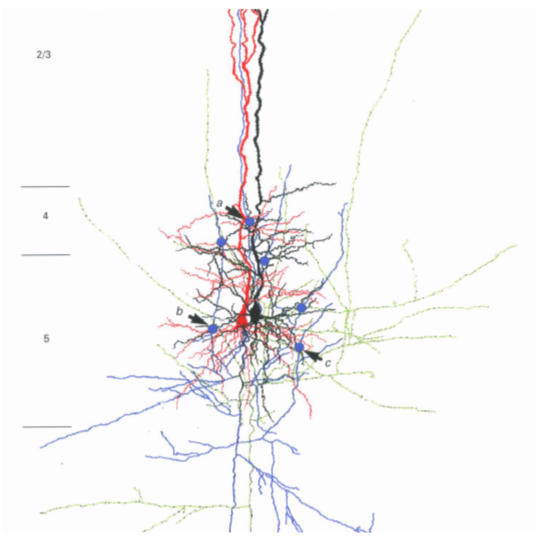
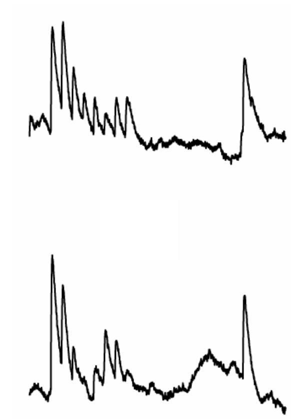
Data Analysis of Short-Term Synaptic Plasticity



Alex Loebel



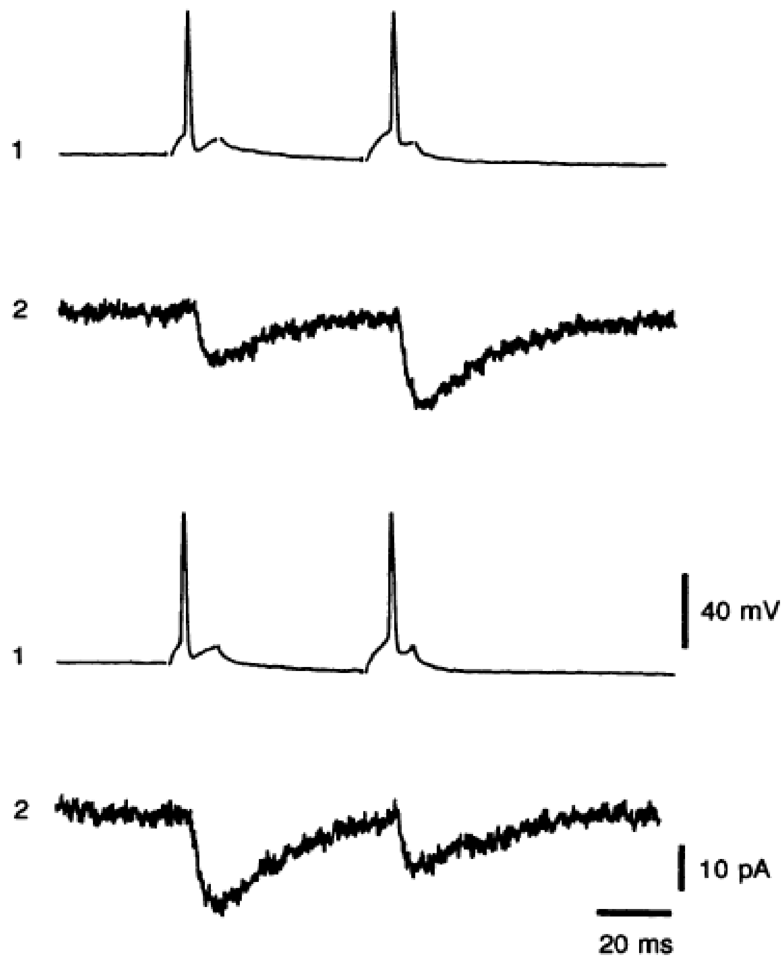
7th G-Node Course in Neural Data Analysis

February, 2015

Goals for today

- Discuss a conceptual way of representing data, i.e., via a mathematical model (in our case, a dynamical system), and see what we can learn from it about our system.
- Learn how to simulate a dynamical system.
- Learn how to fit the free parameters of the model to our data.
- Learn about the Jackknife approach, a statistical method for estimating the confidence interval of our parameters.
- All of the above are general approaches, which we will discuss using the example of short-term synaptic plasticity.

What is STSP?

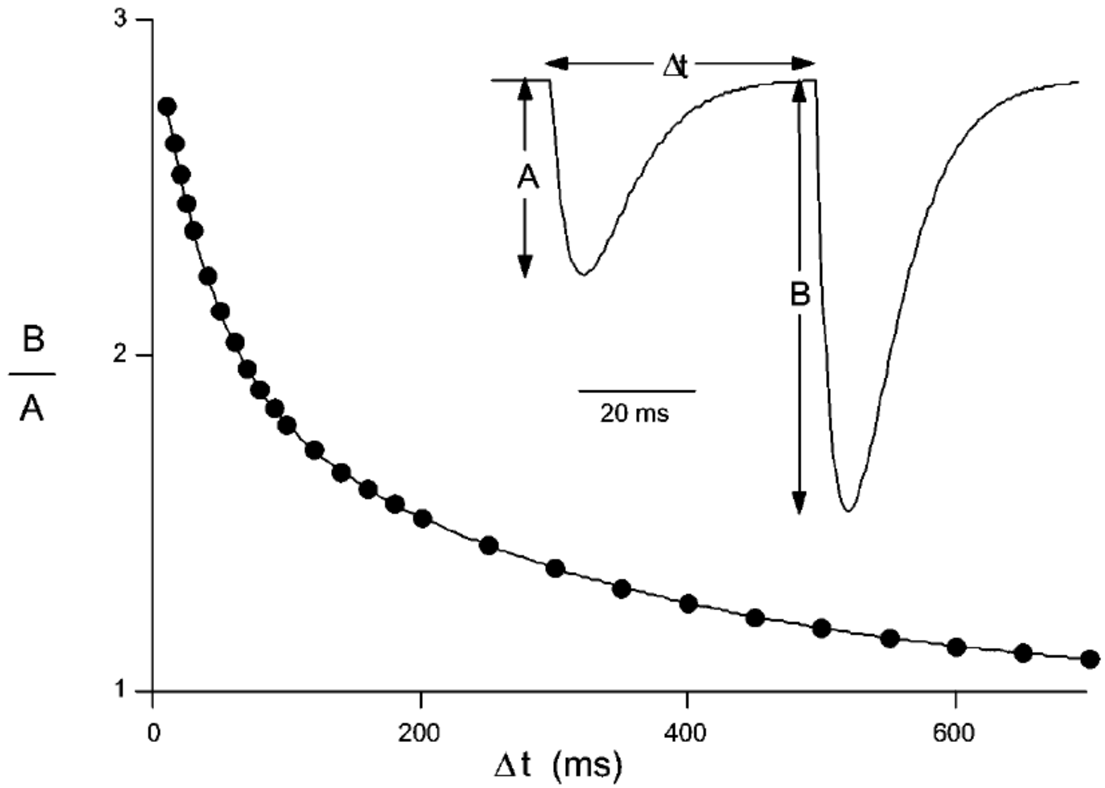


Short-term facilitation

Short-term depression

Debanne et al., 1996

What is STSP?



Zucker and Regehr, 2002

STSP is all over the place!

