Computational Neurobiology

Lecture 8: Plactisity and networks

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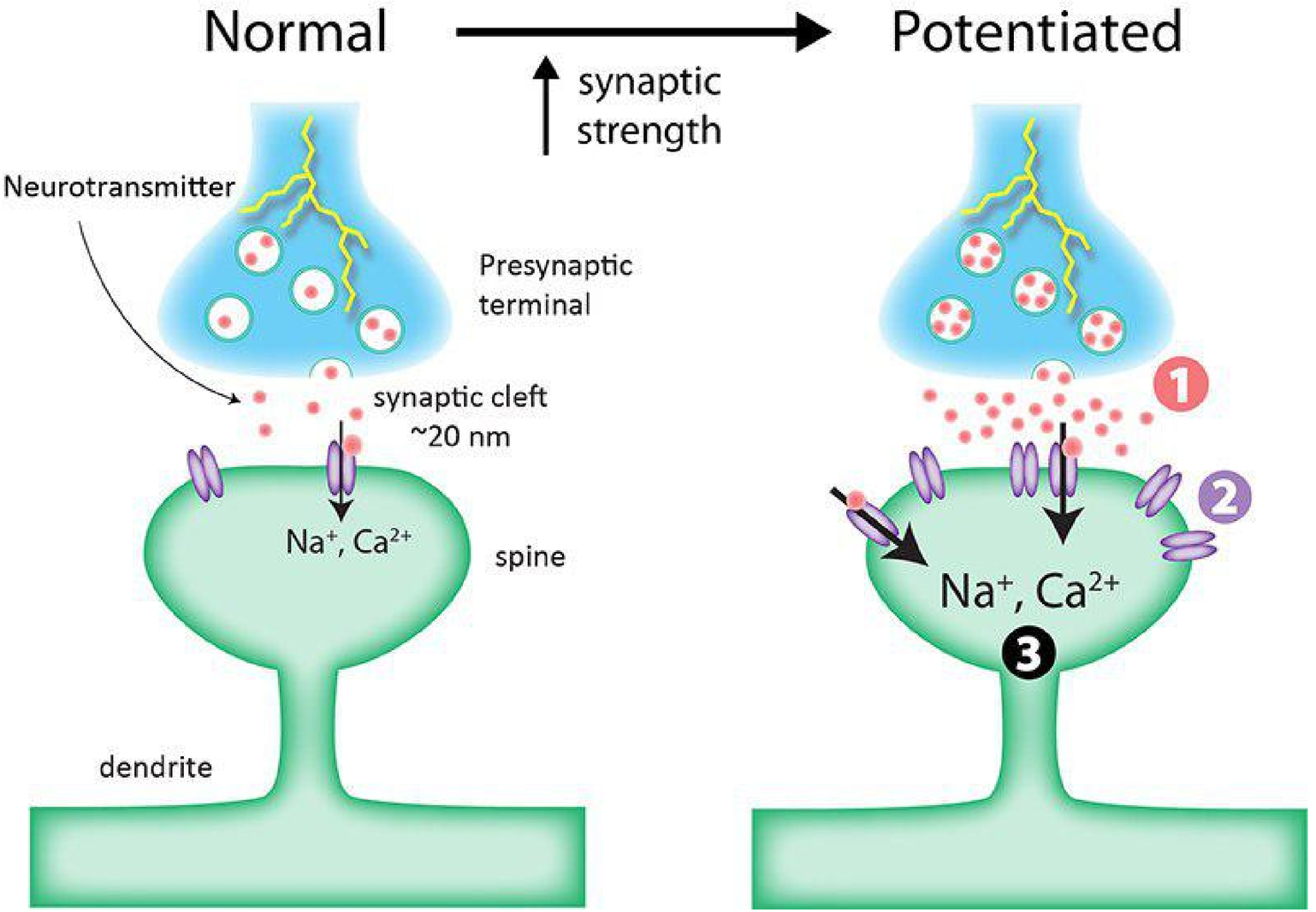
Syllabus

- Synaptic plasticity
    - Hebbian theory
    - Biological mechanisms
    - Spike-timing dependent plasticity
    - Synaptic homeostasis
- Networks
    - Biological structures
    - Firing-rate network models
    - Spiking network models

Synaptic plasticity



Hebbian theory

Postulate: **Cells that fire together, wire together**

- When two joining cells fire simultaneously, the connection between them strengthens (Hebb, 1949)
- Discovered at a biomolecular level by Lomo (1966, long-term potentiation)

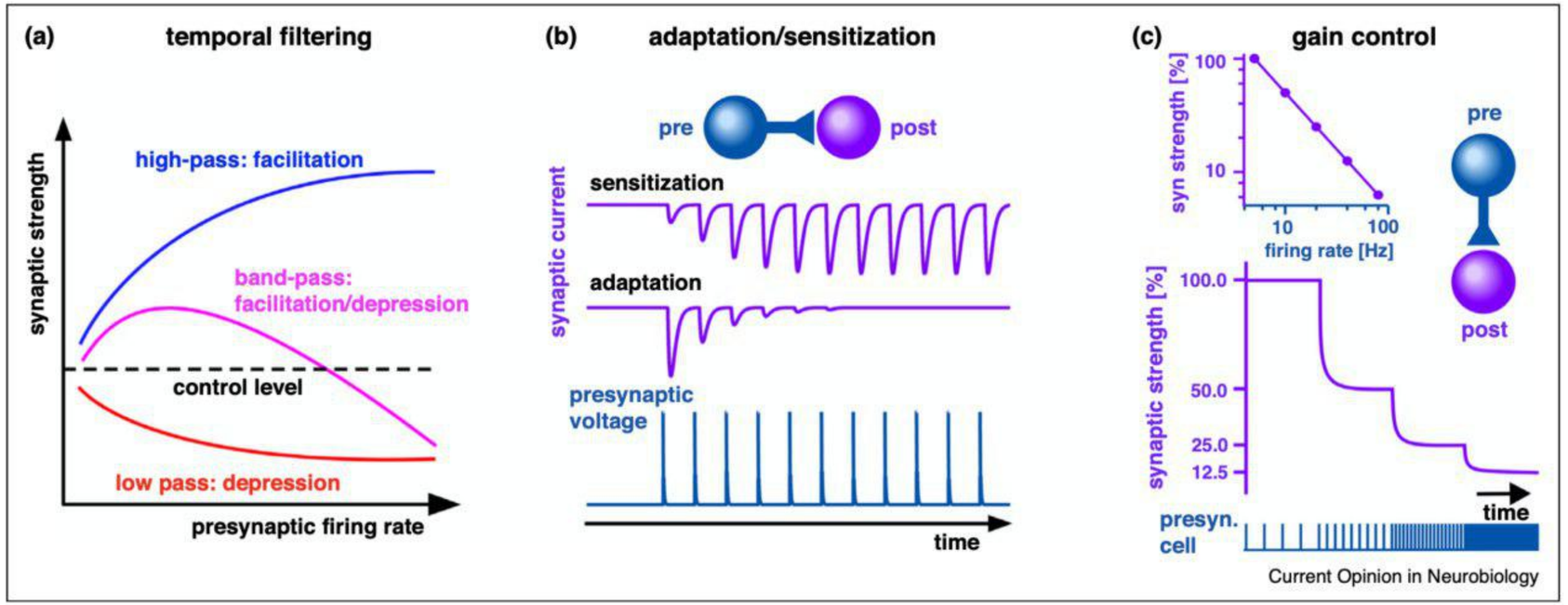
Short-term synaptic plasticity

Timescale: tens of ms - a few minutes

- **Potentiation (STP)**: increased probability of synaptic terminals releasing transmitters in response to pre-synaptic action potentials; increase in the amount of packaged transmitter released in response to each action potential.
- **Depression (STD)**: depletion of the readily releasable vesicles; post-synaptic processes; feedback activation of presynaptic receptors.

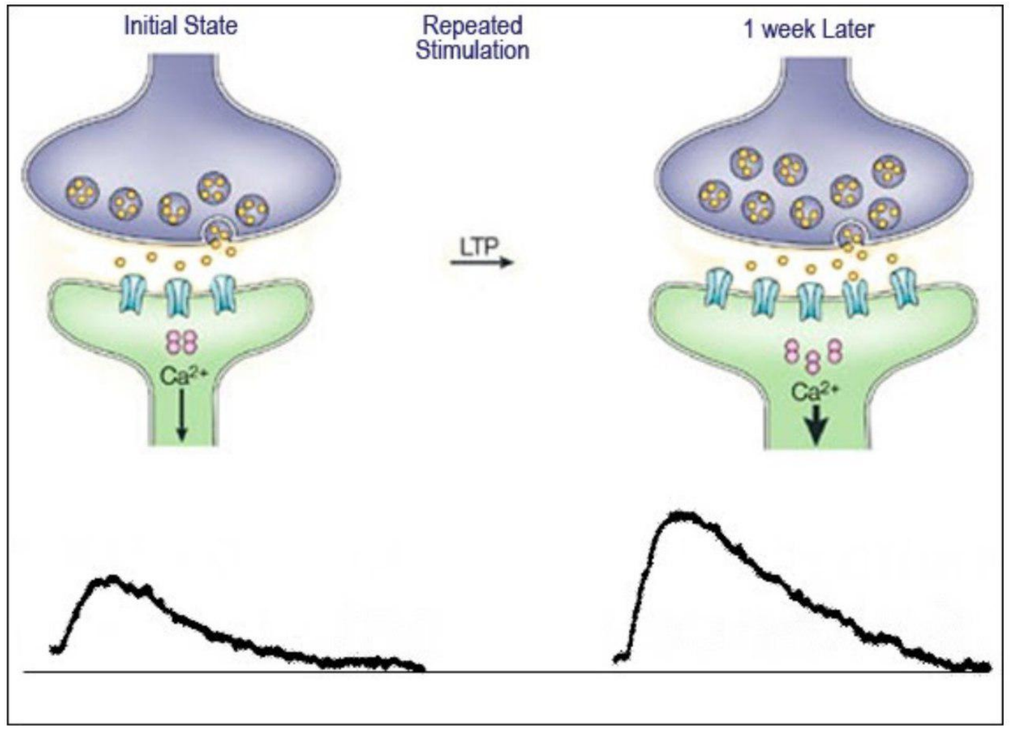
STP and STD act as dynamic control mechanisms through which a sensory system produces adaptation or sensitization.

