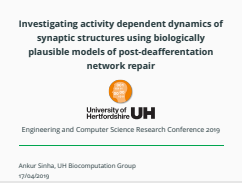
Investigating activity dependent dynamics of synaptic structures using biologically plausible models of post-deafferentation network repair

University of Hertfordshire UH

Engineering and Computer Science Research Conference 2019

Ankur Sinha, UH Biocomputation Group

17/04/2019



The brain: learning, plasticity, stability

2019-04-15

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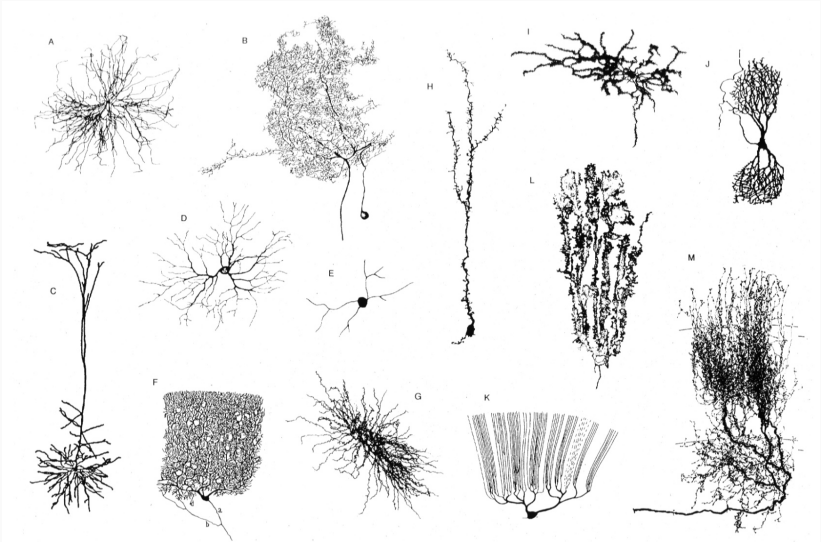
The brain: neurons



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

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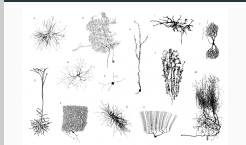

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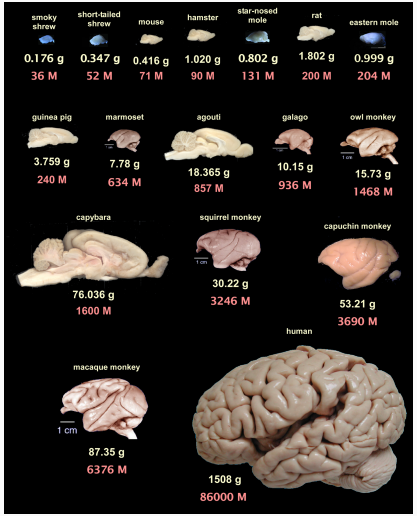
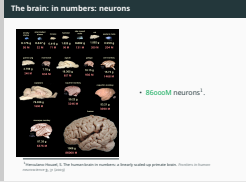
1. The brain is composed of specialised cells that enable it to process information by the use of electrical impulses
2. As the figure shows, these cells, neurons, have specialised into many many types. They serve different functions, include different proteins and markers, and can be classified in many different ways.

The brain: in numbers: neurons



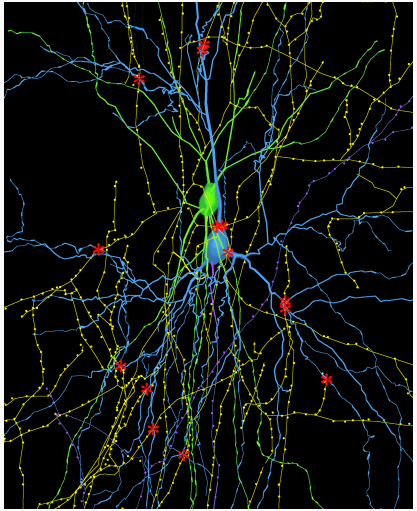
- 86oooM neurons[1].

