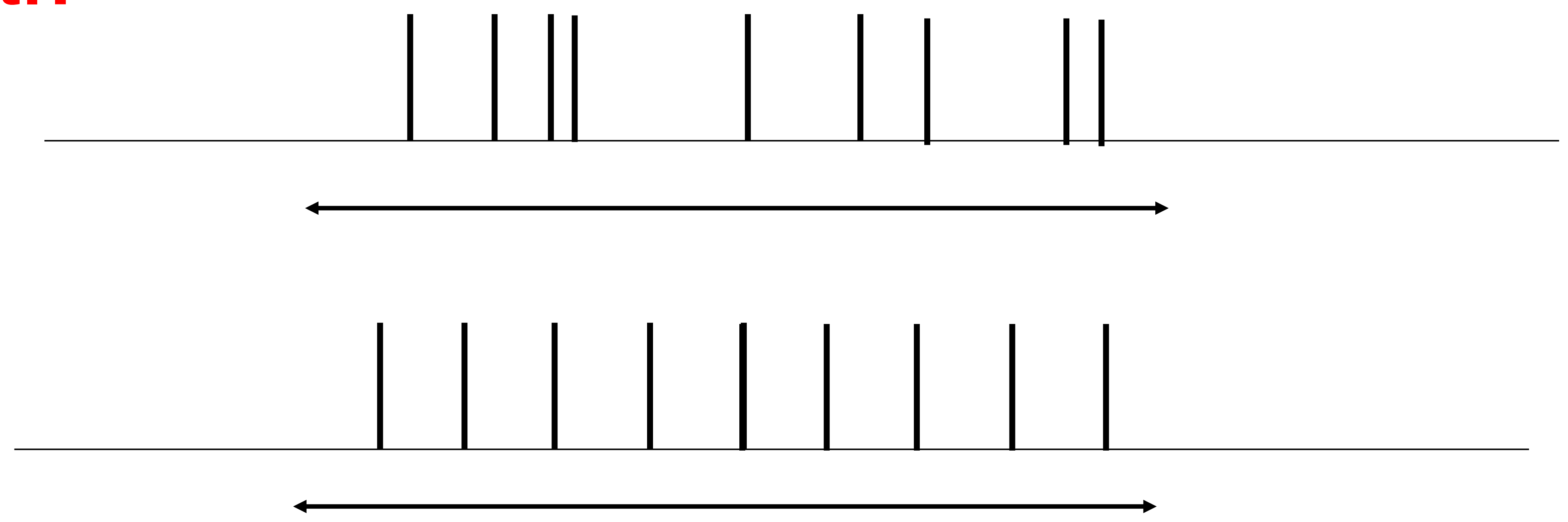
Brain



stim

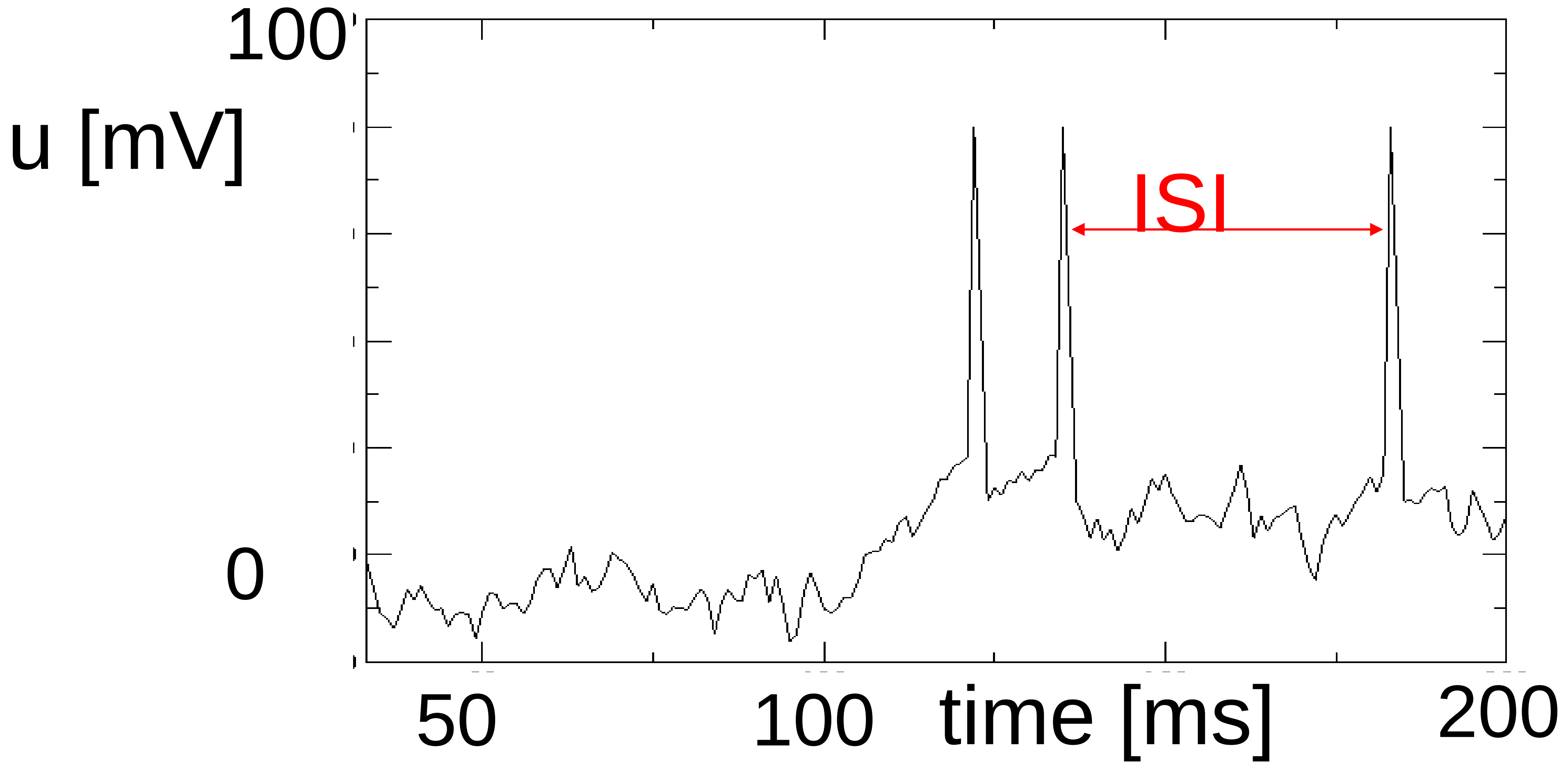
Neuronal Dynamics – 7.3. Rate codes: spike count

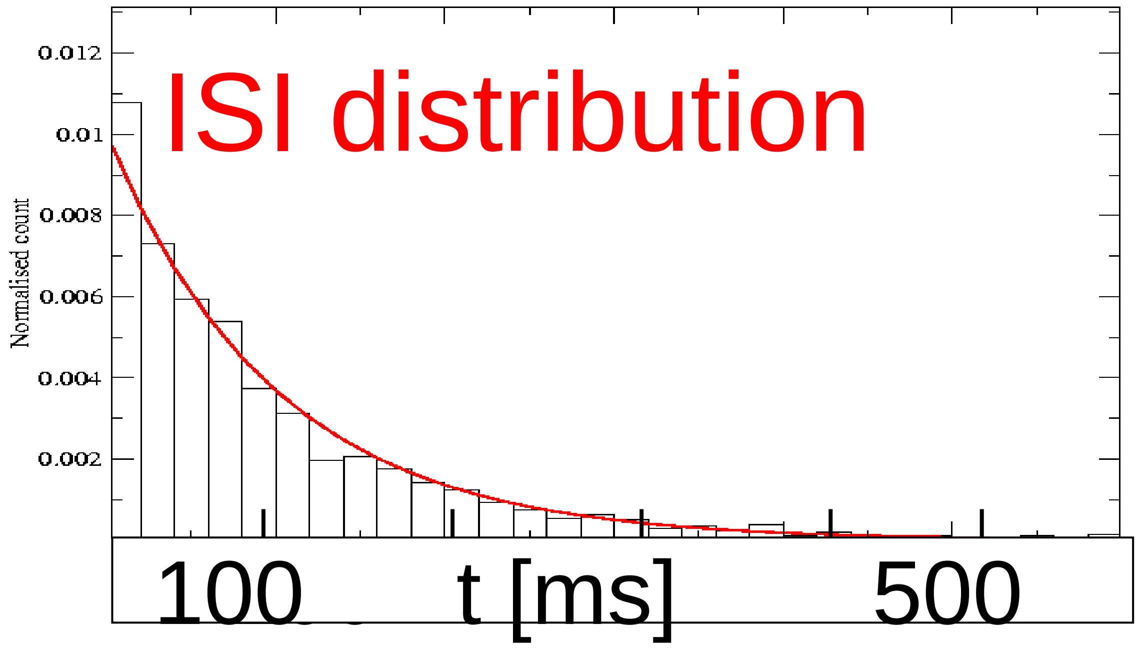
single neuron/single trial:
temporal average



