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Network Physiology Approaches to Natural and Data-Driven Multi-Omics and High-Frequency Networks: Methodologies and Applications to Clinical Medicine

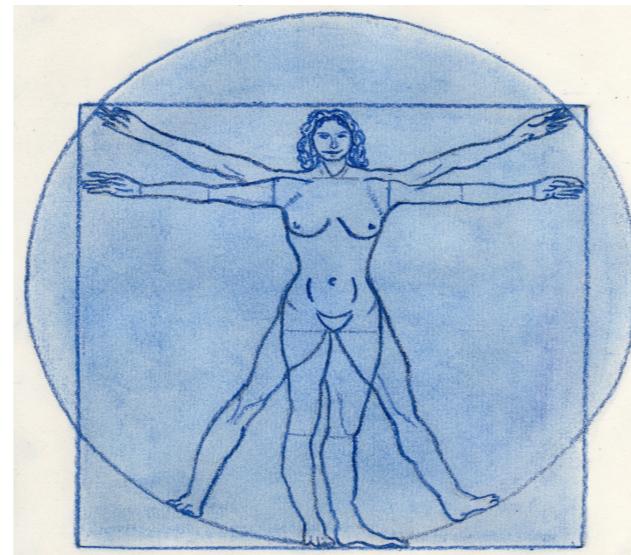
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Home > Frontiers in Network Physiology > Systems Interactions and Organ... > Research Topics > Astrocytes in the Brain Active Mi...

Astrocytes in the Brain Active Milieu

Intelligence and Consciousness in Genetic Neuron-Astrocyte Networks

Work in Progress



Alexey Zaikin
www.zaikinlab.com



What is the difference?



What is the difference?



Intelligence (ability to classify and learn)?
Consciousness (positive Integrated Information)?

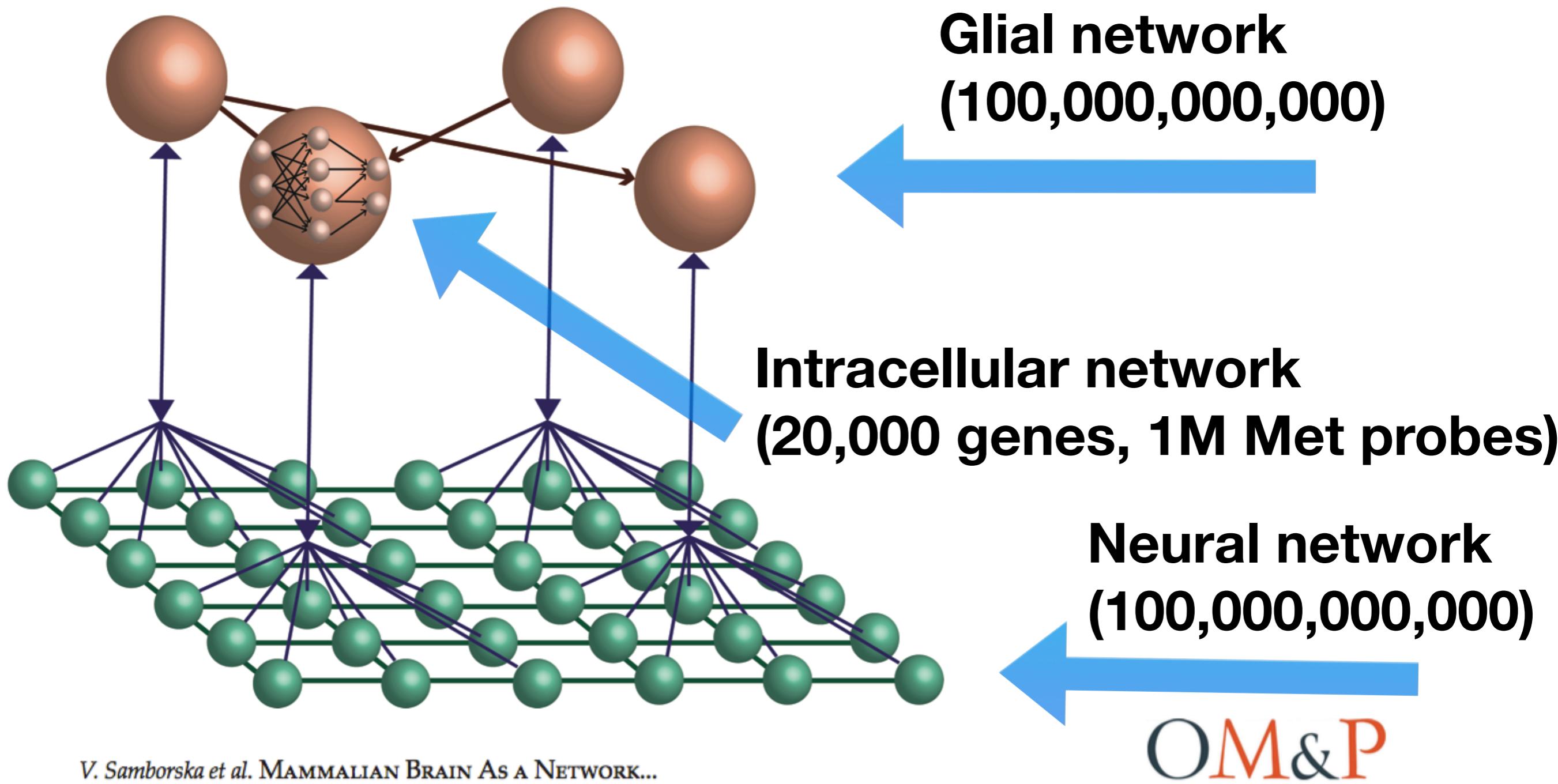
Where is Intelligence and Consciousness?

What is the difference?



Intelligence (ability to classify and learn)?
Consciousness (positive Integrated Information)?

Mammalian Brain: Simplified Scheme

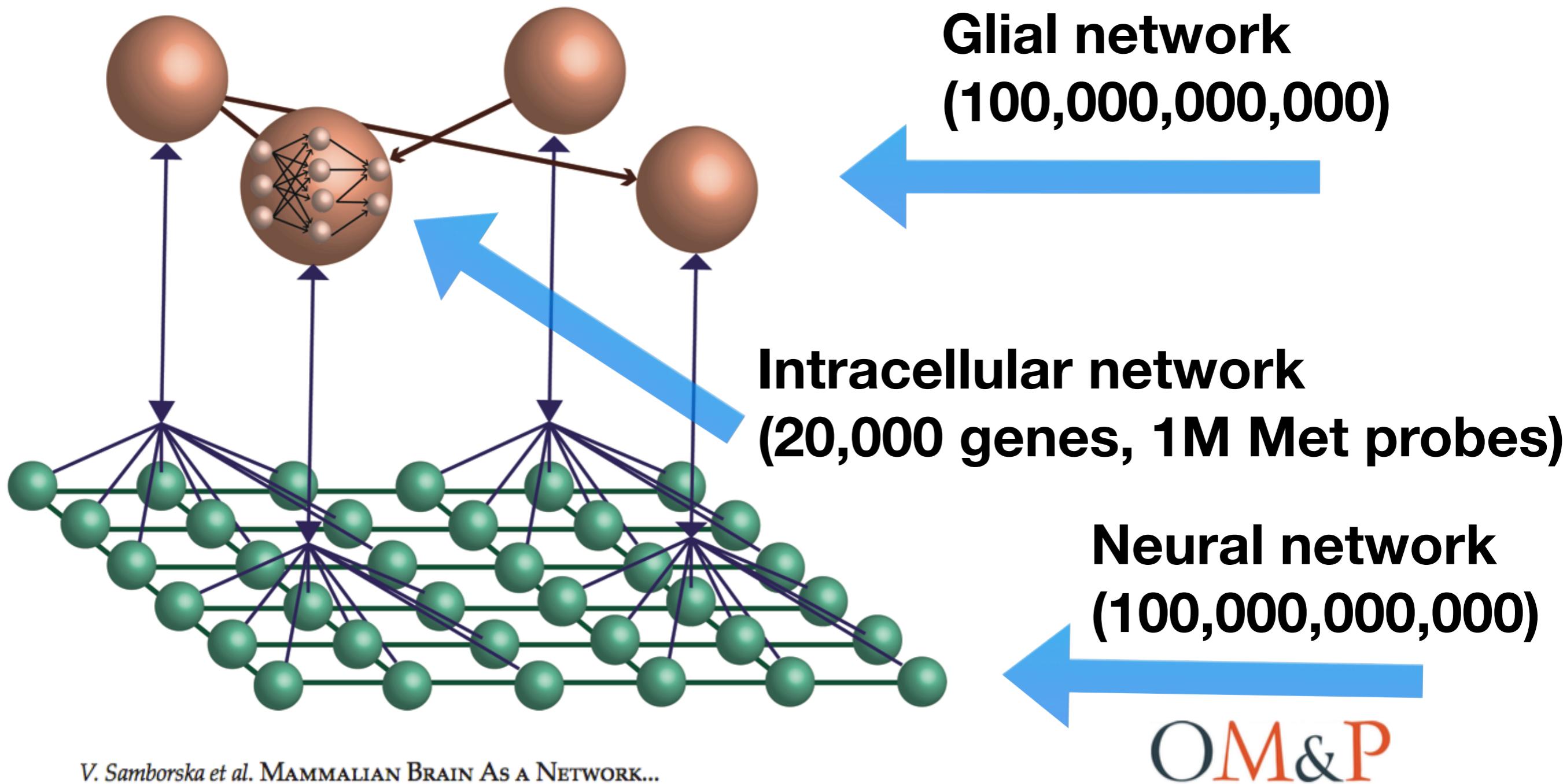


V. Samborska et al. MAMMALIAN BRAIN AS A NETWORK...

MAMMALIAN BRAIN AS A NETWORK OF NETWORKS

Veronika Samborska ¹, Susanna Gordleeva ², Ekkehard Ullner ³, Albina Lebedeva ², Viktor Kazantsev ², Mikhail Ivanchenko ² and Alexey Zaikin ^{2,4}

