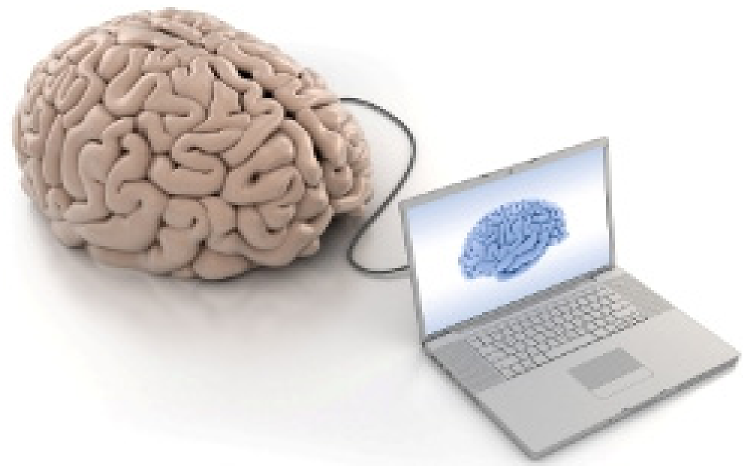
Computational Neuroscience

COSC422 – lecture 13

Revision

Topics for final exam



Resources

- Textbook: *Principles of Computational Modelling in Neuroscience*
  Authors: David Sterratt, Bruce Graham, Andrew Gillies, David Willshaw
  Published by: Cambridge University Press, Cambridge, U.K., 2011.
  - http://www.cambridge.org/us/knowledge/isbn/item6025106/
- Scholarpedia – free encyclopedia of computational neuroscience:
  - http://www.scholarpedia.org/article/Encyclopedia_of_computational_neuroscience
- Wikipedia.

1st topic: computational modelling

- Reading:
  - Lecture 1 handouts
  - Chapter 1, pp. 1 – 9, from the textbook
  - Appendix B, pp. 328 – 331 (up to B.1.2), from the textbook

- 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 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 and compare the resulting model data with the new experimental data to verify that the chosen parameter values are robust.

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.

Solving differential equations

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

- Let us assume we know what is the "something" function, e.g.:

$$\tau_m \frac{dV}{dt} = E_L - V + r_m I_e$$

- Questions: how would you solve this equation numerically?
- Or write a pseudocode for a numerical solution of this equation.
- Answer is in Appendix B.1.1.

Forward Euler method

- Let us rewrite the original equation like this:

$$\frac{dV}{dt} = \frac{1}{\tau_m}\left(E_L - V + r_m I_e\right)$$

- According to the forward Euler method we assume time runs in small discrete steps Δt. The new value of dependent variable is thus calculated as:

$$V(t + \Delta t) = V(t) + \frac{dV}{dt}\Delta t$$

- Thus the new value of V in the next time step is:

$$V(t + \Delta t) = V(t) + \frac{1}{\tau_m}\left(E_L - V(t) + r_m I_e\right)\Delta t$$

2nd topic: neuron and its membrane

- Describe parts of a neuron, composition of the membrane in these different parts and function of these different parts.