Short-term synaptic plasticity



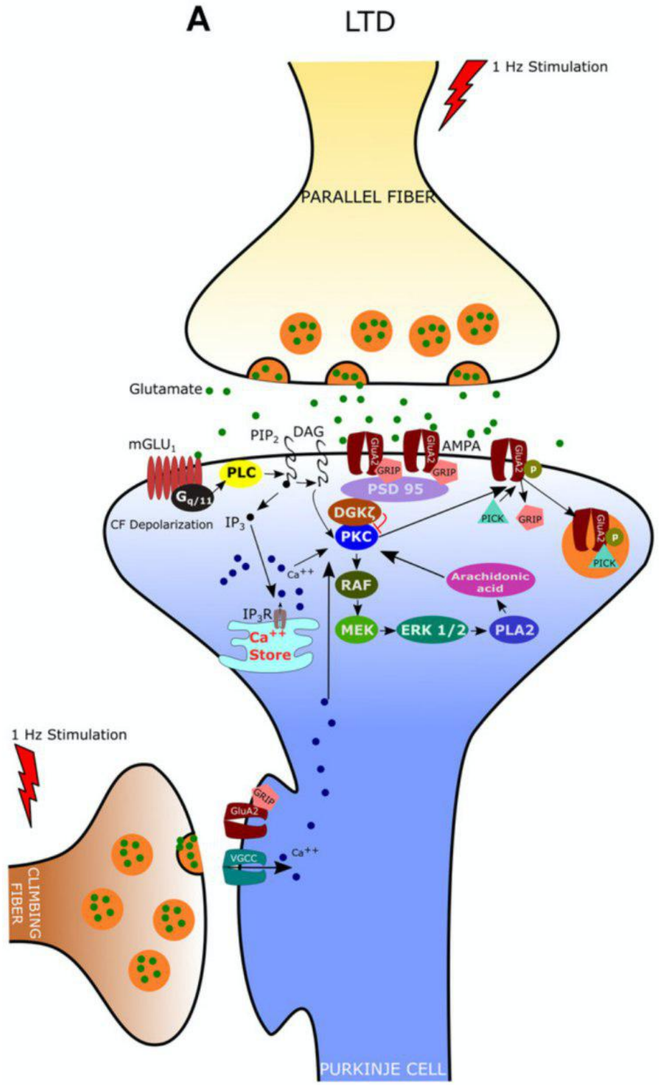
Long-term synaptic plasticity

- Long-term depression (LTD) and long-term potentiation (LTP) are two forms of long-term plasticity, lasting minutes or more. Occur in excitatory synapses.
- Synaptic plasticity can change either the amount of neurotransmitter released or the number of postsynaptic receptors available. Both have the effect of altering how much electrical current flows through the ion channels.



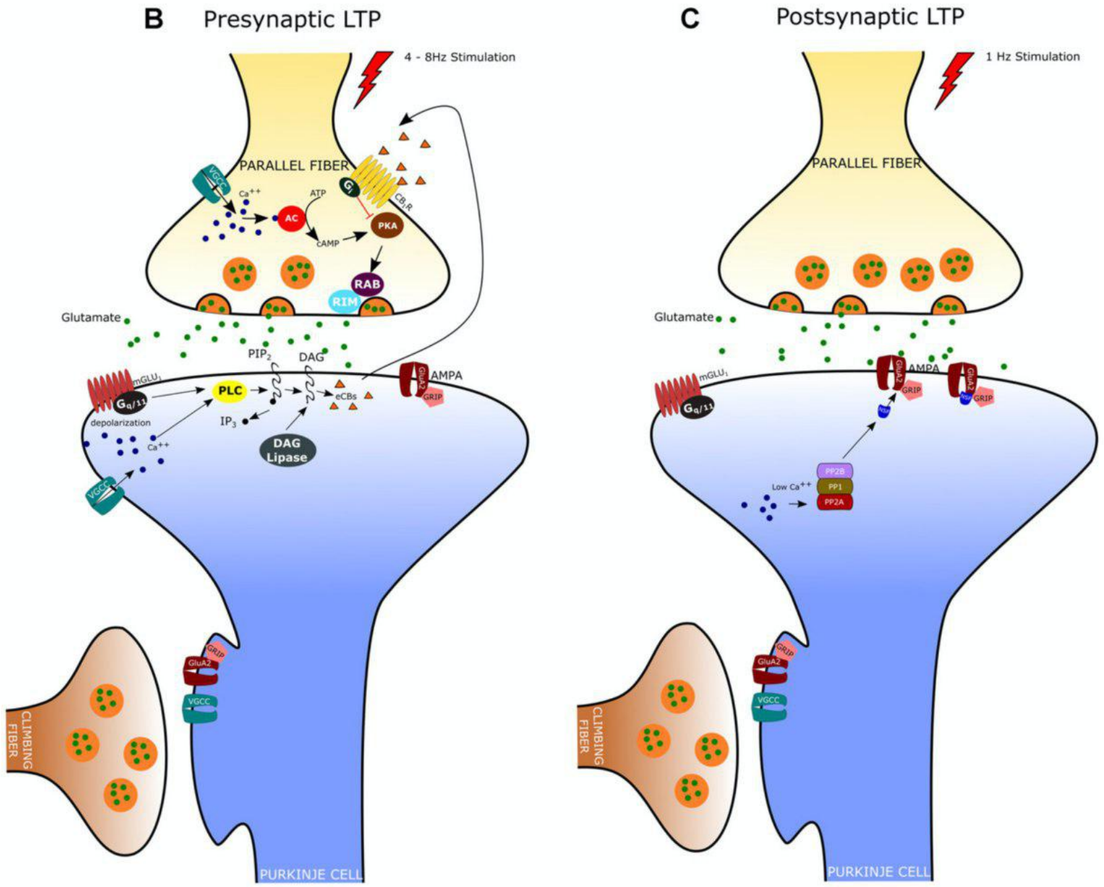
Long-term depression (LTD)

- Ca2+ entry (from EPR or from the outside) and other secondary messengers activate PKC
- PKC induces the phosphorylation of AMPA receptors, which results in the elimination of the receptor from the dendritic spines via clathrin-mediated endocytosis
- This is the key change for LTD expression since it is responsible for the reduced responsiveness to glutamate

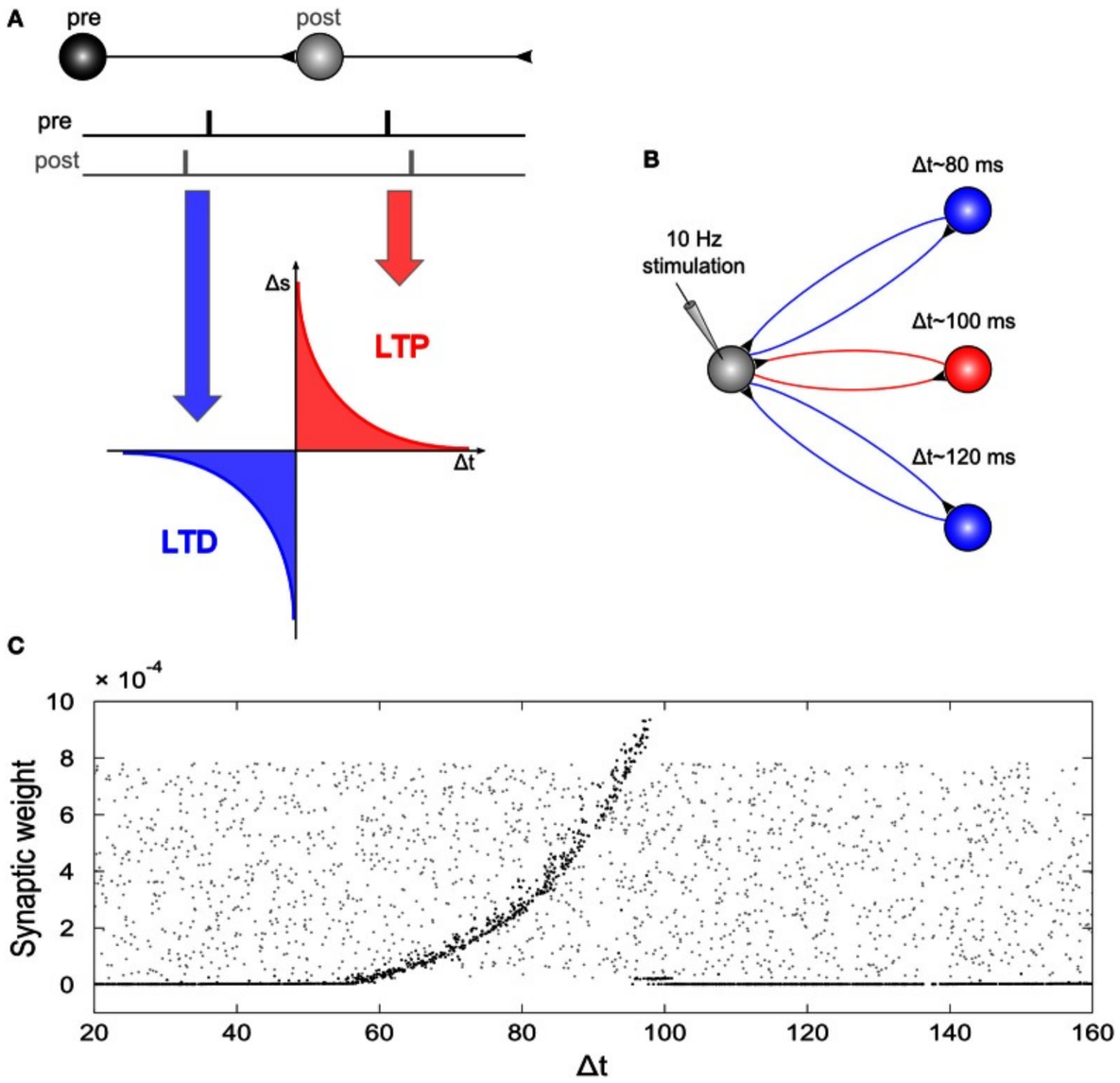


Long-term potentiaton (LTP)