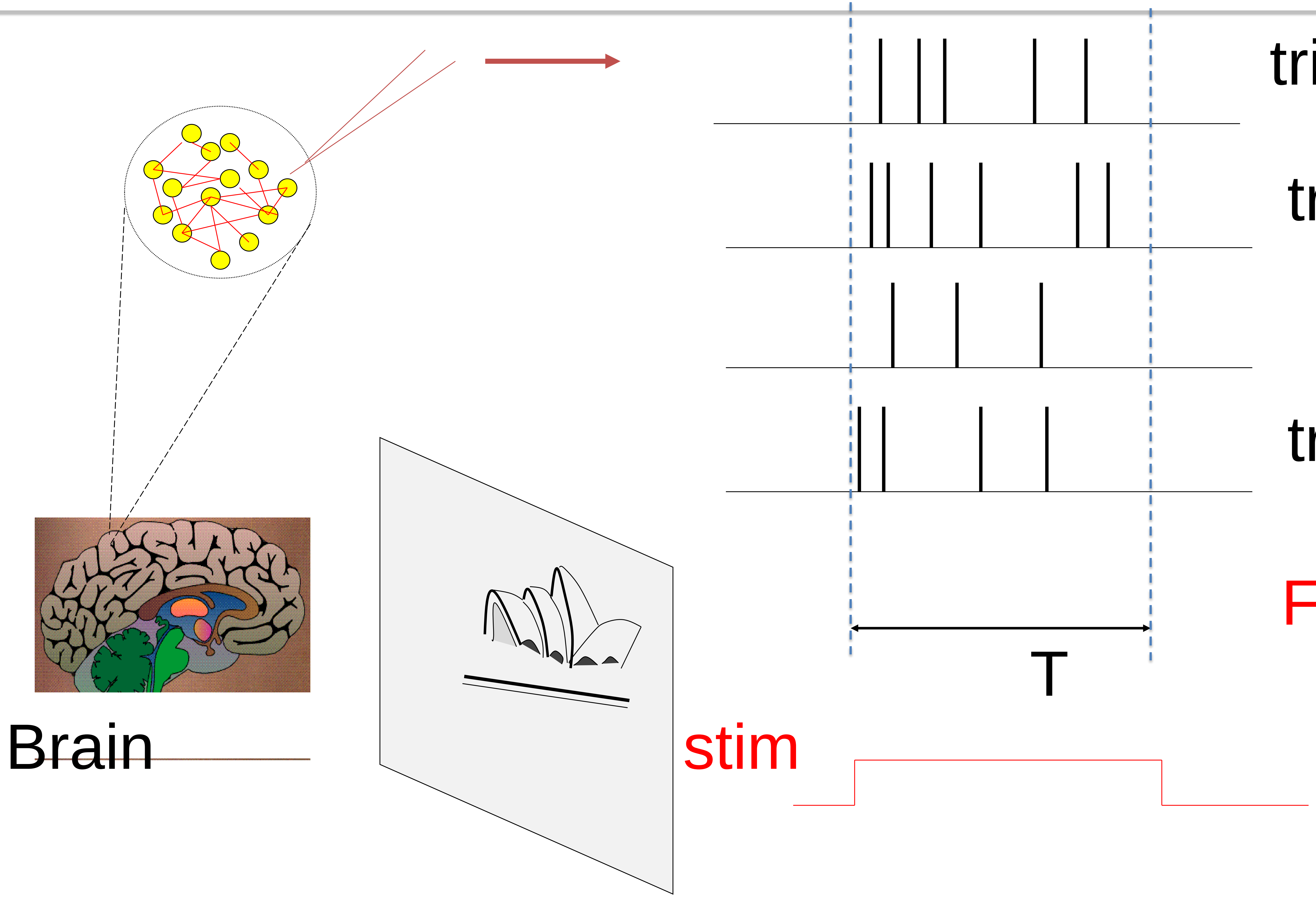
$$\nu(t) = \frac{n^{sp}}{T}$$

Variability of interspike intervals (ISI) measure regularity





Neuronal Dynamics – 7.3. Spike count: FANO factor



trial 1 $\quad n_1^{sp} = 5$

trial 2 $\quad n_2^{sp} = 6$

trial K $\quad n_K^{sp} = 4$

Fano factor

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

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)

3 definitions

√ -Temporal averaging

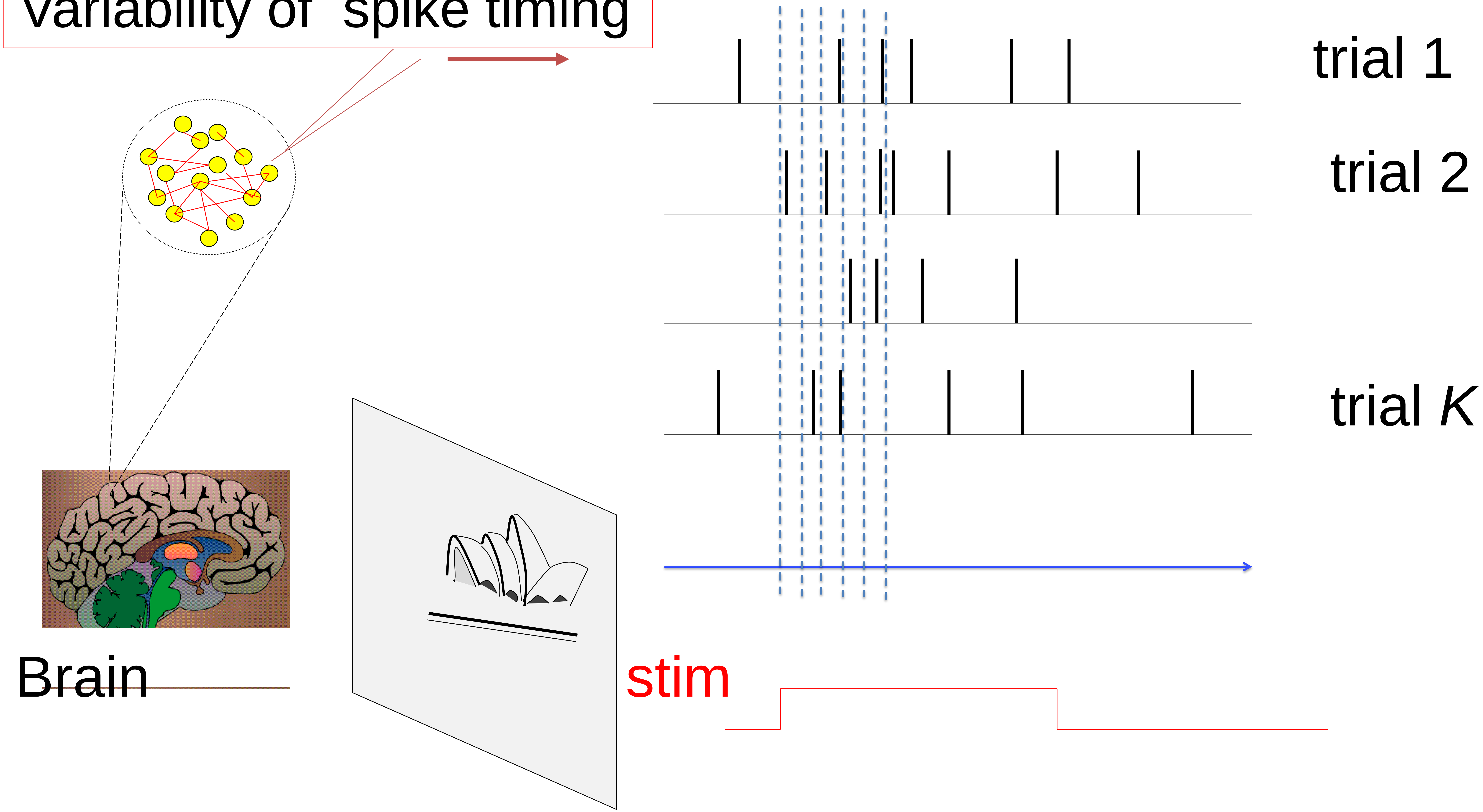
Problem: slow!!!

- Averaging across repetitions

- Population averaging

Neuronal Dynamics – 7.3. Rate codes: PSTH

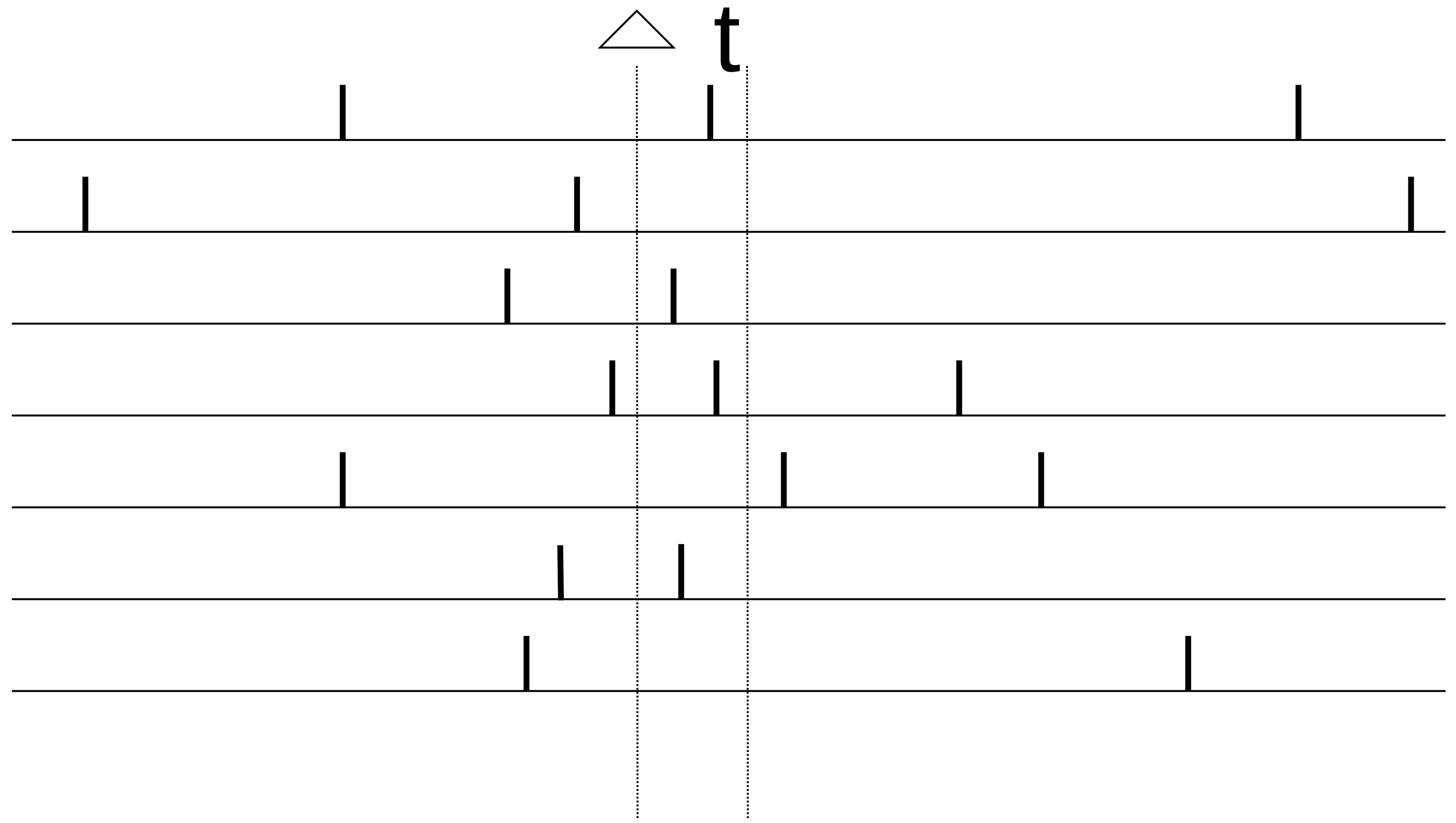
Variability of spike timing



Averaging across repetitions

single neuron/many trials: average across trials

K repetitions

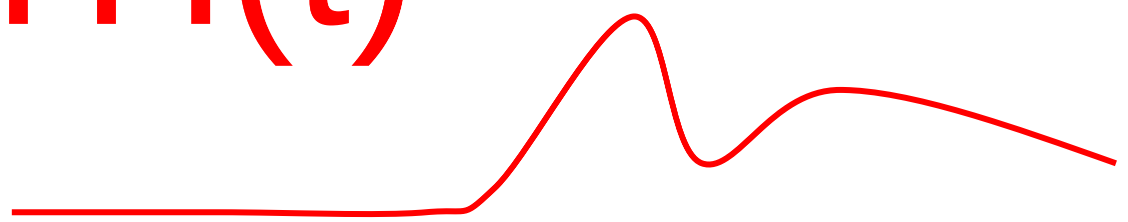


$$PSTH(t) = \frac{n(t;t+\Delta t)}{K\,\Delta t}$$

Stim(t)

K=50 trials

PSTH(t)



