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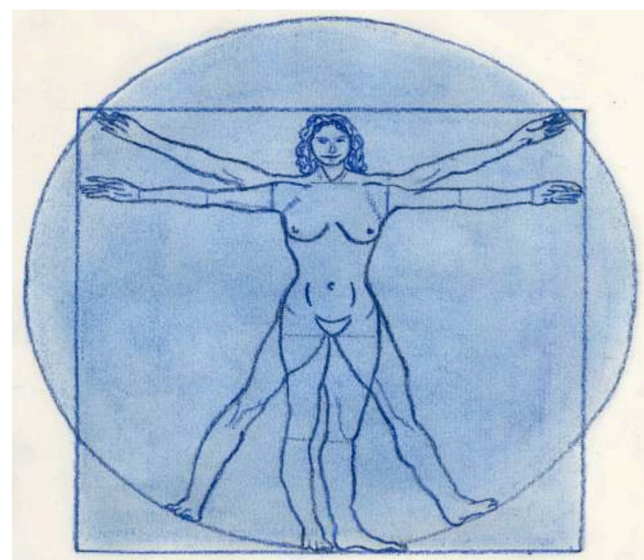
Astrocytes in the Brain Active Milieu

Intelligence and Consciousness in Genetic Neuron-Astrocyte Networks

Work in Progress



Alexey Zaikin

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UCL

ЦАСС Центр анализа сложных систем

Сеченовский Университет

Университет Лобачевского

What is the difference?

What is the difference?

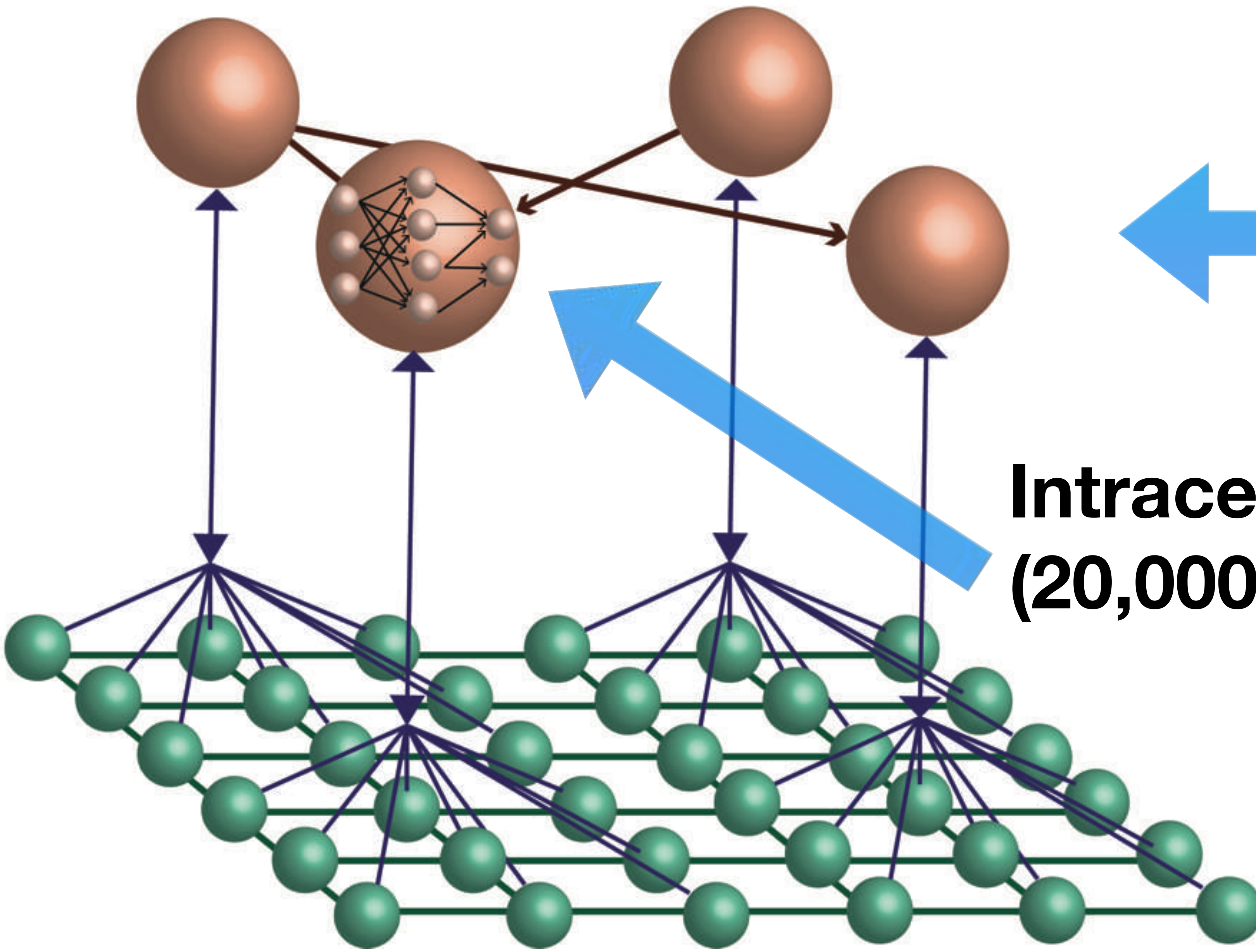
Intelligence (ability to classify and learn)?
Consciousness (positive Integrated Information)?

Where is Intelligence and Consciousness?

What is the difference?

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

Mammalian Brain:
Simplified Scheme



Glial network (100,000,000,000)

Intracellular network (20,000 genes, 1M Met probes)

Neural network (100,000,000,000)

OM&P

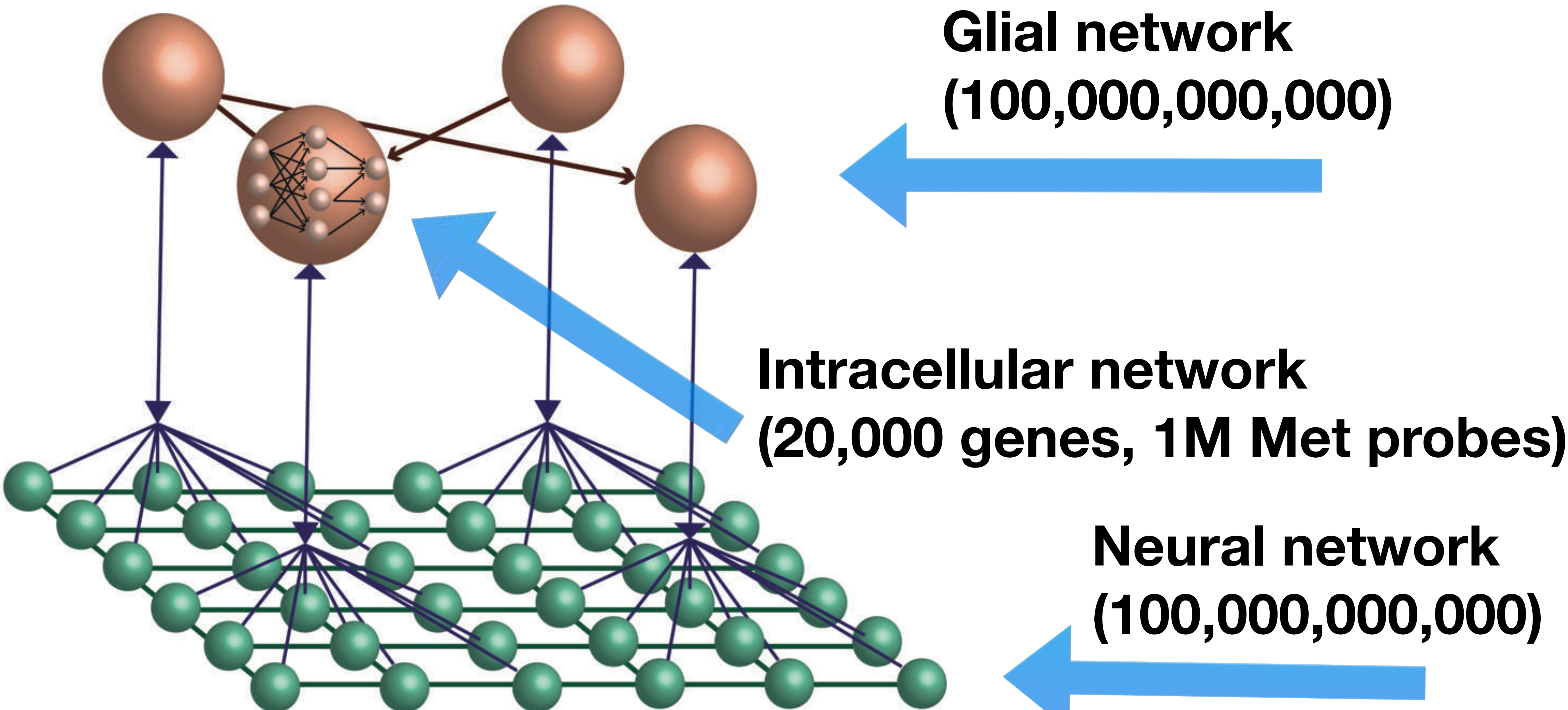
V. Samborska et al. Mammalian Brain As a Network...

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]

Opera Medica & Physiologica 1 • 23-38 • January 2016

Mammalian Brain:
Very Simplified Scheme



OM&P

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]

