Nonlinear Dynamics of Neuronal Systems

Synaptic channels

- Synaptic channels
- Synaptic dynamics
- Short term plasticity: depression and facilitation

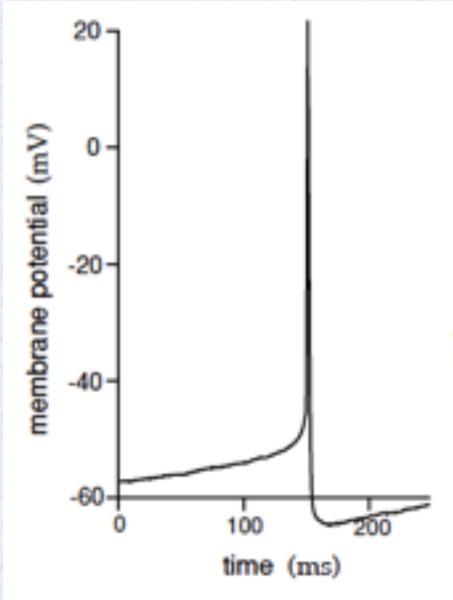
Bibliography:

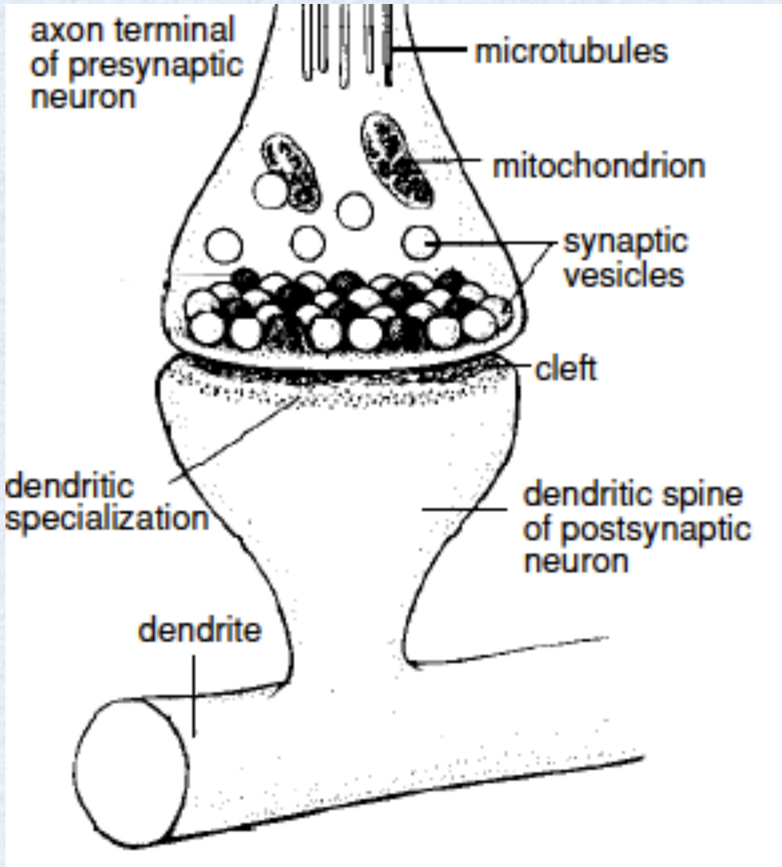
"Mathematical Foundations of Neuroscience" – G. B. Ermentrout & D. Terman (Springer, 2010).

Synaptic channels

Membrane channels

- Voltage-gated
- Ion-gated
- Synaptic





Opening of synaptic channels

- Action potential (AP) travels down the axon
- AP terminates at presynaptic sites (many)
- AP invades synaptic terminals (containing Ca)
- Depolarization release Ca
- Ca activates a Ca-binding protein
- Transmitter release (binding to vesicles containing the transmitter)
- Vesicles (“docked”) release the transmitter into the synaptic cleft
- Transmitter diffusion through the cleft
- Binding to receptors on the postsynaptic neuron (spines)
- Receptors open channels, causing
  - Depolarization
  - Hyperpolarization

Synaptic channels

Transmitter release

- Affected by neuromodulators (chemicals)
- Probabilistic
- Quantal (occurs in discrete amounts)
- Potentiation or facilitation (increase of transmitter over successive firings of APs)
- Depression (decrease of transmitter over successive firings of APs)

Main transmitters:

- Glutamate (“excitation”)
- GABA (“inhibition”)