- STSP is expressed all over the nervous system, from the spinal cord, to the brain stem, thalamo-cortical connections, intra-cortical connections (hippocampus, neocortex)…
- In the neocortex, it has been shown that STSP is area specific, as well as cell type specific.

Specificity of STSP

- Somato-sensory area:

  $E \rightarrow E$ Depressing

  $I \rightarrow E$ Depressing

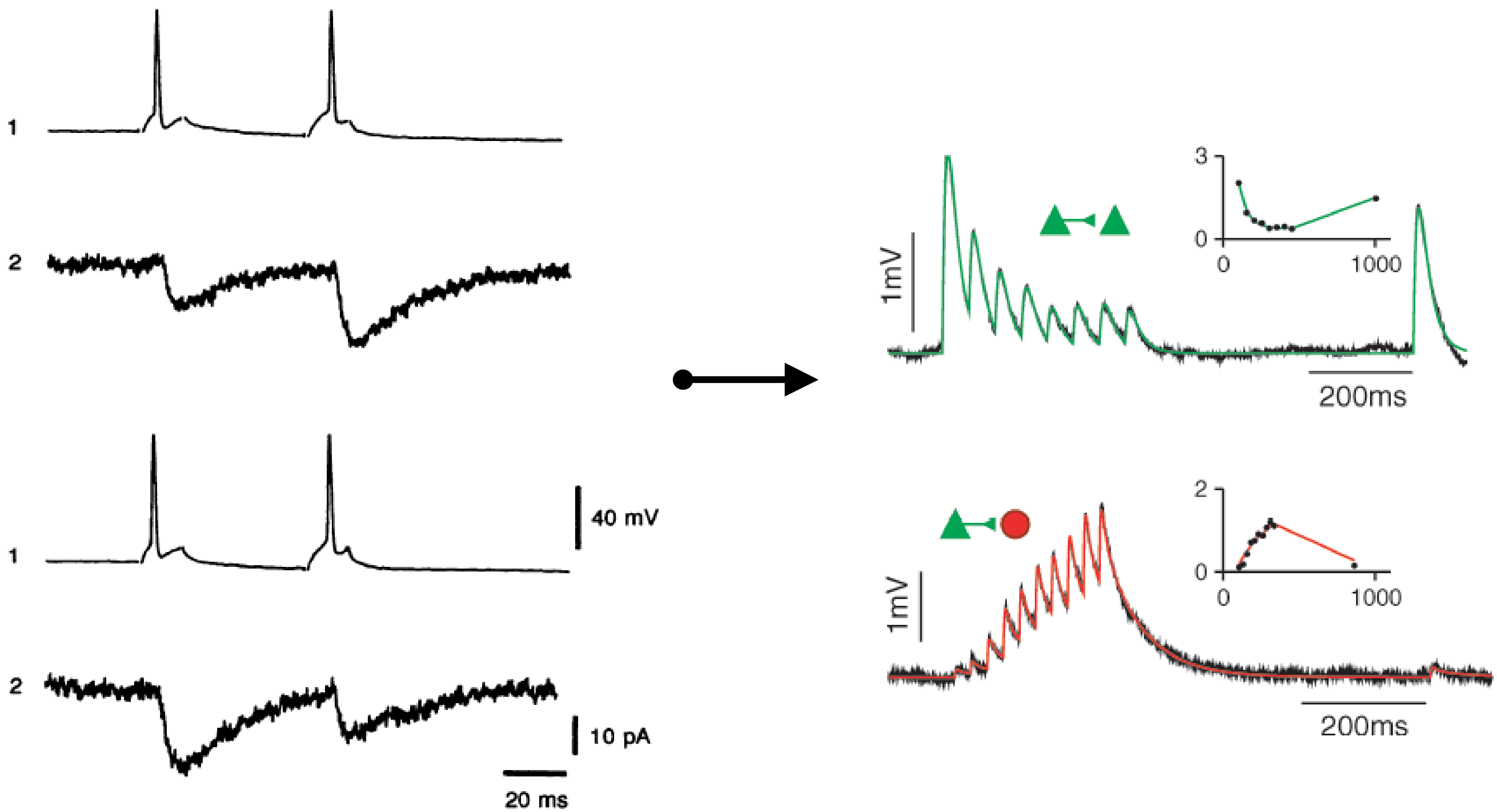
  $E \rightarrow I$ Facilitating

  $I \rightarrow I$ Facilitating

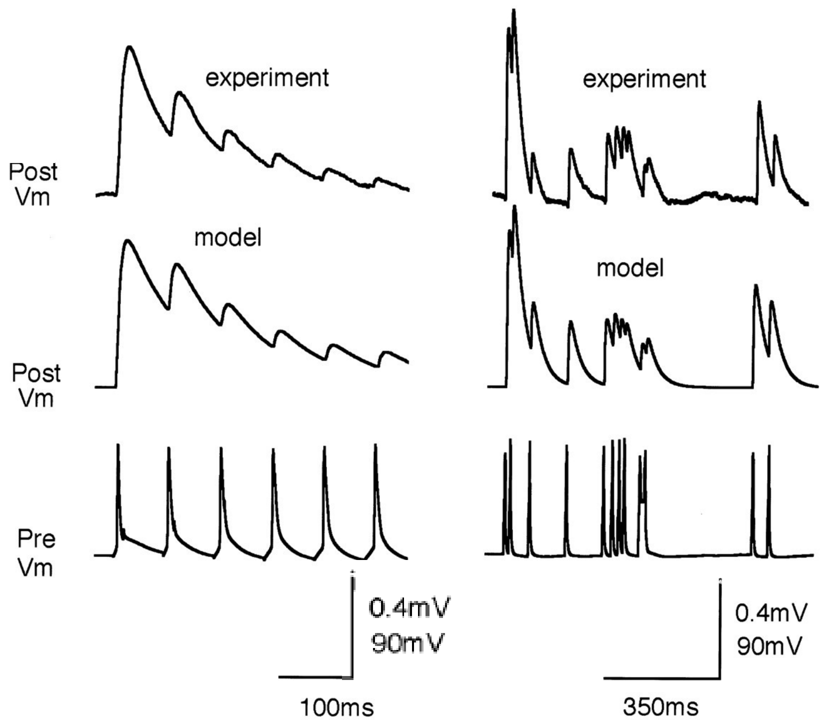
- But in the Prefrontal-cortex, the relations are different, and, for example:

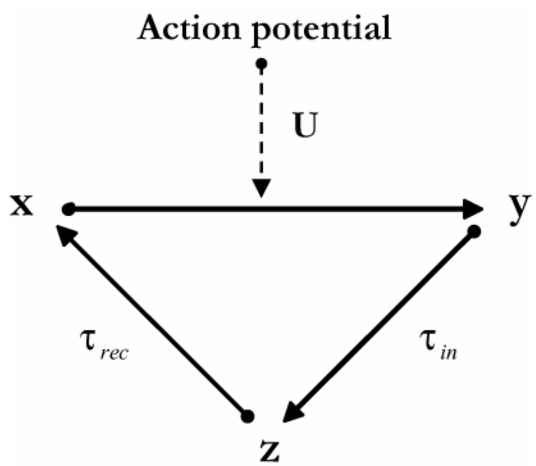
  $E \rightarrow E$ Facilitating

The model, and analysis


1
2
1
2
40 mV
10 pA
20 ms
1mV
200ms
3
0
0
1000
1mV
200ms
2
0
0
1000

Short-term synaptic depression: The model

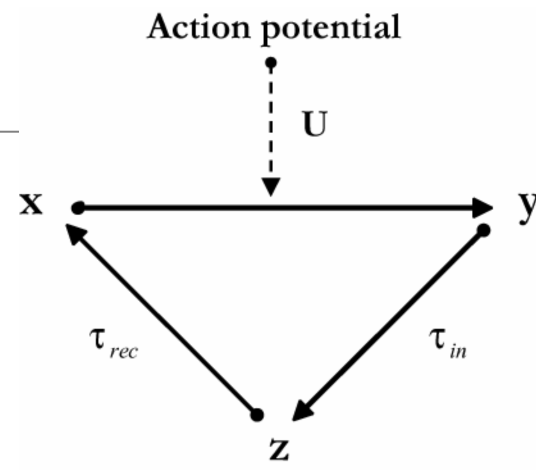


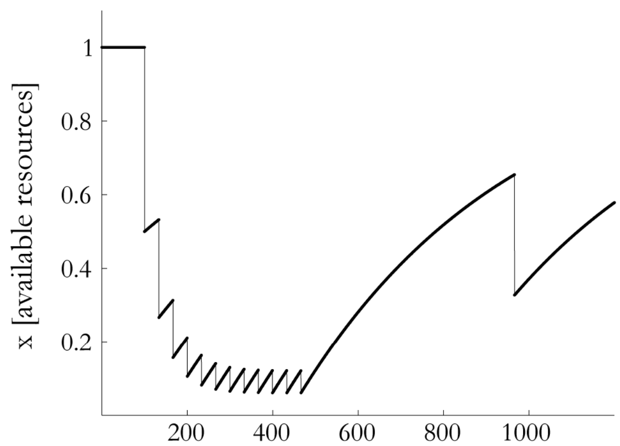


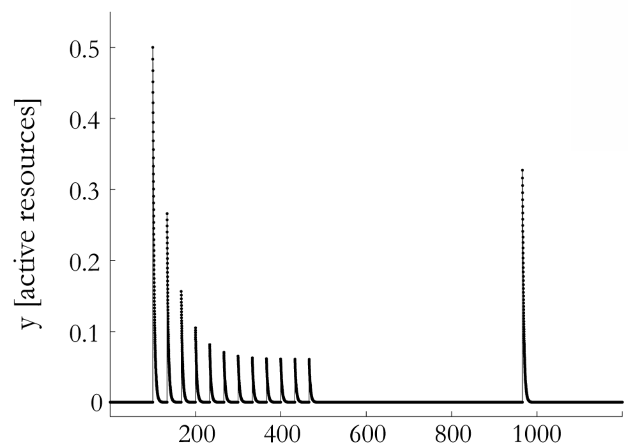
The scaling parameter: A

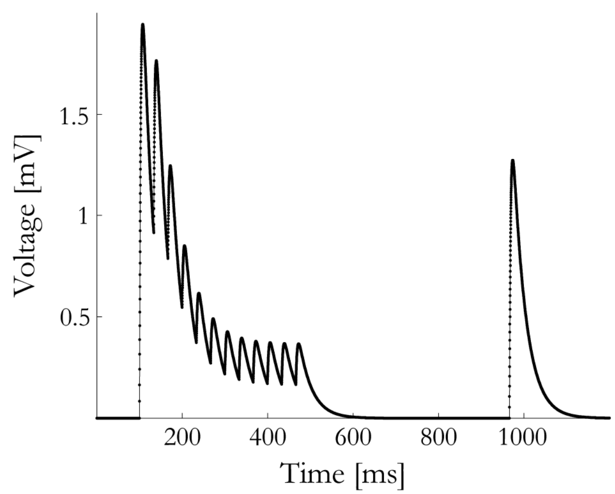
(Tsodyks and Markram, 1997; Abbott et al, 1997)

Short-term synaptic depression









Exc. 1

Underlying physiology

N → Number of vesicles

p → probability of release

q → post-synaptic quantal contribution

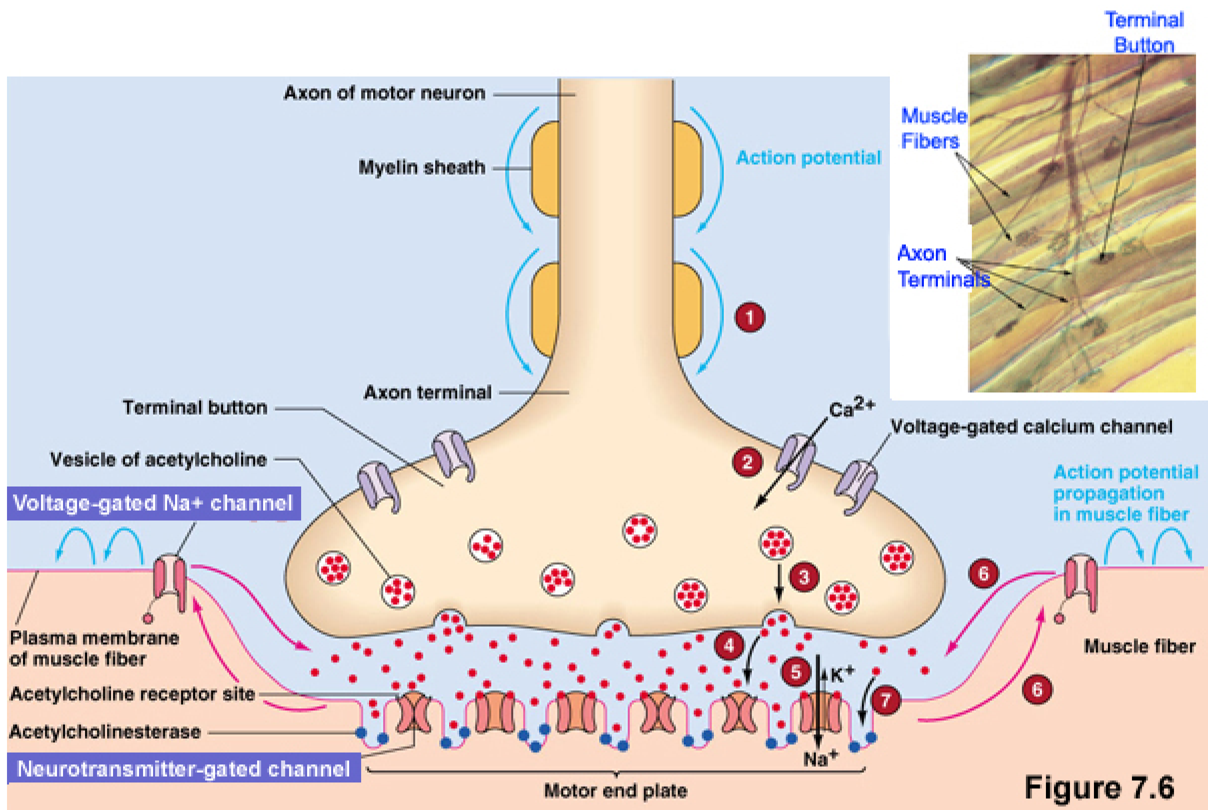
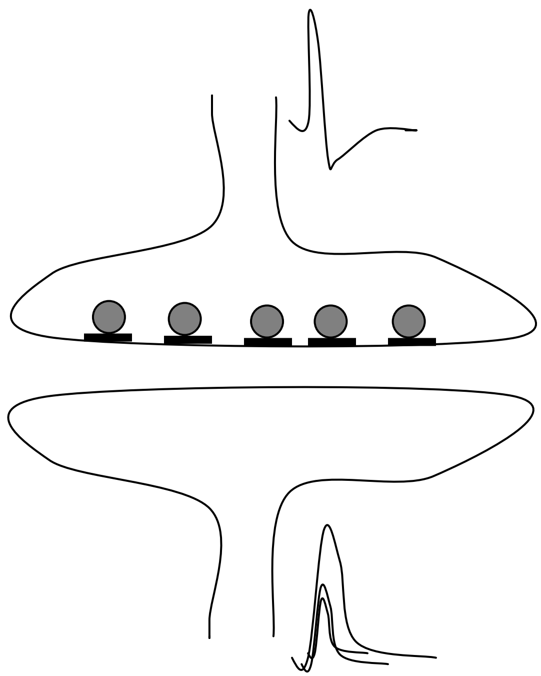


