# Inferring synaptic connections from spike data of multiple neurons

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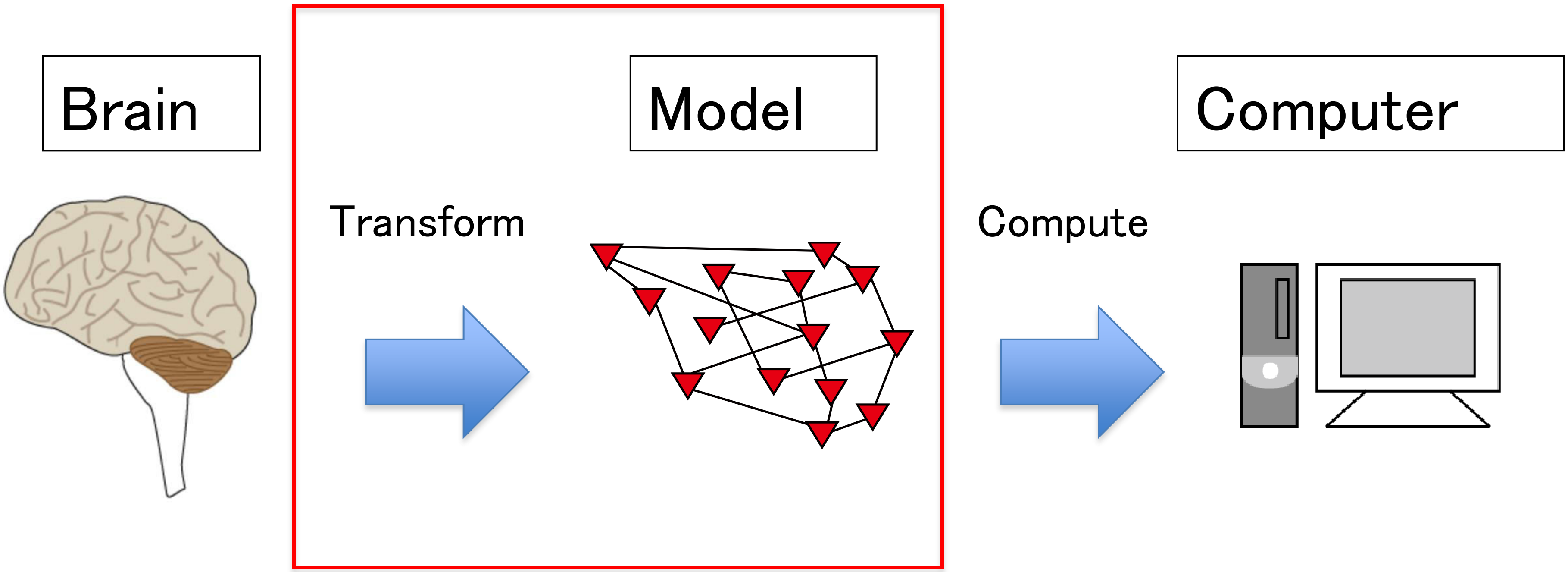
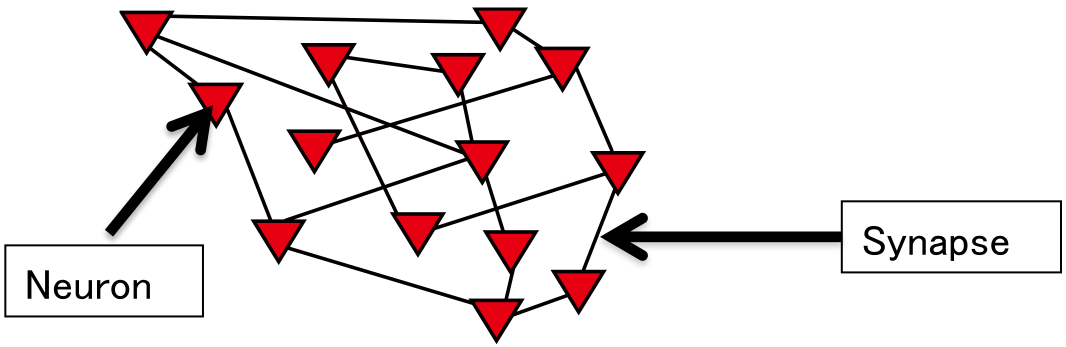
# Modeling the brain



