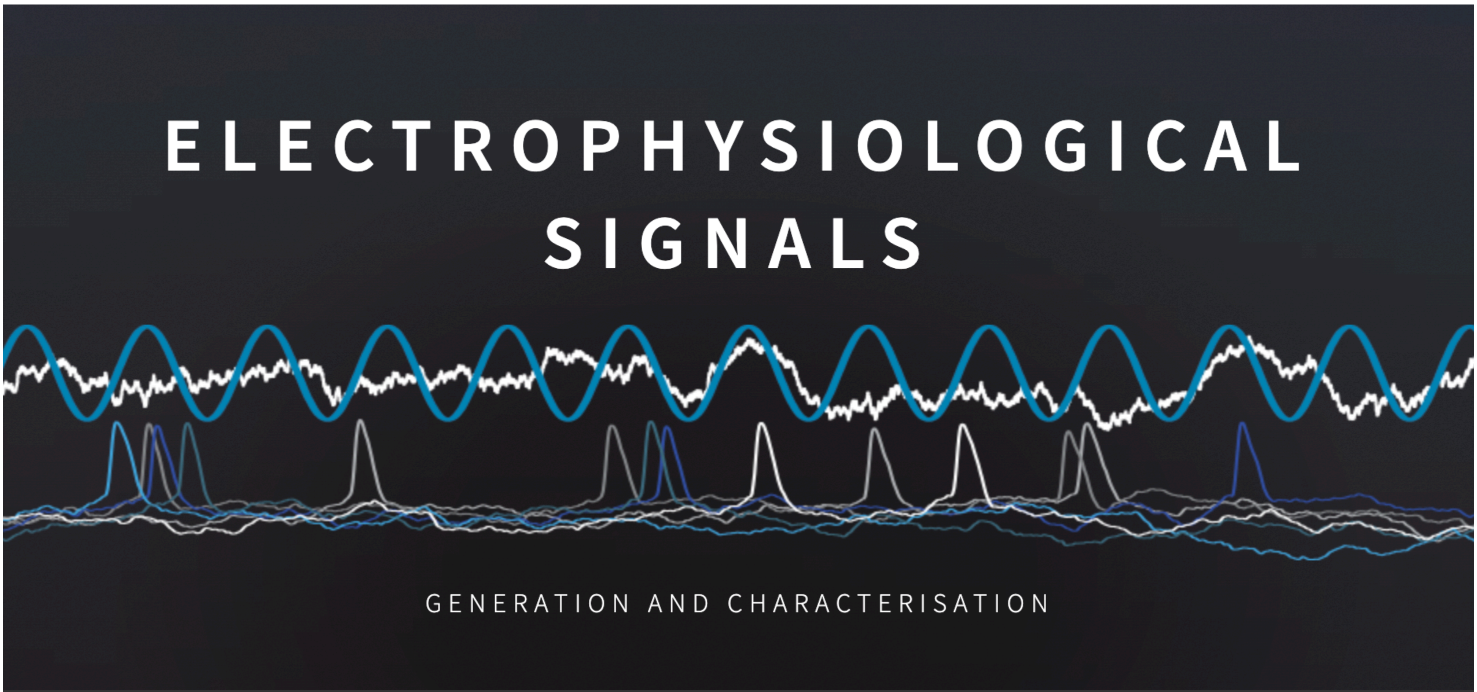
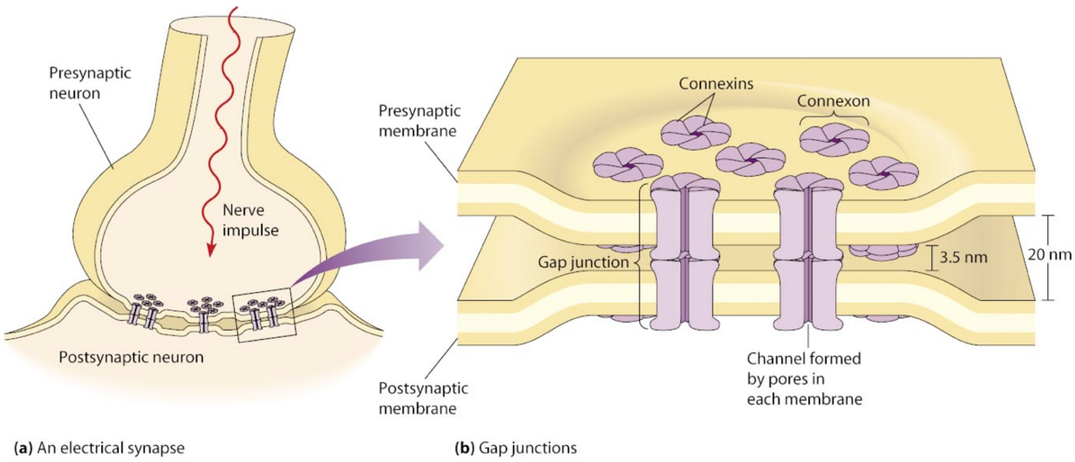