Figure 7.6

(del Castillo and Katz, 1954)

Underlying physiology



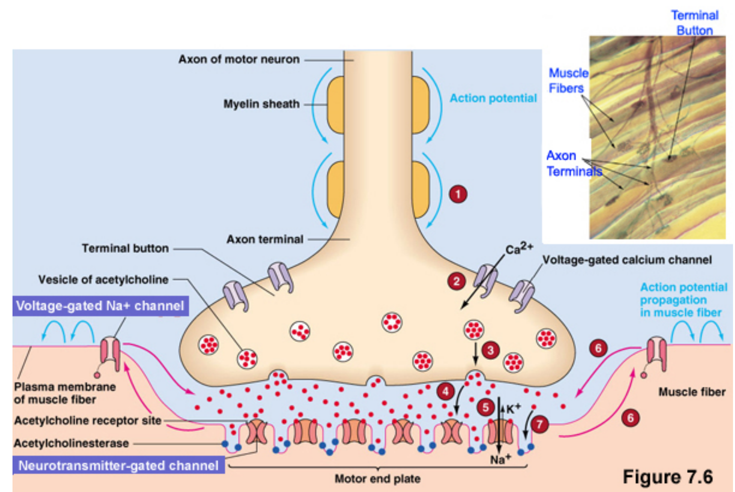
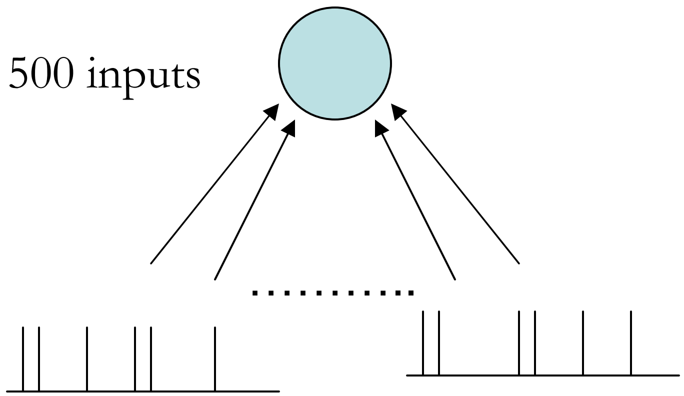
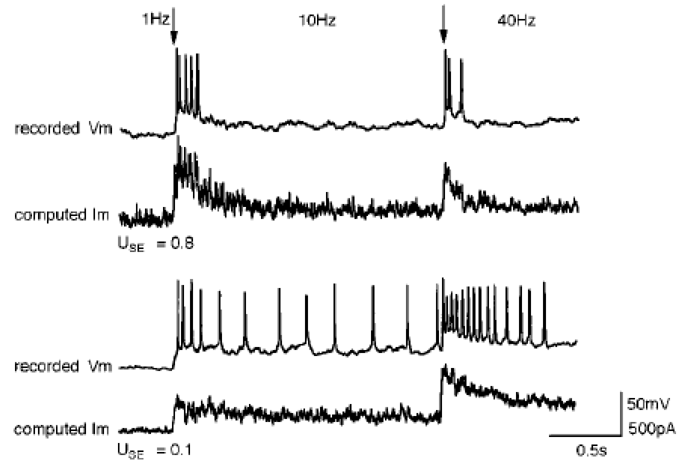


