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本資料をご利用する際には、その定めるところに従ってください。

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- I 複製及び複製物の頒布、譲渡、貸与
- II 上映
- III インターネット配信等の公衆送信
- IV 翻訳、編集、その他の変更
- V 本資料をもとに作成された二次的著作物についての I から IV

ご利用にあたっては、次のどちらかのクレジットを明記してください。

東京大学 UTokyo OCW 学術俯瞰講義

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# 計算神経科学—モデルと解析

## 第一回：脳活動を表現する数式

豊泉太郎

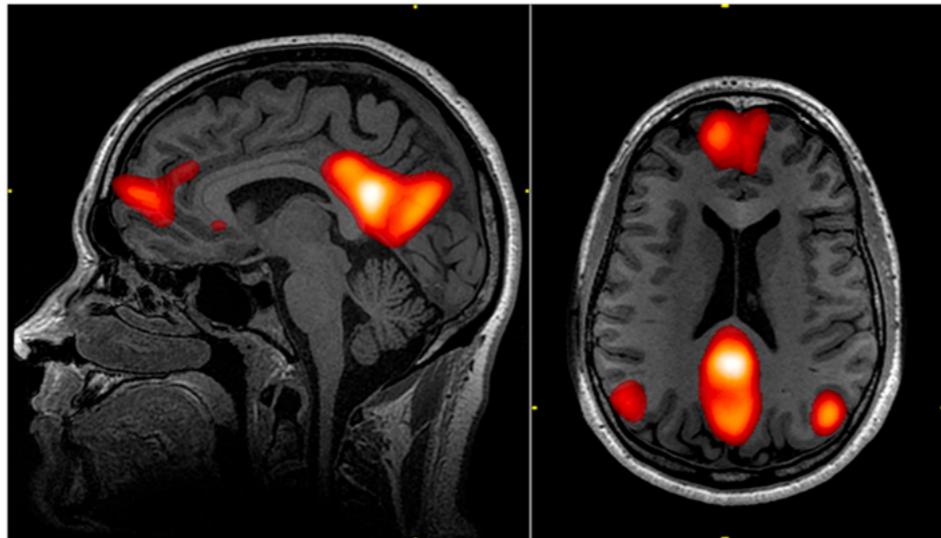
理化学研究所 脳科学総合研究センター

# Background:

Technological advance in neuroscience

# Imaging brain activity

fMRI



calcium imaging

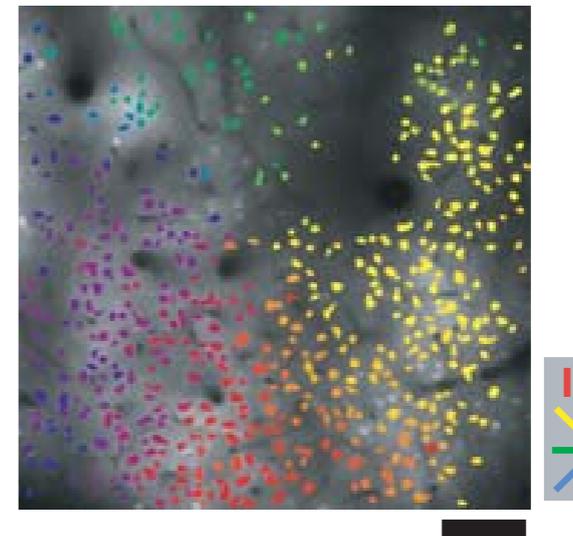
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calcium imaging

Takahashi et al. (2012)

Locally Synchronized Synaptic Inputs,  
Science 335 (6066): 353-356, p. 354 Fig. 1C.

<http://www.sciencemag.org/content/335/6066/353.full>



Ohki et al. (2006)

Highly ordered arrangement of single neurons in orientation pinwheels,  
Nature 442(7105): 925-928, p. 926 Fig. 1e.

<http://www.nature.com/nature/journal/v442/n7105/full/nature05019.html>

# The Connectome

## Electron microscopy

### The C. elegans wiring diagram

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線虫 C. elegans のコネクトーム  
<http://connectomethebook.com/?portfolio=the-c-elegans-connectome>  
The C. elegans connectome  
Credit: Mitya Chklovskii



photo by Omegatron, from Wikipedia  
[https://commons.wikimedia.org/wiki/File:Adult\\_Caenorhabditis\\_elegans.jpg](https://commons.wikimedia.org/wiki/File:Adult_Caenorhabditis_elegans.jpg)  
CC BY-SA 2.5

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### 電子顕微鏡の映像

This beautiful data was published  
Friday, July 30th 2015 in Cell  
<http://www.sciencedirect.com/science/article/pii/S0092867415008247>

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### 神経のCG画像

Jeong et al. (2009)  
Scalable and Interactive Segmentation  
and Visualization of Neural Processes in  
EM Datasets, IEEE Transactions on  
Visualization and Computer Graphics 15  
(6): 1505-1514 p. 1505

Fig. 1: NeuroTrace allows neuroscientists  
to interactively explore and segment  
neural processes in high-resolution EM  
data.

<http://ieeexplore.ieee.org/xpls/icp.jsp?arnumber=5290767>

### Diffusion spectrum imaging



\* V Gewin (2013) Neuroscience: A head start for brain imaging, Nature 503 (7474): 153–155, p. 153 Fig. The neuronal pathways in the brain's white matter are picked out in this magnetic resonance image.  
<http://www.nature.com/nature/journal/v503/n7474/full/nj7474-153a.html>

# Virtual reality

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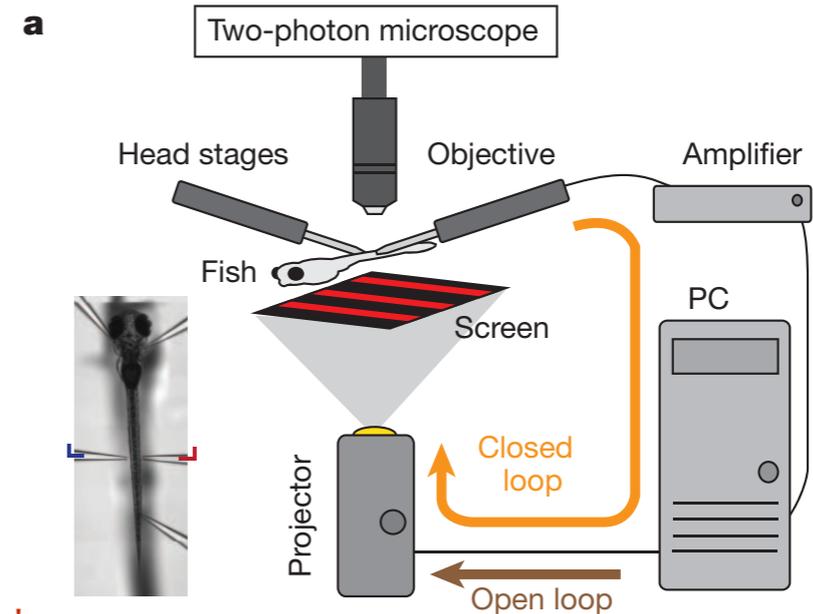
ネズミを使った実験の模式図

Dombeck et al. (2007) Imaging Large-Scale Neural Activity with Cellular Resolution in Awake, Mobile Mice, *Neuron* 56(1): 43–57, p. 44 Fig. 1A.

<http://www.sciencedirect.com/science/article/pii/S0896627307006149>



\*

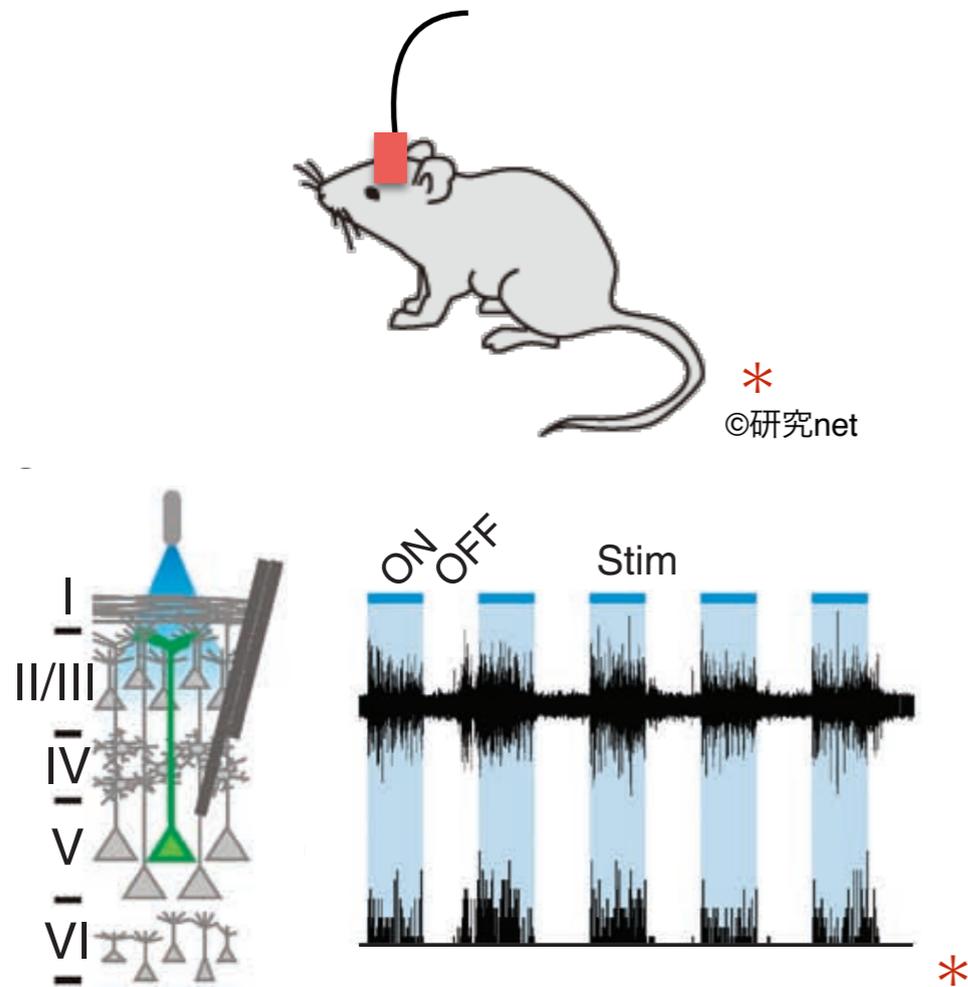


\*

Ahrens et al. (2012) Brain-wide neuronal dynamics during motor adaptation in zebrafish, *Nature* 485 (7399): 471–477, p. 472 Fig. 1a. <http://www.nature.com/nature/journal/v485/n7399/full/nature11057.html>

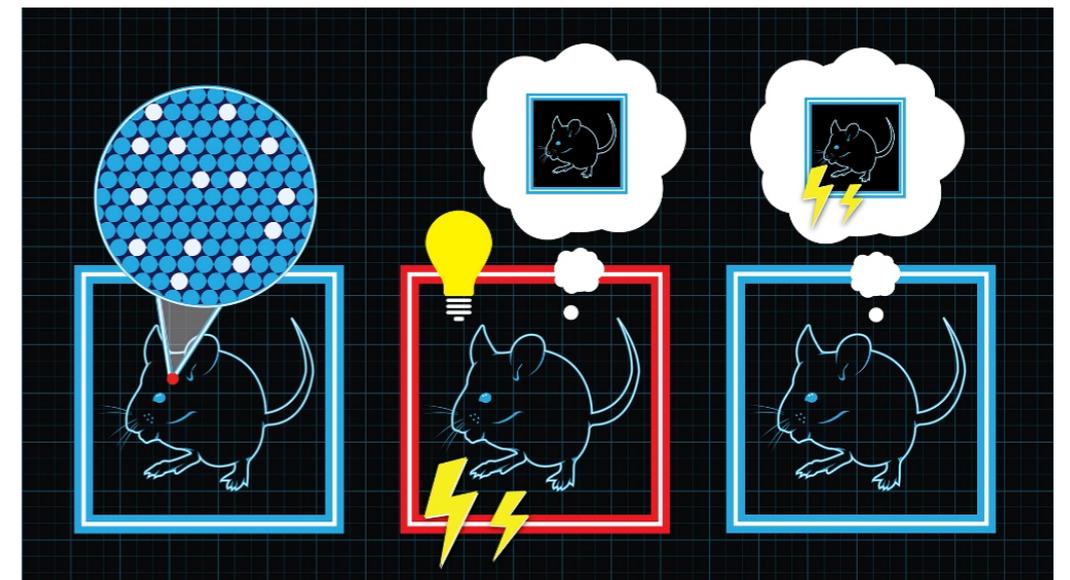
# Optogenetics

## Optical stimulation of specific neurons



Beltramo et al. (2013) Layer-specific excitatory circuits differentially control recurrent network dynamics in the neocortex, *Nature Neuroscience* 16(2): 227–234, p. 230 Fig. 3a, 3d  
<http://www.nature.com/neuro/journal/v16/n2/abs/nn.3306.html>

## Incepting a memory

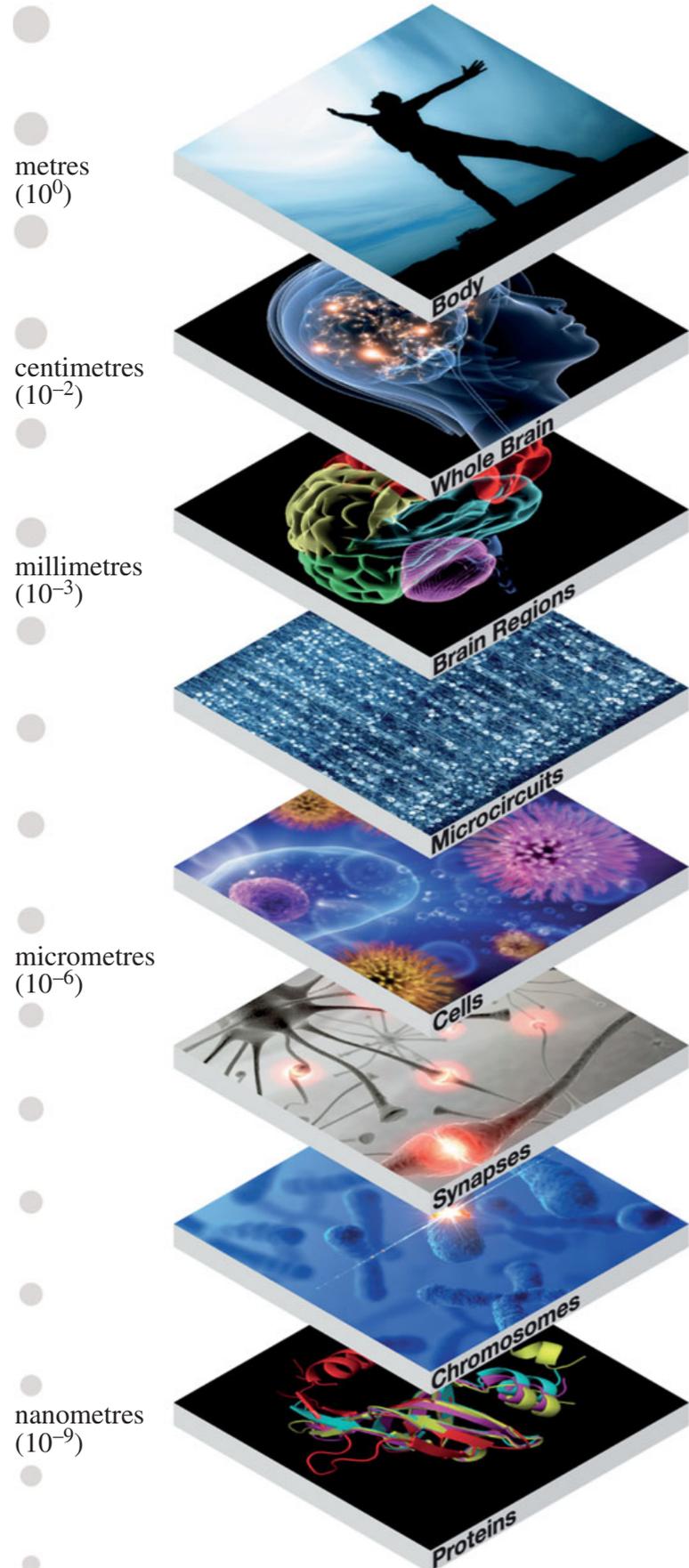


**What is the impact on computational neuroscience?**

**More theoretical concepts have become experimentally testable and got practical applications.**

# Outline

spatial scales



## Analyzing

- A single neuron
- A network of neurons
- A whole brain

## Topics include

- Modeling
- Data analysis
- Encoding and decoding

# Textbooks

著作権等の都合により、  
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た

書籍の表紙

Kandel et al. Principles of Neural Science,  
Fourth edition, McGraw-Hill, 2000.

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た

書籍の表紙

Bear et al. Neuroscience: Exploring the  
Brain, 3rd Edition. Lippincott Williams and  
Wilkins, 2006.

