Continual learning in Neuroscience

What modifications reflect learning in a biological neural network ?

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- The brain is an ensemble of complex and dynamical processes that we study using imperfect tools and without any baseline as to what we are suppose to look for.
- The information we gather is incomplete, messy because of noise and unknown factors, and we only get to tiny little pieces with every experiments.

Learning in the brain

or our best approximation of how the brain encode information

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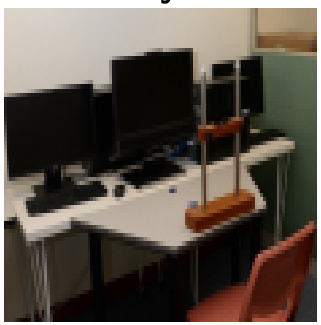
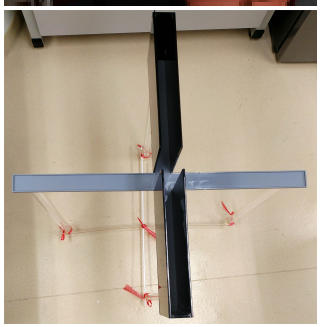
$\Rightarrow$ The challenge is to reconcile all of these levels and come up with a coherent view that can integrate informations from multitude sources.

Learning in the brain

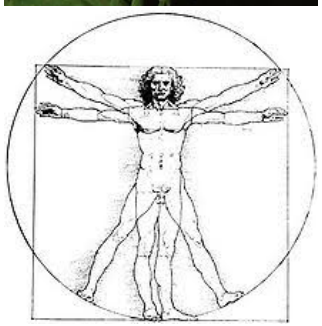
The behavioral level

Many different learning tasks and paradigms in a lot of different species







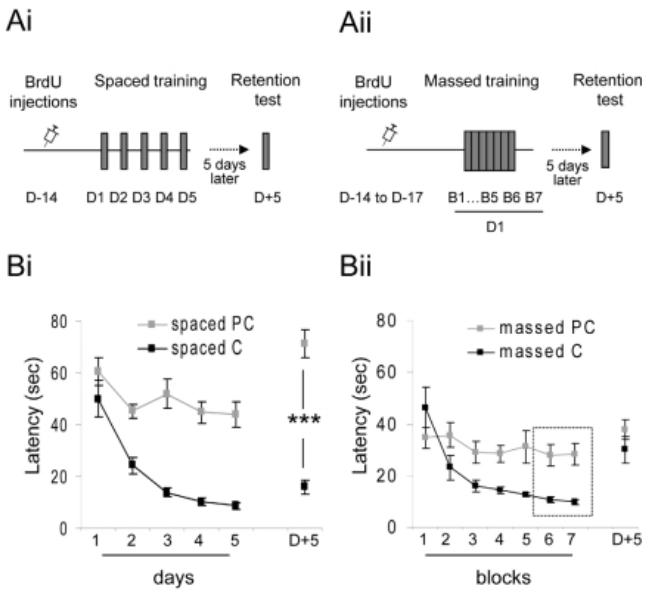



images from: https://ubsn.polyu.edu.hk/Equipment/Index and wikipedia

Learning in the brain

The behavioral level

Behavioral training can be massed or spaced which results in different memory length.



Most paradigms cannot be one-shot learned but some can: e.g. fear conditioning.

⇒ Depending on what you want to look at, the choice of learning tasks is crucial.

Kermen et al. 2010

image from: https://c3v9f5e2.stackpathcdn.com/wp-content/uploads/2017/05/fear-conditioning-maze.png

Learning in the brain

Brain structures and their interactions

Memories don't necessarily reside in the same brain region forever.