Figure 7.6

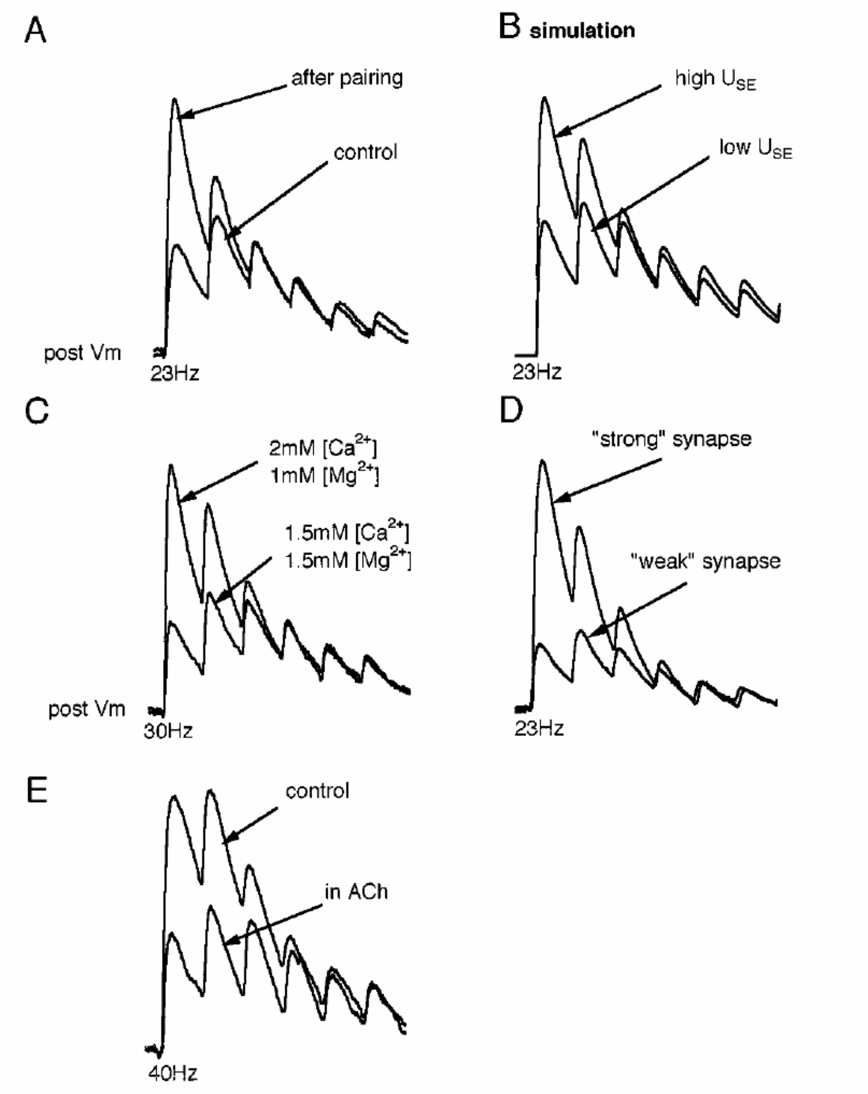
Temporal coding vs. Rate coding





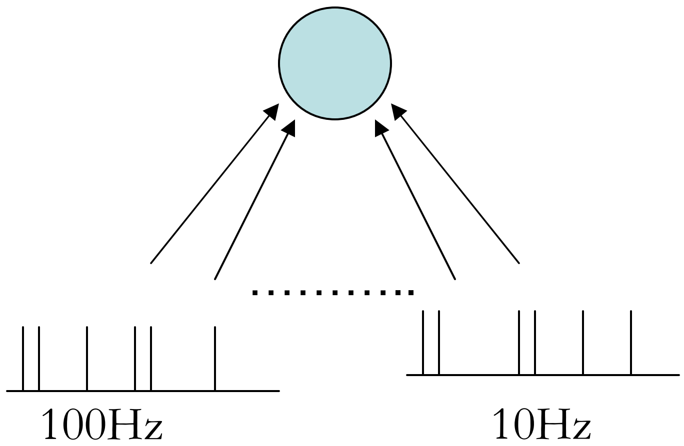
Tsodyks and Markram, 1997

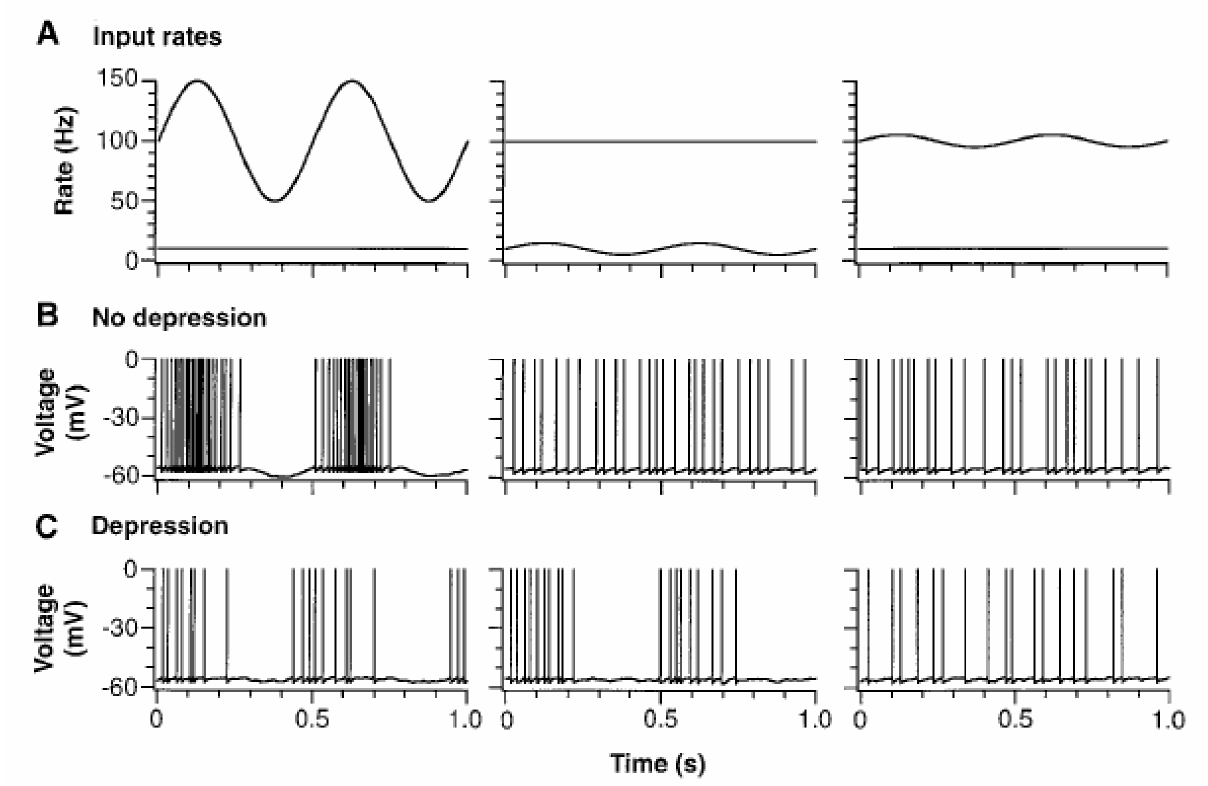
Regulating the neural code



Tsodyks and Markram, 1997

Gain control





Abbott et al., 1997

Weber-Fechner law

differential change
in stimulus

$$dP \propto \frac{dS}{S}$$

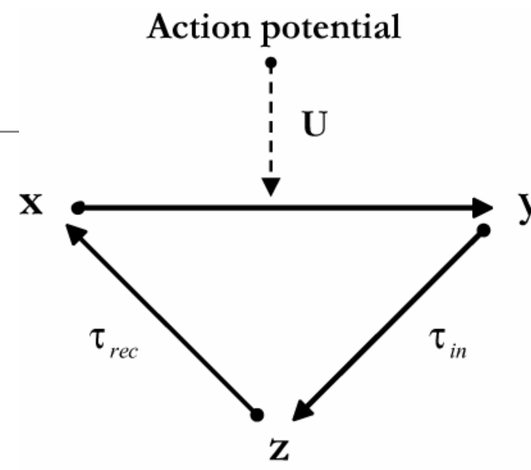
differential change
in perception

stimulus at time
of change

Why STSP? applications and predictions

- Long term changes to synaptic efficacy can occur by changing either the strength of a connection, or its dynamics with different functional roles (e.g., Tsodyks and Markram, 1997).
- Rate coding (weak depression) vs. Temporal coding (strong depression) (Tsodyks and Markram, 1997).
- STSP can serve as a dynamic gain control of synaptic efficacy (Abbott et al., 1997).
- STSP can serve as a mechanism for direction selectivity and contrast adaptation in V1 (Chance et al., 1998).
- With STSP the redundancy of synaptic inputs can be reduced (Goldman et al., 2002).
- A model for the primary auditory cortex (Loebel et al., 2007).
- A model for working memory (Mongillo et al., 2008).

Short-term synaptic depression



$$\dot{x} = \frac{z}{\tau_{rec}} - Ux\delta(t - \vec{t}_{sp})$$

$$x(t_{sp}-) \rightarrow x(t_{sp}-) - x(t_{sp}-) \cdot U$$

$$\dot{z} = \frac{y}{\tau_{in}} - \frac{z}{\tau_{rec}}$$

$$\tau_{mem}\dot{V} = -V + Ay(t)$$

The spike timings:

$$\vec{\boldsymbol{t}}_{sp} = \{\boldsymbol{t}^1_{sp}, \boldsymbol{t}^2_{sp}, \ldots, \boldsymbol{t}^9_{sp}\}$$

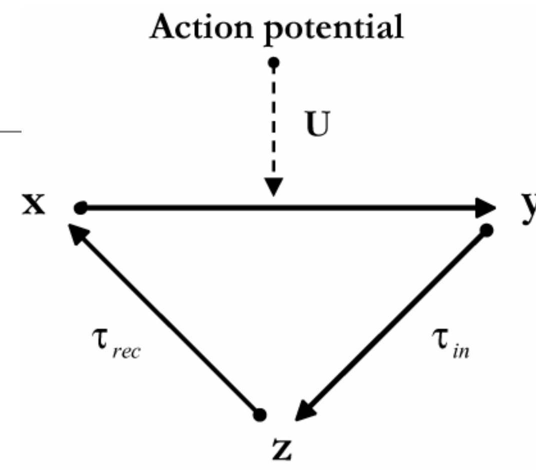
The synaptic parameters:

$$\boldsymbol{A}, \boldsymbol{U}, \tau_{rec}, \tau_{in}$$

The cell parameter:

$$\tau_{mem}$$

Short-term synaptic depression



$$x + y + z = 1$$

$$\dot{x} = \frac{1 - x - y}{\tau_{\mathrm{rec}}} - Ux\delta(t - \vec{t}_{\mathrm{sp}})$$

$$\dot{y} = -\frac{y}{\tau_{\mathrm{in}}} + Ux\delta(t - \vec{t}_{\mathrm{sp}})$$

$$\tau_{\mathrm{mem}}\dot{V} = -V + Ay$$

The spike timings:

$$\vec{\boldsymbol{t}}_{sp} = \{\boldsymbol{t}_{sp}^{1}, \boldsymbol{t}_{sp}^{2}, \ldots, \boldsymbol{t}_{sp}^{9}\}$$

