From Spike Trains to Behavior: an introduction to point processes

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LVIII Cracow School of Theoretical Physics 2018, Zakopane

100 years nencki institute of experimental biology

Laboratory of Neuroinformatics

Nencki Institute of Experimental Biology
Polish Academy of Sciences

In 2017:

- ~350 employees
  - ~110 researchers
  - ~240 support staff
- ~200 PhD students

Laboratory of Neuroinformatics
http://neuroinflab.pl

- Data analysis
  - Spike trains
  - Local field potentials
  - Behavior
  - Images
- Modeling
  - Neural system activity
  - Electric field in the brain
  - Animal behavior
  - Structural connectivity
- Infrastructure for large-scale data management and sharing

I have deeply regretted that I did not proceed
far enough at least to understand
something of the great leading
principles of mathematics;
for men thus endowed seem
to have an extra sense.

Charles Darwin

Mathematics Is Biology's Next Microscope, Only Better; Biology Is Mathematics' Next Physics, Only Better

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December 2004 | Volume 2 | Issue 12 | e439

Joel E. Cohen

Here are five biological challenges that could stimulate, and benefit from, major innovations in mathematics.

(1) Understand cells, their diversity within and between organisms, and their interactions with the biotic and abiotic environments. The complex networks of gene interactions, proteins, and signaling between the cell and other cells and the abiotic environment is probably incomprehensible without some mathematical structure perhaps yet to be invented.

(2) Understand the brain, behavior, and emotion. This, too, is a system problem. A practical test of the depth of our understanding is this simple question: Can we understand why people choose to have children or choose not to have children (assuming they are physiologically able to do so)?

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Here are five mathematical challenges that would contribute to the progress of biology.

(1) Understand computation. Find more effective ways to gain insight and prove theorems from numerical or symbolic computations and agent-based models. We recall Hamming: "The purpose of computing is insight, not numbers" (Hamming 1971, p. 31).

(2) Find better ways to model multi-level systems, for example, cells within organs within people in human communities in physical, chemical, and biotic ecologies.

(3) Understand probability, risk, and uncertainty. Despite three centuries of great progress, we are still at the very beginning of a true understanding. Can we understand uncertainty and risk better by integrating frequentist, Bayesian, subjective, fuzzy, and other theories of probability, or is an entirely new approach required?

(4) Understand data mining, simultaneous inference, and statistical de-identification (Miller 1981). Are practical users of simultaneous statistical inference doomed to numerical simulations in each case, or can general theory be improved? What are the complementary limits of data mining and statistical de-identification in large linked databases with personal information?

(5) Set standards for clarity, performance, publication and permanence of software and computational results.

VIEWPOINT

Introductory Science and Mathematics Education for 21st-Century Biologists

William Bialek[1,3] and David Botstein[2,3]*

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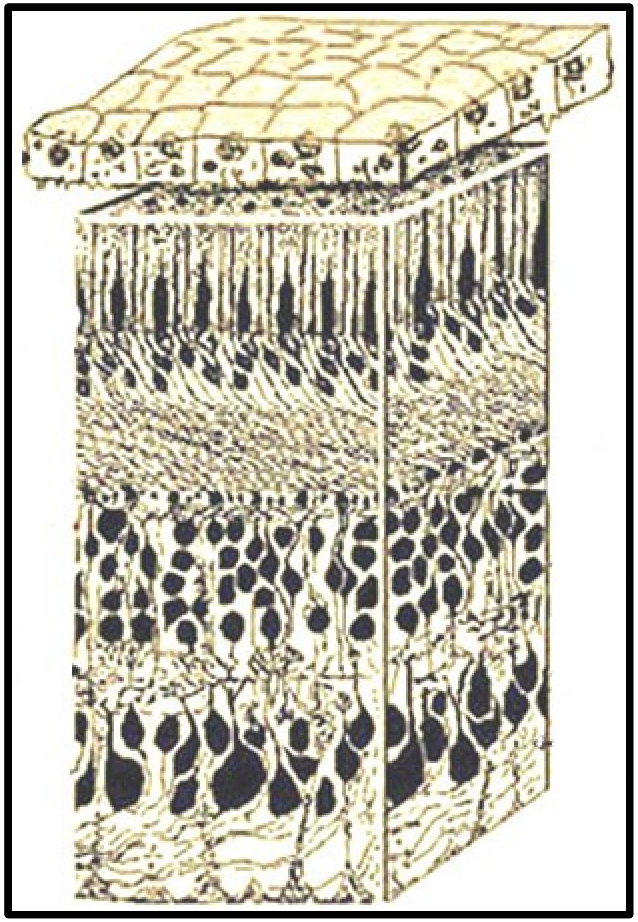
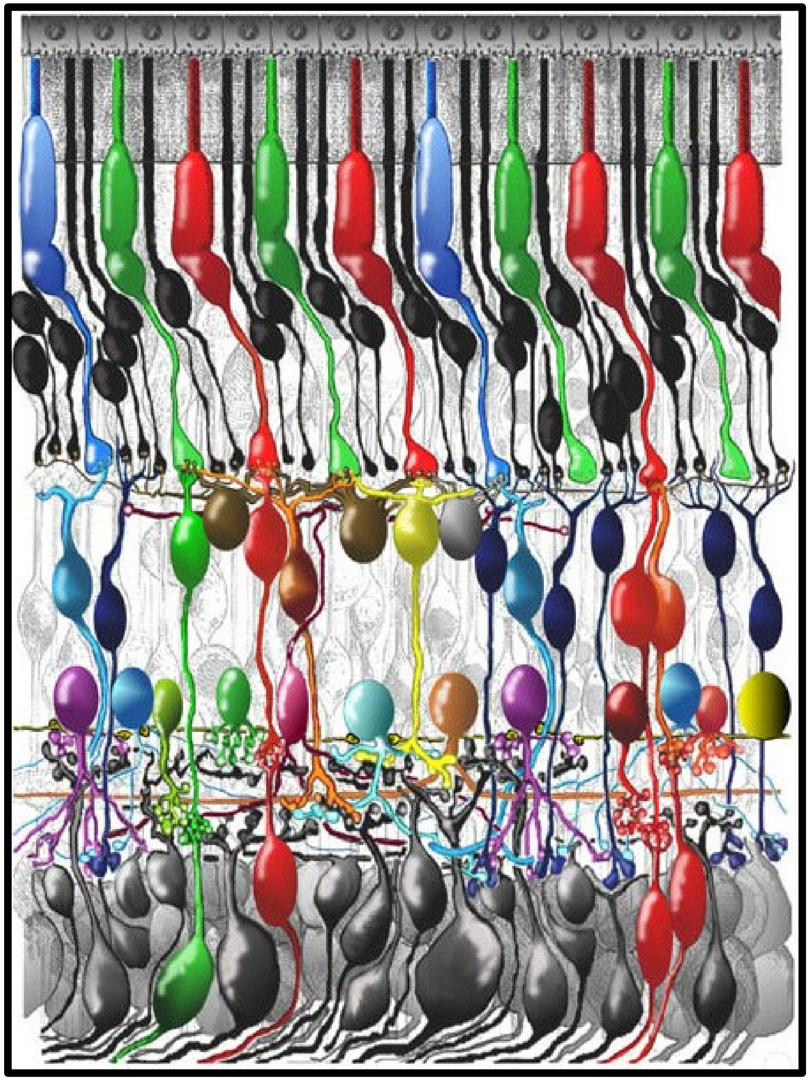
Galileo wrote that "the book of nature is written in the language of mathematics"; his quantitative approach to understanding the natural world arguably marks the beginning of modern science. Nearly 400 years later, the fragmented teaching of science in our universities still leaves biology outside the quantitative and mathematical culture that has come to define the physical sciences and engineering. This strikes us as particularly inopportune at a time when opportunities for quantitative thinking about biological systems are exploding. We propose that a way out of this dilemma is a unified introductory science curriculum that fully incorporates mathematics and quantitative thinking.

Retina:
entry to the visual system



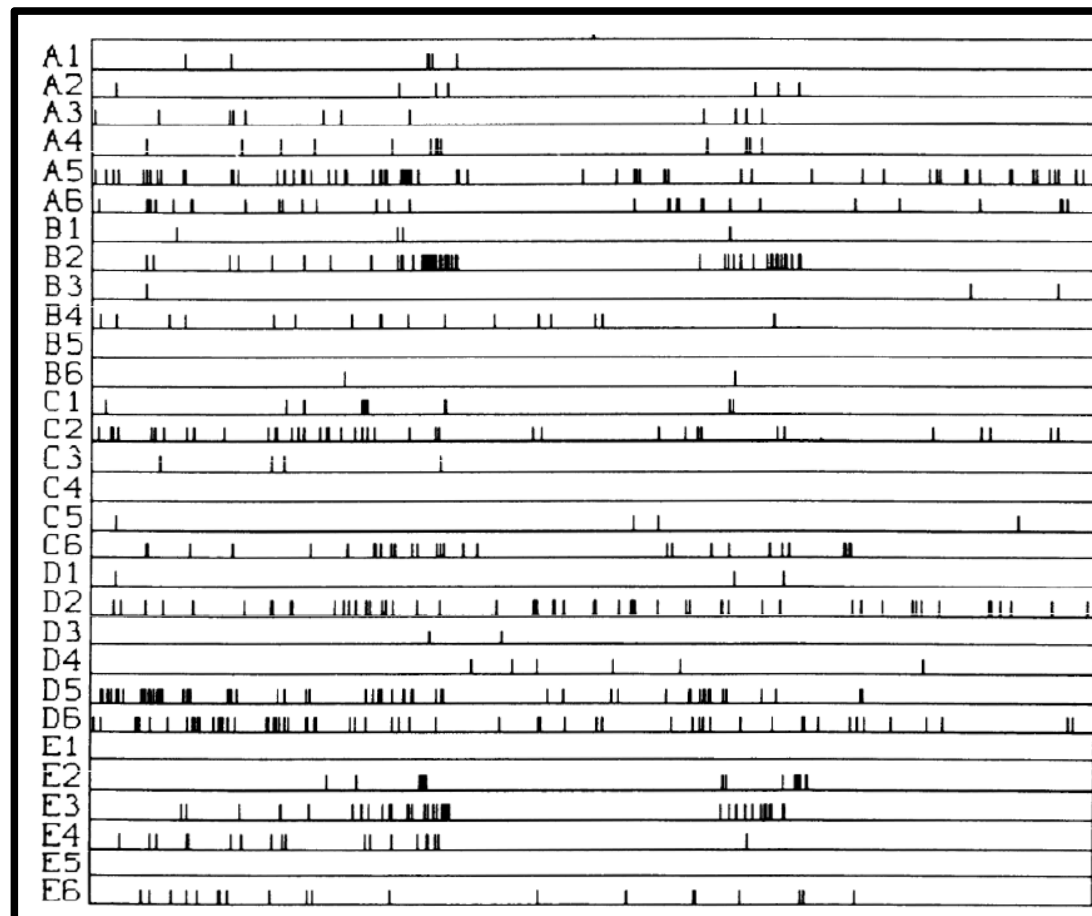
input:
125 milions
receptors

output:
1 milion
ganglion
cells



Coding

All the sensory stimuli are turned into sequences of identical impulses – spike trains



Spikes – Rieke et

Edgar Douglas Adrian
1889-1977

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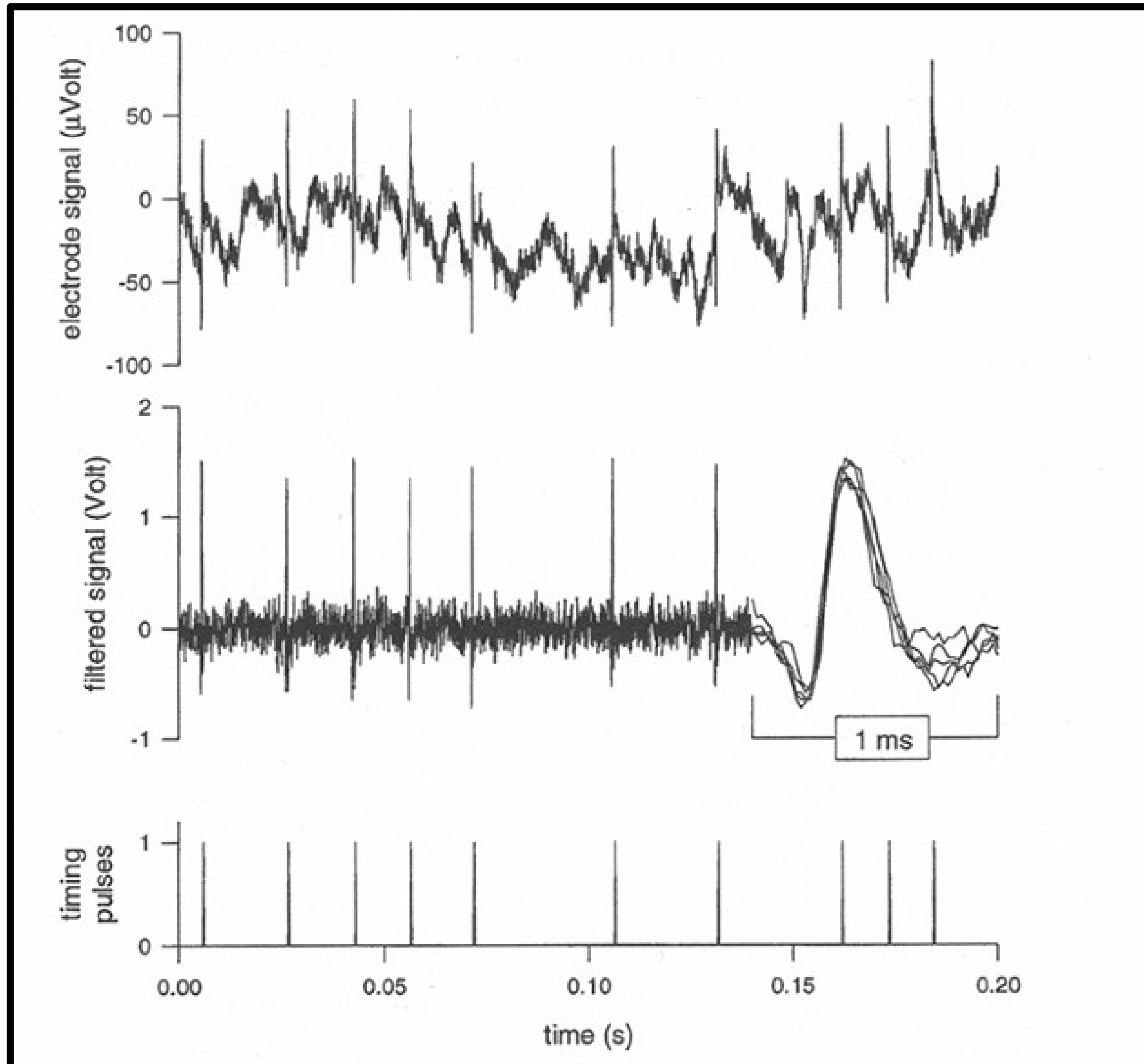
1889-1977

I had arranged electrodes on the optic nerve of a toad in connection with some experiments on the retina. The room was nearly dark and I was puzzled to hear repeated noises in the loudspeaker attached to the amplifier, noises indicating that a great deal of impulse activity was going on. It was not until I compared the noises with my own movements around the room that I realized I was in the field of vision of the toad's eye and that it was signaling what I was doing.

Neural impulses encode sensory information

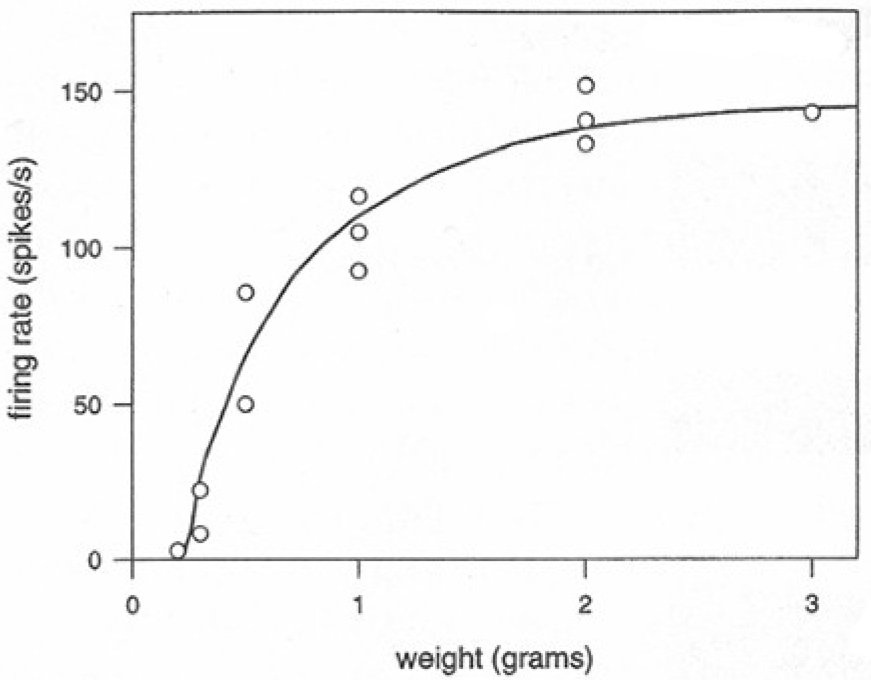
Sensory neurons generate stereotypical impulses (action potentials, spikes)

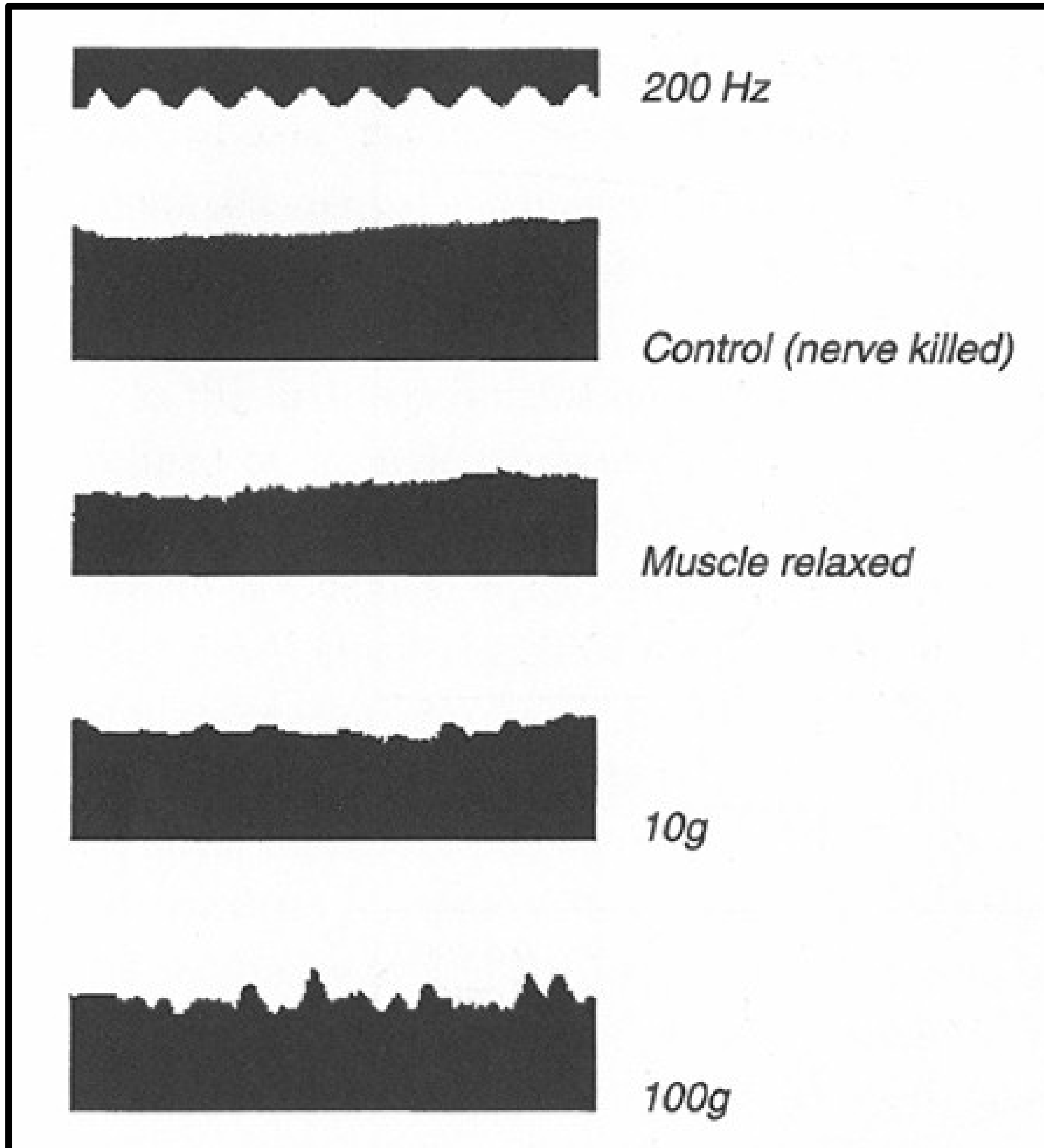
All-or-nothing generation



Spikes – Rieke et

Pulse frequency encodes stimulus amplitude

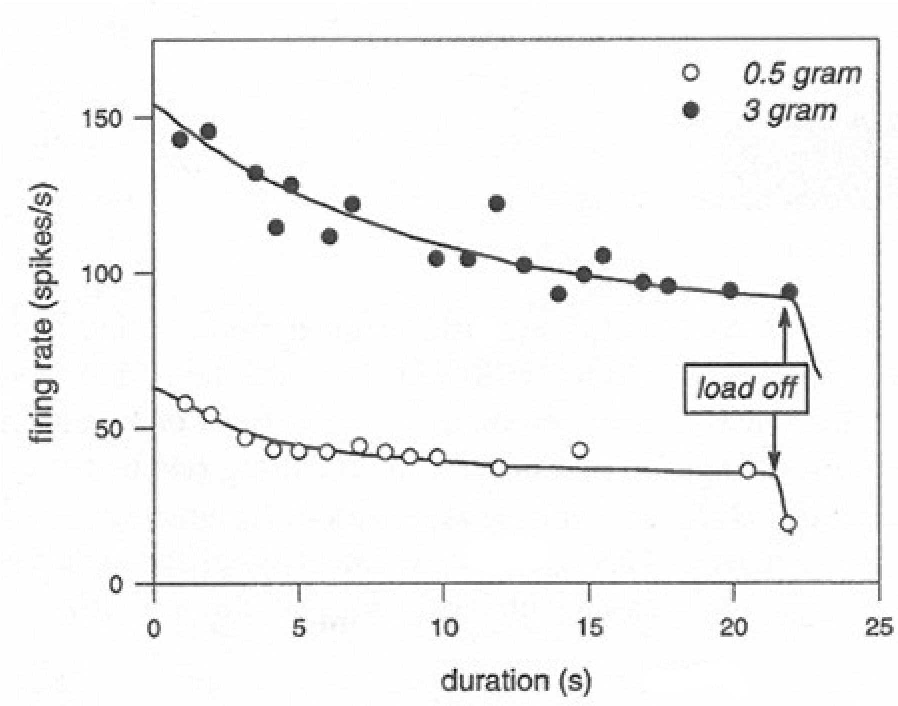




Cell activity grows with the stimulus amplitude

Spikes – Rieke et al.

Adaptation



Long stimulus leads to a
decrease in spiking activity

Spikes – Rieke et al.

