Computational Neuroscience

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Lecture 10

Topics for final exam

Centre for Cognitive Science
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Final written exam (worth 40%)

- Time allowed: **2 hours**
- No supplementary material will be provided for the examination.
- **Closed book exam**:
  - No reference books, no notes, nor other written material allowed.
- I will not ask anything that was not covered in the **theory** lectures.

Resources

- Lecture slides and selected chapters from the textbook: *Principles of Computational Modelling in Neuroscience*, by D. Sterratt, B. Graham, A. Gillies, & D. Willshaw, Cambridge Uni. Press, Cambridge, U.K., 2011.
  - Available at http://dai.fmph.uniba.sk/courses/comp-neuro/
- Scholarpedia – free encyclopedia of computational neuroscience:
  - http://www.scholarpedia.org/article/Encyclopedia_of_computational_neuroscience
- Wikipedia!
  - https://en.wikipedia.org/wiki/Main_Page

1st topic: computational modelling

- Relation between theory, model and experiment / observation
  - Theory: cause –> effect, predictions, block schemes,
  - Model: 4 steps, see the next slide
  - experiment / observation, disproval or validation.

- Why do computational modelling in neuroscience?
  - Aid to reasoning and development of new theories
  - Removal of ambiguity from existing theories
  - Testing new hypotheses / theories
  - Replacement or supplement to neuroscience experiments
  - Prediction of outcome and design of new biological experiments

Steps in creating the model

- **Step 1**: Verbally state the assumptions on which the model will be based. These assumptions should describe the relationship among the variables to be studied.
- **Step2**: Describe variables and parameters to be studied in the model.
- **Step 3**: Use the assumptions formulated in Step 1 to derive math equations relating the quantities in Step 2.
- **Step 4:** use mathematical knowledge and/or computer program to solve the equations and make predictions about the evolution of studied quantities in the future.

How do we fix the model parameter values?

- Step 1: Fix the known parameters (e.g., V_0, E_L, etc.) and make educated guesses for the remaining unknown parameter values.
- Step 2: Use the model to simulate experiments, producing model data.
- Step 3: Compare the model data with experimental data.
- Step 4: Adjust one or more parameter values and repeat from Step 2 until the simulated data sufficiently matches experimental data.
- Step 5: Use the model to simulate new experiments not used in the steps above to verify validity of the model. This may involve to find new values of some parameters.

Equation, i.e., derivative = *k* something

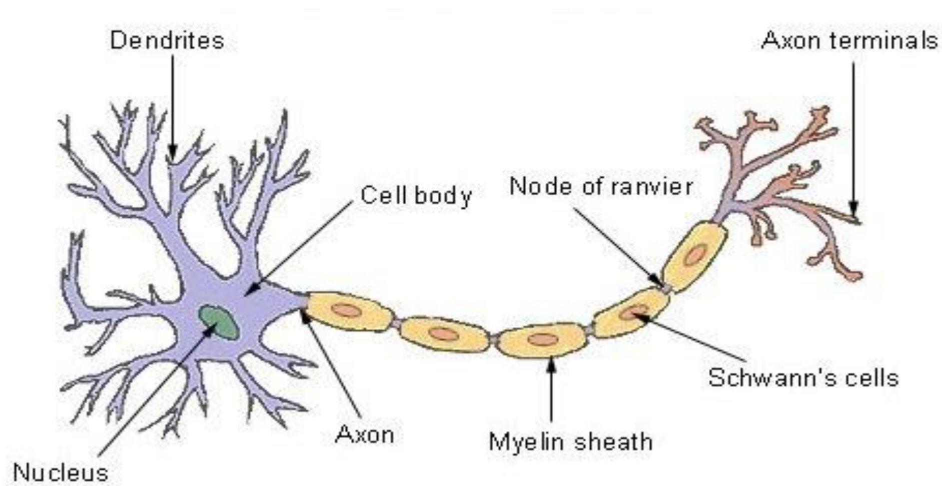
- The equation: $$\frac{d(\text{dependent variable})}{dt} = k\ \text{something}$$

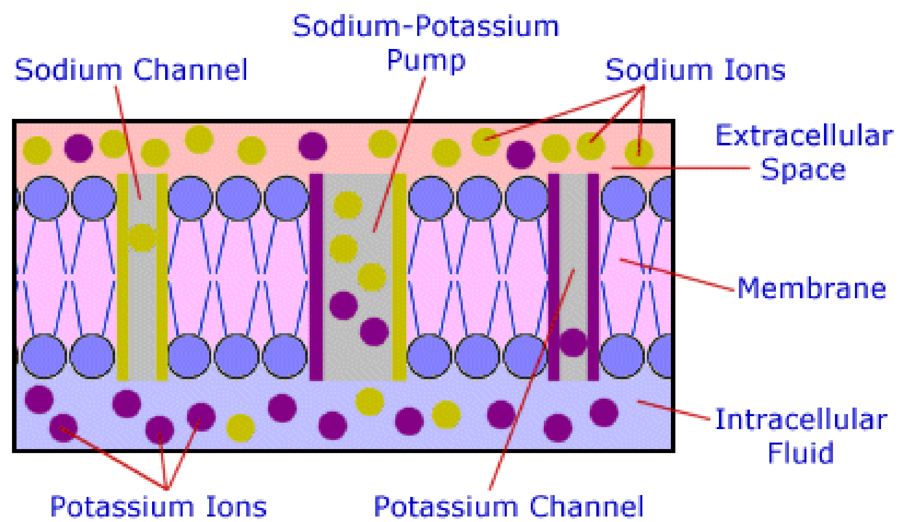
- is at the core of all models in computational neuroscience.

- Dependent variable can be anything from
  - Voltage or electric current,
  - number of synapses,
  - concentration of neurotransmitter,
  - number of ion channels or receptors, etc.

Neuronal membrane and its function

- Parts of a neuron, composition of the membrane in these different parts, function of axon, dendrites, synapses.
- Which types of proteins and what's their function?
- Which factors affect the movement of ions across the membrane?
- Explain voltage-gated, ligand-gated, equilibrium potential, resting potential, and such.





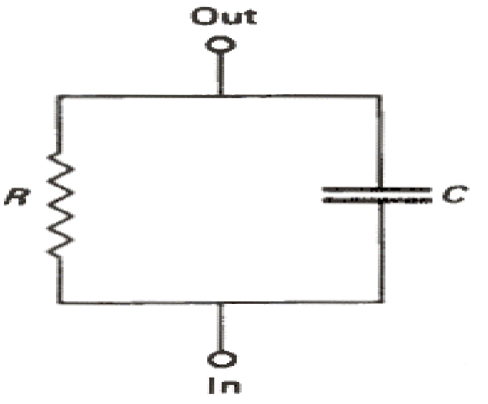
Explain variables in the given equation

$$i_m = g_{Na} m^3 h (V - E_{Na}) + g_K n^4 (V - E_K) + g_L (V - E_L)$$

- What this equation describes?
- What do all the variables in the equation denote?
- How do we calculate or measure them?
- Describe the four phases of generation of action potential (AP).
- Describe the propagation of AP along the axon.

