DONDERS INSTITUTE

How to measure information transfer in the brain?

Neural dynamics and deep learning
UvA

December 3rd, 2024

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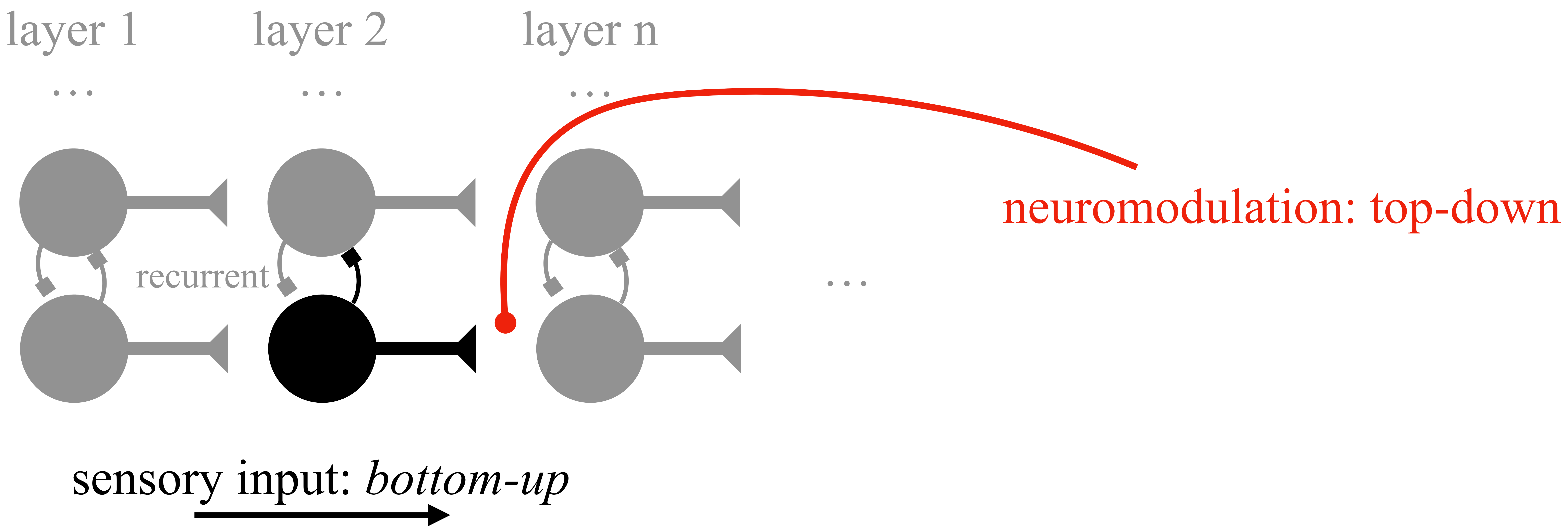
Radboud University Radboudumc


Buff

Perception is an active process

Brain continually adapts (unlike computers)

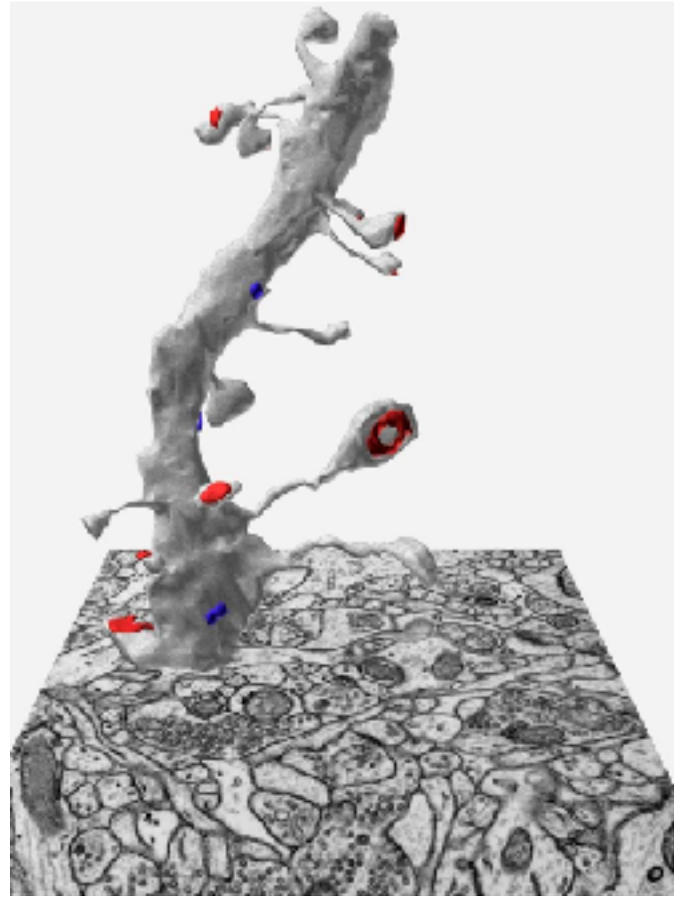
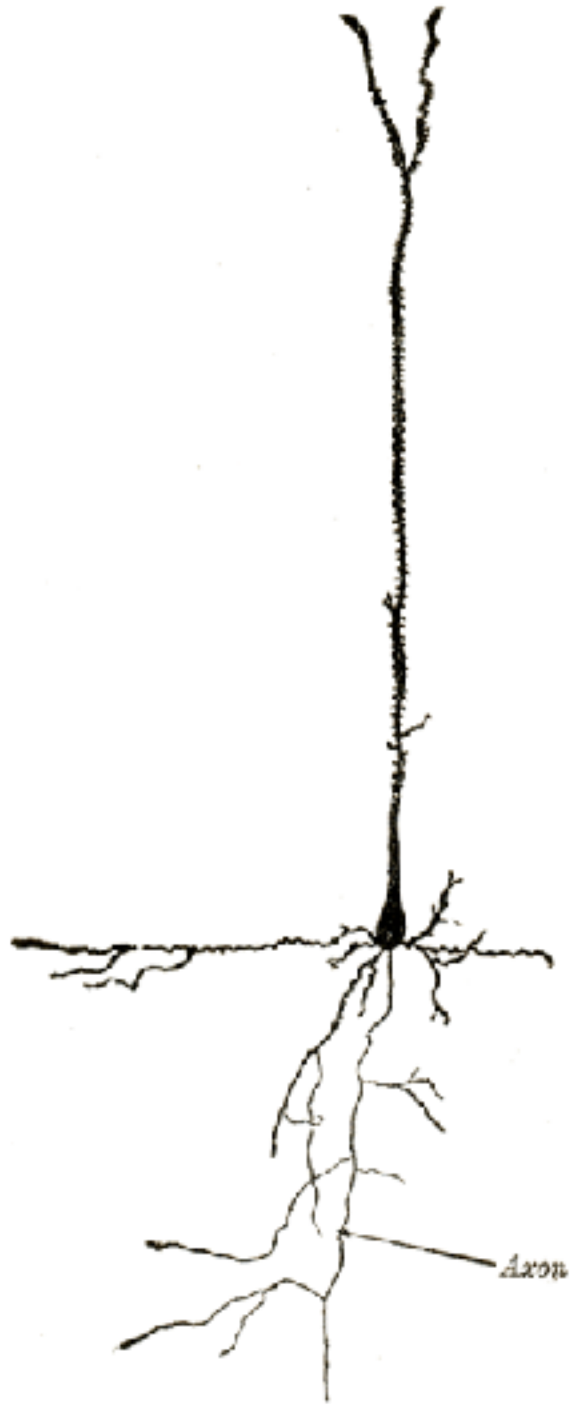
How does the brain adapt?

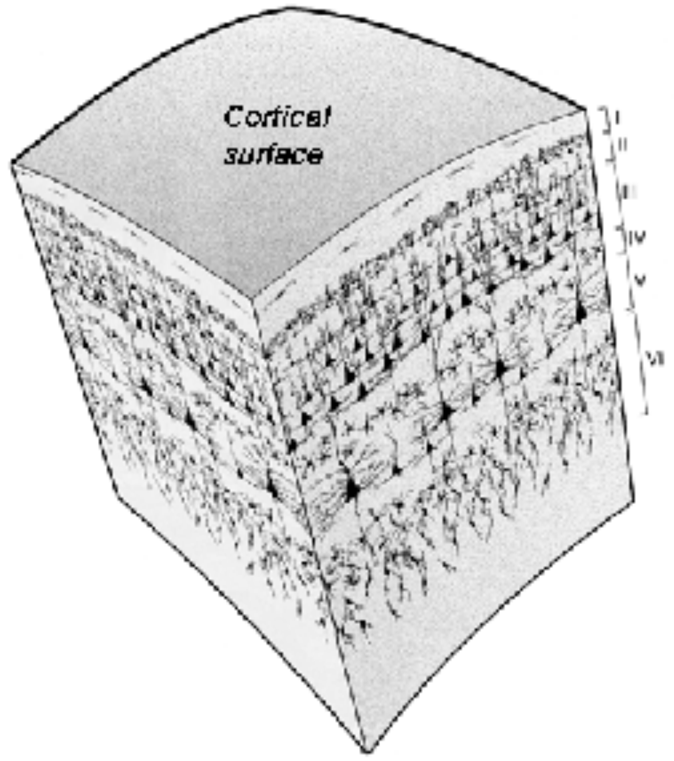


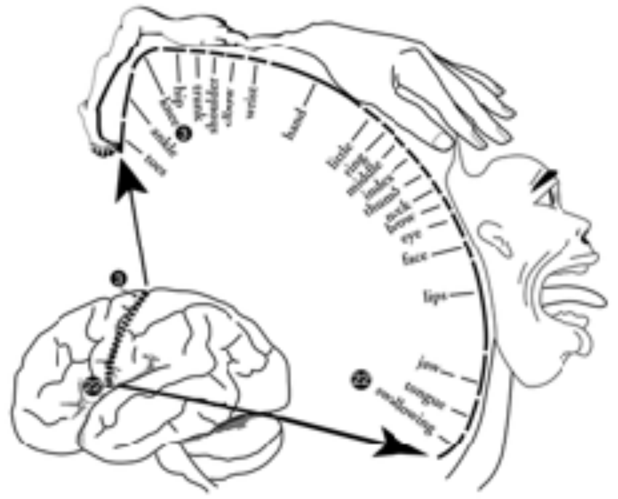
How and why do neuromodulators influence sensory processing?
→ Computational modelling

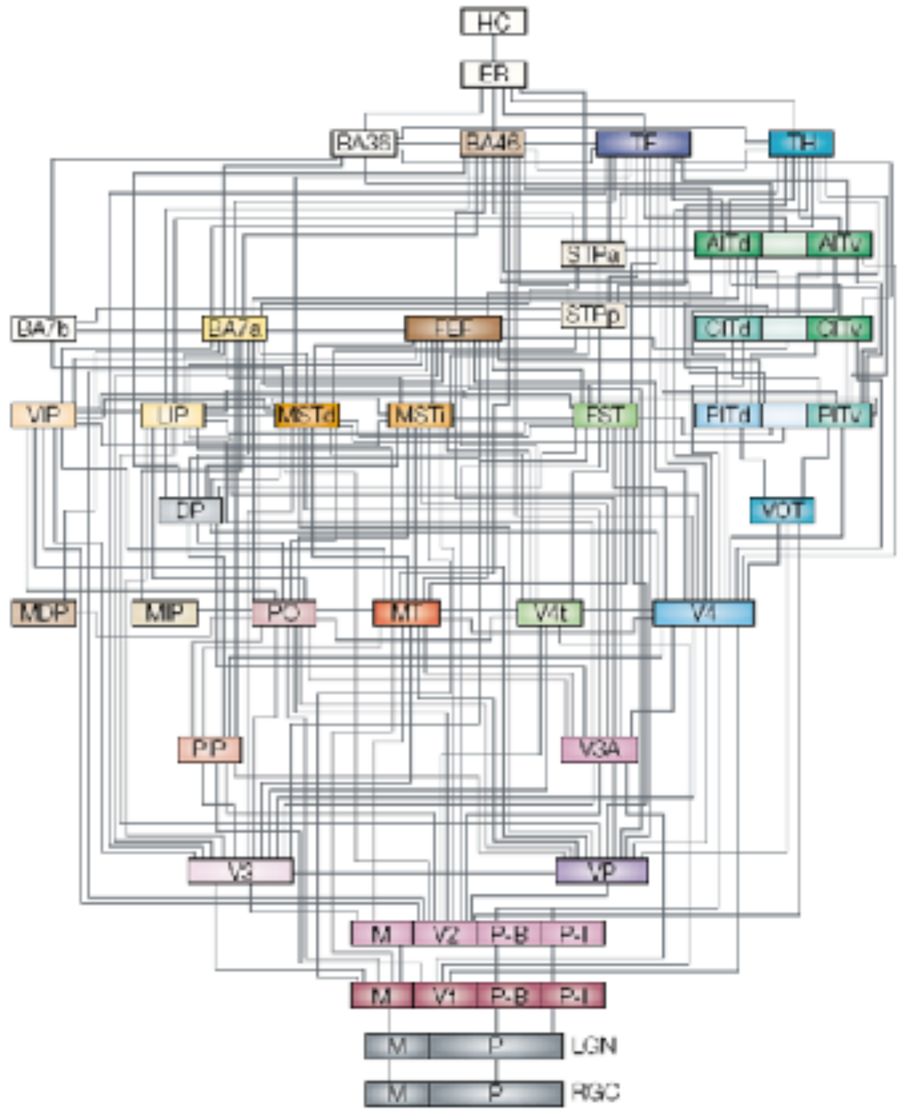
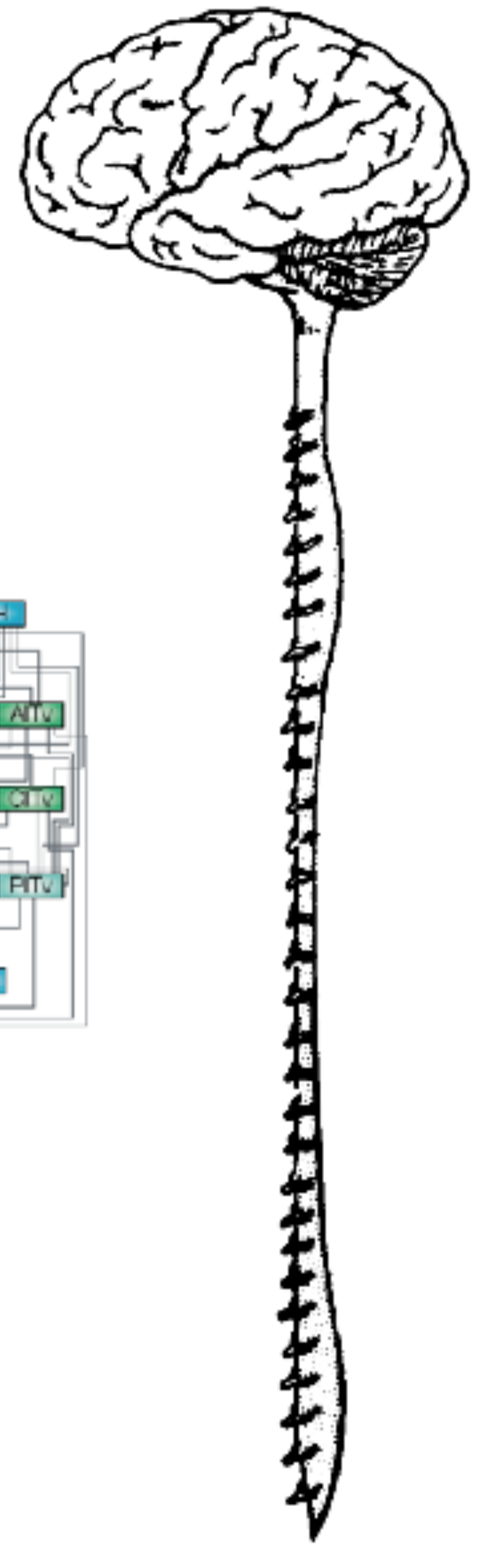
Neural mechanisms of sensorimotor control

Molecules	Synapses	Neurons	Networks	Maps	Systems	CNS
1Å	1μm	100 μm	1 mm	1 cm	10 cm	1 m





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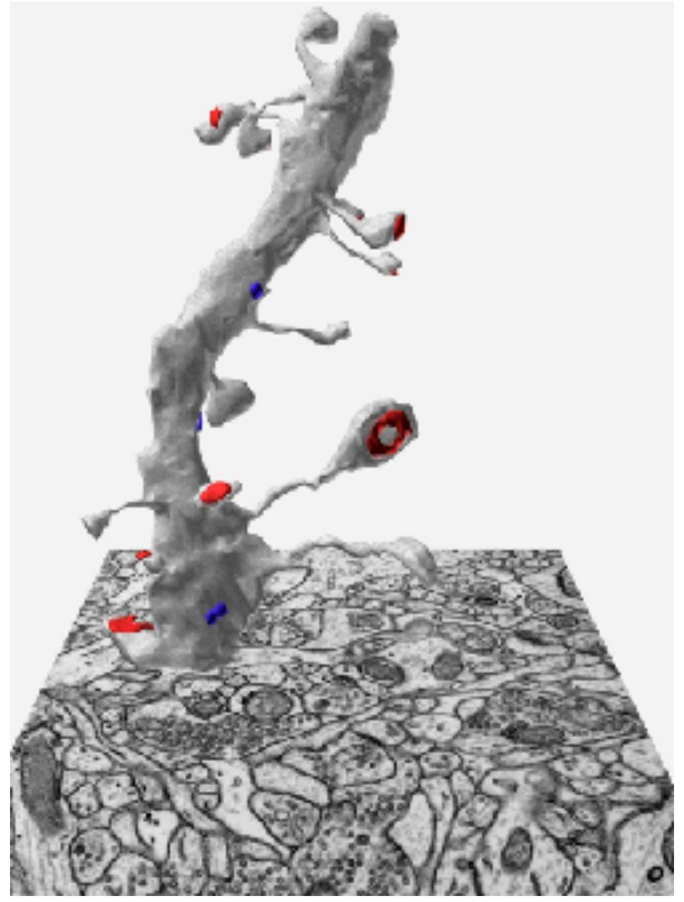

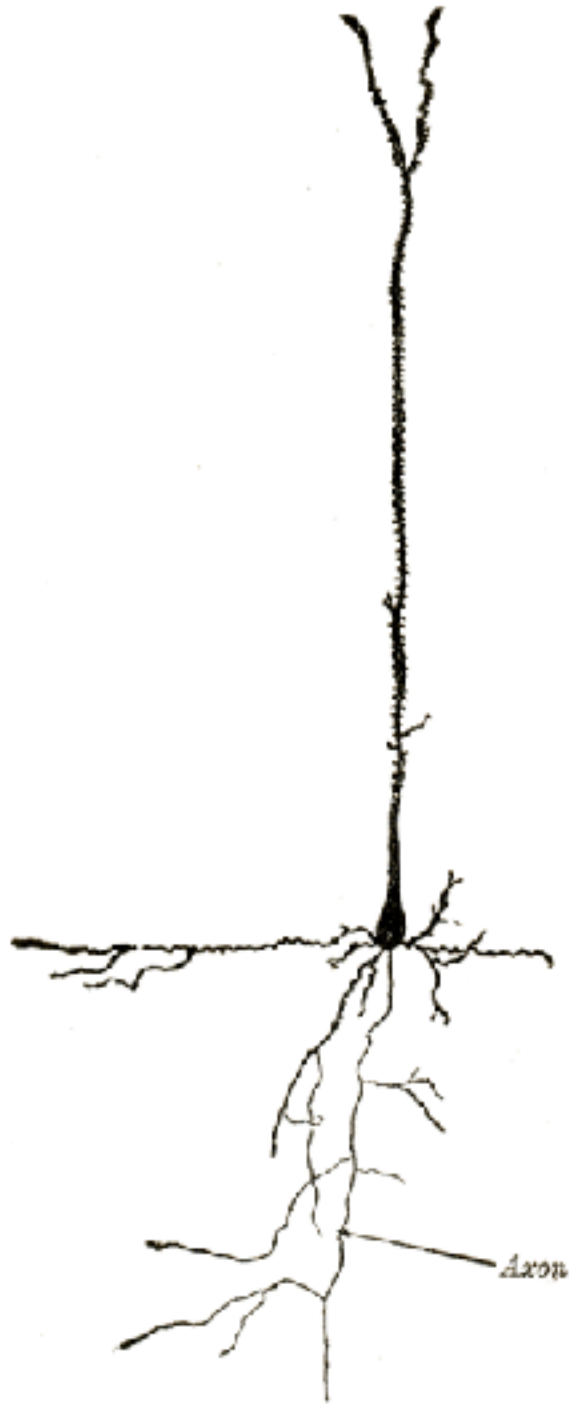

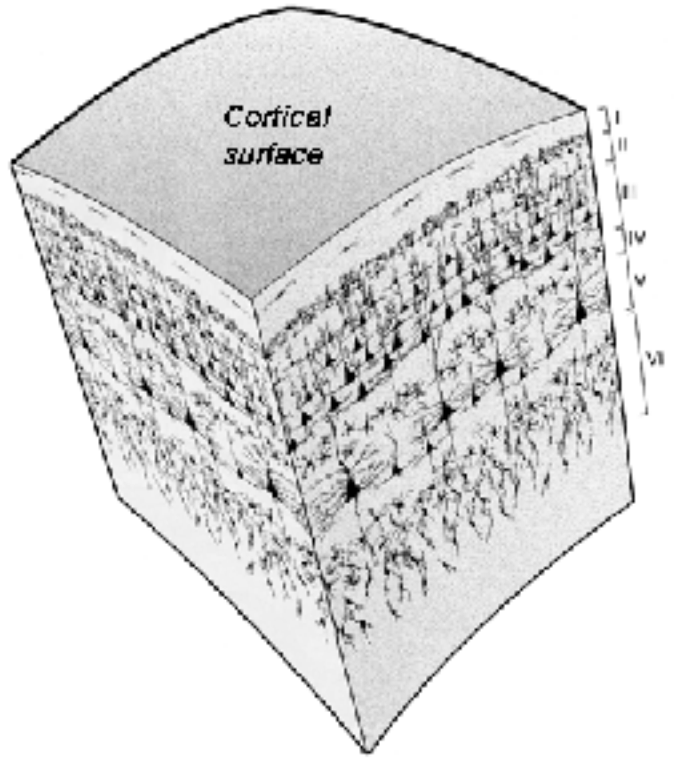

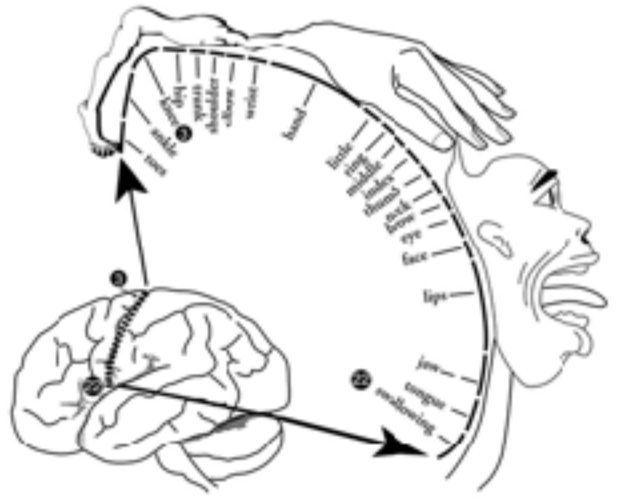

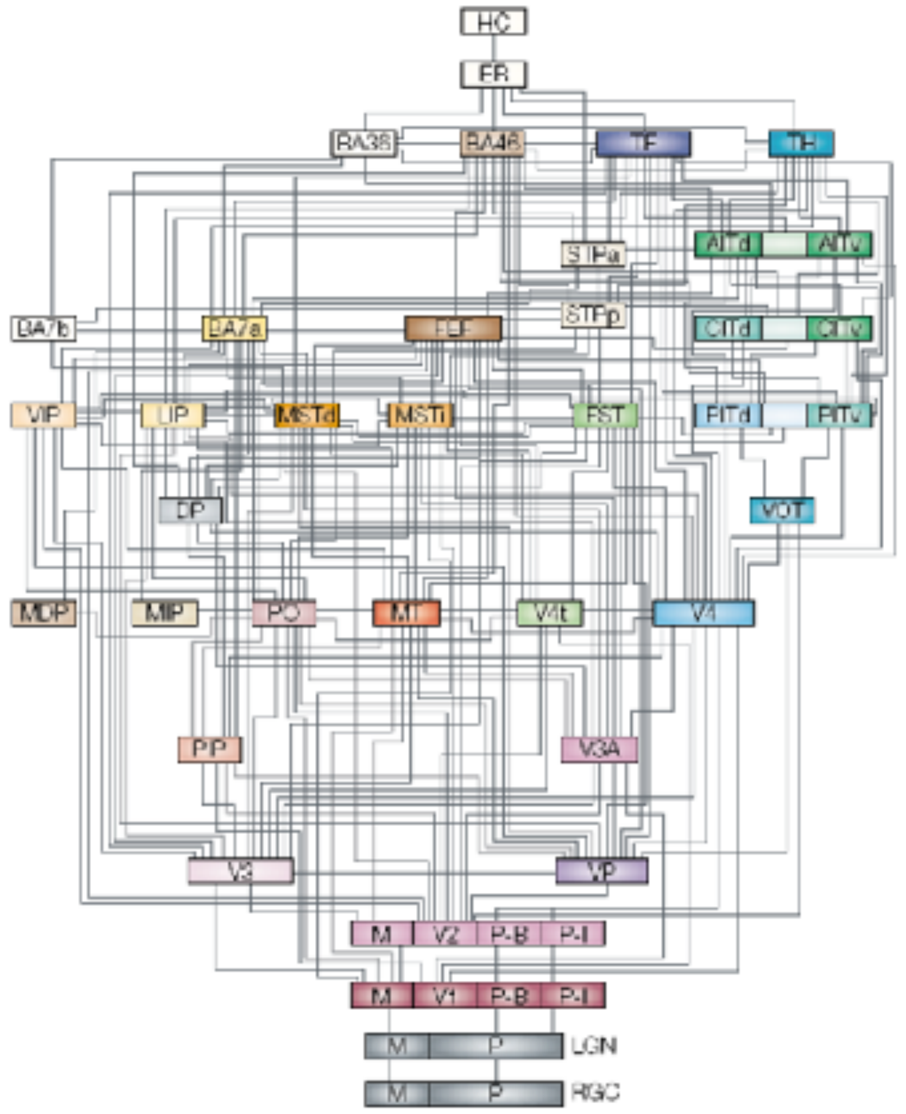

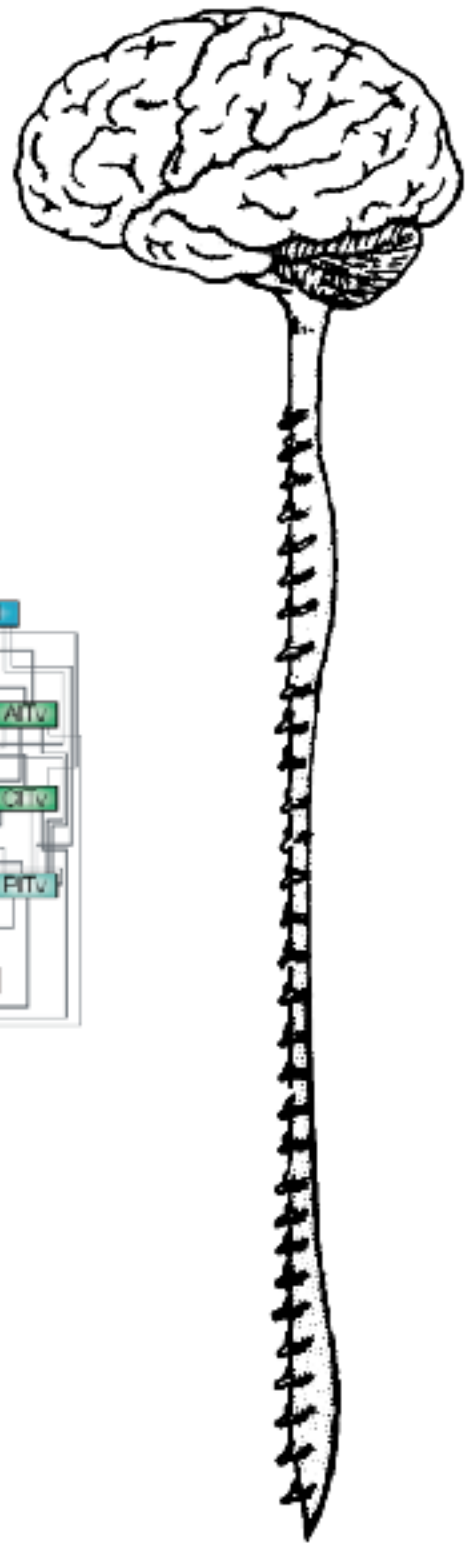

Physical properties ⇔ Computation

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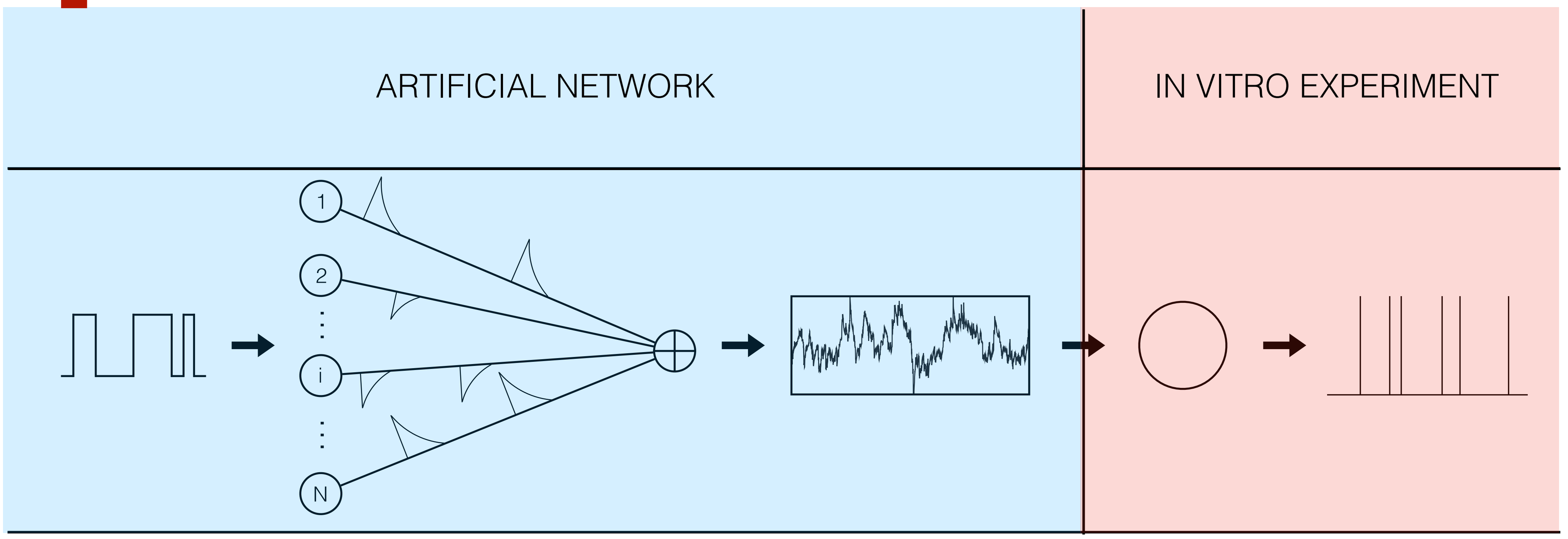
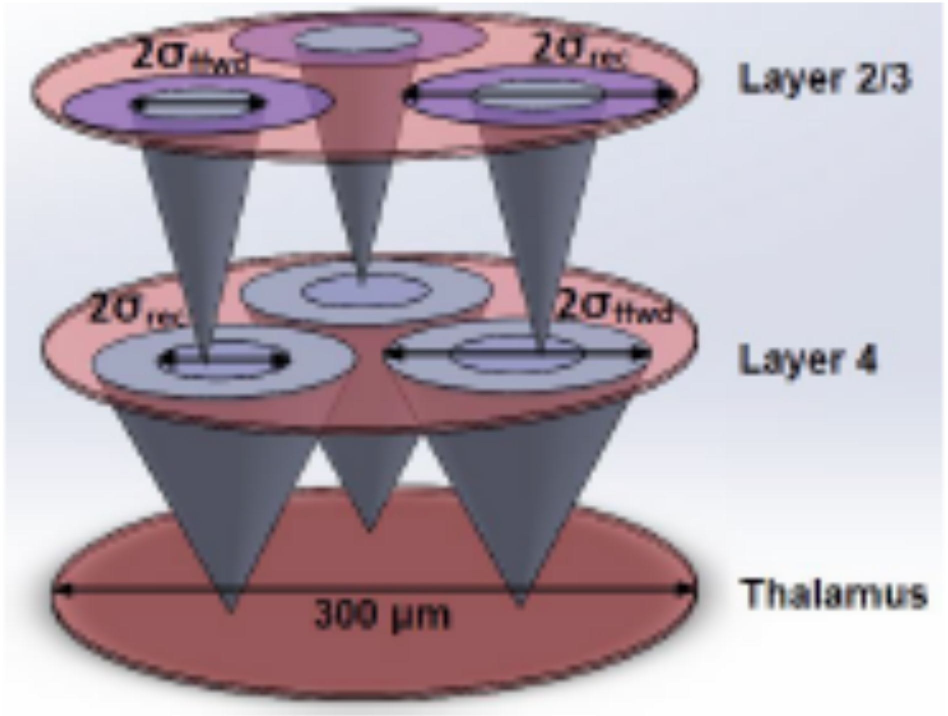
Molecules	Synapses	Neurons	Networks	Maps	Systems	Behaviour

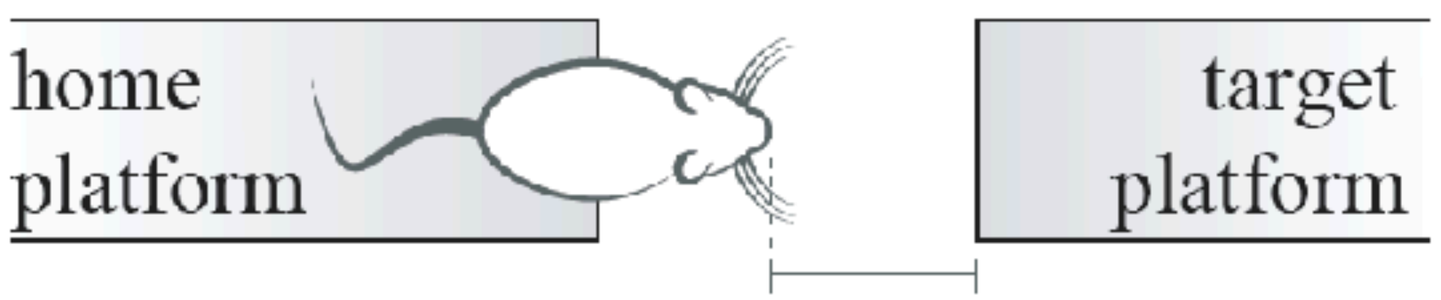
1 Advanced (information) methods / analysis



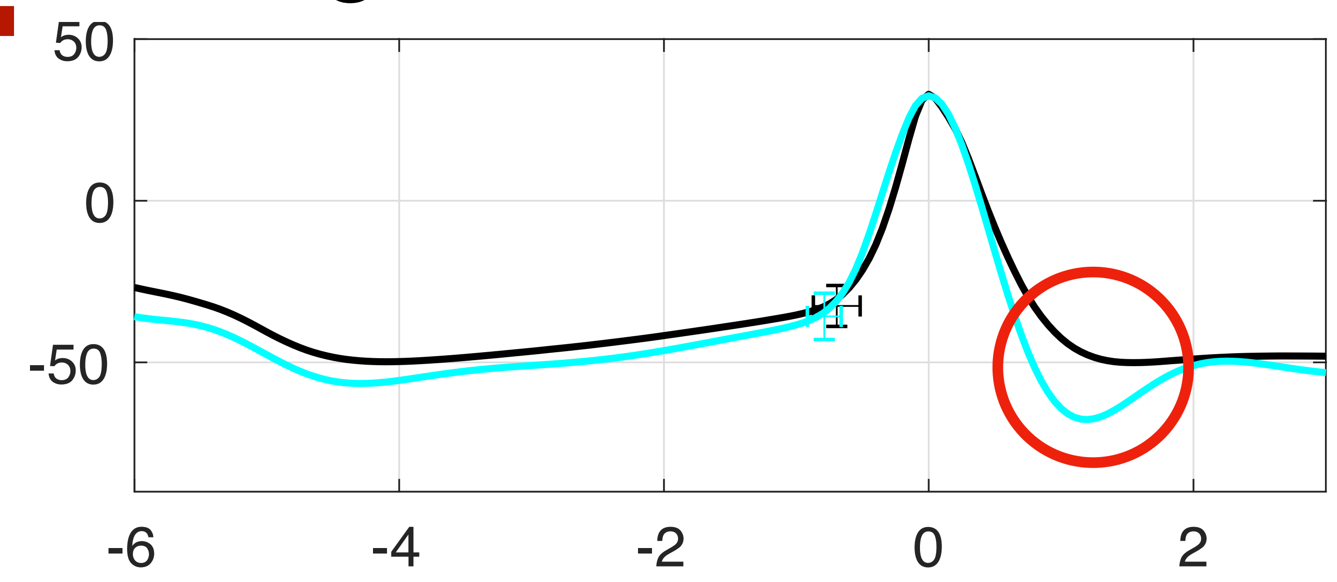
3 Biophysical network models



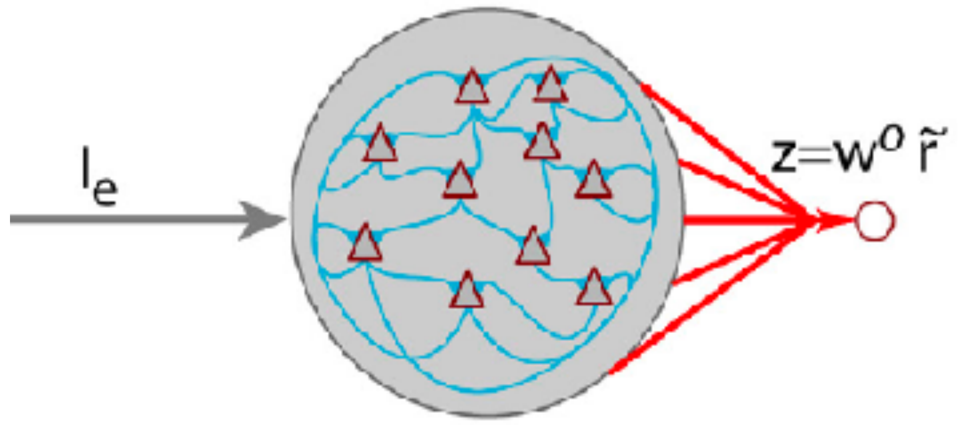
5 Behavioural data



2 Single neuron models



4 Coding models



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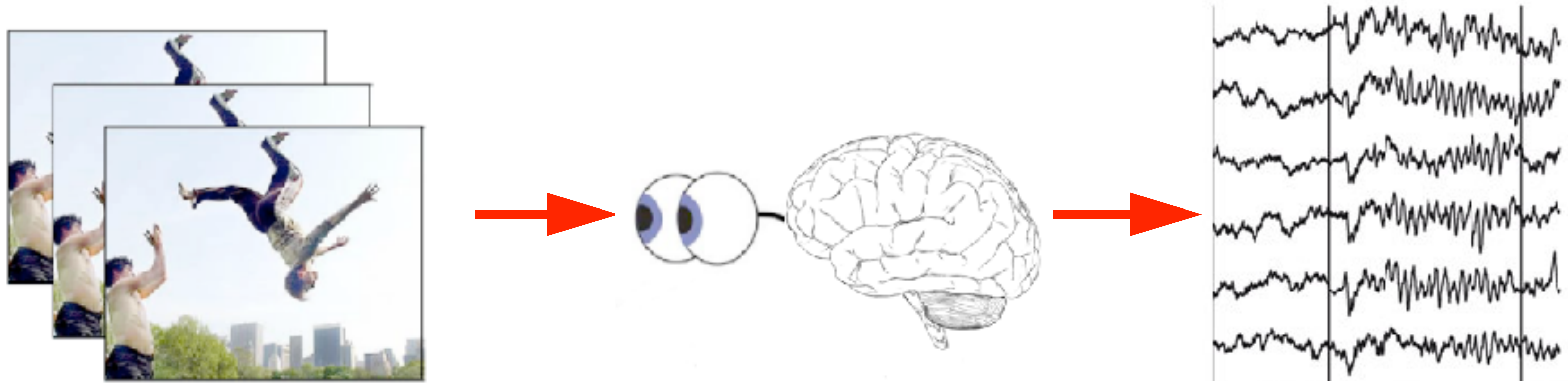
Neural coding

There is a relation between the world, neural activity, our behaviour and perception.

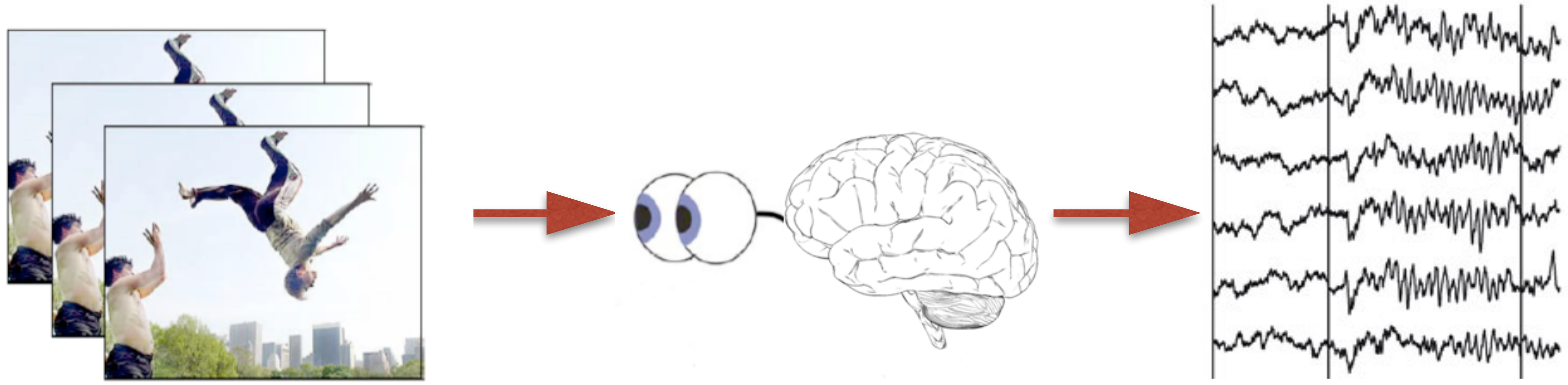
What is this relation? **Neural coding**

Representations: how are the things we perceive represented by neural activity?

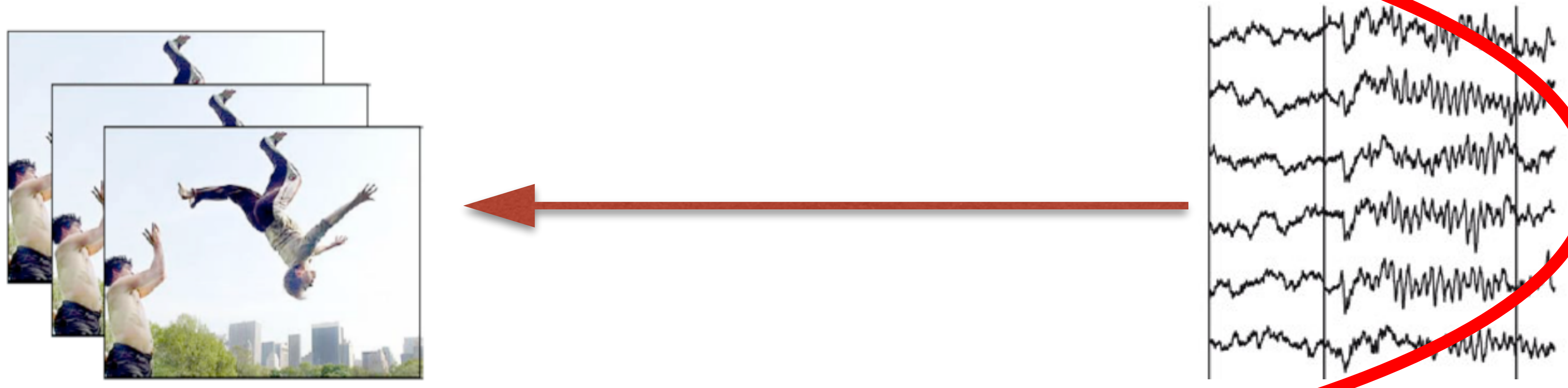


Encoding and decoding

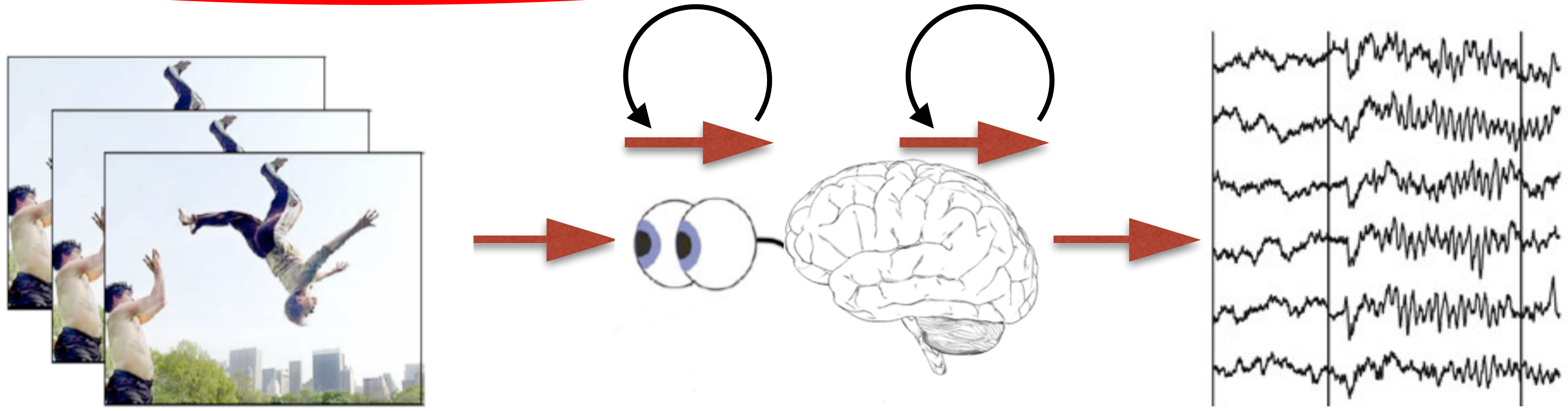
encoding: how does the brain generate activity in response to stimuli?



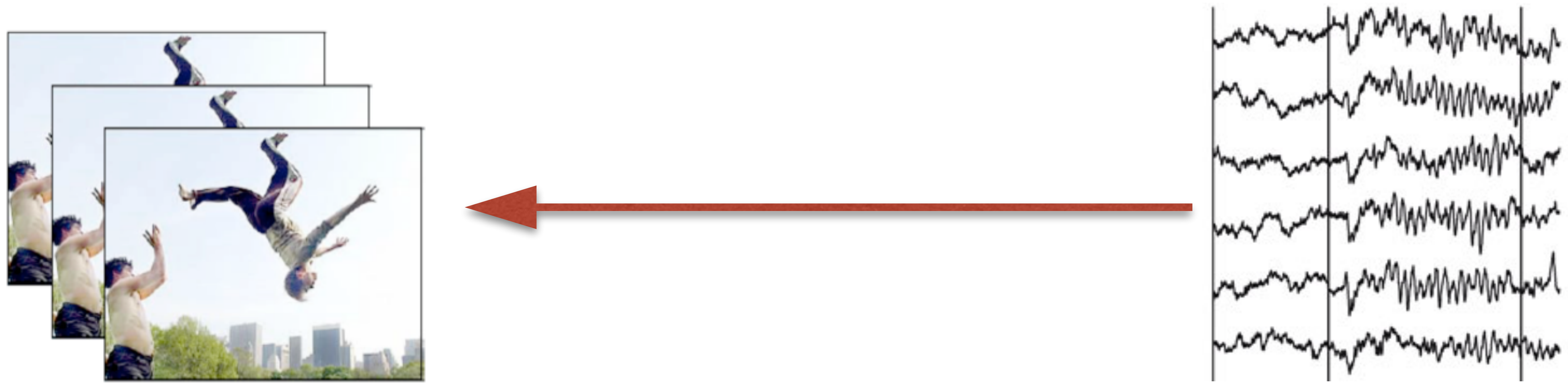
decoding: what does the neural activity tell me about the stimulus?



of course both happen in the brain!



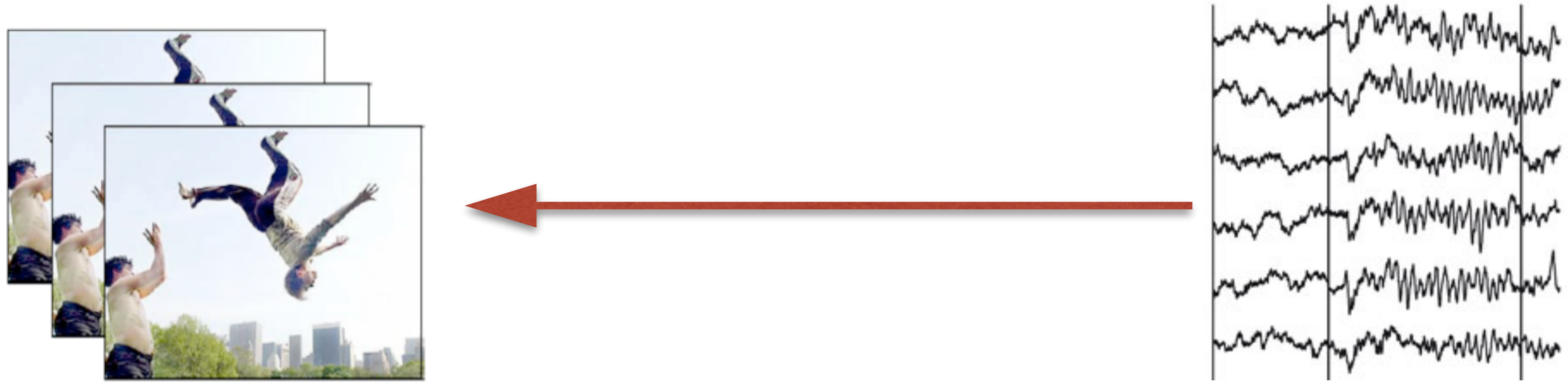
Information transfer



Decoding: what does the neural activity tell me about the stimulus?

- *What* information is encoded by the brain (and what information is discarded)
- *How much* information is transferred (or lost).
    - *How well* can we reconstruct a stimulus from neural activity?
    - What is the relation biophysics ↔ information?

Information transfer



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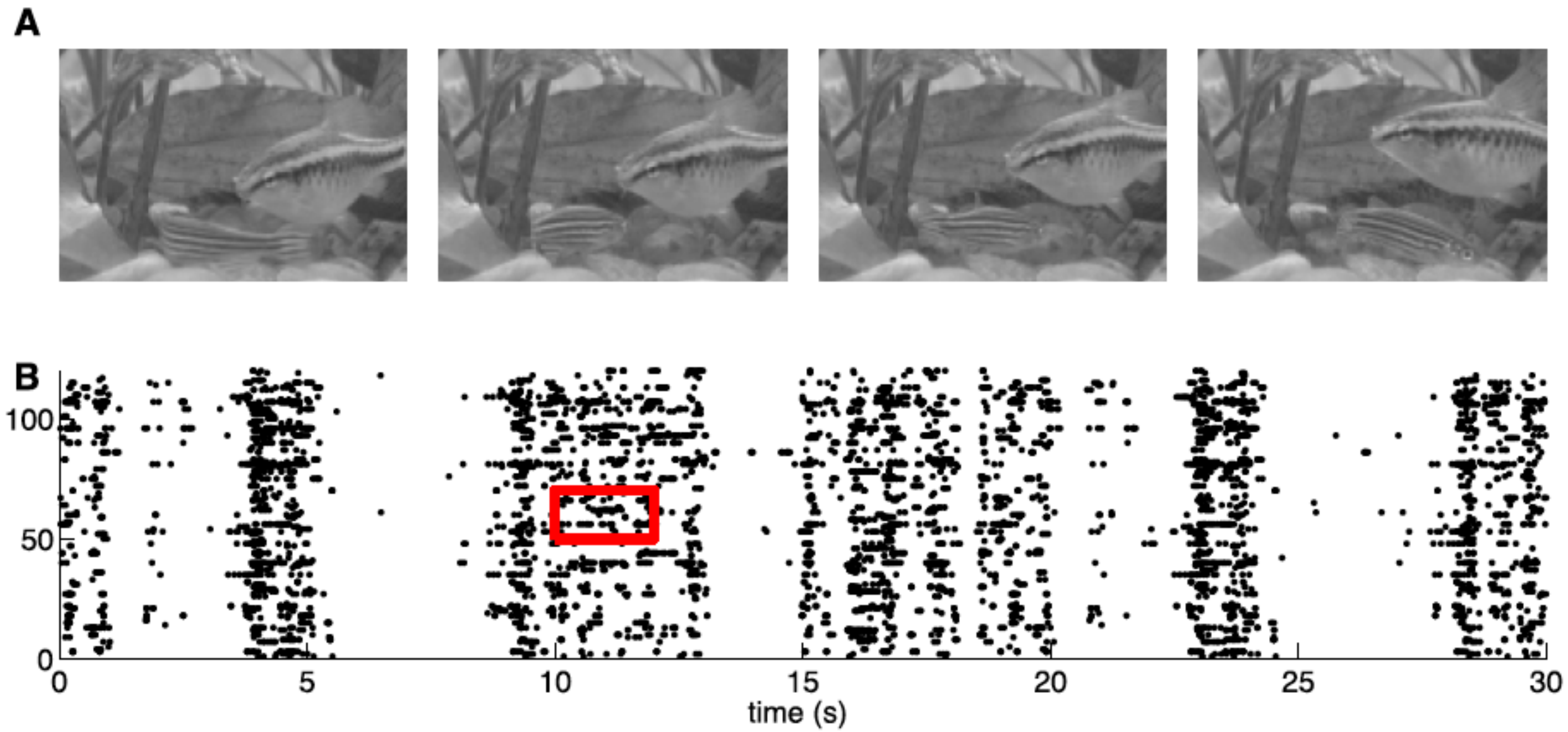
Example experiment

Retinal (salamander) recordings on a MEA, showing natural movie

How much information does the neural activity give me about the input?

How does one quantify this?



Tkačik et al., PLoS Comp Bio, 2014

Information theory

How to quantify information?

What is 1 bit ?

Mathematical language: probabilities

All based on work of Claude Shannon

https://aeon.co/videos/the-father-of-information-theory-claude-shannon-brought-us-our-digital-world

Today

- Lecture 1: Introduction information theory
  - Entropy
  - Information
- Lecture 2: How to measure information in single neurons and what do we know about the network level?

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Entropy

If I throw a die, how surprising is a 6?

Depends on

- number of sides of the die
- probability of a 6

Entropy = ‘surprise’, ‘uncertainty'

How to quantify surprise?

