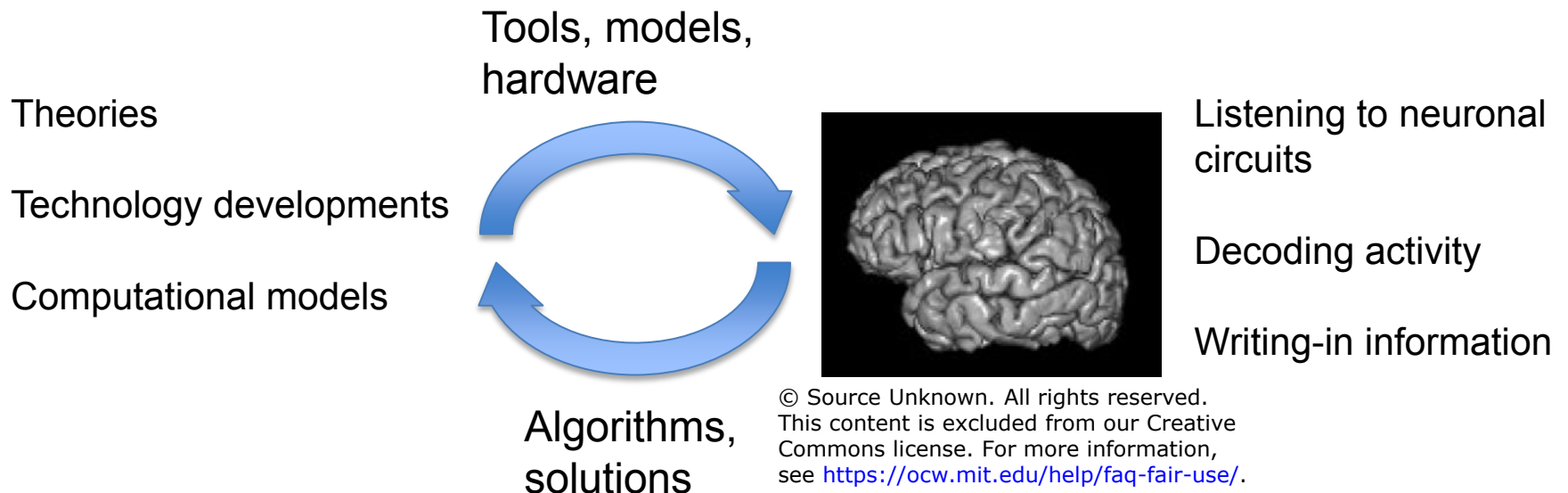


# Outline

1. Introduction to neural circuits
2. Computational roles of feedback signals
3. Open questions, challenges, opportunities

# Biologically-inspired computation

*Claim (without proof):  
over millions of years of evolution, “interesting” solutions to  
difficult problems have emerged through changes in neuronal  
circuits*



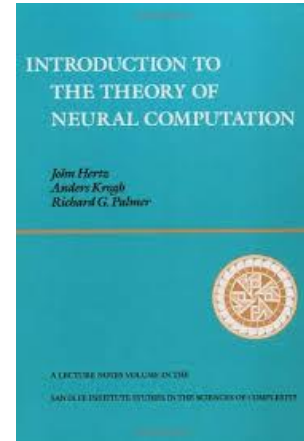
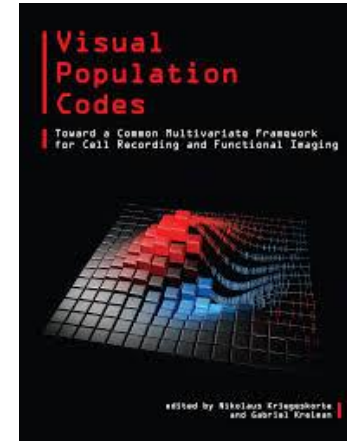
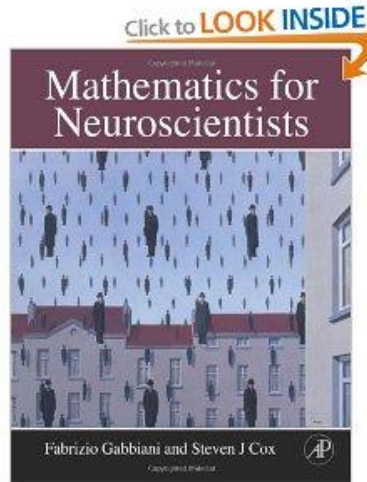
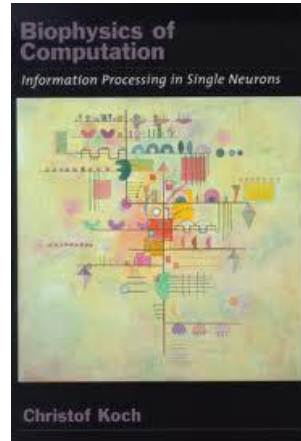
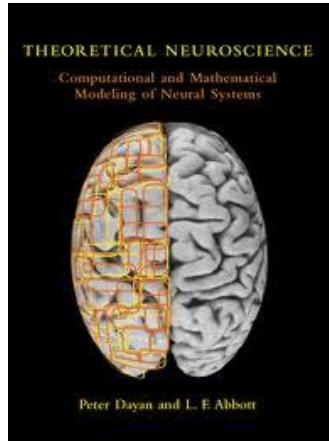
# Some features of brain-based computations

- Hardware and software that work for many decades
- Parallel computation (with serial bottlenecks)
- Reprogrammable architecture
- Single-shot learning
- “Discover” structure in data
- Fault tolerance
- Robustness to sensory transformations
- Component interaction and integration of sensory modalities

# Why study neural circuits?

- We can begin to explore high-level at the neural circuit level
- Golden age for neural circuits: opportunity to manipulate, disrupt and interact with neural circuits at unprecedented resolution
- Theories can be rigorously tested at the neural level
- Empirical findings can be readily translated into algorithms

# Recommended books



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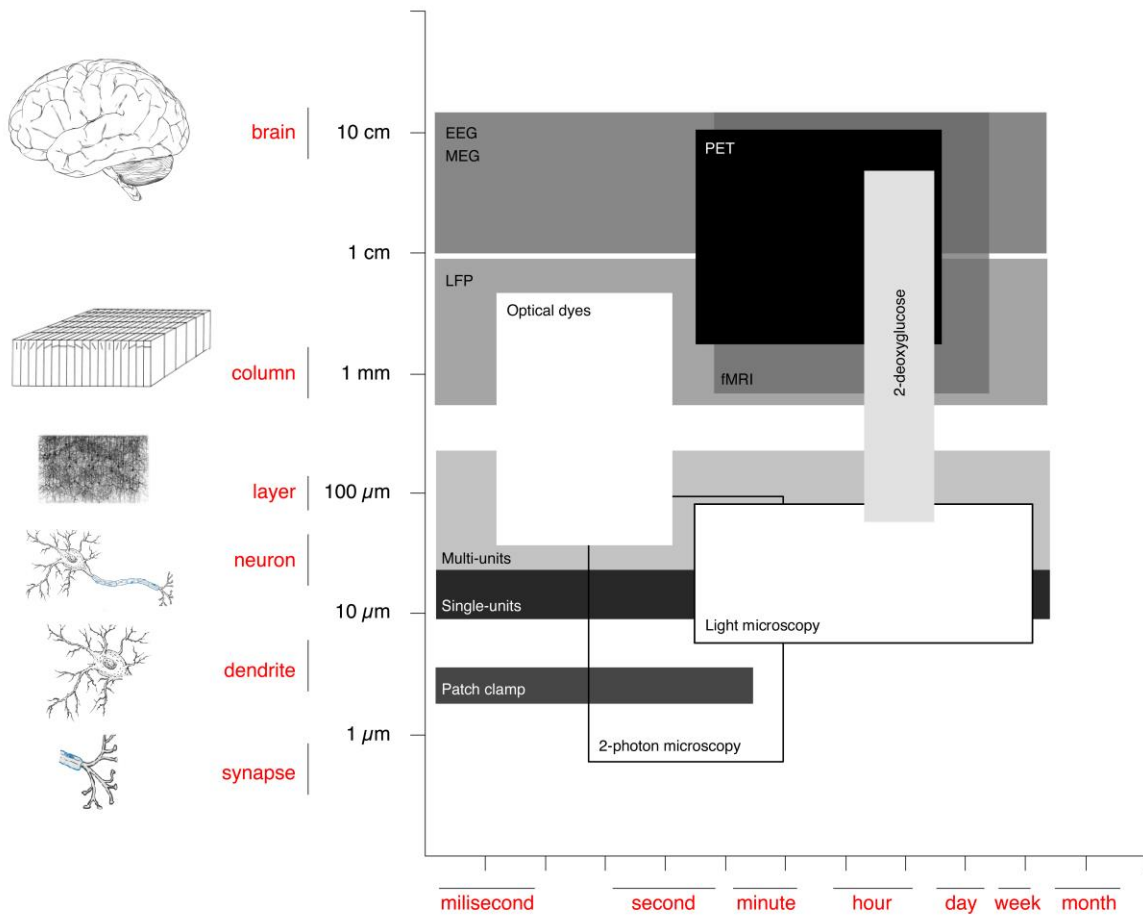
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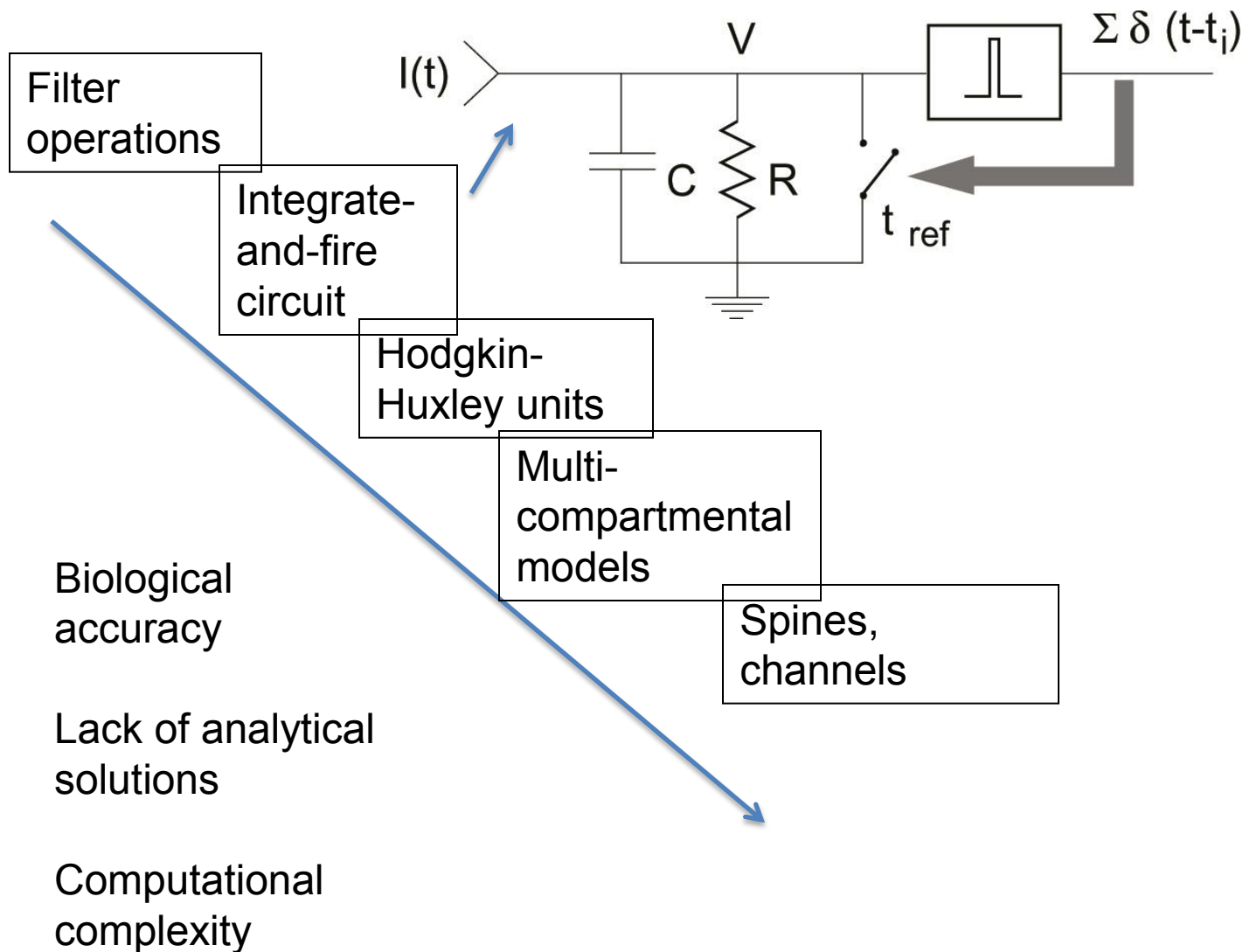
- Abbott and Dayan. Theoretical Neuroscience - Computational and Mathematical Modeling of Neural Systems [2001] (ISBN 0-262-04199-5). MIT Press.
- Koch. Biophysics of Computation [1999] (ISBN 0-19-510491-9). Oxford University Press.
- Gabbiani and Cox. Mathematics for Neuroscientists. [2010] (ISBN 978-0-12-374882-9). Academic Press.
- Kriegeskorte and Kreiman. Visual Population Codes. [2010] (ISBN 9780262016247). MIT Press.
- Hertz, Krogh, and Palmer. Introduction to the Theory of Neural Computation. [1991] (ISBN 0-20151560-1). Santa Fe Institute Studies in the Sciences of Complexity.

# Methods to study the brain at different scales

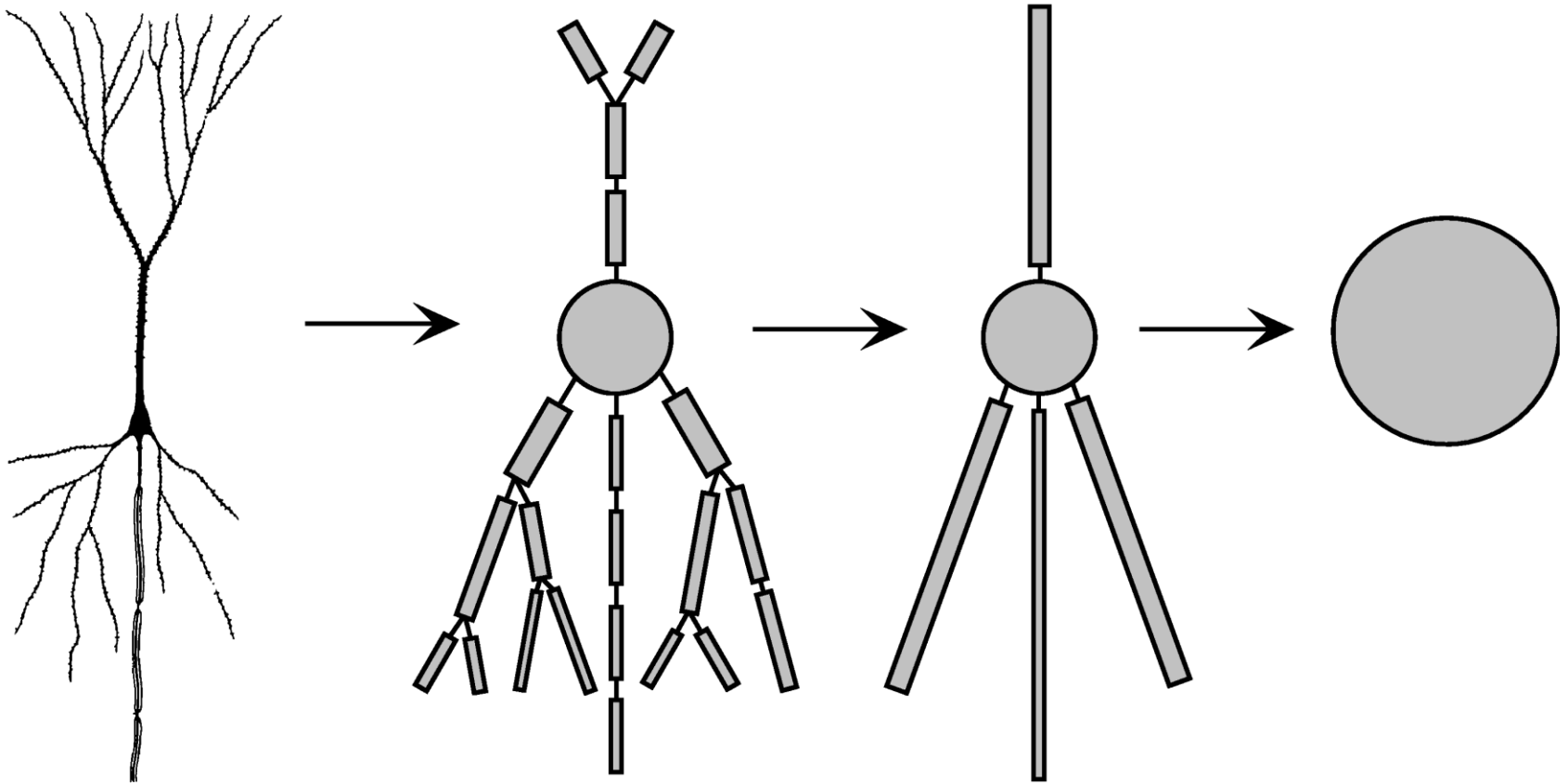


Courtesy of Elsevier, Inc., <http://www.sciencedirect.com>. Used with permission.  
 Source: Kreiman, Gabriel. "Neural coding: computational and biophysical perspectives." *Physics of Life Reviews* 1, no. 2 (2004): 71-102.

