From Spike Trains to Behavior: an introduction to point processes

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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
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)?
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 environment and systems of cells and signaling molecules. How similar are they to computer circuitry and how can we understand and manipulate them?

(2) Understand inter-level interactions. How do local activities in one level impacts another, and how can we understand the dynamics of these interactions? How do we understand the development and evolution of biological systems, and how do they have come to be as they are?

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.
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 millions receptors

output: 1 million ganglion cells
Coding

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

Spikes – Rieke et
Edgar Douglas Adrian
1889-1977

I had arranged electrodes on the optic nerve of a toad in connection with some experiments on the retina.
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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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Here I must refer to the previous Waynflete Lectures given by Professor E. D. Adrian, on *The Physical Background of Perception*, because the results of physiological investigations seem to me in perfect agreement with my suggestion about the meaning of reality in physics. The messages which the brain receives have not the least similarity with the stimuli. They consist in pulses of given intensities and frequencies, characteristic for the transmitting nerve-fiber, which ends at a definite place of the cortex. All the brain 'learns' [...] is a distribution or 'map' of pulses. From this information it produces the image of the world by a process which can metaphorically be called a consummrate piece of combinatorial mathematics: it sorts out of the maze of indifferent and varying signals invariant shapes and relations which form the world of ordinary experience.
Response variability

Variable responses

Structure preserved

Probabilistic approach necessary
Probabilistic perspective on coding

\[ P[\{s(t)\}; \{t_i\}] \]
The CODING problem

Find out conditional probability $P[r \mid s]$ 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 $P[s \mid r]$ 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

spontaneous

W. Waleszczyk
G. Mochol
M. Wypych
Raster plot – result of several repetitions

Spike times

Recorded responses

stimulus
Response variability

Variable responses

Structure preserved

Probabilistic approach necessary
Information contained in spike trains

Spike times

Gerstein, 1960
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 $t$

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

$N_{0:t}$ 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
Stochastic intensity

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- Impractical and unnecessary for the description of spiking activity
Stochastic intensity

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  - 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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- Problem:
  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
\[ \text{PSTH} = \text{inhomogeneous Poisson process} \]
Poisson process: properties

Divide experiment time \((0, T]\) into \(M\) intervals \(\delta t\)

\[
\begin{align*}
0 & \quad t_1 & \quad t_2 & \quad t_n & \quad T \\
\end{align*}
\]
Poisson process: properties

Divide experiment time \((0,T]\) into \(M\) intervals \(\delta t\)

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

\[
\prod_{j=1}^{s} (1 - \lambda(t_j)\delta t)
\]
Poisson process: properties

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

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

\[ p(N_0:T) = \lim_{M \to \infty} \frac{\Pr[\text{spikes in int. cont. } t_1, t_2, \ldots, t_s]}{(\delta t)^s} \]
\[ = \prod_{j=1}^{s} \lambda(t_j) \cdot \lim_{M \to \infty} \prod_{n=1}^{M} \left[ 1 - \lambda \left( \left( n - \frac{1}{2} \right) \delta t \right) \delta t \right] \]
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] =
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Poisson process: properties

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\[
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\]

\[
\approx \sum_{n=1}^{M} \left[ -\lambda \left( \left( n - \frac{1}{2} \right) \delta t \right) \delta t + o(\delta t^2) \right]
\]

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

\[
\xrightarrow[M \to \infty]{\text{ }} - \int_{0}^{T} \lambda(t) dt
\]
Poisson process: properties

Compute the logarithm of the last term

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

\[
p(N_0:T) = \prod_{j=1}^{s} \lambda(t_j) \cdot \lim_{M \to \infty} \prod_{n=1}^{M} \left[ 1 - \lambda \left( \left( n - \frac{1}{2} \right) \delta t \right) \delta t \right]
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\]

\[
\rightarrow_{M \to \infty} - \int_{0}^{T} \lambda(t) dt = -T \bar{\lambda}
\]

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 (\( \lambda = \text{const.} \))

\[ p(N_{0:T}) = \lambda^s e^{-\lambda T} \]
Poisson process: properties

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

\[
P_{(0,T]}[n] = \int_0^T dt_1 \int_{t_1}^T dt_2 \cdots \int_{t_{n-1}}^T dt_n \lambda^n e^{-\lambda T}
\]

\[
= \lambda^n e^{-\lambda T} \int_0^T dt_1 \int_{t_1}^T dt_2 \cdots \int_{t_{n-1}}^T dt_n
\]

\[
= \lambda^n e^{-\lambda T} \frac{T^n}{n!}
\]
We obtain the Poisson distribution (hence the name)

\[ P_{(0,T)}[n] = \frac{(\lambda T)^n}{n!} e^{-\lambda T} \]
Poisson process: properties

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

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?