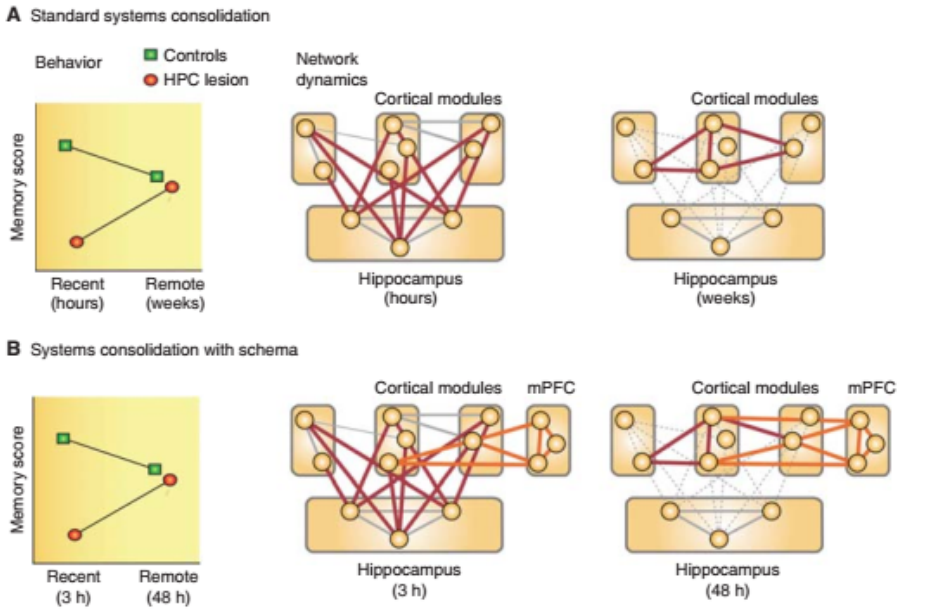


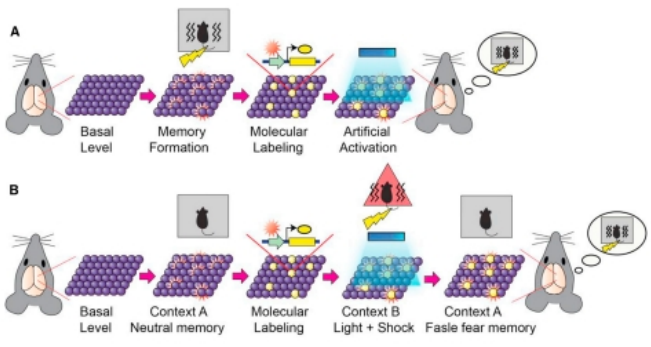
Figure 3. Hypothetical models of hippocampal–neocortical interactions during memory consolidation. (*A*) The standard model supposes that information is stored simultaneously in the hippocampus and in multiple cortical modules during learning and that, after learning, the hippocampal formation guides a process by which cortical modules are gradually bound together over time. This process is considered to be slow, occurring across weeks, months, or even longer (based on Frankland and Bontempi 2005). (*B*) In situations in which prior knowledge is available and, thus, cortical modules are already connected at the start of learning, a similar hippocampal–neocortical-binding process takes place. However, this process may involve the assimilation of new information into an existing "schema" rather than the slower process of creating intercortical connectivity (based on van Kesteren et al. 2012). HPC, hippocampus; mPFC, medial prefrontal cortex.

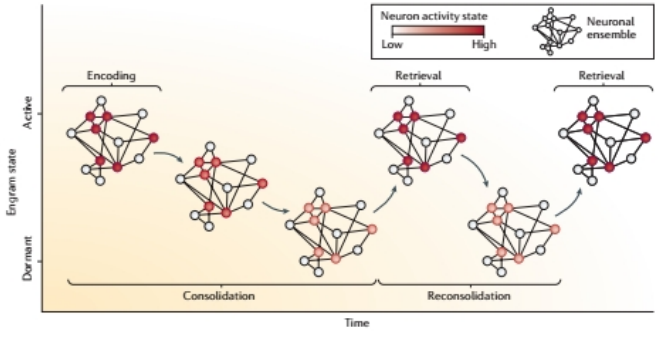
Squire et al. 2015

Learning in the brain

Neuronal populations

The brain has a higly sparse activity.
When encoding memories only specific subpopulations of neurons endure long-lasting physical and chemical changes : they constitute the memory engram = the physical substrate of a specific memory.