Michele GIUGLIANO

Synaptic transmission

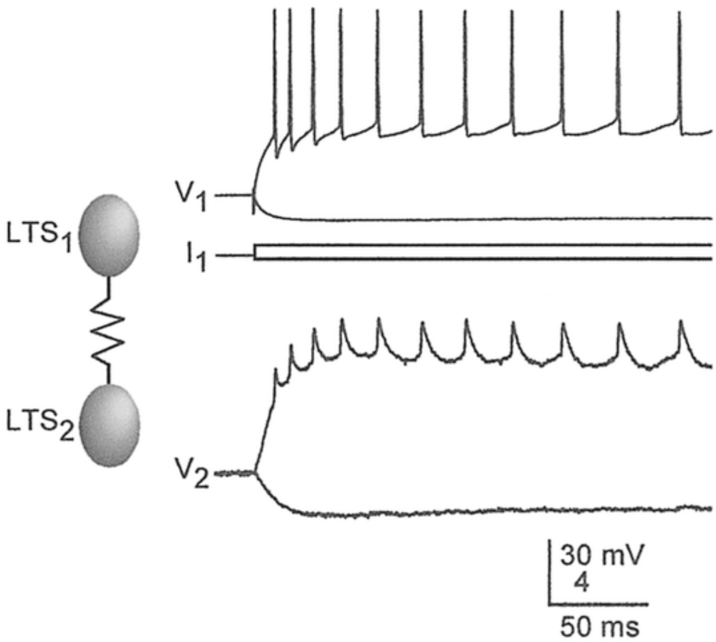
- Electrical synaptic transmission
- Chemical Synaptic Transmission
- Nomenclature and classes of postsynaptic receptors
- *Excitatory* and *Inhibitory* synapses

Electrical synaptic transmission
[bidirectional, slow, without “sign”]

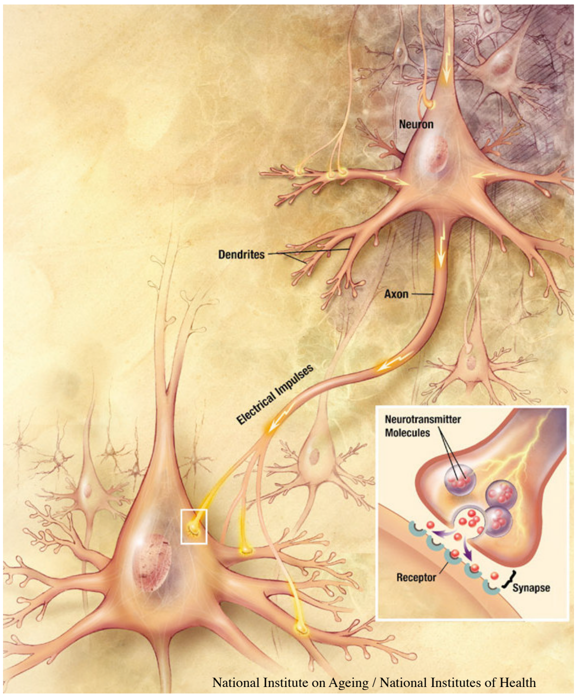


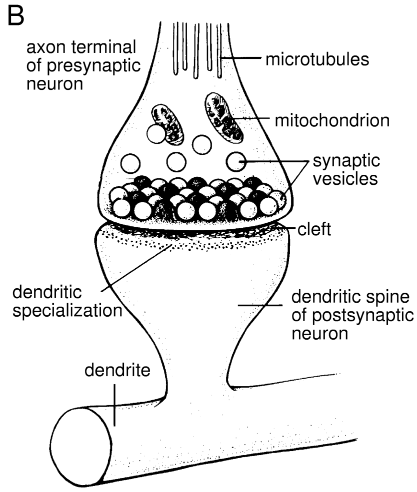
(a) An electrical synapse (b) Gap junctions

Electrical synaptic transmission
[bidirectional, slow, without “sign”]



Chemical synaptic transmission
[unidirectional, fast, with "sign"]

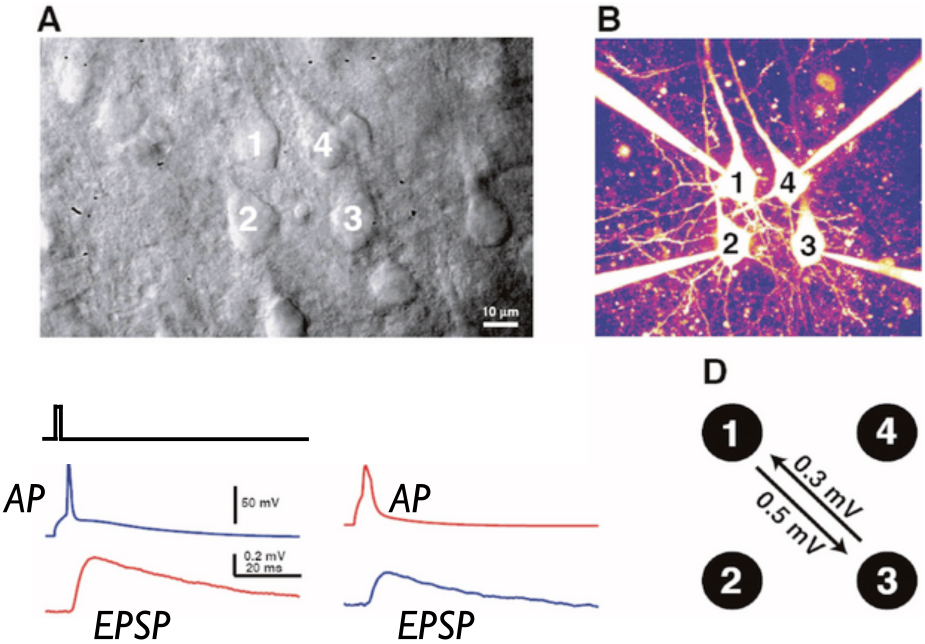




Simultaneous whole-cell patch-clamp recordings from several neurons simultaneously

Song *et al.* [2005]

Simultaneous whole-cell patch-clamp recordings
from several neurons simultaneously