Mammalian Brain: **Very Simplified Scheme**



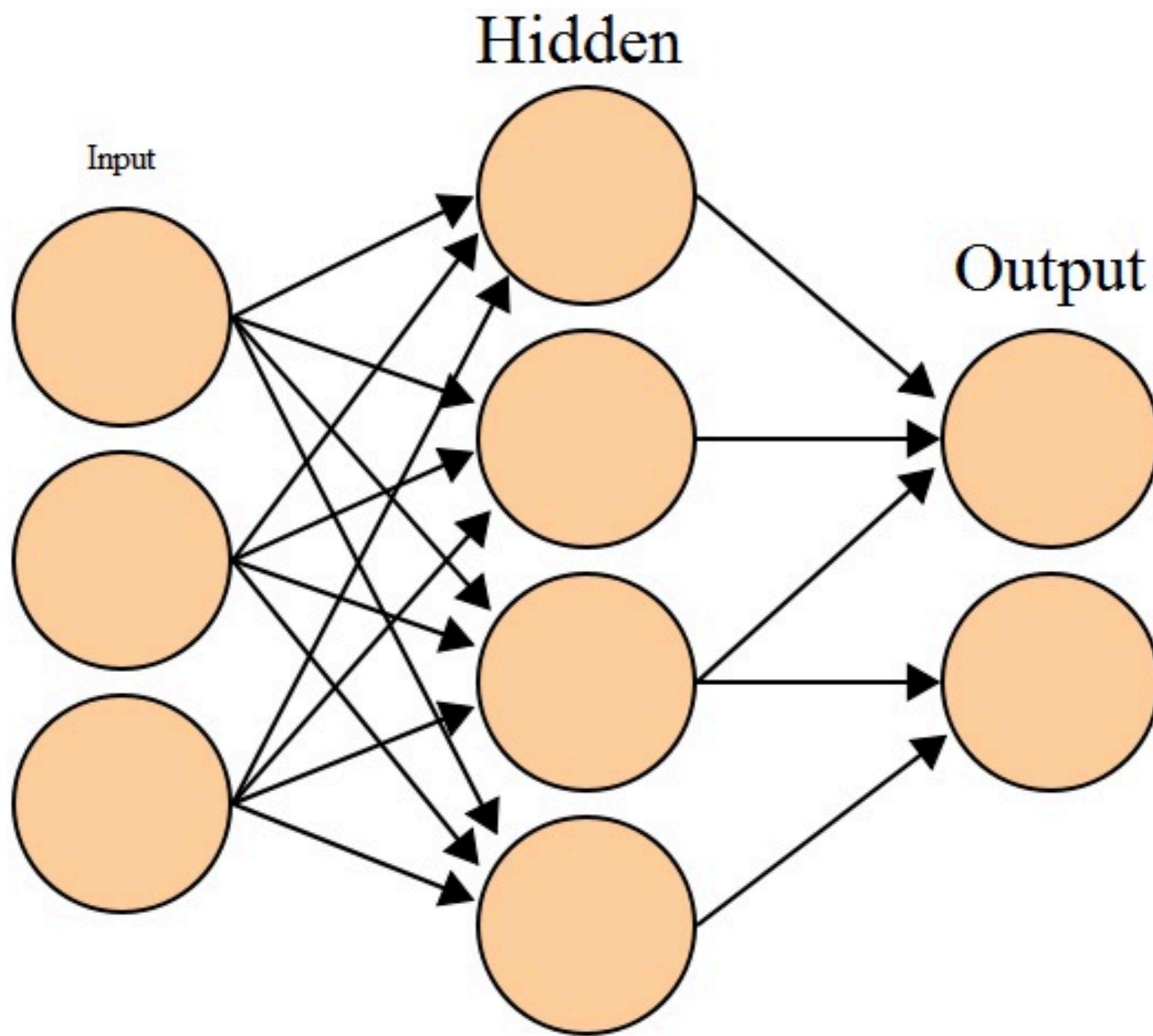
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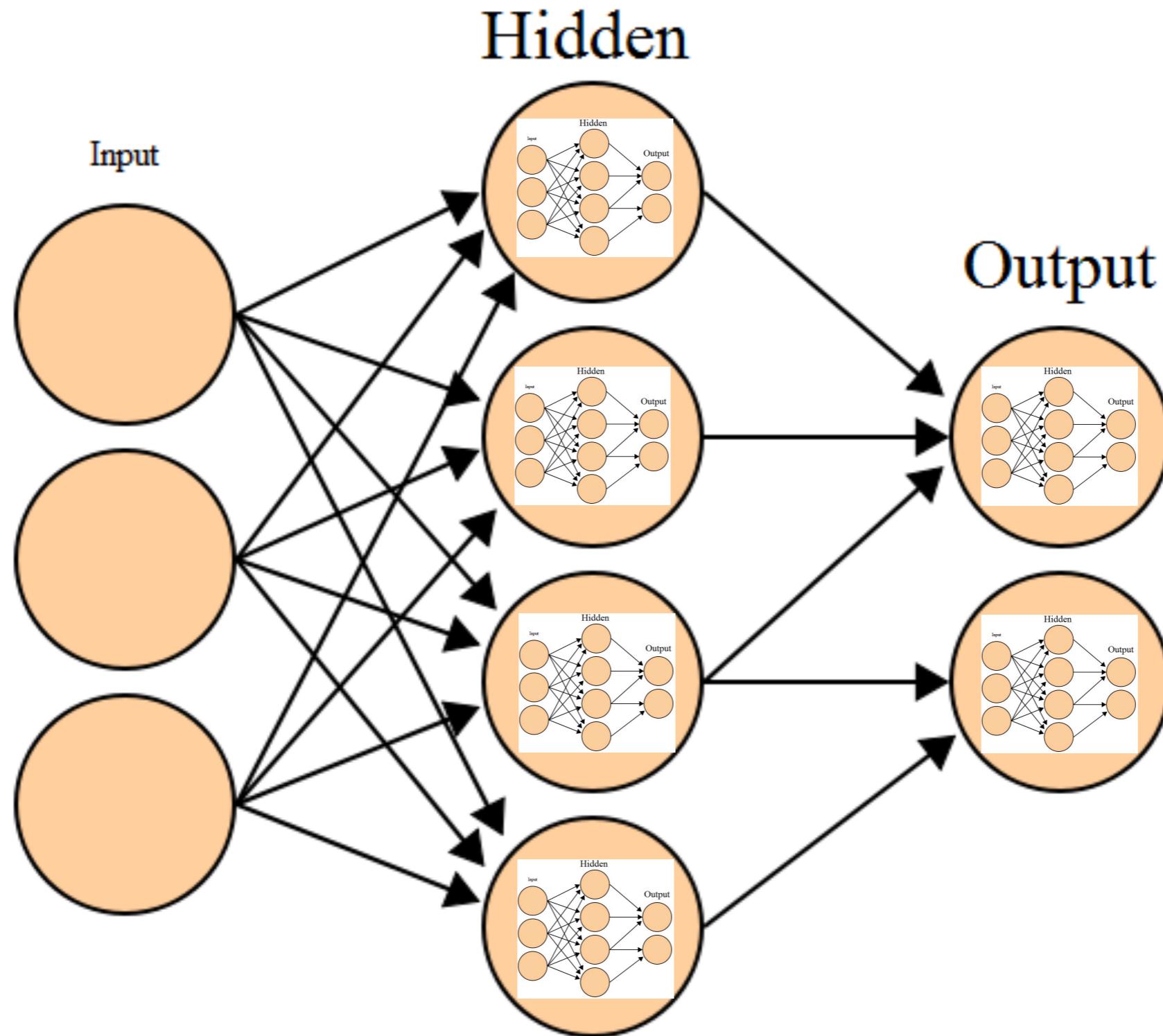
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Intelligence

Multicellular intelligence



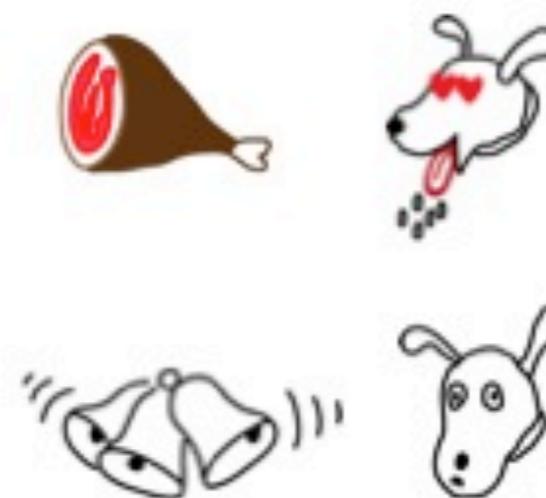
Intracellular intelligence



Paradigms of artificial Intelligence

Associative perceptron:

Two inputs



Learning the association



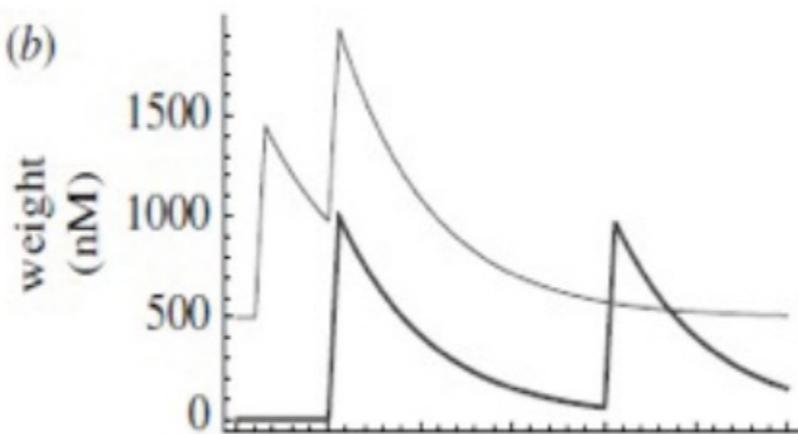
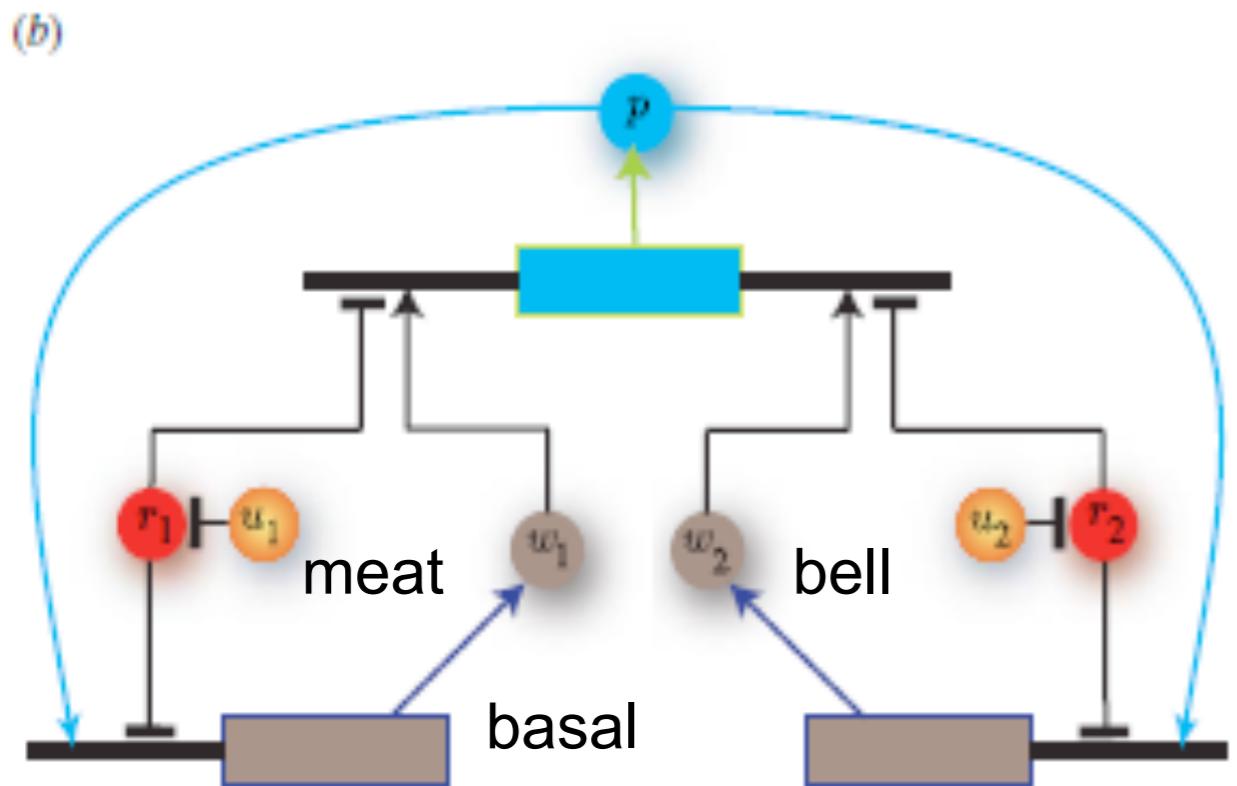
Reaction to learned association



Molecular circuits for associative learning in single-celled organisms

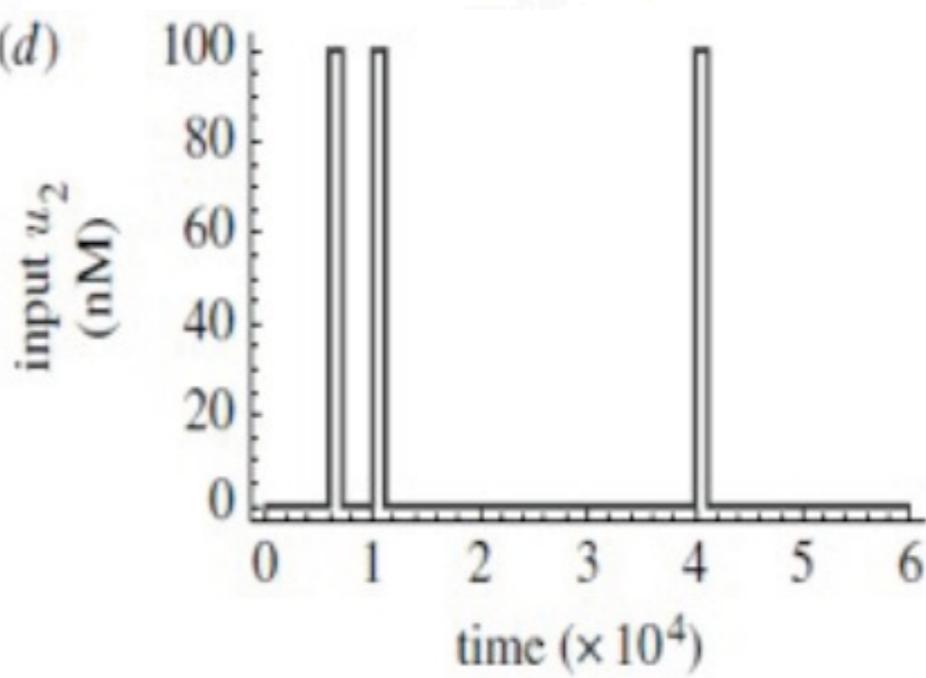
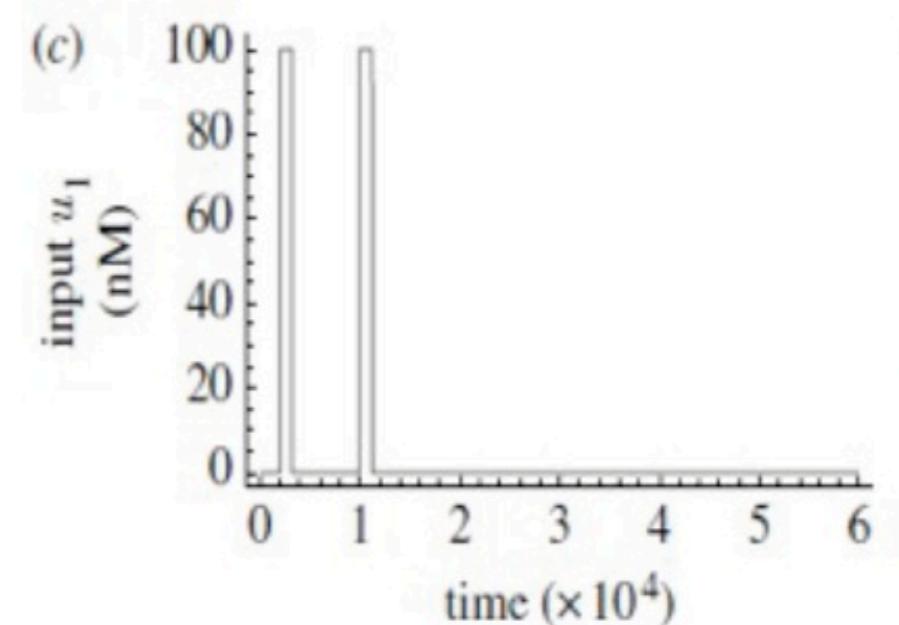
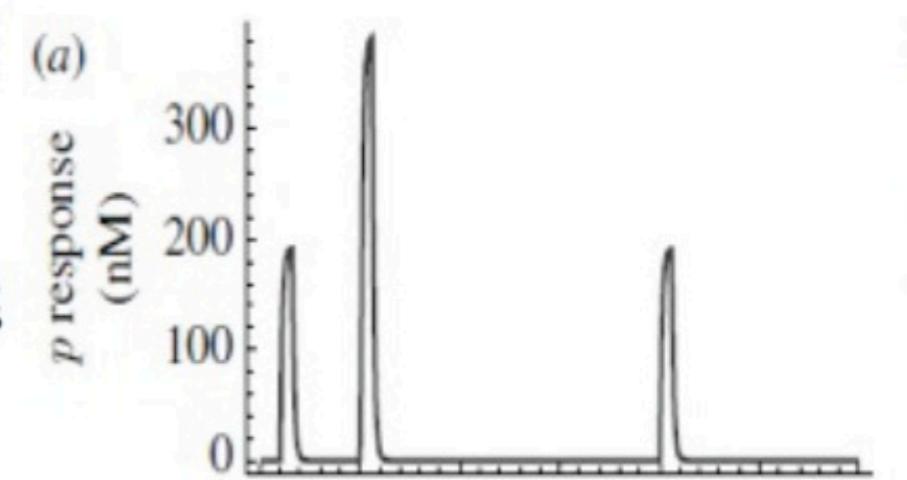
Chrisantha T. Fernando^{1,2,*}, Anthony M. L. Liekens³, Lewis E. H. Bingle¹, Christian Beck⁴, Thorsten Lenser⁴, Dov J. Stekel¹ and Jonathan E. Rowe⁵