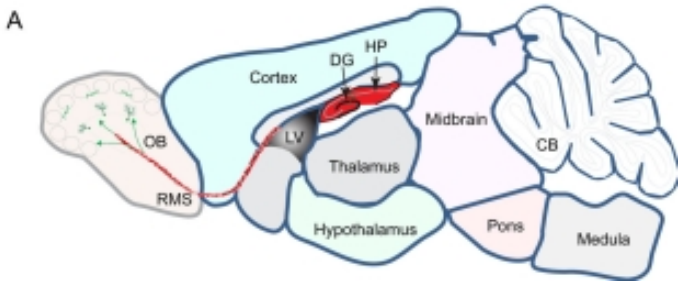


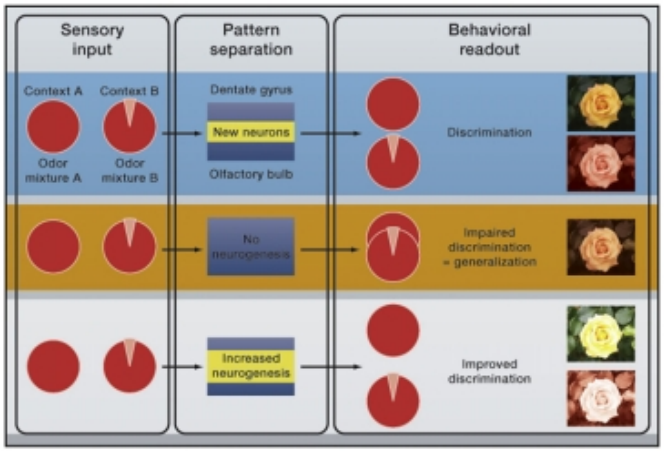
Tonegawa et al. 2015
Josselyn et al. 2015

Learning in the brain

Neuronal populations

In some specific neuronal regions things are even more complex with new neurons being constantly created de-novo: it's a process called adult-neurogenesis. These neurons integrate a pre-existing circuit without destabilizing it.





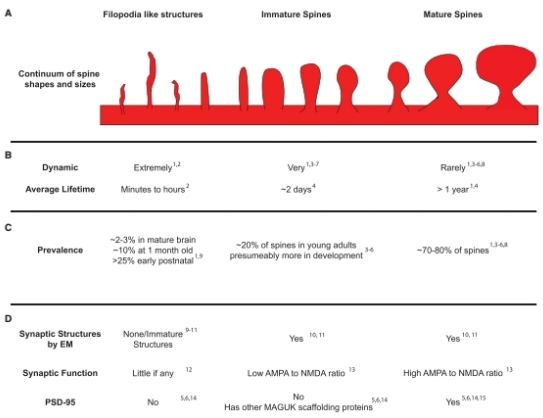
Ming and Song 2011
Sahay et al. 2011

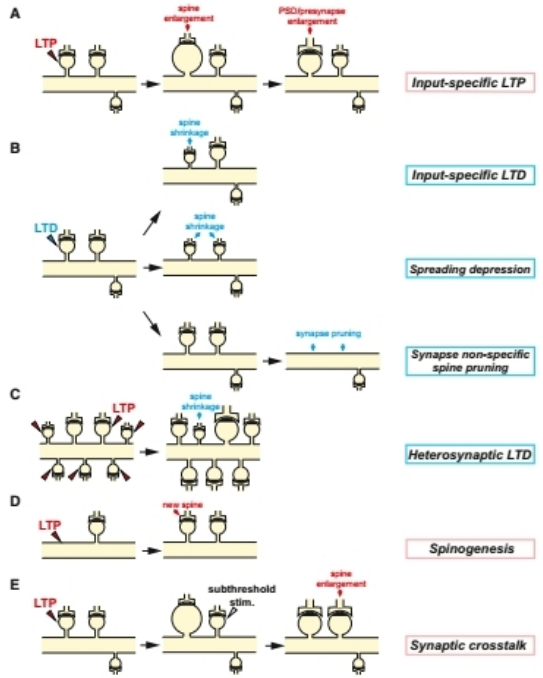
Learning in the brain

Neurons and both their functional and structural modifications

Structural plasticity

Neurons have a highly dynamic structures, notably at the dendritic spines level (however not exclusively!)





