

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



University of
Hertfordshire **UH**

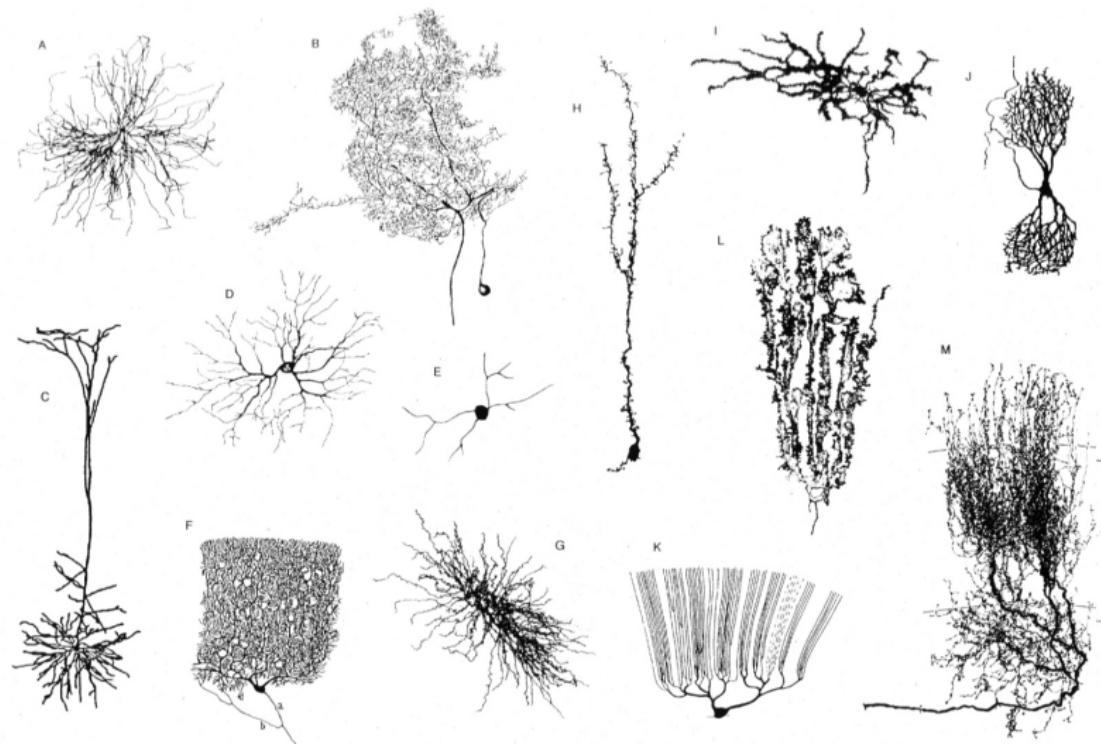
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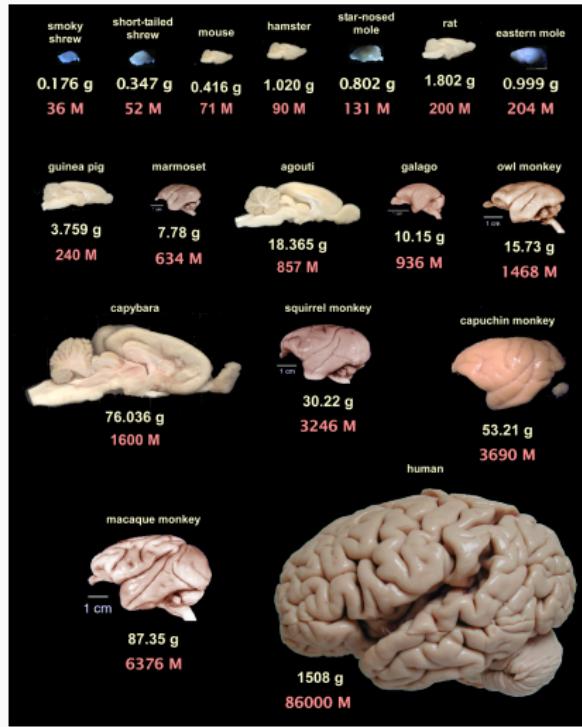
The brain: numbers, learning, plasticity and stability.