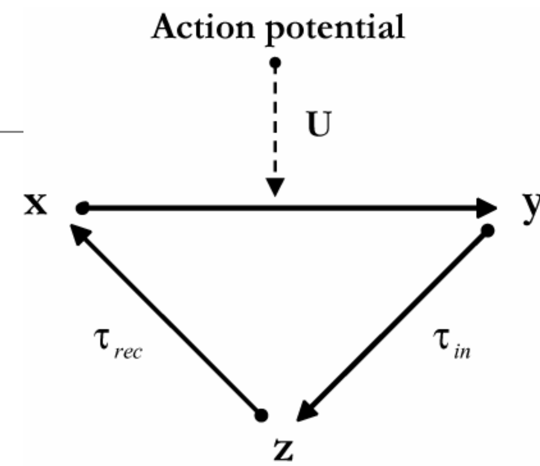
The synaptic parameters:

$$\boldsymbol{A}, \boldsymbol{U}, \boldsymbol{\tau}_{rec}, \boldsymbol{\tau}_{in}$$

The cell parameter:

$$\boldsymbol{\tau}_{mem}$$

Short-term synaptic depression



$$\tau_{\mathrm{in}} << \tau_{\mathrm{rec}}$$

$$\dot{\mathrm{x}} = \frac{1-\mathrm{x}}{\tau_{\mathrm{rec}}} - \mathrm{U}\mathrm{x}\delta(\mathrm{t}-\vec{\mathrm{t}}_{\mathrm{sp}})$$

$$\dot{\mathrm{y}} = -\frac{\mathrm{y}}{\tau_{\mathrm{in}}} + \mathrm{U}\mathrm{x}\delta(\mathrm{t}-\vec{\mathrm{t}}_{\mathrm{sp}})$$

$$\tau_{\mathrm{mem}}\dot{\mathrm{V}} = -\mathrm{V} + \mathrm{A}\mathrm{y}$$

The spike timings:

$$\vec{\boldsymbol{t}}_{\boldsymbol{sp}} = \{\boldsymbol{t}^1_{\boldsymbol{sp}}, \boldsymbol{t}^2_{\boldsymbol{sp}}, \ldots, \boldsymbol{t}^9_{\boldsymbol{sp}}\}$$

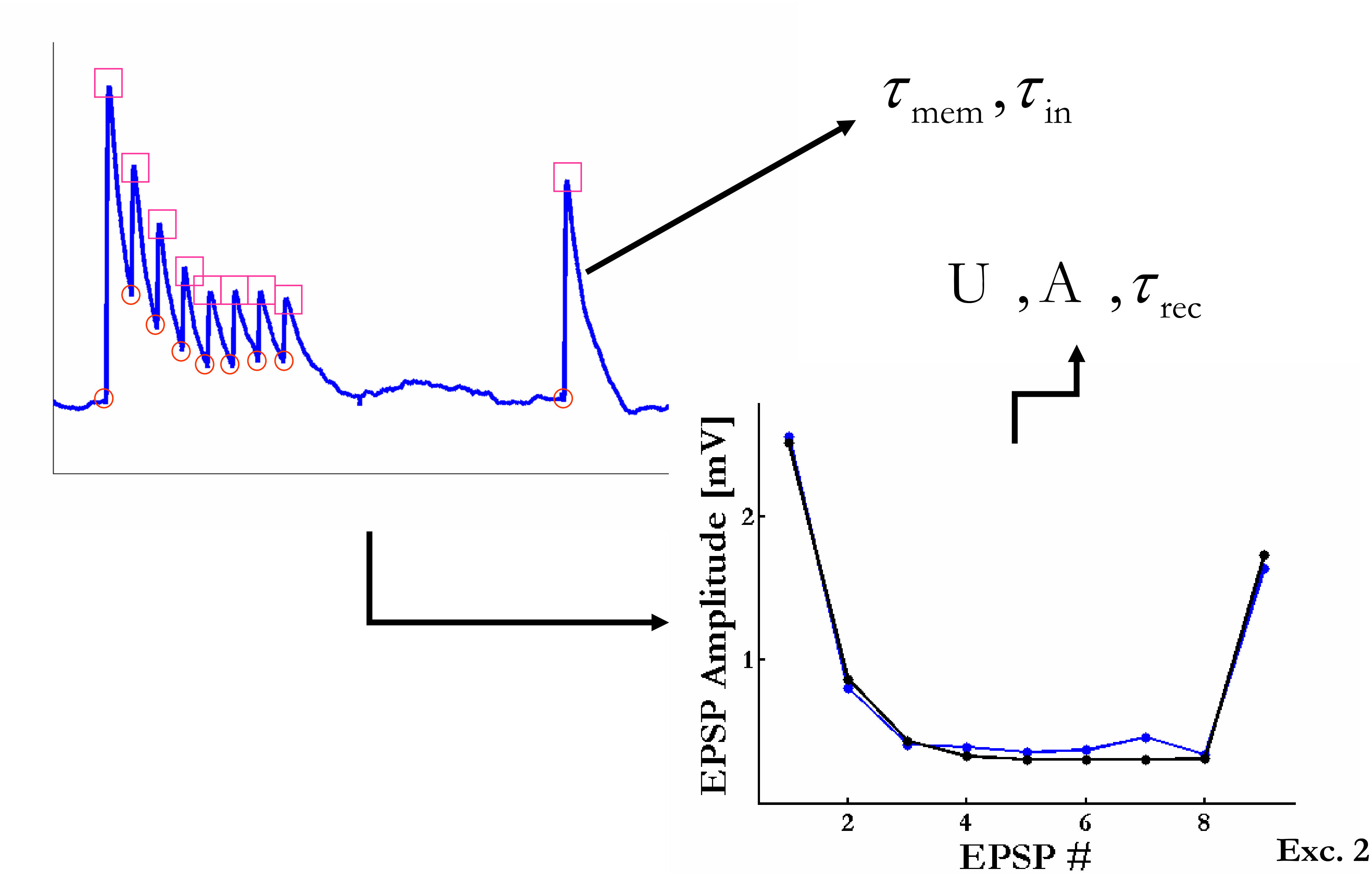
The synaptic parameters:

$$\boldsymbol{A}, \boldsymbol{U}, \boldsymbol{\tau}_{\boldsymbol{rec}}, \boldsymbol{\tau}_{\boldsymbol{in}}$$