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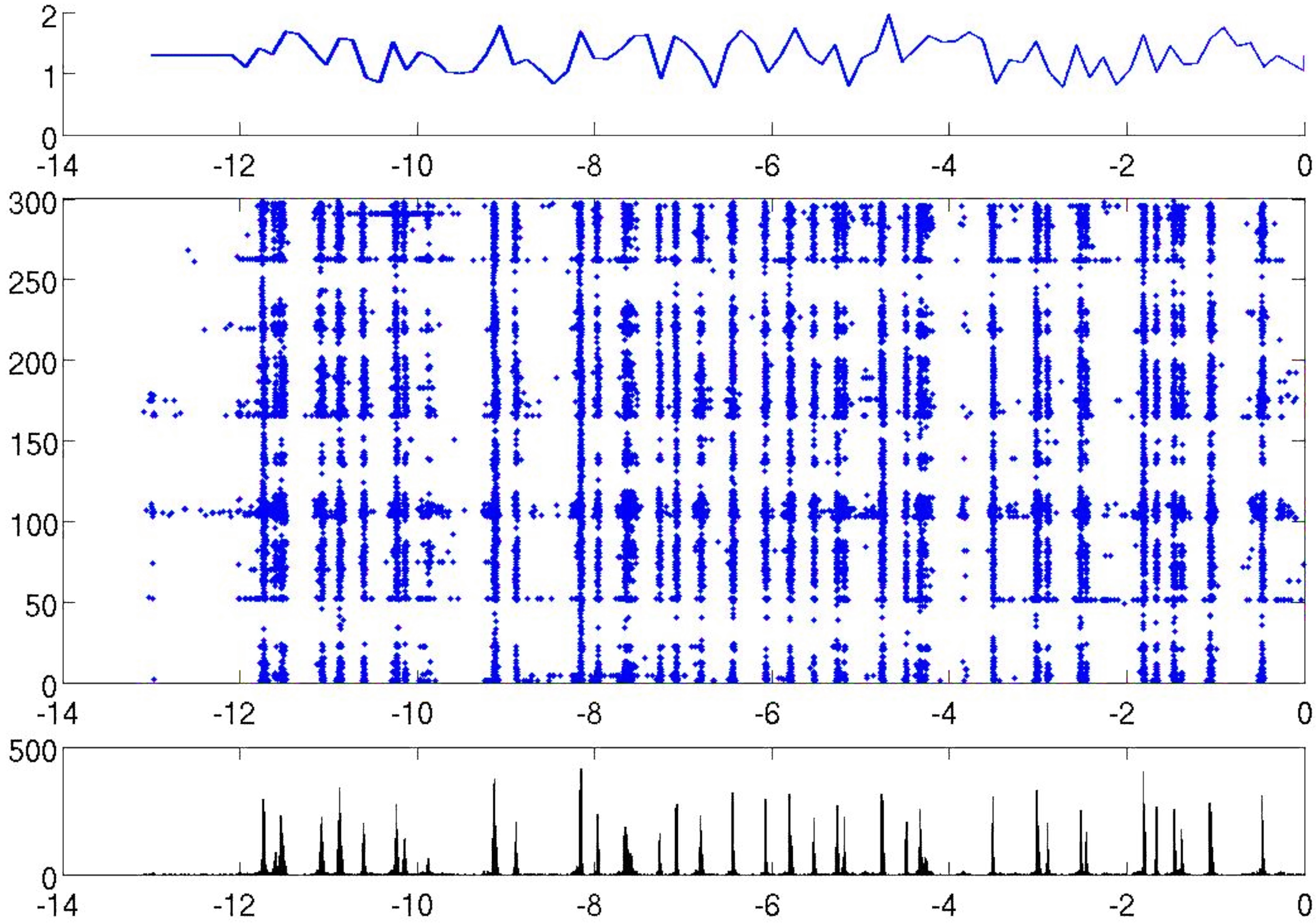
Response variability

Variable responses

Structure preserved

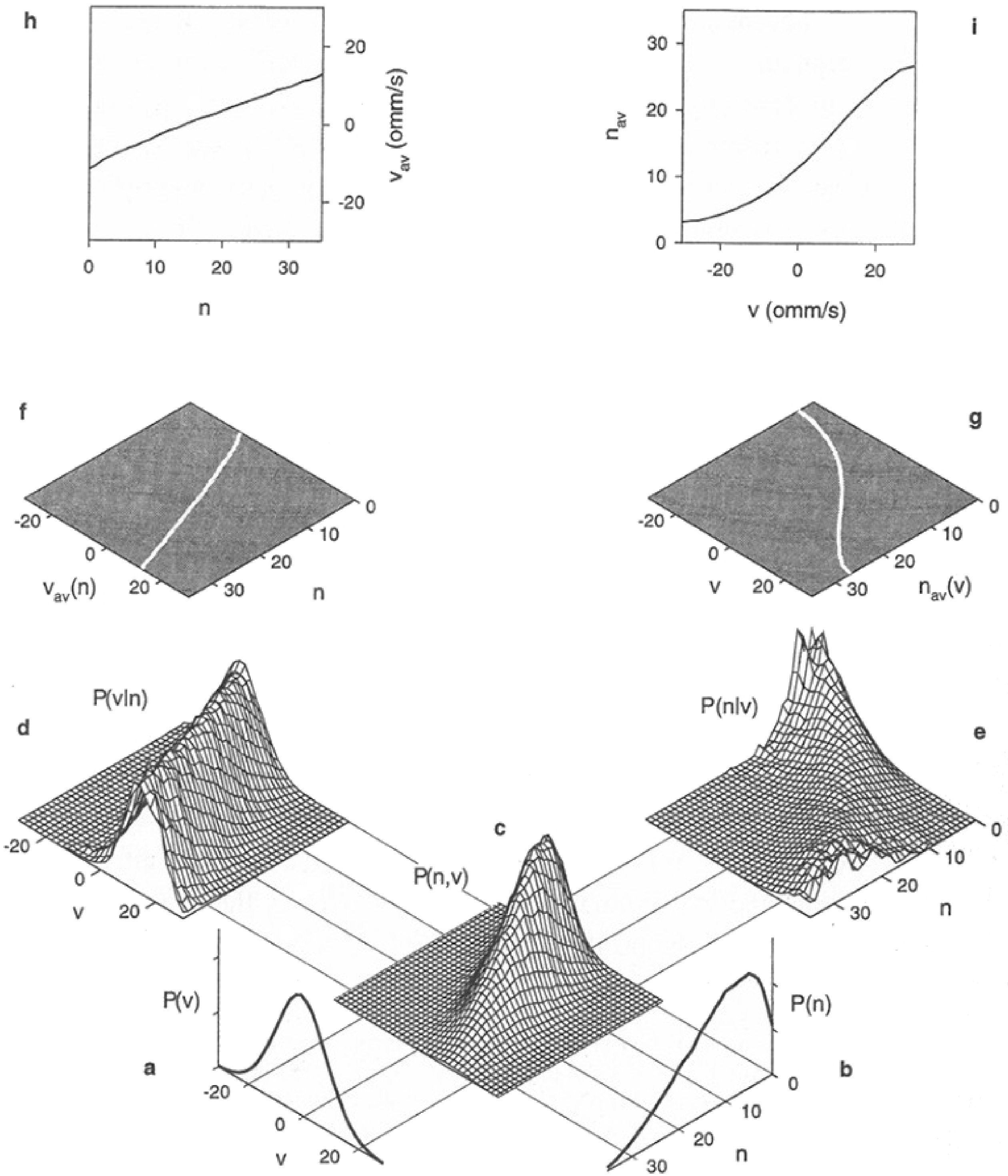
Probabilistic approach necessary



Wioletta Waleszczyk, Gabriela Mochol, Marek Wypych

Probabilistic perspective on coding

$$P[\{s(t)\};\{t_i\}]$$

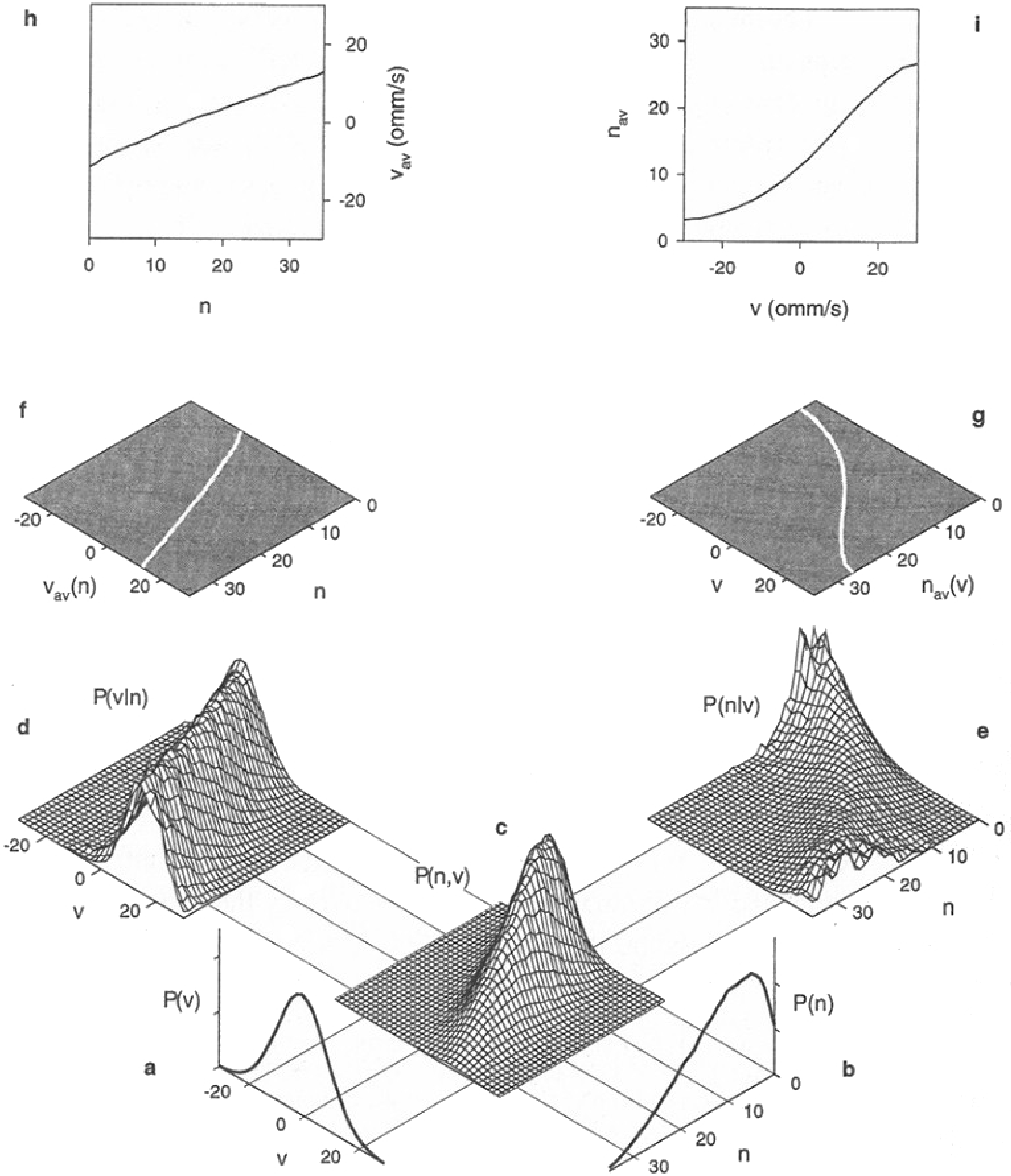


Spikes – Rieke et al.

The CODING problem

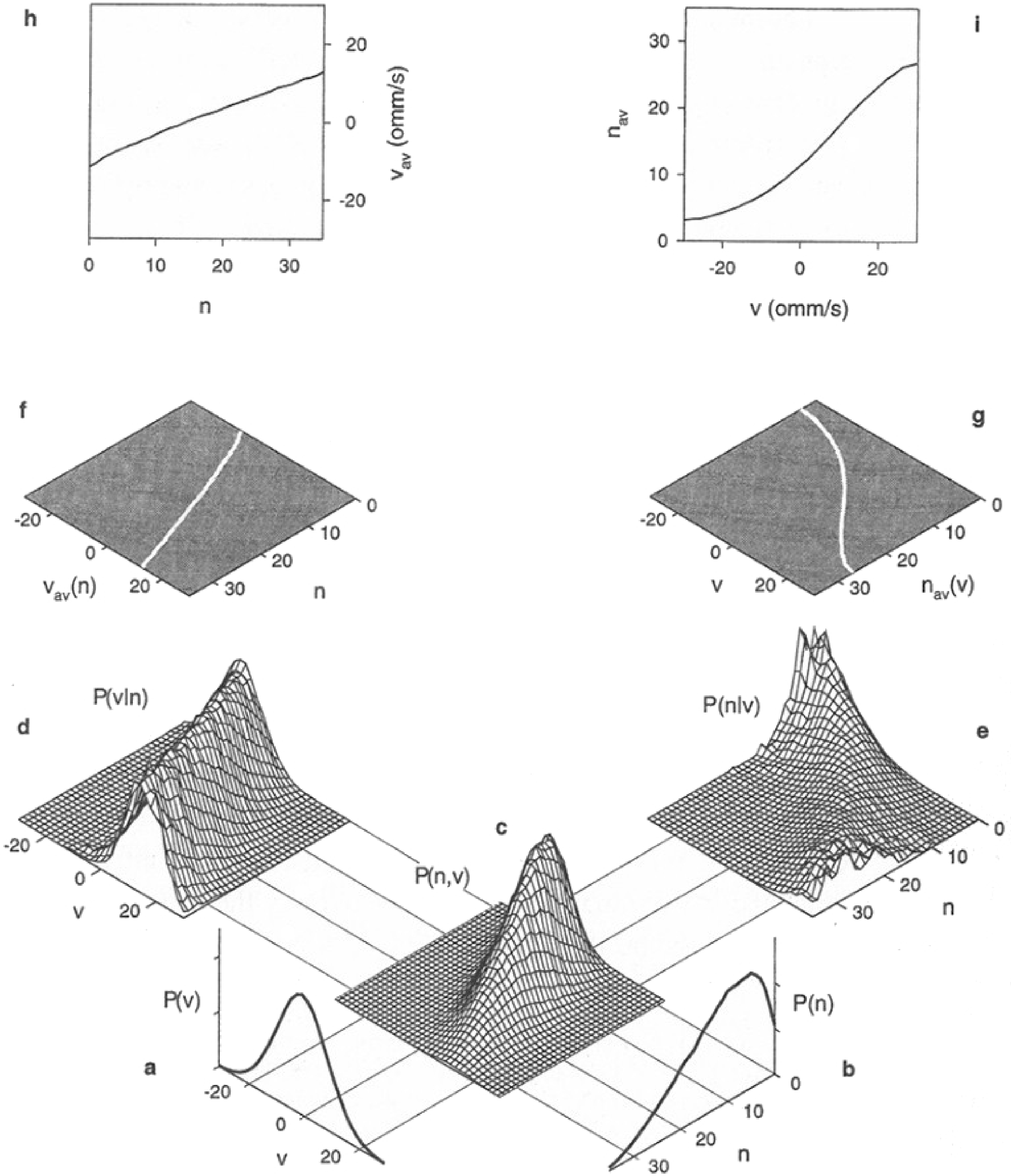
Find out conditional probability P[r | s] to generate response r to stimulus s.

The problem of **researcher**: we give the same stimulus many times and study the statistics of the responses.



Spikes – Rieke et al.

The DECODING Problem



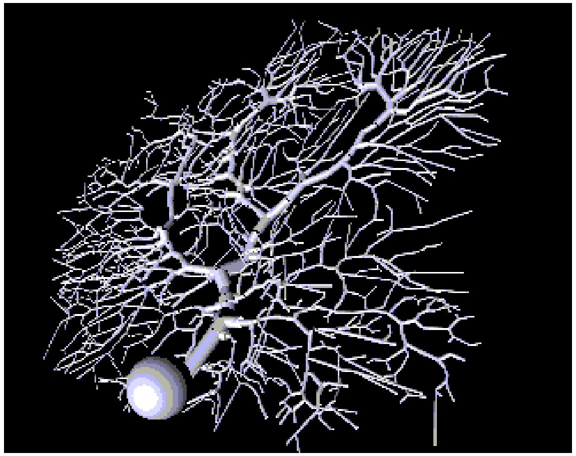
Find out conditional probability P[s | r] Of the stimulus s, which generated response r.

The problem of the **brain**: we get a spike train and want to guess the stimulus.

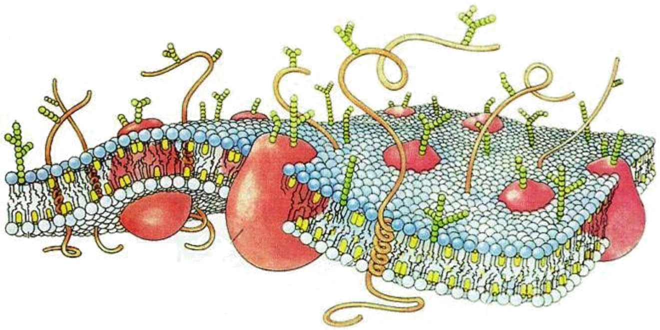
Spikes – Rieke et al.