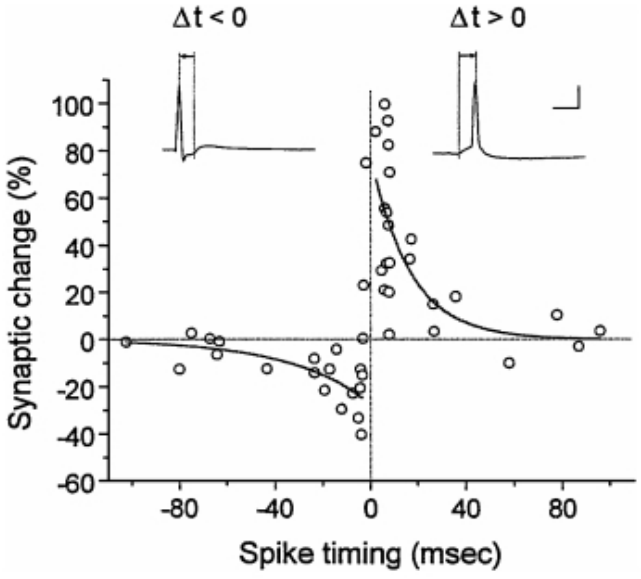
Nishiyama and Yasuda 2015
Berry and Nevidi 2017

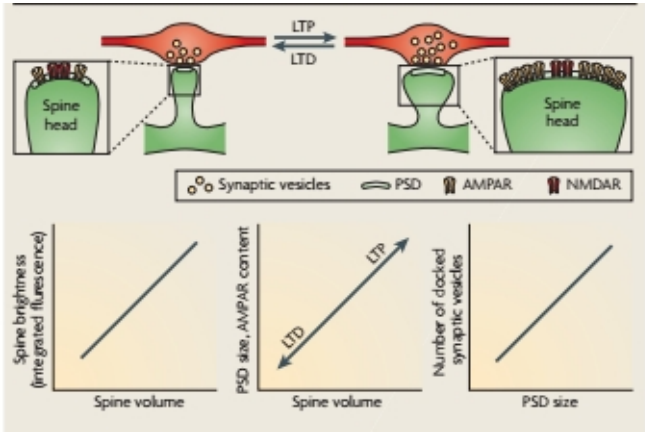
Learning in the brain

Neurons and both their functional and structural modifications

Functional modifications

Hebbian plasticity i.e. long-term potentiation and long-term depression are biological ways of increasing or decreasing synaptic strengh.





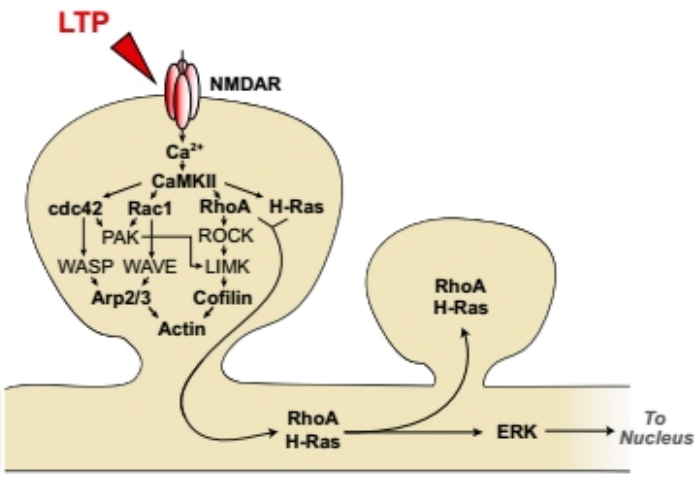
Bi and Poo 2001
Holtmaat and Scoboda 2009

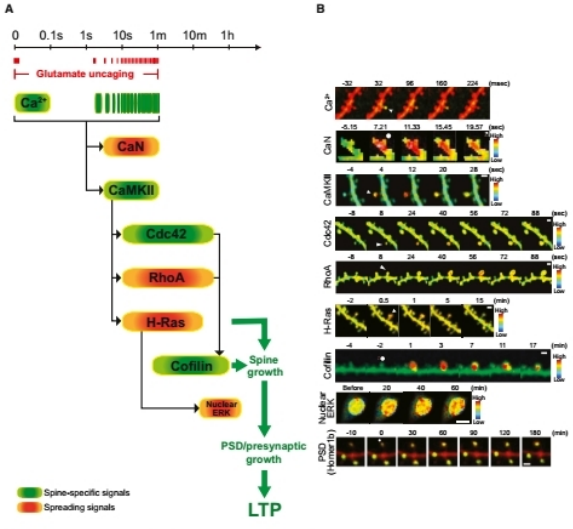
Learning in the brain

Molecular pathways and protein modifications

Cascade of activation and synapse complexity

These functional modifications are underlined by untertwined molecular cascade of vast complexities.





