Investigating activity dependent dynamics of synaptic structures using biologically plausible models of post-deafferentation network repair

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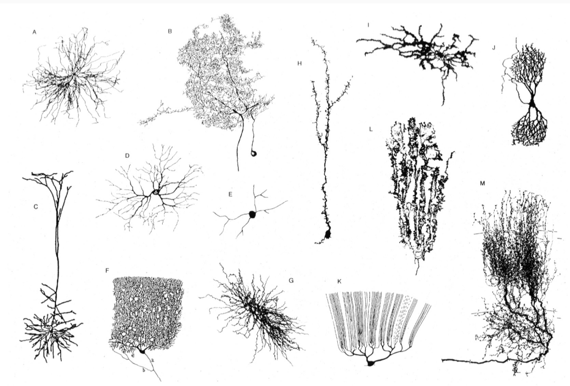
Notes

The brain: numbers, learning, plasticity and stability.

Notes

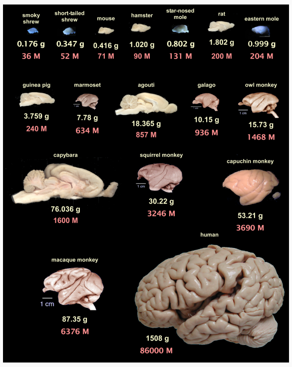
The brain: neurons



Dendrites, Oxford University Press, 2015; Modified from Mel, B.W. Neural Computation, 1994.

Notes

The brain: in numbers: neurons

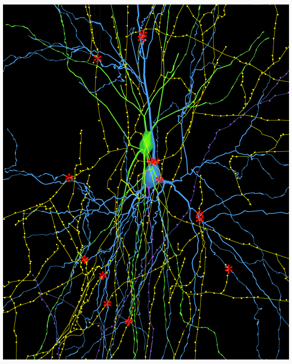


- 86B neurons[1].

[1] Herculano-Houzel, S. The human brain in numbers: a linearly scaled-up primate brain. *Frontiers in human neuroscience* **3**, 31 (2009)

Notes

The brain: in numbers: synapses



- Thousands of connections (synapses)[2].
- Synapses can be excitatory or inhibitory.
- Synapses underlie learning[3].

[2] Image from The Gao lab, College of Medicine, Drexel University.
[3] Hebb, D. O. *The organization of behavior: A neuropsychological theory.* 1949

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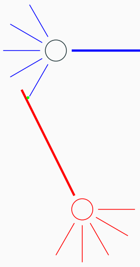
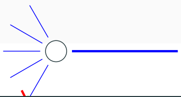
The brain: learning via changes in synapses (plasticity)



Food



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The brain: plasticity and stability?

- Learning occurs all the time.
- In fact, whole synapses are formed and removed all the time[4]: **structural plasticity**.
- Unregulated brain activity causes disorders: epilepsy.
- So, how does the brain remain stable despite changing all the time?
- Suggests the existence of stabilising (homeostatic) processes[5].

[4] Holtmaat, A. J. G. D. *et al.* Transient and Persistent Dendritic Spines in the Neocortex In Vivo. *Neuron* **45,** 279–291. ISSN: 0896-6273 (2005)
[5] Turrigiano, G. G. Homeostatic plasticity in neuronal networks: the more things change, the more they stay the same. *Trends in neurosciences* **22,** 221–227 (1999)

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Smell A

Our research focus: Homeostatic Structural Plasticity

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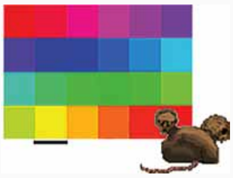
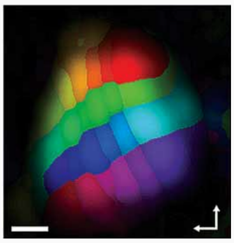
Studying homeostatic structural plasticity: biologists

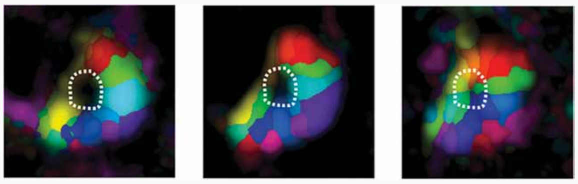




[1] Keck, T. *et al.* Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* **11,** 1162–1167 (2008)

Notes

after injury . . .



[6] Keck, T. *et al.* Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* **11,** 1162–1167 (2008)

Notes

Our investigations: computational modelling

- We made a new computer model of a small part of the brain.
- We replicated what biologists observed in their laboratories.
- We tested different ways in which homeostatic structural plasticity may occur.
- Iterative process: we send our ideas back to biologists for validation.

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Our new model: replicates biological observations

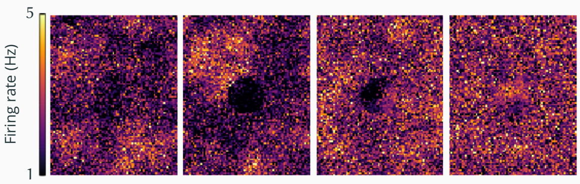

Figure 1: 1000 neurons. From left to right: normal network, network after injury, network during repair, network after repair.
Simulation duration: 7 days on the cluster[7] with 128 CPU nodes to simulate ~5 hours of real brain time.

[7] UH High Performance Cluster: https://uhhpc.herts.ac.uk

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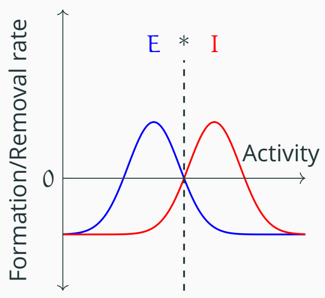
Our model suggests that



- Neurons modify their dendrites (inputs) to maintain their activity.
- More than necessary: reduce excitatory inputs, increase inhibitory inputs.
- Less than necessary: vice versa.

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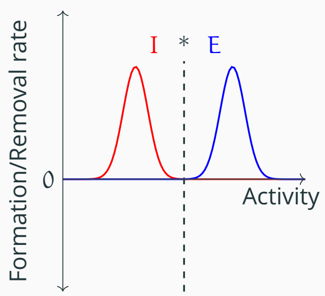
Our model suggests that: II



- Neurons modify their axons (outputs) to make other neurons match their activity.
- More than necessary: pass on excitation.
- Less than necessary: pass on inhibition.

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What next?

- Investigate functional consequences of homeostatic structural plasticity: does the part of the brain behave the same after repair?
- Further investigation with more detailed modelling: move from simple point neuron models to more realistic multi-compartmental models.

Notes

Summary

- The brain is plastic but stable.
- Neurons form and remove synapses all the time—continuously modifying brain networks.
- We investigated how the brain remains stable.
  - Homeostatic Structural Plasticity.
  - We developed a new, realistic computer model of brain injury.
  - Our simulations suggest that neurons maintain their own activity by forming and removing inputs, and transferring their states to other neurons.

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