Entropy: possible information

quantify ‘surprise’ S:

1. S is **positive**

2. S **decreases** with likelihood: S(P(x)) is a decreasing function; S(1) = 0

3. **summation**: for two ***independent*** events the surprise is the sum of the two surprises: S(P(x)*P(y)) = S(P(x))+S(P(y))

Only the log function follows all three rules!

$$S(P[x]) = S(X) = -\sum_x P(x) \log_2 P(x)$$

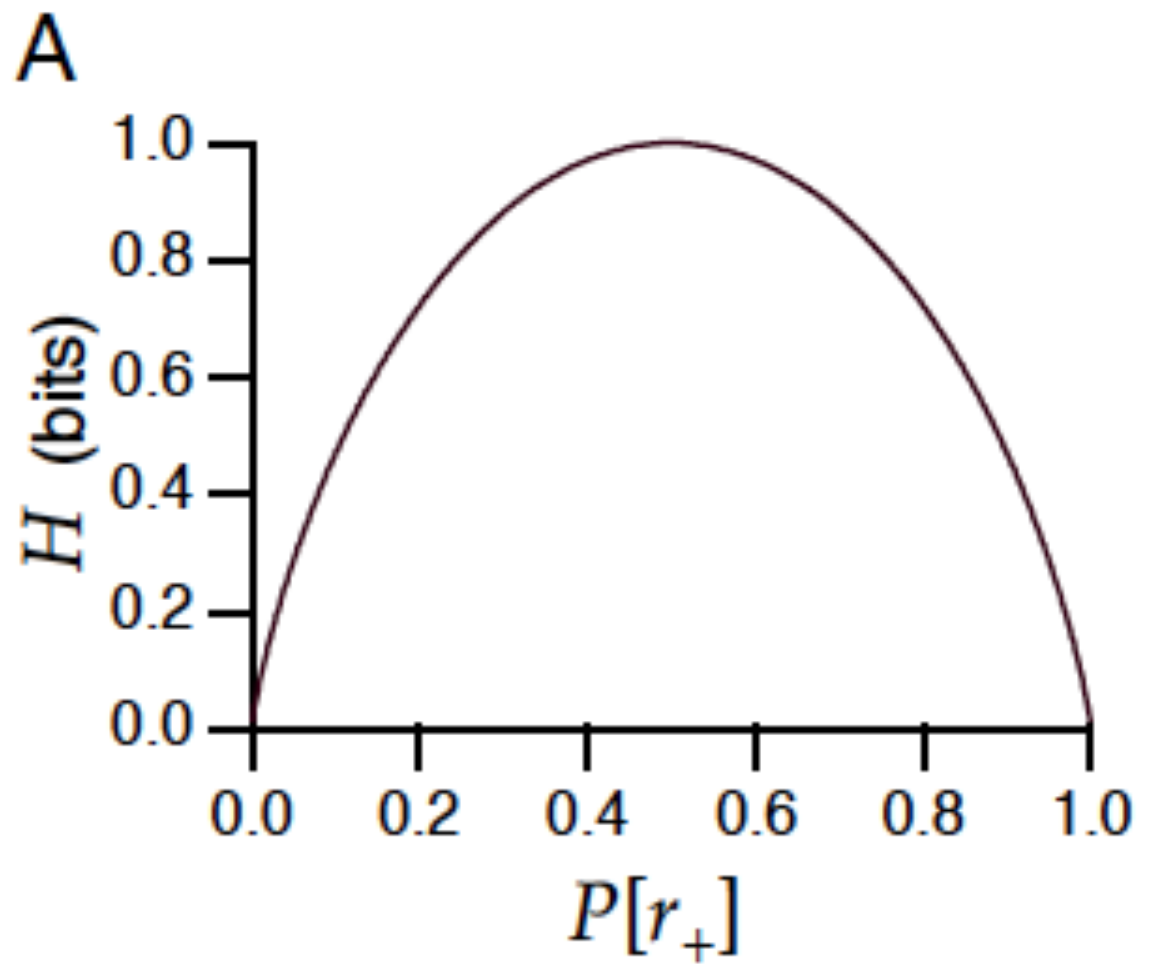
Entropy: example

Coin toss

Entropy S = -(P(heads) $\log_2$ P(heads) + P(tails) $\log_2$ P(tails))

Entropy S = -(P(heads) $\log_2$ P(heads) + (1-P(heads)) $\log_2$ (1-P(heads))) = 1 bit

What if I change the probability P(heads)?



Entropy maximal if P(heads) = P(tails) = 0.5

$$S(P[x]) = S(X) = -\sum_x P(x) \log_2 P(x)$$

Image: Dayan&Abbott, 2001

Entropy: example

Dice

1 die:

- P(each number) = 1/6
- S = -6*(1/6 * $\log_2$ 1/6) = -$\log_2$ 1/6 = 2,6 bit

2 dice, independent

- P(each combination) = 1/36
- S = -36*(1/36 * $\log_2$ 1/36) = -$\log_2$ 1/36 = 5,2 bit

- Conclusion: two dice have more entropy than one

$$S(P[x]) = S(X) = -\sum_x P(x) \log_2 P(x)$$

Entropy: example

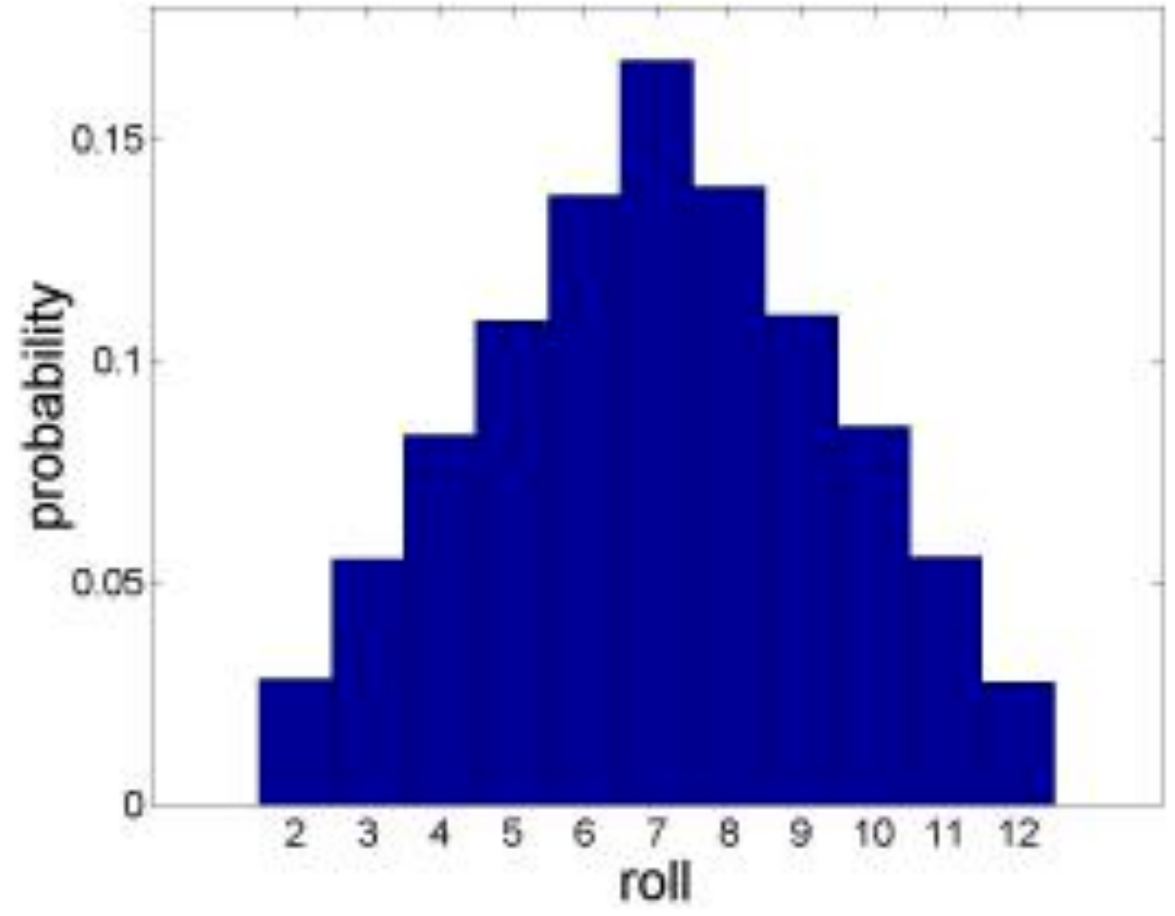
Horse race

Storm as a chance of 1/4 to win, Thunderbolt too, Speedy 1/2. What is the entropy?

- $S = -1/4 * \log_2 1/4 - 1/4 * \log_2 1/4 - 1/2 * \log_2 1/2 =$
  $-1/2 (\log_2 1/4 + \log_2 1/2) = 1{,}5$ bit

2 dice, sum

- 36 possible combinations, sum = 2,3, …,12
- probability sum equals 2 is 1/36, sum=3 is 2/36, etc
- so $S = -6/36 * \log_2 6/36$
  $-2(1/36 * \log_2 1/36 + \ldots)$
  $= 3{,}3$ bit



Which one has the highest entropy?

Entropy and information

Entropy: ‘number of possibilities’, ‘uncertainty’, ‘possible’ information, ‘surprise’

- a die with 20 sides has a higher entropy than a die with 6 sides
- A ‘fair’ coin toss has a higher entropy than an ‘unfair’ one
- Entropy measures the variability of the input or output

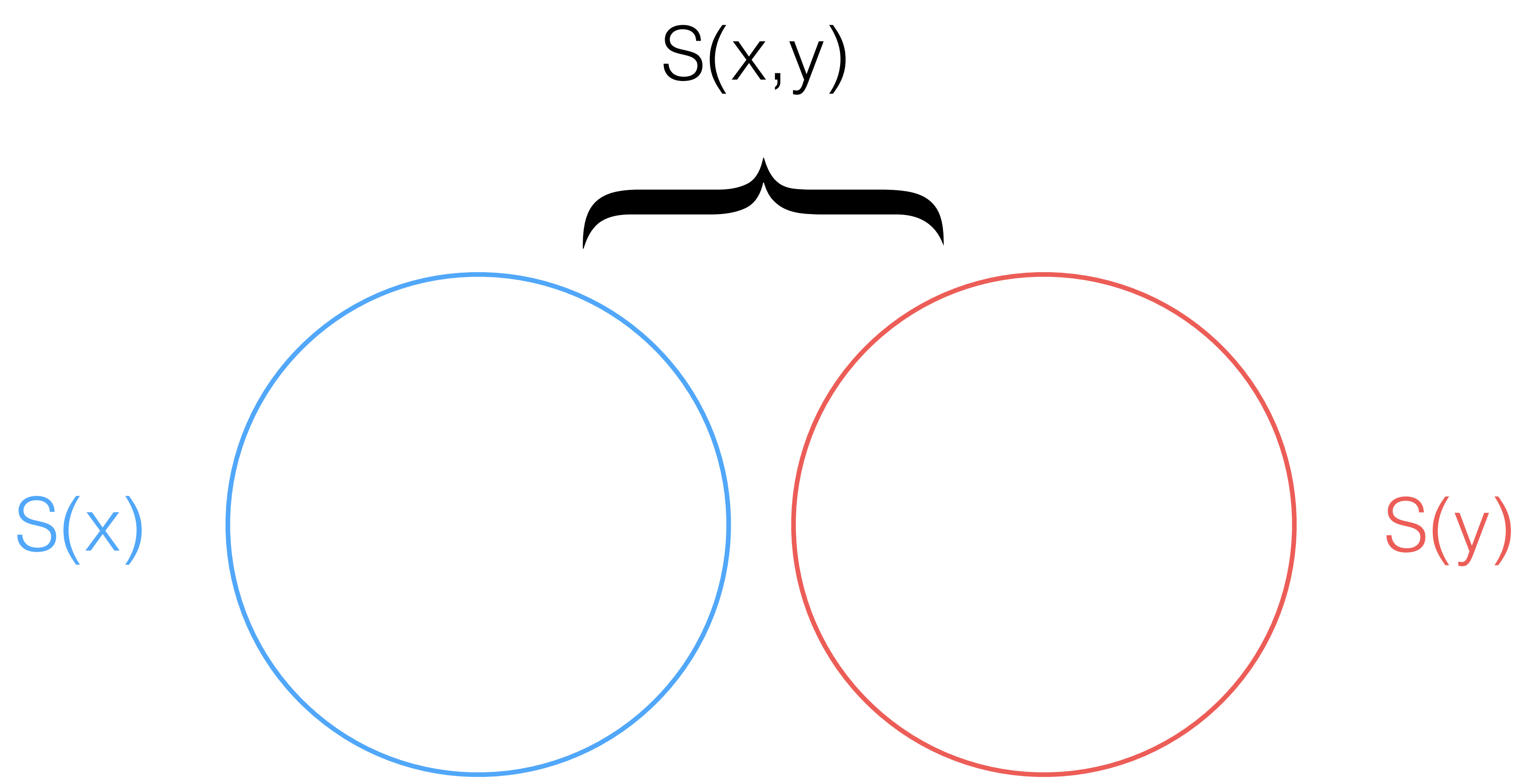
$$S(P[x]) = S(X) = -\sum_x P(x) \log_2 P(x)$$

- So what is information?

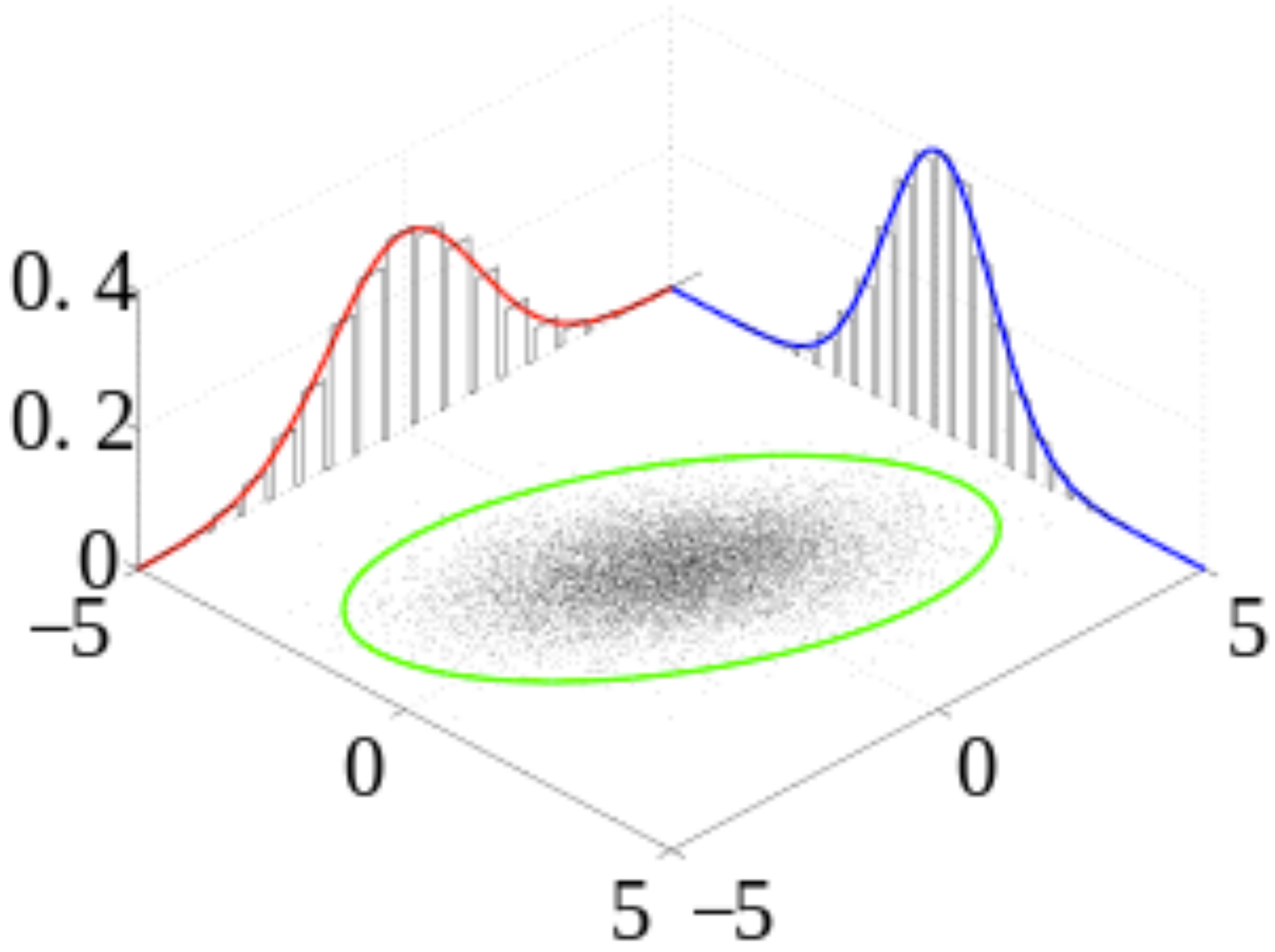
Joint Entropy

Joint Entropy: Entropy of two variables

- Independent variables: sum $S(x,y) = S(x) + S(y)$



Joint Probability Distribution



Joint Entropy

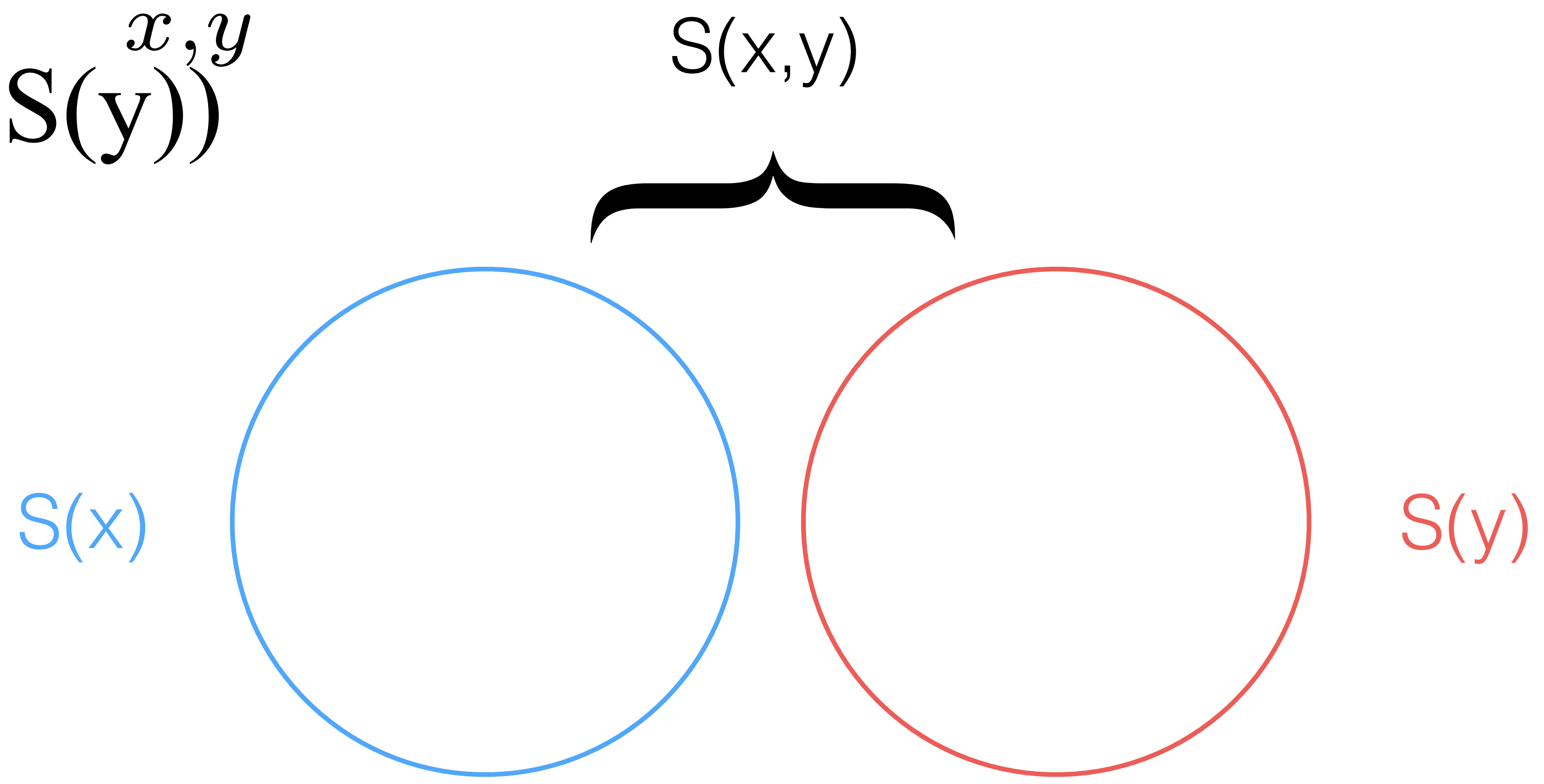
Joint Entropy: Entropy of two variables

- Independent variables: sum S(x,y) = S(x) + S(y)

- Dependent variables: be careful of the ‘overlap’!

$$S(P[x], P[y]) = S(X, Y) = -\sum_{x,y} P(x,y) \log_2 P(x,y)$$

- S(x)+S(y) ≧ S(x,y) ≧ max(S(x), S(y))



Joint Entropy: weather example

In summer, the chance of warm weather is higher on sunny days than on rainy days, so the outside temperature and rain/sun are not independent

Suppose: P(sun, warm) = 1/2; P(sun, cool) = 1/12, P(rain, warm) =1/6, P(rain, cool) = 1/4

P(sun) = 1/2+1/12 = 7/12; P(rain) = 1/6+1/4 = 5/12
S(weather) = -7/12 * $\log_2$ (7/12) - 5/12 * $\log_2$ (5/12) = 0,98 bit

P(warm) = 1/2+1/6 = 2/3; P(cool) = 1/12+1/4 = 1/3
S(temperature) = -2/3 * $\log_2$ (2/3) - 1/3 * $\log_2$ (1/3) = 0,92 bit

The joint entropy equals
S(weather, temperature) = -1/2 * $\log_2$ (1/2) - 1/12 * $\log_2$ (1/12) - 1/6 * $\log_2$ (1/6) - 1/4 * $\log_2$ (1/4) = 1,7 bit

So S(weather)+S(temperature) ≧ S(weather, temperature)

Conditional Entropy

What if I know one of the variables?

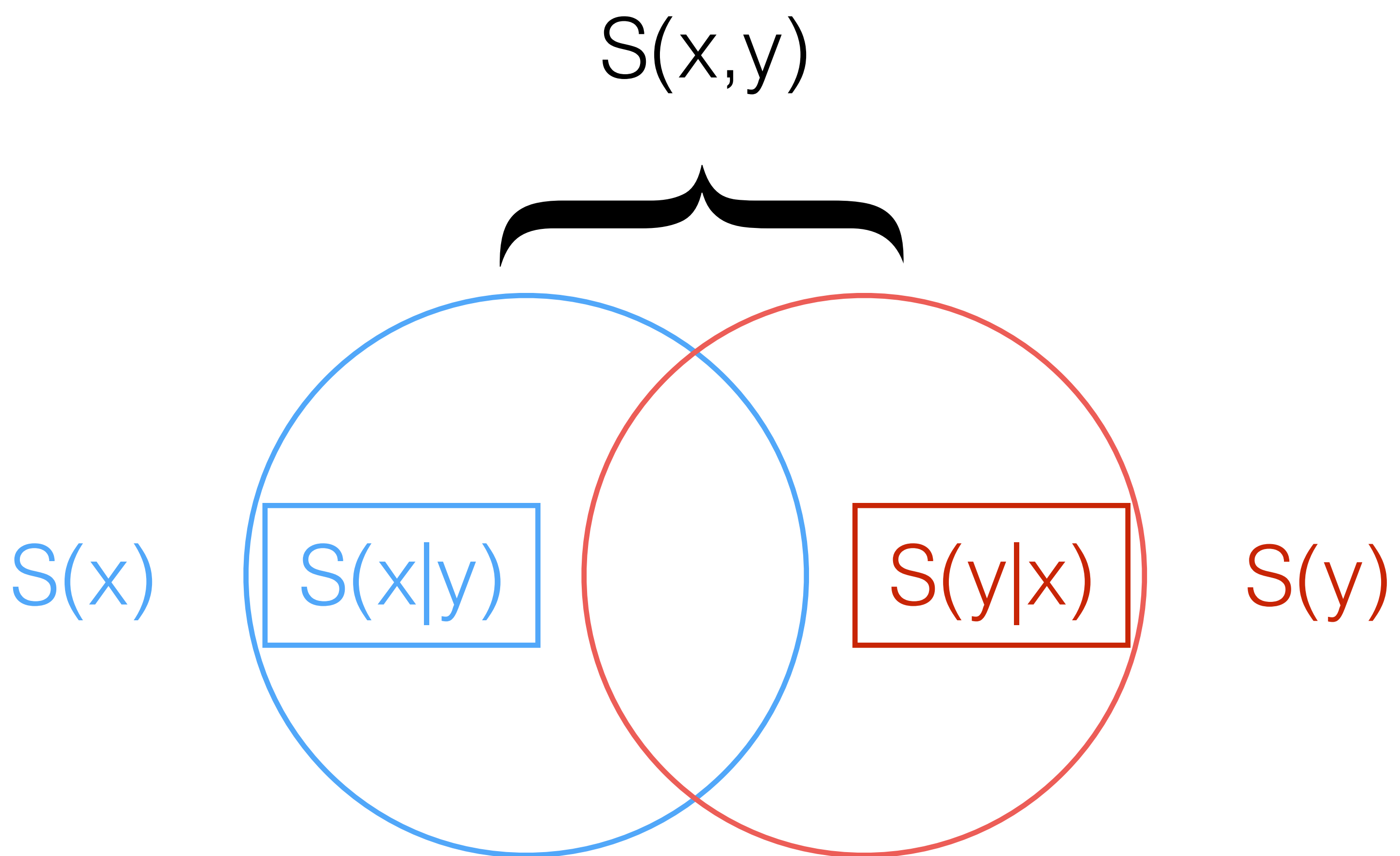
Examples:

- What is the entropy of the temperature if I know it is sunny?
- What is the entropy of the response if I know the input?

$$S(X|Y) = -\sum_{x,y} P(y)P(x|y)\log_2 P(x|y) = S(X,Y) - S(Y)$$

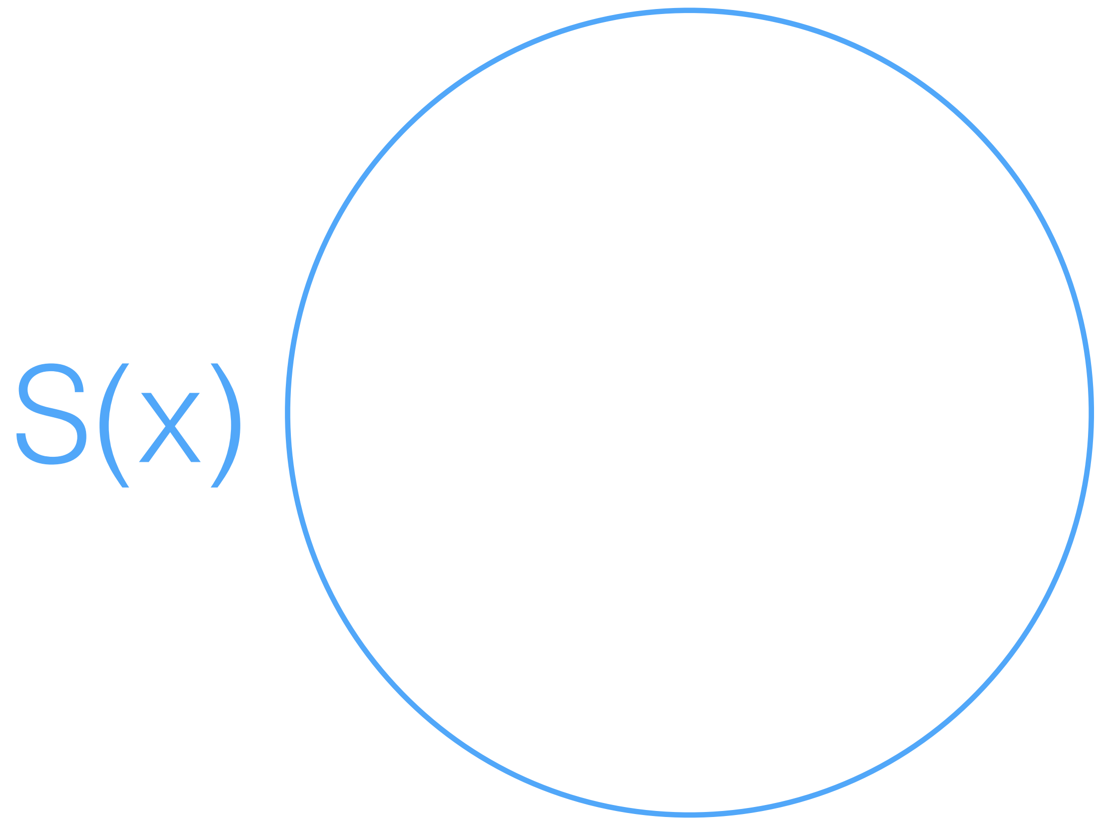
- Also: 'noise entropy' (x=response neuron, y=input): entropy from noise in the system!

- Always smaller than or equal to S(X): reduction of entropy!



Conclusion Entropy

- Entropy = ‘number of possibilities’, ‘uncertainty’, ‘possible’ information, ‘surprise’ → possible information, coding space



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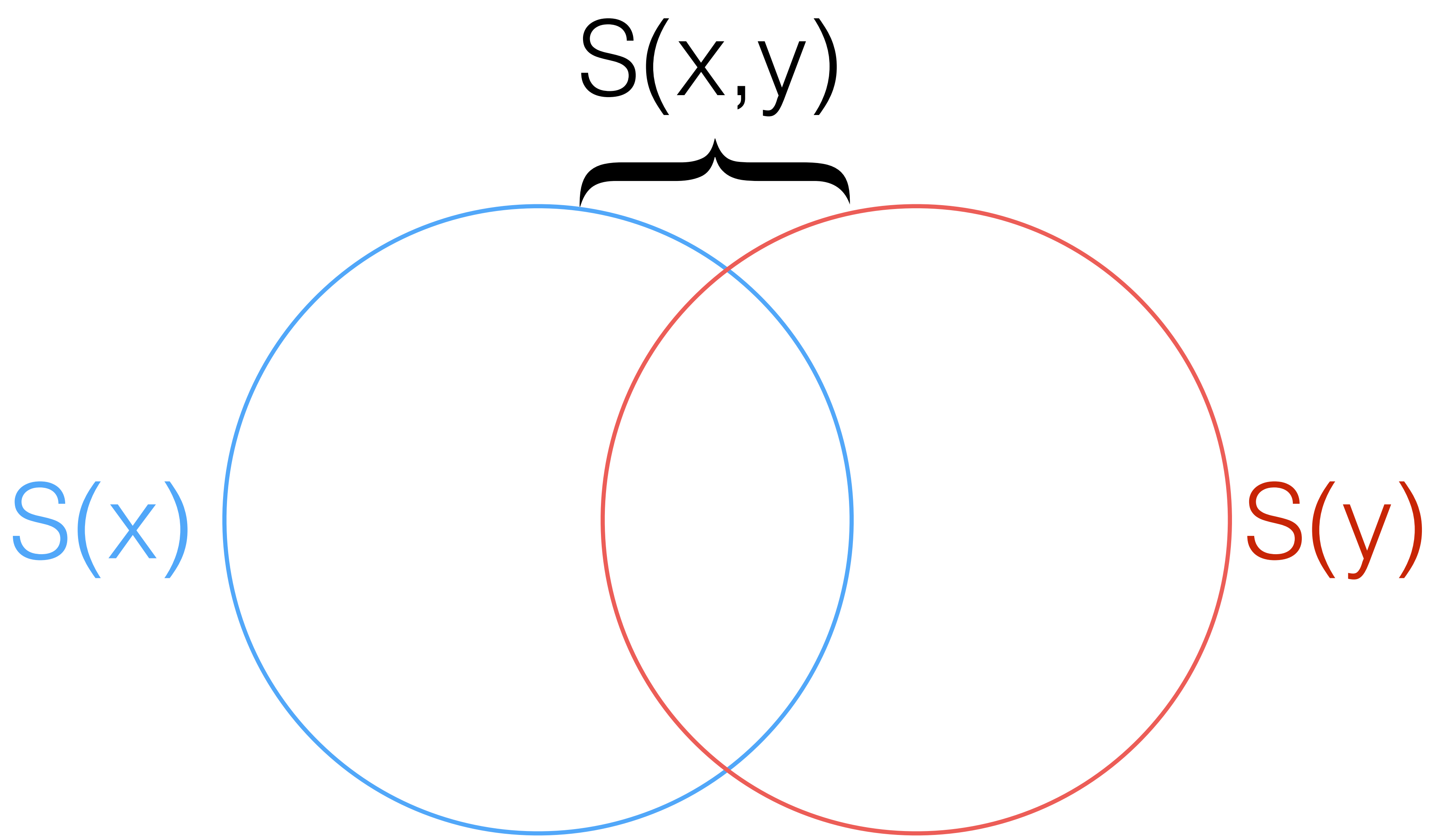
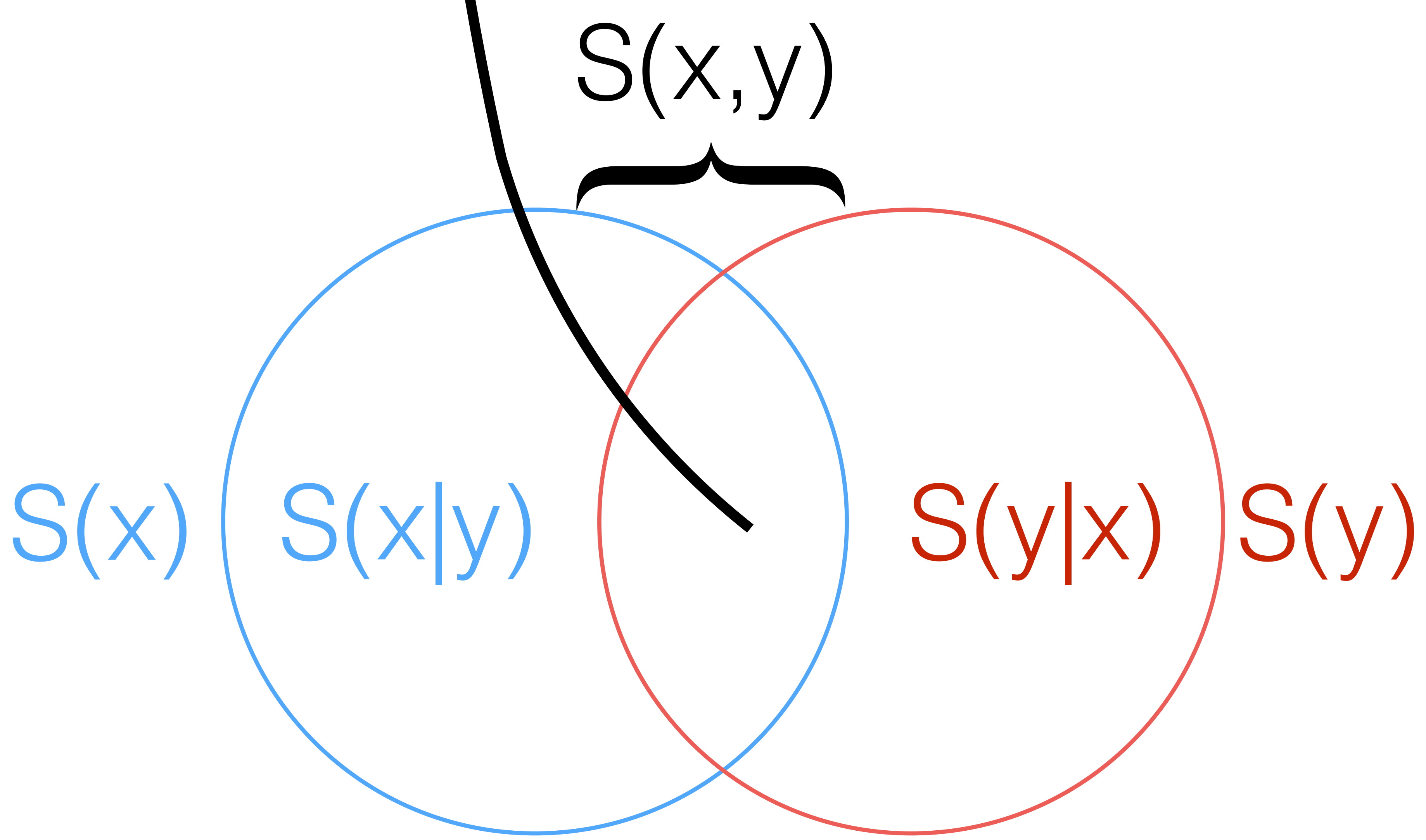


Conclusion Entropy

- Entropy = ‘number of possibilities’, ‘uncertainty’, ‘possible’ information, ‘surprise’ → possible information, coding space
- Joint Entropy = Entropy of two variables
- Conditional Entropy: what if I know one of the variables?

What’s that in the middle?



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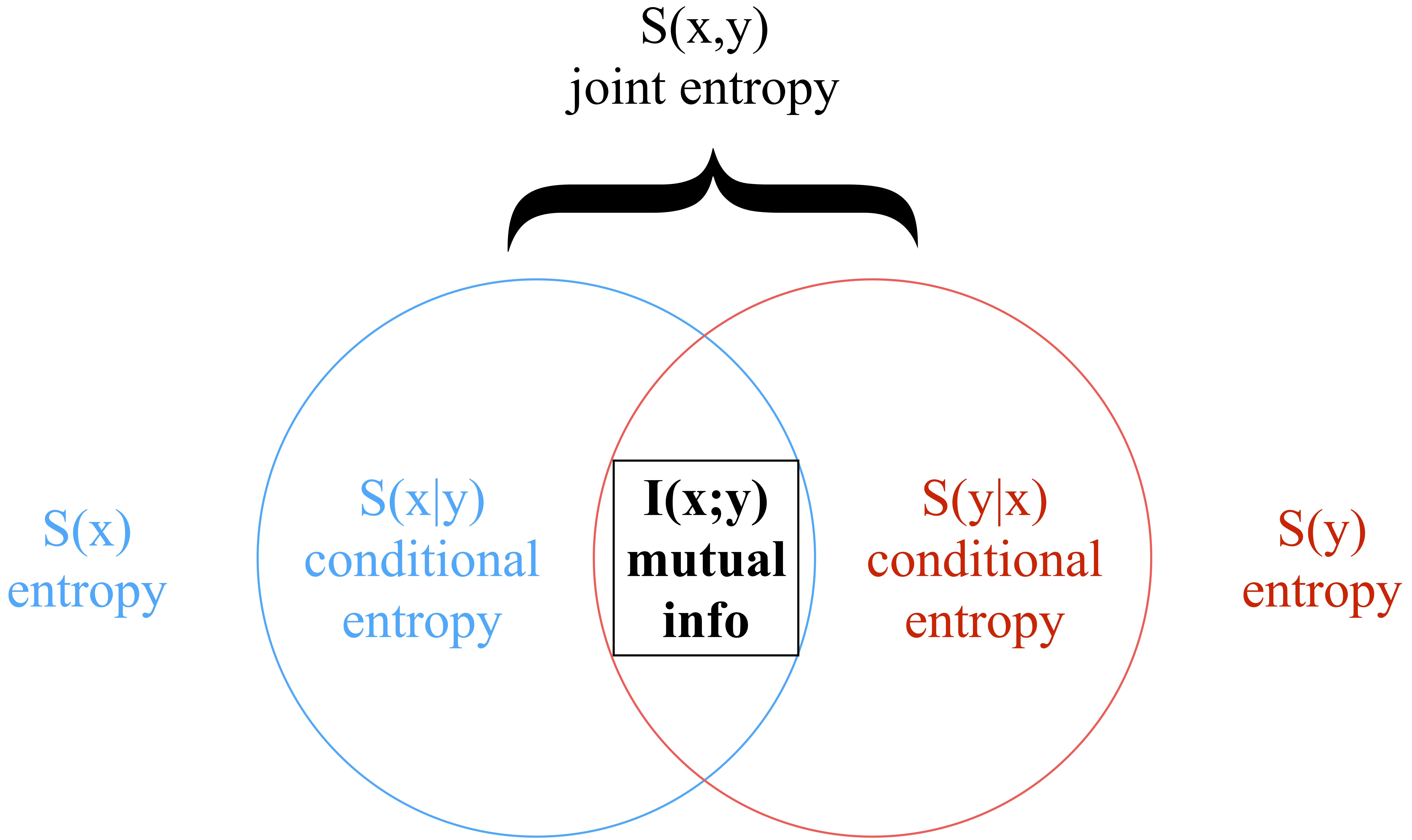
Mutual Information



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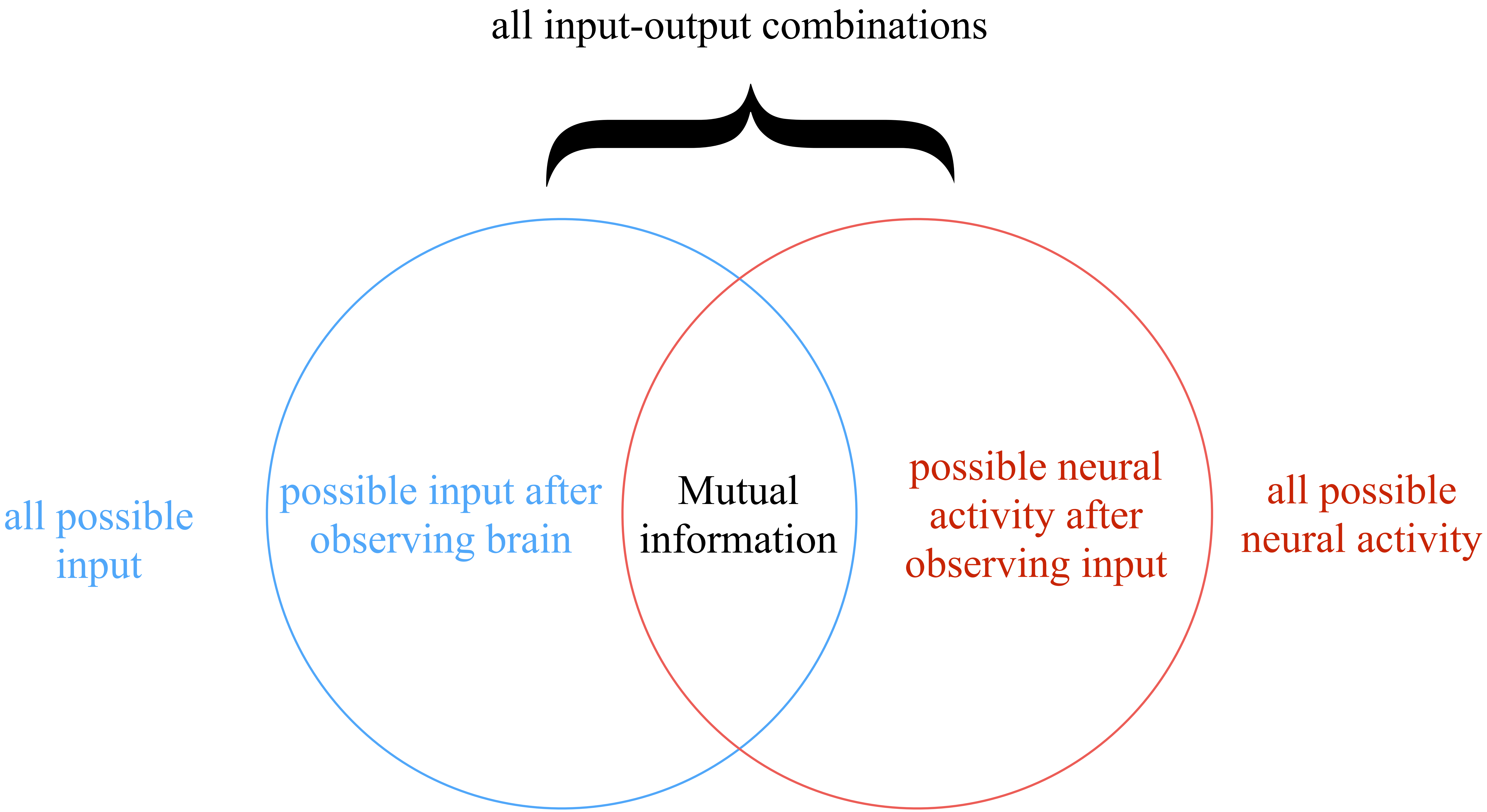

Entropy and information

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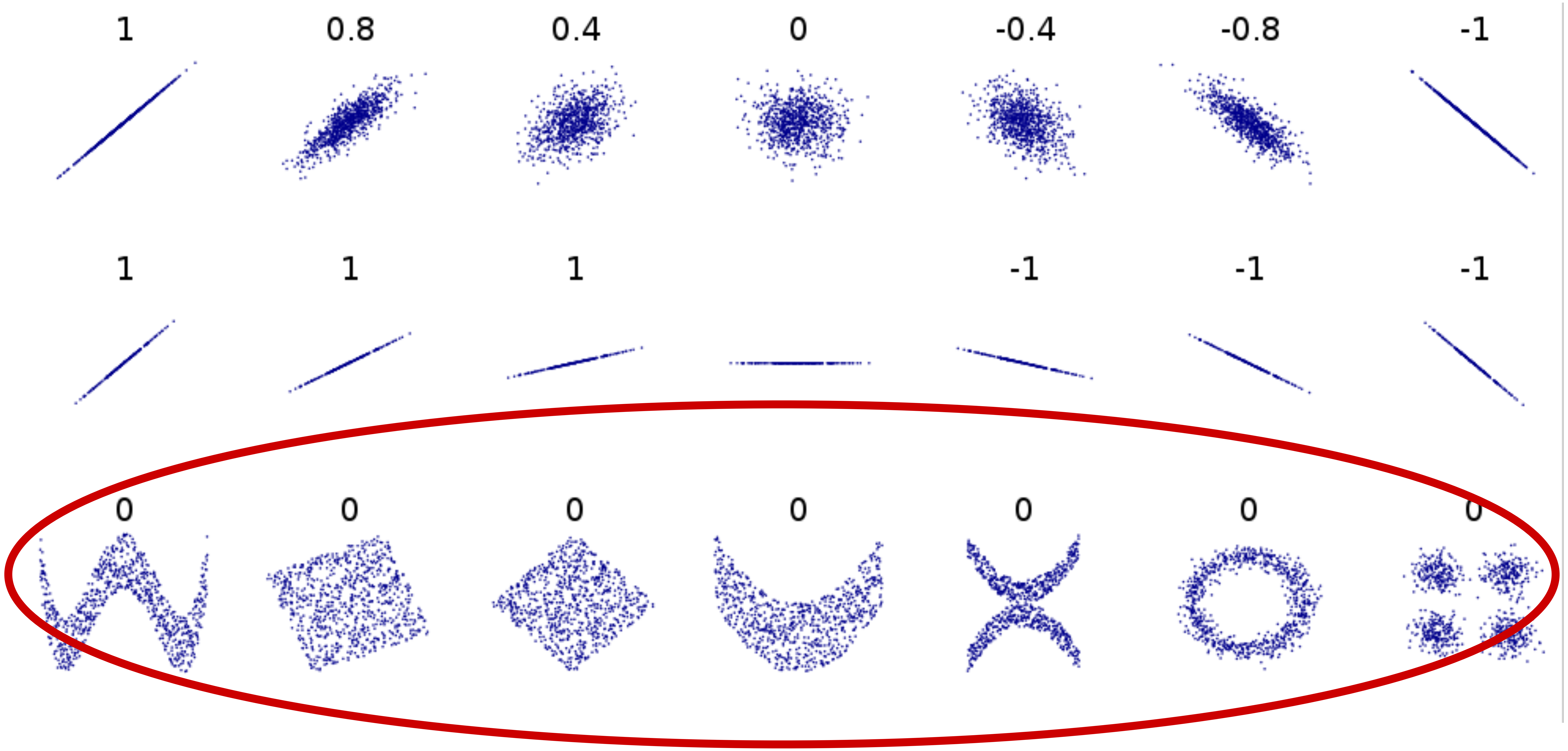
$$S(P[x]) = S(X) = -\sum_x P(x)\log_2 P(x)$$

Information between two variables:

- reduction in entropy in input after observing the neural activity
- reduction in entropy in neural activity after observing the input

$$I(X;Y) = \sum_{x,y} P(x,y)\log_2 \frac{P(x,y)}{P(x)P(y)} = S(X) - S(X|Y)$$

Mutual Information



correlation = 0; MI >0

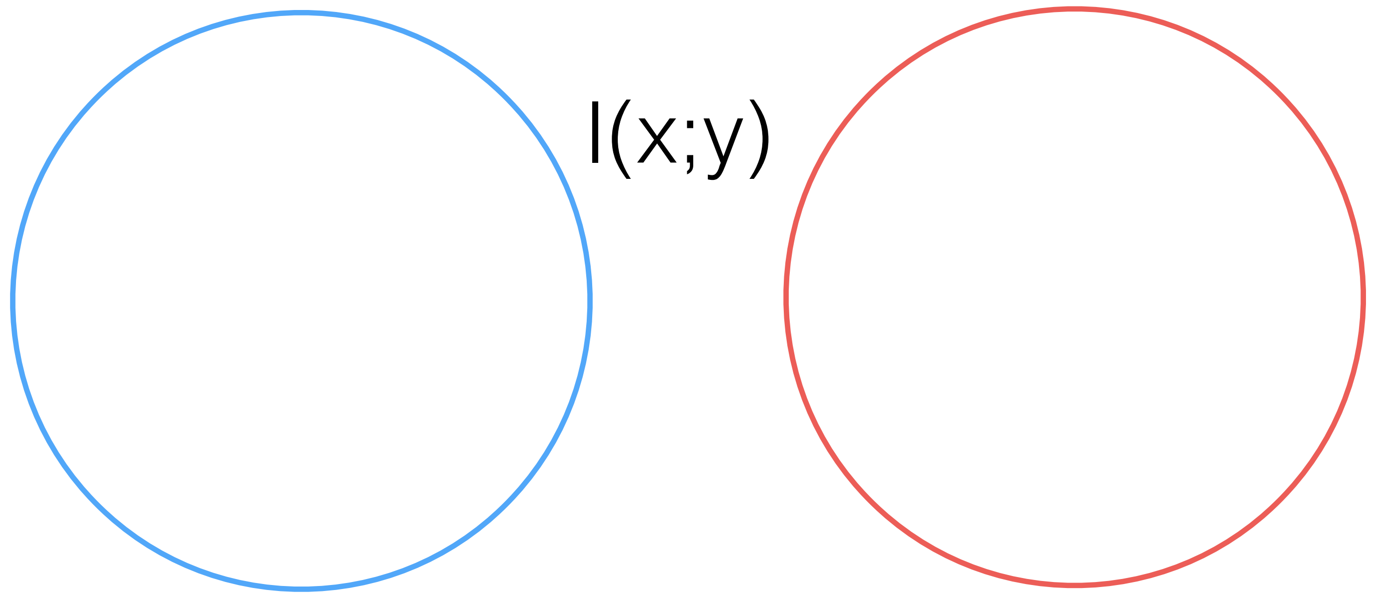
Wikipedia: Correlation and dependence

Mutual Information: neuron example 1

Suppose a neuron is not influenced by the stimulus.

Independent variables, so P(r,s) = P(r)P(s)

$$
\begin{aligned}
I(R;S) &= \sum_{r,s} P(r,s) \log_2 \frac{P(r,s)}{P(r)P(s)} \\
&= \sum_{r,s} P(r)P(s) \log_2 \frac{P(r)P(s)}{P(r)P(s)} \\
&= \sum_{r,s} P(r)P(s) \log_2 1 = 0
\end{aligned}
$$



Mutual Information: neuron example 2

Experiment visual cortex V1

- 2 stimuli: red dot and blue dot
- measure firing frequency of a pyramidal cell in response to stimuli
- 20 experiments

Often, the neuron has a higher firing frequency with the red stimulus

1. What is the entropy of the input?
2. What is the probability of a high frequency response?
3. What is the mutual information between input and response?

stimulus → response ↓	red dot	blue dot
high r>15 Hz	7/20	5/20
low r<15 Hz	3/20	5/20

Mutual Information: neuron example 2

1. S(Input)?
   P(red) = 7/20 + 3/20 = 1/2
   P(blue) = 1/2
   S(input) = 1 bit

2. P(high)=
   7/70+5/20 = 12/20 = 3/5;
   P(low) = 2/5

stimulus → response ↓	red dot	blue dot
high r>15 Hz	7/20	5/20
low r<15 Hz	3/20	5/20

3. MI(input; response)?

$$I(stim;response) = P(red,high)\log_2\frac{P(red,high)}{P(red)P(high)} + ...red,low... + ...$$

$$= 7/20\log_2\frac{7/20}{1/2*3/5} + 3/20\log_2\frac{3/20}{1/2*2/5}$$

$$+ 5/20\log_2\frac{5/20}{1/2*3/5} + 5/20\log_2\frac{5/20}{1/2*2/5}$$

$$= 0.03 \text{ bit}$$

Mutual Information: properties

1. Symmetric: $I(x;y) = I(y;x)$

2. Data processing inequality: you cannot create information from nothing:
   - $MI \geqq 0$
   - $S(X) \geqq S(X|Y)$
   - $S(X) \geqq MI$ (information is always smaller than or equal to entropy of the input)
   - If Z is a variable that depends only on Y, then $I(X;Z) \leq I(X;Y)$.

