Short-term Synaptic Plasticity

褚天昊

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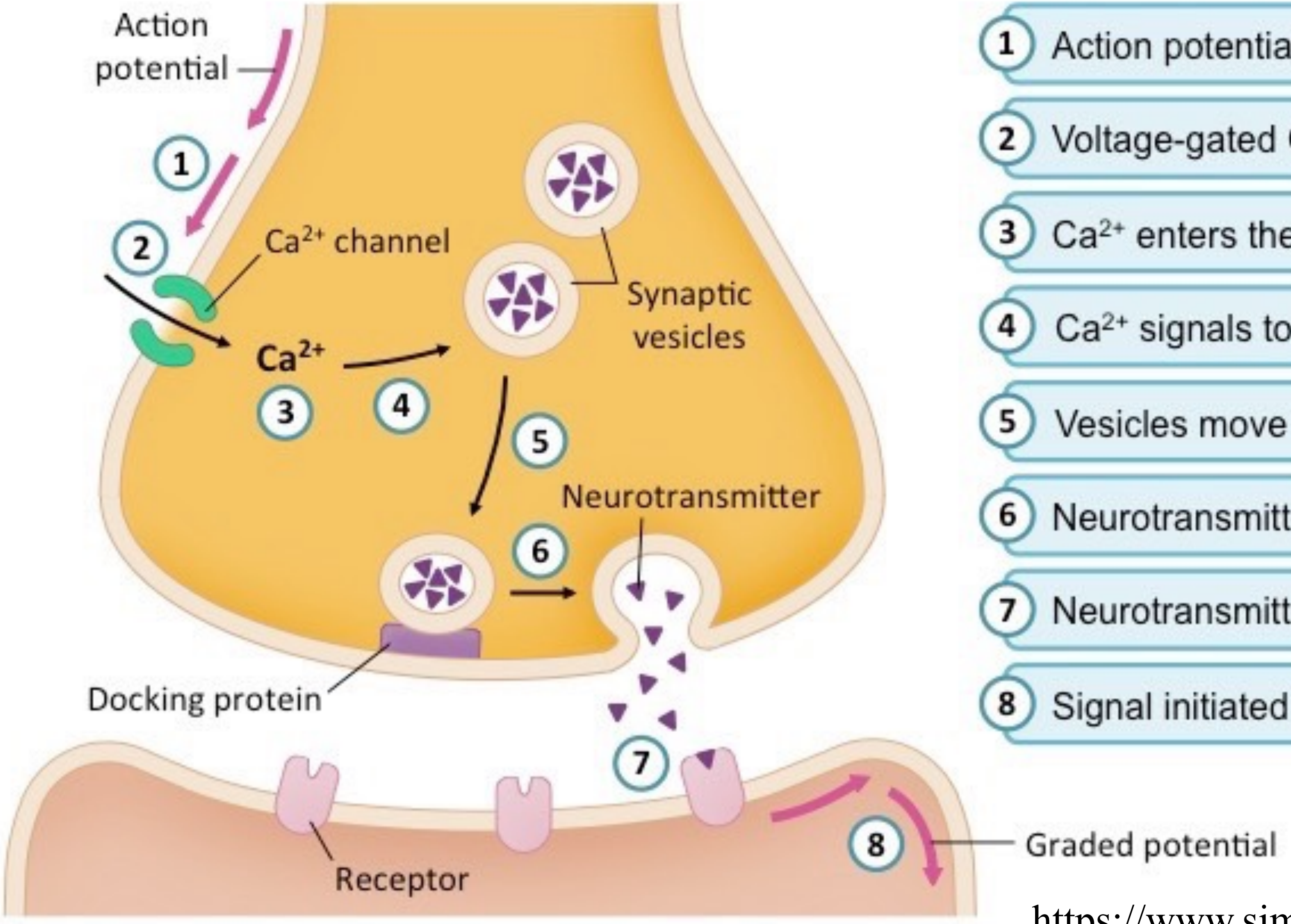
01

Synaptic transmission and plasticity

Process of Chemical synaptic transmission



1. Action potential arrives at axon terminal
2. Voltage-gated Ca^{2+} channels open
3. Ca^{2+} enters the presynaptic neuron
4. Ca^{2+} signals to neurotransmitter vesicles
5. Vesicles move to the membrane and dock
6. Neurotransmitters released via exocytosis
7. Neurotransmitters bind to receptors
8. Signal initiated in postsynaptic cell

https://www.simplypsychology.org/synapse.html

EPSP and EPSC

EPSP: Excitatory Post Synaptic Potential

EPSC: Excitatory Post Synaptic Current

Post synaptic current:

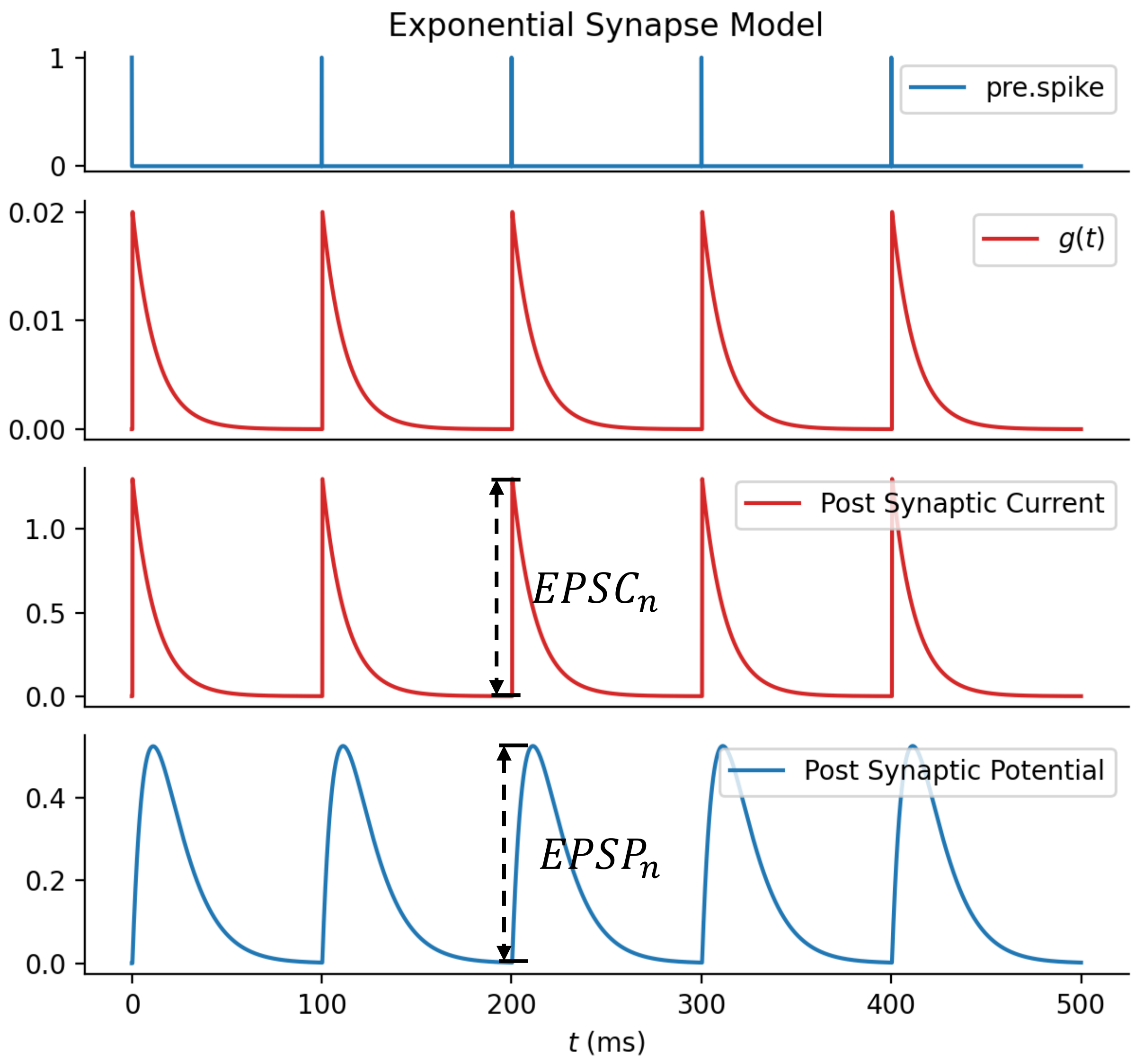
$$I(t) = g(t)\left[V_{\mathrm{post}}(\mathrm{t}) - E_{reversal}\right]$$

Dynamics of post-synaptic conductance (exponential model):

$$\frac{dg(t)}{dt} = -\frac{g(t)}{\tau_S} + A\delta\left(t - t_{sp}\right)$$

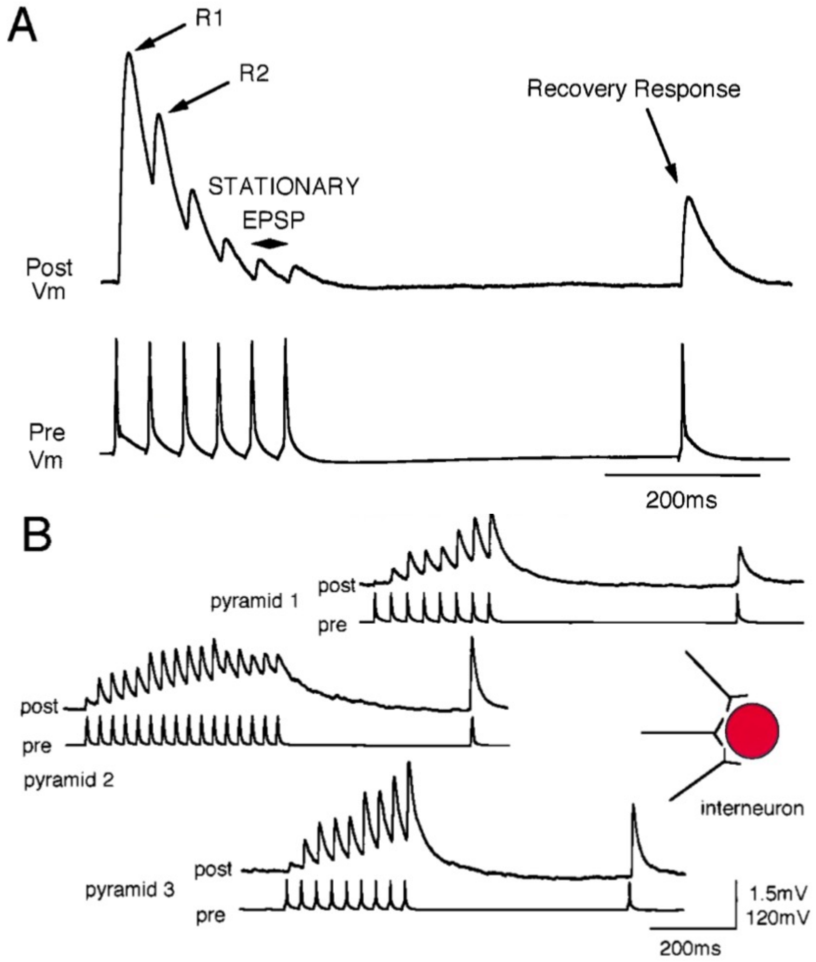
The synaptic strength is characterized as EPSC, which refers to the post synaptic current increment at each spike,

$$EPSC_n = A(V_{\mathrm{rest}} - E_{reversal})$$

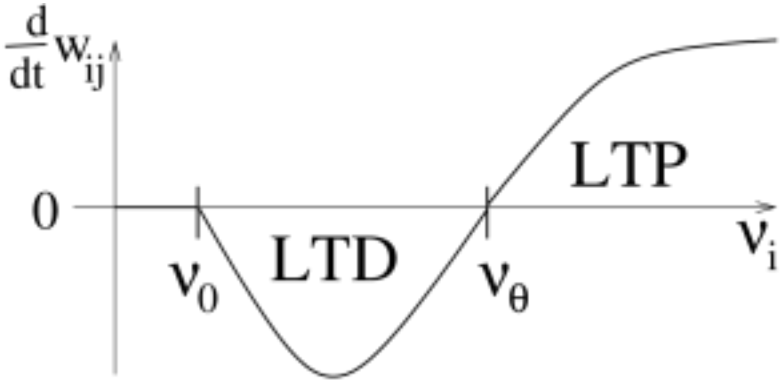


Synaptic plasticity

Short-term plasticity
(timescale: 1ms-1s)



Long-term plasticity
(timescale: > 1mins)