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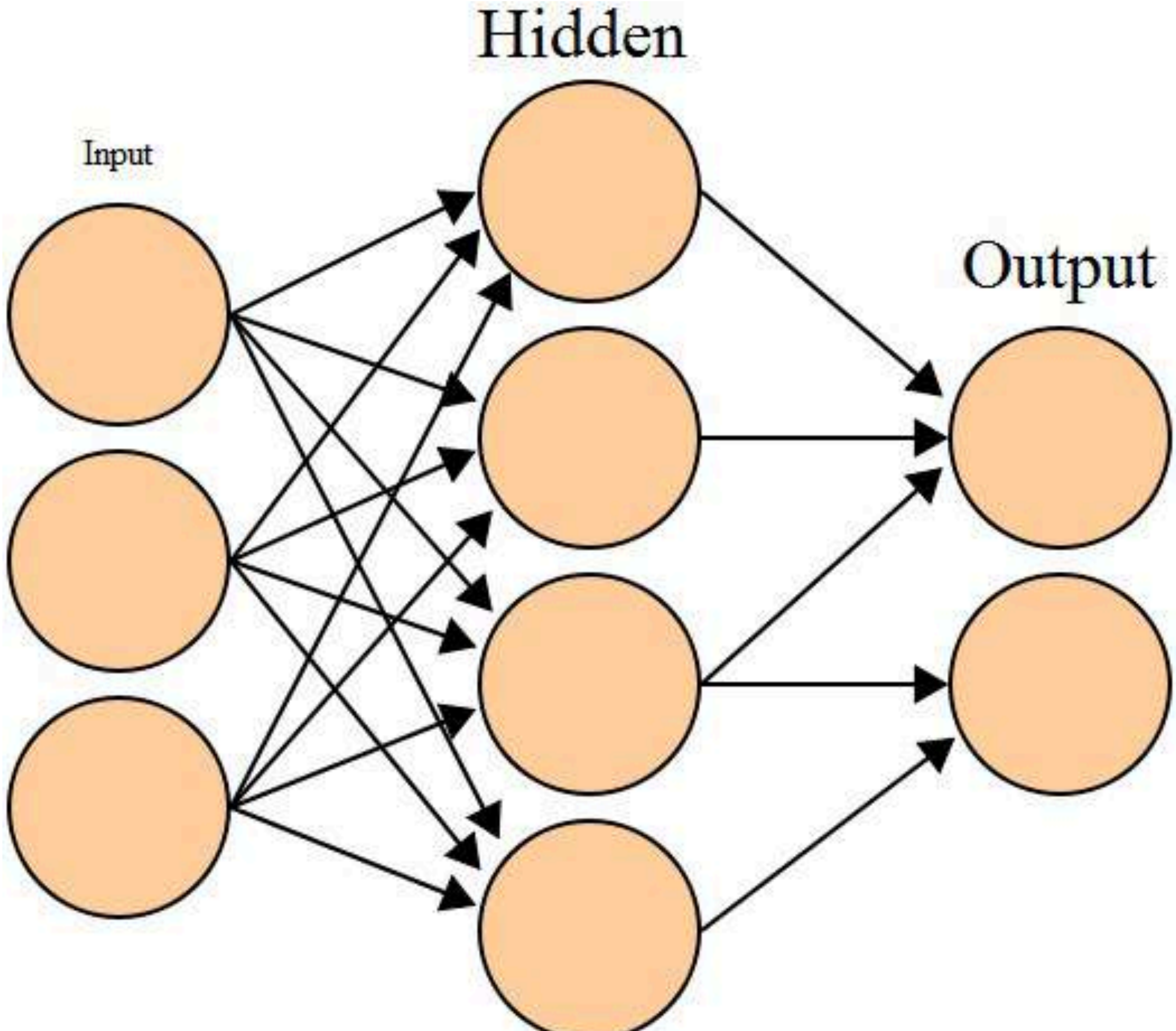
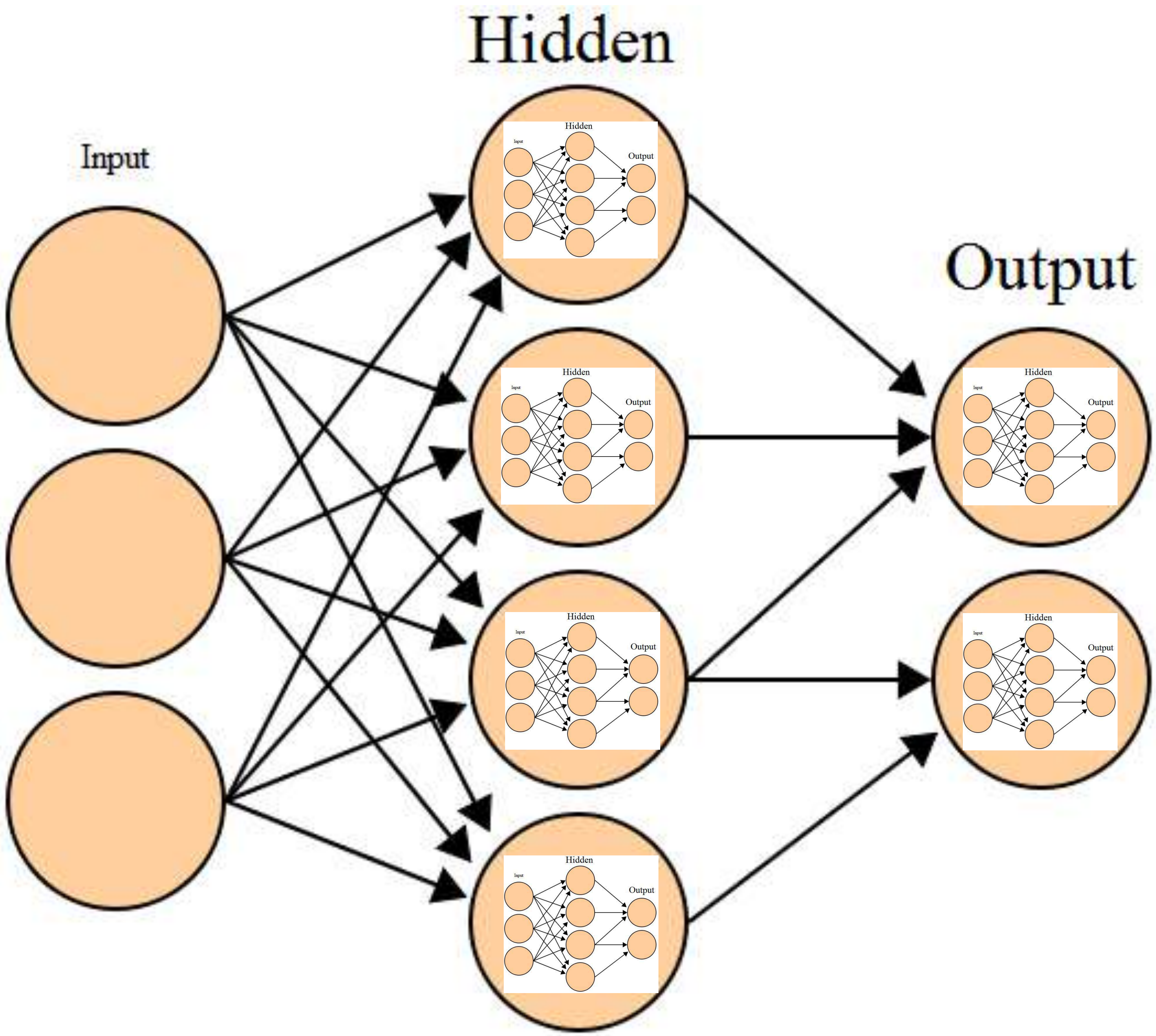
Intelligence

Multicellular intelligence



Intracellular intelligence



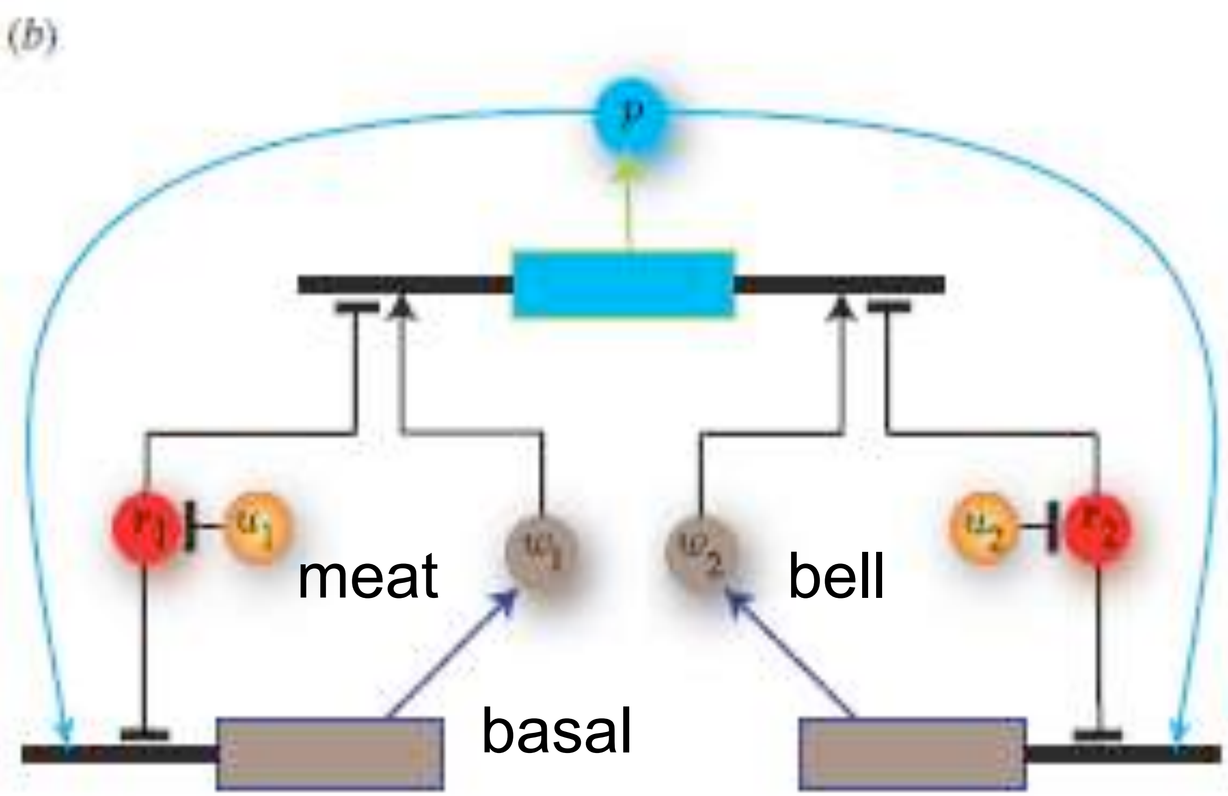
Paradigms of artificial Intelligence

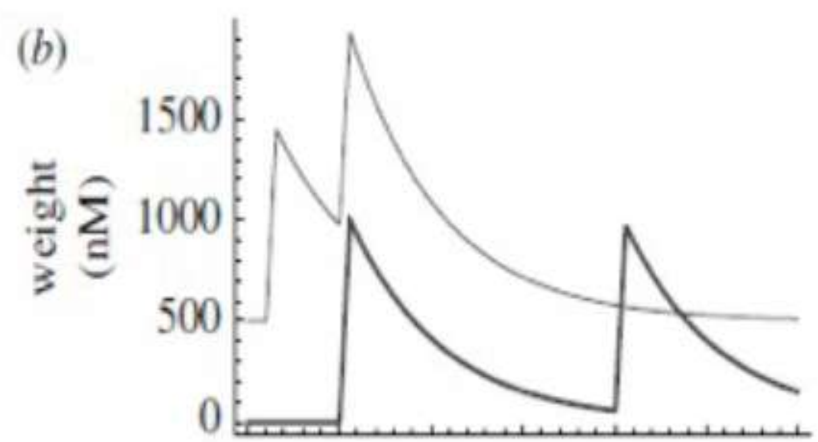
Associative perceptron:

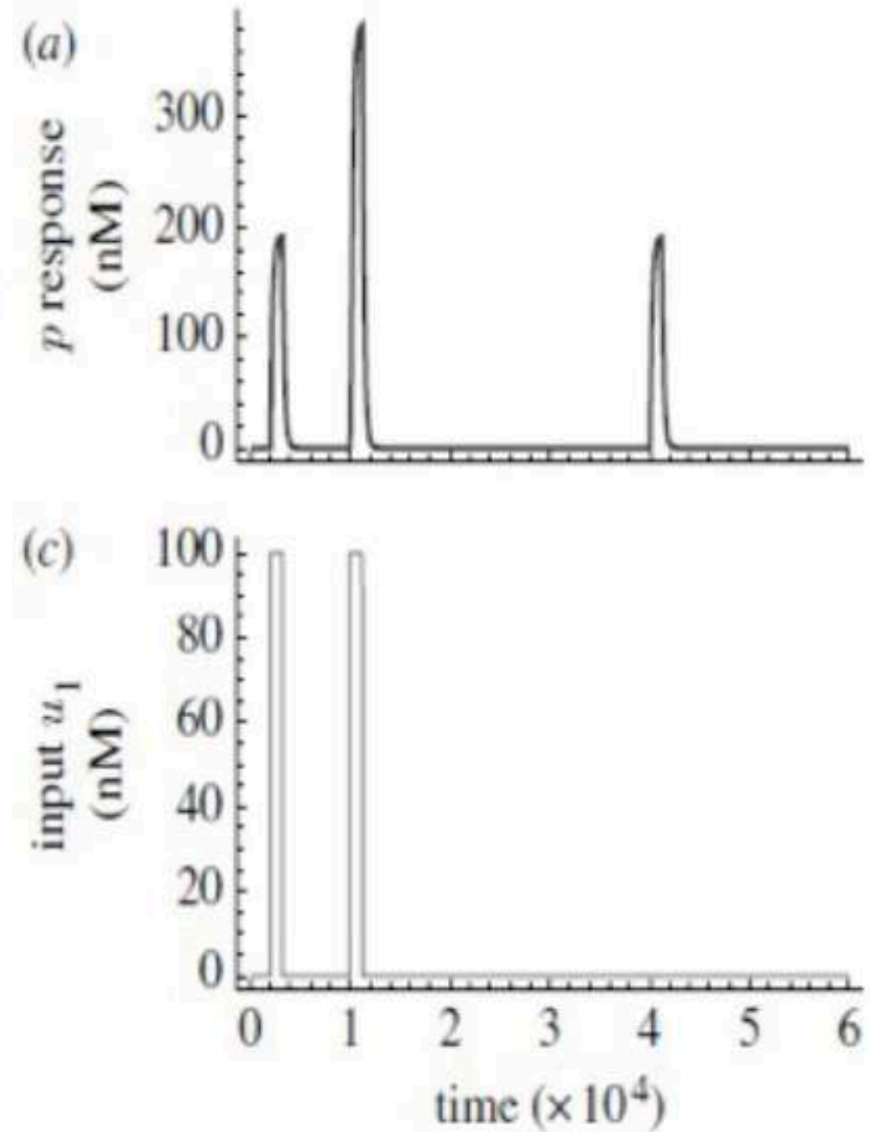
Molecular circuits for associative learning in single-celled organisms

Chrisantha T. Fernando[1,2,*], Anthony M. L. Liekens[3], Lewis E. H. Bingle[1], Christian Beck[4], Thorsten Lenser[4], Dov J. Stekel[1] and Jonathan E. Rowe[5]