# Simulating single neurons: A nested family of models



# Geometrically accurate models vs. spherical cows with point masses

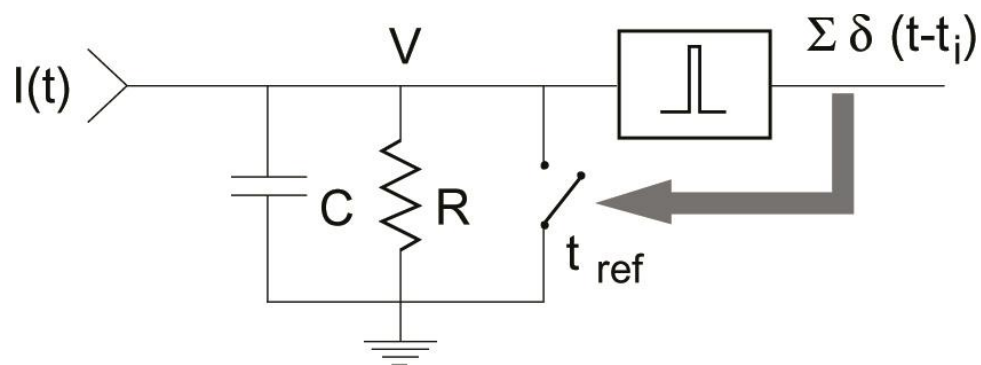


A central question in Theoretical Neuroscience:  
What is the “right” level of abstraction?



# The leaky integrate-and-fire model

- Lapicque 1907
- Below threshold, the voltage is governed by:
$$C \frac{dV(t)}{dt} = -\frac{V(t)}{R} + I(t)$$
- A spike is fired when  $V(t) > V_{thr}$  (and  $V(t)$  is reset)
- A refractory period  $t_{ref}$  is imposed after a spike
- Simple and fast
- Does not consider:
  - spike-rate adaptation
  - multiple compartments
  - sub-ms biophysics
  - neuronal geometry



# Leaky I&F neurons: a simple implementation

$$C \frac{dV(t)}{dt} = -\frac{V(t)}{R} + I(t)$$

```
function [V,spk]=simpleiandf(E_L,V_res,V_th,tau_m,R_m,I_e,dt,n)
```

```
% ultra-simple implementation of integrate-and-fire model
% inputs:
% E_L = leak potential      [e.g. -65 mV]
% V_res = reset potential  [e.g. E_L]
% V_th = threshold potential [e.g. -50 mV]
% tau_m = membrane time constant [e.g. 10 ms]
% R_m = membrane resistance [e.g. 10 MOhm]
% I_e = external input     [e.g. white noise]
% dt = time step          [e.g. 0.1 ms]
% n = number of time points [e.g. 1000]
%
% outputs:
% V = intracellular voltage [n x 1]
% spk = 0 or 1 indicating spikes [n x 1]
```



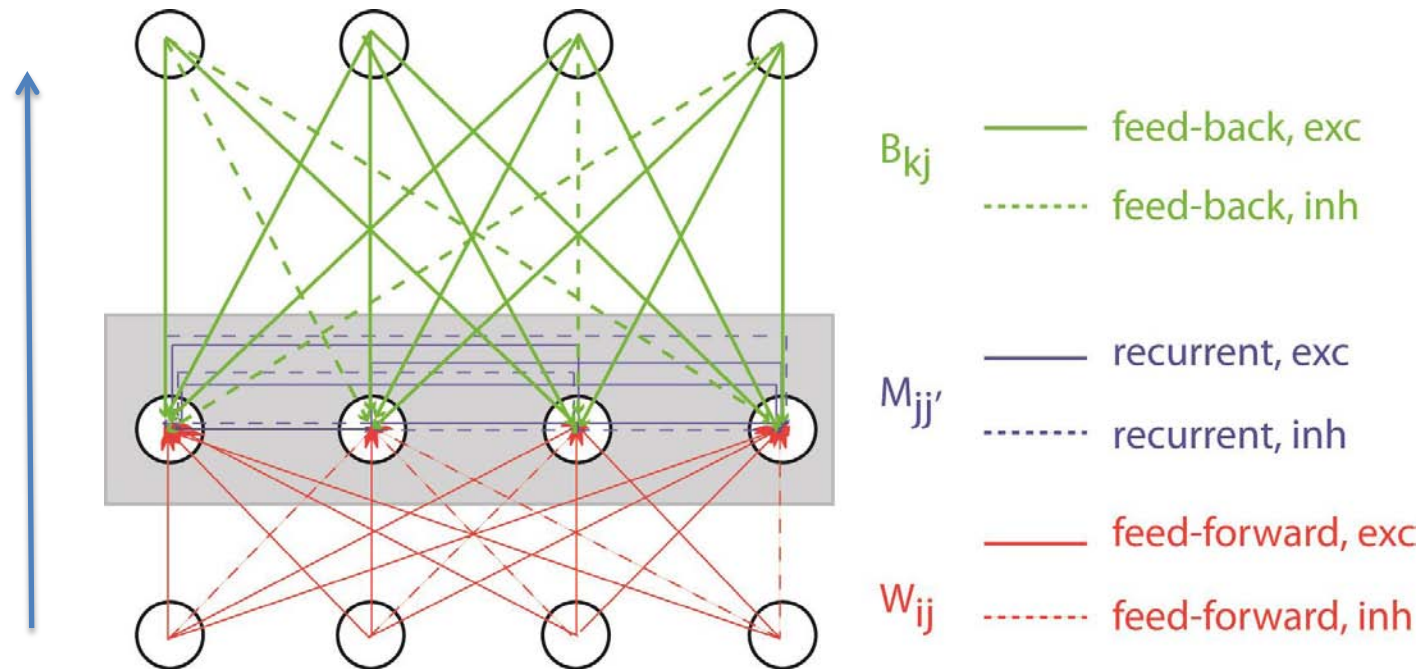
All of these lines are comments

```
V(1)=V_res; % initial voltage
spk=zeros(n,1);
for t=2:n
    V(t)=V(t-1)+(dt/tau_m) * (E_L - V(t-1) + R_m * I_e(t)); % Change in voltage at time t
    if (V(t)>V_th) % Emit a spike if V is above threshold
        V(t)=V_res; % And reset the voltage
        spk(t)=1;
    end
end
```



This is the key line integrating the differential equation

# Circuits – some basic definitions



## Notes:

1. Connectivity does not need to be all-to-all
2. There are excitatory neurons and inhibitory neurons (and many types of inhibitory neurons)
3. Most models assume balance between excitation and inhibition
4. Most models do not include layers and the anatomical separation of forward and back pathways
5. There are many more recurrent+feedback connections than feed-forward connections (the opposite is true about models...)



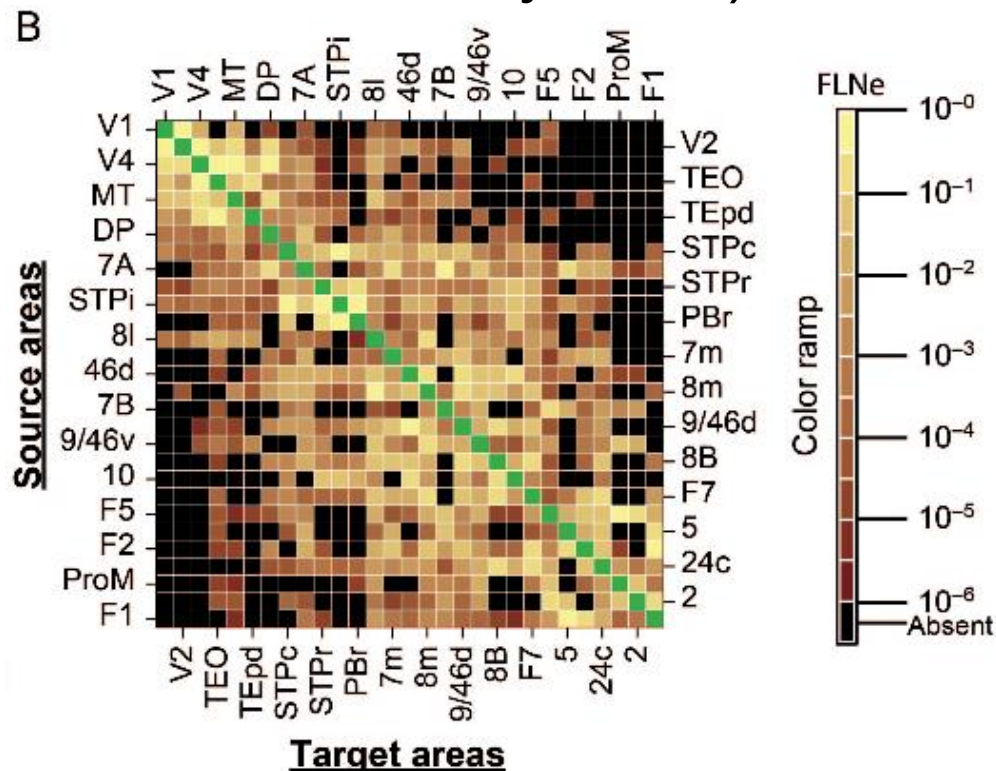
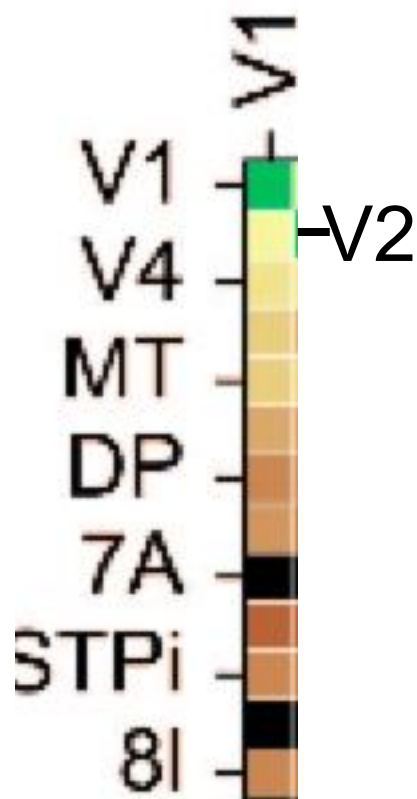


# First order approximation: “Immediate” recognition as a hierarchical feed-forward process

1. Behavior: We can recognize objects within ~150ms (e.g. Potter et al 1969, Thorpe et al 1996)
2. Physiology: Visually selective responses to complex shapes arise within ~150 ms (e.g. Keyser et al 2001, Hung et al 2005, Liu et al 2009)
3. Computation: Bottom up computational models perform relatively well in basic object recognition (e.g. Fukushima 1980, Riesenhuber and Poggio 1999)

# Why are there so many feedback connections?

There are more horizontal + top-down projections than bottom-up ones (e.g. Douglas 2004, Callaway 2004)



Markov et al 2012

© Oxford University Press. All rights reserved. This content is excluded from our Creative Commons license. For more information, see <https://ocw.mit.edu/help/faq-fair-use/>. Source: Markov, Nikola T., M. M. Ercsey-Ravasz, AR Ribeiro Gomes, Camille Lamy, Loic Magrou, Julien Vezoli, P. Misery et al. "A weighted and directed interareal connectivity matrix for macaque cerebral cortex." *Cerebral cortex* (2012): bhs270.

What are feedback signals doing?  
When?  
Why?  
How?

# Computational roles of feedback signals

1. **Fundamental computations in V1**
2. Visual search
3. Pattern completion



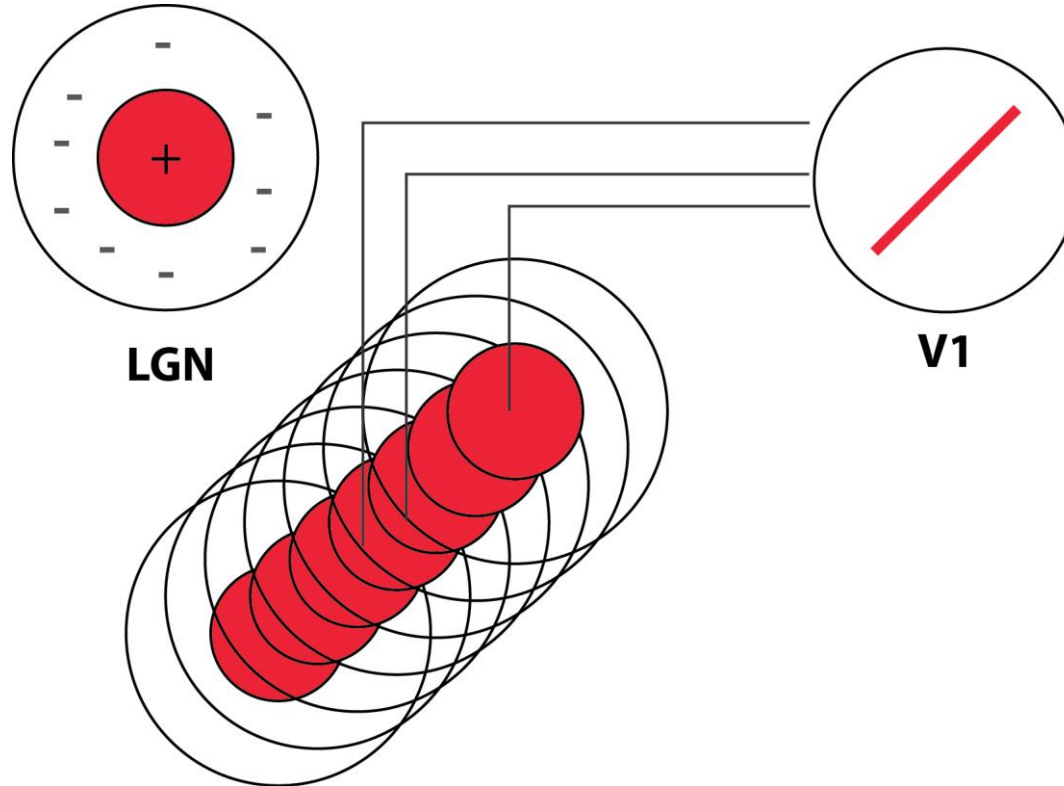
# Neurons in primary visual cortex show orientation tuning

Gabor function

$$D(x,y) = \frac{1}{2\pi\sigma_x\sigma_y} \exp\left[-\frac{x^2}{2\sigma_x^2} - \frac{y^2}{2\sigma_y^2}\right] \cos(kx - \phi)$$

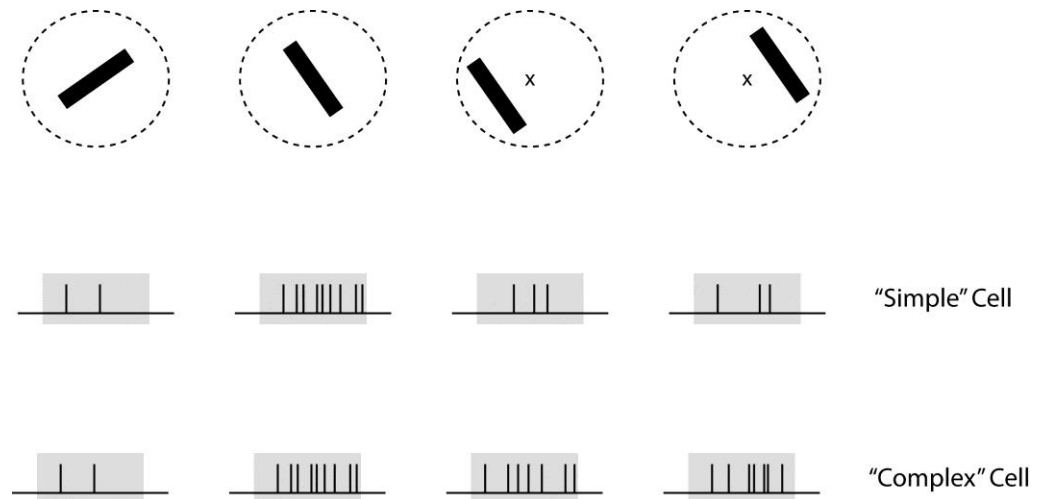
Image removed due to copyright restrictions. Please see the video.  
Source: Eye, Brain, and Vision. David H. Hubel. New York : Scientific American  
Library : Distributed by W.H. Freeman, c1988. ISBN: 0716750201.