3 definitions

√ -Temporal averaging

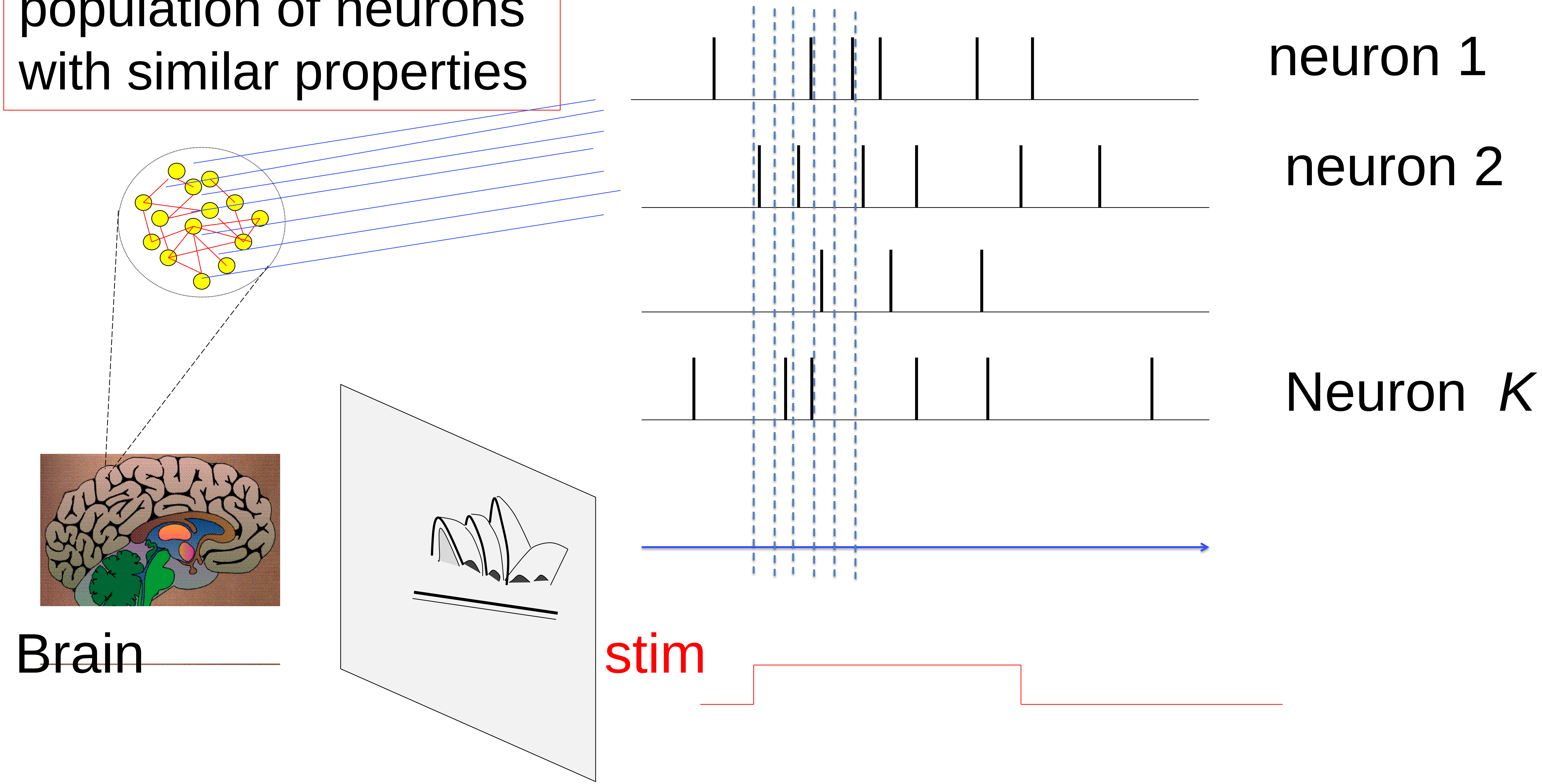
√ - Averaging across repetitions

Problem: not useful for animal!!!

- Population averaging

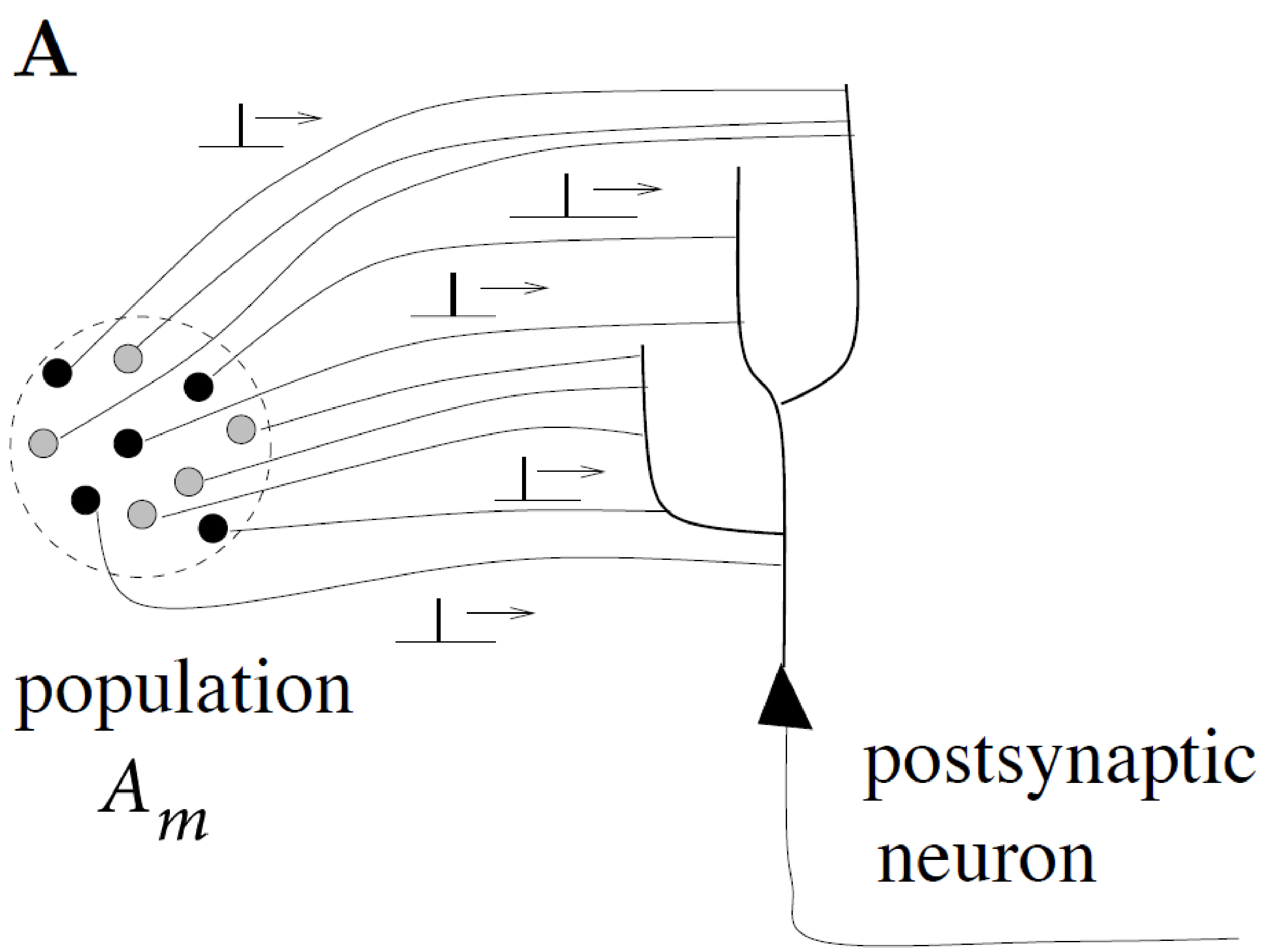
Neuronal Dynamics – 7.3. Rate codes: population activity

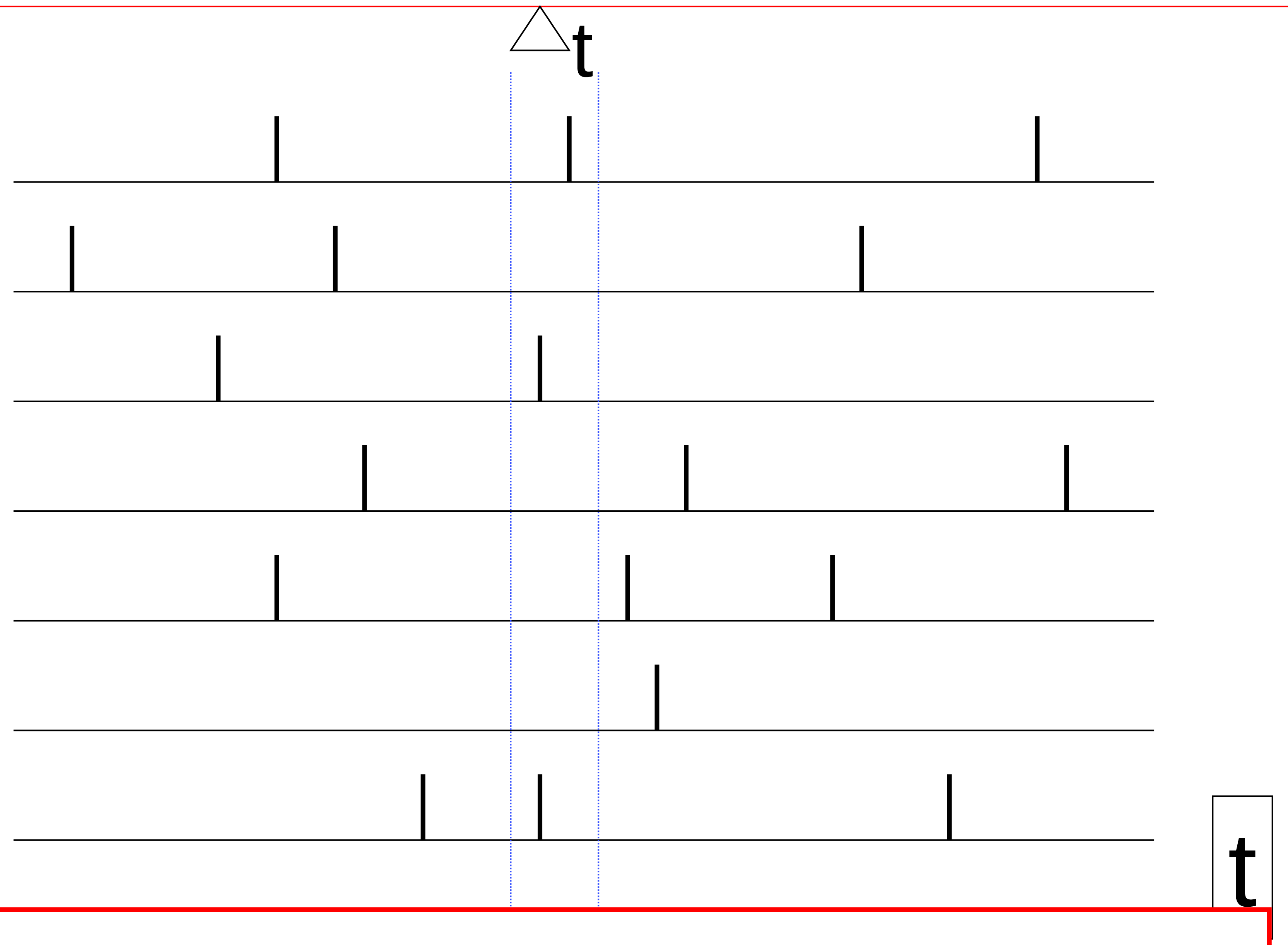
population of neurons
with similar properties



Neuronal Dynamics – 7.3. Rate codes: population activity

population activity - rate defined by population average





'natural readout'

population activity

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

Three averaging methods

-over time

Too slow for animal!!!