The Model Network



meat

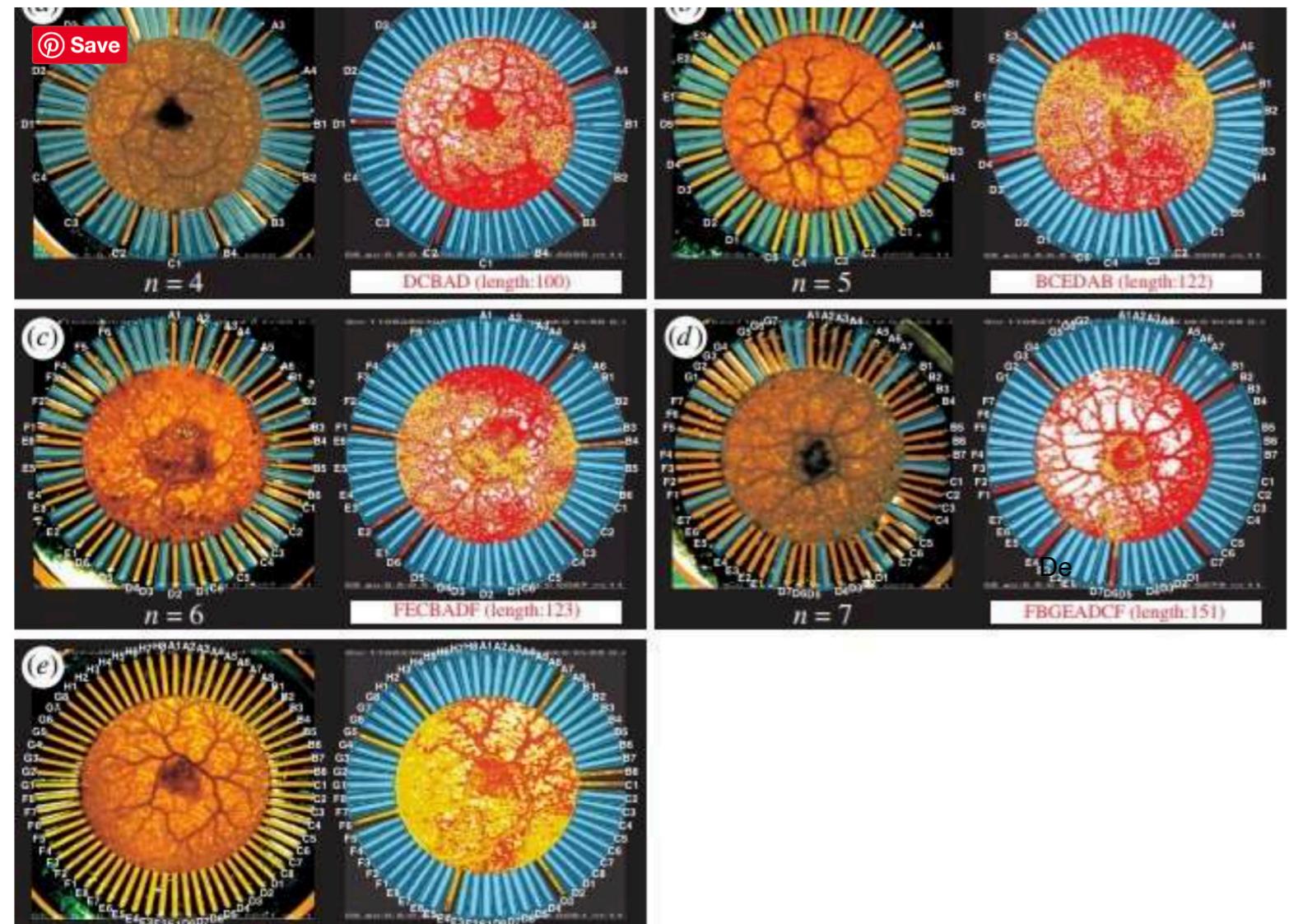
bell



December 2018:

Amoeba finds approximate solutions to NP-hard problem in linear time

December 20, 2018 by Lisa Zyga, Phys.org feature



TSP solutions obtained by the amoeba-based computing system for 4, 5, 6, 7, and 8 cities. Credit: Zhu et al. ©2018 Royal Society Open Science

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Research



Cite this article: Zhu L, Kim S-J, Hara M, Aono M. 2018 Remarkable problem-solving ability of unicellular amoeboid organism and its mechanism. *R. Soc. open sci.* **5**: 180396. <http://dx.doi.org/10.1098/rsos.180396>

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How Computationally Complex Is a Single Neuron?

Beniaguev et al., 2021, *Neuron* 109, 2727–2739
September 1, 2021 © 2021 Elsevier Inc.
<https://doi.org/10.1016/j.neuron.2021.07.002>

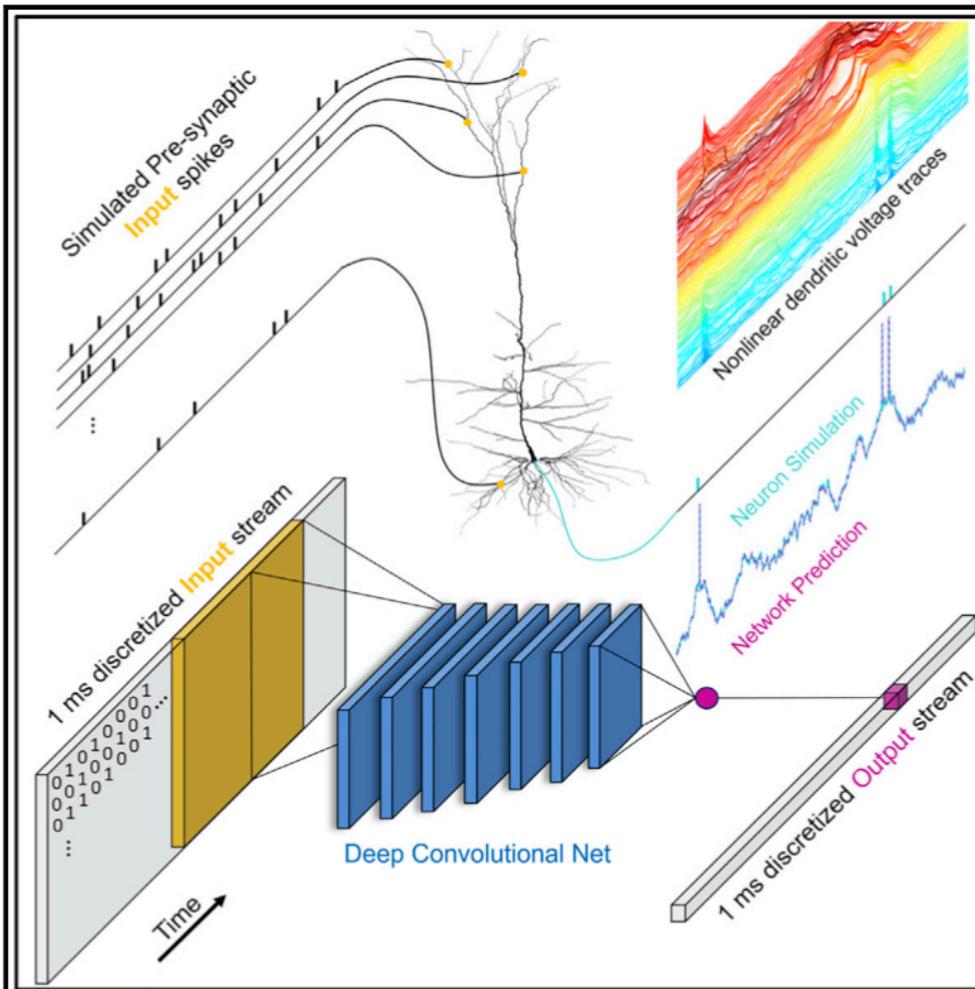


Article

Neuron

Single cortical neurons as deep artificial neural networks

Graphical abstract



Authors

David Beniaguev, Idan Segev,
Michael London

Correspondence

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In brief

Using a modern machine learning approach, we show that the I/O characteristics of cortical pyramidal neurons can be approximated, at the millisecond resolution (single spike precision), by a temporally convolutional neural network with five to eight layers. This computational complexity stems mainly from the interplay between NMDA receptors and dendritic morphology.

Beniaguev et al., 2021, Neuron 109, 2727–2739

September 1, 2021 © 2021 Elsevier Inc.

<https://doi.org/10.1016/j.neuron.2021.07.002>

Highlights

- Cortical neurons are well approximated by a deep neural network (DNN) with 5–8 layers
- DNN's depth arises from the interaction between NMDA receptors and dendritic morphology
- Dendritic branches can be conceptualized as a set of spatiotemporal pattern detectors
- We provide a unified method to assess the computational complexity of any neuron type

Recurrence-based information processing in gene regulatory networks

Marçal Gabalda-Sagarra, Lucas B. Carey, and Jordi Garcia-Ojalvo^{a)}

Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona Biomedical Research Park, 08003 Barcelona, Spain

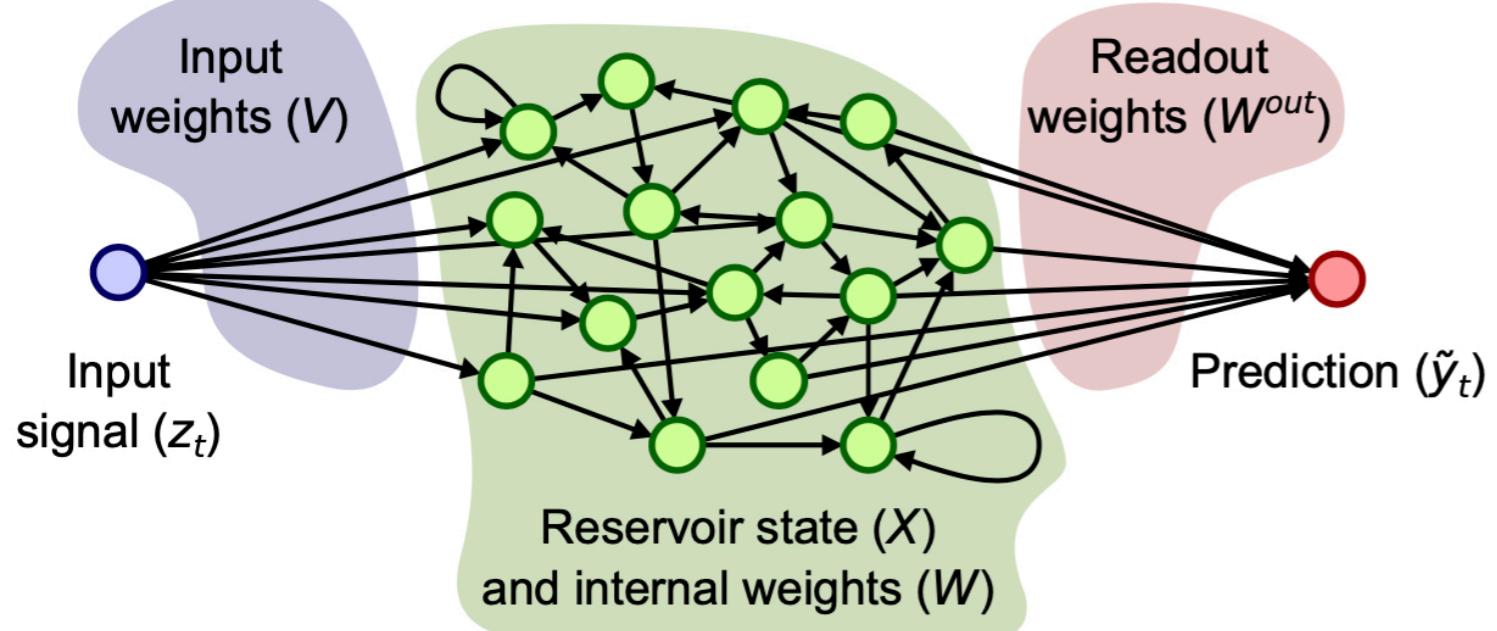


Figure 3.4: Setup to test the memory of a network. A reservoir is built with a connectivity matrix W that defines the topology of a given network. A signal z_t arrives to the nodes of the reservoir with different strengths defined by the input weight vector V . Then, one or more readout nodes compute a weighted sum of the state of the reservoir X . The weight vector W^{out} is tuned so that the output \tilde{y}_t of the readout approximates a target output signal.