# A simple model for simple cells



A feed-forward model for orientation selectivity in V1  
(by no means the only model)

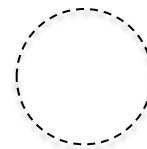
# Complex cells show position tolerance



Stimulus: black bar



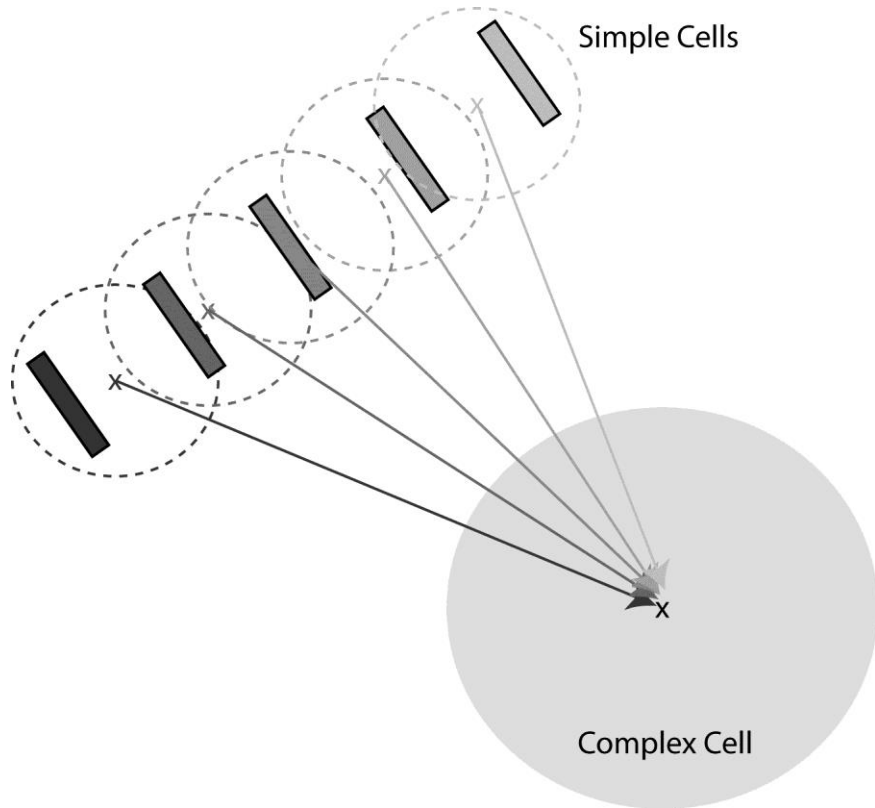
Stimulus presentation time



Receptive field

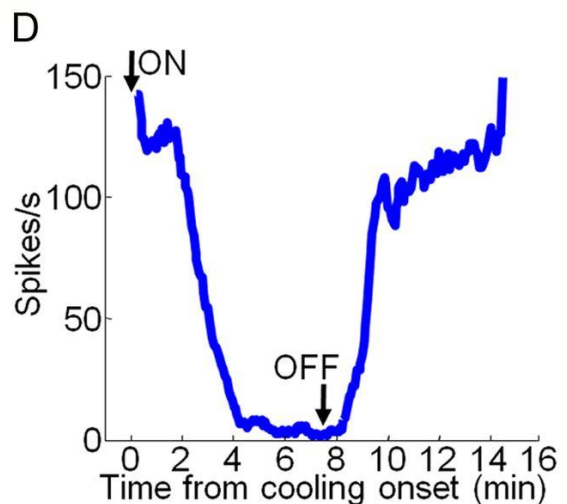
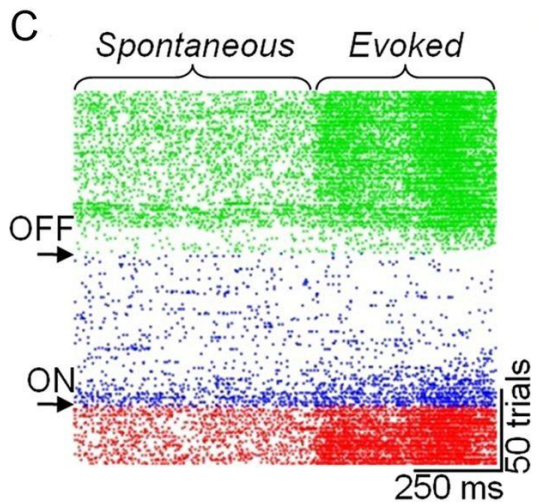
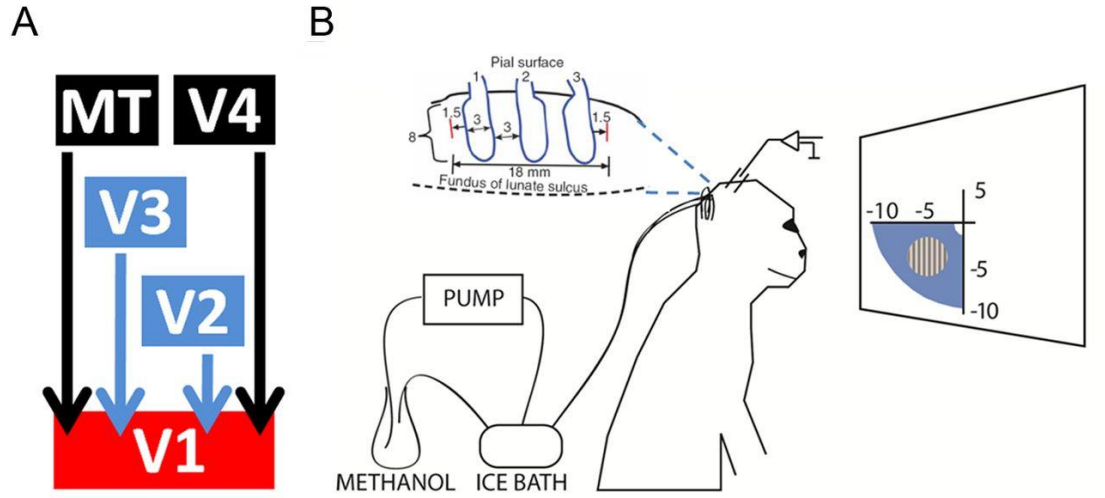
© Wiley. All rights reserved. This content is excluded from our Creative Commons license. For more information, see <https://ocw.mit.edu/help/faq-fair-use/>. Source: Hubel, David H., and Torsten N. Wiesel. "Receptive fields, binocular interaction and functional architecture in the cat's visual cortex." *The Journal of physiology* 160, no. 1 (1962): 106-154.

# A model to describe tolerance in complex cells



A feed-forward model  
describing the responses of  
complex cells arising from  
non-linear (e.g. OR, max)  
combination of inputs from  
multiple simple cells  
(by no means the only model)

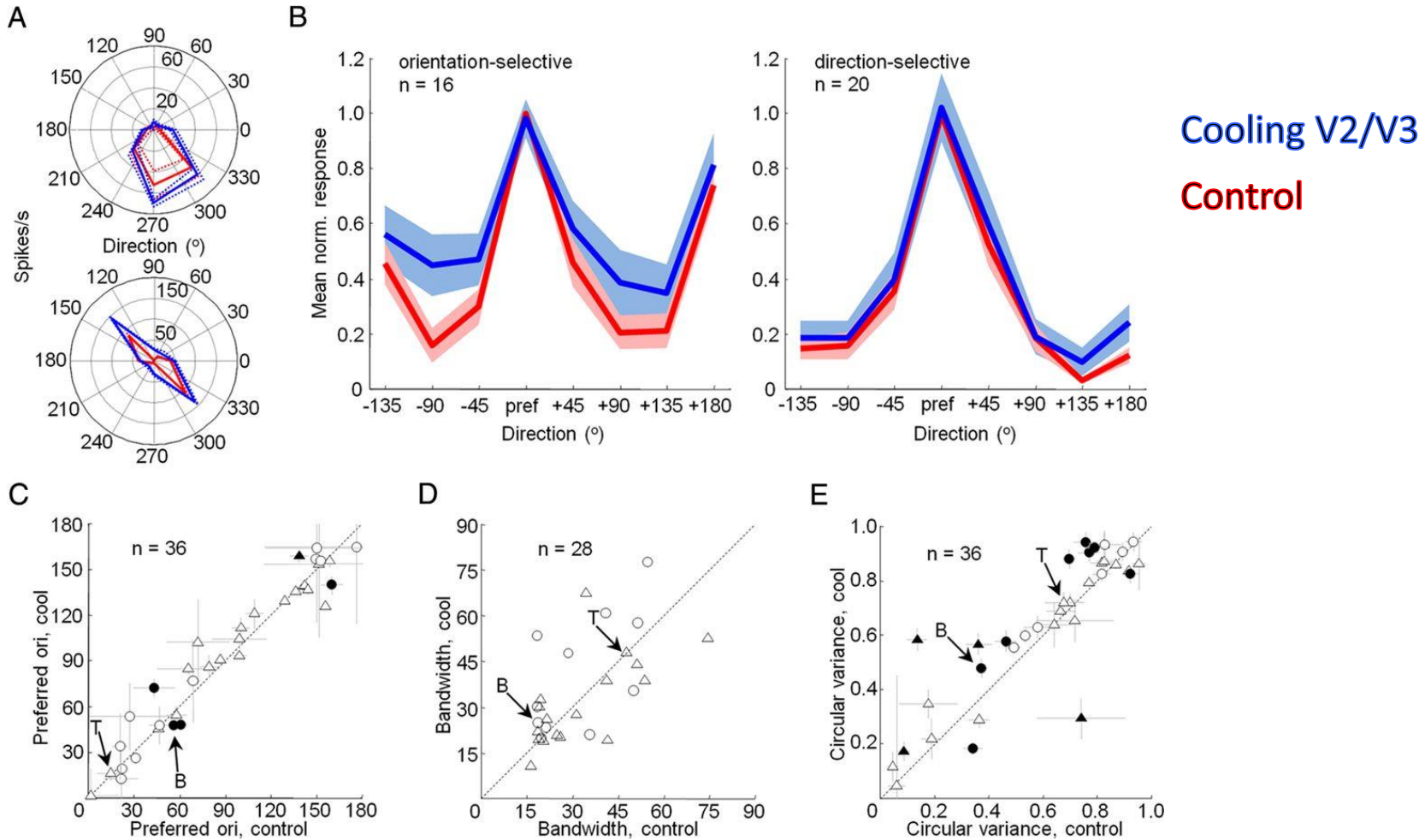
# Reversible inactivation of V2/V3



Courtesy of Society for Neuroscience. License CC BY NC SA.  
 Source: Nassi, Jonathan J., Stephen G. Lomber, and Richard T. Born.  
 "Corticocortical feedback contributes to surround suppression in V1 of  
 the alert primate." *Journal of Neuroscience* 33, no. 19 (2013): 85048517.

JoJo Nassi and Richard Born

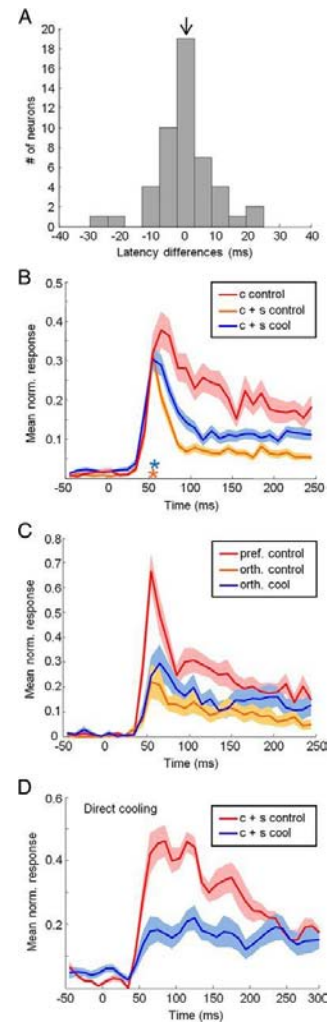
# Feedback inactivation does not change orientation or direction selectivity



Courtesy of Society for Neuroscience. License CC BY NC SA.  
Source: Nassi, Jonathan J., Stephen G. Lomber, and Richard T. Born.  
"Corticocortical feedback contributes to surround suppression in V1 of  
the alert primate." *Journal of Neuroscience* 33, no. 19 (2013): 85048517.

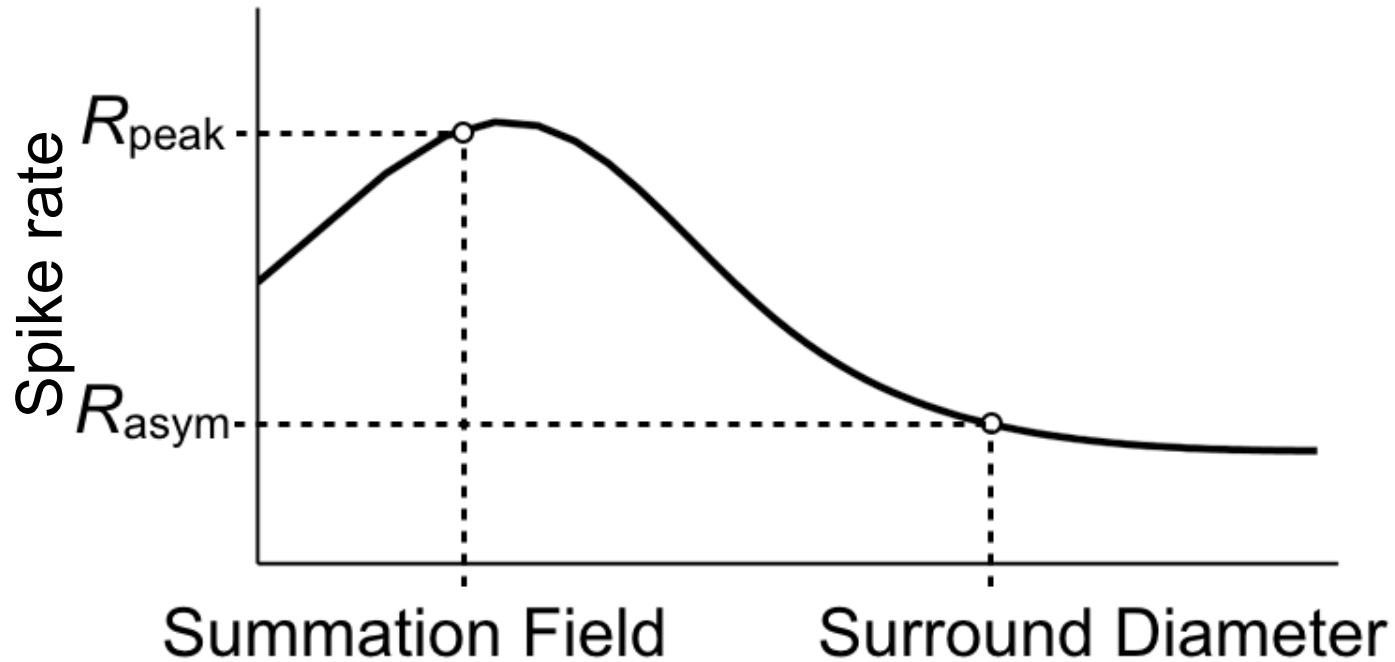
**Nassi et al 2013**

# Temporal dynamics of feedback inactivation effects



Courtesy of Society for Neuroscience. License CC BY NC SA.  
Source: Nassi, Jonathan J., Stephen G. Lomber, and Richard T. Born.  
"Corticocortical feedback contributes to surround suppression in V1 of the alert primate." *Journal of Neuroscience* 33, no. 19 (2013): 85048517.