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

In the Poisson process:

\[ E[N(t)] = \sum_{n=1}^{\infty} nP_{0:t}[n] = \]

\[ = \sum_{n=1}^{\infty} n \frac{1}{n!} \left( \int_{0}^{t} \lambda(\tau) \, d\tau \right)^n \exp \left[ - \int_{0}^{t} \lambda(\tau) \, d\tau \right] = \int_{0}^{t} \lambda(\tau) \, d\tau \]
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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

• $\tau$ – time from the last spike

• The basic quantity: 
  distribution of inter-spike intervals (ISI)

\[
P(\tau) \Delta t := \Pr(\text{spike during}(\tau, \tau + \Delta t) \cap \\
\cap \text{no spikes during}(0, \tau))
\]
Example 2: renewal processes

- $\tau$ – time from the last spike

- The basic quantity: *distribution of inter-spike intervals* (ISI)

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

- Another useful notion: *survival function*

\[
S(\tau) := \Pr(\text{no spikes until } \tau) \\
= \int_\tau^\infty d\tau' P(\tau') \\
= 1 - \int_0^\tau d\tau' P(\tau')
\]
Example 2: renewal processes

- Conditional intensity

\[ \lambda(\tau)\Delta t := \Pr(\text{spike during } (\tau, \tau + \Delta t) \mid \text{no spikes during}(0, \tau)) \]
Example 2: renewal processes

- **Conditional intensity**

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

- **Relation between \( \lambda \), \( P \) and \( S \)**

  \[
  P(\tau) \Delta t = \Pr(\text{spike during } (\tau, \tau + \Delta t) \cap 0 \text{ spikes until } \tau) \\
  = \Pr(\text{spike during } (\tau, \tau + \Delta t) \mid 0 \text{ spikes until } \tau) \cdot \Pr(0 \text{ spikes until } \tau) \\
  = \lambda(\tau) \Delta t \cdot S(\tau)
  \]
Example 2: renewal processes

- Conditional intensity

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

- Relation between \( \lambda, P \) and \( S \)

\[
\begin{align*}
P(\tau) \Delta t &= \Pr(\text{spike during } (\tau, \tau + \Delta t) \cap 0 \text{ spikes until } \tau) \\
&= \Pr(\text{spike during } (\tau, \tau + \Delta t) \mid 0 \text{ spikes until } \tau) \cdot \Pr(0 \text{ spikes until } \tau) \\
&= \lambda(\tau) \Delta t \cdot S(\tau)
\end{align*}
\]

- Thus

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

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

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 $\tau$ since the last spike

  \[ \lambda = \lambda(t, \tau) \]

  We call such model the IMI model
Example 3: IMI model – Inhomogeneous Markov Interval

- Assume we only know the current time $t$ and the time $\tau$ 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
We have two factors in the model:

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

- 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 $\lambda_2$

- Find a fragment of the recording with „spontaneous” activity. There $\lambda_1 = \text{const}$ 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

- red – experimental distribution
- blue – smoothed with gaussian kernel
- black – best fit of a parametric model (gamma distribution)
\( \lambda_2 \) obtained

- blue – smoothed with gaussian kernel
- black – best fit of a parametric model (gamma distribution)
Estimation of $\lambda_1$ from $\lambda_2$

- Probability to generate a spike in i-th response
Estimation of $\lambda_1$ from $\lambda_2$

- 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 $\tau$ is the time since the last spike before $t$
Estimation of $\lambda_1$ from $\lambda_2$

- 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 $\tau$ is the time since the last spike before $t$

- From here, approximately
  \[ \lambda_1(t) = \frac{\bar{r}([t, t + \delta t])}{\langle \lambda_2(\tau_i) \rangle_i} \]
\[ \lambda_1(t) = \frac{\bar{r}(\tau \in [t, t + \delta t])}{{\langle \lambda_2(\tau_i) \rangle}_i} \]

- **v=10**
- **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 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 $\tau_k$ 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 $z_k$'s.
- If the model is correct, resulting curve will be diagonal
Test of the model quality

Cumulative Distribution Function

Quantiles

ent3u7 v=100
Test of the model quality

Cumulative Distribution Function

ent5u3 v=1000

Quantiles

imi
gamma imi
poisson
Be careful!!!
Problem 1

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

Cell: Sc8u12

Blue: left → right
Red: right → left
Spontaneous? – sometimes no!

Cell: ent3u7

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)

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.

| Morris Water Maze | 1 week | mixed genotypes • group learning • individual learning | 3 weeks | IntelliCage • group learning • individual learning | separated genotypes
**Procedure**

**ANIMALS:**
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<table>
<thead>
<tr>
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<th>1 week</th>
<th>3 weeks</th>
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<tbody>
<tr>
<td>Morris Water Maze</td>
<td>mixed genotypes</td>
<td></td>
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</tbody>
</table>
|               | • group learning
|               | • individual learning |
| IntelliCage | separated genotypes |
|               | • group learning
|               | • individual learning |
IntelliCage

- Microprocessor
- Bottles with liquid
- 4 Learning corners with dual reward

NewBehavior
Learning corner
Group learning

Setup of experiments in IntelliCage

mixed

separated

WT, wild-type mice
APP.V717I mice
sweet water
plain water
Group learning

% visits in corner with sugar water

**mixed**

- **WT young**
- **APP.V717I young**

**separated**

1st 5th 1st 5th 1st 5th

***
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]
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 $1 - \alpha$ mouse makes a decision based on its own experience

- **Social influence**
  - With probability $\alpha$ 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
wtbodyta  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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- Ewelina Knapska
- Tomasz Werka
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- Fred van Leuven
- Leszek Kaczmarek

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- Marek Wypych
- Andrzej Wróbel
- Wit Jakuczun