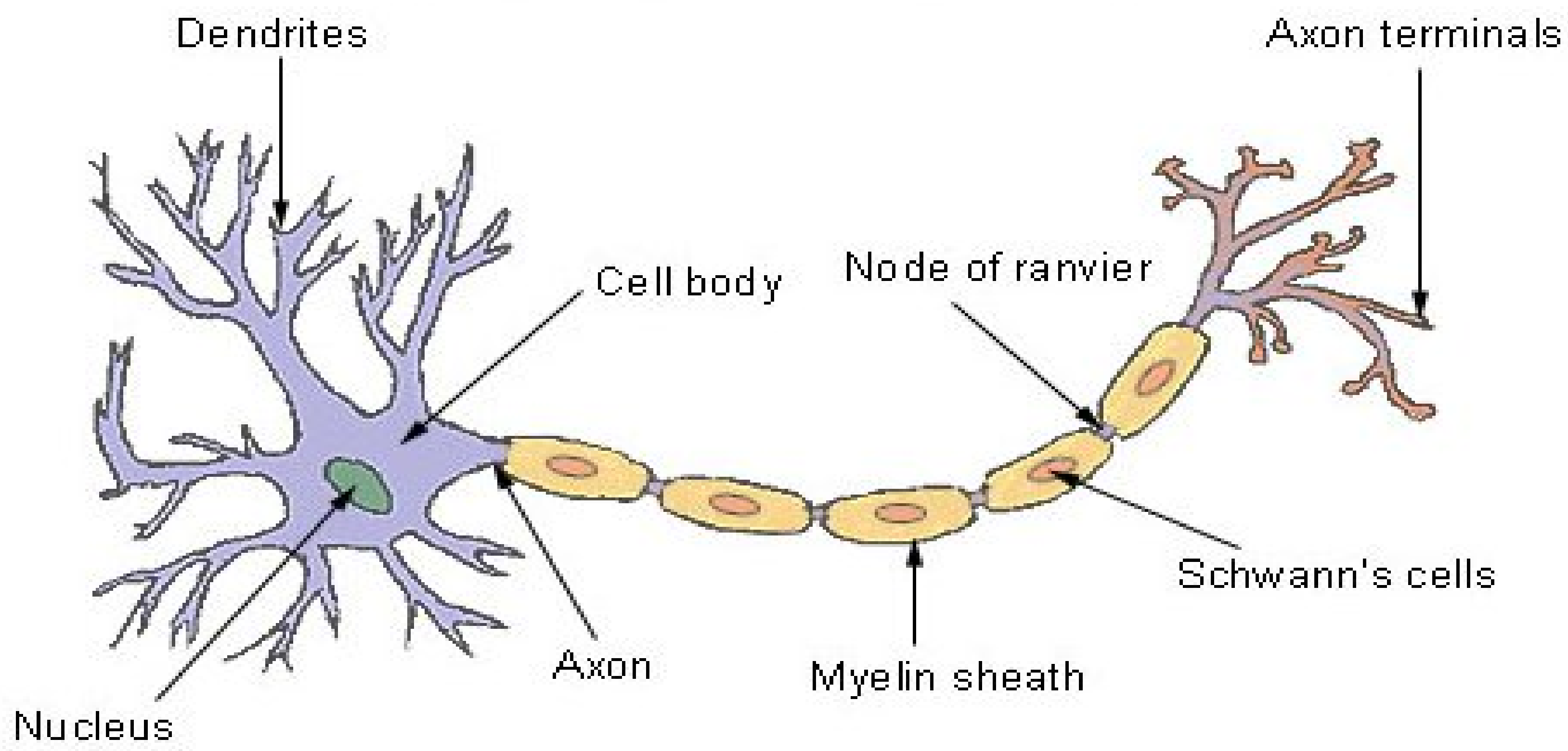
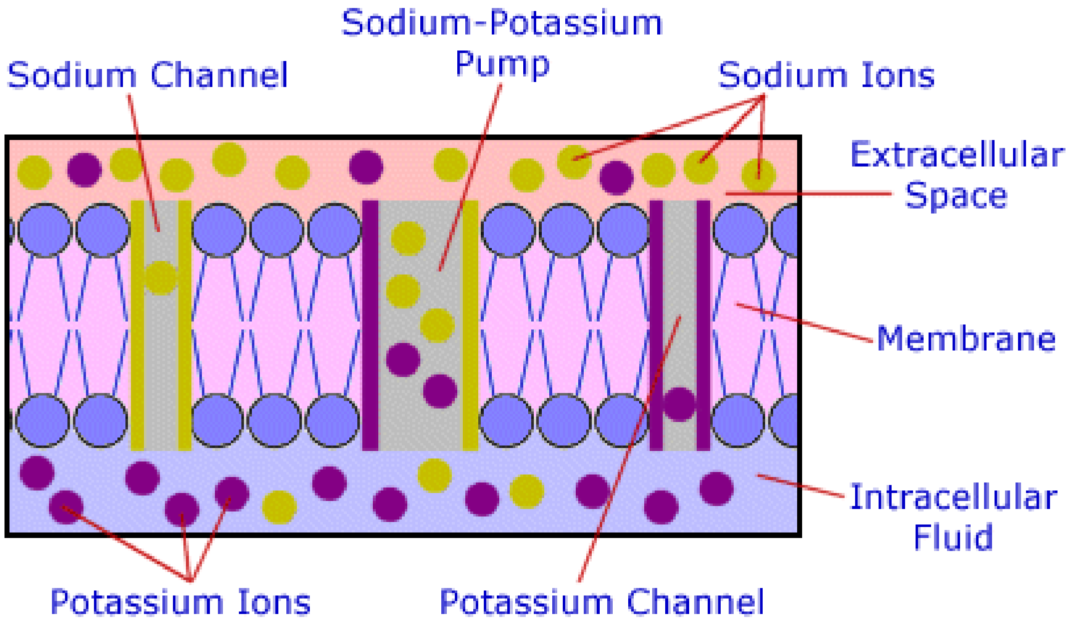


Image source: http://www.daviddarling.info/encyclopedia/N/neuron.html

Neuronal membrane and its function

- Separates inside from outside, contains various proteins – which types and what's their function?
- Which factors affect the movement of ions across the membrane?
- Reading:
  - Lecture 2, 4, and 8.
  - Chapter 2, pp. 13 – 20, from the textbook.



