

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



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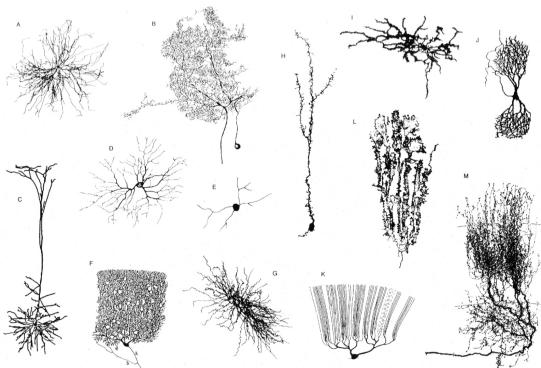
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Notes

The brain: numbers, learning, plasticity and stability.

Notes

The brain: neurons

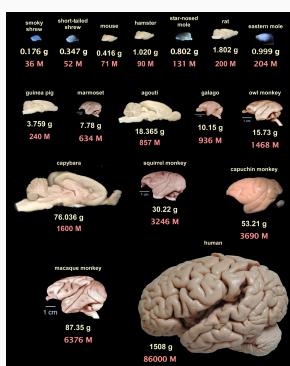


Dendrites, Oxford University Press, 2015; Modified from Mel, B.W. Neural Computation, 1994.

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Notes

The brain: in numbers: neurons



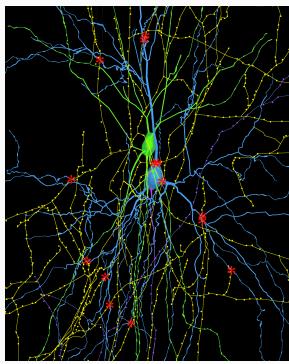
• 86000M neurons¹.

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

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The brain: in numbers: synapses



- Thousands of connections (synapses) between pairs².
- Synapses can be excitatory or inhibitory.
- Synapses underlie learning³.

²Image from The Gao lab, College of Medicine, Drexel University.

³Hebb, D. O. *The organization of behavior: A neuropsychological theory*. 1949

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Notes

The brain: learning via changes in synapses (plasticity)

Food: curry!



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Notes

The brain: plasticity and stability?

- Learning occurs all the time.
- In fact, whole synapses are formed and removed all the time⁴: **structural plasticity**.
- Unregulated brain activity causes disorders: **epilepsy**.
- So, how does the brain remain stable despite changing all the time?
- Stabilising (**homeostatic**) processes⁵?

⁴Holtmaat, A. J. G. D. et al. Transient and Persistent Dendritic Spines in the Neocortex In Vivo. *Neuron* **45**, 279–291.
ISSN: 0896-6273 (2005)

⁵Turrigiano, 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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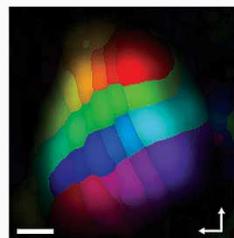
Smell A

Our research focus:
Homeostatic Structural Plasticity

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Studying homeostatic structural plasticity: biologists

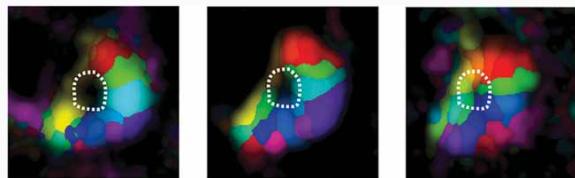


¹Keck, T. et al. Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* 11, 1162–1167 (2008)

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after injury ...



²Keck, T. et al. Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nature neuroscience* 11, 1162–1167 (2008)

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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

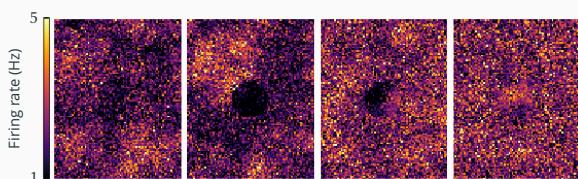
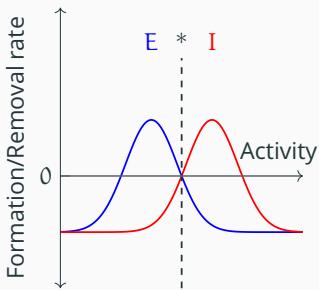


Figure 1: 1000 neurons. Simulation duration: 7 days on the cluster⁷ with 128 CPU nodes to simulate ~5 hours of real brain time.

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Our model suggests that: I

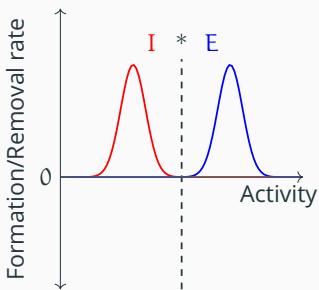


- Neurons modify their **dendrites (inputs)** to maintain their activity.
- Too much: reduce excitatory inputs, increase inhibitory inputs.
- Too less: vice versa.

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Our model suggests that: II



- Neurons modify their **axons (outputs)** to transfer their activity.
- Too much excitation: pass on to neighbours.
- Too much inhibition: pass on to neighbours.

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Notes

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.

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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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