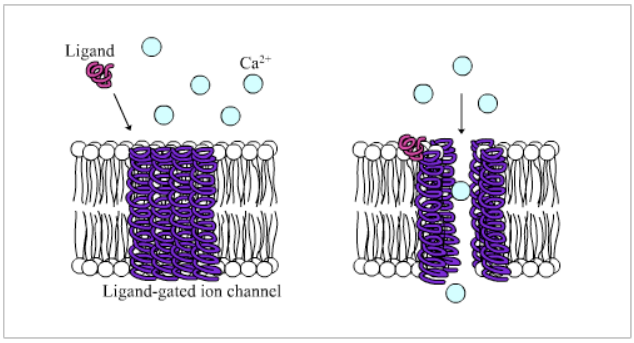
Song *et al.* [2005]

Chemical synaptic transmission:
release of neurotransmitter upon arrival of an AP

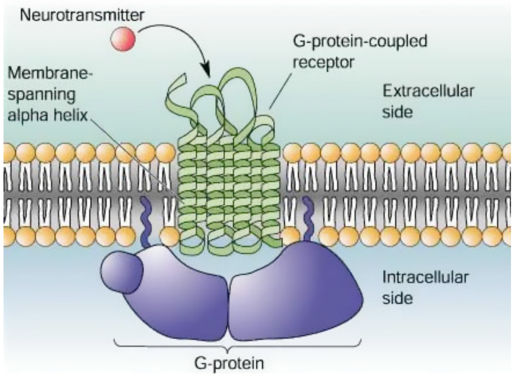
EPSCs - excitatory postsynaptic currents
EPSPs - excitatory postsynaptic potentials
[IPSCs - inhibitory postsynaptic currents]
[IPSPs - inhibitory postsynaptic potentials]

Synaptic receptors
[located on the membrane of the postsynaptic - i.e. target - neuron]

Ionotropic receptors
[i.e. pore]



Metabotropic receptors
[i.e. no pore exists!]



Excitatory Synaptic transmission
mediated by receptors permeable to Na+ and/or Ca++

Mediated by
"fast-activating" receptors

receptors are ligand-gated
ion channels
[i.e. ionotropic receptors]

AMPAr
NMDAr
ACh r

Mediated by
"slow-activating" receptors

receptors are ligand-activated
protein that trigger an intracellular
cascade of reactions leading to
[intracellular-side] gating of channels
[i.e. metabotropic receptors]

mGLUr

$$E_{syn} = \frac{R\ T}{z\ F} \log\left(\frac{C_{out}}{C_{in}}\right) > V_{rest}$$

Inhibitory Synaptic transmission
mediated by receptors permeable to K+ or Cl-

Mediated by
"fast-activating" receptors

receptors are ligand-gated
ion channels
[i.e. ionotropic receptors]

GABA-A r
Gly r

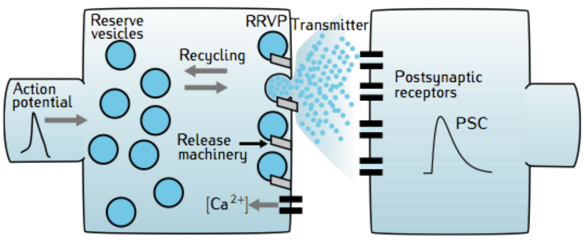
Mediated by
"slow-activating" receptors

receptors are ligand-activated
protein that trigger an intracellular
cascade of reactions leading to
[intracellular-side] gating of channels
[i.e. metabotropic receptors]

GABA-B r

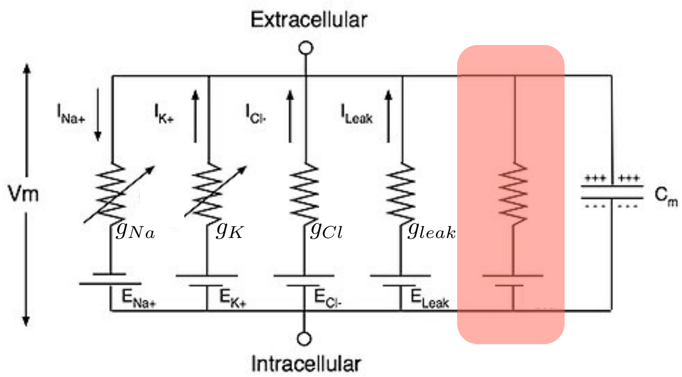
$$E_{syn} = \frac{R\ T}{z\ F} \log\left(\frac{C_{out}}{C_{in}}\right) < V_{rest}$$

Chemical synaptic transmission
[unidirectional, fast, with "sign"]



from Sterratt et al., 2011

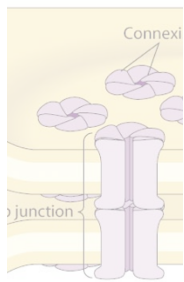
$$I_{syn} = g_{syn}(t)\ (E_{syn} - V_m)$$