The brain: neurons



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

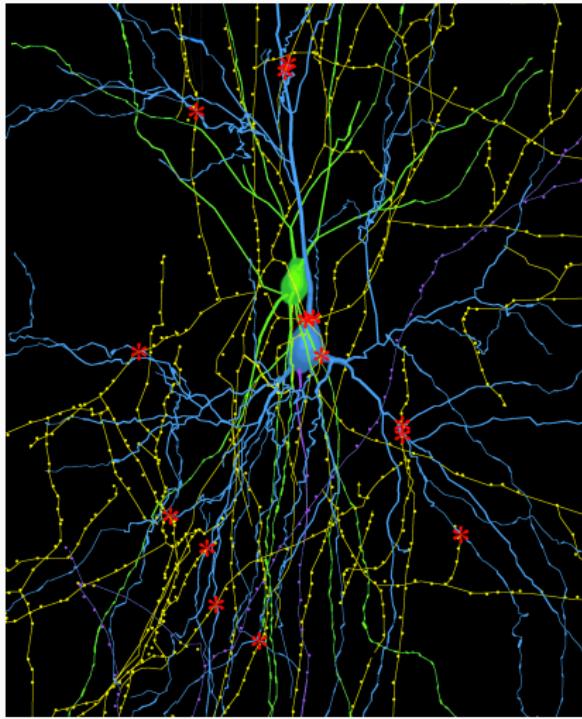
The brain: in numbers: neurons



- 86000M neurons¹.

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

The brain: in numbers: synapses



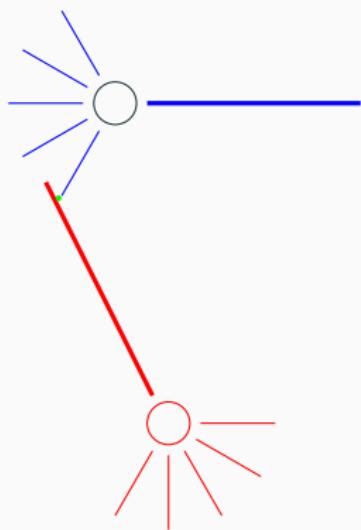
- Thousands of connections (synapses) between pairs².
- Synapses can be excitatory or inhibitory.
- Synapses underlie learning³.

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

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

The brain: learning via changes in synapses (plasticity)

Food: curry!



Smell A

Food: curry!



The brain: plasticity and stability?

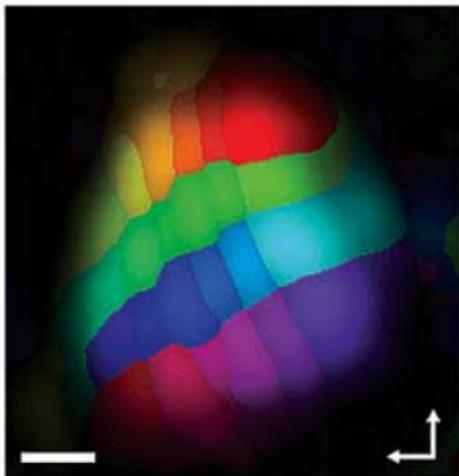
- Learning occurs **all the time**.
- In fact, **whole synapses are formed and removed** all the time⁴: **structural plasticity**.
- Unregulated brain activity causes disorders: **epilepsy**.
- So, how does the brain remain **stable** despite changing all the time?
- Stabilising (**homeostatic**) processes⁵?

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)

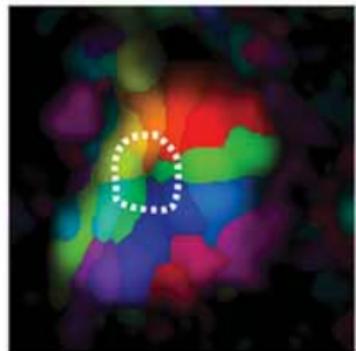
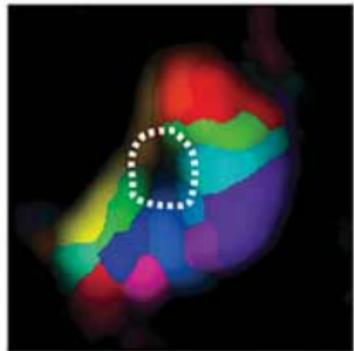
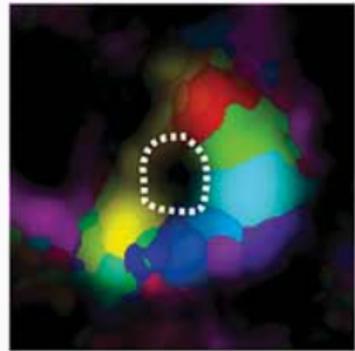
Our research focus:
Homeostatic Structural Plasticity

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)

after injury ...