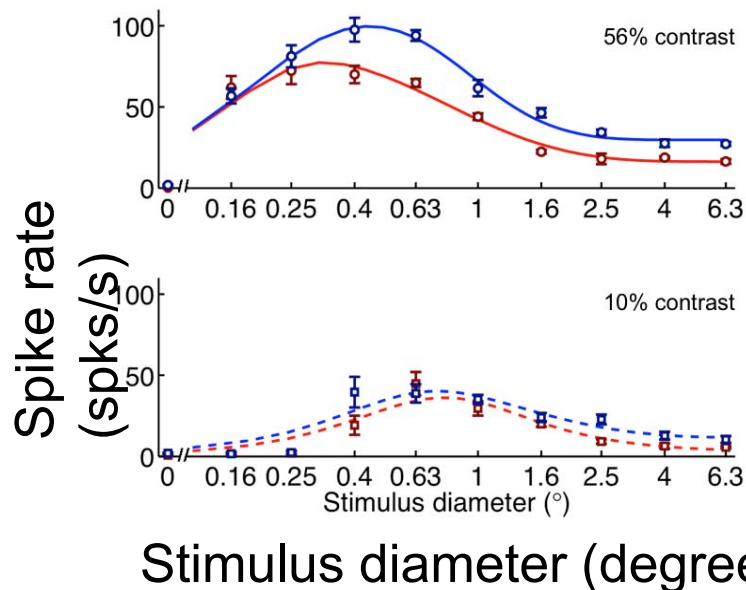
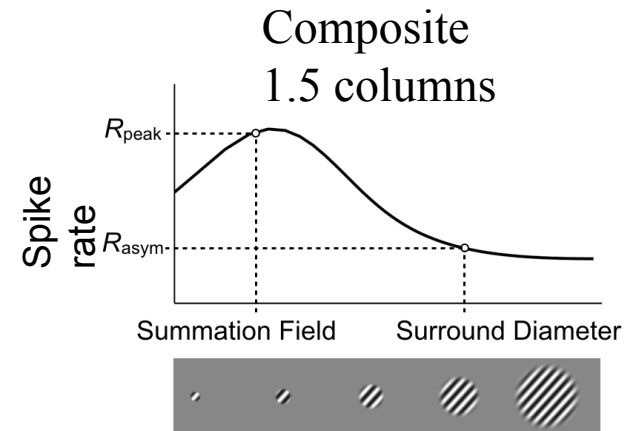
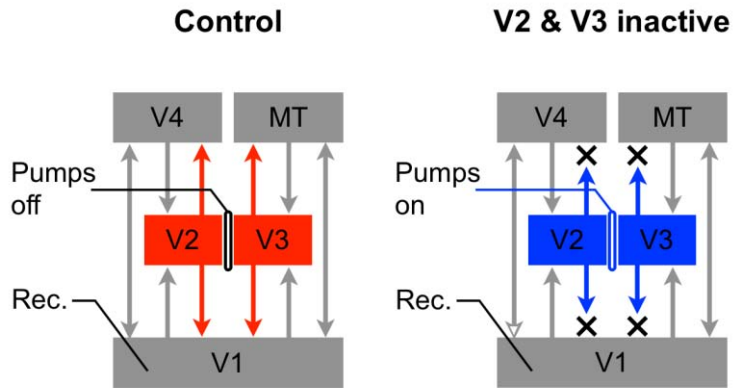
# Area summation curve in V1



Courtesy of Frontiers in Systems Neuroscience. Used with permission.  
Source: Nassi, Jonathan J., Camille Gómez-Laberge, Gabriel Kreiman, and Richard T. Born. "Corticocortical feedback increases the spatial extent of normalization." *Frontiers in systems neuroscience* 8 (2014): 105.



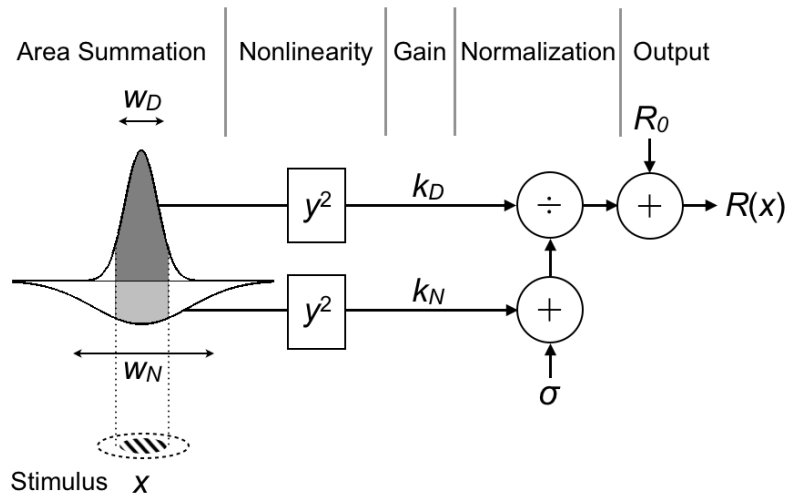
# Feedback inactivation leads to reduced surround suppression



Courtesy of Frontiers in Systems Neuroscience. Used with permission.

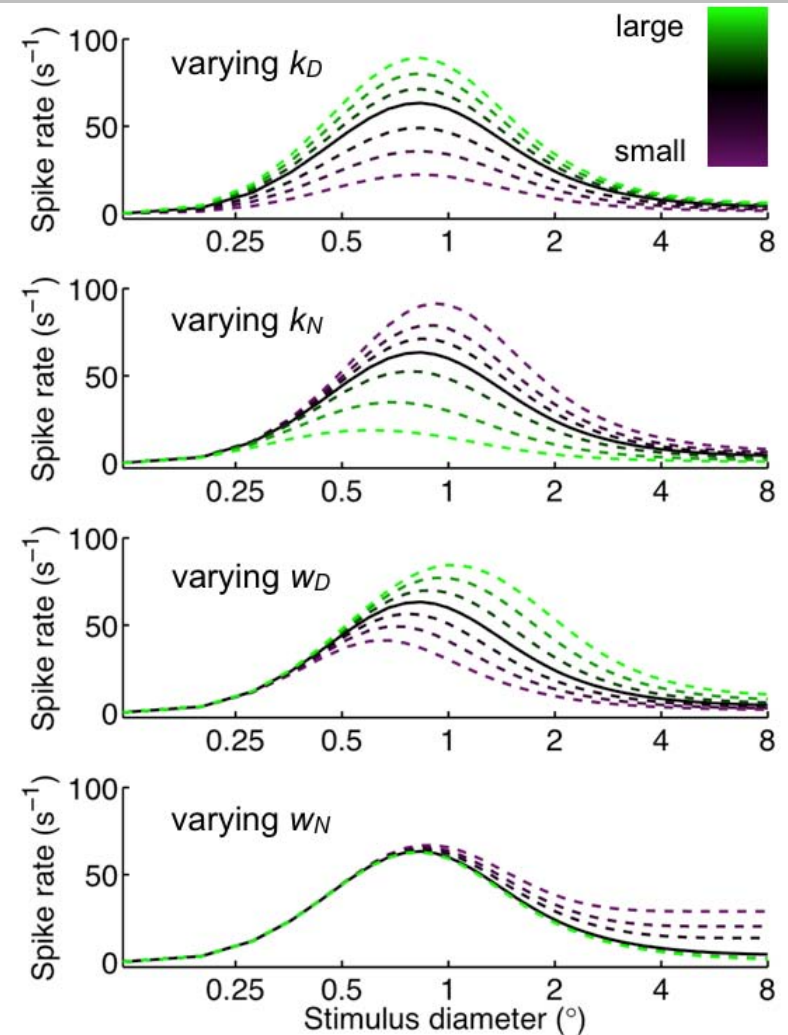
Source: Nassi, Jonathan J., Camille Gómez-Laberge, Gabriel Kreiman, and Richard T. Born. "Corticocortical feedback increases the spatial extent of normalization." *Frontiers in systems neuroscience* 8 (2014): 105.

# A simple normalization model to explain area summation curves



$$R_{ROG}(x) = R_0 + \frac{D(x)}{\sigma + N(x)}$$

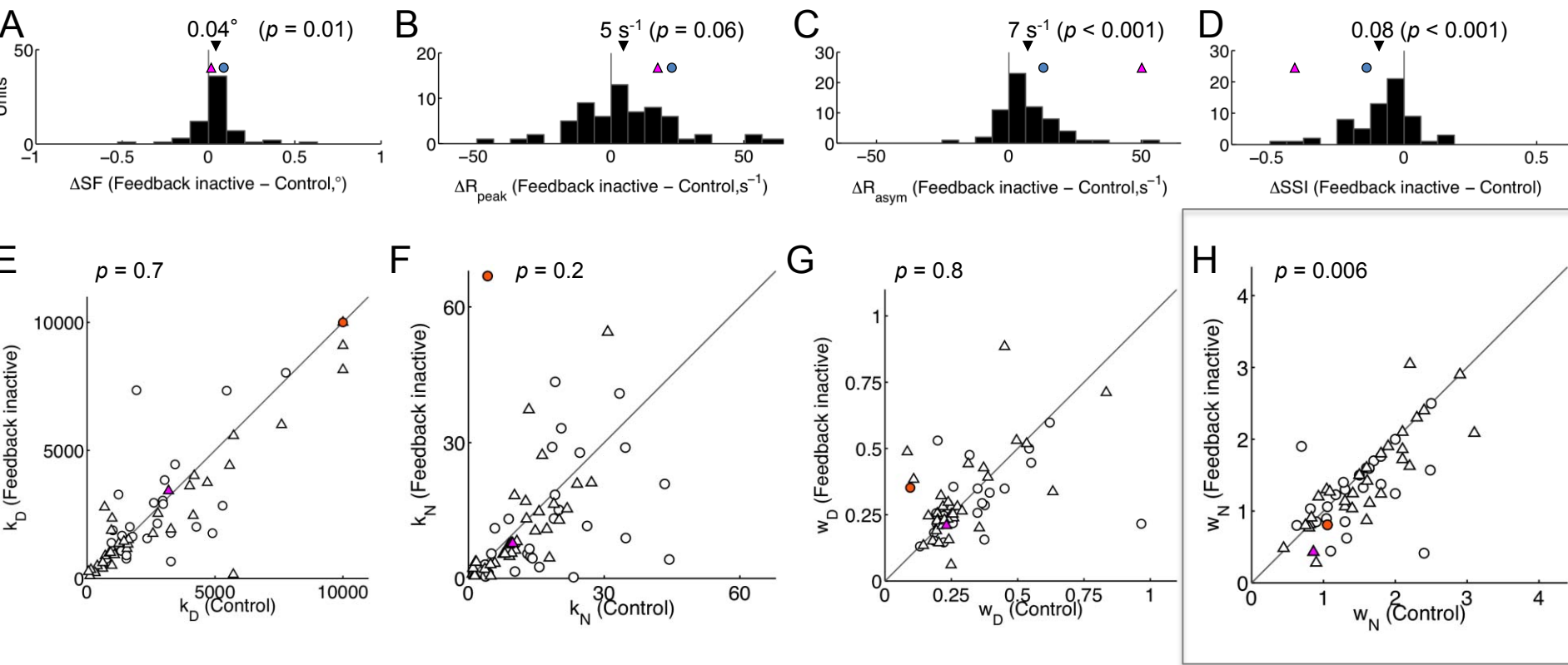
$$R_{ROG}(x) = R_0 + \frac{k_D [w_D \operatorname{erf}(x/2w_D)]^2}{\sigma + k_N [w_N \operatorname{erf}(x/2w_N)]^2}$$



Courtesy of Frontiers in Systems Neuroscience. Used with permission.

Source: Nassi, Jonathan J., Camille Gómez-Laberge, Gabriel Kreiman, and Richard T. Born. "Corticocortical feedback increases the spatial extent of normalization." *Frontiers in systems neuroscience* 8 (2014): 105.

# Feedback increases the normalization width: $w_N$



Courtesy of Frontiers in Systems Neuroscience. Used with permission.  
 Source: Nassi, Jonathan J., Camille Gómez-Laberge, Gabriel Kreiman, and Richard T. Born. "Corticocortical feedback increases the spatial extent of normalization." *Frontiers in systems neuroscience* 8 (2014): 105.

# Computational roles of feedback signals

1. Fundamental computations in V1
- 2. Visual search**
3. Pattern completion

Picture of Waldo removed due to copyright restrictions

# Feedback signals in visual search

Figure removed due to copyright restrictions. Please see the video.  
Source: Miconi, Thomas, Laura Groomes, and Gabriel Kreiman.  
"There's Waldo! A normalization model of visual search predicts  
single-trial human fixations in an object search task." *Cerebral  
Cortex* (2015): bhv129.

# The model can search for objects in cluttered images

Figure removed due to copyright restrictions. Please see the video.  
Source: Miconi, Thomas, Laura Groomes, and Gabriel Kreiman.  
"There's Waldo! A normalization model of visual search predicts  
single-trial human fixations in an object search task."Cerebral  
Cortex (2015): bhv129.

# The model's performance is comparable to human performance in the same visual search task

Figure removed due to copyright restrictions. Please see the video.  
Source: Miconi, Thomas, Laura Groomes, and Gabriel Kreiman.  
"There's Waldo! A normalization model of visual search predicts  
single-trial human fixations in an object search task." *Cerebral  
Cortex* (2015): bhv129.

# Consistency metrics

Figure removed due to copyright restrictions. Please see the video.  
Source: Miconi, Thomas, Laura Grooms, and Gabriel Kreiman.  
"There's Waldo! A normalization model of visual search predicts  
single-trial human fixations in an object search task." *Cerebral  
Cortex* (2015): bhv129.



# Computational roles of feedback signals

1. Fundamental computations in V1
2. Visual search
3. **Pattern completion**



Image by Hanlin Tang

Courtesy of Hanlin Tang. Used with permission.