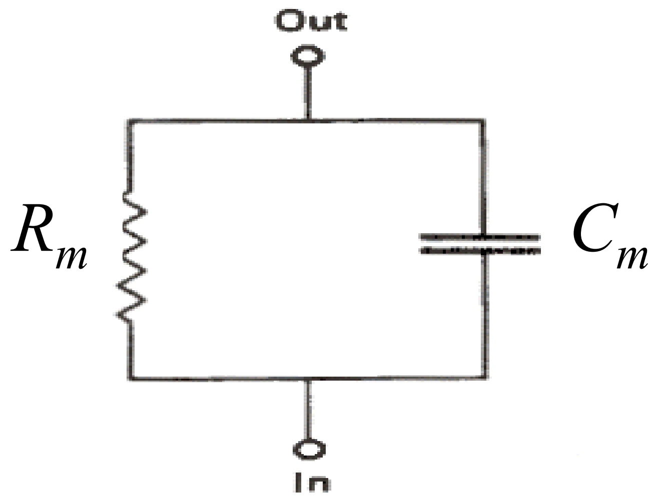
Hodgkin-Huxley model

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

- What do all the variables in the equation mean?
- How do we calculate or estimate them?
- Describe the four phases of generation of action potential (AP).
- Describe the propagation of AP along the axon.
- **Reading**: lecture 2 handouts + Chapter 3 sections 3.3, 3.5, 3.6.

Theory of passive dendritic trees

- Electric circuit of the passive membrane patch:

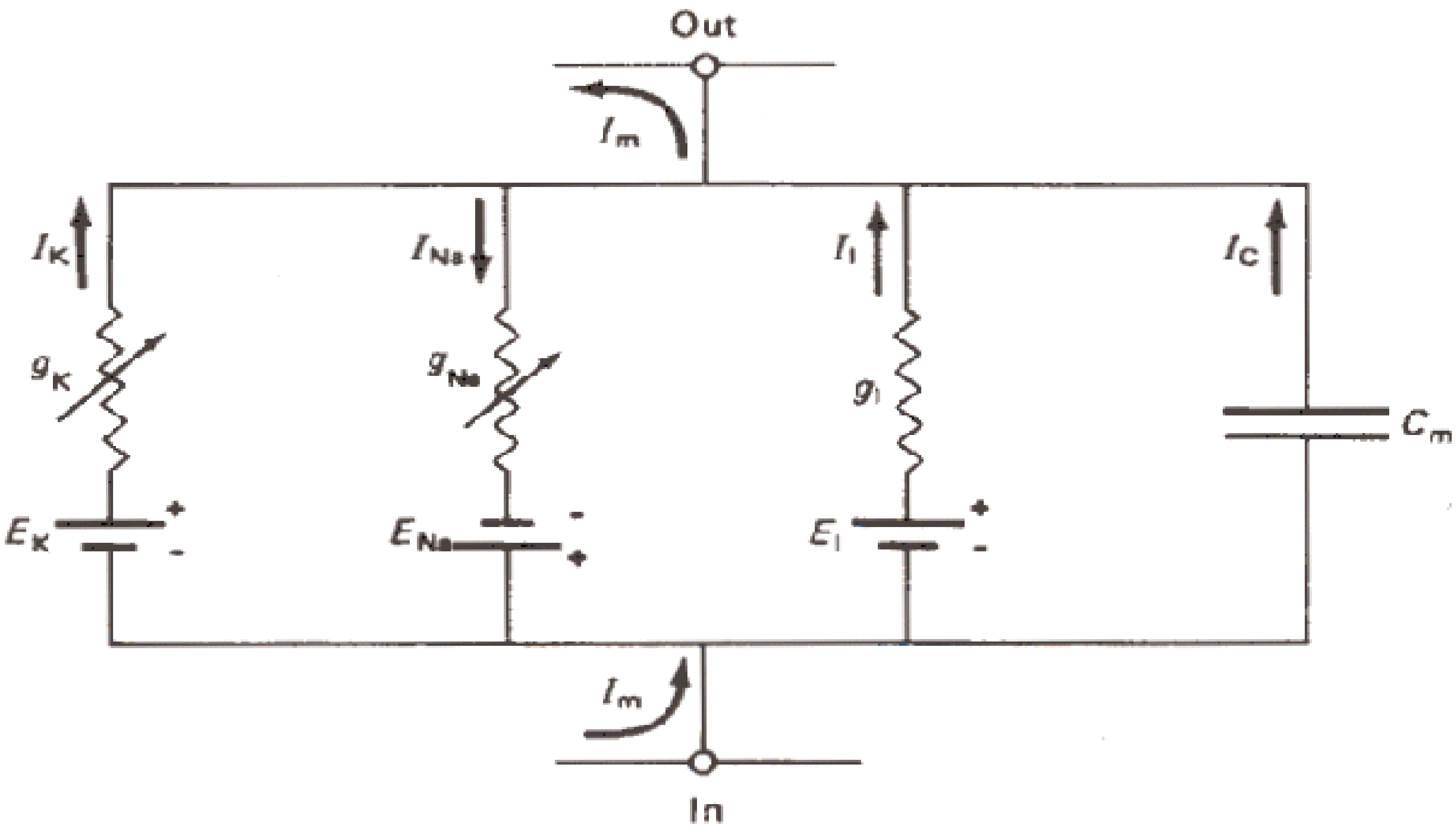


- What is the mathematical expression of electric current flowing through this passive membrane patch?

