Point Process Models in Neuroscience:

From Spike Trains to Behavior

Daniel K. Wójcik

d.wojcik@nencki.gov.pl

Laboratory of the Visual System
Nencki Institute of Experimental Biology

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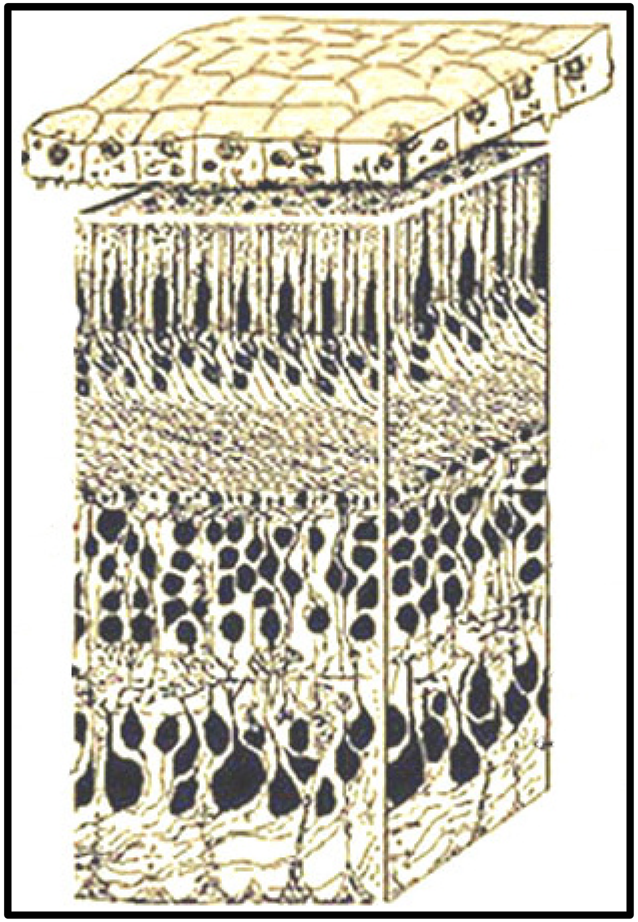
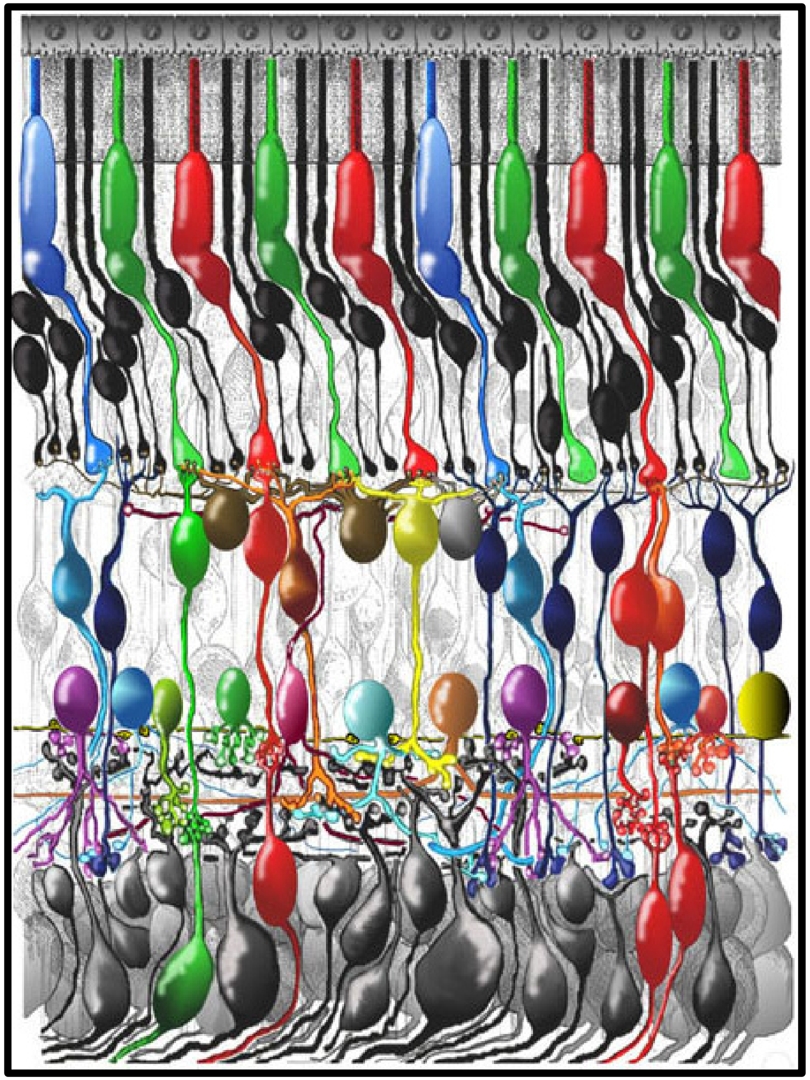
Retina:
entry to the visual system