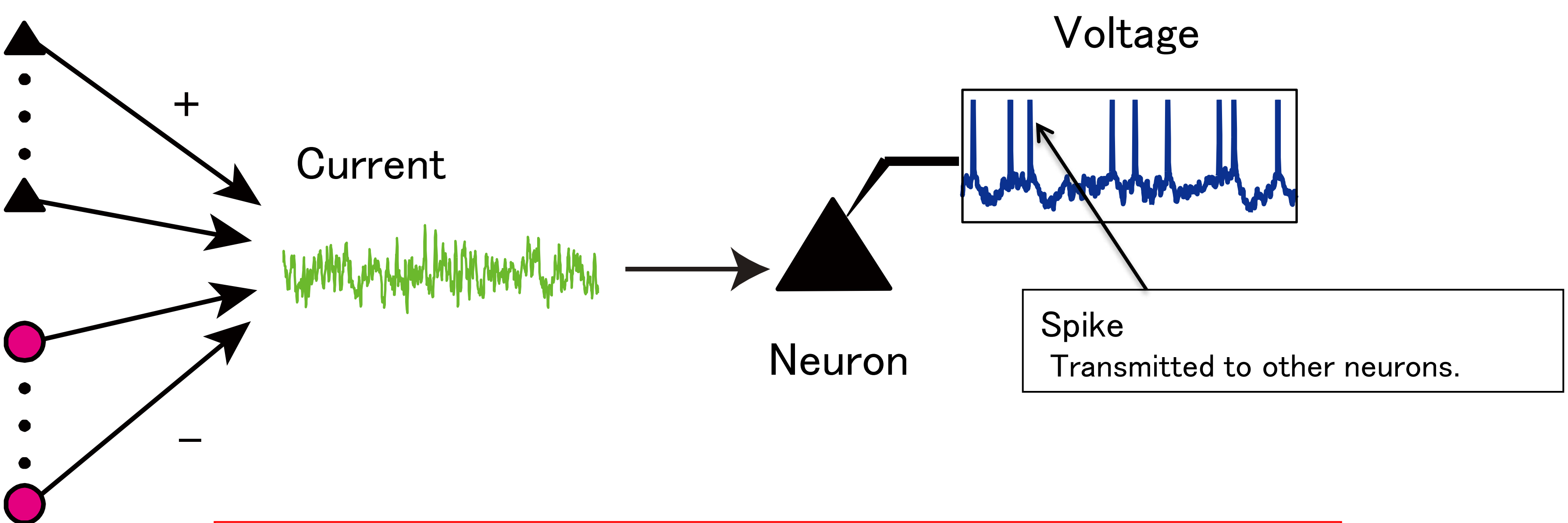
# Components for a brain model




① Neuron

② Synapse

# Neuron



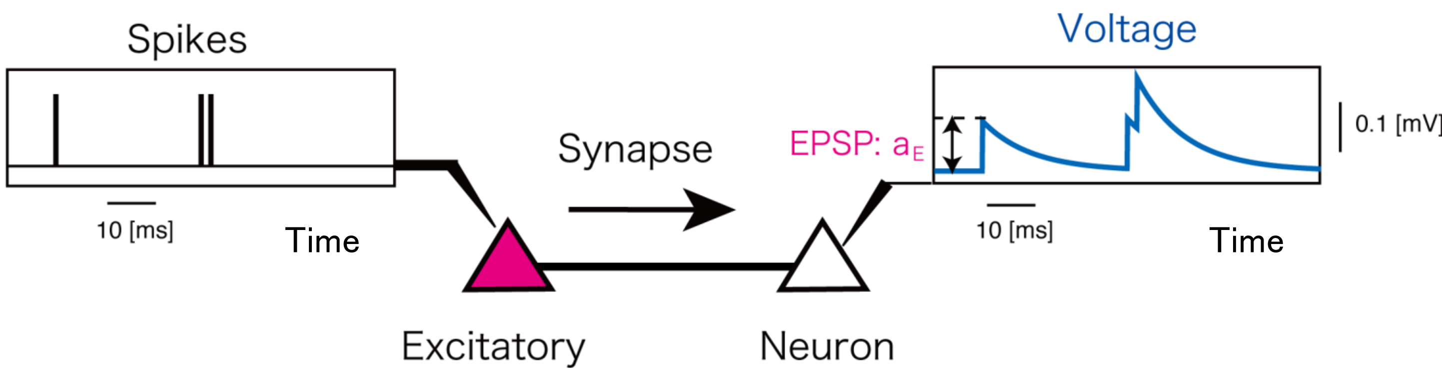

① Basic component of the brain
② Input: Current, Output: Spike.

Neuron model:
Describe the state of the neuron
(Voltage, spike timings etc.)

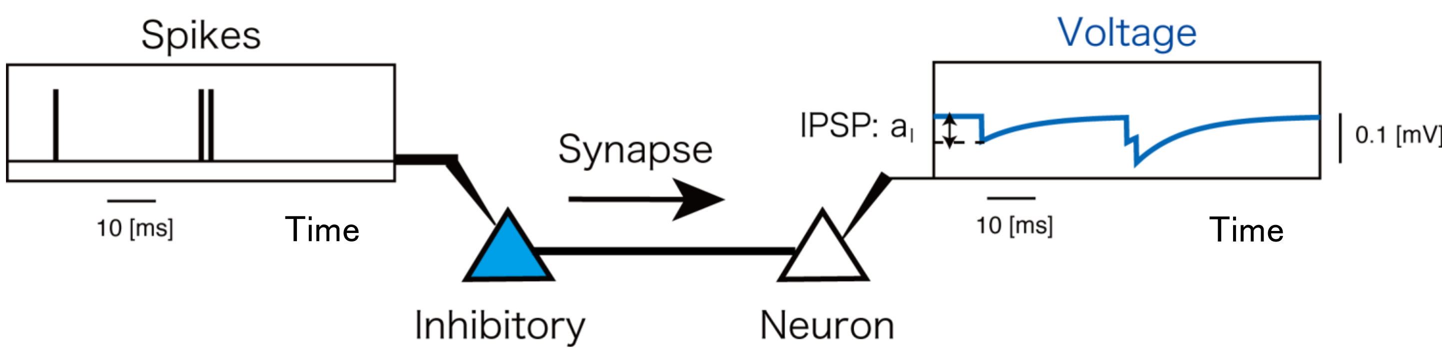
# Synapse

## Communication between neurons

**Pre-synaptic neuron** **Post-synaptic neuron**




Excitatory neurons increase the voltage of a neuron.




Inhibitory neurons increase the voltage of a neuron.

# Outline

① Single neuron model from data.

Propose a neuron model
that can perfectly predict experimental data.

② Network connectivity from data.

Propose a method
that can estimate connections from data.