What information is encoded by a cell? How to identify this code from

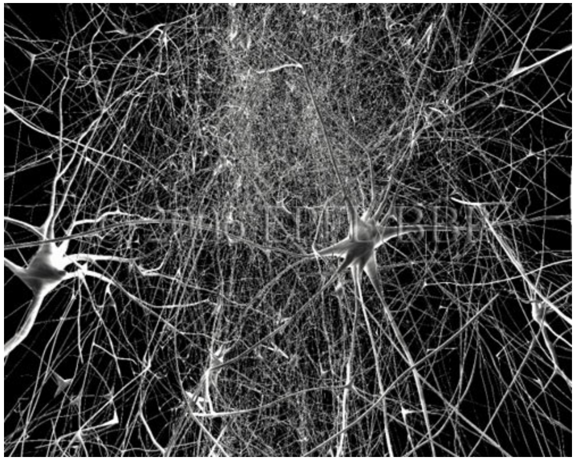
morphology



membrane biophysics



connectome

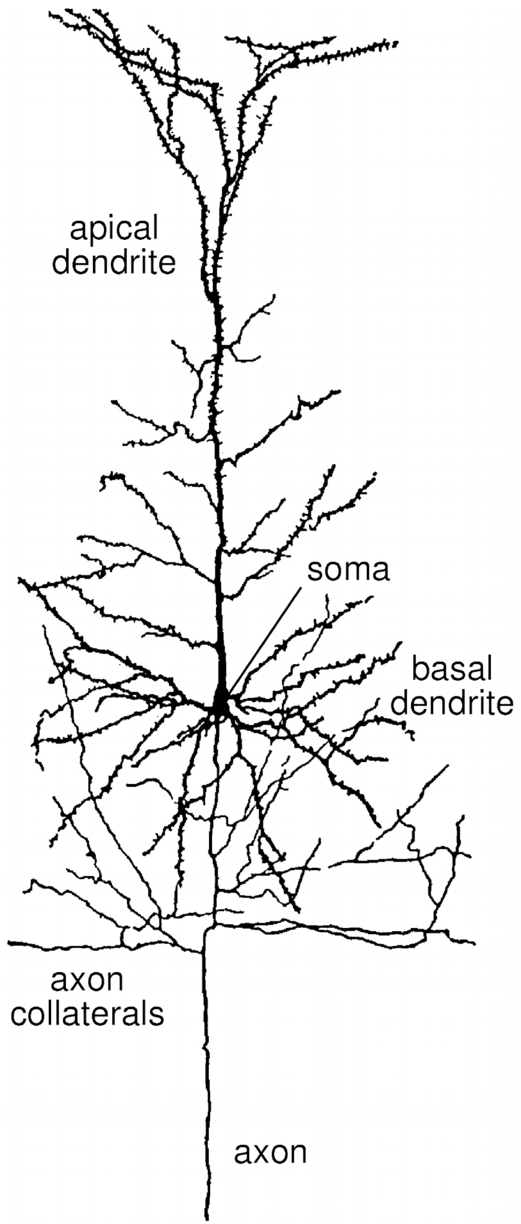


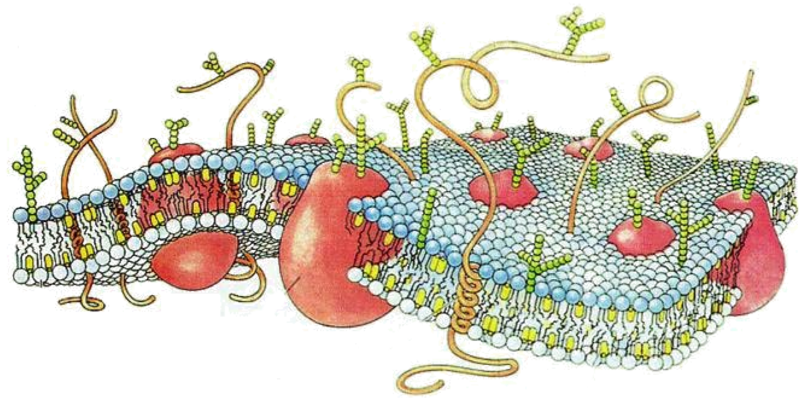
Open problem

E. de Schutter; Wikipedia; Blue Brain Project

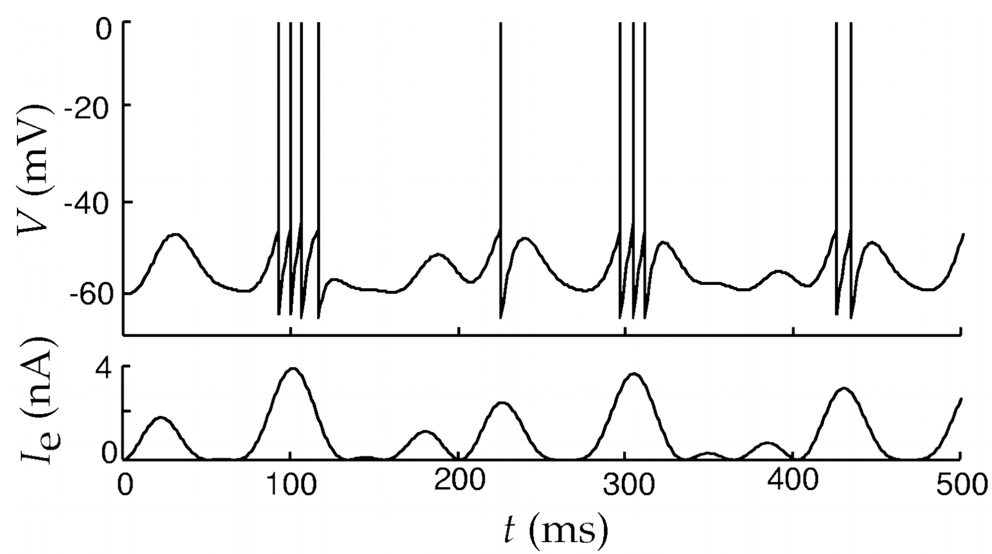
2. Kinematics of spike trains

How neuron works

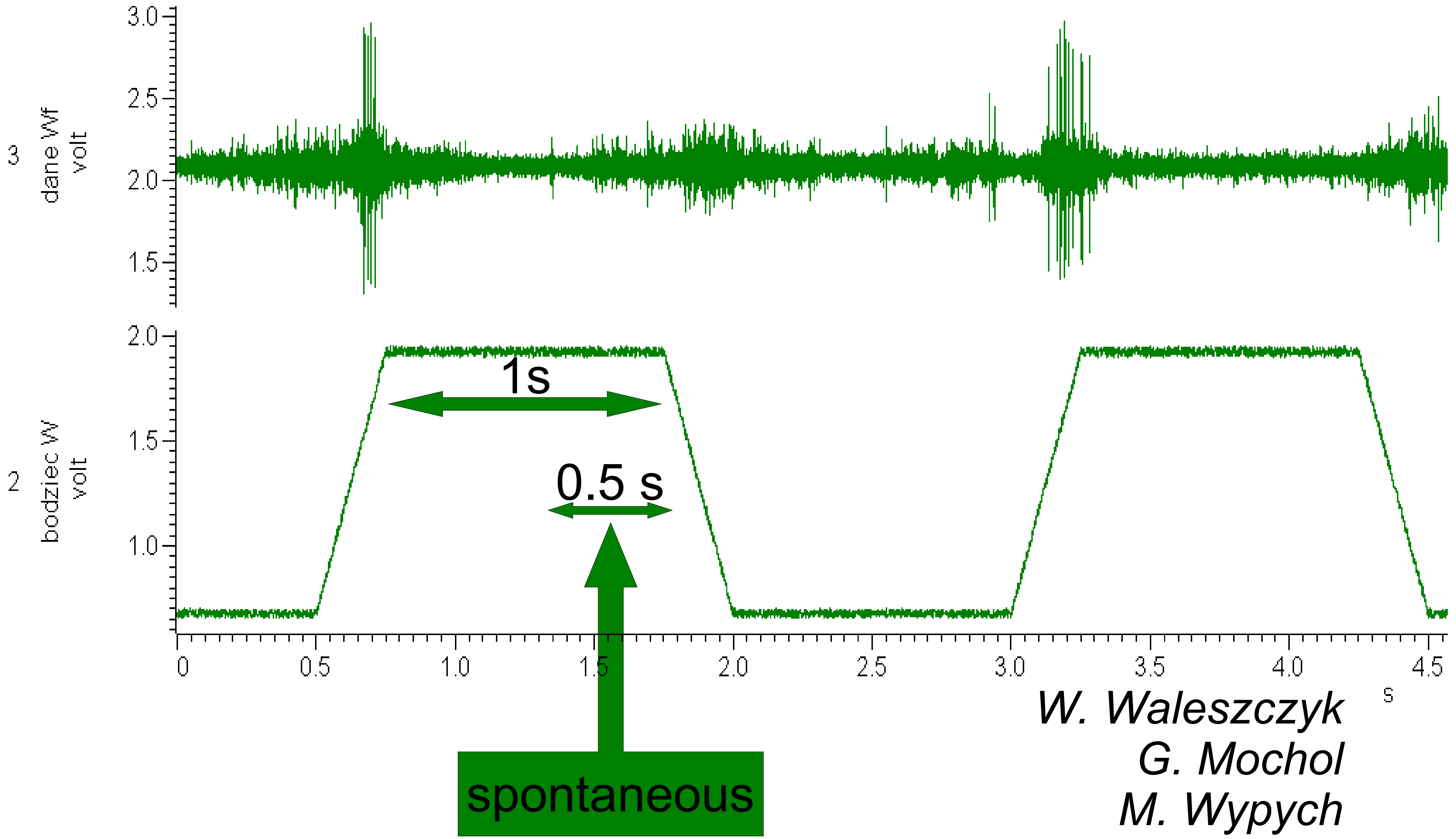




Current entering the cell leads to generation of action potentials



Our experiments



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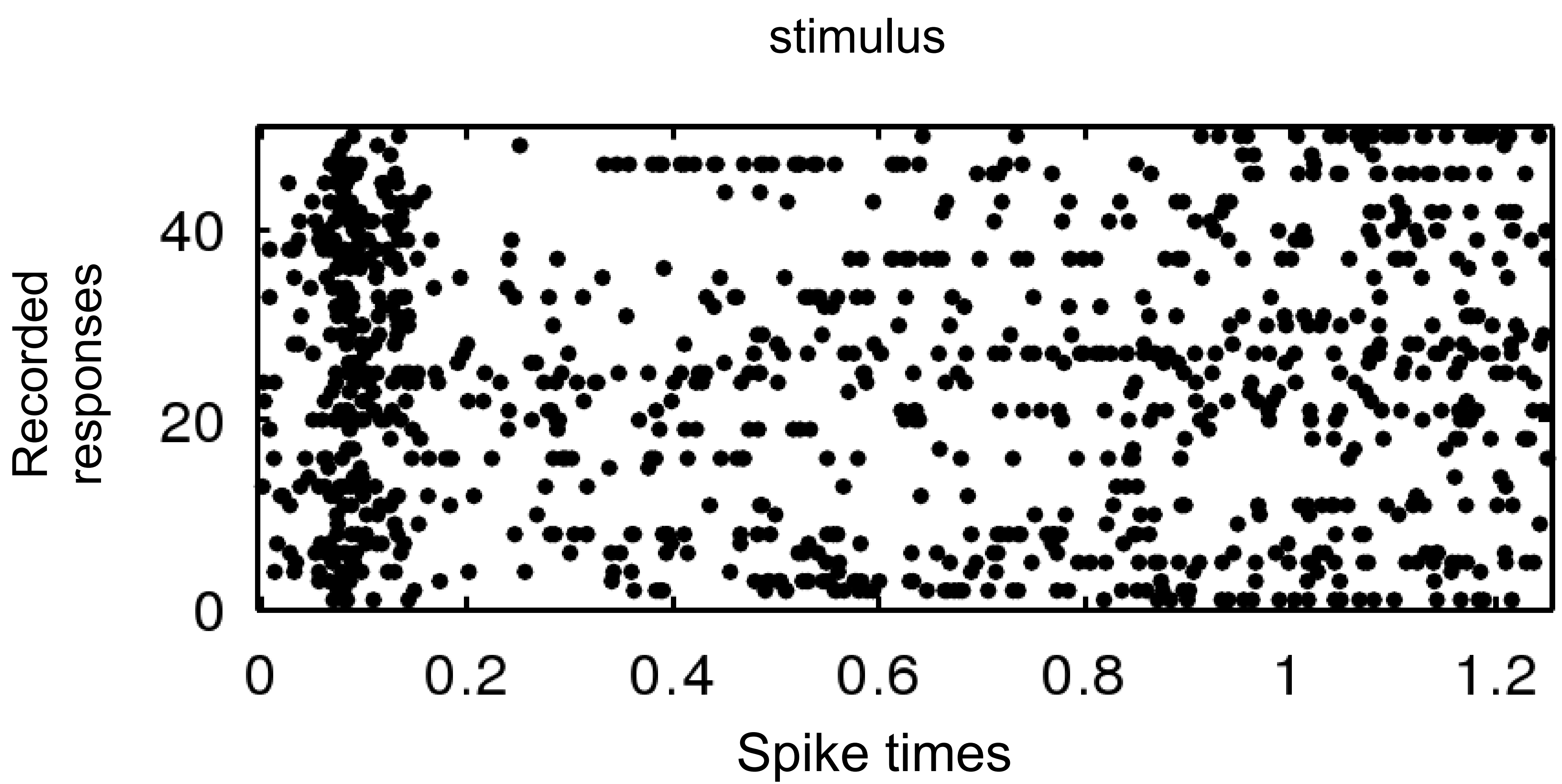
G. Mochol
M. Wypych

Raster plot – result of several repetitions



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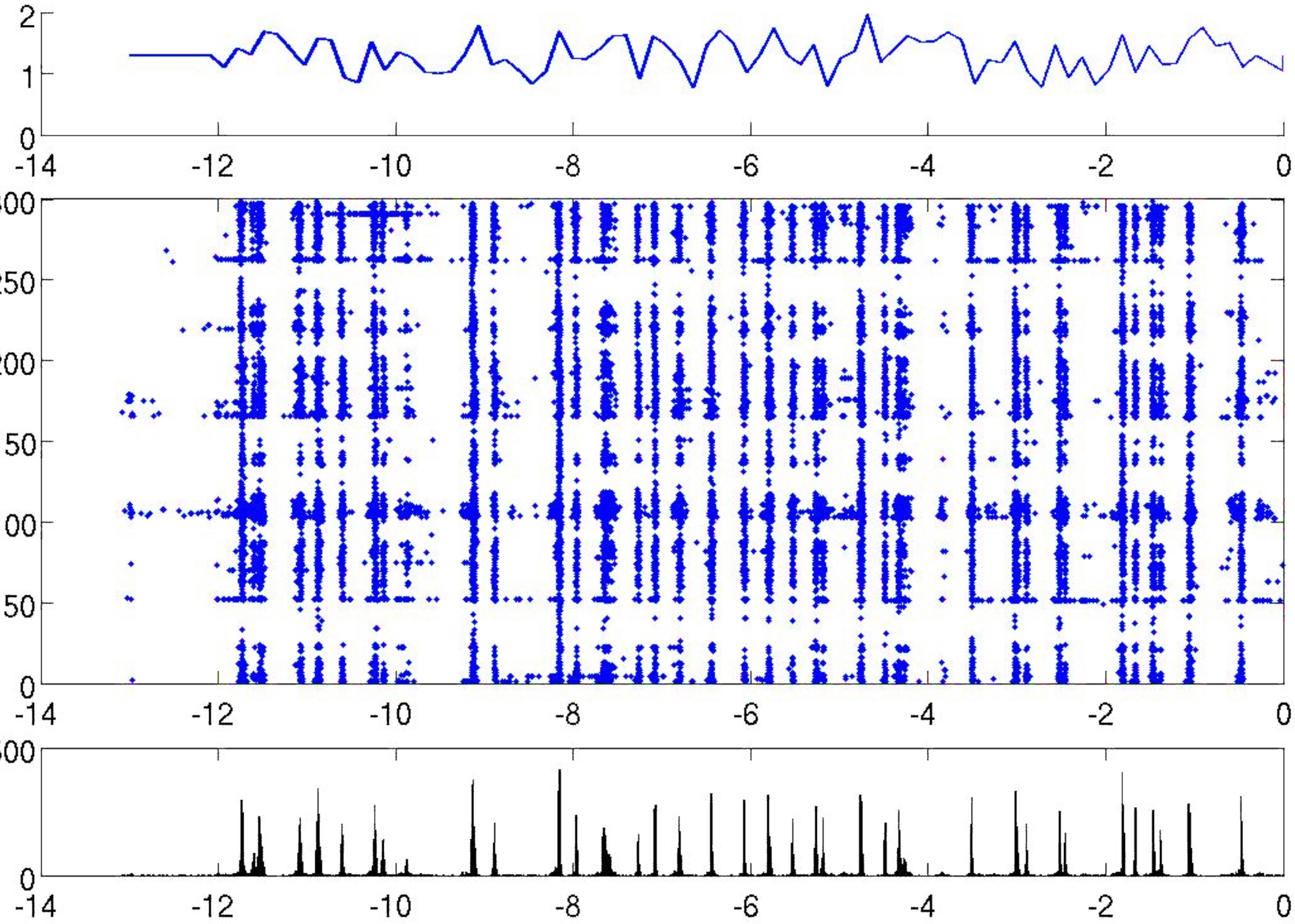

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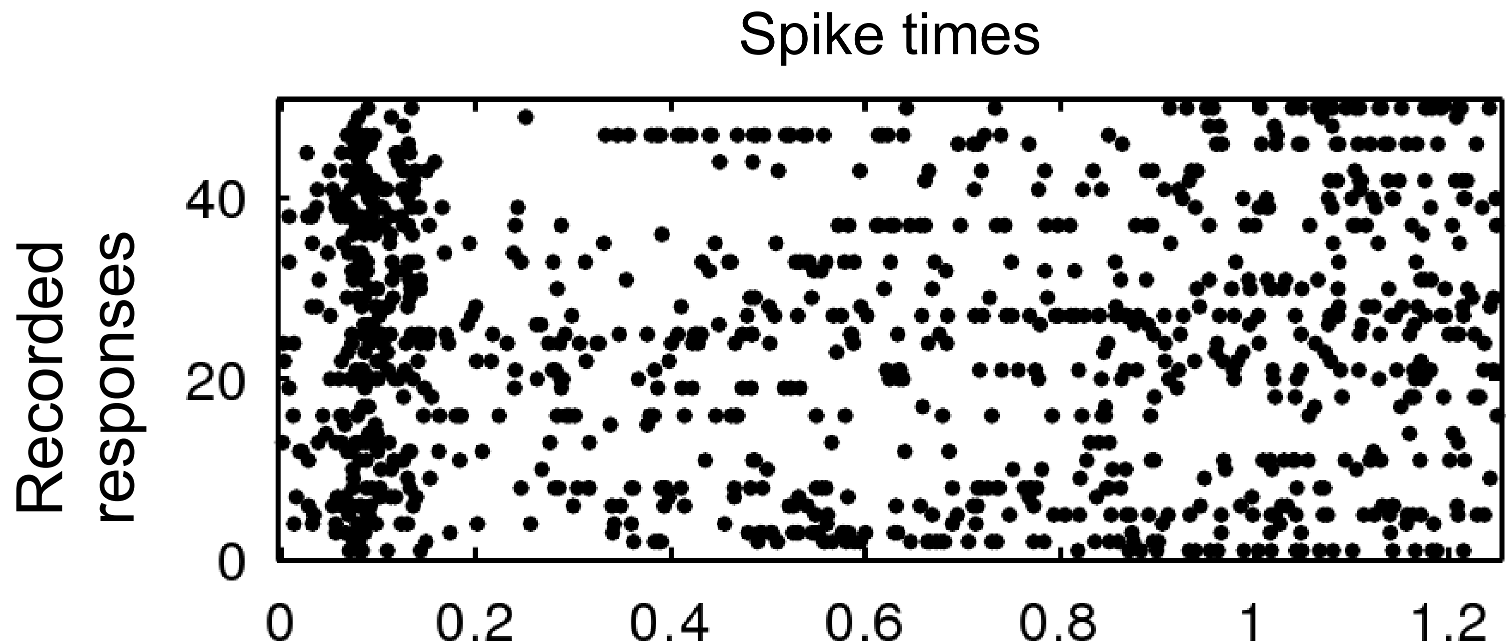
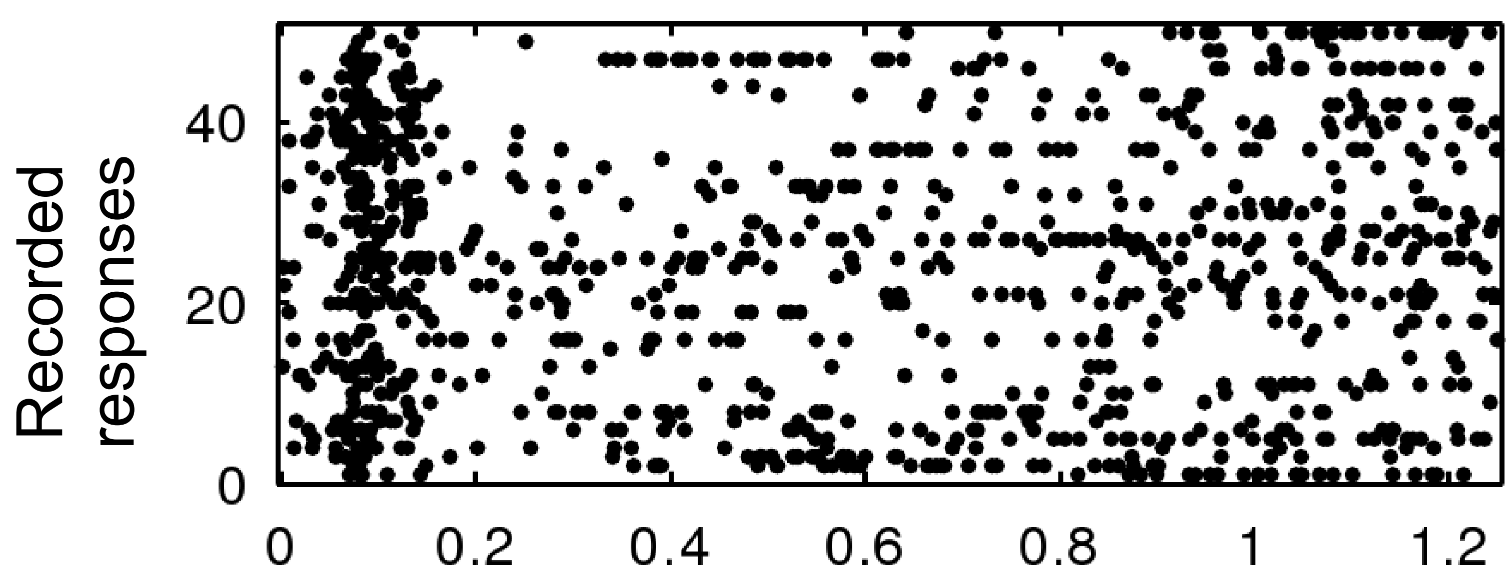
Information contained in spike trains



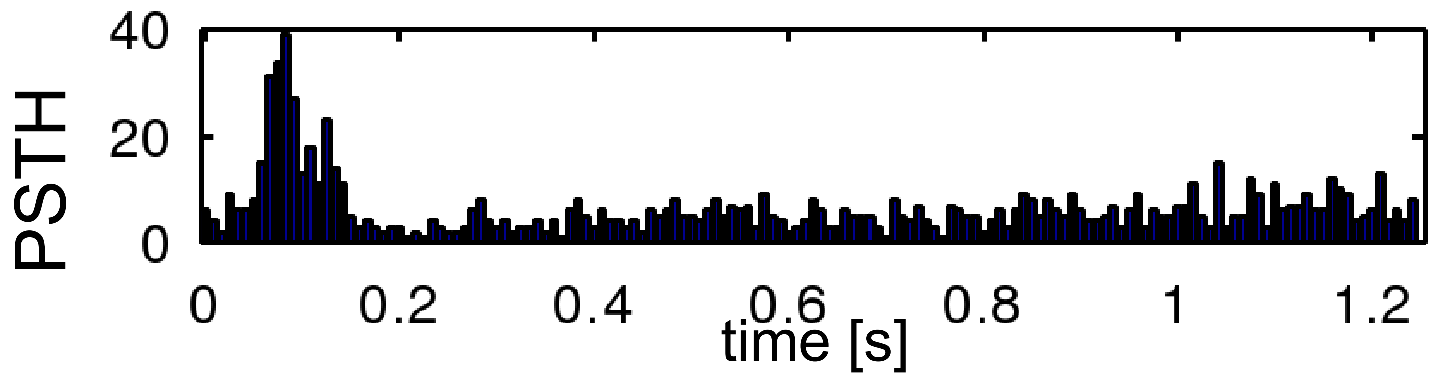
Information contained in spike trains

Spike times



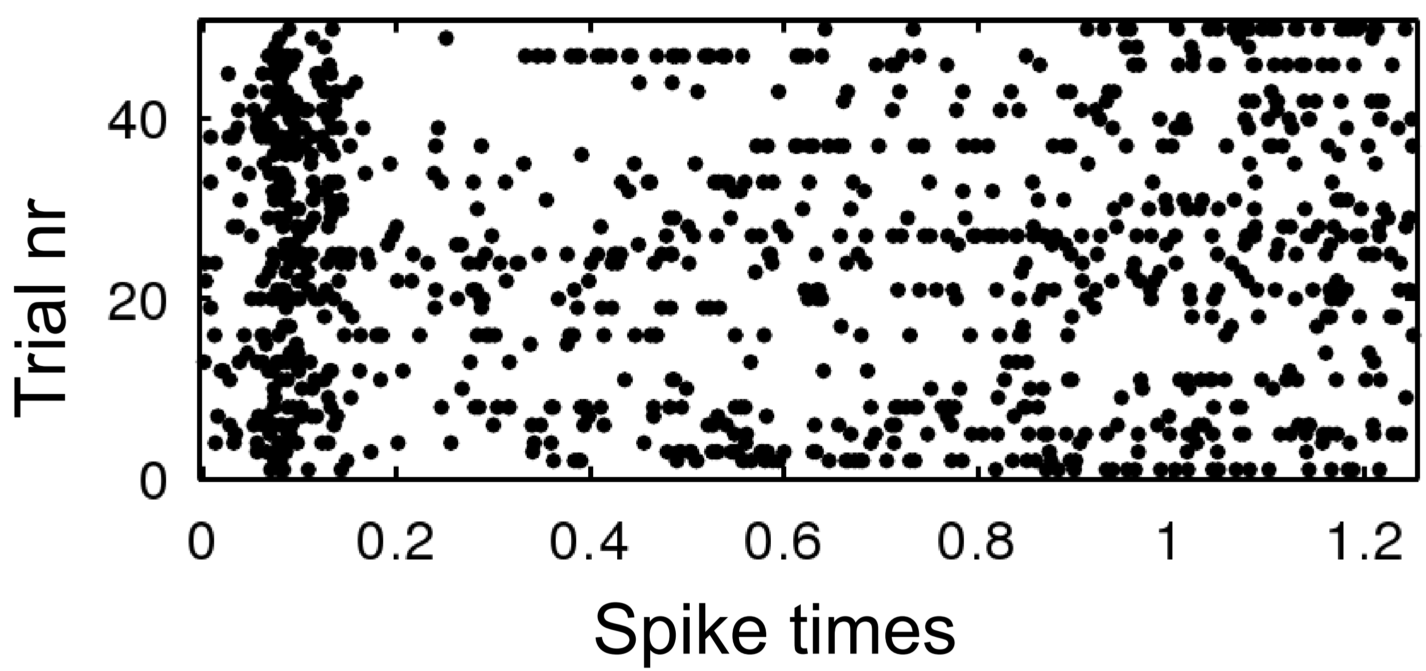
Firing rate

Gerstein, 1960



Stochastic point processes

- Start recording at time 0
- Spikes recorded at times $t_1, t_2, \ldots, t_n$
- Spike times t_k are random variables



Local description in time

- Probability of generating a spike around t

  Pr [1 event in $(t, t+\Delta t)|N_{0:t}$]=: $\lambda(t|N_{0:t})\Delta t$

  $N_{0:t}$ is the total history of spiking:

$$N_{0:t} \equiv \{0 < t_1 < t_2 < \cdots < t_j \leq t \cap N(t) = j\}$$

- We call $\lambda(t; N_{0:t})$ **conditional intensity** or **hazard function**

Stochastic intensity

- $\lambda(t; N_{0:t})$ may depend on:
  - time after the stimulus onset, t
  - the whole history of spike generation

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Stochastic intensity

- $\lambda(t; N_{0:t})$ may depend on:
  - time after the stimulus onset, t
  - the whole history of spike generation
- Impractical and unnecessary for the description of spiking activity
- To simplify, specify the memory model

Example 1: Memoryless model

- Poisson model:
  spike generation depends solely on time

$$\lambda = \lambda(t)$$

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  Incorrect physiologically,
  the spikes can be generated arbitrarily close

Example 1: Memoryless model

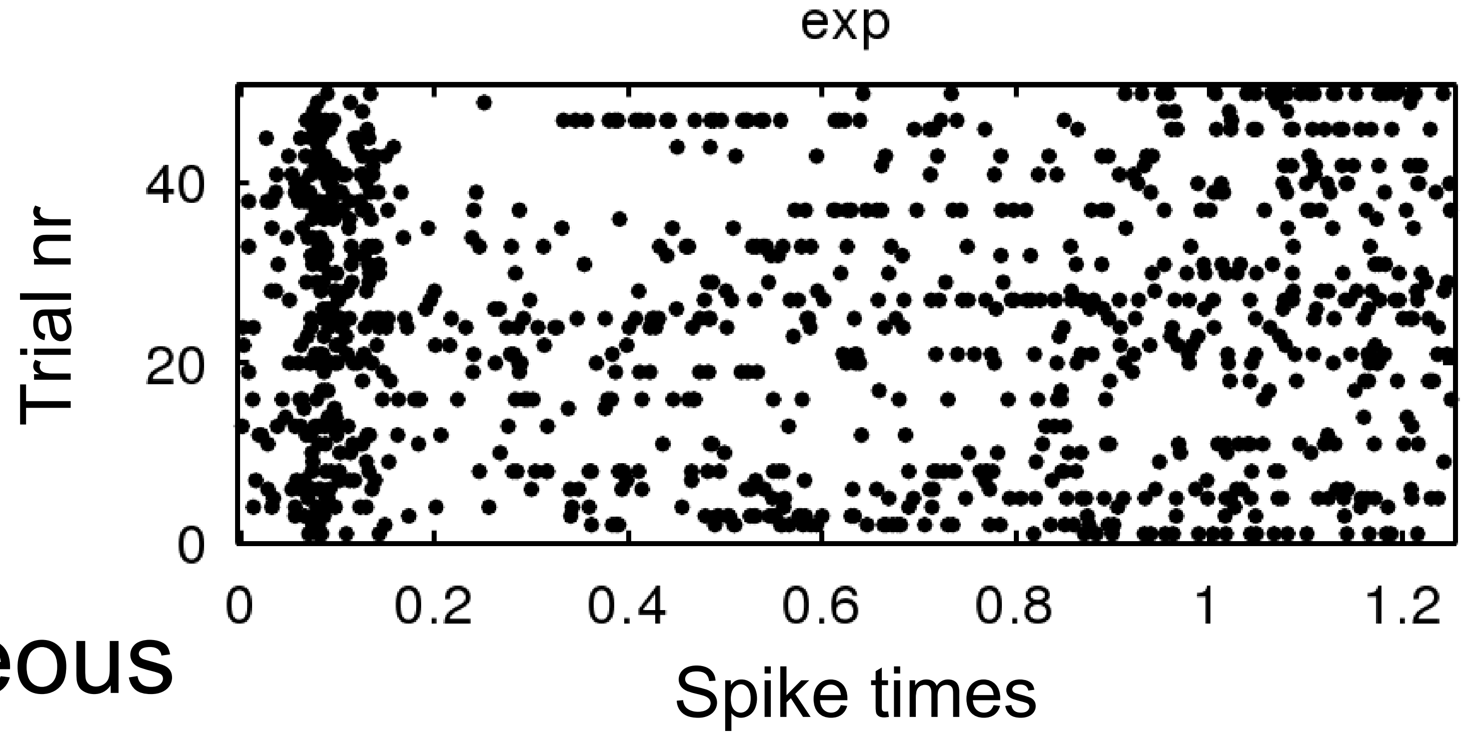
- Poisson model:
  spike generation depends solely on time