single neuron

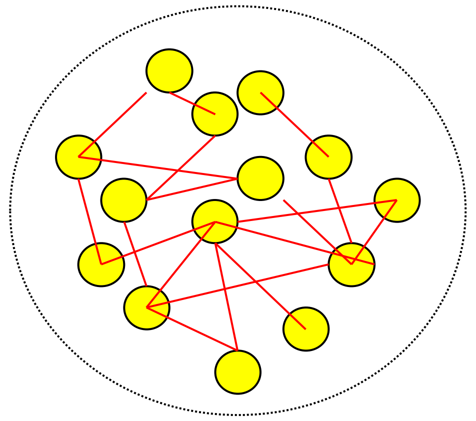
- over repetitions

single neuron

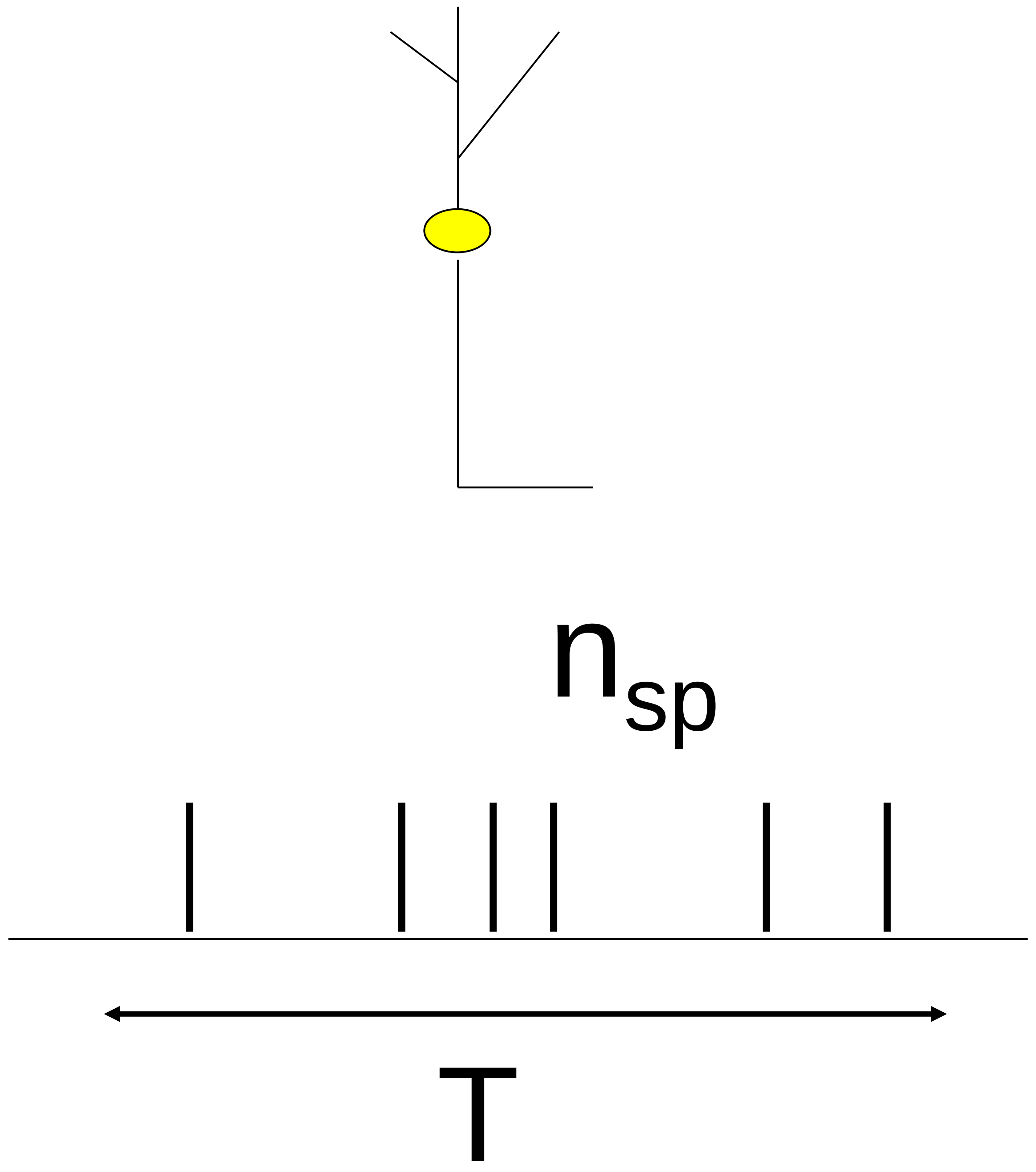
Not possible for animal!!!

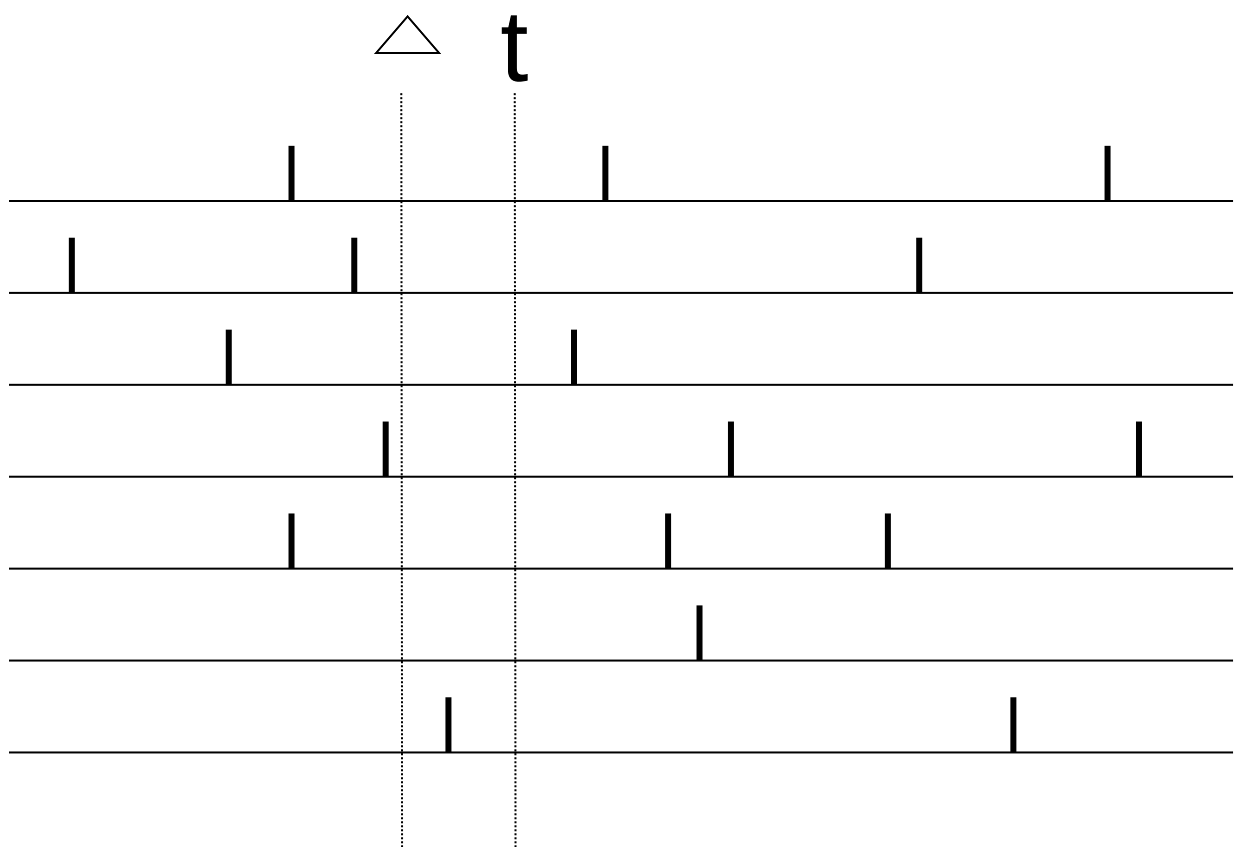
- over population (space)

many neurons

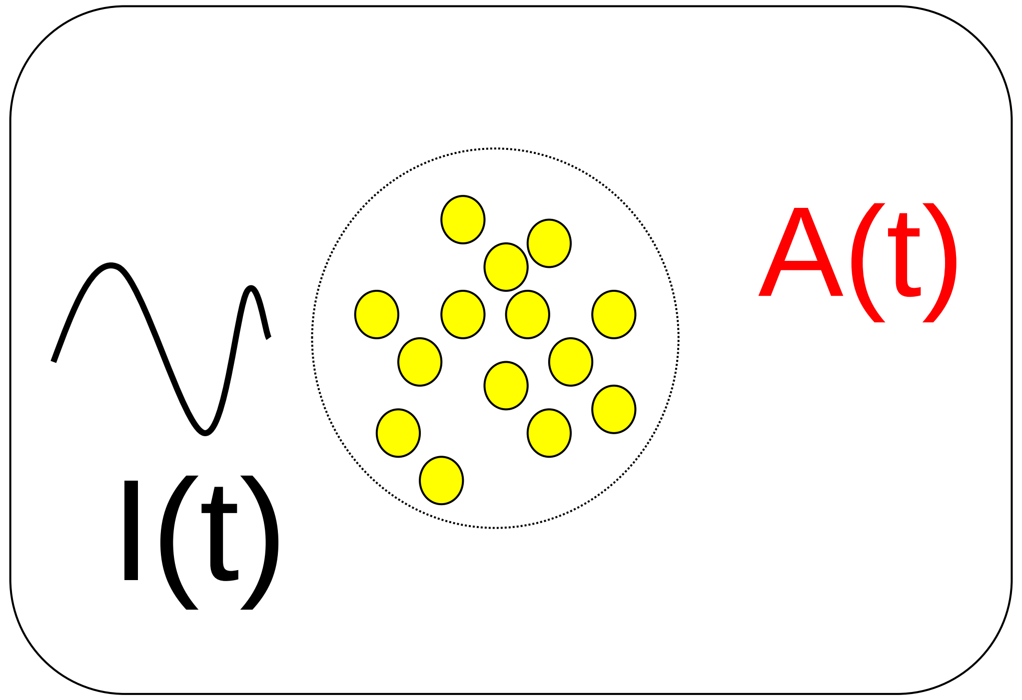


'natural'