Explain variables in the equation and scheme

- Explain variables in the image or scheme:



- Explain variables in the equation. What does this equation expresses?

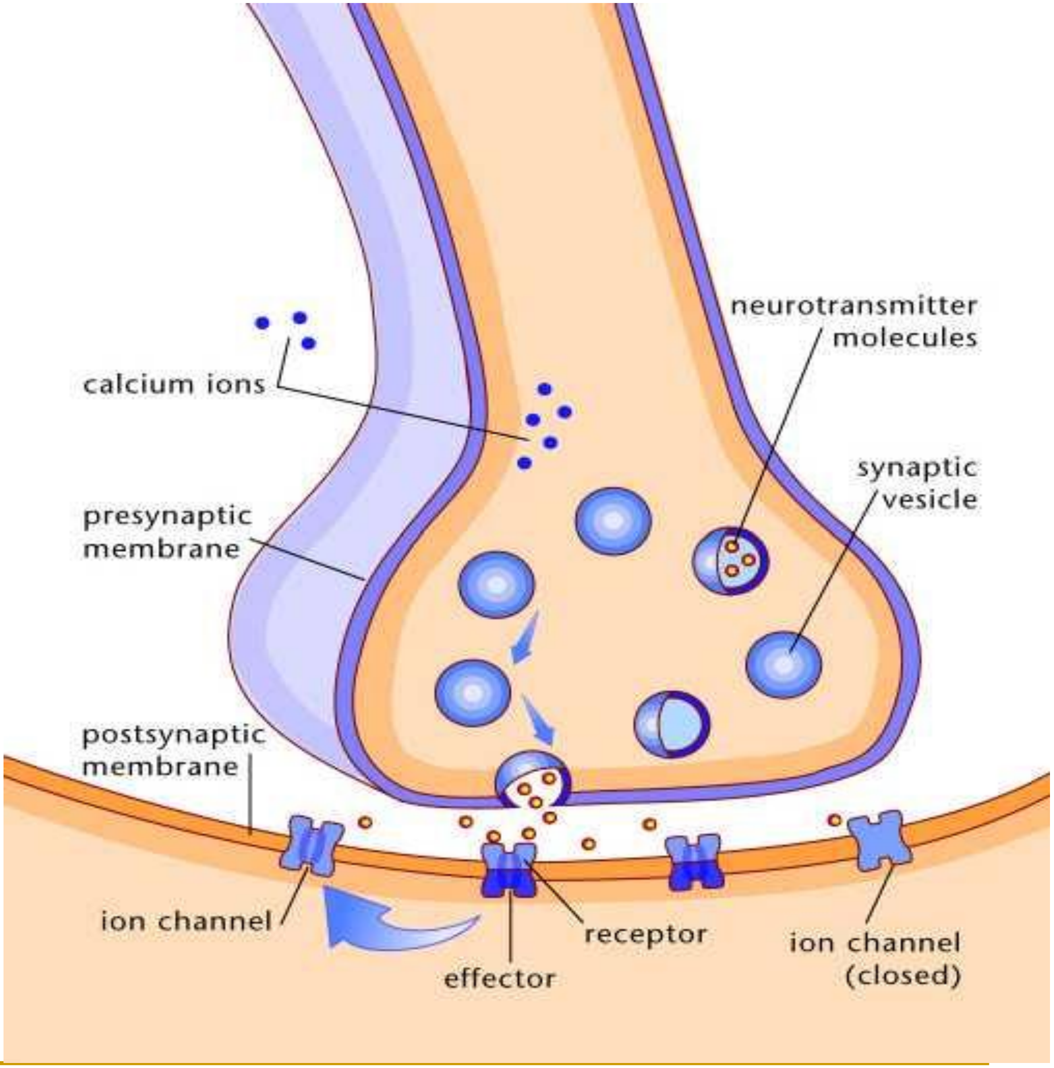
$$I_m = C_m \frac{dV}{dt} = -\frac{V}{R_m}$$

- Explain variables in the equation. What is this equation used for?

$$g_{syn}(t) = g_{\max} \exp\left(-\frac{t - t_s}{\tau}\right)$$

3^{rd} topic: synapse and synaptic plasticity

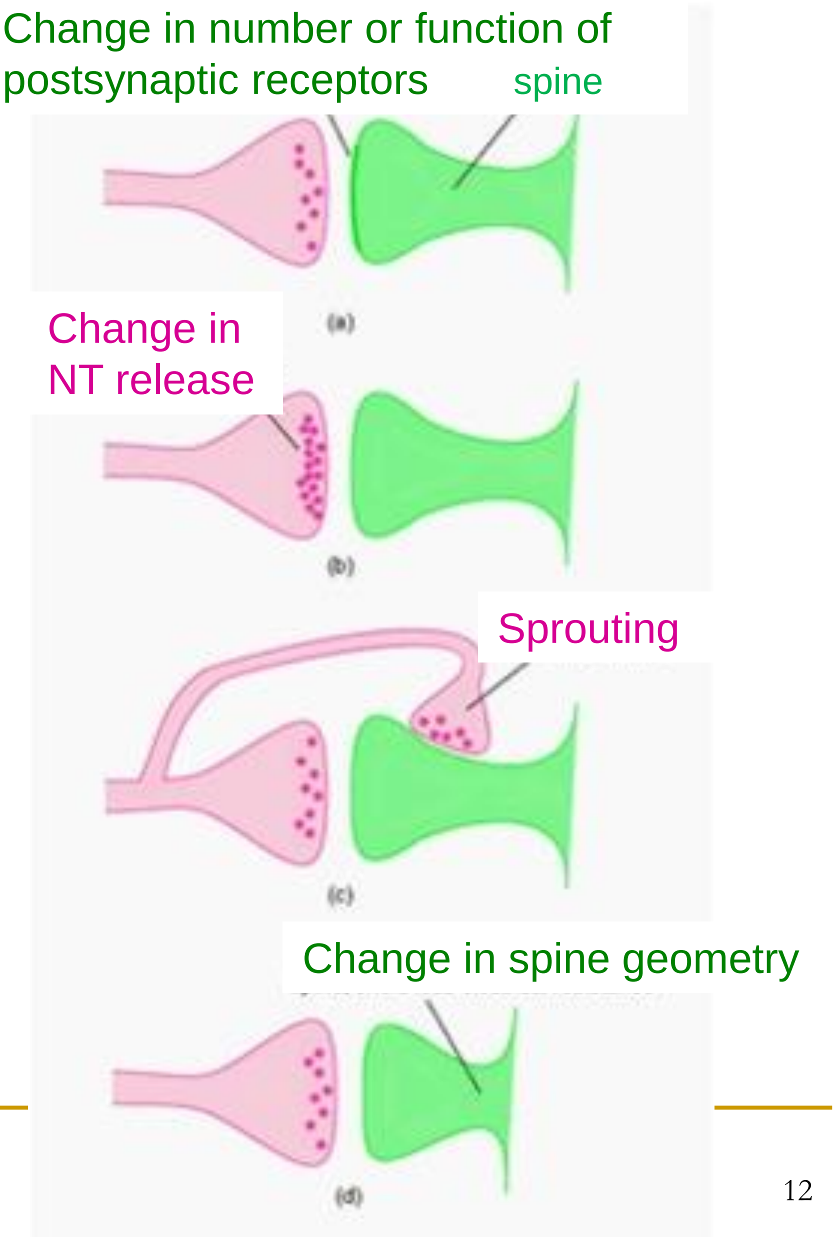
- Parts of a synapse and their function.
- Describe the steps of synaptic transmission in the chemical synapse.
- Excitation vs. inhibition.
- Types of receptors and neurotransmitters.