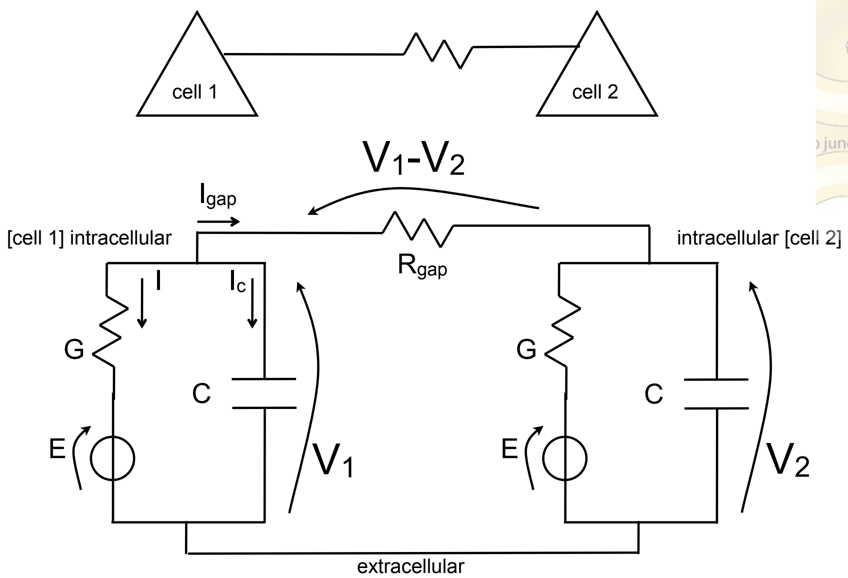


Plan for the day

- Models of Synaptic transmission (electric / chemical)
- Simplified models of synaptic transmission
- Example and relevance for biological phenomena

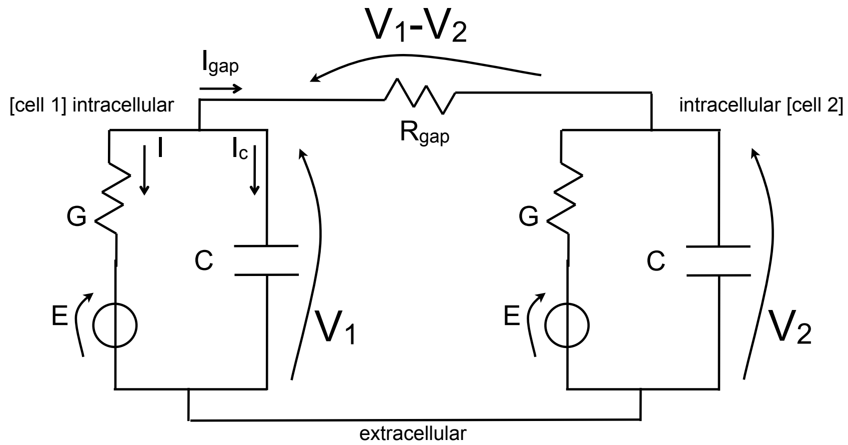
Electrical synaptic transmission [bidirectional, slow, without "sign"]



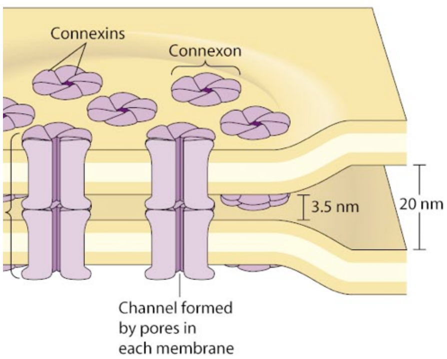


$$C\frac{dV_1}{dt} = G\ (E - V_1) - \boxed{\frac{(V_1 - V_2)}{R_{gap}}}$$

$$C\frac{dV_2}{dt} = G\ (E - V_2) + \boxed{\frac{(V_1 - V_2)}{R_{gap}}}$$



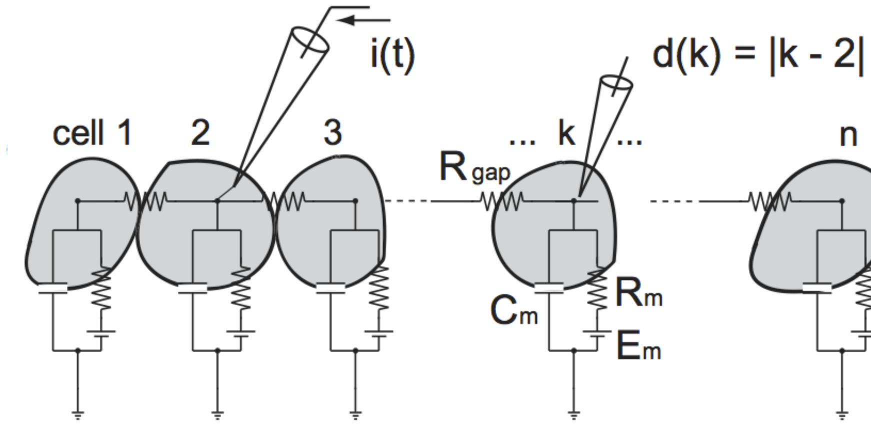
Electrical synaptic transmission
[bidirectional, slow, without "sign"]



$$\boxed{I_{syn} = g_{gap}\ (V_{pre} - V_{post})}$$

Electrical synaptic transmission at the steady-state [i.e., DC regimes]

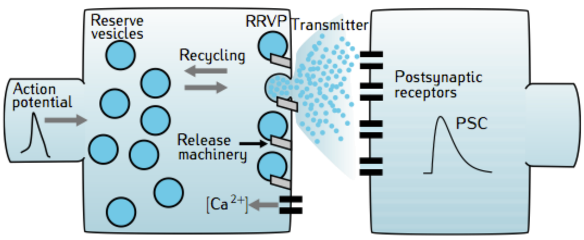
$$\frac{dV_1}{dt} = \frac{dV_2}{dt} = 0$$



A cascade of gap-junction coupled neurons is like a **series** of resistors....