- Both pre- and postsynaptic LTP can be induced by presynaptic cell stimulation at different frequencies (high vs low, respectively)
- A retrograde signaling mechanism mediated by cannabinoids regulates **presynaptic LTP**. Ca2+ and other secondary messengers also involved. Increased glutamate release is the result
- **Postsynaptic LTP**: induced by lower-freq. stimulation, depends on lower Ca2+ transients than LTD, requires activation of protein phosphatases which stabilize the AMPA receptors to the membrane



Spike-timing dependent plasticity (STDP)



Synaptic homeostasis

- Motivation for studies of homeostatic plasticity is the concern that Hebbian networks are potentially unstable because of positive feedback loops

  → There are probably additional types of plasticity, complementary to STDP, that may serve to constrain synaptic weights and/or neuronal firing

- These are collectively known as “homeostatic plasticity”

- Include schemes that control the total synaptic strength of a neuron, modulate its intrinsic excitability as a function of average activity, or make the ability of synapses to undergo Hebbian modification depend upon their history of use.

Synaptic homeostasis:

- Operates at a much slower time scale than more acute forms of plasticity, such as LTP and LTD
- Is a critical mechanism by which the cell tunes the strength of its synaptic inputs up or down
- Counteracts normal or pathological activity perturbations
- Contributes to the restoration of baseline neuronal output

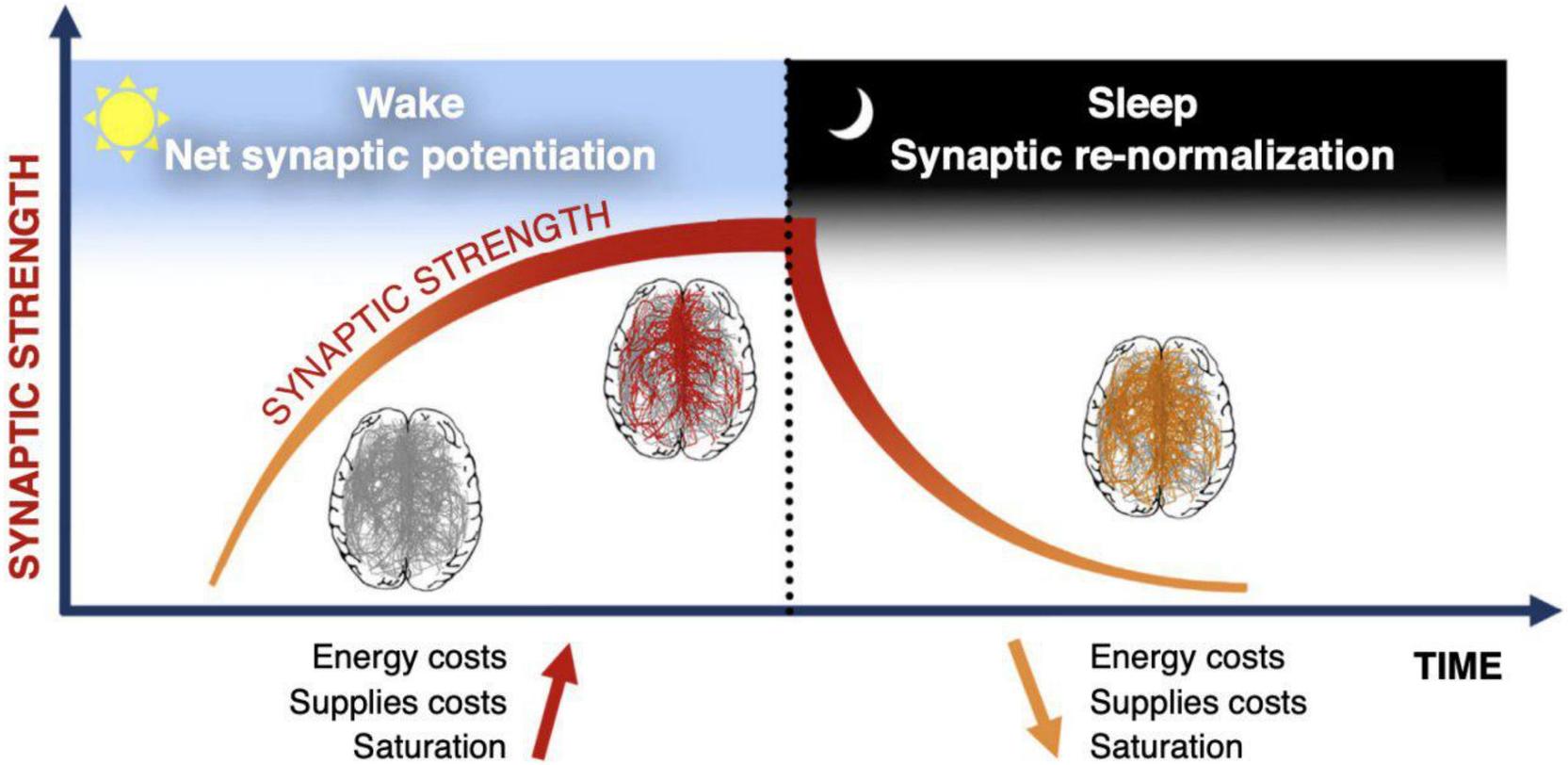
Possible mechanisms of synaptic homeostasis

- **Synaptic scaling:** directly regulates the strength of synapses
- **Homeostatic Intrinsic Plasticity:** neurons and circuits maintain appropriate levels of electrical activity through overall shifts in cellular excitability. Activity manipulation affects channel density, but also localization and gating characteristics.
- **Metaplasticity:** the capacity of synapses to undergo Hebbian modification depend upon their history of use or upon the history of neuronal activity