Synaptic Dynamics

Model: First approach

$$I_{\text{syn}} = g(t)(V_{\text{post}} - V_{\text{rev}})$$

$$g(t) = \bar{g}\sum_k \alpha(t - t_k)$$

$$\alpha(t) = \frac{a_d a_r}{a_r - a_d}(\mathrm{e}^{-a_d t} - \mathrm{e}^{-a_r t})$$

- g(t): synaptic conductance
- a_r: rise time
- a_d: decay time

$$z'' + (a_r + a_d)z' + a_r a_d z = a_r a_d \sum_k \delta(t - t_k)$$

Synaptic Dynamics

Model:

$$I_{\text{syn}} = g(t)(V_{\text{post}} - V_{\text{rev}})$$

- [T]: Concentration of transmitter released into the synaptic cleft by a presynaptic spike
- s(t): Fraction of open channels
- a_r: rise time
- a_d: decay time

$$\frac{\mathrm{d}s}{\mathrm{d}t} = a_r[T](1-s) - a_d s$$

$$[T](V_{\text{pre}}) = \frac{T_{\max}}{1+\exp(-(V_{\text{pre}} - V_{\text{T}})/K_p)}$$

$T_{\max}$ =1 mM, V_{T} = 2, and K_p = 5 mV.

Synaptic Dynamics

Excitation (chemical)

- AMPA/kainate (very fast)
- NMDA (implicated in memory and long-term potentiation)

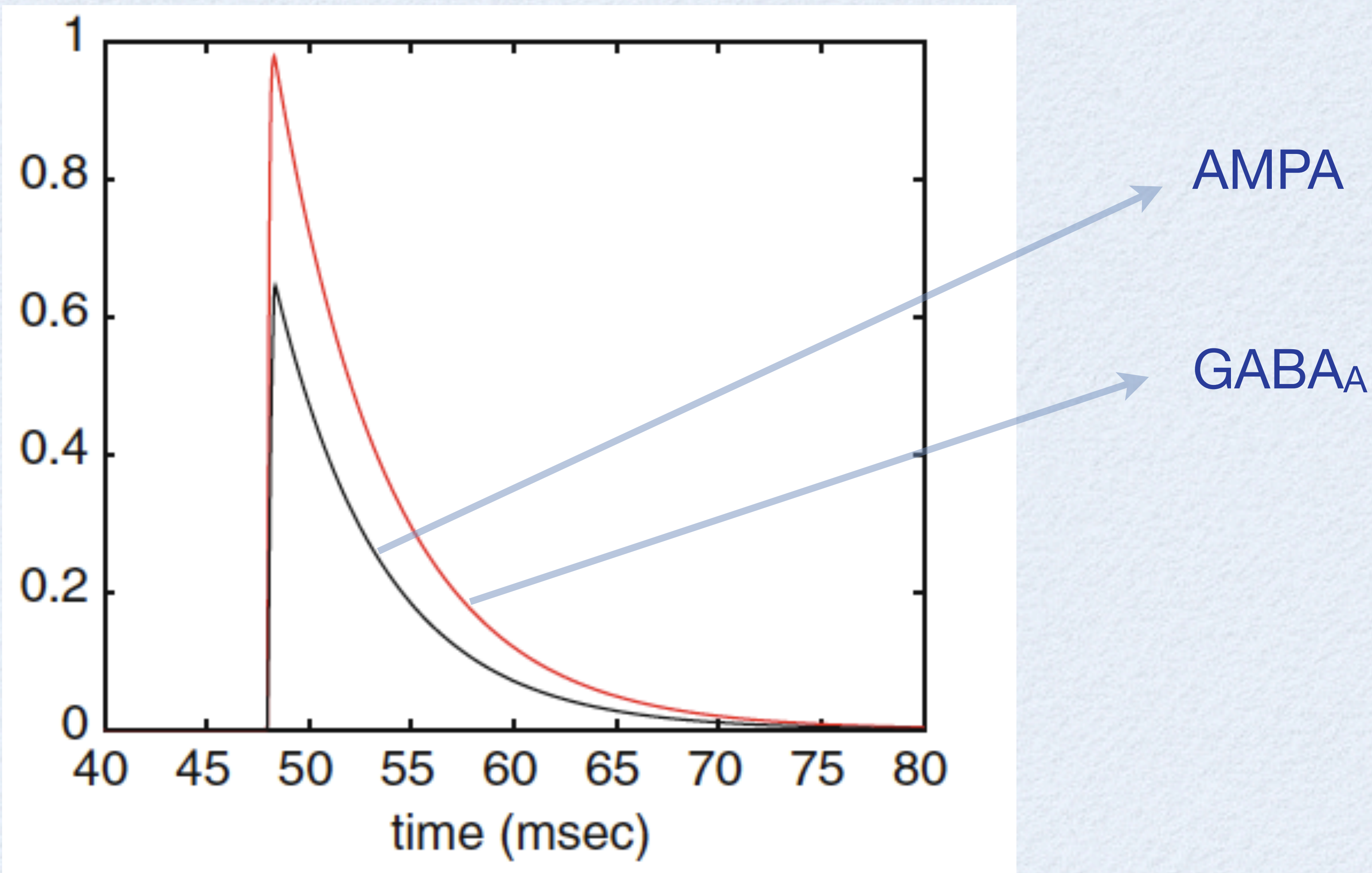
Inhibition (chemical)