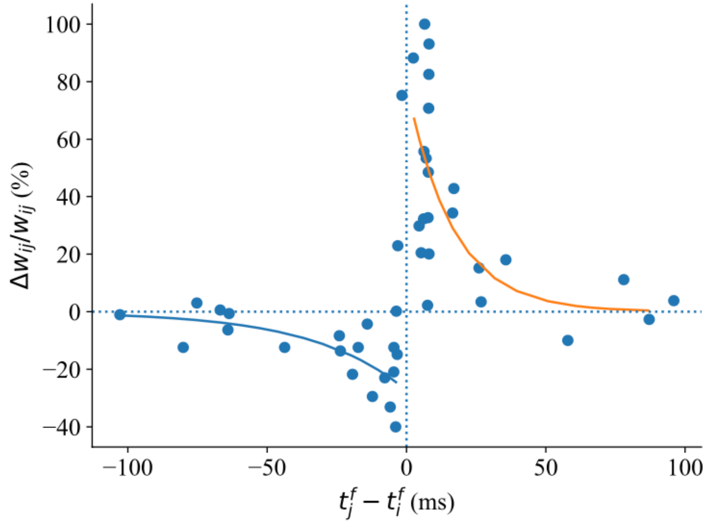


图 5.3: 脉冲时序依赖可塑性[34]

02

Phenomenological model of Short-term Plasticity

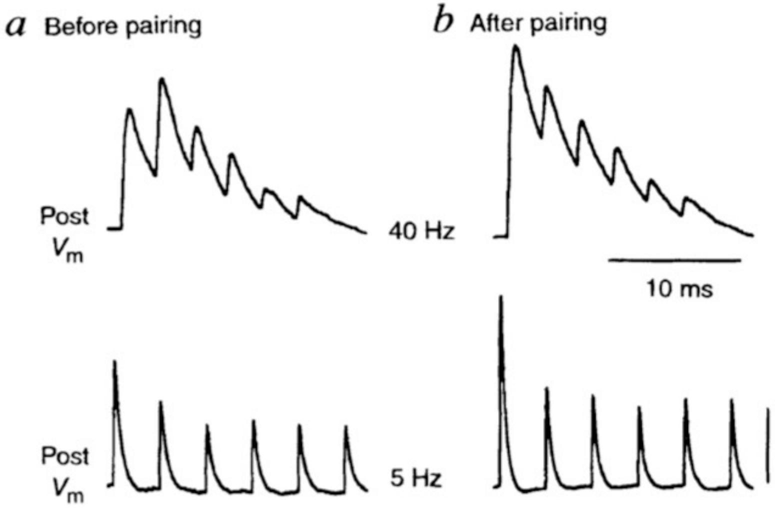
Short-term depression observed between pyramidal cells

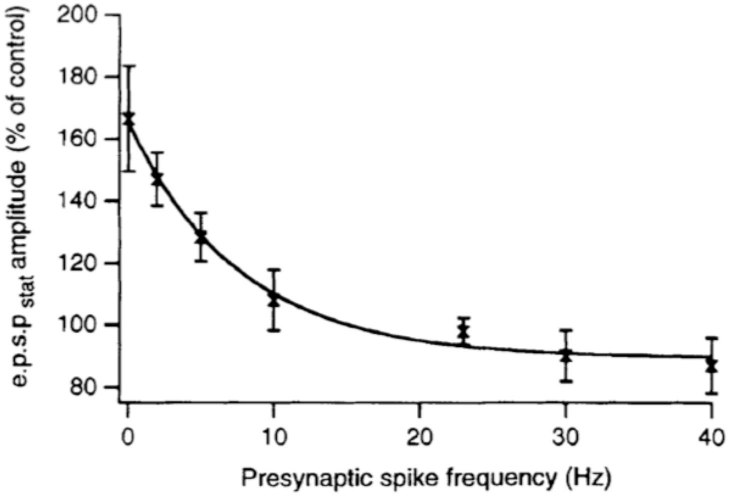
Pyramidal cell – Pyramidal cells

Redistribution of synaptic efficacy between neocortical pyramidal neurons

Henry Markram & Misha Tsodyks

Department of Neurobiology, The Weizmann Institute for Science, Rehovot 76100, Israel





Markram et al., 1996, Nature

Modeling neuro-transmitter consumption

Dynamics of three-factor STD:

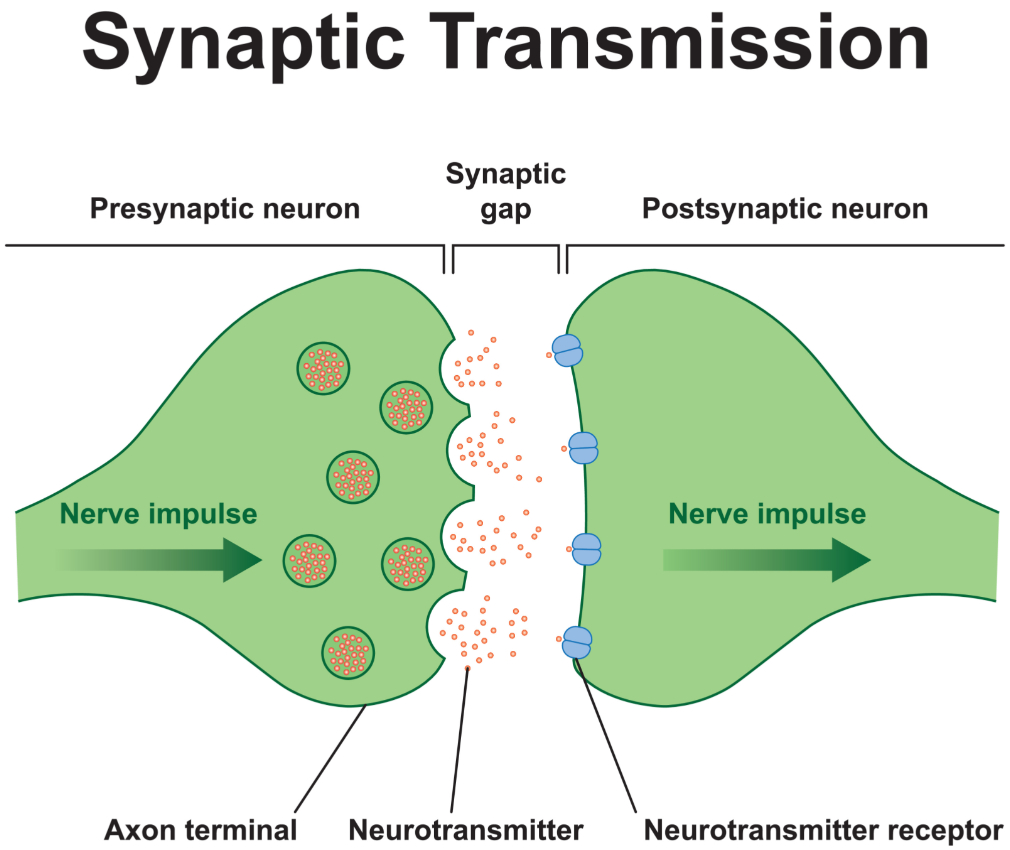
$$\frac{dx(t)}{dt} = \frac{z(t)}{\tau_{rec}} - U_{SE}x(t)\delta(t - t_{sp}),$$

$$\frac{dy(t)}{dt} = -\frac{y(t)}{\tau_{in}} + U_{SE}x(t)\delta(t - t_{sp}),$$

$$x(t) + y(t) + z(t) = 1,$$

$$\frac{dg(t)}{dt} = -\frac{g(t)}{\tau_s} + g_{max}y(t),$$

x: Fraction of available neuro-transmitter
y: Fraction of active neuro-transmitter
z: Fraction of inactive neuro-transmitter
U_{se}: Release probability of active neuro-transmitter
t_{sp}: Pre-synaptic spike time
g(t): Post-synaptic conductance,
A: total amount of neuro-transmitter
τ_{in} & τ_{rec}&τ_s: Time constants



https://www.simplypsychology.org/synapse.html

Simulate the three-factor STD

Dynamics of three-factor STD:

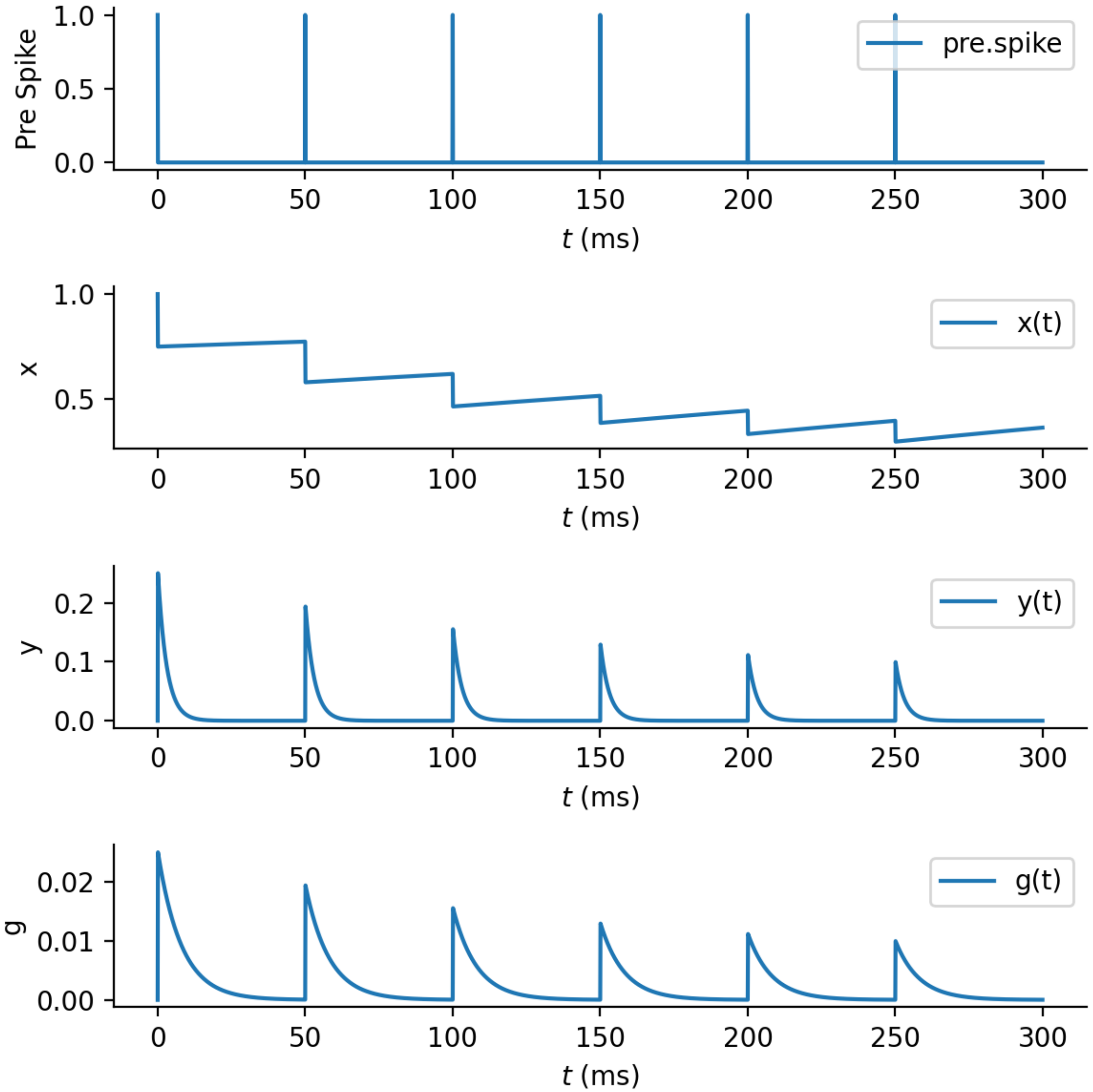
$$\frac{dx(t)}{dt} = \frac{z(t)}{\tau_{rec}} - U_{SE}x(t)\delta(t - t_{sp}),$$