3. Related to Signal-to-Noise Ratio

Mutual Information: Noise

- Idea: there is **noise** between the world (input) and its representation (neural activity)

- noise = ‘real' input - input that can be reconstructed from representation (neural activity)

- Signal-to-Noise Ratio (**SNR**) = var(signal) / var(noise)

- Relation Information and SNR: more noise means a smaller SNR and less information

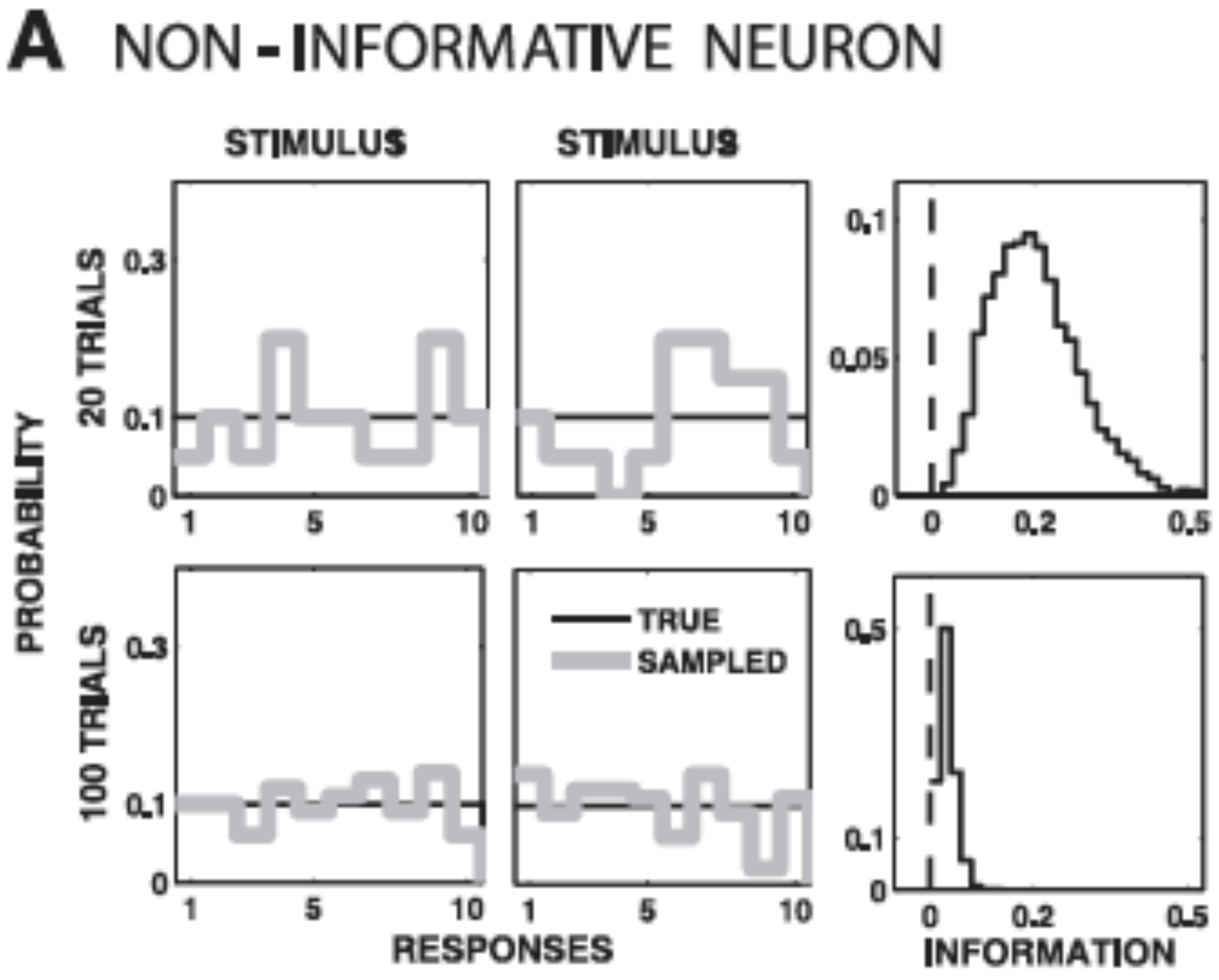
 (MI= 0.5 log2 (1+SNR) under certain Gaussian assumptions)

Mutual Information: bias from undersampling

- P(x,y) often difficult to measure experimentally. This means measuring every possible stimulus-response pairs several times!

- In practice: limited number of measurements → ‘measured' probabilities deviate from ‘real' probabilities

- This results in a **bias**: **overestimation** of mutual information



Panzeri et al. 2007

Conclusion Mutual information

Decoding: how much does the neural activity tell me about the stimulus?

Entropy: ‘number of possibilities’, ‘uncertainty’, ‘possible’ information, ‘surprise’

Information between two variables: ‘advanced correlation’
reduction in entropy in input after observing the neural activity (or vice versa)

Relation **SNR**: more noise means a smaller SNR and less information

P(x,y) often difficult to measure experimentally. This means measuring every possible stimulus-response pairs several times! A limited number of measurements → ‘measured' probabilities deviate from ‘real' probabilities → **bias**: **overestimation** of mutual information

Break

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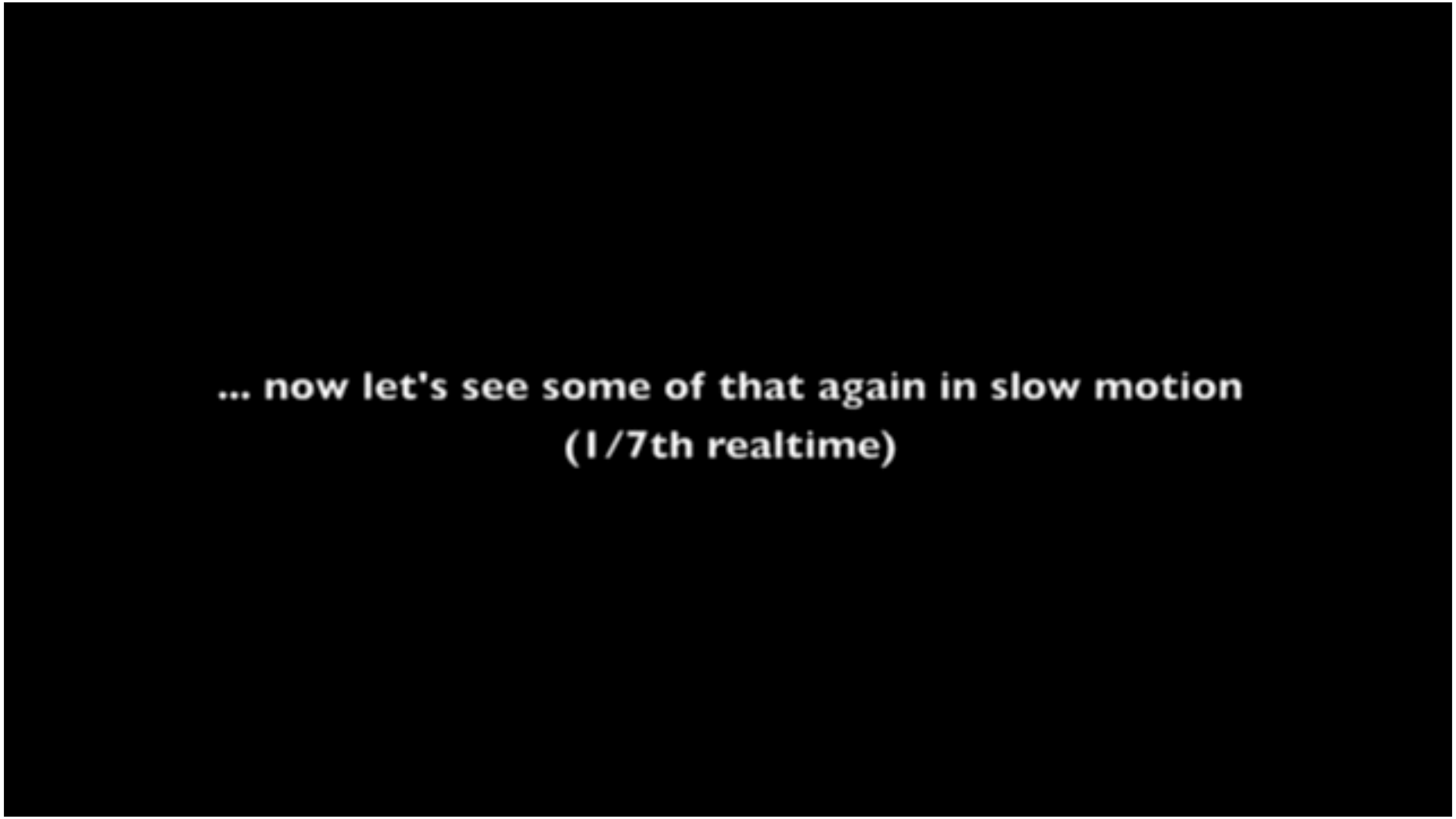
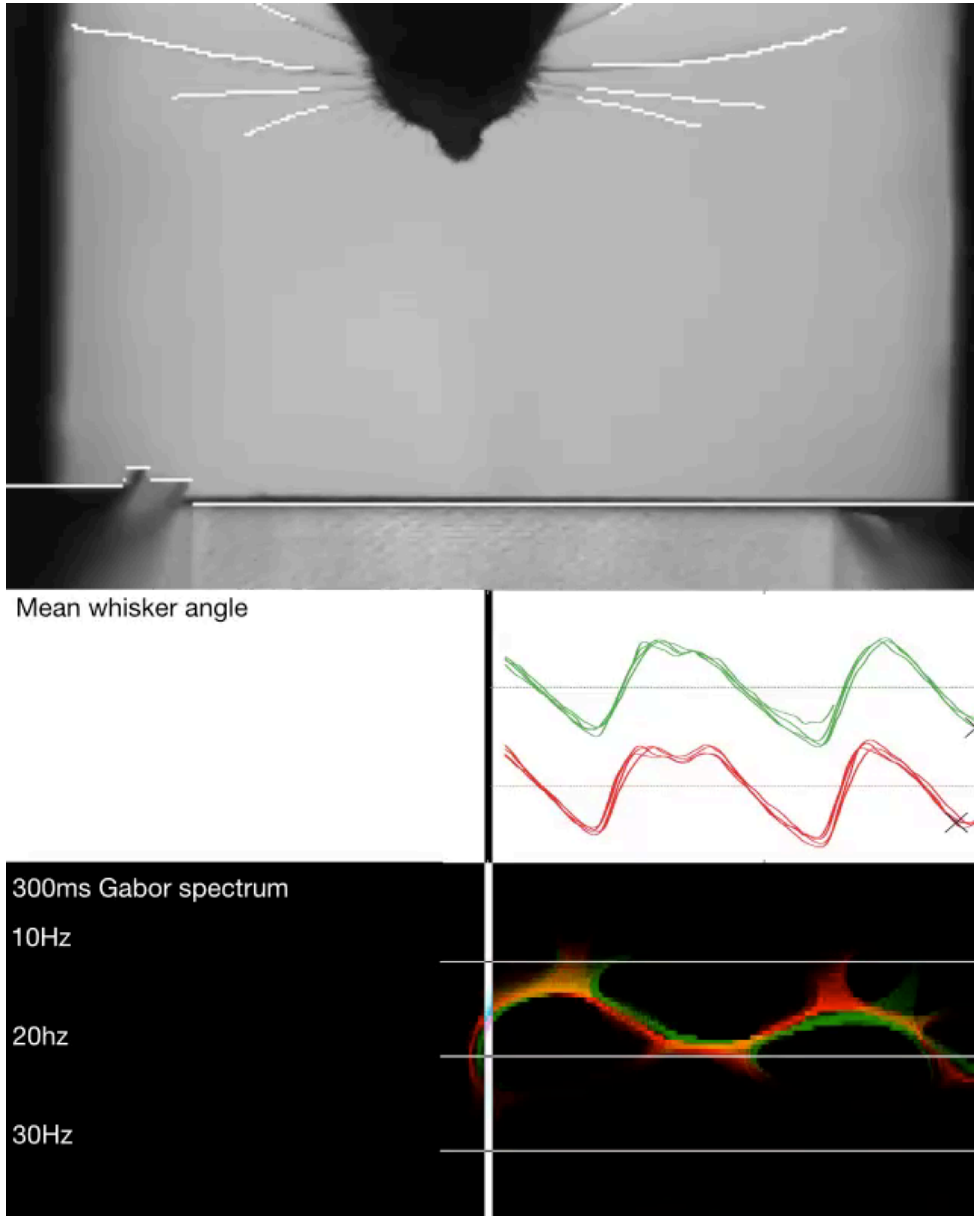
Rodents use their whiskers as we our fingers (video Prescott lab)



Rodents use their whiskers as we our fingers

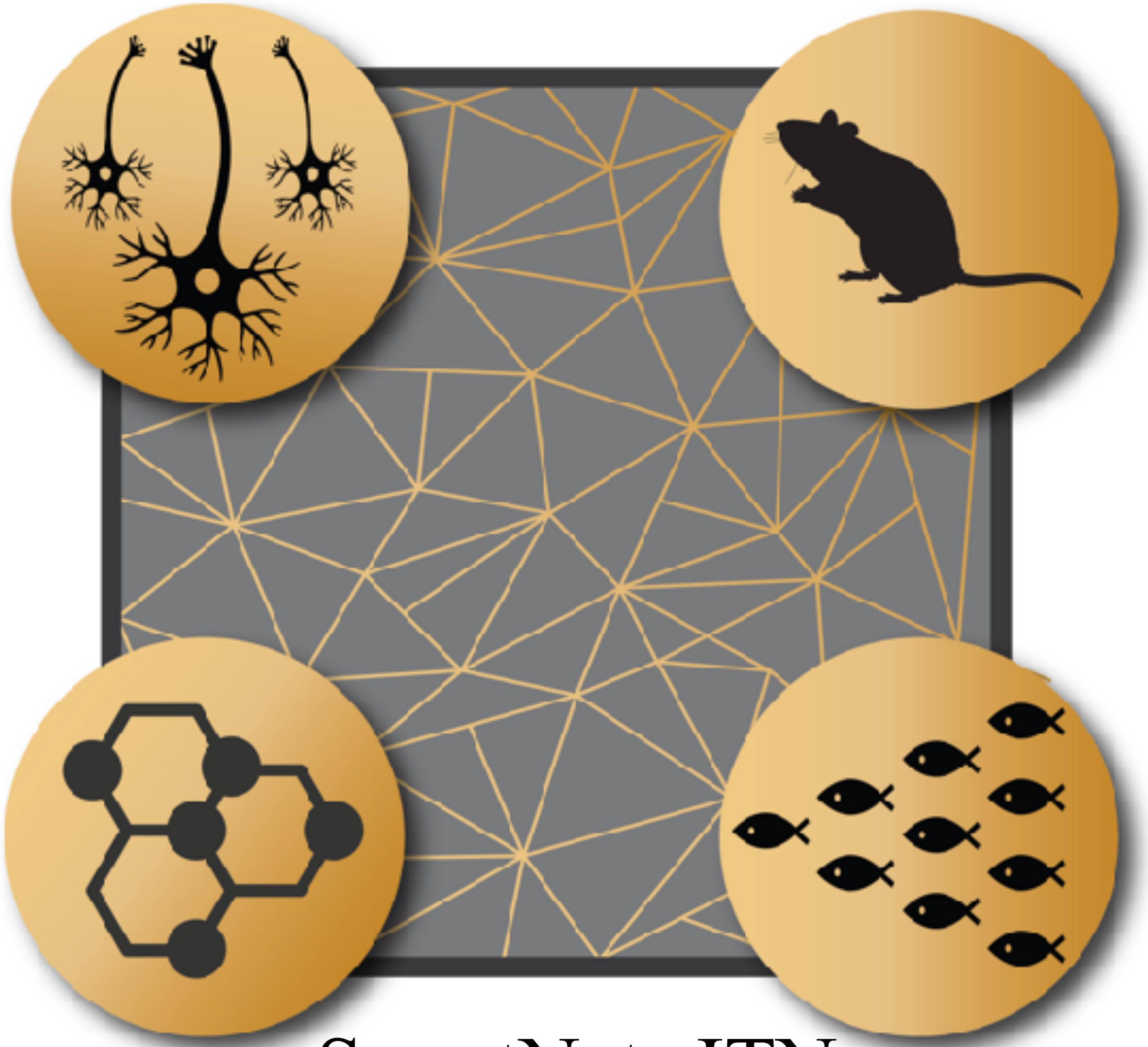
- Easy to observe
- Very similar to other sensory systems, even in other animals
- Control neural activity (optogenetics)
- Active sense: Mice control whisker position to target predicted position object (Voigts et al. (2015))



Structure ↔ Function

How does structure (cell properties / network properties) influence (efficiency of) information transfer and vice versa?

- overarching principles in networks (not only the brain, think also about animal collectives or molecular networks)
- influence of
    1. node properties (neurons)
    2. connectivity
    3. implementation of necessary function



SmartNets ITN

Inhibitory and excitatory neurons - what we know

Differences inhibitory (interneurons) and excitatory (PC) cells:

Network
- PCs connect **between networks** (layers, areas)
- interneurons connect (mostly) **locally**
- interneurons connect **unspecifically;** PCs **specifically**

	Excitatory (PC)	***Inhibitory (interneuron)***
Connectivity	***specific projecting***	***unspecific local***
Tuning	***specific***	***broad***

Functional
- PCs respond to **specific stimuli**

How do *intrinsic* differences between inhibitory and excitatory neurons influence information transfer?

In-vitro experiments

How do *intrinsic* differences between inhibitory and excitatory neurons influence information transfer?

Measure the information transfer of a single neuron

How do biophysical properties (conductances) influence information transfer?

How much information is lost by the spike generating process?

- maximum duration experiment: ~ 1 hour (shorter for strong stimuli)
- test multiple conditions (pharmacology, protocols)
- ‘naturalistic’ stimulus

How would one do this?

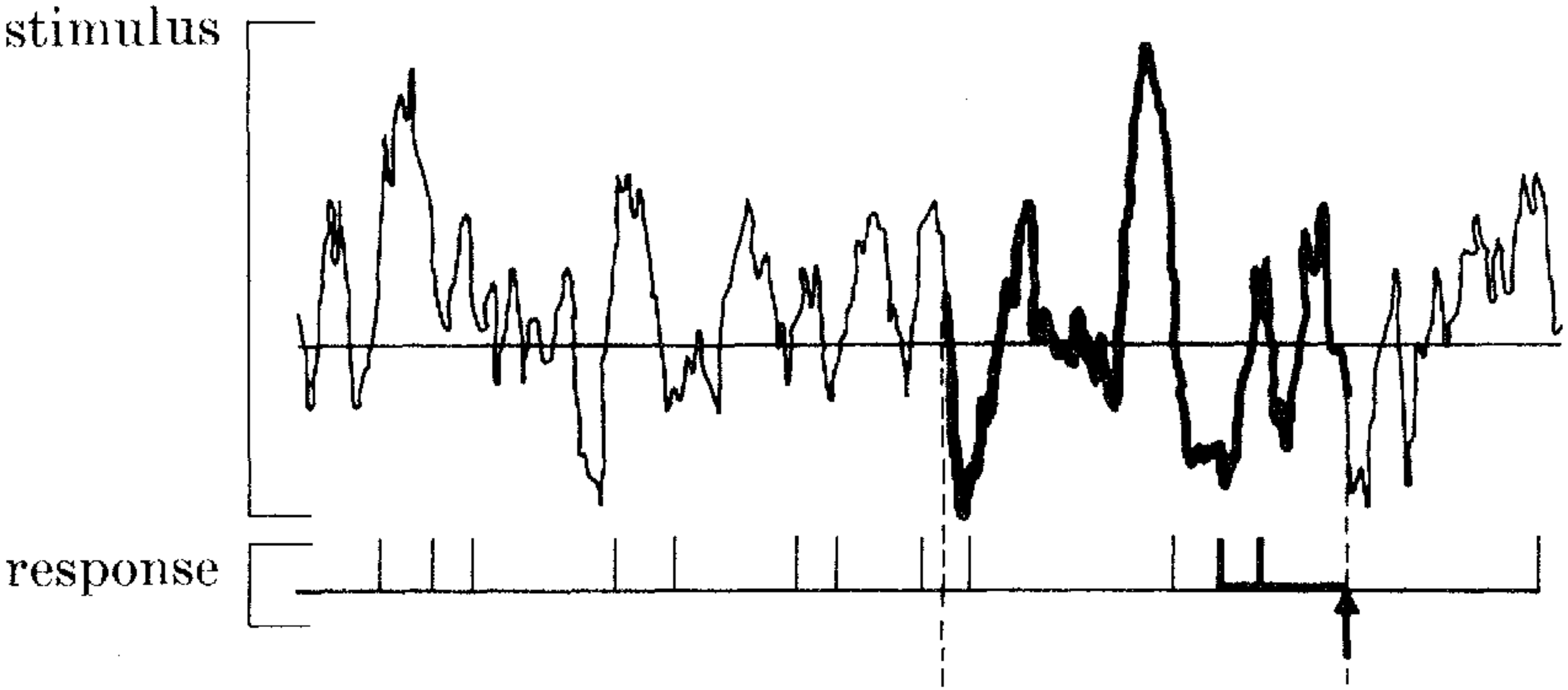
Today

- Lecture 1: Introduction information theory
  - Entropy
  - Information
- Lecture 2:
  - How to measure information in single neurons?
    - Classical methods
      - reverse correlation
      - ‘direct method'
    - Zeldenrust et al. method
  - What does that mean for networks?

Method 1: reverse correlation

de Ruyter van Steveninck & Bialek, 1988;

- **stimulus**: time-varying angular velocity random pattern
- **recordings**: motion sensitive neurons blowfly

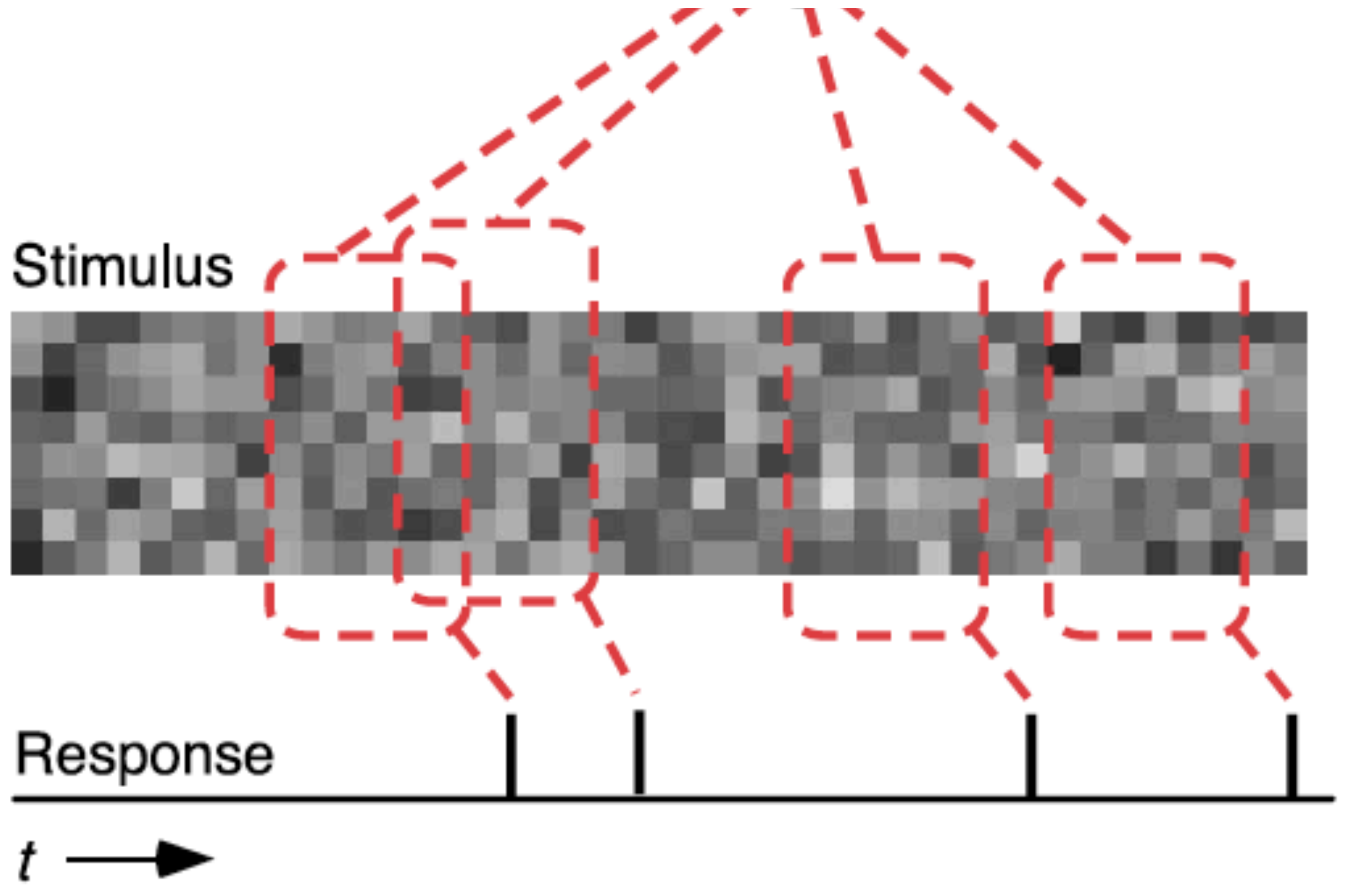


also: Bialek et al., 1991; Rieke et al., 1997

Method 1: reverse correlation

de Ruyter van Steveninck & Bialek, 1988;

- **stimulus**: time-varying angular velocity random pattern
- **recordings**: motion sensitive neurons blowfly
- **method**:
  1. reconstruct stimulus
     A. Every time a neuron fires: record stimulus



Schwartz et al. 2006

Methode 1: reverse correlation

de Ruyter van Steveninck & Bialek, 1988;

- **stimulus**: time-varying angular velocity random pattern
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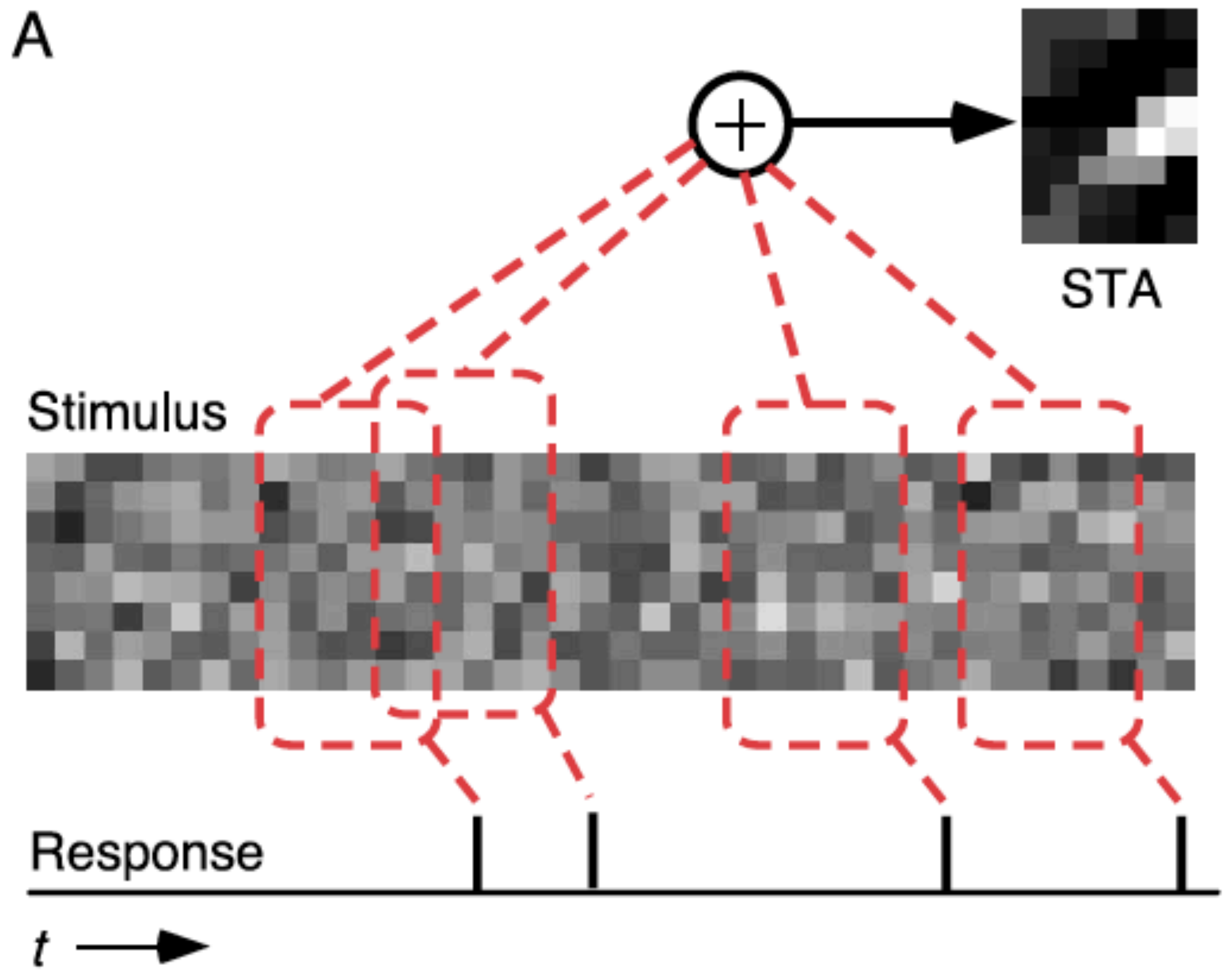
- **method**:
  1. reconstruct stimulus
     A. Every time a neuron fires: record stimulus
     B. the average over all these stimulus bits is the 'receptive field'



Schwartz et al. 2006

Methode 1: reverse correlation

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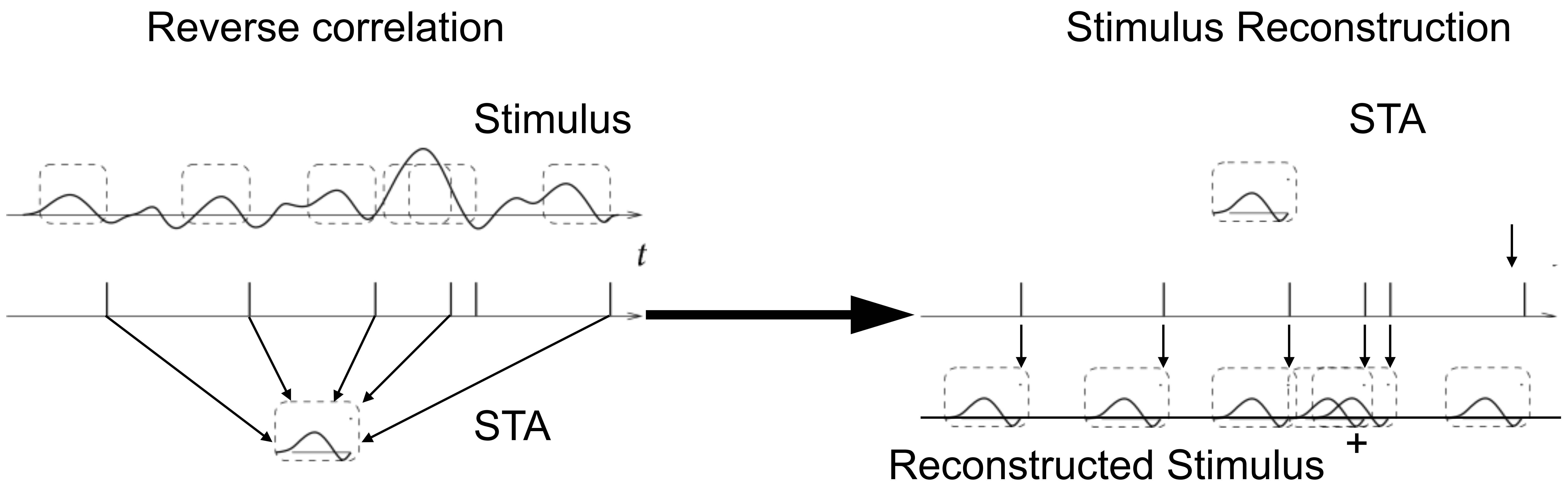
- **stimulus**: time-varying angular velocity random pattern
- **recordings**: motion sensitive neurons blowfly
- **method**:
  1. reconstruct stimulus
     A. Every time a neuron fires: record stimulus
     B. the average over all these stimulus bits is the ‘receptive field’
     C. reconstruct the stimulus by putting a ‘receptive field’ before each spike

Method 1: reverse correlation



Method 1: reverse correlation

de Ruyter van Steveninck & Bialek, 1988;

- **stimulus**: time-varying angular velocity random pattern
- **recordings**: motion sensitive neurons blowfly
- **method**:
  1. reconstruct stimulus
  2. real stimulus (s) - reconstructed stimulus (s_{est}) = noise (N)
  3. Signal to Noise Ratio

$$\mathrm{SNR} = \frac{P_s}{P_N} \; .$$

  4. Information

$$I = \frac{1}{2}\log_2\left(1 + SNR\right)$$

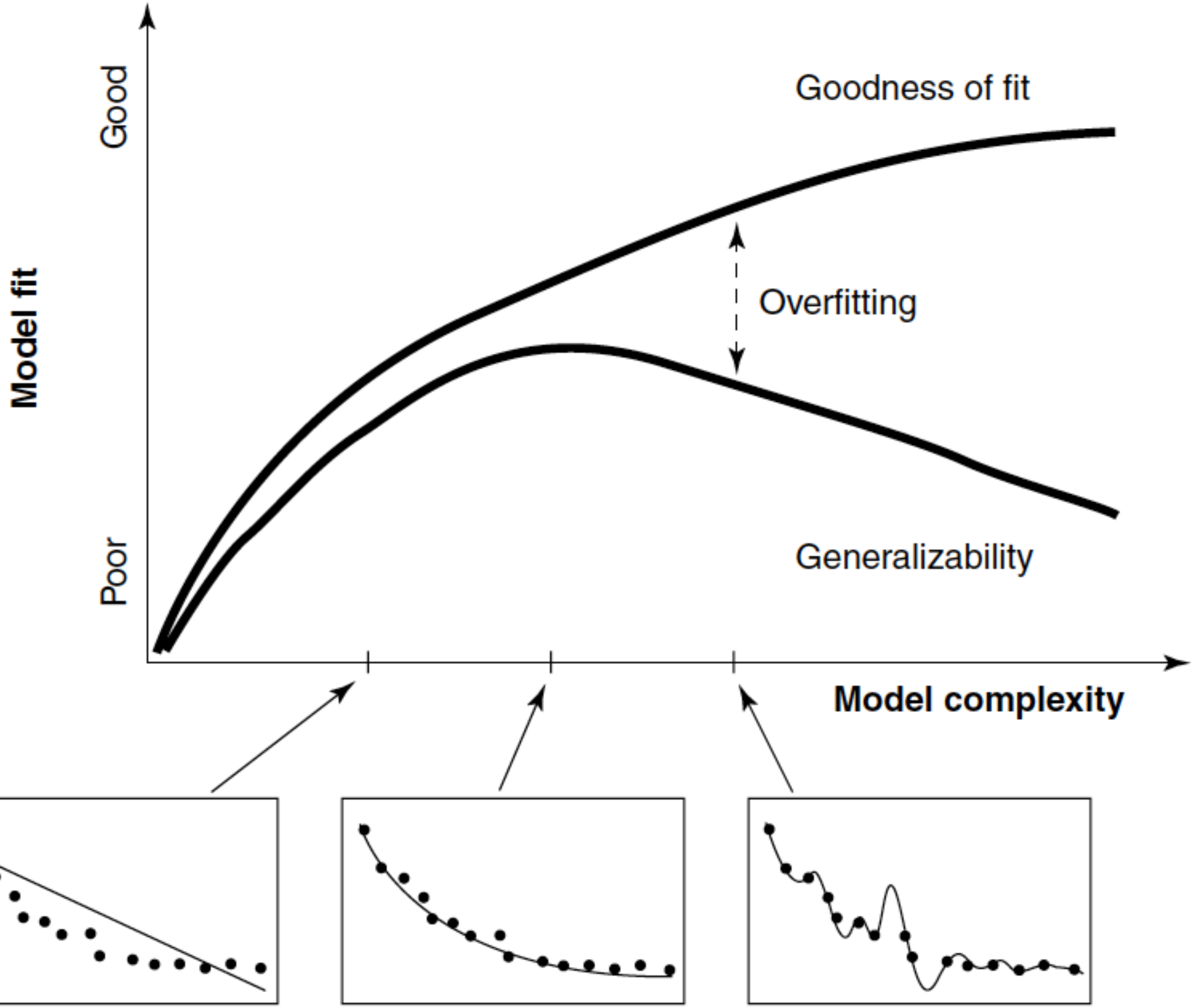
also: Bialek et al., 1991; Rieke et al., 1997

Intermezzo: avoid ‘overfitting’

Overfitting (fitting of noise)

- **generalizability**: the ability of a model to fit all data samples generated by the same process, not just the currently observed sample
- **flexibility / complexity**: the property of a model that enables it to fit diverse patterns of data
- **overfitting**: the case where, in addition to fitting the main trends in the data, a model also fits the microvariation from this main trend at each data point

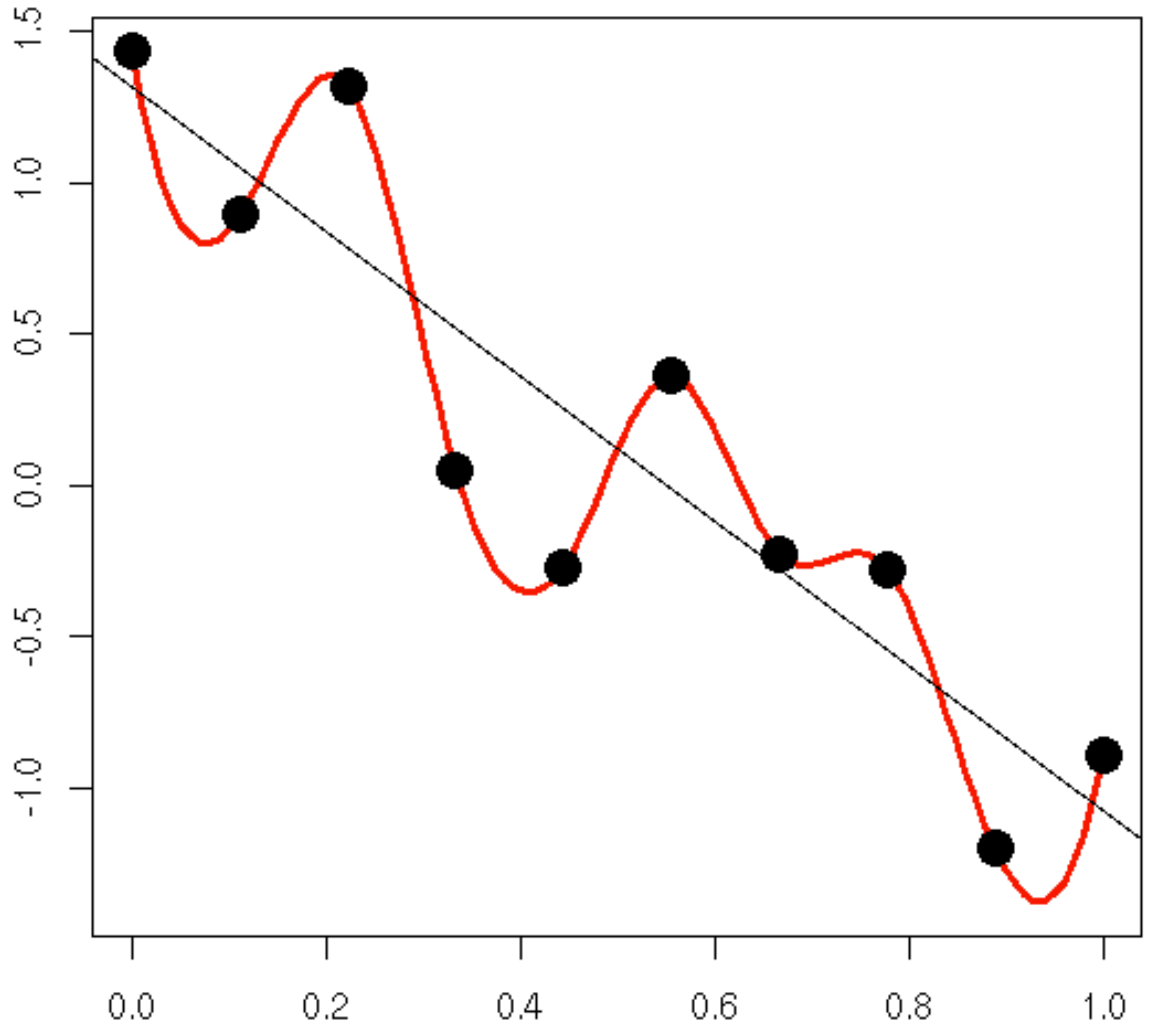
Intermezzo: avoid ‘overfitting’



Pitt & Myung, 2002

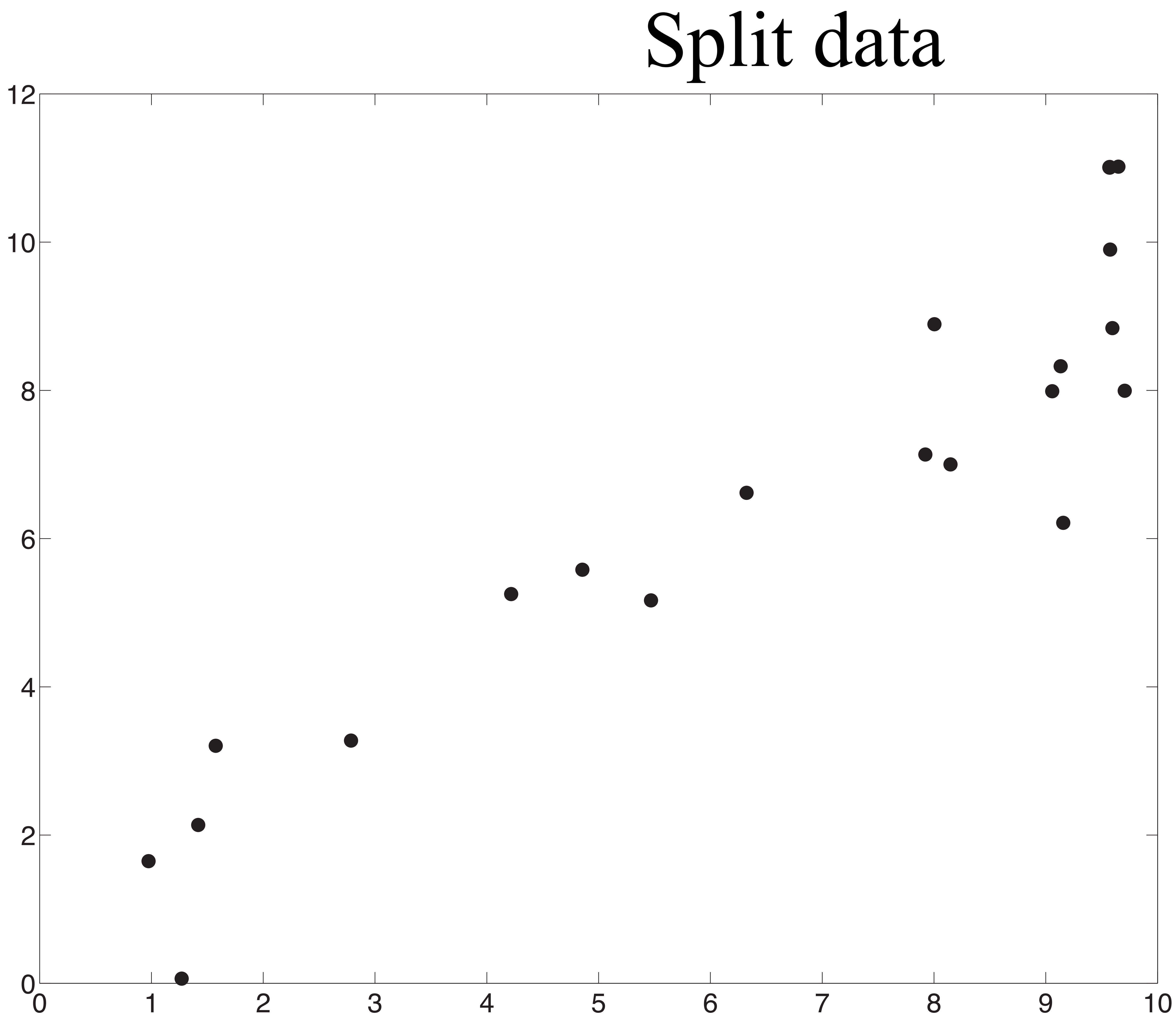
Intermezzo: avoid ‘overfitting’

Which model is better?



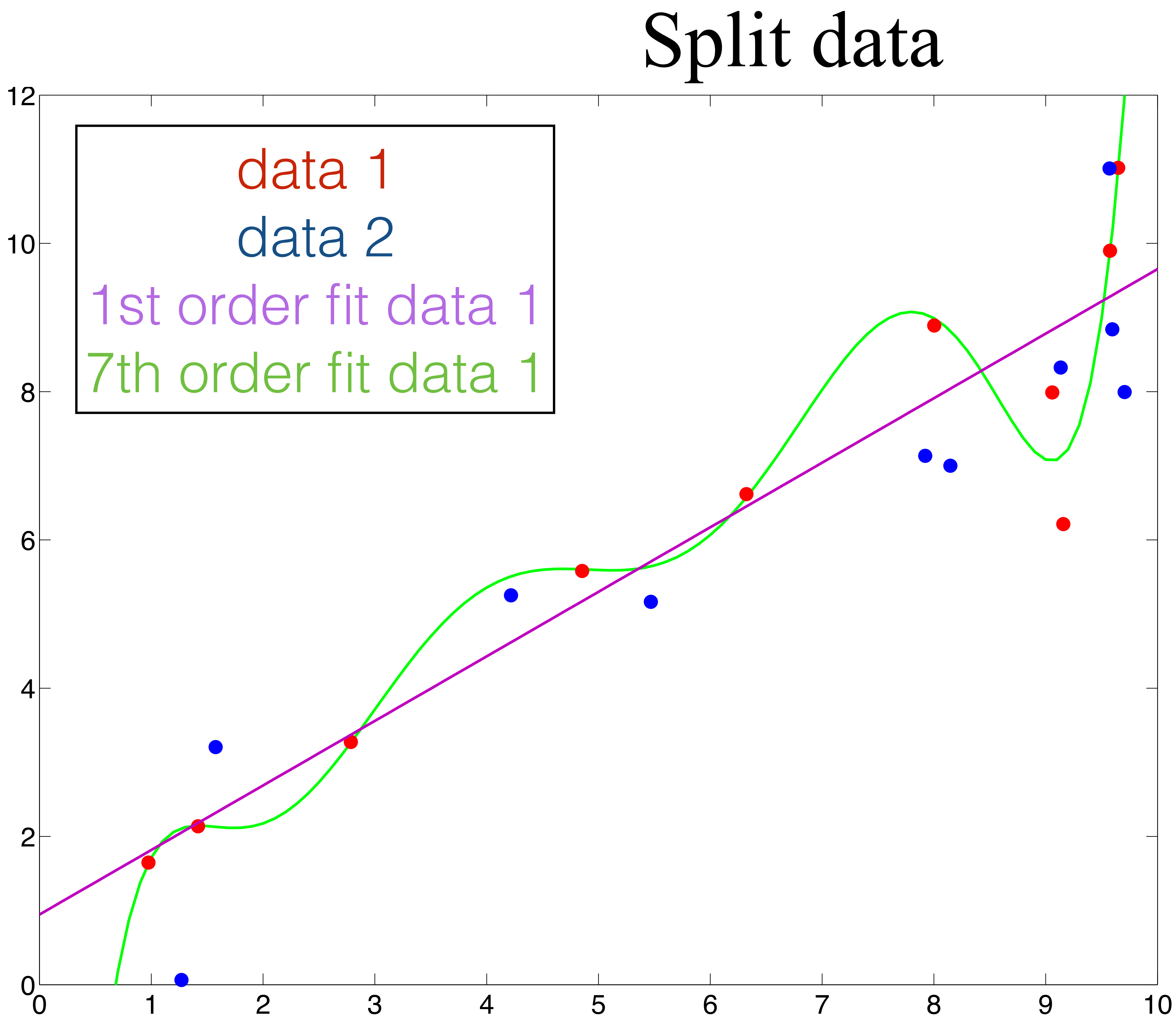
- error = 0, lage generalisability ⟶ overfitting
- error > 0, betere generalisability

Intermezzo: avoid ‘overfitting’



Split data
- ‘fit' part
- ‘test' part

Intermezzo: avoid ‘overfitting’

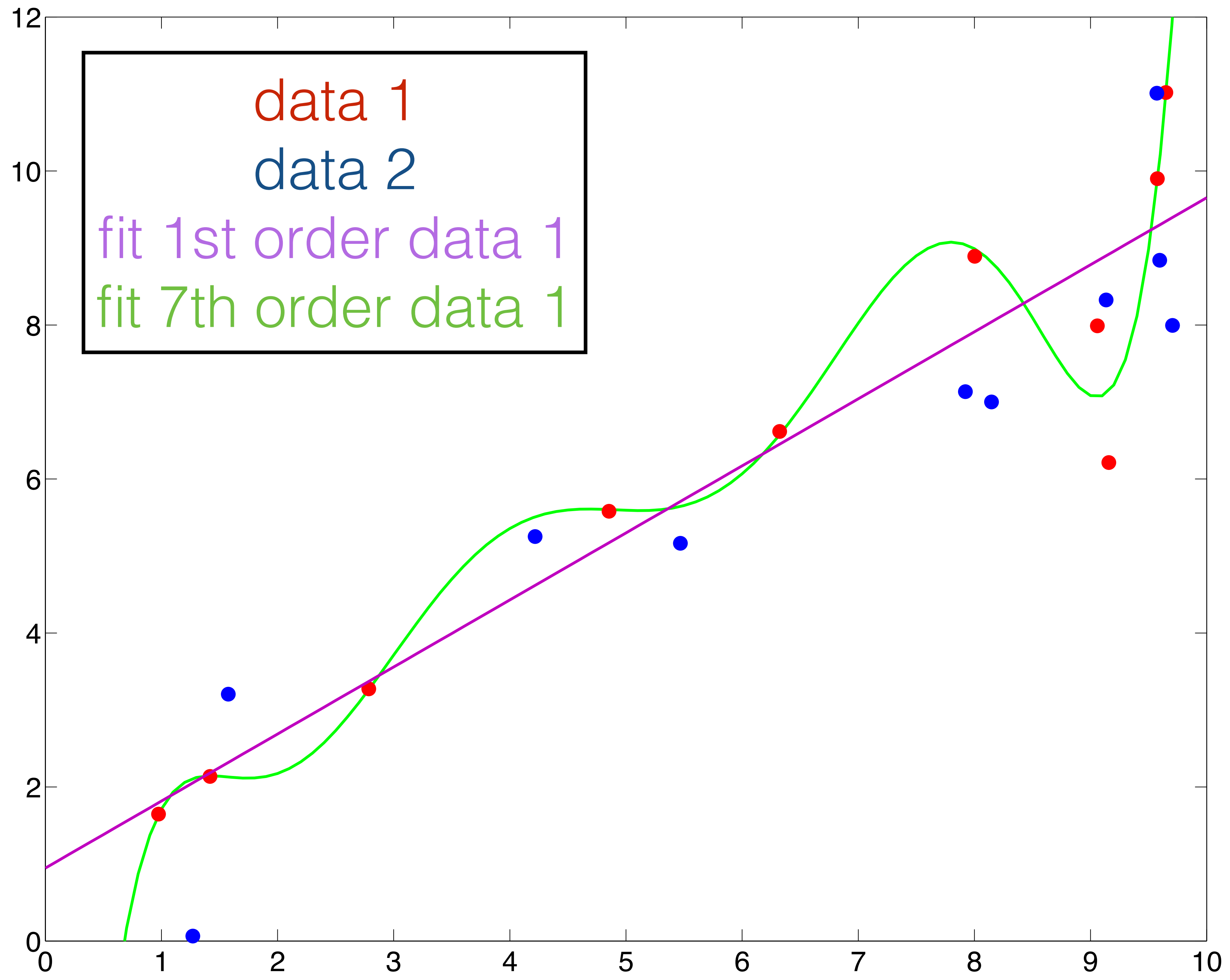


Split data
- ‘fit' part
- ‘test' part

Intermezzo: avoid ‘overfitting’

Overfitting: error test-data >> error fit-data

error (RMSE)	1e orde	7e orde
fitdata	1.24	0.93
testdata	1.25	4.1



Method 1: reverse correlation

de Ruyter van Steveninck & Bialek, 1988;

- **stimulus**: time-varying angular velocity random pattern
- **recordings**: motion sensitive neurons blowfly
- **method**: reconstructions using inverse correlation
- Needed:
  - much data for reverse correlation (fit-data)
  - even more data voor measuring information (test-data)
  - result: **1 hour** recordings needed for 1 MI measurement!

But: the maximum recording time is about 1 hour. So how to test different conditions?

also: Bialek et al., 1991; Rieke et al., 1997

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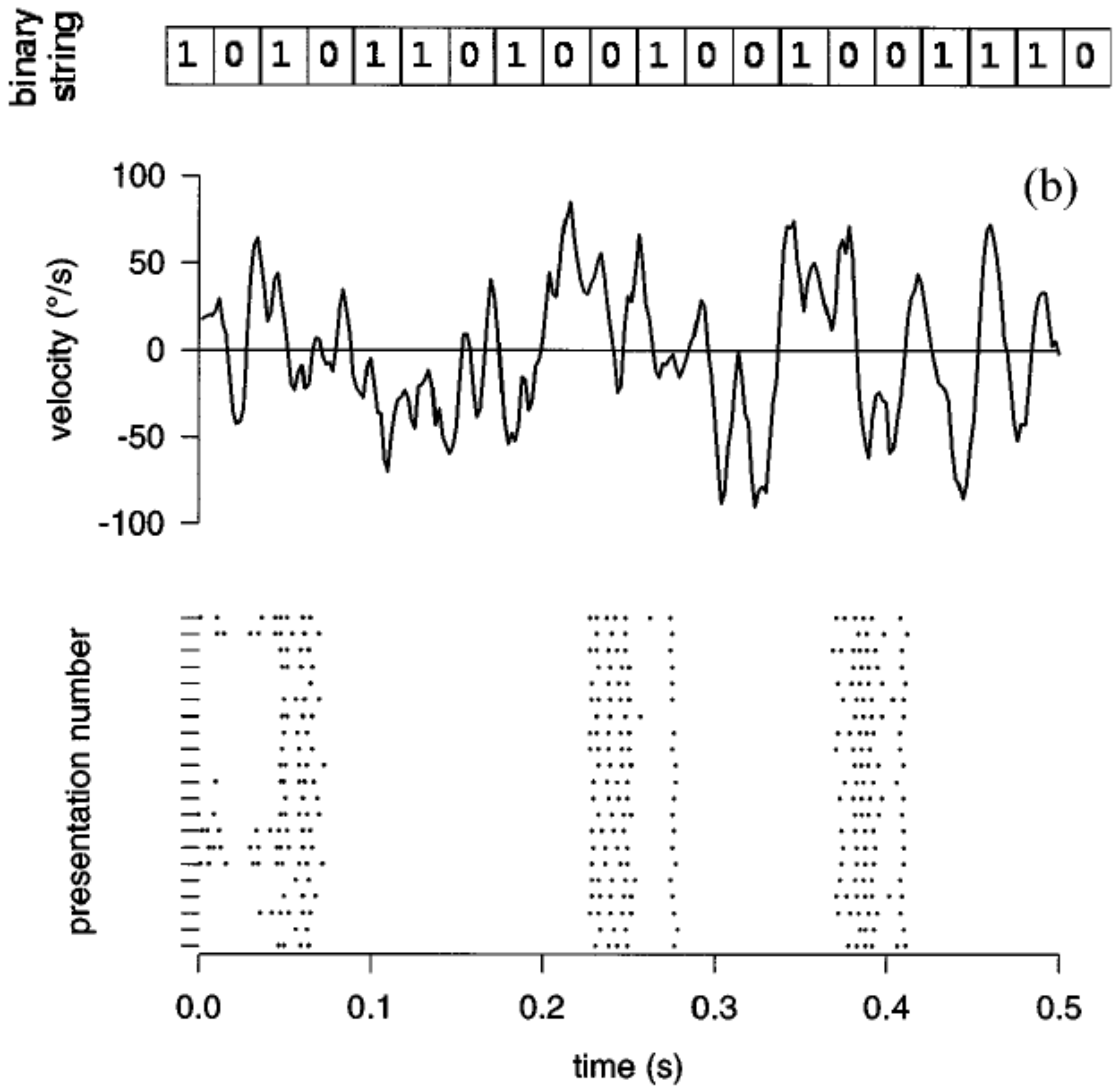
    - What does that mean for networks?

How to measure information?