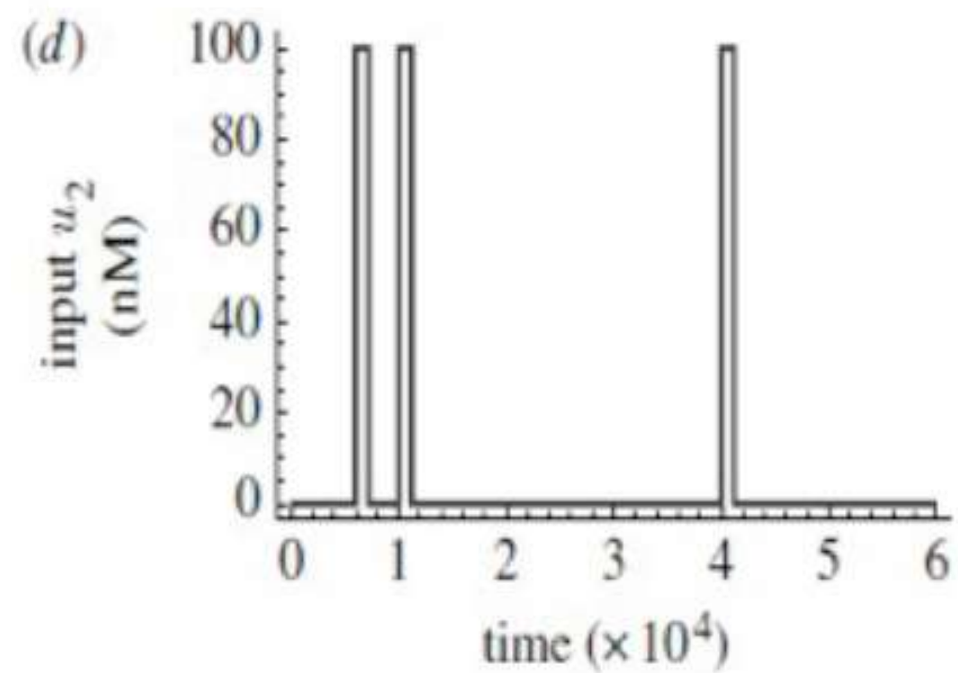
The Model Network







meat

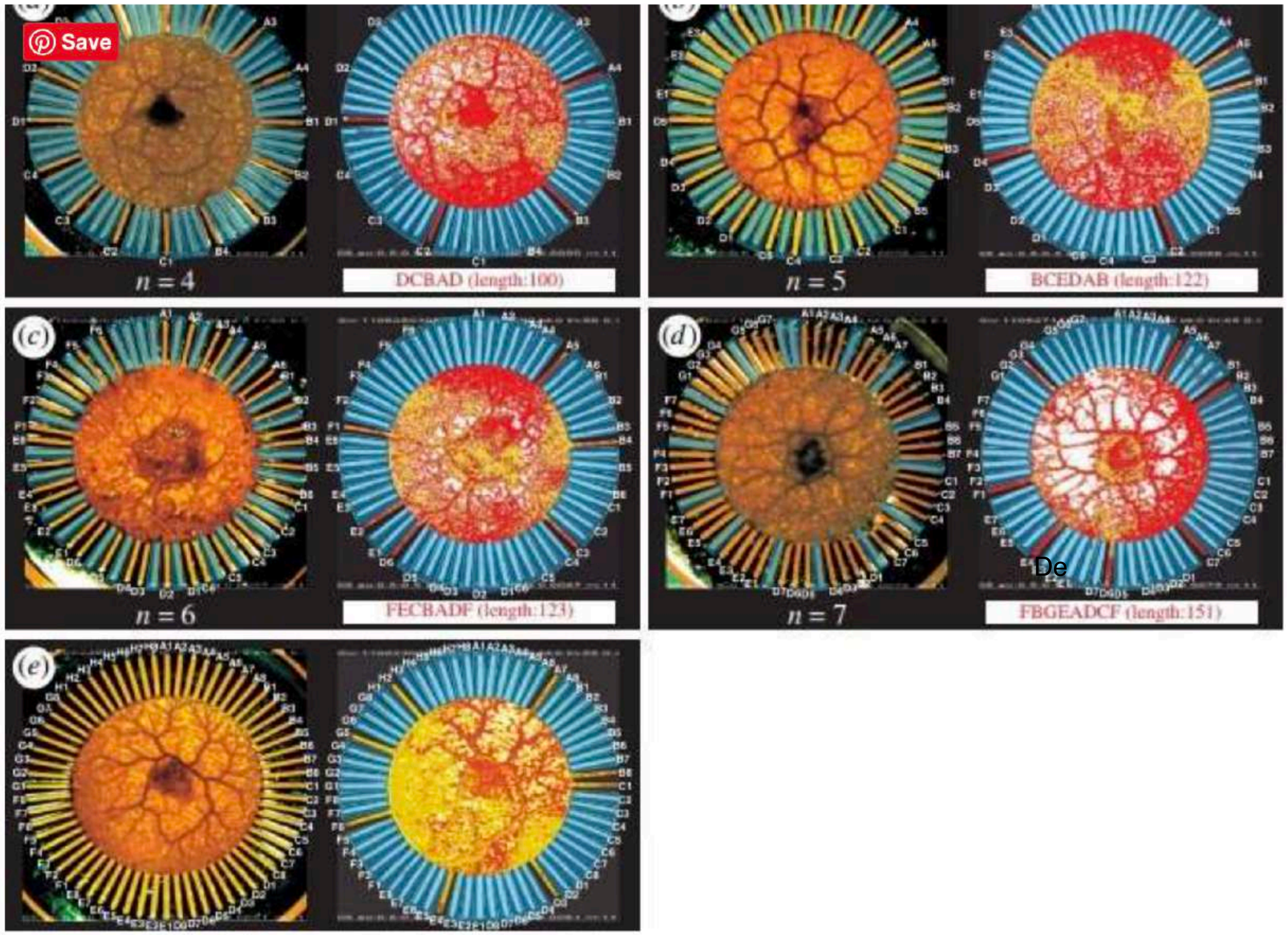


bell

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

Check for updates

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

Received: 14 March 2018
Accepted: 14 November 2018

NEURONS

How Computationally Complex Is a Single Neuron?

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

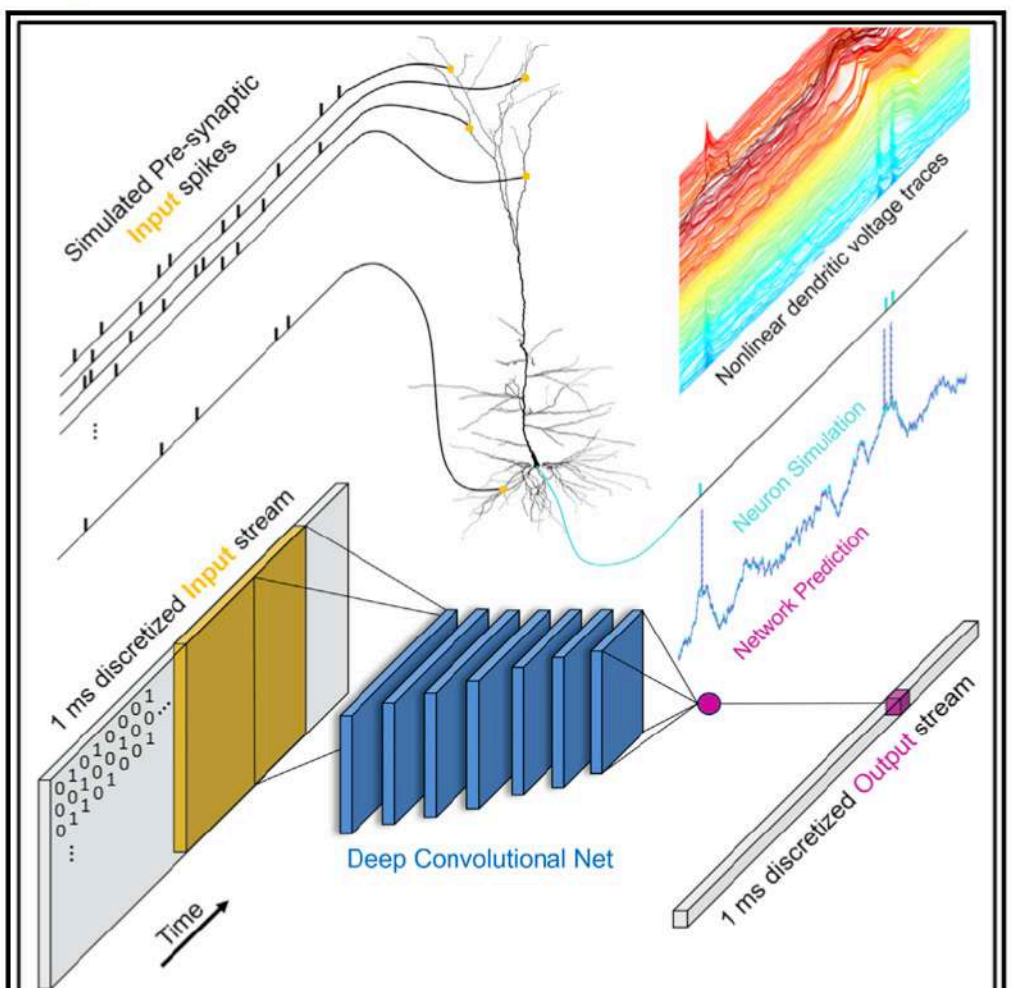
https://doi.org/10.1016/j.neuron.2021.07.002

Article

Neuron

Single cortical neurons as deep artificial neural networks

Graphical abstract



Authors

David Beniaguev, Idan Segev, Michael London

Correspondence

david.beniaguev@gmail.com

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

CHAOS **28**, 106313 (2018)

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

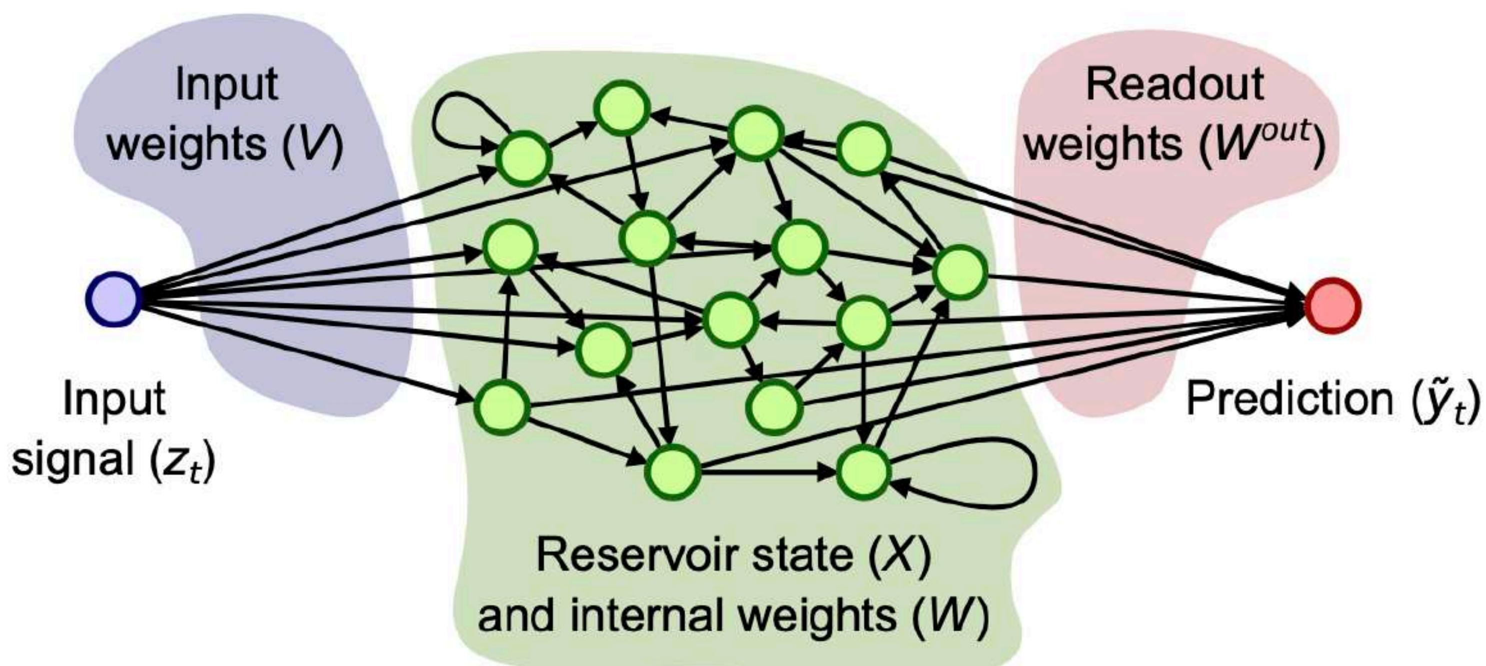


Figure 3.4: Setup to test the memory of a network. A reservoir is built with a connectivity matrix W that defines the topology of a given network. A signal z_t arrives to the nodes of the reservoir with different strengths defined by the input weight vector V. Then, one or more readout nodes compute 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.