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

- Derive an ODE for the voltage: $$\frac{dV}{dt} = -\frac{V}{R_m C_m}$$

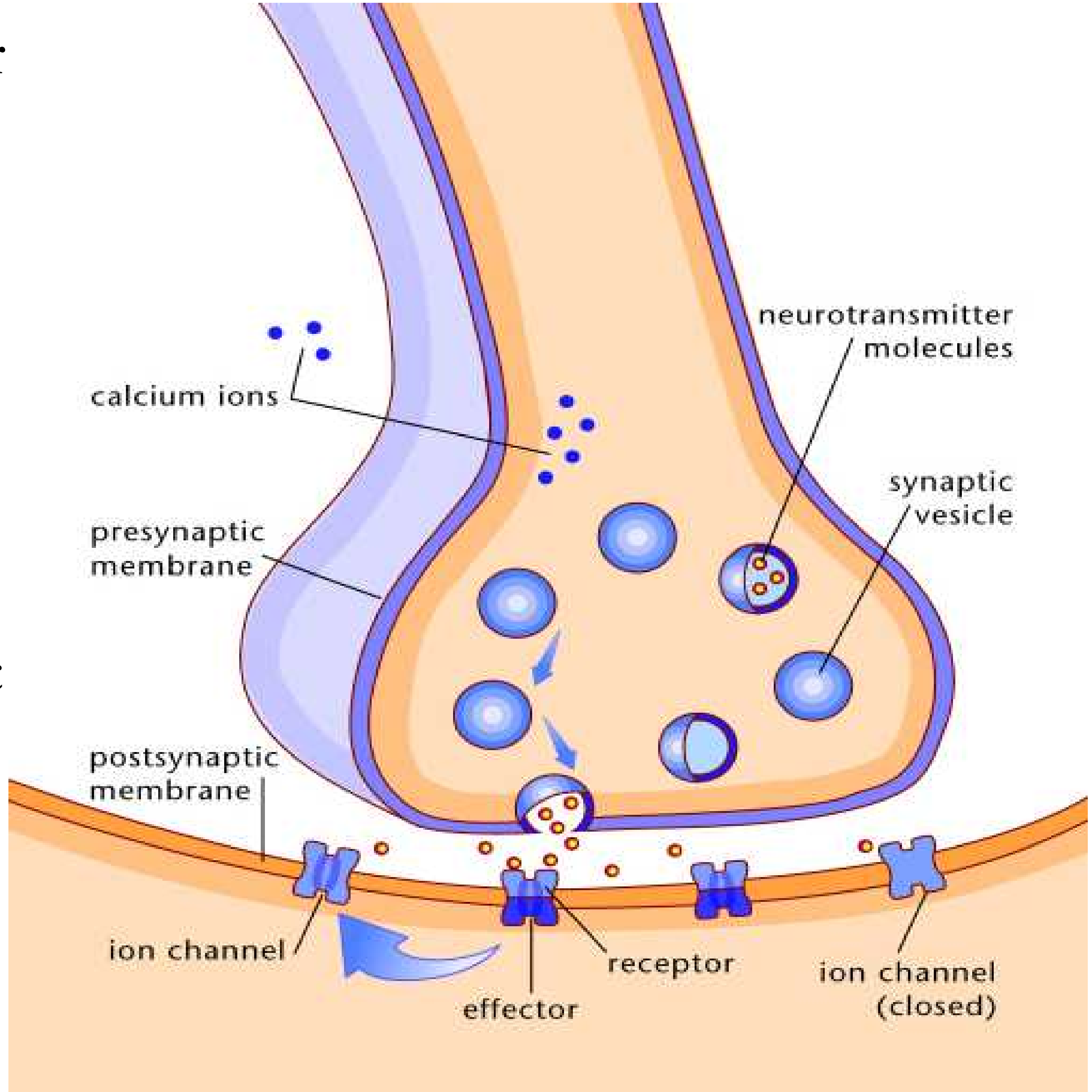
Patch of the membrane with V-gated ion channels



- Write equation(s) for the membrane current I_m and potential V.
- **Reading**: lecture 4 + Chapter 2, pp. 29 – 35 (up to section 2.7)

3rd topic: synapse and synaptic plasticity

- **Reading**: lecture 8 + Chapter 7, pp. 172 – 190 up to equation 7.37.
- Parts of synapse and their function.
- Describe the steps of synaptic transmission in the chemical synapse.
- Excitation vs. inhibition.