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た

書籍の表紙

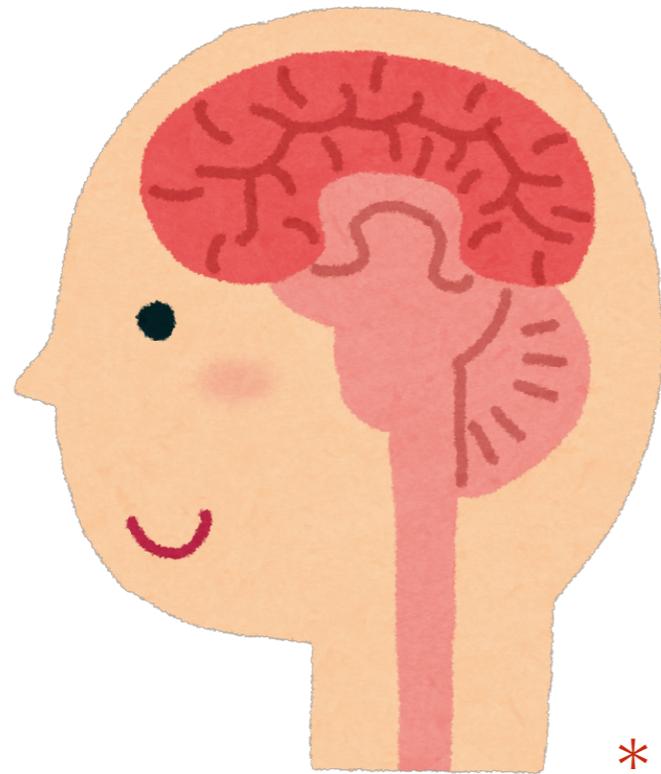
Abbott and Dayan, Theoretical  
Neuroscience: Computational and  
Mathematical Modeling of Neural  
Systems, The MIT Press, 2001.

著作権等の都合により、  
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た

書籍の表紙

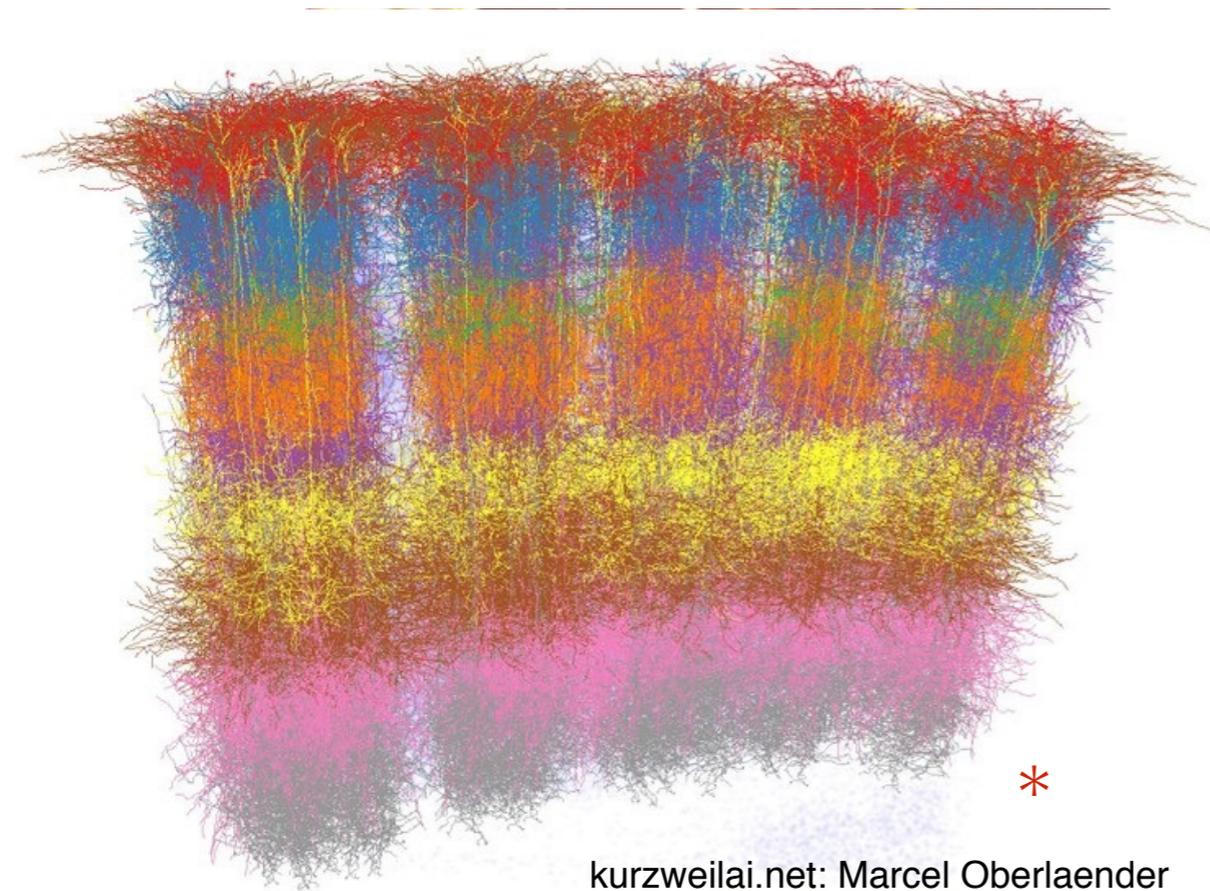
Gerstner and Kistler, Spiking Neuron  
Models: Single Neurons, Populations,  
Plasticity, Cambridge University Press,  
2002.

# How a single neuron works in the brain?



©いらすとや

# How a single neuron works in the brain?



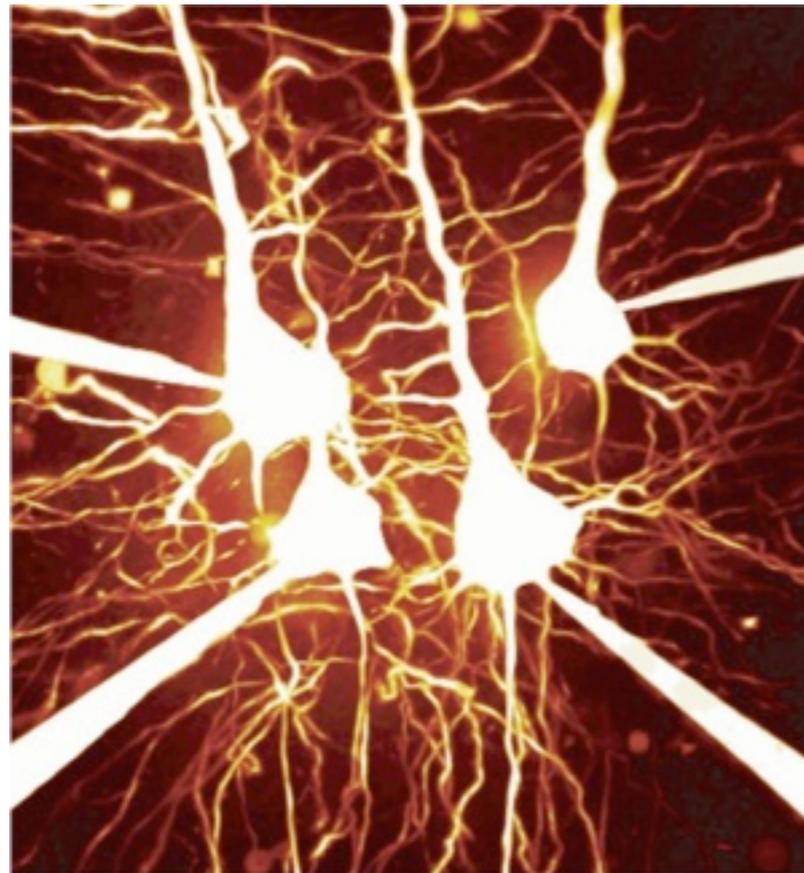
kurzweilai.net: Marcel Oberlaender

Cortex In Silico - Reconstruction of cortical columns in rat barrel cortex"; Image provided by Dr. M. Oberlaender, Research Center caesar, Bonn, Germany

# How a single neuron works in the brain?

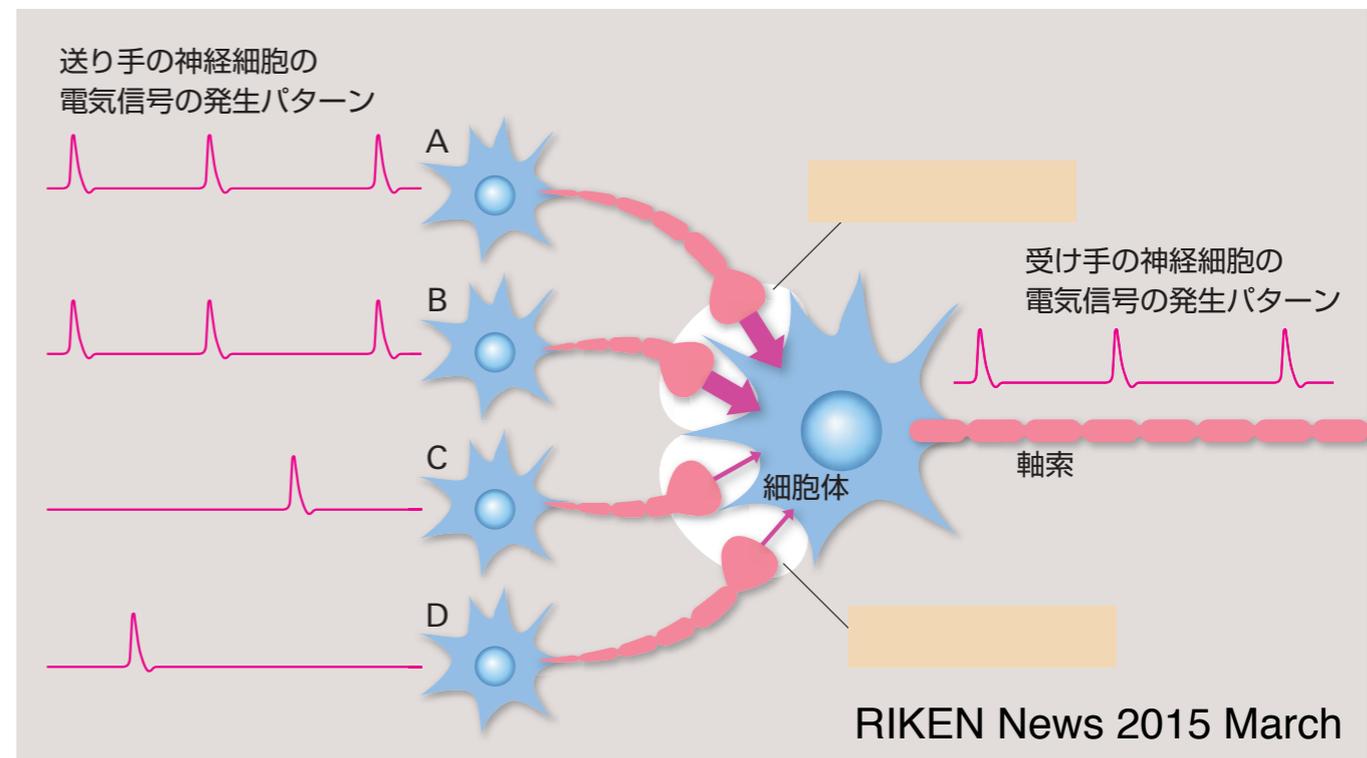
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ニューロンの電気信号の波形図



\*

Jesper Sjostrom and Michael Hausser, University College London



\*

『理研ニュース』2015年3月号より転載（提供：理化学研究所）

# Single-neuron analysis

# A model of a neuron: The Hodgkin-Huxley equation

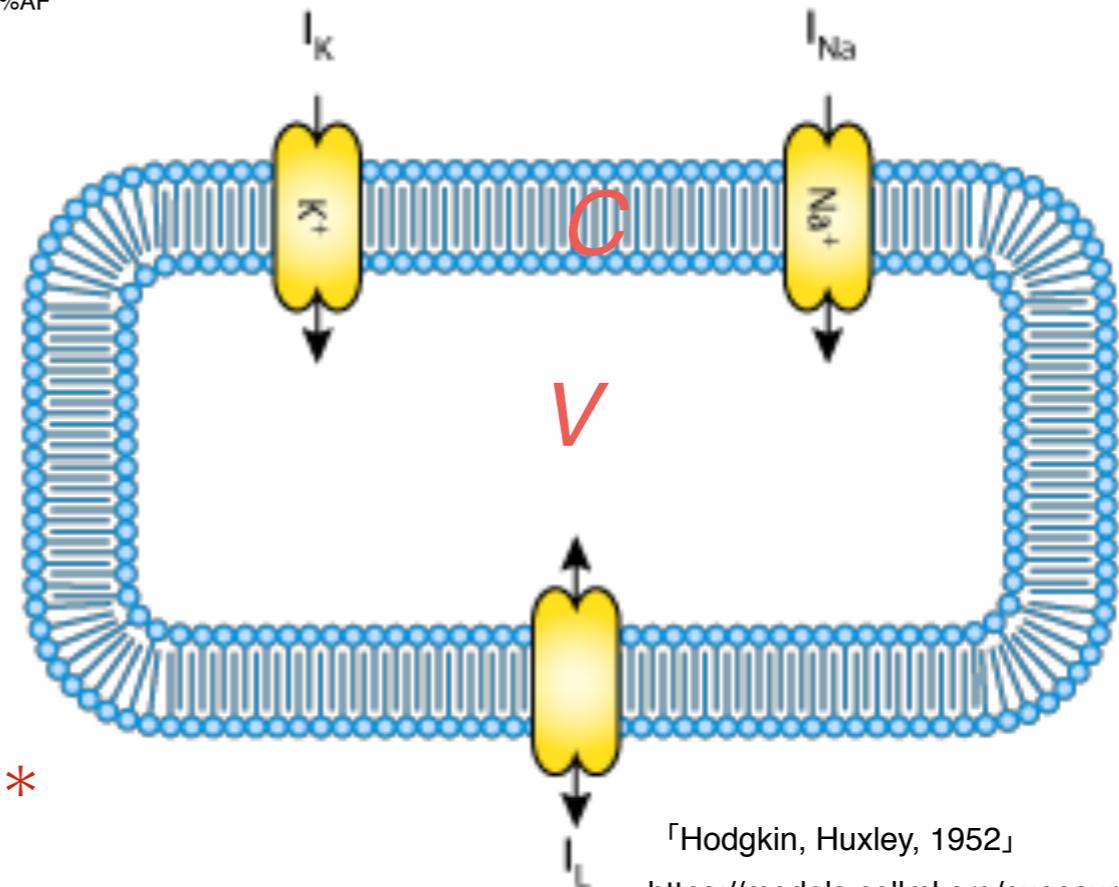
Photo by Vmadeira, from Wikipedia  
[https://ja.wikipedia.org/wiki/%E3%82%A2%E3%83%B3%E3%83%89%E3%83%AA%E3%83%A5%E3%83%BC%E3%83%BB%E3%83%95%E3%82%A3%E3%83%BC%E3%83%AB%E3%83%87%E3%82%A3%E3%83%B3%E3%82%B0%E3%83%BB%E3%83%8F%E3%82%AF%E3%82%B9%E3%83%AA%E3%83%BC#/media/File:Andrew\\_huxley\\_trinity.png](https://ja.wikipedia.org/wiki/%E3%82%A2%E3%83%B3%E3%83%89%E3%83%AA%E3%83%A5%E3%83%BC%E3%83%BB%E3%83%95%E3%82%A3%E3%83%BC%E3%83%AB%E3%83%87%E3%82%A3%E3%83%B3%E3%82%B0%E3%83%BB%E3%83%8F%E3%82%AF%E3%82%B9%E3%83%AA%E3%83%BC#/media/File:Andrew_huxley_trinity.png)  
 CC BY-SA 3.0



Photo by Australian National University, from Wikipedia  
[https://ja.wikipedia.org/wiki/%E3%82%B8%E3%83%A7%E3%83%B3%E3%83%BB%E3%83%BB%E3%82%A8%E3%83%83%E3%82%AF%E3%83%AB%E3%82%B9#/media/File:Eccles\\_lab.jpg](https://ja.wikipedia.org/wiki/%E3%82%B8%E3%83%A7%E3%83%B3%E3%83%BB%E3%83%BB%E3%82%A8%E3%83%83%E3%82%AF%E3%83%AB%E3%82%B9#/media/File:Eccles_lab.jpg)  
 CC BY 3.0