Synaptic plasticity

- Definition: synaptic plasticity is the ability of the synapse to change its strength (weight).

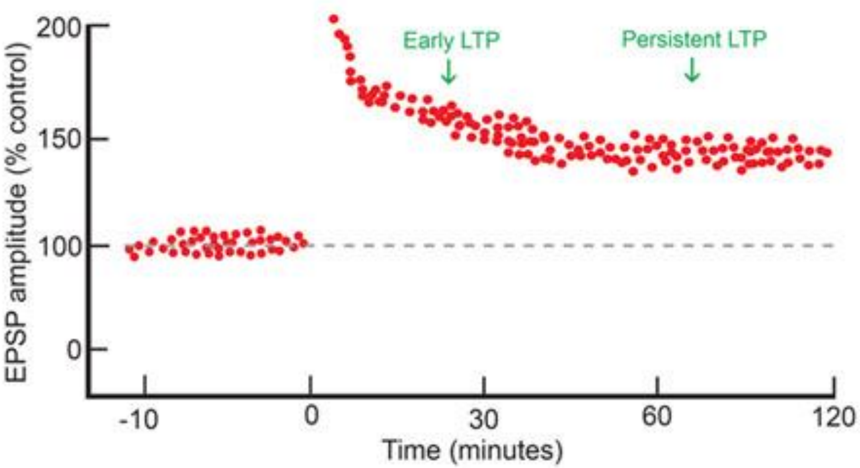
- Various mechanisms:
  - change in number/functionality of postsynaptic receptors (medium-term),
  - change in the amount of released neurotransmitter (short-term),
  - morphological changes like axonal sprouting and spine size changes (long-term).

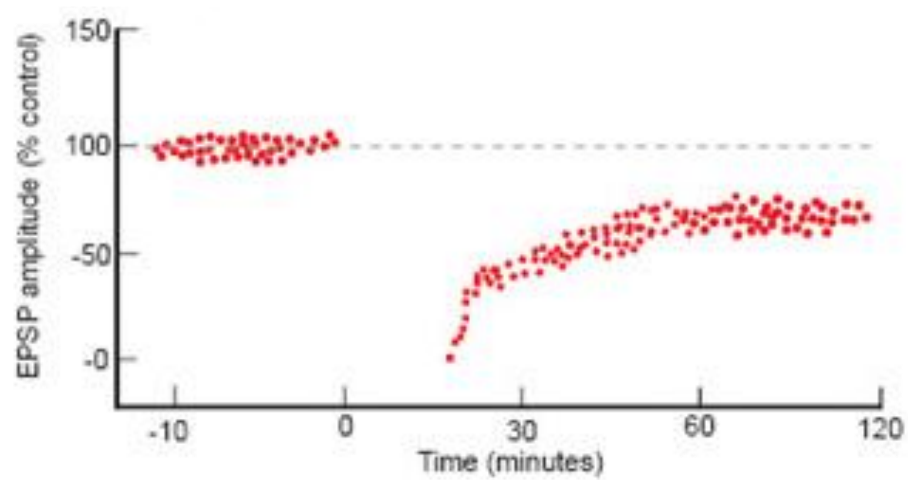


Synaptic plasticity: LTP and LTD

- What's LTP and LTD? Describe the stimulation protocol of their induction.

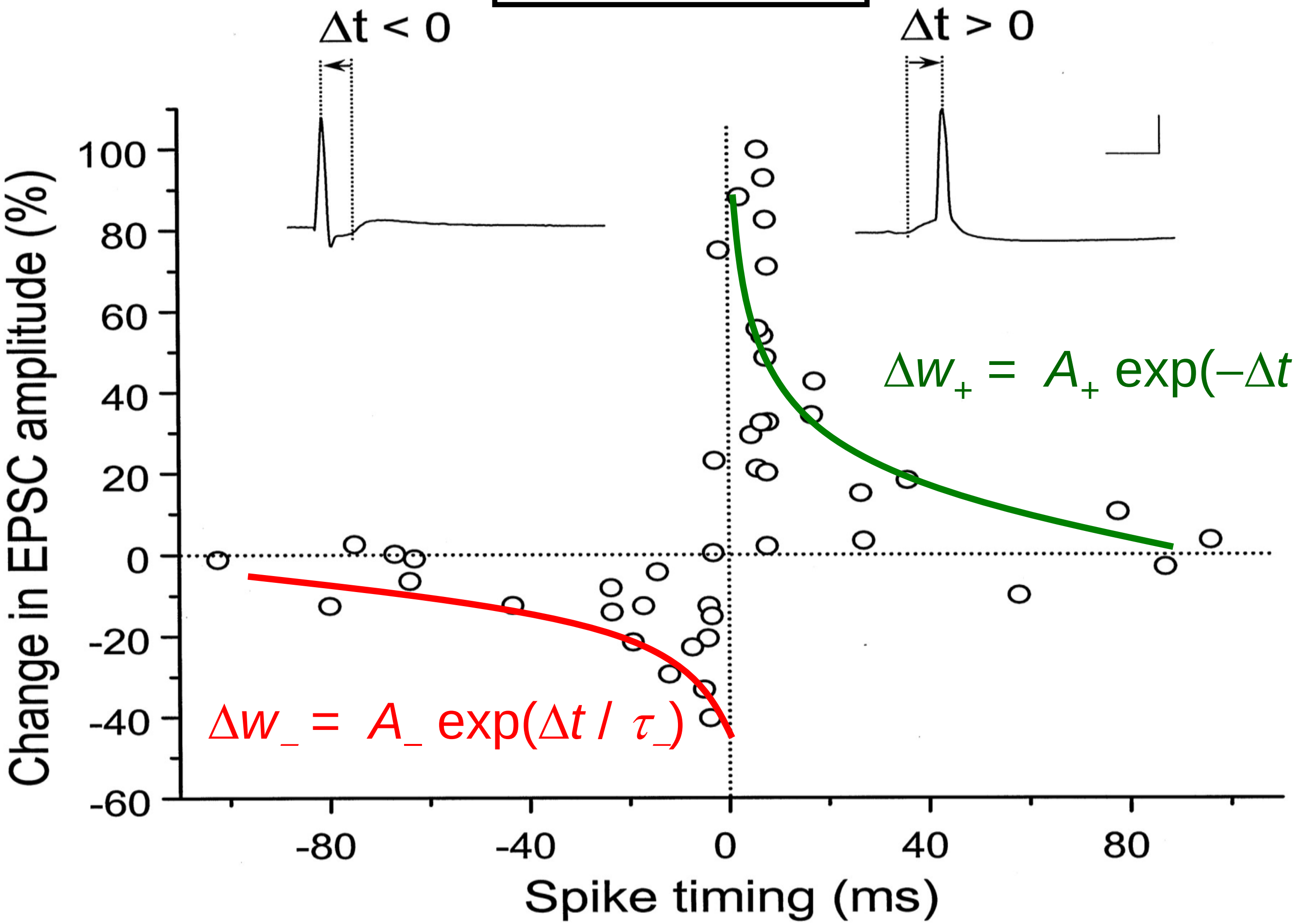
- Describe the BCM rule of synaptic plasticity, metaplasticity and theory of LTD/LTP threshold.