$$\frac{dy(t)}{dt} = -\frac{y(t)}{\tau_{in}} + U_{SE}x(t)\delta(t - t_{sp}),$$

$$x(t) + y(t) + z(t) = 1,$$

$$\frac{dg(t)}{dt} = -\frac{g(t)}{\tau_s} + Ay(t),$$

$$\tau_{rec} = 500ms, \qquad \tau_{in} = 3ms, \qquad fr = 20hz$$

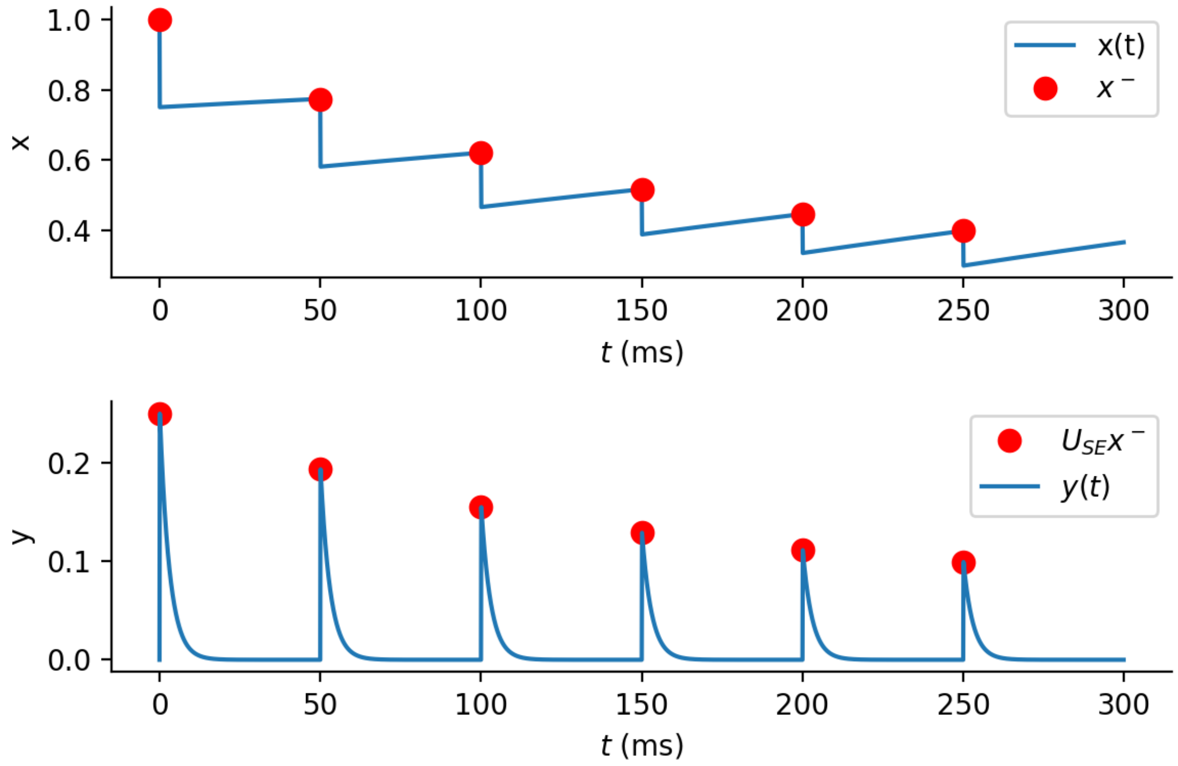


Simplify the dynamics of neuro-transmitter consumption

In general, the inactivation time constants is much shorter (3ms) than the spike time interval, i.e., $\tau_{in} \ll \Delta t$, so the formulation can be approximately simplified,

$$\frac{dy(t)}{dt} = -\frac{y(t)}{\tau_{in}} + U_{SE}x(t)\delta(t - t_{sp})$$

$$\Rightarrow \left\{ \begin{array}{l} y(t) = U_{SE}x^{-}\delta_1(t - t_{sp}), \\ x^{-} = \lim_{t - t_{sp} \to 0^{-}} x(t) \end{array} \right.$$



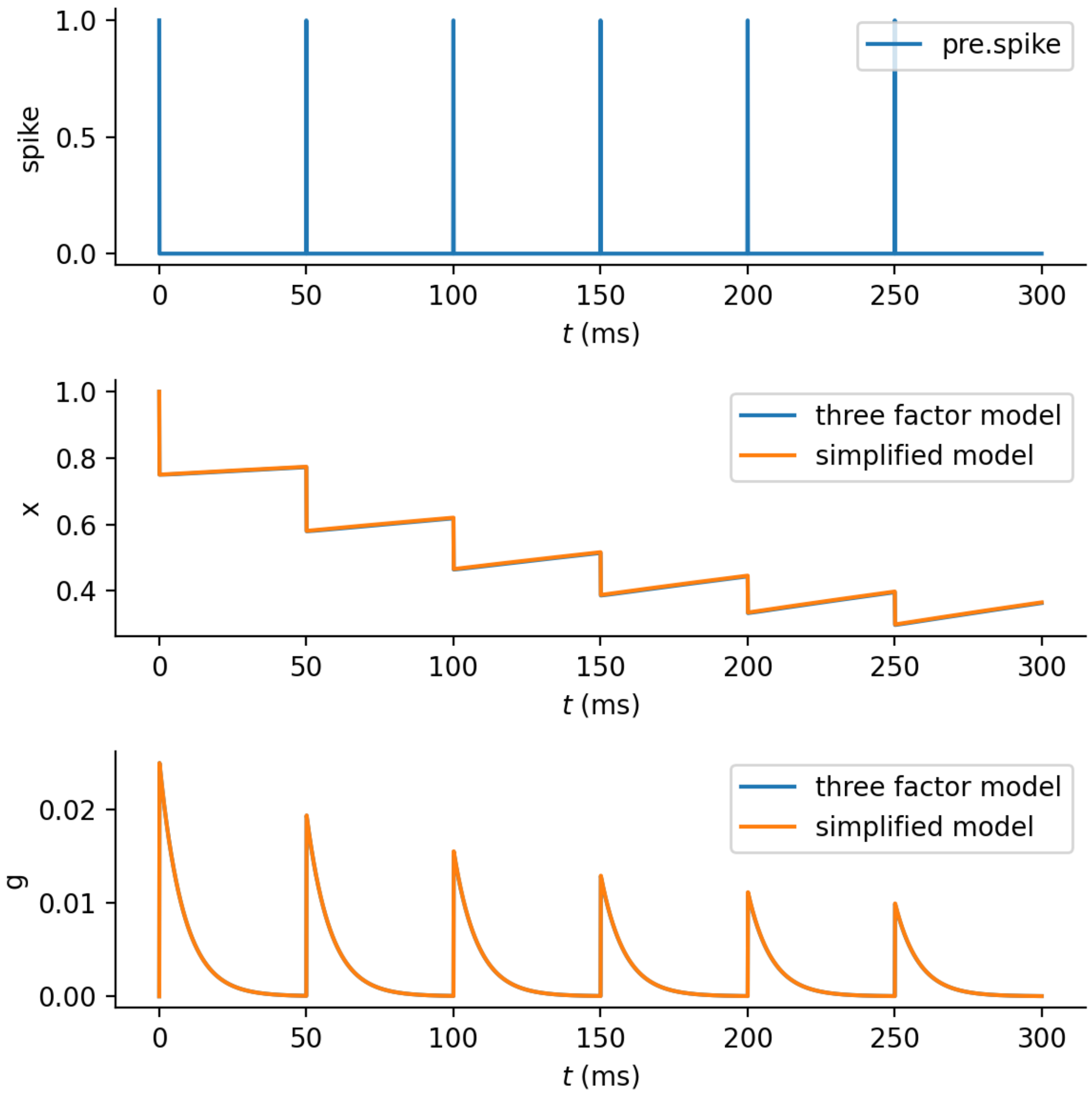
Simulate STD using simplified dynamics

Simplified model:

$$\frac{dx(t)}{dt} = \frac{1 - x(t)}{\tau_{rec}} - U_{SE} x^- \delta(t - t_{sp}),$$

$$\frac{dg(t)}{dt} = -\frac{g(t)}{\tau_s} + A U_{SE} x^- \delta(t - t_{sp}),$$

$$EPSC = A U_{SE} x^-,$$



Infer model parameters from experimental data

Short term depression model:

$$\frac{dx(t)}{dt} = \frac{1 - x(t)}{\tau_{rec}} - U_{SE} x^{-} \delta(t - t_{sp}),$$

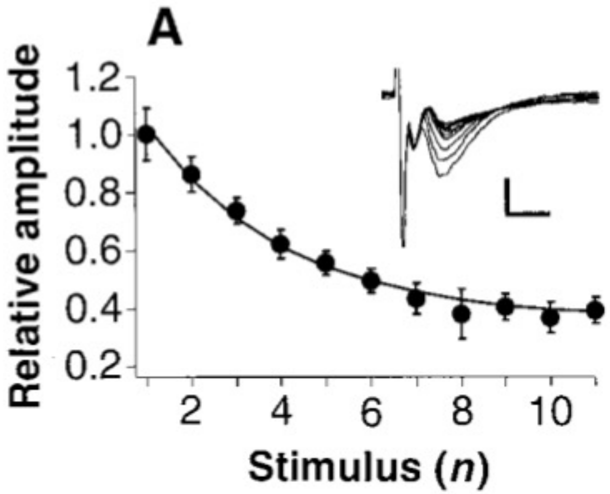
$$EPSC = AU_{SE} x^{-},$$

Iterative expression for EPSCs:

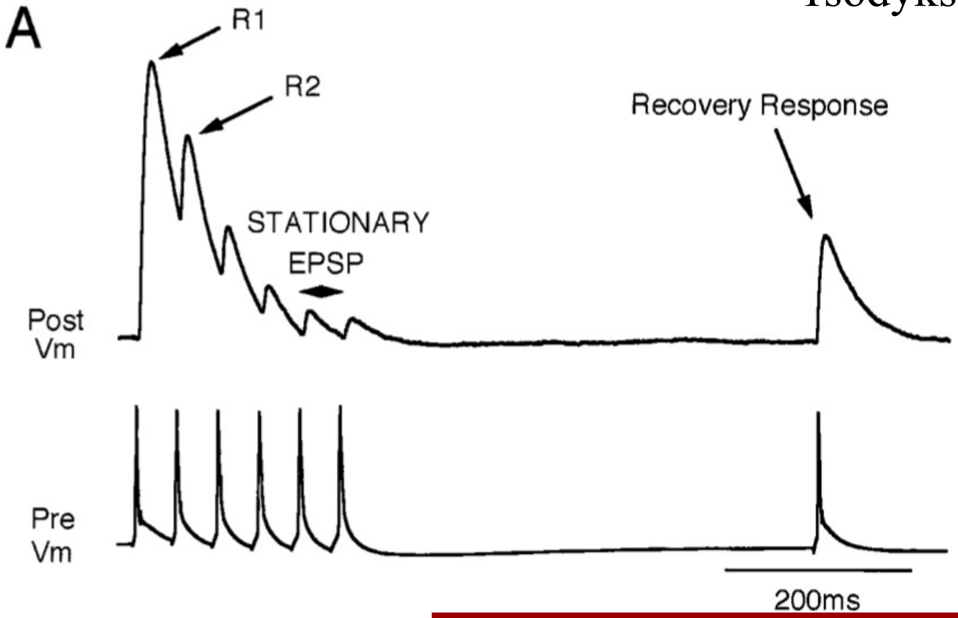
$$x_1^{-} = 1, \qquad EPSC_1 = AU_{SE},$$

$$x_{n+1}^{-} = 1 - x_n^{-}(1 - U_{SE}) \mathrm{e}^{-\frac{\Delta t}{\tau_{rec}}}$$