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アラン・ロイド・ホジキンの肖像



\*

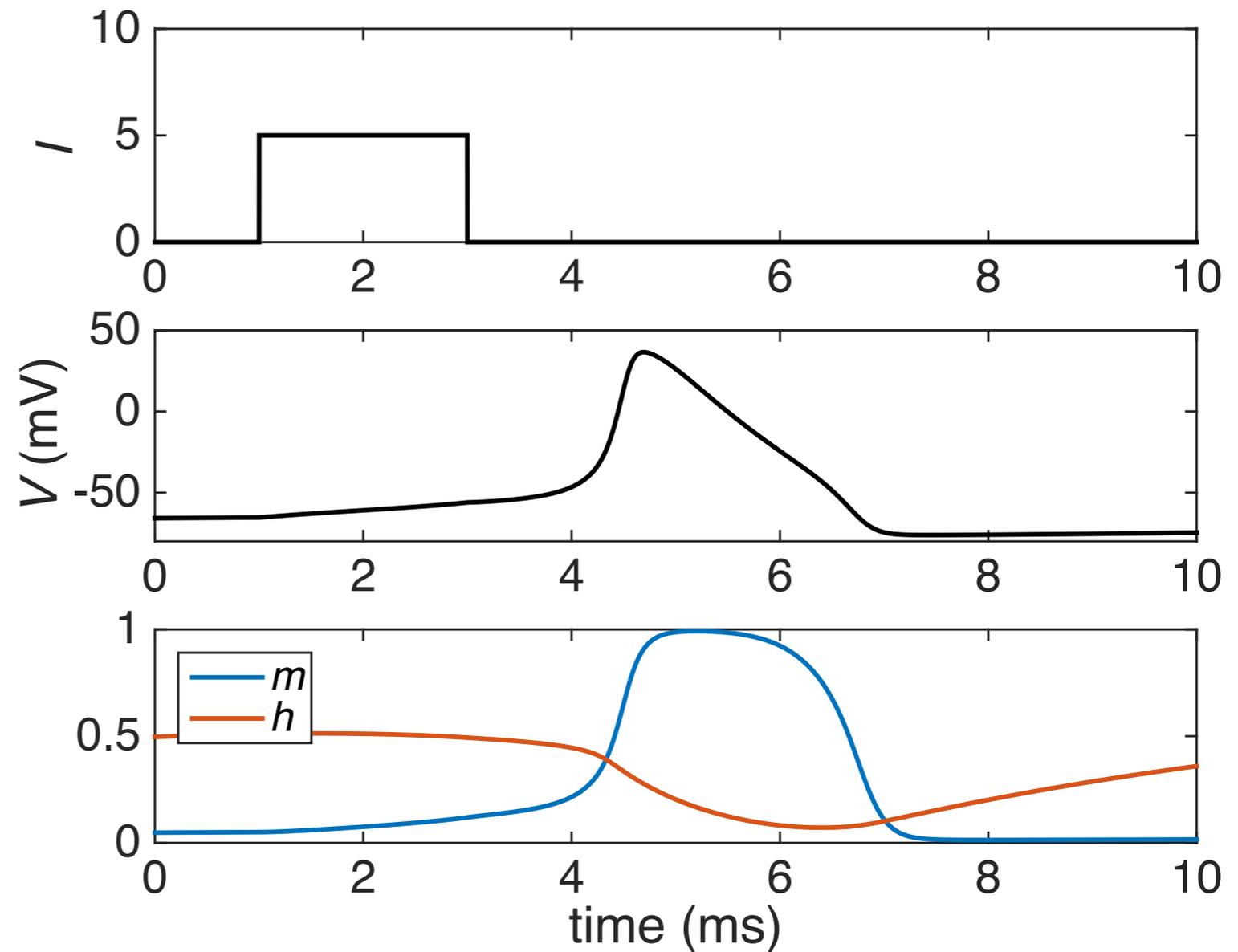
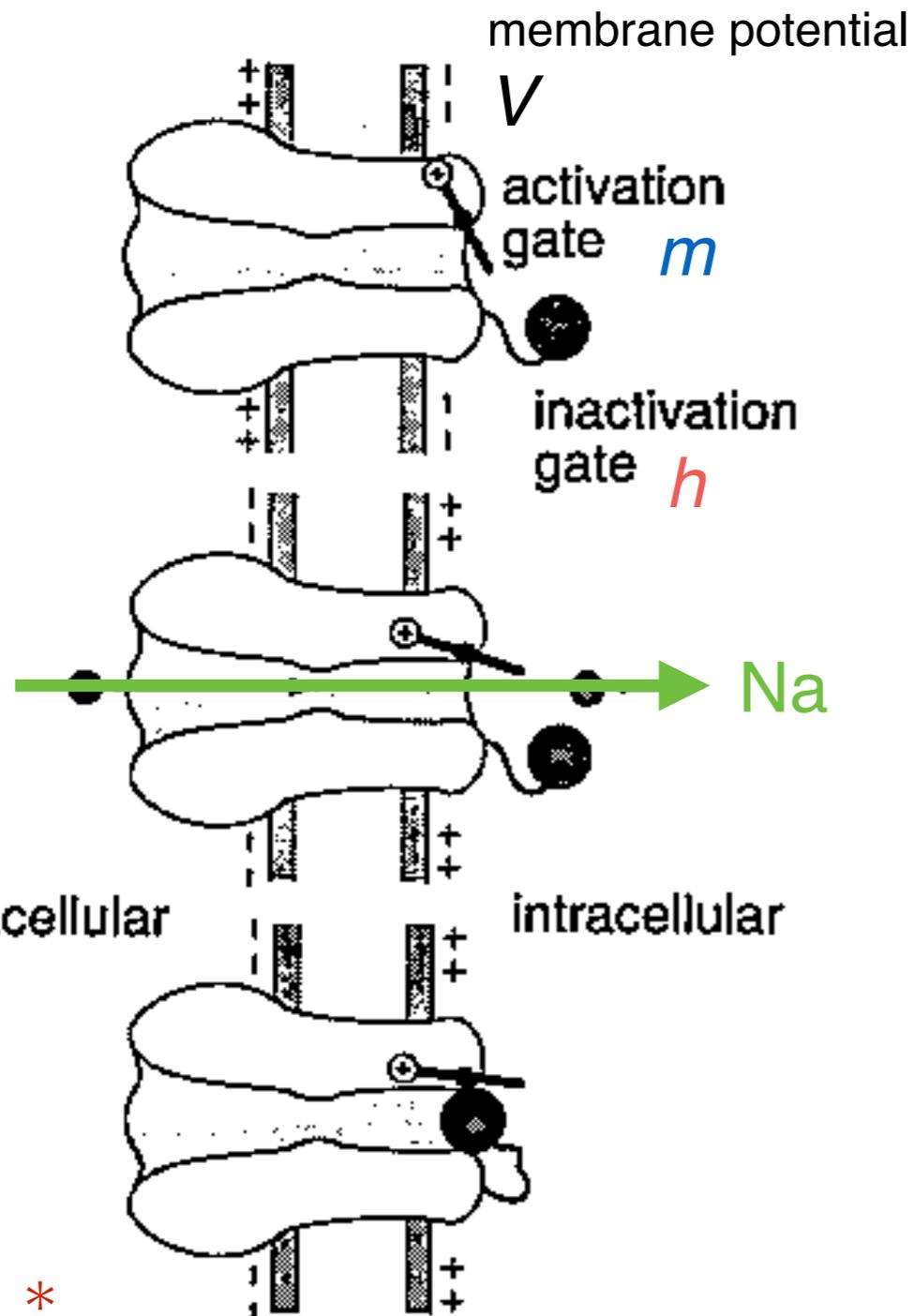
「Hodgkin, Huxley, 1952」

<https://models.cellml.org/exposure/5d116522c3b43ccaeb87a1ed10139016/view>  
 A schematic cell diagram describing the current flows across the cell membrane that are captured in the Hodgkin Huxley model.  
 CC BY 3.0

$$C \frac{dV}{dt} = I_L + I_{Na} + I_K + I_{ext}$$

# The Hodgkin-Huxley model of action potential generation

$$I_{Na} = g_{Na} m^3 h (V_{Na} - V)$$



\*  
 Dayan and Abbott, *Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems*, MIT Press, 2001, p. 169 Fig. 5.8 B. A cartoon of the gating of a transient conductance.  
 (From Kandel et al. *Principles of Neural Science*, Third edition, McGraw-Hill, 1991)

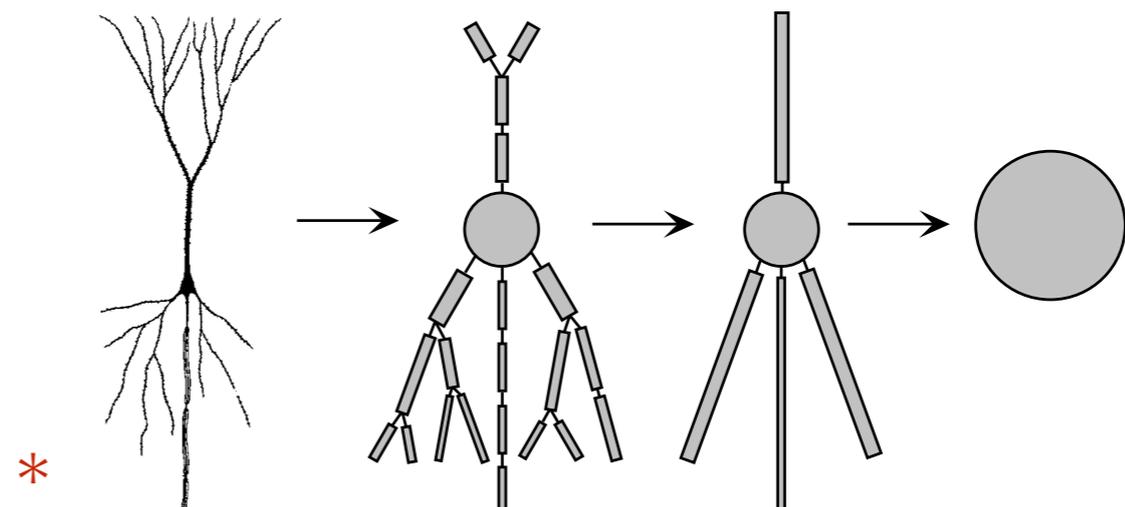
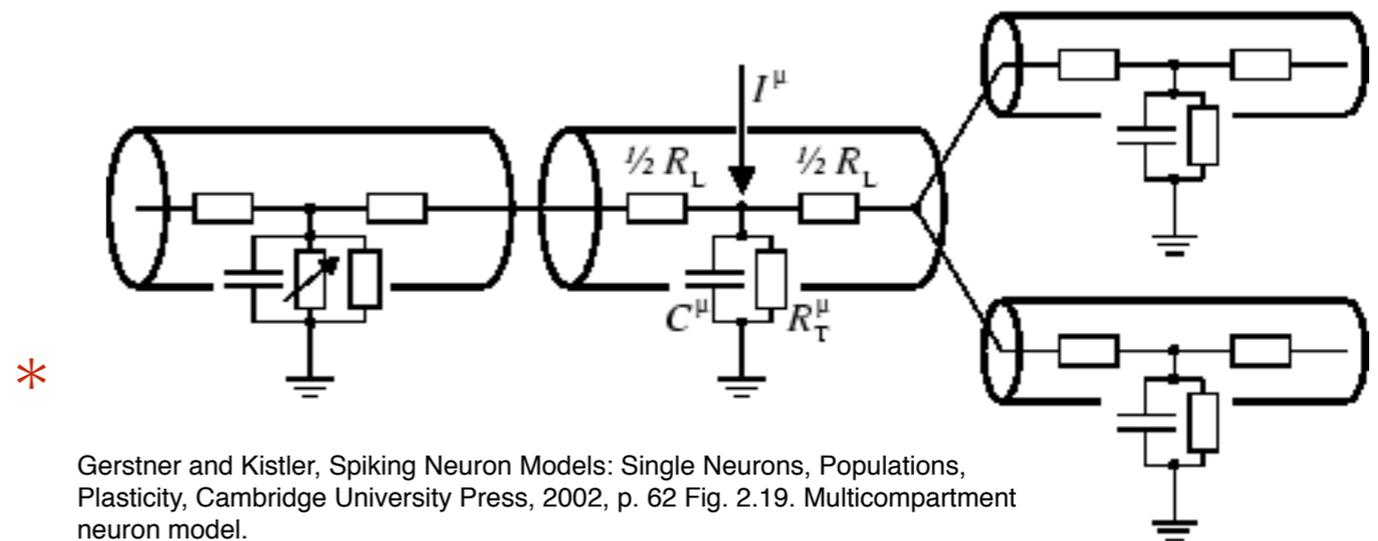
# Morphology: cable transmission and compartments

## Action potential conduction along axons

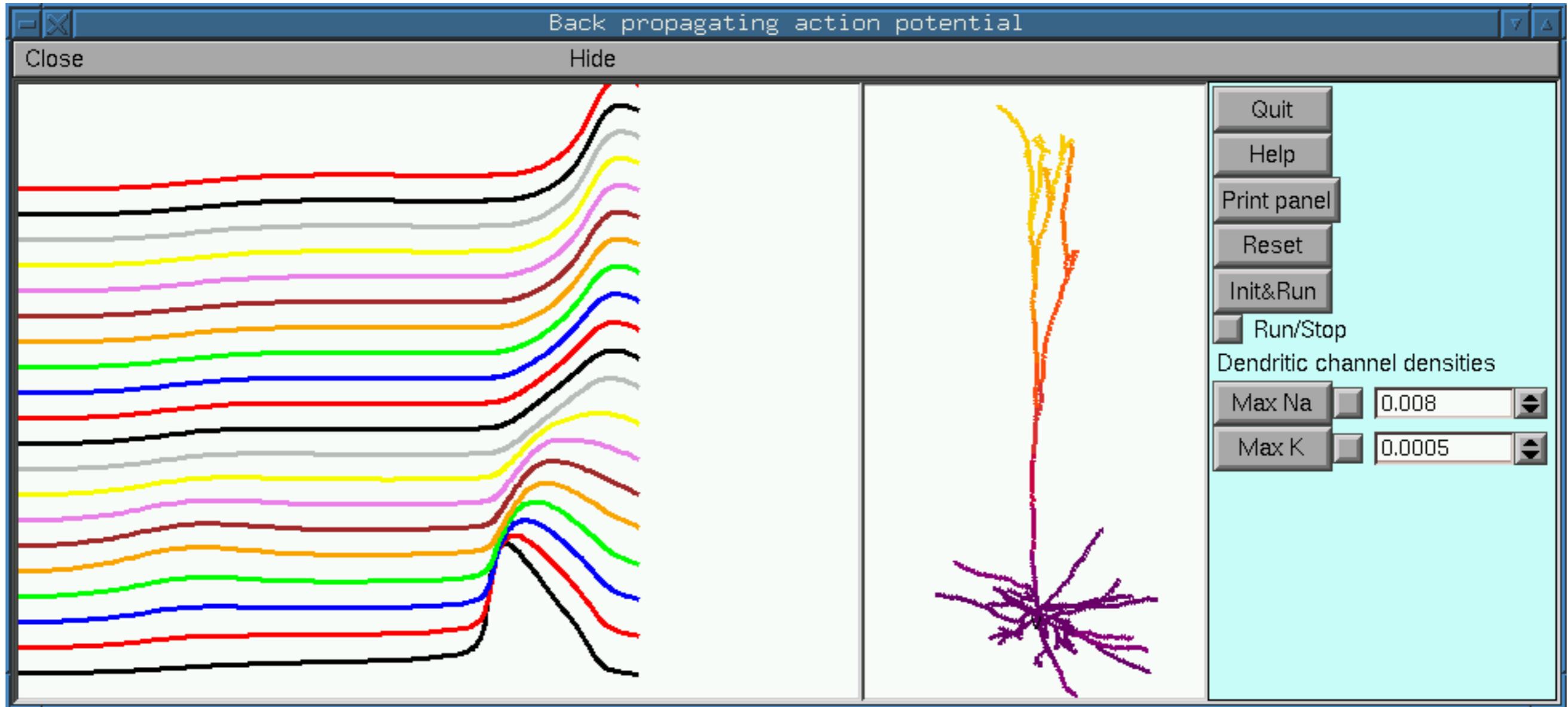
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Action potential conduction along axons  
Bear et al. Neuroscience: Exploring the Brain, Third edition, Lippincott Williams & Wilkins, 2001, p. 93 Fig. 4.11: Action potential conduction.