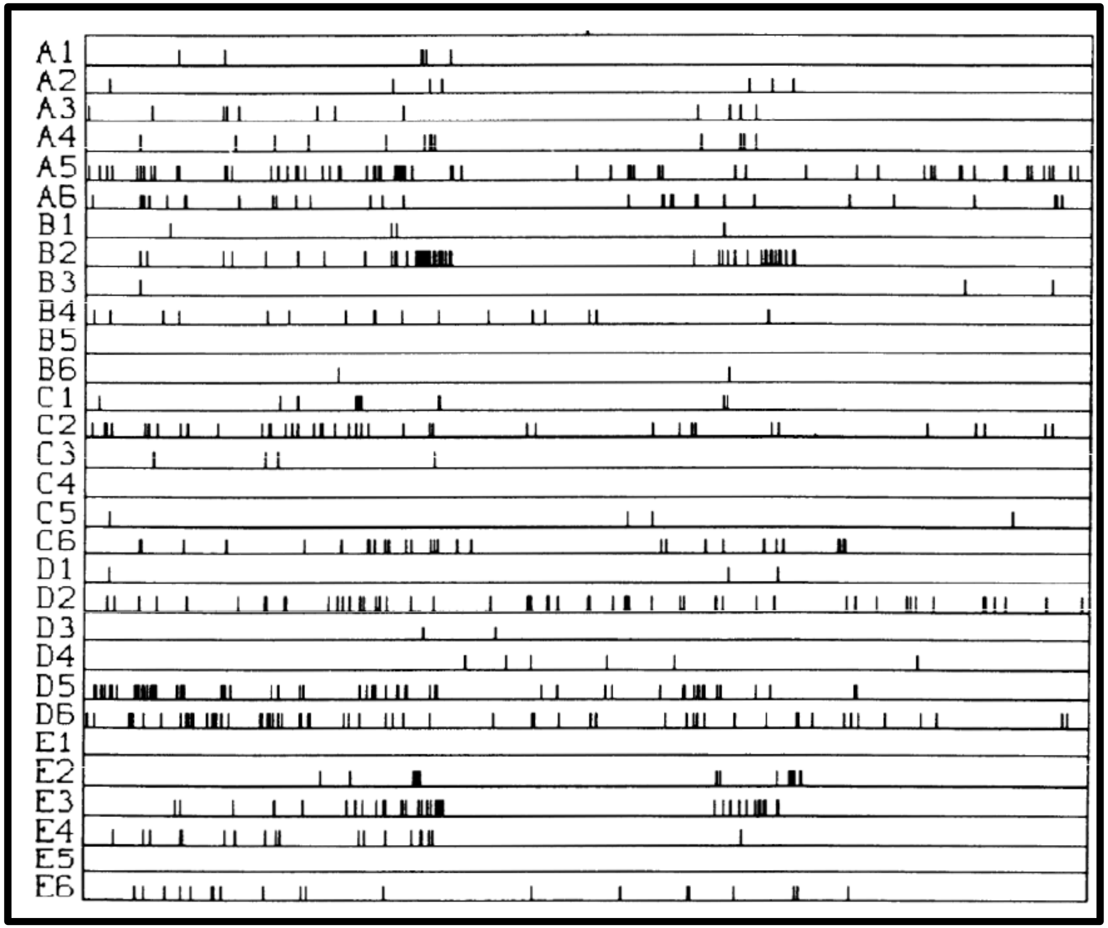
input:
125 milions
receptors

output:
1 milion
ganglion
cells

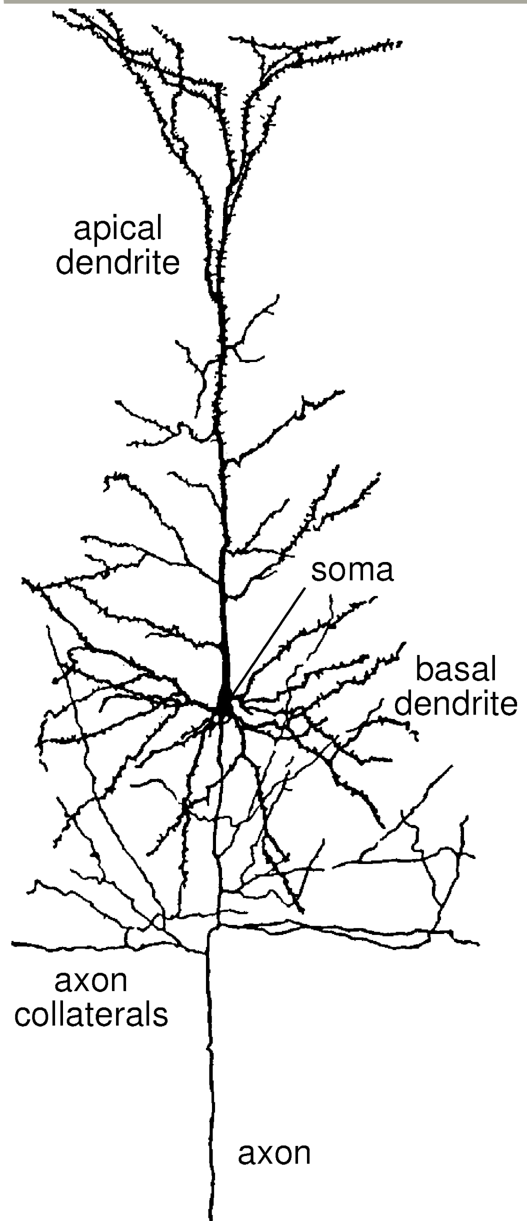


Coding

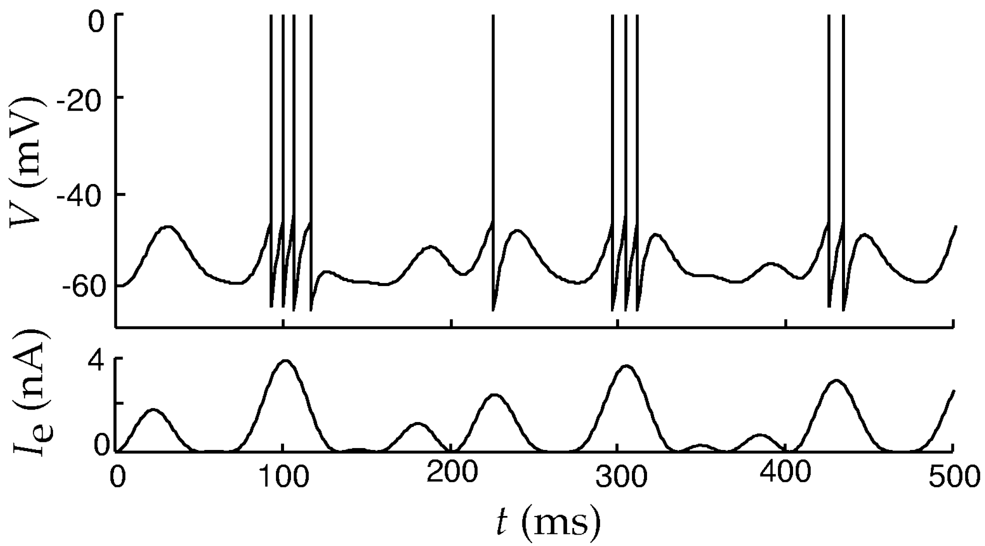
All the sensory stimuli are turned into sequences of identical impulses – spike trains