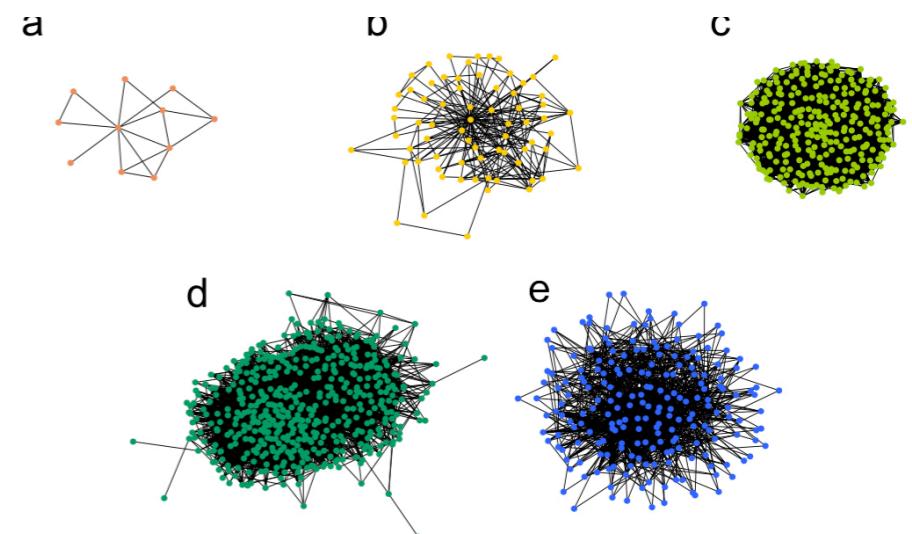


FIG. 3. Recurrent cores of the gene regulatory networks: *Bacillus subtilis* (a), *Escherichia coli* (b), *Saccharomyces cerevisiae* (c), *Drosophila melanogaster* (d), and *Homo sapiens* (e). All nodes in these subgraphs have both out-degree and in-degree larger than 0.

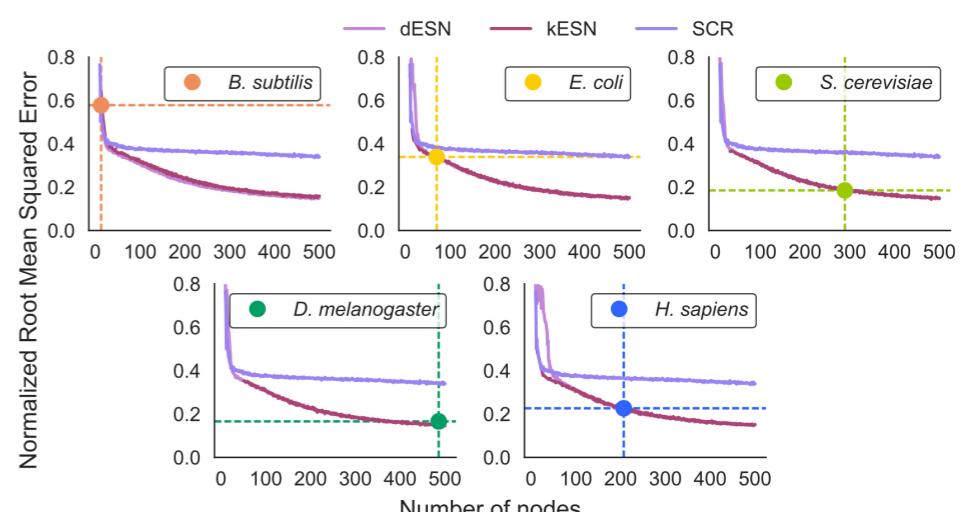
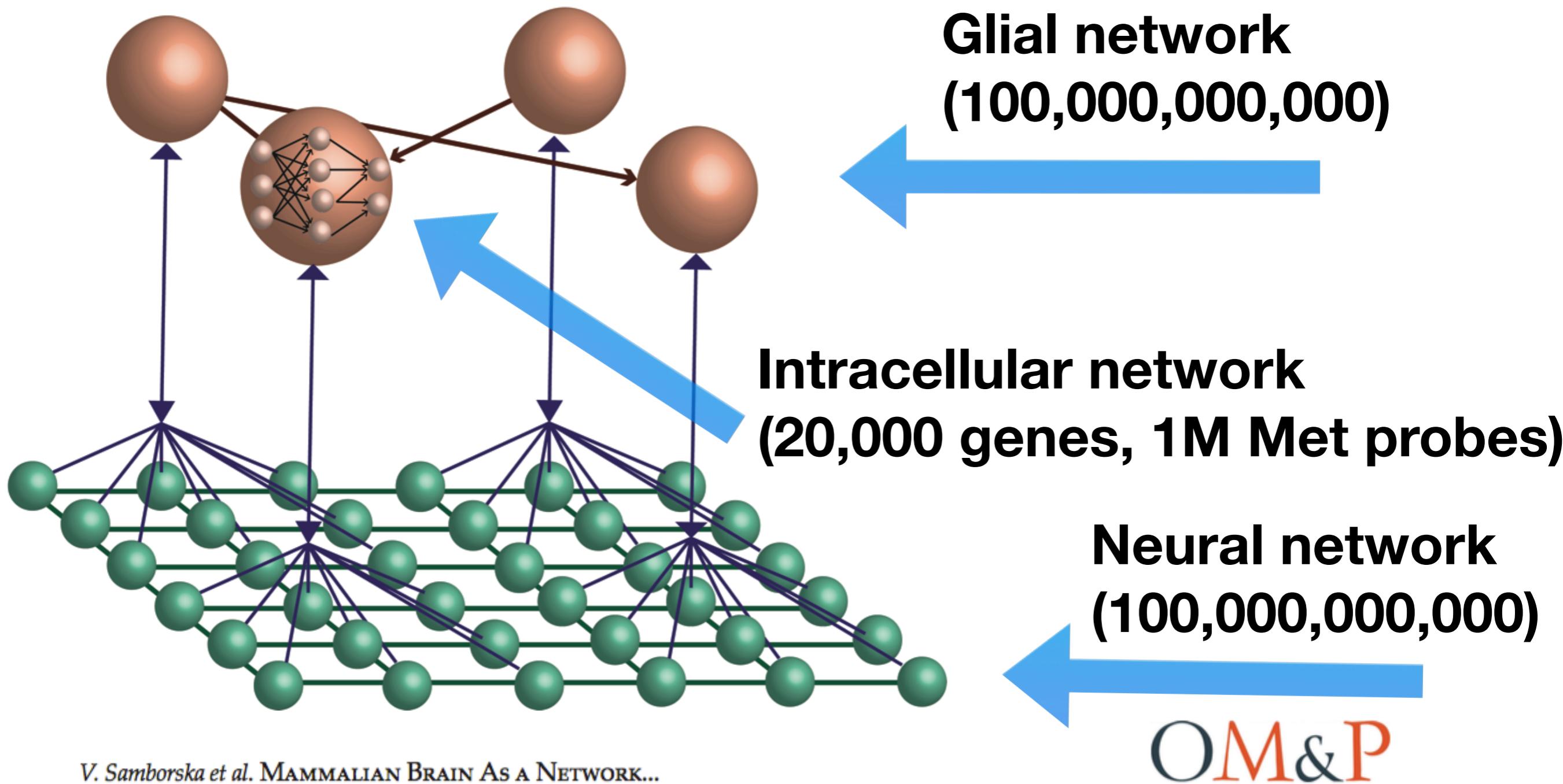


FIG. 6. Performance of the biological reservoirs compared with control topologies. Performance is evaluated with the Normalized Root Mean Squared Error (NRMSE) between expected and reconstructed outputs. The NRMSE value shown for each biological network topology corresponds to the median of 10 000 trials (with edge weights and data series randomization). The values plotted for each control network (dESN, kESN, and SCR) correspond to the median value of 100 trials for each network size from 10 to 500 nodes.

Mammalian Brain: Simplified Scheme



V. Samborska et al. MAMMALIAN BRAIN AS A NETWORK...

MAMMALIAN BRAIN AS A NETWORK OF NETWORKS

Veronika Samborska ¹, Susanna Gordleeva ², Ekkehard Ullner ³, Albina Lebedeva ², Viktor Kazantsev ², Mikhail Ivanchenko ² and Alexey Zaikin ^{2,4}

Astrocytes? Astrocytes Organize Associative Memory



in Cellular Neuroscience

ORIGINAL RESEARCH
published: 31 March 2021
doi: 10.3389/fncel.2021.631485

Modeling Working Memory in a Spiking Neuron Network Accompanied by Astrocytes

Susanna Yu. Gordleeva^{1,2*}, Yuliya A. Tsybina¹, Mikhail I. Krivonosov¹,
Mikhail V. Ivanchenko¹, Alexey A. Zaikin^{1,3,4}, Victor B. Kazantsev^{1,2,5} and
Alexander N. Gorban^{1,6}

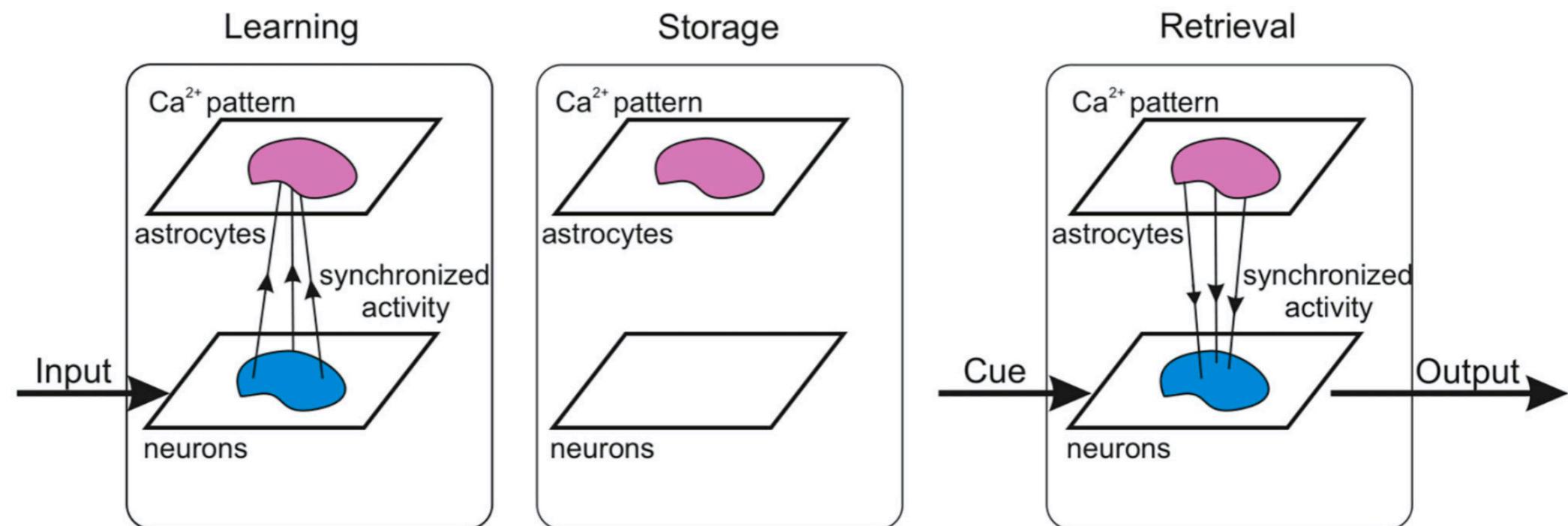
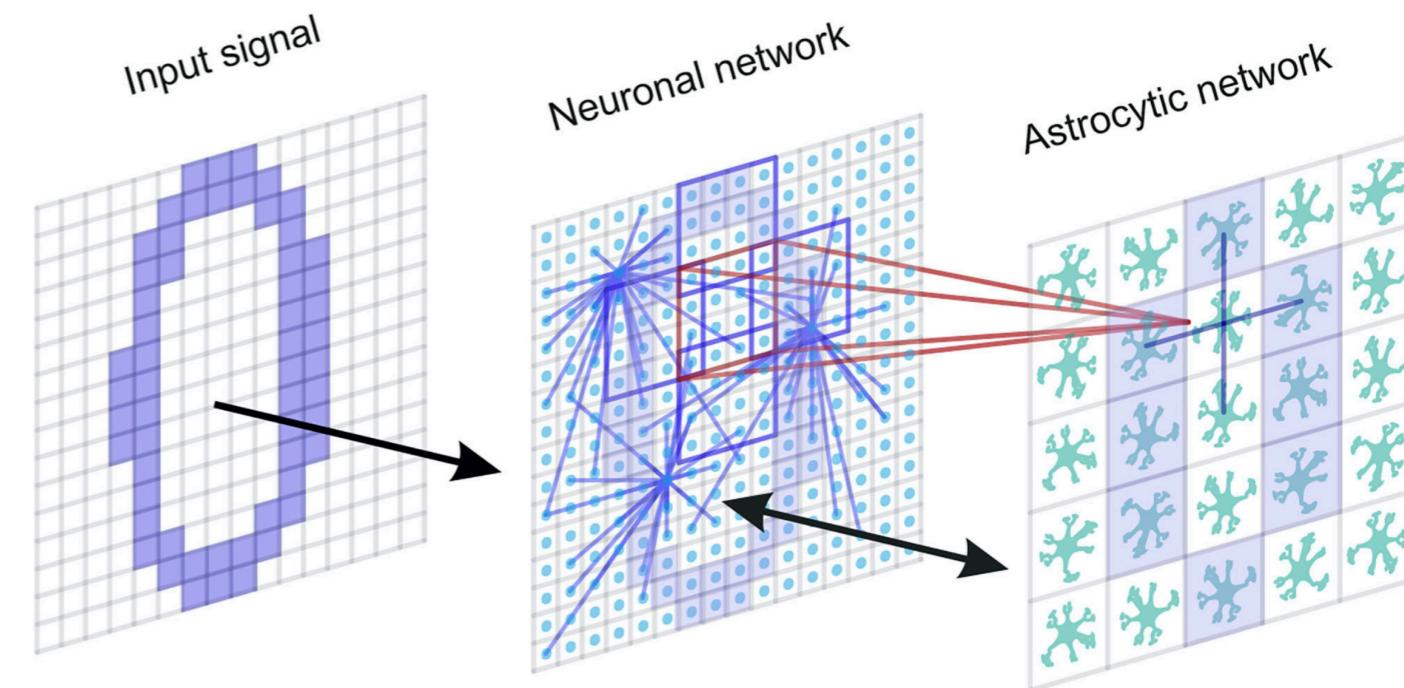


FIGURE 13 | Concept of WM operation in the spiking neuron network model accompanied by astrocytes.