- $GABA_A$ (fast)
- $GABA_B$

Gap junctions (electrical)

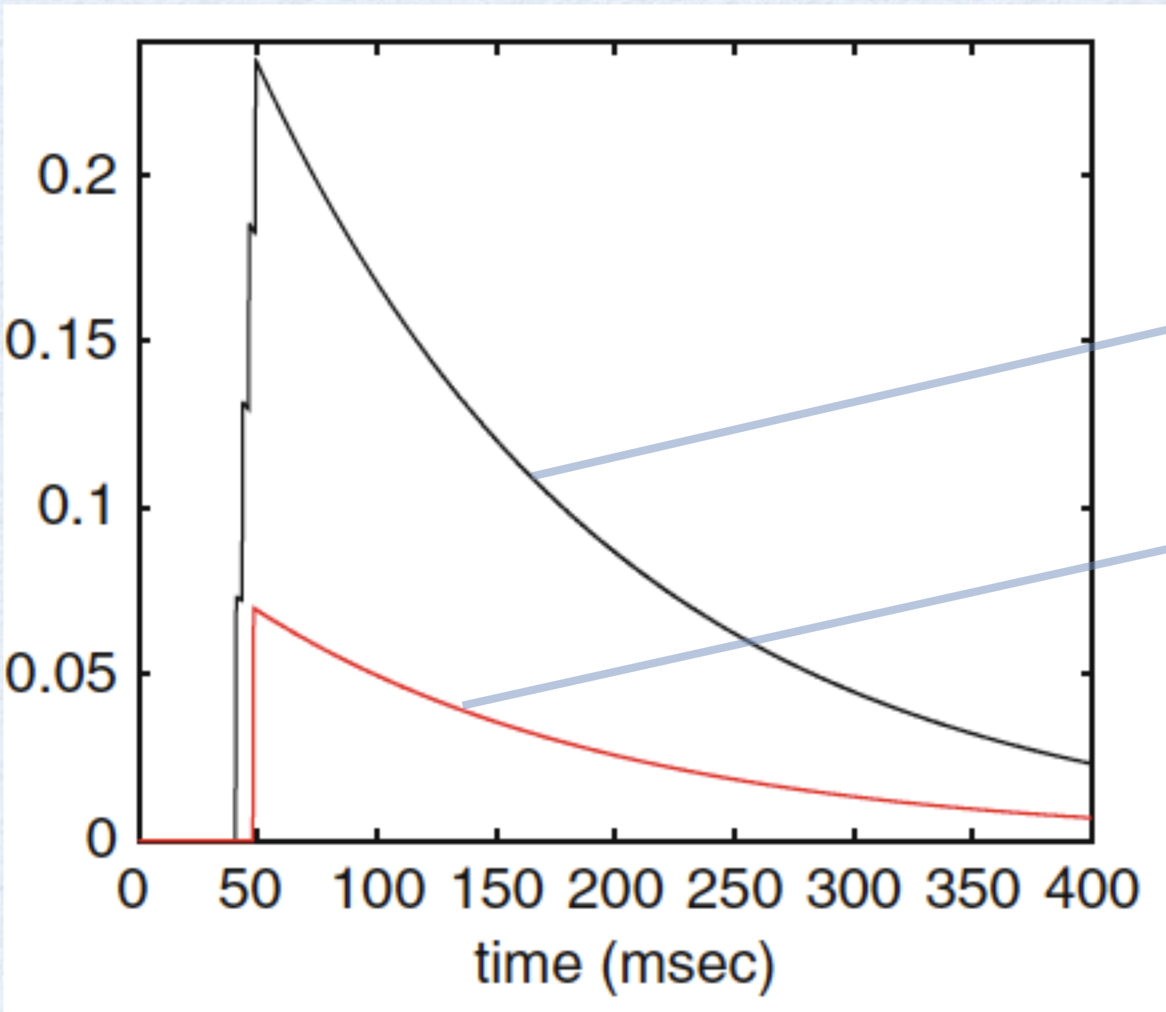
Synaptic Dynamics

Model:



Synaptic Dynamics

Model:

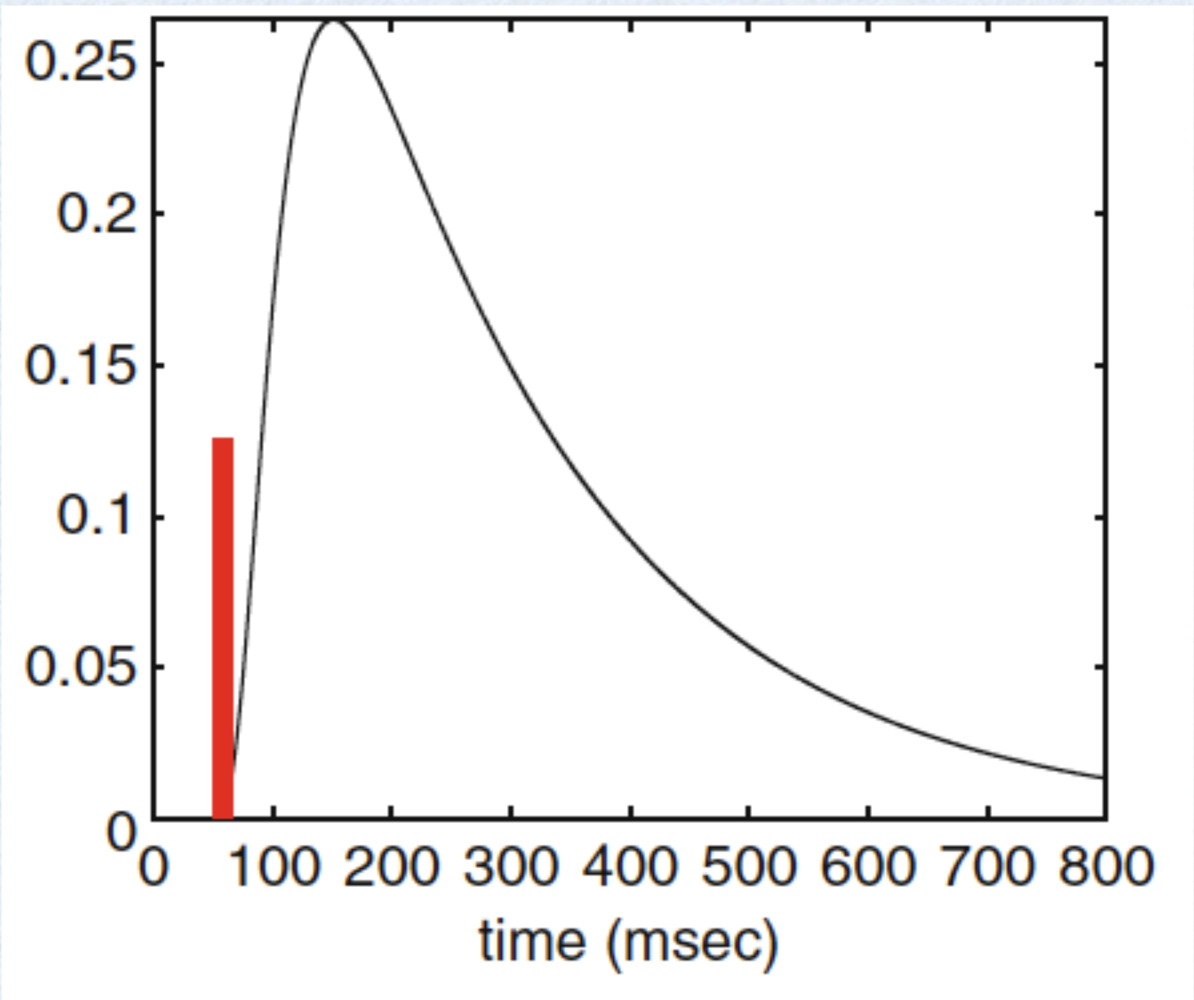


NMDA (4 spikes)

NMDA (1 spike)

Synaptic Dynamics

Model:



GABA$_B$ (8 spikes)