# Inference and pattern completion as a hallmark of intelligence

A, C, E, G,



I

1, 2, 3, 5, 7, 11,



13

V-s-a- R-c-g-i-i-n



Visual Recognition

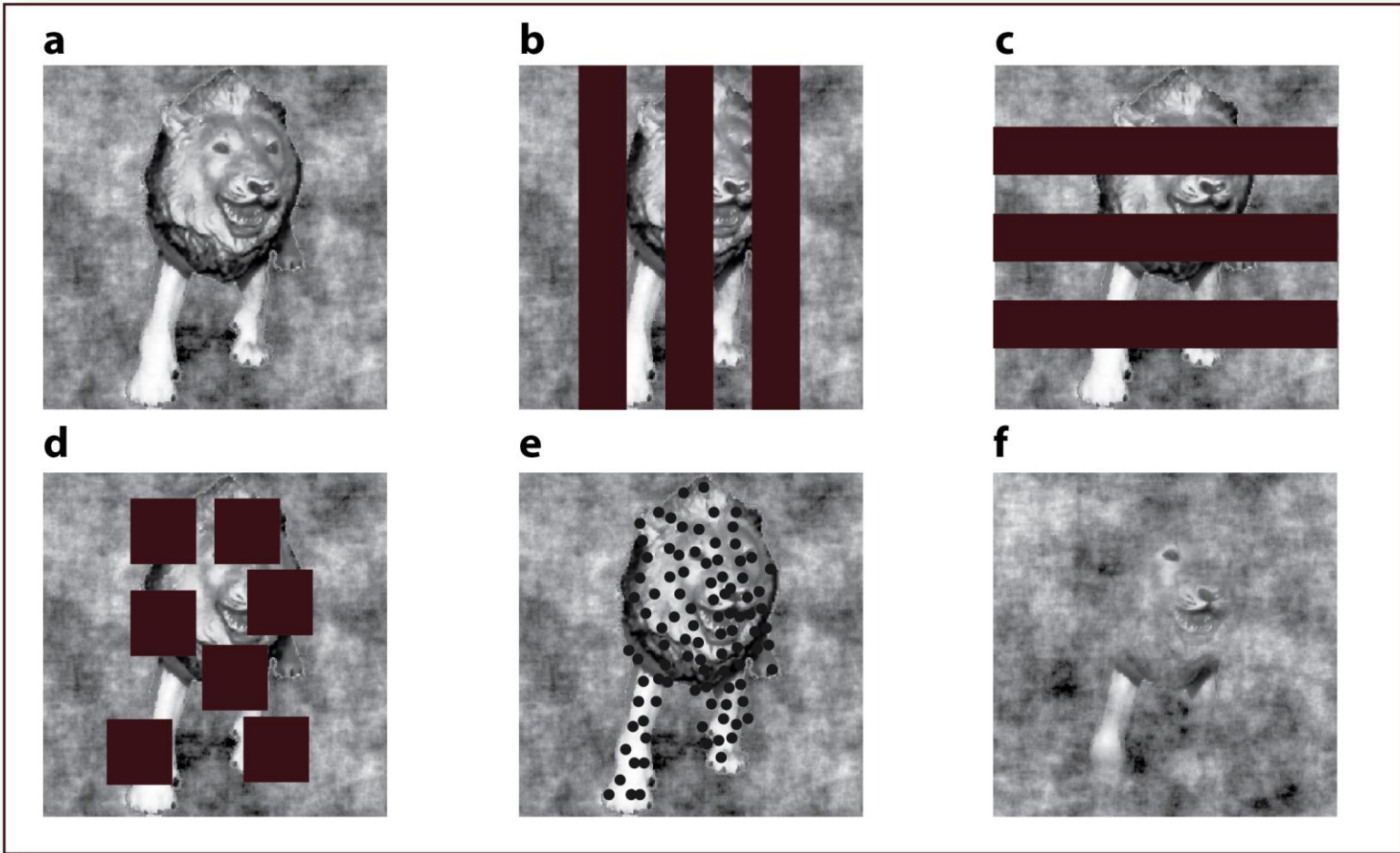
Even though it was raining heavily,  
Jonathan decided to go out without  
an




Umbrella

**Also:**  
**Other sensory modalities**  
**Music**  
**Social interactions**


# Objects can be recognized from partial information




20 bubbles




10 bubbles



6 bubbles



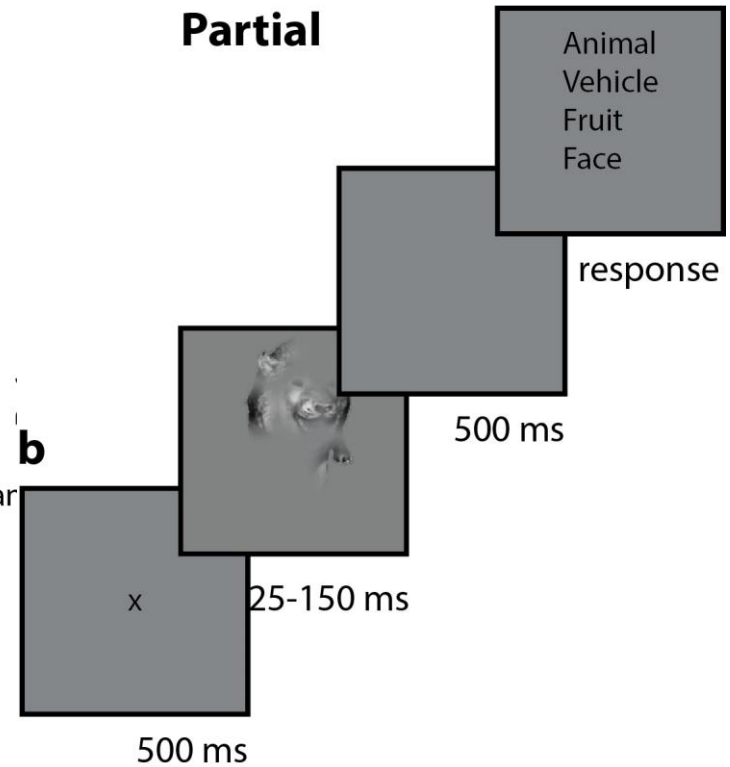
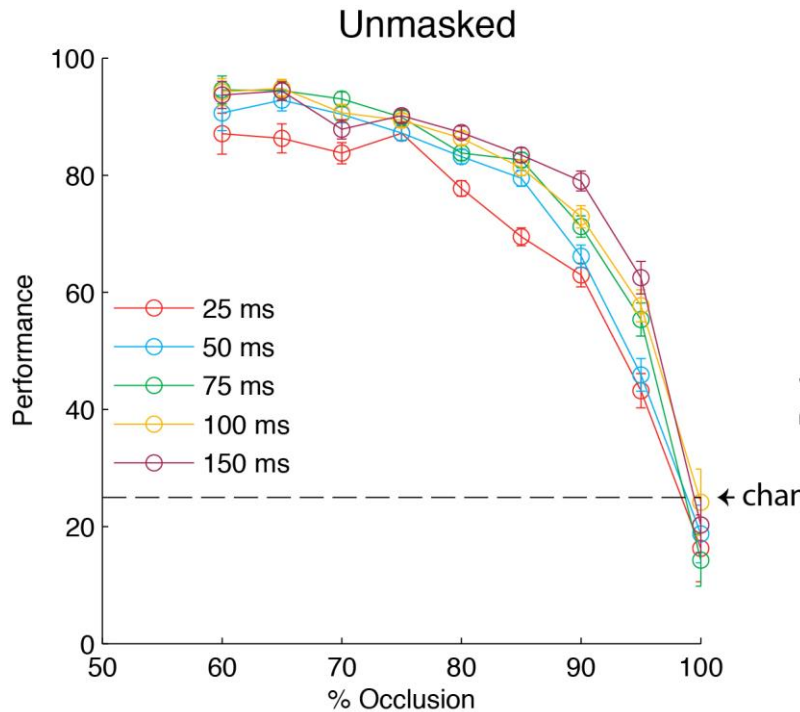
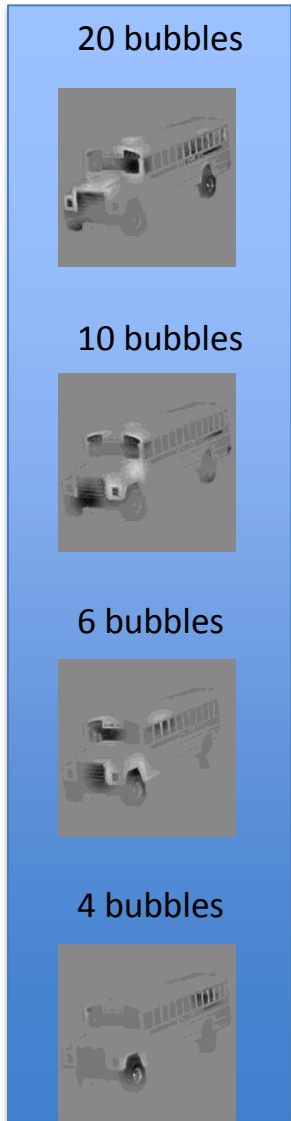
4 bubbles



A vertical blue bar on the right side of the slide contains four bus icons, each associated with a number of bubbles: 20, 10, 6, and 4. The bus icons are rendered in a light gray color.

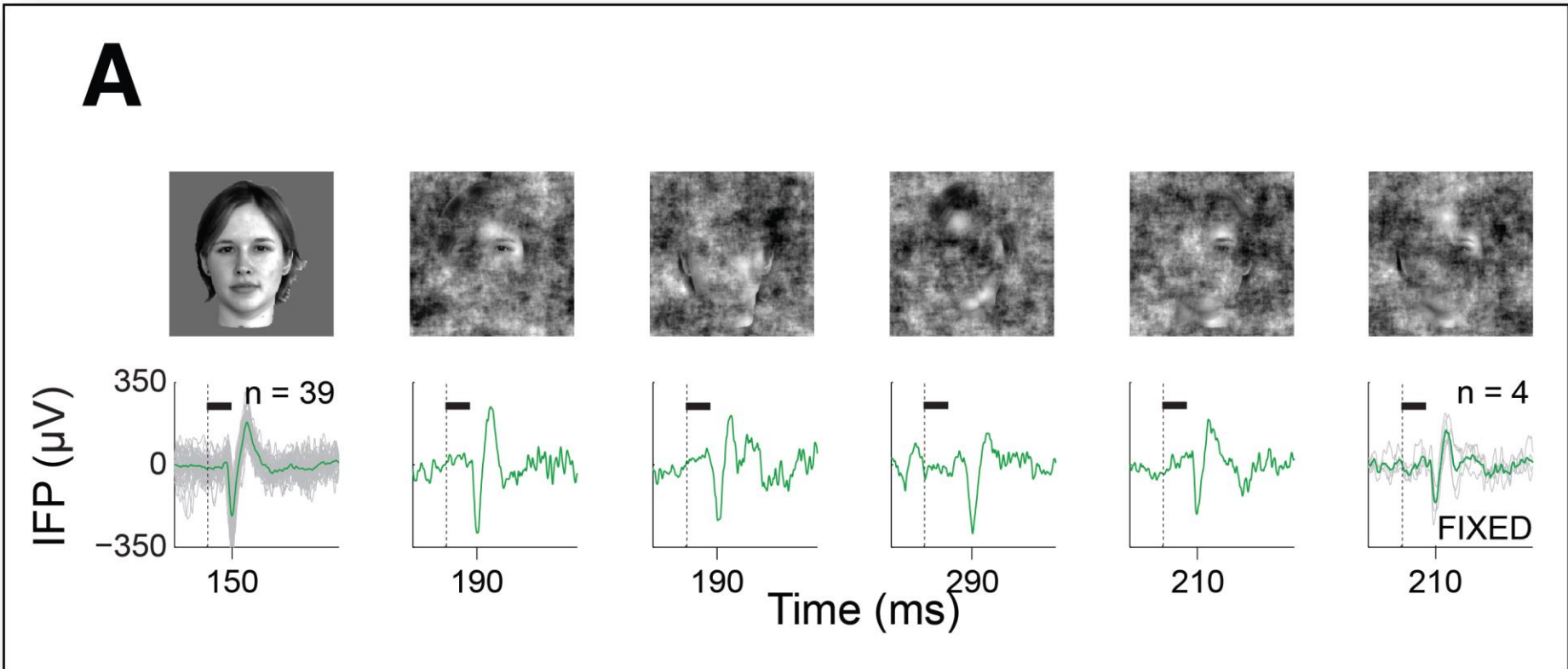
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# Behavior: Robustness to presentation of partial image information



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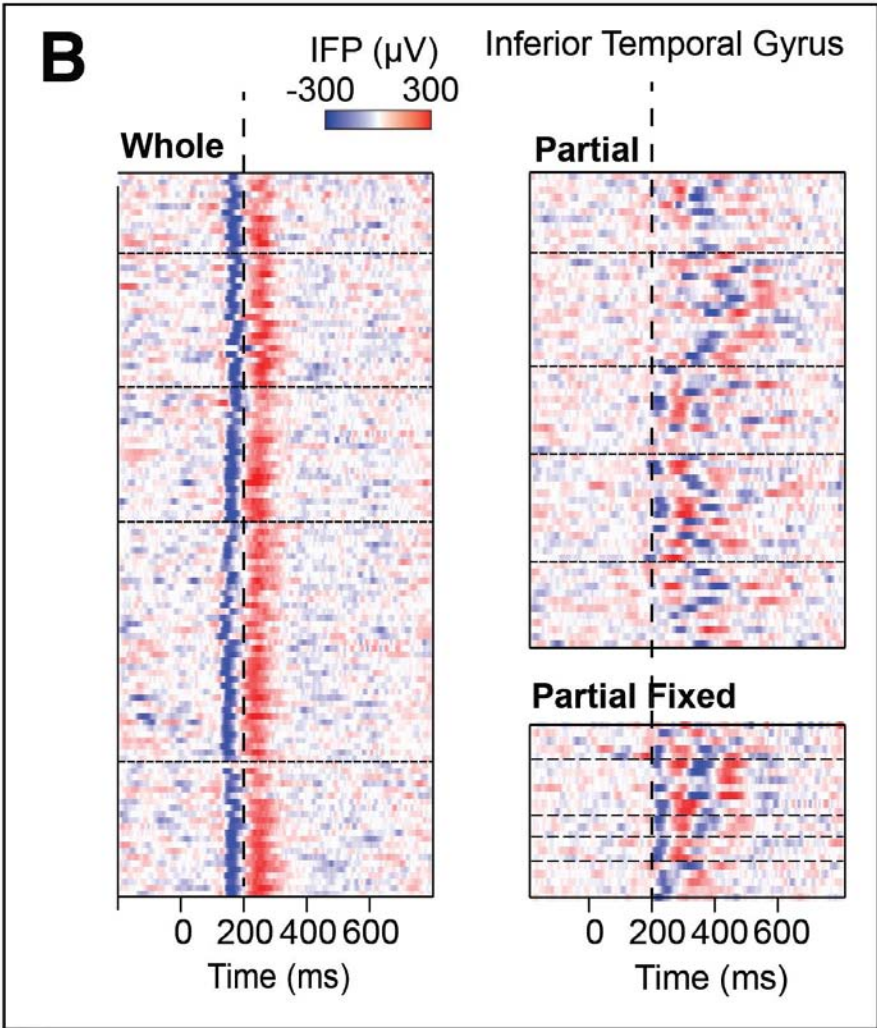
# Example responses during object completion



Courtesy of Elsevier, Inc., <http://www.sciencedirect.com>. Used with permission.  
Source: Tang, Hanlin, Calin Buia, Radhika Madhavan, Nathan E. Crone, Joseph R. Madsen, William S. Anderson, and Gabriel Kreiman. "Spatiotemporal dynamics underlying object completion in human ventral visual cortex." *Neuron* 83, no. 3 (2014): 736-748.

Tang et al,  
*Neuron* 2014

# Example responses during object completion



Courtesy of Elsevier, Inc., <http://www.sciencedirect.com>. Used with permission.  
Source: Tang, Hanlin, Calin Buia, Radhika Madhavan, Nathan E. Crone, Joseph R. Madsen, William S. Anderson, and Gabriel Kreiman. "Spatiotemporal dynamics underlying object completion in human ventral visual cortex." *Neuron* 83, no. 3 (2014): 736-748.