Describe STDP: Spike Timing-Dependent Plasticity

$$\Delta t = t_{post} - t_{pre}$$

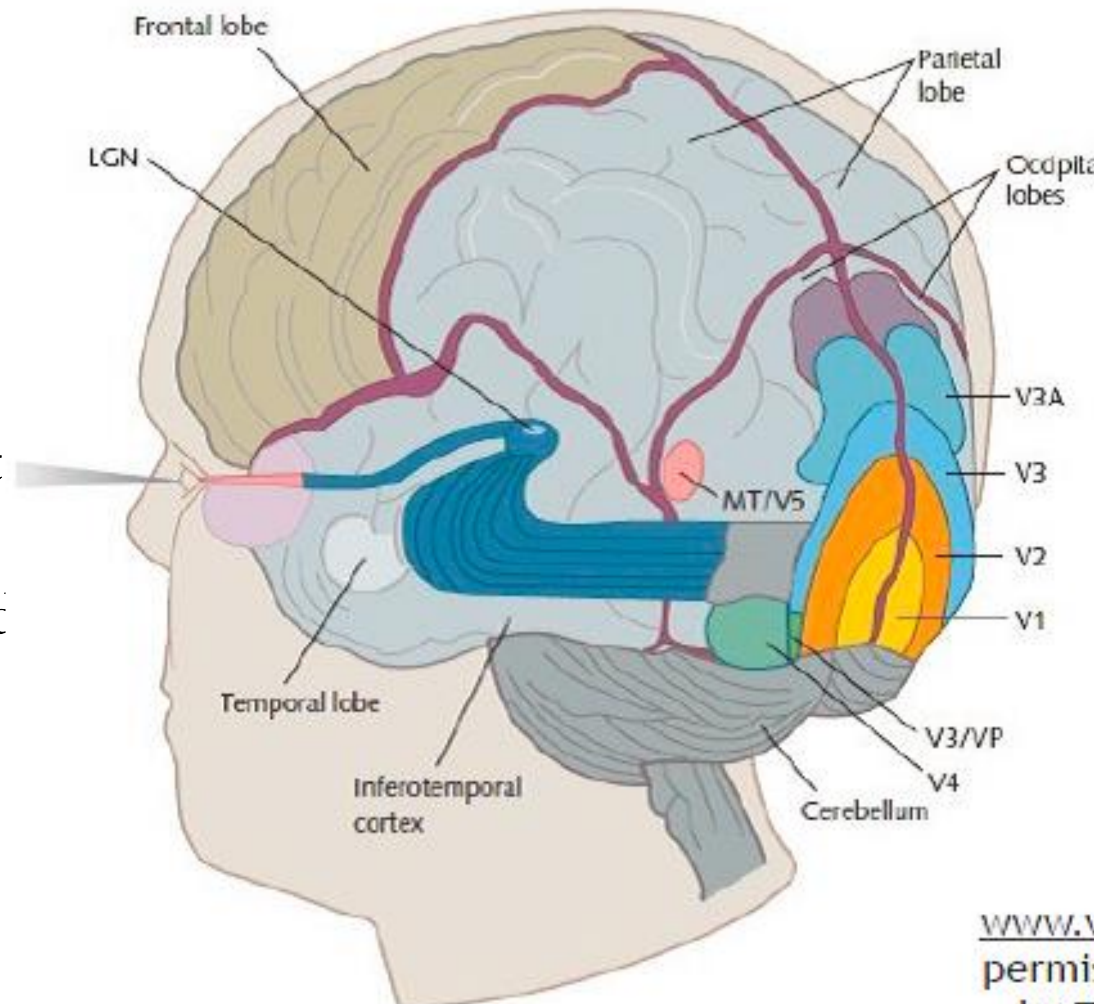


$$\Delta w_+ = A_+ \exp(-\Delta t / \tau_+)$$

$$\Delta w_- = A_- \exp(\Delta t / \tau_-)$$

How is the information coded in the brain?

- Visual signals travel from eyes to LGN and from there to primary visual cortex V1.
- Information from the left halves of eye retinas goes to the left hemisphere and
- Information from the right halves of eye retinas goes to the right hemisphere.



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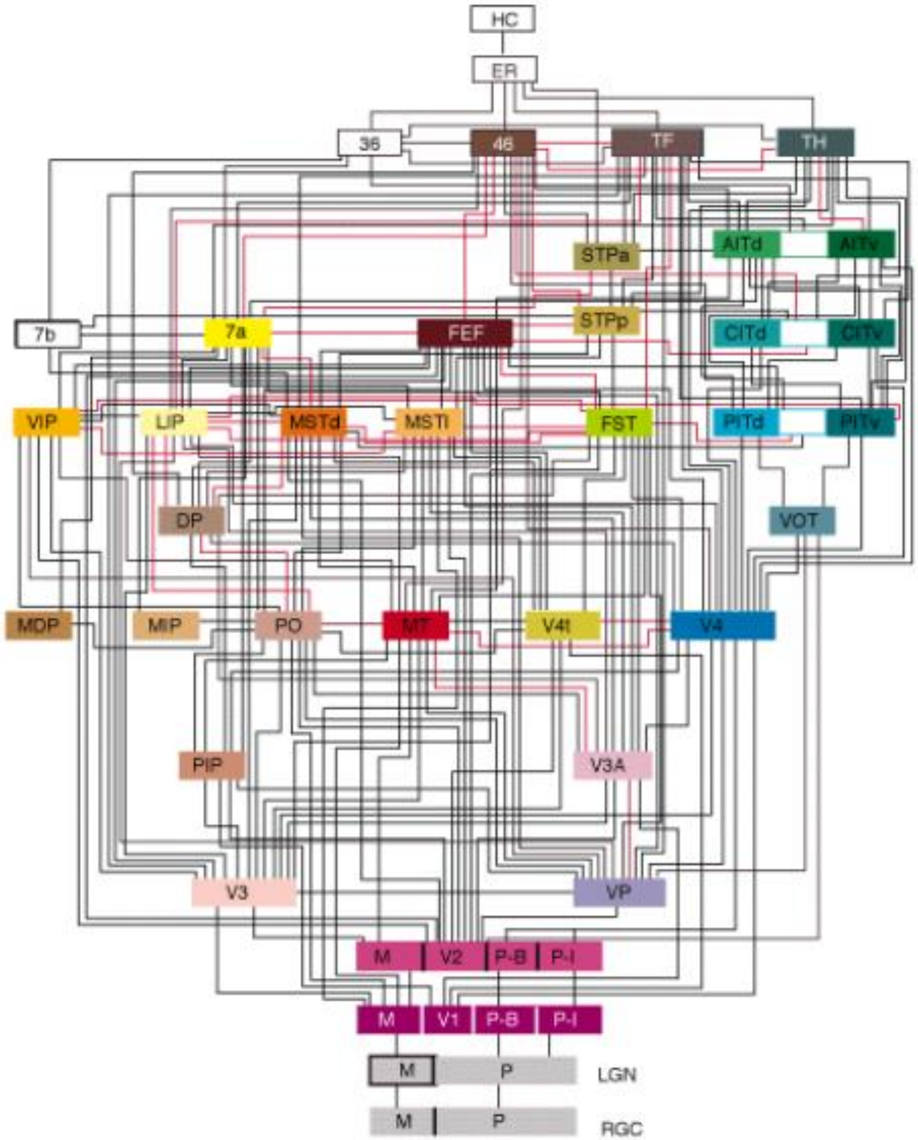
Circuit diagram of macaque visual system