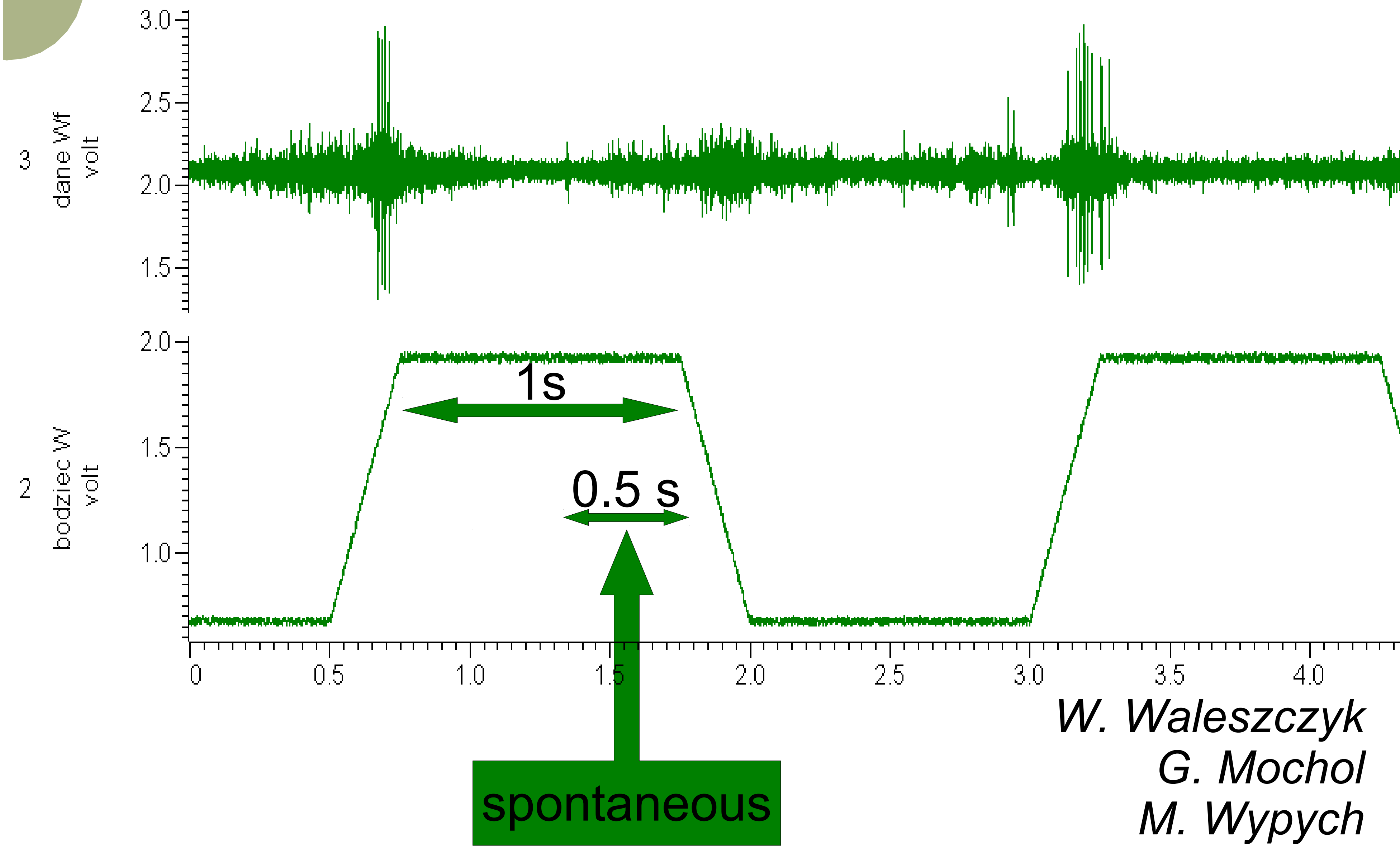
How neuron works



Current entering the cell leads to generation of action potentials

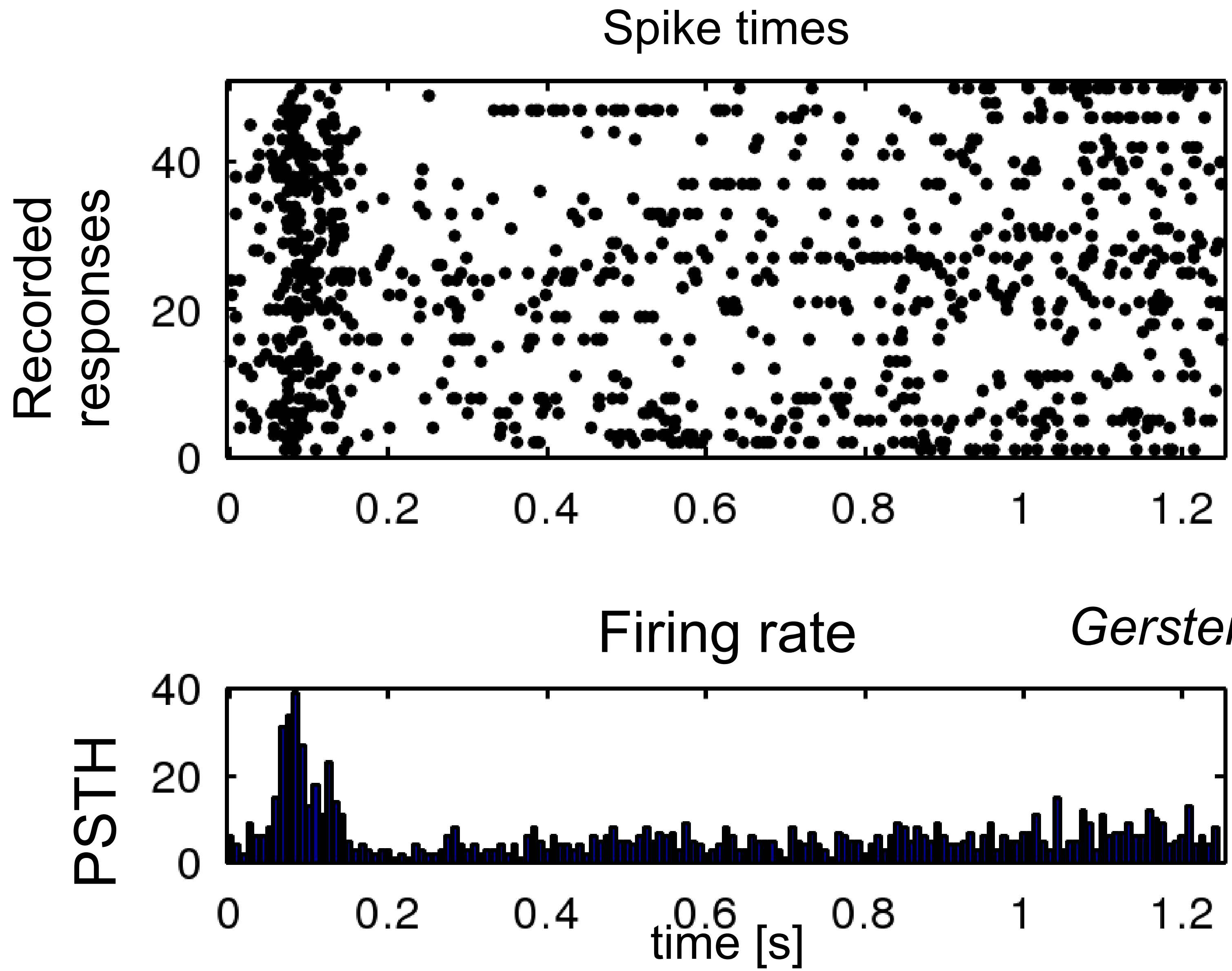


Our experiments



W. Waleszczyk
G. Mochol
M. Wypych

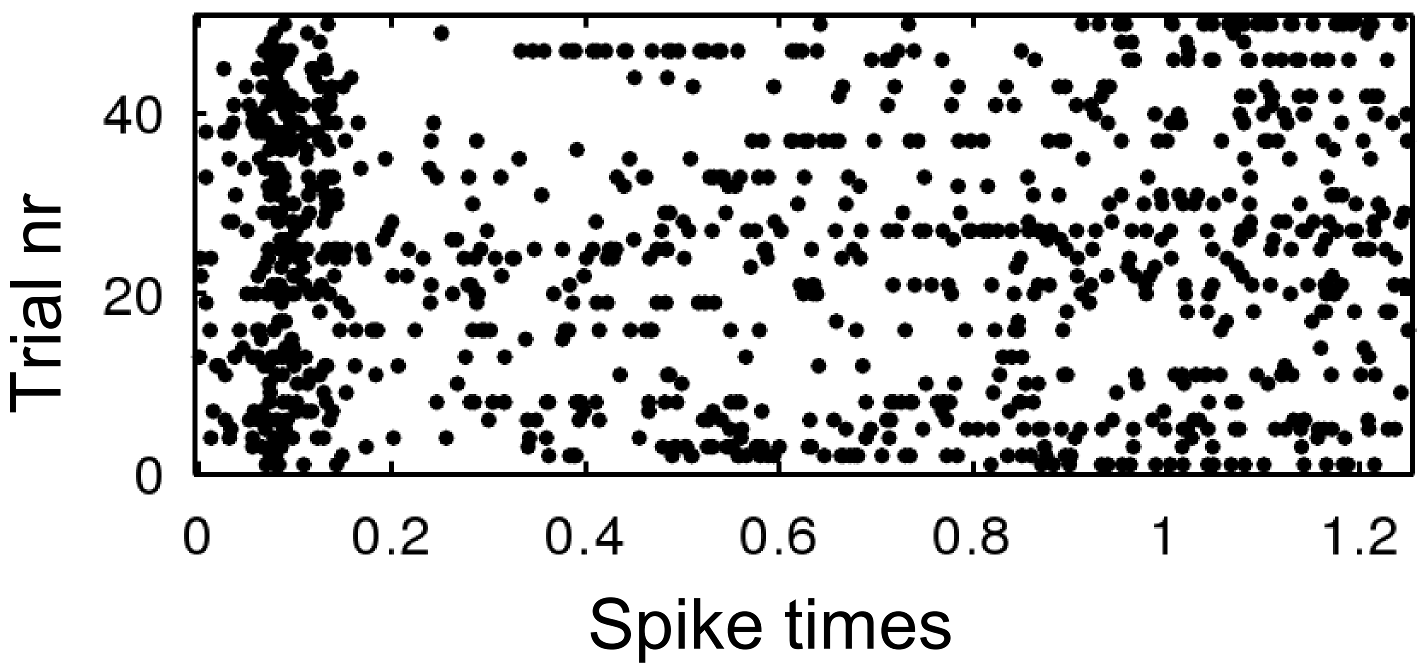
Information contained in spike trains



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**

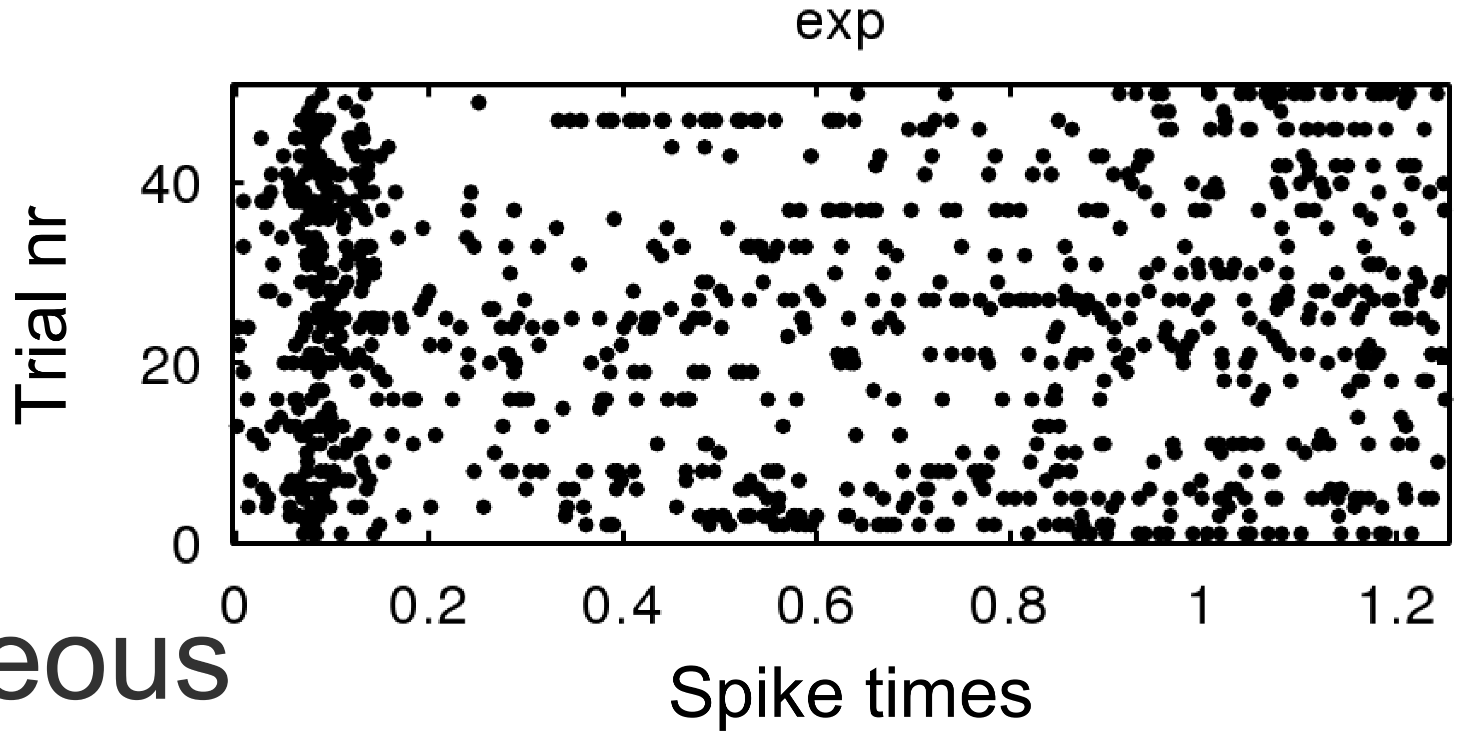
Stochastic intensity

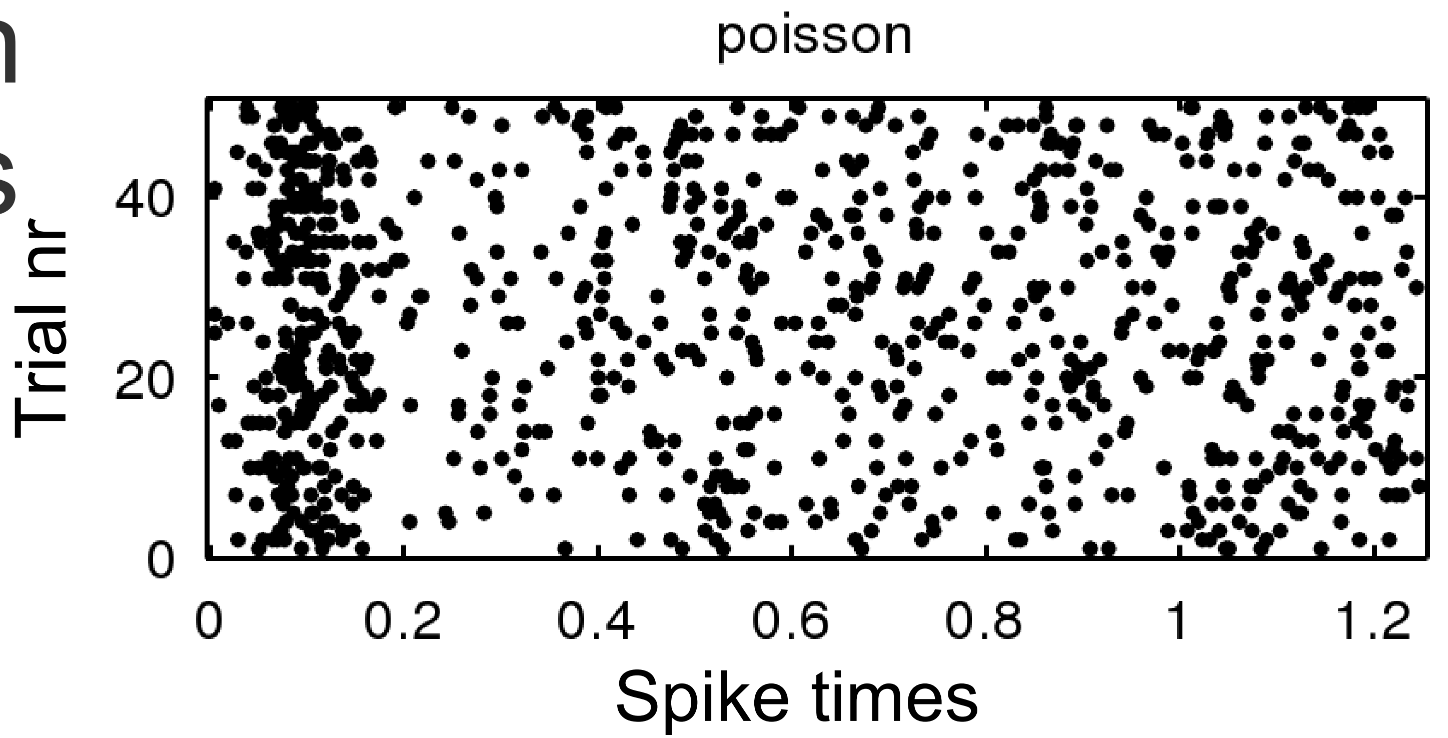
- $\lambda(t; N_{0:t})$ may depend on:
  - time after the stimulus onset, t
  - the whole history of spike generation
- Impractical and unnecessary
  for the description of spiking activity
- To simplify, specify the memory model