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



1. The most recent estimate puts the number of neurons in the human brain at 86B.

The brain: in numbers: synapses



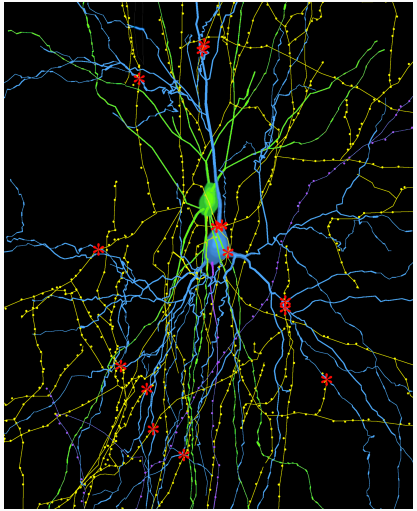
- Thousands of connections (synapses) between pairs[2].

[2] Image from The GAO lab

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

1. Each neuron connects with thousands of other neurons, forming a massive network.
2. This is especially important because we now know that it is in these synapses that learning occurs.

The brain: in numbers: synapses



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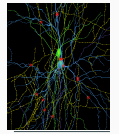

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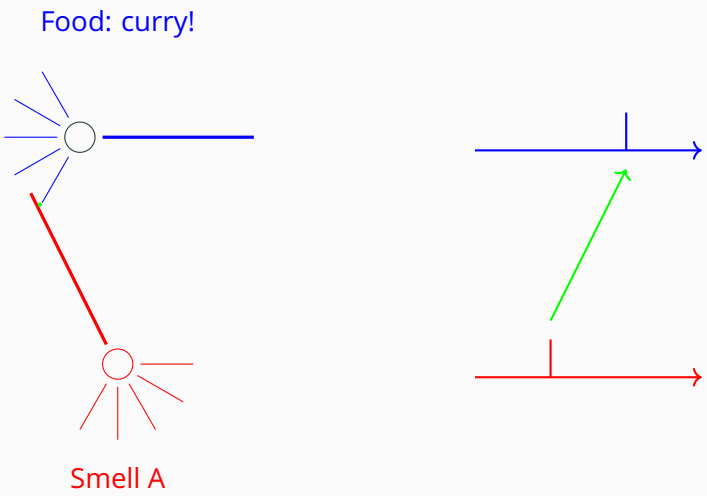
The brain: plasticity and learning



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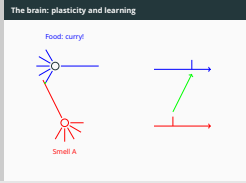

1. We learn when synapses change in the brain
2. As an example, let's say we have a neuron that was activated by a smell.
3. Later, we found out that that was the smell of some food, say curry.
4. Because these neurons fired one after the other here, this synapse is strengthened.
5. When this happens repeatedly, the synapse is strengthened again and again.
6. Until, the faintest whiff of the smell reminds you of the food!

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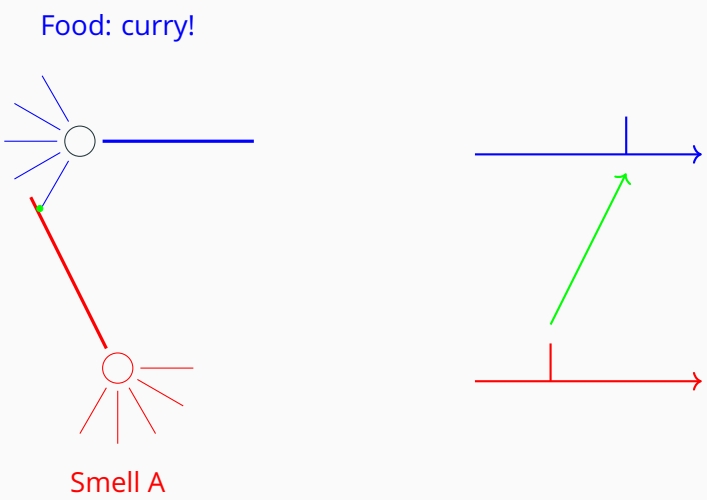

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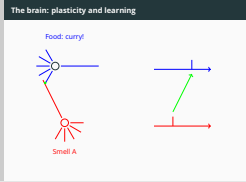