Postsynaptic potential (PSP)

- To model the time course of postsynaptic conductance change for the time t after arrival of presynaptic spike t_s, we use these waveforms:

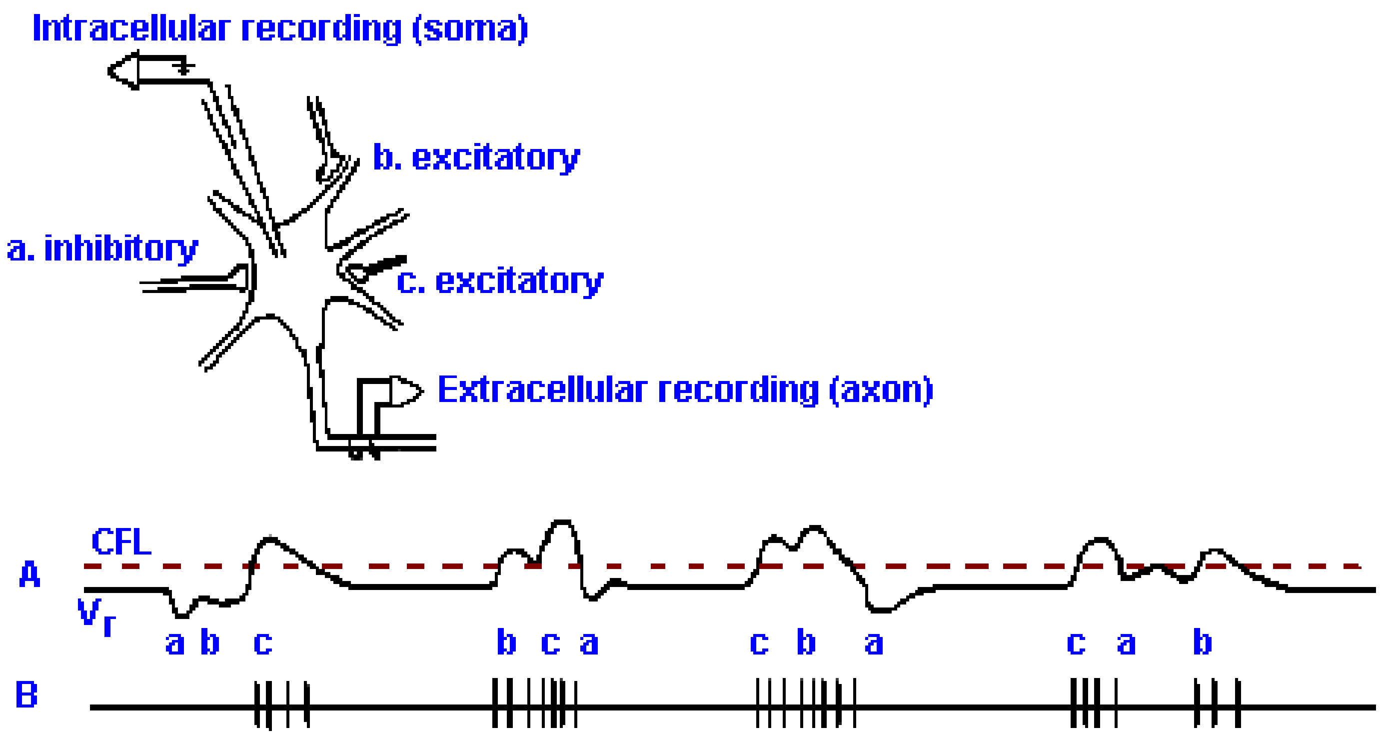
- Single exponential decay: $$g_{syn}(t) = g_{\max} \exp\left(-\frac{t-t_s}{\tau}\right)$$

- Alpha function (Rall, 1967): $$g_{syn}(t) = g_{\max} \frac{t-t_s}{\tau} \exp\left(-\frac{t-t_s}{\tau}\right)$$

- Dual (double) exponential function:

$$g_{syn}(t) = g_{\max} \frac{\tau_1 \tau_2}{\tau_1 - \tau_2} \left[\exp\left(-\frac{t-t_s}{\tau_1}\right) - \exp\left(-\frac{t-t_s}{\tau_2}\right)\right]$$