Synaptic Dynamics

AMPA/kainate

$$I_{\text{AMPA}} = \bar{g}_{\text{AMPA}} s (V - V_{\text{AMPA}})$$

$$V_{\text{AMPA}} = 0$$

$a_r = 1.1\ \text{mM}^{-1}\ \text{ms}^{-1}$ and $a_d = 0.19\ \text{ms}^{-1}$

Synaptic Dynamics

NMDA

- Faster than AMPA
- Partially blocked by Mg under normal conditions
- Mg block can be removed if the postsynaptic neuron is depolarized
- Both the pre- and post-synaptic cells must be active for I_{NMDA} to flow
- Memory encoding (long term changes, Ca)
- Persistent activity (short term memory)

$$I_{\mathrm{NMDA}} = \bar{g}_{\mathrm{NMDA}} s B(V)(V - V_{\mathrm{NMDA}})$$

$$B(V) = \frac{1}{1 + \mathrm{e}^{-(V - V_{\mathrm{T}})/16.13}}$$

$$V_{\mathrm{T}} = 16.13 \ln \frac{[\mathrm{Mg}^{2+}]}{3.57}$$

At the physiological concentration of 2 mM, $V_{\mathrm{T}} \approx -10\,\mathrm{mV}$

$$V_{\mathrm{NMDA}} = 0\,\mathrm{mV}$$

$$a_r = 0.072\ \mathrm{mM}^{-1}\,\mathrm{ms}^{-1},\ a_d = 0.0066$$

Synaptic Dynamics

$GABA_A$

$$I_{\mathrm{GABA_A}} = \bar{g}_{\mathrm{GABA_A}} s(V - V_{\mathrm{GABA_A}})$$

$V_{\mathrm{GABA_A}}$ varying between -81 and -60 mV

$$a_r = 5\ \mathrm{mM^{-1}\,ms^{-1}},\ a_d = 0.18\ \mathrm{ms^{-1}}$$

- Carried by Cl^-
- Dependent on the physiological conditions and the developmental stage of the neuron

Synaptic Dynamics

- Direct synapses: AMPA / kainate, NMDA, $GABA_A$ (ion channel and receptor are the same protein
- Indirect synapses: $GABA_B$ (activator of the receptor sets off a cascade of intracellular events which alter the conductivity of an ion channel)

$GABA_B$

- Transmitter binding to a receptor protein
- Activation of an intracellular complex (G-protein)
- Activation of a K channel (membrane hyperpolarization)

- Slow responses
- Non-linear responses
- Long lasting responses

Synaptic Dynamics

GABA$_B$

$$I_{\mathrm{GABA_B}} = \bar{g}_{\mathrm{GABA_B}} \frac{s^n}{K_d + s^n}(V - E_K)$$

$$\frac{\mathrm{d}r}{\mathrm{d}t} = a_r[T](1-r) - b_r r,$$

$$\frac{\mathrm{d}s}{\mathrm{d}t} = K_3 r - K_4 s.$$

r: receptor
s: ion channel

$a_r = 0.09\ \mathrm{mM^{-1}ms^{-1}}$, $a_d = 0.0012\ \mathrm{ms^{-1}}$

$n = 4$, $K_d = 100$, $K_3 = 0.18\ \mathrm{ms^{-1}}$, and $K_4 = 0.034\ \mathrm{ms^{-1}}$

Synaptic Dynamics

Gap junctions

- Communication via tight junctions between membranes
- Act as resistors
- Always keep the cells in communication
- No need of a presynaptic AP