## Multi-compartment models



# Computer simulations



\*

<http://www.neuron.yale.edu/>

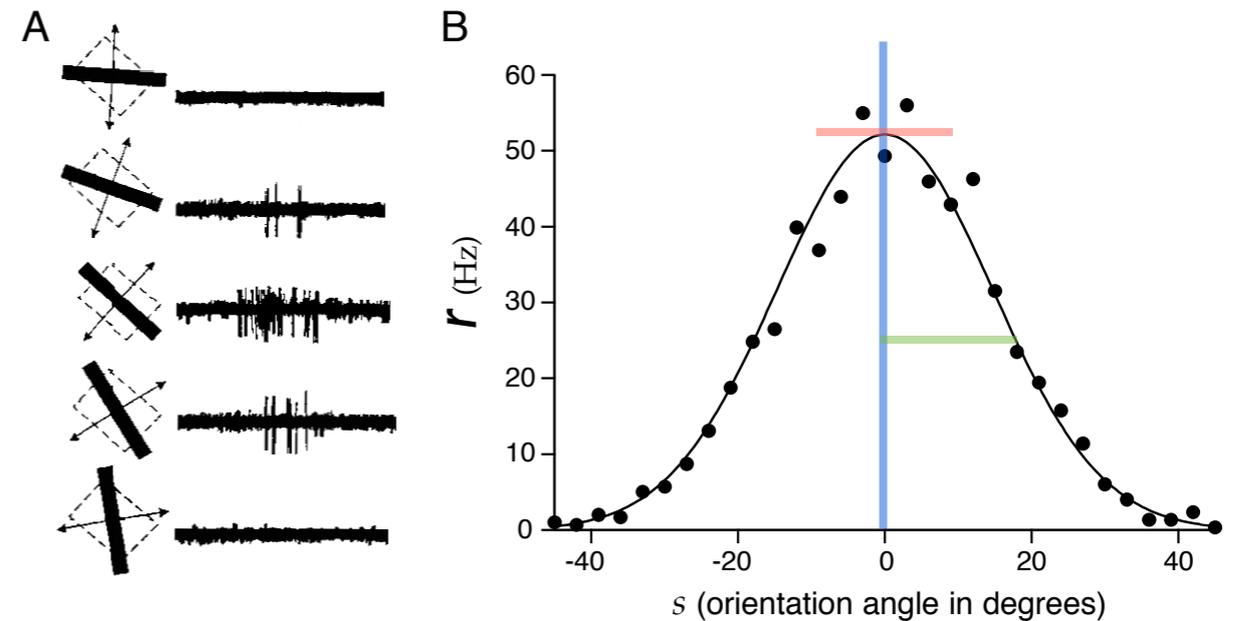
# Neural coding

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Neural coding  
Bialek et al. (1991) Reading a neural code, Science  
252 (5014): 1854-1857, p. 1855 Fig. 1. Schematic  
view of the decoding process.  
[http://science.sciencemag.org/content/  
252/5014/1854.short](http://science.sciencemag.org/content/252/5014/1854.short)

# Neural coding of visual stimuli and hand-reaching direction

## Primary visual cortex



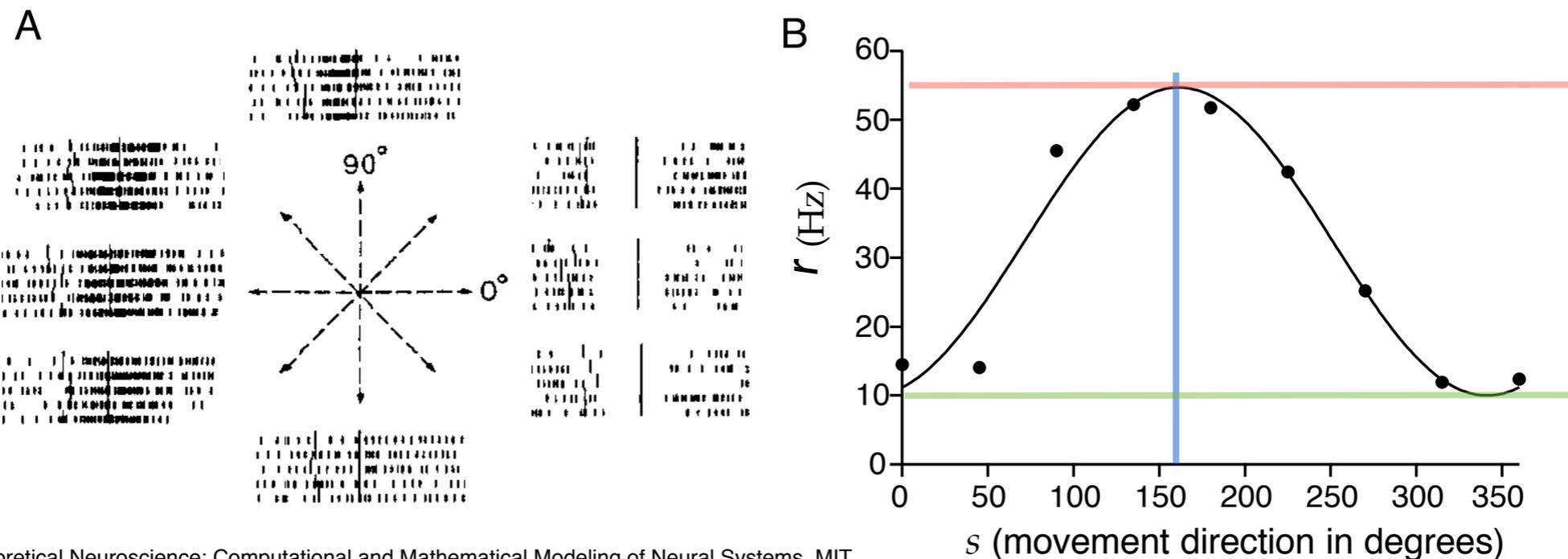
Hubel and Wiesel 1968

Henry et al. 1974

\*

Dayan and Abbott, Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems, MIT Press, 2001, p. 15 Fig. 1.5: (A) Recordings from a neuron in the primary visual cortex of a monkey; (B) Average firing of a cat V1 neuron plotted as a function of the orientation angle of the light bar stimulus.

## Motor cortex



\*

Dayan and Abbott, Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems, MIT Press, 2001, p. 16, Fig. 1.6. (A) Recordings from the primary motor cortex of a monkey performing an arm-reaching task; (B) Average firing rate plotted as a function of the direction in which the monkey moved its arm.

Georgopoulos et al. 1982

# The encoding step: system identification

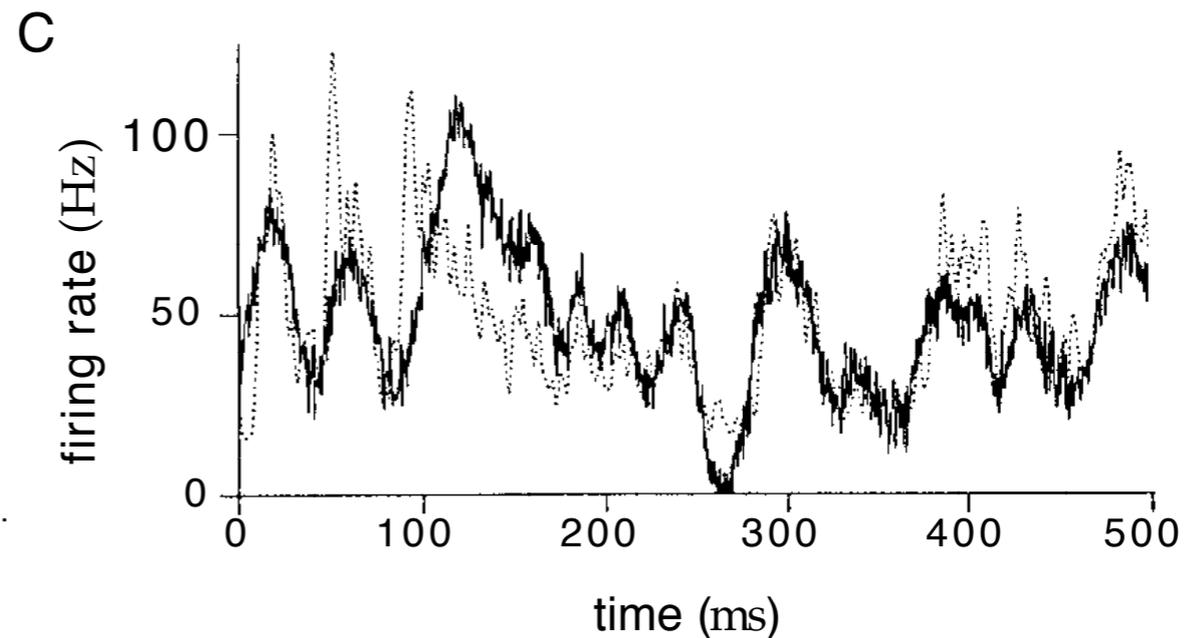
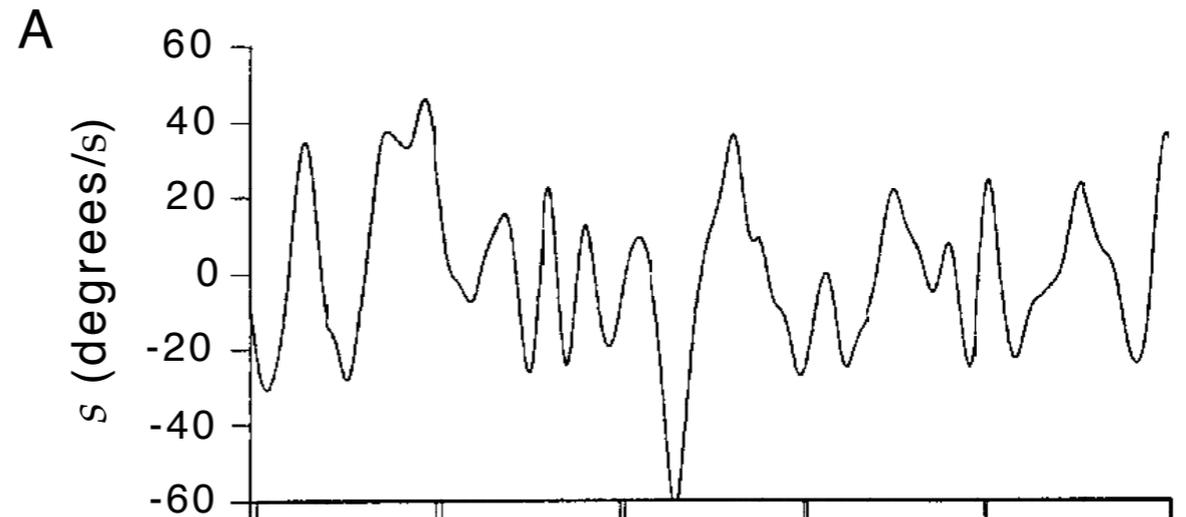
## A linear neuron model

$$r_{\text{model}}(t) = r_0 + \int A(u)s(t-u)du$$

Find the optimal parameters ( $A$  and  $r_0$ ) that minimize the square error

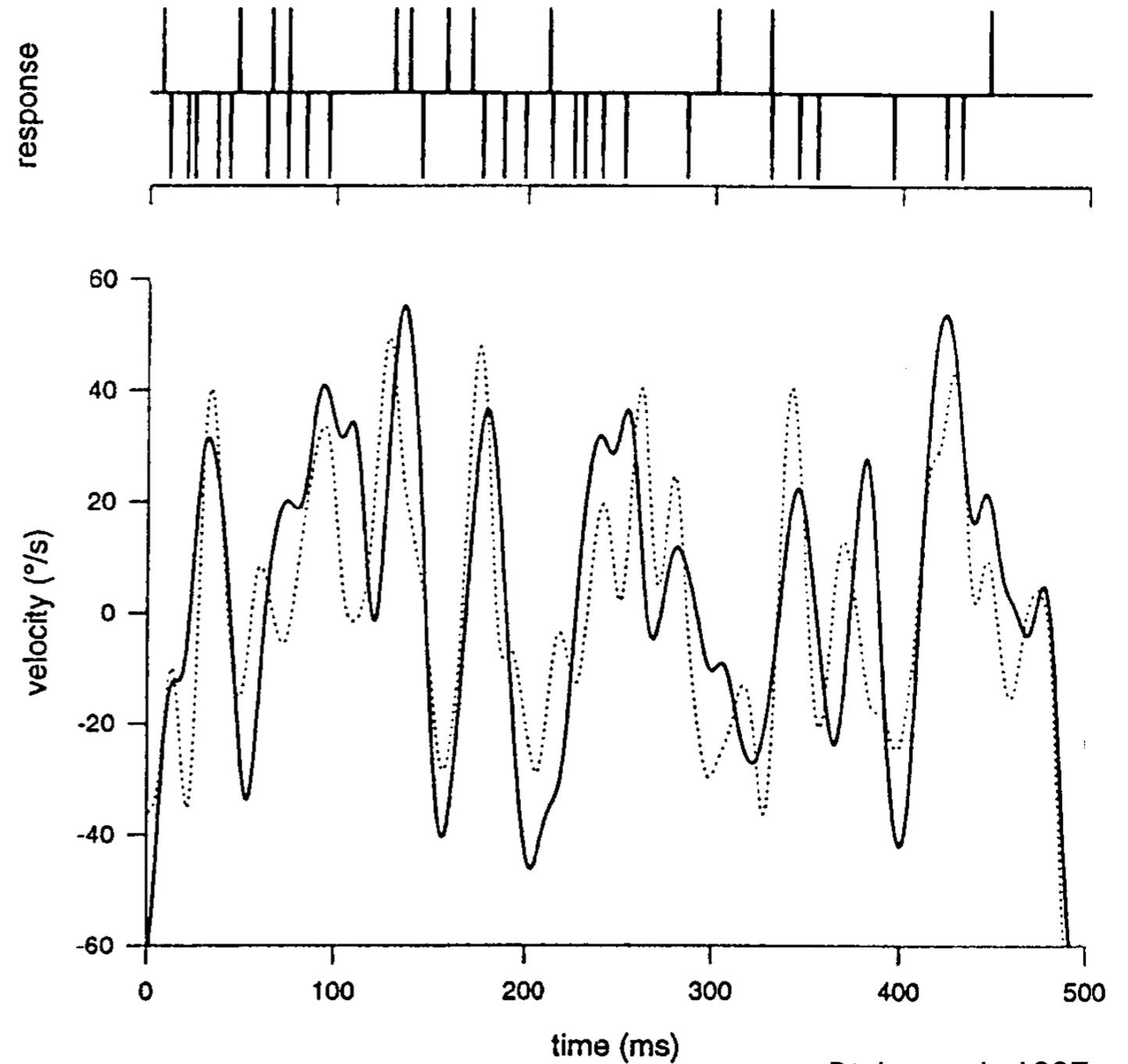
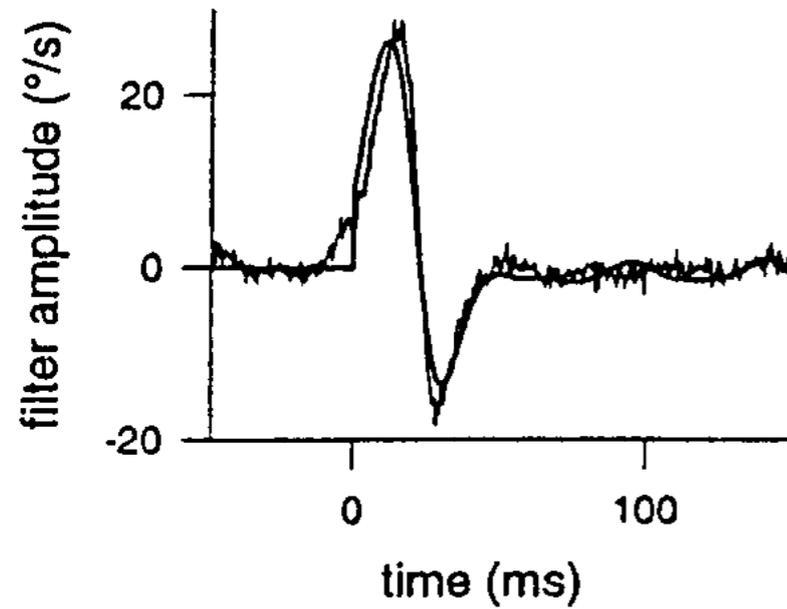
$$\frac{1}{T} \int [r(t) - r_{\text{model}}(t)]^2 dt$$

↑  
experimental observation



Dayan and Abbott, *Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems*, MIT Press, 2001, p. 48, Fig. 2.1: Prediction of the firing rate for an H1 neuron responding to a moving visual image. (Adapted from Rieke et al. *Spikes: Exploring the Neural Code*, MIT Press, 1997, ) \*

# The decoding step: spike decoding



\*

Dayan and Abbott, *Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems*, MIT Press, 2001, p. 118, Fig. 3.14: Decoding the stimulus from an H1 neuron of the fly. (Adapted from Rieke et al. *Spikes: Exploring the Neural Code*, MIT Press, 1997.)