③ Other projects

# Spike timing prediction

## Quantitative modeling of a single neuron

Joint work with

Yasuhiro Tsubo and Shigeru Shinomoto

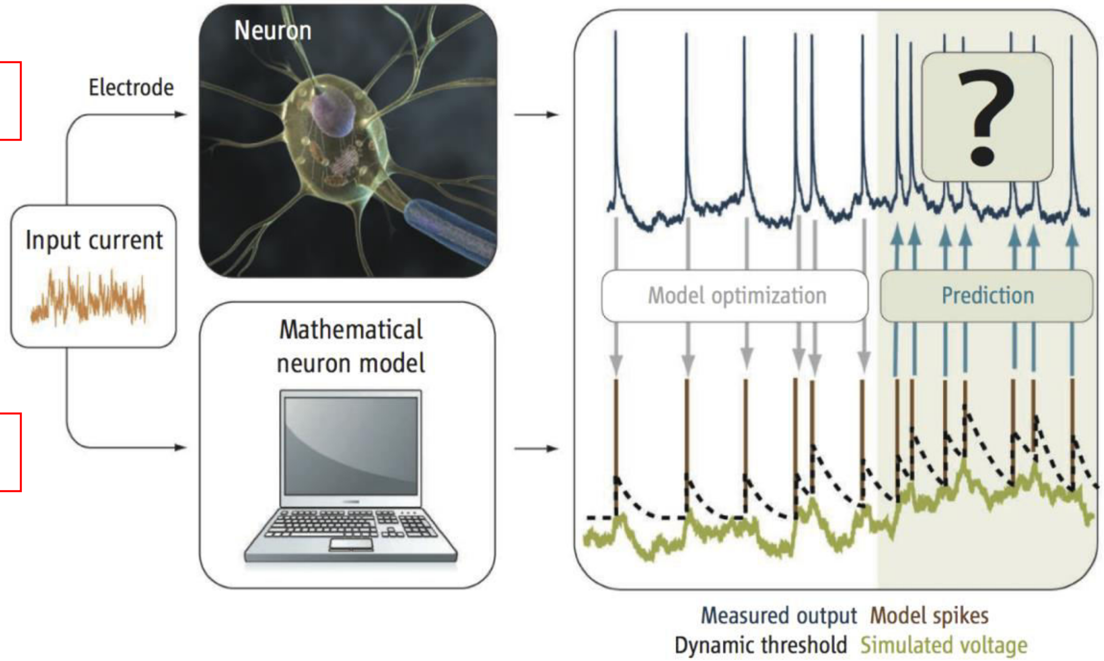
(Kobayashi et al., Front Comput Neurosci 2009)

# Spike timing prediction
## Quantitative modeling of a single neuron

Develop a model that can predict all spike timings.

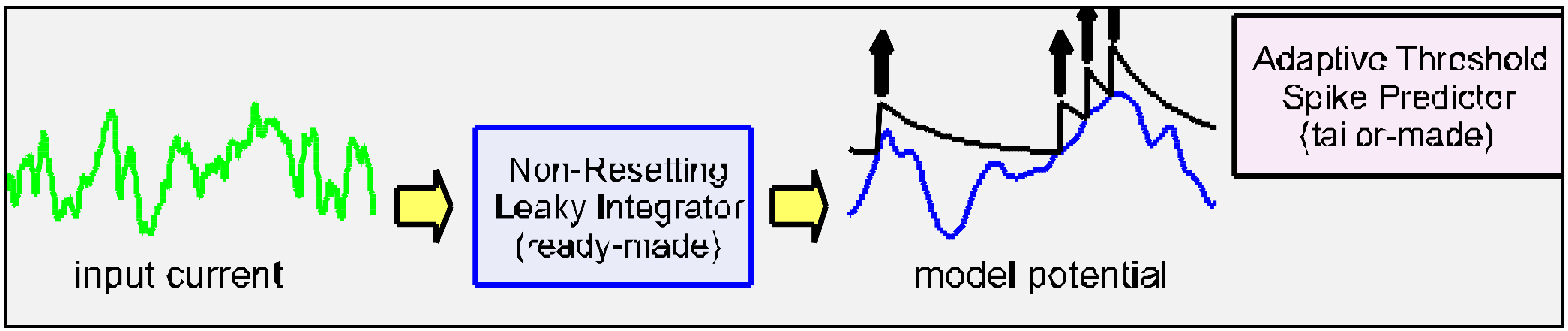
Experiment

Model




Gerstner & Naud, Science, 2009

# Multi-timescale Adaptive Threshold (MAT) model



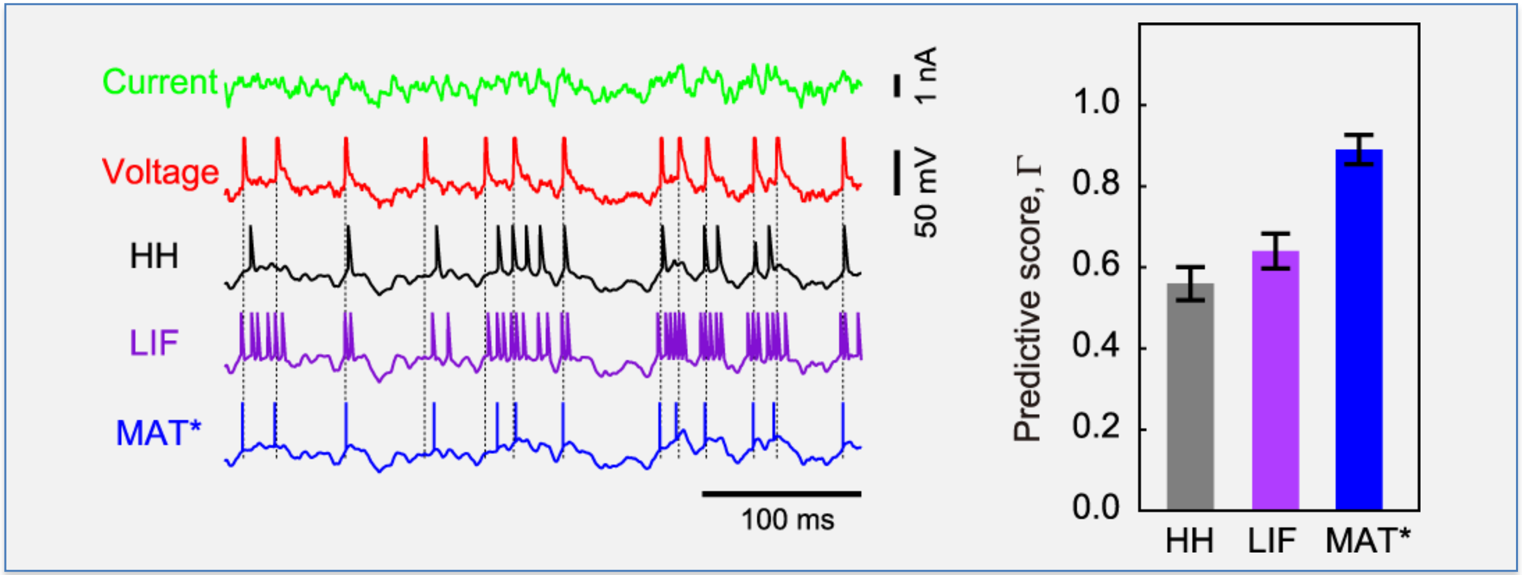

$$C_m \frac{du}{dt} = -g_L(u - E_L) + I(t), \text{ if } u(t) > \boxed{\theta(t)} \rightarrow \text{"Spike generated"}$$

$$\boxed{\theta(t) = \boxed{\theta_\infty} + \sum_{k:t_k<t} \boxed{\alpha_1} e^{-(t-t_k)/\tau_1} + \boxed{\alpha_2} e^{-(t-t_k)/\tau_2}}$$

Kobayashi, Tsubo, Shinomoto. Front. Comput. Neurosci. (2009) 3:9

**Parameters**: fitted from data

# Predictive Performance




- 90 % of reliable spikes can be predicted. (34 cells)
- More accurate than LIF and HH model.