Example 1: Memoryless model

- Poisson model:
  spike generation depends solely on time
  $$\lambda = \lambda(t)$$
- **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





Example 2: 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

- 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:

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

- $\lambda_1(t)$ – 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

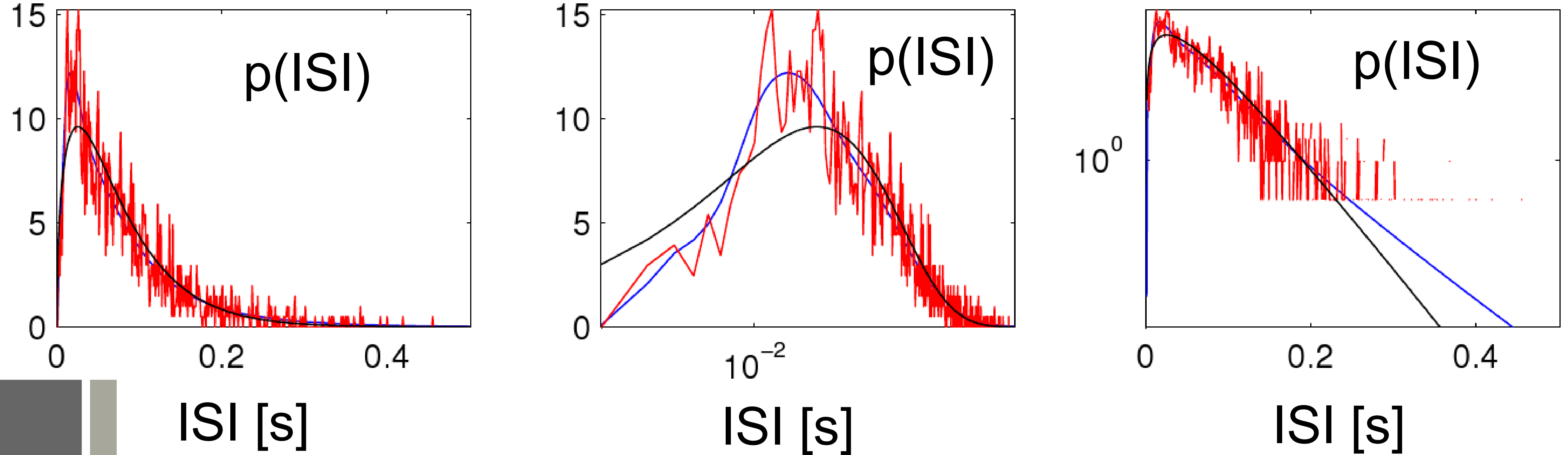
- Find a fragment of the recording with „spontaneous” activity. There $\lambda_1 = const$ and ISI distribution describes $\lambda_2(\tau)$ *[renewal process]*
- The connection between $\lambda_2(\tau)$ and the probability distribution of ISI $P(\tau)$ is

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

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

Perkel, Gerstein Moore 1967

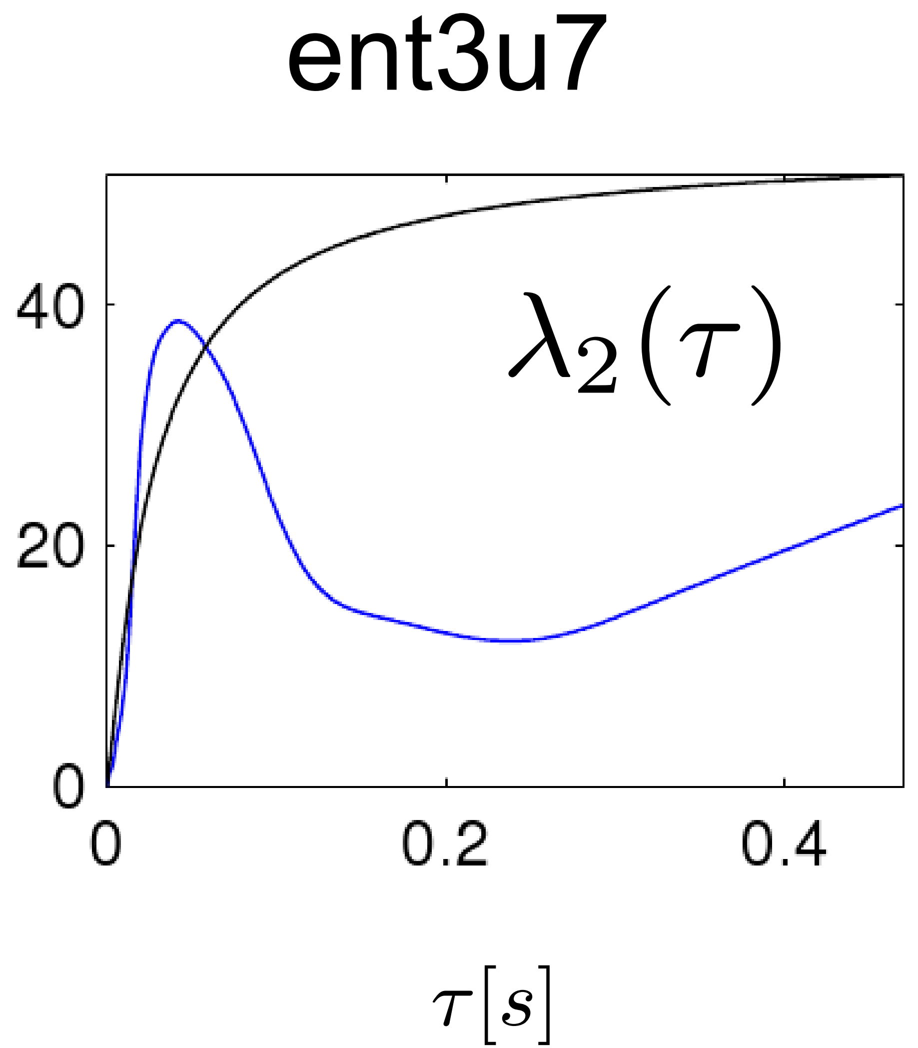
Example ISI distribution



- 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)



Estimation of λ_1 from λ_2

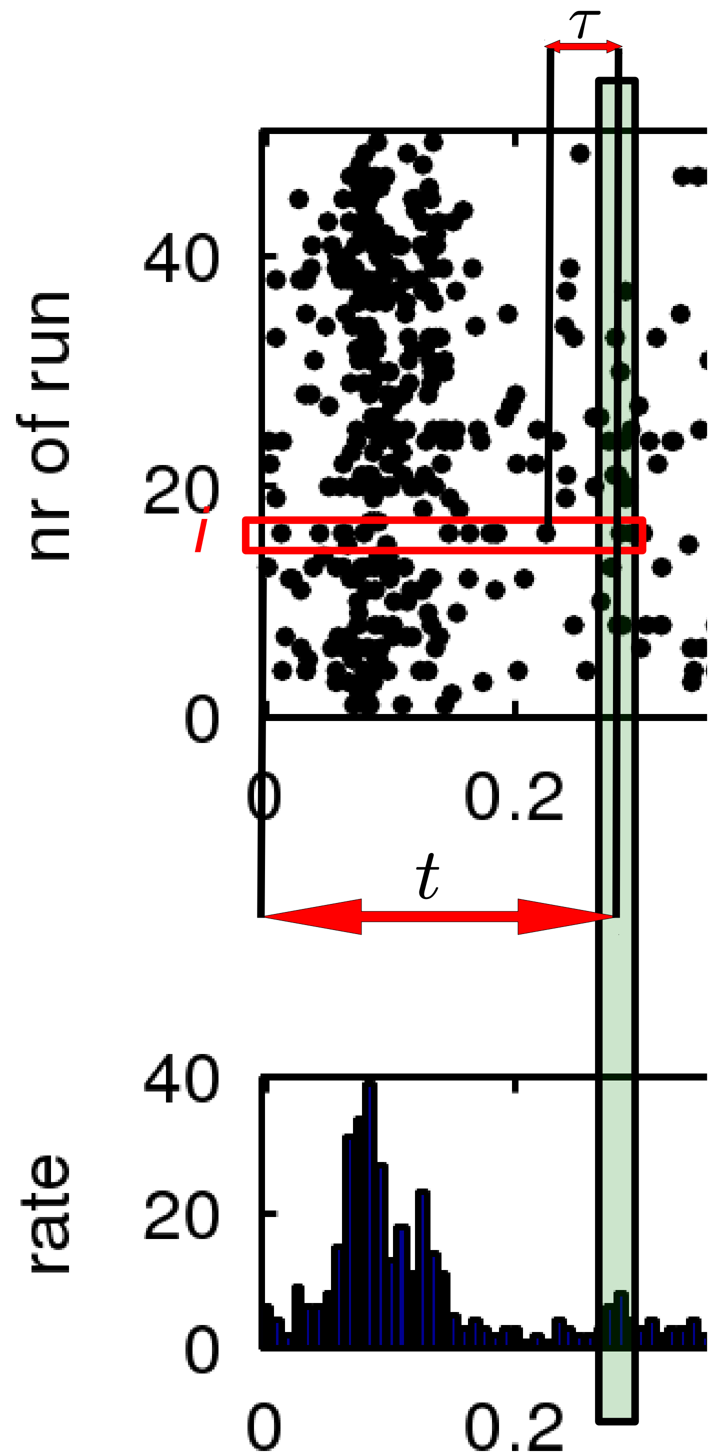
- Probability to generate a spike in i-th response is