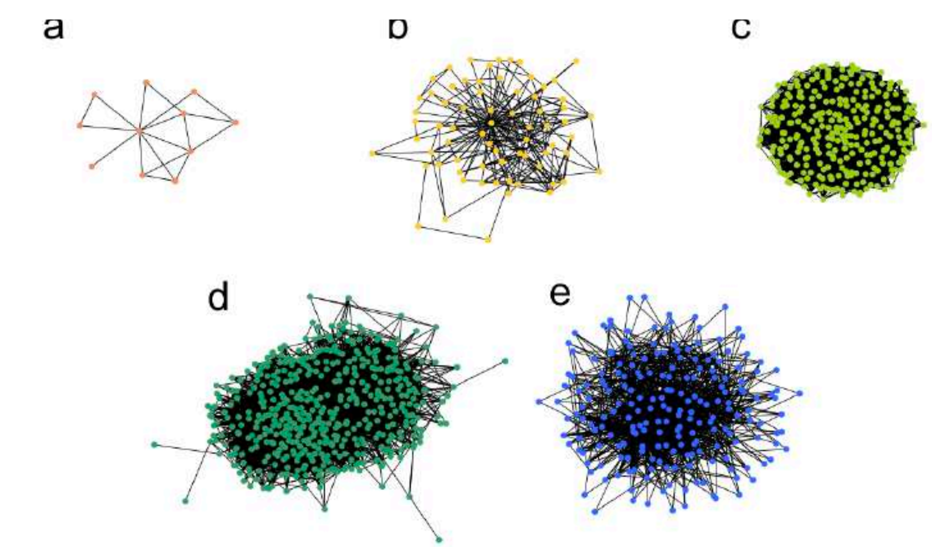


FIG. 3. Recurrent cores of the gene regulatory networks: *Bacillus subtilis* (a), *Escherichia coli* (b), *Saccharomyces cerevisiae* (c), *Drosophila melanogaster* (d), and *Homo sapiens* (e). All nodes in these subgraphs have both out-degree and in-degree larger than 0.

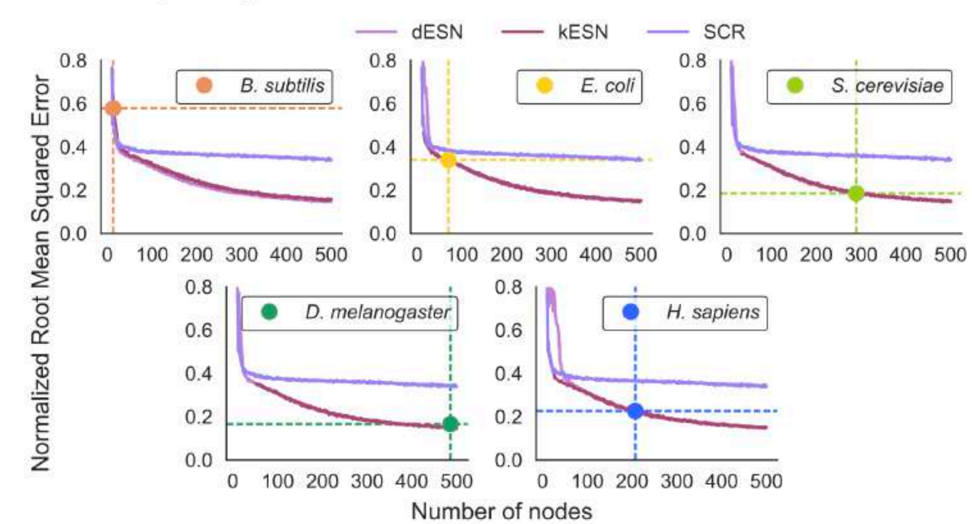
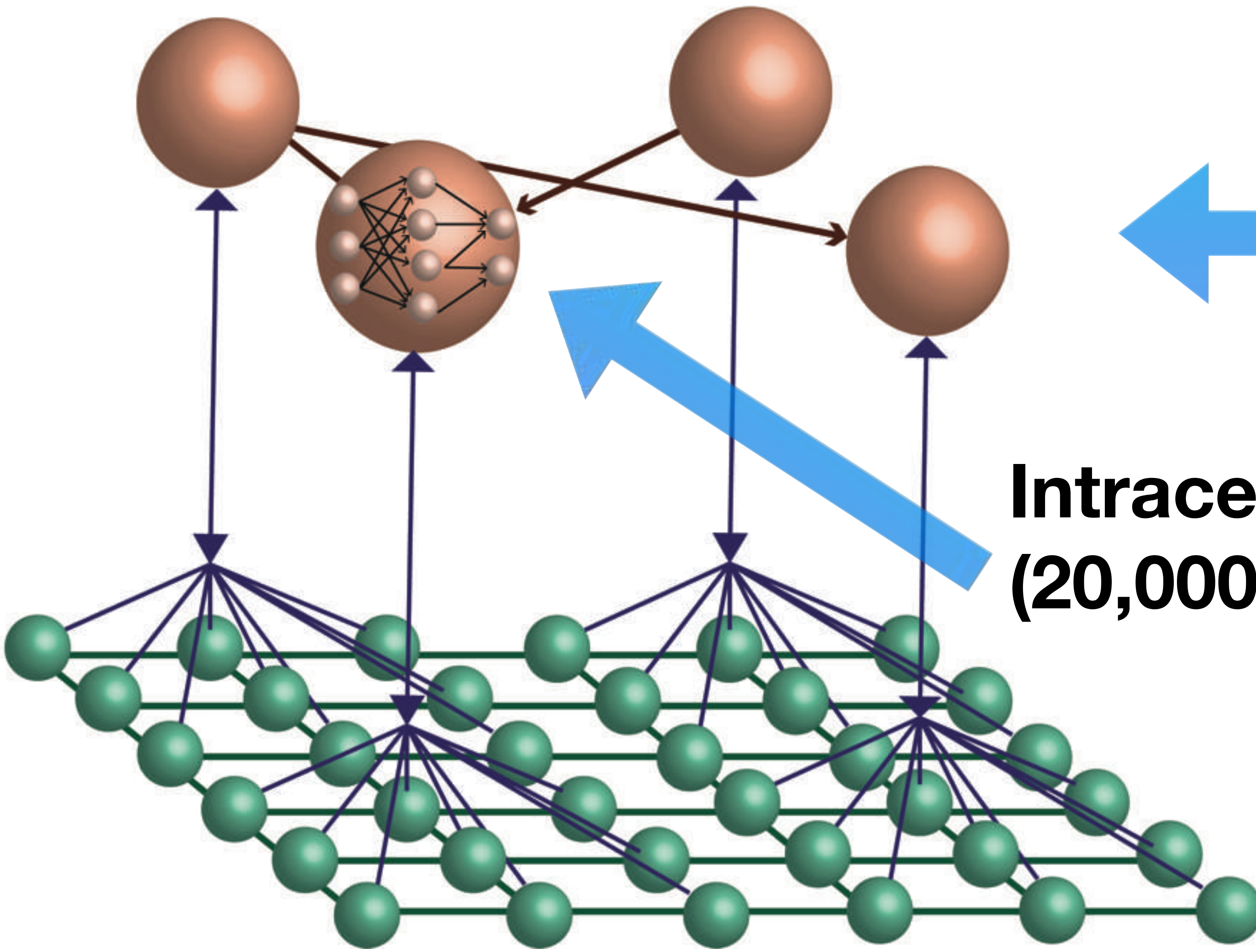


FIG. 6. Performance of the biological reservoirs compared with control topologies. Performance is evaluated with the Normalized Root Mean Squared Error (NRSME) between expected and reconstructed outputs. The NRMSE value shown for each biological network topology corresponds to the median of 10 000 trials (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



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OM&P

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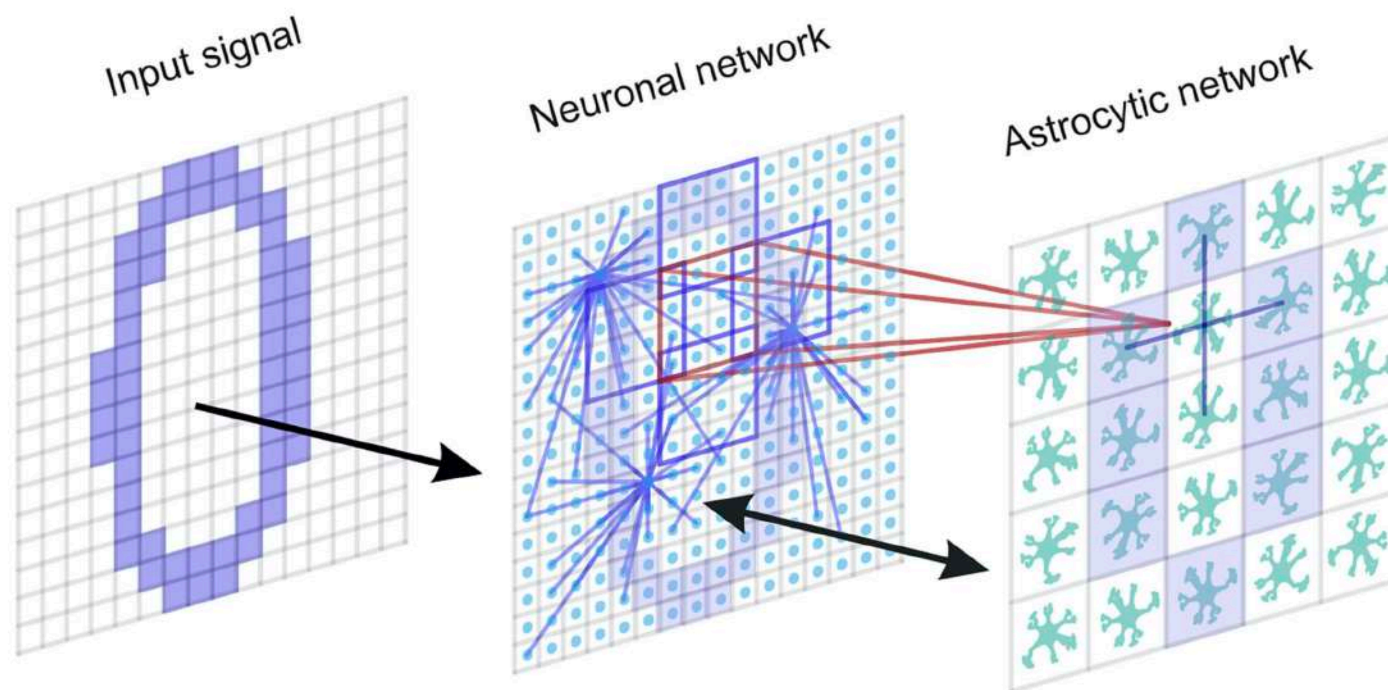
Opera Medica & Physiologica 1 • 23-38 • January 2016

Astrocytes?

Astrocytes Organize Associative Memory

frontiers 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. Tsybina [1], Mikhail I. Krivonosov [1], Mikhail V. Ivanchenko [1], Alexey A. Zaikin [1,3,4], Victor B. Kazantsev [1,2,5] and Alexander N. Gorban [1,6]*

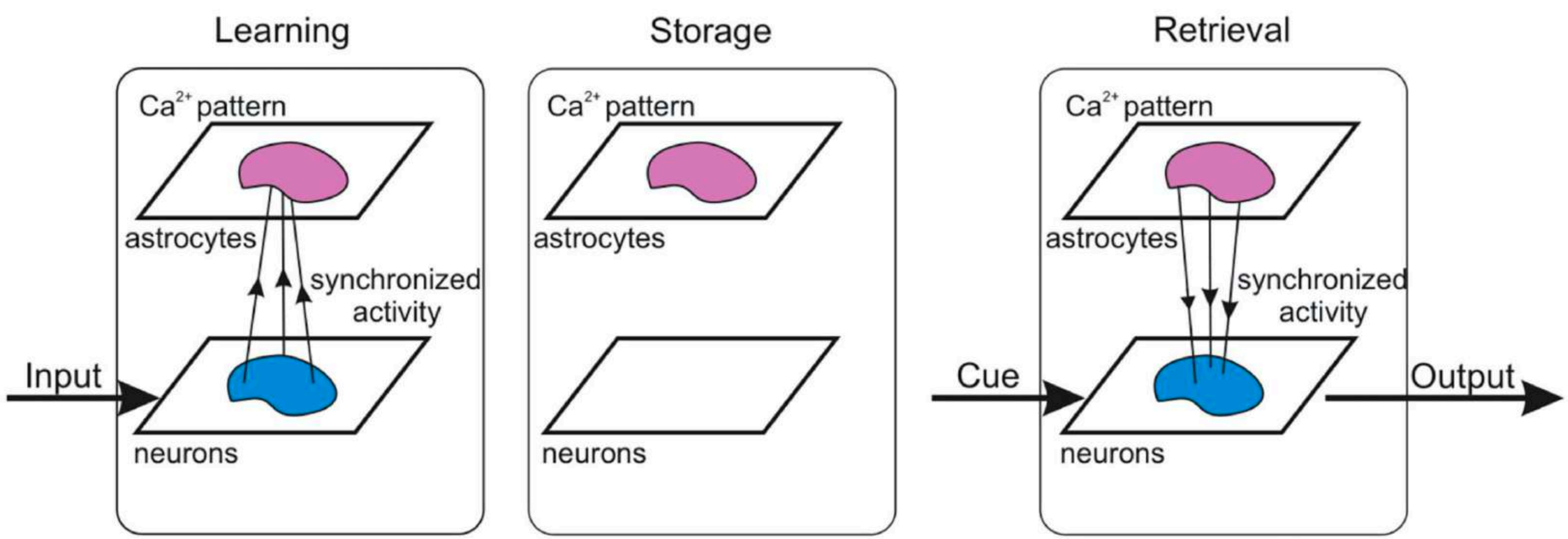


FIGURE 13 | Concept of WM operation in the spiking neuron network model accompanied by astrocytes.