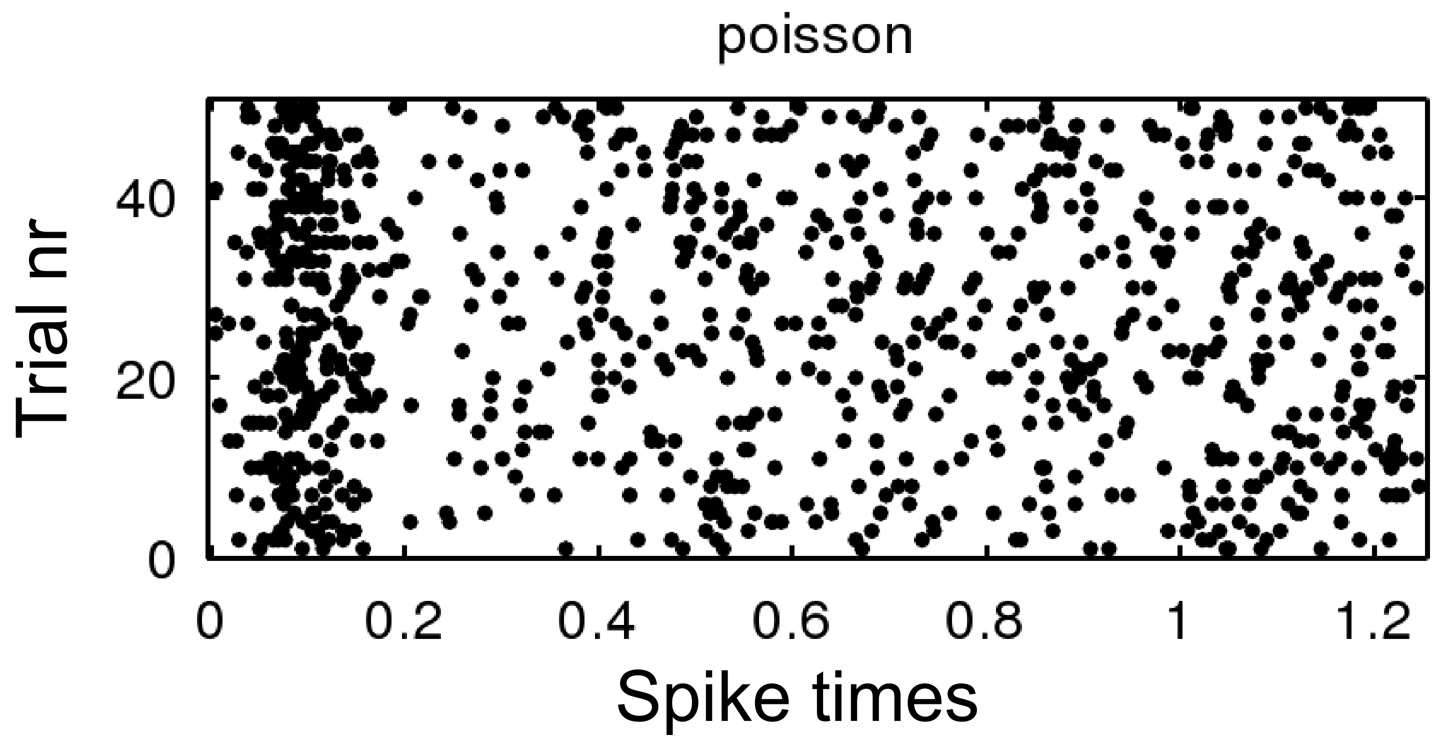
$$\lambda = \lambda(t)$$

- **Problem:**
  Incorrect physiologically,
  the spikes can be generated arbitrarily close

- **Advantage:**
  Easy to estimate; despite lack of refraction
  it can well reflect the true spiking activity

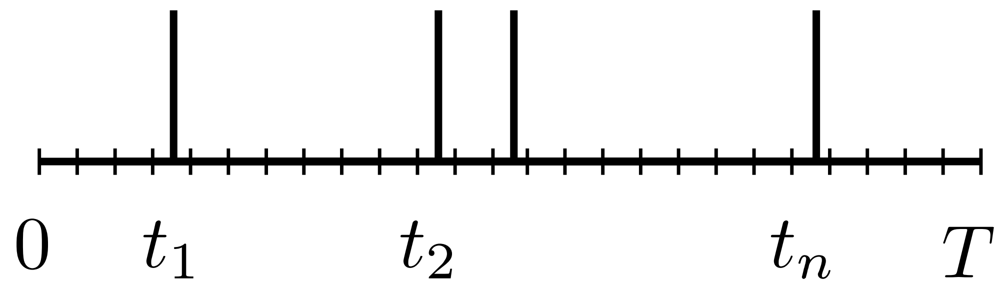
PSTH
=
inhomogeneous
Poisson
process





Poisson process: properties

Divide experiment time (0,T] into *M* intervals δt



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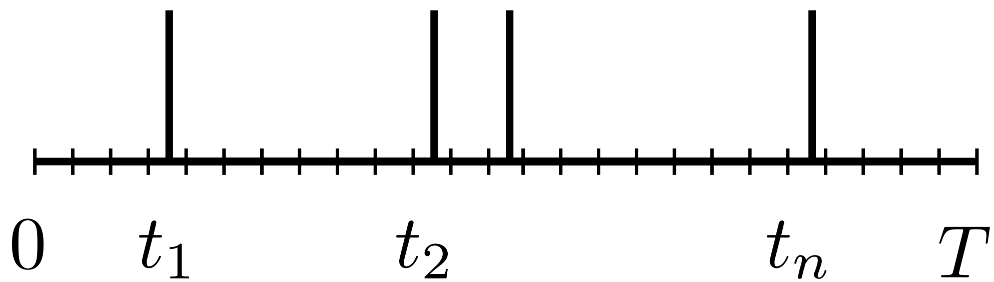

$$\Pr[\text{spikes in intervals containing } t_1, t_2, \ldots, t_s] = \frac{\prod_{j=1}^{s} (\lambda(t_j)\delta t) \cdot \prod_{n=1}^{M} \left[1 - \lambda\left(\left(n - \frac{1}{2}\right)\delta t\right)\delta t\right]}{\prod_{j=1}^{s} (1 - \lambda(t_j)\delta t)}$$

Poisson process: properties

$$\Pr[\text{spikes in intervals containing } t_1, t_2, \ldots, t_s] =$$

$$\frac{\displaystyle\prod_{j=1}^{s} (\lambda(t_j)\delta t) \cdot \prod_{n=1}^{M} \left[1 - \lambda\left(\left(n - \frac{1}{2}\right)\delta t\right)\delta t\right]}{\displaystyle\prod_{j=1}^{s} (1 - \lambda(t_j)\delta t)}$$

Thus the probability density to observe a specific spike train history is

$$\begin{aligned} p(N_{0:T}) &= \lim_{M\to\infty} \frac{\Pr[\text{spikes in int. cont. } t_1, t_2, \ldots, t_s]}{(\delta t)^s} \\ &= \prod_{j=1}^{s} \lambda(t_j) \cdot \lim_{M\to\infty} \prod_{n=1}^{M} \left[1 - \lambda\left(\left(n - \tfrac{1}{2}\right)\delta t\right)\delta t\right] \end{aligned}$$

Poisson process: properties

Compute the logarithm of the last term

$$\ln \prod_{n=1}^{M} \left[1 - \lambda\left(\left(n - \frac{1}{2}\right)\delta t\right)\right] =$$

Poisson process: properties

Compute the logarithm of the last term

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$$= \quad \textstyle\sum_{n=1}^{M} \ln \left[1 - \lambda\left(\left(n - \frac{1}{2}\right)\delta t\right)\delta t\right]$$

Poisson process: properties

Compute the logarithm of the last term

$$\ln \prod_{n=1}^{M} \left[1 - \lambda \left(\left(n - \frac{1}{2} \right) \delta t \right) \right] =$$

$$\begin{aligned}
&= && \sum_{n=1}^{M} \ln \left[1 - \lambda \left(\left(n - \tfrac{1}{2} \right) \delta t \right) \delta t \right] \\
&\approx && \sum_{n=1}^{M} \left[-\lambda \left(\left(n - \tfrac{1}{2} \right) \delta t \right) \delta t + o(\delta t^2) \right] \\
&\approx && -\delta t \sum_{n=1}^{M} \lambda \left(\left(n - \tfrac{1}{2} \right) \delta t \right) \\
&\xrightarrow{M \to \infty} && -\int_0^T \lambda(t) dt
\end{aligned}$$

Poisson process: properties

Compute the logarithm of the last term

$$\ln \prod_{n=1}^{M} \left[1 - \lambda \left(\left(n - \frac{1}{2} \right) \delta t \right) \right] =$$

$$\begin{aligned} &= \sum_{n=1}^{M} \ln \left[1 - \lambda \left(\left(n - \tfrac{1}{2} \right) \delta t \right) \delta t \right] \\ &\approx \sum_{n=1}^{M} \left[-\lambda \left(\left(n - \tfrac{1}{2} \right) \delta t \right) \delta t + o(\delta t^2) \right] \\ &\approx -\delta t \sum_{n=1}^{M} \lambda \left(\left(n - \tfrac{1}{2} \right) \delta t \right) \\ &\overset{M \to \infty}{\longrightarrow} -\int_0^T \lambda(t) dt \end{aligned}$$

Thus

$$p(N_{0:T}) = \prod_{j=1}^{s} \lambda(t_j) \cdot \lim_{M \to \infty} \prod_{n=1}^{M} \left[1 - \lambda \left(\left(n - \frac{1}{2} \right) \delta t \right) \delta t \right]$$

Poisson process: properties

Compute the logarithm of the last term

$$\ln \prod_{n=1}^{M} \left[1 - \lambda \left(\left(n - \frac{1}{2} \right) \delta t \right) \right] =$$

$$\begin{aligned}
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&\approx -\delta t \sum_{n=1}^{M} \lambda \left(\left(n - \tfrac{1}{2} \right) \delta t \right) \\
&\xrightarrow{M \to \infty} -\int_0^T \lambda(t) dt = -T\overline{\lambda}
\end{aligned}$$

Thus

$$p(N_{0:T}) = \left(\prod_{j=1}^{s} \lambda(t_j) \right) \exp \left[- \int_0^T \lambda(t) dt \right]$$

Poisson process: properties

Therefore

$$p(N_{0:T}) = \left(\prod_{j=1}^{s} \lambda(t_j) \right) \exp\left[-\int_0^T \lambda(t) dt \right]$$

For a homogeneous Poisson process $(\lambda = const.)$

$$p(N_{0:T}) = \lambda^s \, e^{-\lambda T}$$

Poisson process: properties

What is the probability to observe exactly *n* spikes during the time of experiment (0,T]?

$$
\begin{aligned}
P_{(0,T]}[n] &= \int_0^T dt_1 \int_{t_1}^T dt_2 \cdots \int_{t_{n-1}}^T dt_n \, \lambda^n e^{-\lambda T} \\
&= \lambda^n e^{-\lambda T} \int_0^T dt_1 \int_{t_1}^T dt_2 \cdots \int_{t_{n-1}}^T dt_n \\
&= \lambda^n e^{-\lambda T} \frac{T^n}{n!}
\end{aligned}
$$

Poisson process: properties

We obtain the Poisson distribution (hence the name)

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For inhomogeneous process:

$$P_{(0,T]}[n] = \frac{1}{n!} \left(\int_0^T \lambda(t) dt \right)^n \exp\left[- \int_0^T \lambda(t) dt \right]$$

$$P_{(0,T]}[n] = \frac{(\bar{\lambda} T)^n}{n!} e^{-\bar{\lambda} T}$$

What is the firing rate?

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$$= \sum_{n=1}^{\infty} n \frac{1}{n!} \left(\int_0^t \lambda(\tau) d\tau \right)^n \exp\left[- \int_0^t \lambda(\tau) d\tau \right] = \int_0^t \lambda(\tau) d\tau$$

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Thus

$$r(t) = \lim_{\delta t \to 0^+} \frac{\int_t^{t+\delta t} \lambda(t) dt}{\delta t} = \lambda(t)$$

Example 2: renewal processes

- τ – time from the last spike
- The basic quantity:
  distribution of inter-spike intervals (ISI)

$$P(\tau)\Delta t := \Pr(\text{spike during}(\tau, \tau + \Delta t) \cap$$
$$\cap \, \text{no spikes during}(0, \tau))$$

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$$\cap \, \text{no spikes during}(0, \tau))$$

- Another useful notion: *survival function*

$$\begin{aligned} S(\tau) &:= \Pr(\text{no spikes until } \tau) \\ &= \int_\tau^\infty d\tau' \, P(\tau') \\ &= 1 - \int_0^\tau d\tau' \, P(\tau') \end{aligned}$$

Example 2: renewal processes

- Conditional intensity

$$\lambda(\tau)\Delta t := \Pr(\text{spike during } (\tau, \tau + \Delta t) \,|\, \text{no spikes during}(0, \tau))$$

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$$\begin{aligned} P(\tau)\Delta t &= \Pr(\text{spike during } (\tau, \tau + \Delta t) \cap 0 \text{ spikes until } \tau) \\ &= \Pr(\text{spike during}(\tau, \tau + \Delta t) \,|\, 0 \text{ spikes until } \tau) \cdot \\ &\quad \cdot \Pr(0 \text{ spikes until } \tau) \\ &= \lambda(\tau)\Delta t \cdot S(\tau) \end{aligned}$$

Example 2: renewal processes

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- Thus

$$\boxed{P(\tau) = \lambda(\tau) \cdot S(\tau)}$$

Example 2: renewal processes

$$P(\tau) = \lambda(\tau) \cdot S(\tau)$$

We can now express any of these quantities in terms of any other.

Examples:

$$S(\tau) = 1 - \int_0^\tau ds\, P(s) = \int_\tau^\infty ds\, P(s)$$

$$\lambda(\tau) = \frac{P(\tau)}{1 - \int_0^\tau ds P(s)}$$

$$P(\tau) = \lambda(\tau) \exp\left[- \int_0^\tau ds\ \lambda(s) \right]$$

$$P(\tau) = -\frac{dS(\tau)}{d\tau}$$

What is the firing rate?

$$r(t) = \lim_{\delta t \to 0^+} \frac{E[N(t + \delta t) - N(t)]}{\delta t}$$

Alternatively:

$$\nu = \frac{1}{\langle \tau \rangle} = \left[\int_0^\infty \tau P(\tau) \right]^{-1} = \left[\int_0^\infty S(\tau) \right]^{-1}$$

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In the homogeneous Poisson process:

$$\nu = \left[\int_0^\infty e^{-\lambda \tau} \right]^{-1} = \left[\frac{1}{\lambda} \right]^{-1} = \lambda$$

The equality between firing rate and intensity holds only for the Poisson process!!! In general – no.

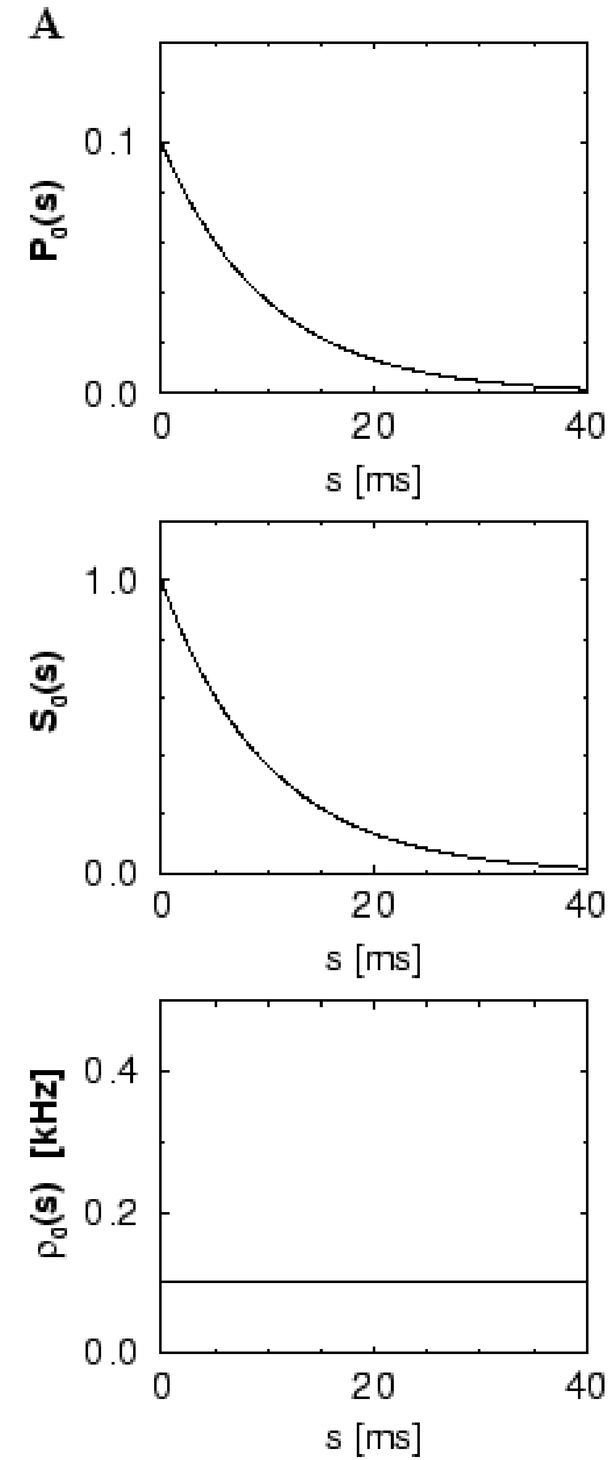
Example 2.1: Poisson process

In a uniform Poisson process with intensity λ the survival function is

$$S(s) = e^{-\lambda s}$$

Inter-spike interval distribution is exponential

$$P(s) = \lambda e^{-\lambda s}$$



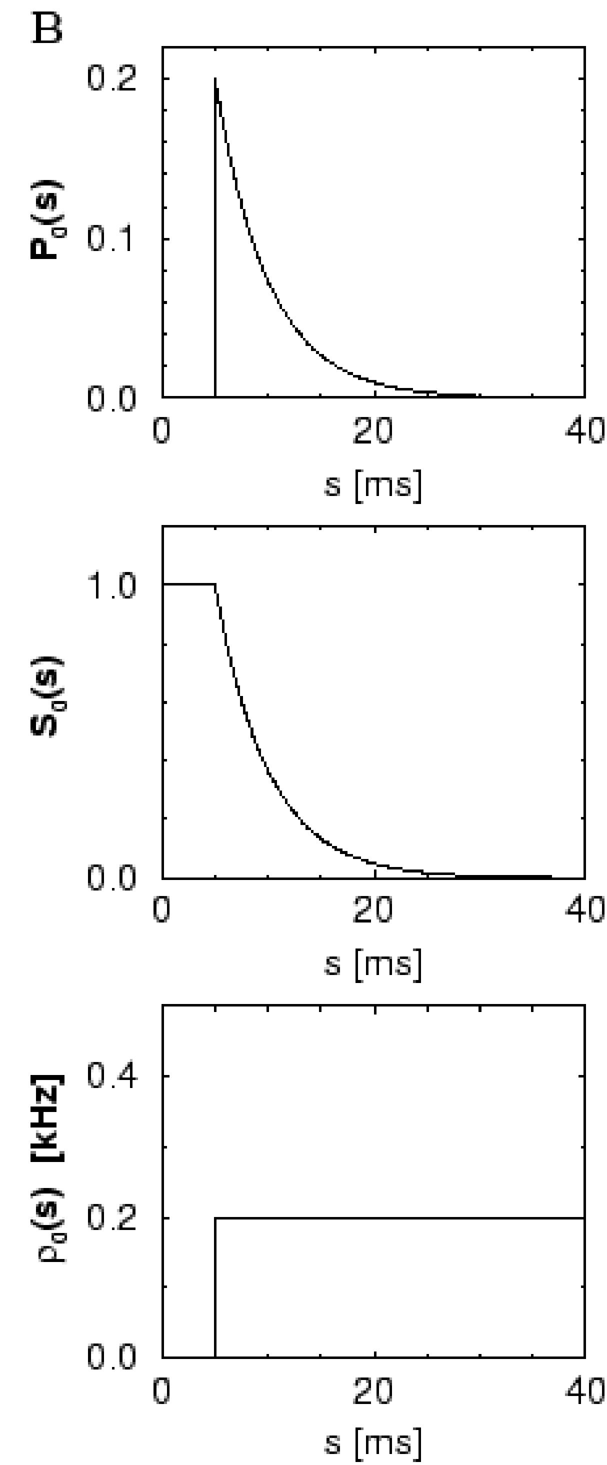
Example 2.2: Poisson process with refraction

If we add refractory period to the Poisson process

$$\lambda(s) \equiv \varrho_0(s) = \begin{cases} 0 & \text{for} \quad s < \Delta^{\text{abs}} \\ r & \text{for} \quad s > \Delta^{\text{abs}} \end{cases}$$

Inter-spike interval distribution takes the form

$$P(s) = \begin{cases} 0 & \text{for } s < \Delta^{\text{abs}} \\ r \exp[-r(s - \Delta^{\text{abs}})] & \text{for } s > \Delta^{\text{abs}} \end{cases}$$



Gerstner, Kistler, 2002

Example 3: IMI model – Inhomogeneous Markov Interval

- Assume we only know the current time t and the time τ since the last spike

$$\lambda = \lambda(t, \tau)$$

We call such model the IMI model

Kass, Ventura, 2001

Example 3: IMI model – Inhomogeneous Markov Interval

- Assume we only know the current time t and the time τ since the last spike

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- We shall limit ourselves to multiplicative IMI models:

$$\lambda(t, \tau) = \lambda_1(t)\lambda_2(\tau)$$

Kass, Ventura, 2001

IMI model

- We have two factors in the model:

$$\lambda(t, \tau) = \lambda_1(t)\lambda_2(\tau)$$

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- $\lambda_1(t)$ – response to the stimulus, receptive field or equivalent properties of the cell

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$$\lambda(t, \tau) = \lambda_1(t)\lambda_2(\tau)$$

- $\lambda_1(t)$ – response to the stimulus, receptive field or equivalent properties of the cell

- $\lambda_2(\tau)$ – local modulation of this activity, e.g. due to refractive properties of cell membrane

Estimation – proposition: first get λ_2

- Find a fragment of the recording with „spontaneous” activity. There $\lambda_1 = const$ and ISI distribution describes $\lambda_2(\tau)$ *[renewal process]*