$$EPSC_{n+1} = AU_{SE} - EPSC_n (1 - U_{SE}) e^{-\frac{\Delta t}{\tau_{rec}}}$$

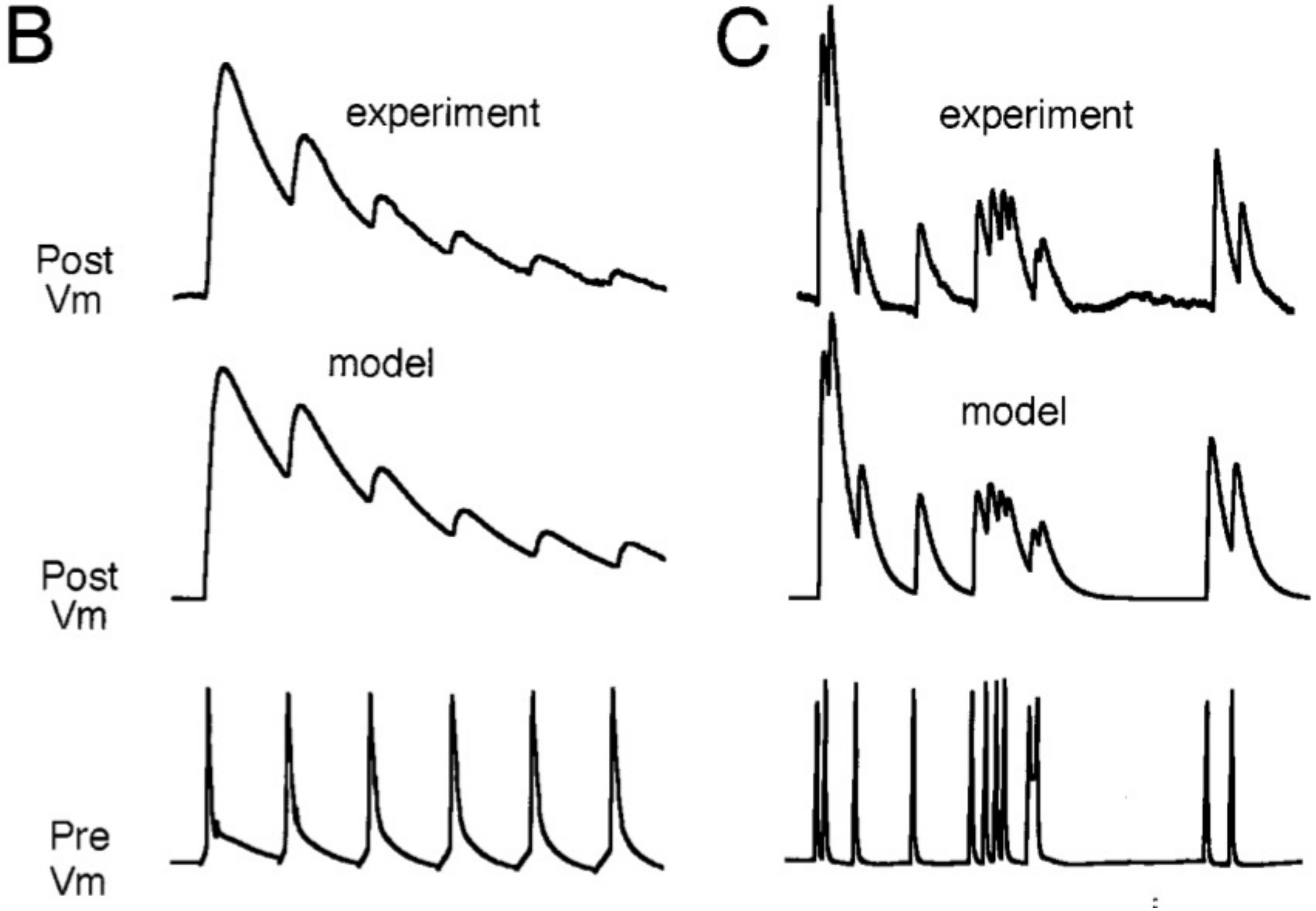


Abbott et al., 1997, Nature
Tsodyks et al., 1997, PNAs



Prediction for complex post-synaptic patterns

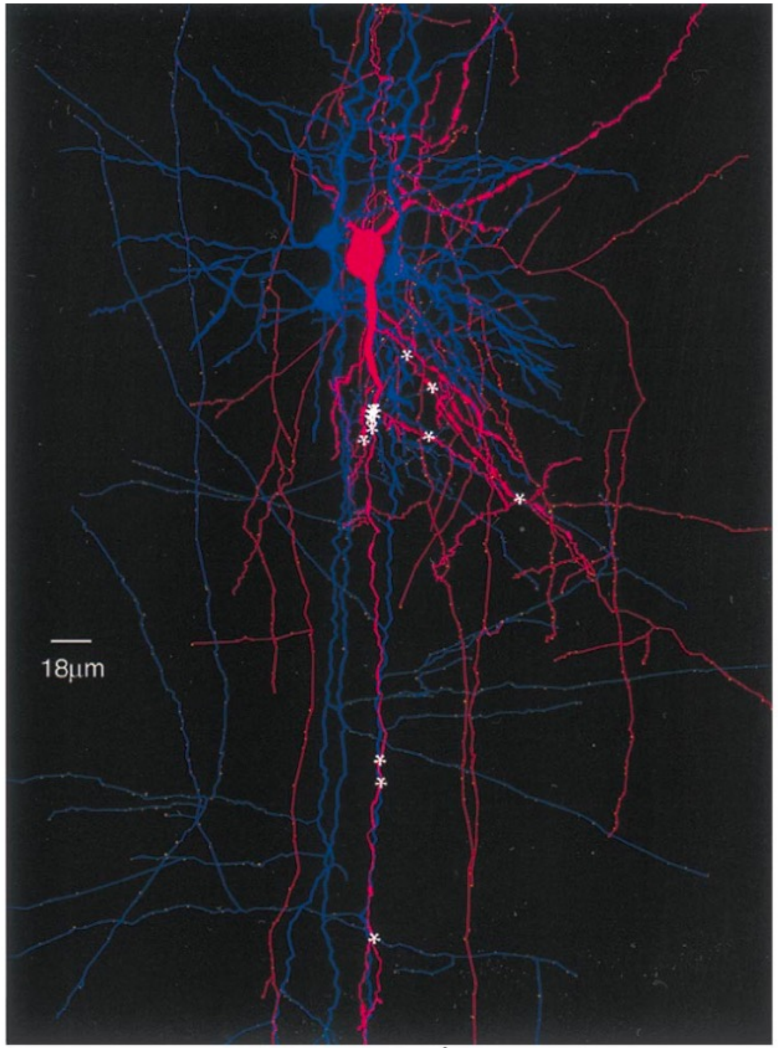
Simulate with complex pre-synaptic spike trains and compare with vitro experimental results (patch-clamp)



Tsodyks et al., 1997, PNAs

Short-term facilitation observed between pyramidal cells and interneurons

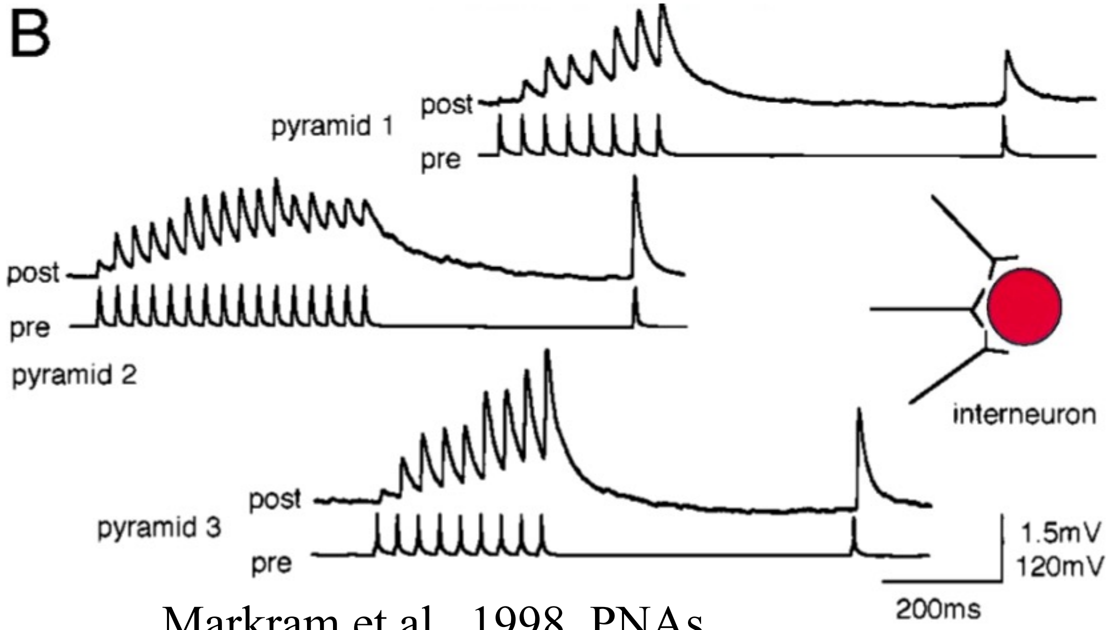
pyramidal cell – interneurons



Proc. Natl. Acad. Sci. USA
Vol. 95, pp. 5323–5328, April 1998
Neurobiology

Differential signaling via the same axon of neocortical pyramidal neurons

HENRY MARKRAM*, YUN WANG, AND MISHA TSODYKS



Markram et al., 1998, PNAs

Modeling neuro-transmitter release probability

The release probability can also be modelled as a dynamical variable $u(t)$,

$$\frac{du(t)}{dt} = \frac{-u(t)}{\tau_f} + U_{SE}(1 - u^-)\delta(t - t_{sp}),$$

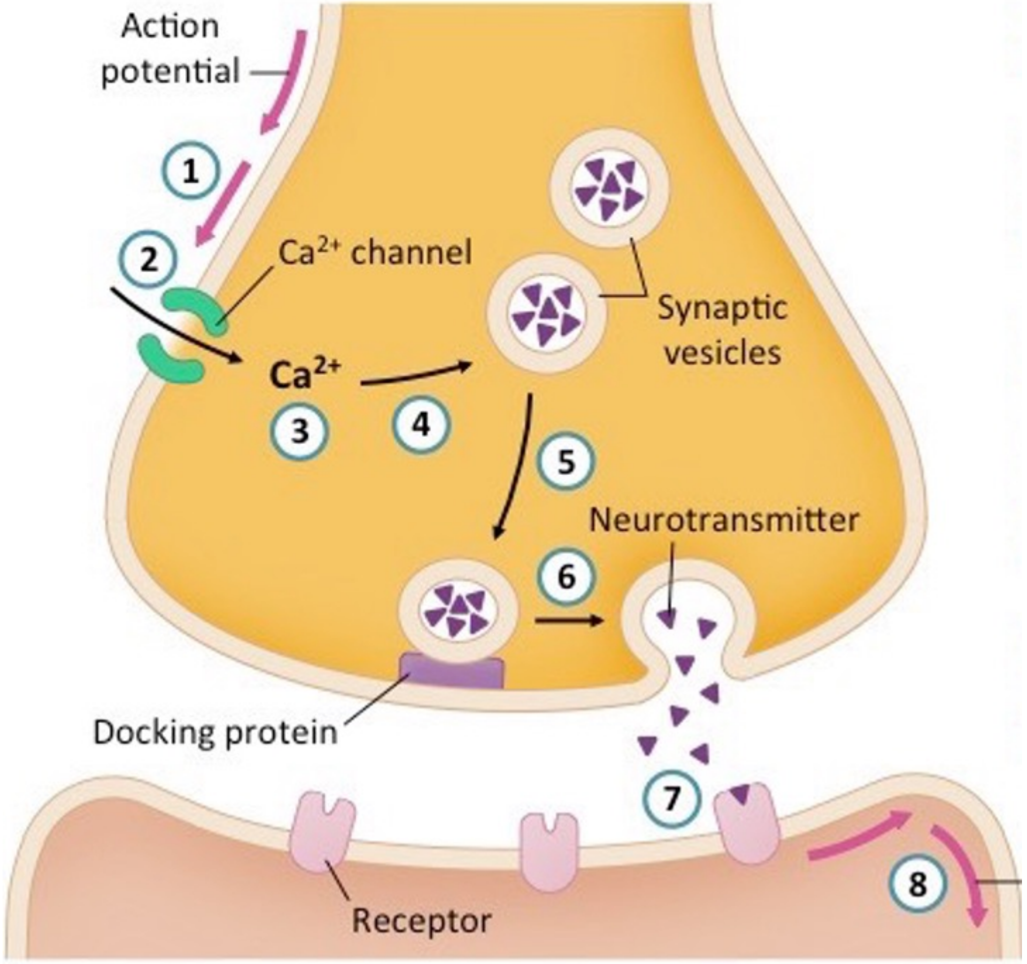
$$\frac{dx(t)}{dt} = \frac{1 - x(t)}{\tau_d} - u(t)x^-\delta(t - t_{sp} + \delta t),$$

$$\frac{dg(t)}{dt} = -\frac{g(t)}{\tau_s} + Au(t)x^-\delta(t - t_{sp} + \delta t),$$