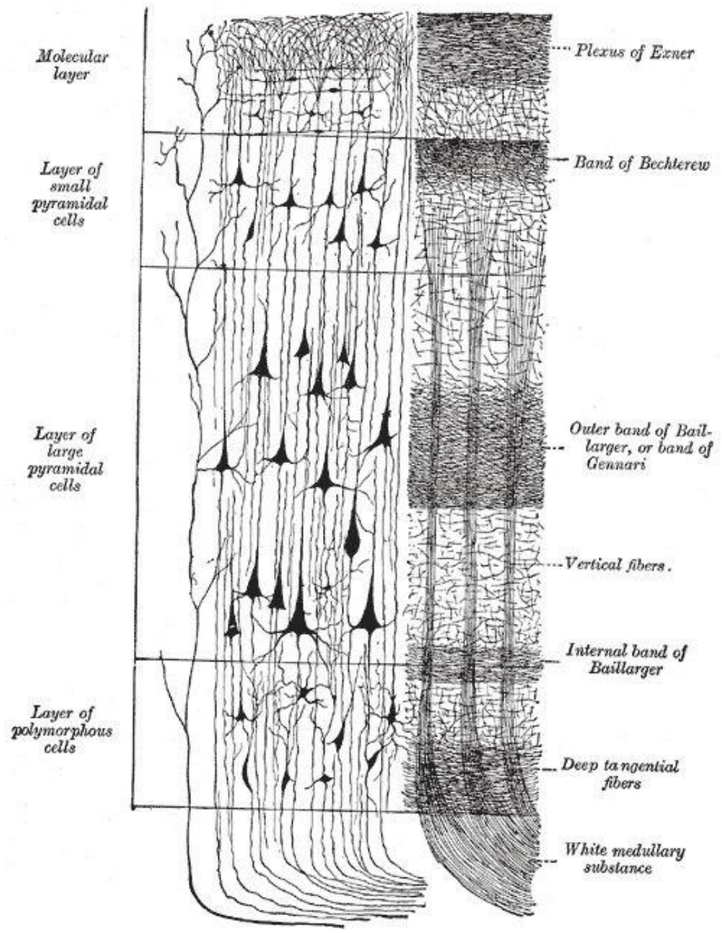
Synaptic scaling

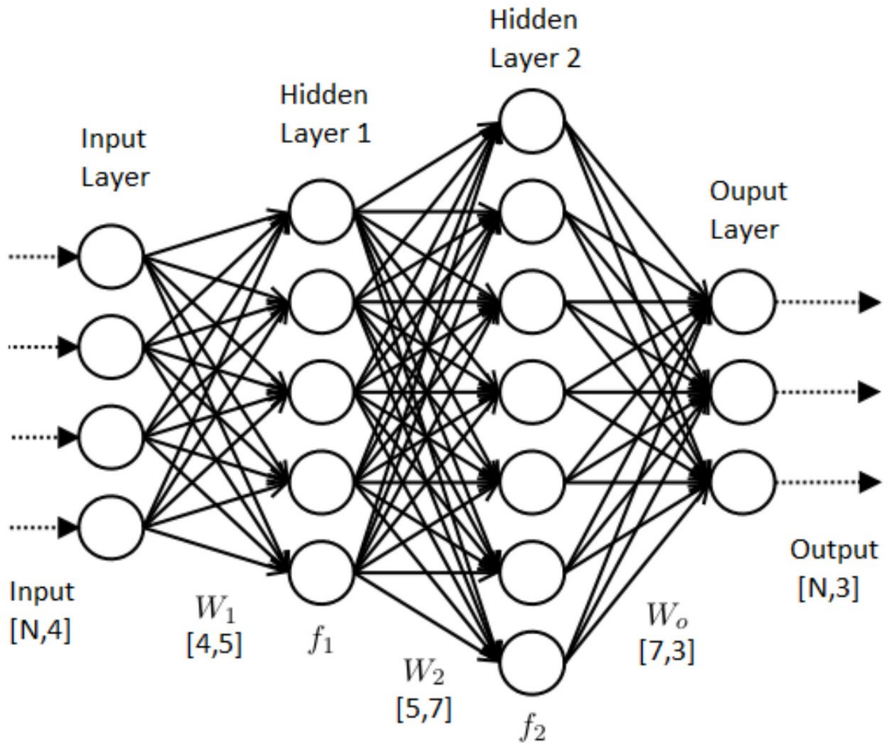
- One of the best-studied homeostatic plasticity mechanisms
- It directly regulates the strength of synapses (the same synapses that, undergoing synaptic plasticity like STDP, are likely to be among the sources of destabilization of a neuron’s firing rate)
- With scaling, a neuron can keep its synapses within some optimal size range: energetically advantageous
- Like in LTP, **calcium** acts as the signal that affects a change in AMPA receptors at synapses. Other signaling molecules also appear to be involved.
- How these signaling mechanisms interact remains to be determined

Sleep?

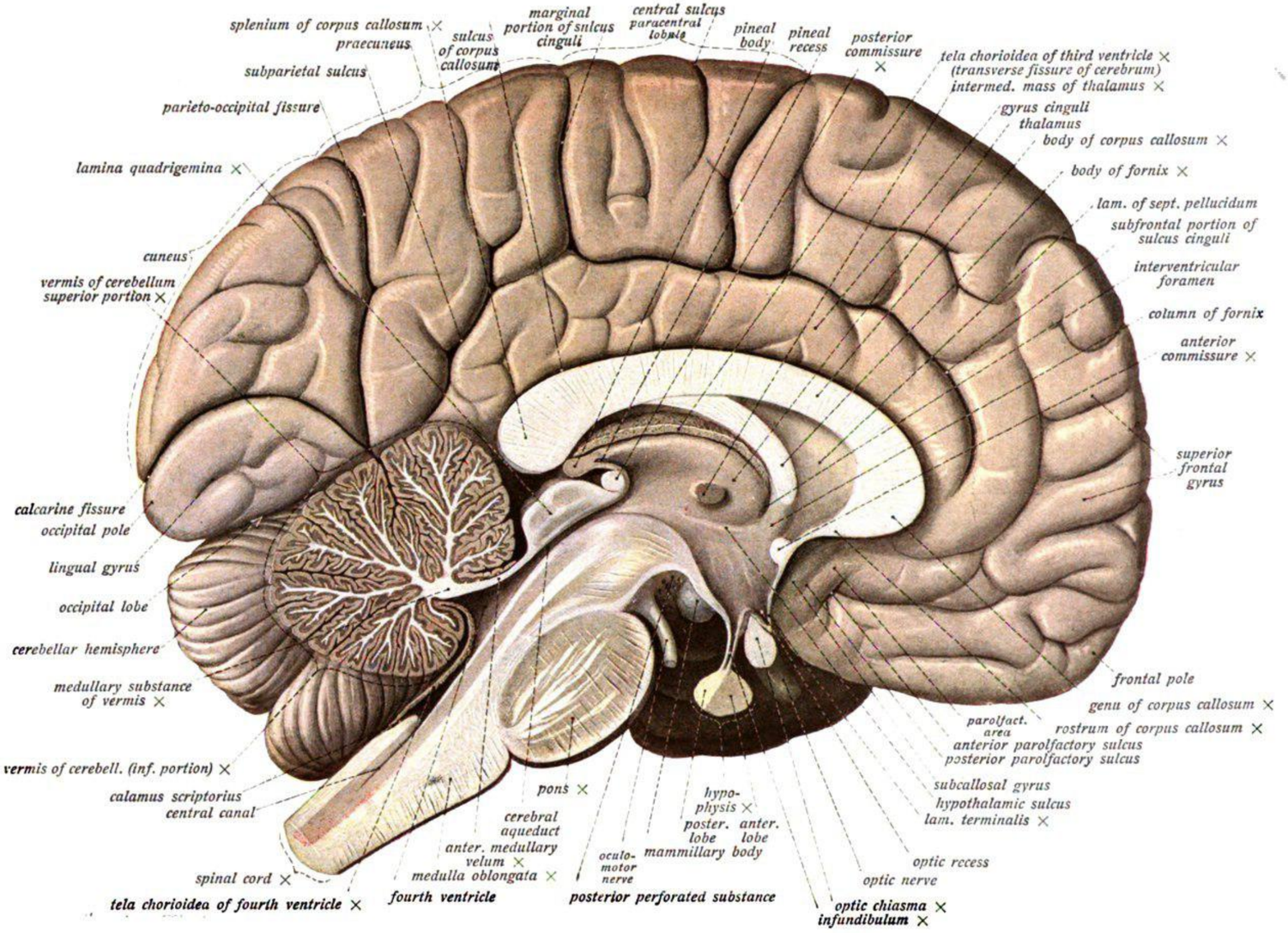

Wake
Net synaptic potentiation
Sleep
Synaptic re-normalization
SYNAPTIC STRENGTH
SYNAPTIC STRENGTH
Energy costs
Supplies costs
Saturation
Energy costs
Supplies costs
Saturation
TIME

Networks

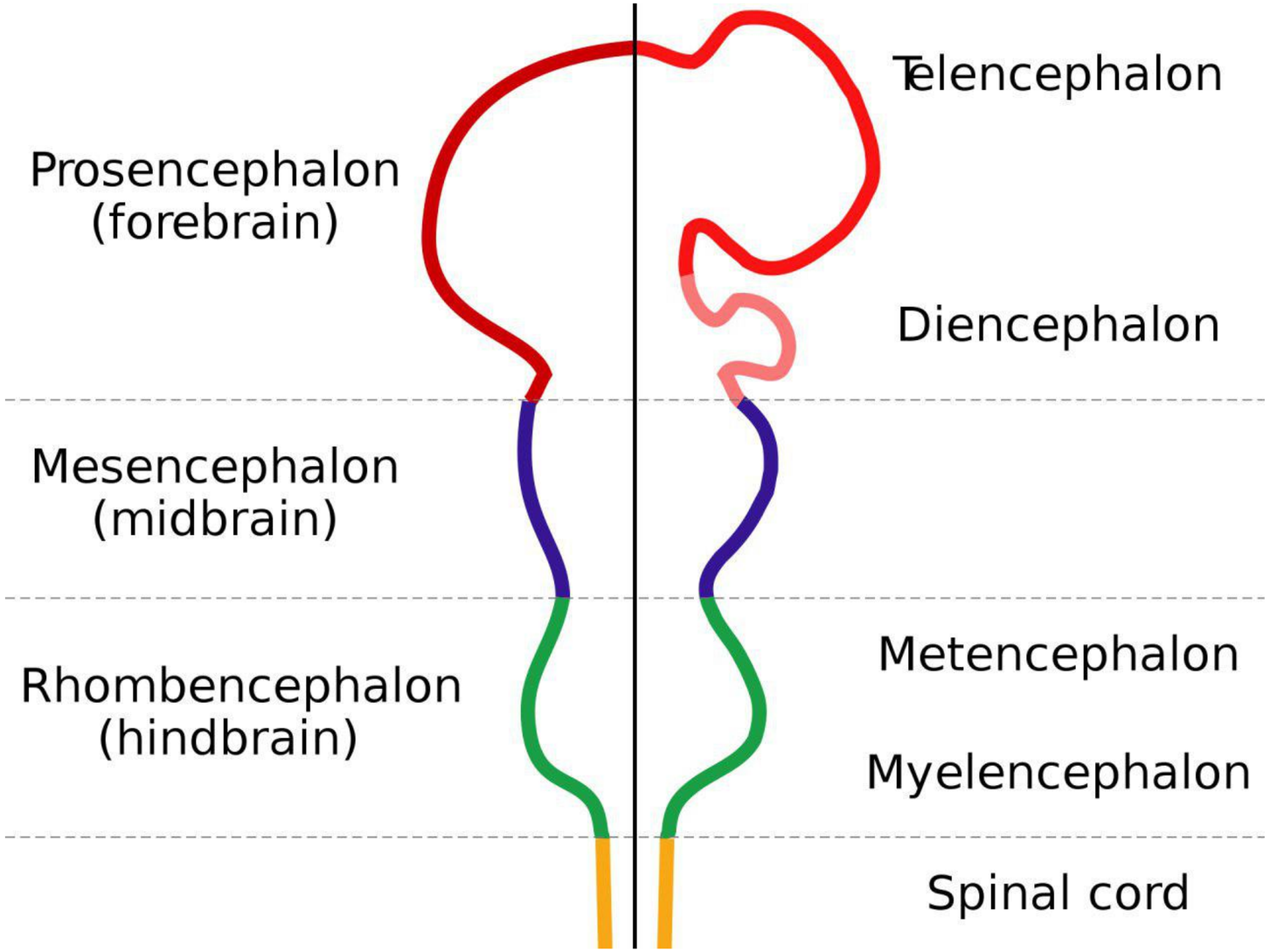

Molecular layer
Layer of small pyramidal cells
Layer of large pyramidal cells
Layer of polymorphous cells
Plexus of Exner
Band of Bechterew
Outer band of Bail-larger, or band of Gennari
Vertical fibers.
Internal band of Baillarger
Deep tangential fibers
White medullary substance