Situation-associated memory in neuromorphic model of spiking neuron-astrocyte network

Susanna Gordleeva^{a,b,*}, Yuliya A. Tsybina^a, Mikhail I. Krivonosov^a, Ivan Y. Tyukin^{a,f}, Victor B. Kazantsev^{a,b,e}, Alexey A. Zaikin^{a,c,d}, Alexander N. Gorban^{a,f}

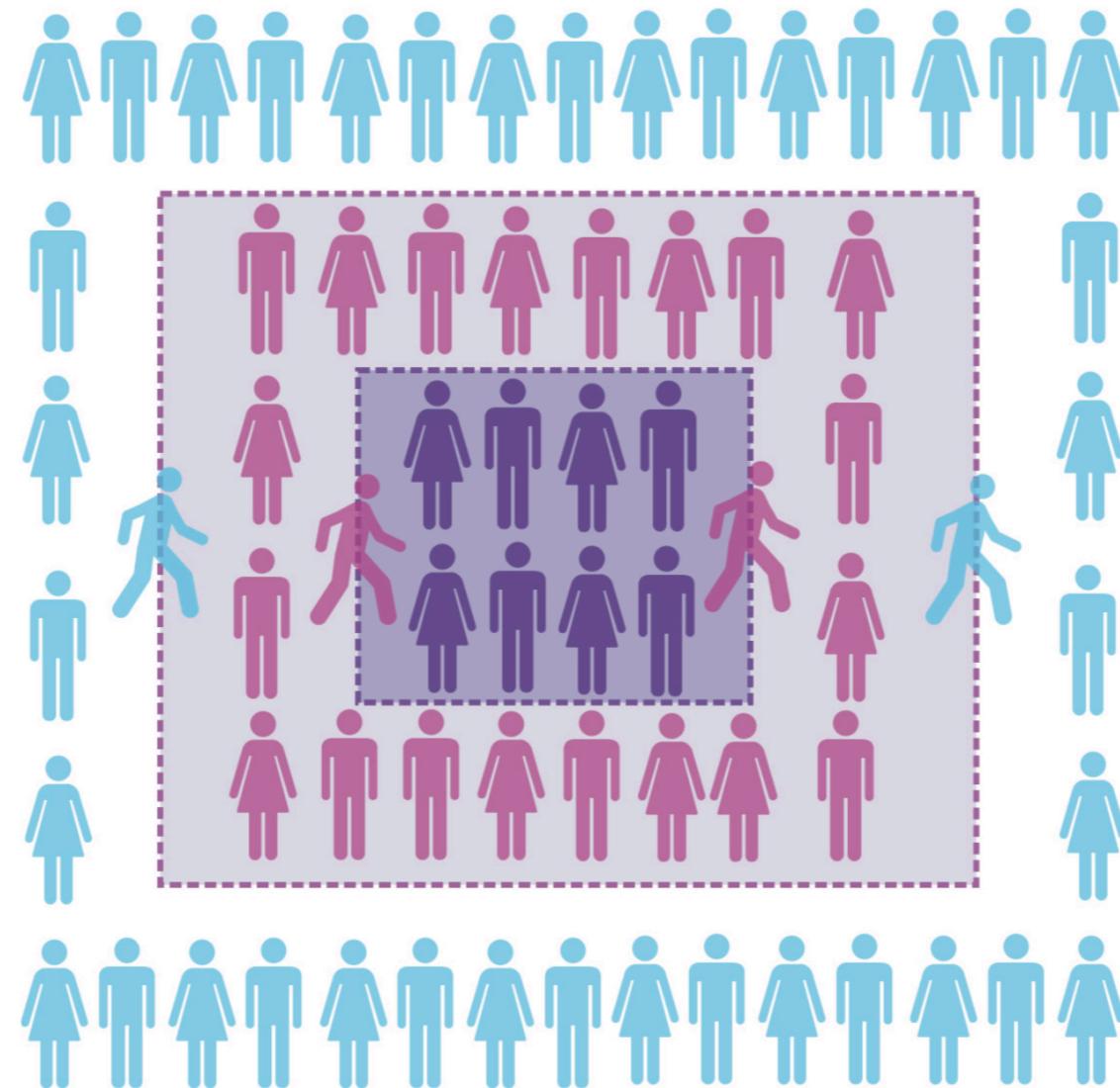
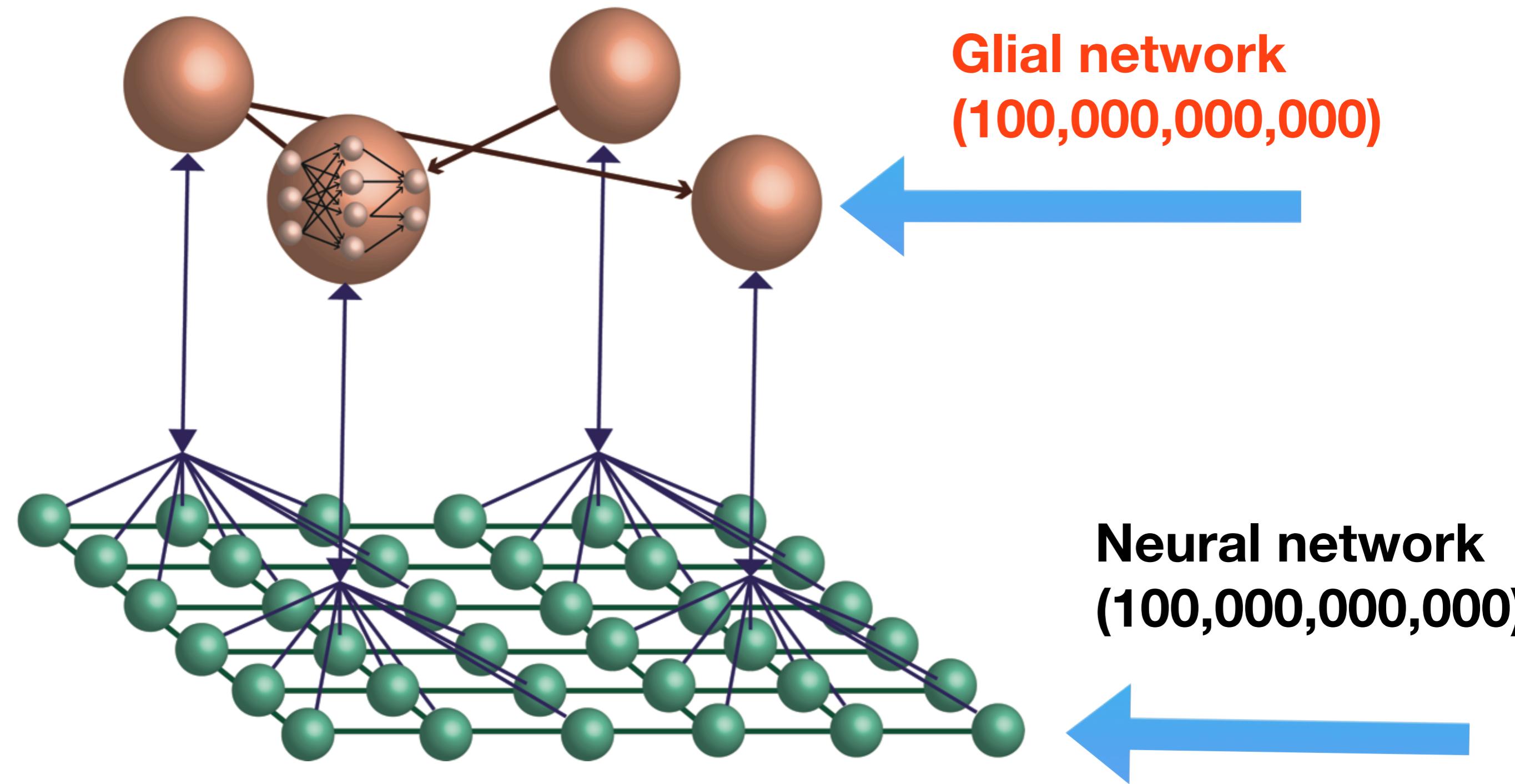


Figure 1: Situation based organisation of data or patterns is structured with three pools of patterns.

Consciousness

Mammalian Brain as Network of Networks

Where is consciousness?



Integrated information

BMC Neuroscience



Research article

An information integration theory of consciousness

Giulio Tononi*

Open Access

Published: 02 November 2004

OPINION

**Integrated information theory:
from consciousness to its physical
substrate**

450 | JULY 2016 | VOLUME 17

www.nature.com/nrn

Giulio Tononi, Melanie Boly, Marcello Massimini and Christof Koch

OPEN ACCESS Freely available online

PLOS COMPUTATIONAL BIOLOGY

Practical Measures of Integrated Information for Time-Series Data

Adam B. Barrett*, Anil K. Seth

January 2011 | Volume 7 | Issue 1 | e1001052

Integrated information

BMC Neuroscience



Research article

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Published: 02 November 2004

An information integration theory of consciousness

Giulio Tononi*

“Integrated Information quantifies the extent to which a system generates more information than the sum of its parts as it transitions between states”

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Research article

An information integration theory of consciousness

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Published: 02 November 2004

“Integrated Information quantifies the extent to which a system generates more information than the sum of its parts as it transitions between states”

“According to the Integrated Information Theory of Consciousness, this quantity is identical to the quantity of consciousness generated by the system”

Brief tutorial to Mutual Information



Uncertainty = 2



Uncertainty = 6

$$u = \log(n)$$

where *log* is used to achieve the additivity for independent uncertainty. Suppose playing with two dies *n* and *m*:

$$u_{nm} = \log(nm) = \log(n) + \log(m),$$

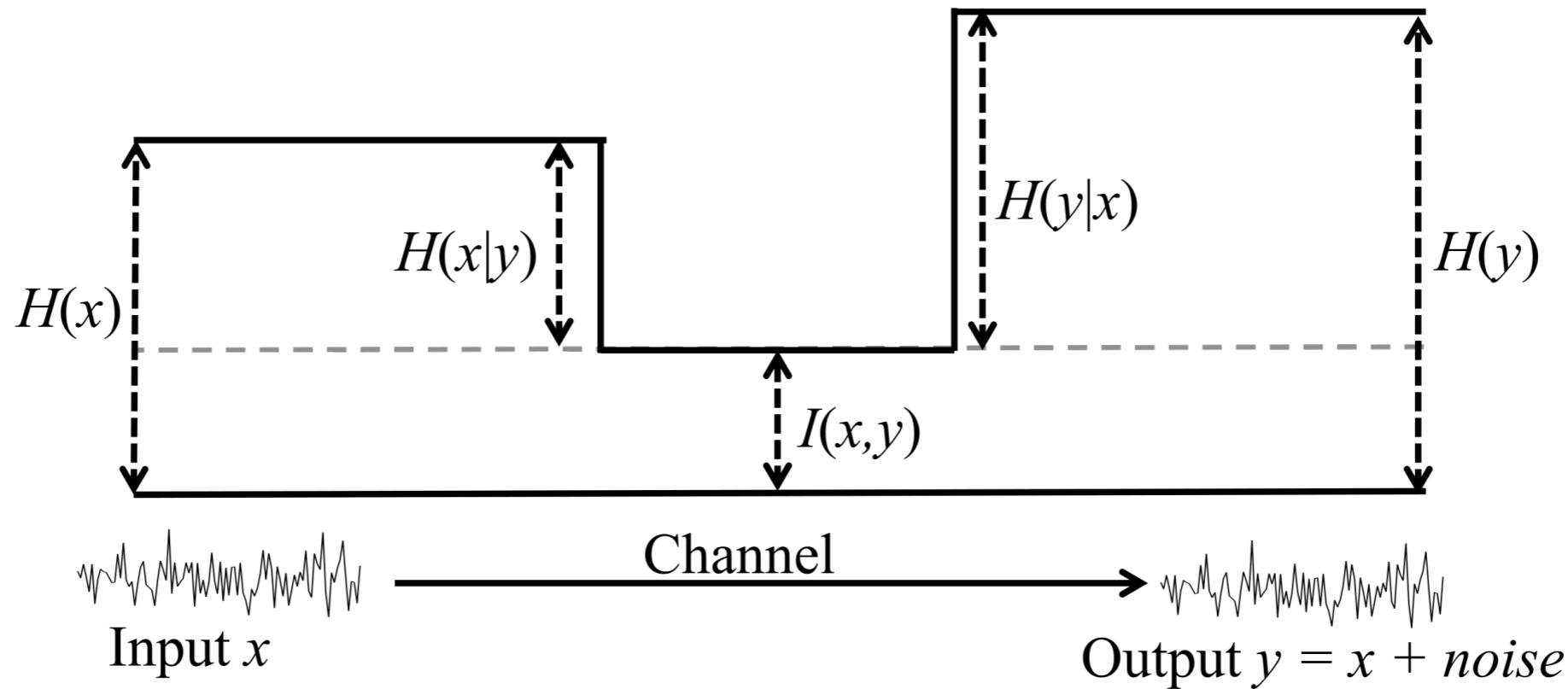
return to playing with one die. Since the probability of each event is $1/n$, we can write

$$u_i = \log\left(\frac{1}{p(x_i)}\right) = -\log(p(x_i))$$

Brief tutorial to Mutual Information

The average uncertainty is then

$$\langle u \rangle = \sum_{i=1}^n p(x_i) u_i = - \sum_{i=1}^n p(x_i) \log(p(x_i)) = H(X)$$



The mutual information is

$$I(x,y) = H(y) - H(y|x)$$

Entropies and mutual informations for parts of x and xy are defined according to (1), (3):

y	x	
0101001111	0100110000	A
1001100011	0100110000	B

$$H(x_A) = - \sum_{x_A} p(x_A) \log p(x_A), \quad (4)$$

$$H(x_B) = - \sum_{x_B} p(x_B) \log p(x_B), \quad (5)$$

$$H(x_Ay_A) = - \sum_{x_Ay_A} p(x_Ay_A) \log p(x_Ay_A), \quad (6)$$

$$H(x_By_B) = - \sum_{x_By_B} p(x_By_B) \log p(x_By_B), \quad (7)$$

$$I(x_A, y_A) = H(x_A) + H(y_A) - H(x_Ay_A), \quad (8)$$

$$I(x_B, y_B) = H(x_B) + H(y_B) - H(x_By_B). \quad (9)$$

Here notations x_Ay_A (x_By_B) mean aggregates of x_A and y_A (x_B and y_B) with the total number of bits in the aggregate being $2|A|$ ($2|B|$). The total numbers of members in the sums over x_A , x_B , x_Ay_A and x_By_B are, respectively, $2^{|A|}$, $2^{|B|}$, $2^{2|A|}$ and $2^{2|B|}$.