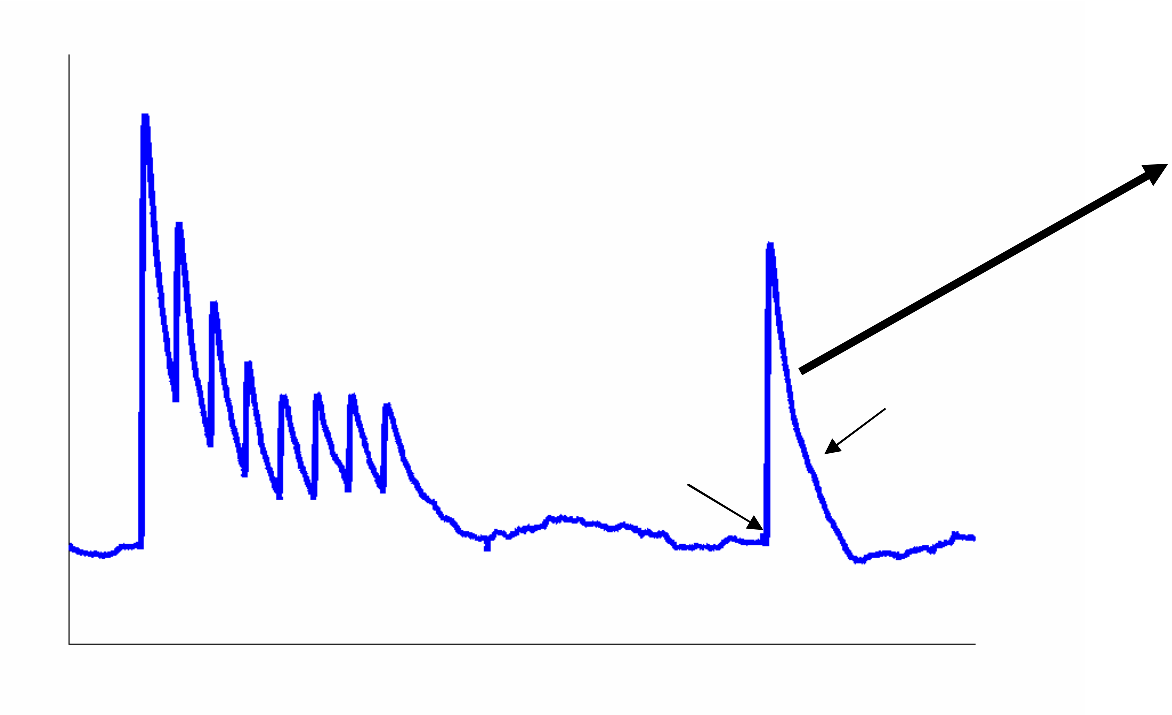
The cell parameter:

$$\boldsymbol{\tau}_{\boldsymbol{mem}}$$

The fitting process



The fitting process



$$\tau_{mem}, \tau_{in}$$

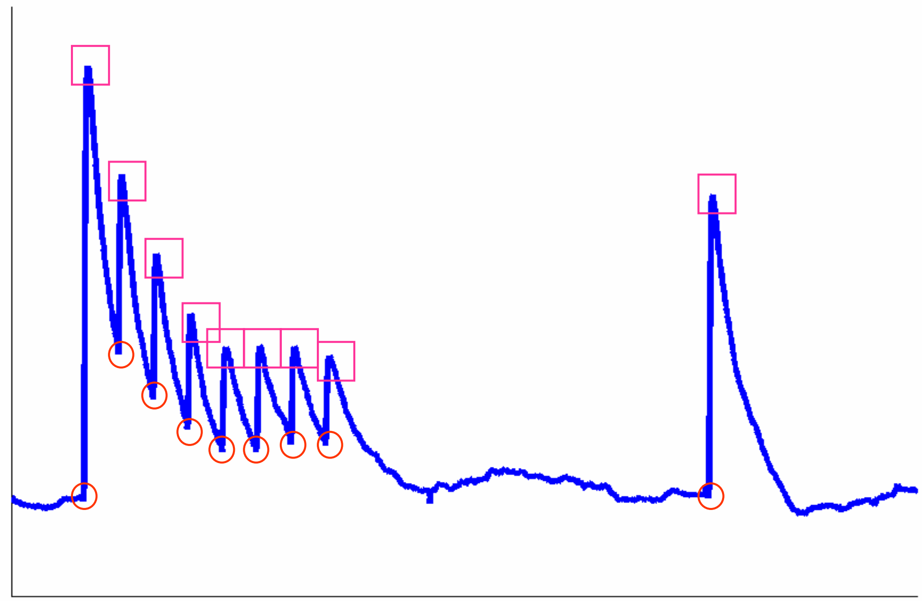
$$\dot{y} = -\frac{y}{\tau_{in}} + Ux\delta(t - \vec{t}_{sp})$$

$$y(t) = y(0) \cdot e^{-\frac{t}{\tau_{in}}}, \quad y(0) = 1$$

$$\tau_{mem}\dot{V} = -V + Ay(t)$$

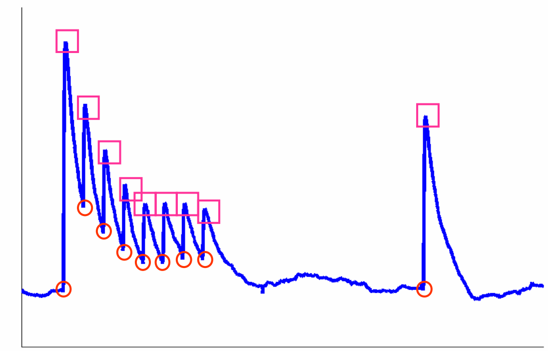
$$V(t) = \frac{B \cdot \tau_{in}}{\tau_{in} - \tau_{mem}} \cdot (e^{-\frac{t}{\tau_{in}}} - e^{-\frac{t}{\tau_{mem}}})$$

The fitting process



$$U, A, \tau_{rec}$$

The fitting process



$$\dot{x} = \frac{1-x}{\tau_{rec}} - Ux\delta(t-\vec{t}_{sp})$$

$$\dot{y} = -\frac{y}{\tau_{in}} + Ux\delta(t-\vec{t}_{sp})$$

$$\tau_{mem}\dot{V} = -V + Ay$$

$$x_1 = 1$$

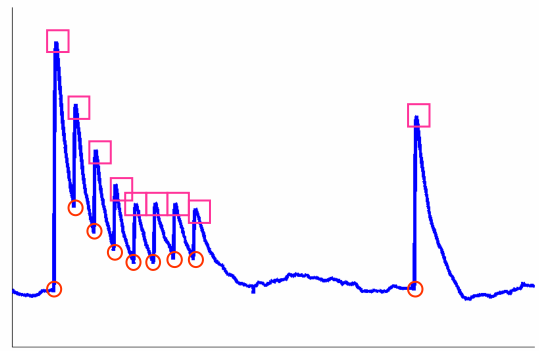
$$\text{for } n = 2:8$$

$$x_n = x_{n-1}\cdot(1-U)\cdot e^{-\frac{\Delta T_1}{\tau_{rec}}} + 1 - e^{-\frac{\Delta T_1}{\tau_{rec}}}$$

$$\text{for } n = 9$$

$$x_n = x_{n-1}\cdot(1-U)\cdot e^{-\frac{\Delta T_2}{\tau_{rec}}} + 1 - e^{-\frac{\Delta T_2}{\tau_{rec}}}$$

The fitting process



$$\alpha_n = A \cdot U \cdot x_n$$

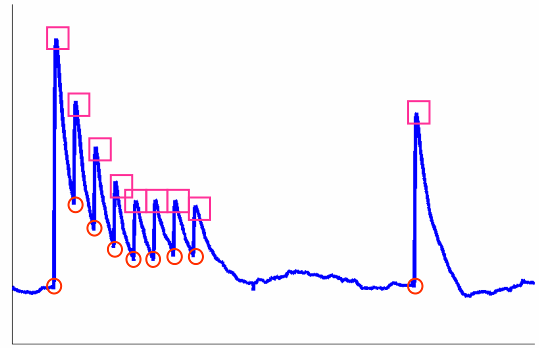
$$V0_1 = 0$$

$$\text{for } n = 2:8$$

$$VMax_{n-1} = \alpha_{n-1} \cdot \left(\frac{\alpha_{n-1} \cdot \tau_{mem}}{\alpha_{n-1} \cdot \tau_{in} - V0_{n-1} \cdot (\tau_{in} - \tau_{mem})}\right)^{\frac{\tau_{mem}}{\tau_{in} - \tau_{mem}}}$$

$$V0_n = V0_{n-1} \cdot e^{-\frac{\Delta T_1}{\tau_{mem}}} + \frac{\alpha_{n-1} \cdot \tau_{in}}{(\tau_{in} - \tau_{mem})} \cdot \left(e^{-\frac{\Delta T_1}{\tau_{in}}} - e^{-\frac{\Delta T_1}{\tau_{mem}}}\right)$$