Input Layer
Hidden Layer 1
Hidden Layer 2
Ouput Layer
Input [N,4]
W_1 [4,5]
f_1
W_2 [5,7]
f_2
W_o [7,3]
Output [N,3]

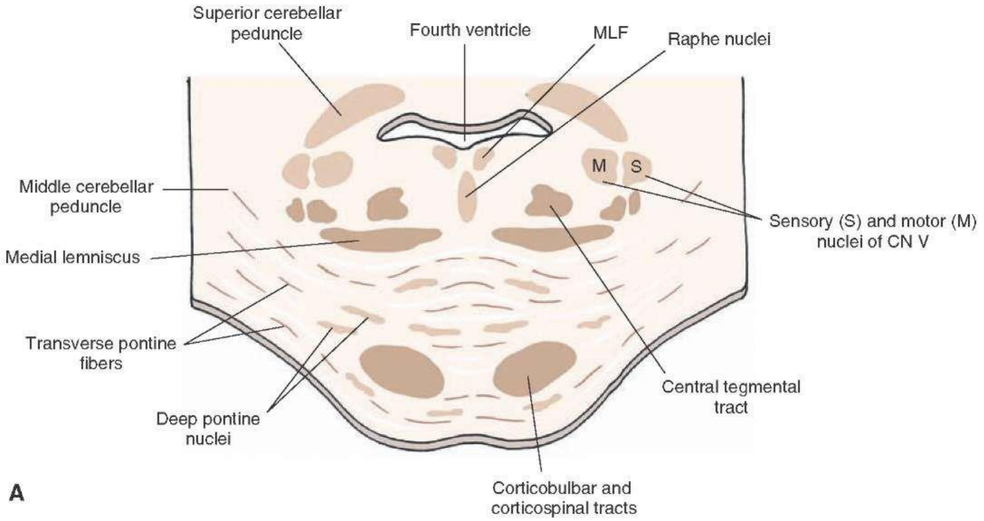
Biological structures

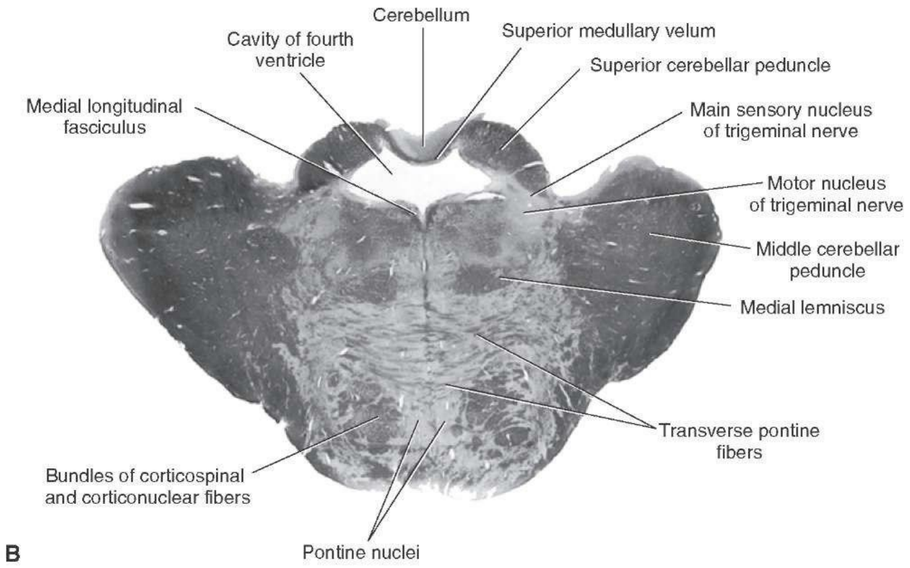


Brain development

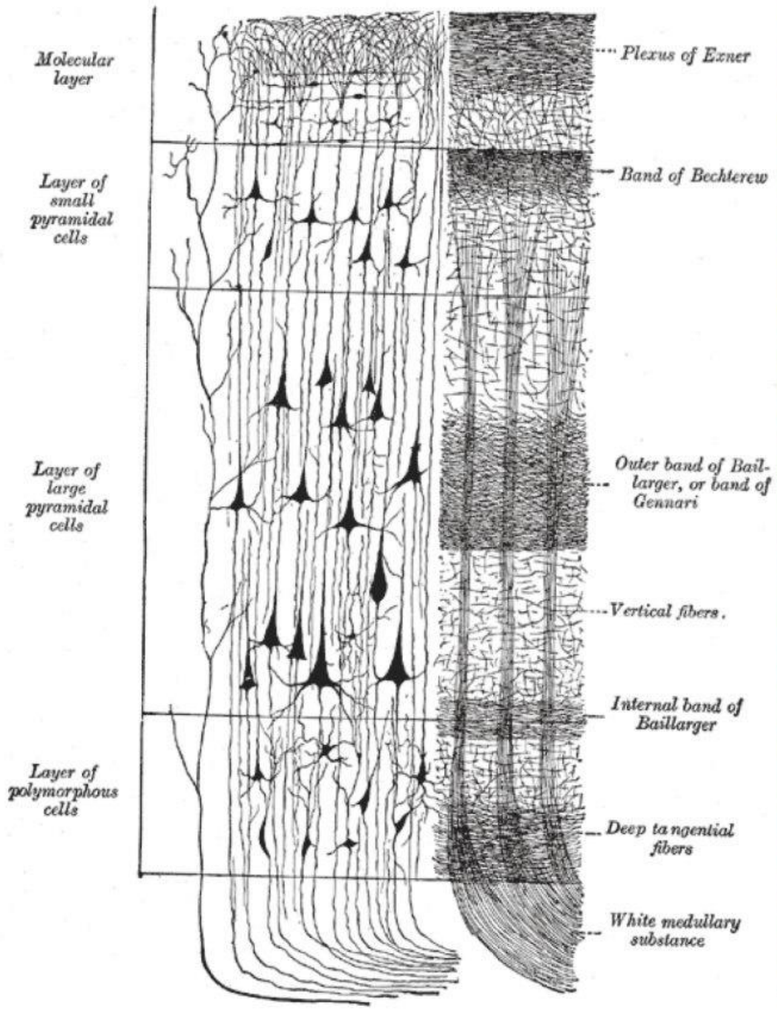


Portine nuclei





Cortex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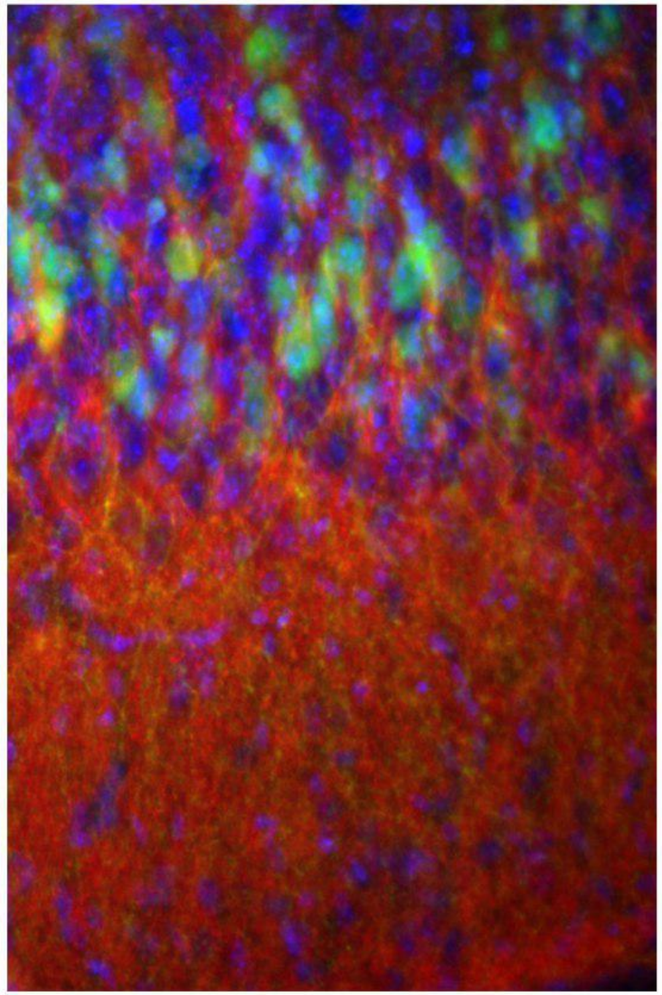