Rieke et al. 1997

# Network / circuit analysis

# Population coding

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ネズミの脳の活動動画

"Imaging Brain Activity Across the Mouse Cortex," posted  
by YaleCampus, from YouTube

<https://www.youtube.com/watch?v=8JhA4ZJ4ZPQ>

0:00-1:00

Youtube: Michael Crair@Yale

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神経の動画

gcamp6 neurons

<https://www.youtube.com/watch?v=GorJM3XbXCw>

Youtube: Ian F Smith

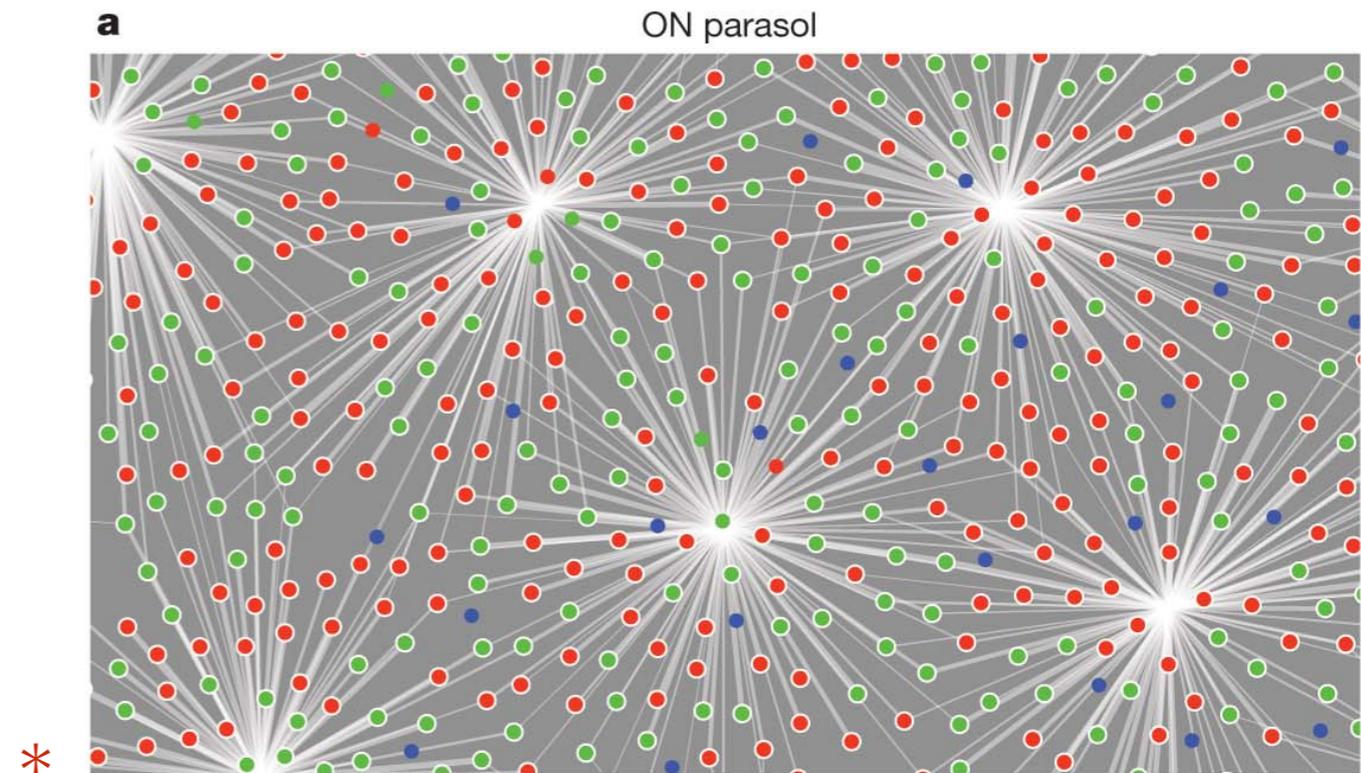
# Retinal encoding: functional connectivity from photoreceptors to ganglion cells

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網膜の回路

「Julia Kuhl\_\_\_Scientific Animation」

<http://www.somedonkey.com/SomeScientificAnimation14.html>



Field et al. 2010

Field et al. (2010) Functional connectivity in the retina at the resolution of photoreceptors, Nature 467 (7316): 673–677, p. 675 Fig. 3a: Full functional sampling of cone lattice by four RGC types.  
<http://www.nature.com/nature/journal/v467/n7316/full/nature09424.html>

Response of neuron  $i$  at time  $t$  to visual stimulus at time  $t'$ , color  $c$ , and location  $z$ :

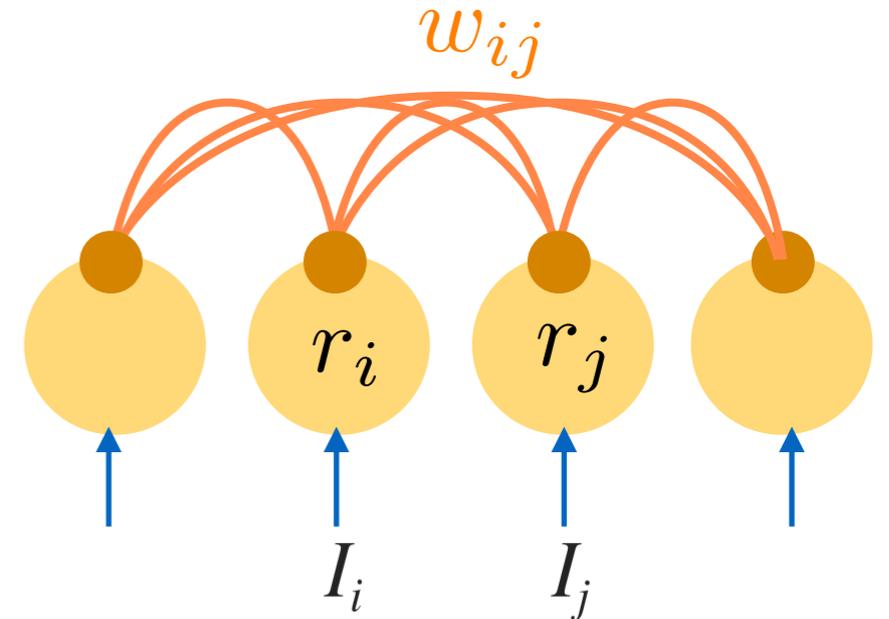
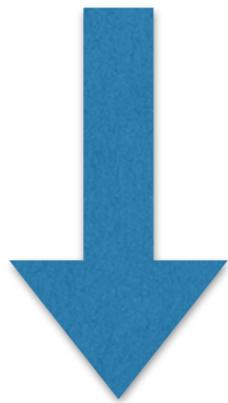
$$h_i(t-t') \sum_j a_{ij} f_j(c, z)$$

↑  
temporal filter of neuron  $i$

↑ ↑  
coupling strength from receptor  $j$  to neuron  $i$     color and spatial sensitivity of receptor  $j$

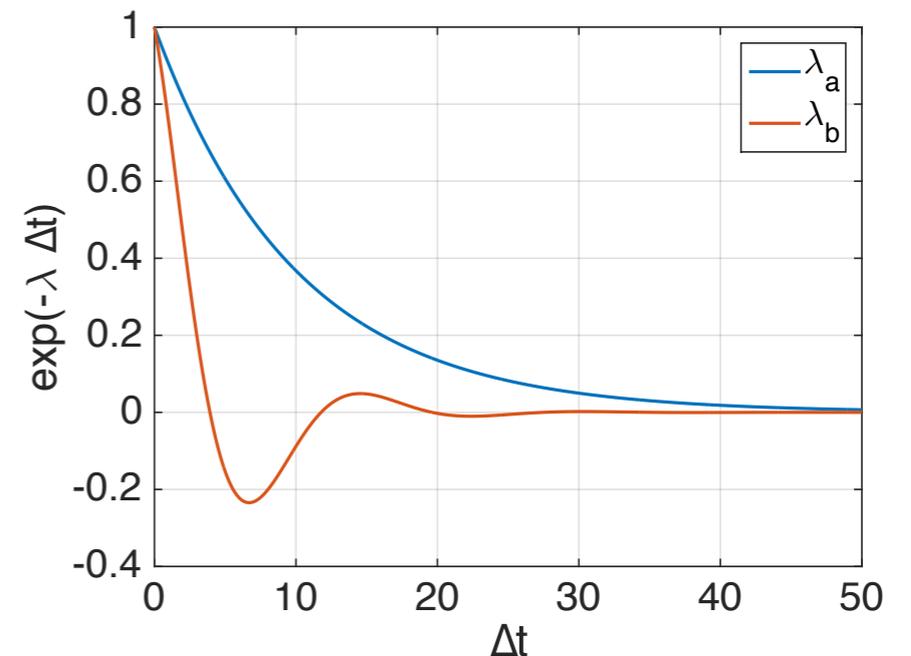
# Linear neural networks

$$\frac{dr_i(t)}{dt} = -r_i(t) + \sum_j w_{ij} r_j(t) + I_i(t)$$

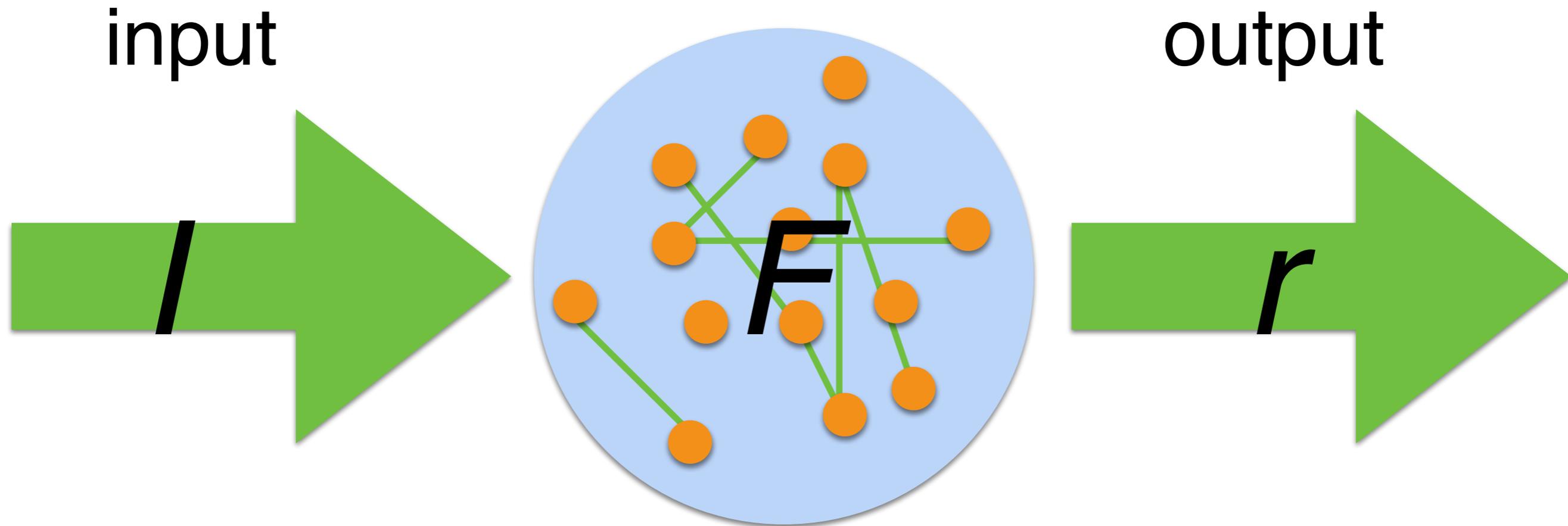


Input  $I_j(t)$  to neuron  $j$  at time  $t$  increases firing rate  $r_i(t+\Delta t)$  by  $F_{ij}(\Delta t) I_j(t)$  regardless of other inputs.

$$F_{ij}(\Delta t) = \sum_a A_{ija} e^{-\lambda_a \Delta t}$$



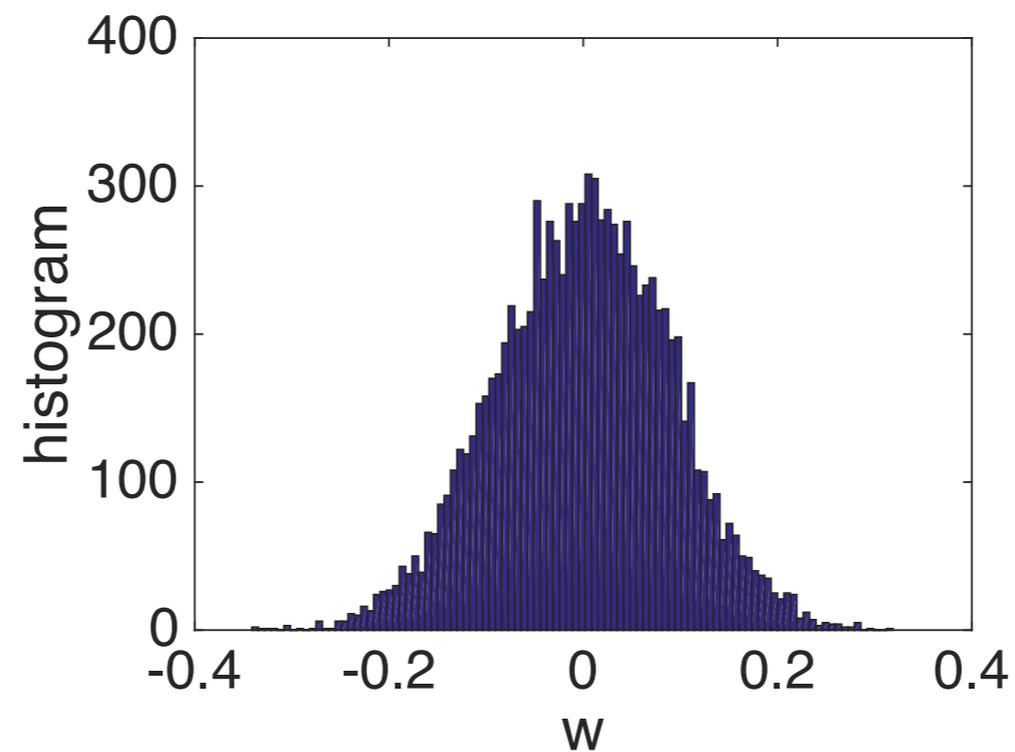
# Interpreting a linear network as an input/output system



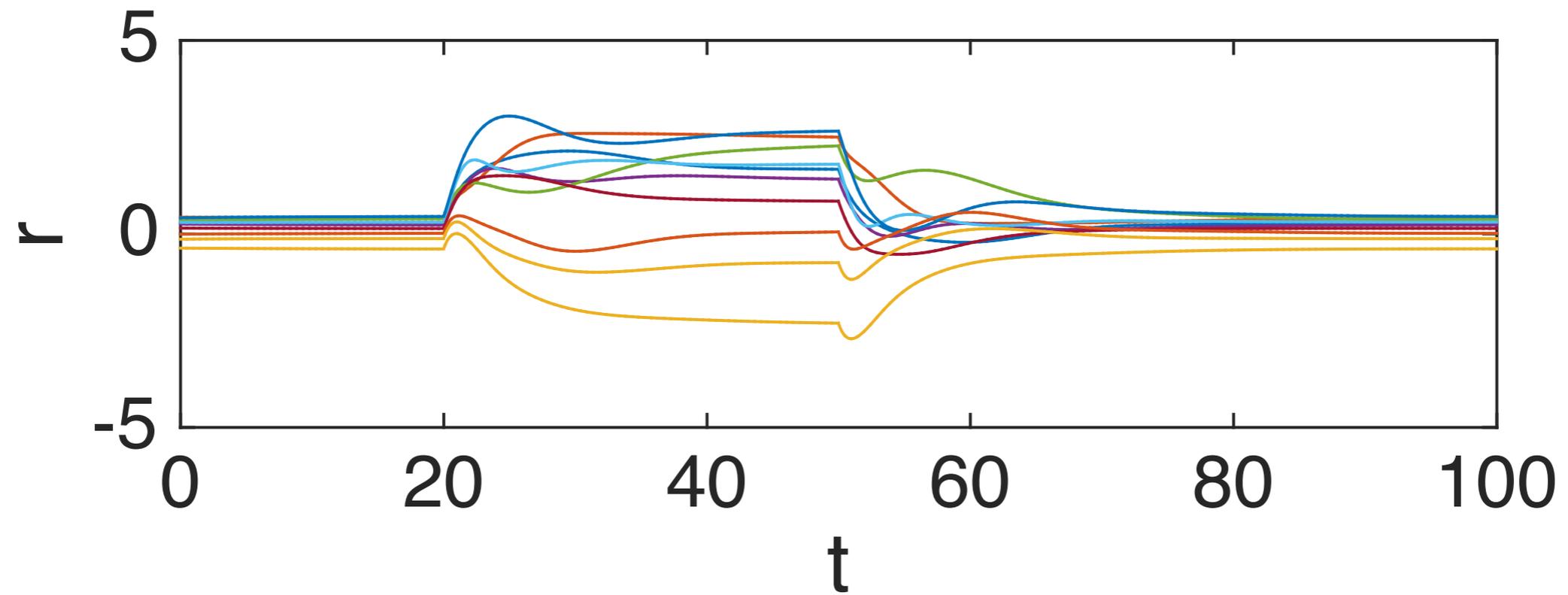
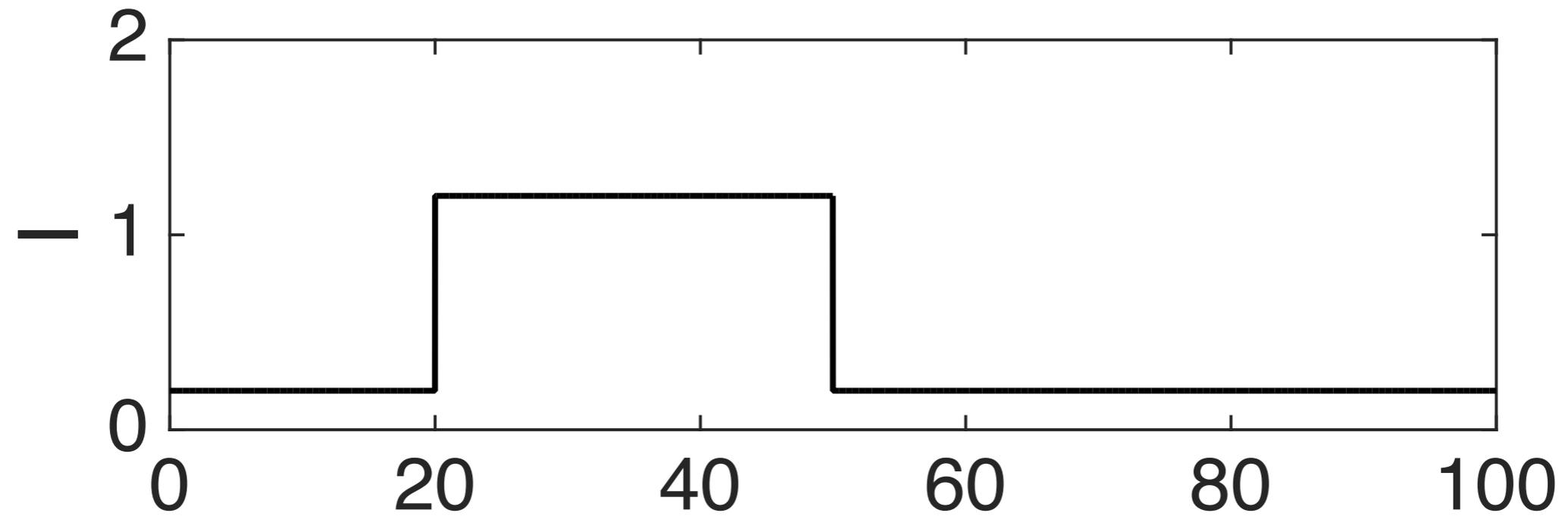
$$r_i(t) = \sum_j F_{ij} * I_j(t)$$