- After V1 there are about 30 visual areas that represent/code different features of visual objects (Fellman & Van Essen, 1991).
- These areas are hierachically organised with millions of feedforward and feedback pathways between layers.
- It is the same in human brain, i.e. we have as many different cortical areas that process different aspects of visual input.



Ultrafast visual classification of objects

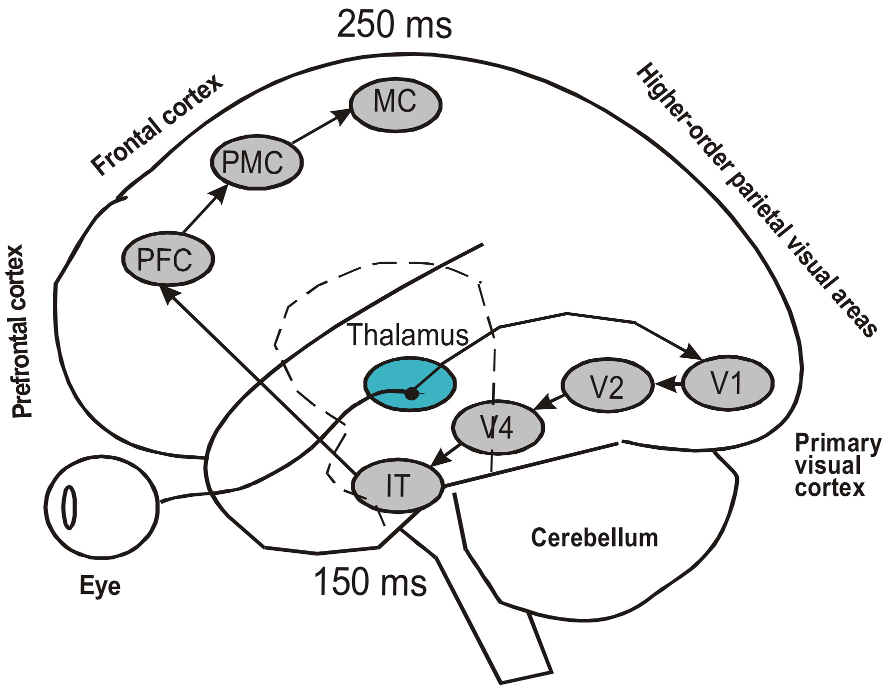
- Simon Thorpe et al. at the University of Toulouse, France, performed an experiment with humans and monkeys, in which subjects were supposed to classify pictures into 2 categories, either an animal category or a non-animal category (Thorpe et al., Science, 1996).

- Hundreds of pictures were shown. Pictures were shown just for 20 ms. In spite of that, humans on average correctly classified the pictures in **94%** cases and monkeys in **91%.**

- Ultra-fast classification did not depend on classes of objects, did not depend on colour, and did not depend on attention or eye fixation.

Brain activity during classification

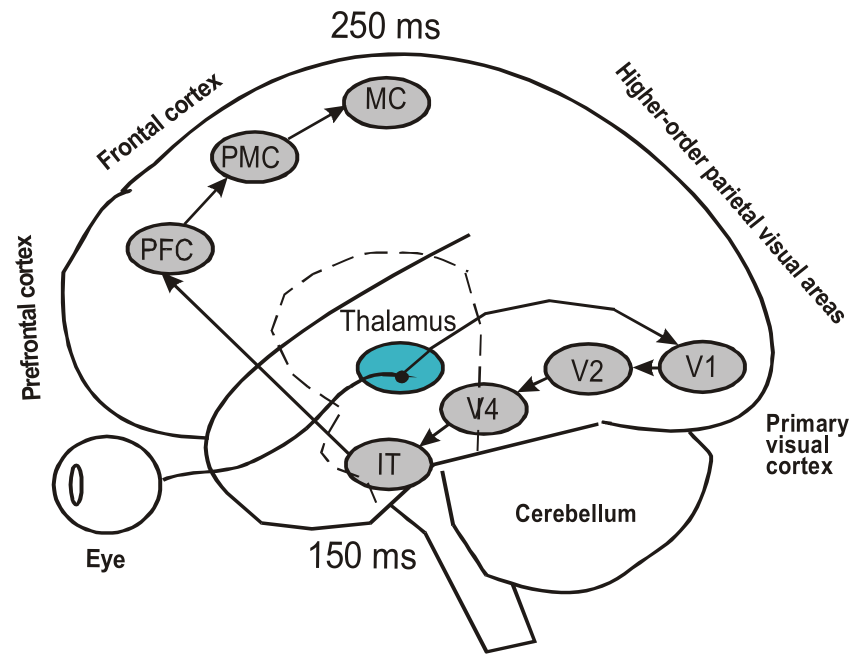
- Reaction time, i.e., time from presentation of a picture to pressing the button = 250 ms in humans, on average.
- Activity in the inferotemporal (IT) cortex occurred on average after 150 ms, so the preparation and execution of motor response took on average 100 ms.
- In monkeys, times were shorter by about 80 ms (smaller brains).