  First prizes in competitions

  See Jolivet et al., 2008; Gerstner & Naud 2009

# Summary:
# Predicting spike timings

Multi-timescale adaptive threshold (MAT) model:

**1) Simple & Efficient for network simulation**

Implemented in NEST (Gewaltig & Diesmann, 2007)

**2) Predict spike timings accurately**

**3) Reproduce a variety of spike patterns**

For details,
Kobayashi, Tsubo, Shinomoto, Front. Comput. Neurosci., 2009

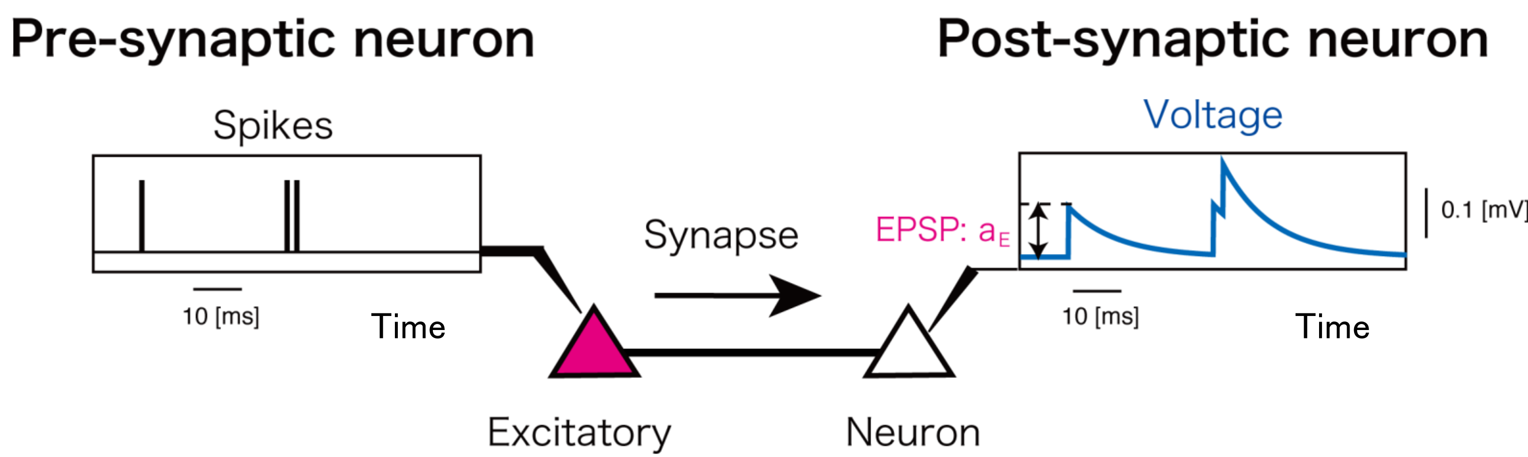
# Inferring synaptic connections from spike data of multiple neurons

Joint work with Katsunori Kitano

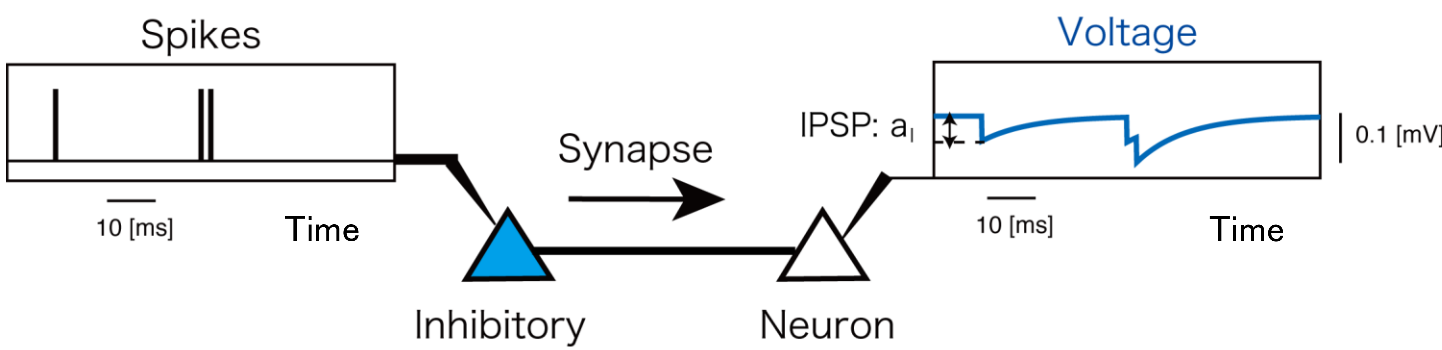
(Kobayashi & Kitano J Comput Neurosci 2013)