Wojcik et al. 2009

Estimation – proposition: first get λ_2

- Find a fragment of the recording with „spontaneous" activity. There $\lambda_1 = const$ and ISI distribution describes $\lambda_2(\tau)$ *[renewal process]*
- The connection between $\lambda_2(\tau)$ and the probability distribution of ISI $P(\tau)$ is

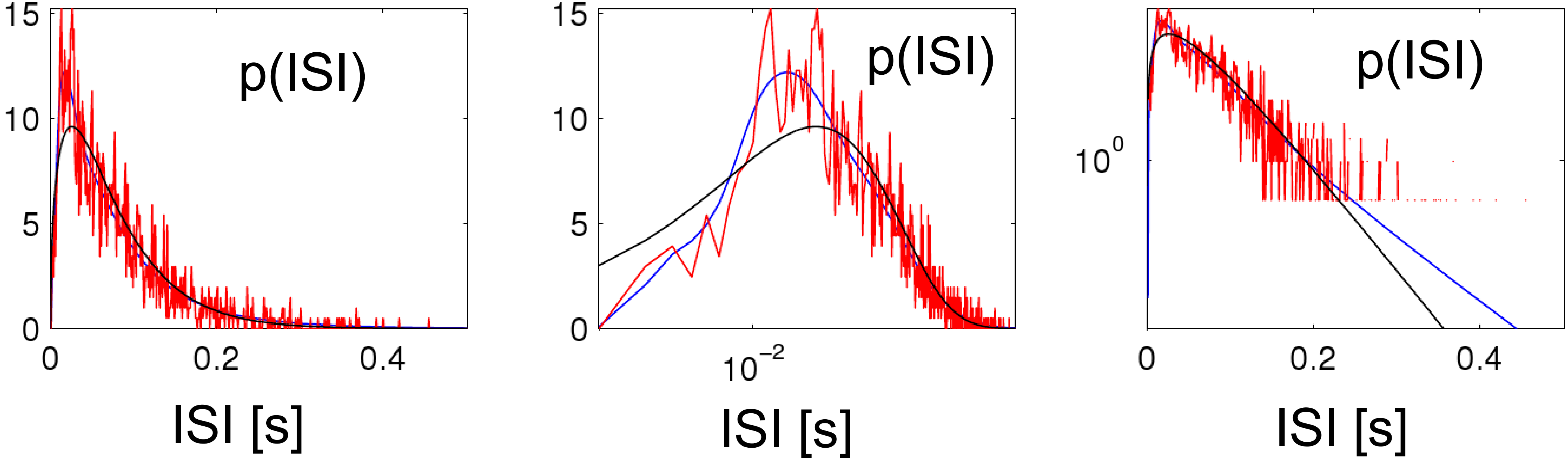
$$\lambda_2(\tau) = \frac{P(\tau)}{1 - \int_0^\tau ds P(s)}$$

$$P(\tau) = \lambda_2(\tau) \exp\left[-\int_0^\tau ds \ \lambda_2(s) \right]$$

Perkel, Gerstein Moore 1967

Wojcik et al. 2009

Example ISI distribution



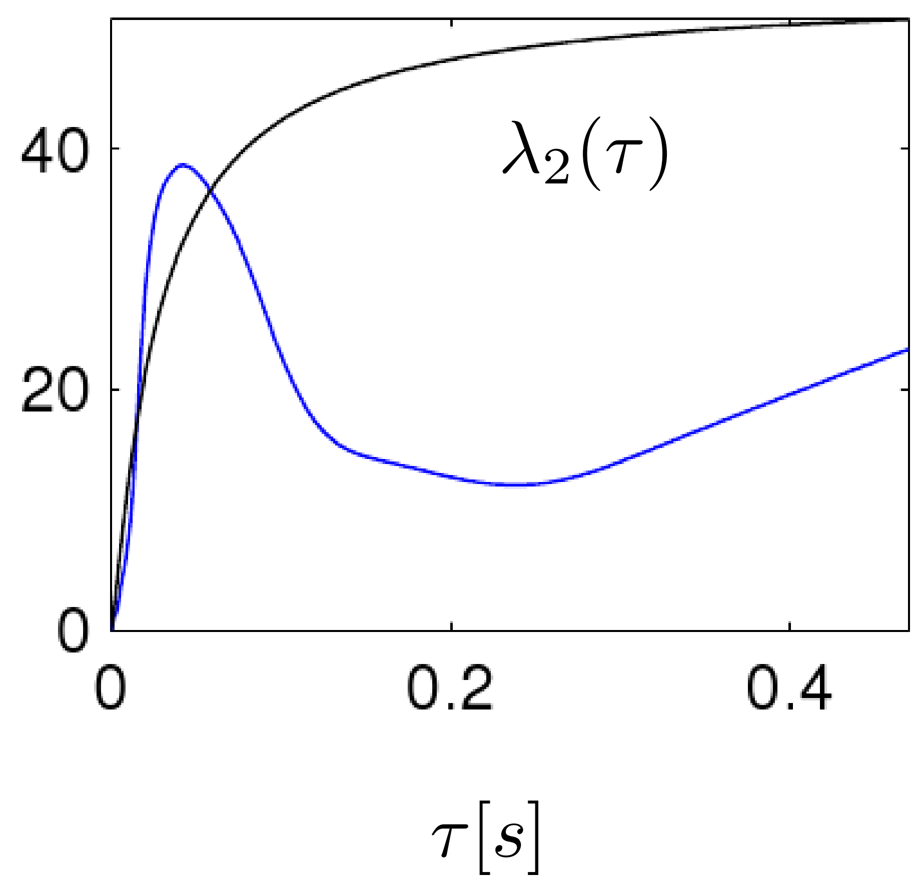
Sc8u12

- red – experimental distribution
- blue – smoothed with gaussian kernel
- black – best fit of a parametric model (gamma distribution)

λ_2 obtained

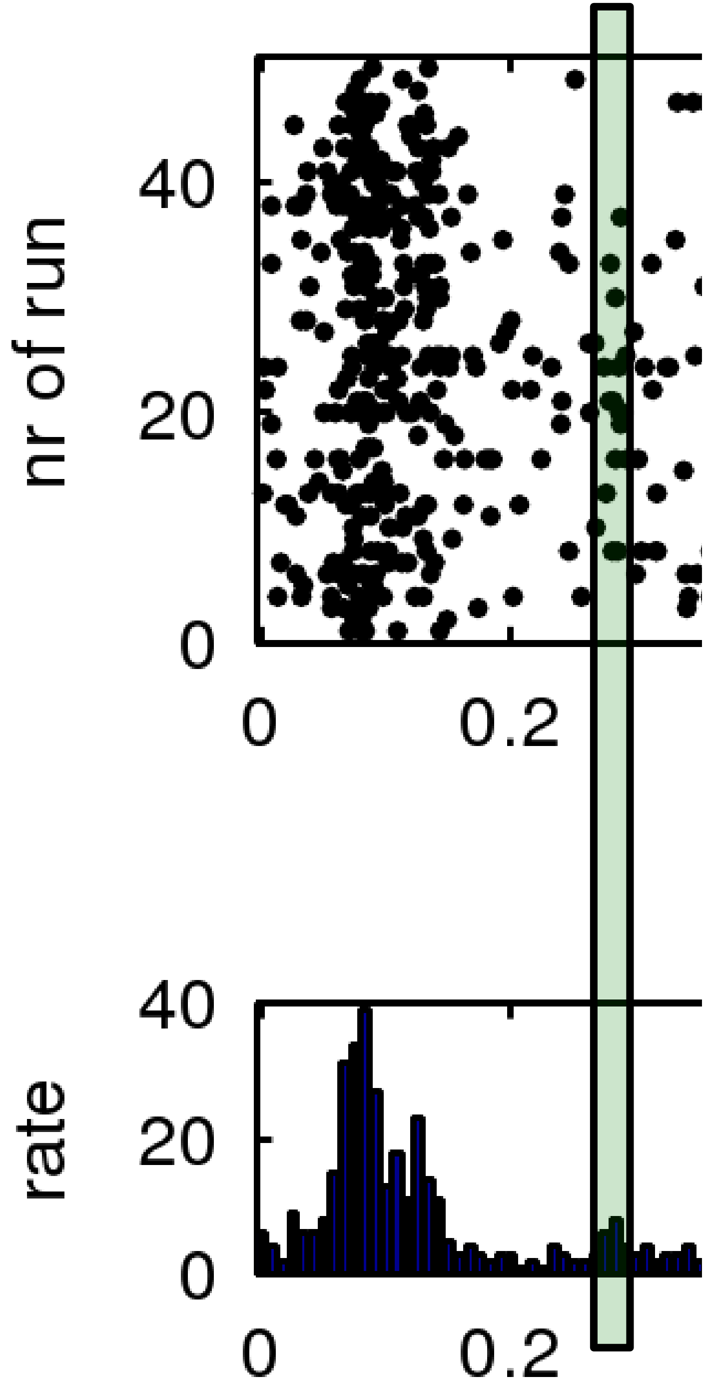
- blue – smoothed with gaussian kernel
- black – best fit of a parametric model (gamma distribution)

ent3u7



Estimation of λ_1 from λ_2

- Probability to generate a spike in i-th response

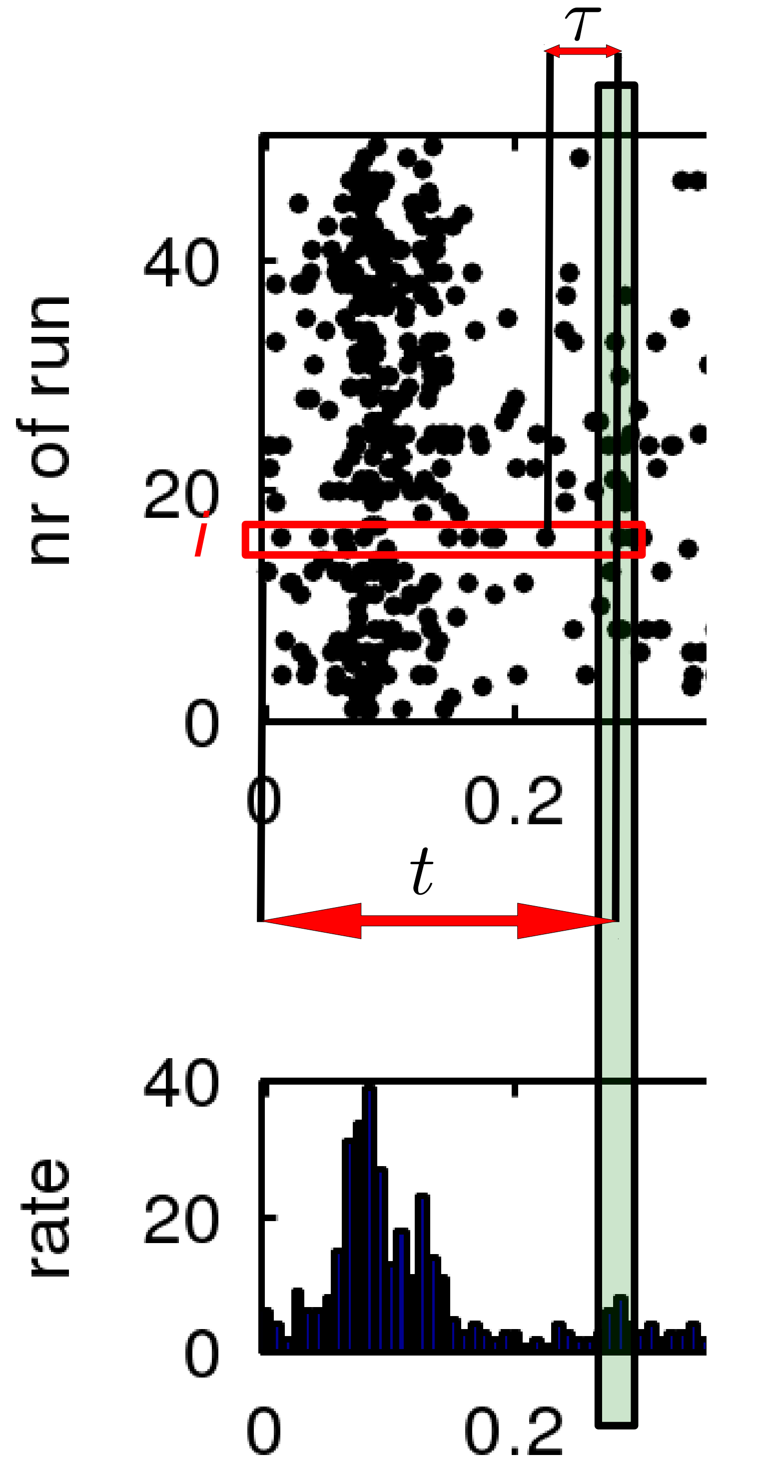


Estimation of λ_1 from λ_2

- Probability to generate a spike in i-th response is

$$p_i([t, t + \delta t]) = \lambda_1(t)\lambda_2(\tau_i)\delta t$$

where τ is the time since the last spike before t



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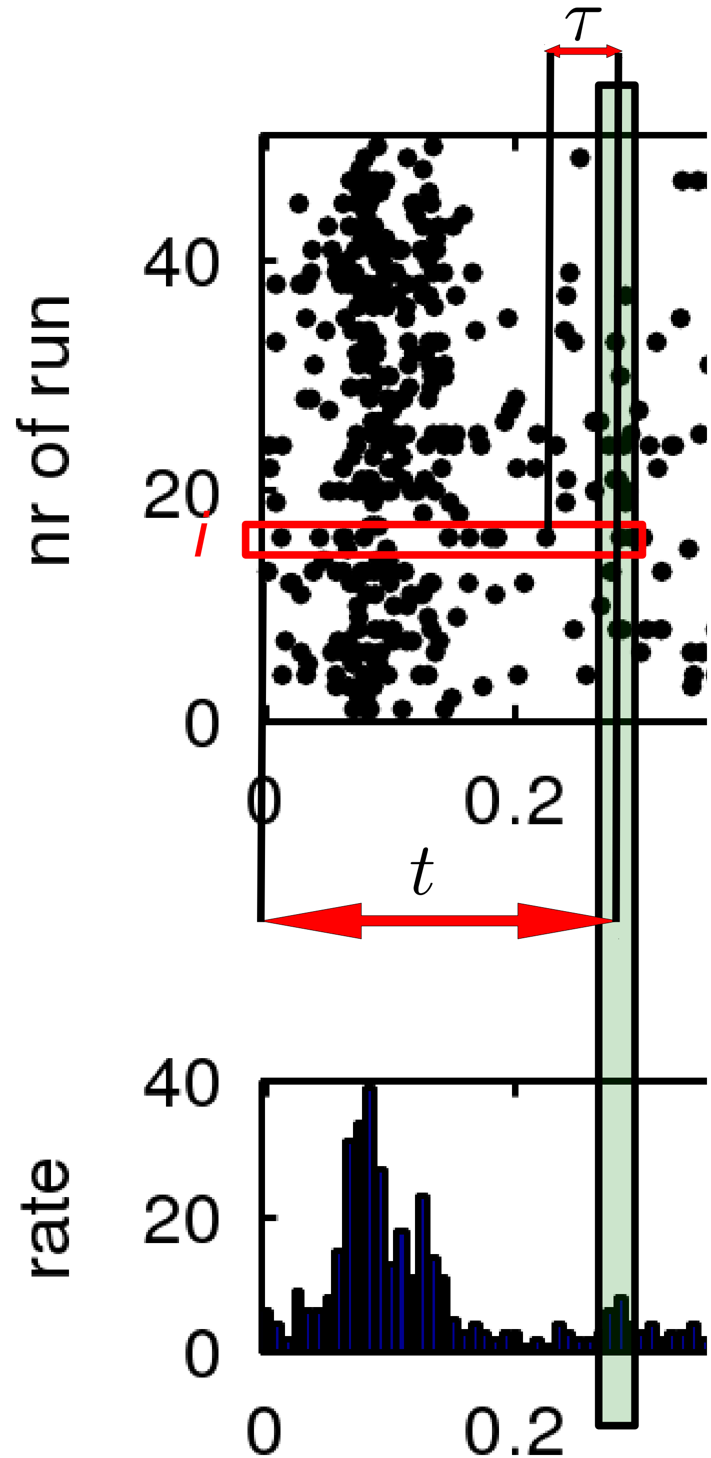
- Probability to generate a spike in i-th response is

$$p_i([t, t+\delta t]) = \lambda_1(t)\lambda_2(\tau_i)\delta t$$

where τ is the time since the last spike before t

- From here, approximately

$$\lambda_1(t) = \frac{\bar{r}([t, t+\delta t])}{\langle \lambda_2(\tau_i) \rangle_i}$$



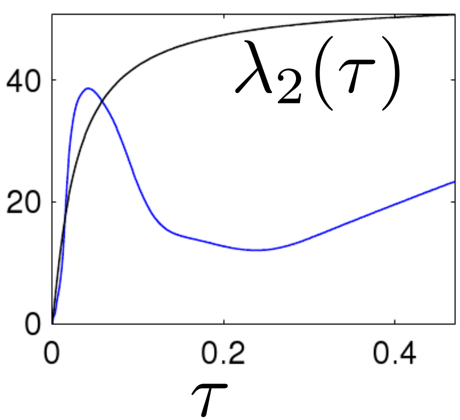
ent3u7

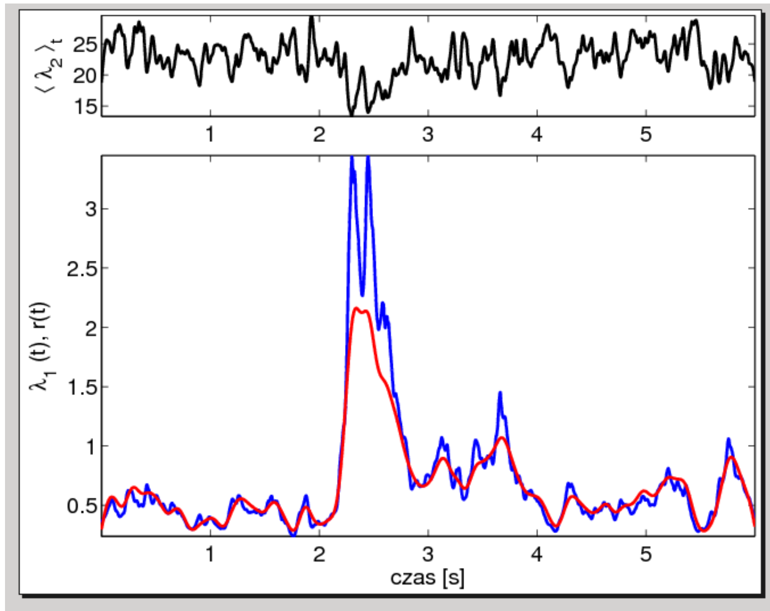
v=10

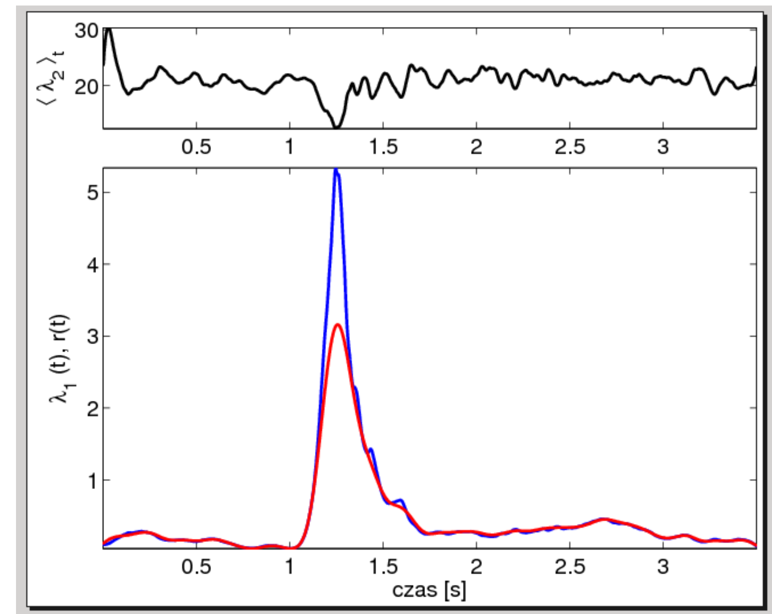
$$\lambda_1(t) = \frac{\bar{r}([t, t+\delta t])}{\langle \lambda_2(\tau_i) \rangle_i}$$

v=20

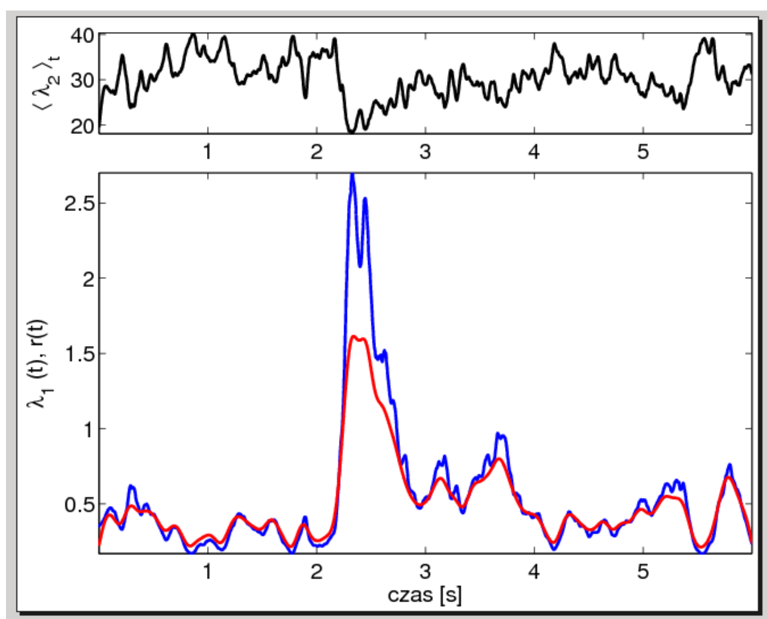
nonparametric

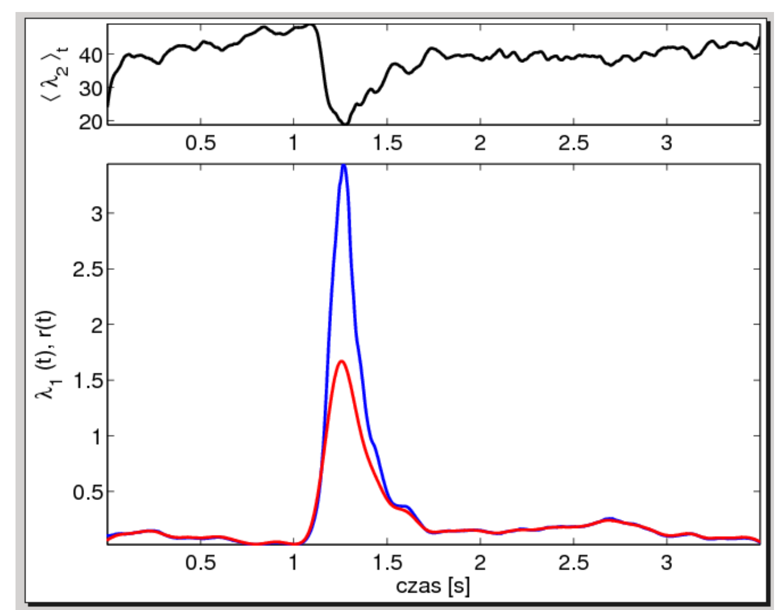




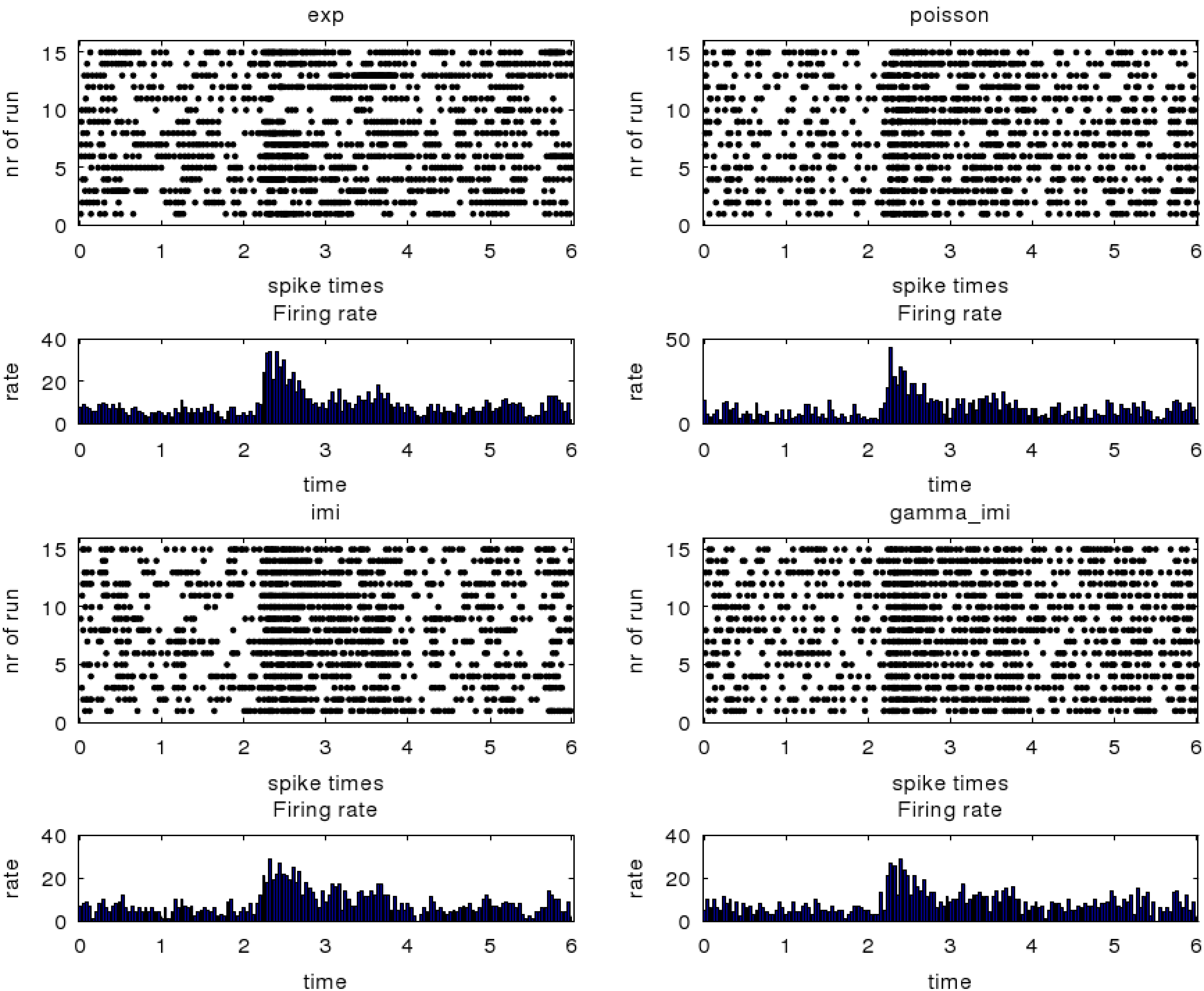


parametric
(gamma)