# Simulating a randomly connected linear network

$$\frac{dr_i(t)}{dt} = -r_i(t) + \sum_j w_{ij} r_j(t) + I_i(t)$$



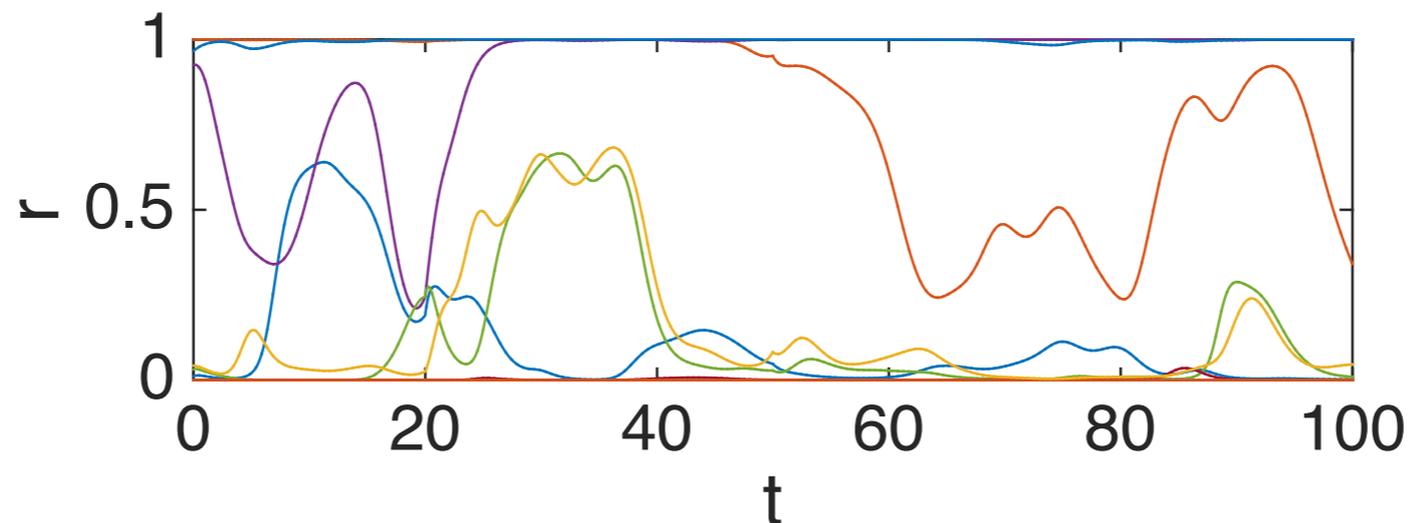
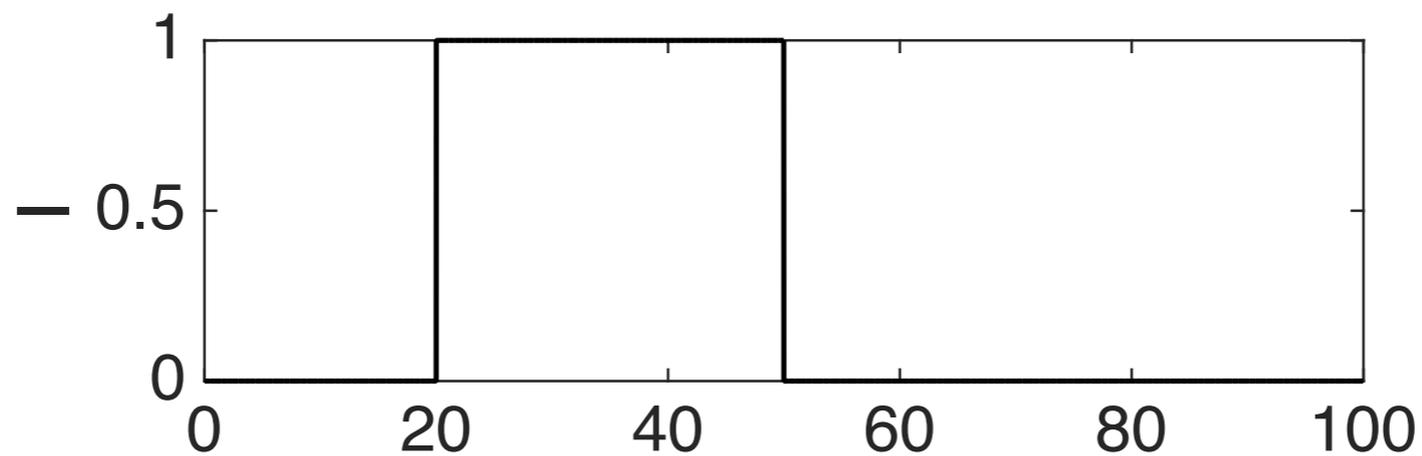
# Simulating a randomly connected linear network



# Is a real neural network a simple input/output system?

Dynamics of randomly connected nonlinear neurons

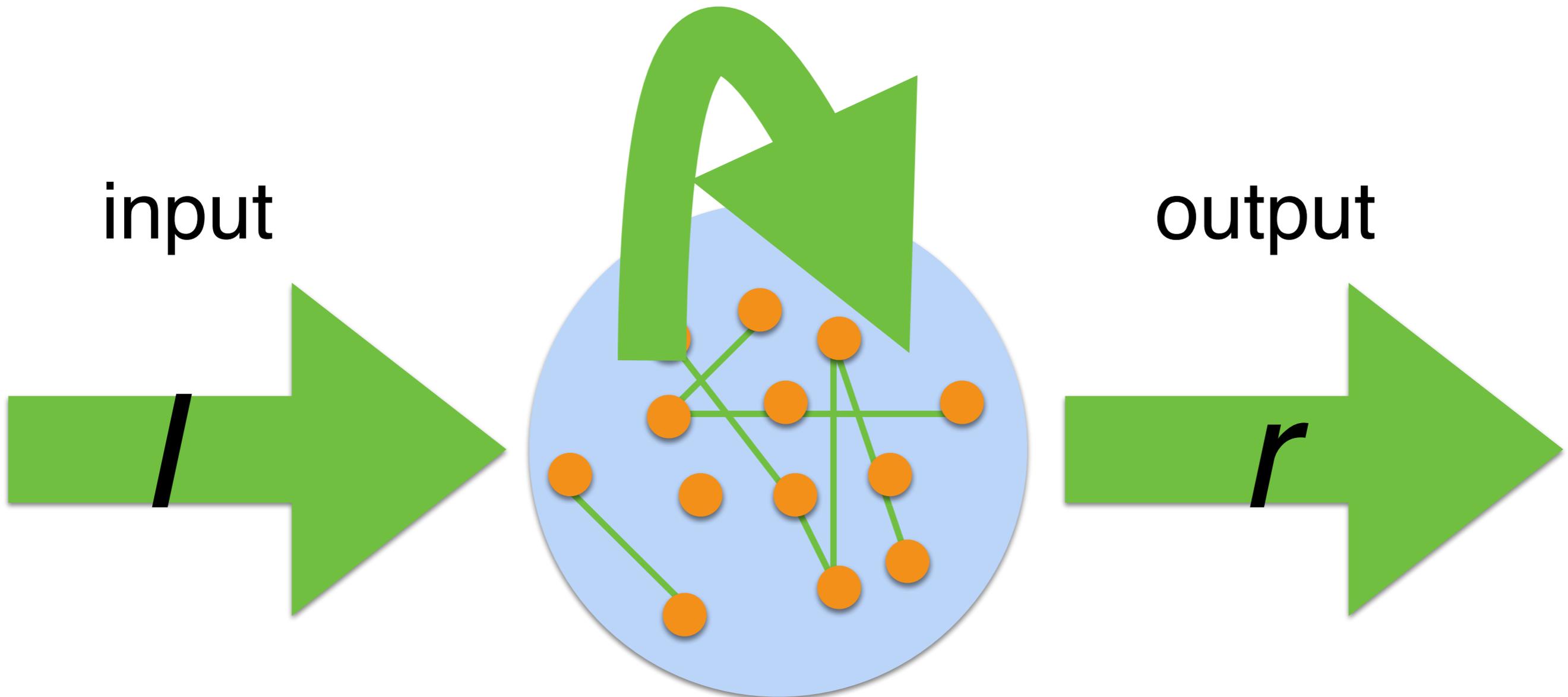
$$\frac{dr_i(t)}{dt} = -r_i(t) + f\left(\sum_j w_{ij}r_j(t) + I_i(t)\right)$$



# Is a real neural network a simple input/output system?

Dynamics of randomly connected nonlinear neurons

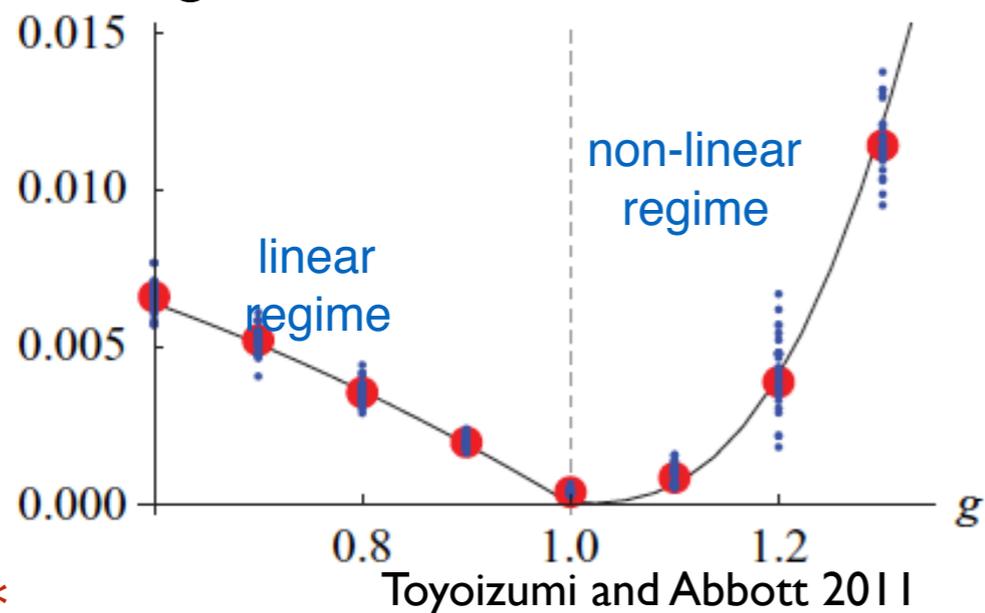
$$\frac{dr_i(t)}{dt} = -r_i(t) + f\left(\sum_j w_{ij}r_j(t) + I_i(t)\right)$$



# What are complex ongoing dynamics good for?

## Robust information coding in the nonlinear regime

Decoding error



\*

Toyozumi and Abbott (2011) Beyond the edge of chaos: Amplification and temporal integration by recurrent networks in the chaotic regime, *Physical Review E* 84 (051908), p. 4 Fig. 4.  
<http://journals.aps.org/pre/abstract/10.1103/PhysRevE.84.051908>

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Coherent pattern generation in the nonlinear regime

Sussillo and Abbott (2009) Generating Coherent Patterns of Activity from Chaotic Neural Networks, *Neuron* 63 (4): 544–557, p. 554 Fig. 8. Networks that Generate Both Running and Walking Human Motions.  
<http://www.sciencedirect.com/science/article/pii/S0896627309005479>

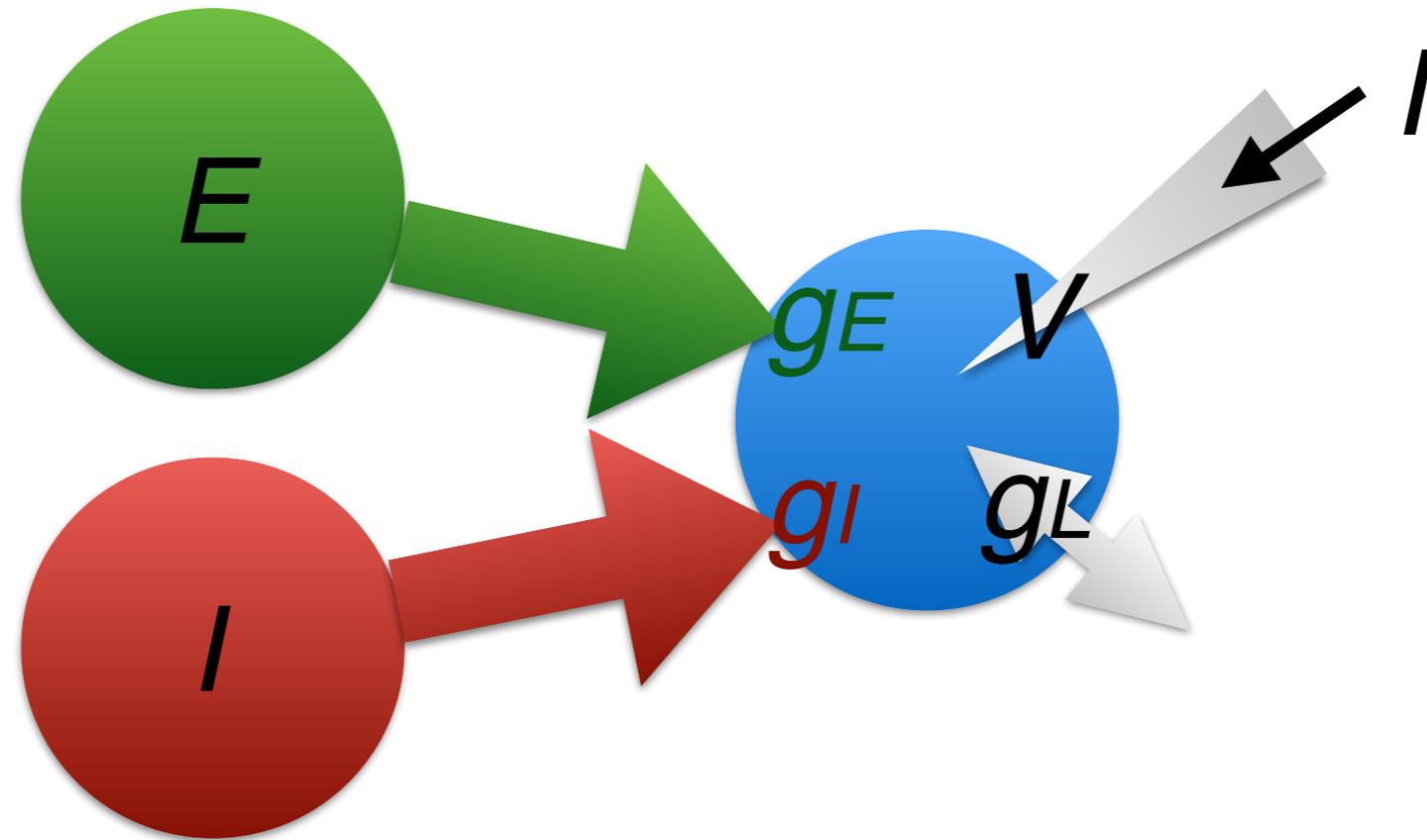
# Is a real neural network a simple input/output system?