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]

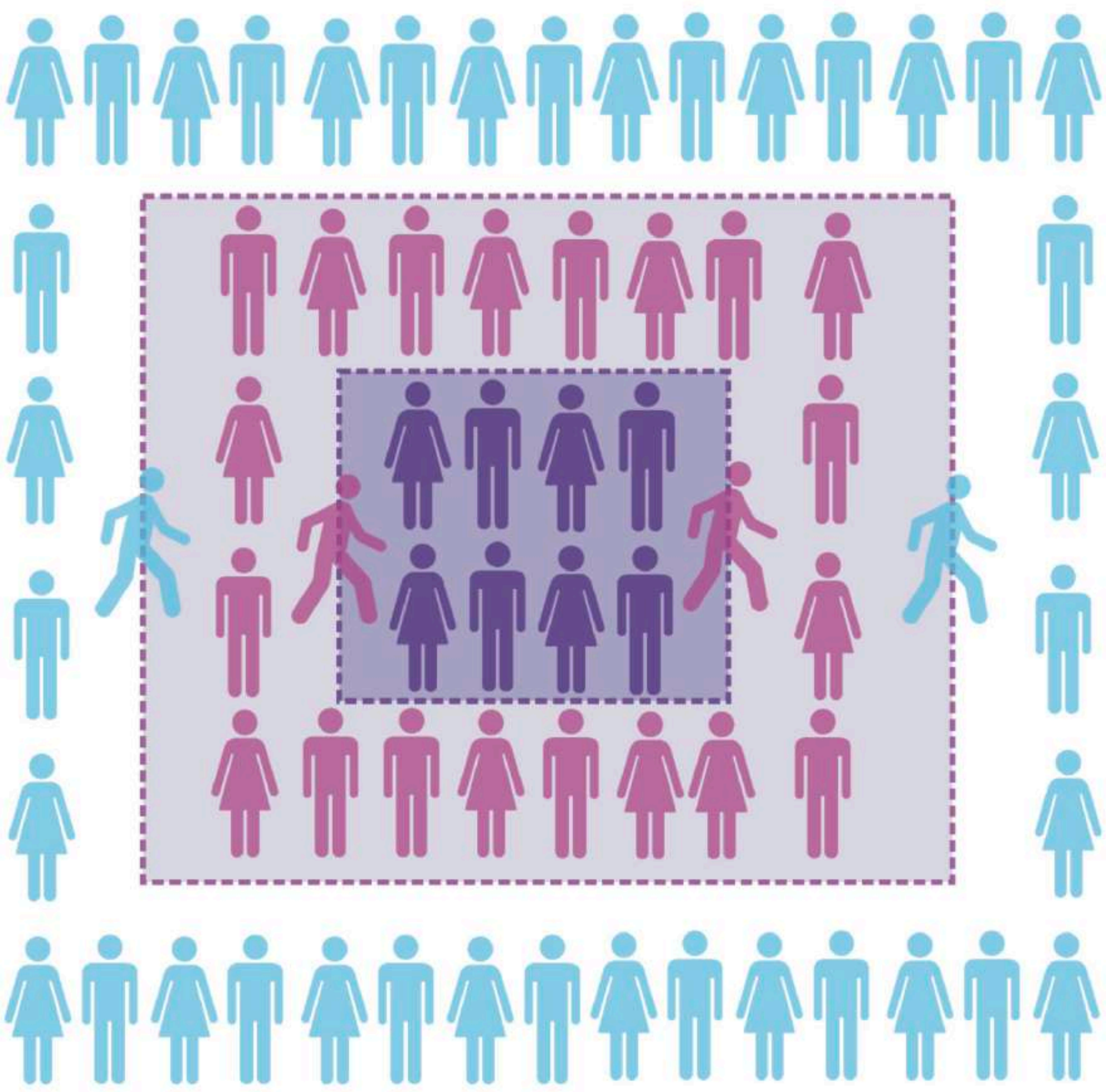
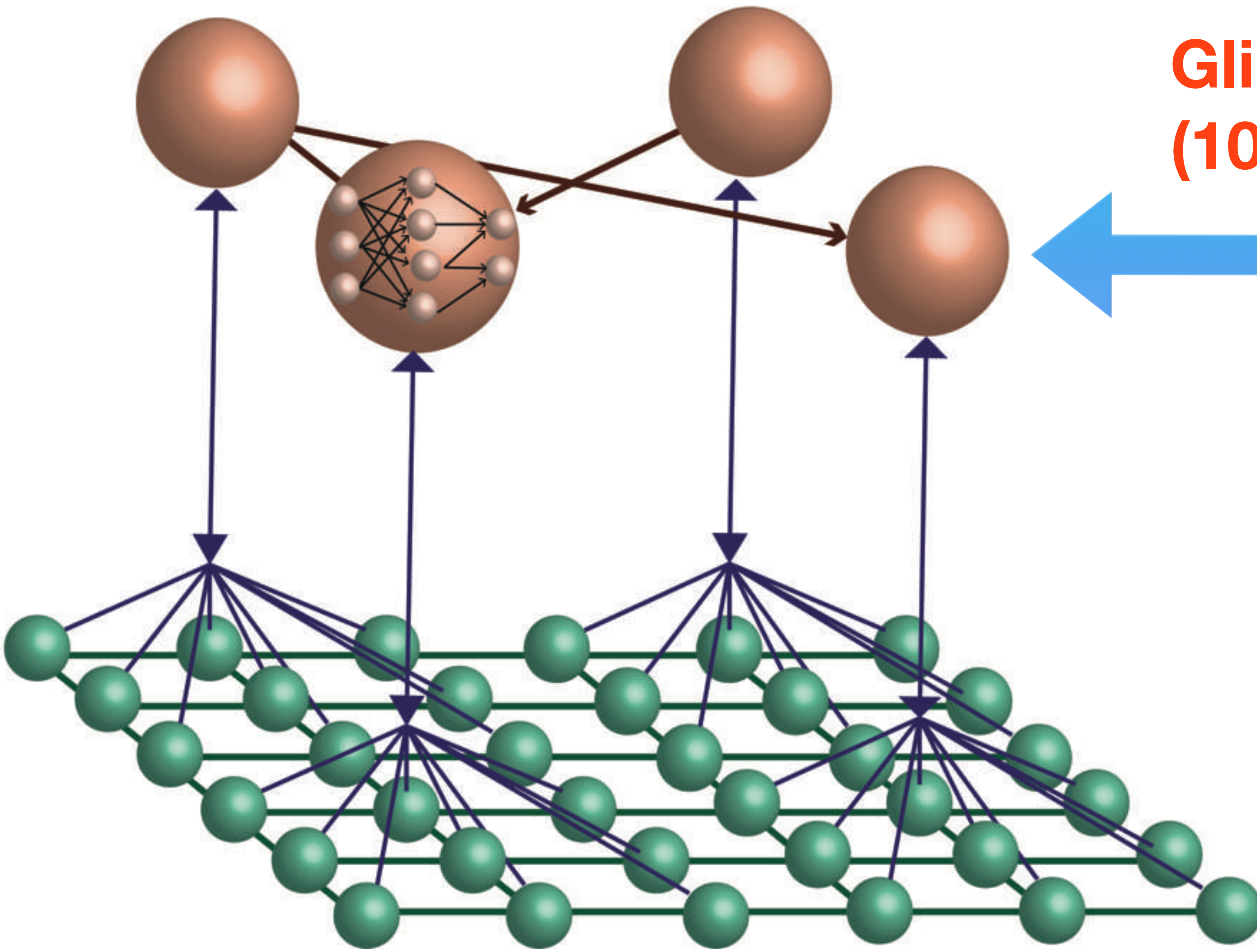


Figure 1: Situation based organisation of data or patterns is structured with three pools of patterns.

Consciousness

Mammalian Brain as Network of Networks

Where is consciousness?



Glial network
(100,000,000,000)

Neural network
(100,000,000,000)

Integrated information

BMC Neuroscience

BioMed Central

Research article

Open Access

Published: 02 November 2004

An information integration theory of consciousness

Giulio Tononi*

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

January 2011 | Volume 7 | Issue 1 | e1001052

Adam B. Barrett*, Anil K. Seth

Integrated information

BMC Neuroscience

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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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An information integration theory of consciousness

Giulio Tononi*

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:

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

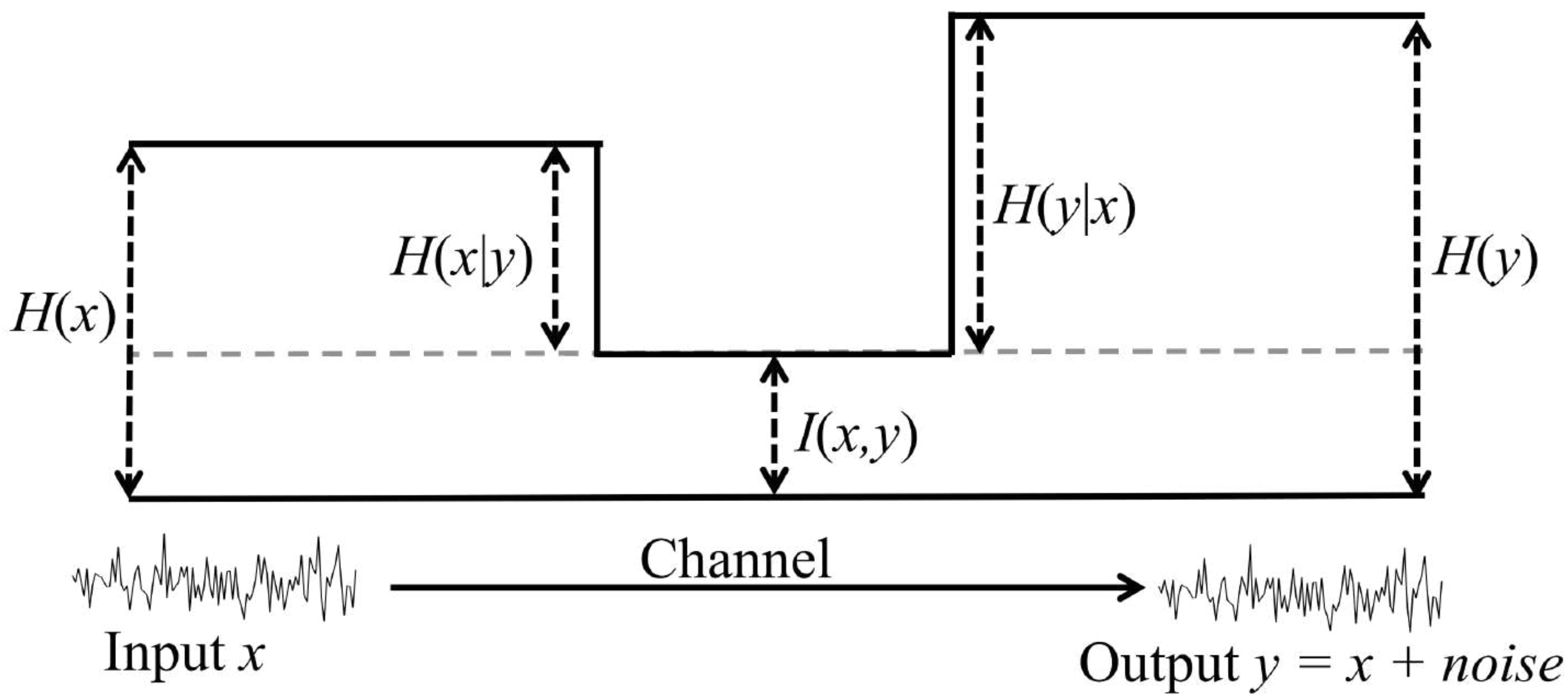
return to playing with one die. Since the probability of each event is $1/n$, we can write

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

Brief tutorial to Mutual Information

The average uncertainty is then

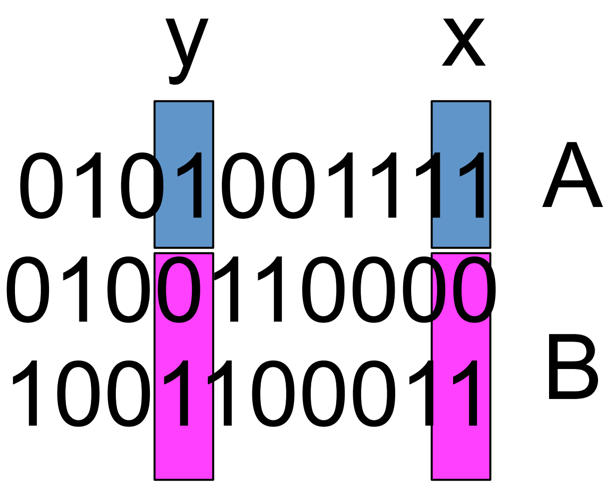
$$< u >= \sum_{i=1} p(x_i)u_i = -\sum_{i=1}^{n} p(x_i)\log(p(x_i)) = H(X)$$



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):



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

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

$$H(x_A y_A) = -\sum_{x_A y_A} p(x_A y_A) \log p(x_A y_A), \tag{6}$$

$$H(x_B y_B) = -\sum_{x_B y_B} p(x_B y_B) \log p(x_B y_B), \tag{7}$$

$$I(x_A, y_A) = H(x_A) + H(y_A) - H(x_A y_A), \tag{8}$$

$$I(x_B, y_B) = H(x_B) + H(y_B) - H(x_B y_B). \tag{9}$$

Here notations $x_A y_A$ ($x_B y_B$) 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, $x_A y_A$ and $x_B y_B$ 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

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

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

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

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

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

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^*.