Tang et al,  
*Neuron* 2014

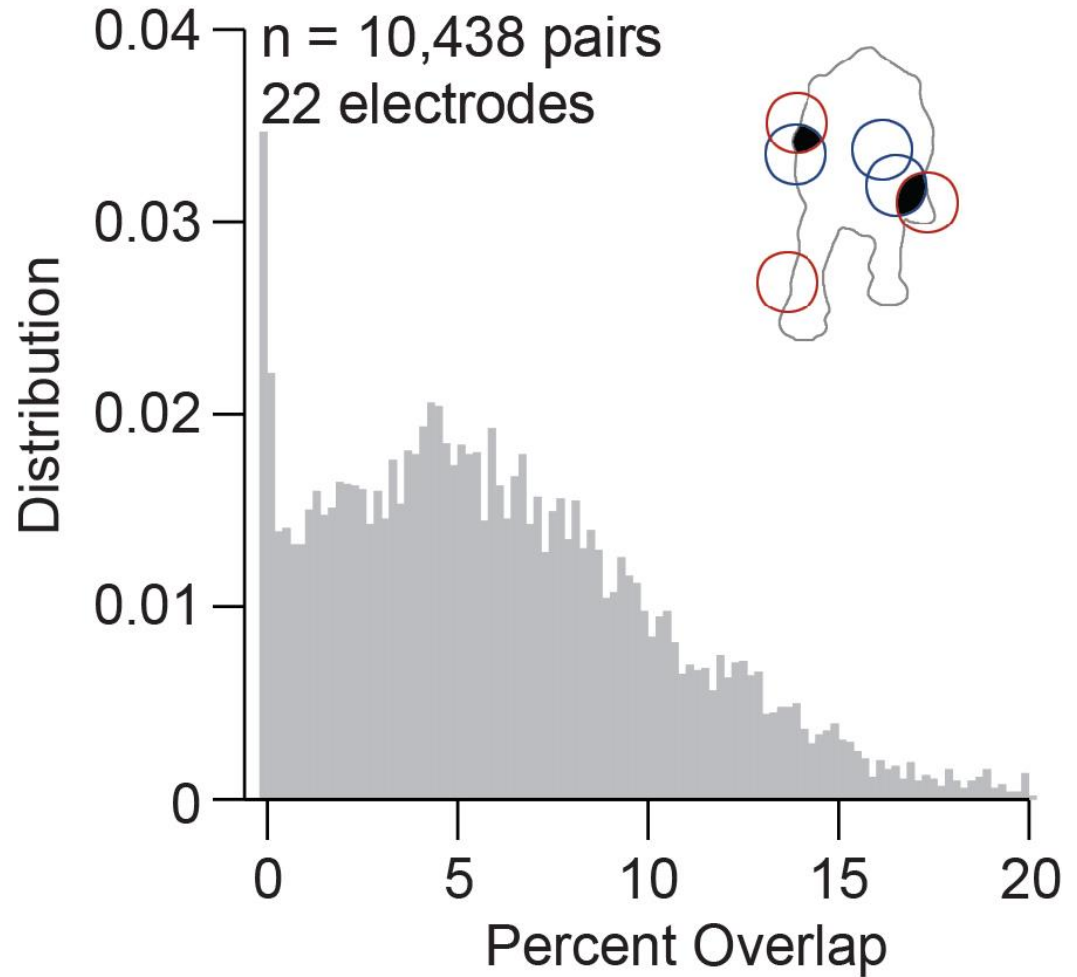
# Limited object completion in feed-forward model

Figure removed due to copyright restrictions. Please see the video.  
Source: Figure 29, Kreiman, Gabriel. "Computational models of visual object recognition." *Principles of Neural Coding 1* (2013): 0.

2000 "C2" units in the model  
Model responds to 25 exemplar objects  
Consider 20 units with high SNR (training data)  
500 repetitions with different bubble locations  
Train classifier with 70% of the repetitions  
Test classifier on remaining 30% of the repetitions  
Identification task (chance=4%)

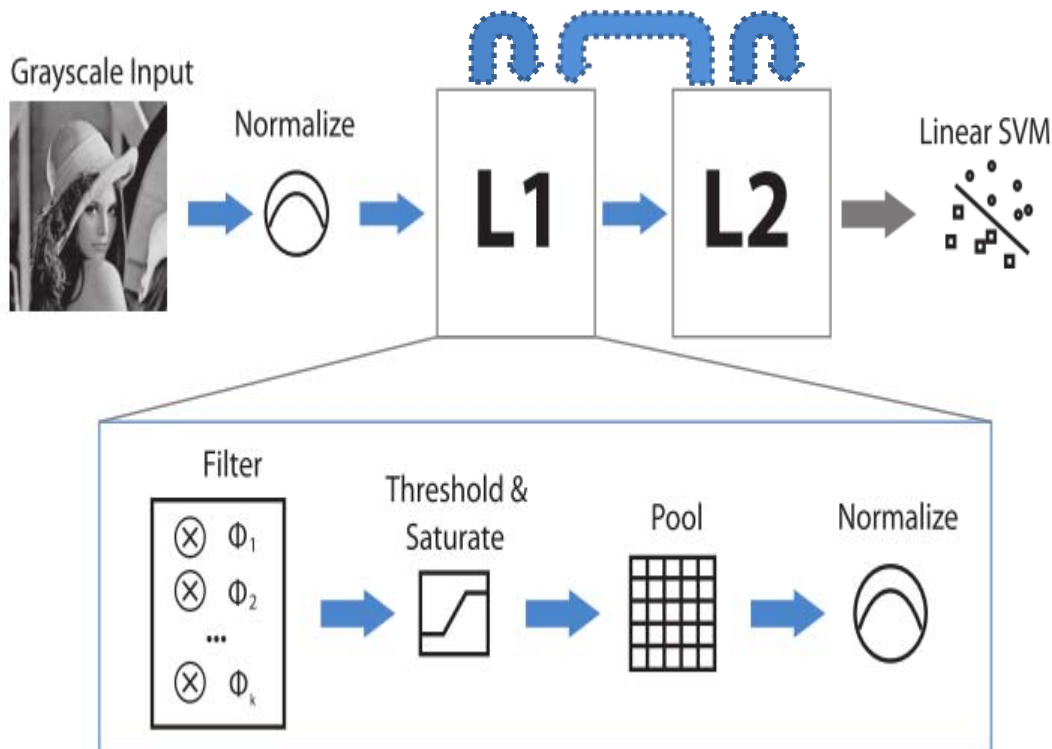
# Holistic responses (?)

**D**



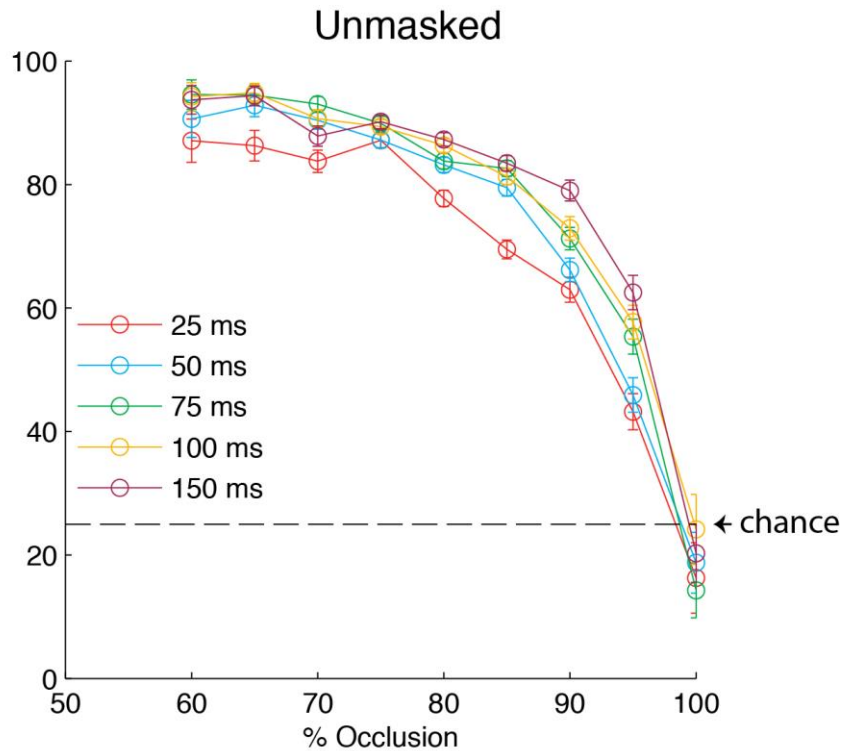


# Adding recurrency to deep network models

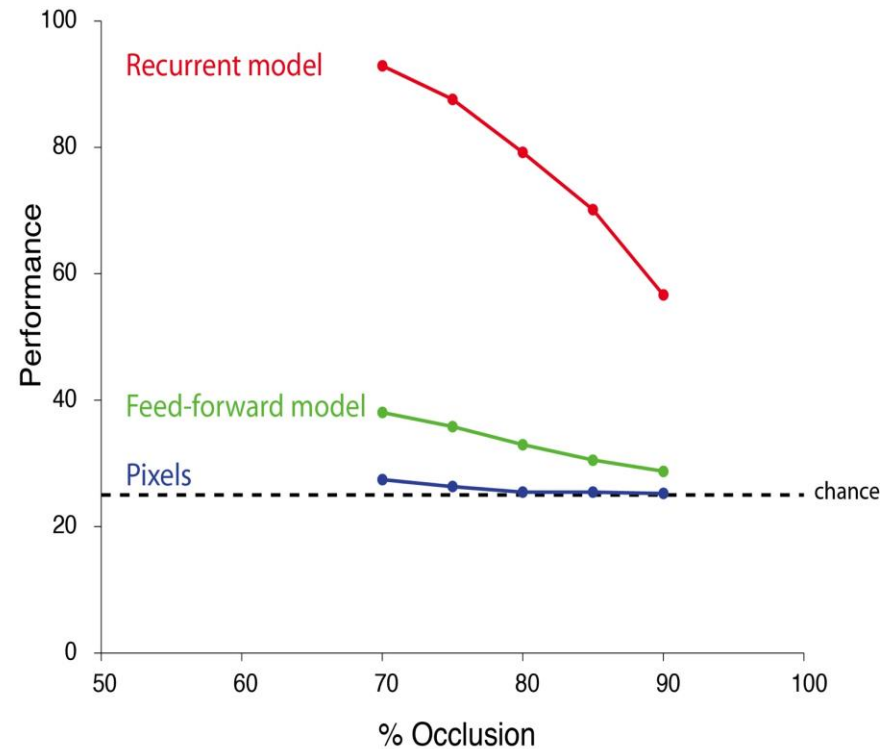


# Preliminary results: Recurrent connections can improve recognition of occluded objects

## Behavior

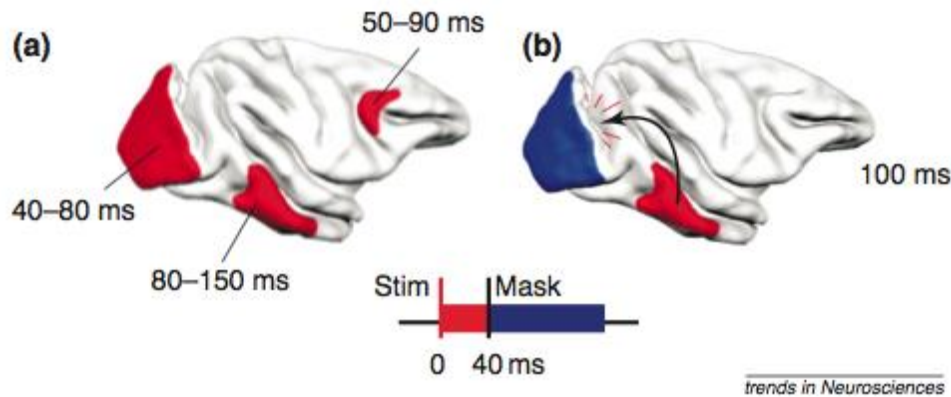


## Recurrent model Trained on whole images

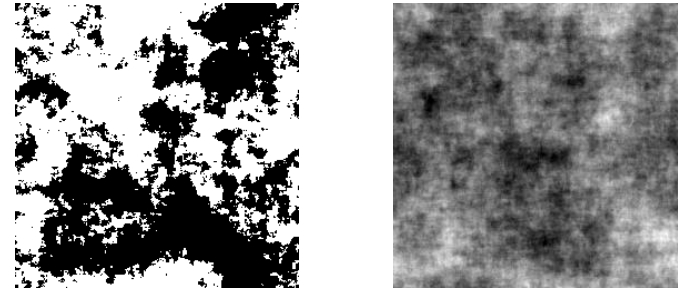


# Backward masking has been proposed to reduce the effects of feedback

## Models:



## Masks:

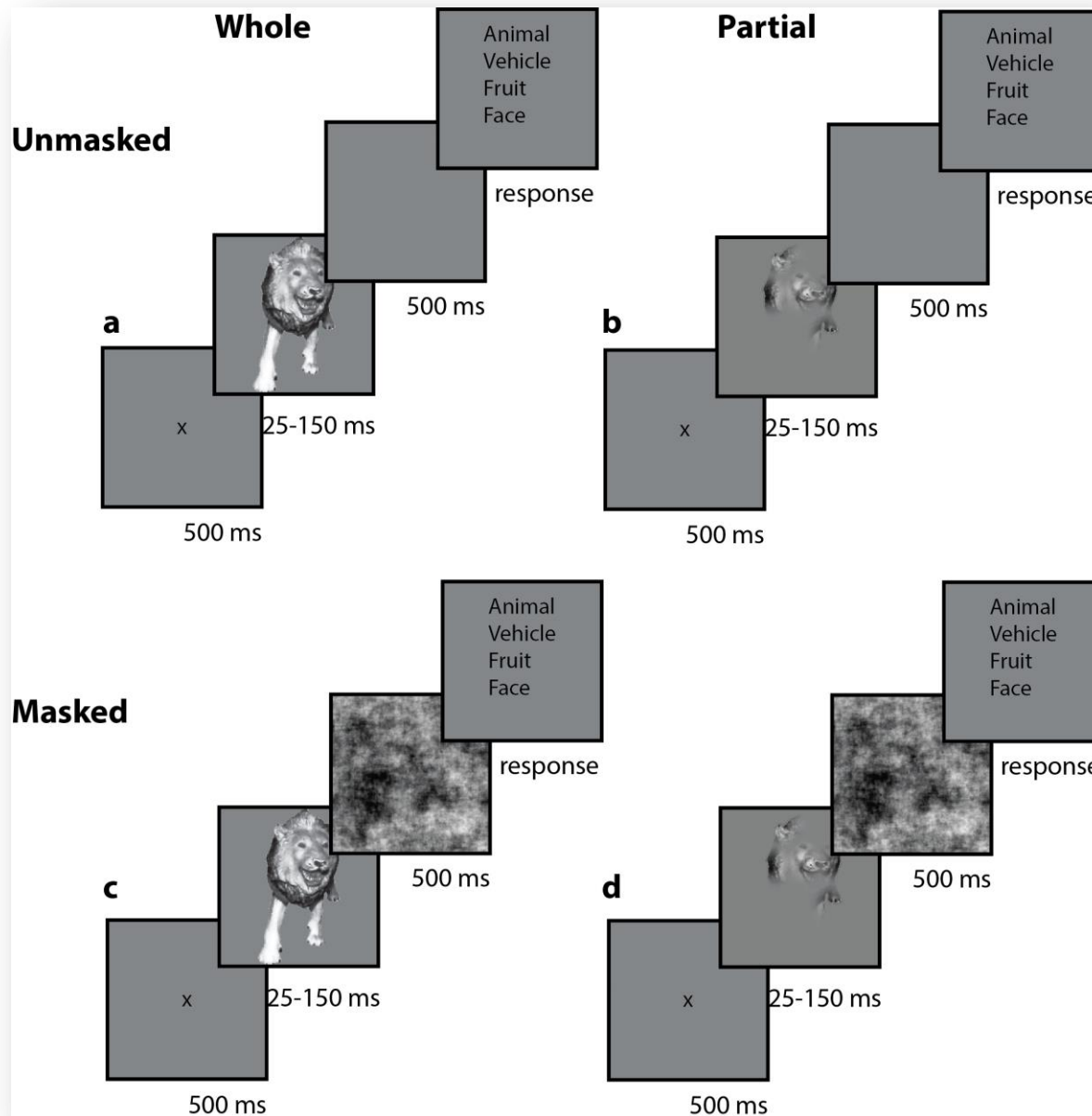


Lamme V, Roelfsema P (2000)

Courtesy of Elsevier, Inc., <http://www.sciencedirect.com>. Used with permission.  
Source: Lamme, Victor AF, and Pieter R. Roelfsema. "The distinct modes of vision offered by feedforward and recurrent processing." Trends in neurosciences 23, no. 11 (2000): 571-579.