Temporal and spatial summation of PSPs

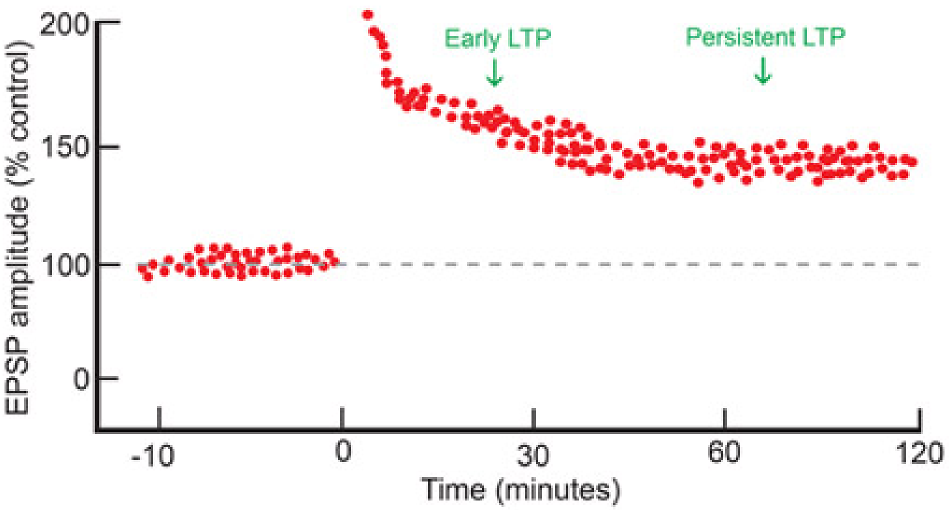


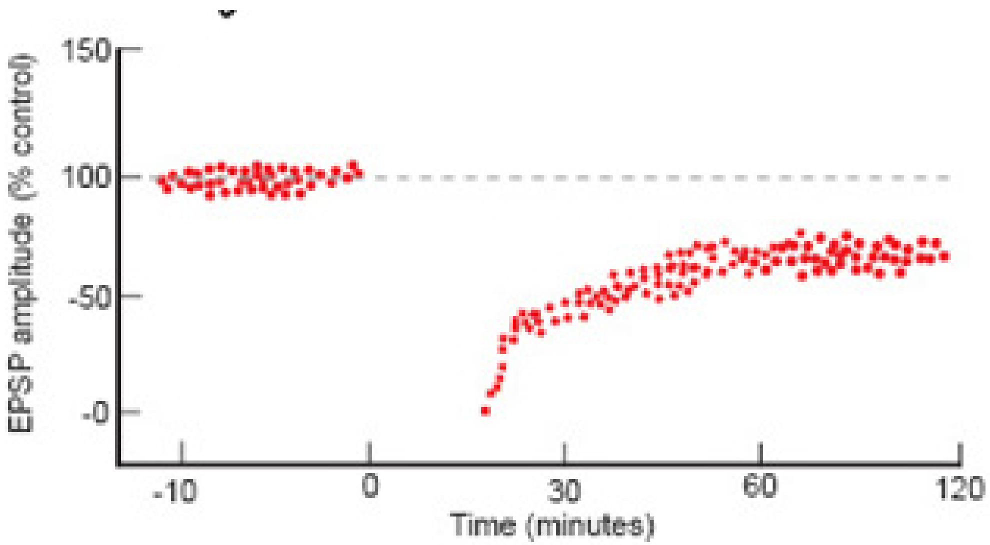
- What is the temporal and spatial summation of PSPs?
- What does the number and frequency of output spikes depend on?

Image source: http://michaeldmann.net/mann13.html

Synaptic plasticity: LTP and LTD

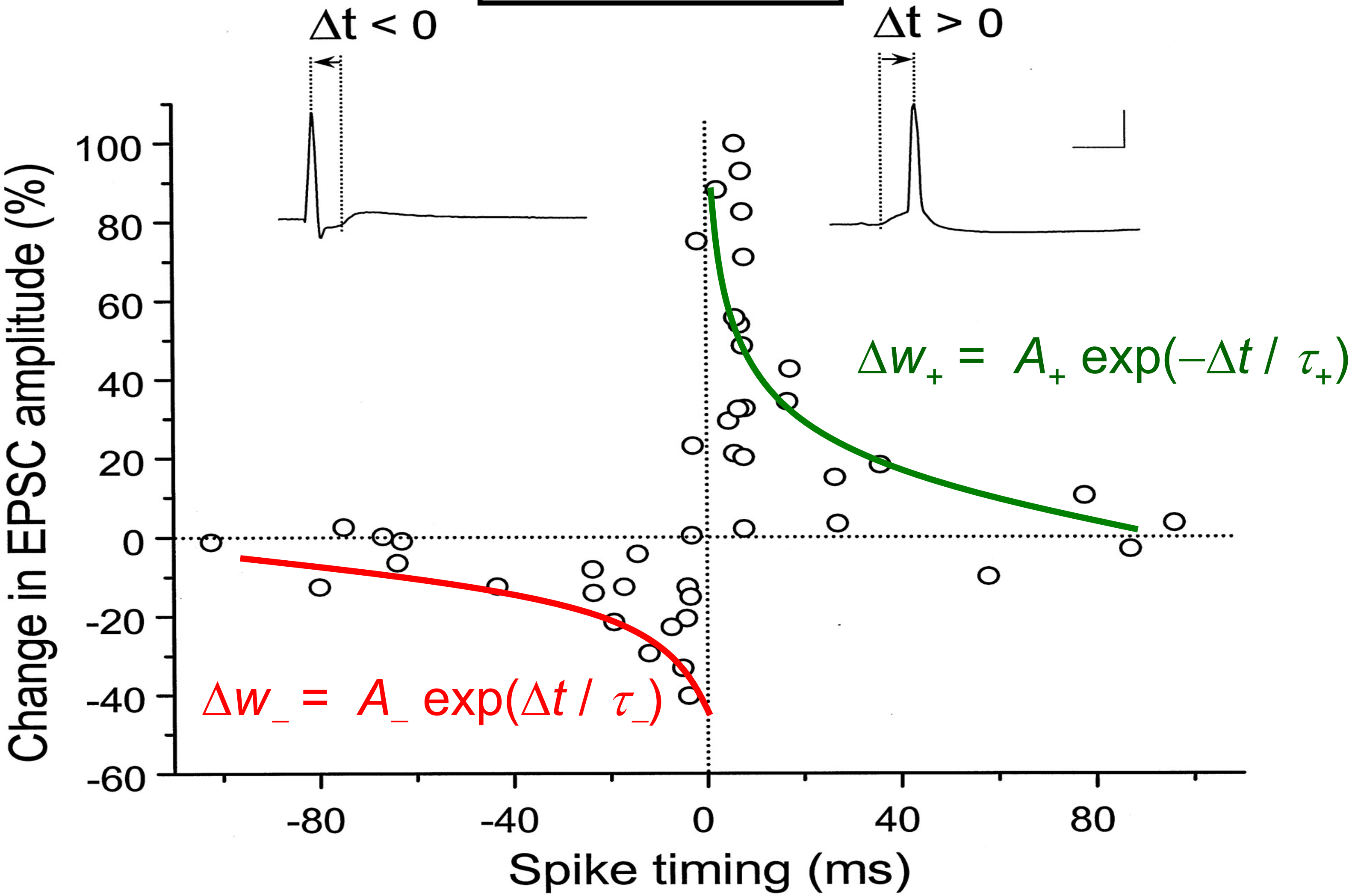
- What's neural mechanisms of learning and memory?
- What's synaptic plasticity (definition).
- What's LTP and LTD? Describe the stimulation protocol of their induction.
- State the Hebb rule of synaptic plasticity.
- What's metaplasticity and theory of LTD/LTP threshold.