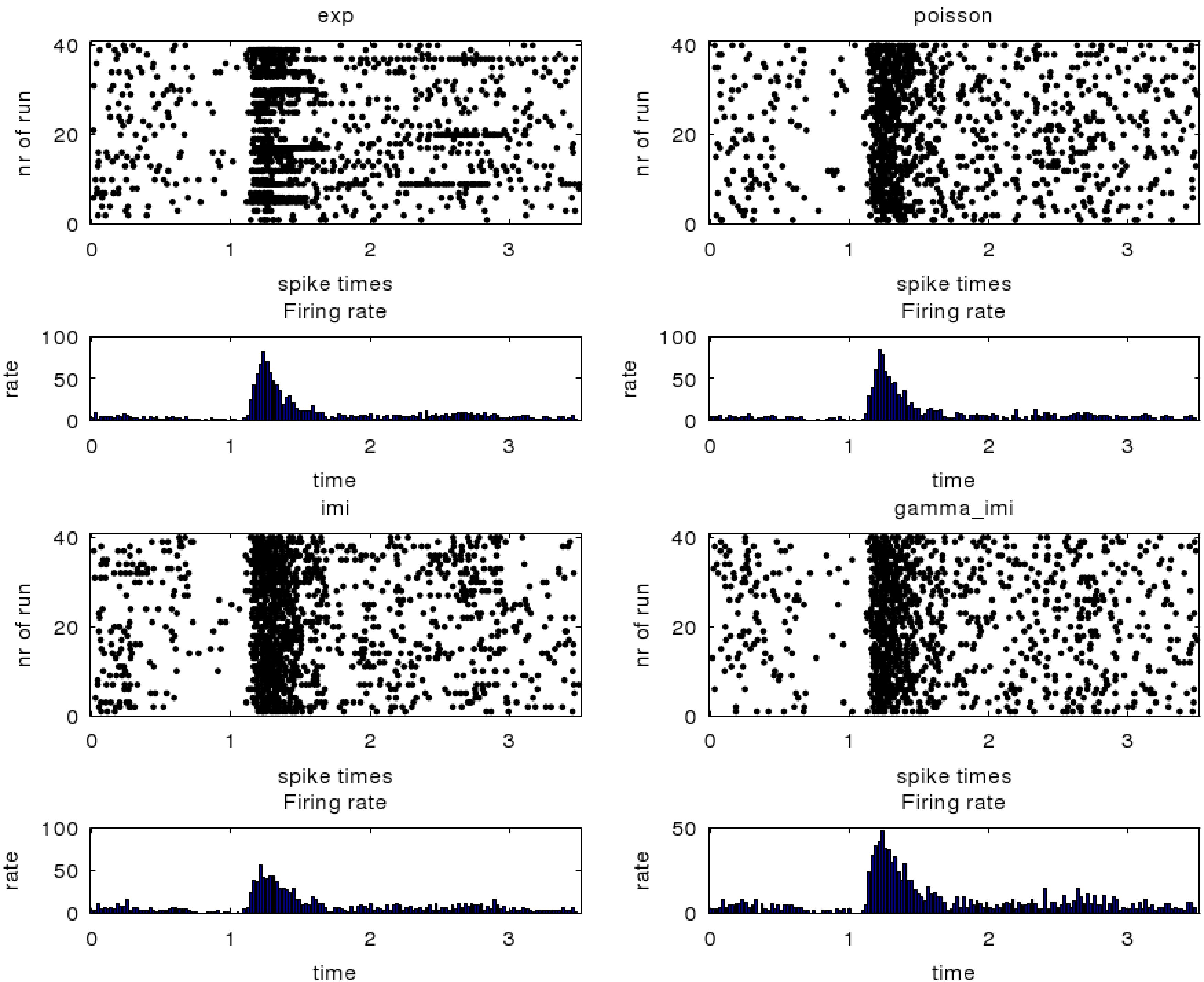




Spike times for cell: ent3u7; velocity: left; stim: 10



Spike times for cell: ent3u7; velocity: left; stim: 20



Time-rescaling theorem

Let $0 < u_1 < u_2 < \cdots < u_n < T$ be a realization of a point process with conditional intensity

$$\lambda(t|N_t)$$

Define a transformation

$$\Lambda(u_k) = \int_0^{u_k} \lambda(u|N_u)\, du,$$

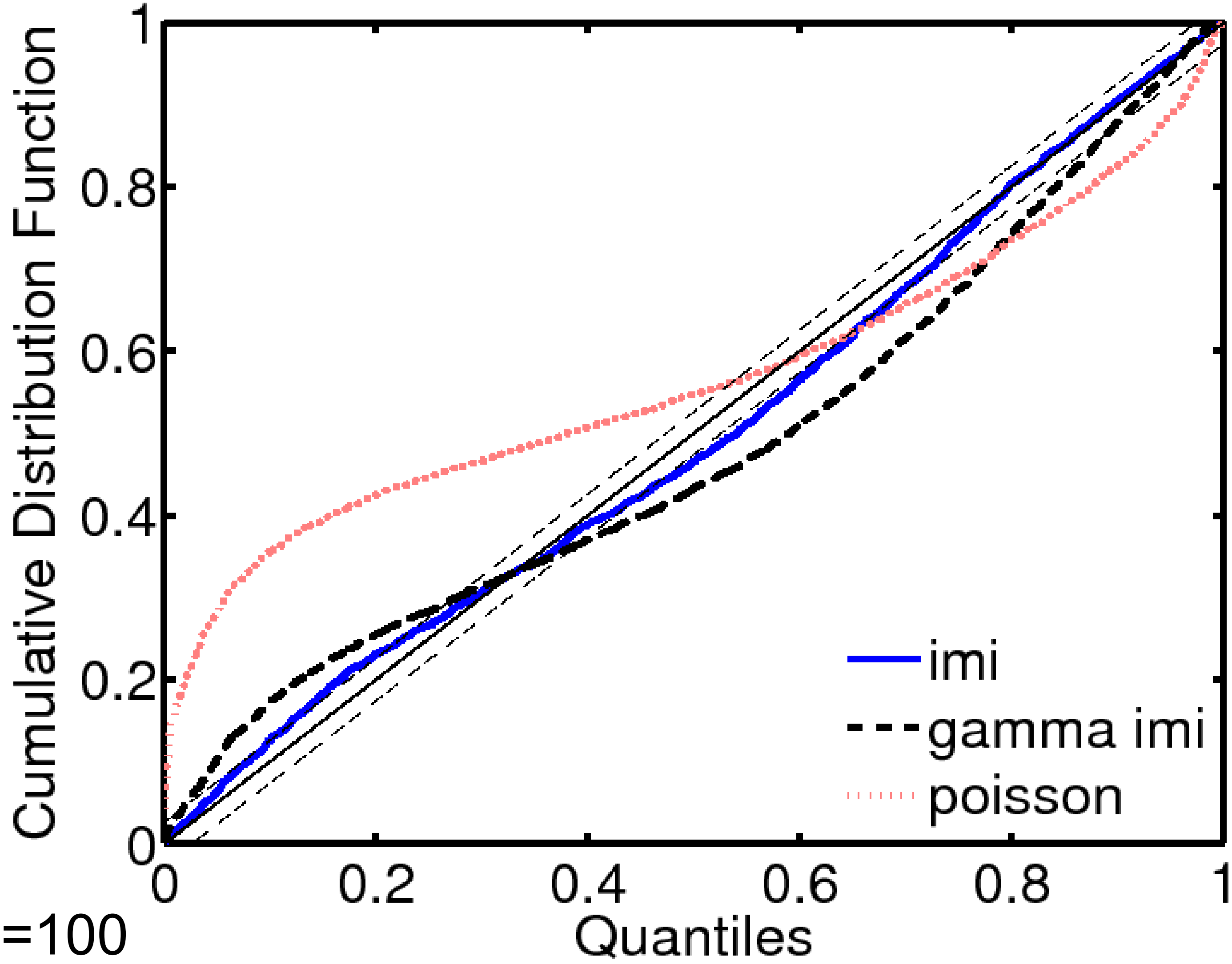
for $k = 1, \ldots, n$. Then $\Lambda(u_k)$ give a homogeneous Poisson process of unit rate.

Brown et al. 2002

Goodness of fit test

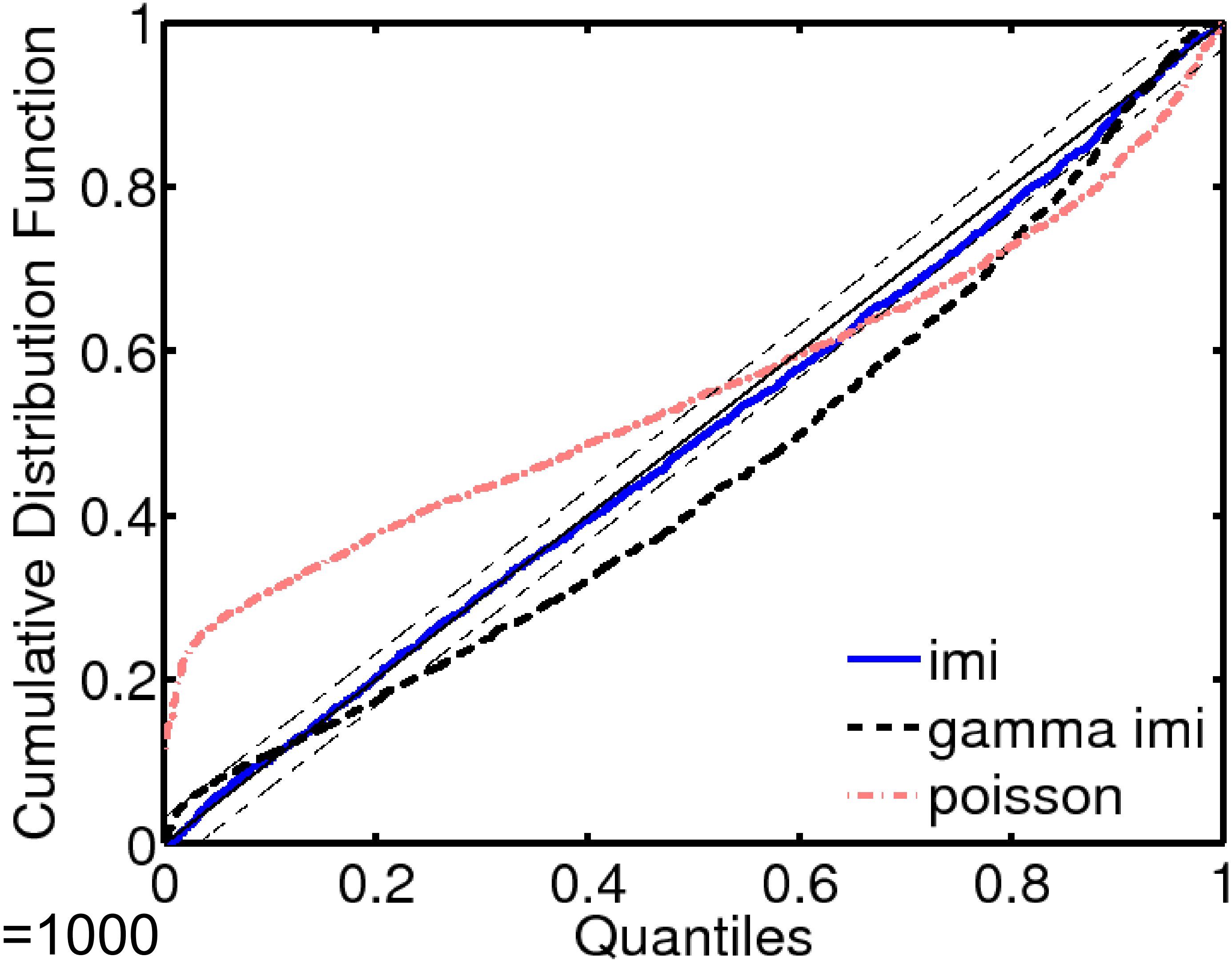
- Compute rescaled ISI: $\tau_k = \Lambda(u_k) - \Lambda(u_{k-1})$
- Transform τ_k to a new variable, $z_k = 1 - \exp(-\tau_k)$
- Then z_k are independent uniform variables on the interval
- Order z_k from smallest to largest and plot cumulative values of uniform density against the ordered z_ks.
- If the model is correct, resulting curve will be diagonal

Test of the model quality



ent3u7 v=100

Test of the model quality



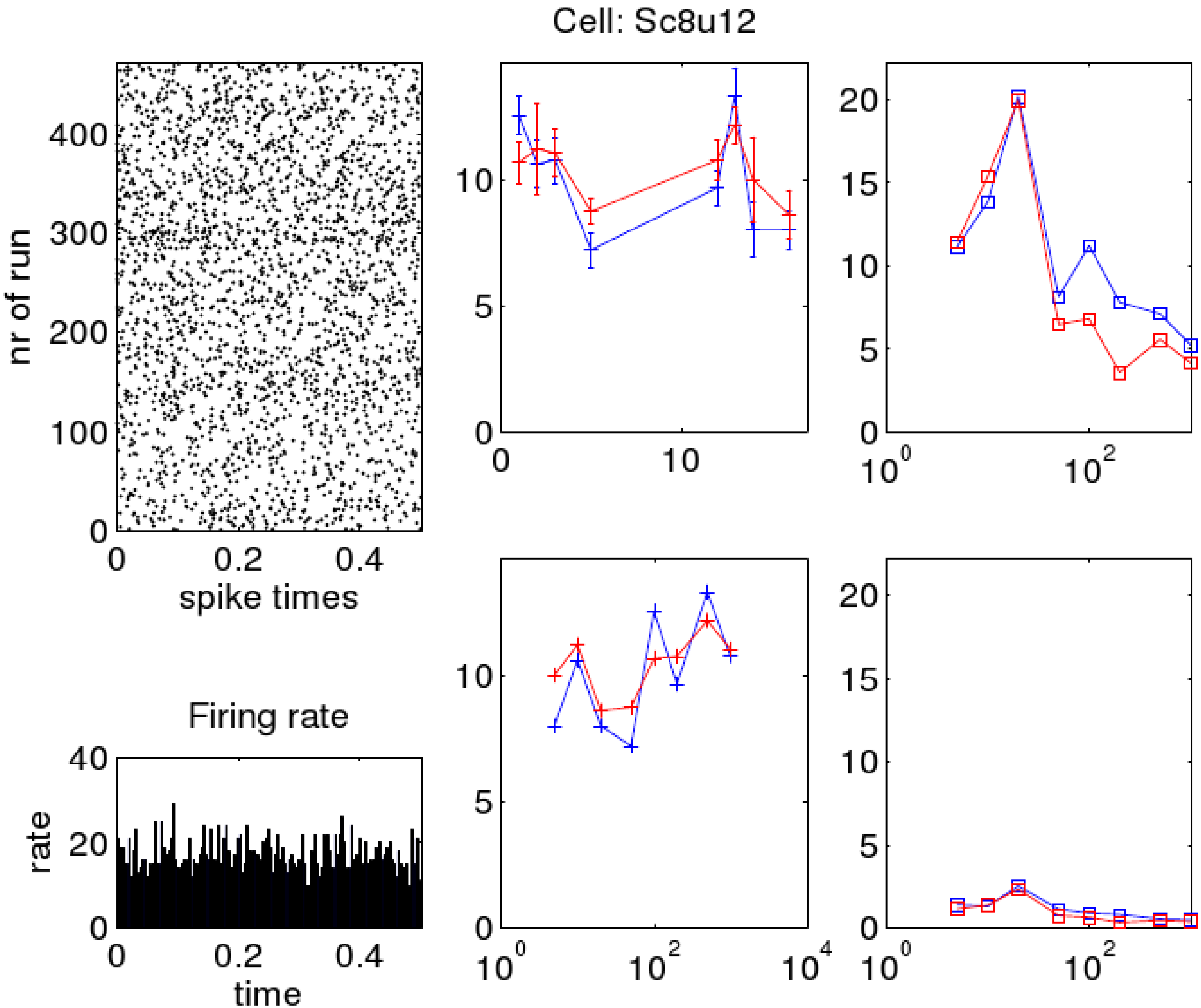
ent5u3 v=1000

Be careful!!!

Problem 1

- We assumed the last 0.5s of our experiment is „spontaneous activity”.
- Is that so?

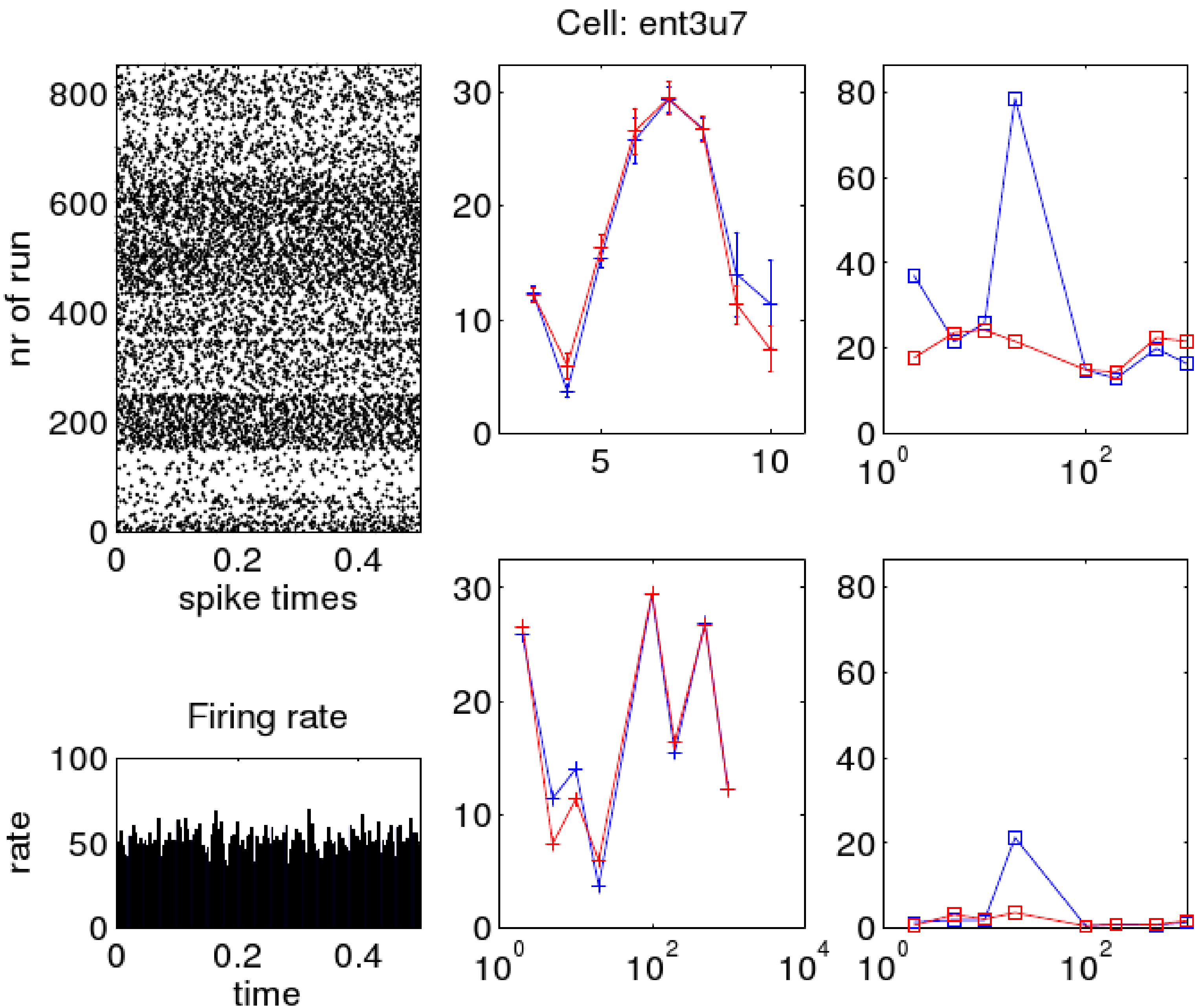
Spontaneous? – sometimes yes!



Blue: left → right

Red: right → left

Spontaneous? – sometimes no!