$$I_{\text{gap}} = \bar{g}_{\text{gap}}(V_{\text{post}} - V_{\text{pre}})$$

Synaptic Dynamics

Short-term plasticity

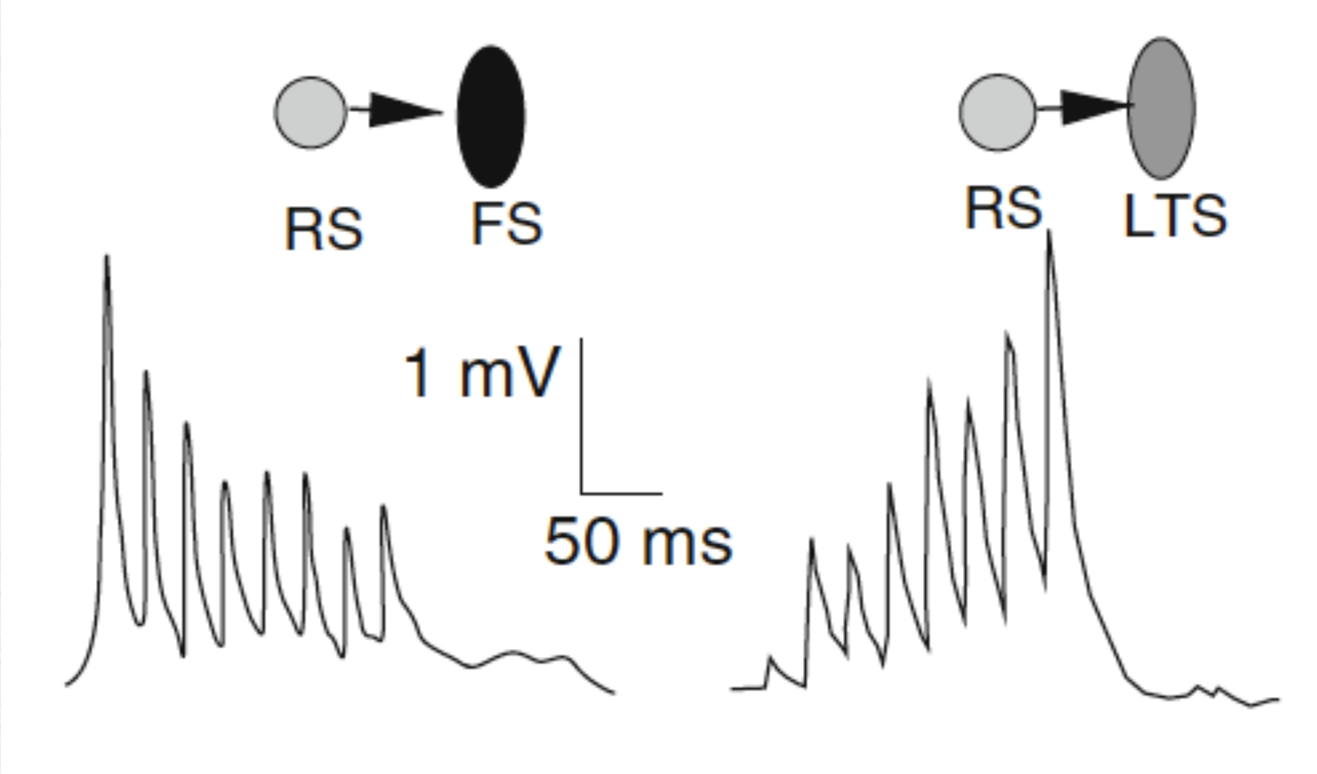


Fig. 7.2 (**a**) Short-term synaptic plasticity in cortical neurons (from [12]). Connections between cortical excitatory cells (RS) and cortical fast spike units (inhibitory) show synaptic depression for 20-Hz stimuli, whereas connections between cortical excitatory cells and low threshold spike (LTS) inhibitory cells show facilitation. (**b–d**) Simulations of (7.13) and (7.14) to periodic stimuli. The parameters for (**b**) are $\tau_d = 300$, $a_d = 0.5$, $d_0 = 1$, $\tau = 10$ and there is no facilitation. The parameters for (**c**) are $\tau_f = 500$, $a_f = 0.2$, $f_0 = 0$, $\tau = 10$ with no depression. The frequency is 20 Hz. (**d**) Both depression and facilitation with $f_0 = 0, d_0 = 1, \tau_f = 50, \tau_d = 400$, $a_f = 0.2, a_d = 0.05$, and $\tau = 5$. The frequency is 100 Hz

Synaptic Dynamics

Model (Dayan & Abbott)

$$M(t) = q(t)\, f(t)$$

- M: Magnitude of synaptic release per presynaptic spike Depression
- q: Depression (between 0 and 1) - d_0: resting value
- f: Facilitation (between 0 and 1) - f_0: resting value

$$\tau_f \frac{\mathrm{d}f}{\mathrm{d}t} = f_0 - f \quad \text{and} \quad \tau_d \frac{\mathrm{d}q}{\mathrm{d}t} = d_0 - q$$

Each time there is a spike, $f(t)$ is increased by an amount $a_f(1 - f)$ and $q(t)$ is decreased by an amount $a_d d$. In both cases, the change is multiplied by a factor which keeps the variables bounded between 0 and 1