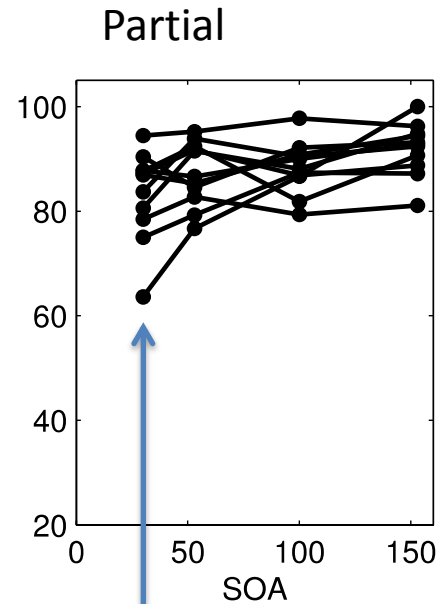
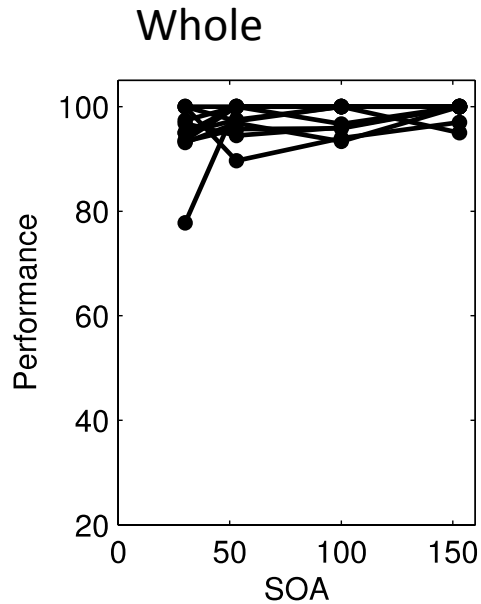
- For short delays ( $SOA < 20ms$ ), the mask reduces visibility of the first stimulus.
- For longer delays, the mask disrupts top-down processing.

# Object completion task (psychophysics)

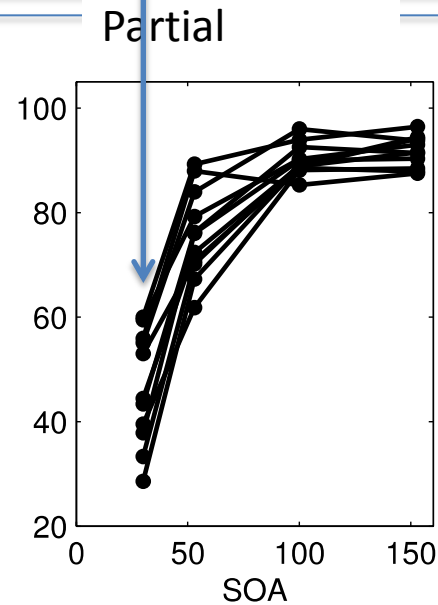
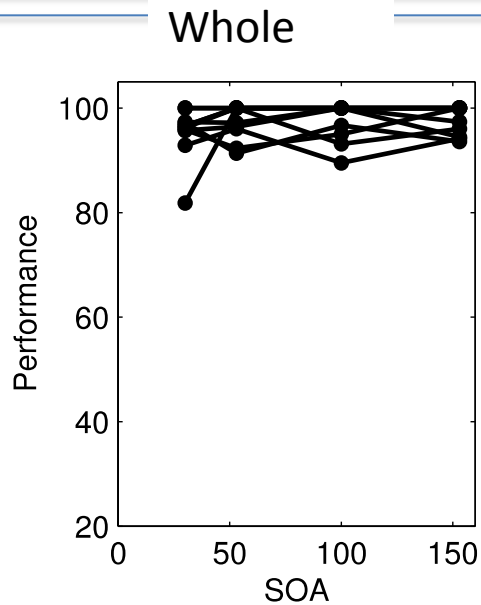


# Backward masking impairs recognition of partial objects at short SOAs

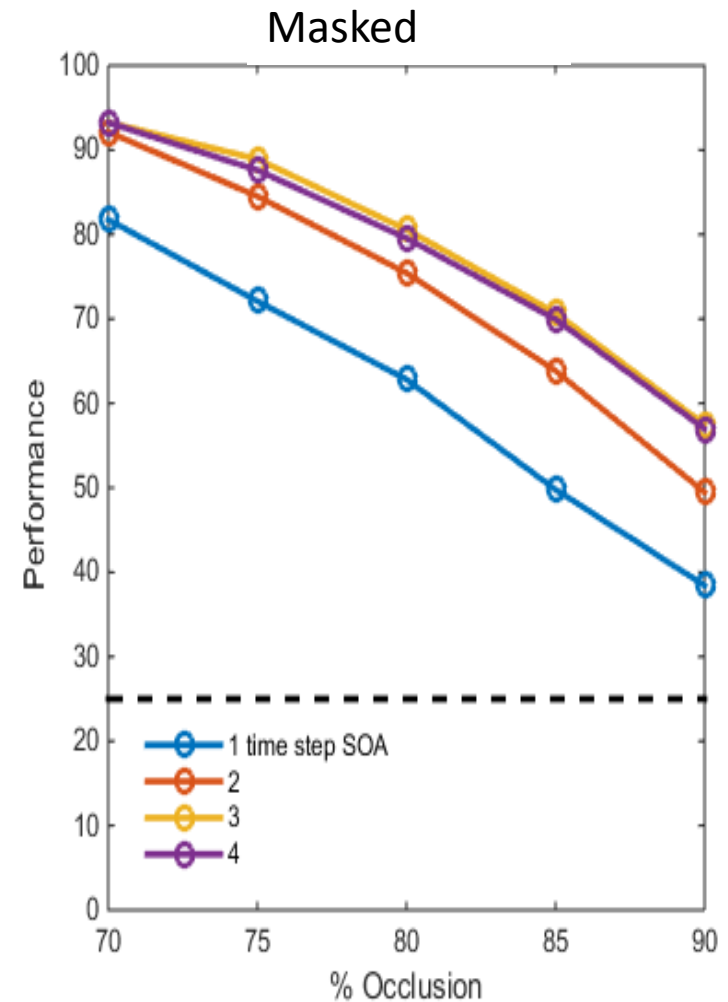
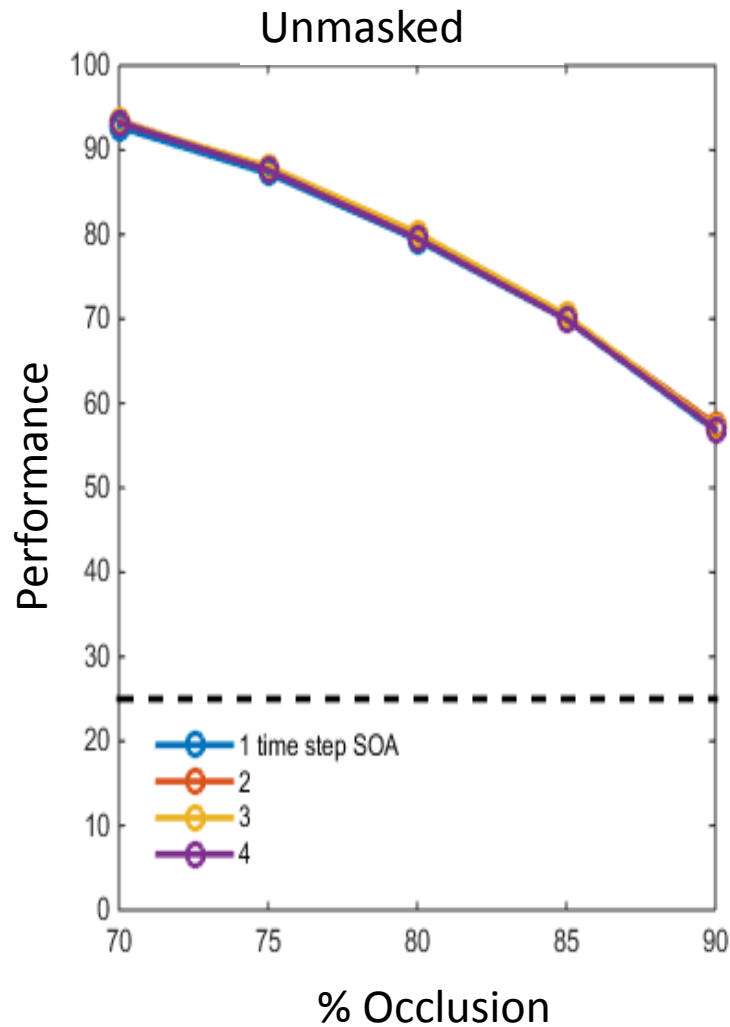
Unmasked



Masked

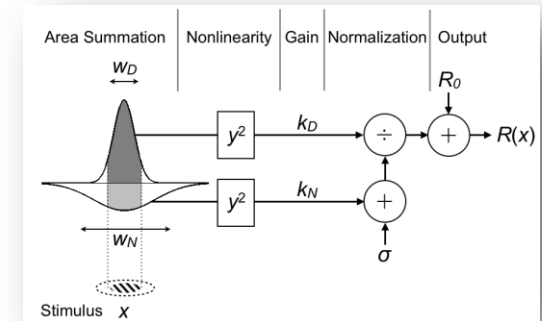


# Model performance in masking experiment

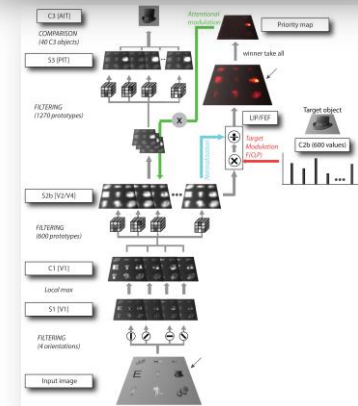


# Summary

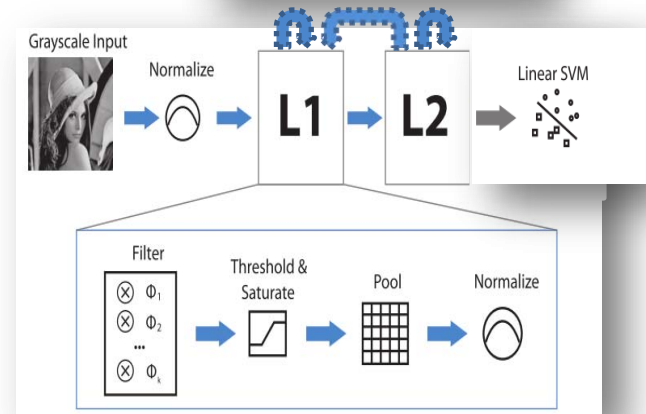
▪ **Basic mechanisms in V1: Feedback signals enhance surround suppression**



▪ **Visual search: Tuned feedback signals can instantiate visual search (and feature-based attention)**  
(Turing question: what will happen next?)



▪ **Pattern completion: Feedback and/or recurrent connections can help recognize heavily occluded objects**  
(Turing question: what is there?)



# Outline

1. Introduction to neural circuits and computational models
2. Computational roles of feedback signals
3. **Open questions, challenges, opportunities**



# Reasons for optimism

- **Wiring diagram**: Rapid progress tracing circuits in humans (low resolution) and animal models (high resolution)
- **Strength in numbers**: Rapid progress recording and mathematically analyzing neurophysiological activity from large ensembles in humans and animal models
- **Source code**: We can manipulate neural circuits (rodents, macaques) to examine necessary and sufficient computational elements

# Wiring diagrams



Courtesy of Professor Sander van den Heuvel and Dr. Mike Boxem. Used with permission.

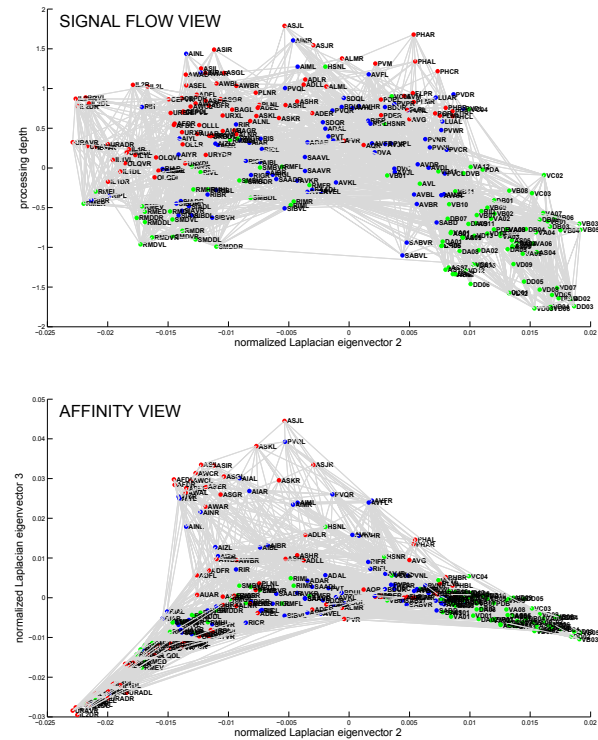
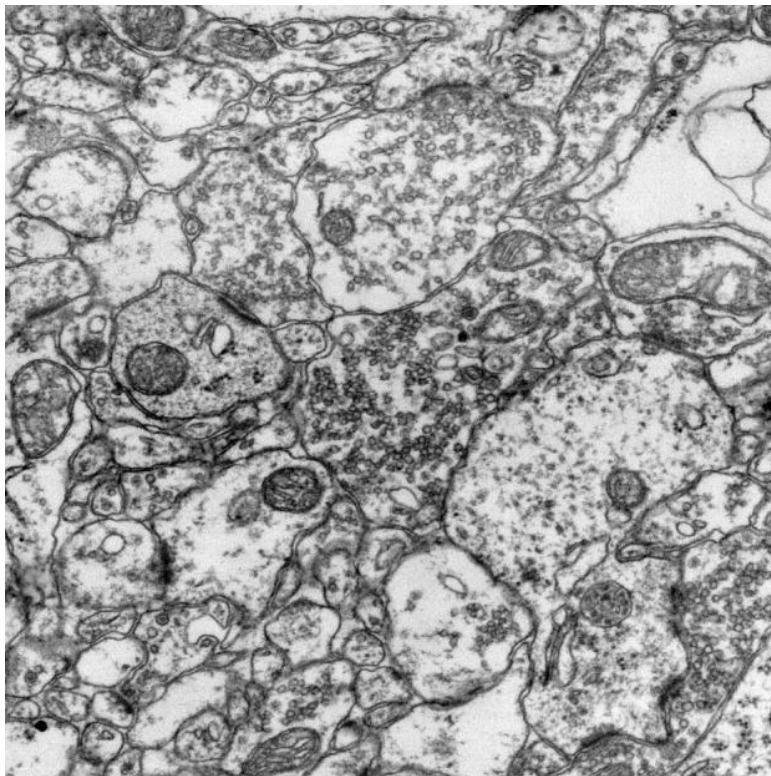
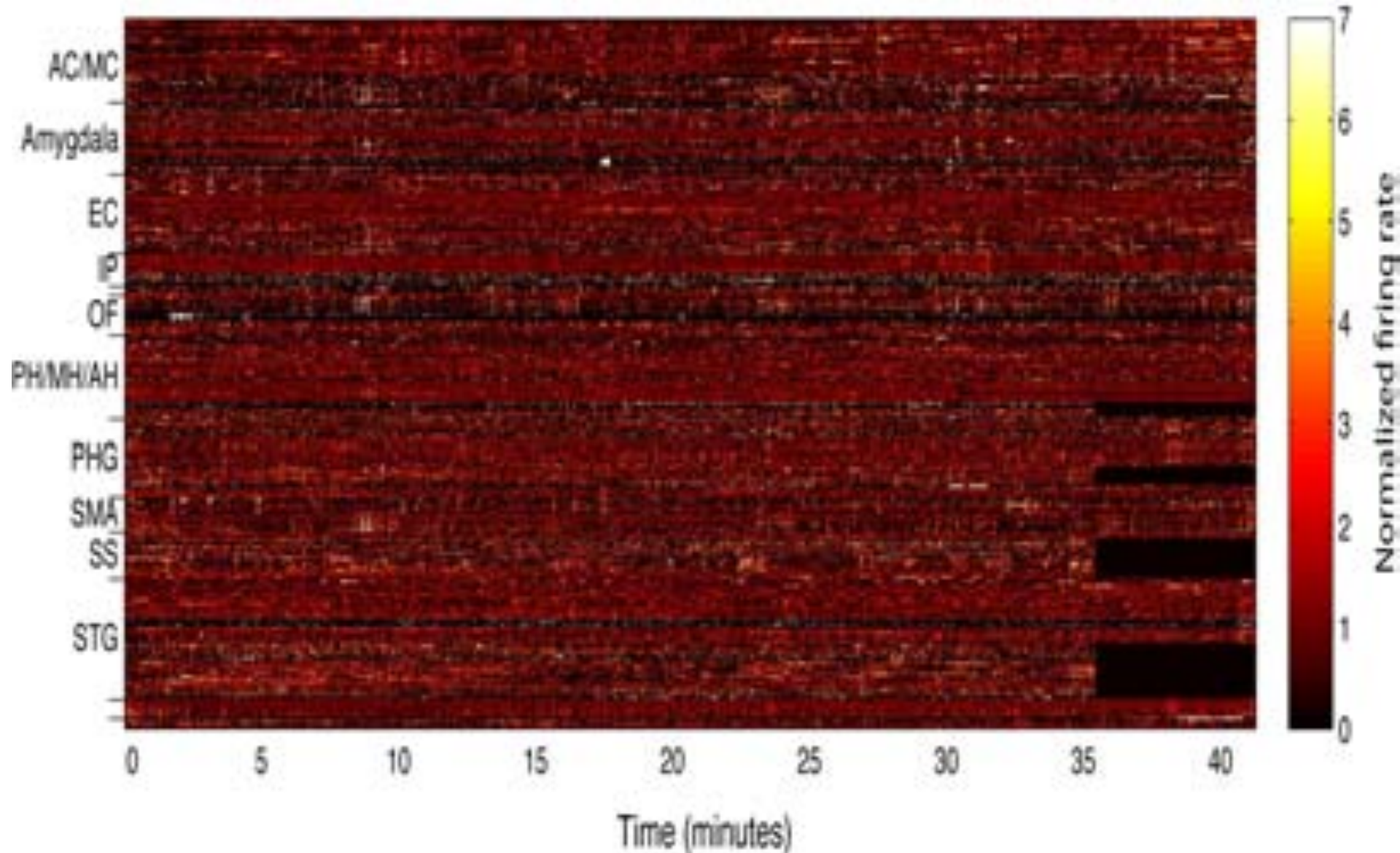


Fig. 2. The *C. elegans* wiring diagram is a network of identifiable, labeled neurons connected by chemical and electrical synapses. Red, sensory neurons; blue, interneurons; green, motoneurons. (a). Signal flow view shows neurons arranged so that the direction of signal flow is mostly downward. (b). Affinity view shows structure in the horizontal plane reflecting weighted non-directional adjacency of neurons in the network.