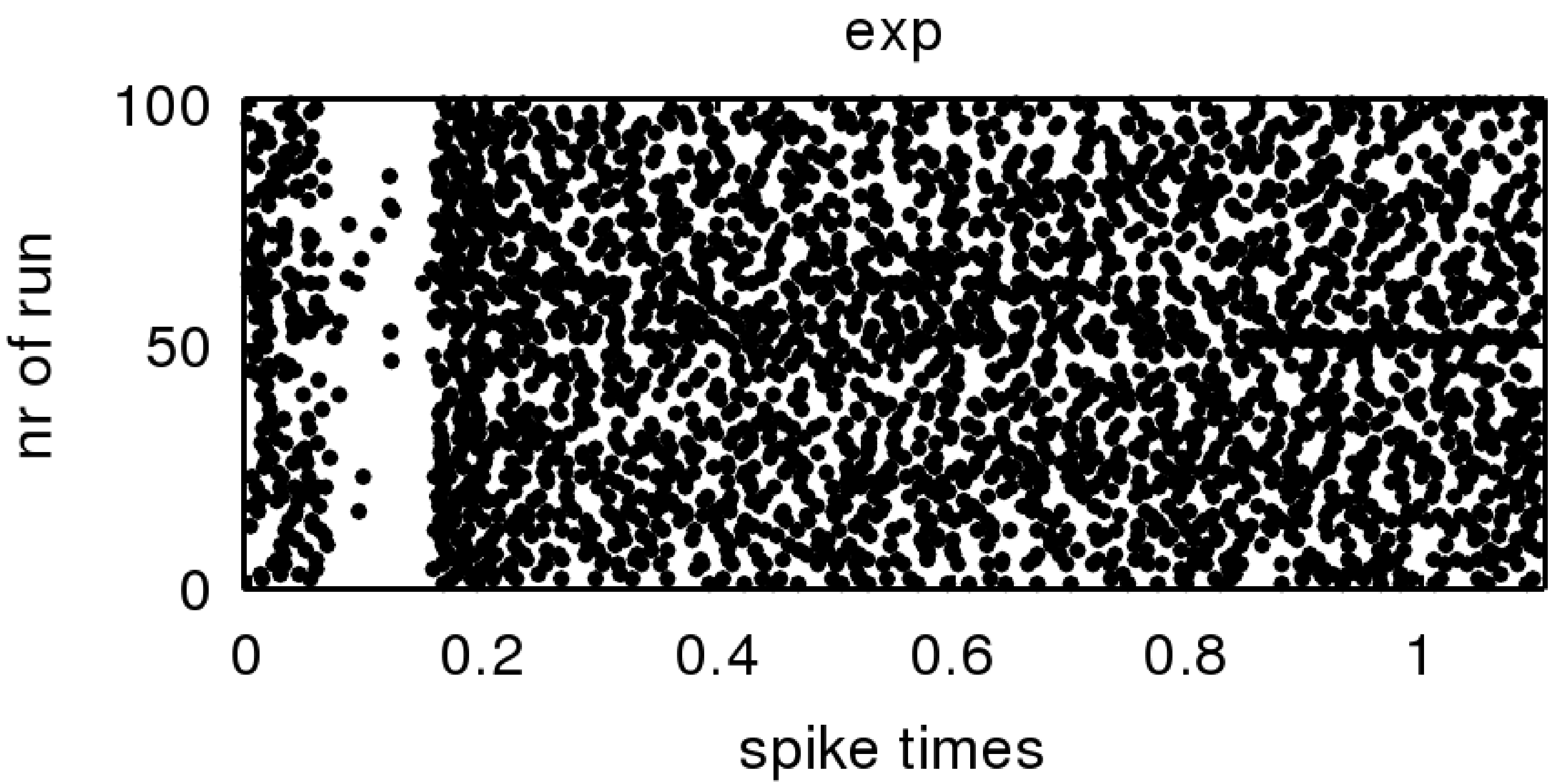


Blue: left → right
Red: right → left

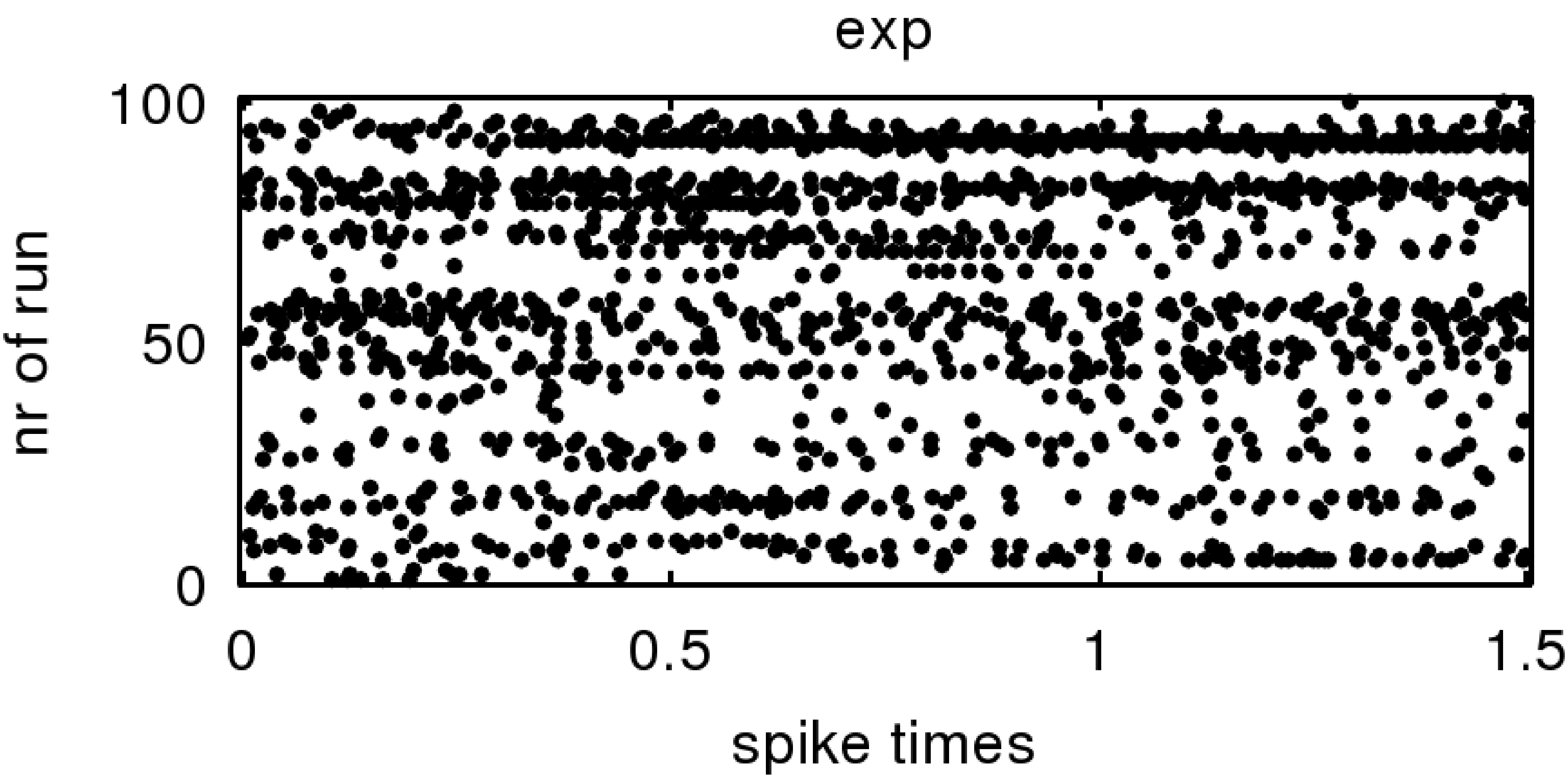
Problem 2

- We assumed our data can be explained by a model dependent on the time of the model and the time from the last spike.
- Is that reasonable?

IMI OK? – sometimes yes!



IMI OK? – sometimes no!



Summary for spike trains

- Spike trains are realizations of point processes
- There is more than Poisson process
- Three issues:
  - How do I think about the data? [the model]
  - How do I estimate the model from data?
  - How do I use the model to generate surrogates?
- Model comparison:
  - Time-rescaling theorem

Challenges

- BRAIN: Record spikes from all the neurons
- Inference from limited system sampling

And now for something totally different

Or not totally?

Point processes can be useful in the description of behavior

Transgenic mice with Alzheimer disease (APP.V717I) learn in a social context, but not individually

Transgenic mice with
Alzheimer disease (APP.V717I)
learn in a social context,
but individually only
when they are sleepy

Procedure

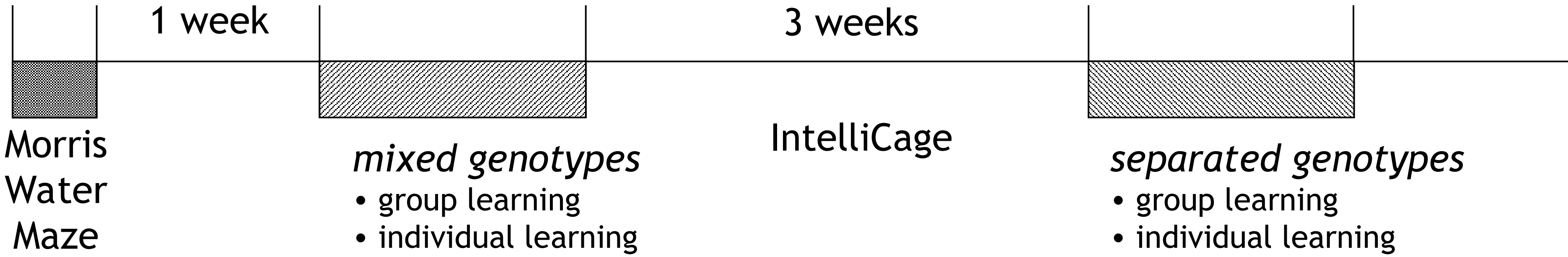
ANIMALS:

Three groups of APP.V717I transgenic mice and their wild type siblings at different age:

1. Young – 5-month old (WT = 12, APP.V717I = 11)
2. Middle-aged – 12-month old (WT = 12, APP.V717I = 12)
3. Old – 18-month old (WT = 10, APP.V717I = 10).

BEHAVIORAL TESTING:

1. Morris Water Maze – to measure individual spatial learning and memory.
2. IntelliCage tests – to measure ability to learning of spatial tasks with appetitive reinforcement:
   - group learning,
   - individual learning.



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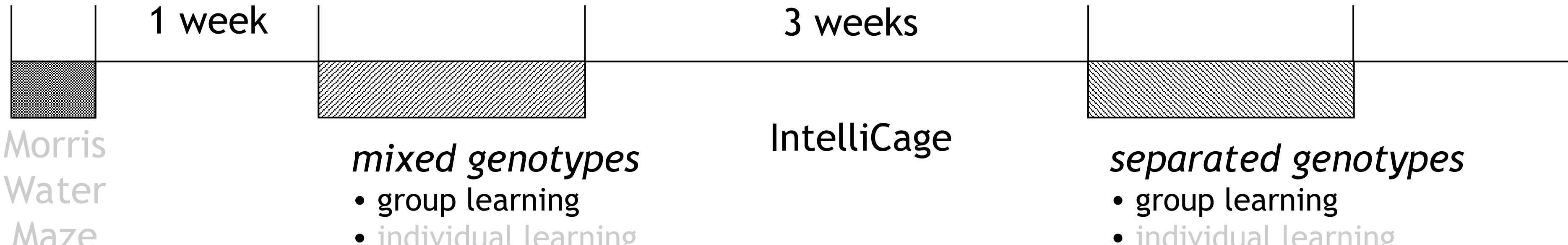
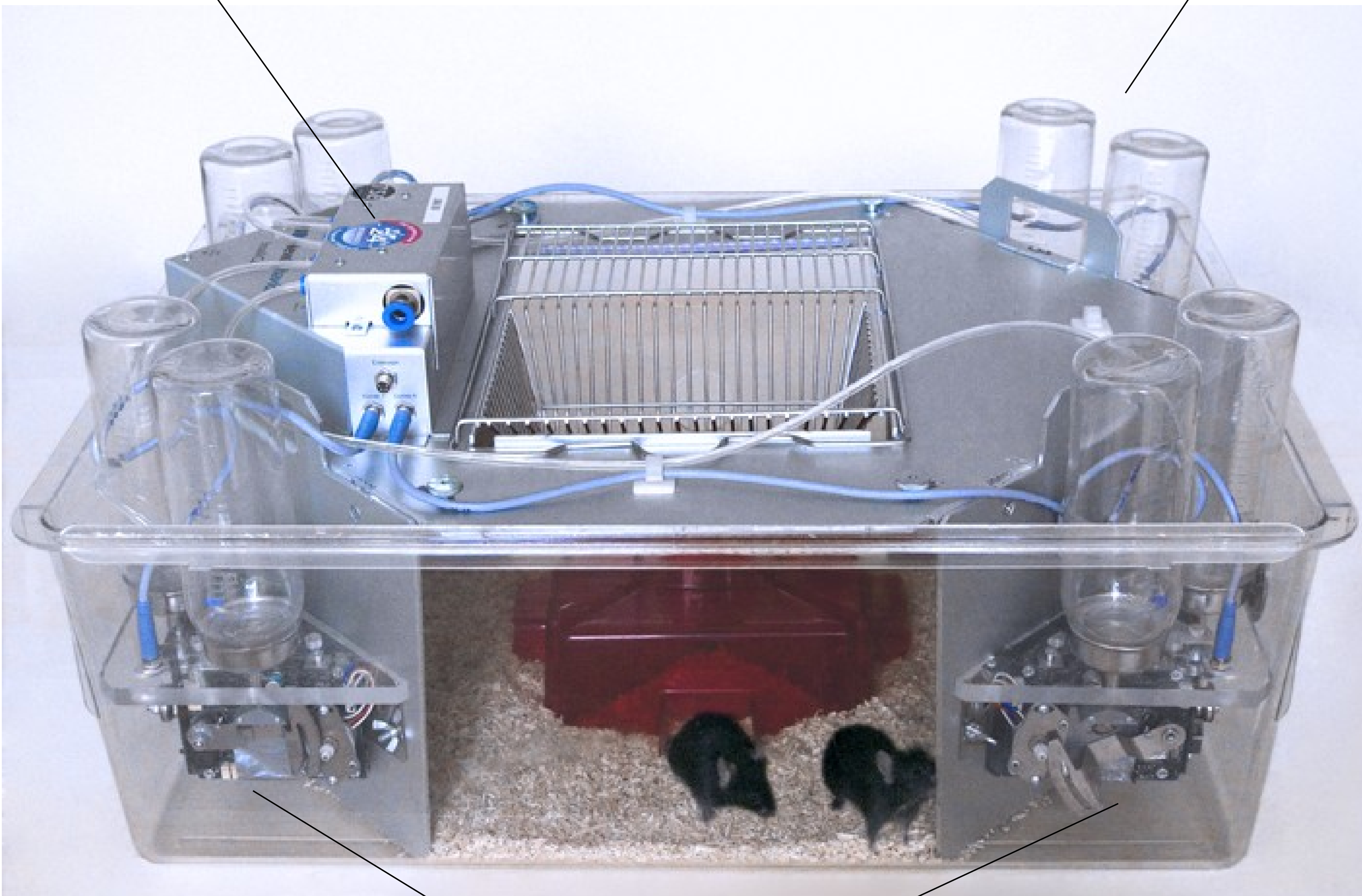