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

where τ is the time since the last spike before t

- From here, approximately

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



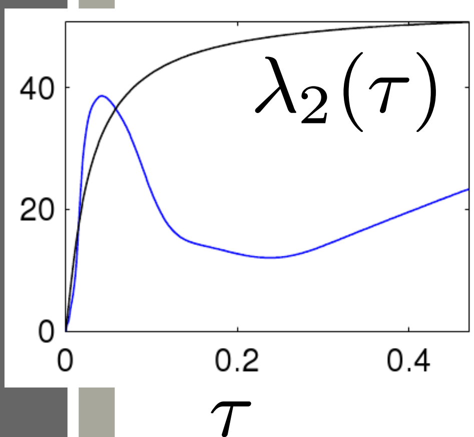
ent3u7

v=10

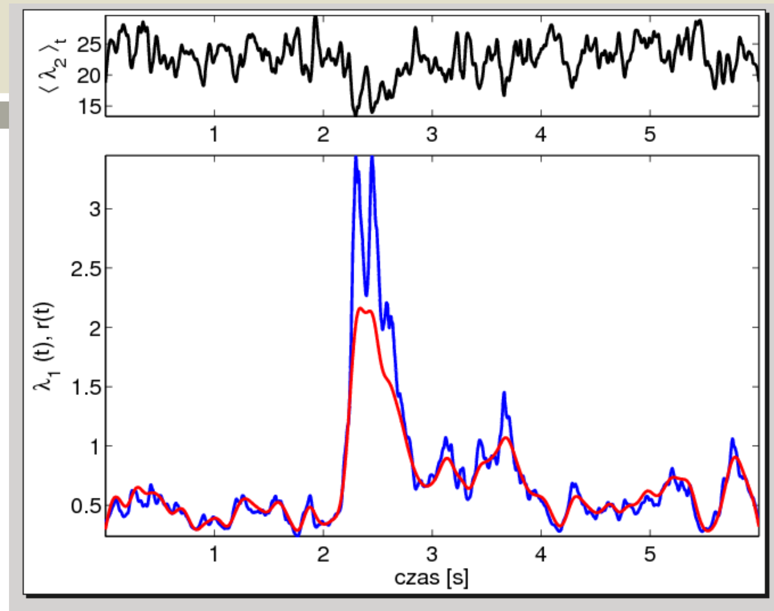
$$\lambda_1(t) = \frac{\bar{r}([t, t+\delta t])}{\langle \lambda_2(\tau_i) \rangle_i}$$

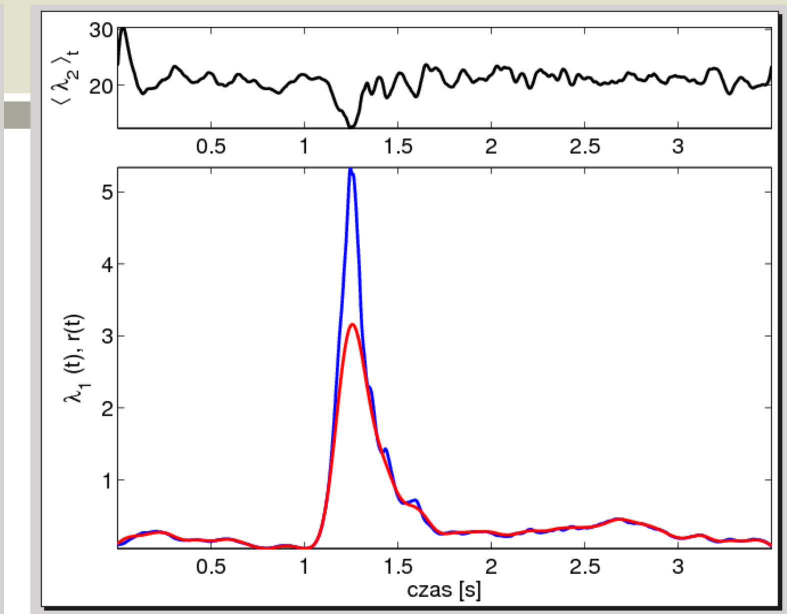
v=20

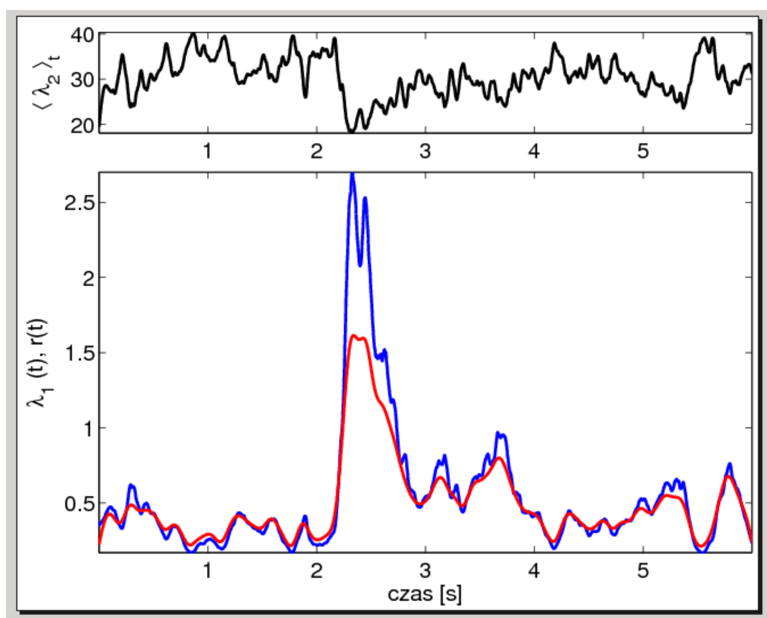
nonparametric

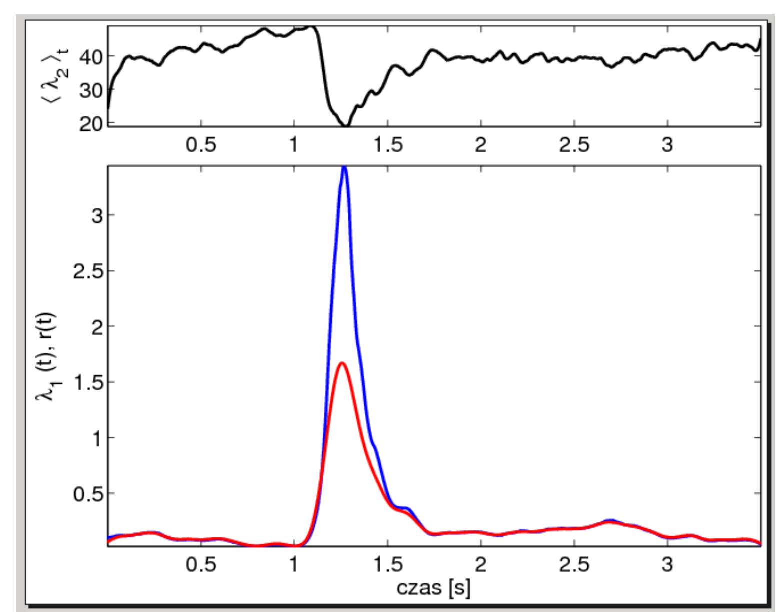


parametric (gamma)