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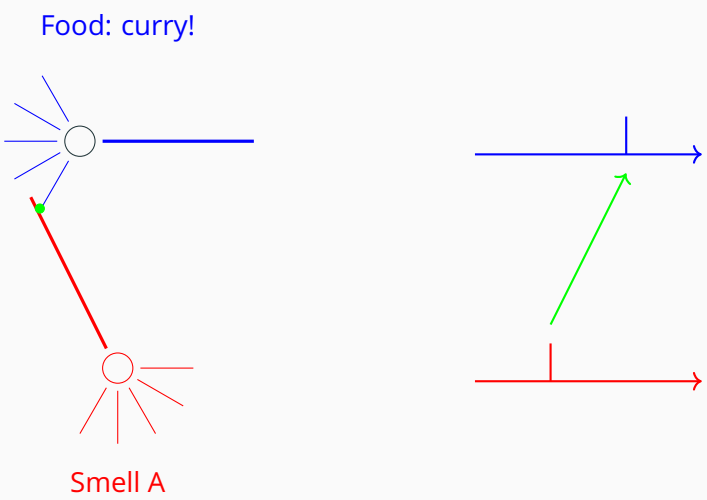

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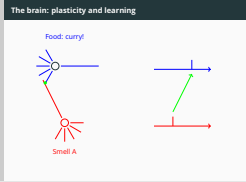

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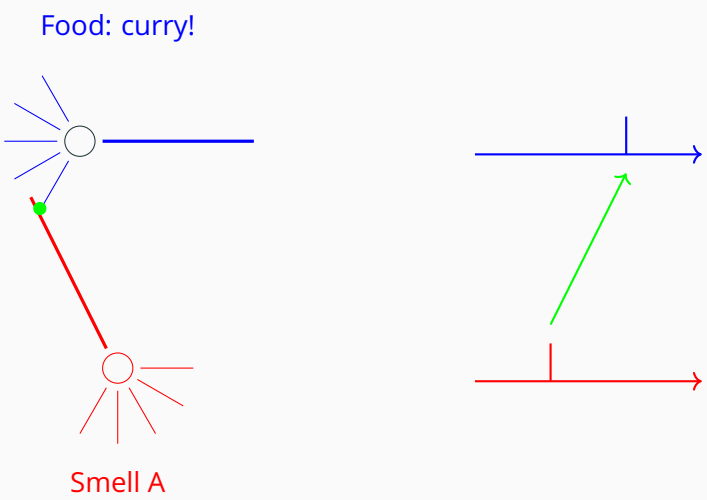

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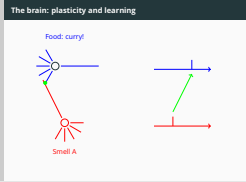

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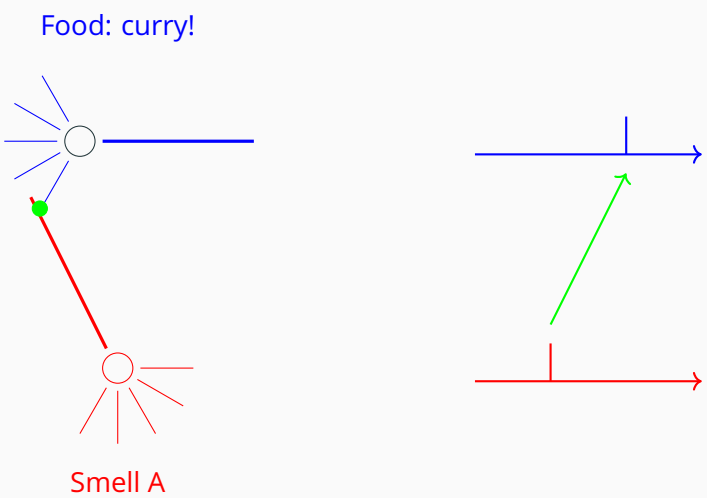

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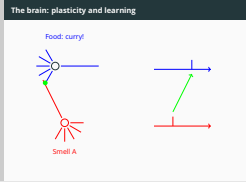

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The brain: plasticity and stability?

- Learning occurs all the time.

[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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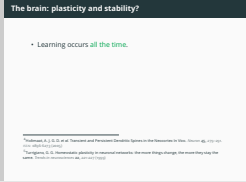

1. Changes in whole synapses change the structure of the networks of neurons, and is referred to as structural plasticity
2. This led researchers to investigate stabilising processes which must work in parallel with learning

The brain: plasticity and stability?