Synaptic Dynamics

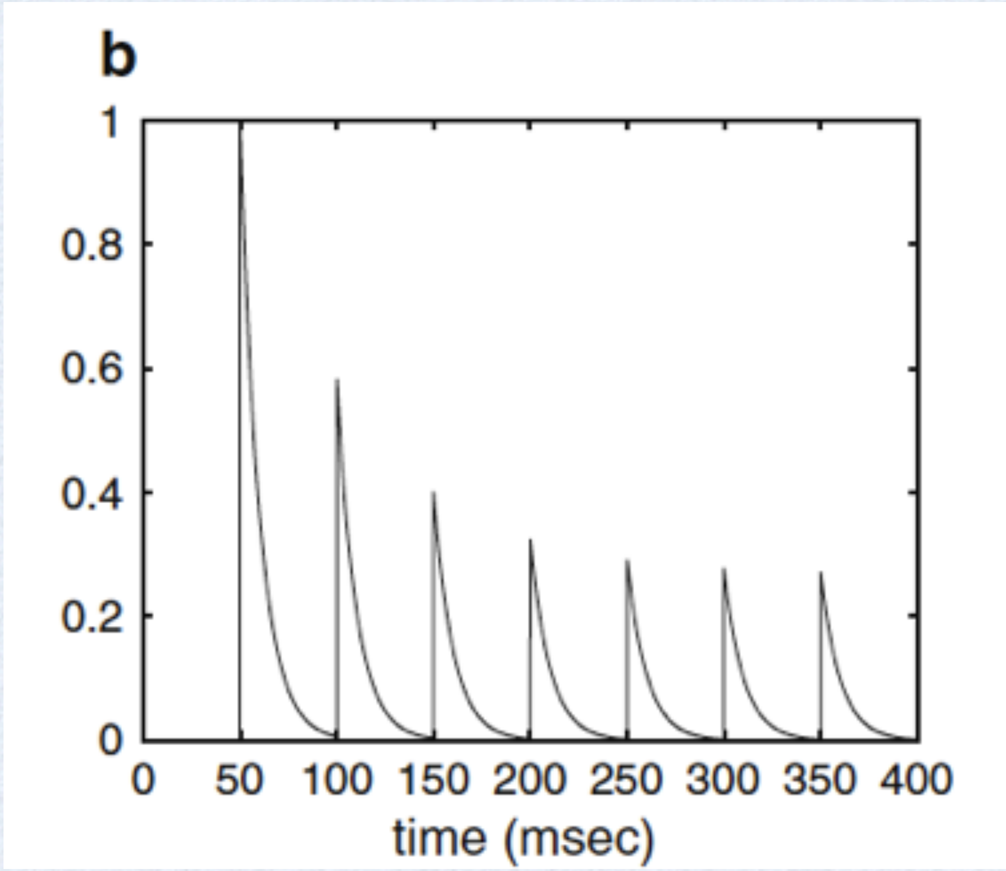
Model (Dayan & Abbott)

$$\frac{\mathrm{d}f}{\mathrm{d}t} = \frac{f_0 - f}{\tau_f} + \left(\sum_j \delta(t - t_j)\right) a_f (1 - f)$$

$$\frac{\mathrm{d}q}{\mathrm{d}t} = \frac{d_0 - q}{\tau_d} - \left(\sum_j \delta(t - t_j)\right) a_d q$$

Synaptic Dynamics

Short-term plasticity



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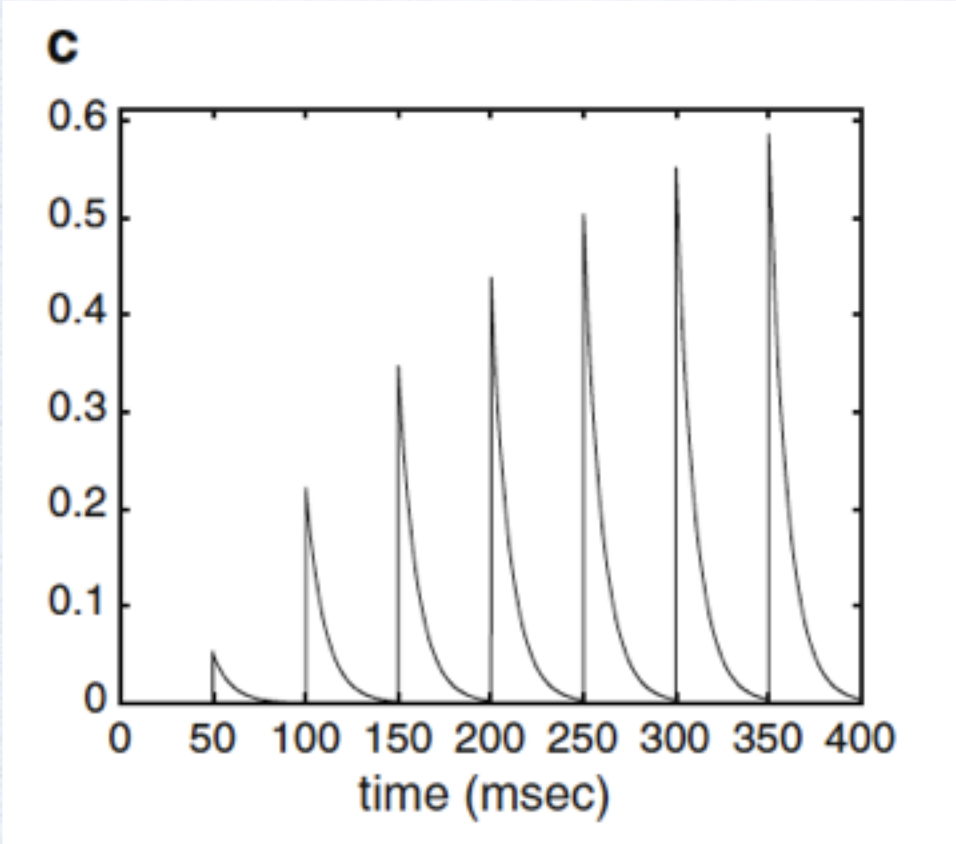
Synaptic Dynamics