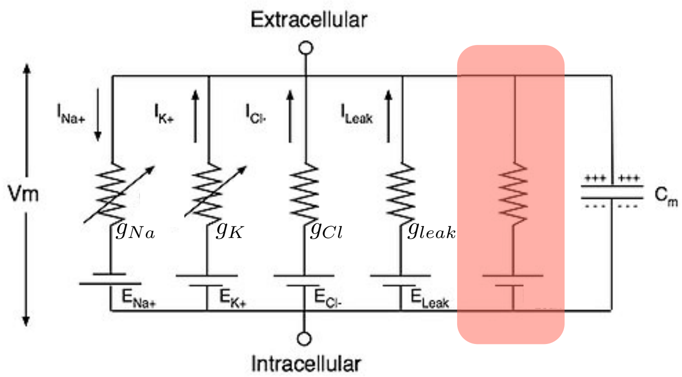
Chemical synaptic transmission

[unidirectional, fast, with "sign"]



from Sterratt et al., 2011

$$I_{syn} = g_{syn}(t)\ (E_{syn} - V_m)$$



Chemical synaptic transmission

[unirectional, fast, with "sign"]
model of a ionotropic receptor

$$C \underset{\beta}{\overset{\alpha[T]}{\rightleftharpoons}} O \qquad\qquad g_{syn}(t) = \overline{g}_{syn} O(t)$$

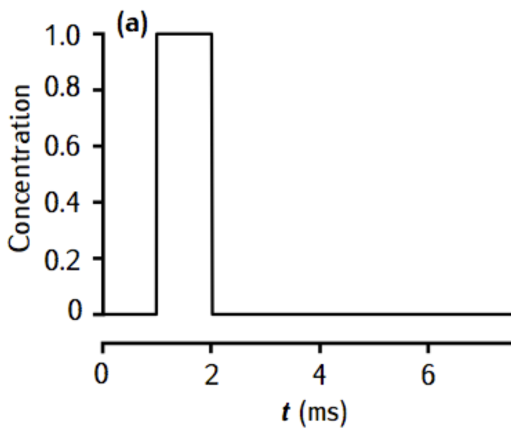
$$\frac{dO(t)}{dt} = -\beta\, O + \alpha\, [T]\, C$$

$$\frac{dC(t)}{dt} = +\beta\, O - \alpha\, [T]\, C$$

$$O(t) + C(t) = 1$$

Destexhe *et al.* [1994]

$$\frac{dO}{dt} = \frac{O_\infty - O}{\tau_O} \qquad O_\infty = \frac{\alpha\, T(t)}{\alpha\, T(t) + \beta} \qquad \tau_O = \frac{1}{\alpha\, T(t) + \beta}$$



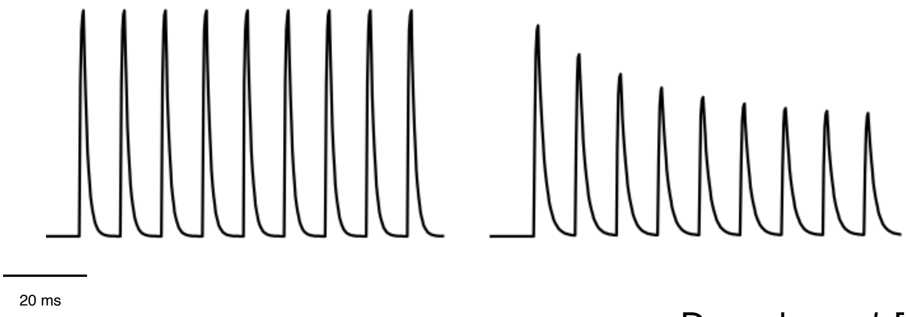
from Sterratt et al., 2011

$$C \underset{\beta}{\overset{\alpha[T]}{\rightleftharpoons}} O$$

$$C_0 \underset{R_{u1}}{\overset{R_b[T]}{\rightleftharpoons}} C_1 \underset{R_{u2}}{\overset{R_b[T]}{\rightleftharpoons}} C_2 \underset{R_c}{\overset{R_o}{\rightleftharpoons}} O$$

$$C_2 \underset{R_r}{\overset{R_d}{\rightleftharpoons}} D,$$

$$I_{syn} \;=\; \bar{g}_{syn}\; O(t)\; (E_{syn} \;-\; V_m)$$



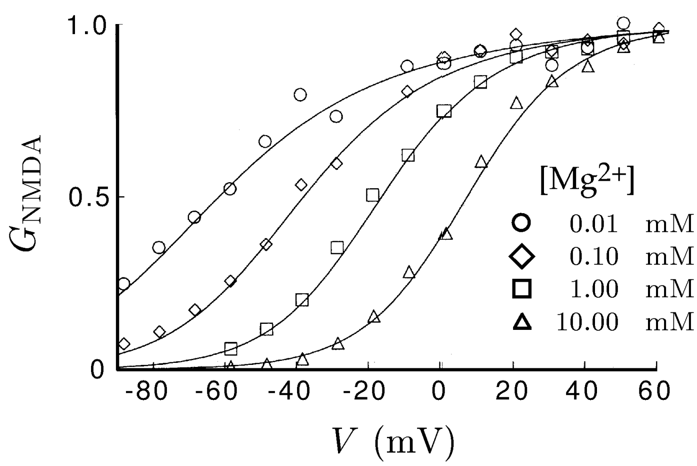
Destexhe *et al.* [1994]

NMDAr: Ligand- and voltage-dependent synaptic currents

[this has the potential for pre/post coincidence-detection]

$$I_{NMDA_R} \;=\; G_{NMDA_R}\; r(t)\; (E_{NMDA_r} \;-\; V_m)$$

$$G_{NMDA_R} \;=\; G_{NMDA_R}(V, [Mg^{2+}])$$



Chemical synaptic transmission

model of a metabotropic receptor

$$R_0 + T \rightleftharpoons R \rightleftharpoons D$$
$$R + G_0 \rightleftharpoons RG \longrightarrow R + G$$
$$G \longrightarrow G_0$$
$$C + nG \rightleftharpoons O,$$