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



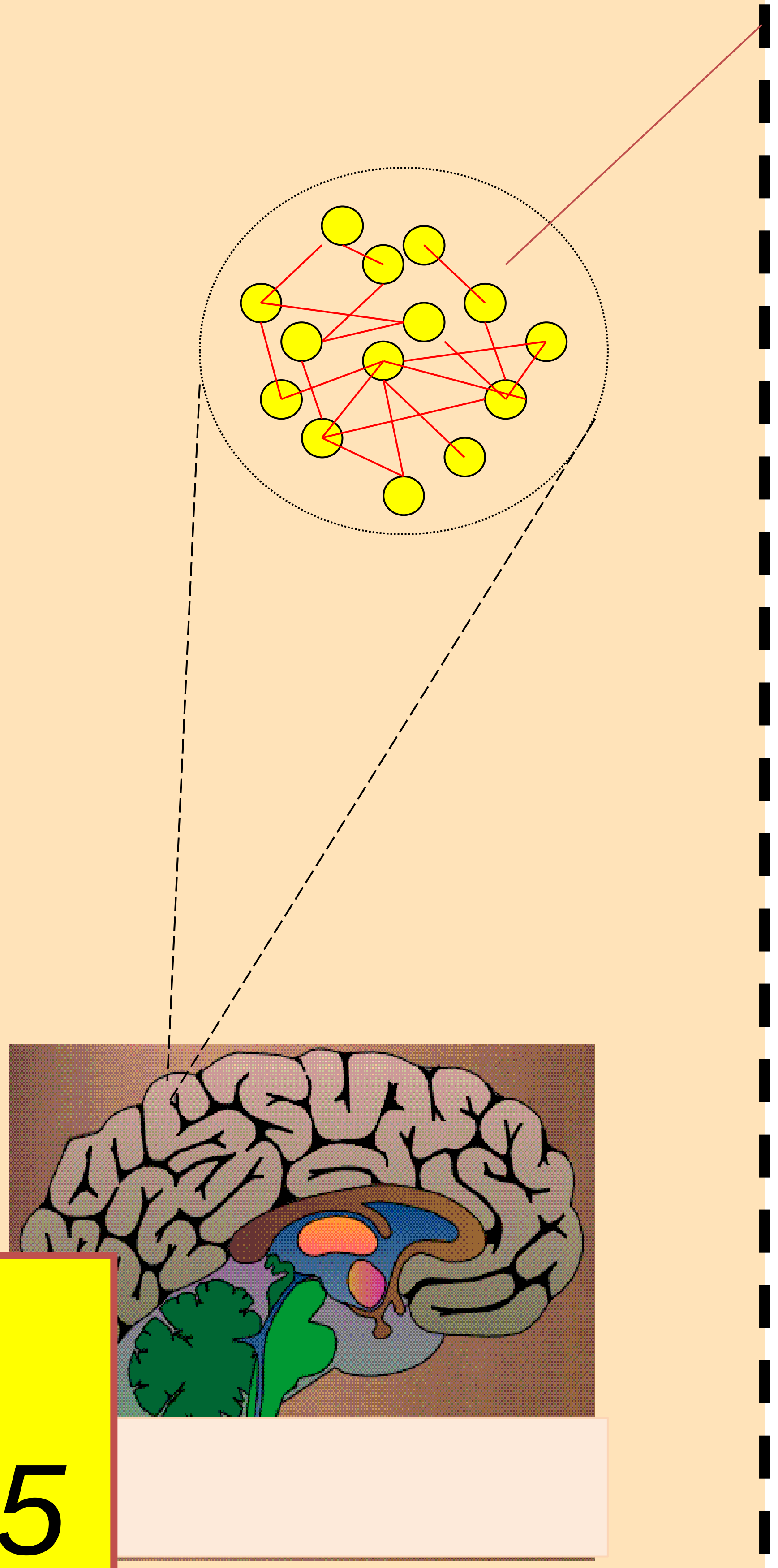
$$A(t) = \frac{n(t;t+\Delta t)}{N\Delta t}$$

population activity

inhomogeneous Poisson model consistent with rate coding

Neuronal Dynamics – Quiz 7.3.

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**. 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. Imagine the brain as a model network containing 100 000 nonlinear integrate-and-fire neurons, 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)

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.

Week 7 – part 4 :Stochastic spike arrival

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Neuronal Dynamics:
Computational Neuroscience of Single Neurons

Week 7 – Variability and Noise:
The question of the neural code

Wulfram Gerstner

EPFL, Lausanne, Switzerland

√ **7.1 Variability of spike trains**
- experiments

√ **7.2 Sources of Variability?**
- Is variability equal to noise?

√ **7.3 Three definitions of Rate code**
- Poisson Model

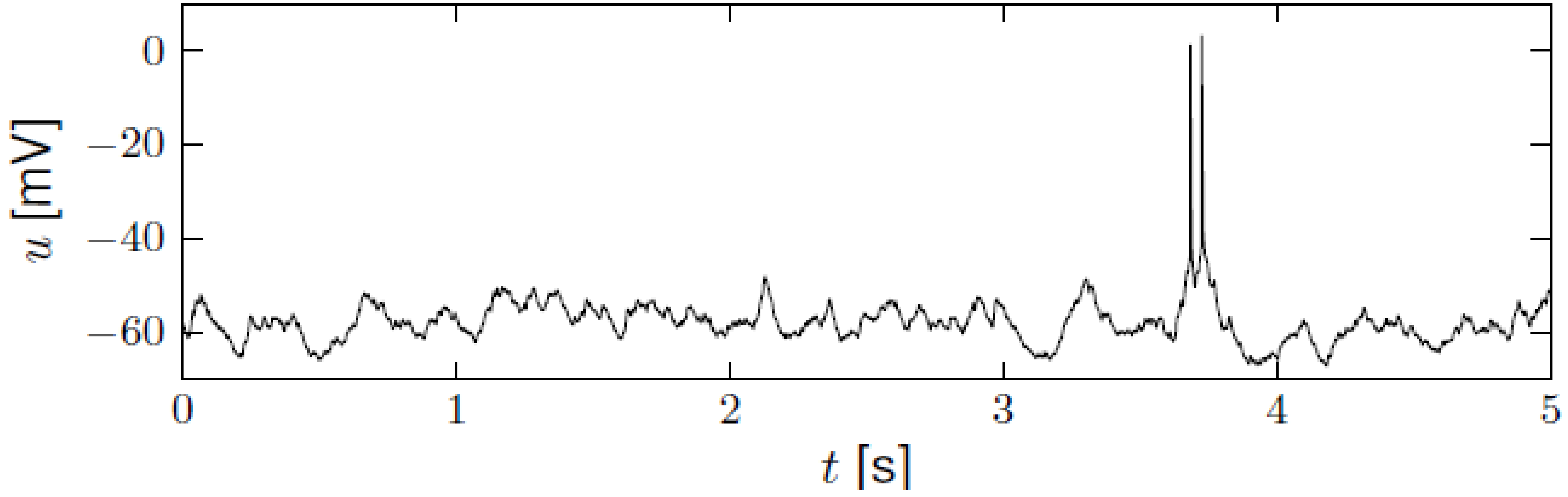
7.4 Stochastic spike arrival
- Membrane potential fluctuations

7.5. Stochastic spike firing
- stochastic integrate-and-fire

Spontaneous activity *in vivo*

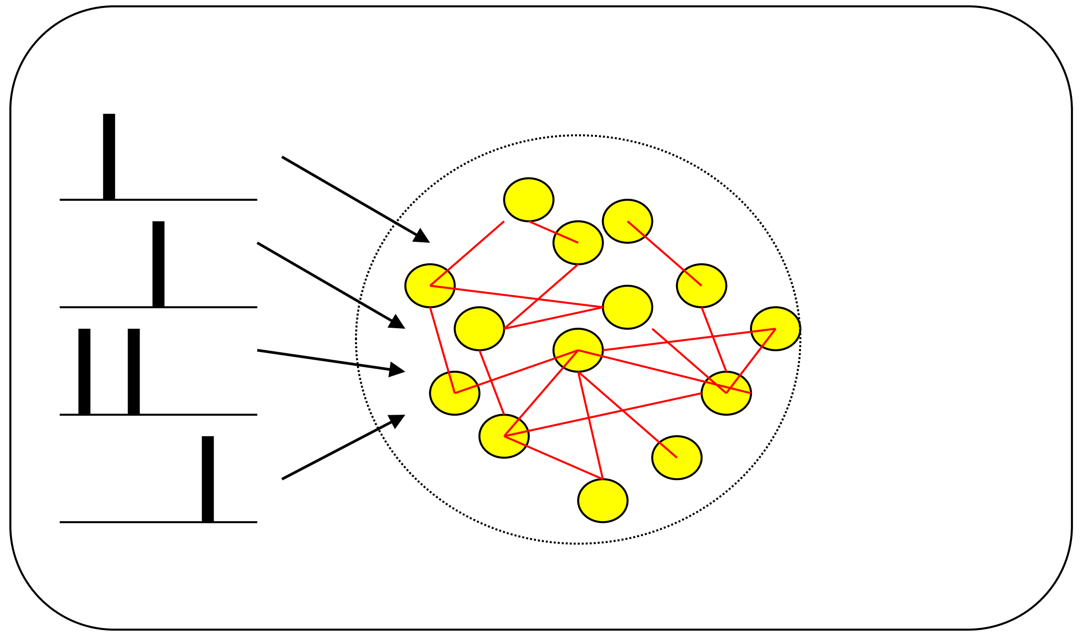
Variability
of membrane potential?

awake mouse, freely whisking,

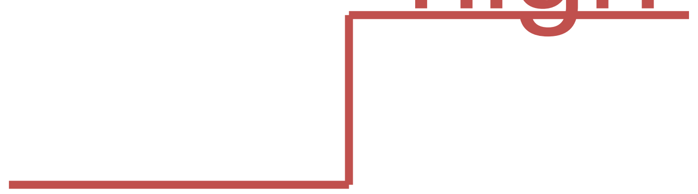


Crochet et al., 2011

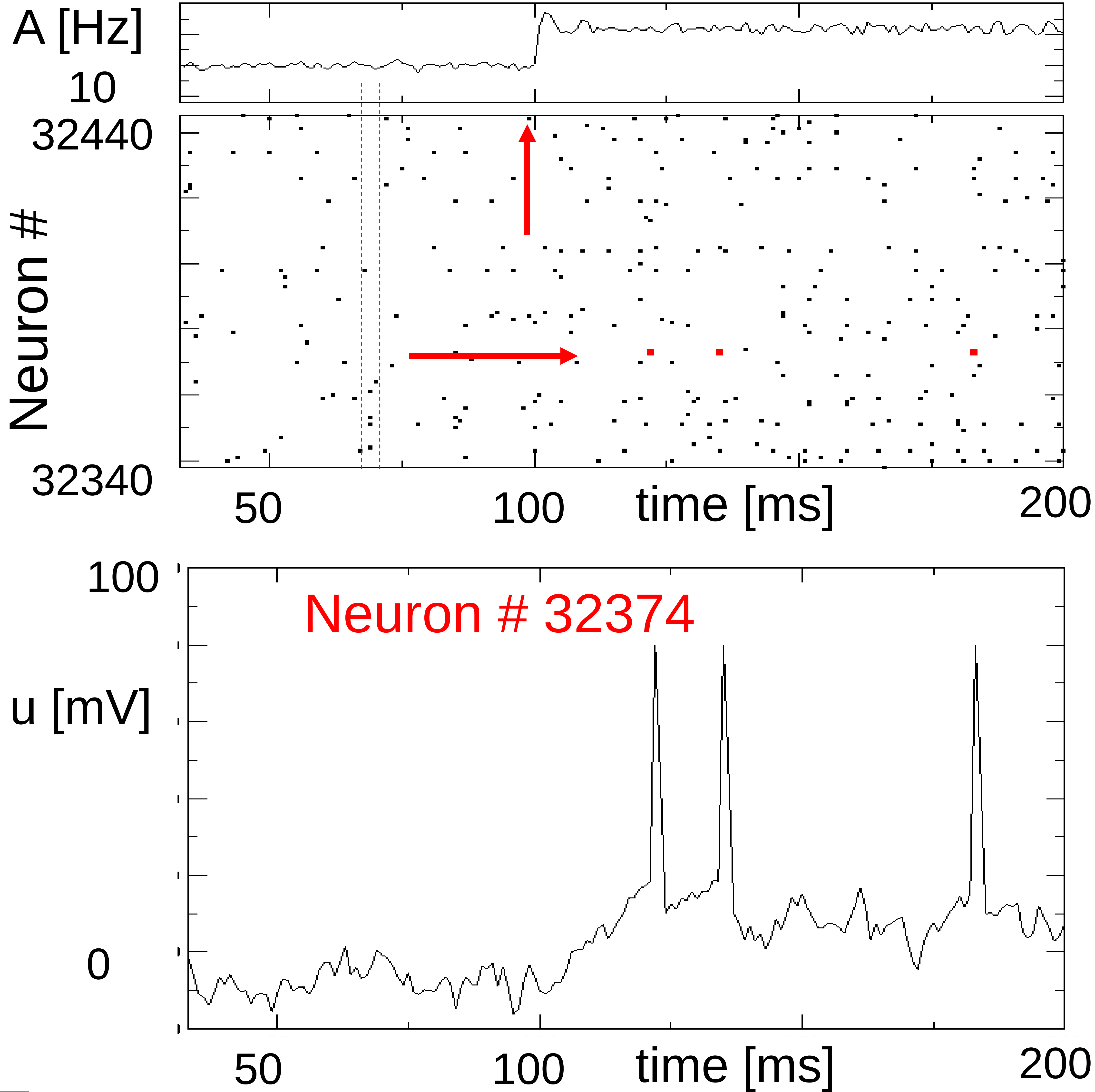
Random firing in a population of LIF neurons