“**Effective information**” between x and y for the specific bipartition AB is defined as

$$I_{\text{eff}}(x, y; AB) = I(x, y) - (I(x_A, y_A) + I(x_B, y_B)). \quad (10)$$

Then **integrated information** between x and y is defined as effective information

$$I_{\text{int}}(x, y) = I_{\text{eff}}(x, y; AB^*) \quad (11)$$

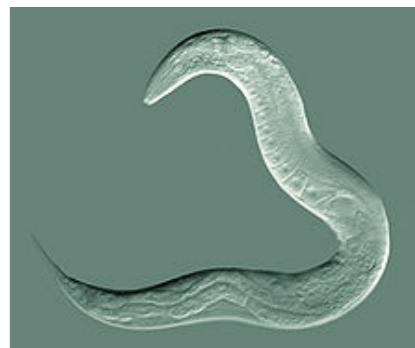
calculated for a specific bipartition AB^* (“minimum information bipartition”) which minimizes normalized effective information:

$$AB^* = \operatorname{argmin}_{AB} \left\{ \frac{I_{\text{eff}}(x, y; AB)}{\min\{H(x_A), H(x_B)\}} \right\}. \quad (12)$$

Note that integrated information itself is not normalized. The normalized effective information is used only as a target function which is minimized by the “minimum information bipartition” AB^* .

Is it just another measure of complexity or smth more?

- II Theory has received both broad criticism and support
- The calculation of even modest-sized system's II is often computationally intractable
- Several proxy measures have been proposed (Barret, Seth, and Oizumi)
- A significant computational challenge in calculating II is finding the Minimum Information Partition of neural system, which requires iterating through all possible network partitions. To solve this problem D. Toker has suggested to use the most modular decomposition of a network and managed to calculate II of the entire *Caenorhabditis elegans* brain.



- A recent study using a less computationally-intensive proxy for II was able to reliably discriminate between varying levels of consciousness in wakeful, sleeping (dreaming vs. non dreaming), anesthetized and comatose patients.

RESEARCH ARTICLE

CONSCIOUSNESS

www.ScienceTranslationalMedicine.org 14 August 2013

A Theoretically Based Index of Consciousness Independent of Sensory Processing and Behavior

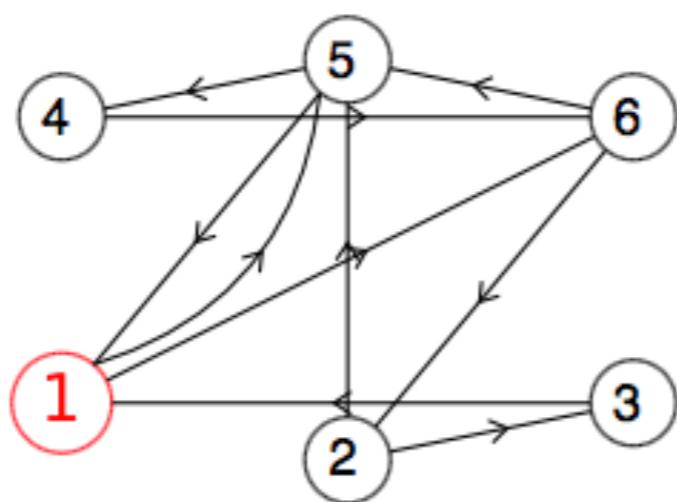
Adenauer G. Casali,^{1,*†} Olivia Gosseries,^{2,*} Mario Rosanova,¹ Mélanie Bozal^{2,4,‡},
Simone Sarasso,¹ Karina R. Casali,^{1,3} Silvia Casarotto,¹ Marie-Aurélie Bruno,²
Steven Laureys,² Giulio Tononi,⁴ Marcello Massimini^{1,5§}

Aim is to show that astrocytes may result in positive II

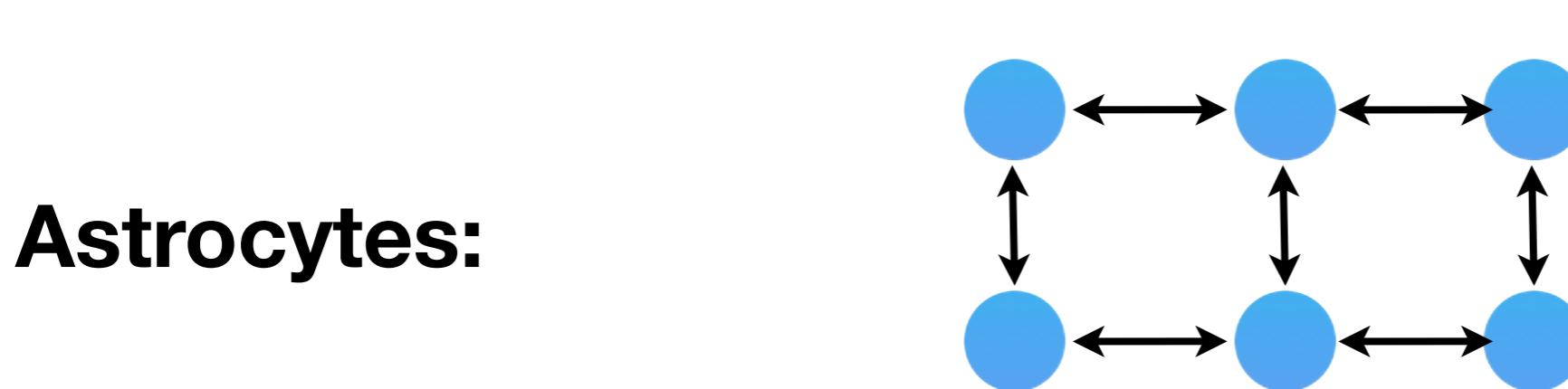
1. Neural network: 6 synaptically coupled Hodgkin-Huxley neurons.
2. 2 versions of network architecture: (i) 1 inhibitory and 5 excitatory neurons with coupling topology obtained by randomly picking 1/3 of the total number of connections out of the full directed graph, excluding self-connections; (ii) all-to-all network of 6 excitatory neurons.
3. Each neuron is stimulated by a Poissonian pulse train with average rate λ , which mimics external spiking inputs.
4. Astrocytes are arranged in a 2×3 lattice with local diffusive interaction. Each astrocyte is connected to a specific neuron, acting on it by upshifting the strength of the neuron's incoming synapses by amount proportional to calcium concentration in the astrocyte. **This interaction is controlled by parameter g_{astro} .**
5. Current influencing production of IP3 depends on the concentration of the neurotransmitters defined by voltage.

**Random
(1 inhibitory)**

Neurons:



**All to all
(all excitatory)**



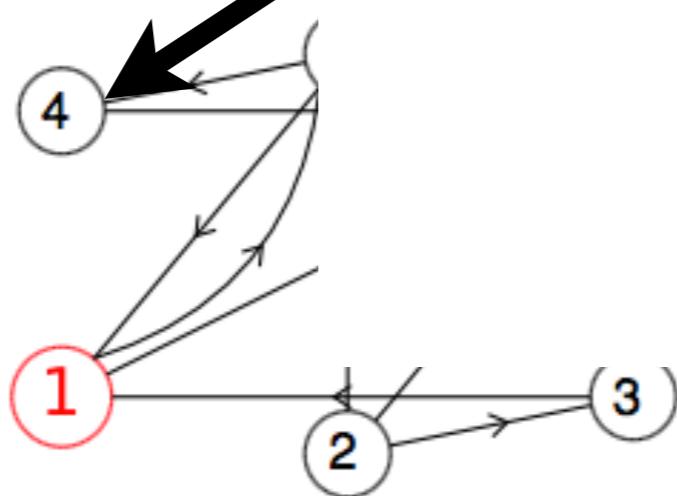
Astrocytes:

The membrane potential of a single neuron:

Rai
(1 inr)

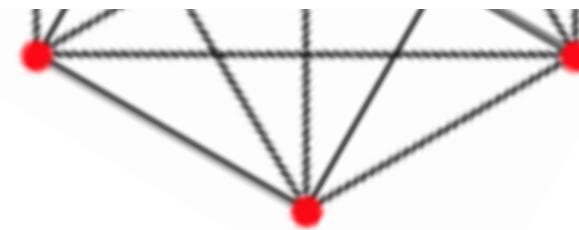
$$C \frac{dV^{(i)}}{dt} = I_{\text{channel}}^{(i)} + I_{\text{app}}^{(i)} + \sum_j I_{\text{syn}}^{(ij)} + I_P^{(i)};$$

Ionic currents (e.g. sodium, potassium and leak currents) are expressed as follows:

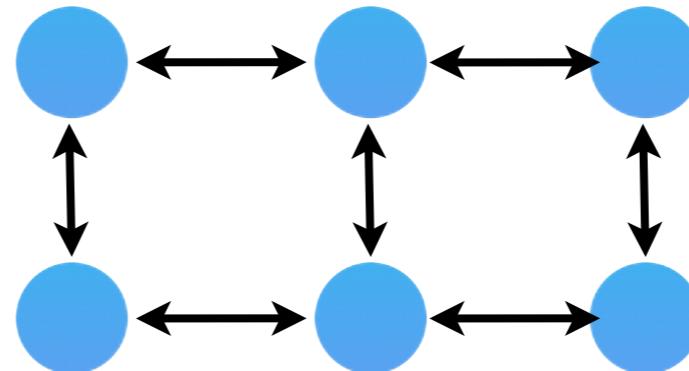


Neurons:

$$I_{\text{channel}} = -g_{Na}m^3h(V - E_{Na}) - g_Kn^4(V - E_K) - g_{\text{leak}}(V - E_{\text{leak}}),$$
$$\frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x, \quad x = m, n, h.$$



Astrocytes:

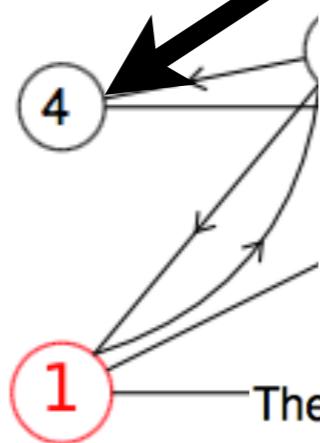


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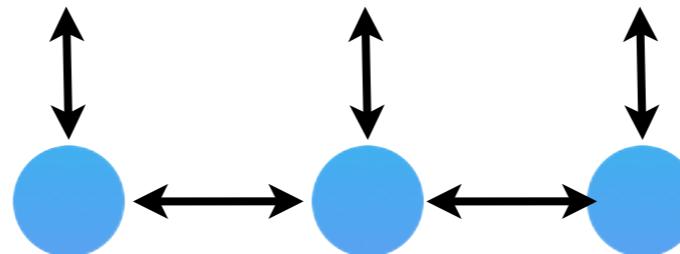
$$\frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x, \quad x = m, n, h.$$

The applied currents $I_{\text{app}}^{(i)}$ control the depolarization level and dynamical regime that can be either excitable, oscillatory or bistable. The synaptic current $I_{\text{syn}}^{(i)}$:

$$I_{\text{syn}}^{(ij)} = \frac{g_{\text{syn}} \text{eff} (V^{(j)} - E_{\text{syn}})}{1 + \exp\left(\frac{-(V^{(i)} - \theta_{\text{syn}})}{k_{\text{syn}}}\right)}; \quad (3)$$

where $E_{\text{syn}} = -90$ mV for the inhibitory synapse and $E_{\text{syn}} = 0$ mV for the excitatory.