$$EPSC = Au(t)x^-,$$

U_{SE} might reflect the concentration of Ca^{2+}

Tsodyks et al., 1998, Neural computation



https://www.simplypsychology.org/synapse.html

Modeling neuro-transmitter release probability

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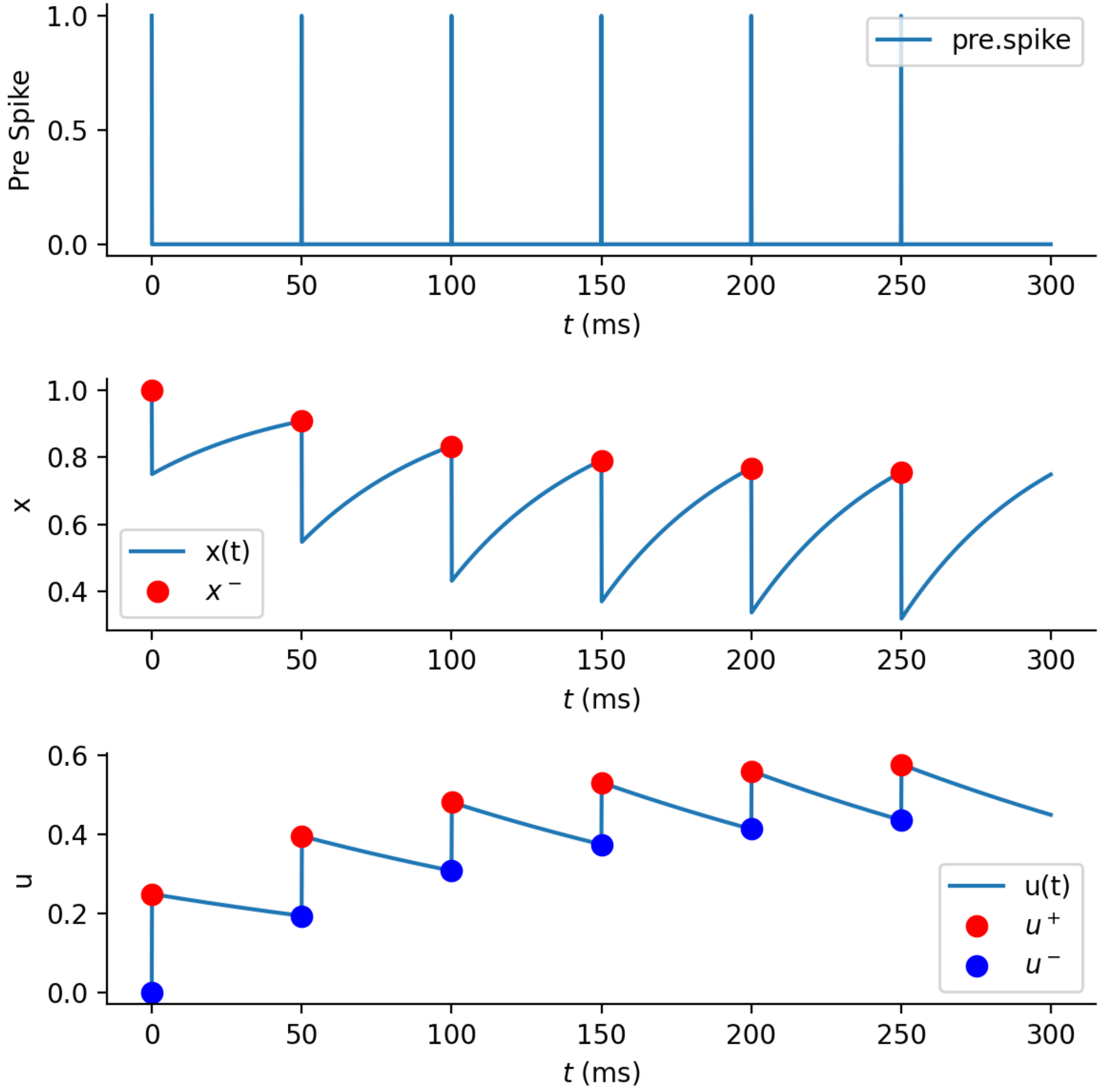
$$\frac{du(t)}{dt} = \frac{-u(t)}{\tau_f} + U_{SE}(1-u^-)\delta(t-t_{sp}),$$

$$\frac{dx(t)}{dt} = \frac{1-x(t)}{\tau_d} - u^+x^-\delta(t-t_{sp}),$$

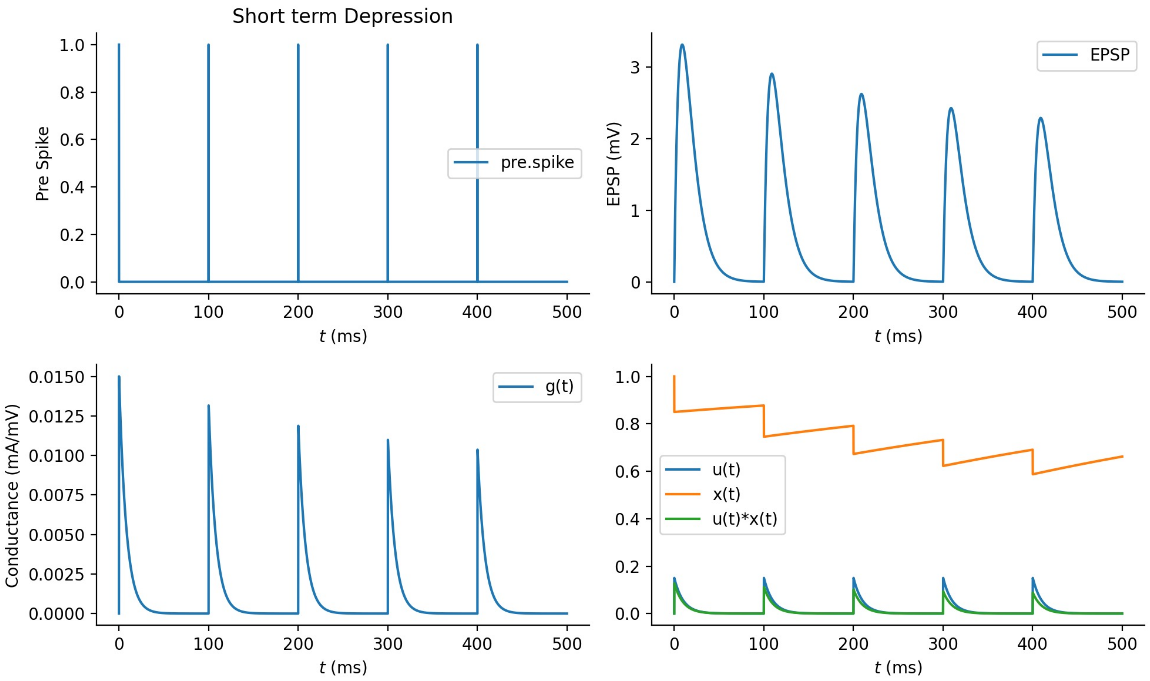
$$\frac{dg(t)}{dt} = -\frac{g(t)}{\tau_s} + Au^+x^-\delta(t-t_{sp}),$$

$$\boxed{EPSC = Au^+x^-, \qquad u^+ = \lim_{t-t_{sp}\to 0^+} u(t),}$$

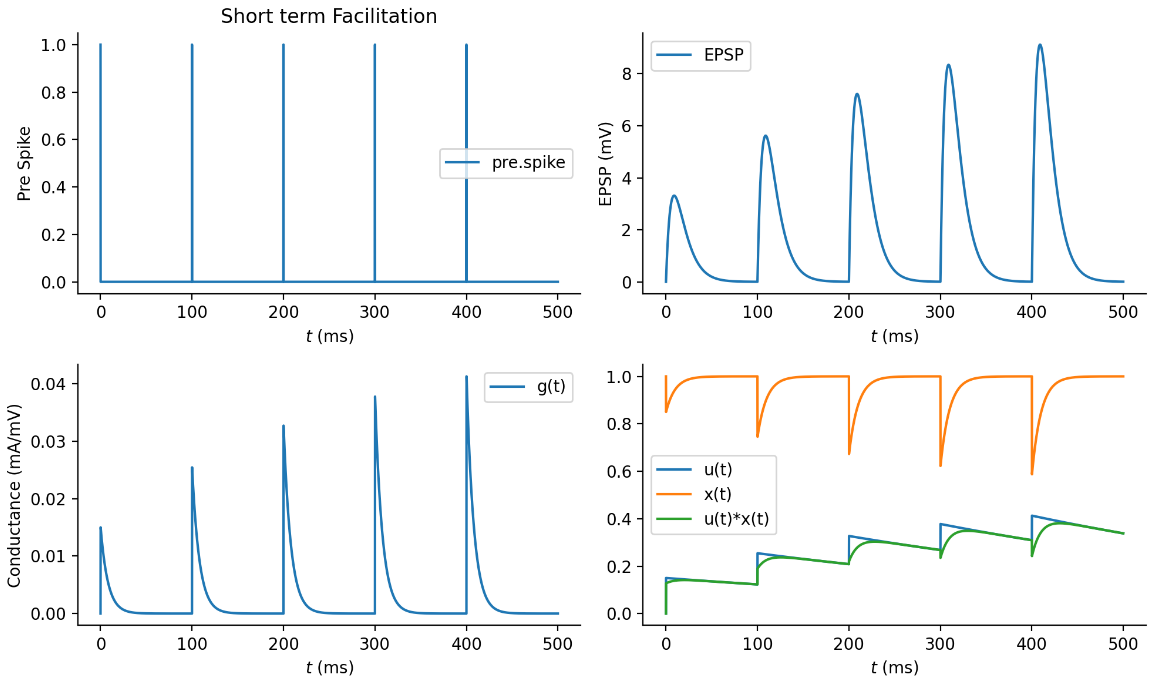


STD and STF under different parameter regime

Short-term depression: $\tau_f = 10ms, \tau_d = 500ms$



Short-term facilitation: $\tau_f = 500ms,\ \tau_d = 10ms$



Derivation of iterative expressions for EPSCs

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Iterative expression for $x_n, u_n, EPSC_n$:

$$u_1^+ = U_{SE}, \qquad x_1^- = 1,$$

$$x_{n+1}^- = 1 - x_n^-(1 - u_n^+)\mathrm{e}^{-\frac{\Delta t}{\tau_{rec}}},$$

$$u_{n+1}^+ = u_n^+ e^{-\frac{\Delta t}{\tau_f}} + U_{SE}\left(1 - u_n^+ e^{-\frac{\Delta t}{\tau_f}}\right),$$

$$EPSC_{n+1} = A u_n^+ x_n^-,$$

Steady state of $x_n, u_n, EPSC_n$:

$$u_{st}^+ = \frac{U_{SE}}{1 - (1 - U_{SE})e^{-\frac{\Delta t}{\tau_f}}} \geq U_{SE} = u_1^+,$$

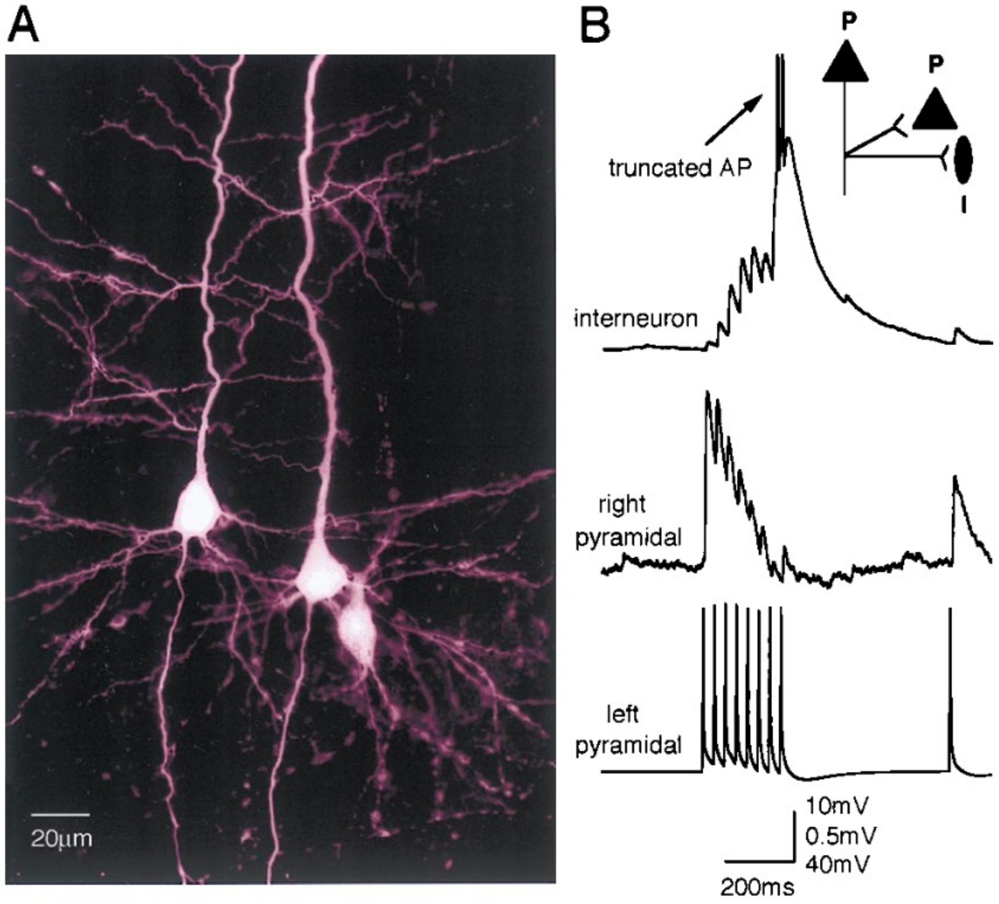
$$x_{st}^- = \frac{1}{1 + (1 - u_{st}^+)\mathrm{e}^{-\frac{\Delta t}{\tau_{rec}}}} \leq 1 = x_1^-,$$