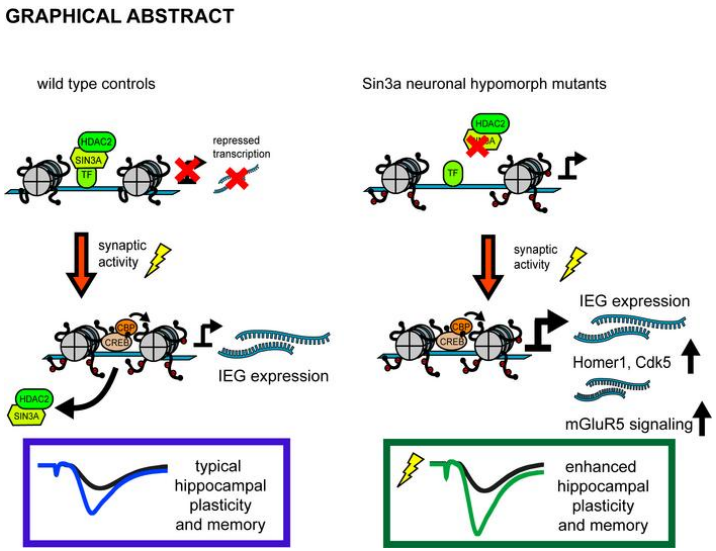
Nishiyama and Yasuda 2015

Learning in the brain

Molecular pathways and protein modifications

Gene activation

Which can have more or less long-lasting changes depending on the up- or downregulation of downstream genes



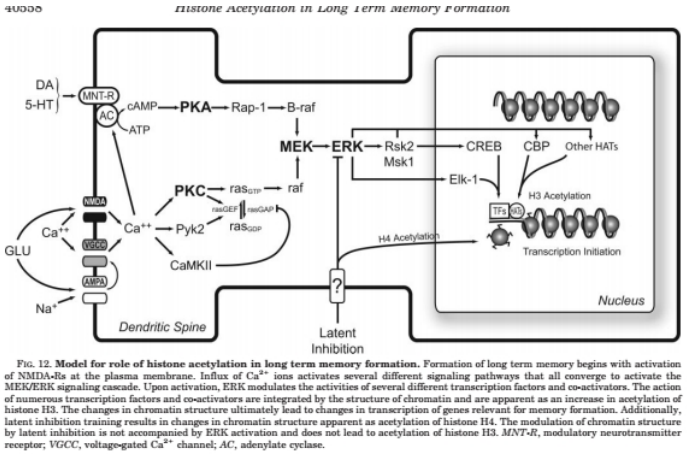


FIG. 12. **Model for role of histone acetylation in long term memory formation.** Formation of long term memory begins with activation of NMDA-Rs at the plasma membrane. Influx of Ca^{2+} ions activates several different signaling pathways that all converge to activate the MEK/ERK signaling cascade. Upon activation, ERK modulates the activities of several different transcription factors and co-activators. The action of numerous transcription factors and co-activators are integrated by the structure of chromatin and are apparent as an increase in acetylation of histone H3. The changes in chromatin structure ultimately lead to changes in transcription of genes relevant for memory formation. Additionally, latent inhibition training results in changes in chromatin structure apparent as acetylation of histone H4. The modulation of chromatin structure by latent inhibition is not accompanied by ERK activation and does not lead to acetylation of histone H3. *MNT-R*, modulatory neurotransmitter receptor; *VGCC*, voltage-gated Ca^{2+} channel; *AC*, adenylate cyclase.

Nishiyama and Yasuda 2015
Levenson et al. 2004

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As said before: The challenge is to reconcile all of these levels and come up with a coherent view that can integrate informations from multitude sources $\Rightarrow$ Modeling will help us refine those biological model and vice versa

Thanks for your attention!