Describe STDP: Spike Timing-Dependent Plasticity

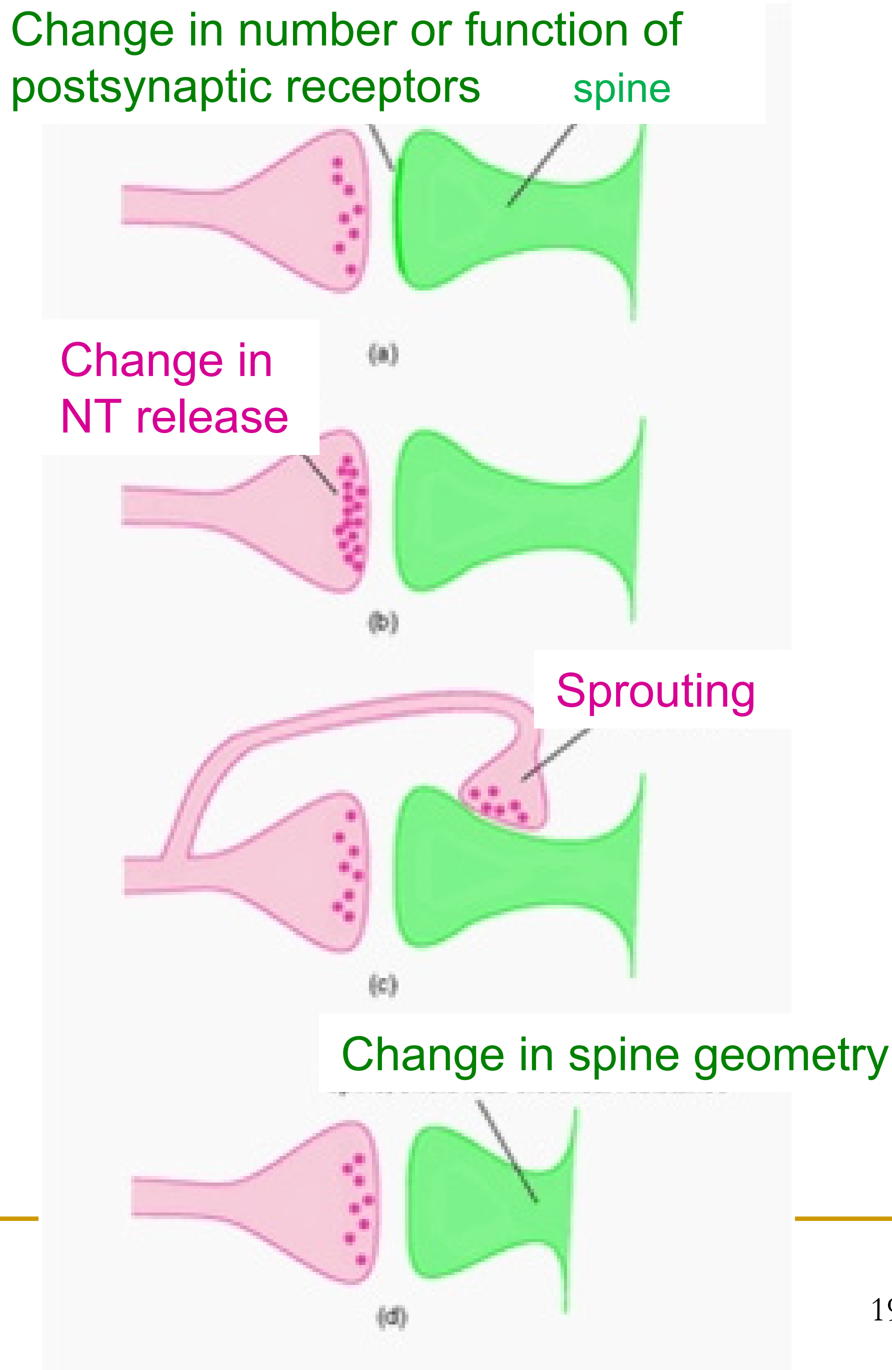
$$\Delta t = t_{post} - t_{pre}$$



Mechanisms of 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,
  - change in the amount of released neurotransmitter (short-term),
  - morphological changes like axonal sprouting and spine size changes (long-term).



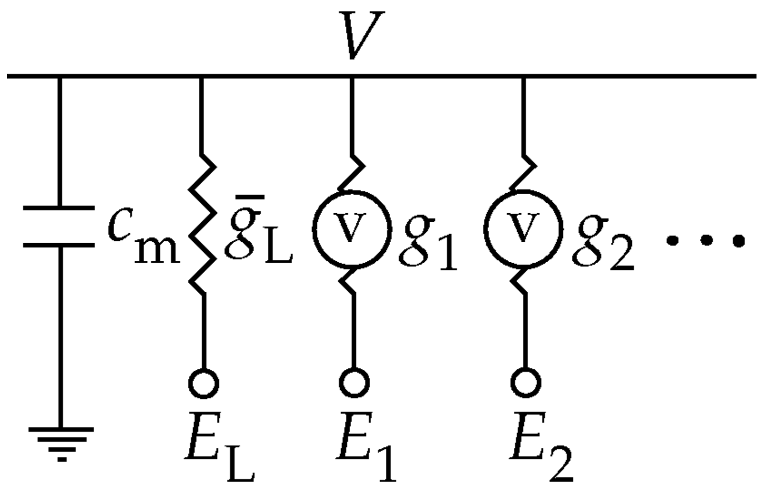
4th topic: neural code and I&F neurons

- **Reading**: lecture 12 + pp. 196 – 205, pp. 226 – 232,
- What is the neural code (i.e. the code that links stimulus and response) that is used by the brain to send information from one neuron to another?
- Four theories:
  - Spike delay code
  - Spatio-temporal code
  - Synchrony code
  - Rate (frequency) code
- Methods of studying brain function (lesions, invasive & noninvasive methods)

"Passive" integrate & fire neuron model

Electric scheme equivalent to an integrate and fire (I&F) neuron model

$$c_m \frac{dV}{dt} = -i_m$$



- Rate of change of the membrane potential *V* is proportional to the electric current entering into neuron, which in turn is the sum of all ion currents that pass through it :

$$i_m = i_L + \sum_k i_k$$

- Three ways how to introduce noise into this model.

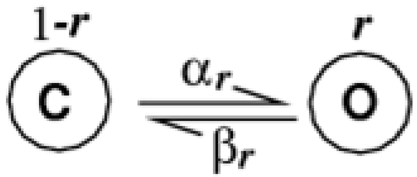
5th topic: gating particle models of ion channels

- Reading: the first 7 slides from lecture 10.