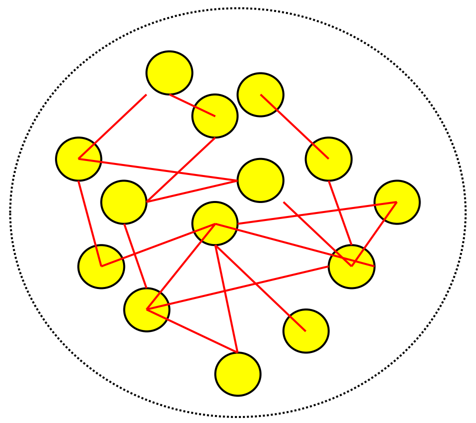


input {low rate / high rate



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

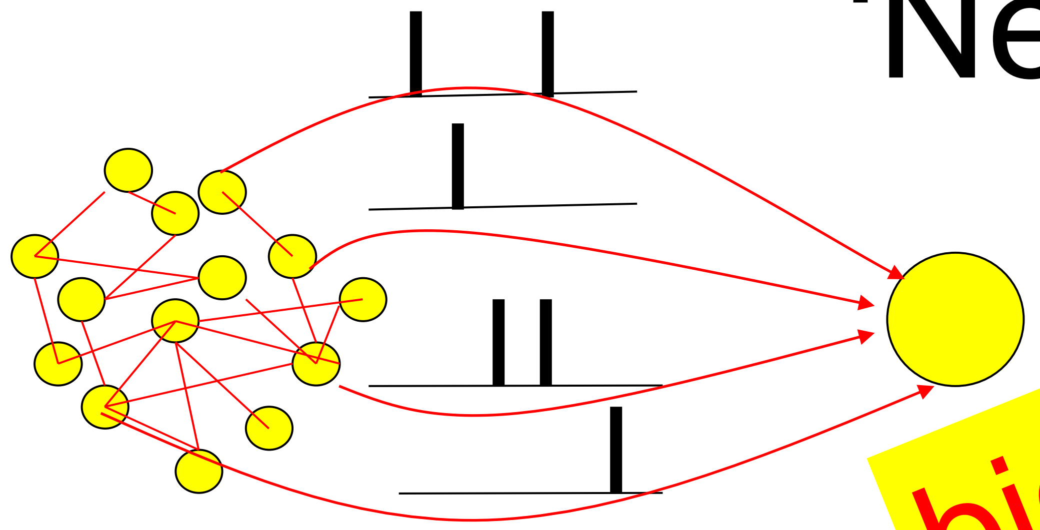




from neuron's point
of view:
stochastic spike arrival

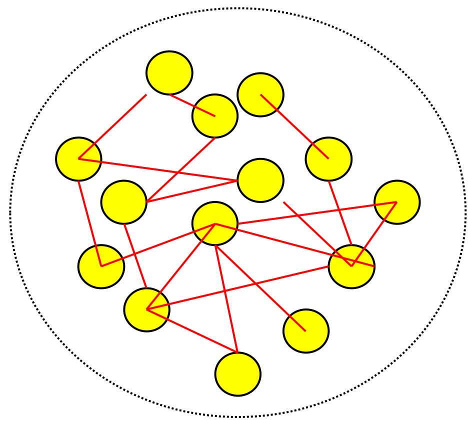
Pull out one neuron

'Network noise'



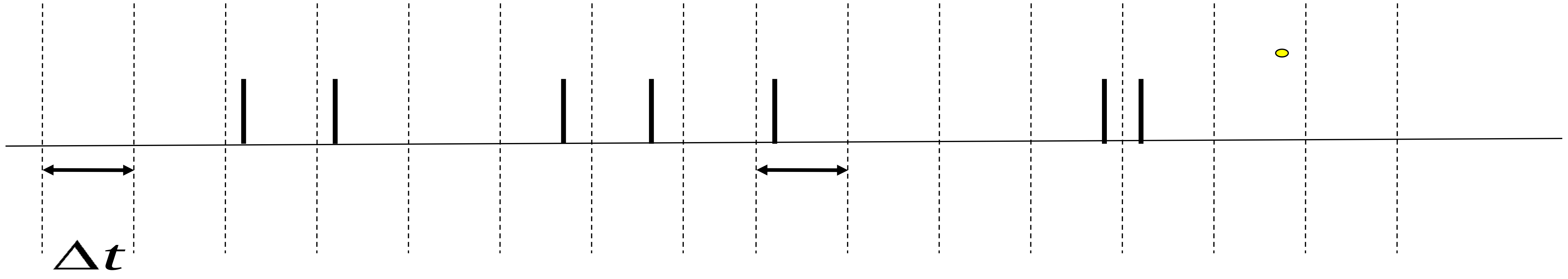
big contribution!

Neuronal Dynamics – 7.4. Stochastic Spike Arrival



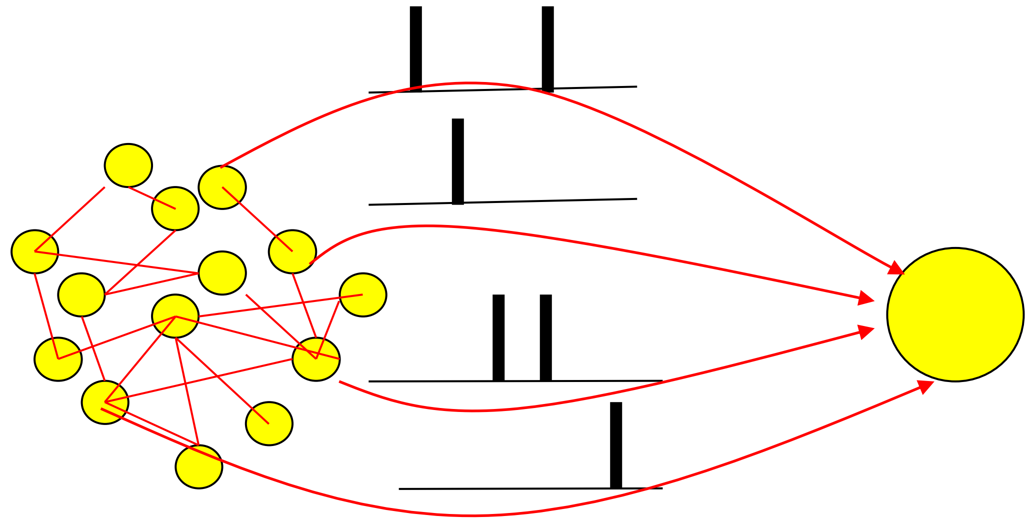
Blackboard now!

Total spike train of K presynaptic neurons



spike train

Pull out one neuron



Probability of spike arrival:

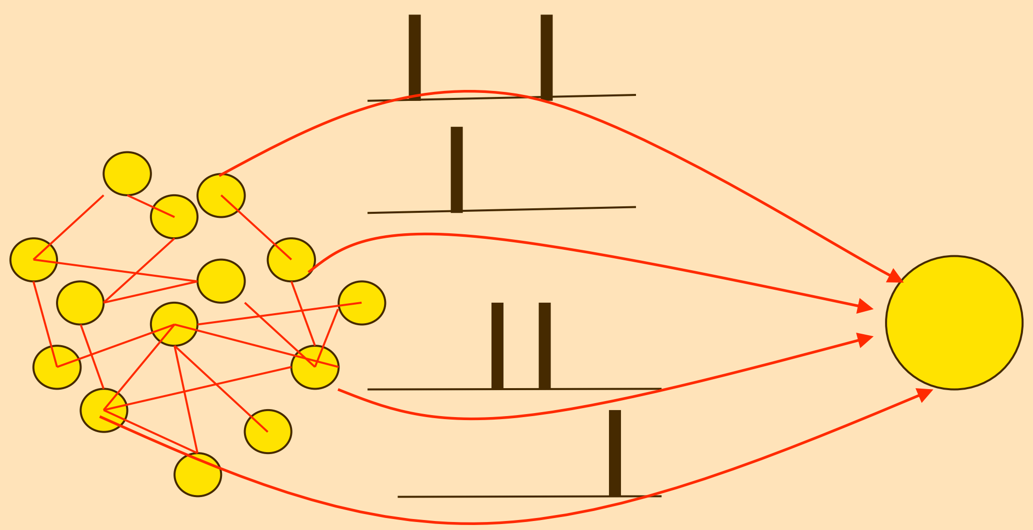
$$P_F = K \rho_0 \, \Delta t$$

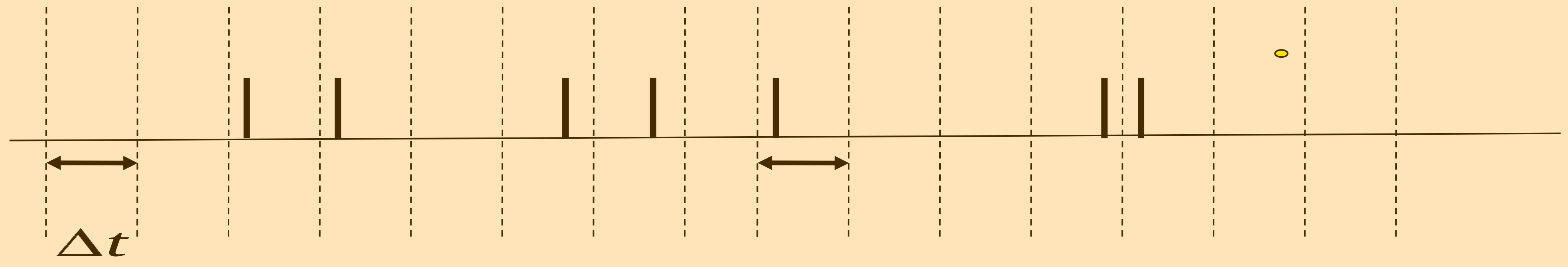
Take $\Delta t \rightarrow 0$

expectation

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

Neuronal Dynamics – Exercise 2.1 NOW





Passive membrane

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

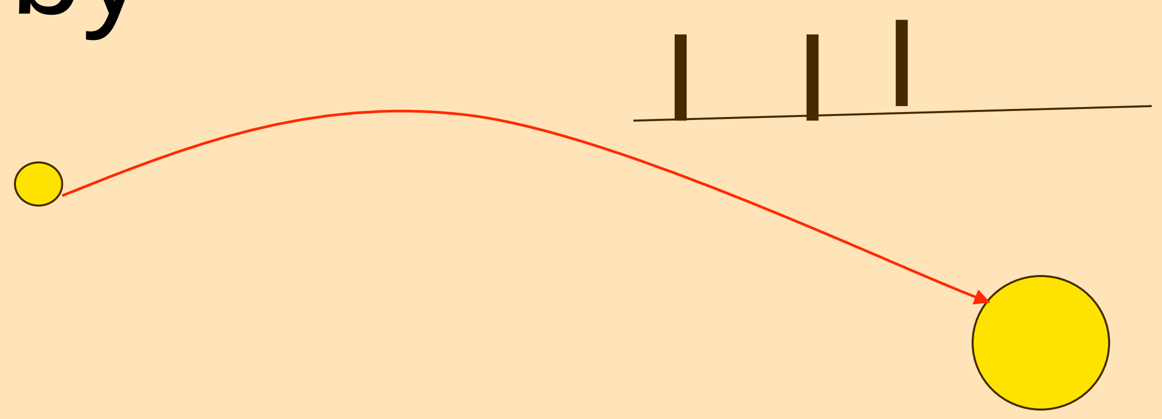
A leaky integrate-and-fire neuron without threshold (=passive membrane) receives stochastic spike arrival, described as a homogeneous Poisson process.
Calculate the **mean membrane potential**. To do so, use the above formula.