'Direct method' (de Ruyter van Steveninck et al., 1997; Strong et al., 1998)

- **stimulus**: time-varying angular velocity random pattern, repeated several times

- **recordings**: motion sensitive neurons blowfly
- **method**: estimate MI from response variability



How to measure information?

method: estimate MI directly from response variability

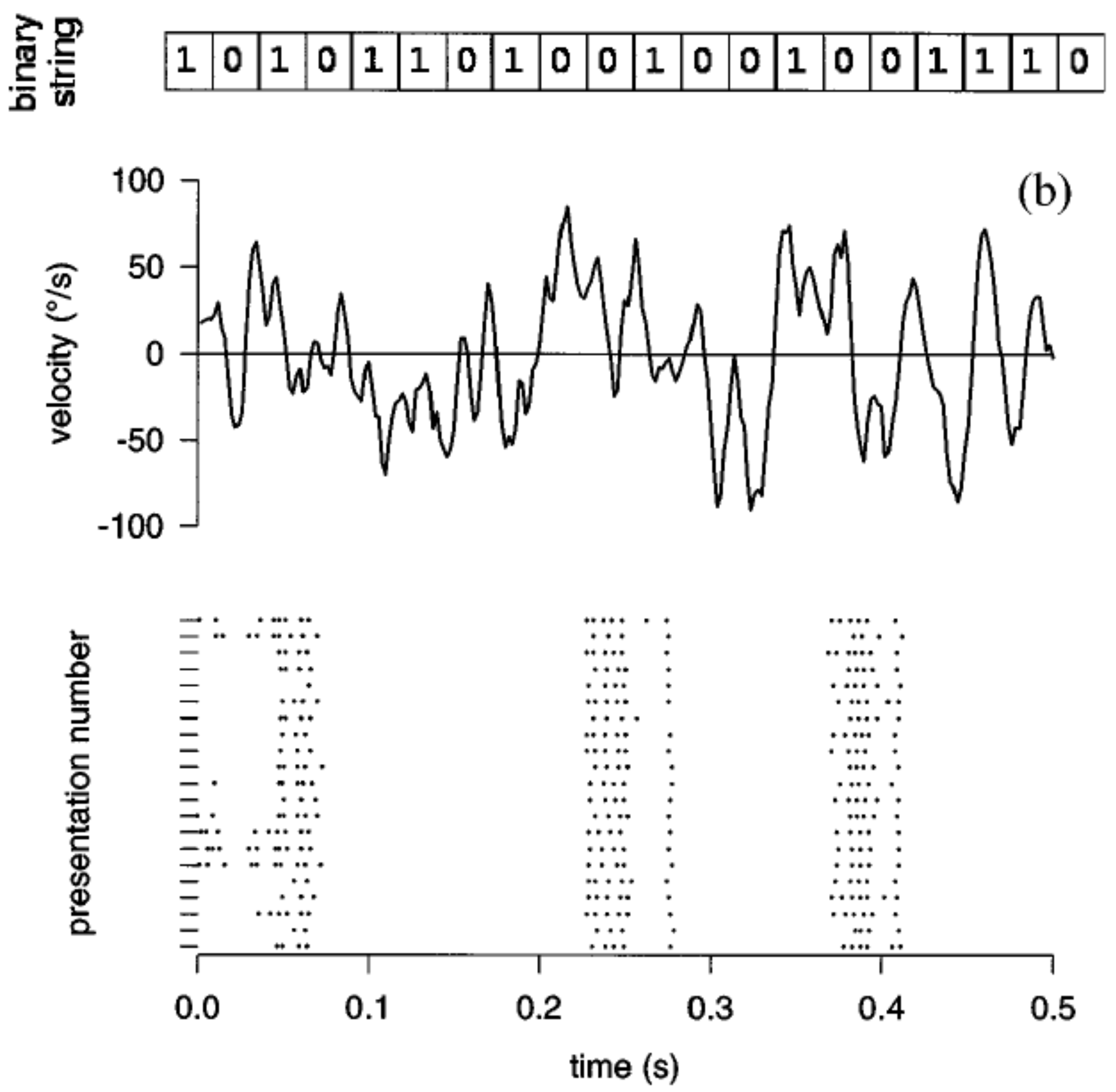
$$I = S(\text{spike train}) - S(\text{spike train}|\text{input})$$

$$S(\text{spike train})$$

variability of the spike train in response to the ensemble of different inputs

$$S(\text{spike train}|\text{input})$$

reliability of the response to repeated presentations of the same inputs (synapses, spike generating mechanism,…): if the same inputs produce the same outputs, it approaches



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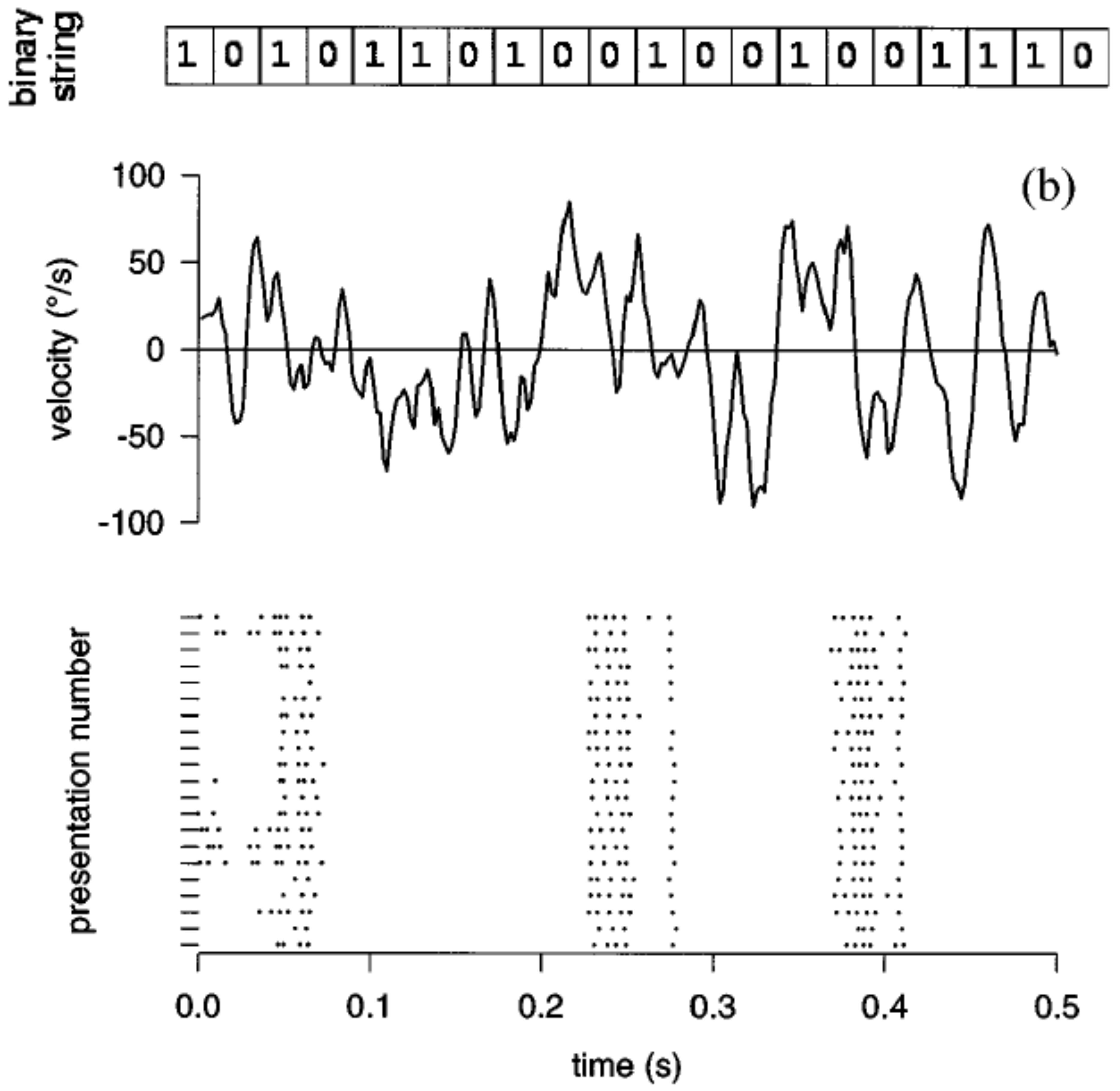

- no reconstruction needed
- MANY repetitions needed
- bias from limited sampling (Treves and Panzeri, 1995; Strong et al., 1998)

Today

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- How can a neuron respond to objects in the outside world (‘carrot’)?
- *Assumption*: Carrot (dis)appears randomly (Markov proces), rates r_{on} and r_{off}
- Neuron does not have acces to ‘the carrot’, only to activity presynaptic neurons

‘Hidden state'

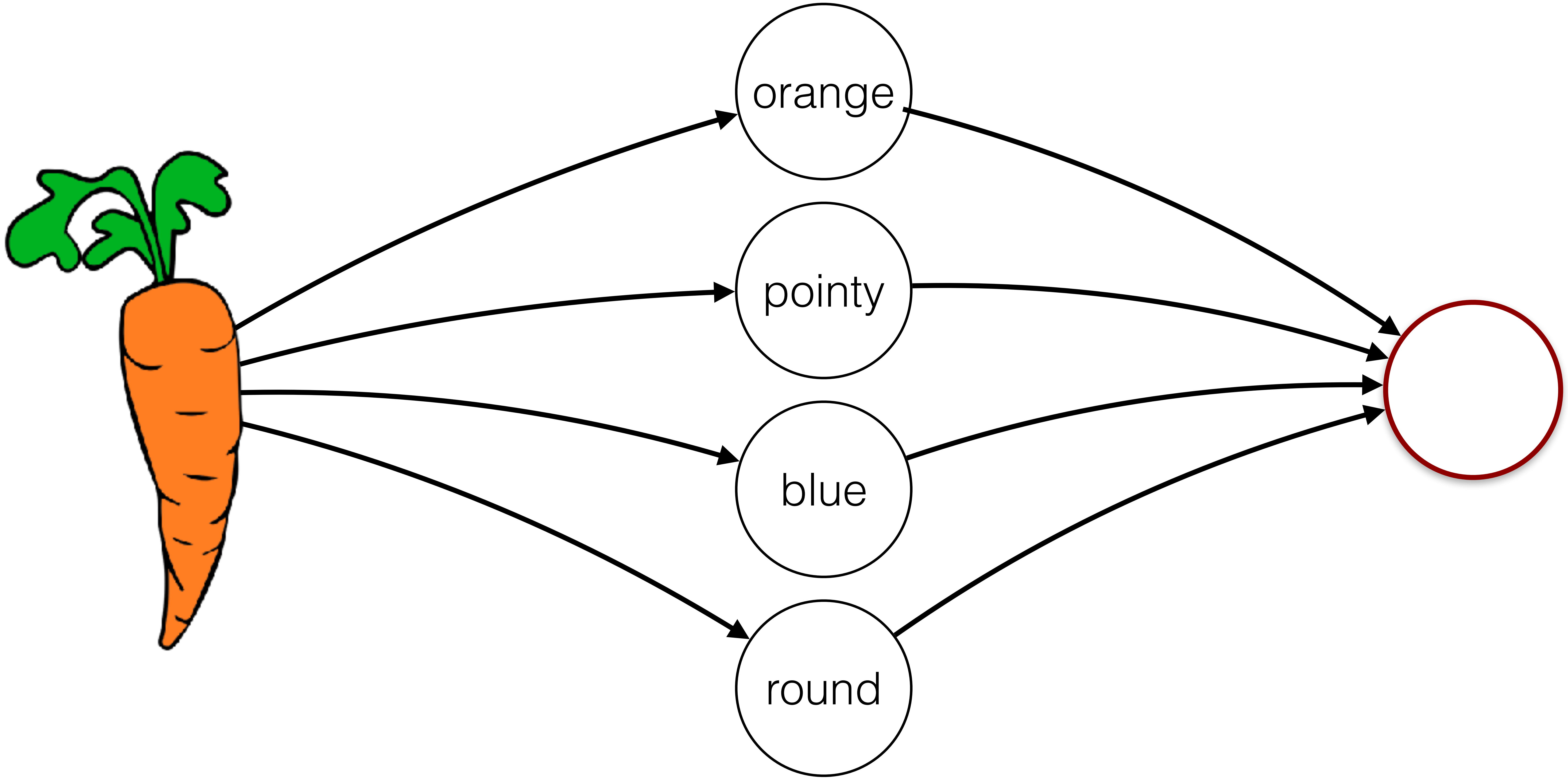
‘Receptors' i

'carrot detector'

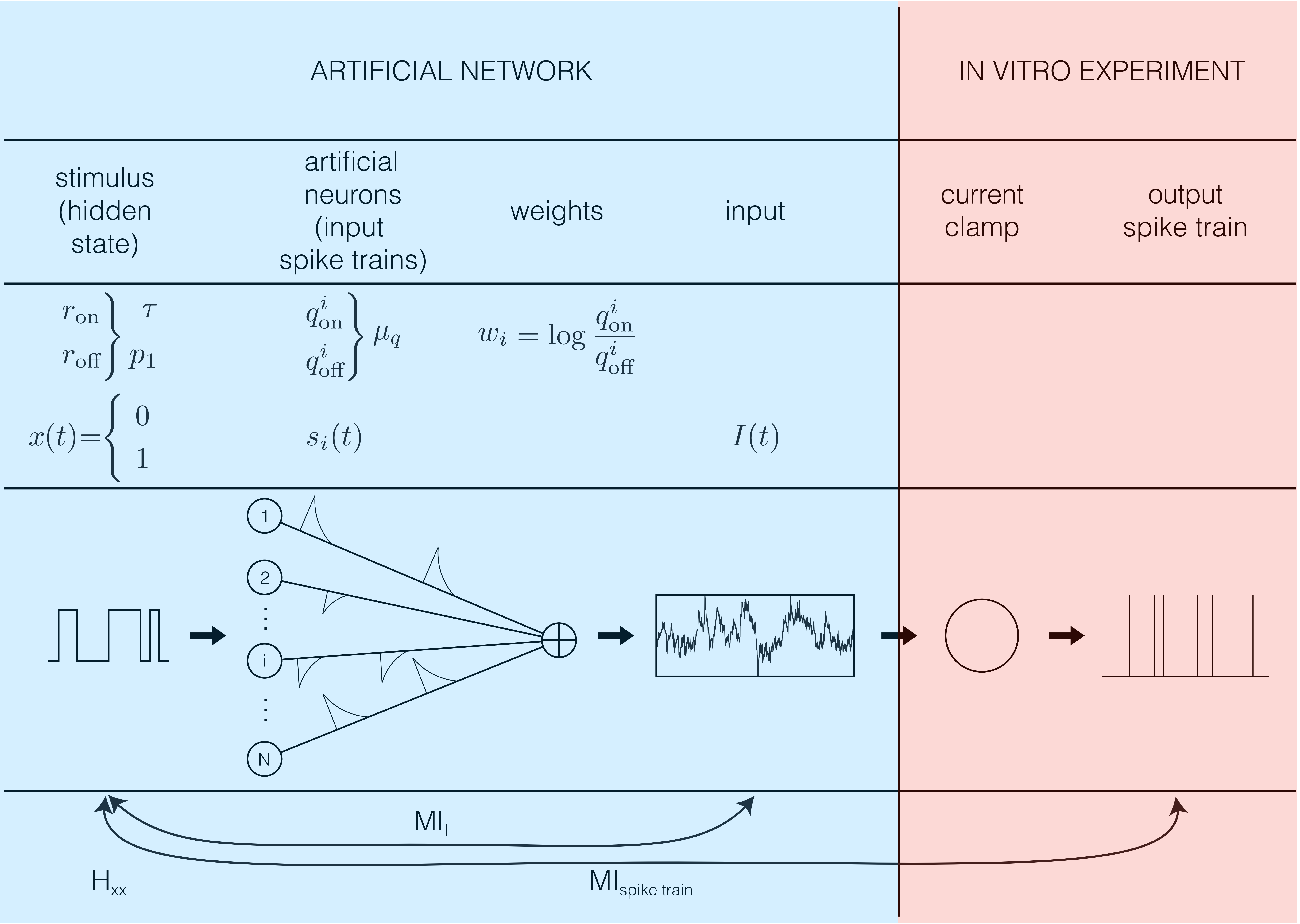
World

Thalamus
lower visual cortex

Higher visual cortex



Input from artificial neural network



Assumptions

1. Neurons respond to a randomly (dis)appearing “preferred stimulus”
2. Neurons only have access to the output of presynaptic neurons
3. Synapses of informative presynaptic neurons are stronger than synapses of non-informative neurons
4. (ergodicity/ stable process) an average over trials can be replaced by an average over time
5. Spike trains are (approximately) Poissonian.

By making a ‘special input’ for the in-vitro experiments, we need shorter recordings to estimate information transfer in single neurons

Conclusions '*frozen noise*' method

Reasoning: neurons extract information from noisy input

Information in the *input* can be controlled

- number of spikes ANN (neurons and firing rates)
- integration time (switching speed hidden state)

Information in the *output* can be estimated (information loss of the spike generation process)

- In about 5 minutes (instead of 1 hour)

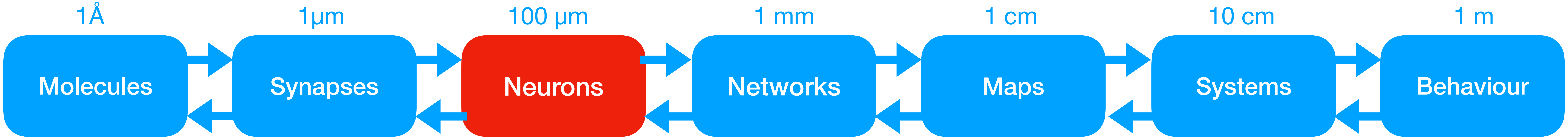
All data can be used for information estimate

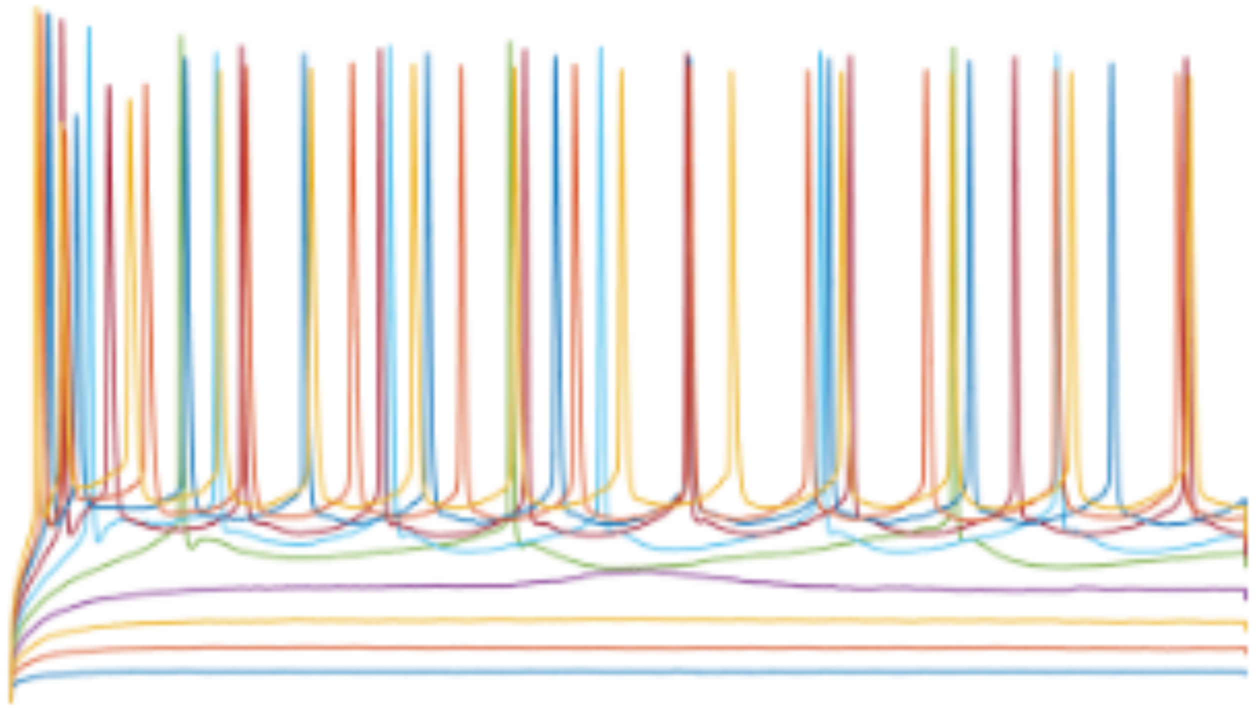
- No trial repetition needed
- No decoding model needs to be fitted

Optimal response model ('Bayesian neuron') for comparison

Zeldenrust et al., Frontiers in Computational Neuroscience, 2017
github.com/fleurzeldenrust/In-vitro-method-for-information-calculation

Databank of single neuron recordings





Supporting data for "A databank for intracellular electrophysiological mapping of the adult somatosensory cortex"

Dataset type: Neuroscience, Electrophysiology

Data released on November 16, 2018

Lantyer Ad; Calcini N; Bijlsma A; Kole K; Emmelkamp M; Peeters M; Scheenen WJJ; Zeldenrust F; Celikel T (2018): Supporting data for "A databank for intracellular electrophysiological mapping of the adult somatosensory cortex" GigaScience Database. http://dx.doi.org/10.5524/100535

DOI 10.5524/100535

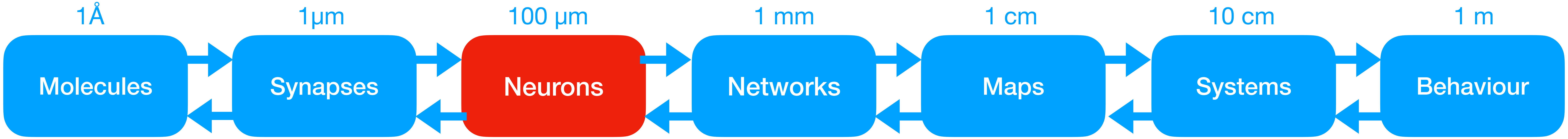
Intracellular whole-cell recording database of the somatosensory cortex:

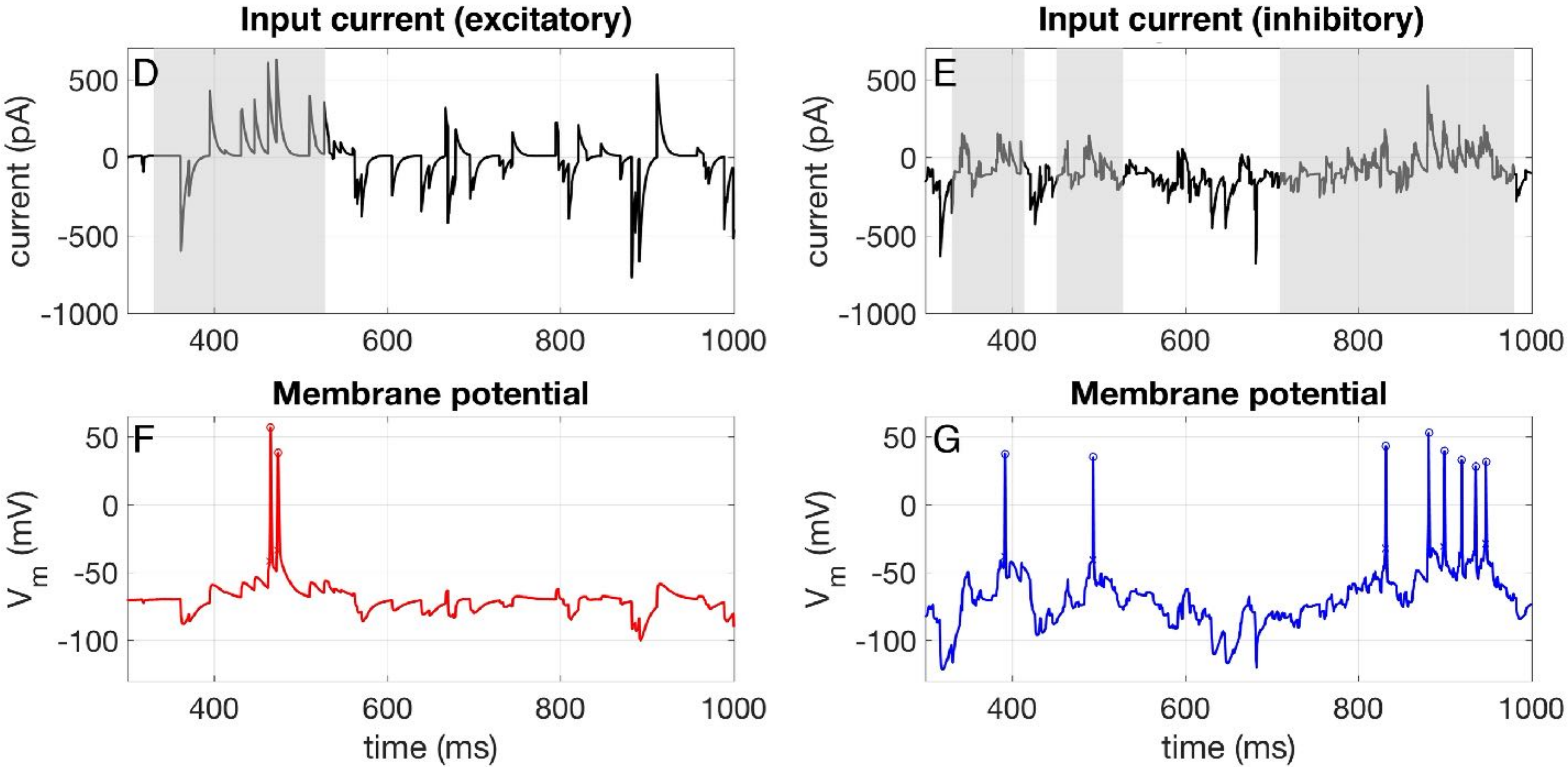
- >850 recordings: current-clamp, voltage-clamp
- 294 neurons from adult mice
- Data is open-source, freely available online

NEURODATA WITHOUT BORDERS

NWB Explorer beta

Single neuron recordings

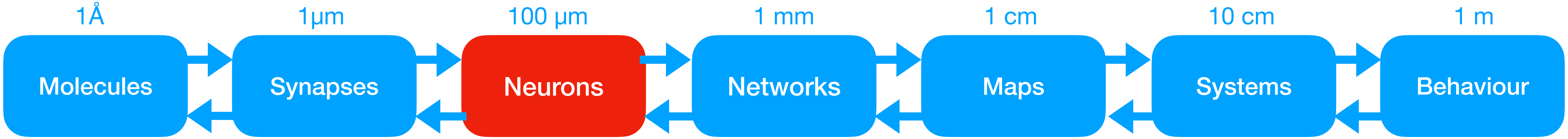


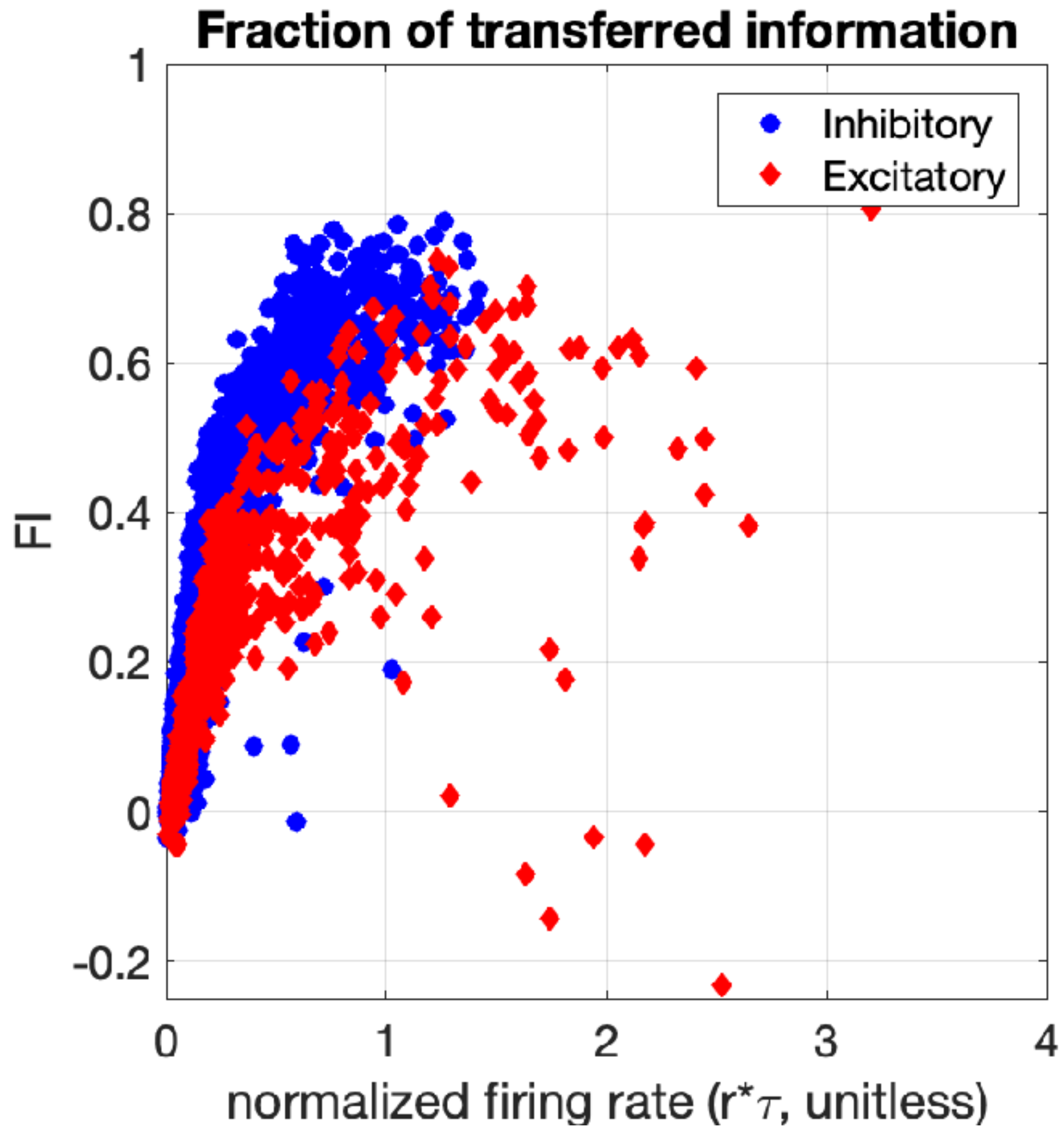


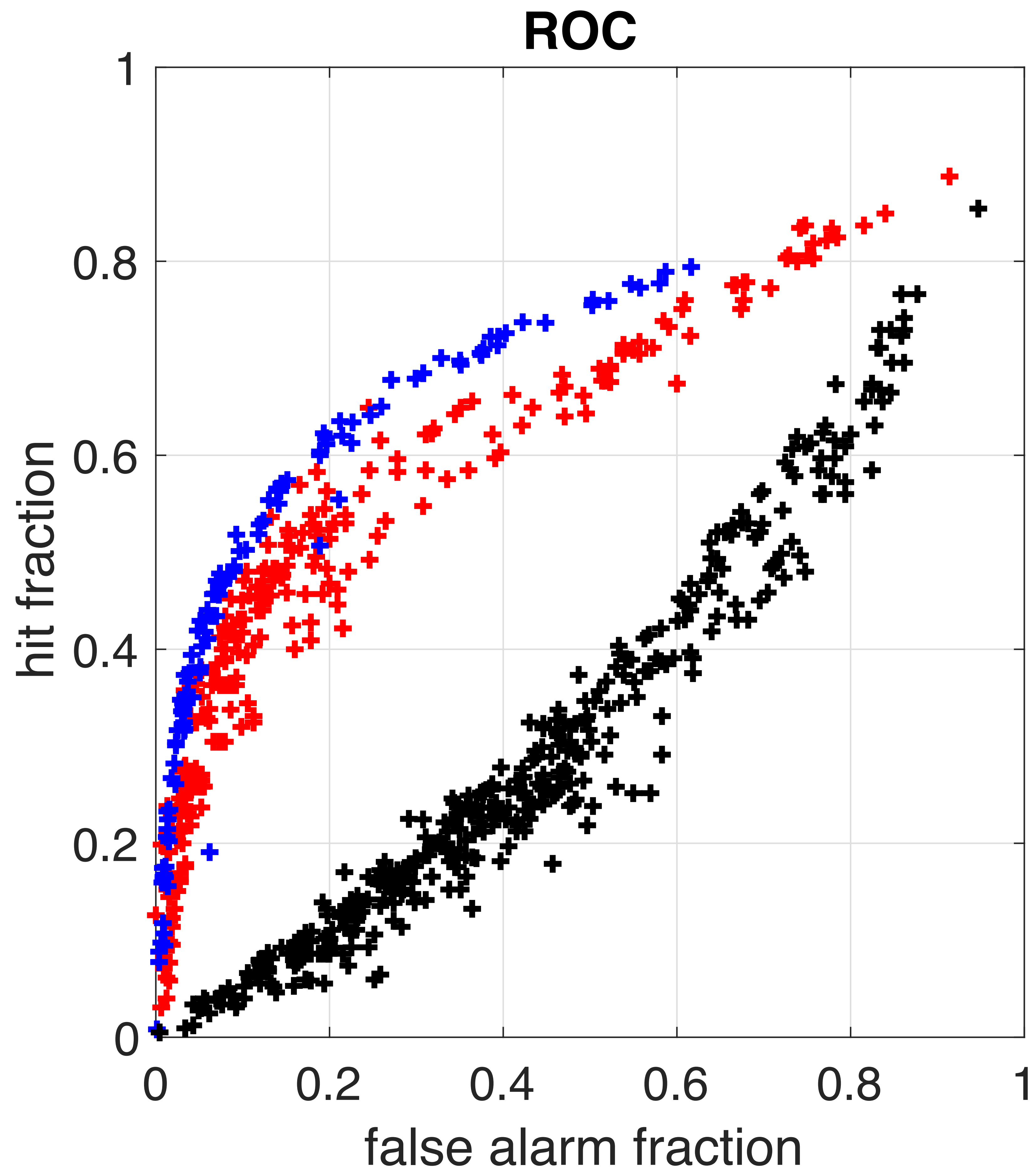
Niccolò Calcini

Zeldenrust, F., Calcini, N., Yan, X., Bijlsma, A., & Celikel, T. (2020). *BioRxiv*

Inhibitory neurons transfer more information





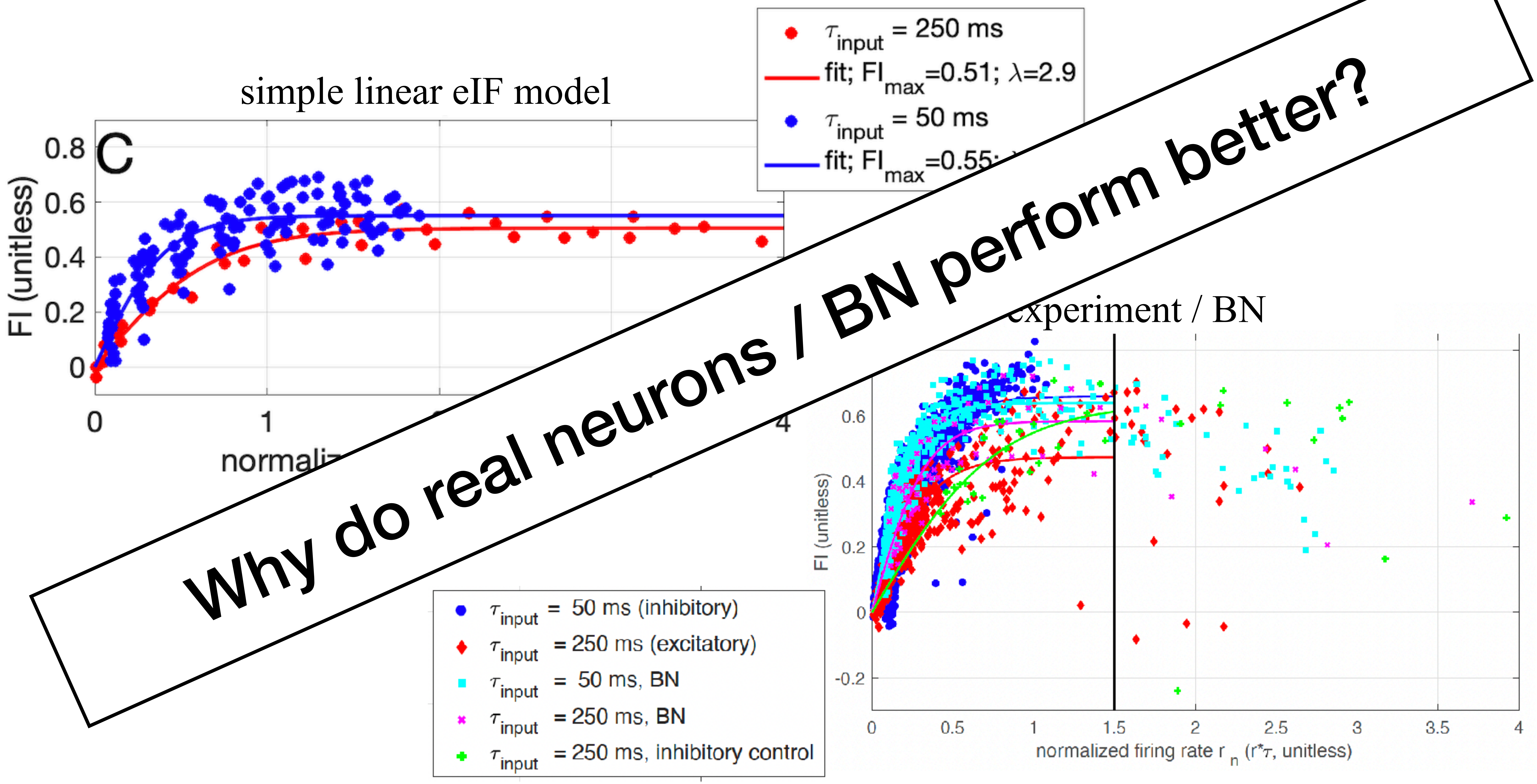


Niccolò Calcini

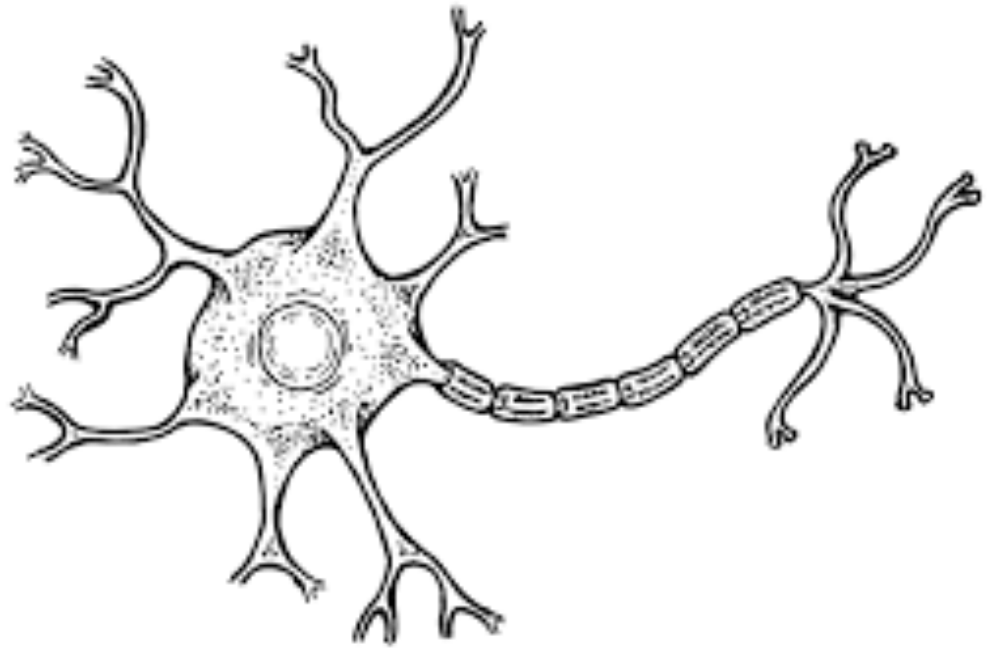
$$FI = \frac{MI_{\text{spike train}}}{MI_{\text{input current}}}$$

Zeldenrust, F., Calcini, N., Yan, X., Bijlsma, A., & Celikel, T. (2024). *PLOS CB*

Can this be captured by a simple (eIF) model?



Why do real neurons / BN transfer more info?



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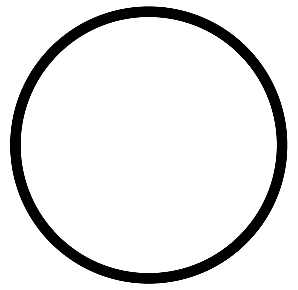
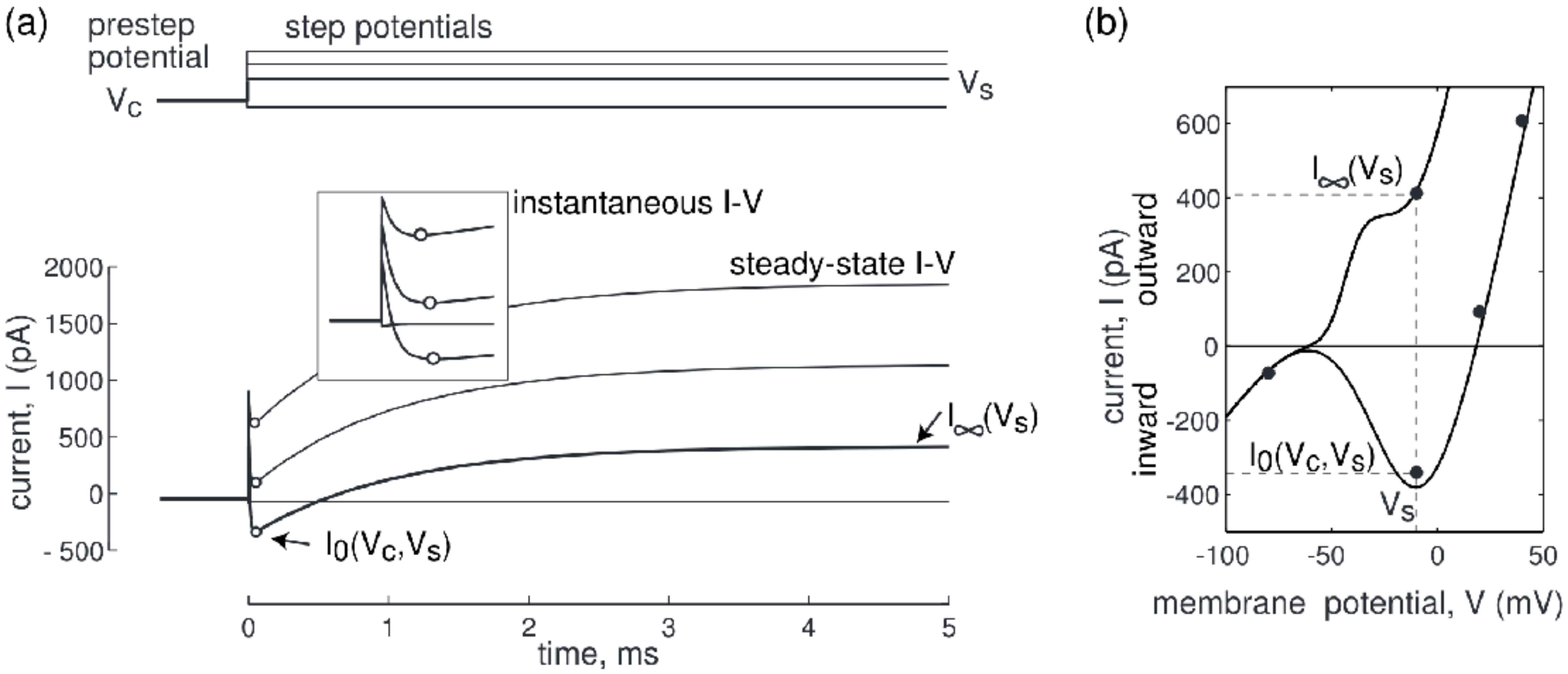


Real neuron / BN

simple eIF neuron

1. Spike frequency adaptation
2. IV curve shape



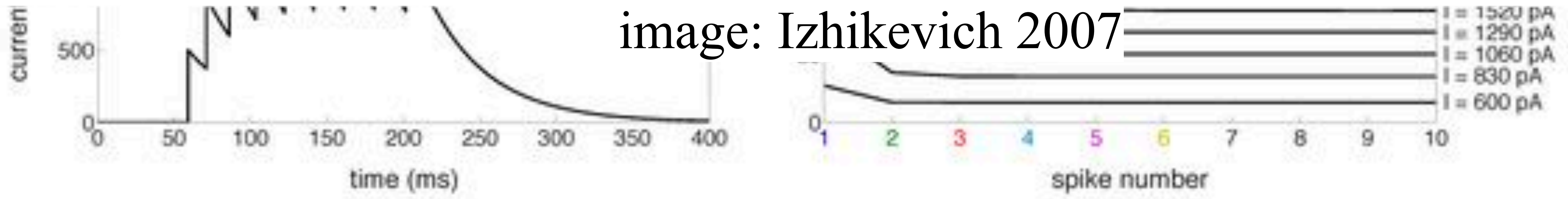


image: Izhikevich 2007

Spike frequency adaptation

Two ways to implement adaptation:

1. Threshold adaptation
   - Every time a neuron spikes, threshold θ goes up
2. Subthreshold adaptation
   - Elevated membrane potential results in hyperpolarizing (potassium) current w

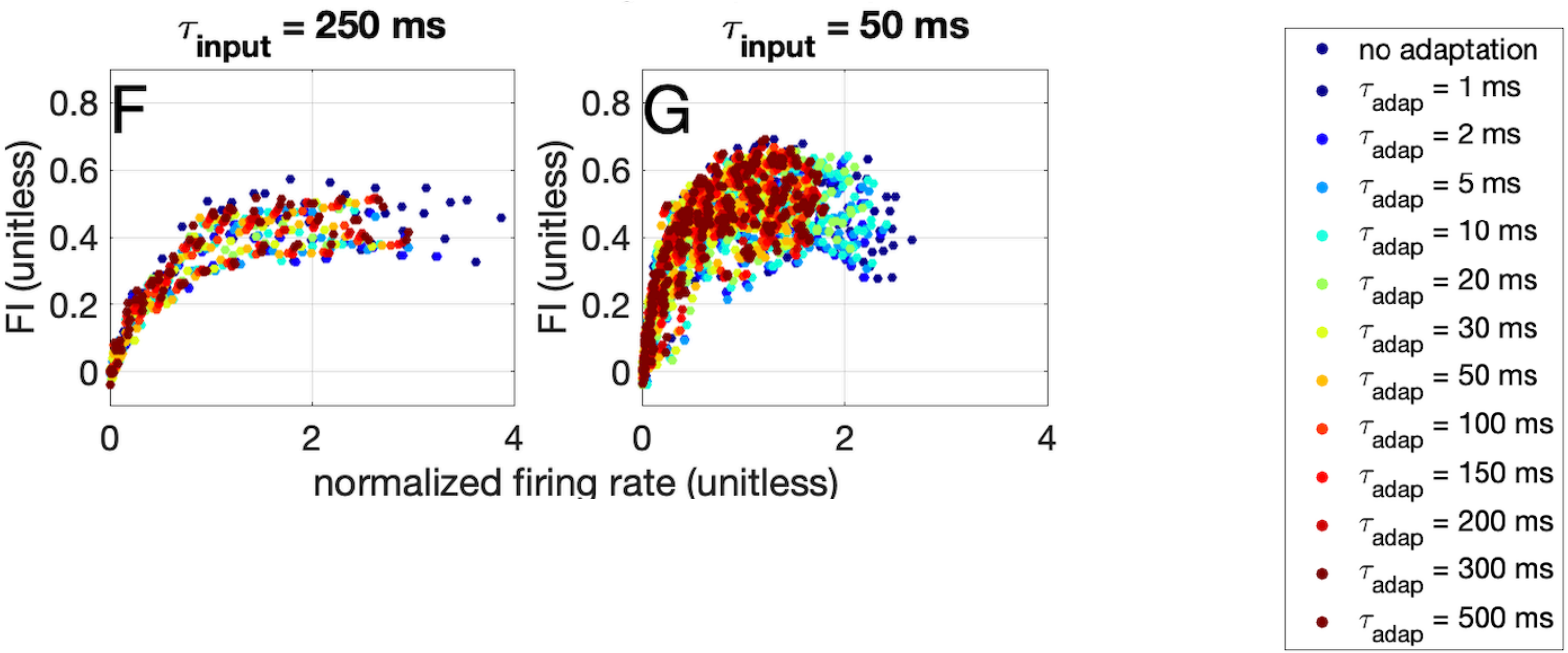
$$C_m \frac{dV_m}{dt} = (g_L(E_L - V_m) + g_L \Delta_T e^{\frac{(Vm-\theta)}{\Delta_T}} + I(t) - w$$

$$\tau_\theta \frac{d\theta}{dt} = \theta_\infty - \theta,$$

$$\tau_w \frac{dw}{dt} = a(V_m - E_L) - w$$

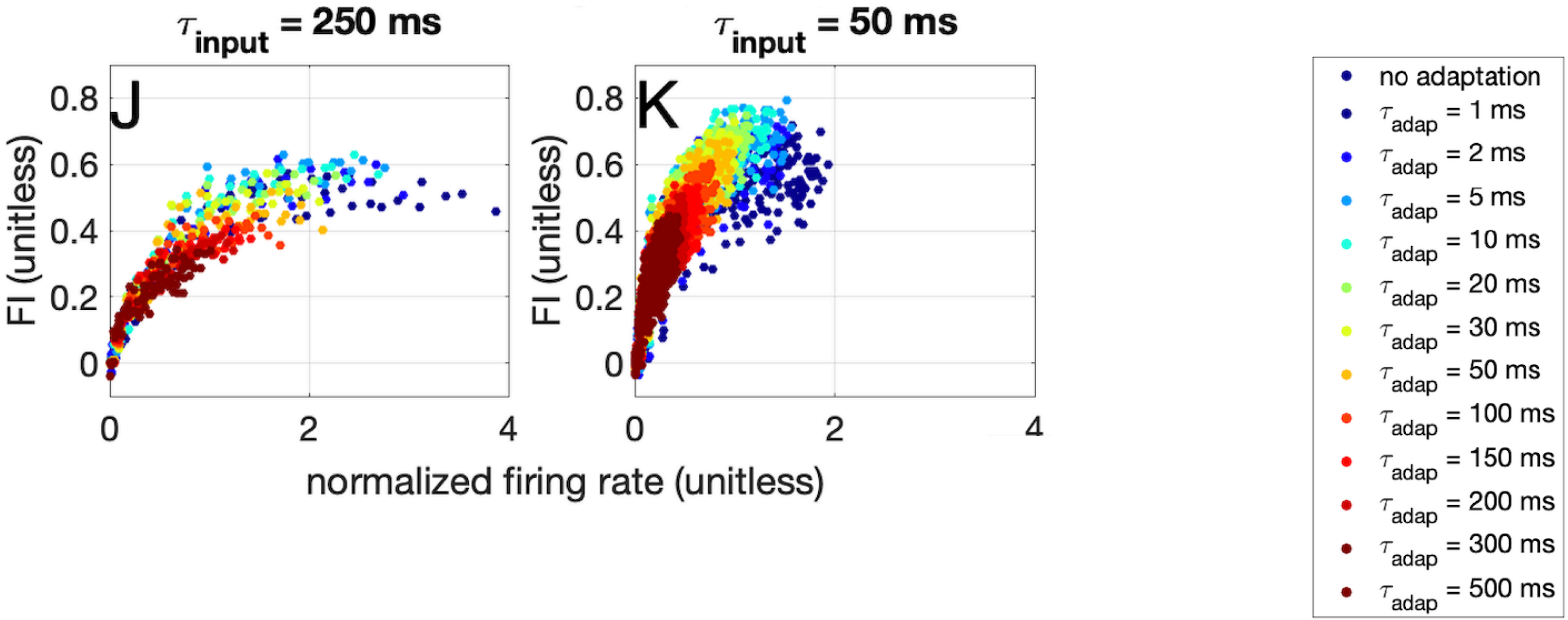
Threshold adaptation

1. Threshold adaptation DOES NOT increase information transfer

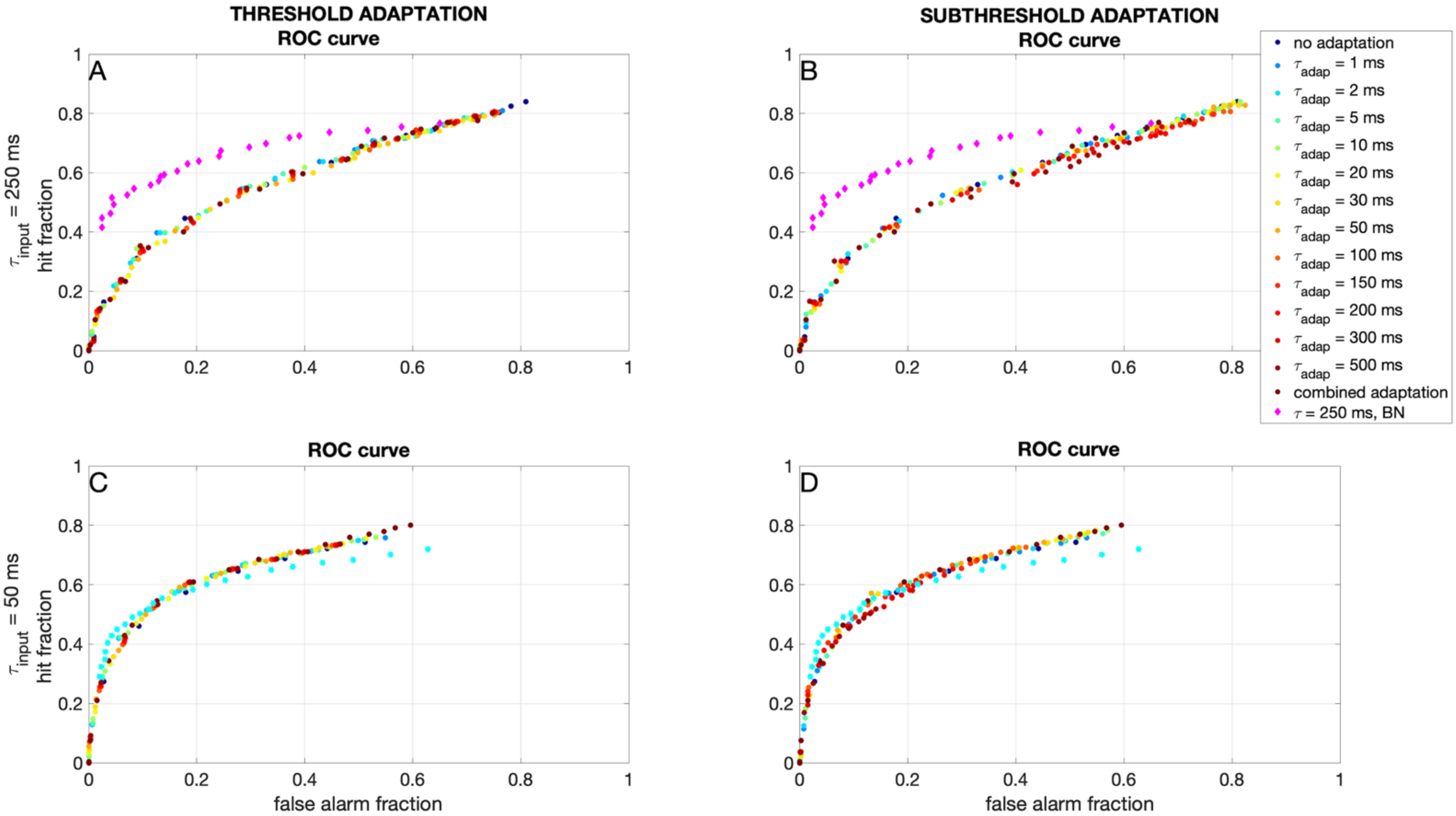


Subthreshold adaptation

1. Subthreshold adaptation DOES increase information transfer



But BN/real neuron still performs better!