# Synapse

## Communication between neurons



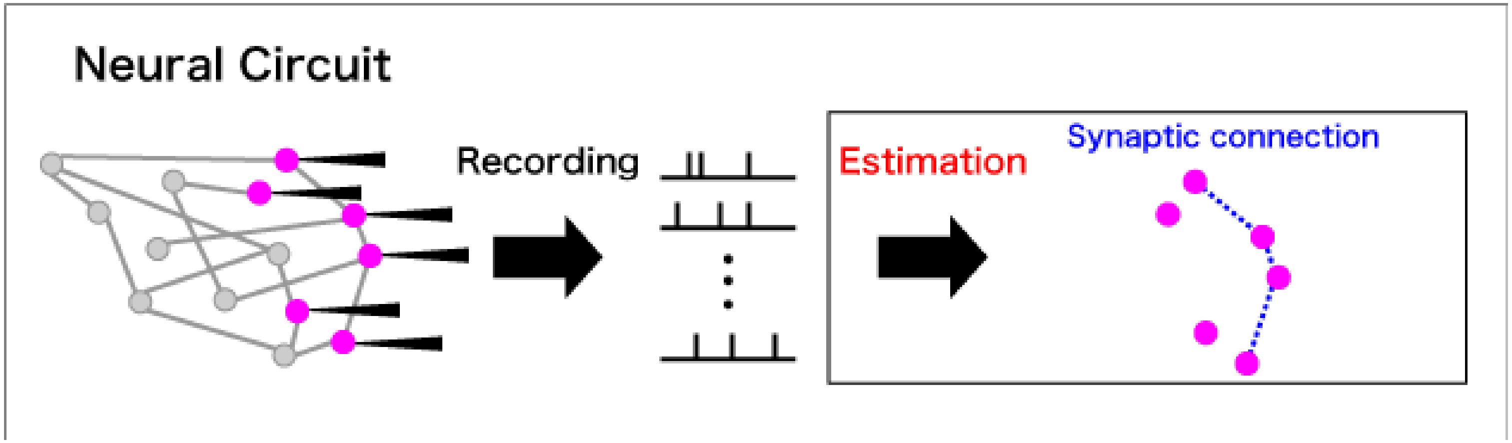

Excitatory neurons increase the voltage of a neuron.




Inhibitory neurons increase the voltage of a neuron.

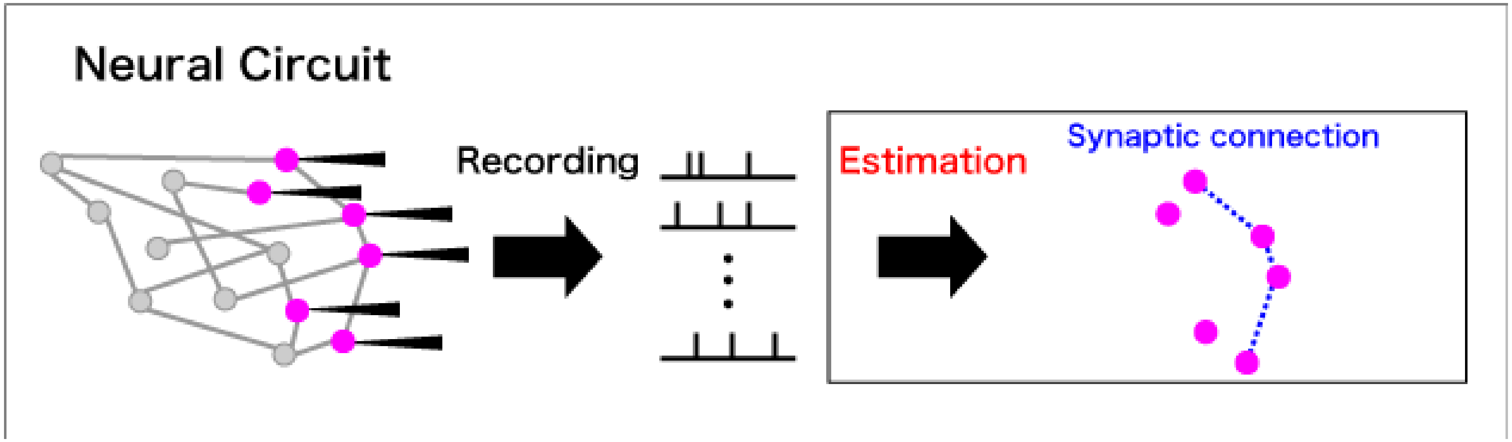
# Estimating synaptic connectivity

Estimate synaptic connectivity from
recorded spike trains of neurons.




Experimentally, it is not possible to record voltage of multiple neurons, but spikes are available.

# Estimataion Problem




Input Data: Neuron ID (k), Spike times, $t^k_j$

Output: Connectivity matrix $w_{ij}$= 0 or 1

# Our approach

1) Develop a method for estimating connectivity.

2) Simulate a realistic neural circuit
with a given connection (connectivity matrix).

3) Apply the estimation method to the simulated data.
Only 2 neurons (in 5,000 neurons) are observable.

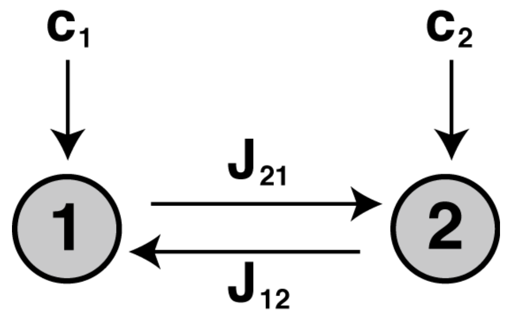
4) Evaluate the performance by a comparison.

# Estimating synaptic connection
# ① Coupled-Escape rate model (CERM)

Extending the escape rate model (Jolivet et. al., 2006; Shinomoto 2009)

$$_1(t) = \exp[c_1 + \ _1 x_1(t) + J_{12} s_2(t)],$$

$$_2(t) = \exp[c_2 + \ _2 x_2(t) + J_{21} s_1(t)],$$




$$\frac{dx_i}{dt} = \frac{x_i}{_m} + \sum_k (t \quad t_{i,k}),$$ Refractory

$$\frac{ds_{ij}}{dt} = \frac{s_{ij}}{_s} + \sum_k (t \quad t_{j,k}).$$ Synaptic input

Parameters $\{c_{1,2}, \ _{1,2}, \boxed{J_{12,21}}\}$ Synaptic strength

Estimation method: Maximum likelihood (Paninski 2004)

# Estimating synaptic connection
# ② Transfer Entropy (TE)

- Information theoretic measure for evaluating predictability between two variables (Schreiber, 2000)

- Let $n_i^t$ be the number of spikes of neuron $i$ within the bin at $t$.
  *Transfer entropy from j to i* $TE_{ij}$:

$$TE_{ij} = H(n_i^{t+1} | n_i^t) \quad H(n_i^{t+1} | n_i^t, n_j^t)$$

where $H(x|y)$ is a conditional entropy.