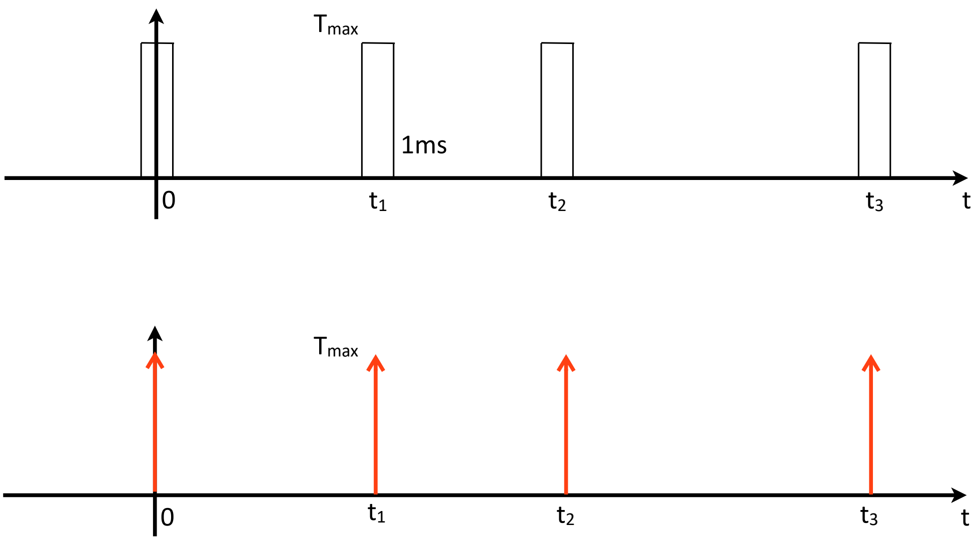
$$g_{syn}(t) = \overline{g}_{syn} O(t)$$

$$I_{syn} = \bar{g}_{syn}\ O(t)\ (E_{syn} - V_m)$$

Chemical synaptic transmission

simplified model of [a population of] ionotropic receptors

- A **train** of presynaptic action potentials leads to [T](t):



Chemical synaptic transmission

<u>simplified</u> model of [a population of] ionotropic receptors

$$C \underset{\beta}{\overset{\alpha[T]}{\rightleftharpoons}} O$$

[dynamical] steady-state??

$$\frac{dO(t)}{dt} = -\beta\, O \;+\; \alpha\; [T]\; C$$

$$\frac{dO}{dt} = -\beta\, O \;+\; \alpha\, T_{max}(1-O)\, \sum_k \delta(t-t_k)$$

$$\frac{dO}{dt} \approx -\beta\, O \;+\; \alpha\, T_{max} \sum_k \delta(t-t_k)$$

$$O(t_{k+1}^{+}) \approx O(t_k^{+}) e^{-\beta\, (t_{k+1}-t_k)} \;+\; \alpha\, T_{max}$$

$$\boxed{O_{SS} \approx \alpha\, T_{max}\, \beta^{-1}\, f}$$

conductance-driven model synapse

$$I_{syn} = \bar{g}_{syn}\, O(t)\, \left(E_{syn} - V_m\right)$$

$$\frac{dO}{dt} \approx -\beta\, O \;+\; \alpha\, T_{max} \sum_k \delta(t-t_k)$$

current-driven model synapse

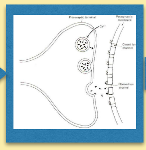
$$I_{syn} \approx \bar{I}\, O(t)$$

$$\boxed{\bar{I} = \bar{g}_{syn}\, \left(E_{syn} - \;< V_m >\right)}$$

$$\frac{dI_{syn}}{dt} \approx -\beta I_{syn} \;+\; W \sum_k \delta\left(t-t_k\right)$$

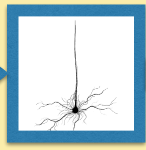
$$W = \bar{g}\alpha T_{max}$$

Very rough (functional) approximation

f  I_0

output

analog variable
proportional to
the driving frequency
[current or conductance]

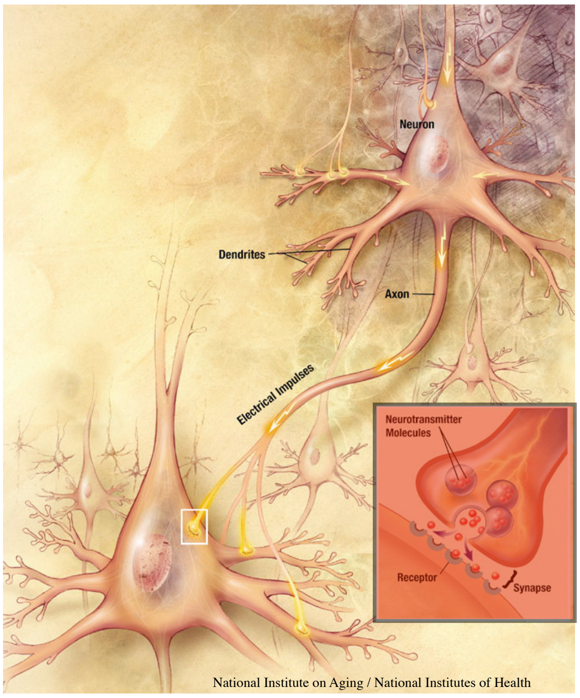
I_0  f

$$O_{SS} \approx \alpha \, T_{max} \, \beta^{-1} \, f$$

$$f(I) \approx \frac{I_0}{C(V_{th} - E)}$$

A synapse is a device that converts input spike trains with a certain ***frequency****, into an average current (****amplitude****).*