Astrocytes:

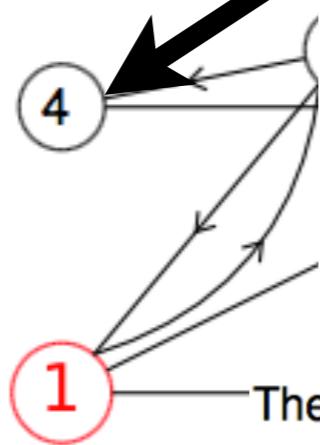


The membrane potential of a single neuron:

Rai
(1 inh)

$$C \frac{dV^{(i)}}{dt} = I_{\text{channel}}^{(i)} + I_{\text{app}}^{(i)} + \sum_j I_{\text{syn}}^{(ij)} + I_P^{(i)};$$

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Neurons:

$$I_{\text{channel}} = -g_{Na}m^3h(V - E_{Na}) - g_Kn^4(V - E_K) - g_{\text{leak}}(V - E_{\text{leak}}),$$

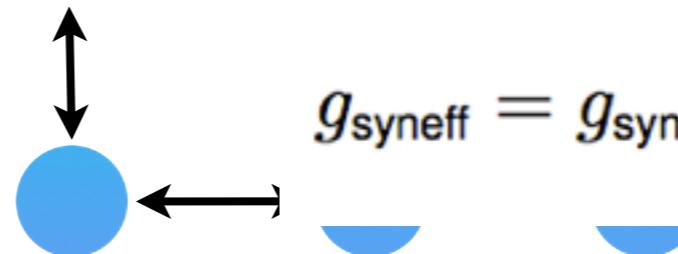
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Astrocytes:

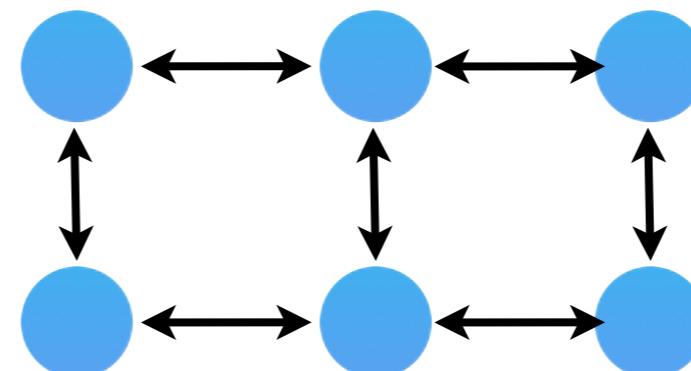


$$g_{\text{syn}} = g_{\text{syn}}(1 + g_{\text{astro}}Ca^{(m,n)});$$

$$\frac{dCa^{(m,n)}}{dt} = J_{\text{ER}}^{(m,n)} - J_{\text{pump}}^{(m,n)} + J_{\text{leak}}^{(m,n)} + J_{\text{in}}^{(m,n)} - J_{\text{out}}^{(m,n)} + J_{C\text{adiff}}^{(m,n)};$$

$$\frac{dIP_3^{(m,n)}}{dt} = \frac{IP_3^* - IP_3^{(m,n)}}{\tau_{IP3}} + J_{\text{PLC}}^{(m,n)} + J_{\text{Glu}}^{(m,n)} + J_{IP3\text{diff}}^{(m,n)};$$

$$\frac{dh^{(m,n)}}{dt} = a_2(d_2 \frac{IP_3^{(m,n)} + d_1}{IP_3^{(m,n)} + d_3} (1 - h^{m,n}) - Ca^{m,n}h^{m,n});$$



Astrocytes:

- [11] V. Volman, E. Ben-Jacob, and H. Levine, Neural Computation **19**, 303 (2007).
- [12] M. De Pitta, V. Volman, H. Berry, and E. Ben-Jacob, PLOS Computational Biology **7**, 1 (2011).

- [13] S. Y. Gordleeva, S. V. Stasenko, A. V. Semyanov, A. E. Dityatev, and V. B. Kazantsev, Frontiers in Computational Neuroscience **6** (2012).

Astrocyte-induced positive integrated information in neuron-astrocyte ensembles

Oleg Kanakov,¹ Susanna Gordleeva,¹ Anastasia Ermolaeva,¹ Sarika Jalan,² and Alexey Zaikin^{1,3,4,*}

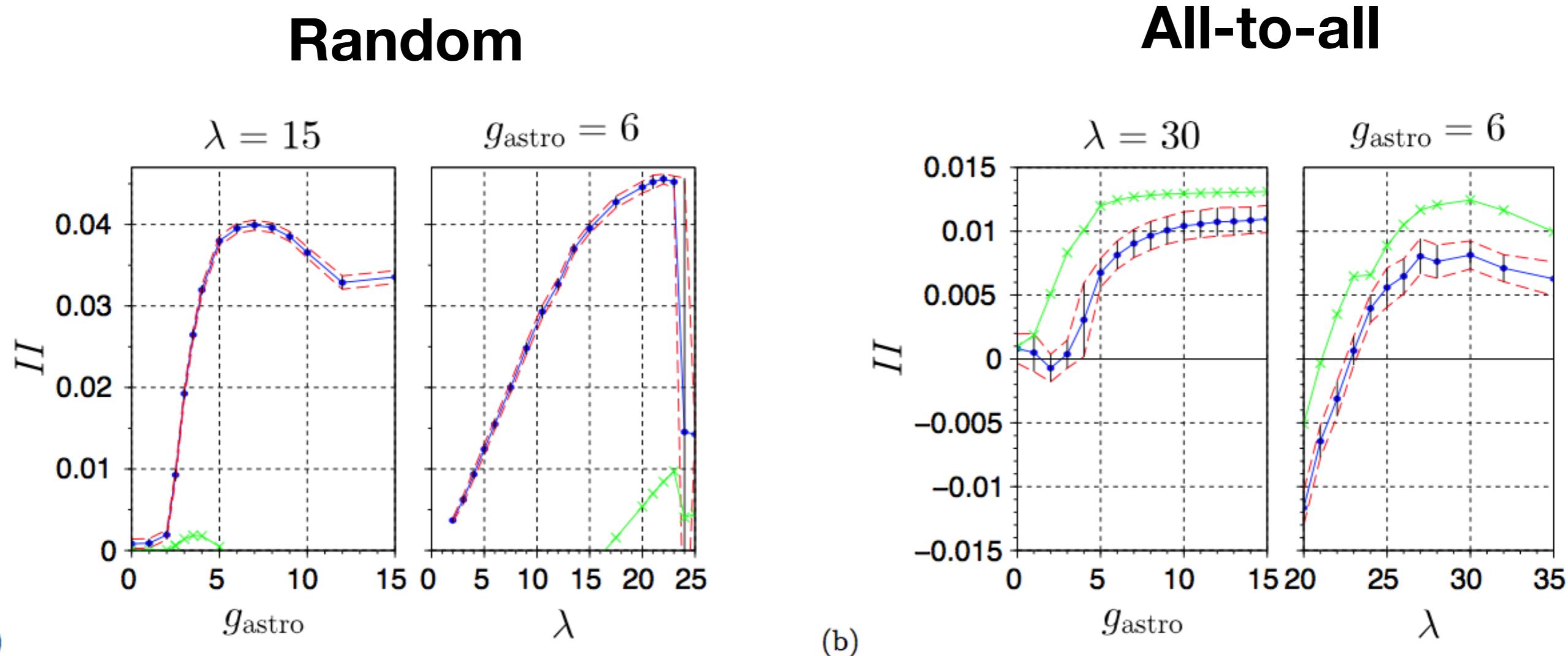


FIG. 2. Dependence of II upon neuro-astrocytic interaction g_{astro} and upon average stimulation frequency λ : (a) — random network (instance shown in FIG. 1); (b) — all-to-all network. Blue solid lines with dot marks — direct calculation by definition from simulation data; red dashed lines — error estimation; green lines with cross marks — analytical calculation for spiking-bursting process with parameters estimated from simulation data.

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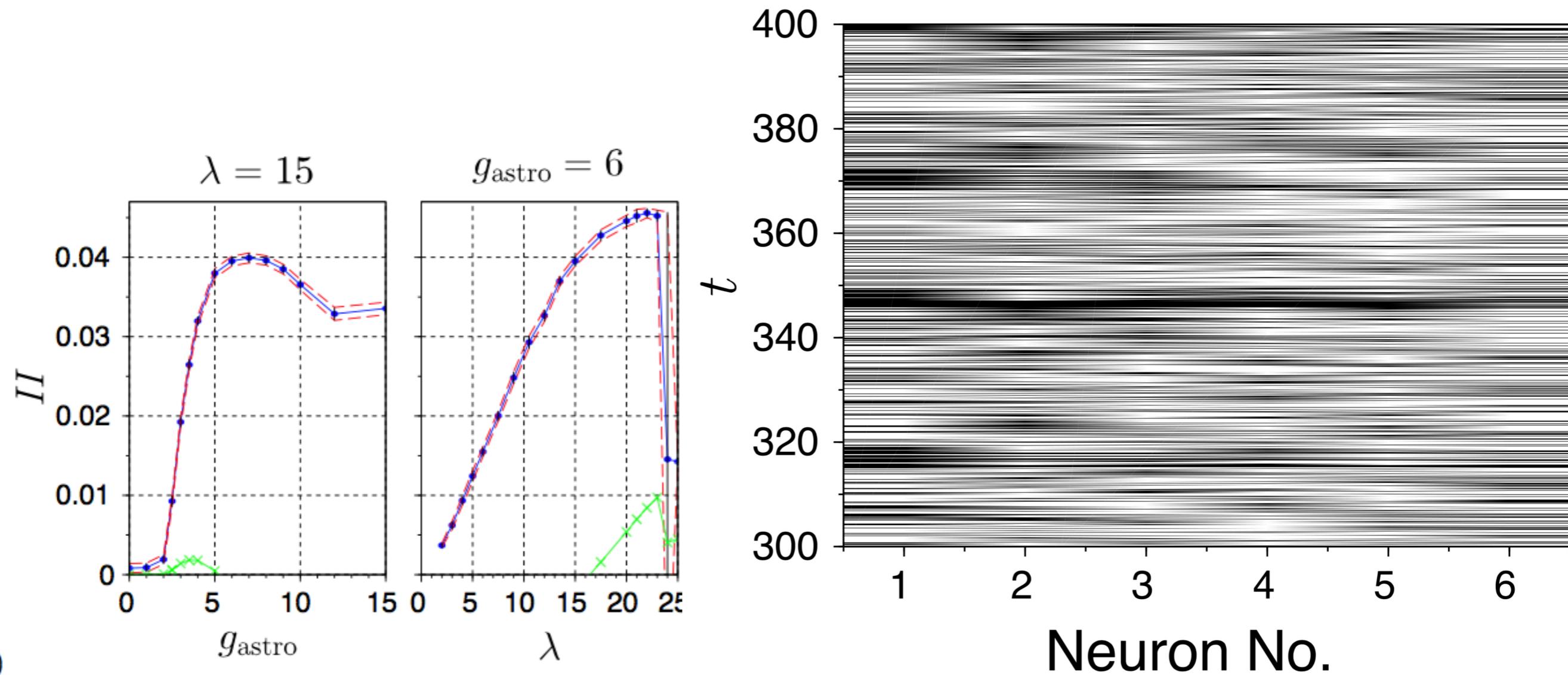


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Estimating integrated information in bidirectional neuron-astrocyte communication

Luis Abrego ,¹ Susanna Gordleeva ,^{2,3} Oleg Kanakov,³ Mikhail Krivonosov ,³ and Alexey Zaikin^{1,3,4,5,*}