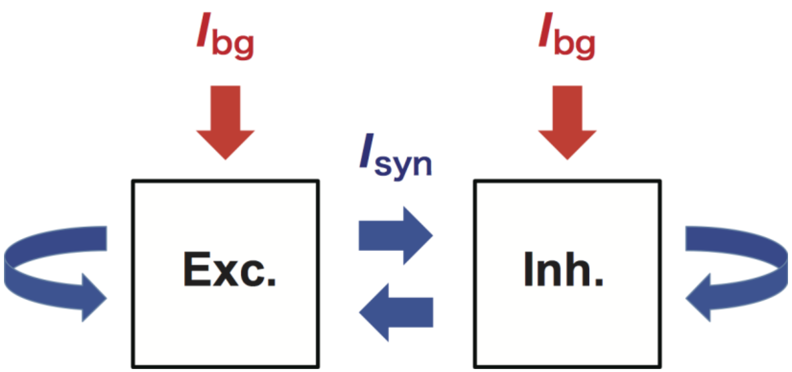
- We used the normalized transfer entropy

$$T_{ij} = \frac{TE_{ij}}{H(n_i^{t+1} \mid n_i^t)}$$

Parameters: $w$ (Bin width)

# Simulation of a micro-neural circuit (1)

## Network model (Kitano & Fukai, J. Comput. Neurosci., 2007)




4096 Excitatory neurons:

$$C_m \frac{dV}{dt} = I_L \quad I_{Na} \quad I_{KDR} \quad I_M \quad I_{syn} \quad I_{bg}$$

1024 Inhibitory neurons:

$$C_m \frac{dV}{dt} = I_L \quad I_{Na} \quad I_{Kv3} \quad I_{syn} \quad I_{bg}$$

$I_{syn}$: AMPA- and GABA-mediated synaptic current

$I_{bg}$: Point conductance model

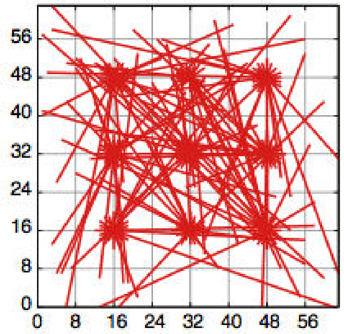
# Simulation of a micro-neural circuit (2)

## Network topology (Kitano & Fukai 2007)

*p*: Rewiring probability

Regular: *p=0.*
Small-world: Small *p*.
Ramdom: *p*=1*.*

Synaptic connection
to nine neurons
– *p= 0.25*




## Connectivity matrix (: we want to estimate)

$$g_{ij} = \begin{cases} g_{\mathrm{exc}} & \text{Exc.Connected} \\ g_{\mathrm{inh}} & \text{Inh.connected} \\ 0 & \text{Not connected} \end{cases}$$

# Evaluation of estimated connectivity

We estimate whether there is a connection or not.

- Real connectivity:

$$c_{ij} = \begin{cases} 1 & \text{Connected} \\ 0 & \text{Not connected} \end{cases}$$

- Predicted connectivity

$$\hat{c}_{ij} = \begin{cases} 1 & J > J_{th} \\ 0 & \text{Otherwise} \end{cases}$$

where $J_{th}$ is the threshold parameter that is determined by maximizing

Metrics of performance (MCC)

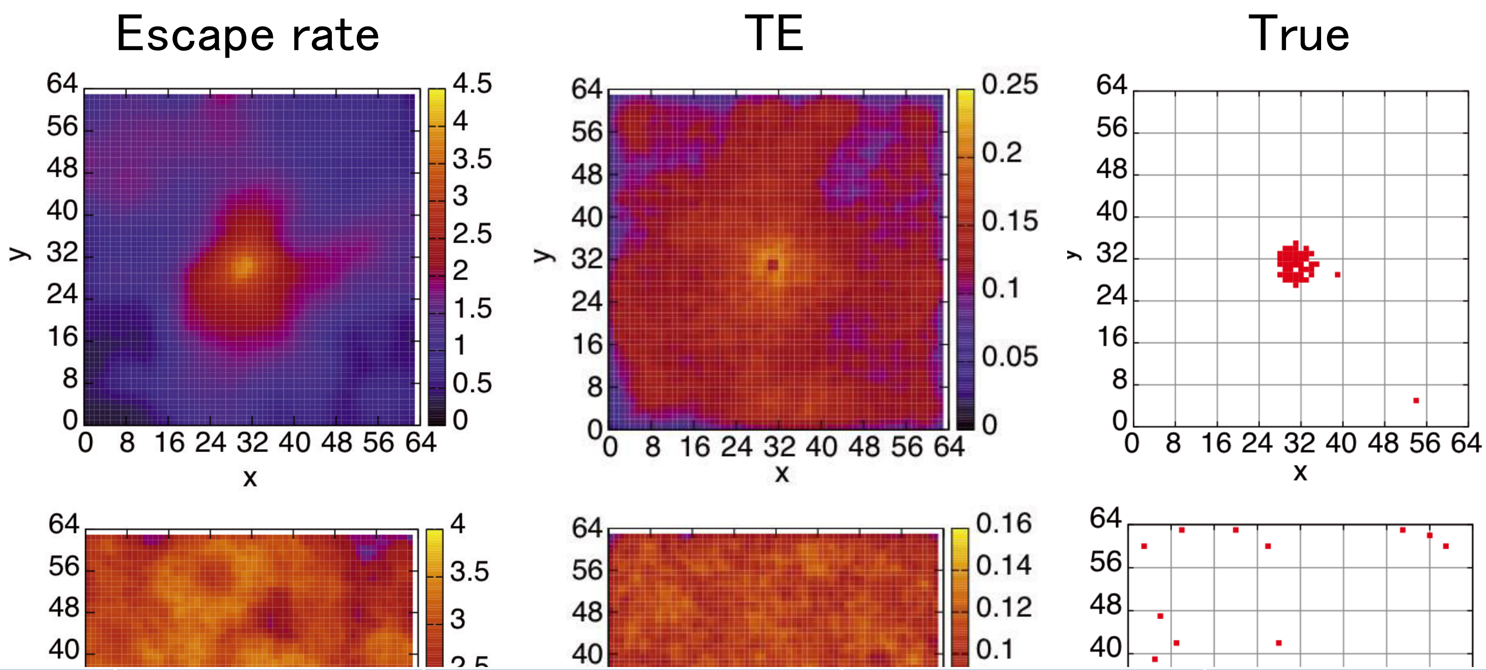
$$MCC = \frac{TP \quad TN \quad FP \quad FN}{\sqrt{(TP+FP)(TP+FN)(TN+FP)(TN+FN)}}$$