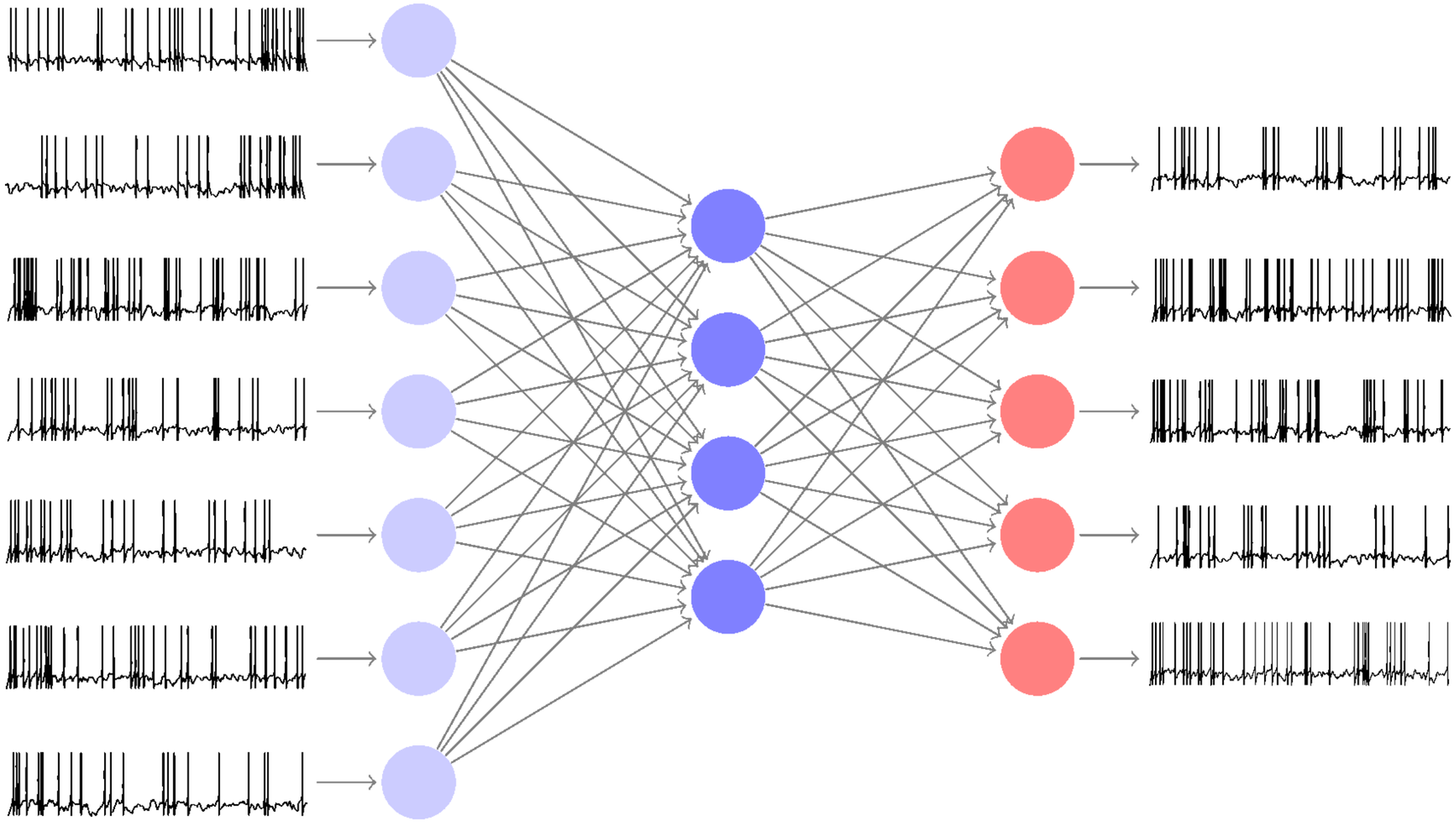
Network models

- Typical neuron in the mammalian neocortex receives thousands of synaptic inputs
- Network models allow us to explore the computational potential of such connectivity, using both analysis and simulations
- Neocortical circuits (cortical columns) are a major focus of interest
- Three main classes of interconnections within cortex
    - Feedforward (early region → late region)
    - Recurrent (interconnect neurons within a particular region, within one column and between columns)
    - Top-down (carry signals back from areas located at later stages)

Firing-rate network models

- Avoid the short time scale dynamics required to simulate action potentials
- Allow us to present analytic calculations of some aspects of network dynamics in comparison to spiking models
- Have less free parameters than spiking models
- Can be used to generate stochastic spike sequences from a deterministically computed rate
- “Averaging” units (neurons) are interconnected more densely than the individual neurons of the actual network

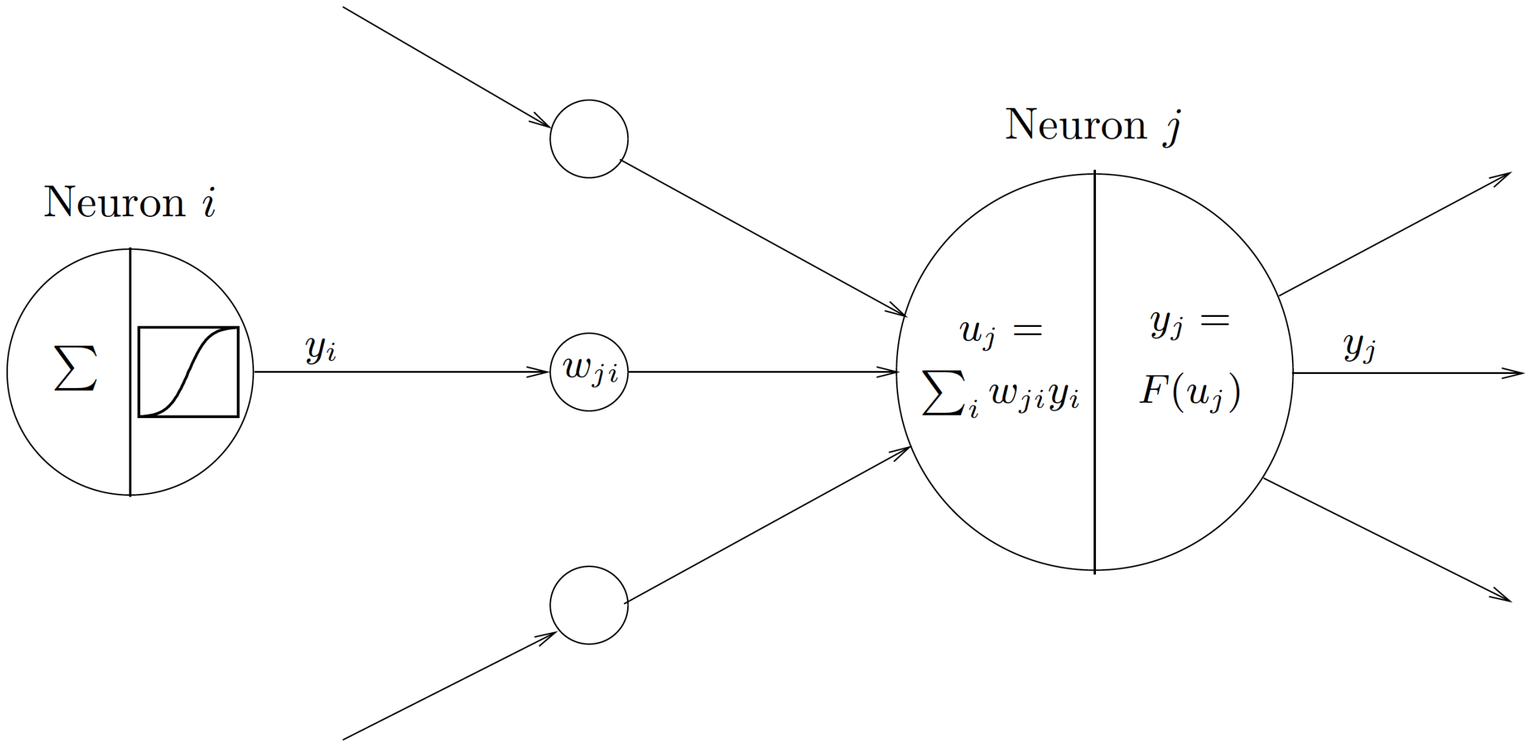
Spiking network models



Spiking neural networks (SNNs)

- Artificial neural networks that more closely mimic natural neural networks
- Incorporate the concept of time into their operating model
- Neurons in the SNN do not fire at each propagation cycle
- Fire only when a membrane potential (variable with decay in time) reaches a specific value
- When a neuron fires, it generates a signal that travels to other neurons
- Current activation level (modeled as a differential equation) is normally considered to be the neuron's state, with incoming spikes pushing this value higher, eventually either firing or decaying
- Various coding methods exist for interpreting the outgoing spike train as a real-value number, relying on either the frequency of spikes, or the interval between spikes, to encode information.

Artificial neuron model

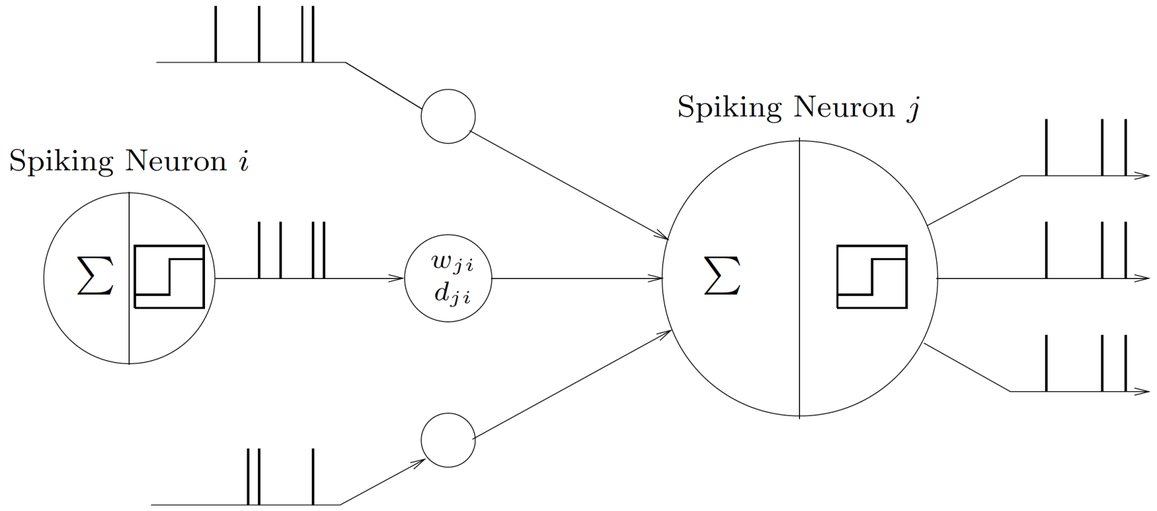


The basic operation-steps of a sigmoidal unit are summation of its input and calculating its activation. The output of neuron i is weighted by the synapse connecting the two neurons giving the weighted input $\omega_{ij} y_i$. This is summed for all inputs-neurons of neuron j to get the potential u_j. Using the sigmoidal function $F(\cdot)$ the activation y_j is calculated. The form of this function is shown in neuron i.