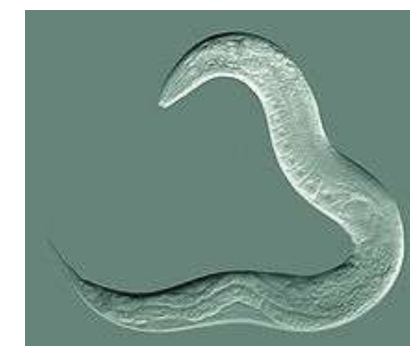
Is it just another measure of complexity or smth more?

- 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 Boly,[2‡] 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§]

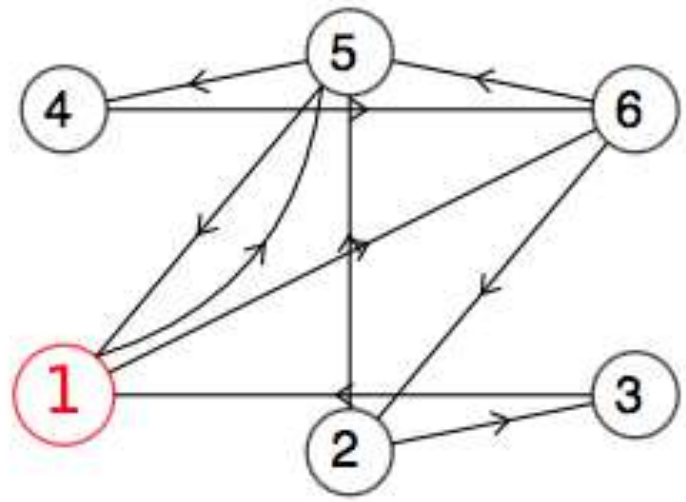
Aim is to show that astrocytes may result in positive II

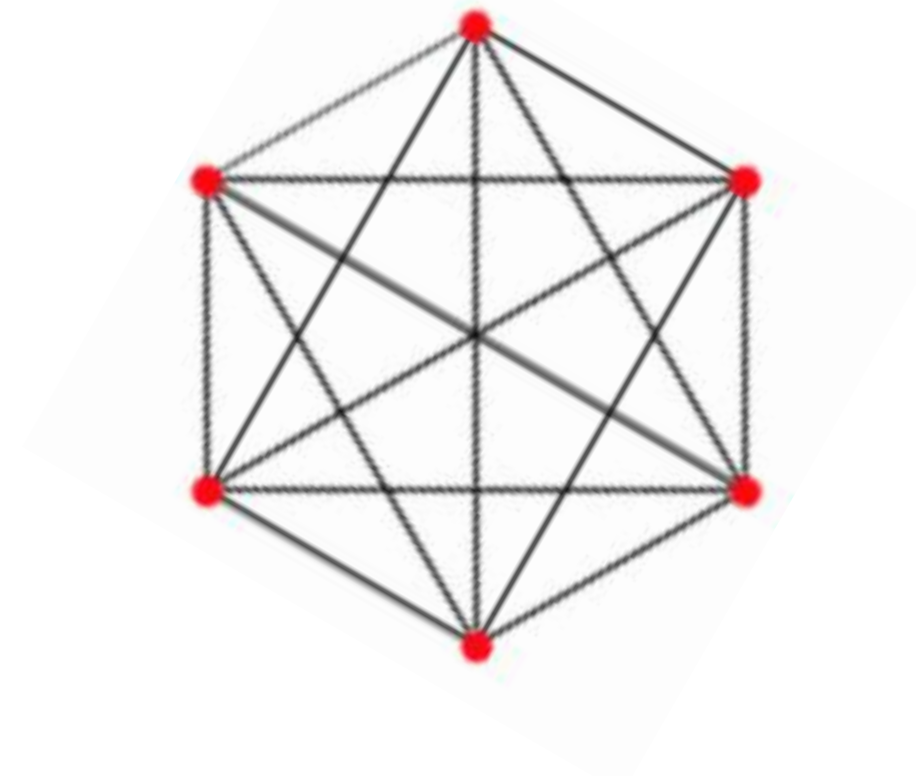
1. Neural network: 6 synaptically coupled Hodgkin-Huxley neurons.
2. 2 versions of network architecture: (i) 1 inhibitory and 5 excitatory neurons with coupling topology obtained by randomly picking 1/3 of the total number of connections out of the full directed graph, excluding self-connections; (ii) 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)

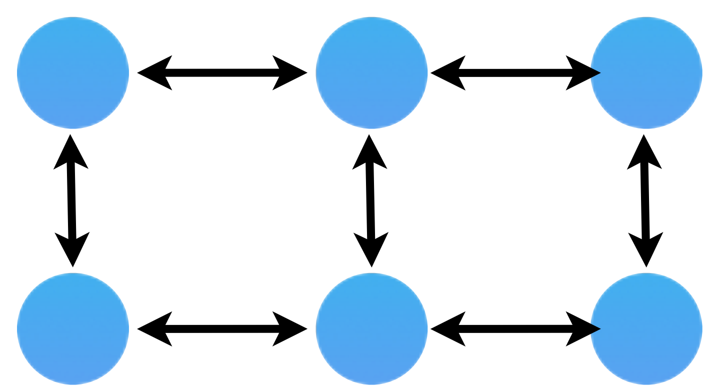
All to all (all excitatory)

Neurons:





Astrocytes:



Ra
(1 inh

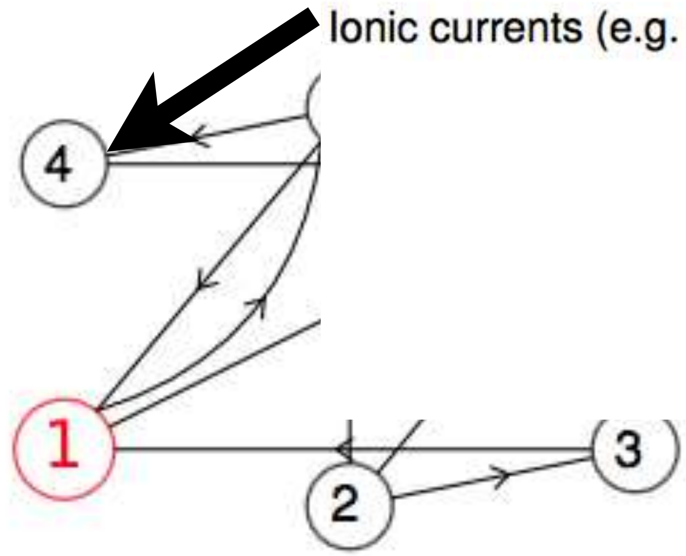
The membrane potential of a single neuron:

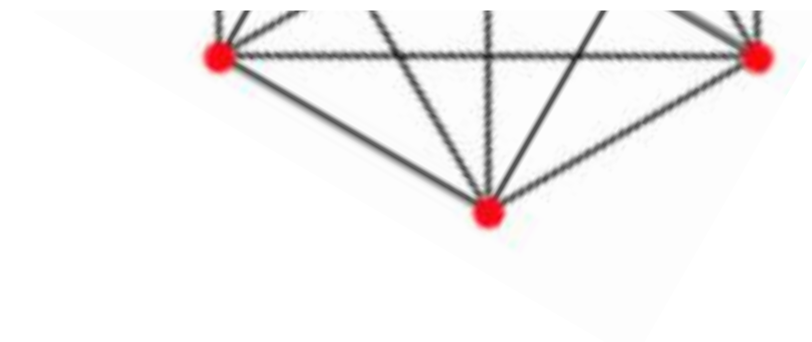
$$C\frac{dV^{(i)}}{dt} = I^{(i)}_{\text{channel}} + I^{(i)}_{\text{app}} + \sum_j I^{(ij)}_{\text{syn}} + I^{(i)}_P;$$

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

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

Neurons:





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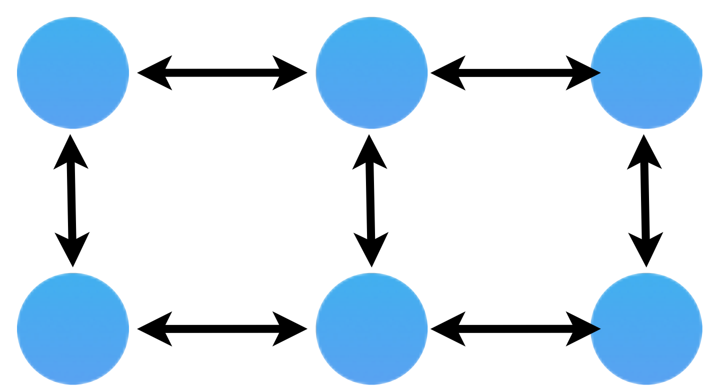

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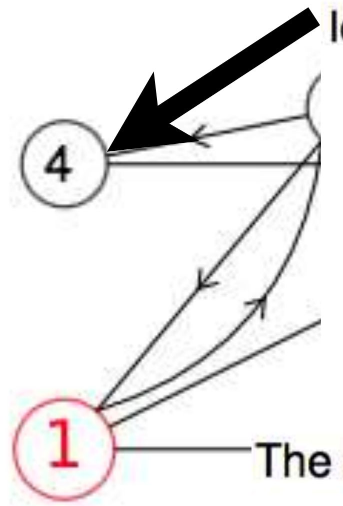

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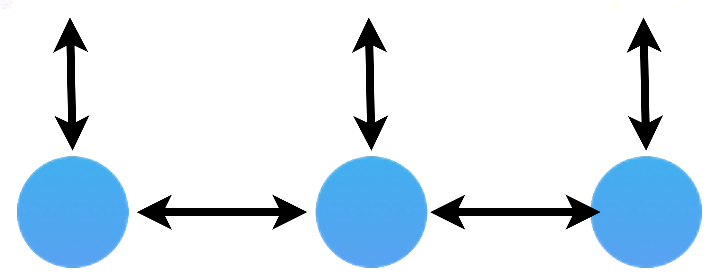
$$\frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x, \quad x = m, n, h.$$

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

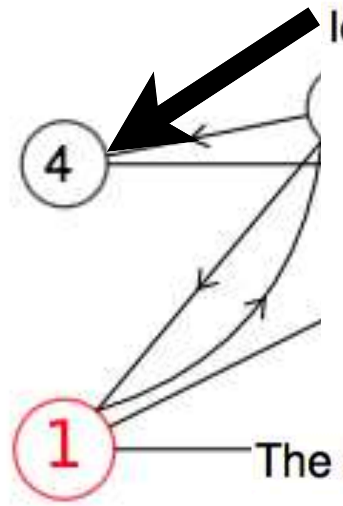
$$I^{(ij)}_{\text{syn}} = \frac{g_{\text{syneff}}(V^{(j)} - E_{\text{syn}})}{1 + \exp\left(\frac{-(V^{(i)} - \theta_{\text{syn}})}{k_{\text{syn}}}\right)}; \tag{3}$$

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

Astrocytes:



Ra
(1 inh



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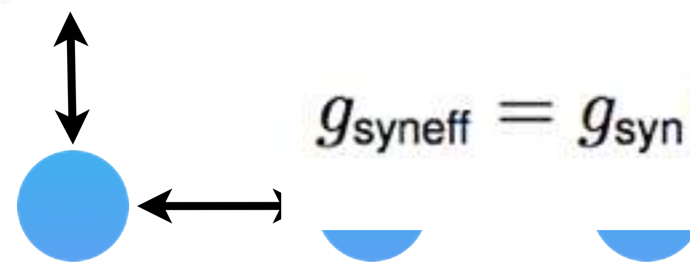
The applied currents $I^{(i)}_{\text{app}}$ control the depolarization level and dynamical regime that can be either excitable, oscillatory or bistable. The synaptic current I_{syn}:

$$I^{(ij)}_{\text{syn}} = \frac{g_{\text{syneff}}(V^{(j)} - E_{\text{syn}})}{1 + \exp(\frac{-(V^{(i)} - \theta_{\text{syn}})}{k_{\text{syn}}})}; \qquad (3)$$

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

Astrocytes:



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

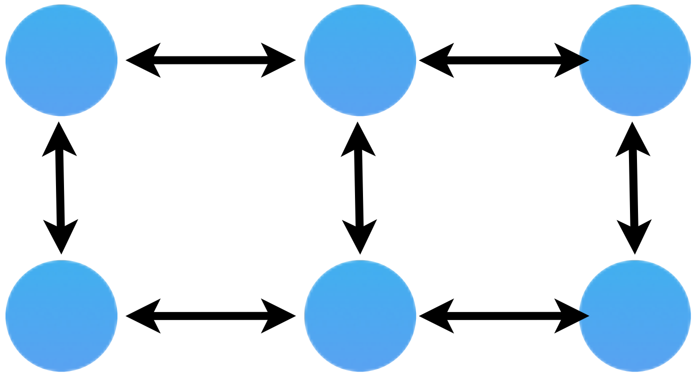
$$\frac{dCa^{(m,n)}}{dt} = J_{\text{ER}}^{(m,n)} - J_{\text{pump}}^{(m,n)} + J_{\text{leak}}^{(m,n)} + J_{\text{in}}^{(m,n)} - J_{\text{out}}^{(m,n)} + $$

$$+J_{Ca\text{diff}}^{(m,n)};$$

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

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

Astrocytes:



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11. ASTROCYTE-INDUCED SYNCHRONIZATION IN NEUROGLIAL NETWORKS

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PHYSICAL REVIEW E **99**, 012418 (2019)

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,*]

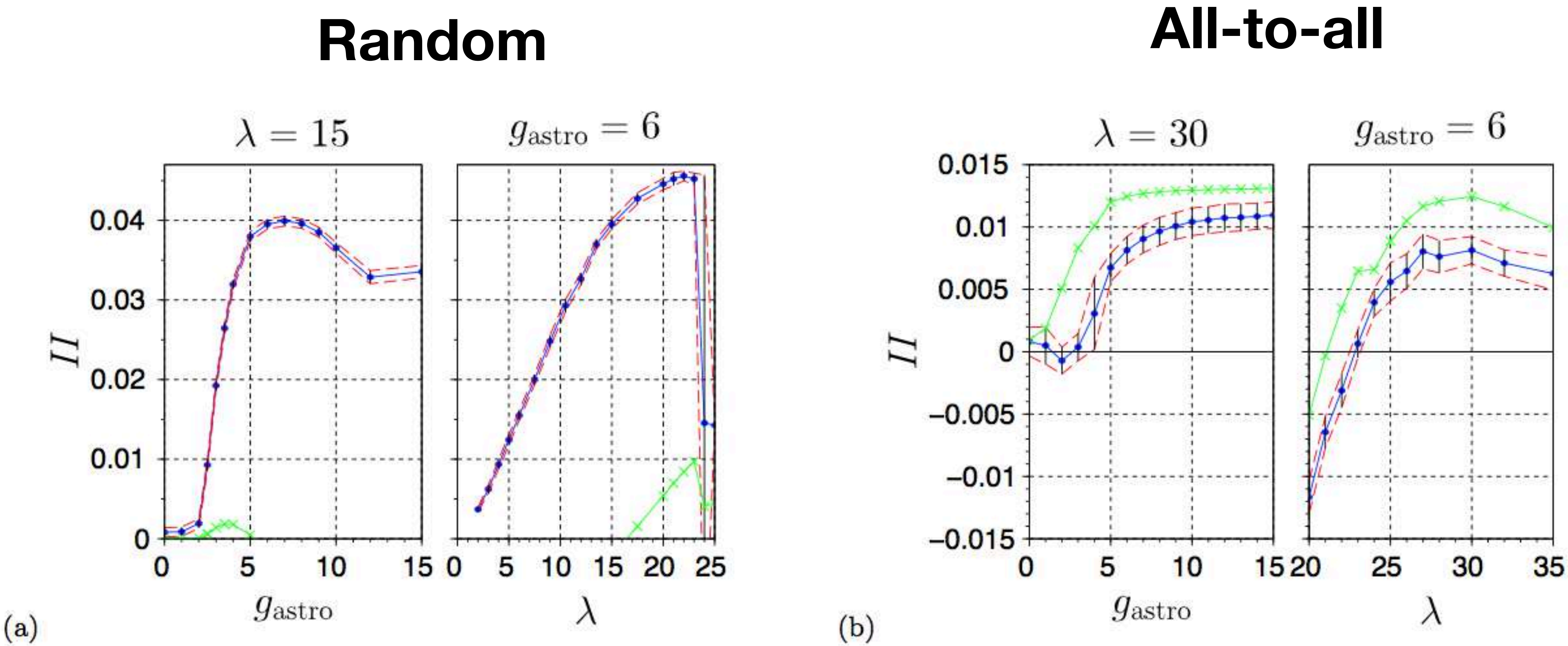
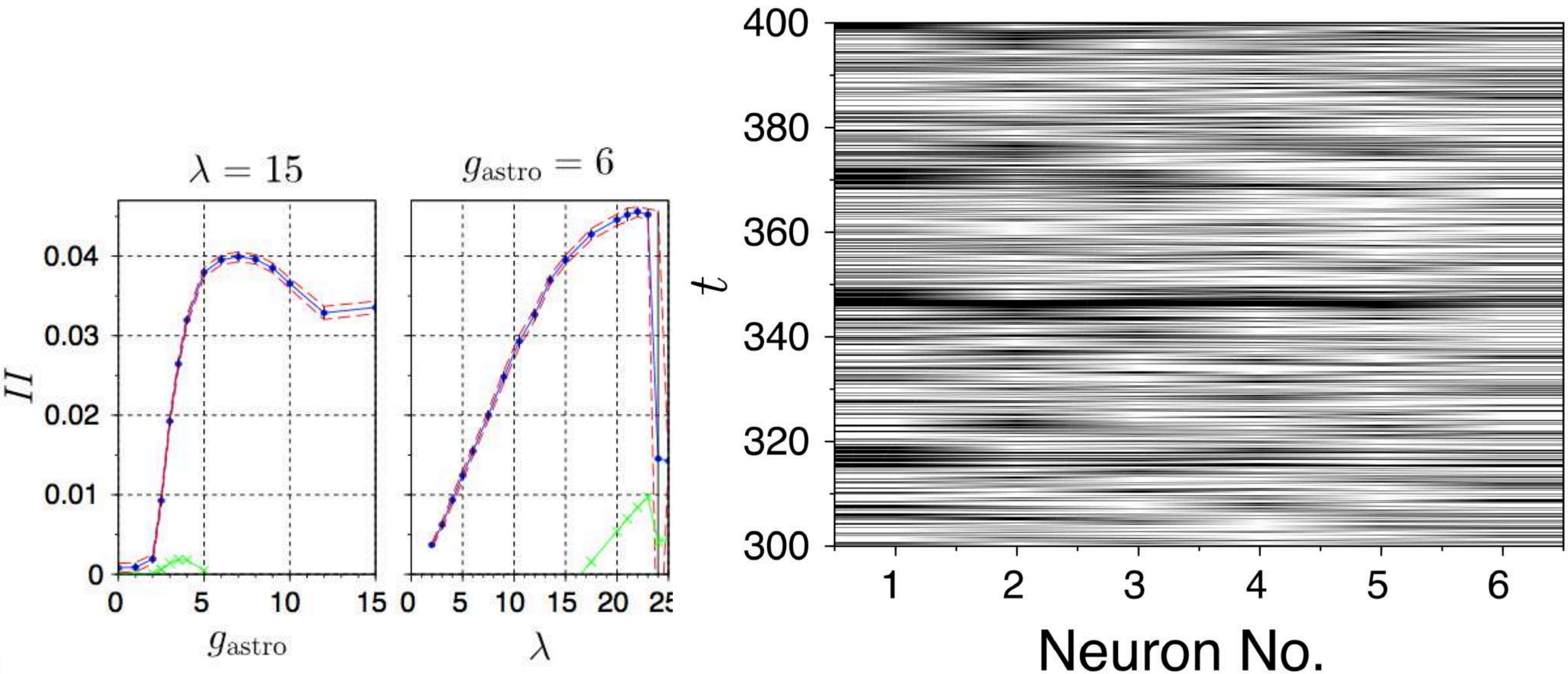


FIG. 2. Dependence of II upon neuro-astrocytic interaction g_{astro} and upon average stimulation frequency λ: (a) — random network (instance shown in FIG. 1); (b) — all-to-all network. Blue solid lines with dot marks — direct calculation by definition from simulation data; red dashed lines — error estimation;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

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,*]



(a)

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.

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,*]