Synaptic connections are more than *connecting plugs*



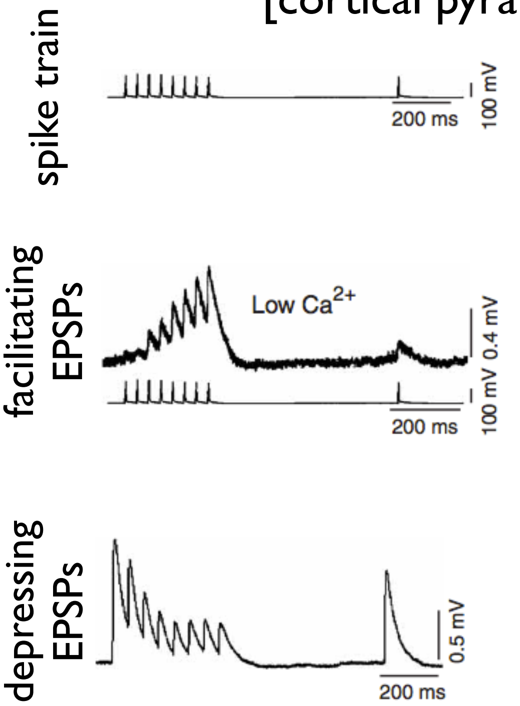
They are physical systems implementing a ***dynamical*** communication channel...

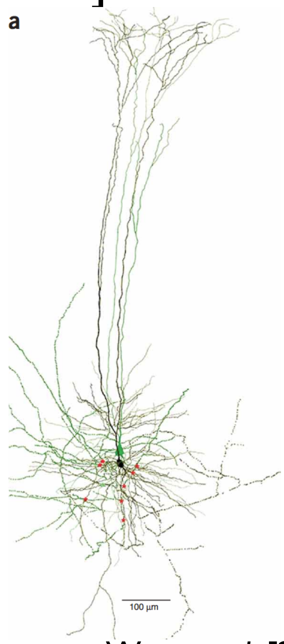
Like all physical system they may show [**transient**] inertia, fatigue, or *depression* during repeated activation.

They may also, on the contrary, [**transiently**] warm up upon use and *facilitate* further communications.

Short-term [homosynaptic] plasticity.
[neuromuscular junction, central syn.]

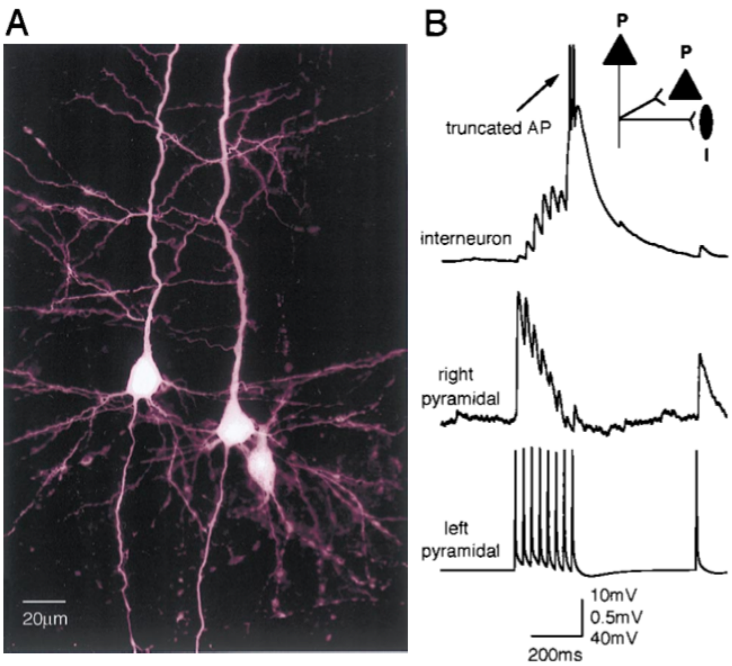
Short-term plasticity: facilitation and depression [cortical pyramidal neurons]





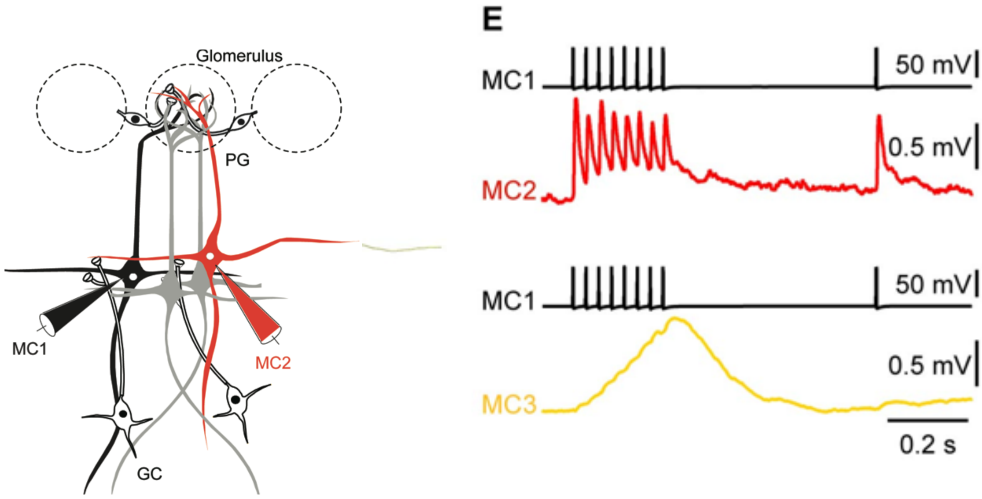
Wang *et al.* [2006]
Tsodyks & Markram[1997]