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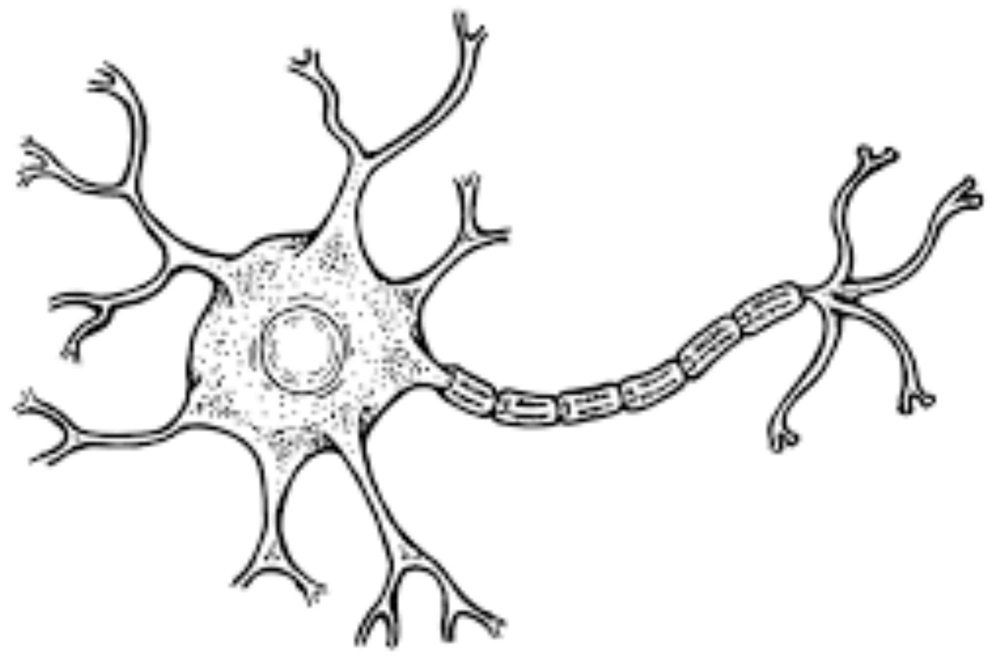
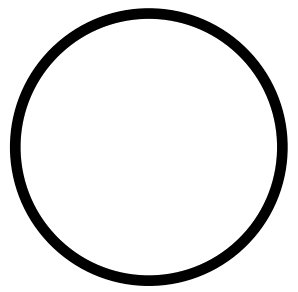


$\Leftrightarrow$

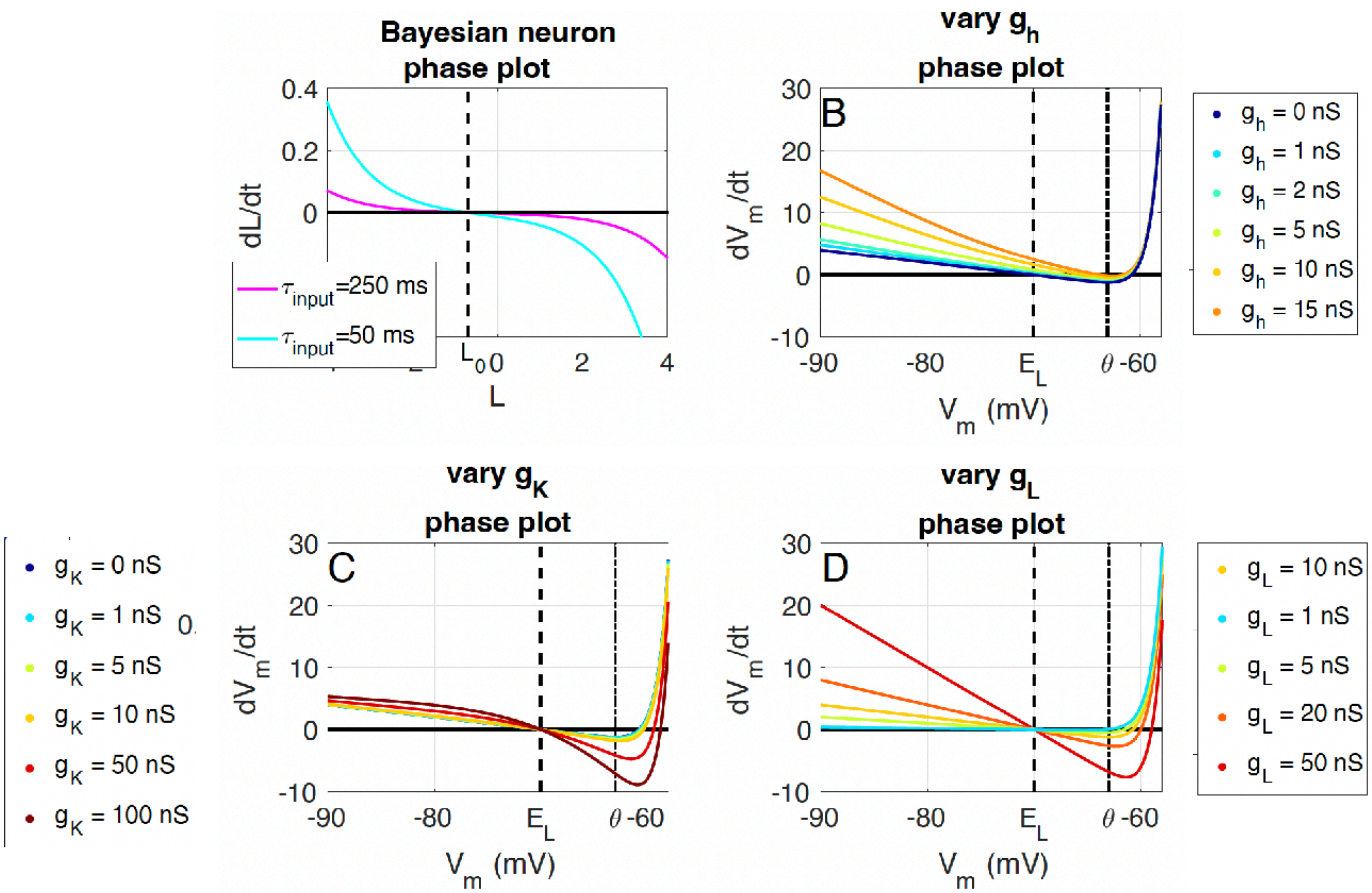


Real neuron / BN

simple eIF neuron

1. Spike frequency adaptation
   - Threshold adaptation increases working range but not info transfer
   - Subthreshold adaptation increases info transfer but not working range
   - Real neuron / BN still performs better (for slow input)
2. IV curve shape

IV curves

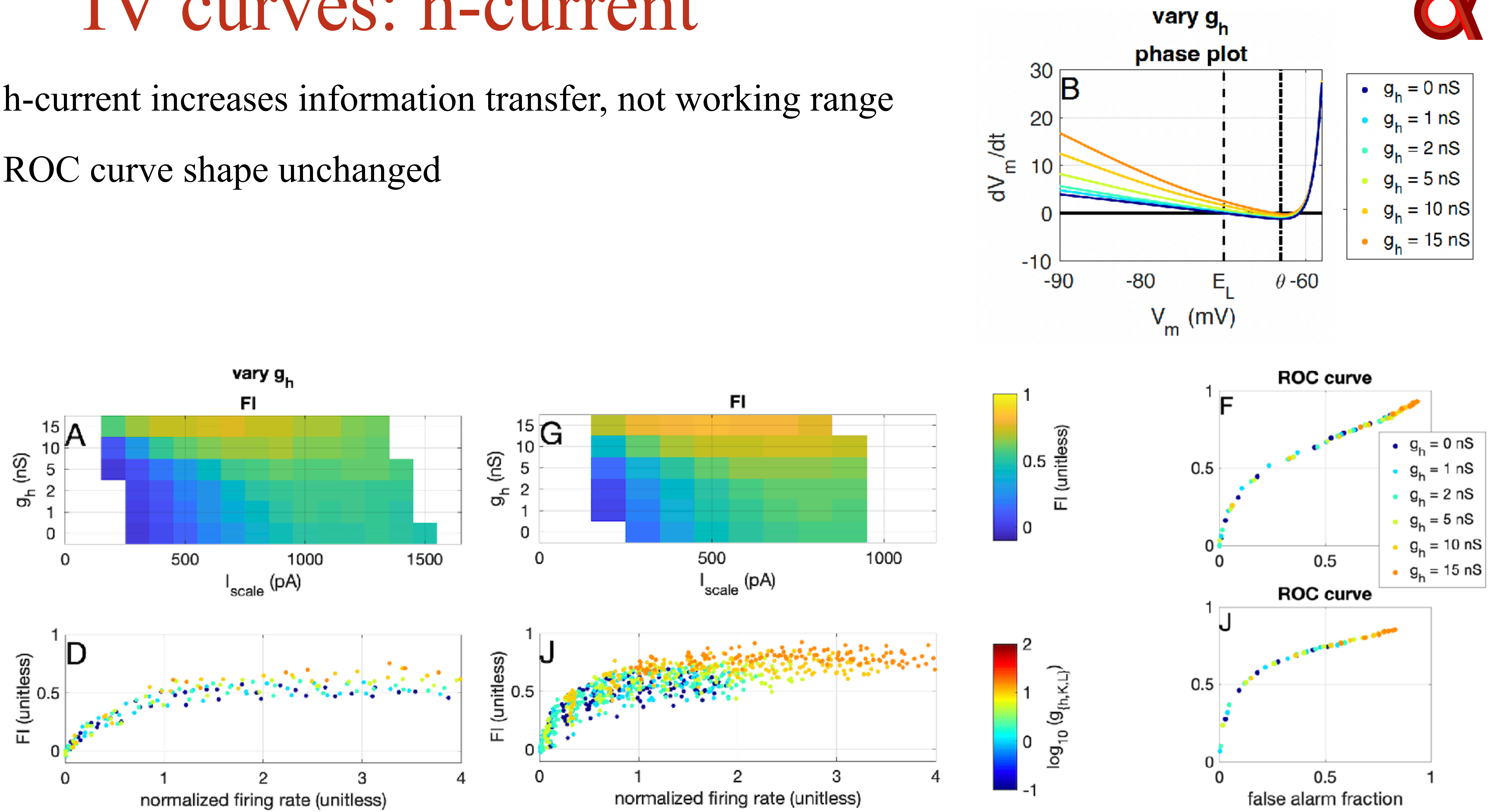


Bayesian neuron
phase plot
0.4
0.2
0
dL/dt
τ_{input}=250 ms
τ_{input}=50 ms
L_0 0
2
4
L
vary g_h
phase plot
30
20
10
0
-10
B
dV_m/dt
-90
-80
E_L
θ -60
V_m (mV)
g_h = 0 nS
g_h = 1 nS
g_h = 2 nS
g_h = 5 nS
g_h = 10 nS
g_h = 15 nS
g_K = 0 nS
g_K = 1 nS
g_K = 5 nS
g_K = 10 nS
g_K = 50 nS
g_K = 100 nS
vary g_K
phase plot
C
dV_m/dt
V_m (mV)
vary g_L
phase plot
D
dV_m/dt
V_m (mV)
g_L = 10 nS
g_L = 1 nS
g_L = 5 nS
g_L = 20 nS
g_L = 50 nS

IV curves: h-current

h-current increases information transfer, not working range

ROC curve shape unchanged



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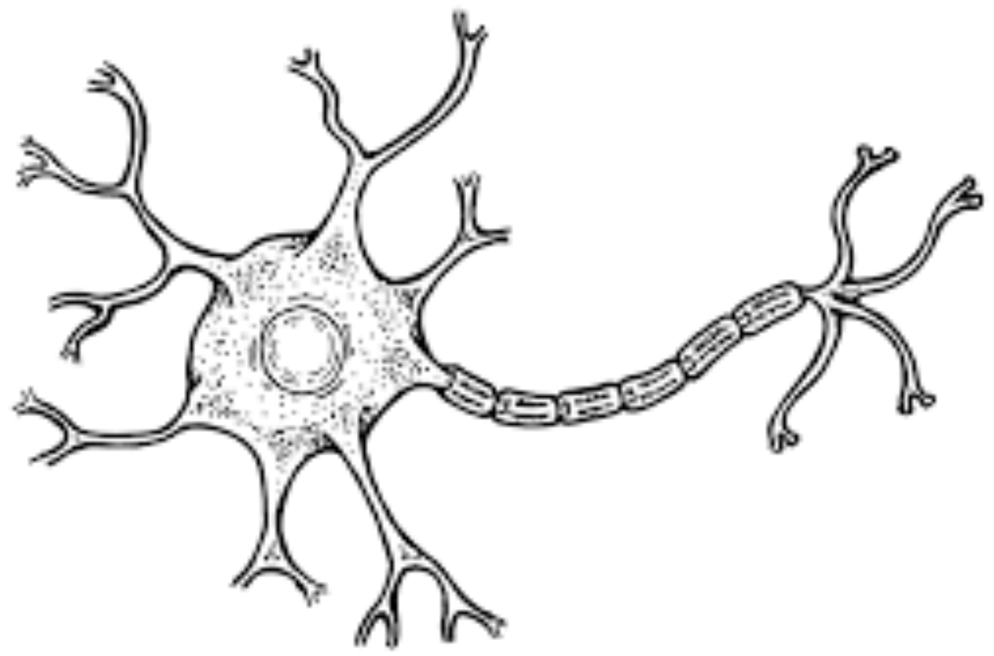

⇔

Real neuron / BN

simple eIF neuron

We still don't know!

Mechanism	Max in[illegible]	[illegible]orking range	ROC curve
threshold adaptation	[illegible]	increased / shift to higher amplitudes	unchanged
subthreshold ad[illegible]	[illegible] properly)	unchanged	unchanged
st[illegible] I[illegible]	[illegible]creased (if tuned properly)	depends on tuning	better detection if tuned properly
hy[illegible] part IV [illegible] (g_h)	increased at the cost of higher firing rate	shift to lower amplitudes	unchanged shape shift towards higher rates
depolarized part IV curve (g_K)	decreased	shift to higher amplitudes	shape unchanged shift towards lower rates

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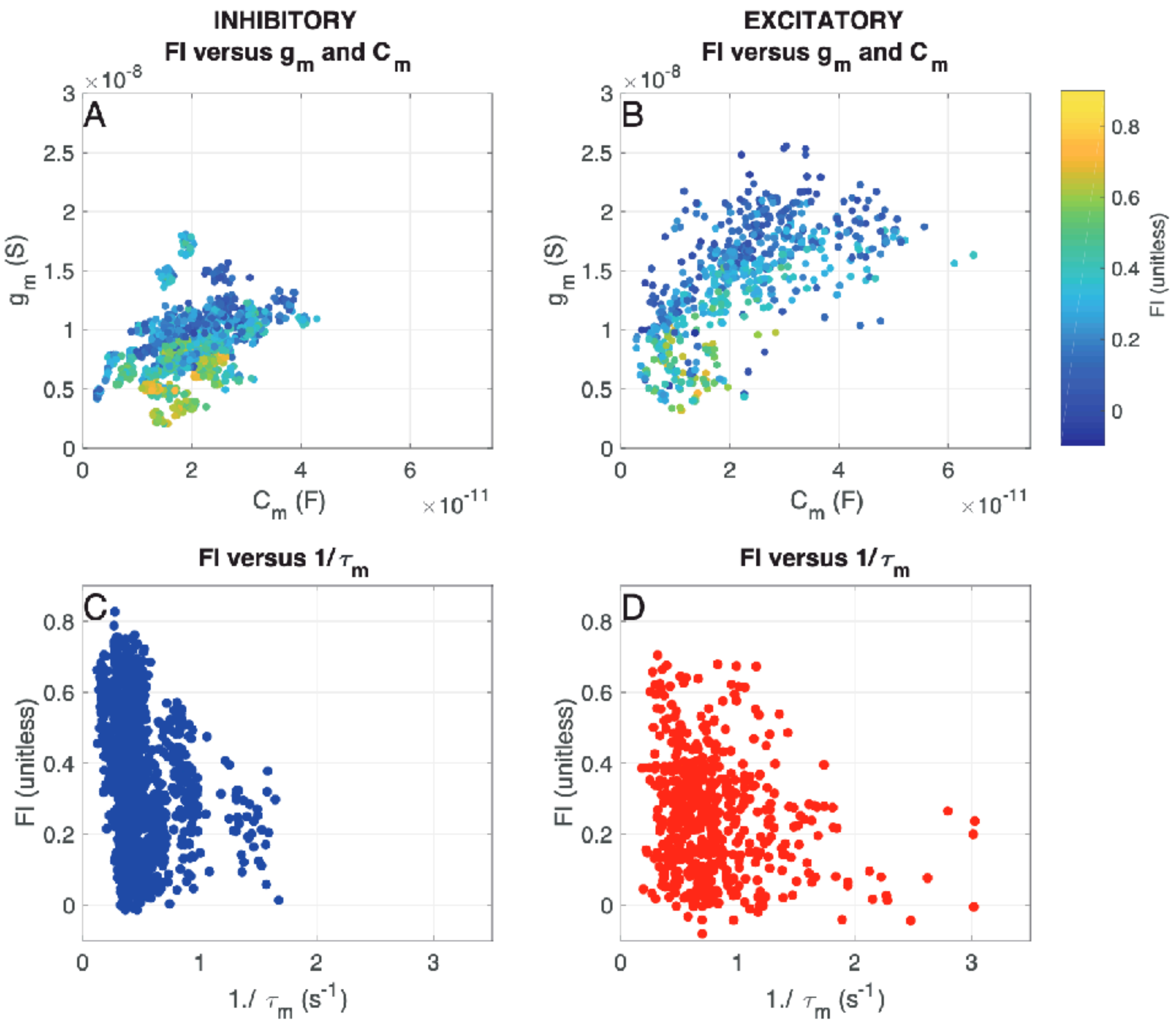
IV-curve in recordings

Badel et al. 2008: dynamic IV curve

Inverse relation FI and slope IV-curve (g)
⇒ same as for leak current in model

Large *variability* of intrinsic properties, in particular for regular spiking excitatory neurons.

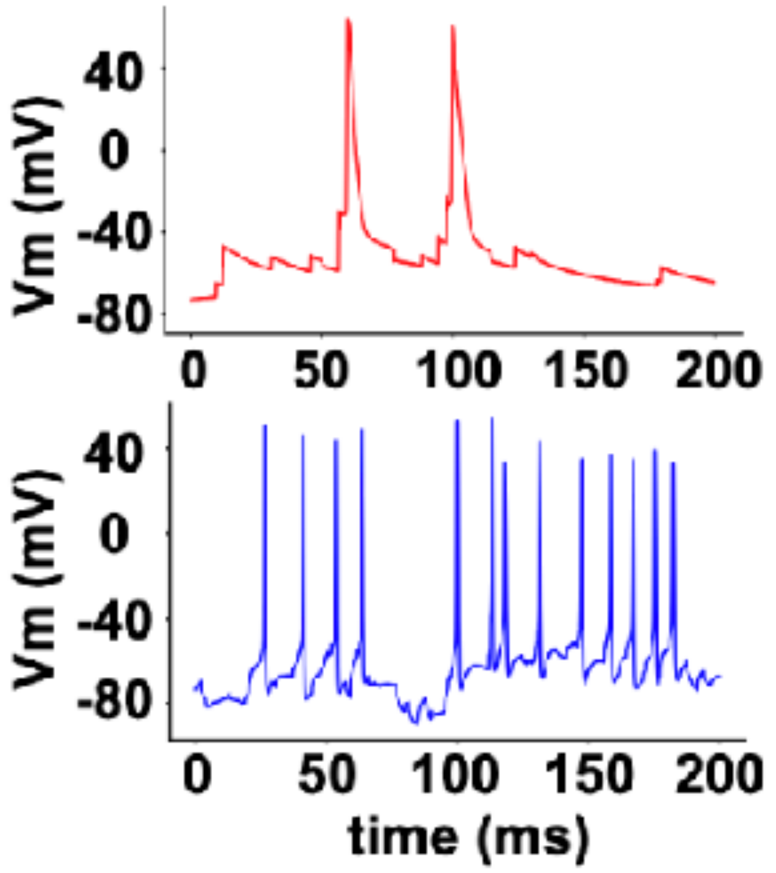


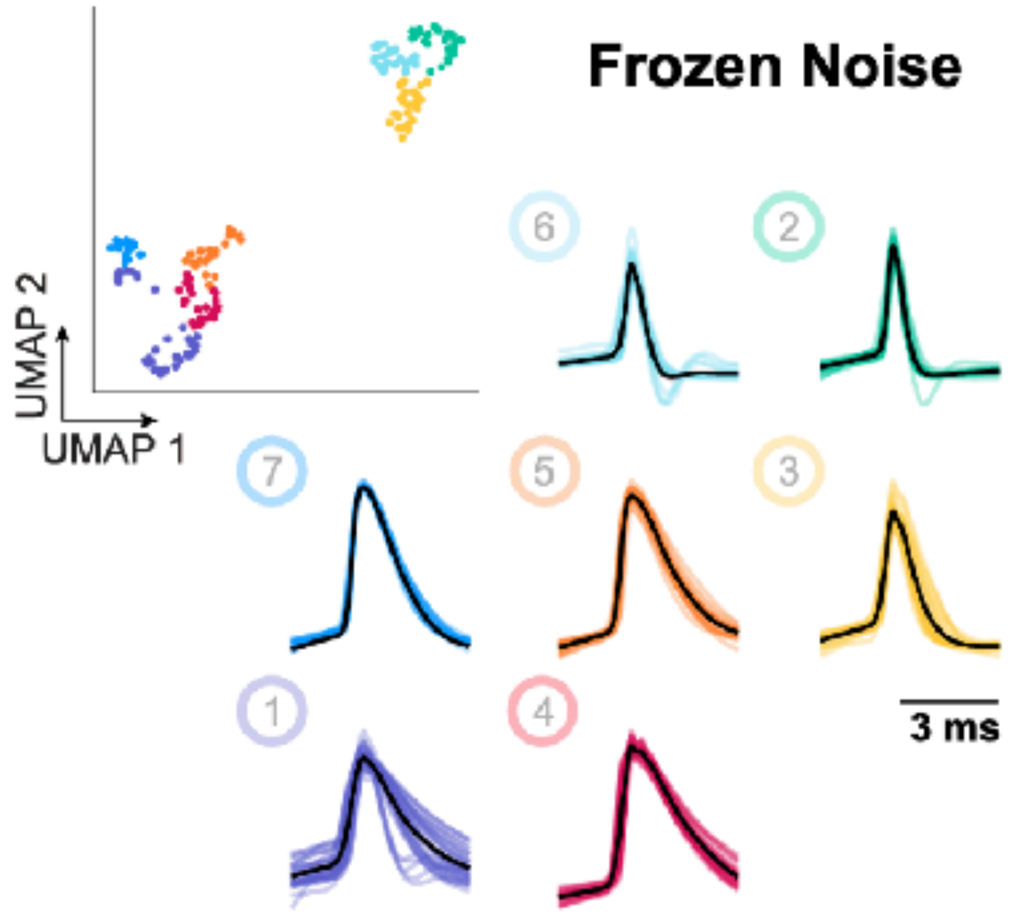
$$\tau_m = \frac{C_m}{g_m}$$

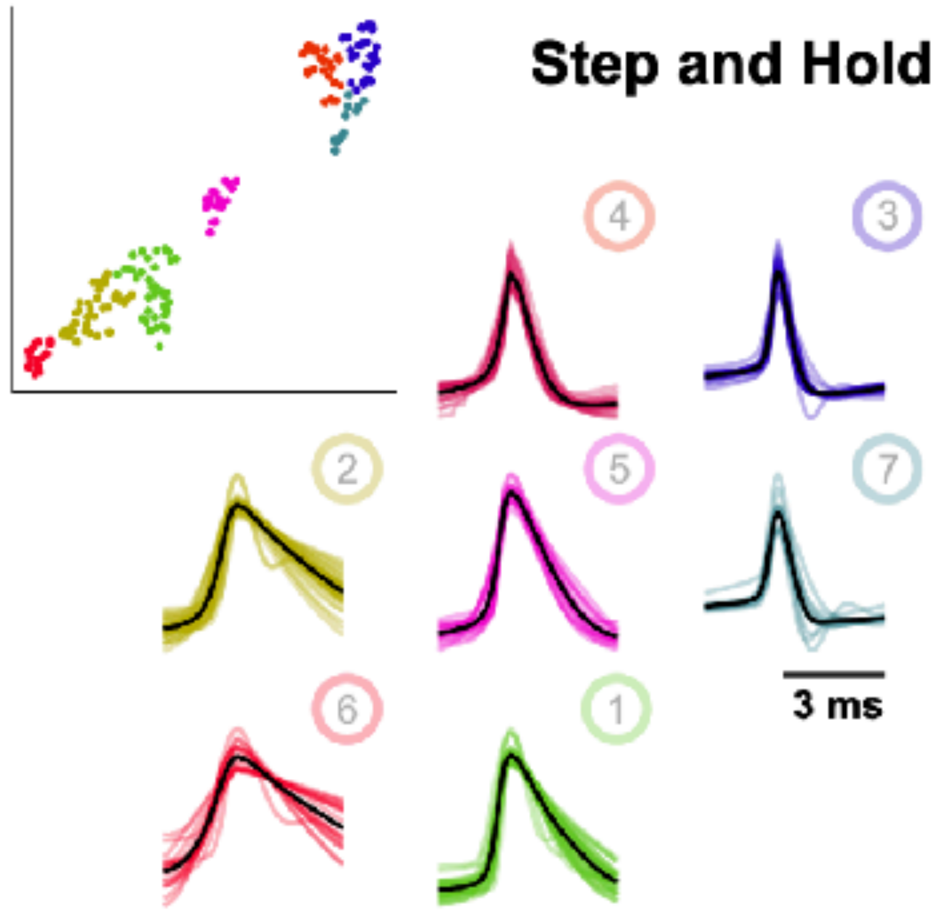
Deeper dive: cell type depends on input

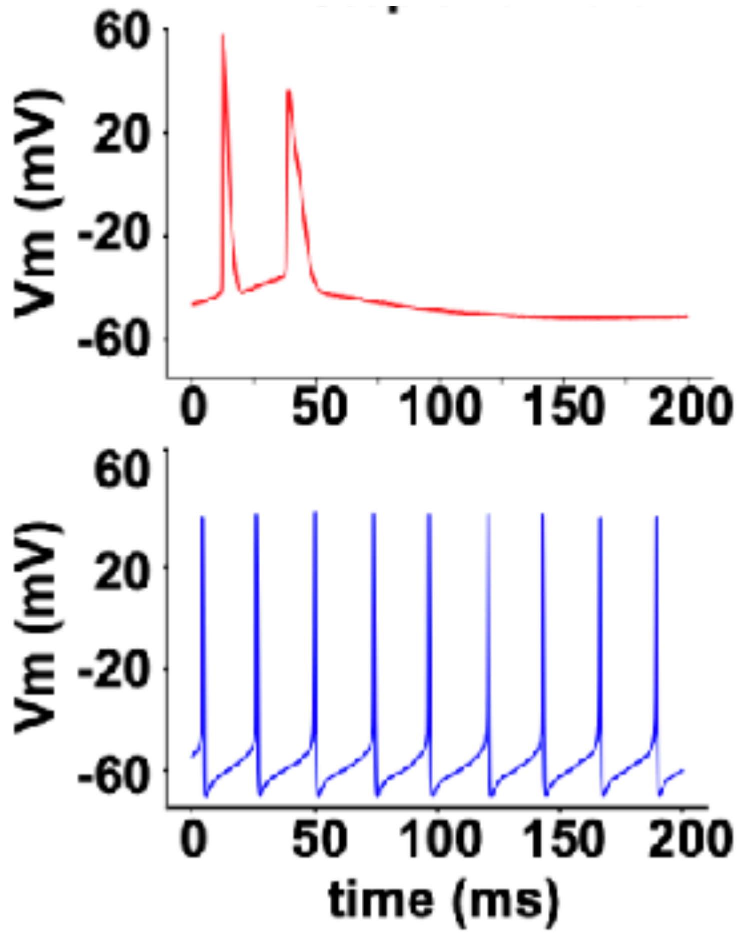
Nishant Joshi

Two types of input, same set of neurons. Same classification?

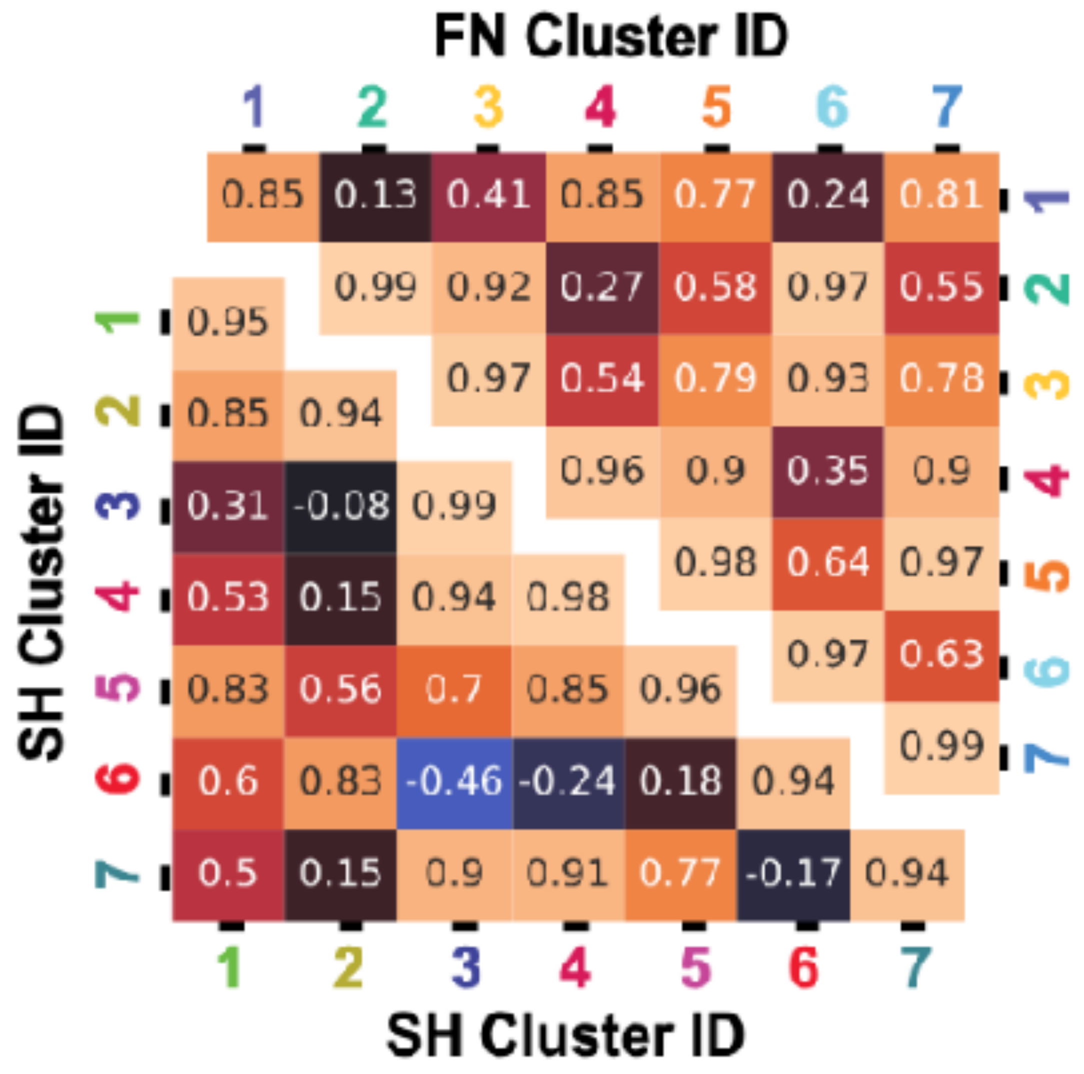


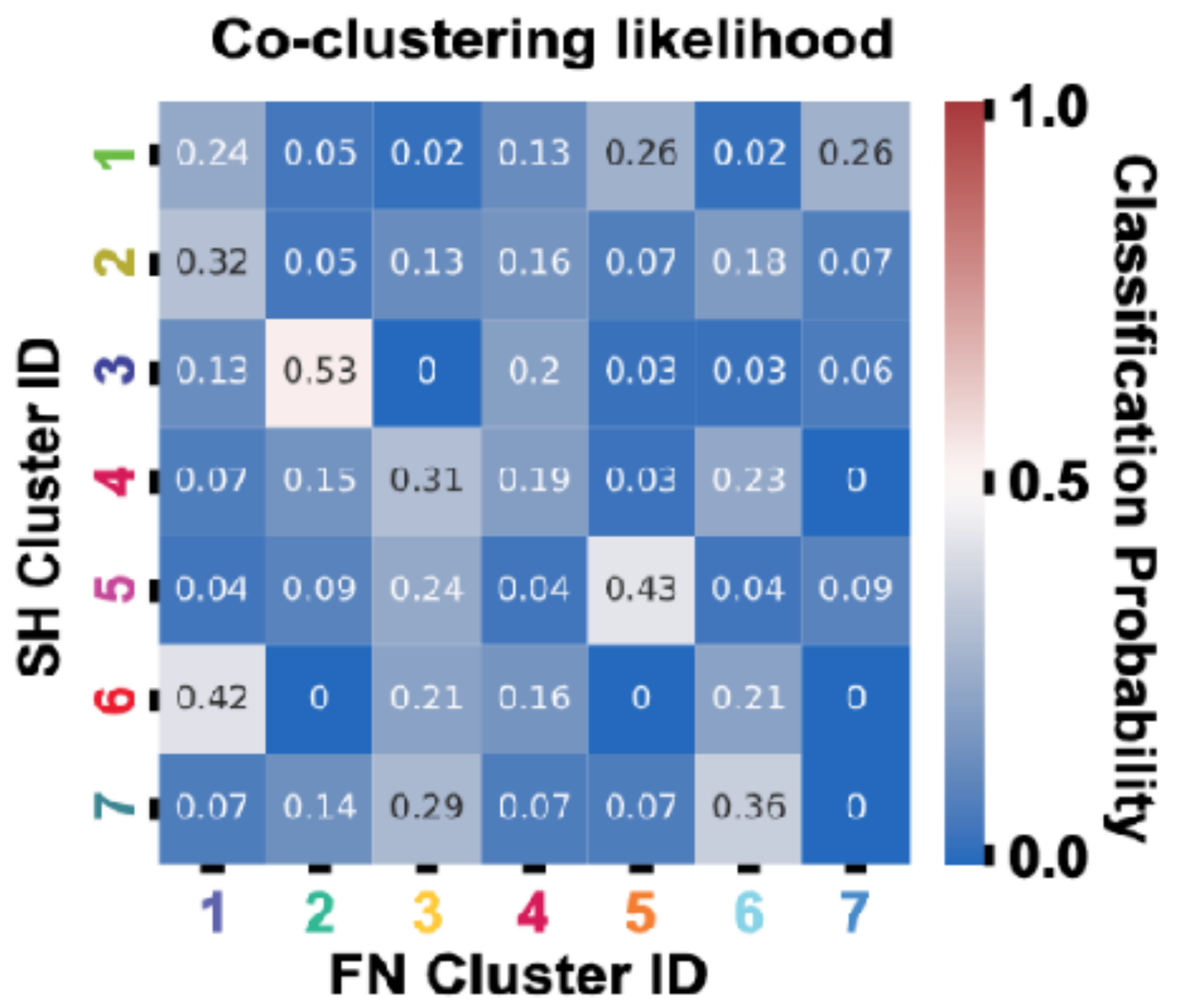






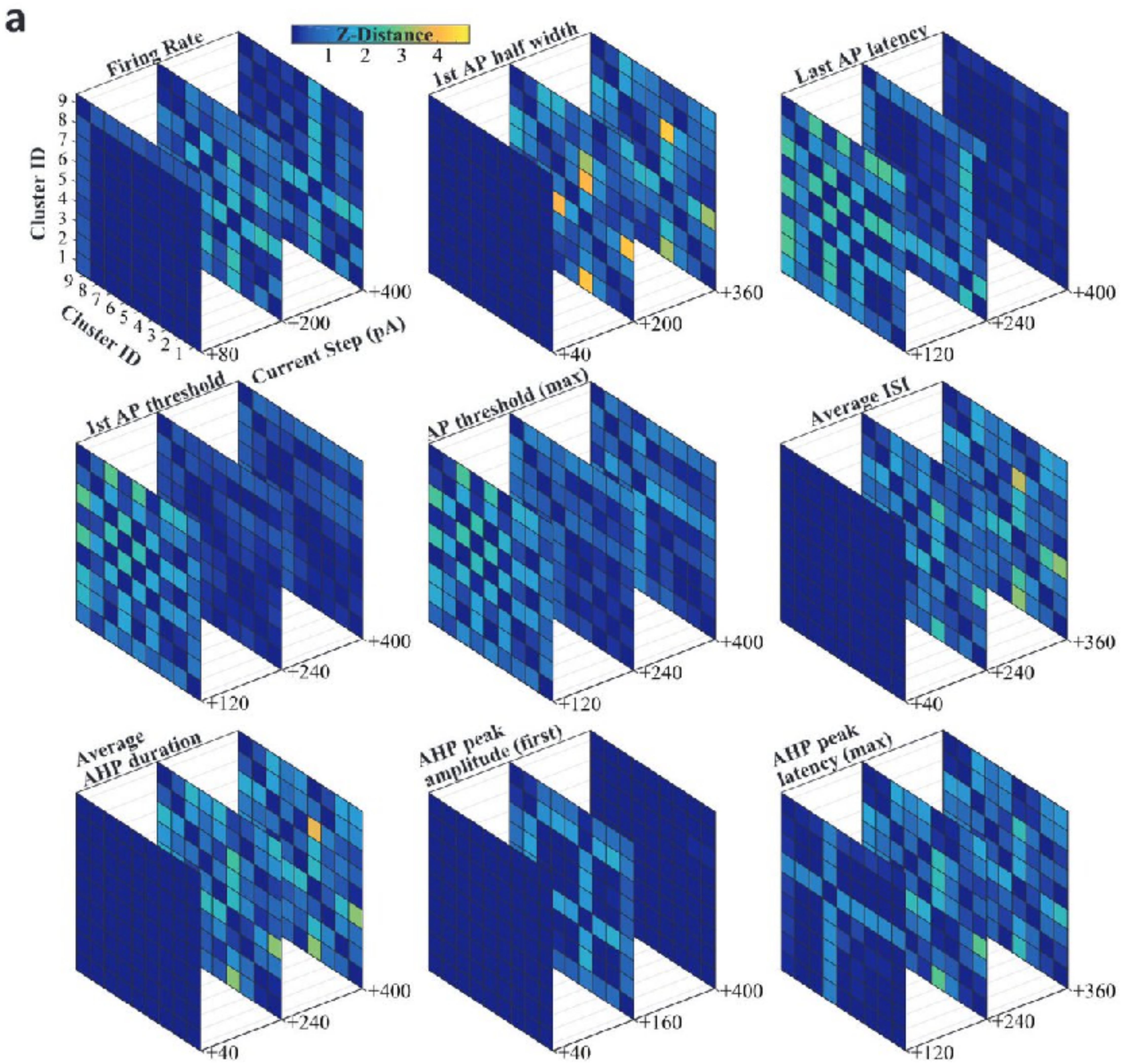
NO!





Joshi, N., van der Burg, S., Celikel, T, Zeldenrust, F., Understanding Neuronal Diversity:Role of Input Dynamics and Selectivity, to appear soon!

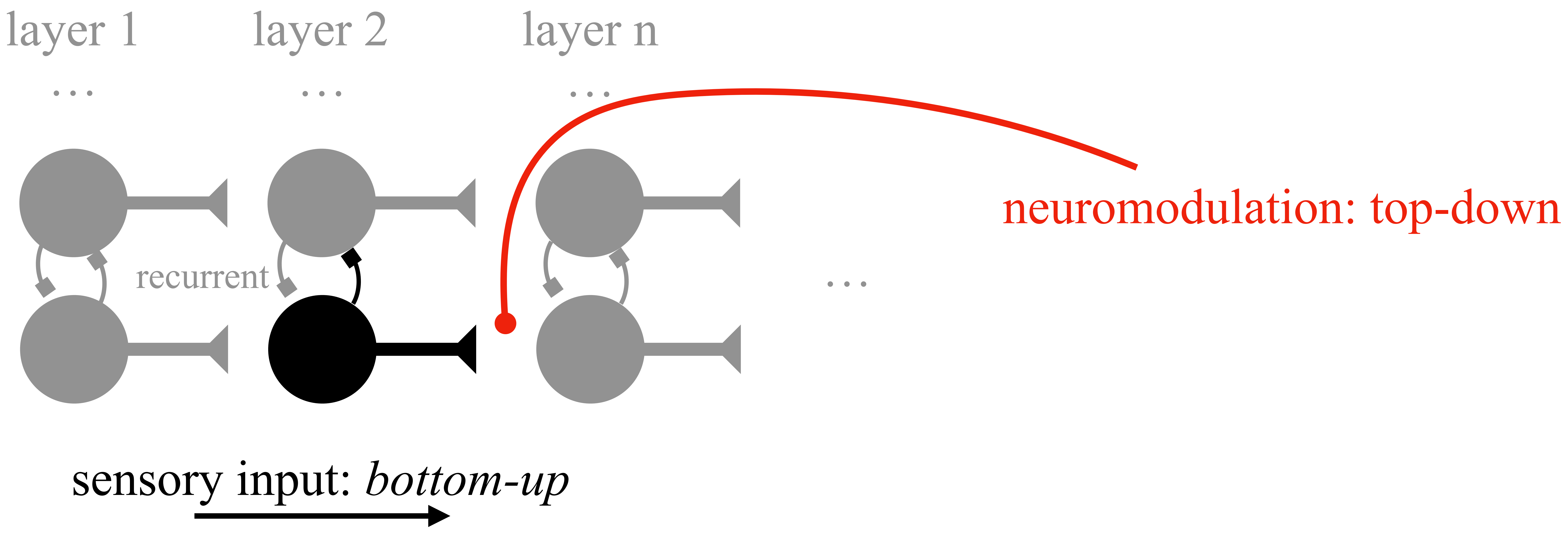
Cell type depends on stimulation amplitude



Niccolò Calcini

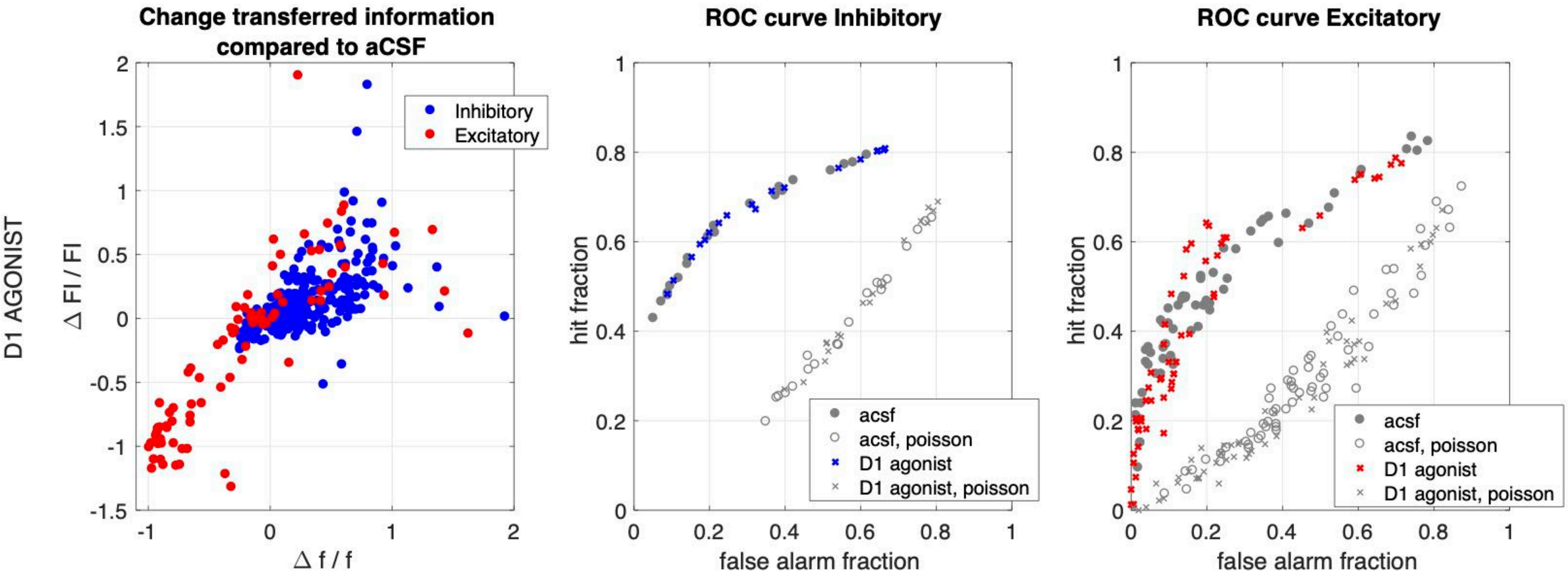
Calcini, N., Zeldenrust, F., & Celikel, T. (2024). *Electrical diversity of neurons in sensory cortices*. https://doi.org/10.1101/2024.10.07.617007

How does the brain adapt?



How and why do neuromodulators influence sensory processing?
→ Computational modelling

D1-agonist increases inhibitory information



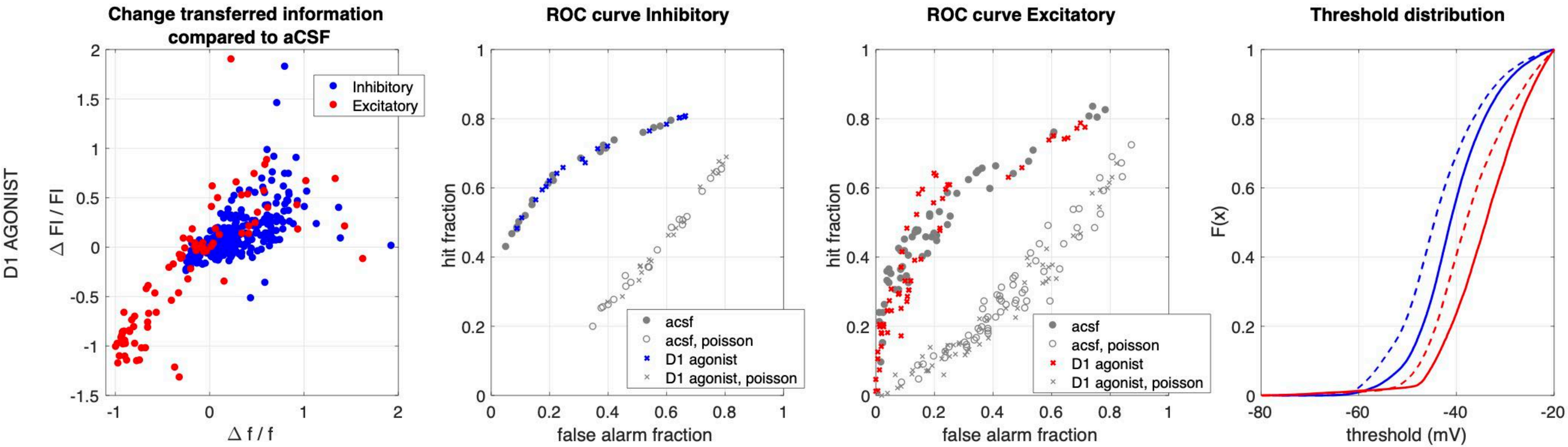
Niccolò
Calcini

Xuan Yan

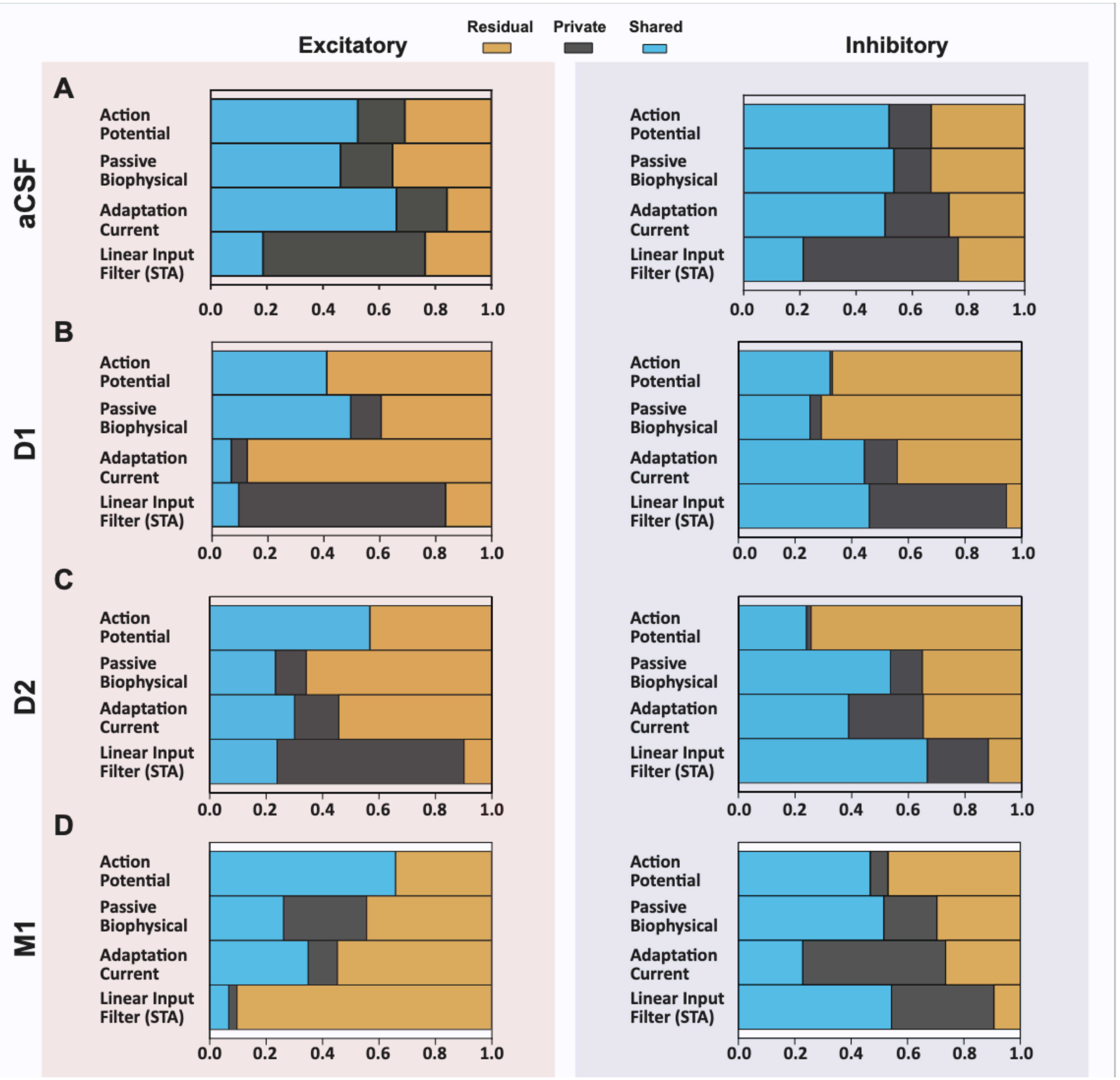
D1-agonist decreases inhibitory threshold

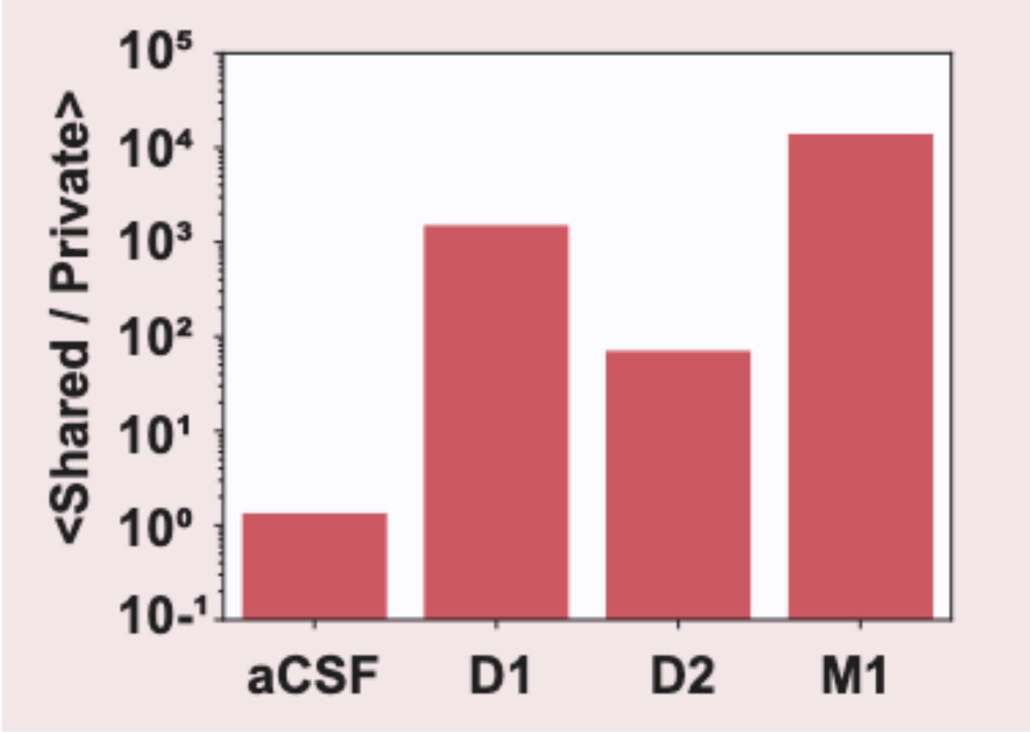
Xuan Yan

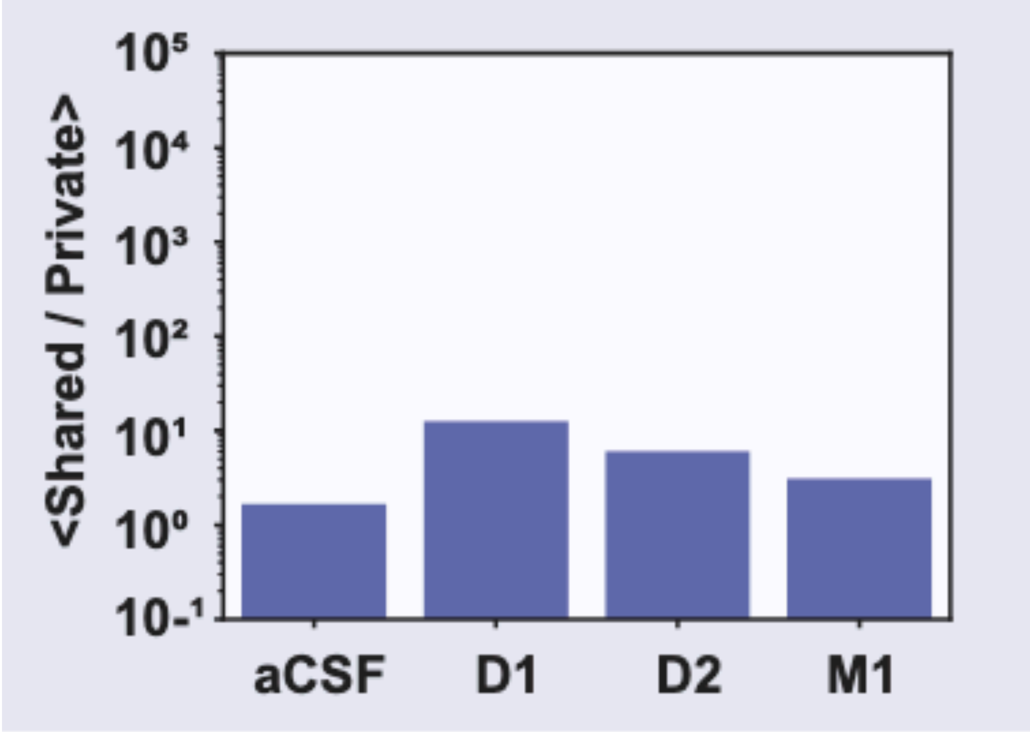
Niccolò Calcini



Heterogeneity changes with modulation







Joshi, N., Burg, S. van der, Celikel, T., & Zeldenrust, F. (2025). *in preparation*

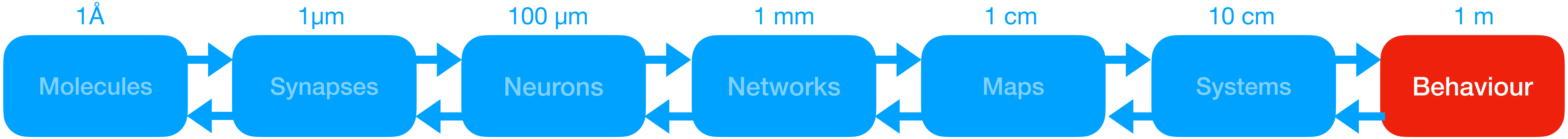
Conclusions

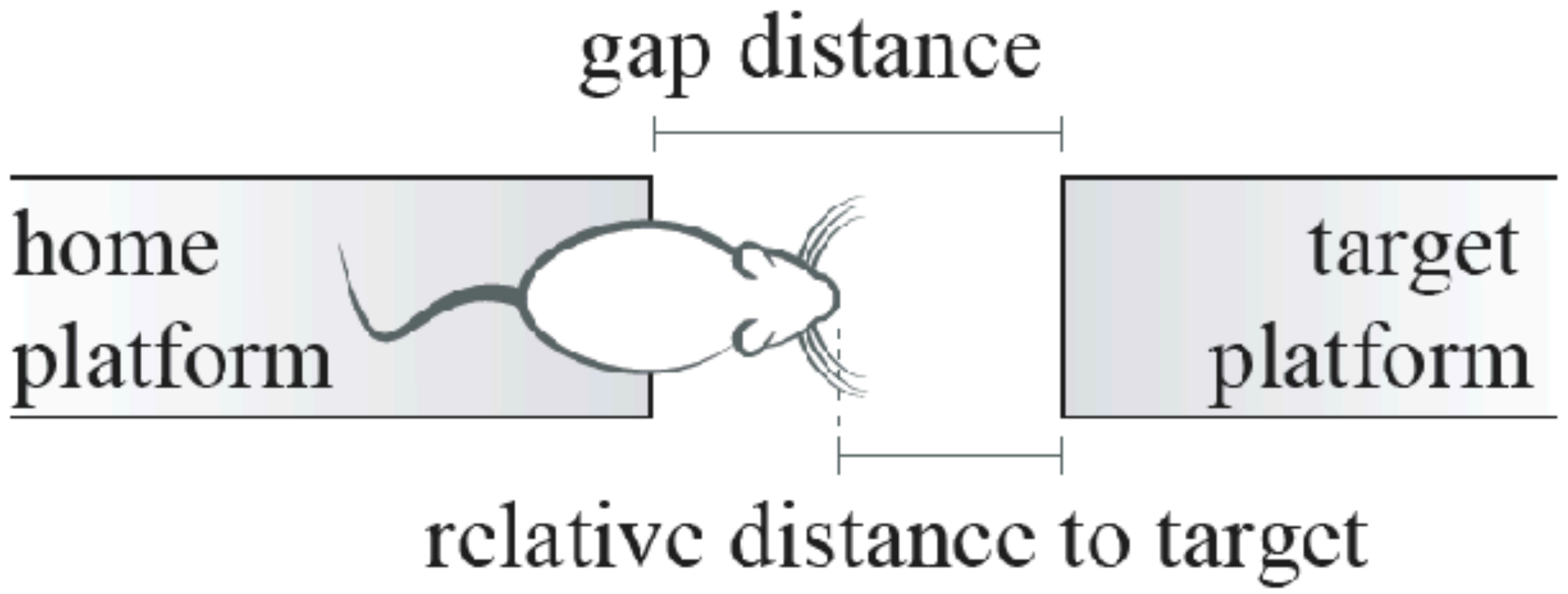
→ Neuron level

- Neurons perform complex, non-linear computations
- Cortical neurons show a large heterogeneity in their properties
- ‘Cell type’ depends on input
- Neuromodulators affect inhibitory and excitatory neurons differentially
- Neuromodulators affect ‘cell type’ and heterogeneity

What are the network level effects of this?