Spiking neuron model

- The state of spiking neuron j in the Spike Response Model (SRM) is described by its potential $u_j(t)$. When this potential crosses a certain constant threshold-value ϑ the neuron fires a spike, that is describes by its spike-time $t^{(f)}$.
- The output of neuron j is thus fully characterized by the array of spike-times:

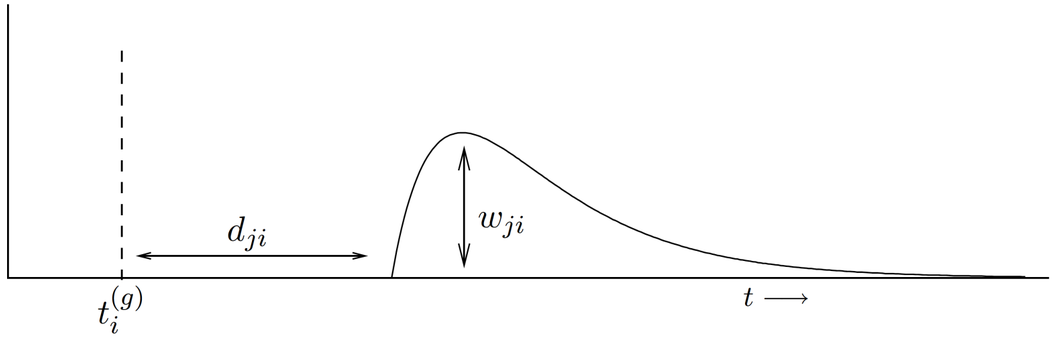
$\mathcal{F}_j = \{t_j^{(f)}; 1 \leq f \leq n\} = \{t | u_j(t) = \vartheta\}$ where the n denotes the number of spikes.



The input and output of a spiking neuron are series of firing-times called spike-trains. The firing-times are represented by vertical bars.

Potential change

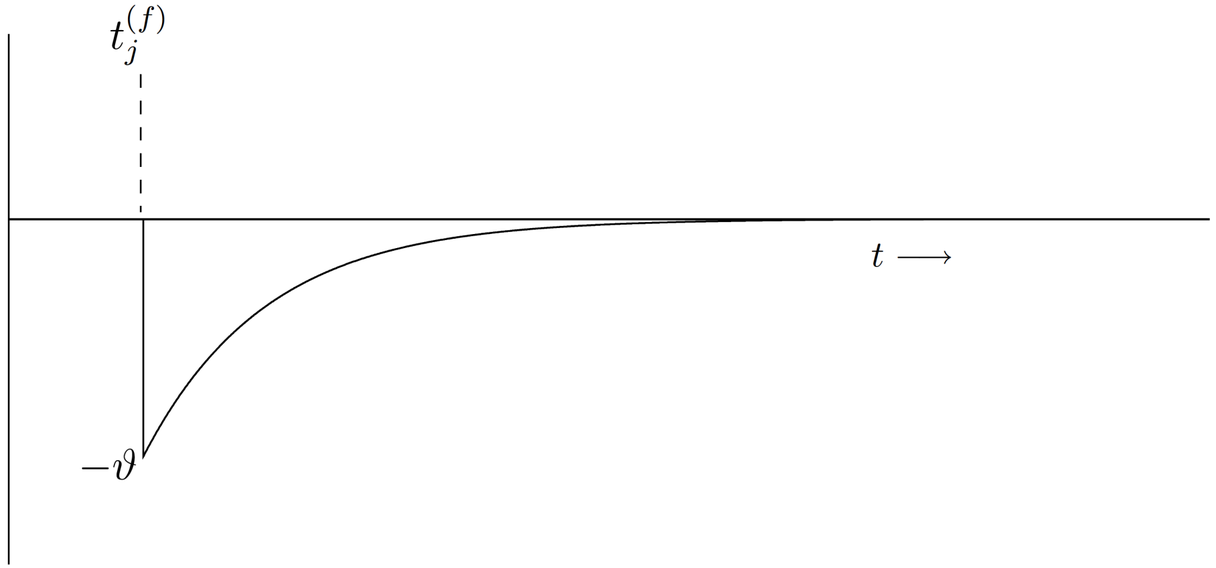
- The potential of a neuron can change due to spikes of its presynaptic neurons $i \in \Gamma_j$, where $\Gamma_j = \{i | i \text{ is presynaptic to } j\}$
- If presynaptic neuron i has fired a spike at time $t^{(g)} \in \mathcal{F}_j$ the potential of postsynaptic neuron j at time t is raised by $\omega_{ij}\varepsilon(t - t_i^{(g)} - d_{ij})$ where ω_{ij} denotes the weight of the connection and d_{ij} denotes the delay of the connection.
- The spike response function ε describes the effect the presynaptic spike has on the potential of the postsynaptic neuron.



The change in the potential of postsynaptic neuron j, given a spike of presynaptic neuron i is given by $\omega_{ij}\varepsilon(t - t_i^{(g)} - d_{ij})$. At time $t_i^{(g)}$ the presynaptic neuron i fires a spike, shown in the figure with the dashed vertical line. After the delay of the connection, d_{ij}, the spike has an effect on neuron j scaled by the weight ω_{ij}. First the potential of postsynaptic neuron j increases fast, followed by a long decay until the spike has no influence anymore.

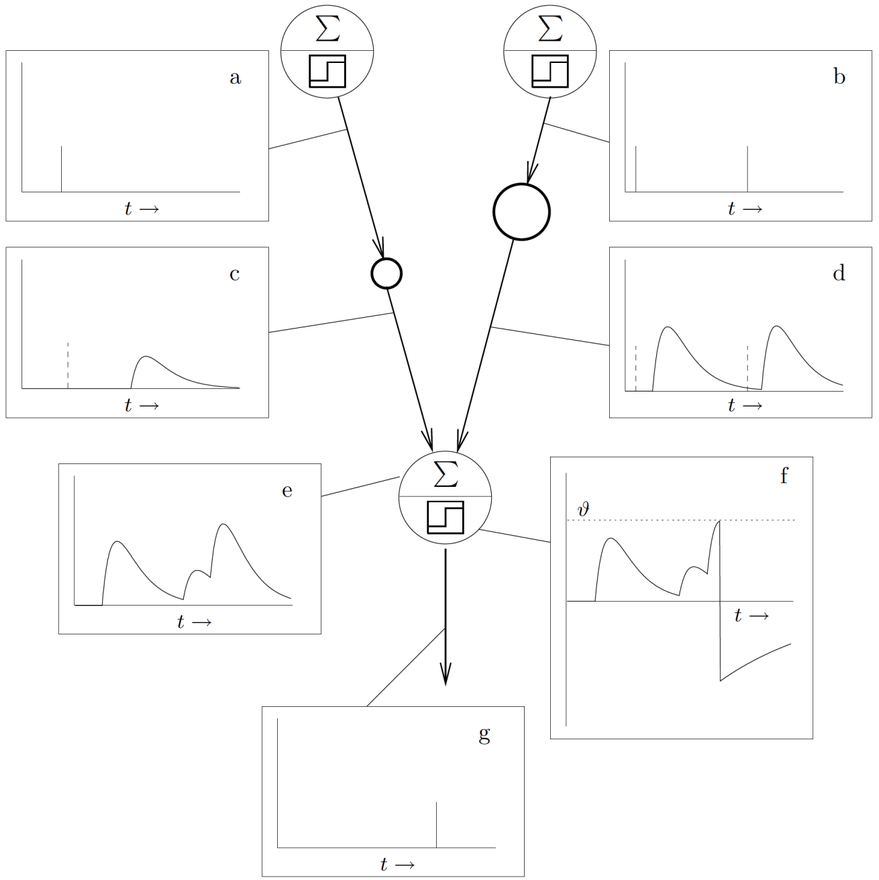
Refraction

- Modeled by the refractory function η
- If neuron j emitted a spike at $t_j^{(f)}$ its potential at t is lowered with $\eta(t - t_j^{(f)})$
- Use of a simple exponential decay