Dynamics of randomly connected nonlinear neurons

$$\frac{dr_i(t)}{dt} = -r_i(t) + f\left(\sum_j w_{ij}r_j(t) + I_i(t)\right)$$

**Data analysis**

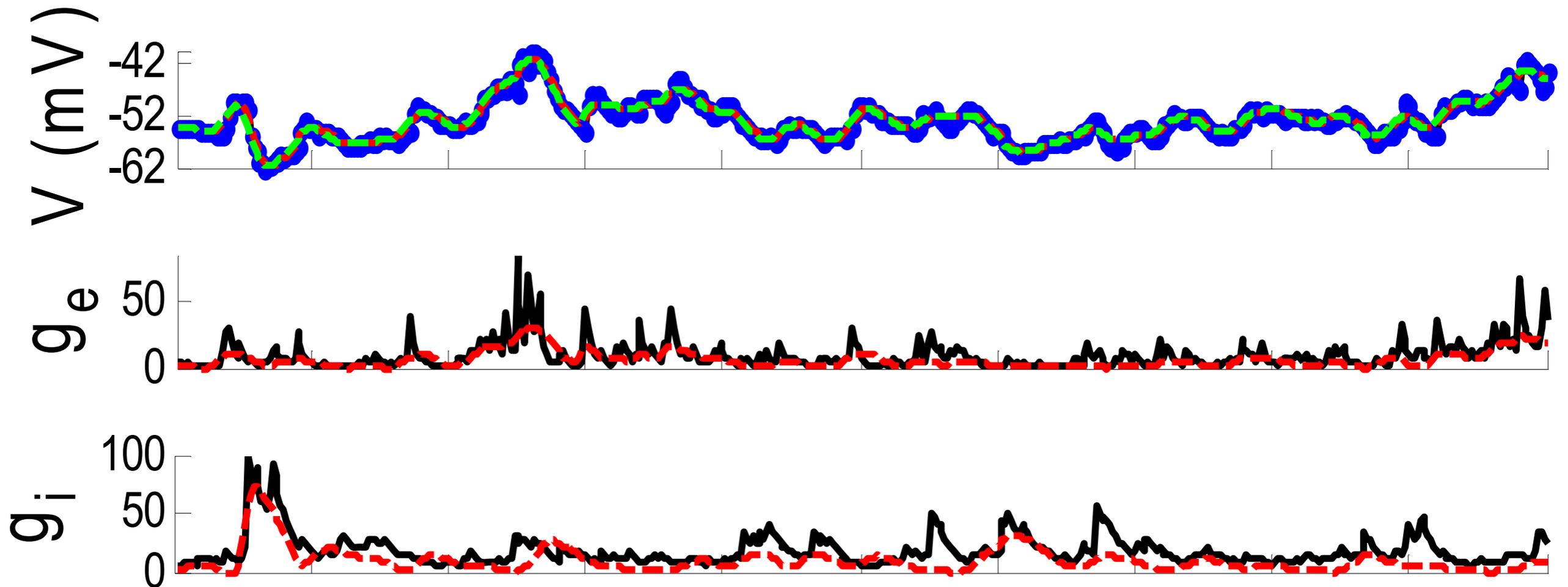
# Visualizing simultaneous excitatory and inhibitory input



$$C \frac{dV}{dt}(t) = g_L(V_L - V(t)) + g_E(t)(V_E - V(t)) + g_I(t)(V_I - V(t)) + I$$

# Visualizing simultaneous excitatory and inhibitory input

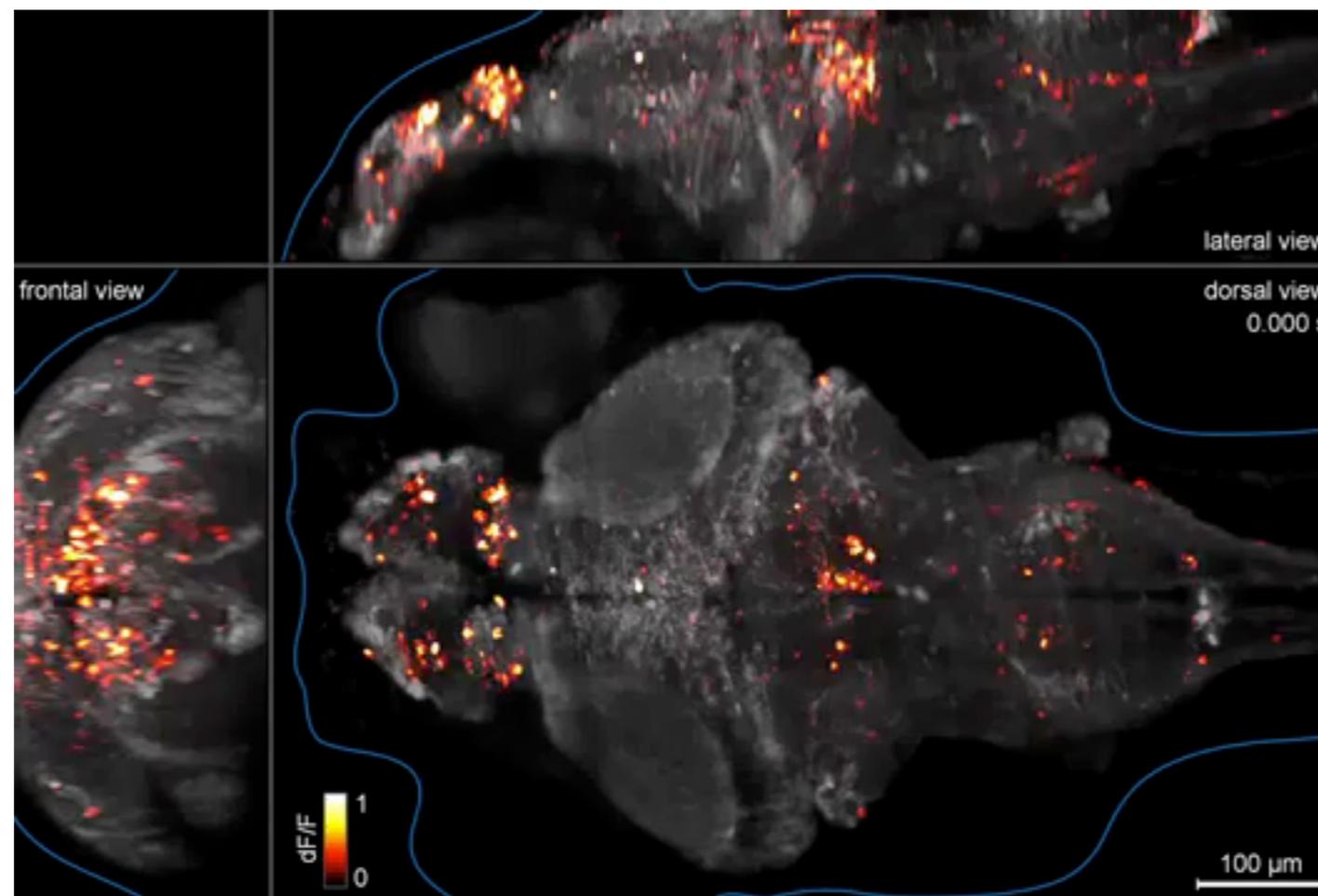
## Simultaneous inference of $g_E$ and $g_I$ by Kalman filtering



Lankarany et al. (2013) Inferring trial-to-trial excitatory and inhibitory synaptic inputs from membrane potential using Gaussian mixture Kalman filtering, *Frontiers in Computational Neuroscience* 7 (109), p. 9 Fig. 8: Estimating synaptic conductances and inputs given a single voltage trace of Example 5 using the GMKF-based (left) and PF-based (right) algorithms.  
<http://journal.frontiersin.org/article/10.3389/fncom.2013.00109/full>  
CC BY

Lankarany and Toyozumi 2013

# Computational approaches to big data analysis



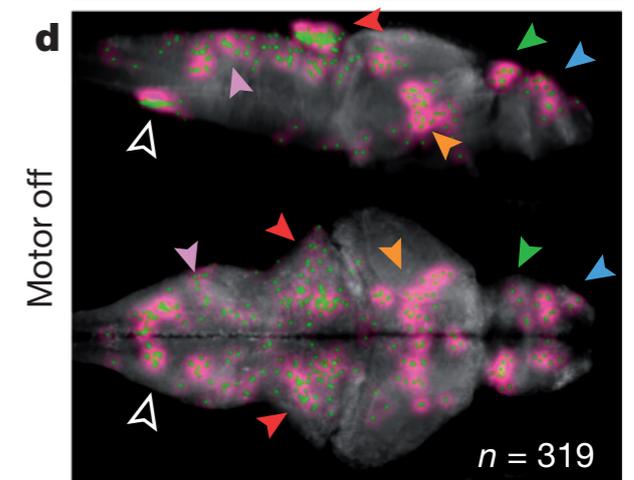
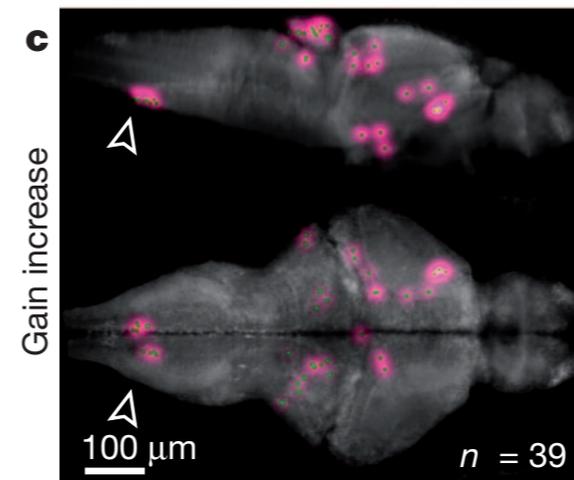
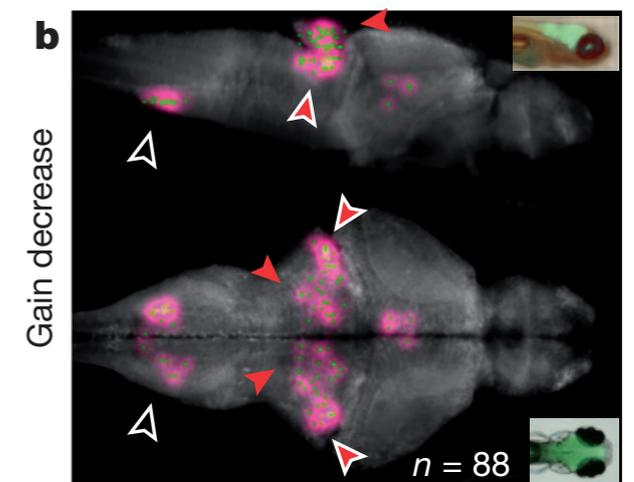
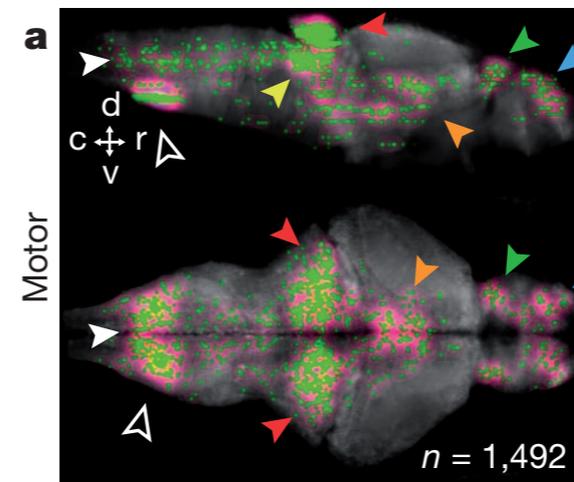
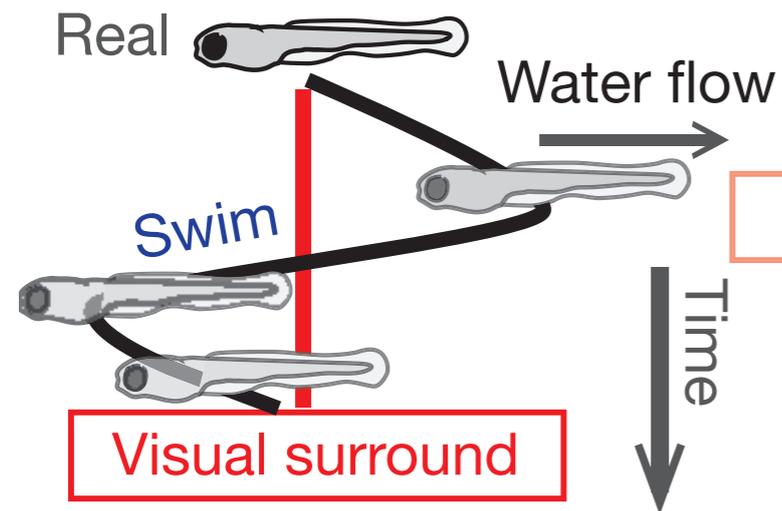
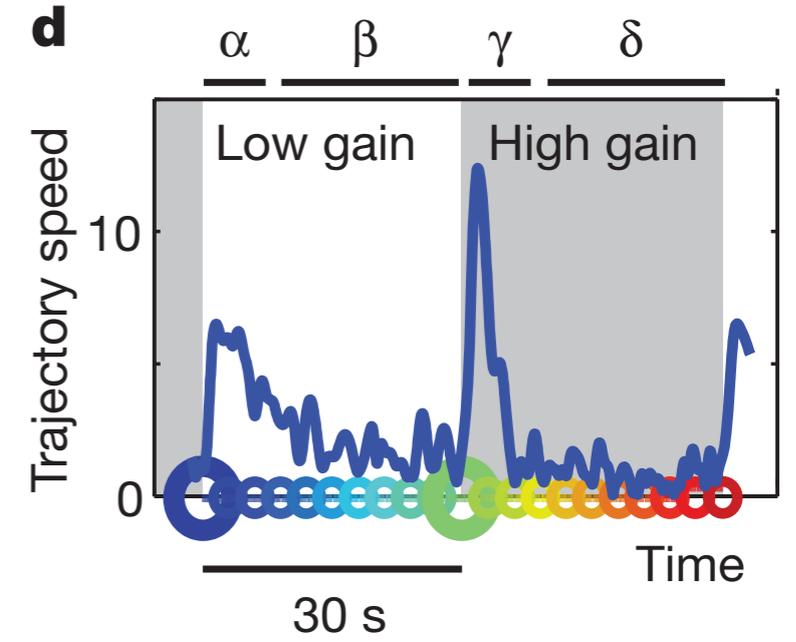
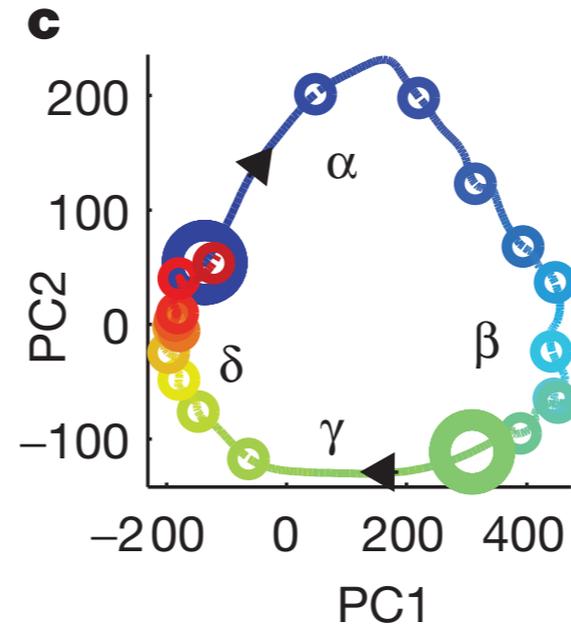
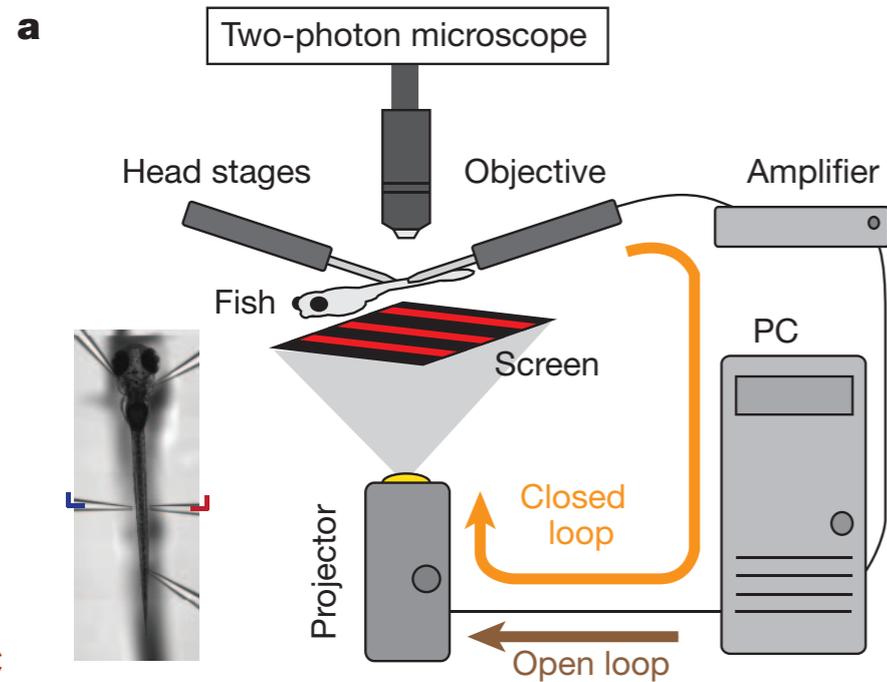
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youtube: Discover Magazine, Ahrens et al@HHMI