Behaviour: gap-crossing task





Voigts, Herman, Celikel (2015): Mice precisely target their whiskers to the distance at which they **expect** objects.

Supporting data for "An open-source high-speed infrared videography database to study the principles of active sensing in freely navigating rodents"

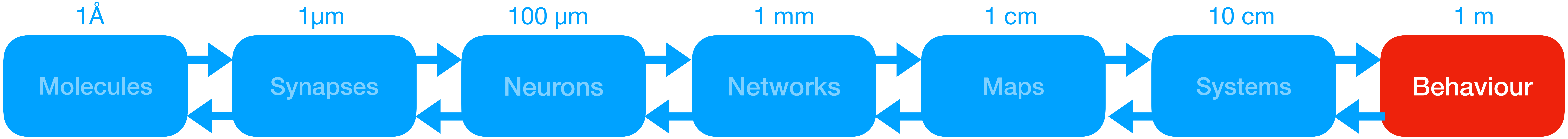
Dataset type: Imaging, Neuroscience

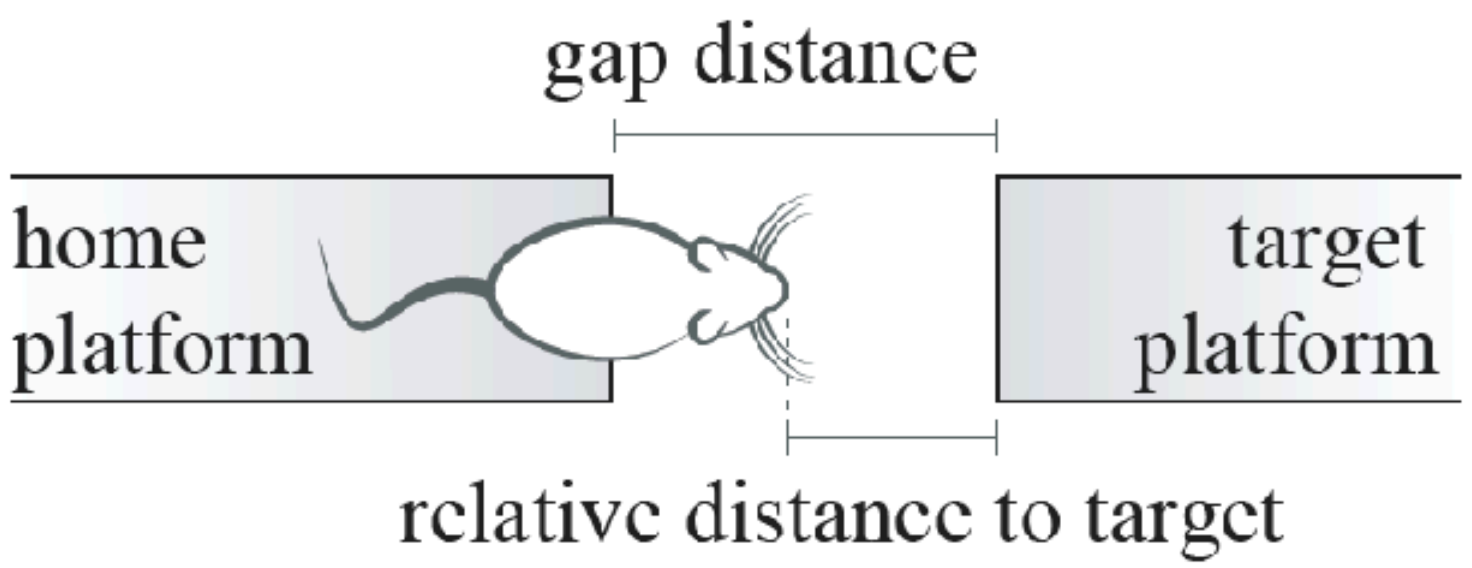
Data released on October 18, 2018

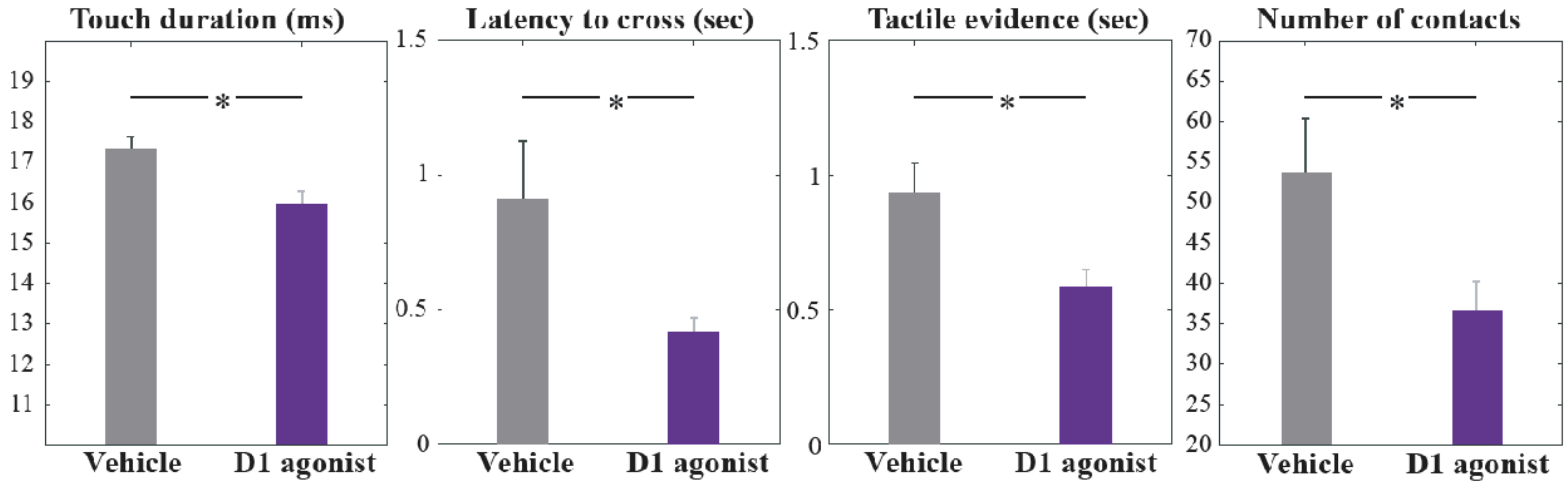
Azarfar A; Zhang Y; Alishbayli A; Miceli S; Kepser L; der Wielen Dv; de Moosdijk Mv; Homberg J; Schubert D; Proville R; Celikel T (2018): Supporting data for "An open-source high-speed infrared videography database to study the principles of active sensing in freely navigating rodents" GigaScience Database. http://dx.doi.org/10.5524/100512

DOI 10.5524/100512

D1 agonist: faster information integration







Calcini, N., Bijlsma, A., Zhang, Y., Lantyer, A. da S., Kole, K., Celikel, T., & Zeldenrust, F. (2019). Cell-type specific modulation of information transfer by dopamine. In Cosyne Abstracts 2019, Lisbon, PT.

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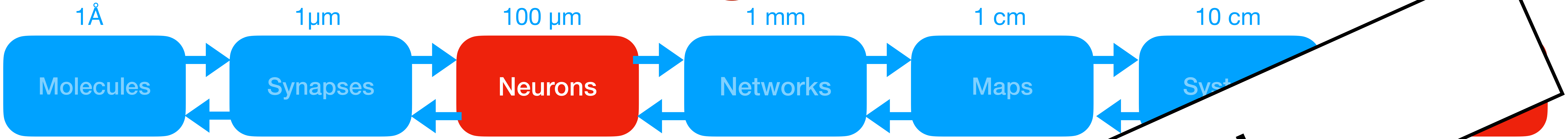
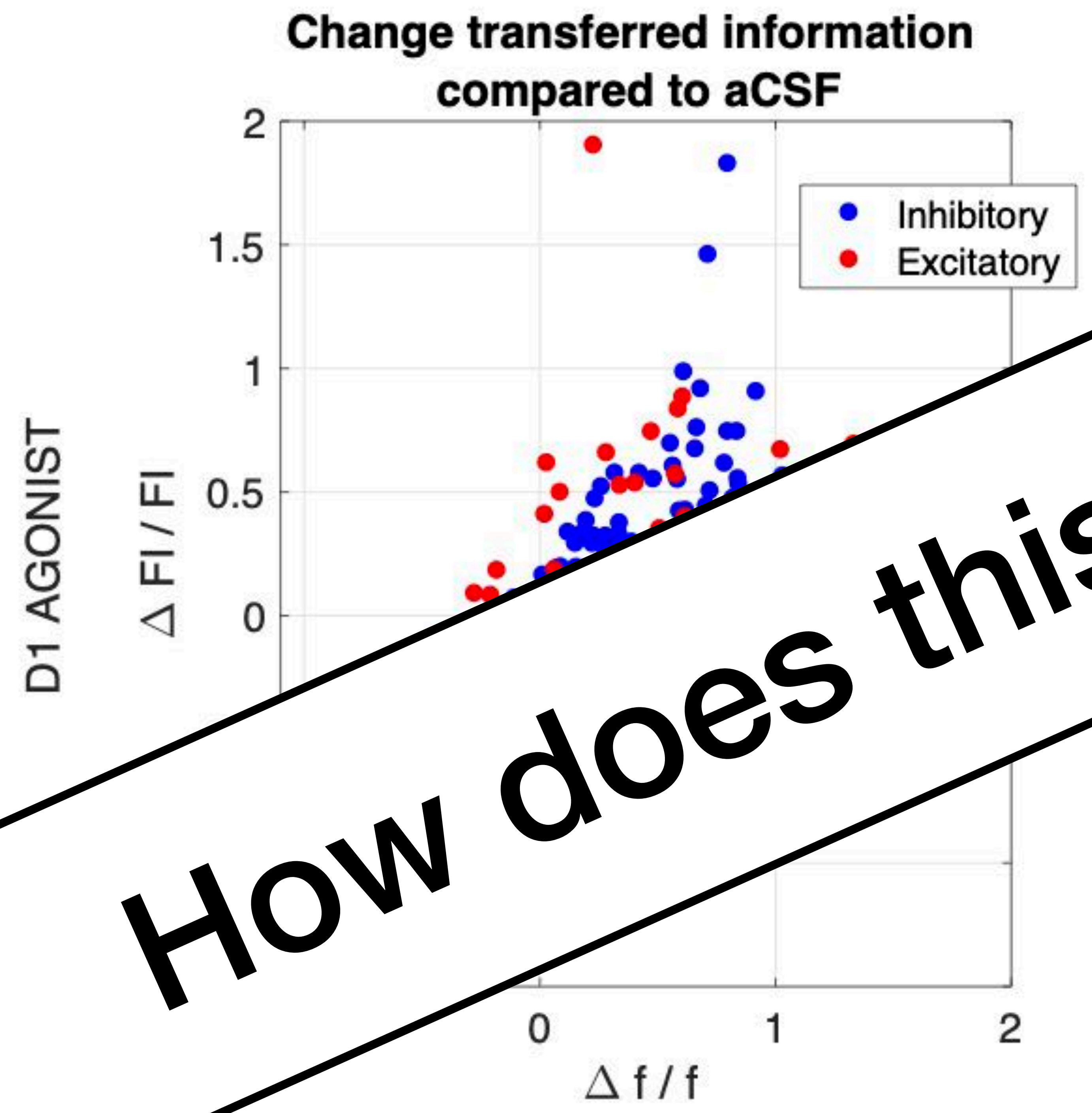
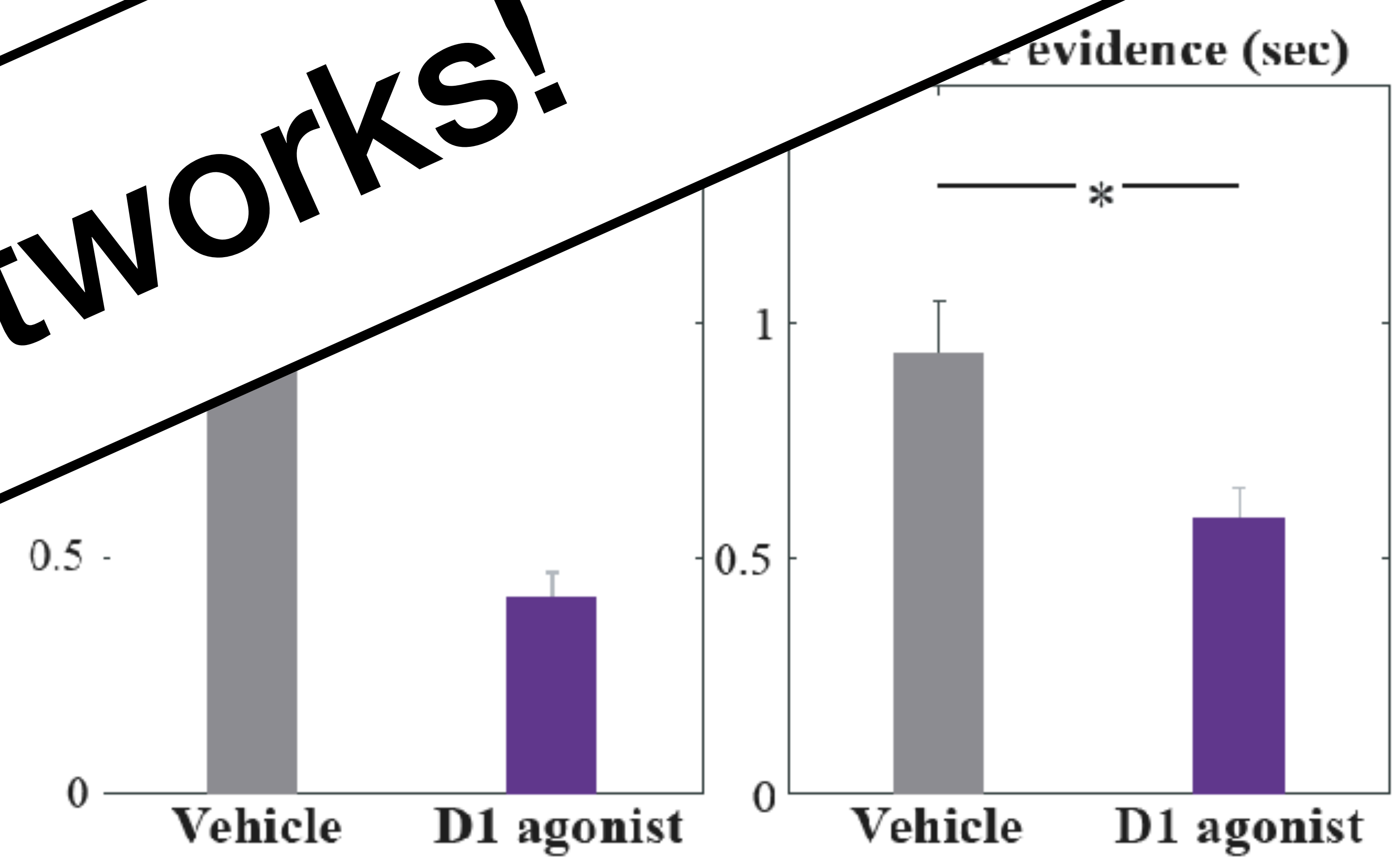
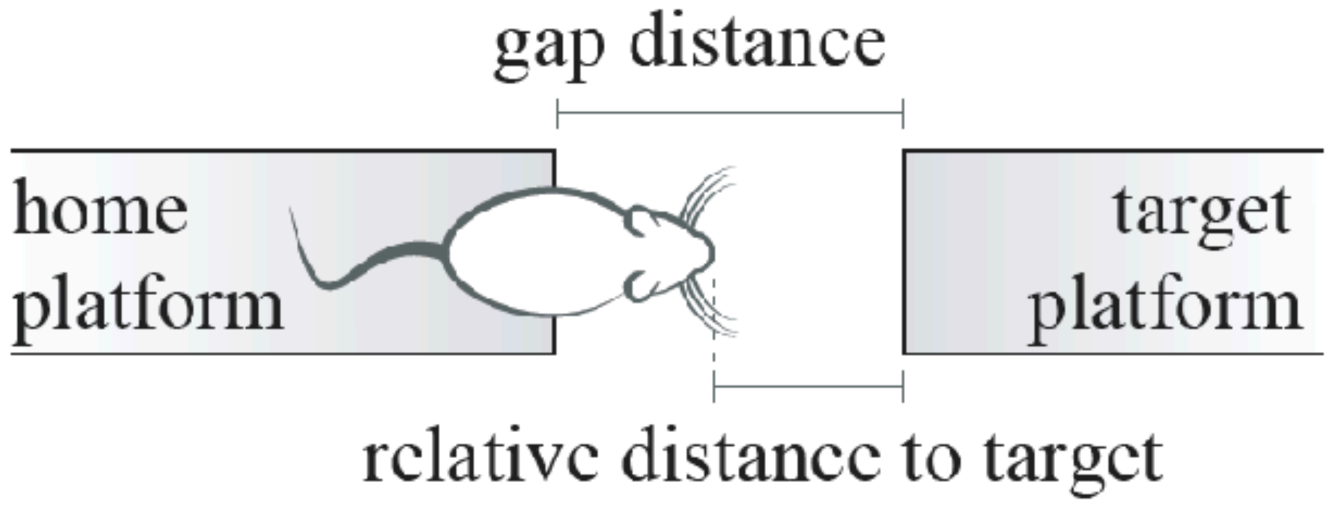




Inhibitory cells:
higher firing, more info





faster information integration

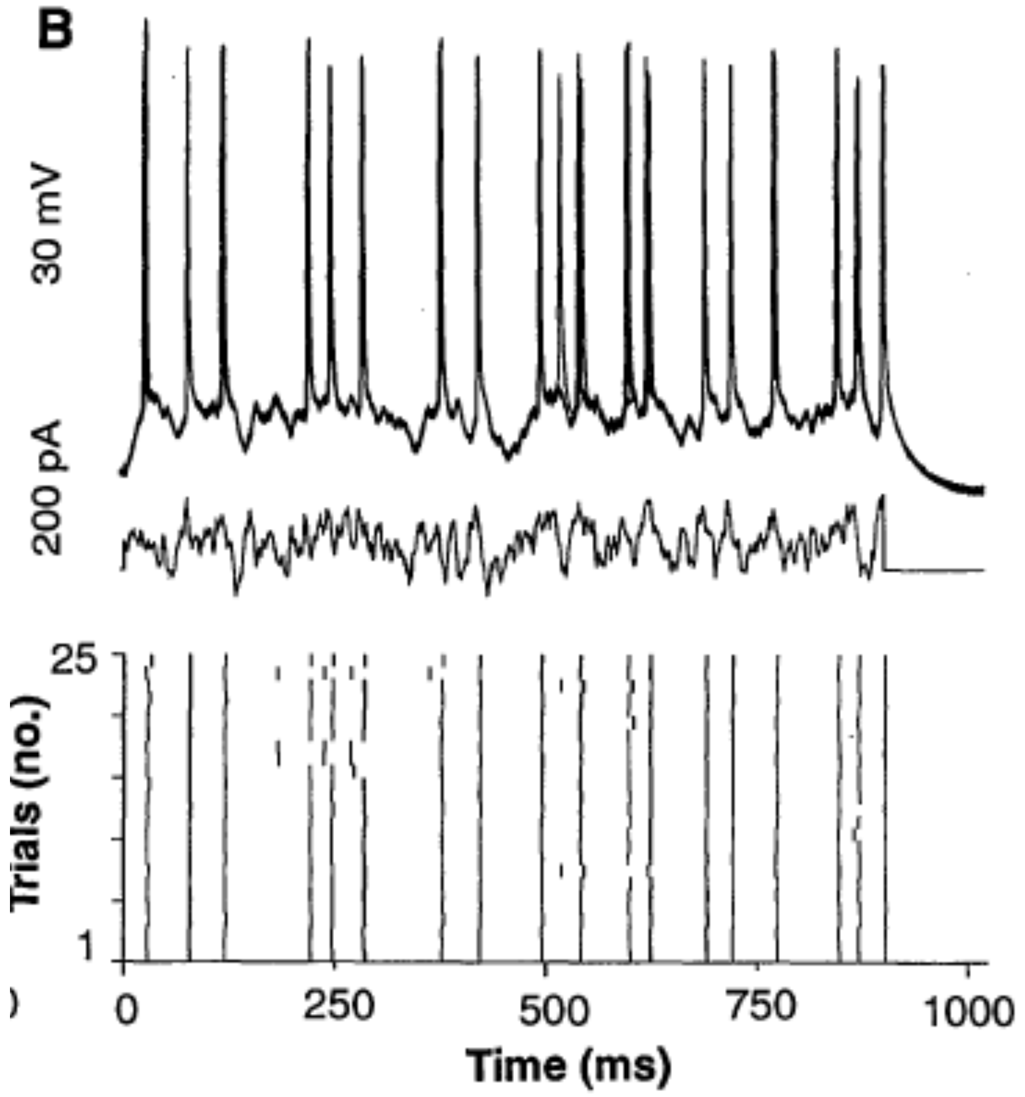
How does this work? Networks!

Calcini, N., Bijlsma, A., Zhang, Y., Lantyer, A. da S., Kole, K., Celikel, T., & Zeldenrust, F. (2019). Cell-type specific modulation of information transfer by dopamine. In Cosyne Abstracts 2019, Lisbon, PT.

Classical networks

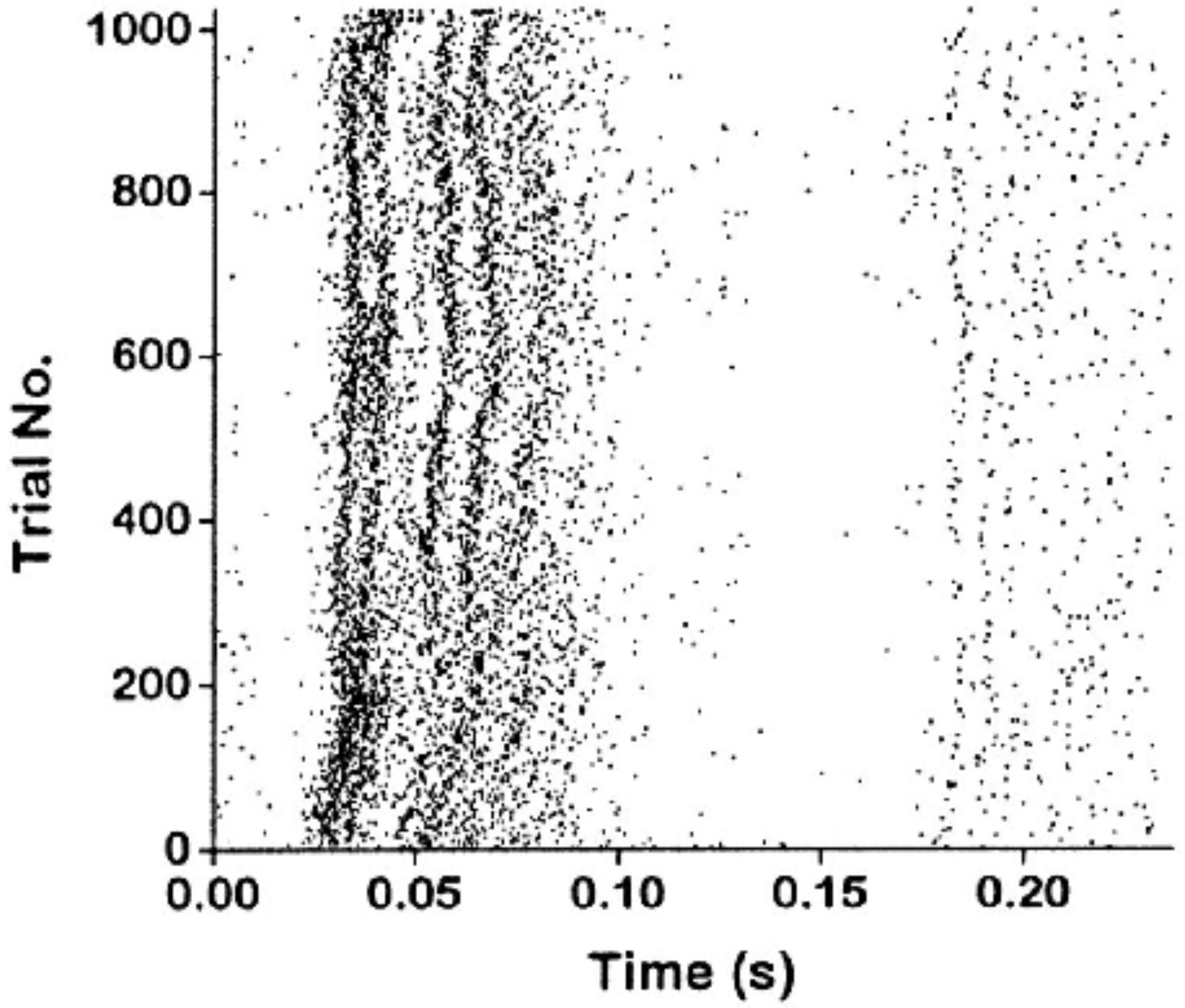
- In vivo neural activity is irregular and unreliable
- This can be explained by a ‘balanced’ (excitation - inhibition) network

In vitro:
- Reliable
- Regular

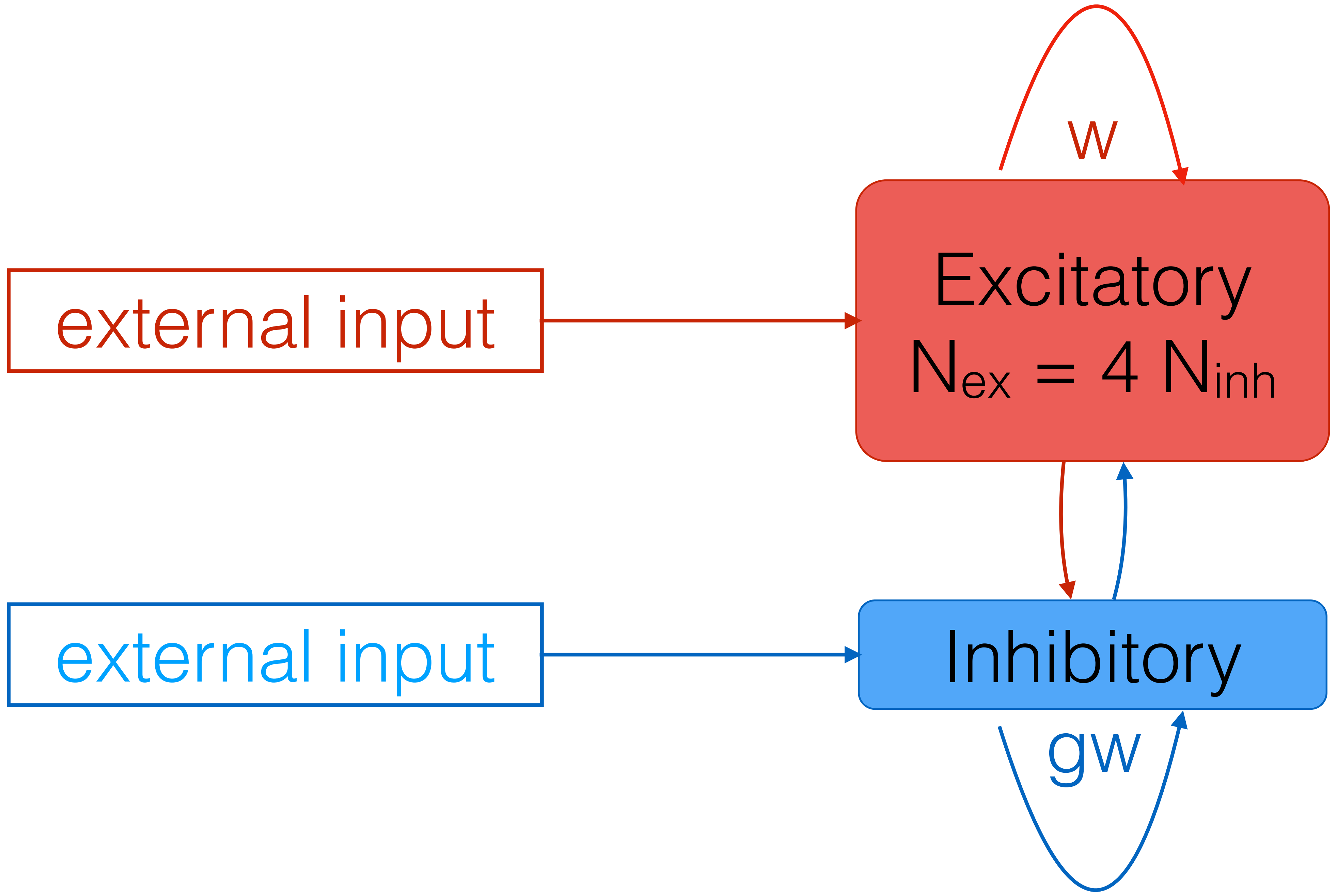


Mainen & Sejnowski, 1995

In vivo:
- Trial-to-trial variability
- Irregular



Reich et al, 1997



van Vreeswijk & Sompolinsky (1996, 1998), Brunel (2000)

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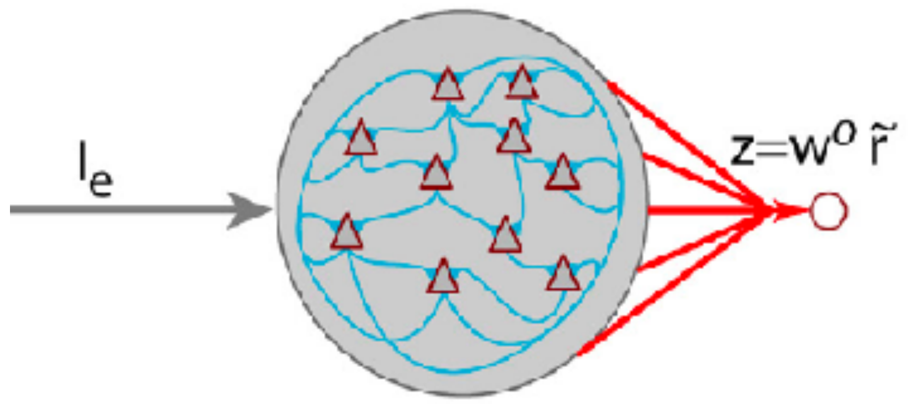

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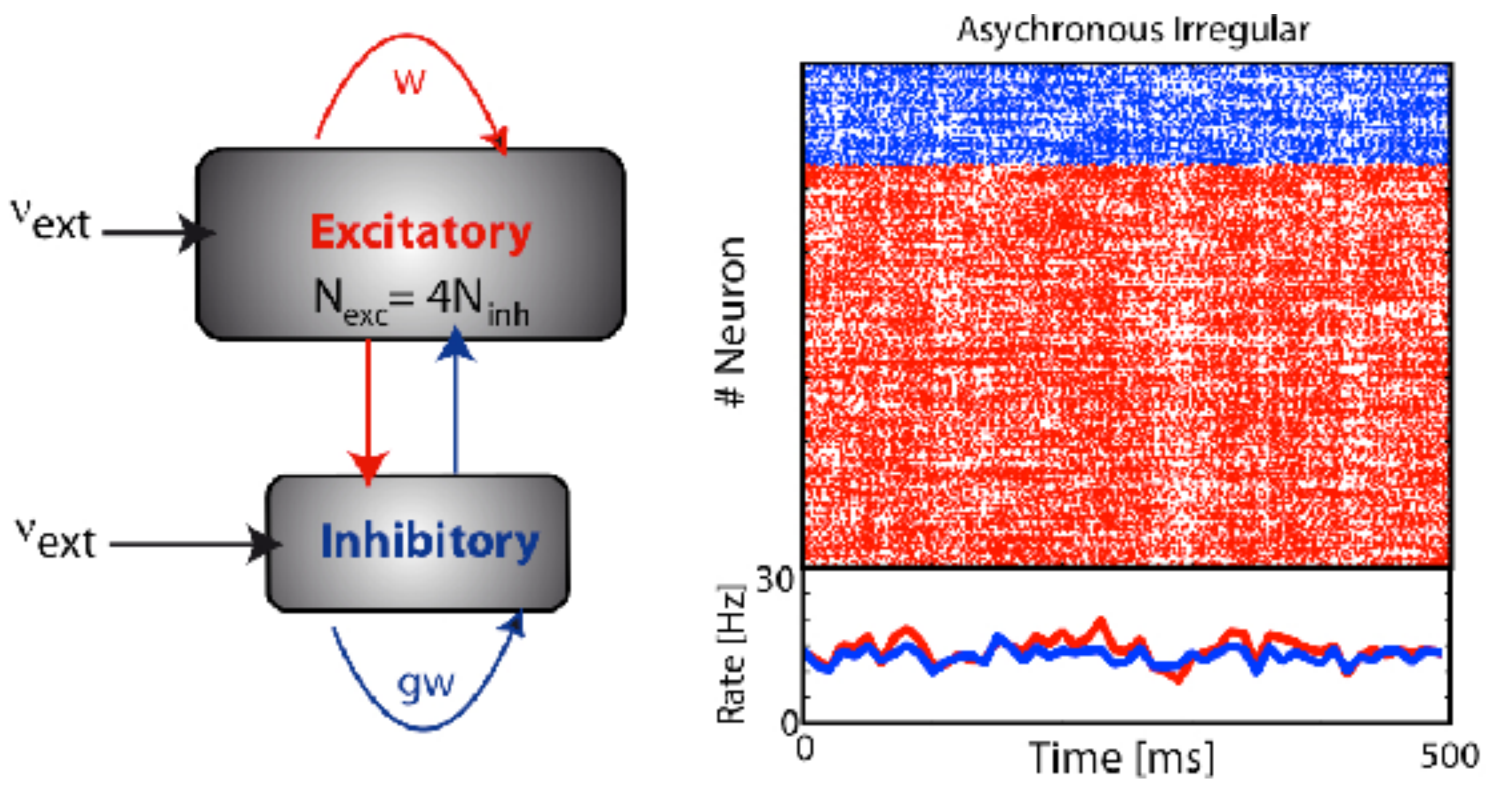


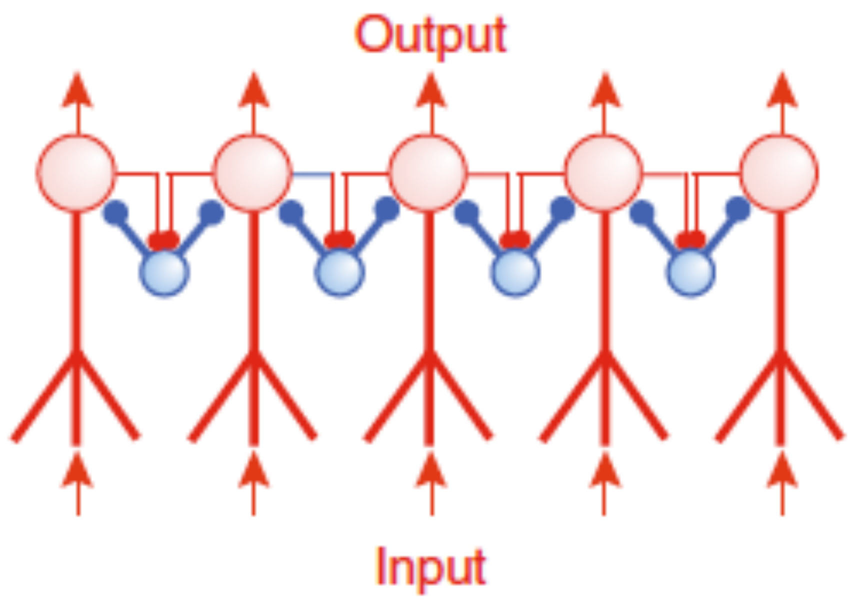


Image: http://www.yger.net/the-balanced-network/

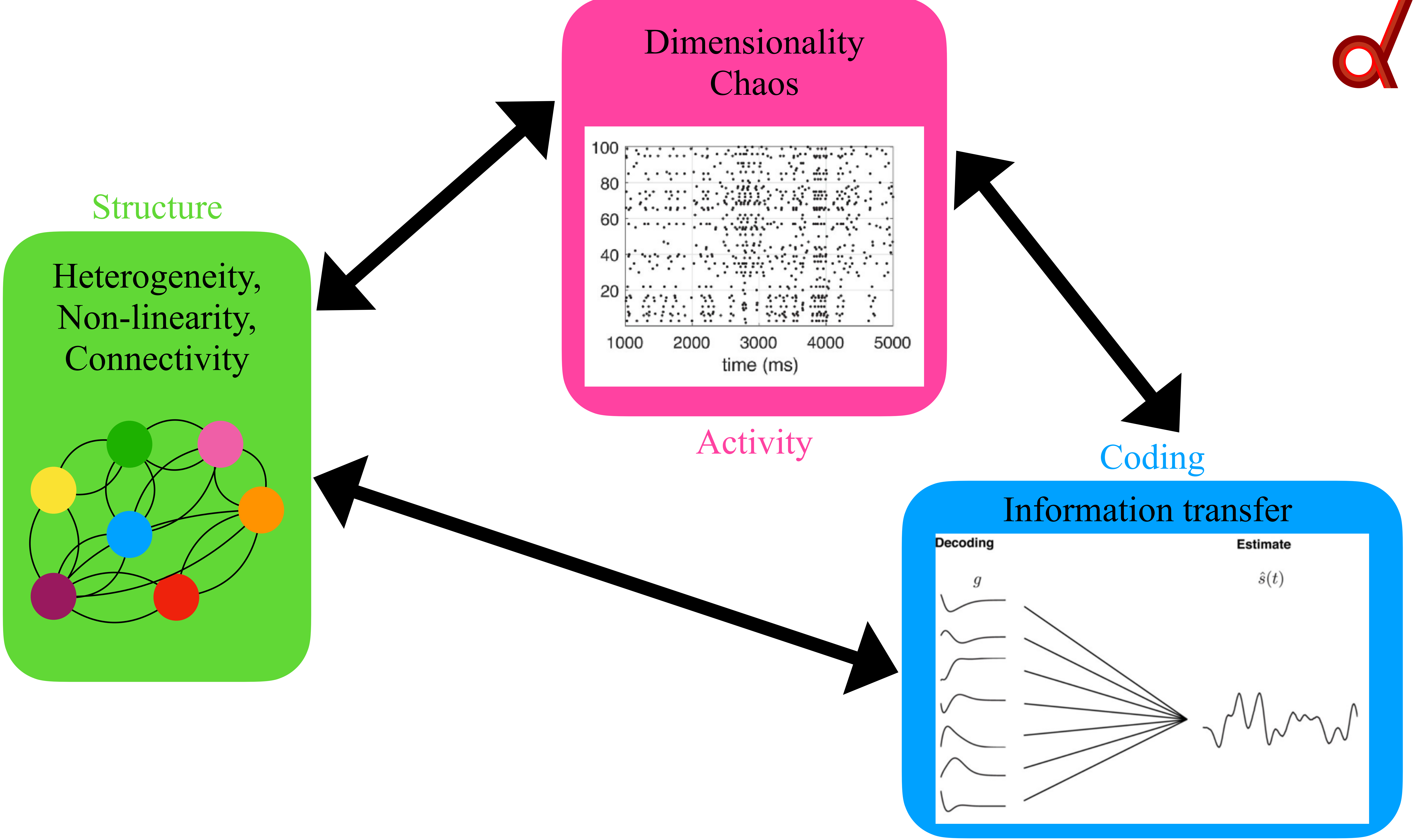
Classical networks

- In vivo neural activity is irregular and unreliable
- This can be explained by a ‘balanced’ (excitation - inhibition) network
- There is a growing body of (circumstantial) evidence for such a balanced state in the brain.
- Mean field approximations very powerful
- These networks have interesting computational properties

BUT

- non-random connectivity
- no 4:1 ratio
- Non-linear neuron properties
- Heterogeneity - cell class stimulus dependent

What does that mean for information transfer / computation?



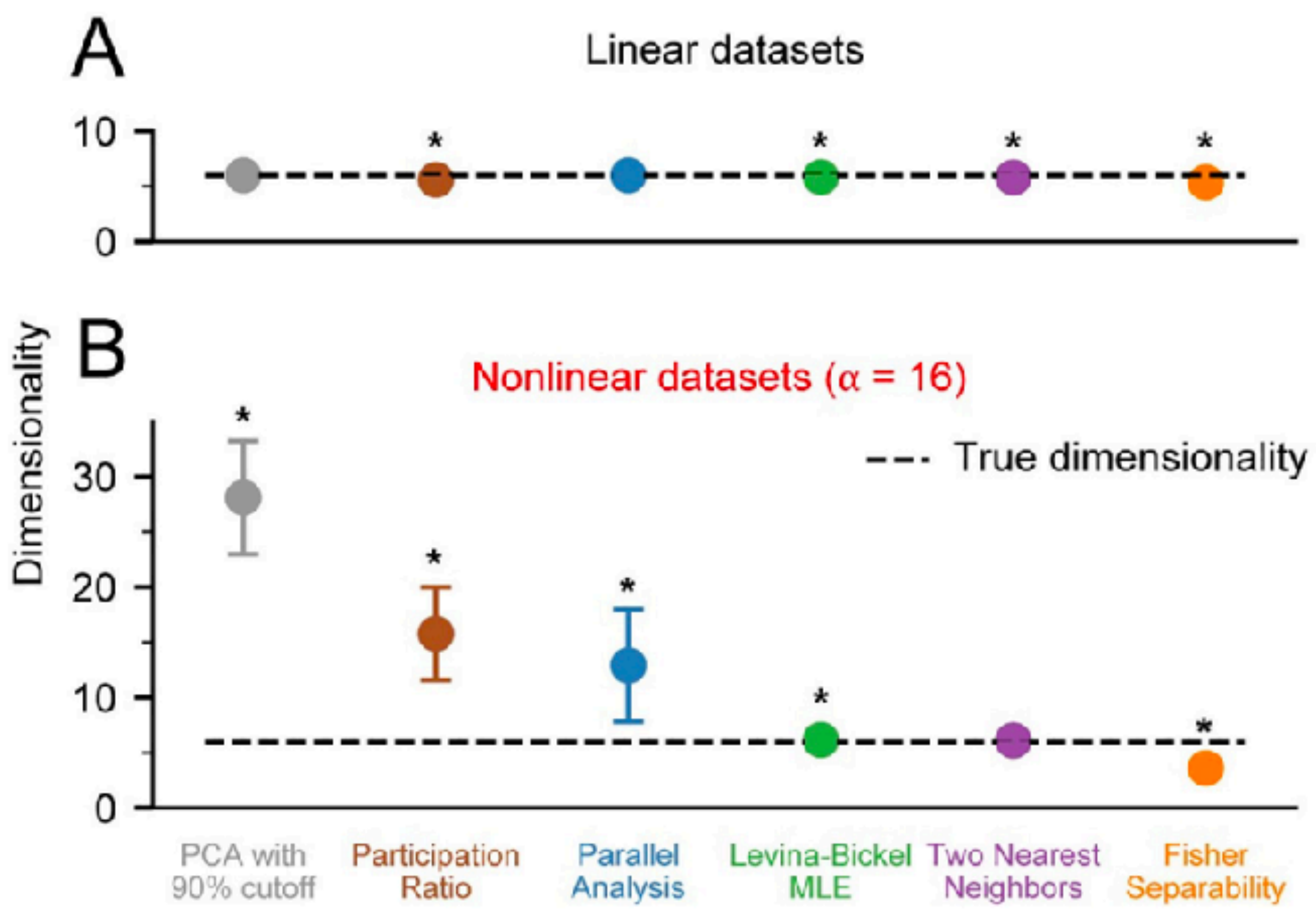
Structure
Heterogeneity,
Non-linearity,
Connectivity
Dimensionality
Chaos
100
80
60
40
20
1000
2000
3000
4000
5000
time (ms)
Activity
Coding
Information transfer
Decoding
Estimate
g
$\hat{s}(t)$

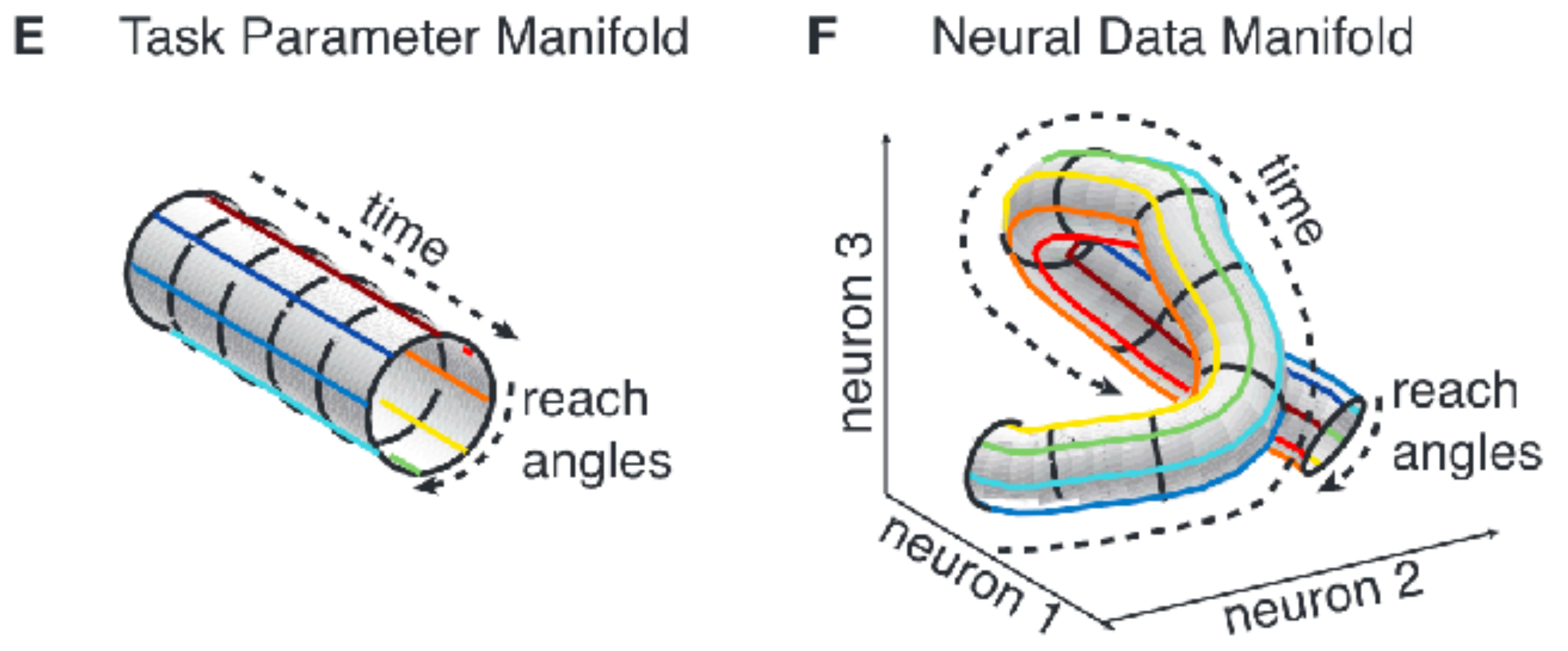
Dimensionality of network response

RESEARCH ARTICLE

Estimating the dimensionality of the manifold underlying multi-electrode neural recordings

Ege Altan[1,2*], Sara A. Solla[1,3], Lee E. Miller[1,2,4,5], Eric J. Perreault[2,4,5]





A theory of multineuronal dimensionality, dynamics and measurement

Peiran Gao[1], Eric Trautmann[2], Byron Yu[3], Gopal Santhanam[4], Stephen Ryu[5,4], Krishna Shenoy[4,1,6,7,8,9] and Surya Ganguli*[10,2,4,8,9]

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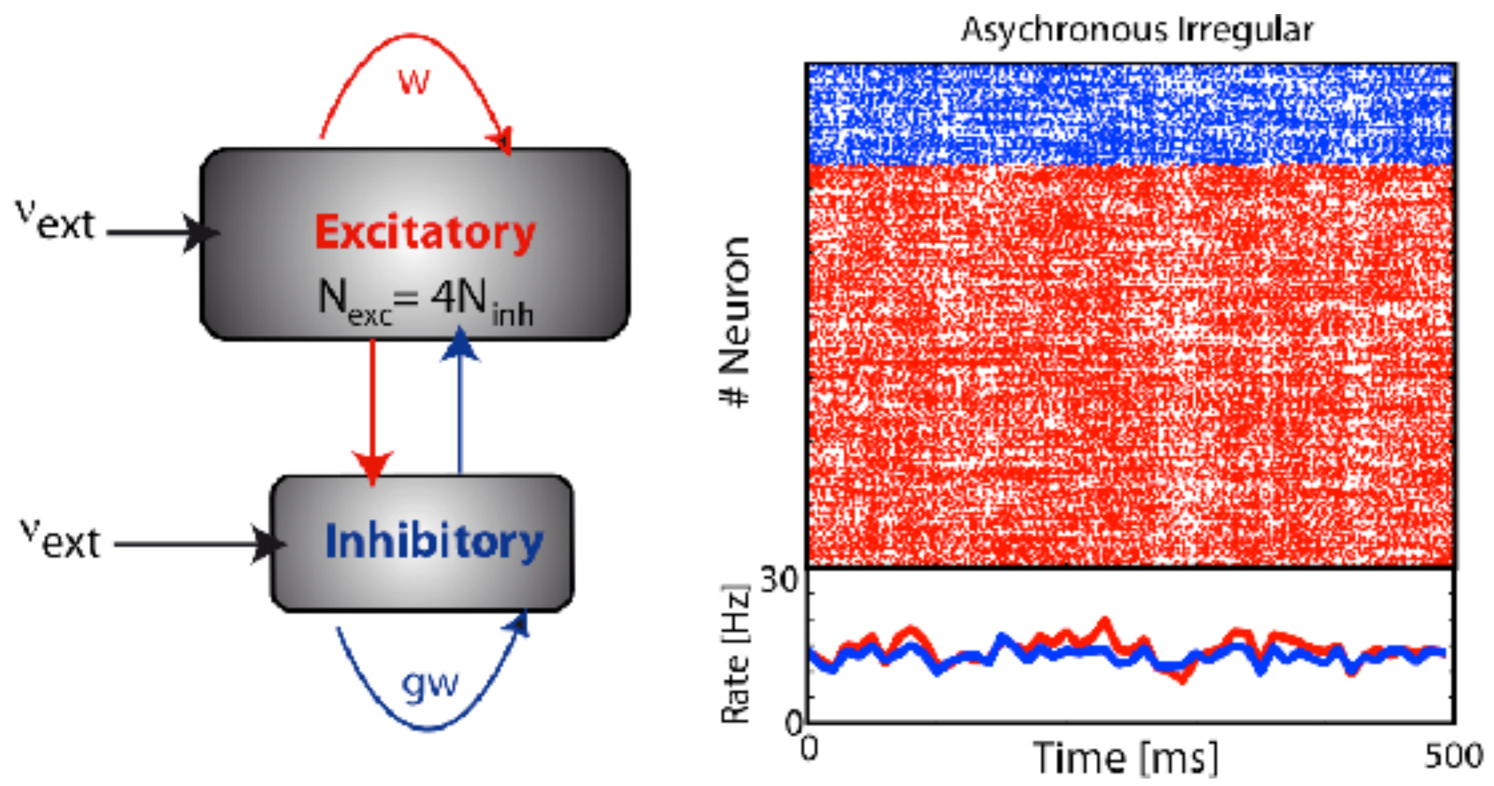