Neurons use few spikes to communicate

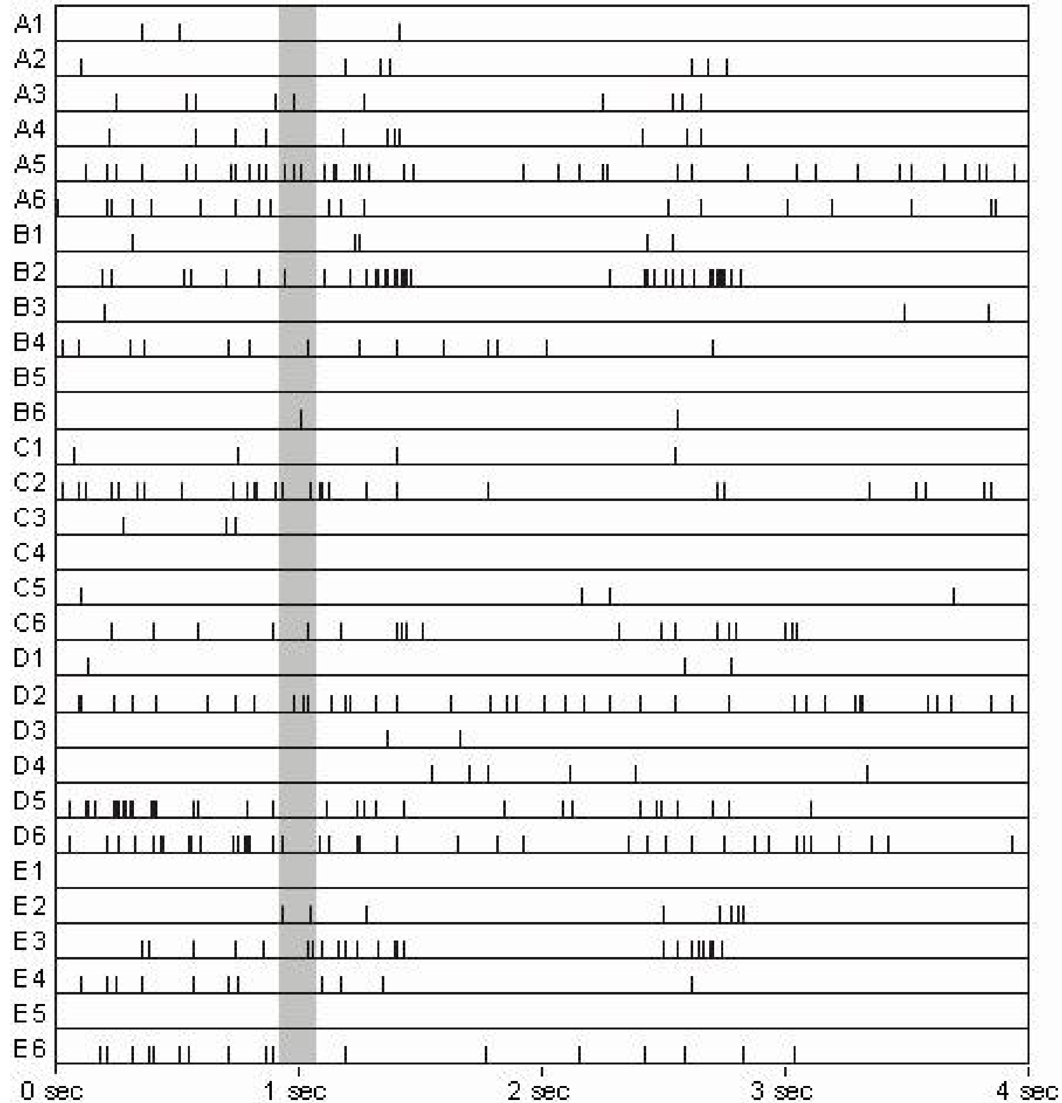
- Projected image stimulates retina for 20 ms. In about 80 ms, the thalamus responds. Thalamic neurons activate neurons in the primary visual cortex (V1). Then, activation proceeds to and through higher-order visual areas, V2, V4 and IT, where activity appears after 150 ms.

- Thus (150-80) / 4 areas = 17.5 ms per area. Even if neurons fired with frequency = 100 Hz, this would mean that each one fired 1-2 spikes within this interval only !



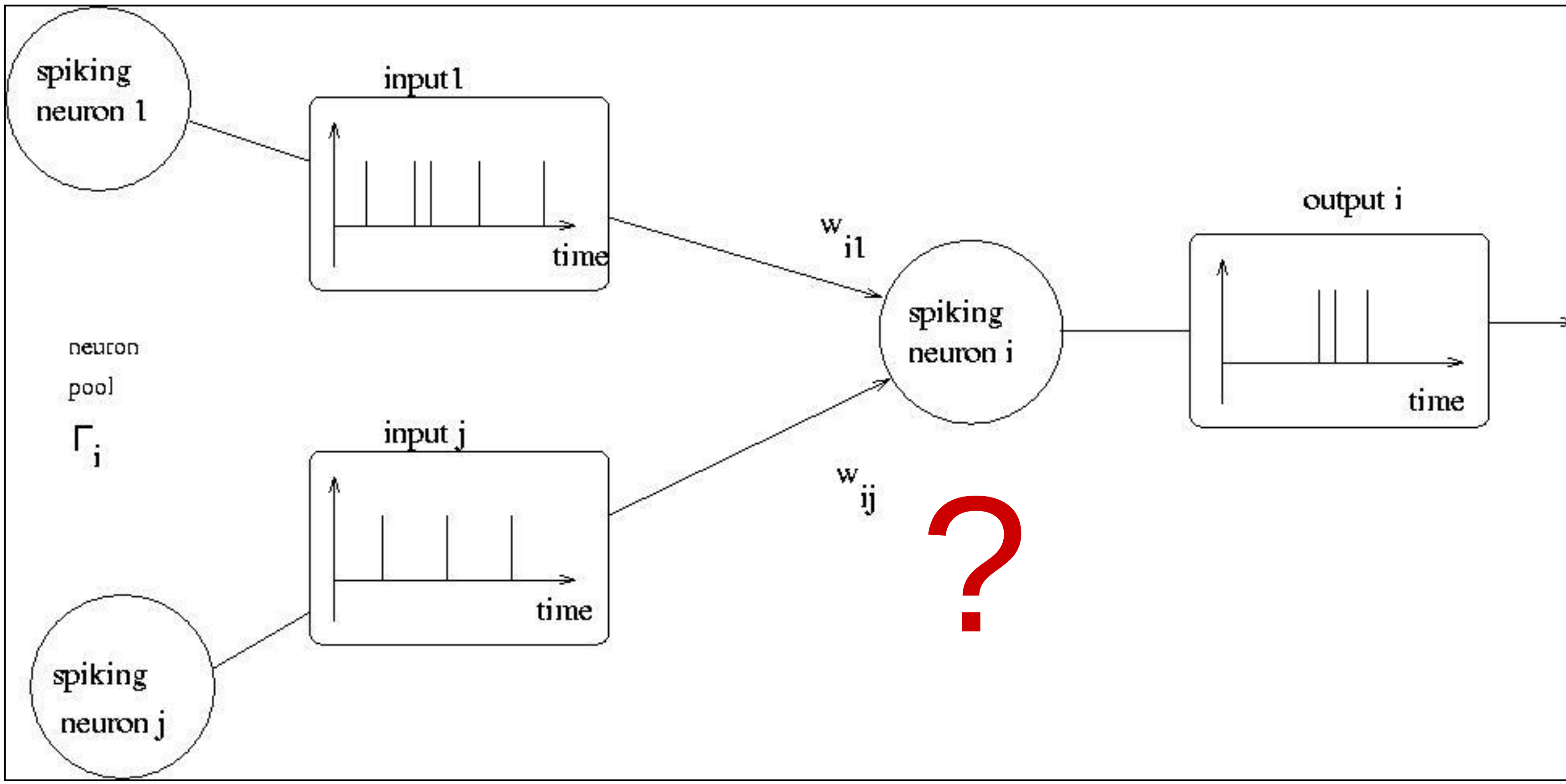
Neurons can use few spikes to solve complex tasks

- Simultaneous recordings of the firing times of 30 neurons from monkey visual cortex (Krüger and Aiple, 1988).
- Each spike is denoted by a vertical bar, with a separate row for each neuron.
- An interval of 150 msec is shaded. This time span is known to suffice for the completion of some very complex computations.