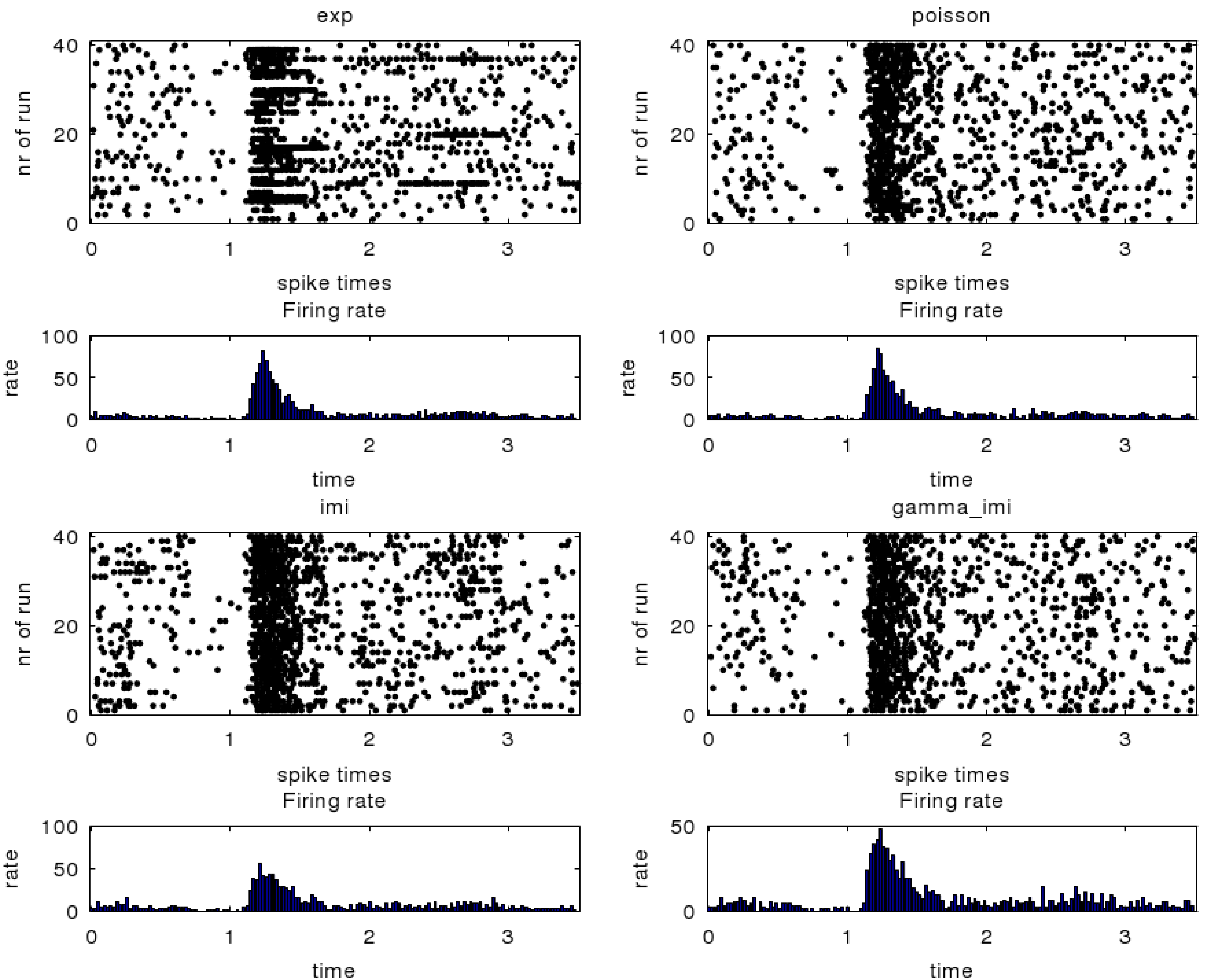








Spike times for cell: ent3u7; velocity: left; stim: 20



Time-rescaling theorem

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

$$\lambda(t|N_t)$$

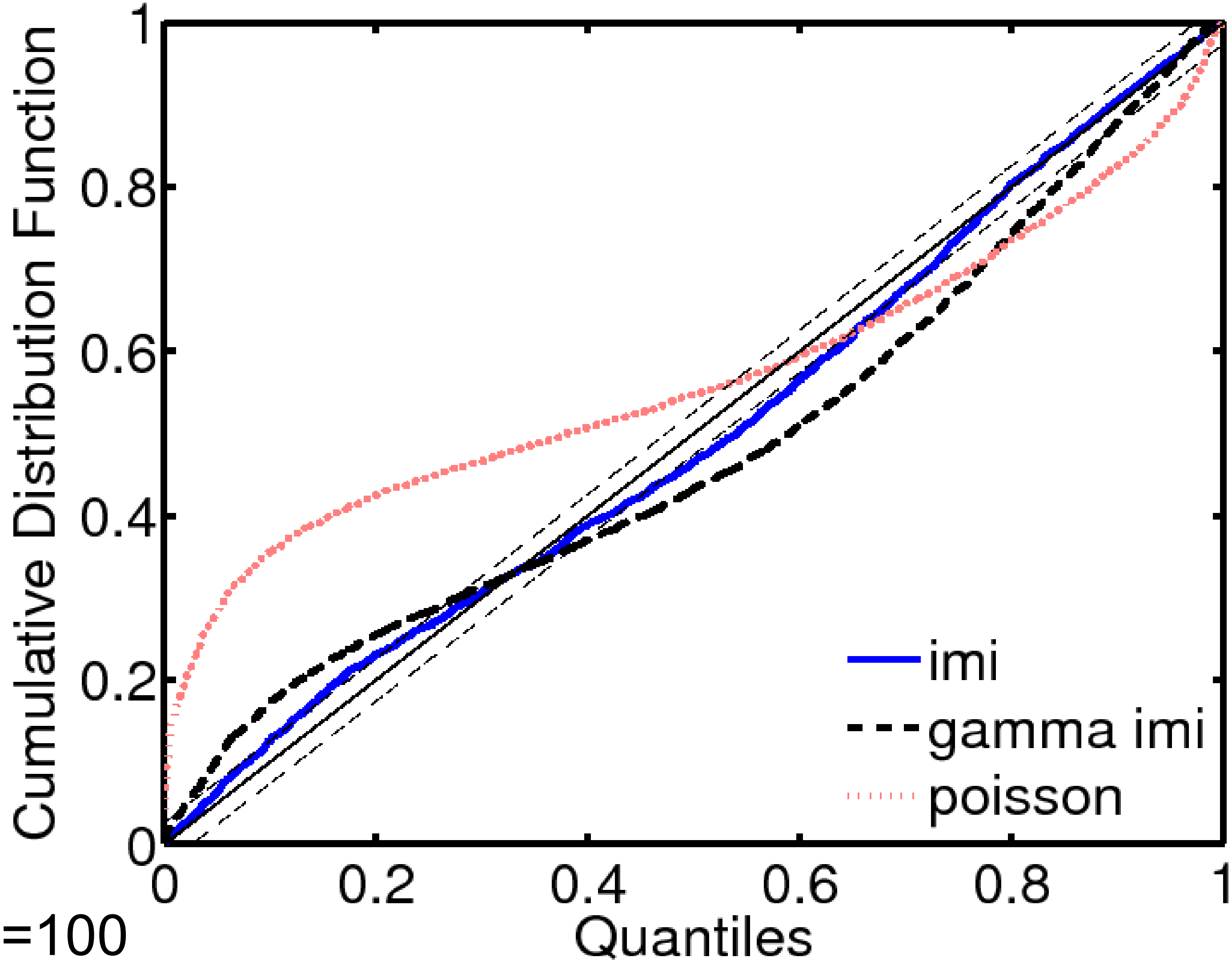
Define a transformation

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

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

Brown et al. 2002

Test of the model quality



ent3u7 v=100

Summary for spike trains

- Spike trains are realizations of point processes
- New method of estimation of Inhomogeneous Markov Interval model
- Example results of modeling responses to visual stimuli of superior colliculus cells of the cat
- At least for some data IMI models perform better than the Poisson model

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

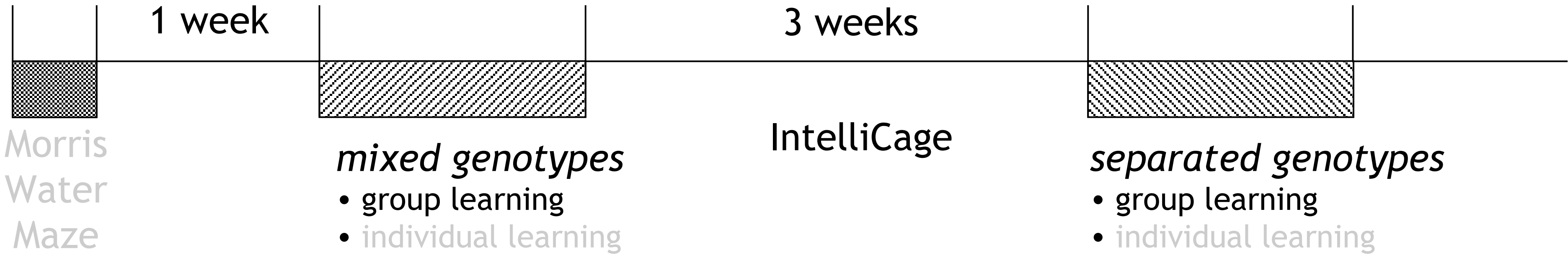
ANIMALS:

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.