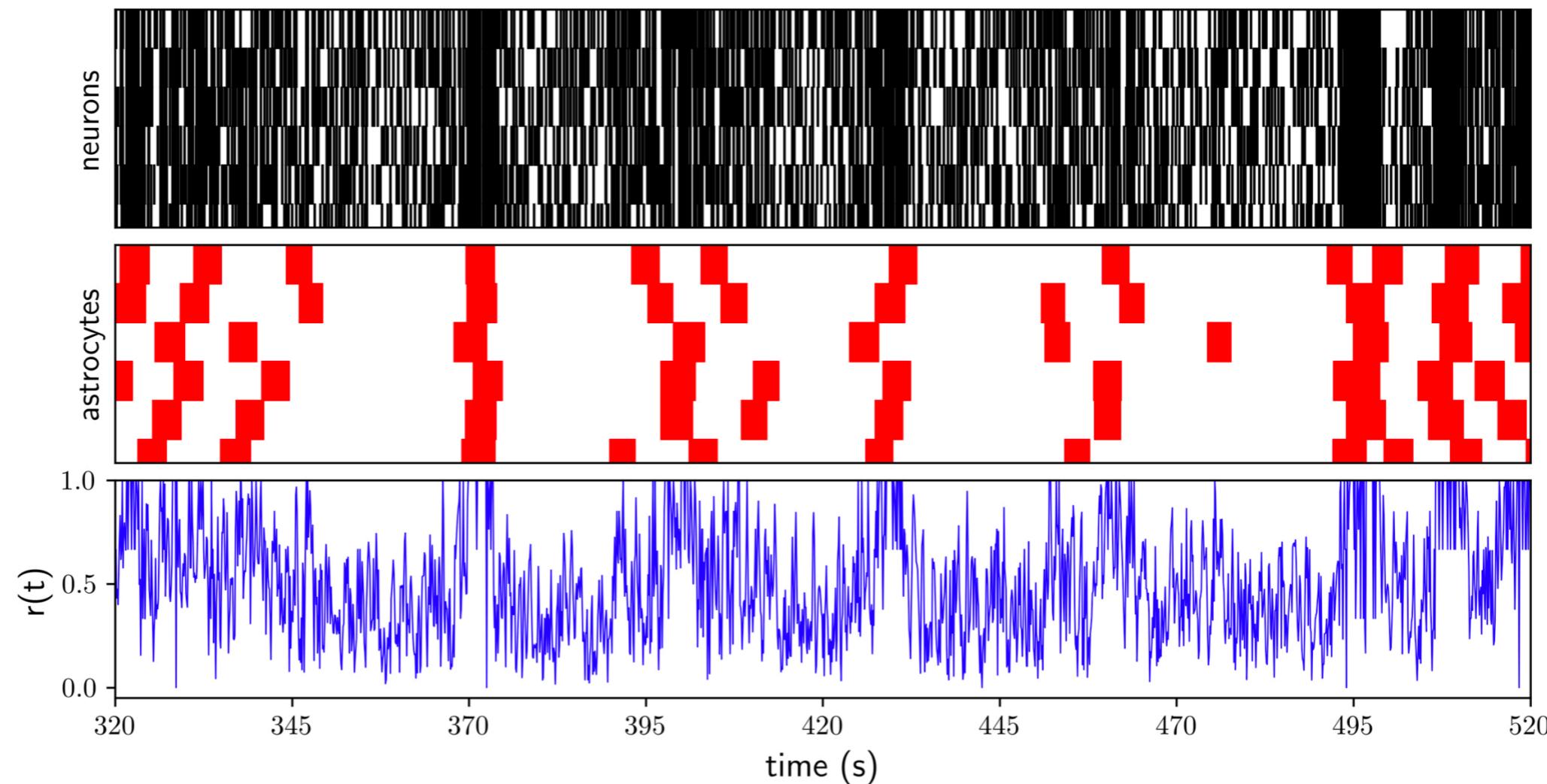
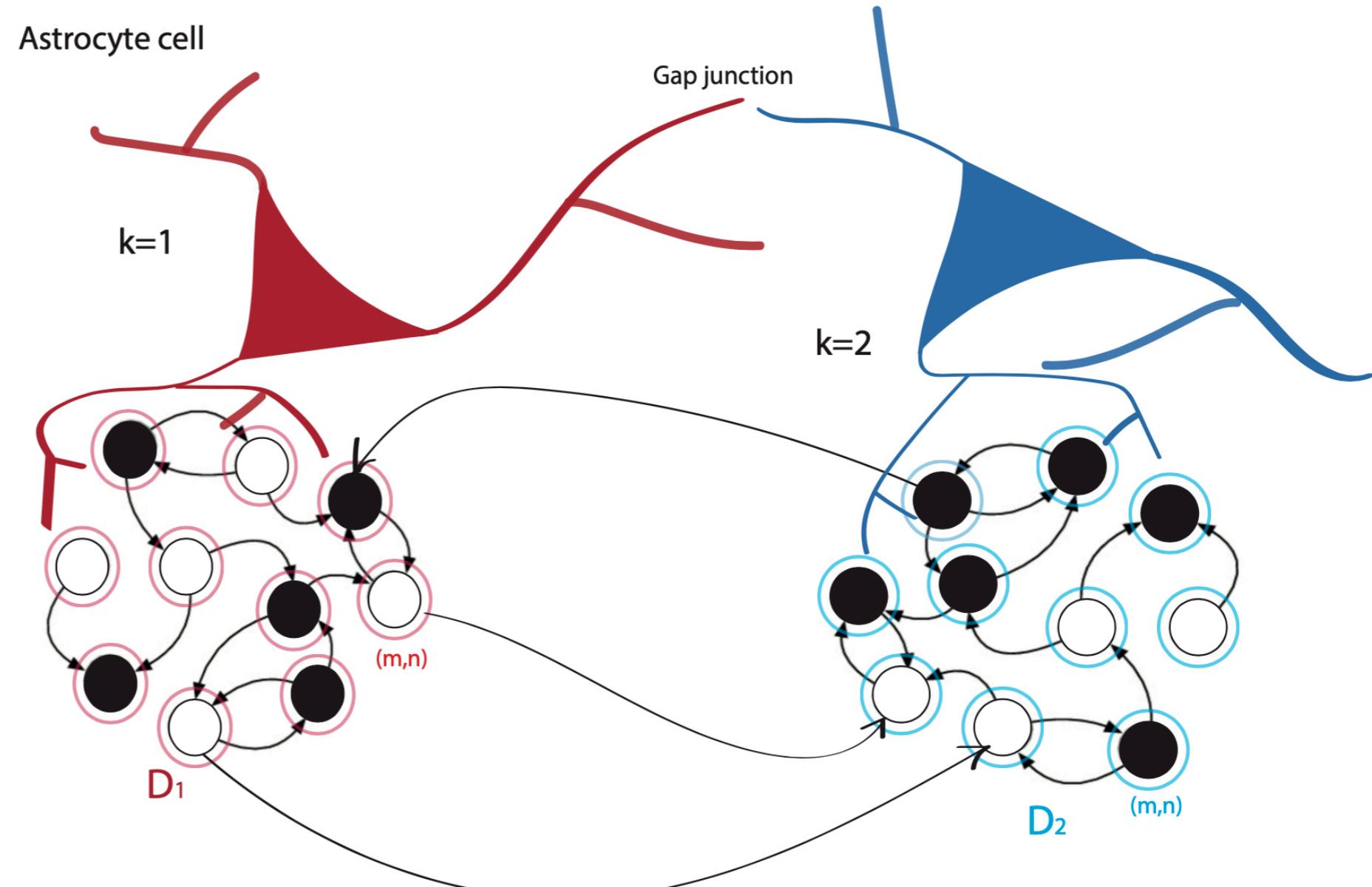


Figure 4.3: Raster plots representing the joint activity of neurons and astrocytes by bidirectional coupling. We set $g_s = 3.4$ and $\lambda = 20$ Hz for excitatory network with all-to-all coupling [exc-full, Fig. 4.1 (a)]. The coordination of the spike trains in the population of neurons is depicted by the instantaneous synchronization r , Eq. (4.22).

Multi-scale modeling of astrocyte-mediated synaptic information transmission



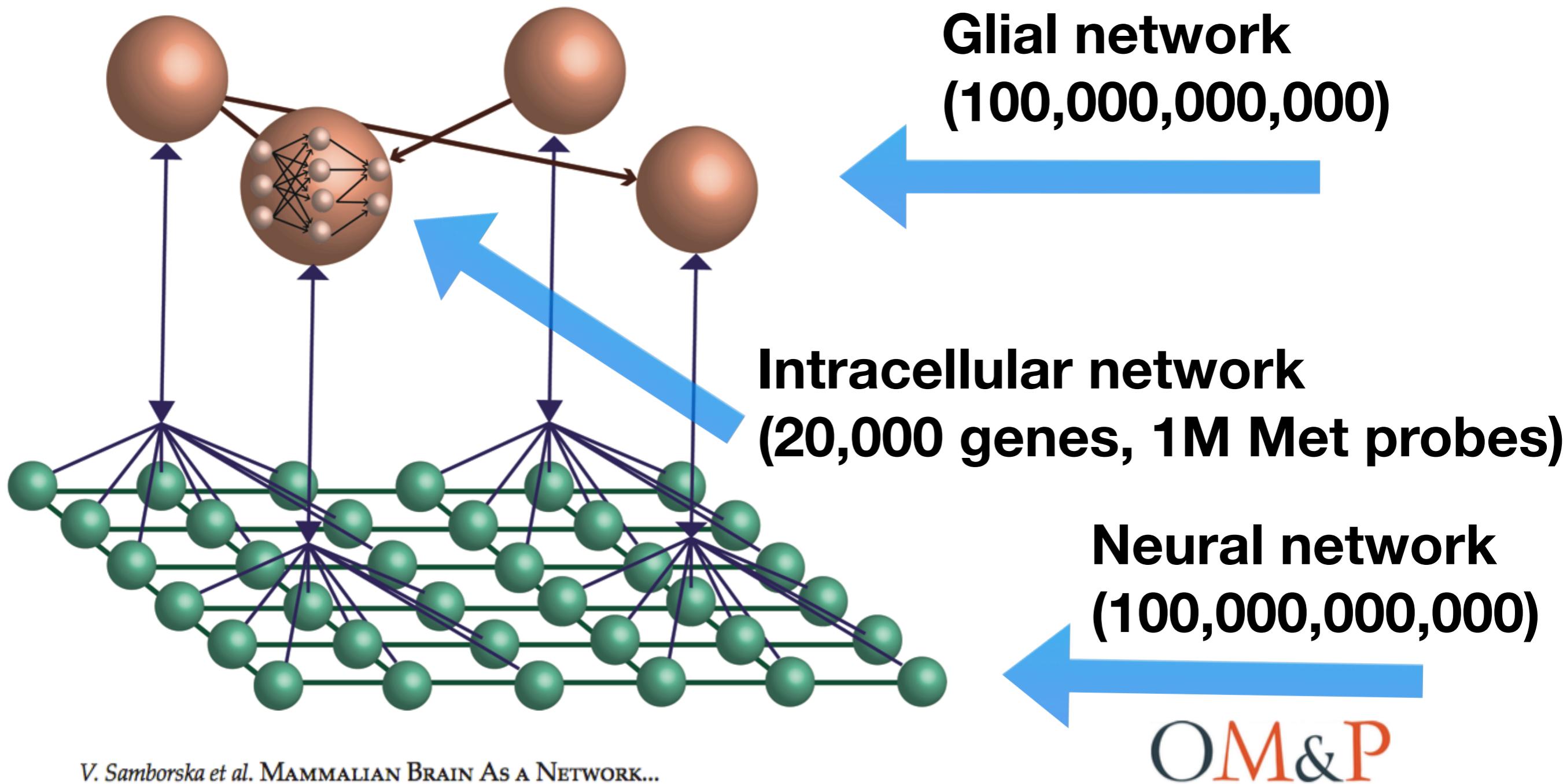
Article

Integrated Information in the Spiking–Bursting Stochastic Model

Entropy **2020**, *22*, 1334

Oleg Kanakov ¹, Susanna Gordleeva ^{2,3} and Alexey Zaikin ^{4,5,6,*}

Mammalian Brain: Simplified Scheme



V. Samborska et al. MAMMALIAN BRAIN AS A NETWORK...

MAMMALIAN BRAIN AS A NETWORK OF NETWORKS

Veronika Samborska ¹, Susanna Gordleeva ², Ekkehard Ullner ³, Albina Lebedeva ², Viktor Kazantsev ², Mikhail Ivanchenko ² and Alexey Zaikin ^{2,4}

Integrated Information as a Measure of Cognitive Processes in Coupled Genetic Repressilators

Luis Abrego ^{1,2} and Alexey Zaikin ^{1,3,4,5*}

Entropy 2019, 21, 382

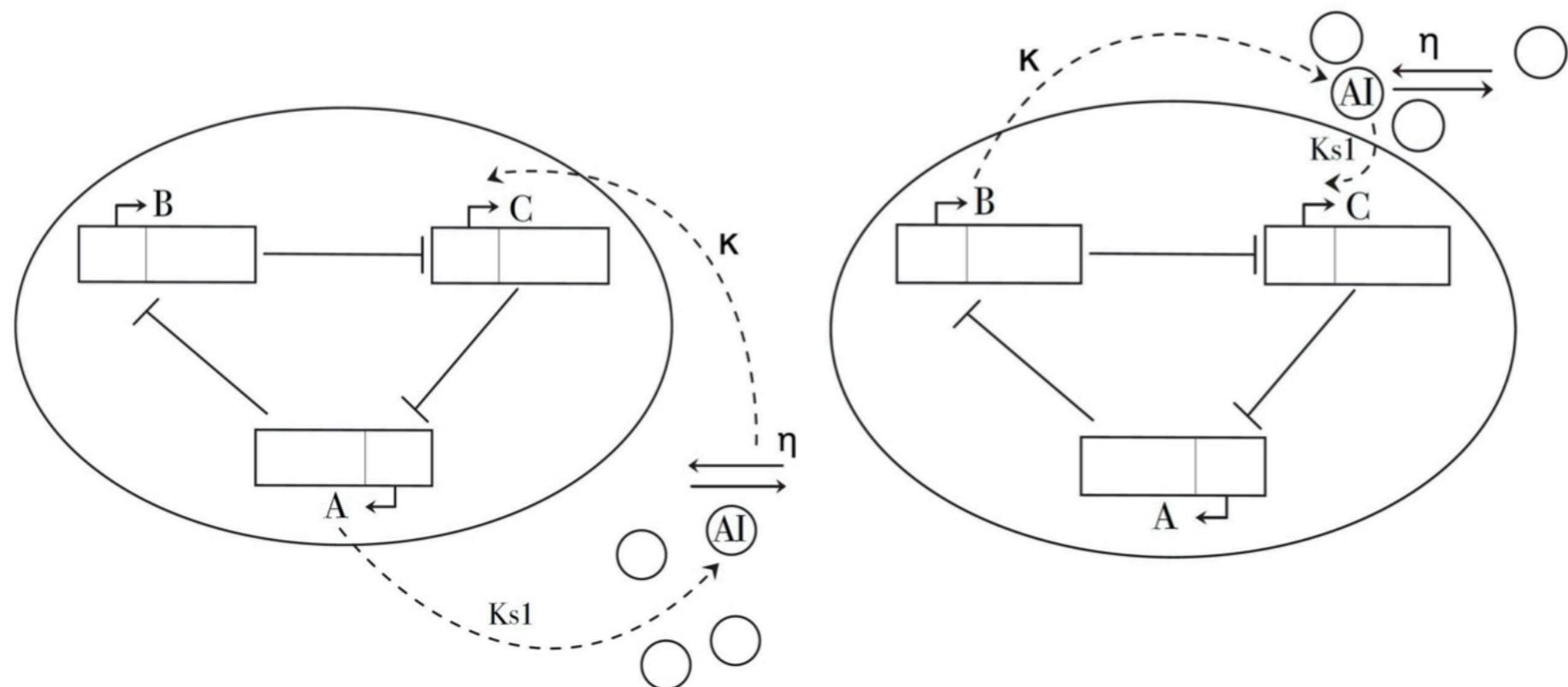


Figure 1. Diagram of the repressor circuit including the quorum sensing mechanism. **Left:** the phase-attractive coupling. **Right:** the phase-repulsive coupling.

Summary

- Both Intelligence and Consciousness could be present on all three levels and, possibly, have important ingredients on all three levels
- Intelligence can be based on gene-to-gene interactions (but too slow?)
- Astrocytes organize associative memory and situation-associated learning
- Astrocyte improve generation of Integrated Information, hence, probably necessary for effective consciousness
- Consciousness theoretically can be based on genetic networks (but not enough power?)
- It is unclear what roles is played by intracellular genetic networks in the organisation of intelligence and consciousness: epigenetic memory?

THANK YOU!!

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