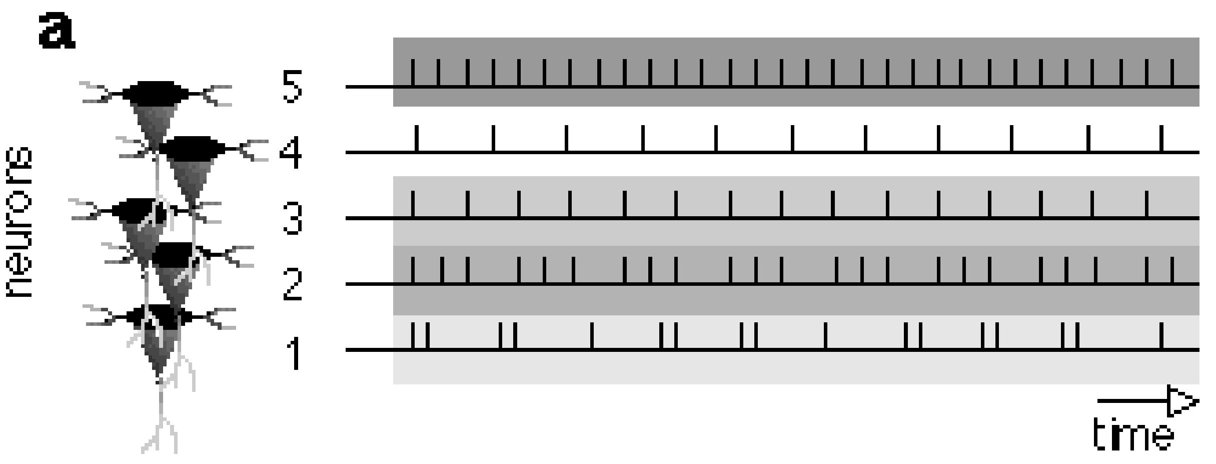


How is the information coded in the brain?

- What is the neural code (which links stimulus and response) that is used by the brain to send information from one neuron to another?



Rate or frequency code

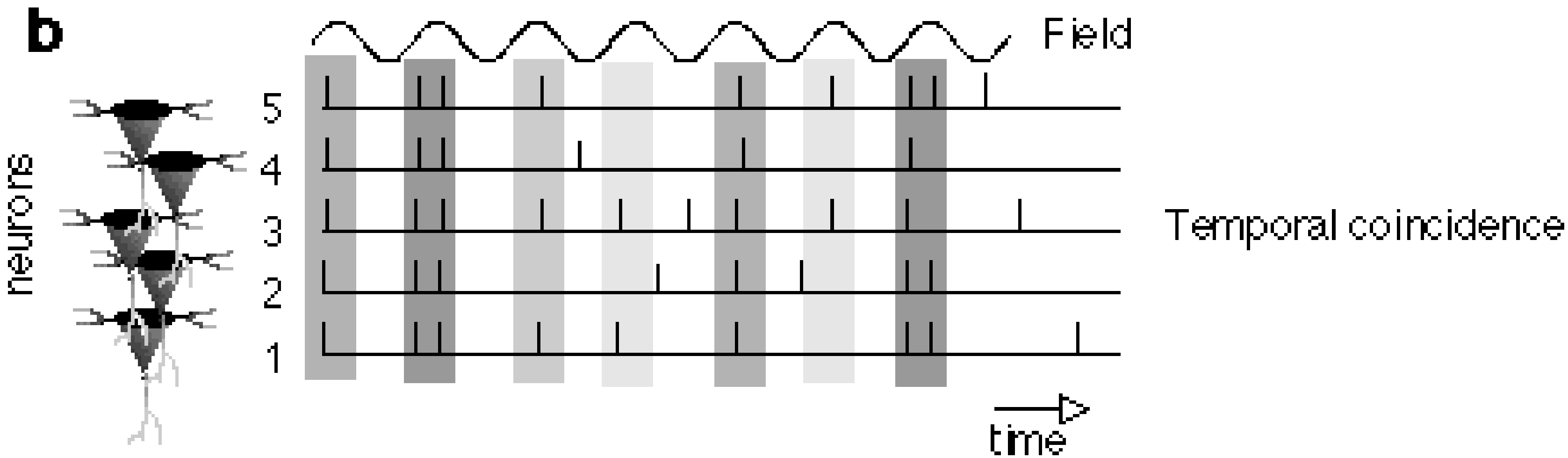


Frequency code

- This hypothesis is based on the idea that a feature of an object is coded by the frequency of spikes.

- In the figure, each of the five neurons codes a different feature of an object (be it colour, orientation, movement, etc.).

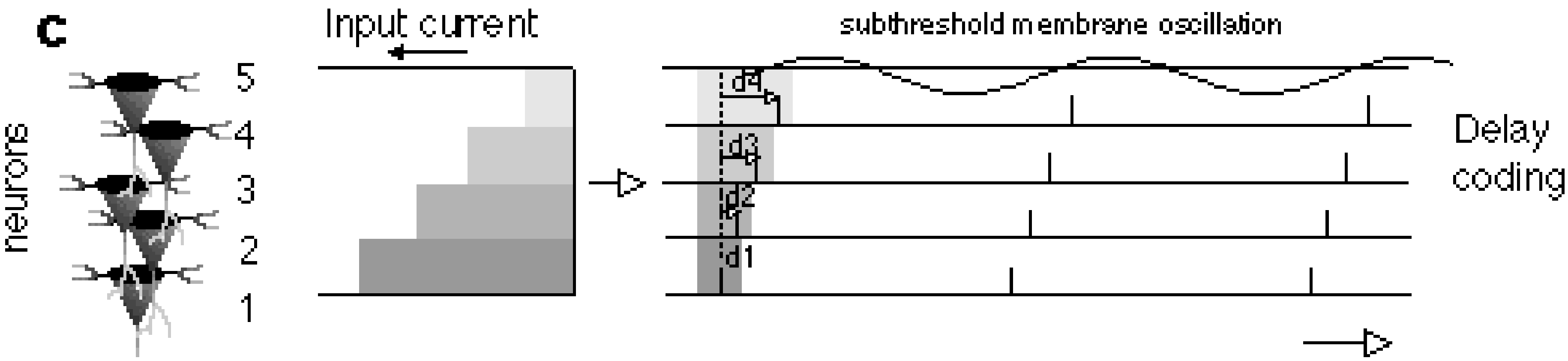
Synchrony code (coincidence detection)



- Features that are represented by particular populations of neurons will synchronize the firing of these neurons if the features belong to the same object (binding by synchrony).