IntelliCage

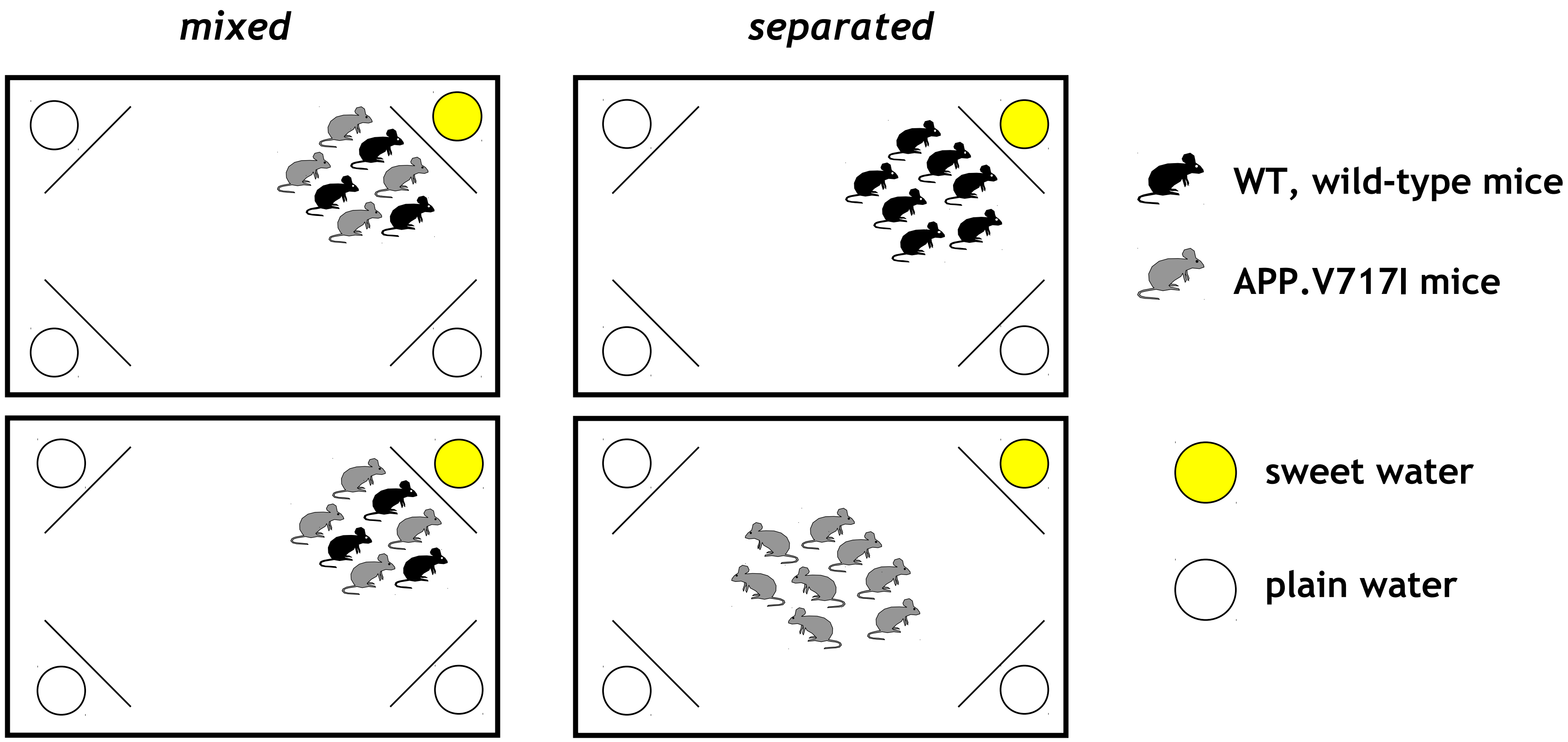
Bottles with liquid

Microprocessor

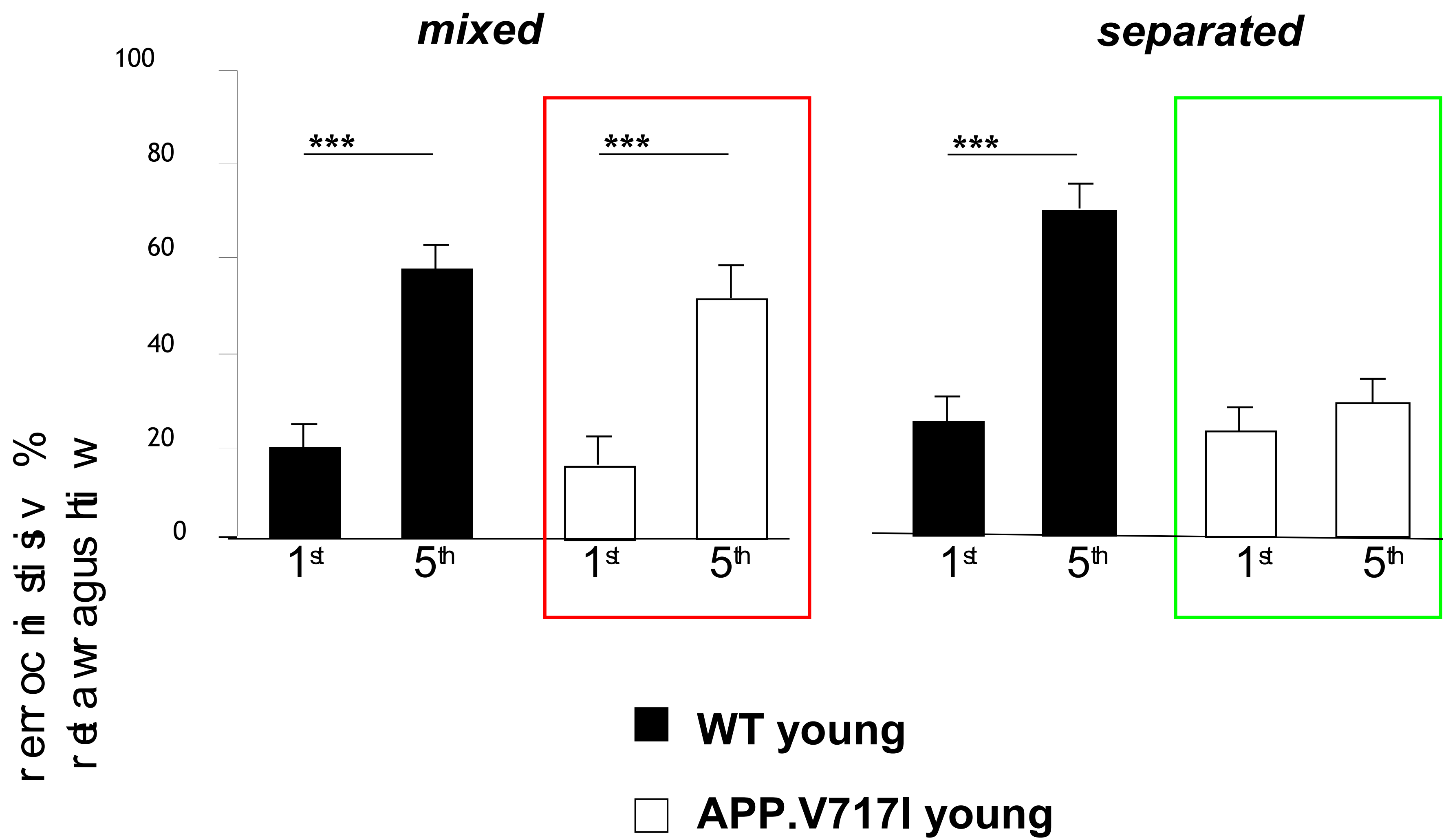
4 Learning corners with dual reward

Group learning

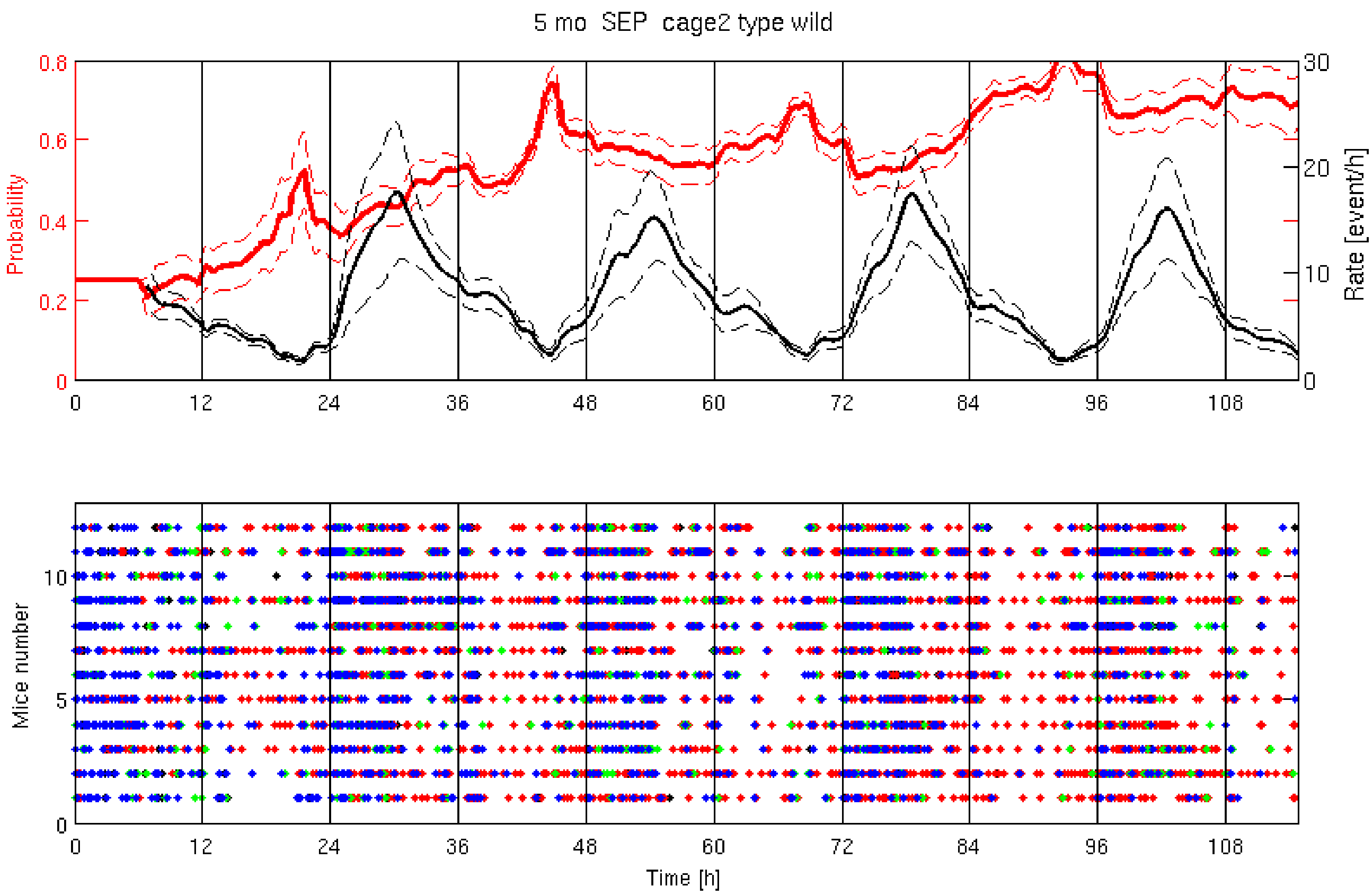
Setup of experiments in IntelliCage



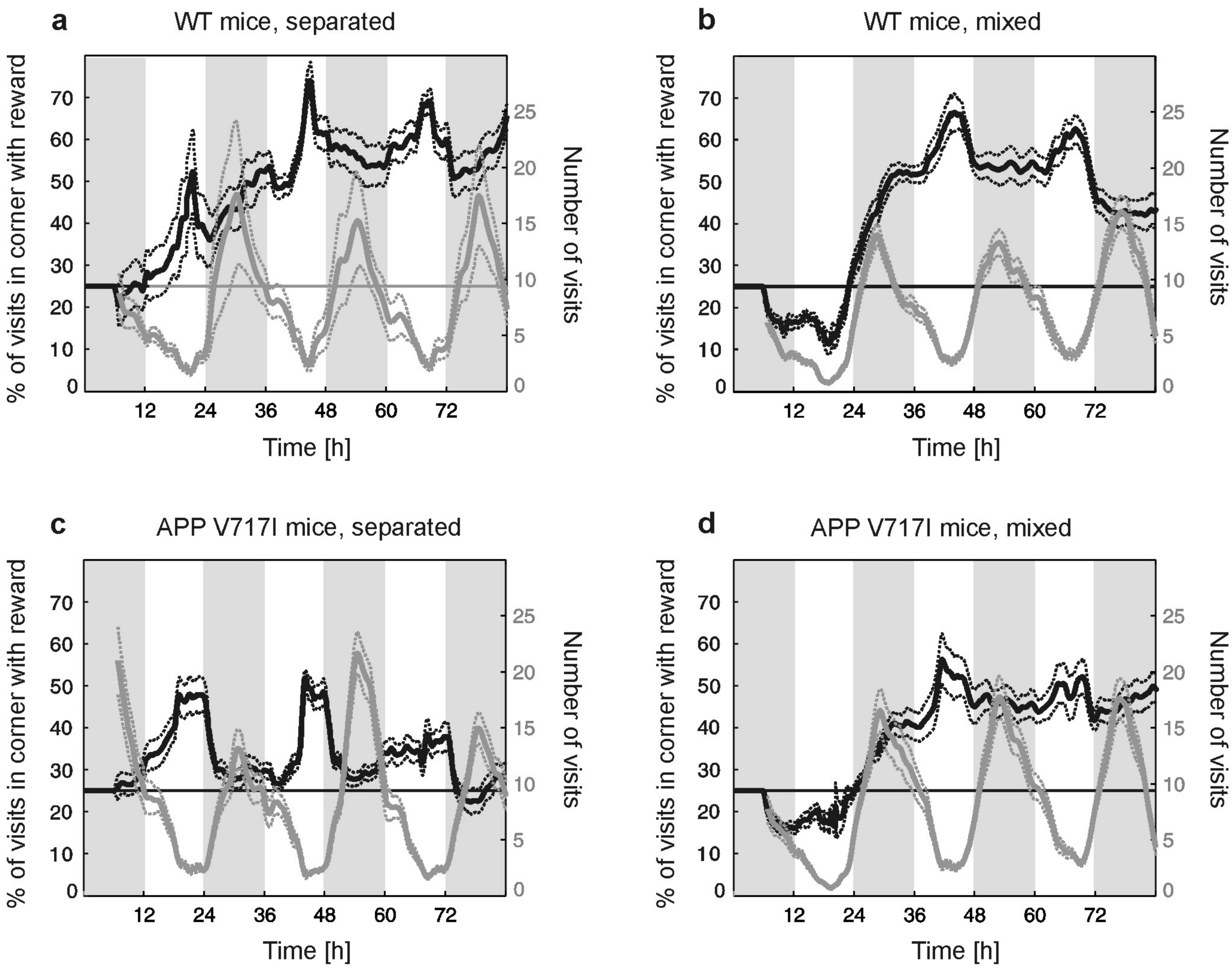
Group learning



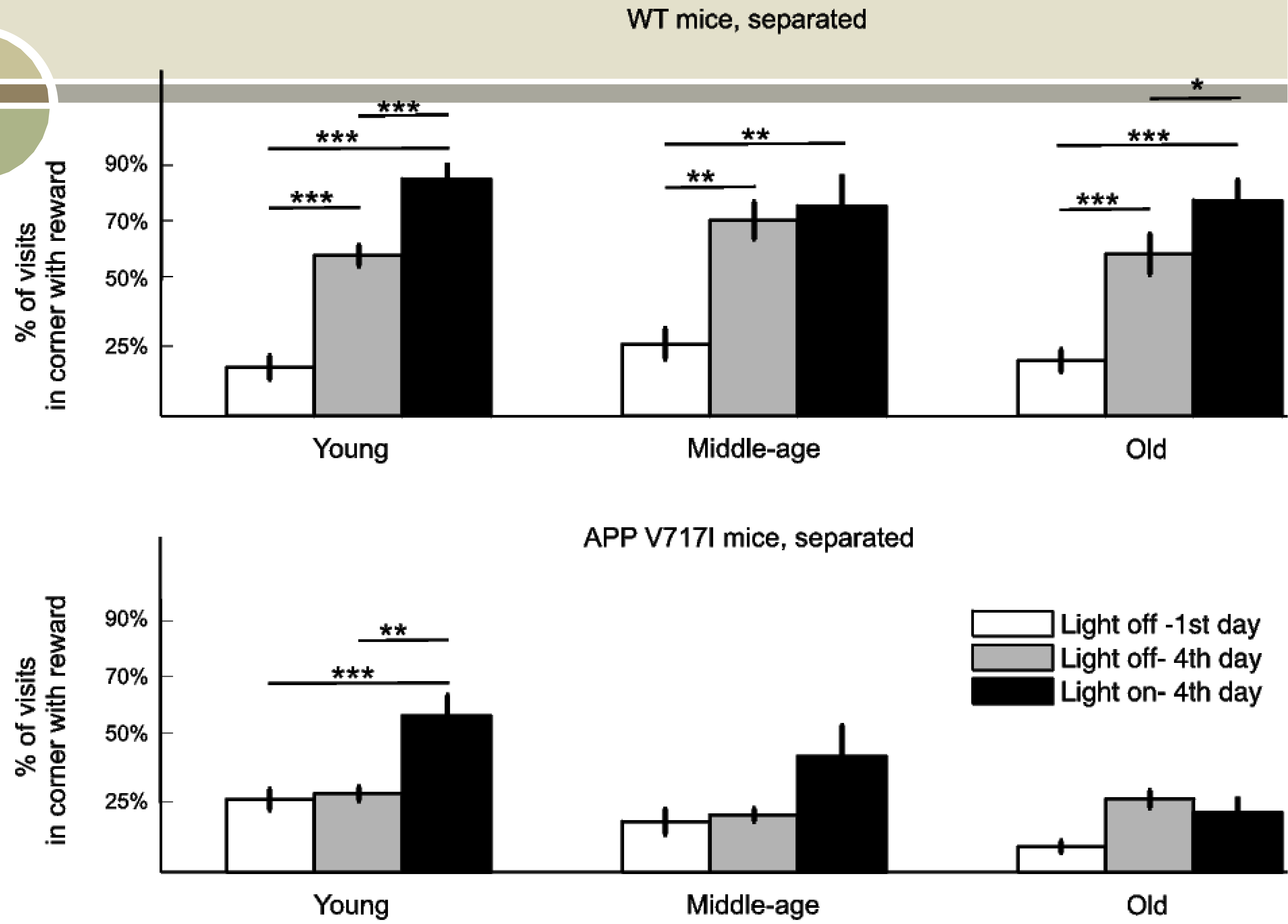
Point process view



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
5
15
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

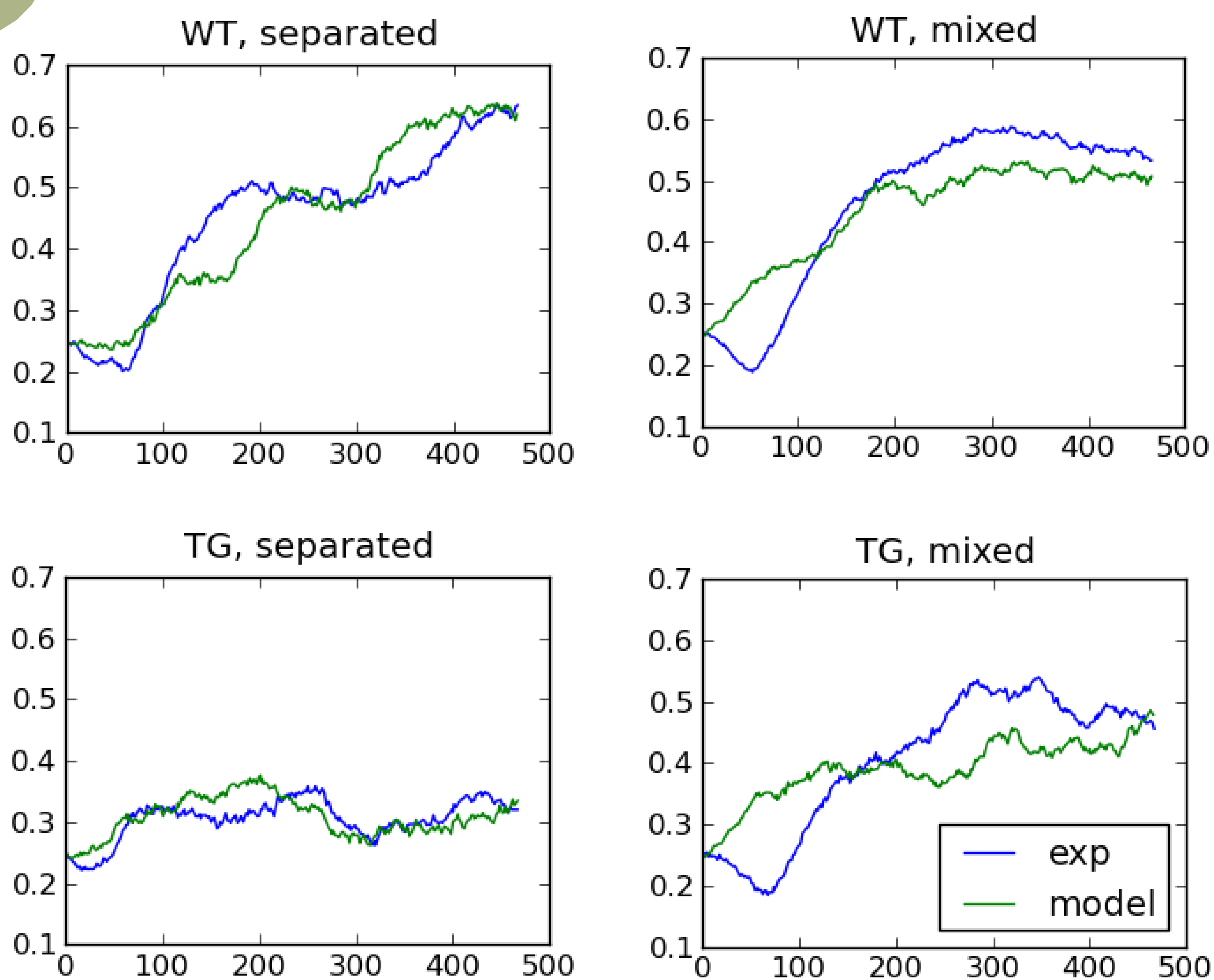
- *Individual learning:*
  - Choose corner with probability depending on learned rewards

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

  - Update learned rewards immediately depending on outcome

- *Social influence:*
  - choose corner with probability depending on history of visits of all 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

Daniel K. Wójcik

d.wojcik@nencki.gov.pl

Collaboration:

Spike trains from SC:

Gabriela Mochol
Wioletta Waleszczyk
Marek Wypych
Andrzej Wróbel

Wit Jakuczun

Mice in Intellicages:

Anna Kiryk
Gabriela Mochol
Szymon Łęski

Robert K. Filipkowski
Marcin Wawrzyniak
Victoria Lioudyno
Ewelina Knapska
Tomasz Werka
Hans-Peter Lipp
Fred van Leuven
Leszek Kaczmarek

Wójcik et al. *"Direct estimation of inhomogenous Markov interval models of spike-trains"*, Neural Computation **21** (2009) 2105-2113