Ahrens et al. (2013) Whole-brain functional imaging at cellular resolution using light-sheet microscopy, Nature Methods 10 (5): 413–420, Supplementary Video 4: Whole-brain imaging of neuronal activity (visualization B, projections). <http://www.nature.com/nmeth/journal/v10/n5/full/nmeth.2434.html#videos>

# Principle component analysis

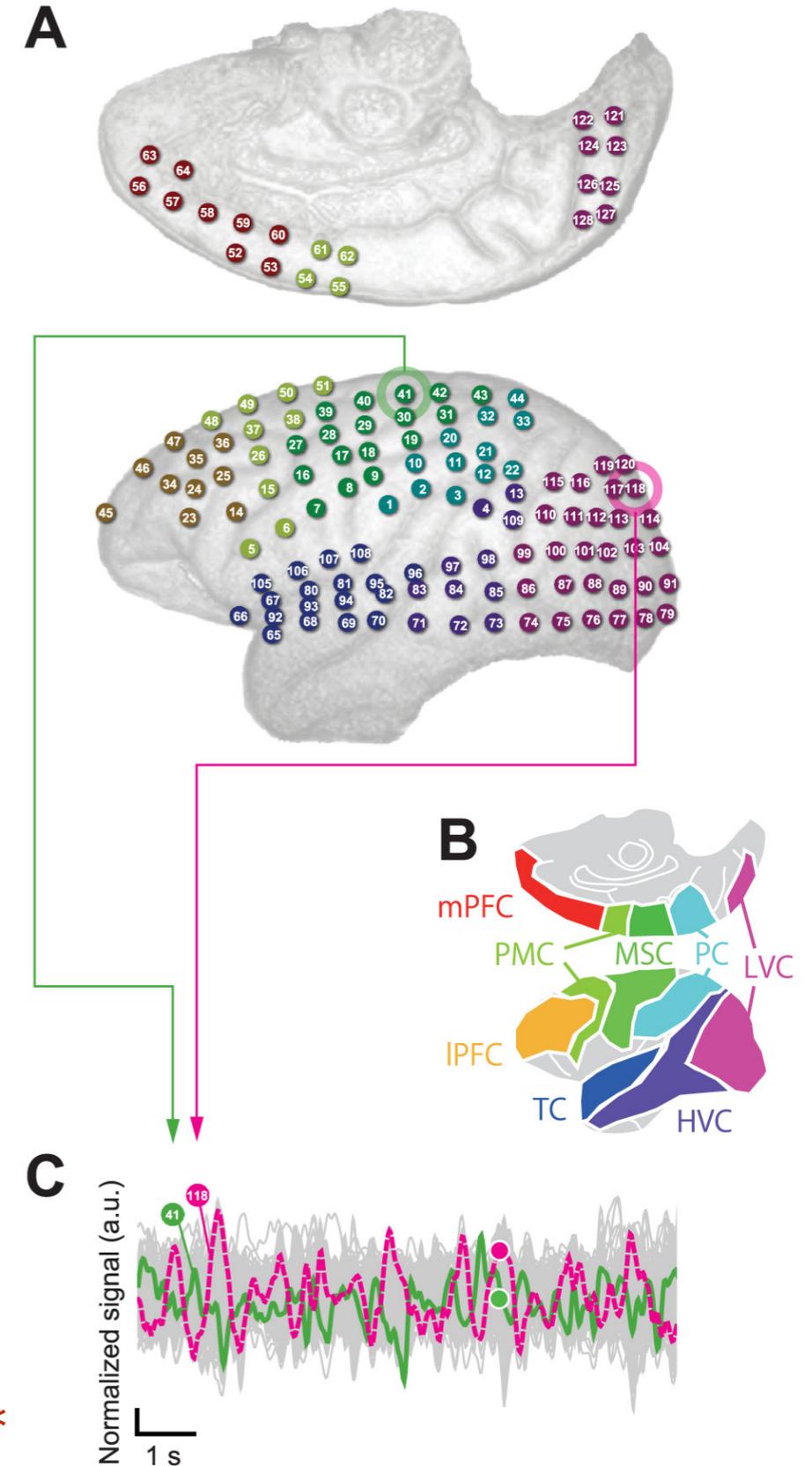
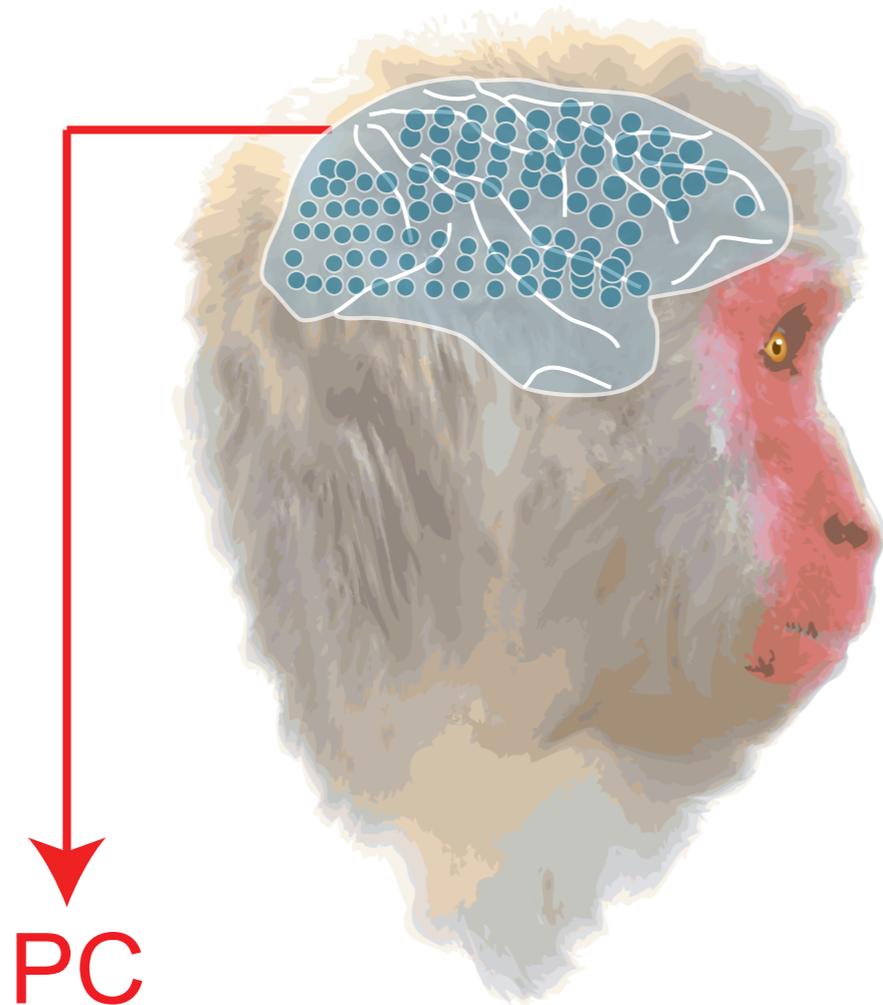
Ahrens et al. (2012) Brain-wide neuronal dynamics during motor adaptation in zebrafish, Nature 485 (7399): 471–477  
<http://www.nature.com/nature/journal/v485/n7399/full/nature11057.html>



Ahrens et al. 2012

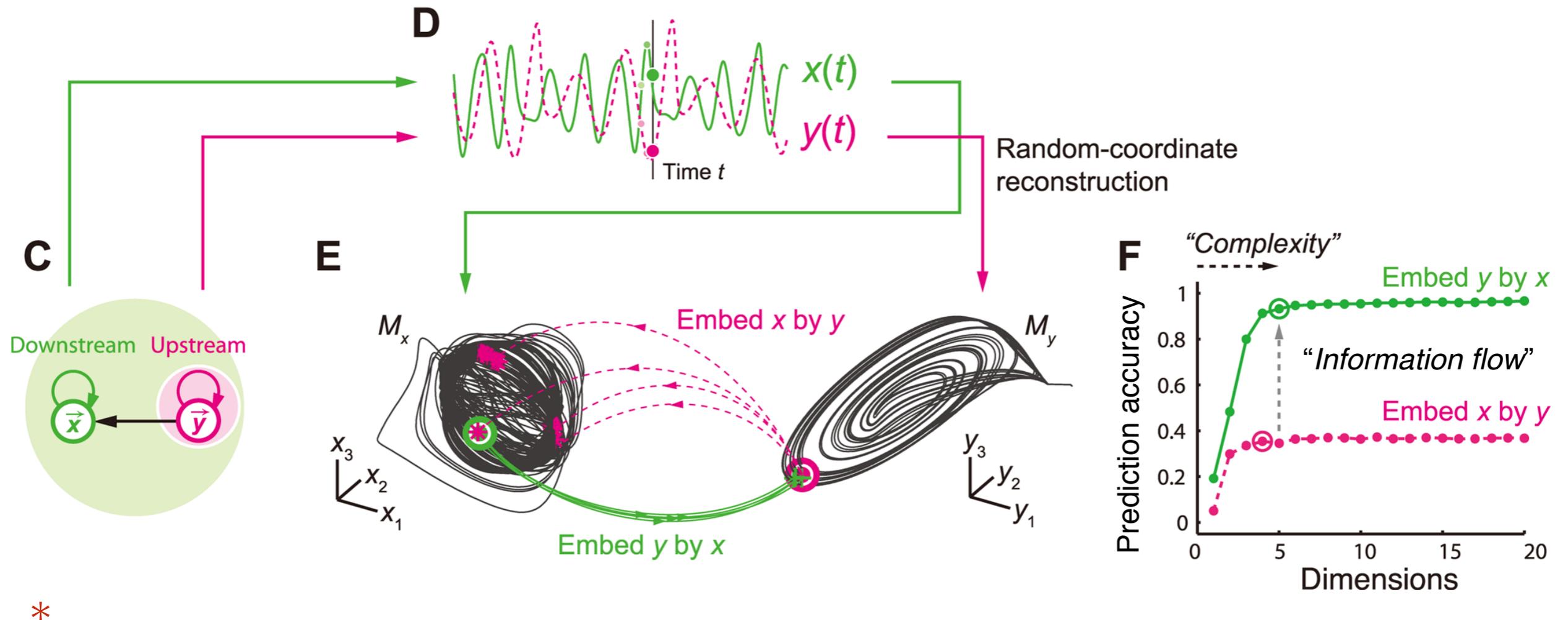
# How to characterize conscious brain dynamics?

## ECoG recording



# Using a mathematical theorem for data analysis: An embedding approach

S. Tajima, T. Yanagawa, N. Fujii, and T. Toyozumi, PLOS Computational Biology 11, e1004537 (2015). DOI:10.1371/journal.pcbi.1004537  
<https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1004537>



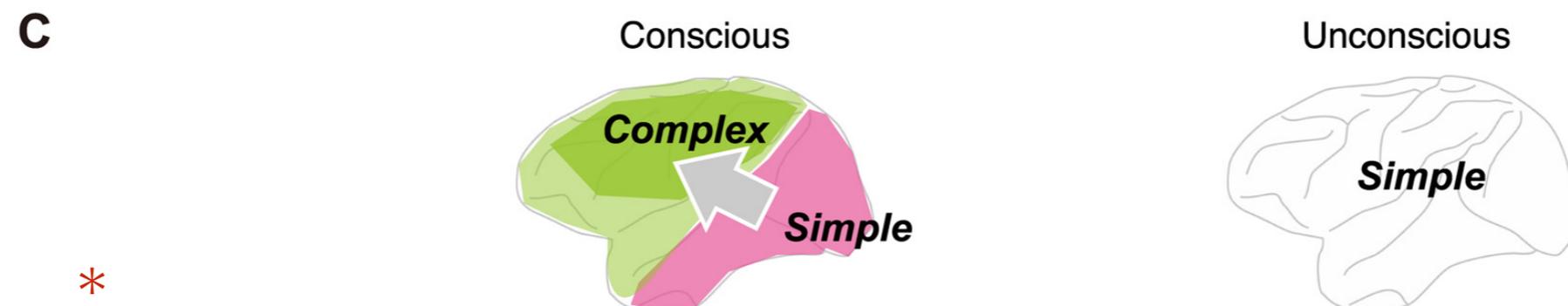
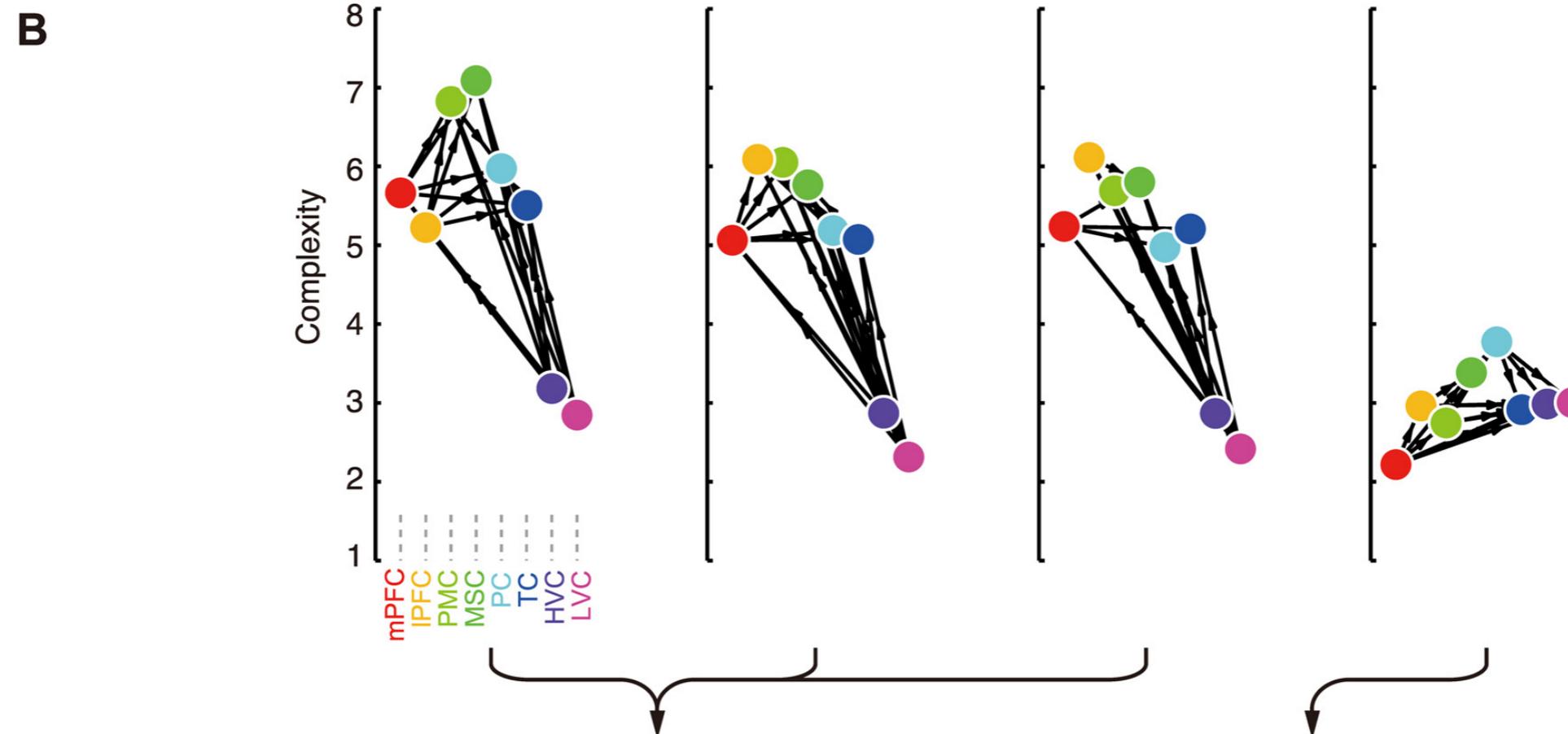
Simultaneous inference of dynamical complexity and information flow

A downstream node must have higher complexity

# A hierarchy of dynamical complexity in the conscious brain

**A**

	Reaching	Awake-Eyes-Open	Awake-Eyes-Closed	Anesthesia
Motor activity	✓	-	-	-
Visual input	✓	✓	-	-
Consciousness	✓	✓	✓	-



\*

次回：「学習」を表現する数式