IntelliCage

Microprocessor

Bottles with liquid



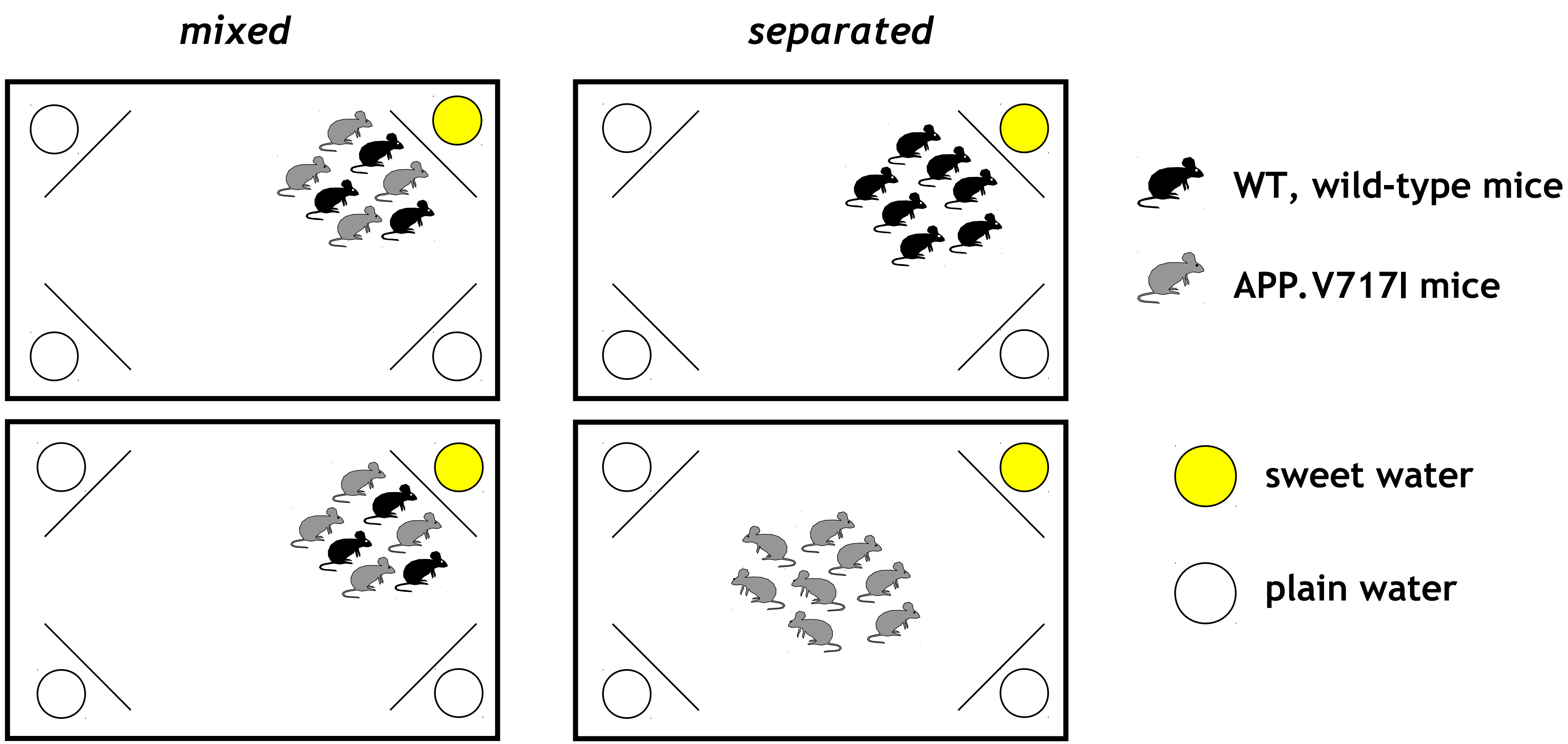
4 Learning corners with dual reward

NewBehavior

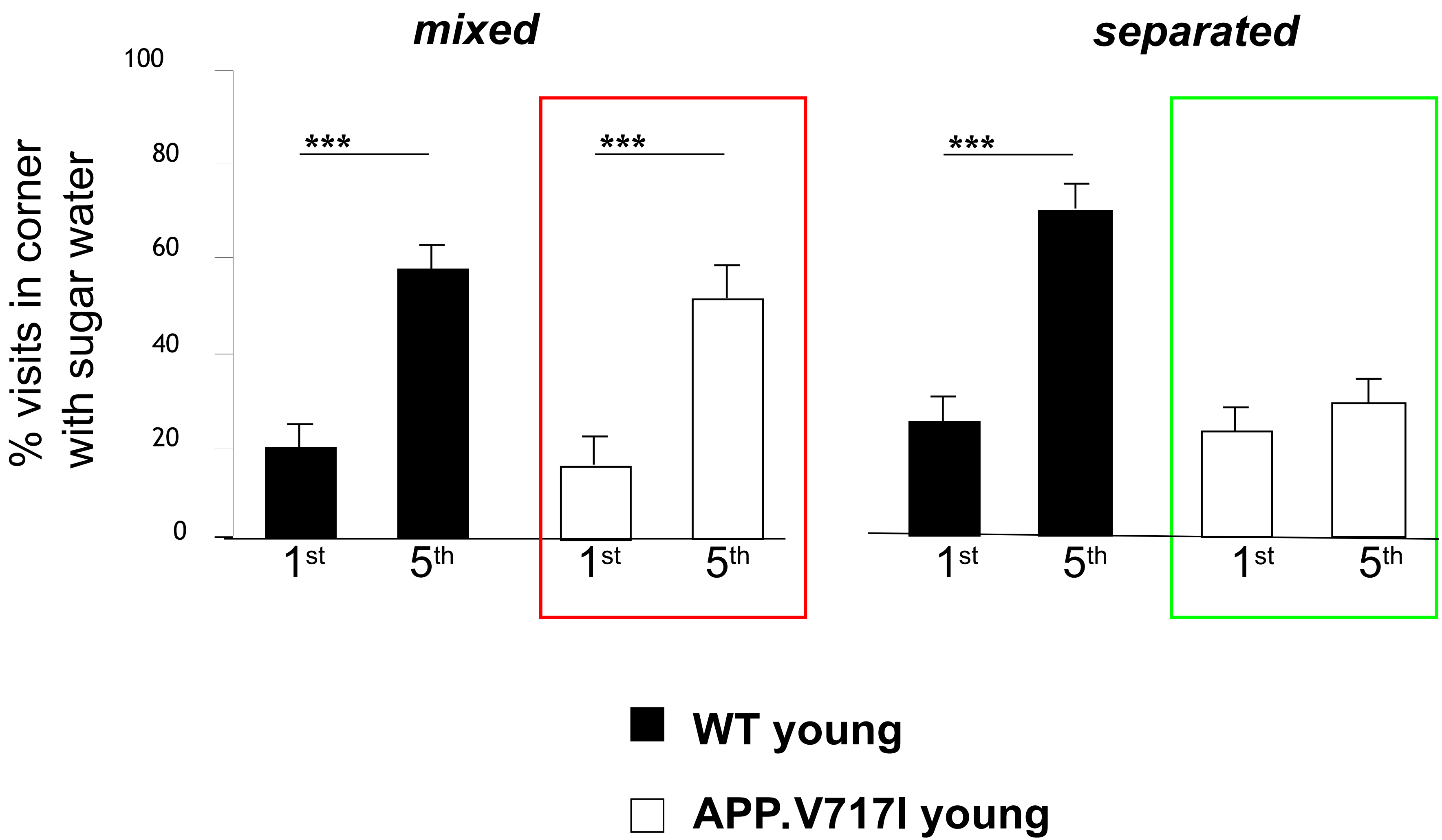
Learning corner

Group learning

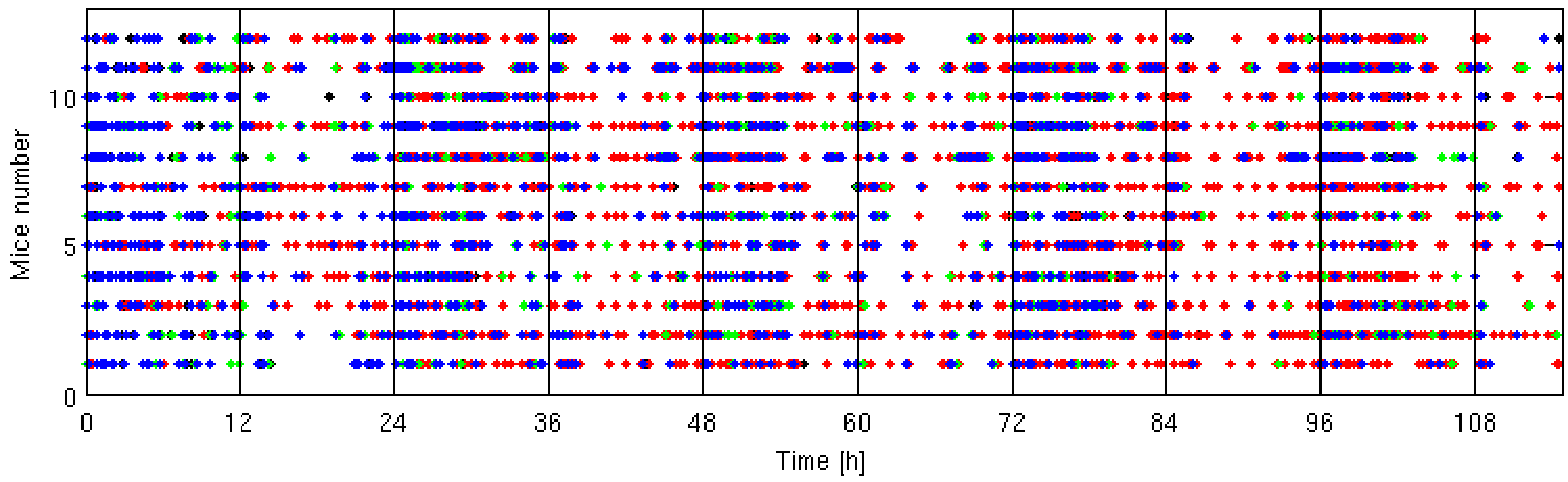
Setup of experiments in IntelliCage



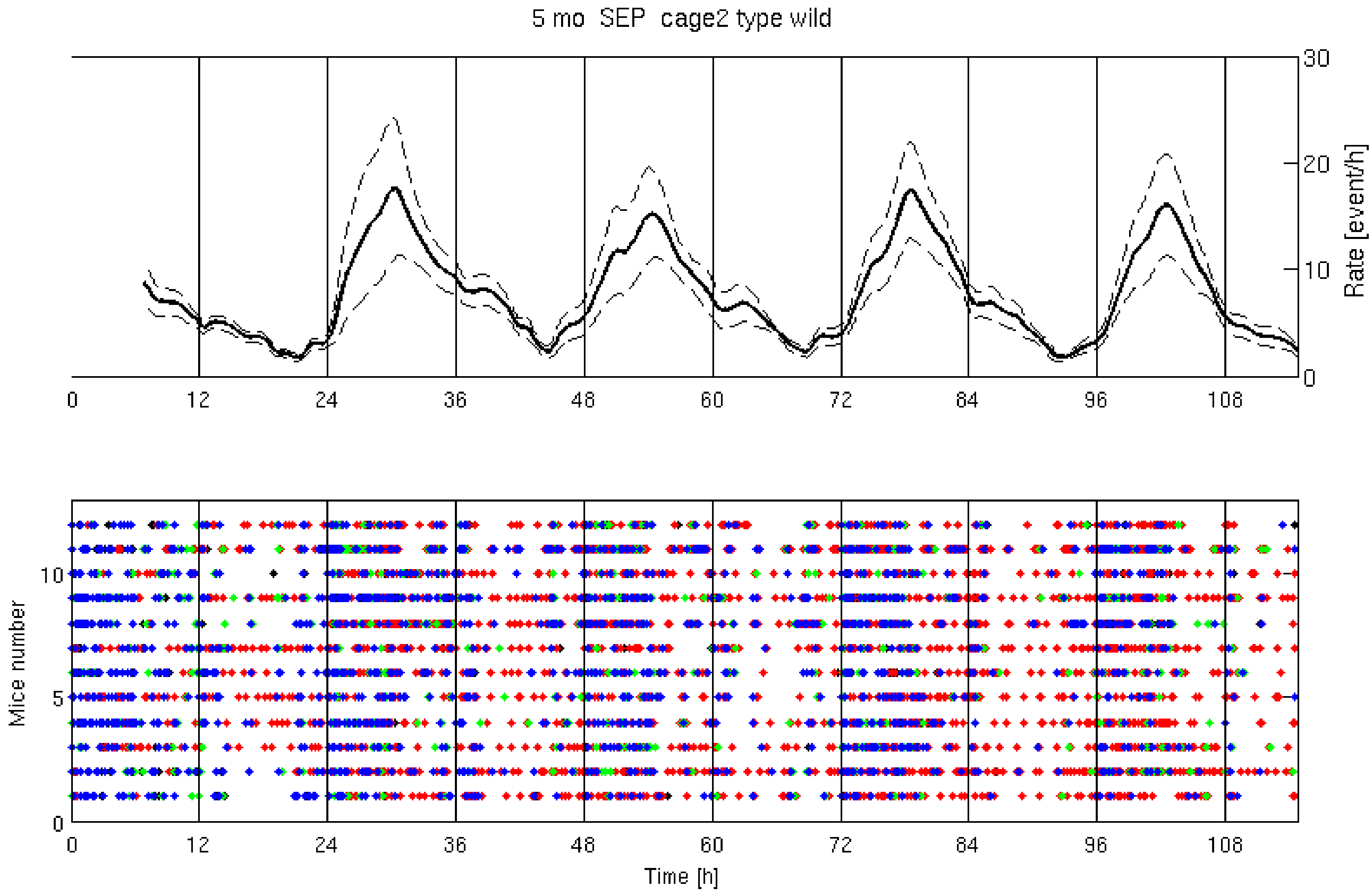
Group learning



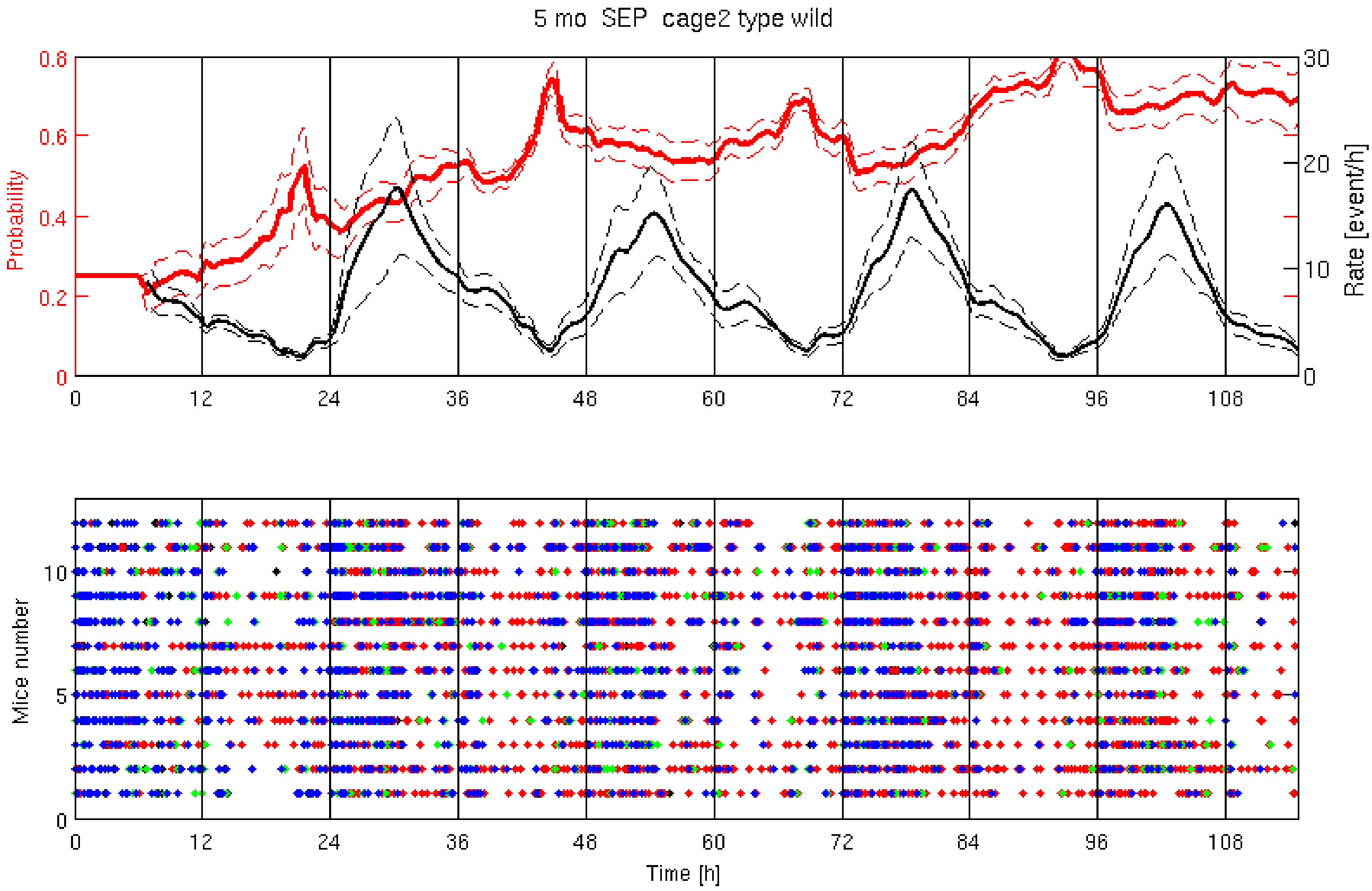
Point process view: raster plot



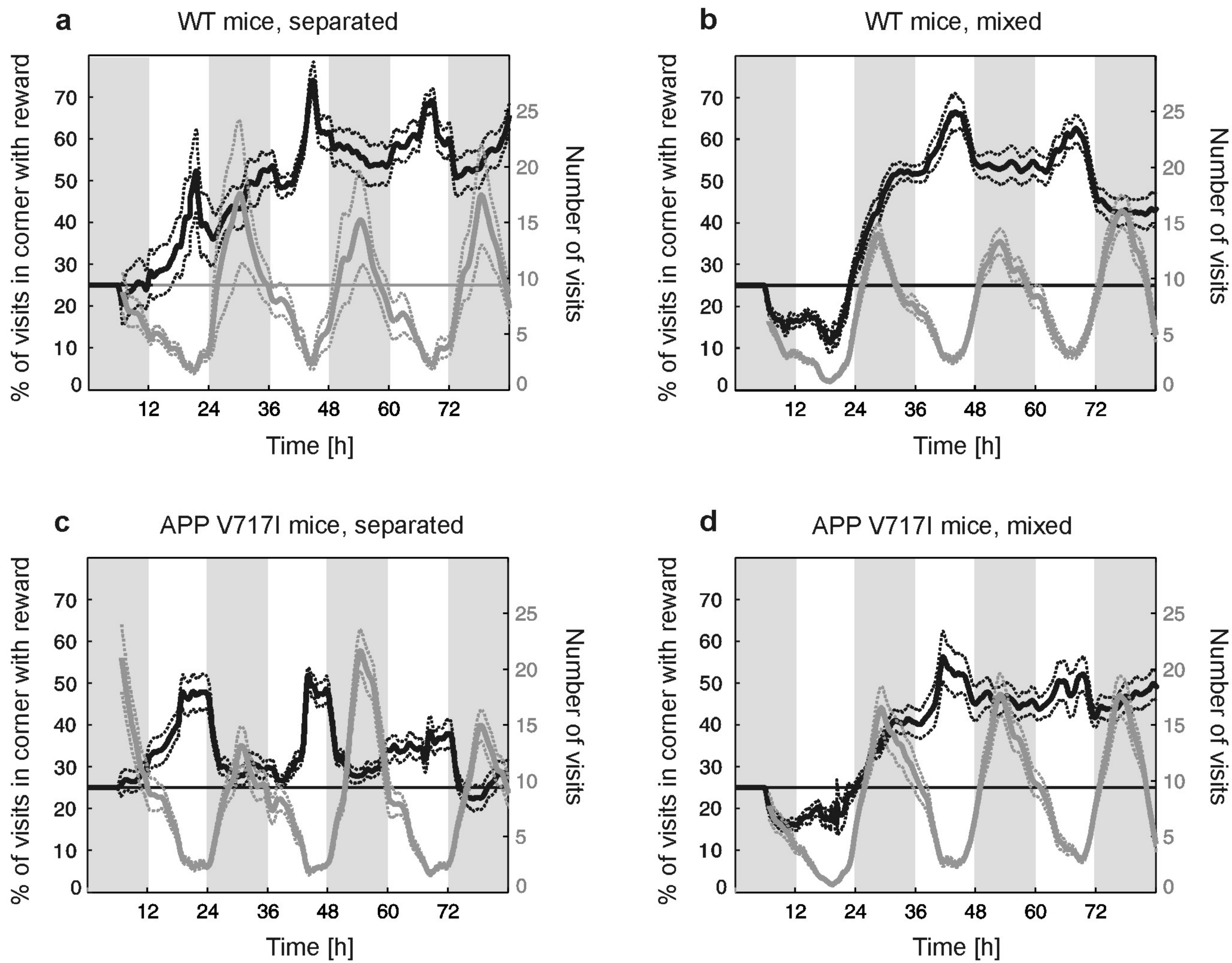
Point process view:
Post Stimulus Time Histogram



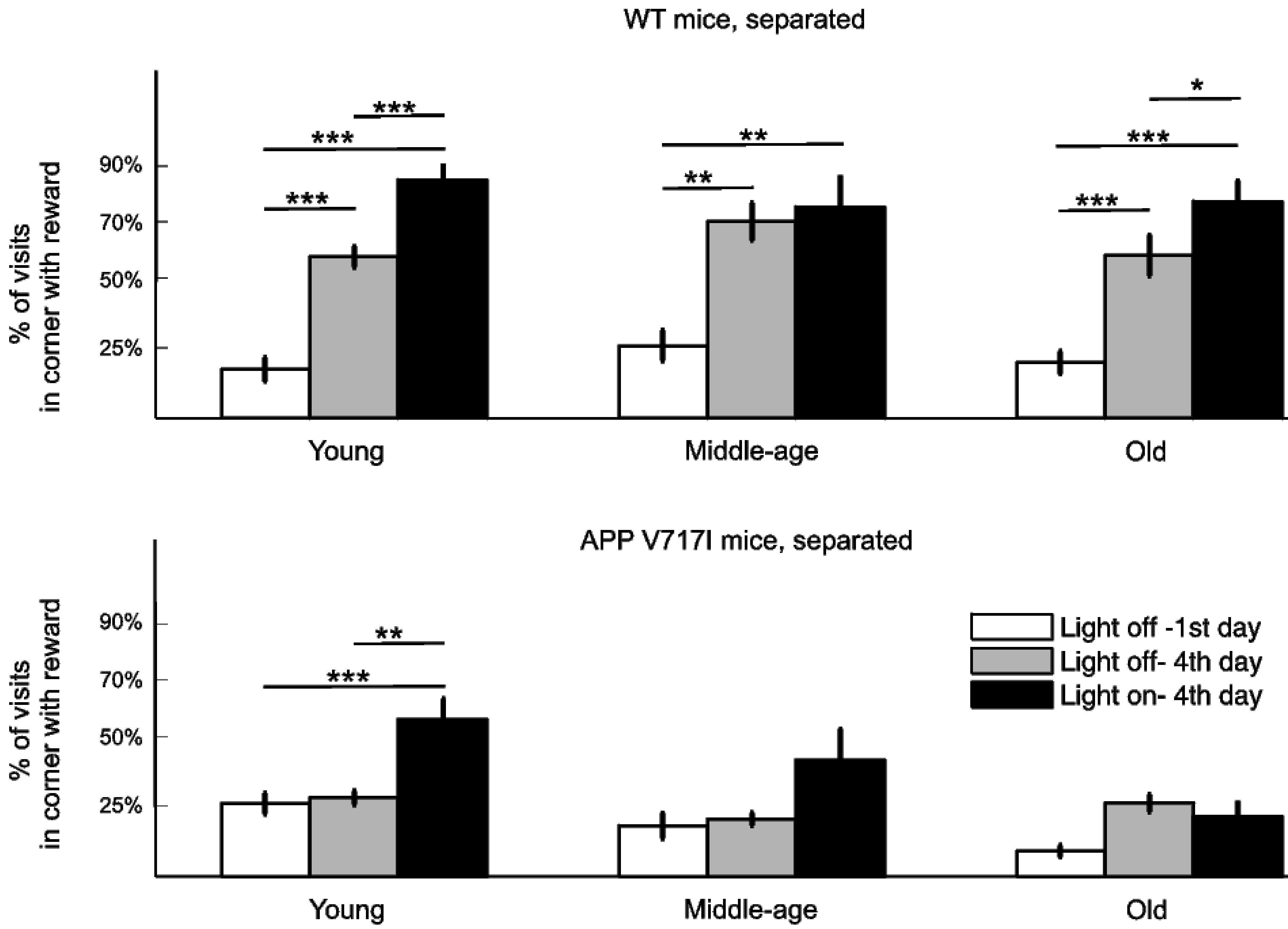
Point process view: learning



APP.V717I



a
WT mice, separated
b
WT mice, mixed
c
APP V717I mice, separated
d
APP V717I mice, mixed
% of visits in corner with reward
Number of visits
Time [h]
0
10
20
30
40
50
60
70
0
5
10
15
20
25
12
24
36
48
60
72



WT mice, separated
% of visits in corner with reward
90%
70%
50%
25%
***
***
***
**
**
*
***
***
Young
Middle-age
Old
APP V717I mice, separated
% of visits in corner with reward
90%
70%
50%
25%
**
***
Light off -1st day
Light off- 4th day
Light on- 4th day
Young
Middle-age
Old

Model of learning and behavior

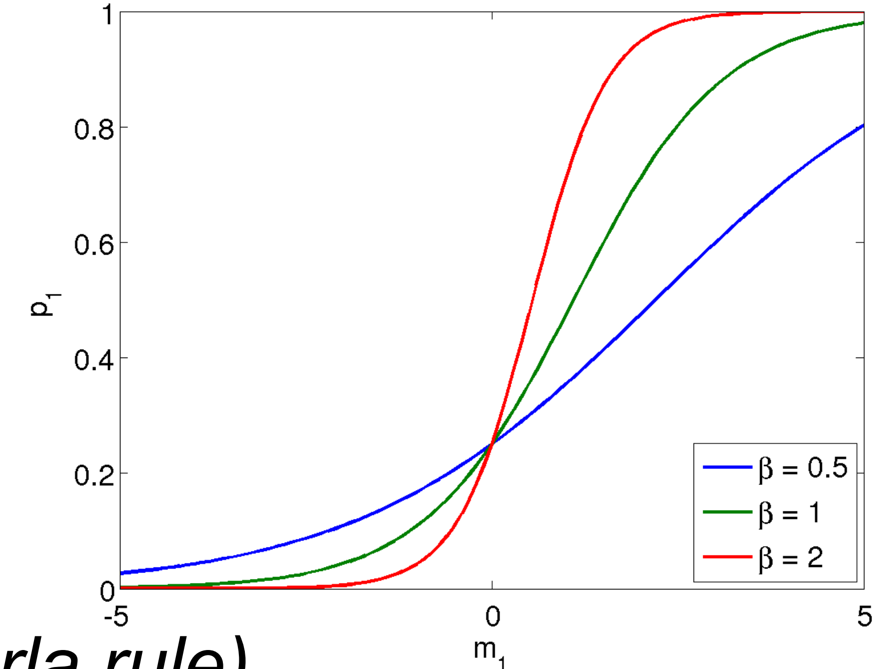
Modeling behavior as a sequence of actions

- Animal makes sequential decisions before action (I go to the corner *n*)
- Action is rewarded immediately after decision („*static action choice*”)
- The reward depends on action taken (e.g. water – 0, sweet water – 4)
- We consider only decisions taken, time is ignored

Model of learning and behavior: decision making

- Select a corner with probability depending on remembered reward (softmax)

$$p_n = \frac{\exp(\beta m_n)}{\sum_{i=1}^{4} \exp(\beta m_i)}$$



- Update the remembered reward m_n immediately depending on the current reward r_n *(Wagner-Rescorla rule)*

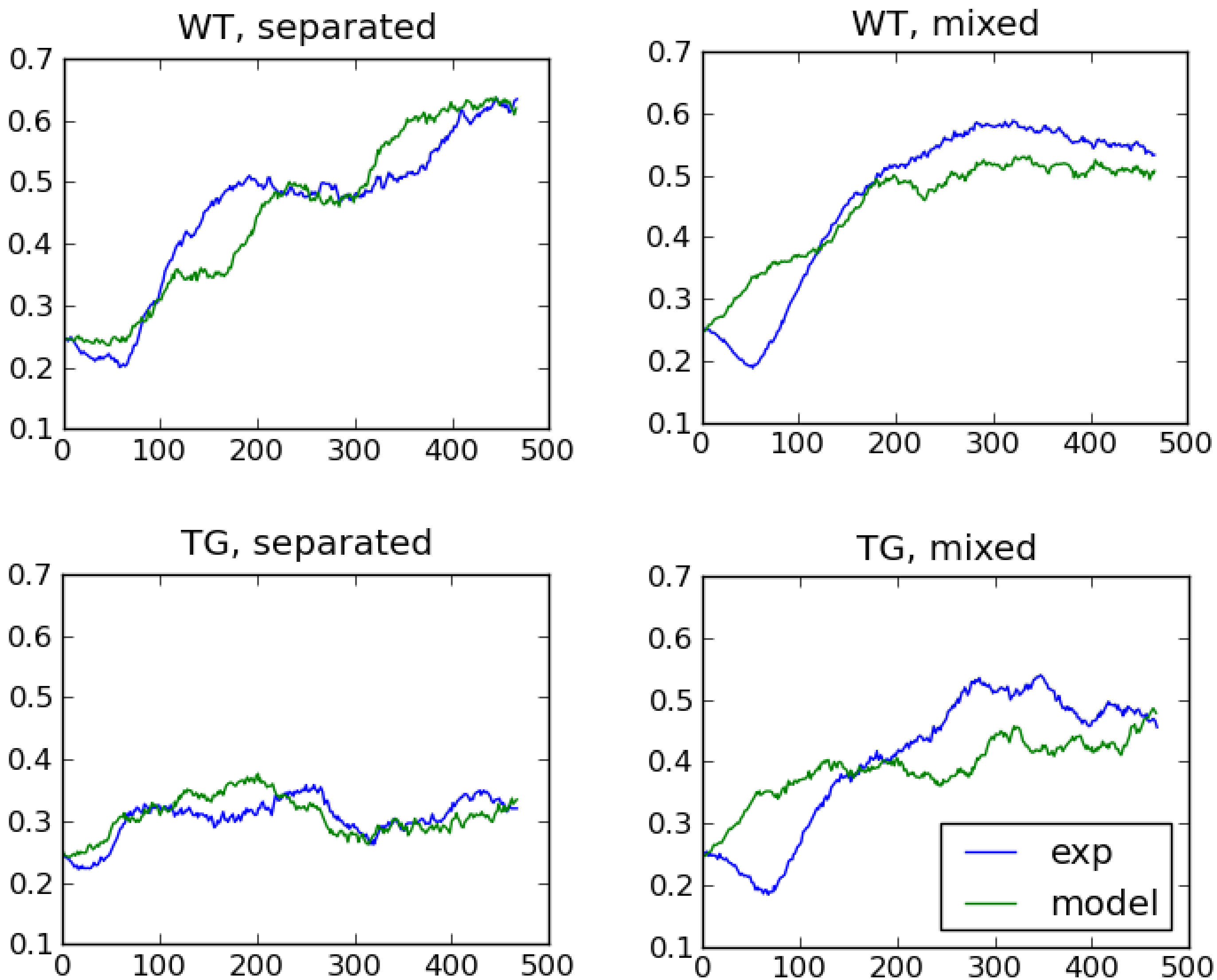
$$m_{n+1} = m_n + \epsilon(r_n - m_n)$$

Model of learning and behavior: decision making

- *Individual learning*
  - With probability *1-*α mouse makes a decision based on its own experience

- *Social influence*
  - With probability α mouse selects a corner depending on the history of visits of all the mice

Model of learning example: young mice



Fitted model parameters

wtplain	1.14
tgplain	1.06
wtsugar	3.73
tgsugar	1.74
wtbeta	0.60
tgbeta	0.59
alpha	0.54
wteps	0.03
tgeps	1.67
wtmstart	1.39
tgmstart	4.00

Conclusions

- Individual examination in the IntelliCage tasks disclosed cognitive impairment in APP.V717I mice as early as at the age of 5 months.
- APP.V717I mice housed in group with wild-type animals, successfully acquired the spatial task in the IntelliCage.
- **APP.V717I mice when separated from their wild-type siblings, showed memory only during inactive phase of day.**
- Social context may alleviate the learning deficit of the APP.V717I mouse model of amyloid pathology in Alzheimer's disease.

Thank you for your attention

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