Start at 11:35,
Discussion at 11:48

Neuronal Dynamics – Quiz 7.4

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

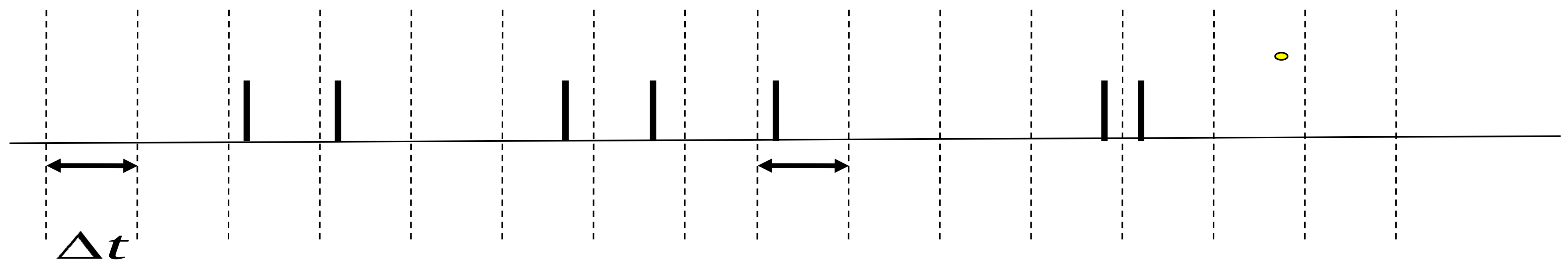
[ ] the constant *a* is equal to u_{rest}

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

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

Neuronal Dynamics – 7.4. 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

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

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

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

Week 7 – part 5 : Stochastic spike firing in integrate-and-fire models

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Biological Modeling and Neural Networks

Week 7 – Variability and Noise:
The question of the neural code

Wulfram Gerstner
EPFL, Lausanne, Switzerland

√ **7.1 Variability of spike trains**
- experiments

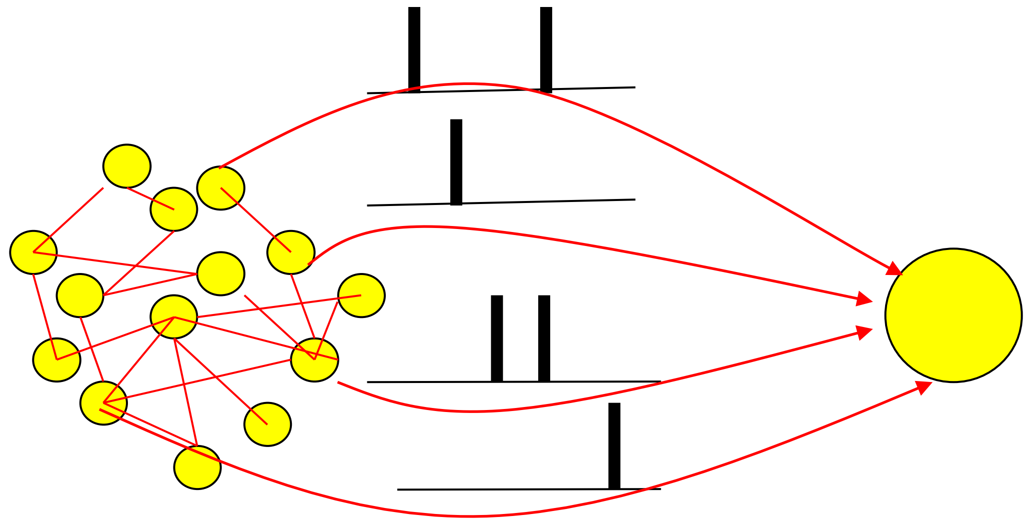
√ **7.2 Sources of Variability?**
- Is variability equal to noise?

√ **7.3 Three definitions of Rate code**
- Poisson Model

√ **7.4 Stochastic spike arrival**
- Membrane potential fluctuations

7.5. Stochastic spike firing
- Stochastic Integrate-and-fire

Neuronal Dynamics – 7.5. Fluctuation of current/potential



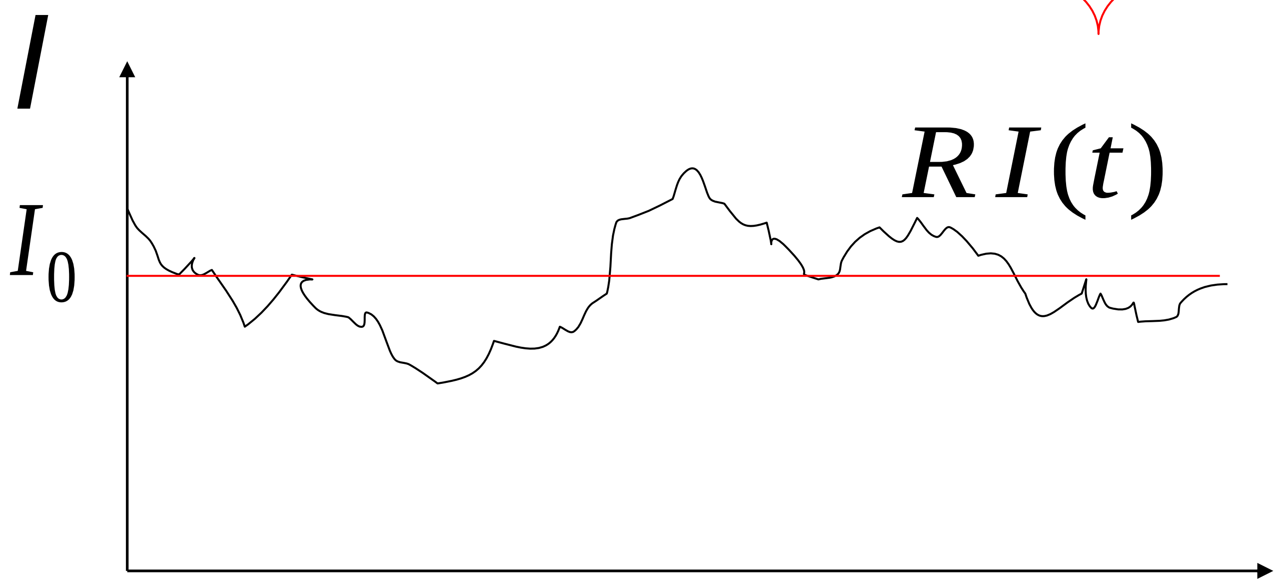
Synaptic current pulses of shape α

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

EPSC

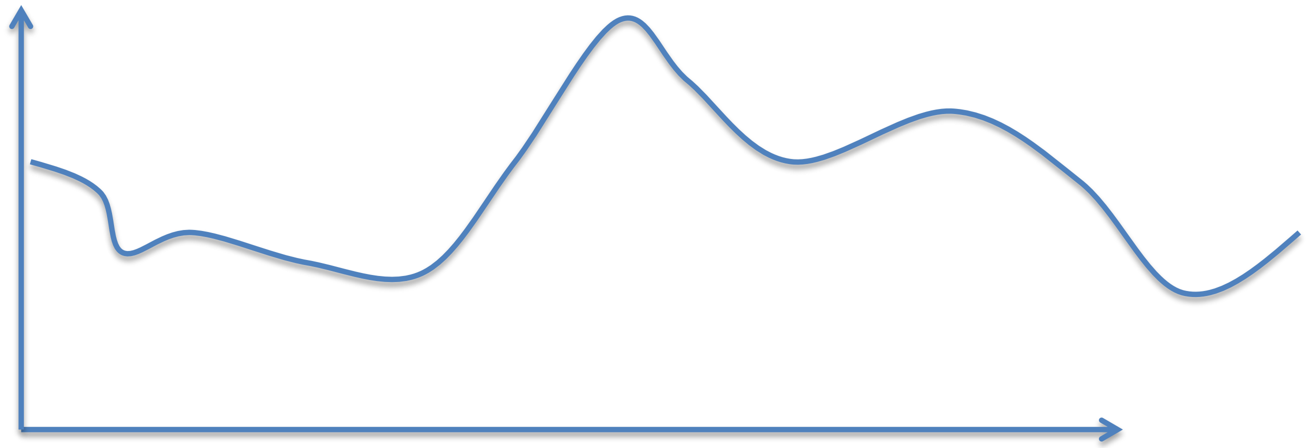
Passive membrane

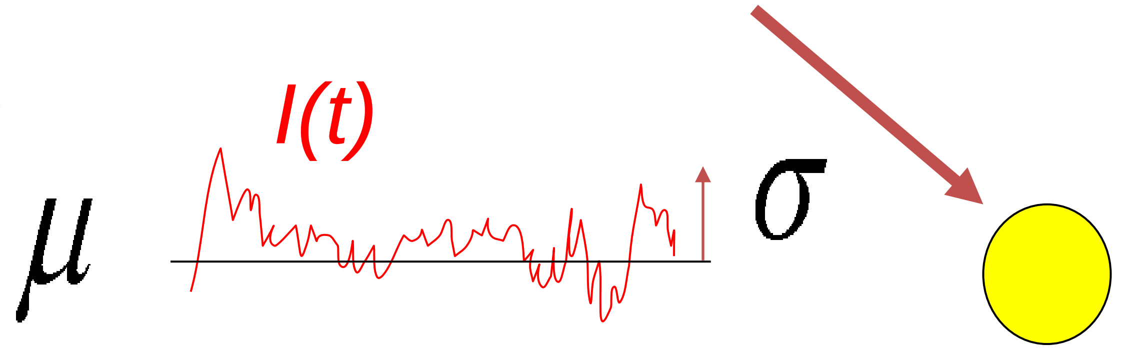
$$\tau \frac{d}{dt} u = -(u - u_{rest}) \quad + R I^{syn}(t)$$