Short-term plasticity



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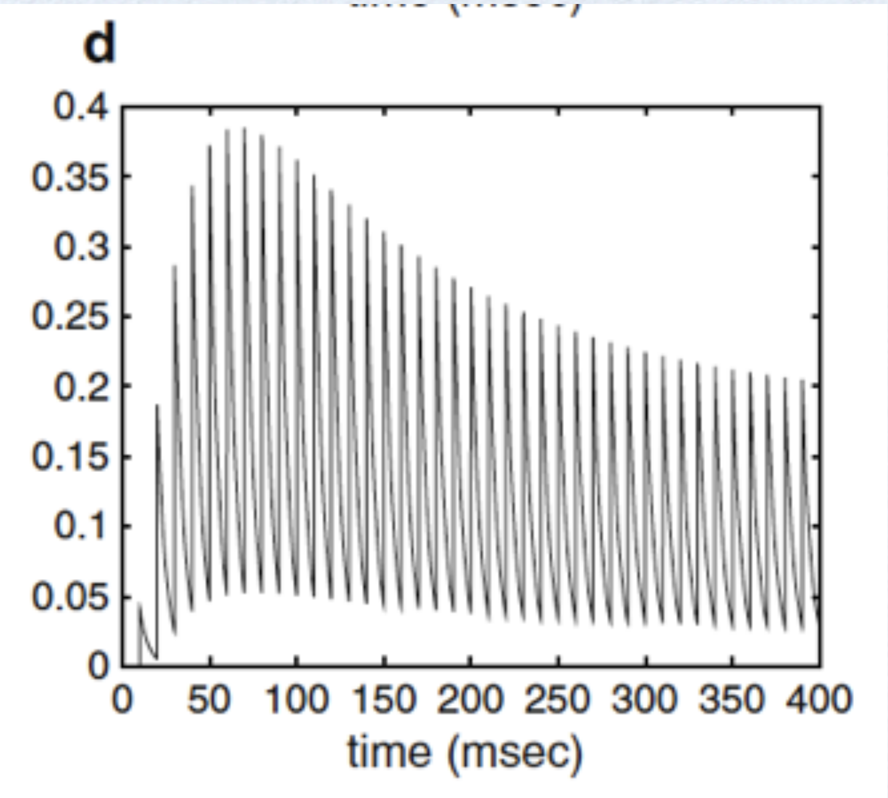
Synaptic Dynamics

Short-term plasticity



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Synaptic Dynamics

Depression model (Manor et al.)

$$\frac{\mathrm{d}q}{\mathrm{d}t} = \frac{q_\infty(V) - q}{\tau_1 + \tau_2 q_\infty(V)},$$

$$q_\infty(V) = \frac{1}{1 + \mathrm{e}^{k(V - V_{\mathrm{thr}})}}$$

$k > 0$ and V_{thr} are parameters

$$\frac{\mathrm{d}s}{\mathrm{d}t} = a_r[T](1 - s) - a_d s$$

$$\bar{g}s(t)q(t)$$

Facilitation:

$$k < 0$$

Synaptic Dynamics

Depression: three-state model

$$A \longrightarrow S,$$
$$S \longrightarrow U,$$
$$U \longrightarrow A.$$

- A: Available transmitter
- S: Conducting state (produces the synaptic conductance)
- U: Transmitter which is unavailable for release

$$\frac{\mathrm{d}s}{\mathrm{d}t} = \alpha(V)(1 - s - u) - \beta s \quad \text{and} \quad \frac{\mathrm{d}u}{\mathrm{d}t} = \beta s - \beta_2 u.$$