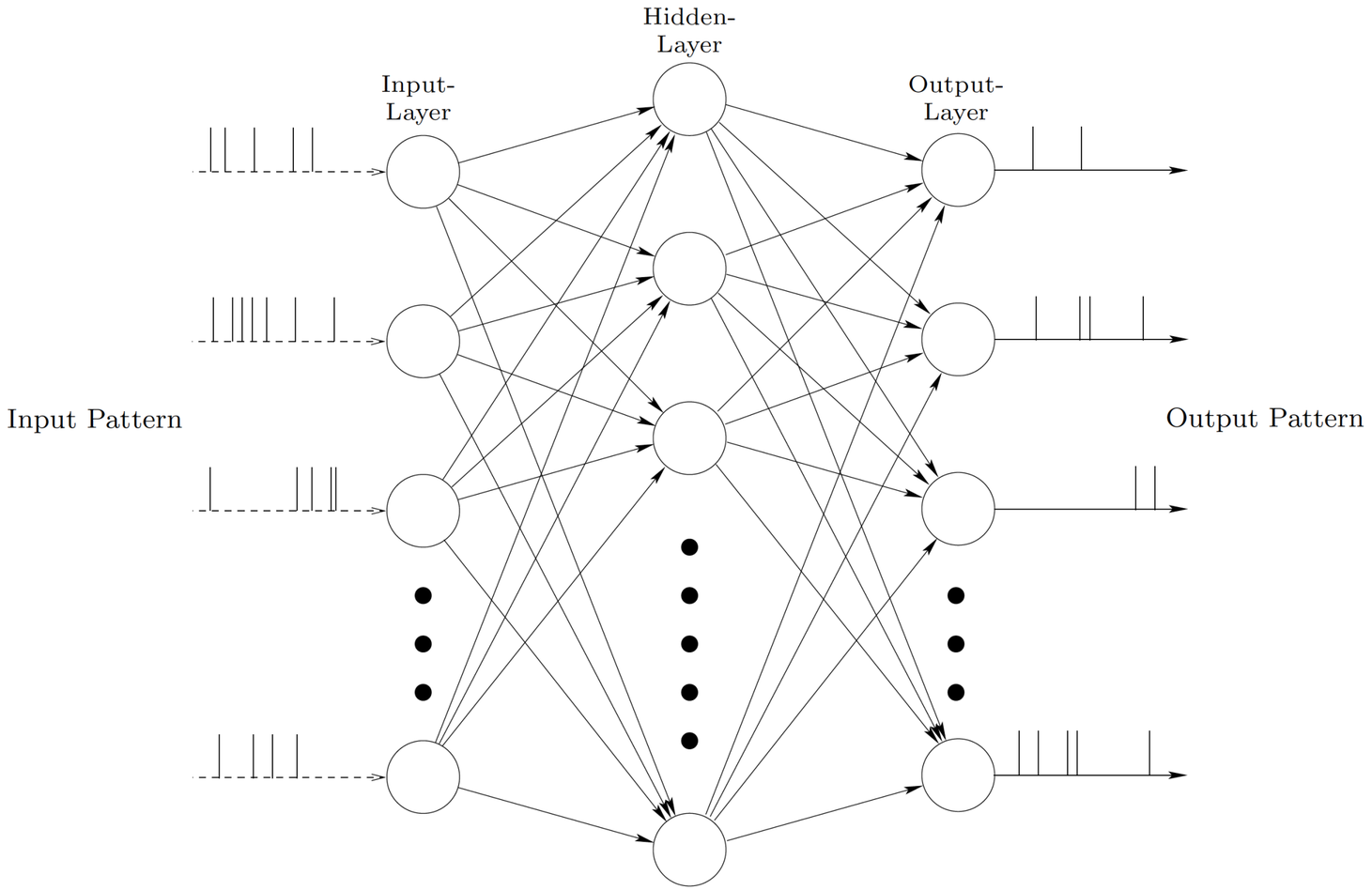
The change in the potential of neuron j given a spike is given by $\eta(t - t_j^{(f)})$. At time $t_j^{(f)}$ neuron j fires a spike, shown in the figure with the dashed vertical line. Immediately after the spike the potential of postsynaptic neuron j drops to $-\vartheta$ and then slowly recovers, followed by a long decay until the spike has no influence anymore.

Spiking neurons connections



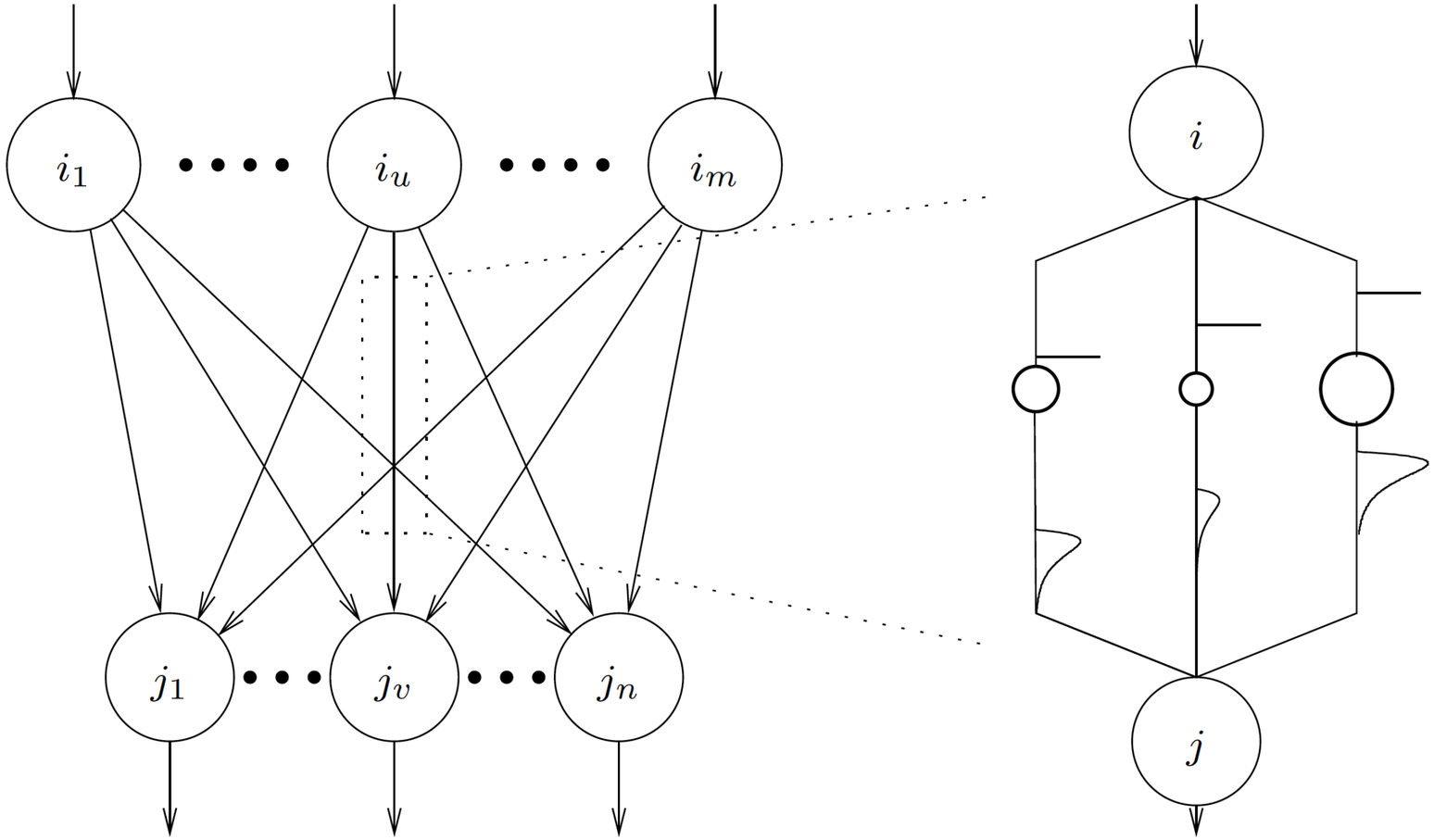
A graphical example explaining the workings of a spiking neuron. a, b: the two top neurons fire spikes, the left fires once, the right fires two times. c, d: the synapses delay and weigh the spikes and then transform them into spike responses using the ε-function; the left synapse has a larger delay then the right synapse, but a smaller weight. e: the incoming spike responses are summed to give the neurons potential. f: the potential is thresholded and because the potential crosses the threshold, the potential drops due to the refractoriness. g: the output of the neuron is a spike at the time the potential reached the threshold.

Feedforward network example



A feedforward network with one hidden layer. The neurons of the input-layer are forced to fire a certain spike-pattern shown with the dashed arrows. The spike-trains of the output-neurons form the output of the network.

Multiple delayed synapses



One connection between two neurons consists of multiple delayed synapses which all have an adjustable weight.

SNN usages

- Neuroscience
    - Modeling of the central nervous system of biological organisms (insect seeking food without prior knowledge of the environment).
    - Analysis and simulations with hypothesised topology of a biological neuronal circuit and its functions.
    - Real and simulation data comparison.
- Industry
    - Auto-associator, pattern-association, classification, clustering
    - Real-time systems
    - Biomedicine and neuroprosthetics

SNN issues

- Stable behavior
- Learning algorithms
- Sync/Async regimes

Hardware

- **SpiNNaker** (Spiking Neural Network Architecture) uses ARM processors as the building blocks of a massively parallel computing platform based on a six-layer thalamocortical model. (University of Manchester)
- **TrueNorth** is a processor that contains 5.4 billion transistors that consumes only 70 milliwatts; most processors in personal computers contain about 1.4 billion transistors and require 35 watts or more. IBM refers to the design principle behind TrueNorth as neuromorphic computing. Its primary purpose is pattern recognition. While critics say the chip isn't powerful enough, its supporters point out that this is only the first generation, and the capabilities of improved iterations will become clear. (IBM)

Links

- Olaf Booij (2004). Temporal Pattern Classification using Spiking Neural Networks (https://obooij.home.xs4all.nl/study/download/booij04Temporal.pdf).
- Mozafari, M., Kheradpisheh, S. R., Masquelier, T., Nowzari-Dalini, A., & Ganjtabesh, M. (2018). First-Spike-Based Visual Categorization Using Reward-Modulated STDP. IEEE Transactions on Neural Networks and Learning Systems (https://doi.org/10.1109/TNNLS.2018.2826721).
- Luziwei Leng, Roman Martel, Oliver Breitwieser, Ilja Bytschok, Walter Senn, Johannes Schemmel, Karlheinz Meier, Mihai A. Petrovici (2017). Spiking neurons with short-term synaptic plasticity form superior generative networks (arXiv:1709.08166 [cs.NE]).
- S.R.Kheradpisheh, etal., Bio-inspired unsupervised learning of visual features leads to robust invariant object recognition, Neurocomputing(2016), http://dx.doi.org/10.1016/j.neucom.2016.04.029