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

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.
- We will now send our ideas back to biologists for validation.

Our new model: replicates biological observations

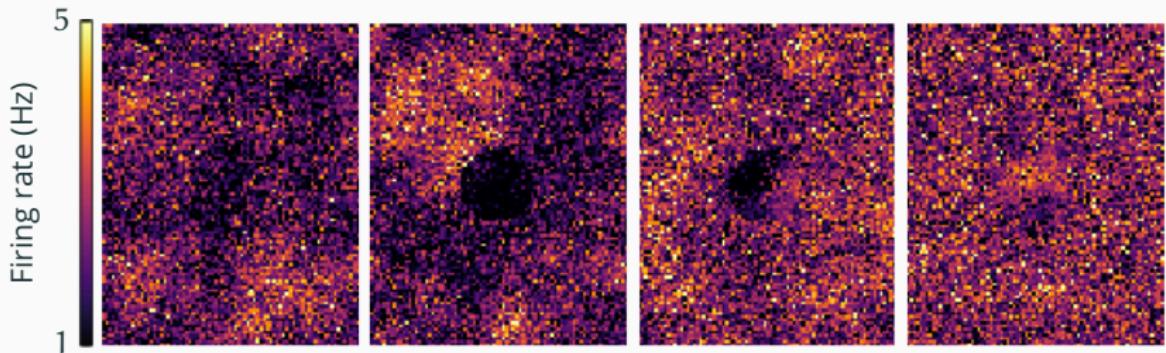
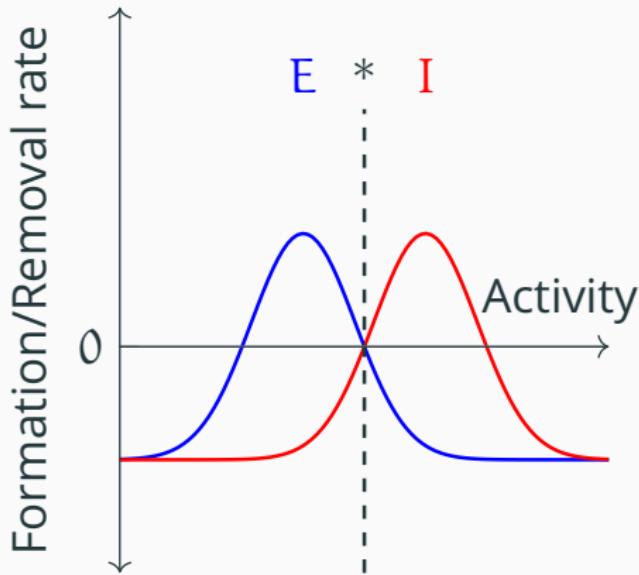


Figure 1: 1000 neurons. Simulation duration: 7 days on the cluster⁷ with 128 CPU nodes to simulate ~5 hours of real brain time.

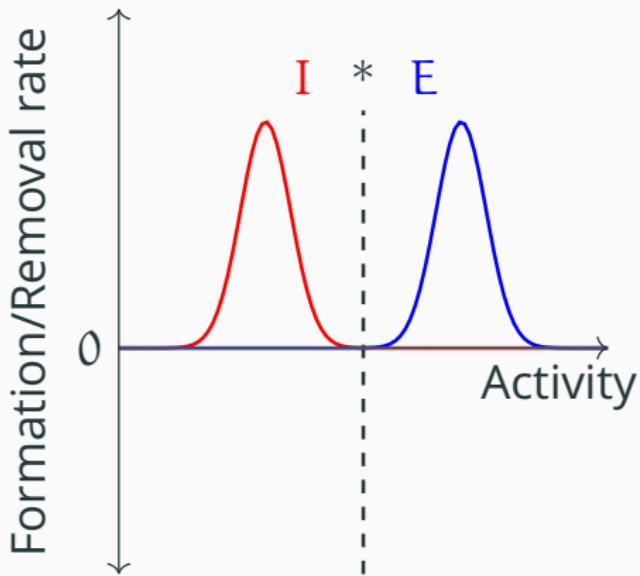
⁷ UH High Performance Cluster: <https://uhhpc.herts.ac.uk>

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.

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.

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.

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.