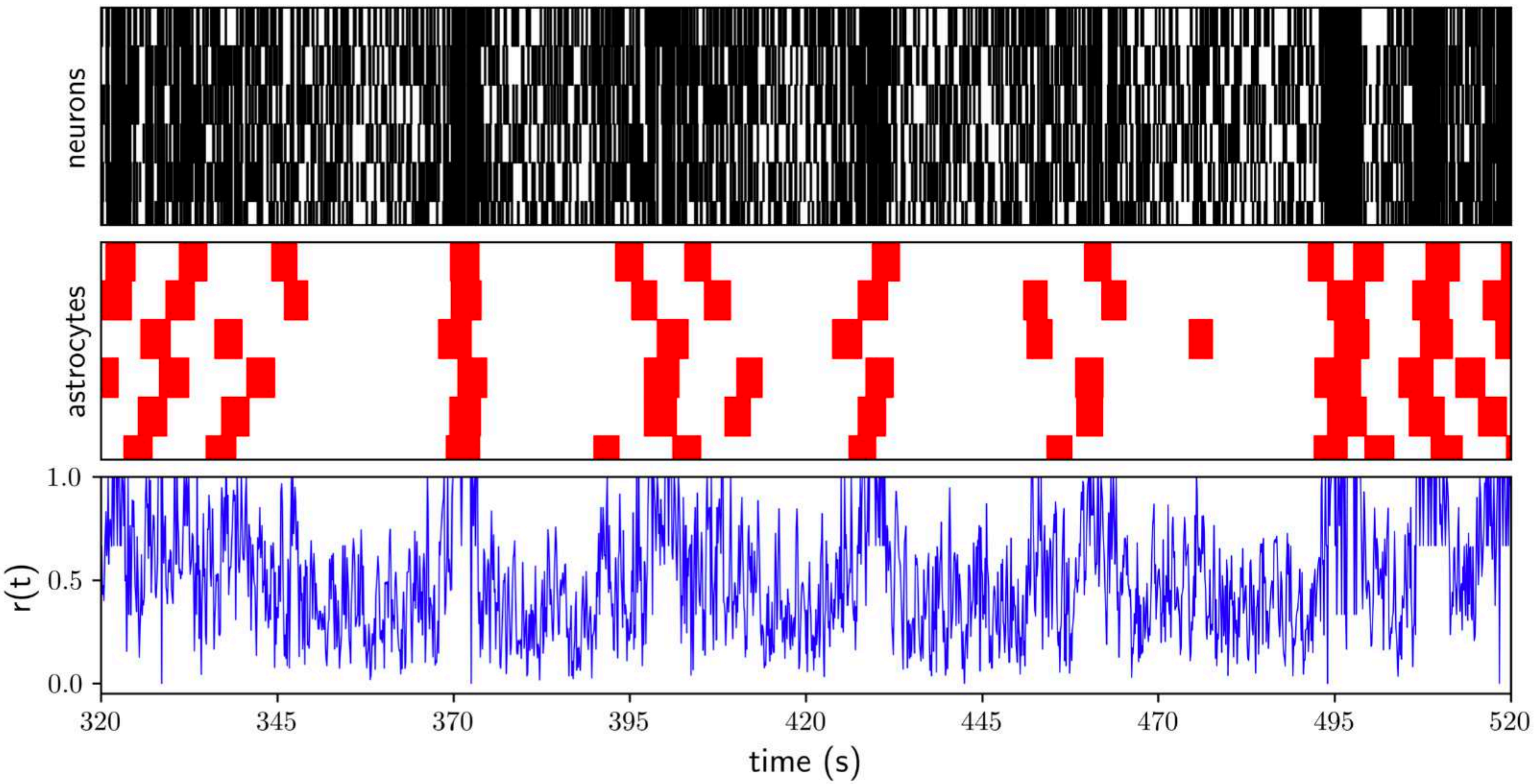
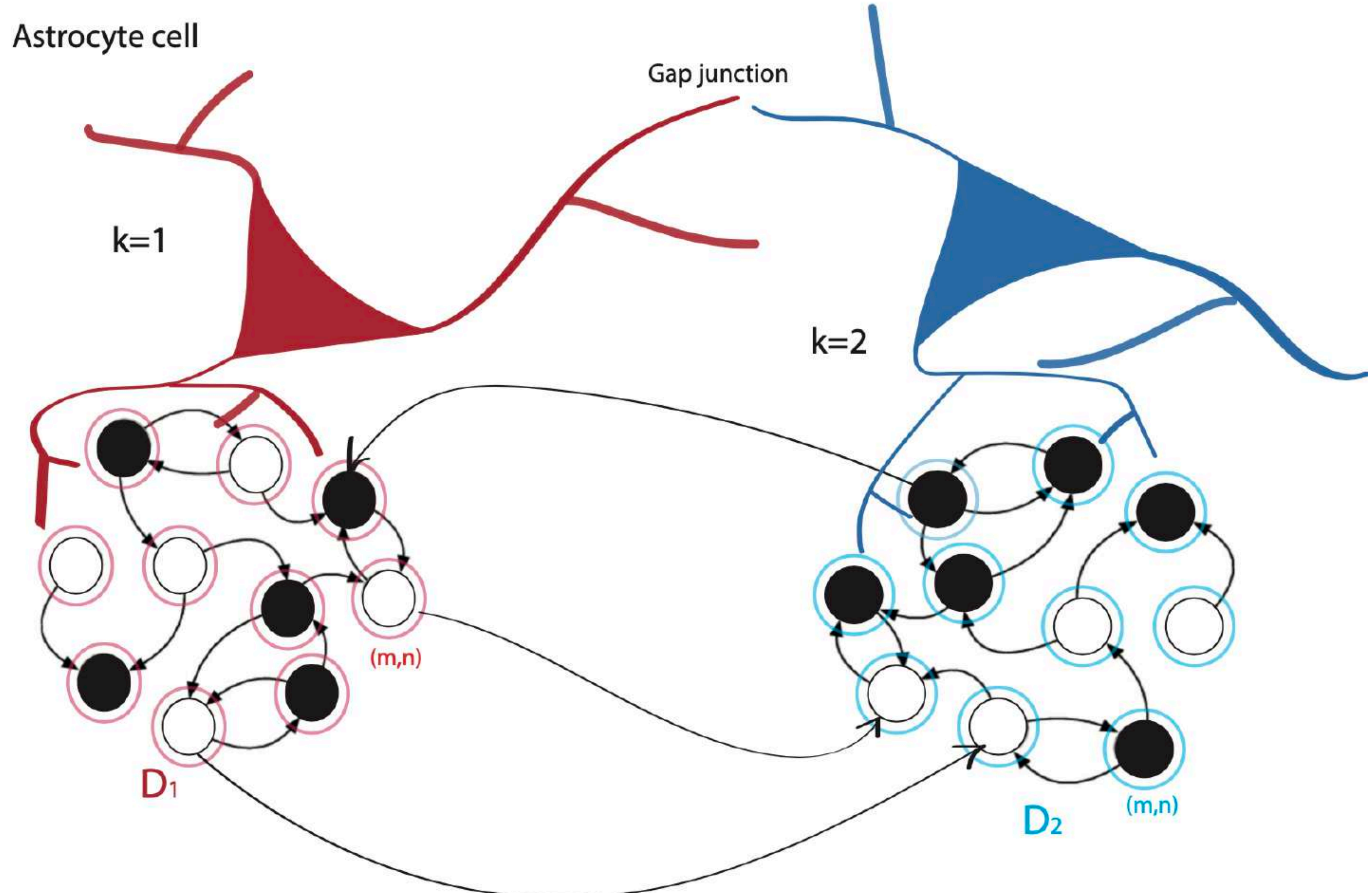


Figure 4.3: Raster plots representing the joint activity of neurons and astrocytes by bidirectional coupling. We set $g_s = 3.4$ and $\lambda = 20$ Hz for excitatory network with all-to-all coupling [exc-full, Fig. 4.1 (a)]. The coordination of the spike trains in the population of neurons is depicted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

Multi-scale modeling of astrocyte-mediated synaptic information transmission



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MDPI

Article

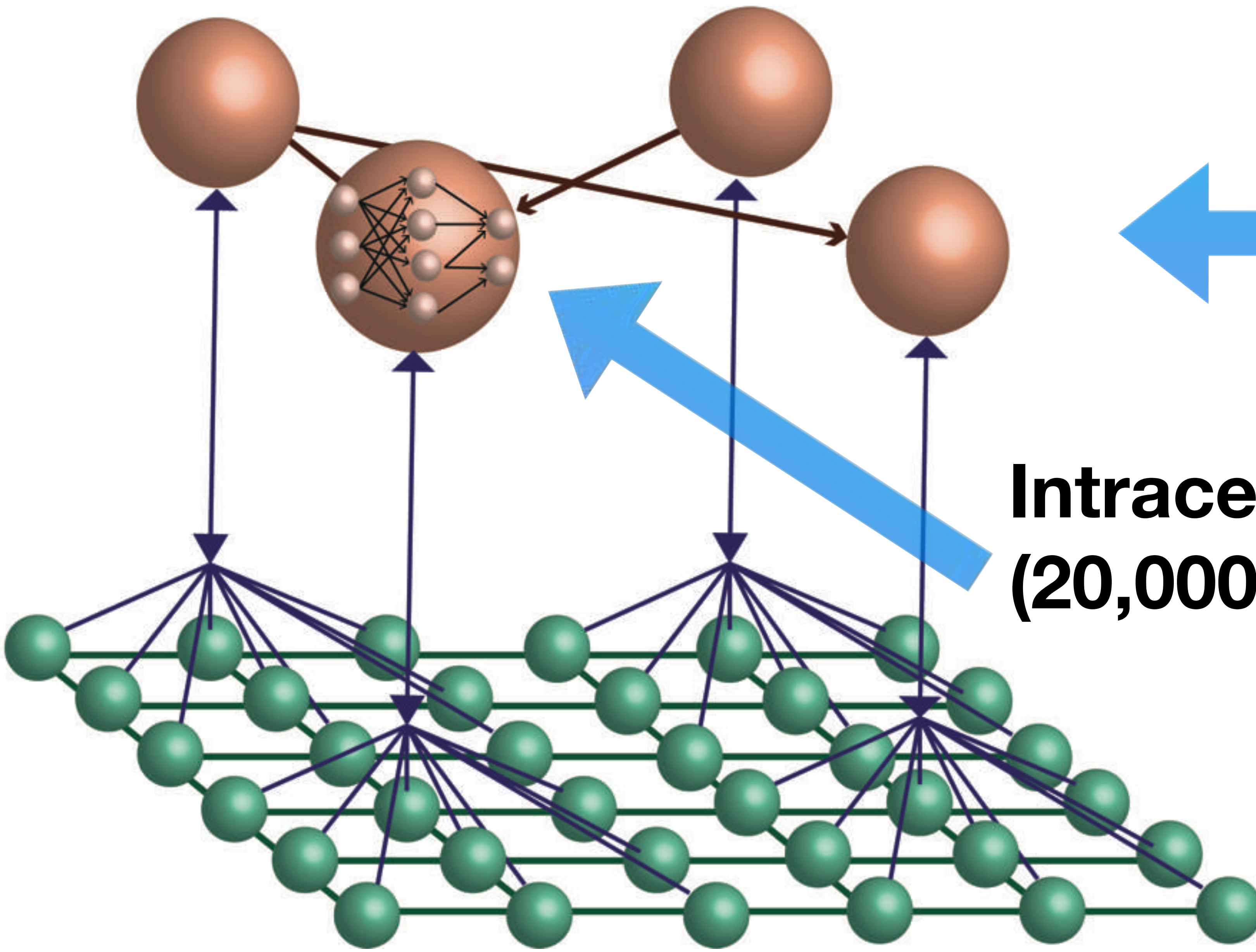
Integrated Information in the Spiking–Bursting Stochastic Model

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

Oleg Kanakov [1], Susanna Gordleeva [2,3] and Alexey Zaikin [4,5,6,*]

Mammalian Brain:

Simplified Scheme



Glial network
(100,000,000,000)

Intracellular network
(20,000 genes, 1M Met probes)

Neural network
(100,000,000,000)

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]

Opera Medica & Physiologica 1 • 23-38 • January 2016

Article

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

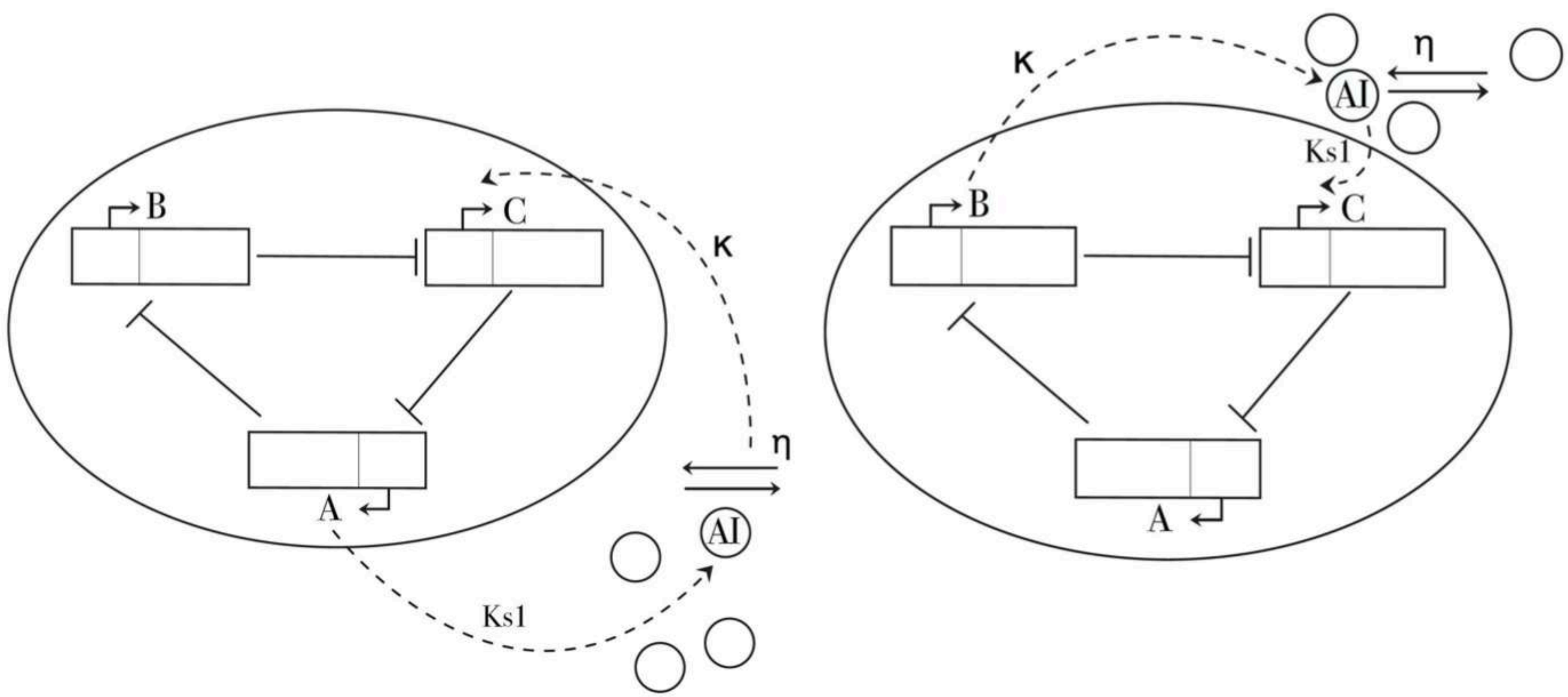


Figure 1. Diagram of the repressilator circuit including the quorum sensing mechanism. **Left**: the phase-attractive coupling. **Right**: the phase-repulsive coupling.

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?

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Jalan, A. Gorban