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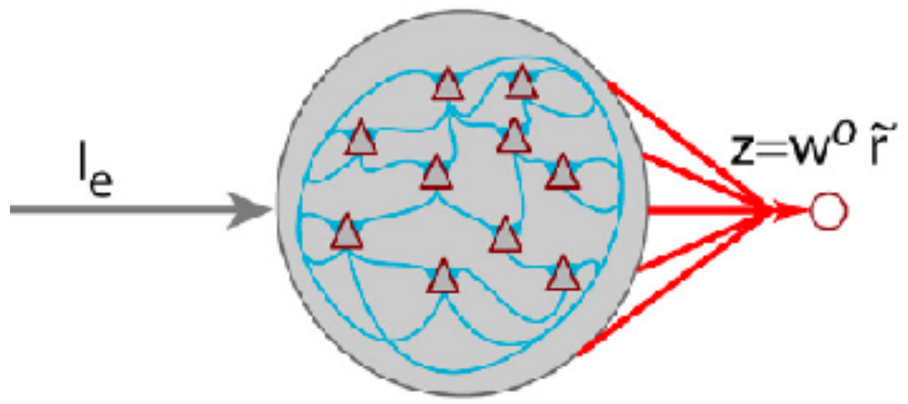

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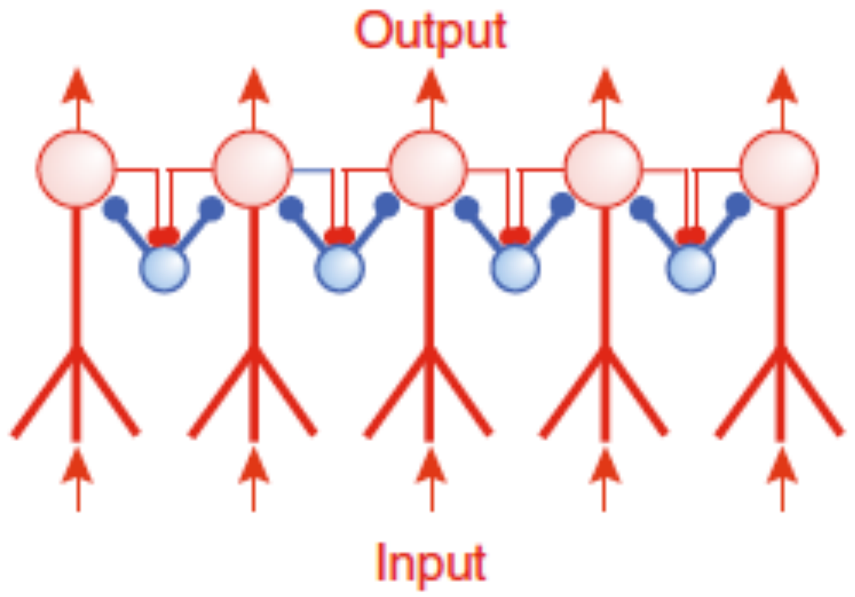
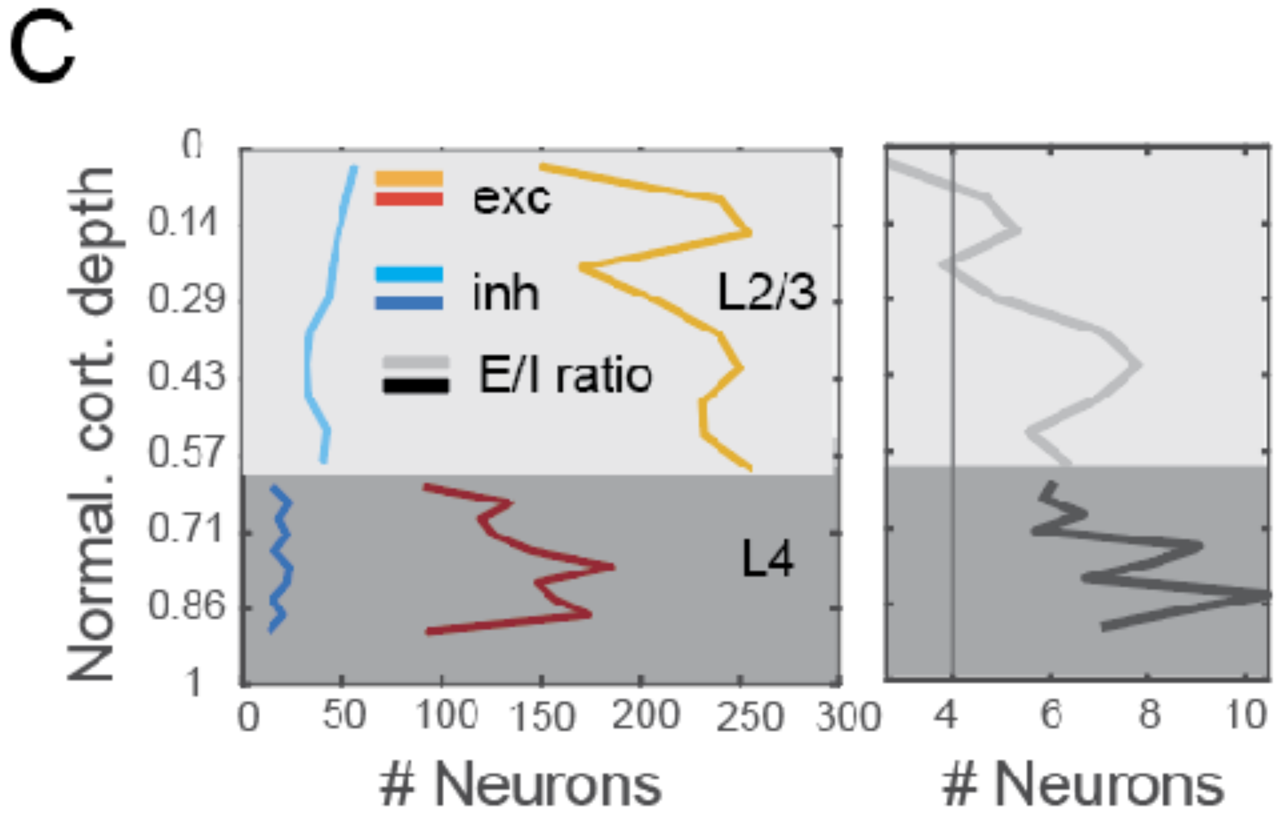
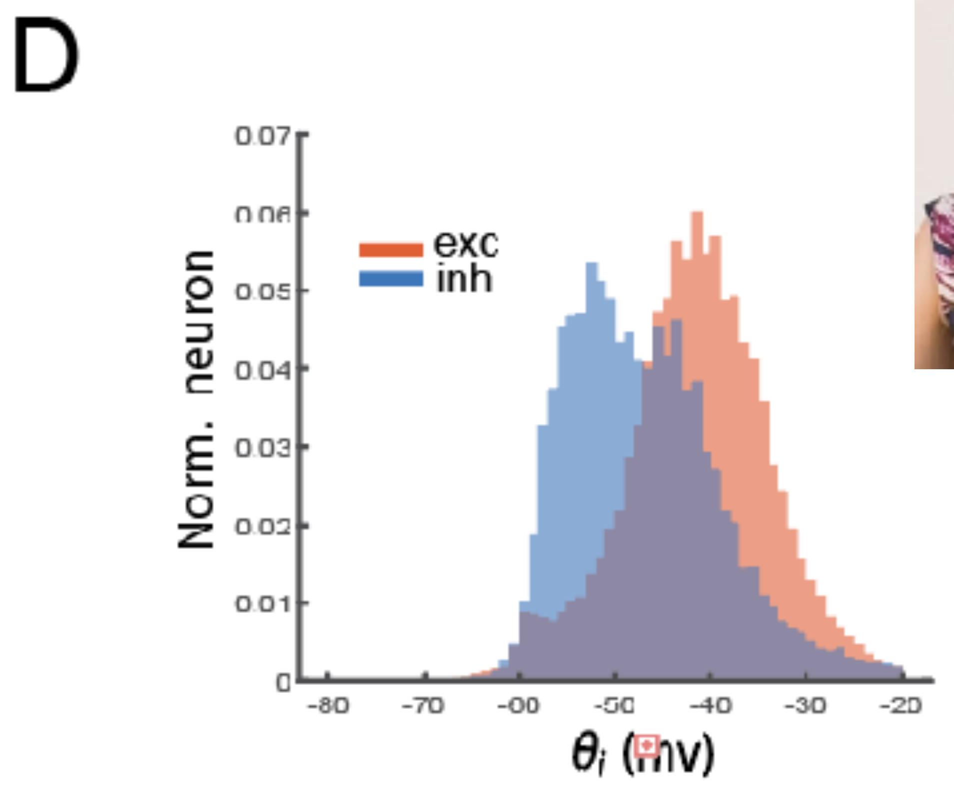


Dimensionality of network response

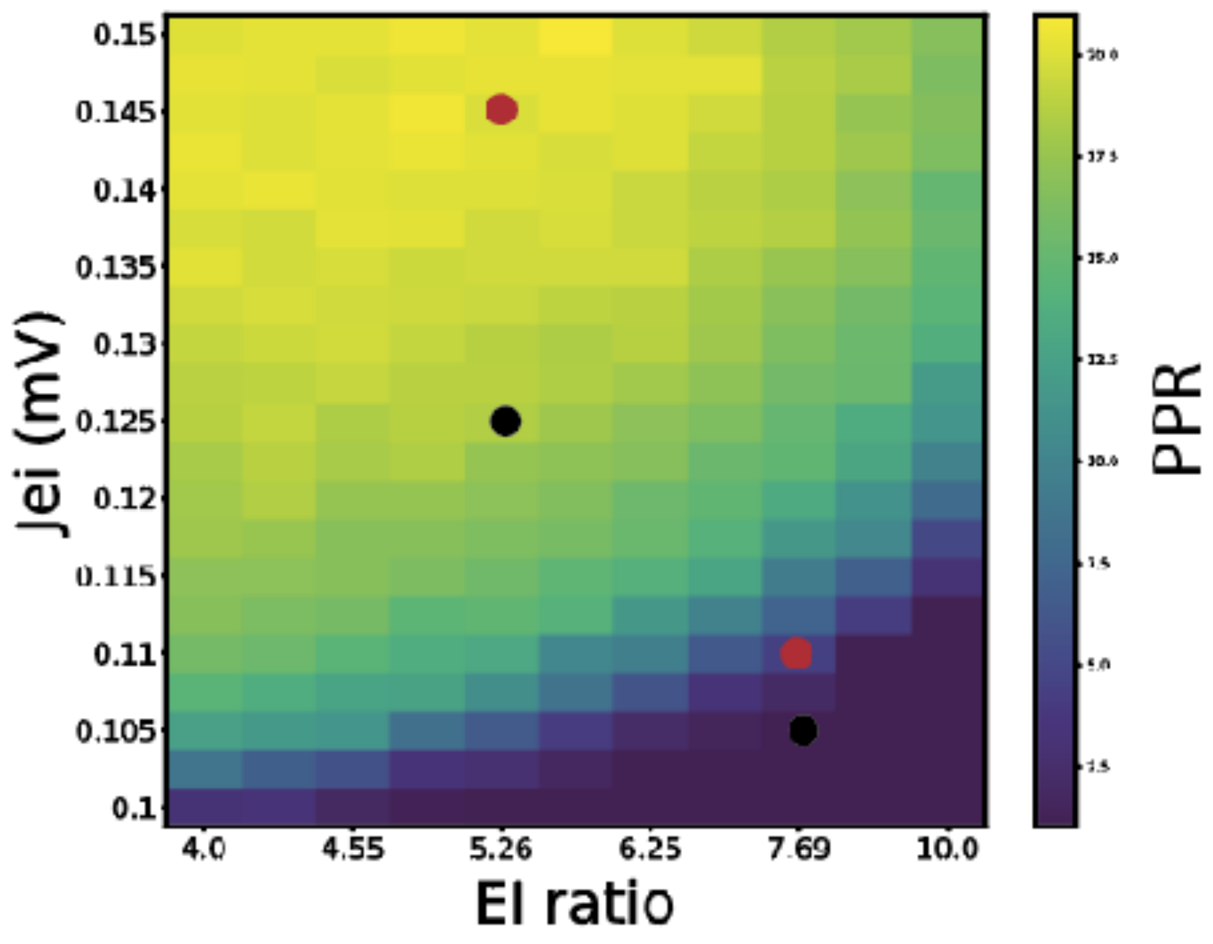
Observations:

- # I neurons depends on network, layer, etc
- threshold I neurons lower than E neurons
- This influences dimensionality…





Arezoo Alizadeh



Alizadeh, A., Englitz, B.,& Zeldenrust, F. (2025). How the layer-dependent ratio of excitatory to inhibitory cells shapes cortical coding in balanced networks. *eLife*

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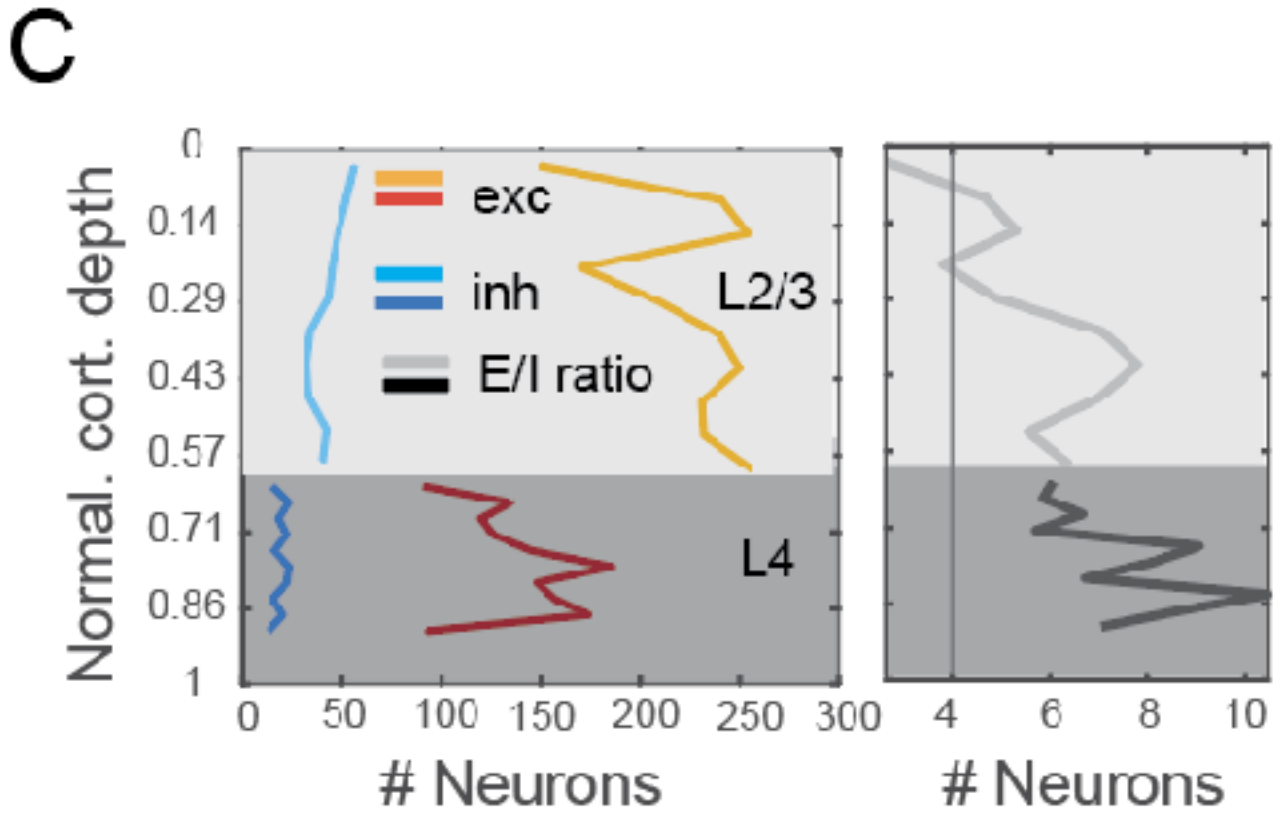
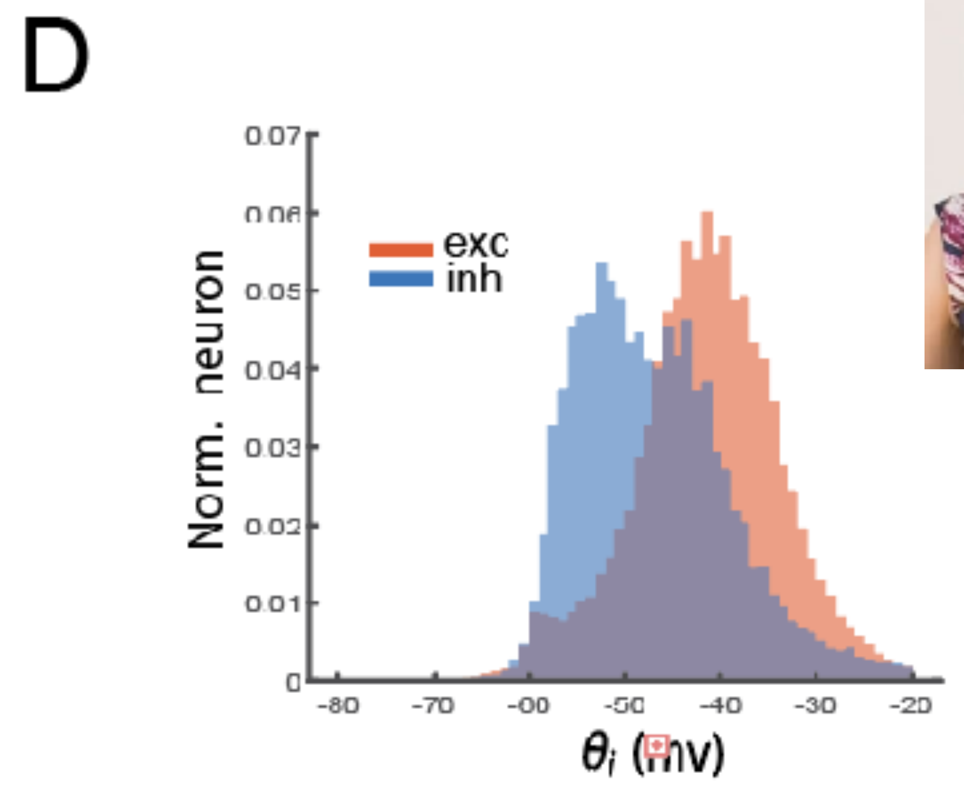
- …and coding!





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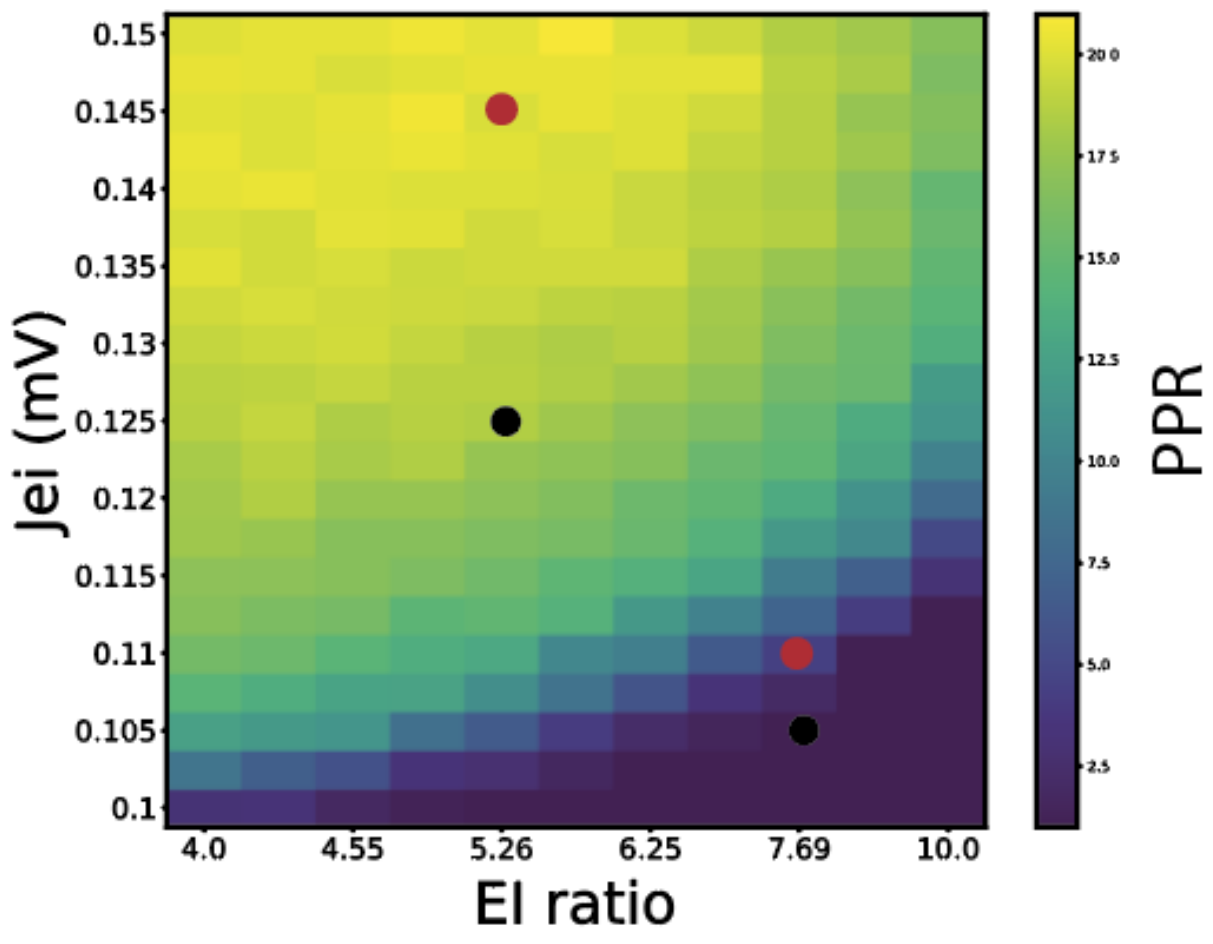

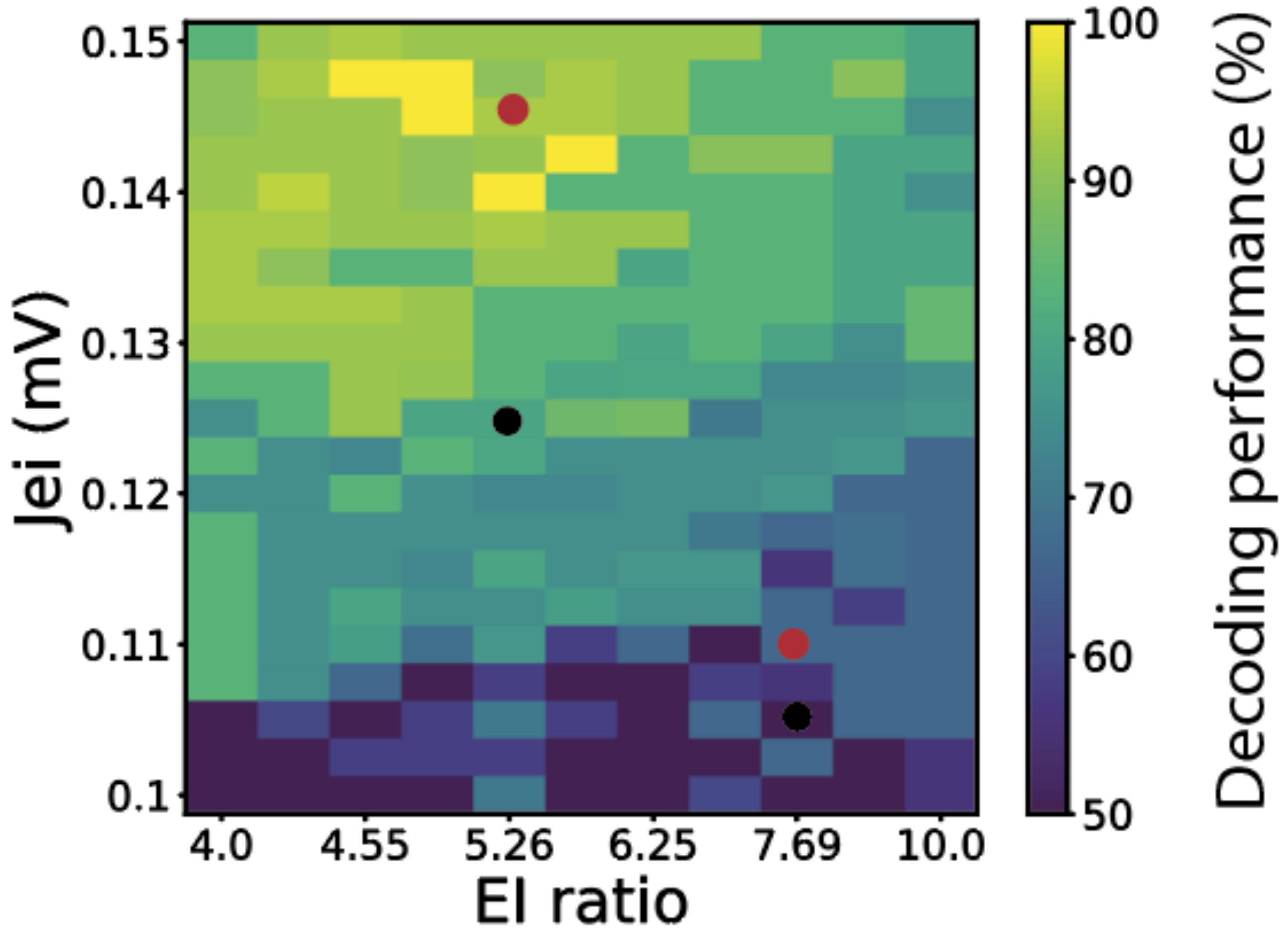

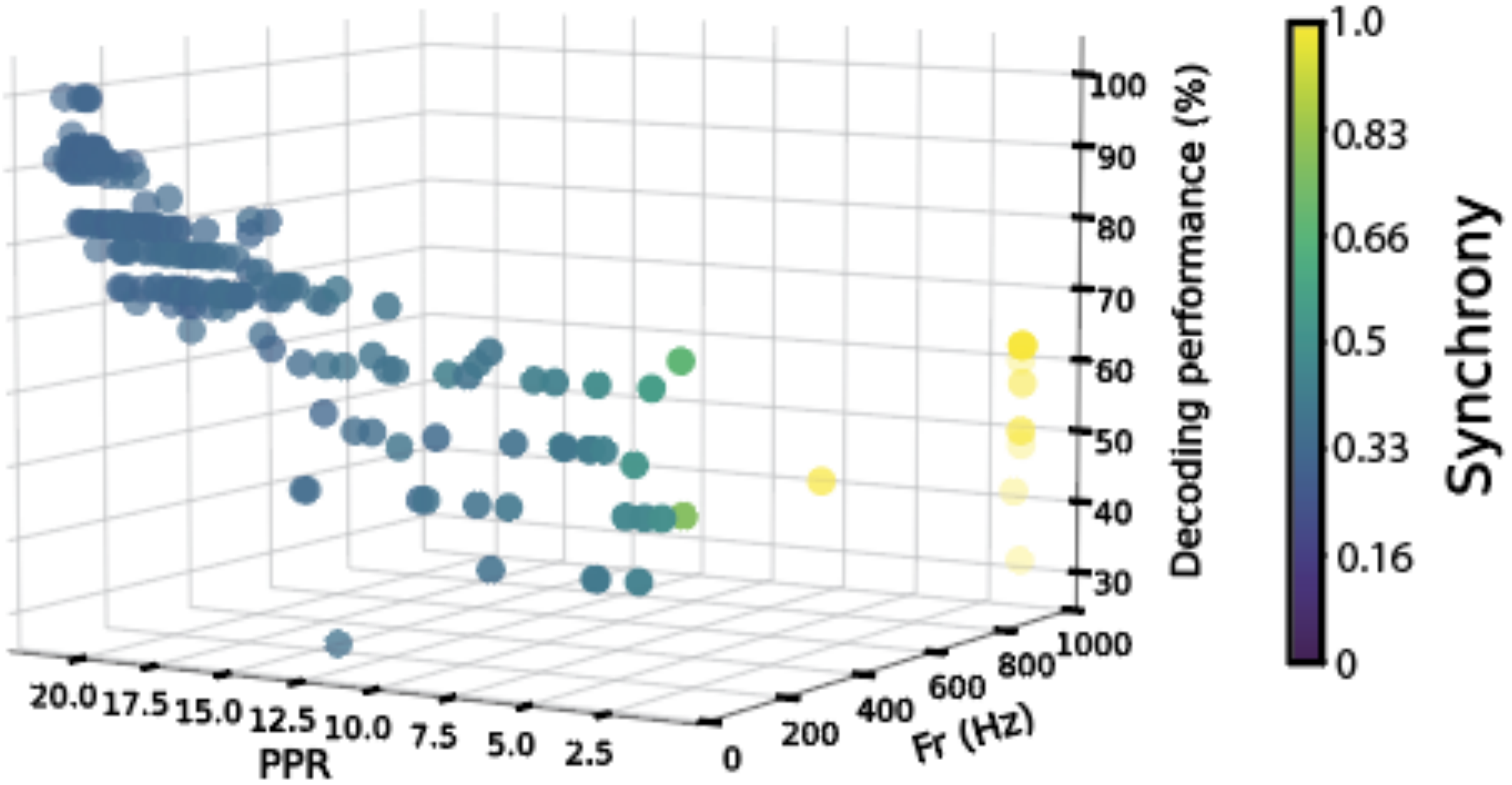

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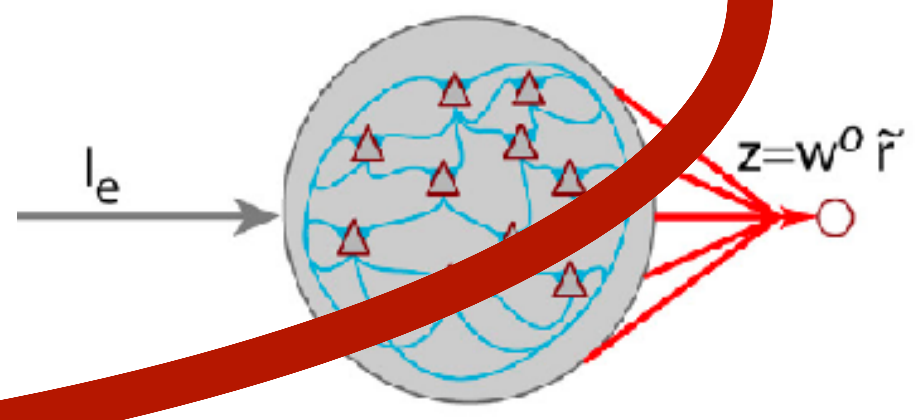

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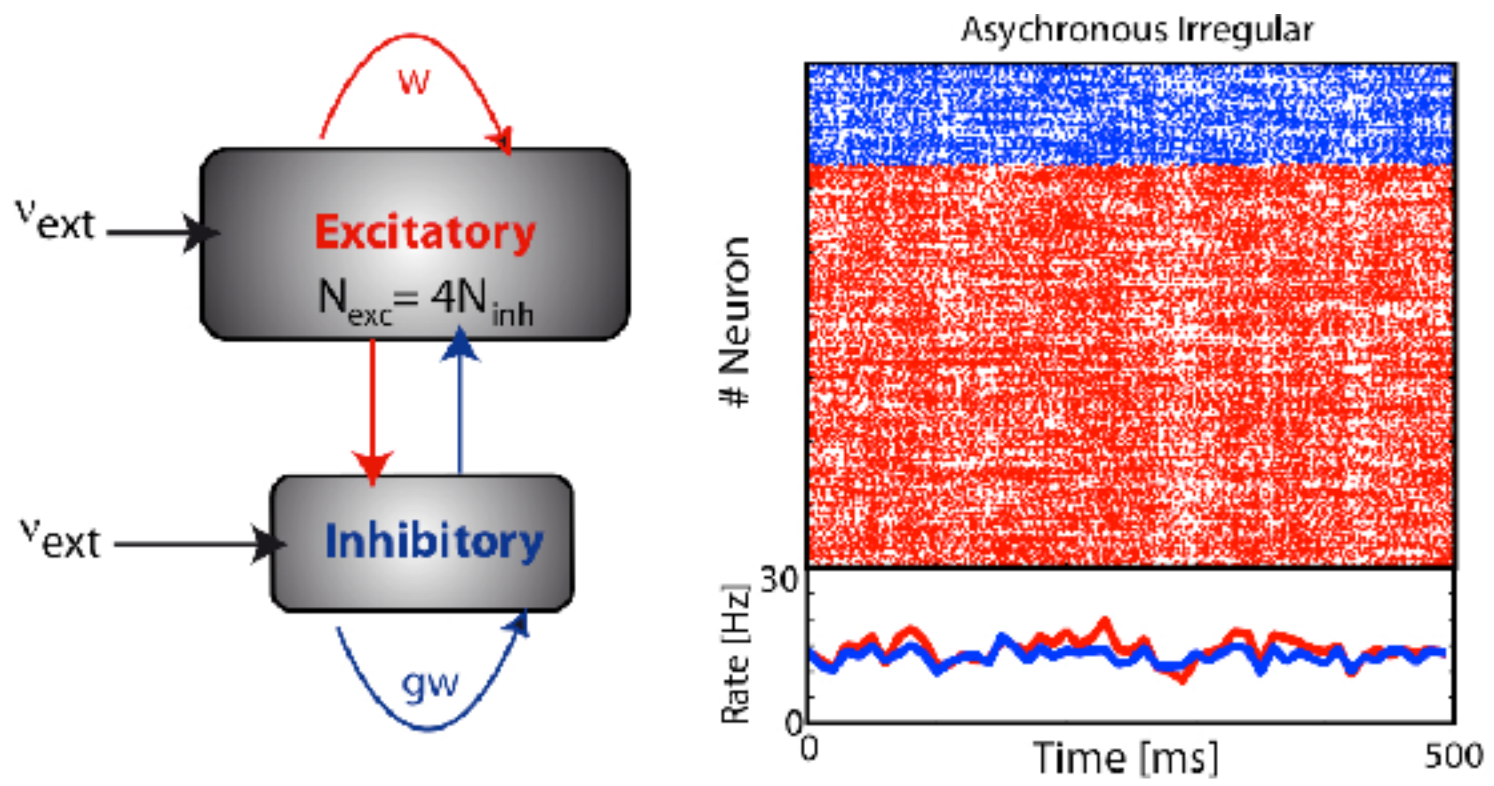

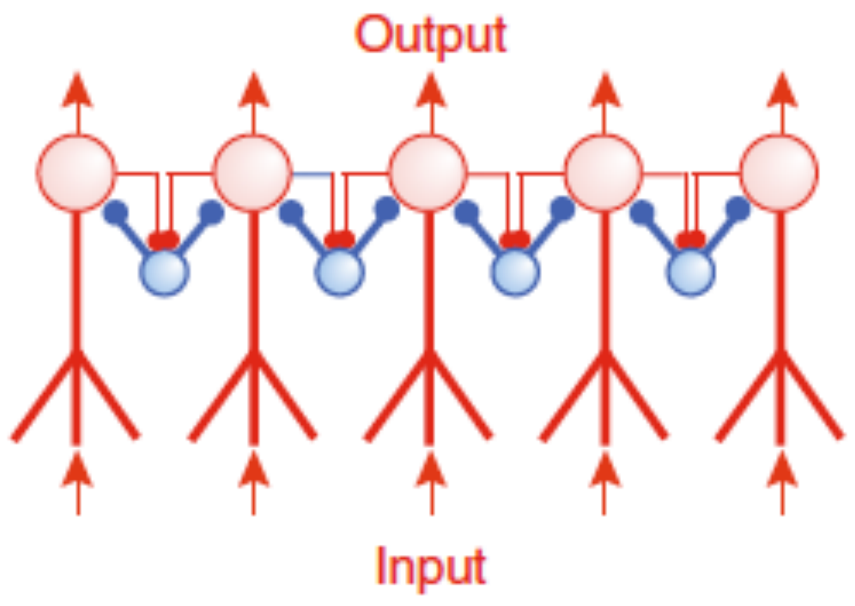

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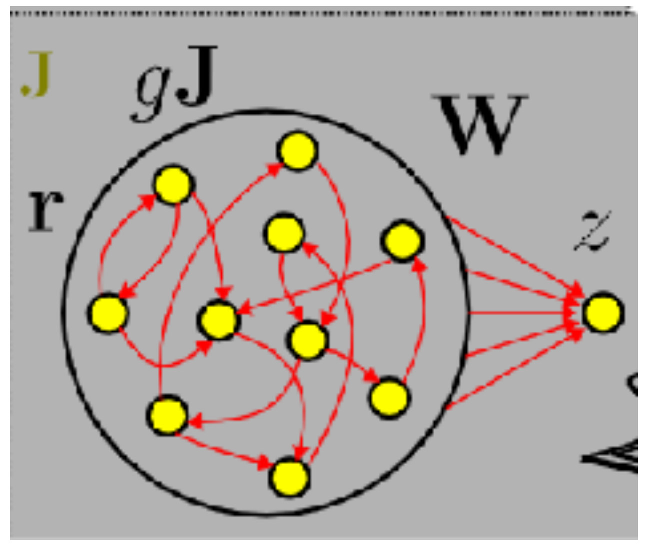
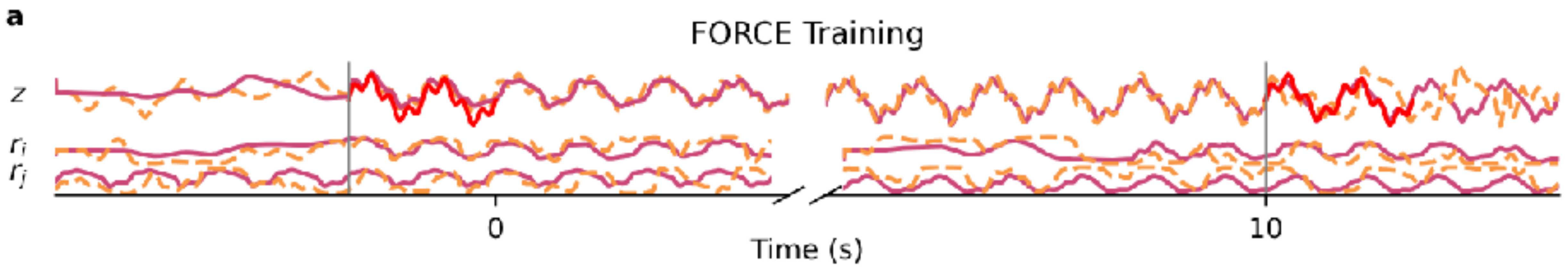
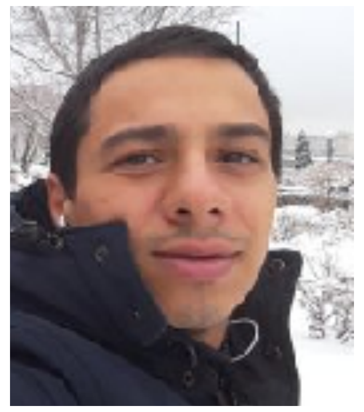
Rate networks: a sweet spot?

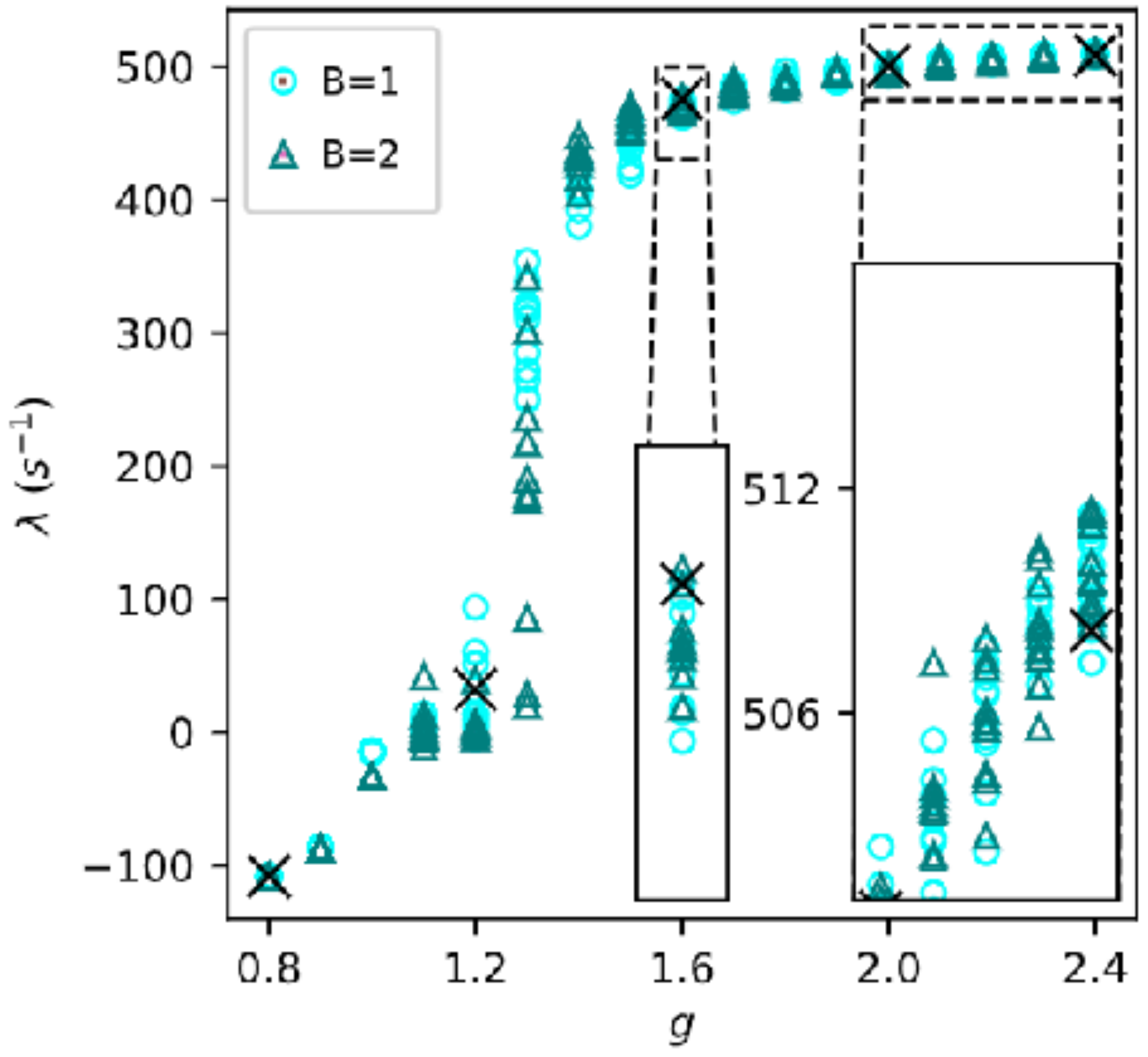




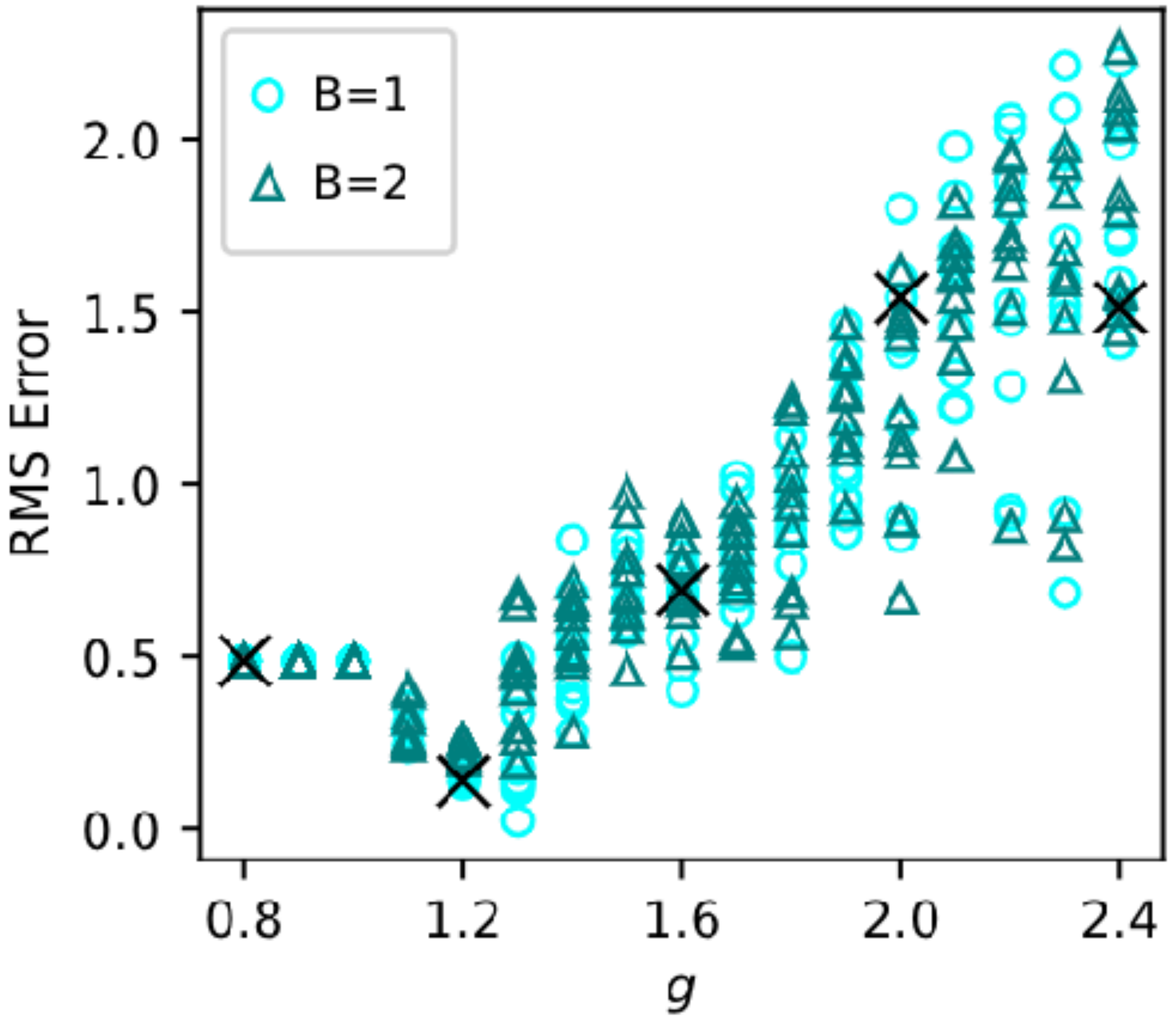


Farhad Razi

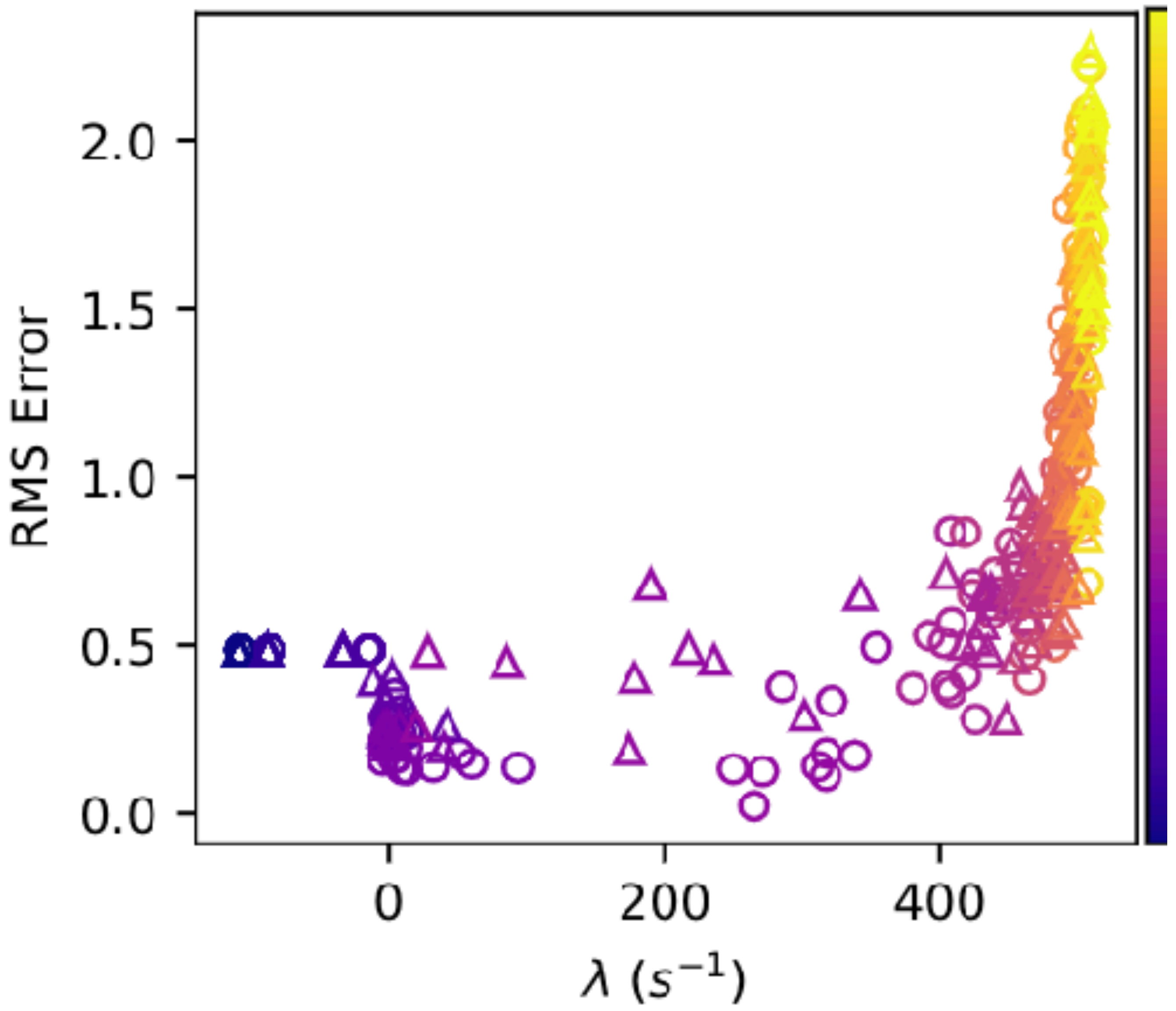
Synaptic upscaling increases chaotic activity



Non-monotonic relation with performance



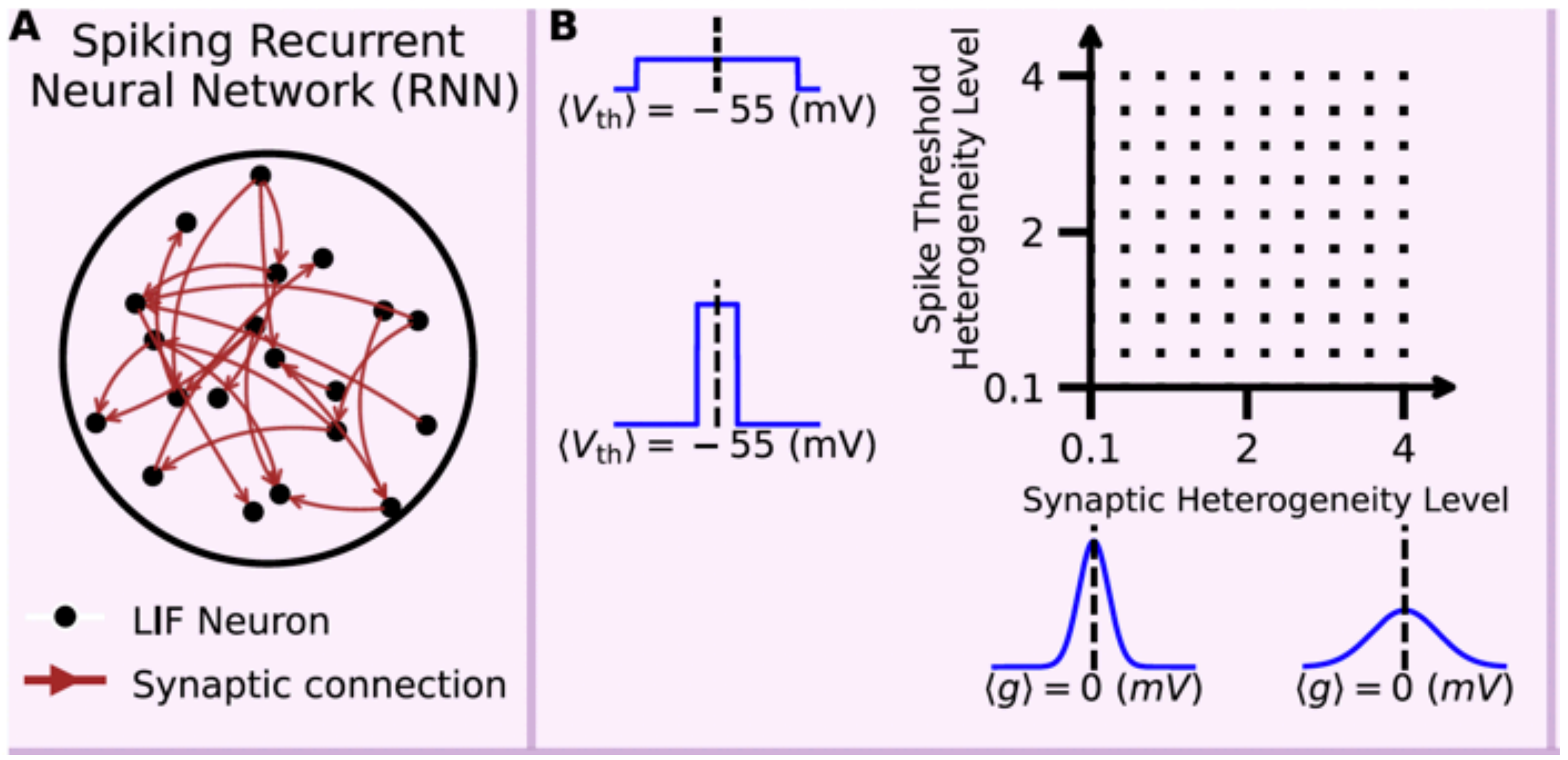
A sweet spot?