0: Random
1: Perfect

# Estimated synaptic connectivity

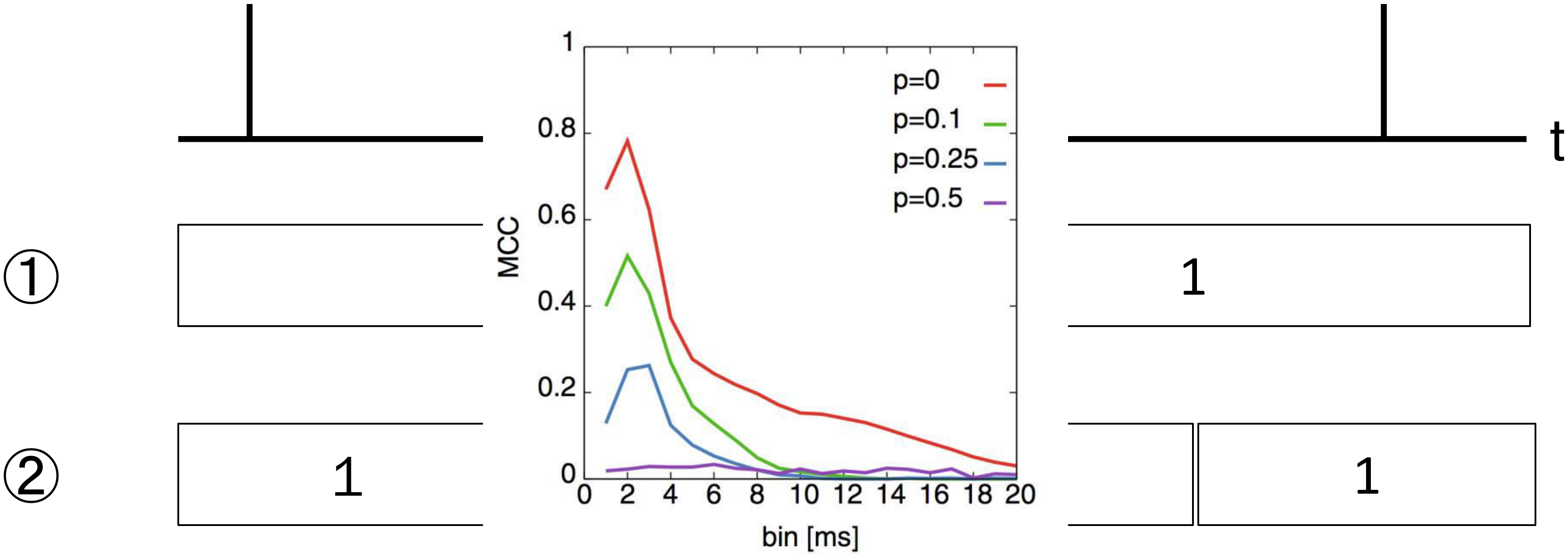
Synaptic connection from neuron (i, j) to neuron (32, 32)

**Small World**
(p =0.1)




| | p=0.0 (Regular) | p= 0.1 (Small World) | p= 0.25 | p= 0.5 (Ramdom) |
|---|---|---|---|---|
| CERM (N=2) | 0.74 | 0.57 | 0.38 | 0.12 |
| TE | 0.65 | 0.37 | 0.10 | 0.02 |

# Binning issue




Binning can be influence the estimation results.

CERM does not require binning.

# Application to the simulated data

Comparison of CERM (N=2) and CERM (N=49)

| | p= 0.1 (Small World) | p= 0.25 | p= 0.5 (Random) |
|---|---|---|---|
| TE | 0.37 | 0.10 | 0.02 |
| CERM: N=2 | 0.64 | 0.55 | 0.12 |
| CERM: N=49 | 0.68 | 0.60 | 0.30 |

CERM (N=49) is better than CERM (N=2).
Especially for Random case.

Kobayashi & Kitano submitted

# Summary:
## Estimation of synaptic connectivity

- Proposed method: Coupled-escape rate model
- Estimation performance using a simulated data

  1) Regular, Small world network: Good!

  2) Random network: Poor!
- Proposed method

  Accurate, robust and does not require binning.
- Extension to N>2 case

  Improve the performance further

Kobayashi & Kitano. J. Comput. Neurosci. (2013).