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

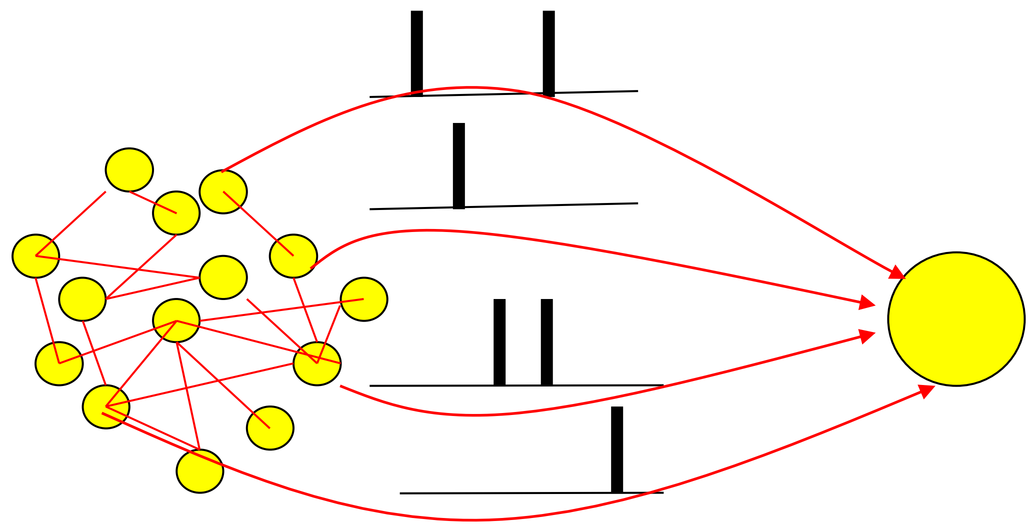
→ Fluctuating potential





Fluctuating input current

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

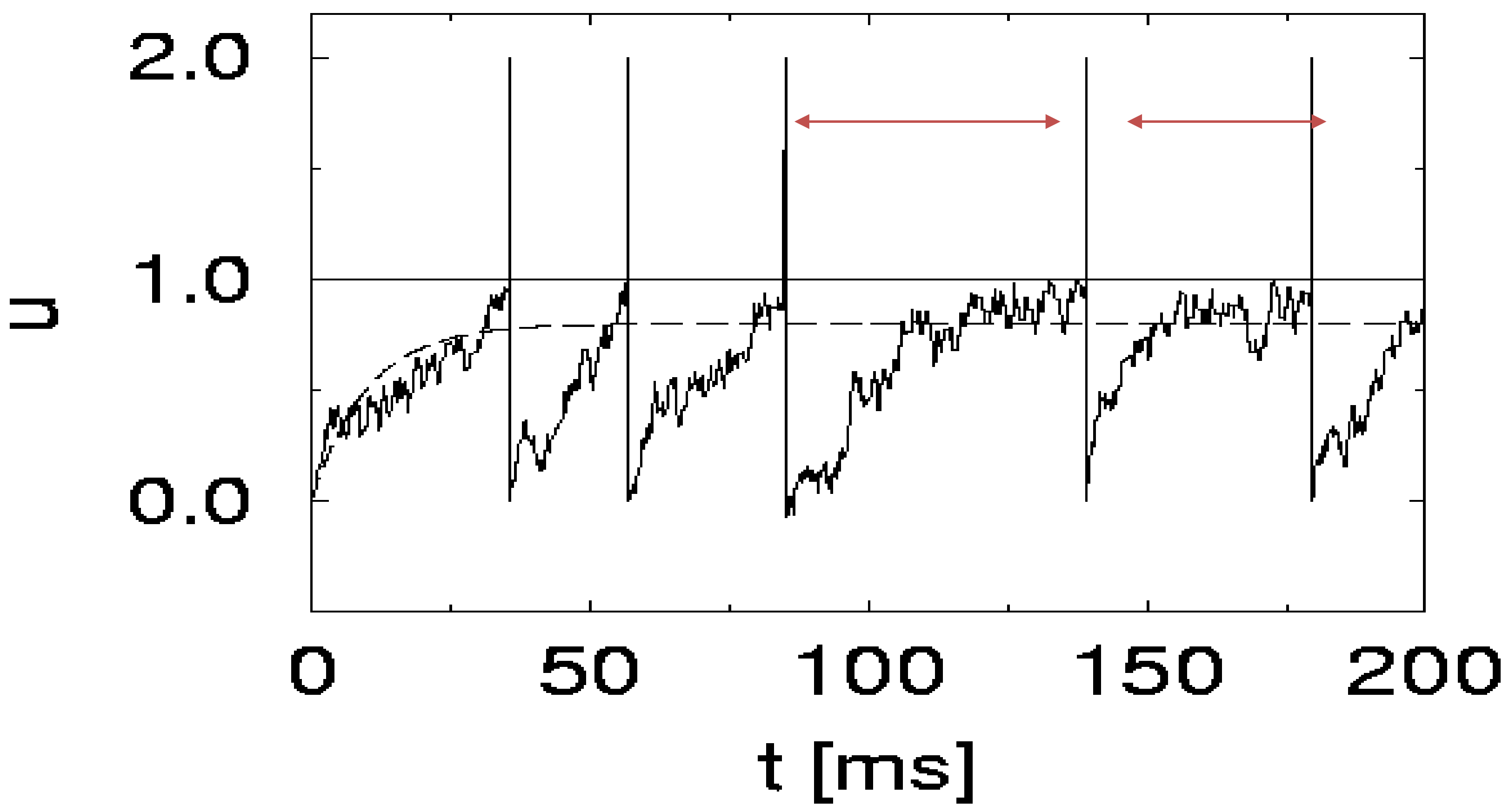


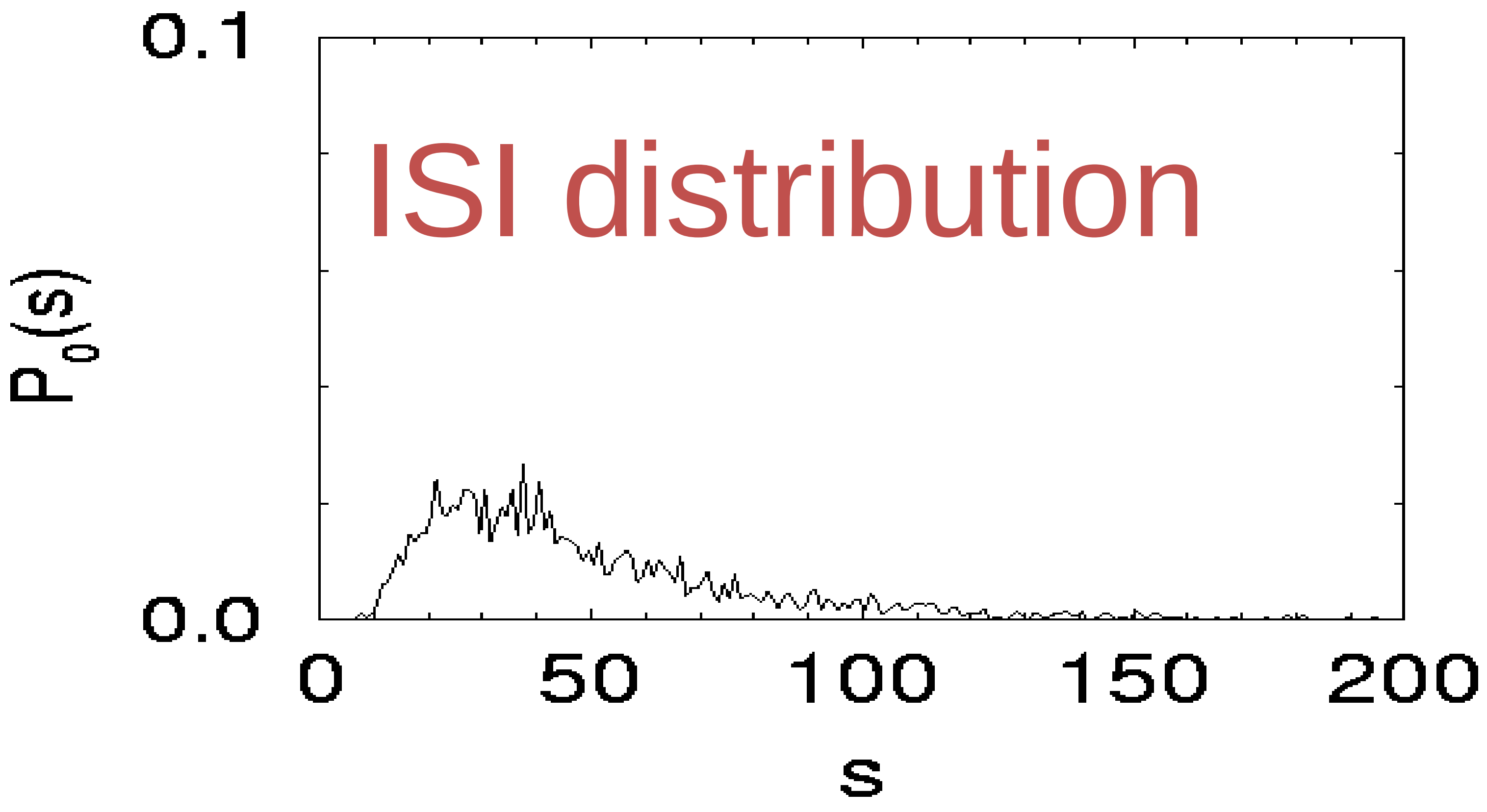
Passive membrane

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

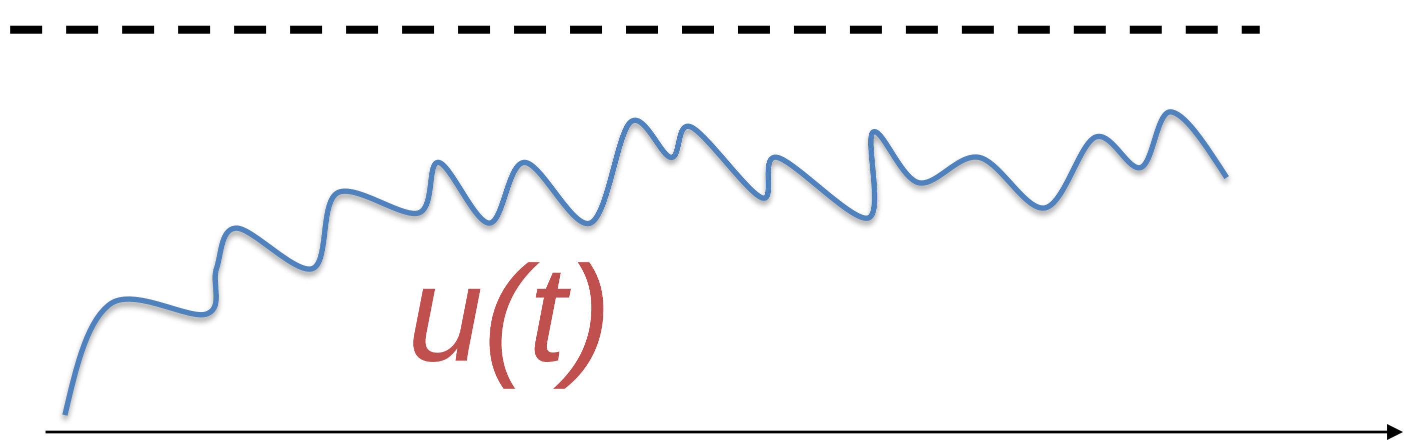
Passive membrane =Leaky integrate-and-fire without threshold

ADD THRESHOLD
→ Leaky Integrate-and-Fire





noisy input/ diffusive noise/ stochastic spike arrival



subthreshold regime:

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

Neuronal Dynamics week 5– 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. 7,8: Cambridge, 2014
OR W. Gerstner and W. M. Kistler, Spiking Neuron Models, Chapter 5, Cambridge, 2002

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THE END