$$EPSC_{st} = A u_{st}^+ x_{st}^-$$

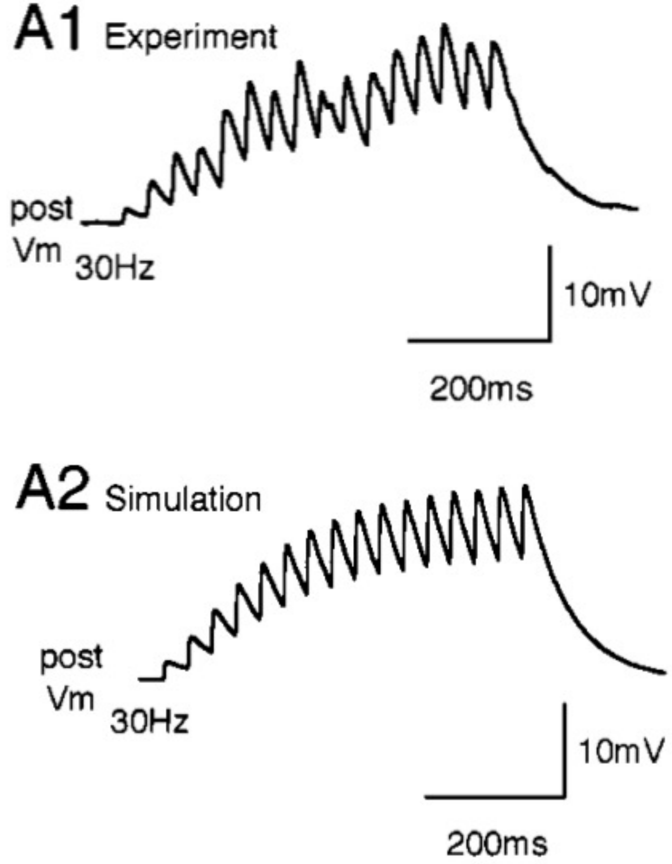
Prediction for complex post-synaptic patterns

Infer model parameters by fitting experiments:

$$EPSC_{n+1} = A u_n x_n$$



Simulate with complex pre-synaptic spike trains and compare with vitro experimental results (patch-clamp)



Markram et al., 1998, PNAs

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03

Effects on Information Transmission

Mean-field Analysis of STP model

STP based on spiking time

$$\frac{du(t)}{dt} = \frac{-u(t)}{\tau_f} + U_{SE}(1-u^-)\delta(t-t_{sp}),$$

$$\frac{dx(t)}{dt} = \frac{1-x(t)}{\tau_d} - u^+x^-\delta(t-t_{sp}),$$

$$\frac{dg(t)}{dt} = -\frac{g(t)}{\tau_s} + Au^+x^-\delta(t-t_{sp}),$$

$$u^+ = \lim_{t-t_{sp}\to 0^+} u(t),$$

time average

STP based on firing rate

$$\frac{du(t)}{dt} = \frac{-u(t)}{\tau_f} + U_{SE}[1-u(t)]R(t),$$

$$\frac{dx(t)}{dt} = \frac{1-x(t)}{\tau_d} - u^+xR(t),$$

$$g(t) = \tau_s A u^+ x R(t),$$

$$u^+ = u(t) + U_{SE}[1-u(t)],$$

Tsodyks et al., 1998, Neural computation

Mean-field Analysis of STP model

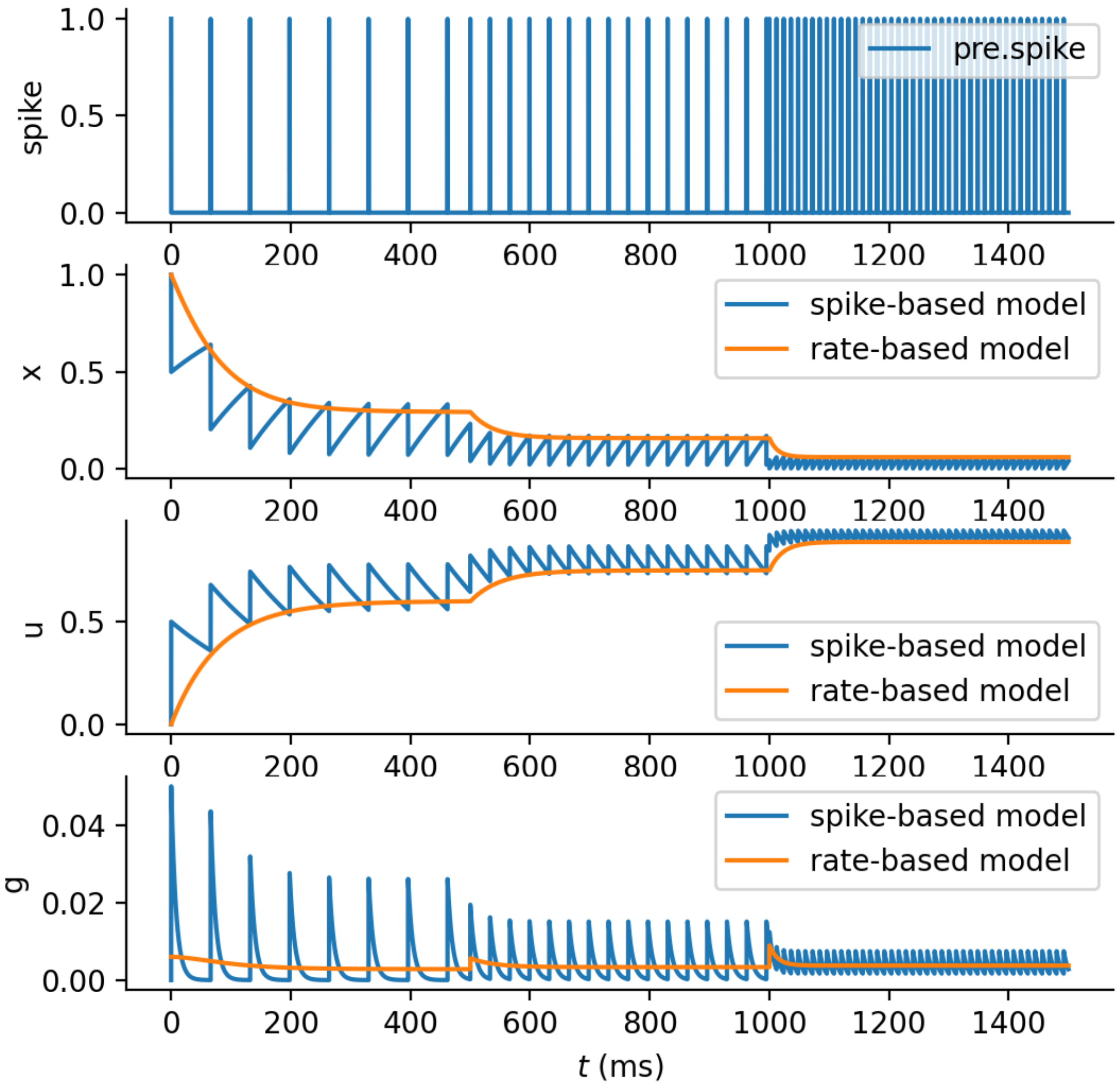
STP based on firing rate

$$\frac{du(t)}{dt} = \frac{-u(t)}{\tau_f} + U_{SE}[1 - u(t)]R(t),$$

$$\frac{dx(t)}{dt} = \frac{1 - x(t)}{\tau_d} - u^+ xR(t),$$

$$g(t) = \tau_s A u^+ xR(t),$$

$$u^+ = u(t) + U_{SE}[1 - u(t)],$$



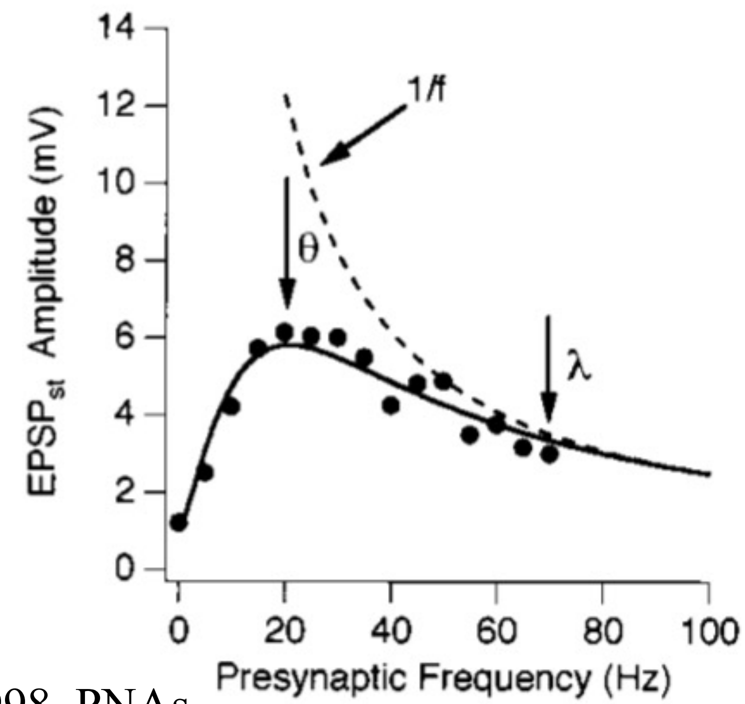
Theoretical analysis of the rate model

Suppose the pre-synaptic firing rate keeps as constant, we can calculate the stationary response

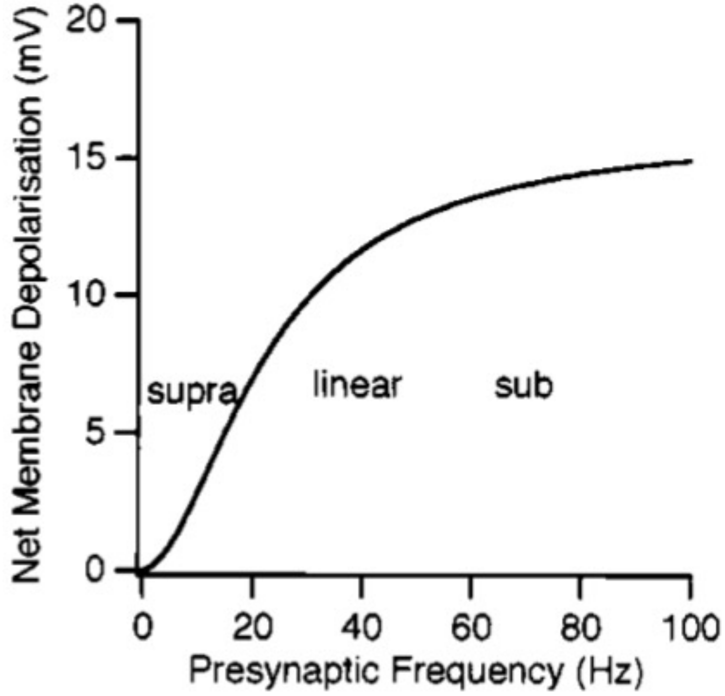
$$u_{st} = \frac{U_{SE} R_0 \tau_f}{1 + U_{SE} R_0 \tau_f}, \qquad u_{st}^{+} = U_{SE} \frac{1 + R_0 \tau_f}{1 + U_{SE} R_0 \tau_f}, \qquad x_{st} = \frac{1}{1 + u_{st}^{+} \tau_d R_0},$$

$$EPSC_{st} = A u_{st}^{+} x_{st} = A \frac{u_{st}^{+}}{1 + u_{st}^{+} \tau_d R_0}, \qquad PSV_{st} \propto g_{st} = \tau_s A u_{st}^{+} x_{st} R_0 = A \frac{u_{st}^{+} R_0}{1 + u_{st}^{+} \tau_d R_0},$$