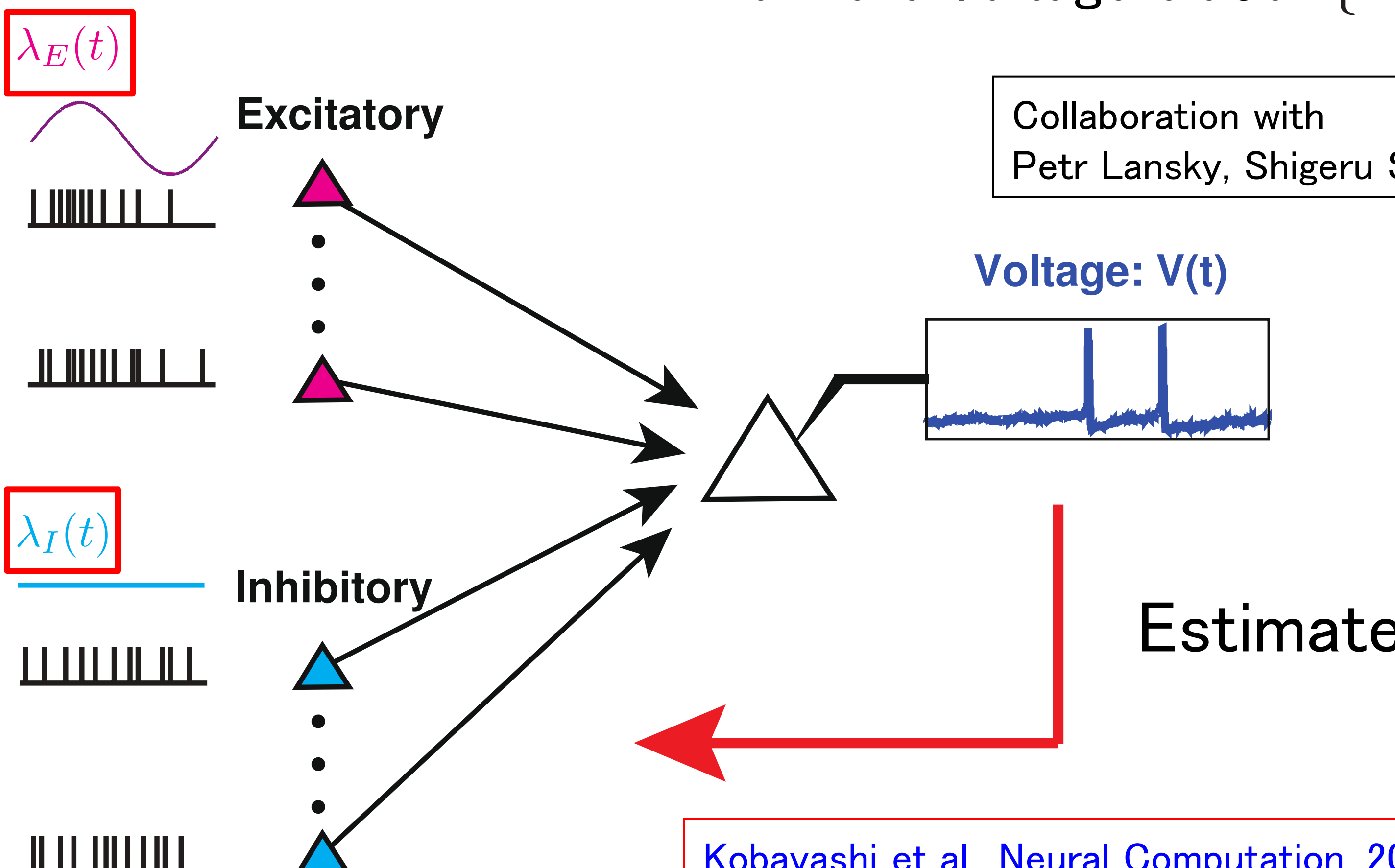
# Other projects

# Estimate input signal to a neuron

Estimate time-varying input rate $\{\lambda_E(t), \lambda_I(t)\}$

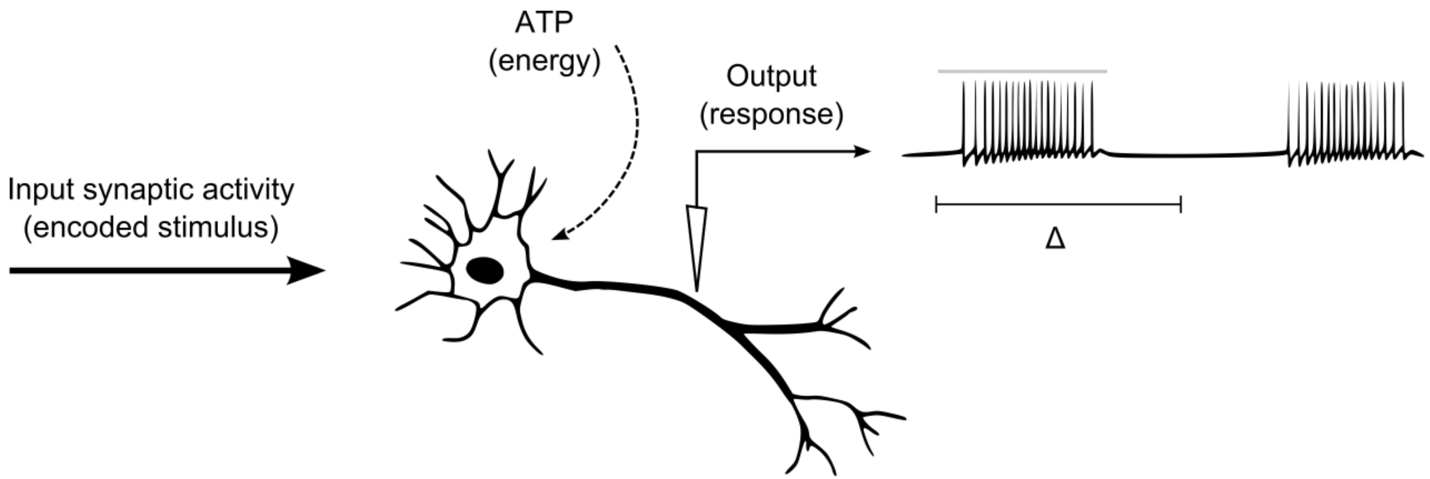
from the voltage trace $\{V(t)\}$

Collaboration with
Petr Lansky, Shigeru Shinomoto.




[Kobayashi et al., Neural Computation, 2011](#)
[Kobayashi et al., NIPS 2011](#)
[Kobayashi et al., Front Comput Neurosci., 2015](#)

# Optimal information transmission through a single neuron




Q. How should a neuron generate spikes
to achieve optimal information transfer?

Collaboration with Lubomir Kostal.

Kostal & Kobayashi, BioSystems, In press

# Thanks for your attention!

Collaborators:

1. Single neuron modeling

    Yasuhiro Tsubo, Shigeru Shinomoto.

2. Estimation of synaptic connectivity

    Katsunori Kitano.

3. Other projects

    ① Input Estimation

    Petr Lansky, Shigeru Shinomoto,
    Yasuhiro Tsubo, Jufang He.

    ② Information transmission of single neurons

    Lubomir Kostal.