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- In fact, whole synapses are formed and removed all the time[4]: **structural plasticity**.

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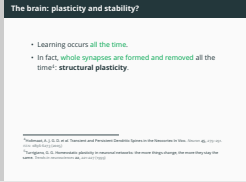

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- So, how does the brain remain stable despite changing all the time?

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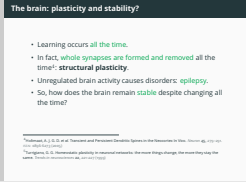

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- Stabilising (homeostatic) processes[5]?

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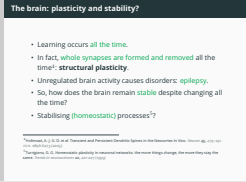

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Our research focus

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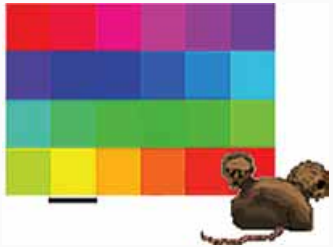
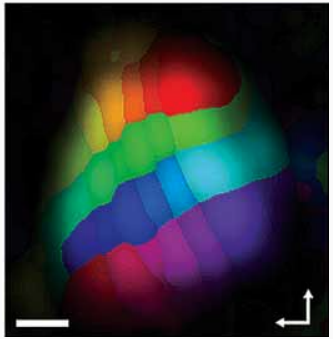
Homeostatic structural plasticity

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)

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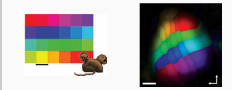
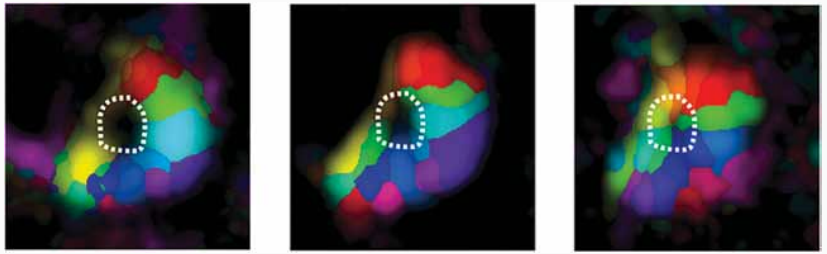


1. The protocol is pretty standard. Here, for a study in the visual cortex, the retinal field of a rat or a mouse is mapped.

after injury . . .



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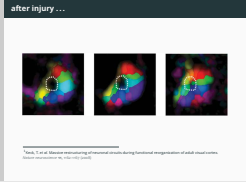

1. Then, a part of the retina is lesioned. This cuts off inputs to a part of the visual cortex, as shown in the first figure. This forms the Lesion Projection Zone (LPZ). By repeated imaging of the region over months, the reorganisation of the network is tracked.
2. Other lesion studies use similar methods: digit removal, whisker trimming, and so on—anything that cuts off projecting activity on to a set of neurons.

Our investigations: computational modelling

- We make models of small parts of the brain on computers.
- We try to replicate what biologists observe in their laboratories.

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Our model: replicates biological observations

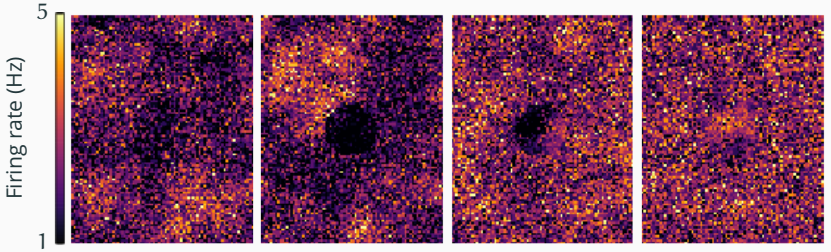

Figure 1: Our model: 1000 neurons. Simulation duration: 7 days on the cluster with 128 CPU nodes.

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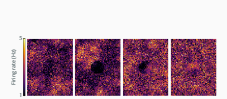

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