$EPSC_{st}\ vs\ R_0$

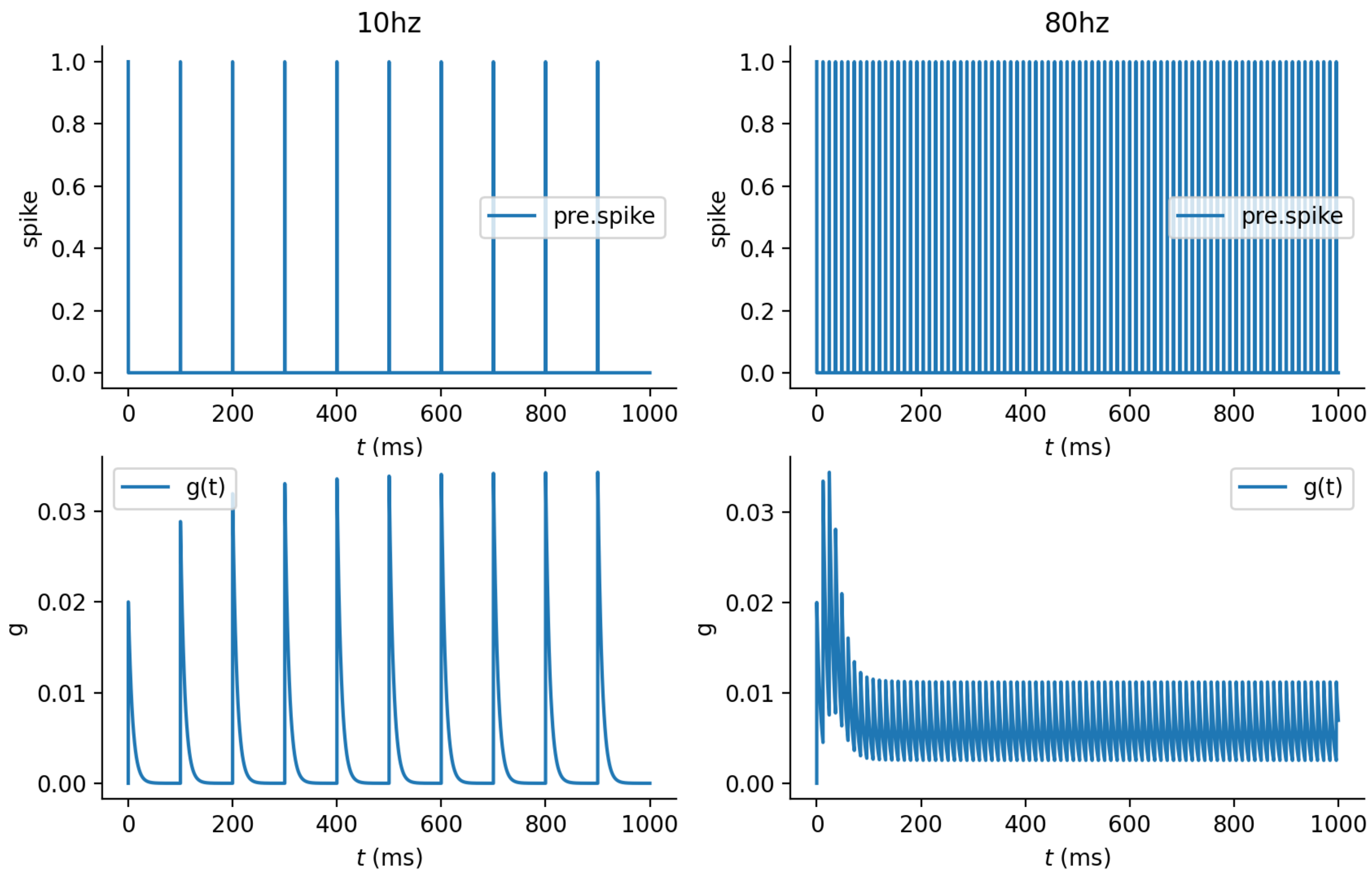


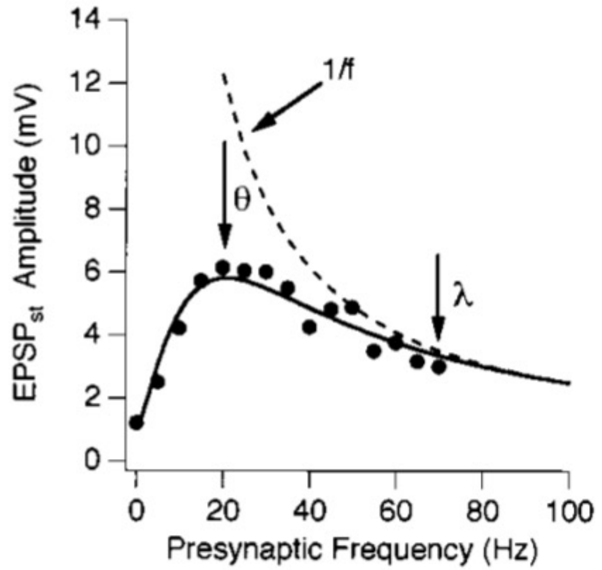
$PSV_{st}\ vs\ R_0$

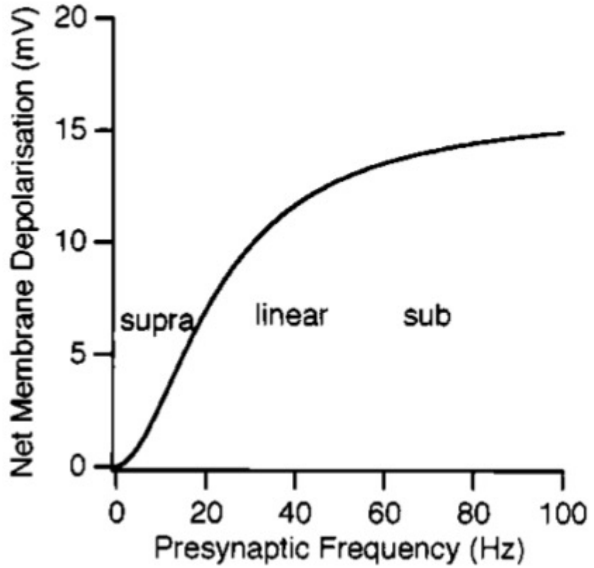


Markram et al., 1998, PNAs

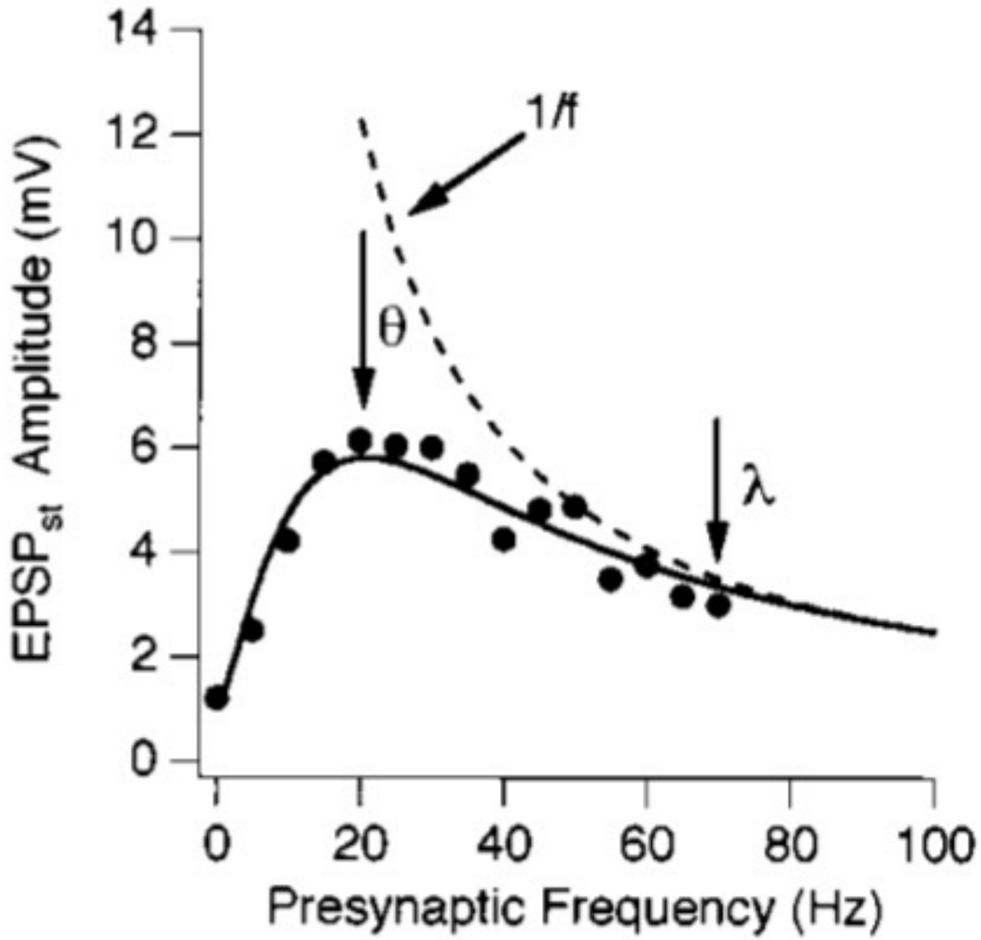
Frequency-dependent facilitation/depression







Frequency-dependent Gain control of spike information



$$u_{st}^{+} = U_{SE}\frac{1+R_0\tau_f}{1+U_{SE}R_0\tau_f},$$

$$x_{st} = \frac{1}{1+u_{st}^{+}\tau_d R_0},$$

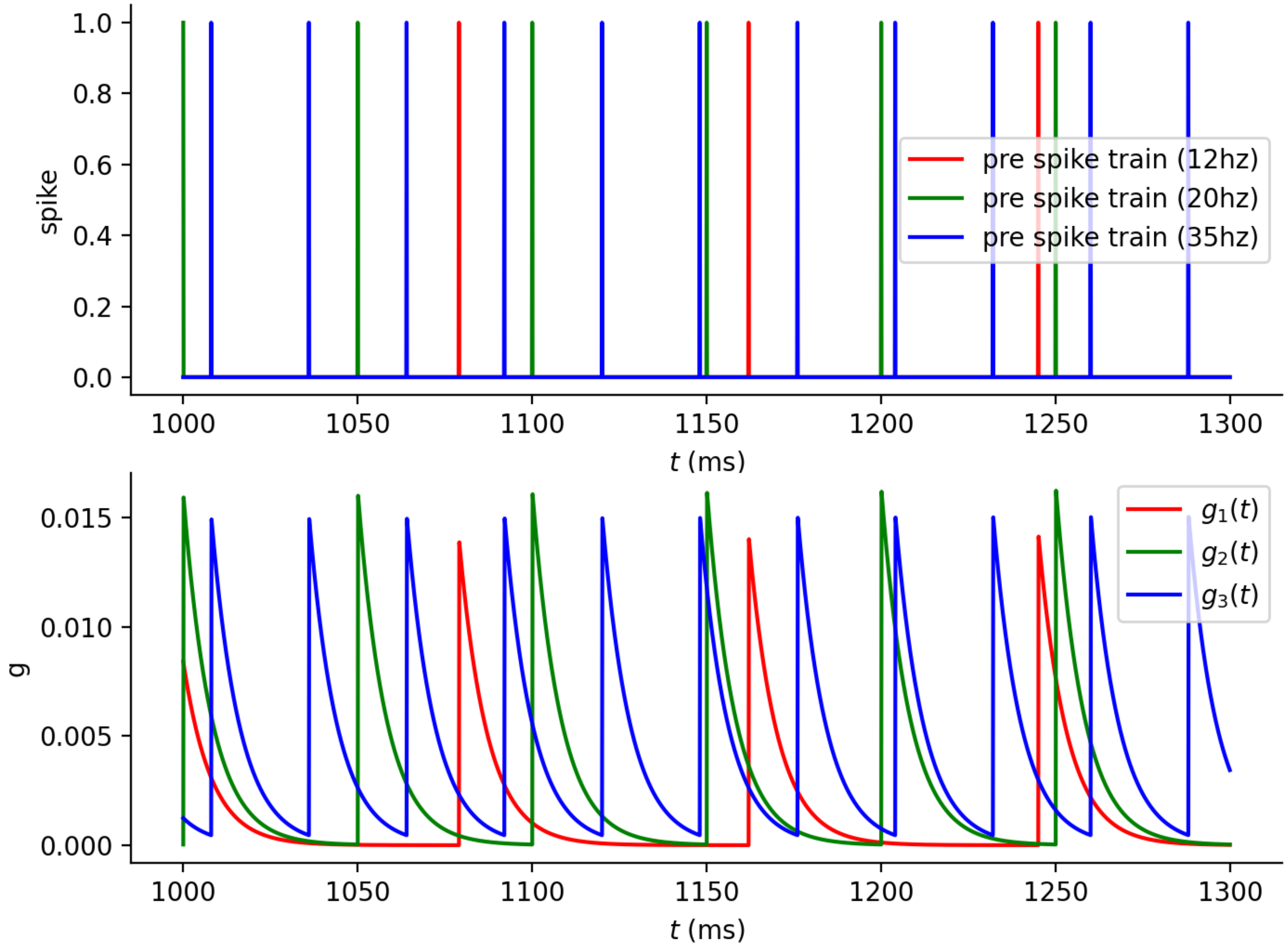
$$EPSC_{st} = Au_{st}^{+}x_{st} = A\frac{u_{st}^{+}}{1+u_{st}^{+}\tau_d R_0},$$