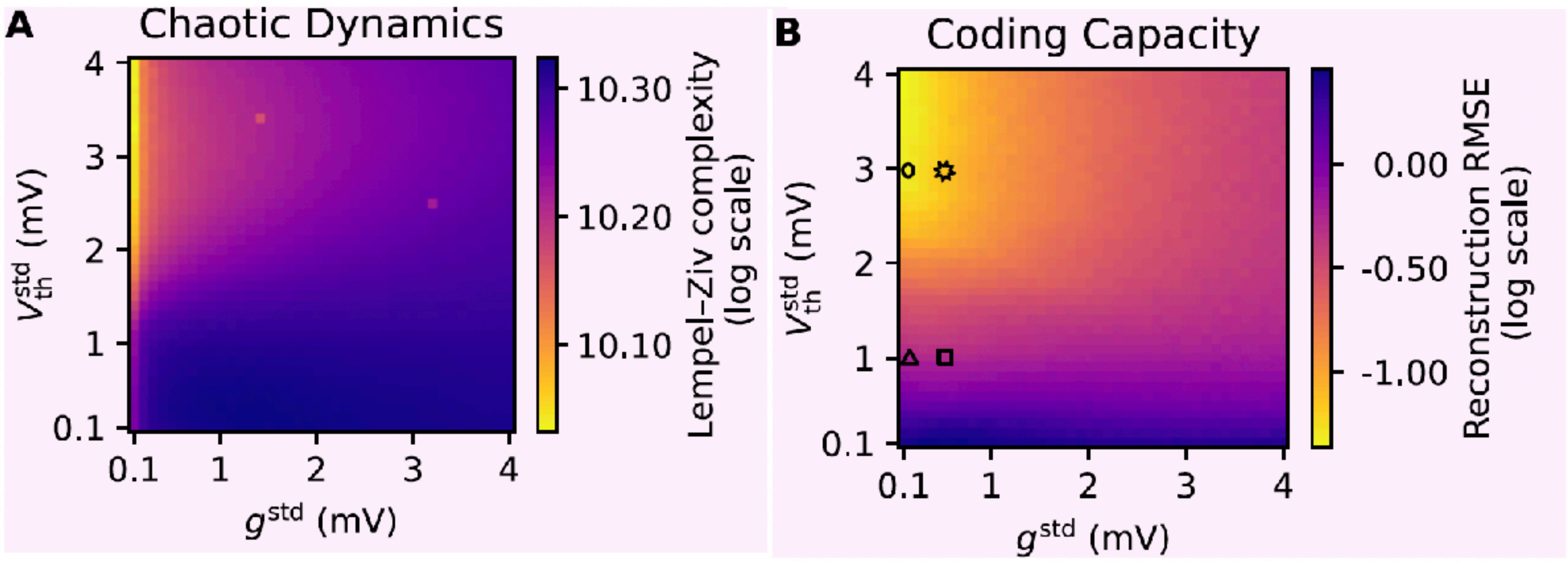


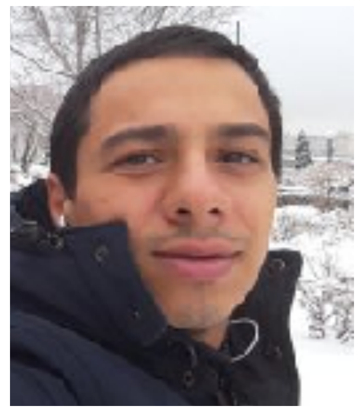
Razi, F., & Zeldenrust, F. Synaptic Upscaling Amplifies Chaotic Dynamics in Recurrent Networks of Rate Neurons. Bernstein Conference 2024. Bernstein Conference 2024. https://doi.org/10.12751/nncn.bc2024.153

Different types of heterogeneity

- Spike **threshold** heterogeneity: reduces trial-to-trial variability
  - by introducing high threshold neurons
  - increases coding capacity
- **Synaptic** heterogeneity: increases trial-to-trial variability







Farhad Razi

Razi, F., & Zeldenrust, F. Higher-Threshold Neurons Boost Information Encoding in Spiking Neural Networks. OCNS 2025. Poster 253

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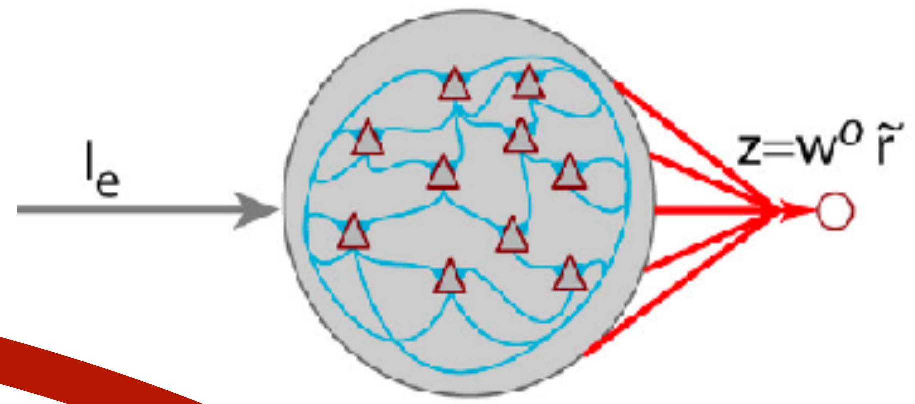

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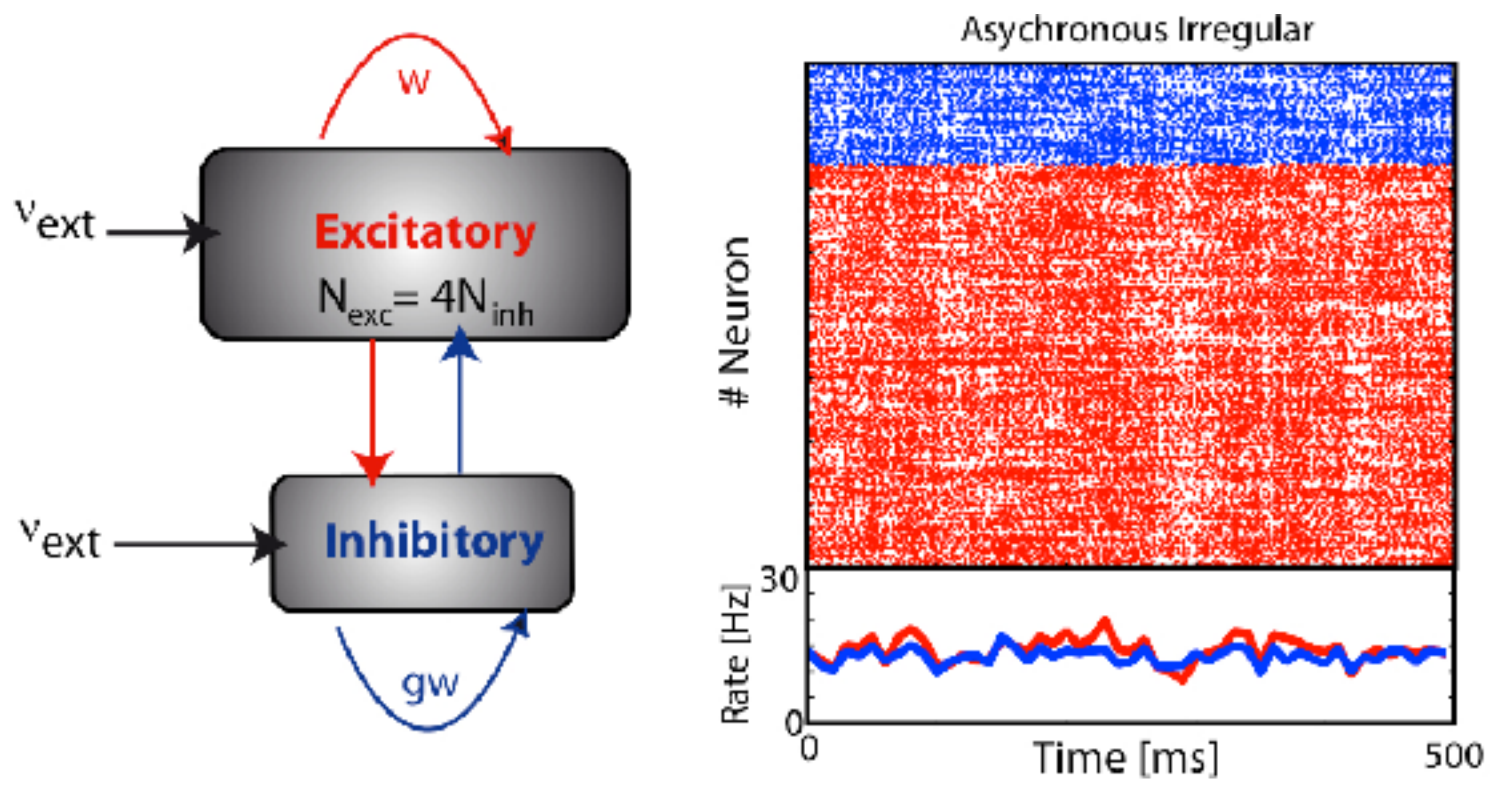


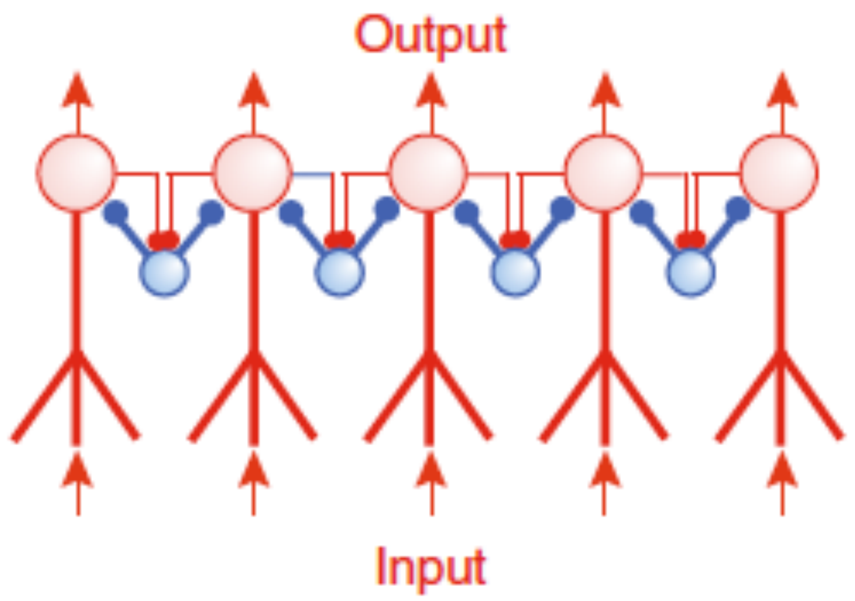
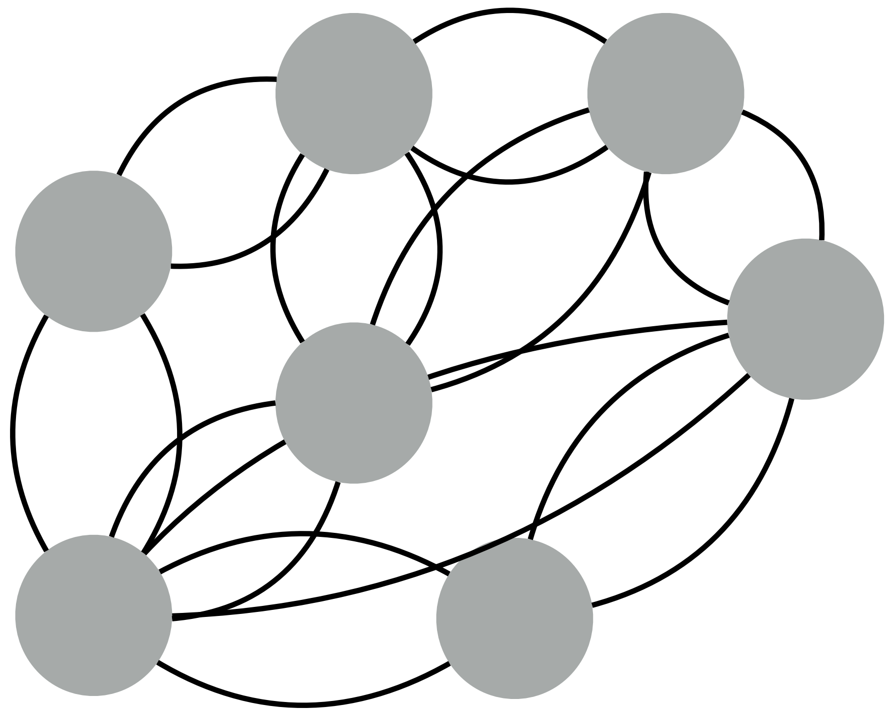
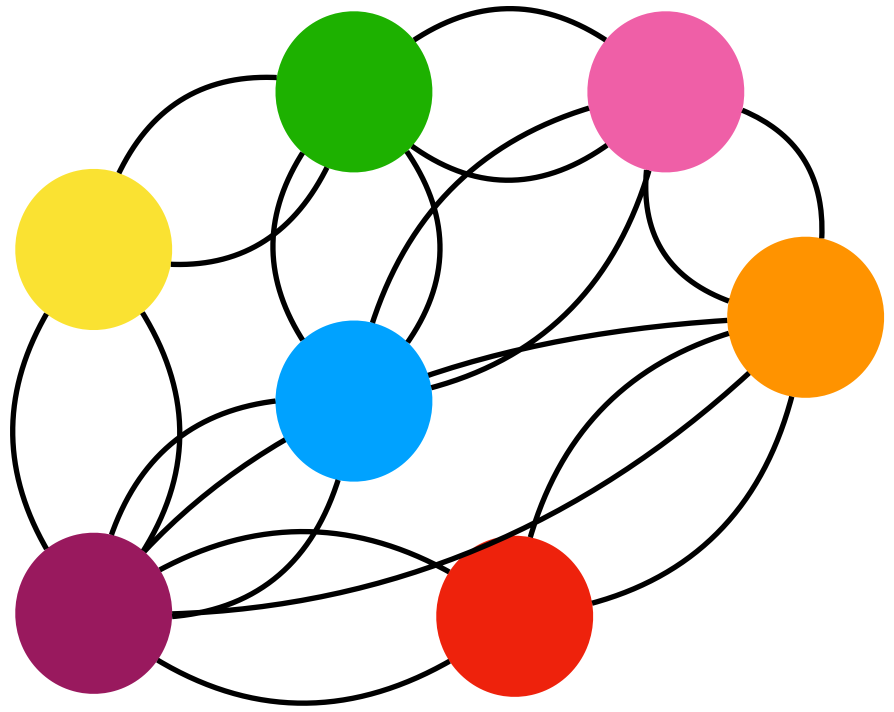


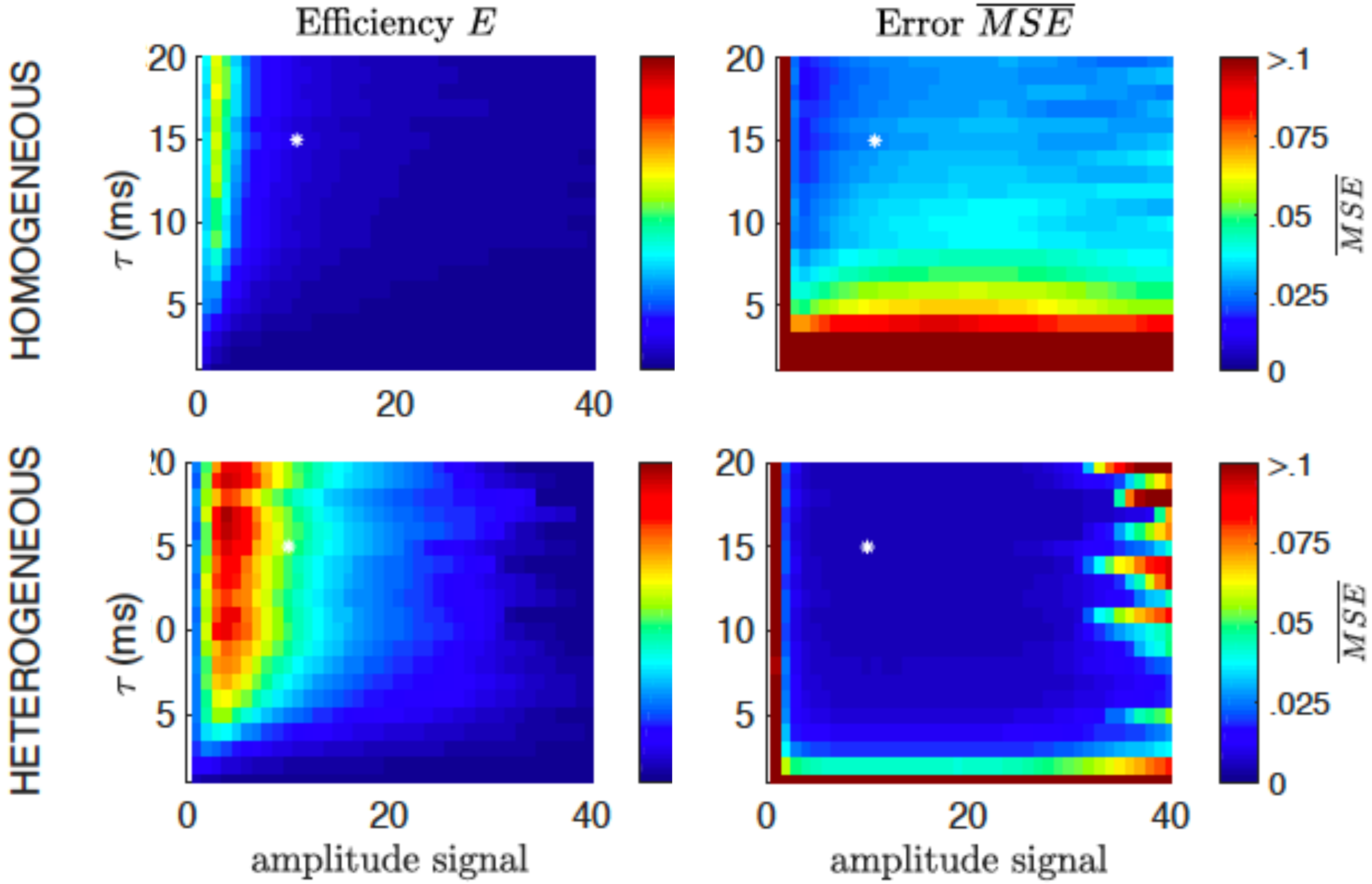
Image: http://www.yger.net/the-balanced-network/

Efficient spike coding networks: Heterogeneity & coding

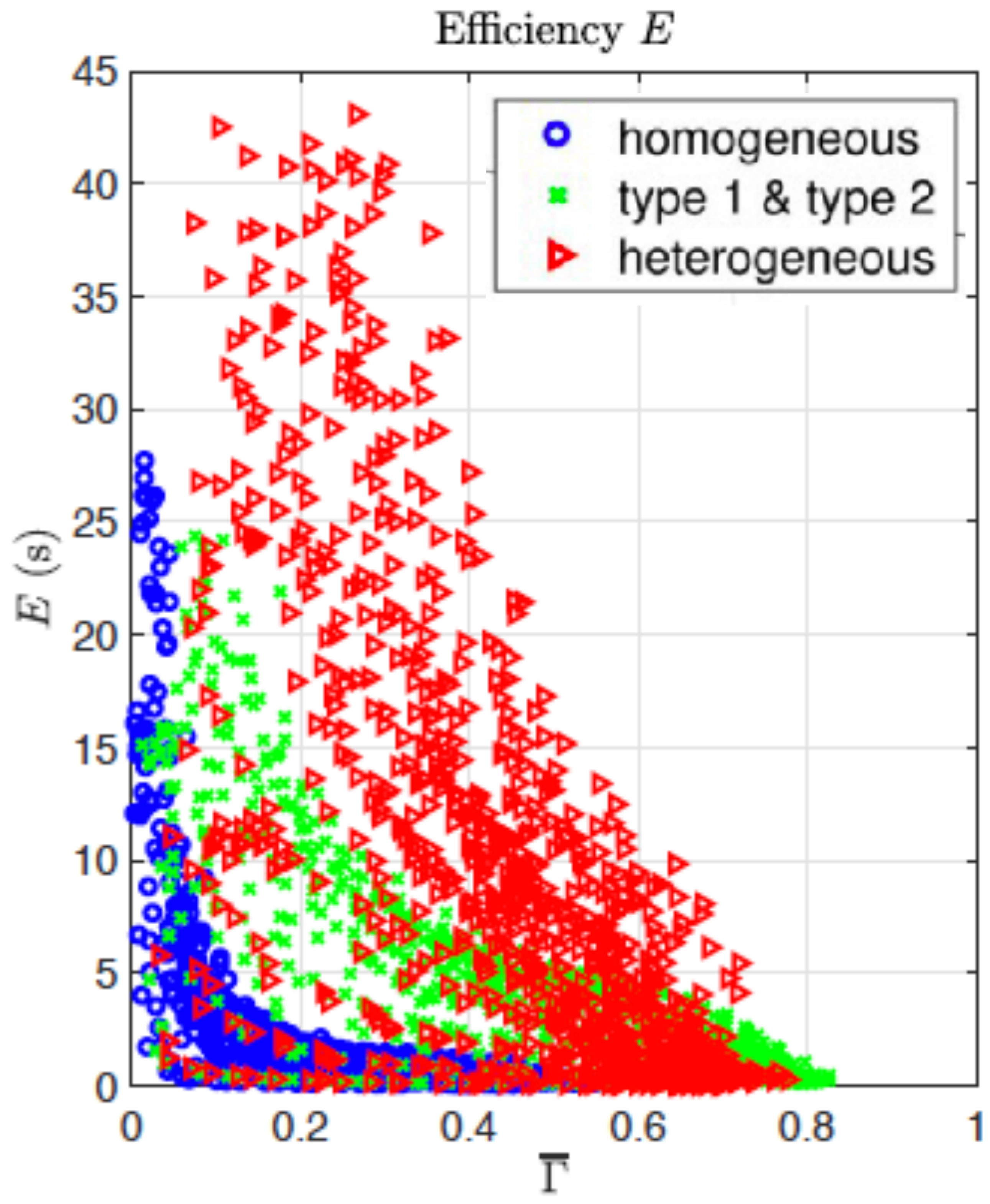
Heterogeneous networks are more *efficient* & *robust* than homogeneous networks





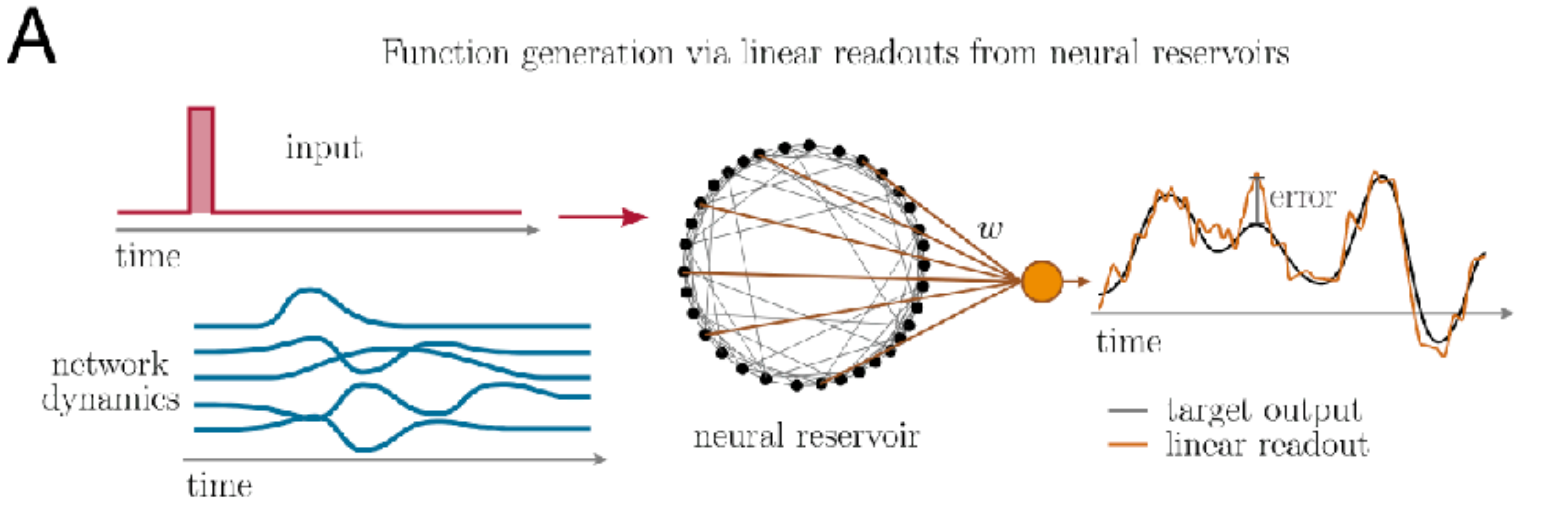


Trial-to-trial variability *increases* with efficiency



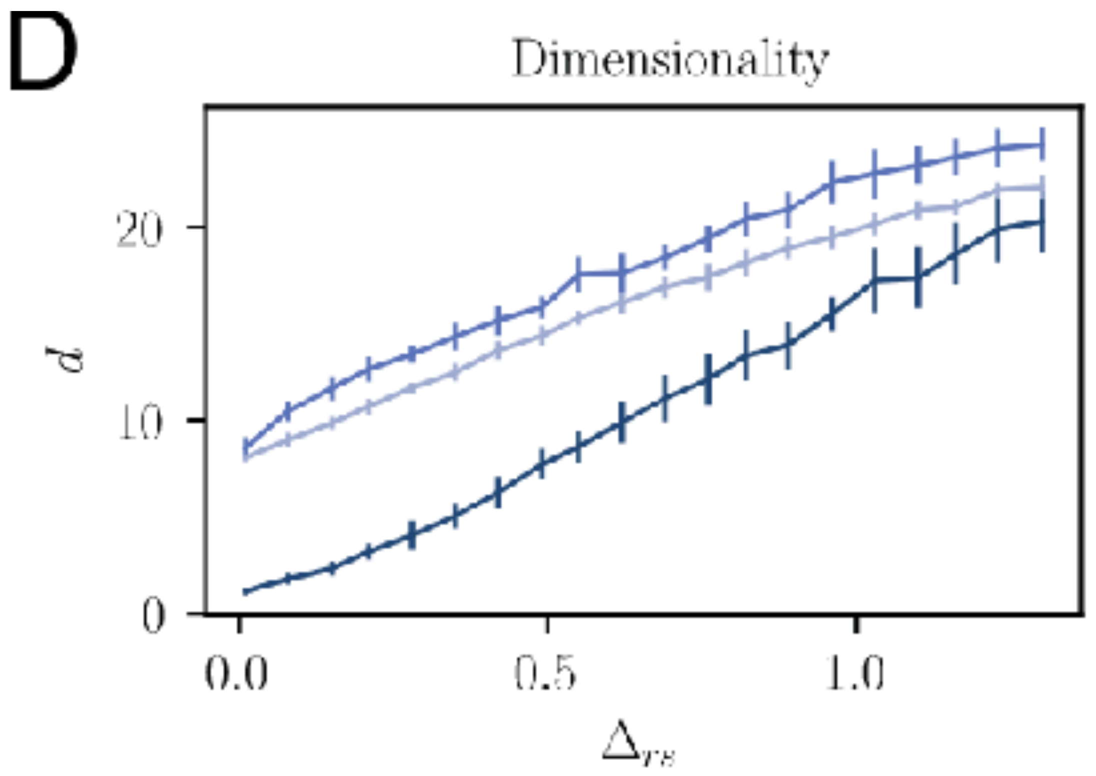
Zeldenrust, Gutkin, Denève, PLOS CB (2021)

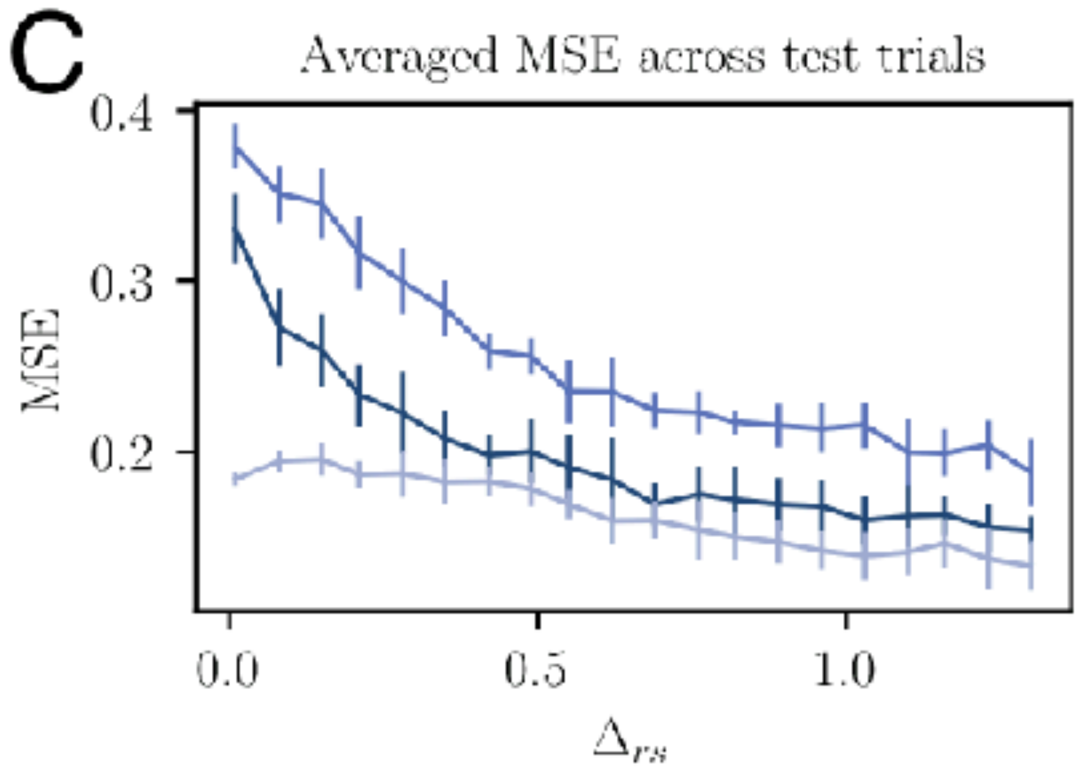
Heterogeneity, dimensionality and coding

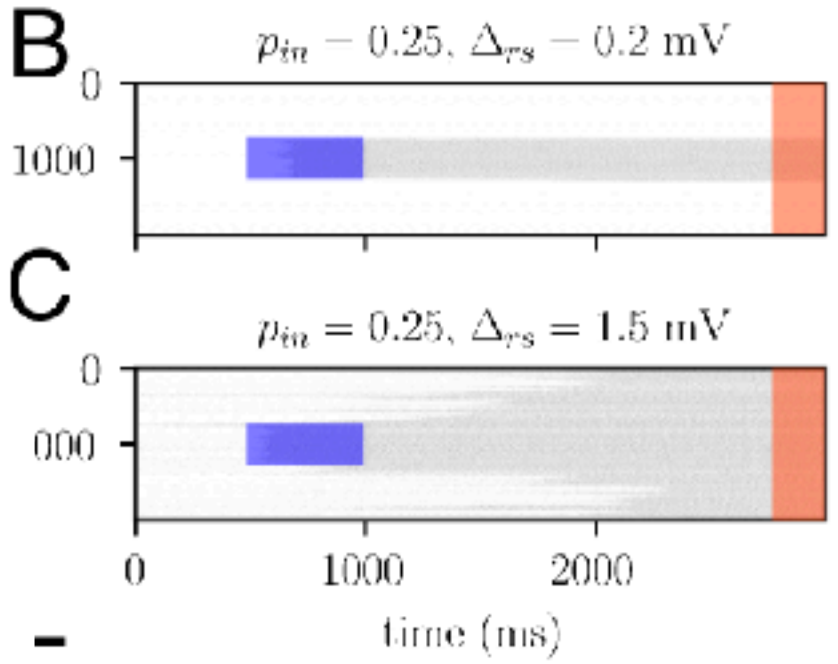


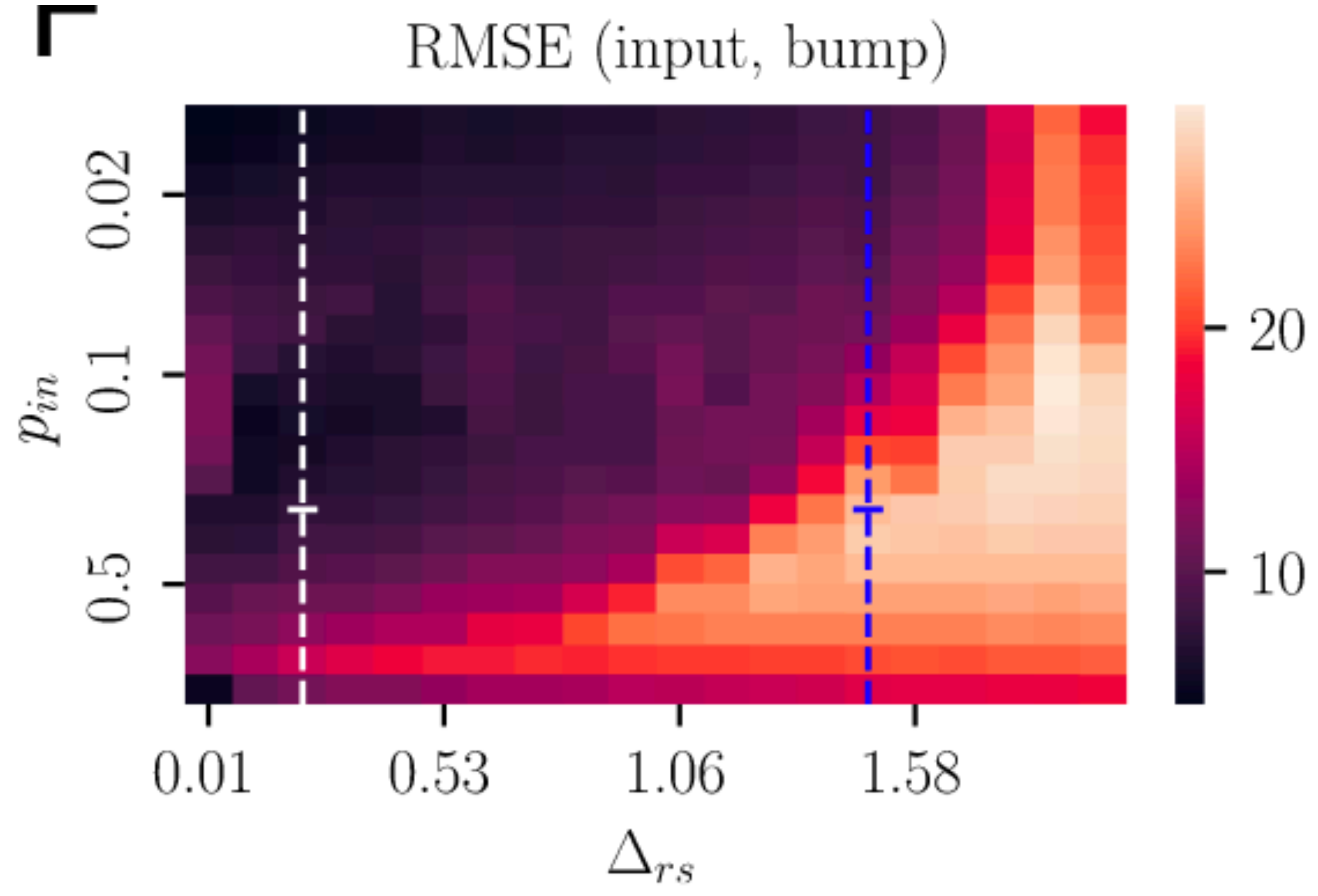
Gast, Solla, and Kennedy. PNAS 2024

- **Heterogeneity** in neuron thresholds increases **dimensionality** of network response
- This goes hand in hand with a **decrease in MSE** for representations
- However, also **increased dispersion** (ie less working memory)



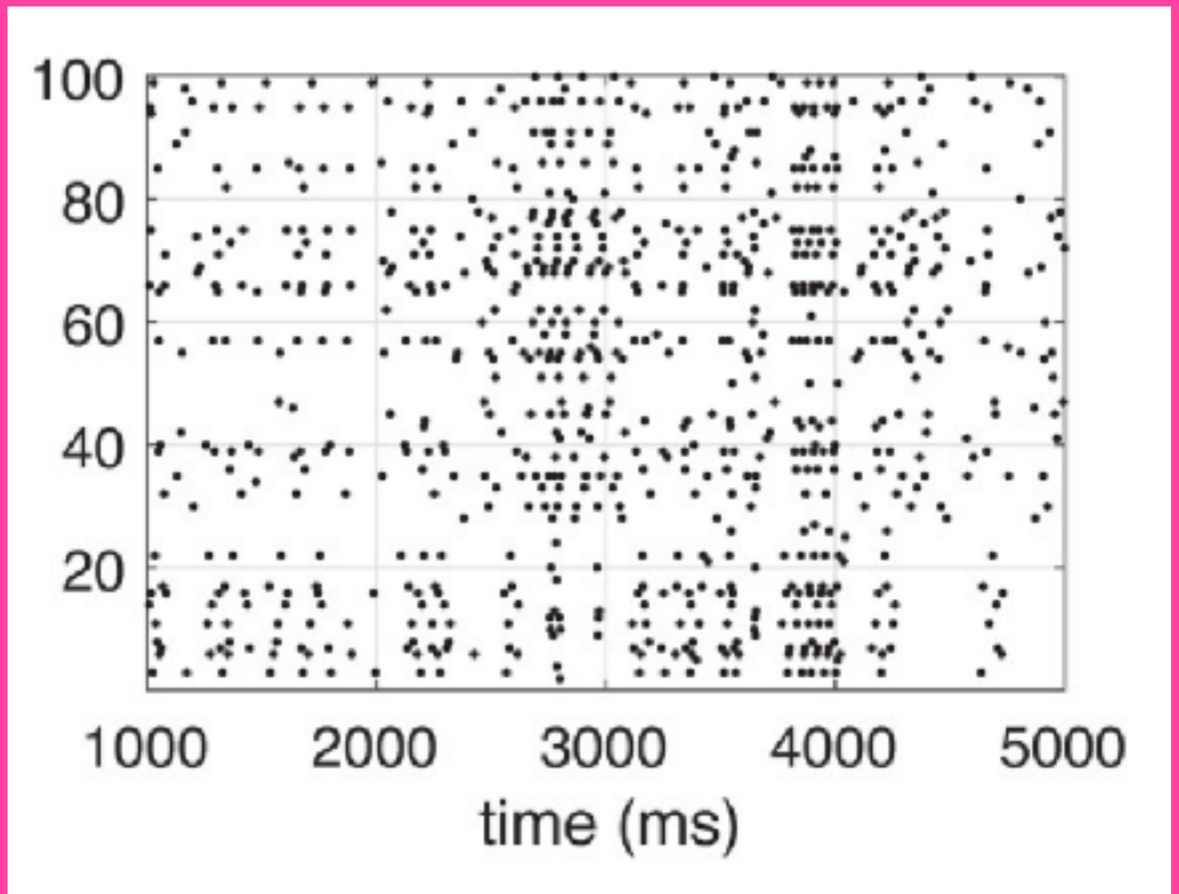






Some (which?) heterogeneity increases dimensionality

Dimensionality
Chaos



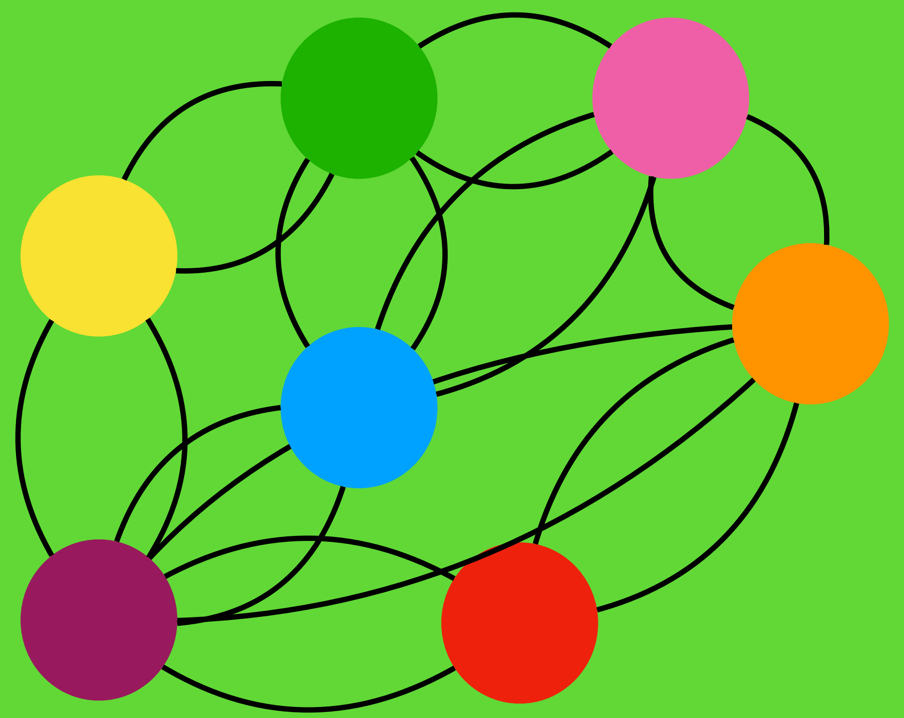
Activity

Dimensionality correlates with coding performance in *some* tasks

Sweet spot?

Structure

Heterogeneity, Non-linearity, Connectivity

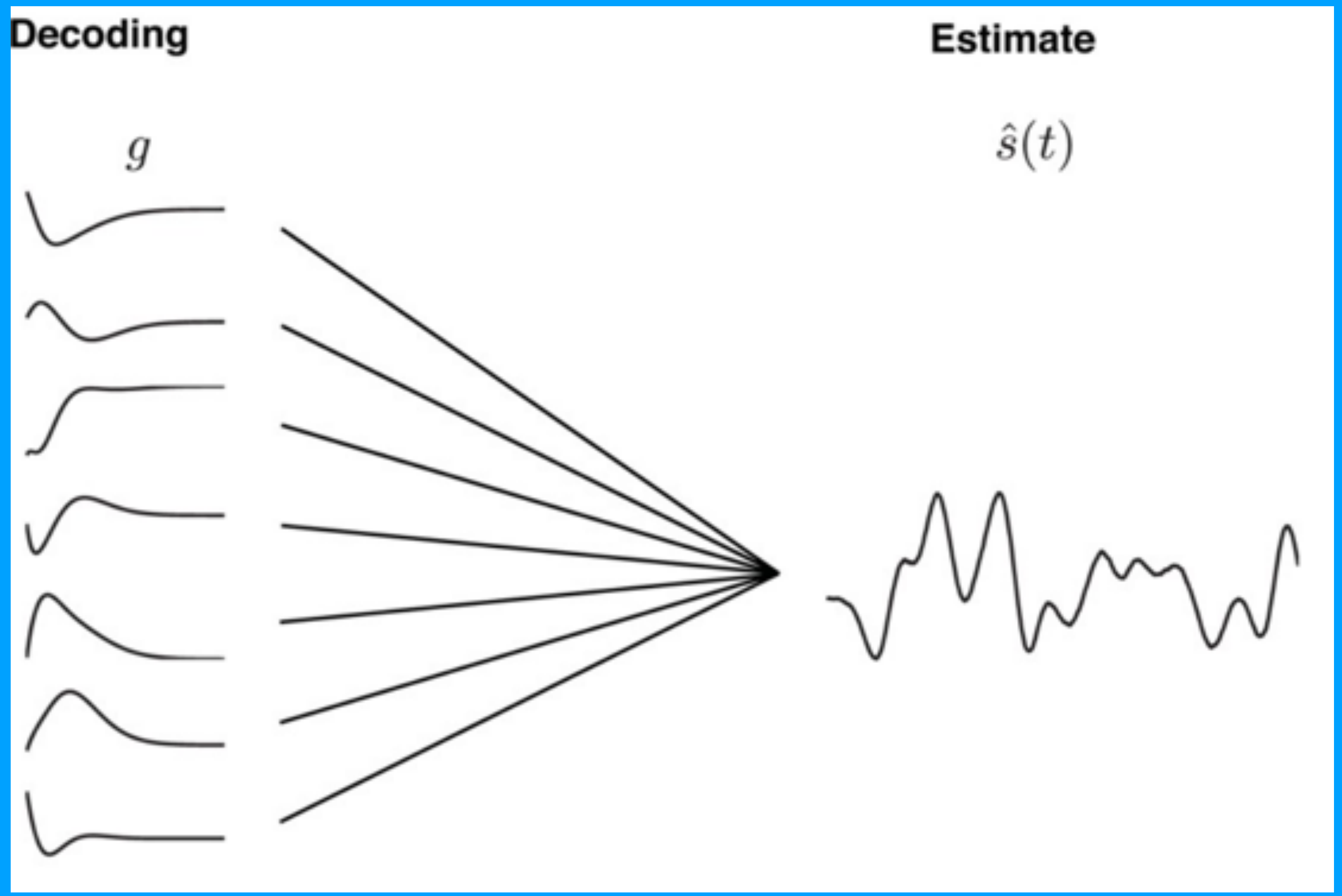


Structural and weight connectivity not the same!

Heterogeneity promotes coding in *some* tasks

Coding

Information transfer



Conclusions

Information transfer in realistic networks

→ Neuron level

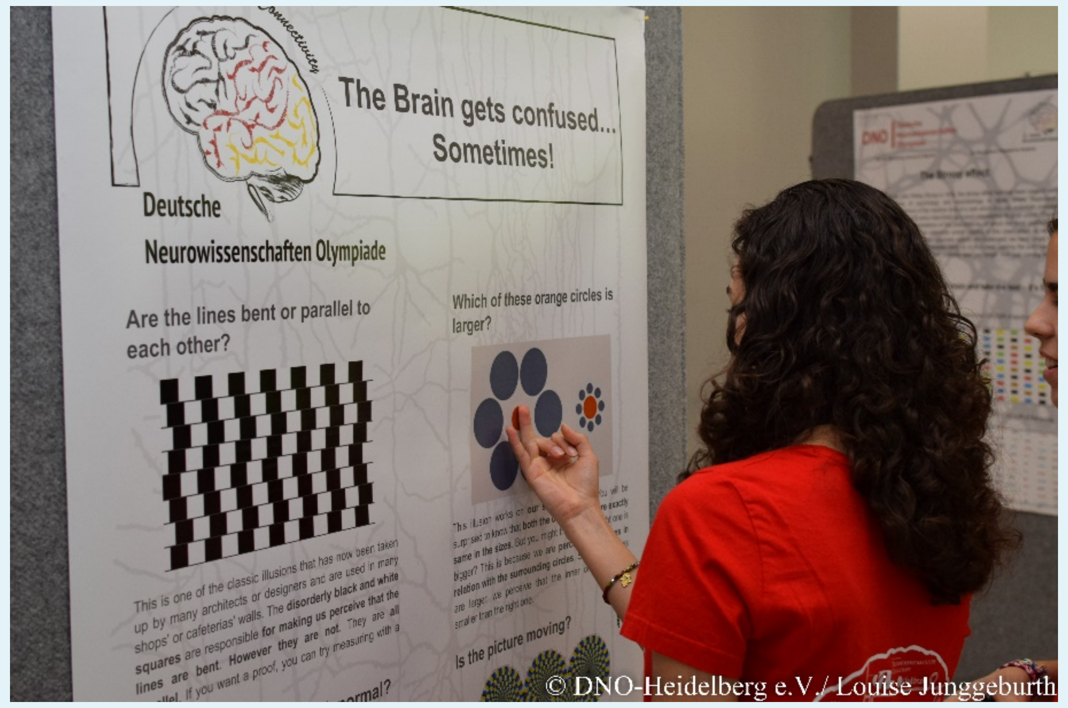
- Neurons perform complex, non-linear computations
- Cortical neurons show a large heterogeneity in their properties
- Neuromodulators affect inhibitory and excitatory neurons differentially
- Neuromodulators affect heterogeneity

→ Network level

- Realistic E/I ratios and neural properties in '**balanced networks**' influence dimensionality and computation (ie **increased dimensionality -> better computation?**)
- **Reservoir computing**: network needs to be high dimensional but not too chaotic (sweet spot?)
- Different heterogeneity effects: threshold (stabilising) and synaptic (destabilising)
- Heterogeneity in neural properties increases efficiency / robustness in **efficient coding networks**
- **Trial-to-trial variability** is a sign of efficient (degenerate) coding?

NEDERLANDSE HERSENOLYMPIADE

Dutch BrainBee: An exciting competition about Neuroscience



- Tell your family/friends to join as a participant (secondary school student)
- **Join the team**
    - present your research and/or
    - help syllabus computational neuroscience & AI
    - help us during the day: join@hersenolympiade.nl

How can I find out which stage of cognitive decline I am in, and how can I prevent Alzheimer's disease or dementia?

How is a neuron

BRAIN HELPDESK

What happens in the brain when you take psychedelics?

Does neuroscience provide better explanations for behaviour than psychology?

Find a question...

What happens in the brain when you feel 'confused'?

What is the purpose of brain research?

What

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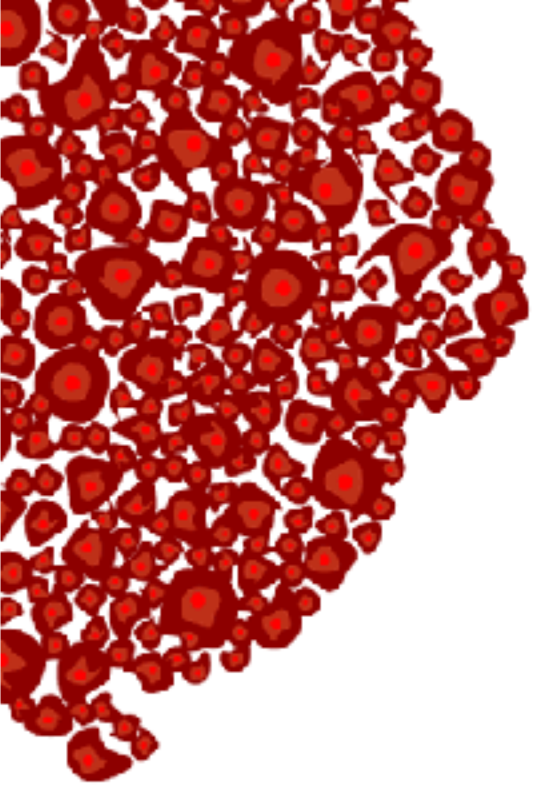

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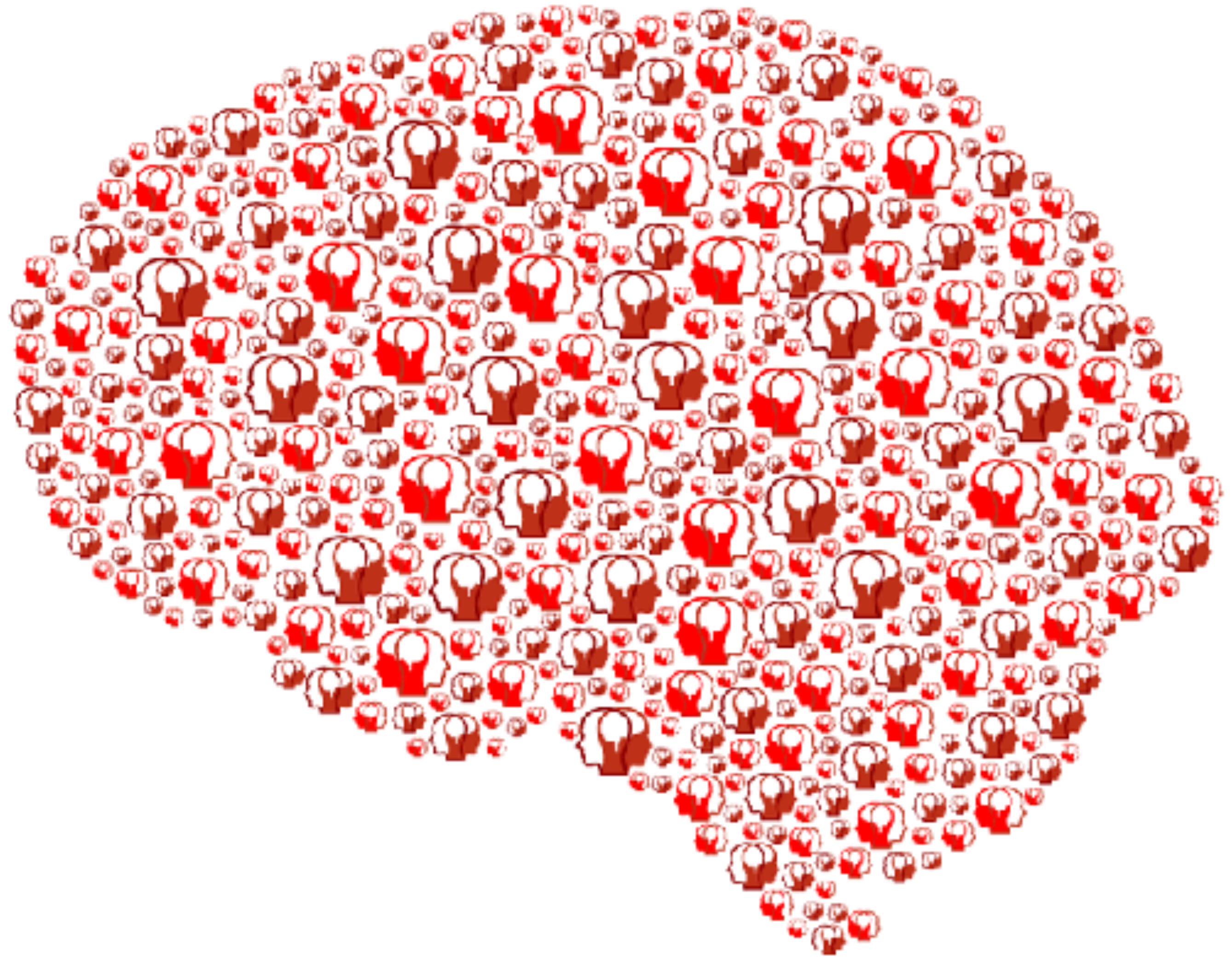
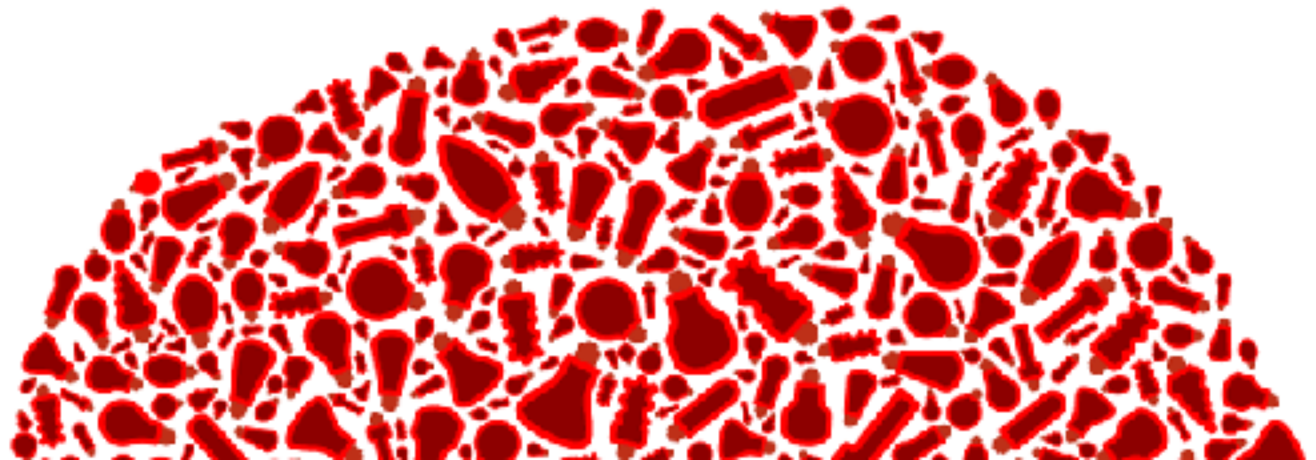
Questions?





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