Short-term plasticity: facilitation and depression



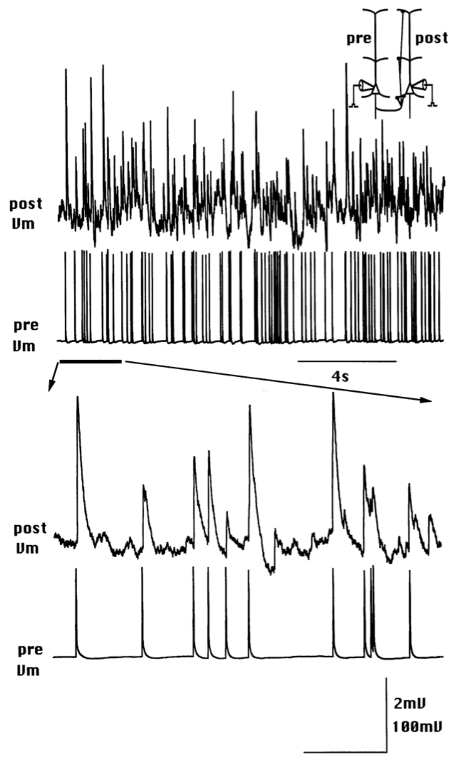
Markram et al. [1998]

Short-term plasticity: facilitation and depression
[olfactory bulb, mitral cells, same glomerulus]



Pignatelli et al.

Impact of short-term synaptic plasticity



Markram et al. [1998]

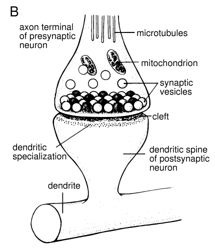
Short-term synaptic depression

$$\begin{tikzcd} R \arrow[rr, bend left, "u"] & & E \arrow[dl, bend left, "\frac{1}{\tau_{inact}}"] \\ & I \arrow[ul, bend left, "\frac{1}{\tau_{rec}}"] & \end{tikzcd}$$

$$\frac{dR}{dt} = -uR + \frac{1}{\tau_{rec}} I$$

$$\frac{dE}{dt} = +uR - \frac{1}{\tau_{inact}} E$$

$$\frac{dI}{dt} = +\frac{1}{\tau_{inact}} E - \frac{1}{\tau_{rec}} I$$

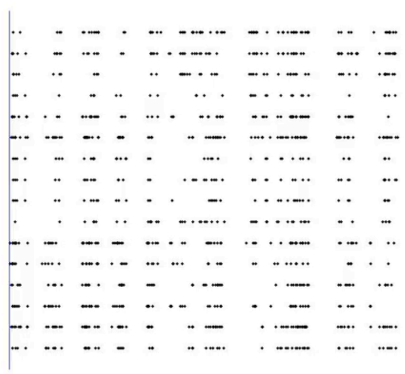


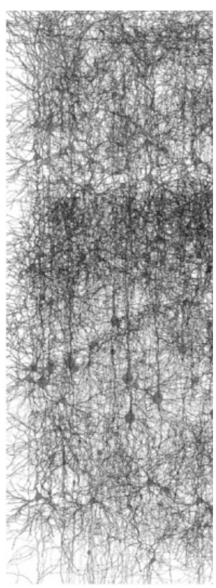
$$\tau_{rec} >> \tau_{inact}$$

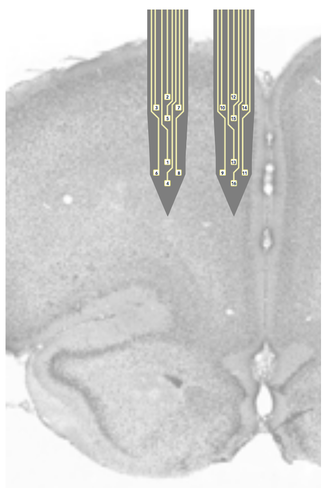
[Pre]synaptic resources [e.g., vesicles]

In vivo cortical networks [transient] synchronisation

J. Couto

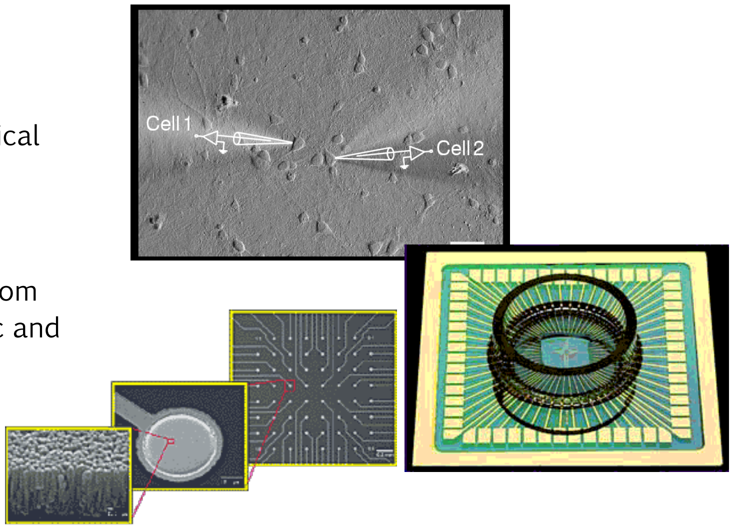






in vitro: spontaneous activity cultured dissociated neurons

- dissociated from the cortical tissue,
- neurons develop ex vivo, reorganising into 2D random networks of glutamatergic and gabaergic cells



Ex vivo cortical networks spontaneous [transient] synchronisation