- Neurons act as coincidence detectors thus responding to and strengthening inputs that are active at the same time.

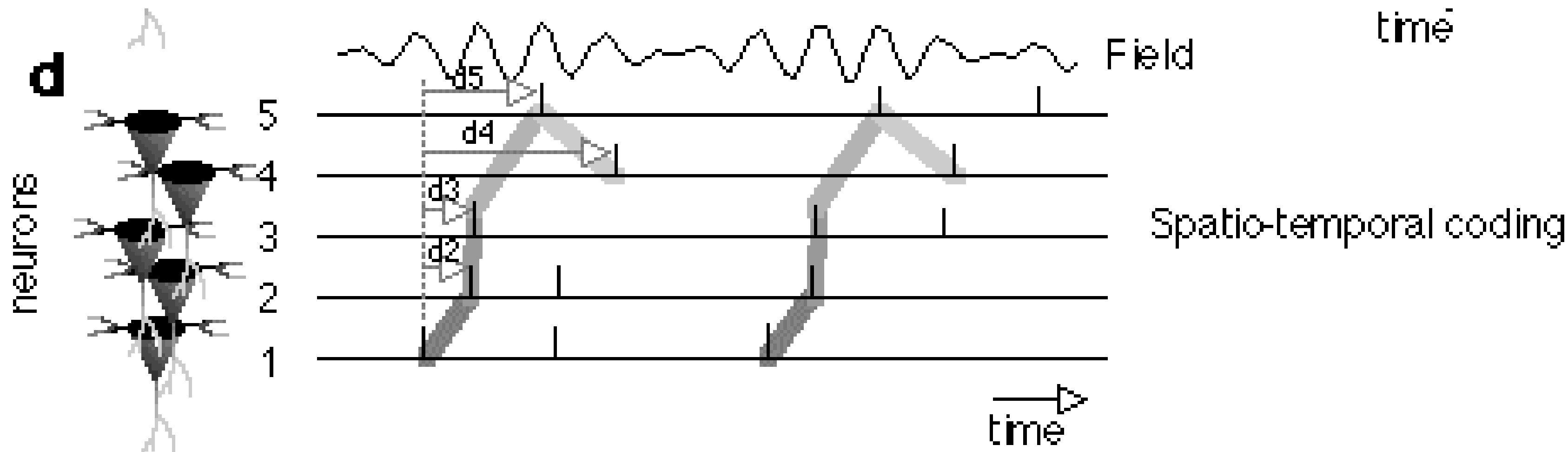
Spike delay code



- Delay coding is based on the idea that neurons will respond to more energetic (salient) input signals by generating a spike earlier, and that this generated spike will arrive at the downstream neuron earlier than other spikes and will thus have a higher impact or 'ranking' relative to later incoming spikes.

- Another variant of the spike delay code is that information is encoded in the phase relationship between the cell's firing activity and the underlying rhythmic oscillations of the whole population of neurons.

Spatio-temporal coding



- Neurons respond to the same stimulus always with the same specific spatio-temporal pattern of spikes.

- Different stimuli evoke different spatio-temporal patterns of spikes in neuronal populations.

Neural code hypotheses

a) *Rate*. Information about the feature is encoded in the frequency of neuron's firing (Adrian 1929, Hubel and Wiesel 1962).

b) *Synchronisation*. Populations of neurons that represent features belonging to one object are bound together by synchronous firing (Singer et al. 1996).

- - Synfire chains: information is carried by waves of synchronously firing neural ensembles (Bienenstock 1995, Abeles 2001).

c) *Delay code*.

- *Phase*. Information about the feature is encoded in the phase of neuron's impulses with respect to the reference background oscillation (Jensen 2001, Hopfield 2005).
- *Time to the first spike*. Neurons that fire the first carry the information about the stimulus features. The rest of neurons and the rest of impulses are ignored (Thorpe et al. 1996).

d) *Spatio-temporal pattern of firing*. Information about the salience of the object feature is encoded in the exact temporal structure of the spike train (Rieke et al. 1996, A. Villa 2005).

Other simulation software

- Compartmental models of neurons and ensembles of neurons: NEURON, GENESIS, HHsim, neuroConstruct, NeuronC, SNNAP, Surf-Hippo (for Hippocampus, CNRS, France).

- Models of subcellular processes: PSICS (Parallel Stochastic Ion Channel Simulator), Copasi, Ecell, MCELL (intracellular signalling).

- Models of spiking networks: BRIAN, Emergent, NEST, NSL, PCSIM.

- Models of neural development: NETMORPH, Topographica, XNBC.

- Databases: ModelDB, NeuroMorpho (digitally reconstructed neurons).

Compartmental: HHsim, NeuronC, neuroConstruct

- HHsim: a graphical simulation of a section of excitable neuronal membrane using the Hodgkin–Huxley equations. It provides full access to the membrane parameters, stimulus parameters and ion concentrations. http://www.cs.cmu.edu/~dst/HHsim

- NeuronC: simulator for large networks with a large number of compartments http://retina.anatomy.upenn.edu/~rob/neuronc.html

- neuroConstruct: neuroConstruct (Gleeson et al., 2007): for creating networks of conductance-based neuronal models, visualising and analysing networks of cells in 3D, managing simulations and analysing network firing behaviour http://www.neuroconstruct.org .

Subcellular models: Copasi, Ecell, MCELL

- Copasi: COmplex PAthway SImulator (Hoops et al., 2006) provides deterministic, stochastic and hybrid solutions for reaction systems. Tools for parameter optimisation. http://www.copasi.org

- Ecell: similar to Copasi. Models of molecular processes in the neuron can be constructed either via a scripting language or graphically (Takahashi et al., 2003). http://www.e-cell.org

- MCell: realistic simulation of cellular signaling, algorithms to track the stochastic behavior of discrete molecules in 3D space and time as they diffuse and interact with ion channels, enzymes, transporters, etc. http://www.mcell.cnl.salk.edu/

Spiking neurons: BRIAN, NEST, NSL, PCSIM

- BRIAN: simulator of spiking neural networks of integrate-and-fire neurons. It is written in Python and runs on many platforms. http://www.briansimulator.org

- NEST: NEural Simulation Technology for large-scale spiking neuronal networks. https://www.nest-simulator.org/

- NSL: The Neural Simulation Language for networks where model neurons are leaky integrators. http://www.neuralsimulationlanguage.org

- PCSIM: Parallel neural Circuit SIMulator is a tool for simulating networks of millions of neurons and billions of synapses. http://www.lsm.tugraz.at/pcsim