Original work: Sydney Brenner  
Image: Doctoral Dissertation Thesis by  
Beth Chen, 2007

Varshney, Lav R., Beth L. Chen, Eric Paniagua, David H. Hall, and Dmitri B. Chklovskii. "Structural properties of the *Caenorhabditis elegans* neuronal network." *PLoS Comput Biol* 7, no. 2 (2011): e1001066. DOI: 10.1371/journal.pcbi.1001066. License CC BY.

# Strength in numbers

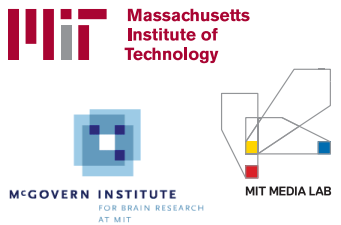


Pseudopopulation: 318 units

Hanlin Tang, Matias Ison, Itzhak Fried

# Strength in numbers: electrode arrays (e.g. Boyden)

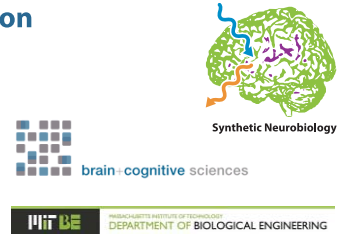
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## Scalable 3-D Microelectrode Recording Architectures for Characterization of Optogenetically Modulated Neural Dynamics

J. Scholvin<sup>1</sup>, S.K. Arfin<sup>1</sup>, J. Bernstein<sup>1</sup>, J. Kinney<sup>1</sup>, C. Moore-Kochlacs<sup>1,2</sup>, P.E. Monaghan<sup>1</sup>, A.N. Zorzos<sup>1</sup>, N. Kopell<sup>2</sup>, C.G. Fonstad<sup>1</sup>, E.S. Boyden<sup>1</sup>

<sup>1</sup> Synthetic Neurobiology Group, MIT Media Lab and MIT McGovern Institute, Departments of Biological Engineering and Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA, <sup>2</sup> Boston University, Boston, MA

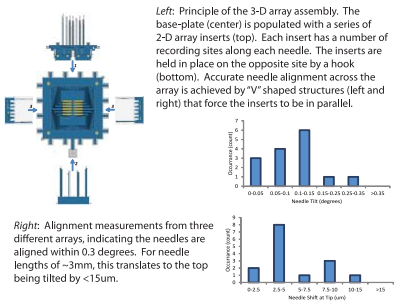


### Introduction

Optogenetics is commonly used for precision modulation of the activity of specific neurons within neural circuits, but assessing the impact of optogenetic neuromodulation on the neural activity of local and global circuits remains difficult. Our collaborative team recently initiated a project (Scholvin et al., SFN 2011) to design and implement 3-D silicon-micromachined electrode arrays with customizable electrode locations, targetable to defined neural substrates distributed in a 3-D pattern throughout a neural network in the mammalian brain, and compatible with simultaneous use of a diversity of existing light delivery devices.

We here describe a series of innovations we have pursued aimed at facilitating the scalability aspect of these probes - that is, aspects of probe design that should enable them to scale up to 1000's of channels of neural recording or more. First, we have developed streamlined electrode fabrication methodologies that enable micromachined probes to be first fabricated using conventional silicon micromachining, then rapidly assembled into custom 3-D arrays, with semi-automated formation of the necessary electrical connections and mechanical constraints. Second, we have developed a set of surgical and insertion technologies towards the goal of enabling the insertion of electrode arrays with a high number of electrode shanks into the brain, while minimizing probe insertion damage. Finally, in order to facilitate scaling of the channel count beyond what is feasible with external amplifiers, we are exploring new approaches for integration of amplifier circuits directly on the probe arrays themselves, to remove bottlenecks associated with connecting of probes to the outside world.

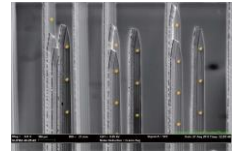
### Design Components



### 3-D Array Construction



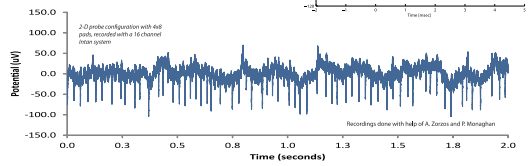
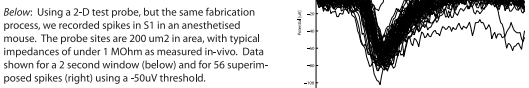
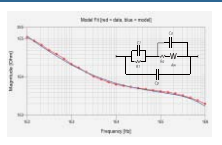
Above, left and center: Assembled 3-D array, demonstrating the construction mechanisms. The above array has 40 needles, with three electrode sites along every needle. Each needle was customized, and in this example designed with a unique length and placed at varying positions along each 2-D insert. The V-shaped alignment bracket mechanism is seen in the center. Right: underside of the 3-D array showing the self-locking assembly mechanism, as well as the electrical connections between the base plate and each array insert.



Above: Close-up of the probe needle tips, with electrode sites highlighted in false color. Here, each needle has three recording sites, and a cross section of 50x50  $\mu\text{m}$ . These dimensions can easily be varied by use of different wafer geometries and lithography tools.

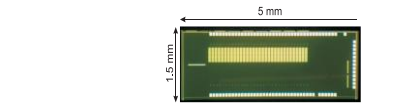
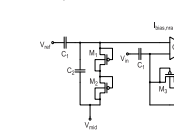
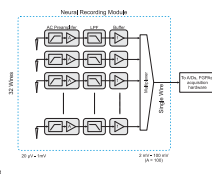
- Below:** Suggested design for a 1000 channel 3-D probe that is capable of recording uniformly throughout the brain. Recording sites are spaced 300  $\mu\text{m}$  in the plane and 110  $\mu\text{m}$  in the vertical.
- Pad arrangement: 10x10x10
  - Volume covered: 2.7 x 2.8 x 3 mm
  - Recording site area: 100  $\mu\text{m}^2$
  - Recording site spacing:
    - ... along needle (Z): 110  $\mu\text{m}$
    - ... needle-to-needle (X): 300  $\mu\text{m}$
    - ... insert to insert (Y): 310  $\mu\text{m}$
  - Needle assembly:
    - ... total length: 1600  $\mu\text{m}$
    - ... length with recording sites: 1000  $\mu\text{m}$
    - ... width: 40  $\mu\text{m}$
    - ... thickness: 15, 30 or 50  $\mu\text{m}$
  - Tissue displacement ratio: 1.5% for 30  $\mu\text{m}$  thickness
  - Expected recording site impedance: 600 kOhm

### Electrical Connections and Testing



### Future Amplifier Integration

**Right:** Amplifier system design for future integration onto the probes. In order to achieve >>1000 channels with on-probe amplification and multiplexing, an integrated amplifier and multiplexer circuit was developed, with system schematic for a 32 channel block (right) and circuit schematic for each channel amplifier (below). A photo of a 32 channel test chip is shown below. The circuit footprint is 90x500  $\mu\text{m}$  per channel.



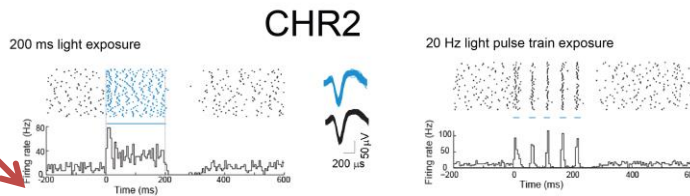
### Acknowledgments

E.S.B. acknowledges funding by Benesse Foundation; Jerry and Marge Burnett; DARPA Living Foundries Program; Department of Defense CDMRP PTSD Program; Google; Harvard/MIT Joint Grants Program in Basic Neuroscience; Human Frontiers Science Program; E.T.A. F. Harvey Prize; Lincoln Labs Campus Collaboration Award; MIT Alumni Club; MIT Intelligence Initiative; MIT McGovern Institute and McGovern Institute Neurotechnology (MINT) Program; MIT Media Lab and Media Lab Consortia (including State Farm and A2Z (Amazon)); MIT Mind-Machine Project; MIT Neurotechnology Fund (8 its generous donors); NARSAD; New York Stem Cell Foundation-Robertson Investigator Award; NIH Director's New Innovator Award (1EP20002020); NIH EUREKA Award (1R01NS075421), NIH Transformative R01 1R01GM104948-01, and NIH Grants 1R01DA029639, 1R4NS070453, 1RC2DE020919, 1RC1MH088182, and 1R01NS067199; NSF CAREER Award (CBET 1053233) and NSF Grants: EFR0835878, DMS0848804, and DMS1041234 (the Cognitive Rhythms Collaborative); Office of the Assistant Secretary of Defense for Research and Engineering; Paul Allen Distinguished Investigator in Neuroscience Award; SKTech; Alfred P. Sloan Foundation; Society for Neuroscience Research Award for Innovation in Neuroscience (RANI); Synthetic Intelligence Project; Wallace H. Coulter Foundation.

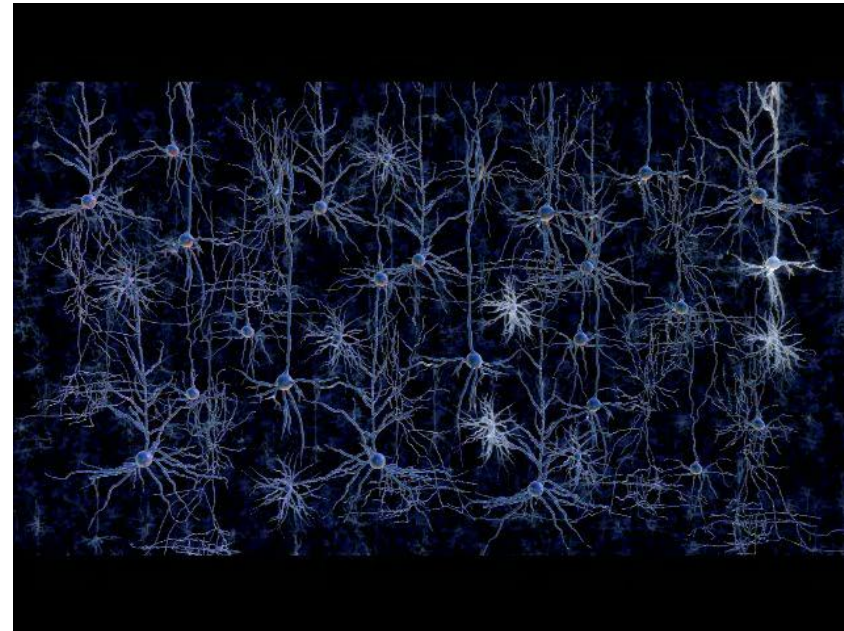
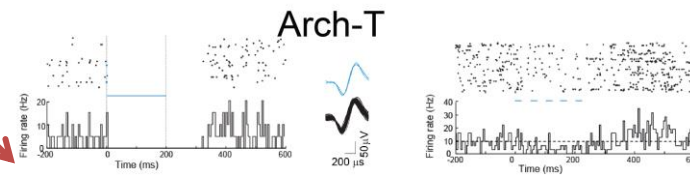
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# Playing with the source code: Using light to modulate neural with high specificity

activate



silence



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Boyden-Desimone

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Source: Han, Xue, Xiaofeng Qian, Jacob G. Bernstein, Hui-hui Zhou, Giovanni Talei Franzesi, Patrick Stern, Roderick T. Bronson, Ann M. Graybiel, Robert Desimone, and Edward S. Boyden. "Millisecond-timescale optical control of neural dynamics in the nonhuman primate brain." *Neuron* 62, no. 2 (2009): 191-198.

# Biological codes to computational codes

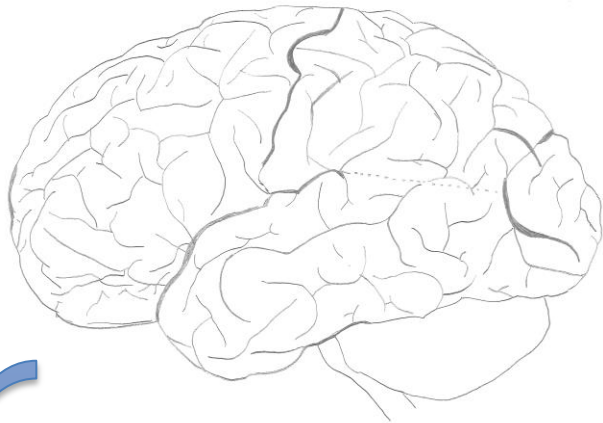
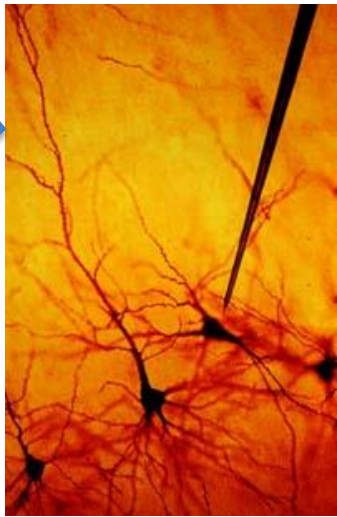
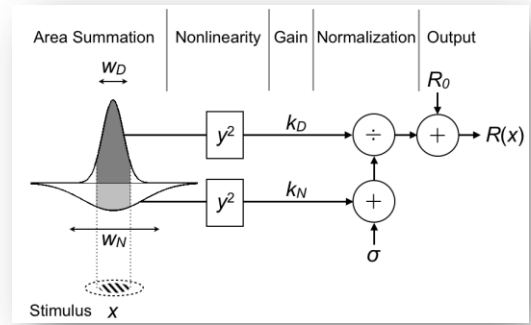
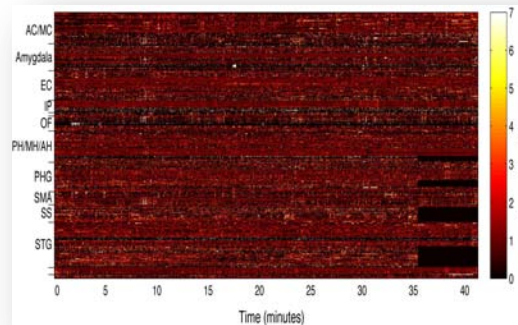


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**Biological  
code**

**Computer  
code**



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