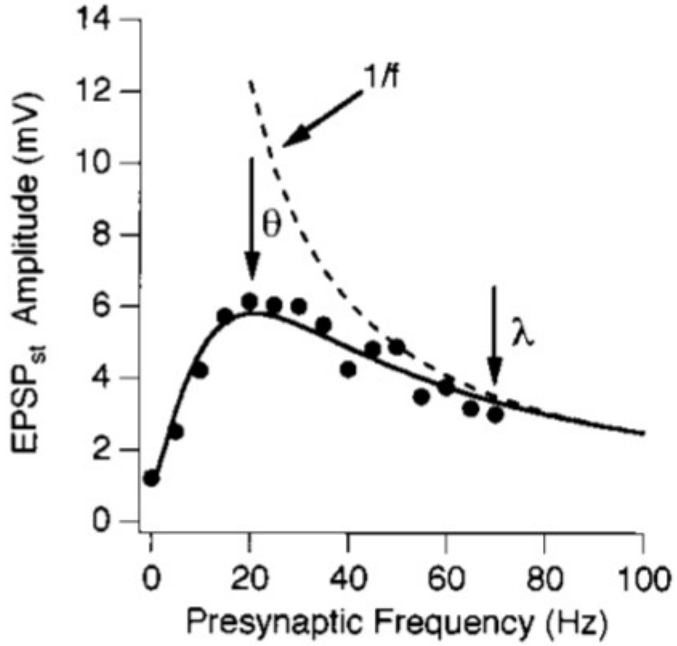
Peak frequency:

$$\theta \sim \frac{1}{\sqrt{U\tau_f\tau_d}}$$

Markram et al., 1998, PNAs

Simulation of Frequency-dependent Gain control

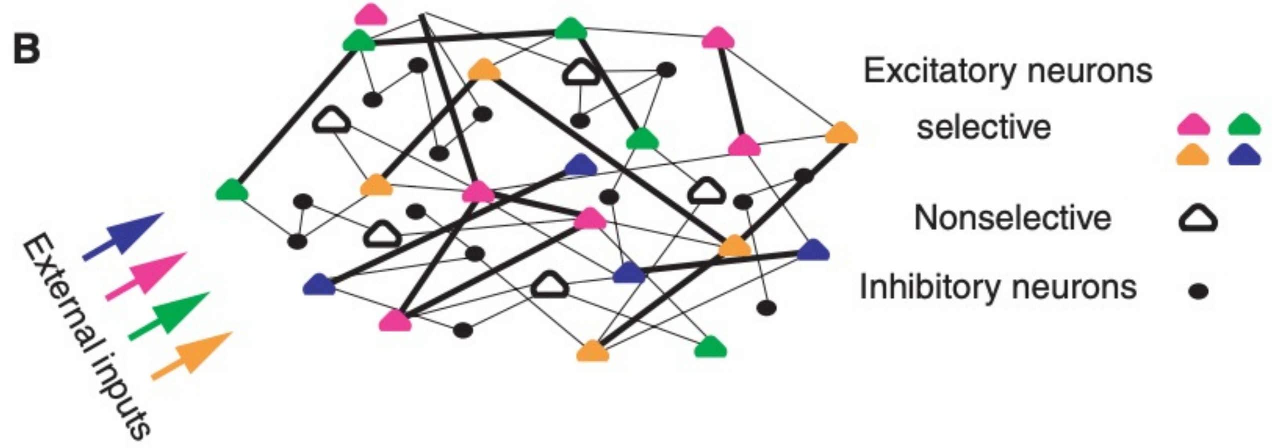


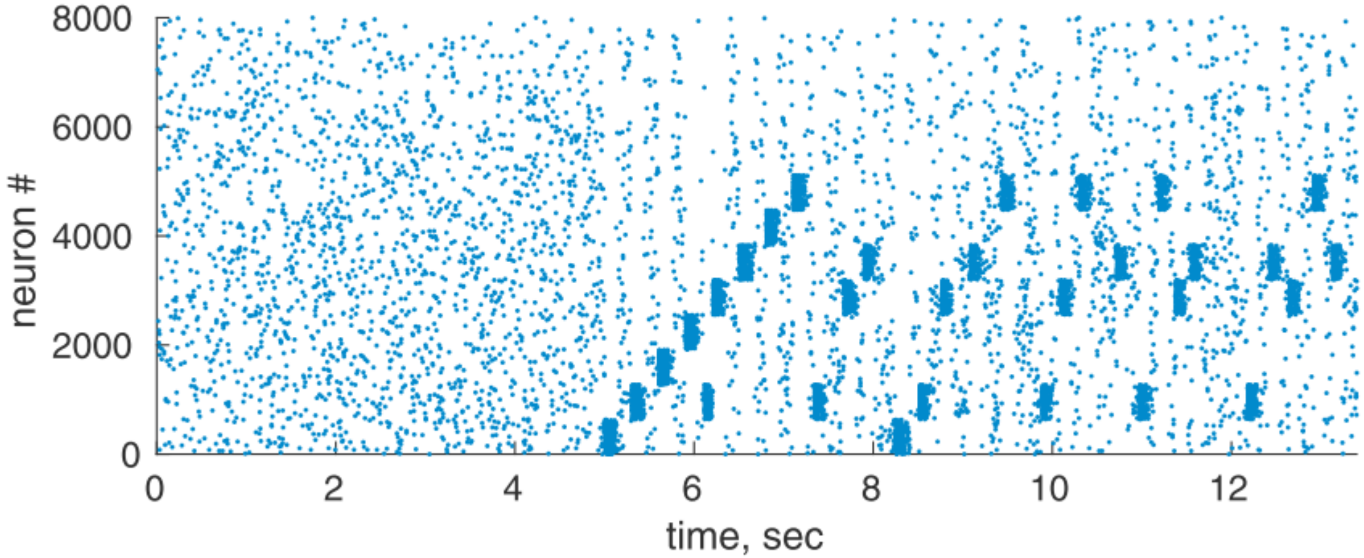


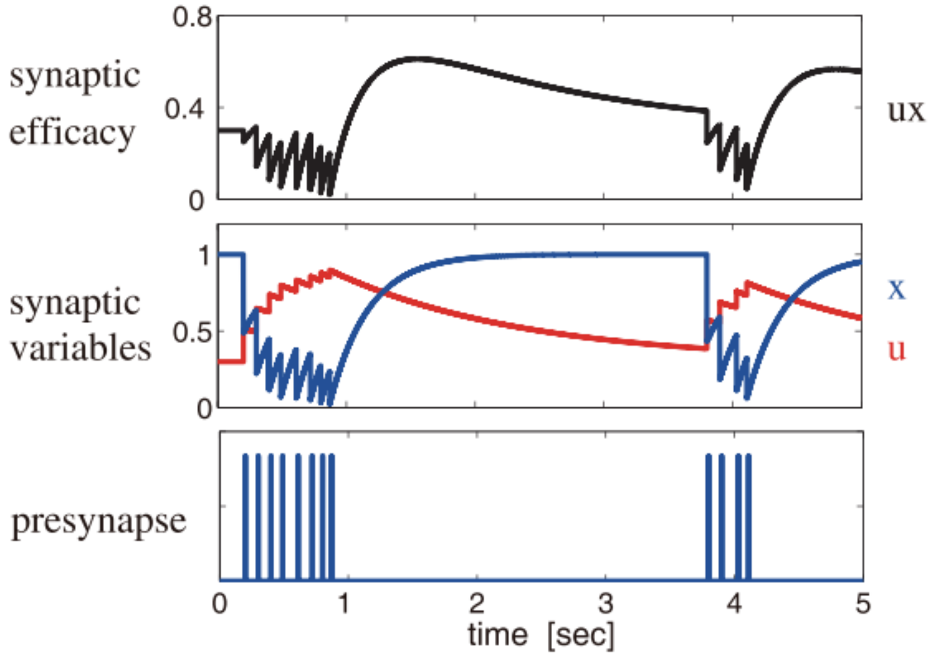
04

Effects on Network dynamics

STP modeling Working memory







Mongillo et al., 2008, Science

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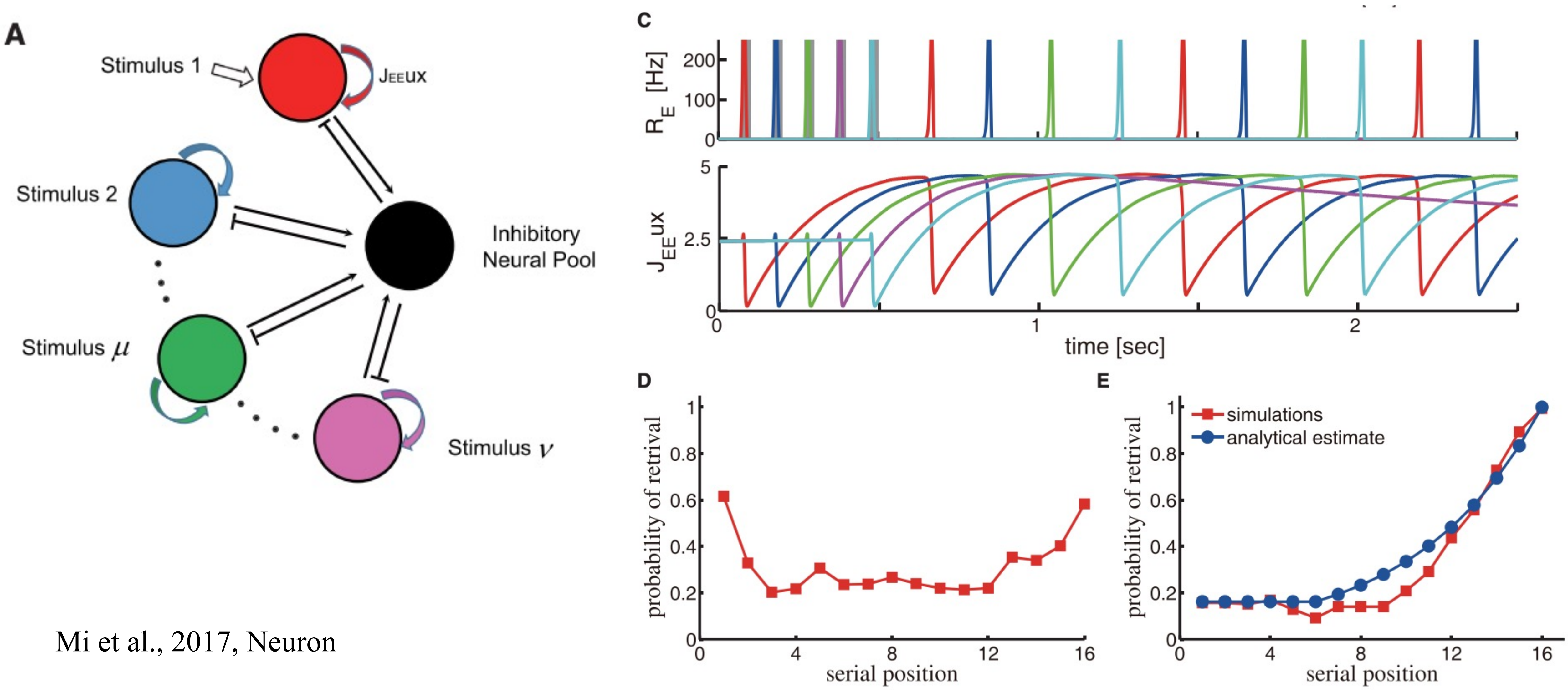
STP modeling Working memory



Mi et al., 2017, Neuron

References

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[2] Tsodyks, M. V., & Markram, H. (1997). The neural code between neocortical pyramidal neurons depends on neurotransmitter release probability. Proceedings of the national academy of sciences, 94(2), 719-723.
[3] Abbott, L. F., Varela, J. A., Sen, K., & Nelson, S. B. (1997). Synaptic depression and cortical gain control. Science, 275(5297), 221-224.
[4] Markram, H., Wang, Y., & Tsodyks, M. (1998). Differential signaling via the same axon of neocortical pyramidal neurons. Proceedings of the National Academy of Sciences, 95(9), 5323-5328.
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[7] Mongillo, G., Barak, O., & Tsodyks, M. (2008). Synaptic theory of working memory. Science, 319(5869), 1543-1546.
[8] Mi, Y., Katkov, M., & Tsodyks, M. (2017). Synaptic correlates of working memory capacity. Neuron, 93(2), 323-330.

Q&A

Thanks for your listening!