- Basic equation for an ion current: $I = g_{(\max)} r^p \ldots r^p \left(V - E\right)$

- State (or gating particle) variables denoted by *r* (*p* means power) obey:

$$\dot{r} = \alpha_r (1 - r) - \beta_r\, r$$



- ODE expresses the channel opening/closing kinetic scheme. Here, *r* is the concentration of open channels, (1 – *r*) is the concentration of closed ones.

- Rate functions α and β can be complex functions of membrane voltage (if the channel is V-gated) or concentration of neurotransmitter (if the channel is receptor gated) or both. In addition, opening/closing can have > 1 transition.

6th topic: design of networks of spiking neurons (SNN)

- Reading: Chapter 9, pp. 227 – 233.

- Which constraints has the modeller take into account when constructing a model of a particular part of the brain?
  - (1) proportion of excitatory versus inhibitory neurons
  - (2) different types of excitatory/inhibitory neurons
  - (3) types of ion channels
  - (4) connectivity patterns
  - (5) which model of neuron (I&F or compartmental, other?)
  - (6) downscaling – how?
  - Etc.
- What's an event based simulation scenario in the context of SNN?

Final exam (worth 40%)

- Time allowed: **3 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 lectures or the indicated reading !

"Just a darn minute! — Yesterday you said that X equals **two**!"