The fitting process



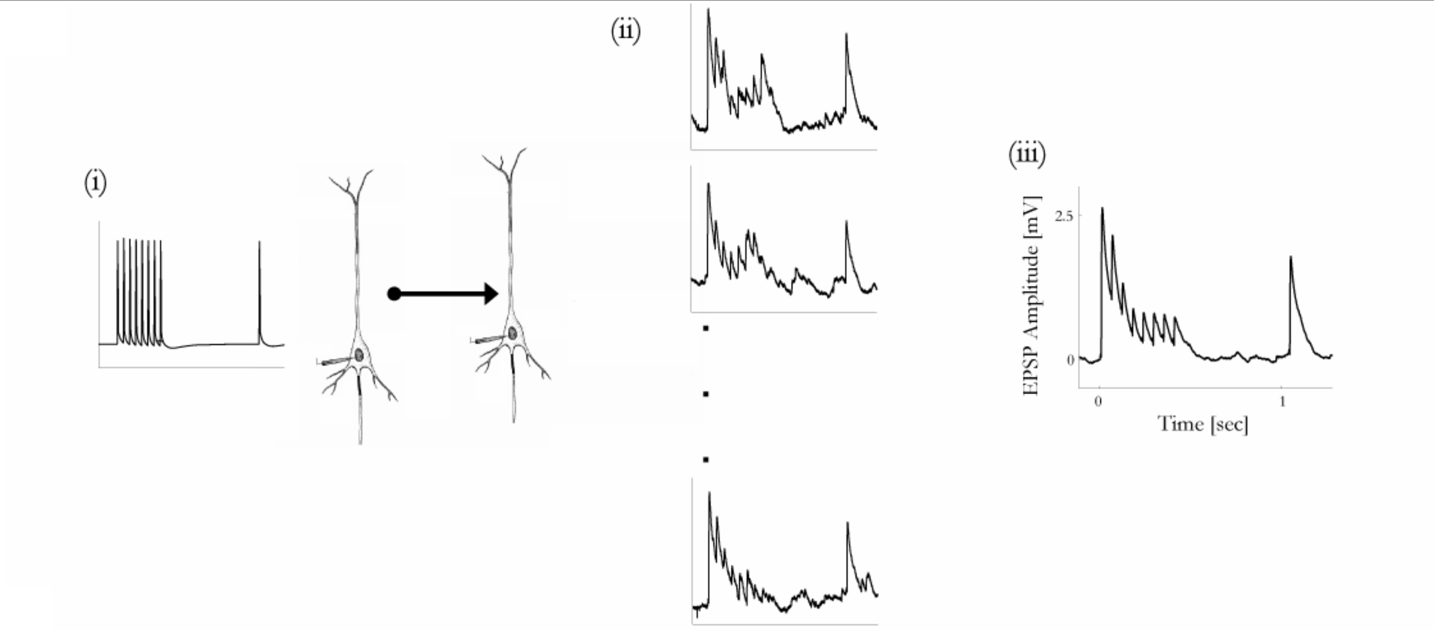
$$\mathrm{VMax}_8 = \alpha_8 \cdot \left(\frac{\alpha_8 \cdot \tau_{\mathrm{mem}}}{\alpha_8 \cdot \tau_{\mathrm{in}} - \mathrm{V0}_8 \cdot (\tau_{\mathrm{in}} - \tau_{\mathrm{mem}})}\right)^{\frac{\tau_{\mathrm{mem}}}{\tau_{\mathrm{in}} - \tau_{\mathrm{mem}}}}$$

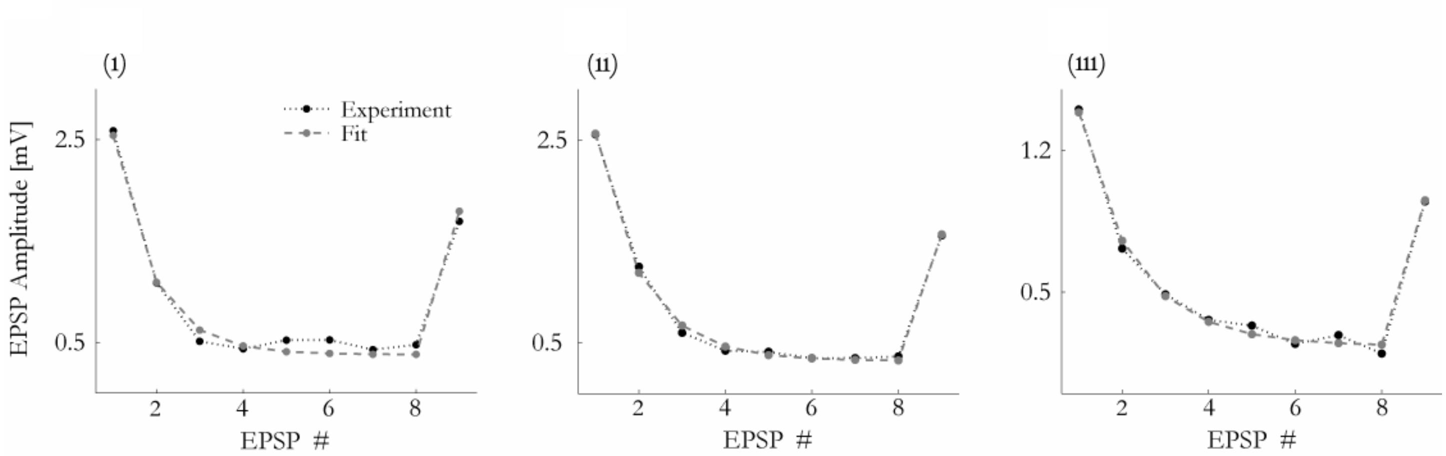
$$\mathrm{V0}_9 = \mathrm{V0}_8 \cdot e^{-\frac{\Delta T_2}{\tau_{\mathrm{mem}}}} + \frac{\alpha_8 \cdot \tau_{\mathrm{in}}}{(\tau_{\mathrm{in}} - \tau_{\mathrm{mem}})} \cdot \left(e^{-\frac{\Delta T_2}{\tau_{\mathrm{in}}}} - e^{-\frac{\Delta T_2}{\tau_{\mathrm{mem}}}}\right)$$

$$\mathrm{VMax}_9 = \alpha_9 \cdot \left(\frac{\alpha_9 \cdot \tau_{\mathrm{mem}}}{\alpha_9 \cdot \tau_{\mathrm{in}} - \mathrm{V0}_9 \cdot (\tau_{\mathrm{in}} - \tau_{\mathrm{mem}})}\right)^{\frac{\tau_{\mathrm{mem}}}{\tau_{\mathrm{in}} - \tau_{\mathrm{mem}}}}$$

$$\mathrm{Amp} = \mathrm{VMax} - \mathrm{V0}$$

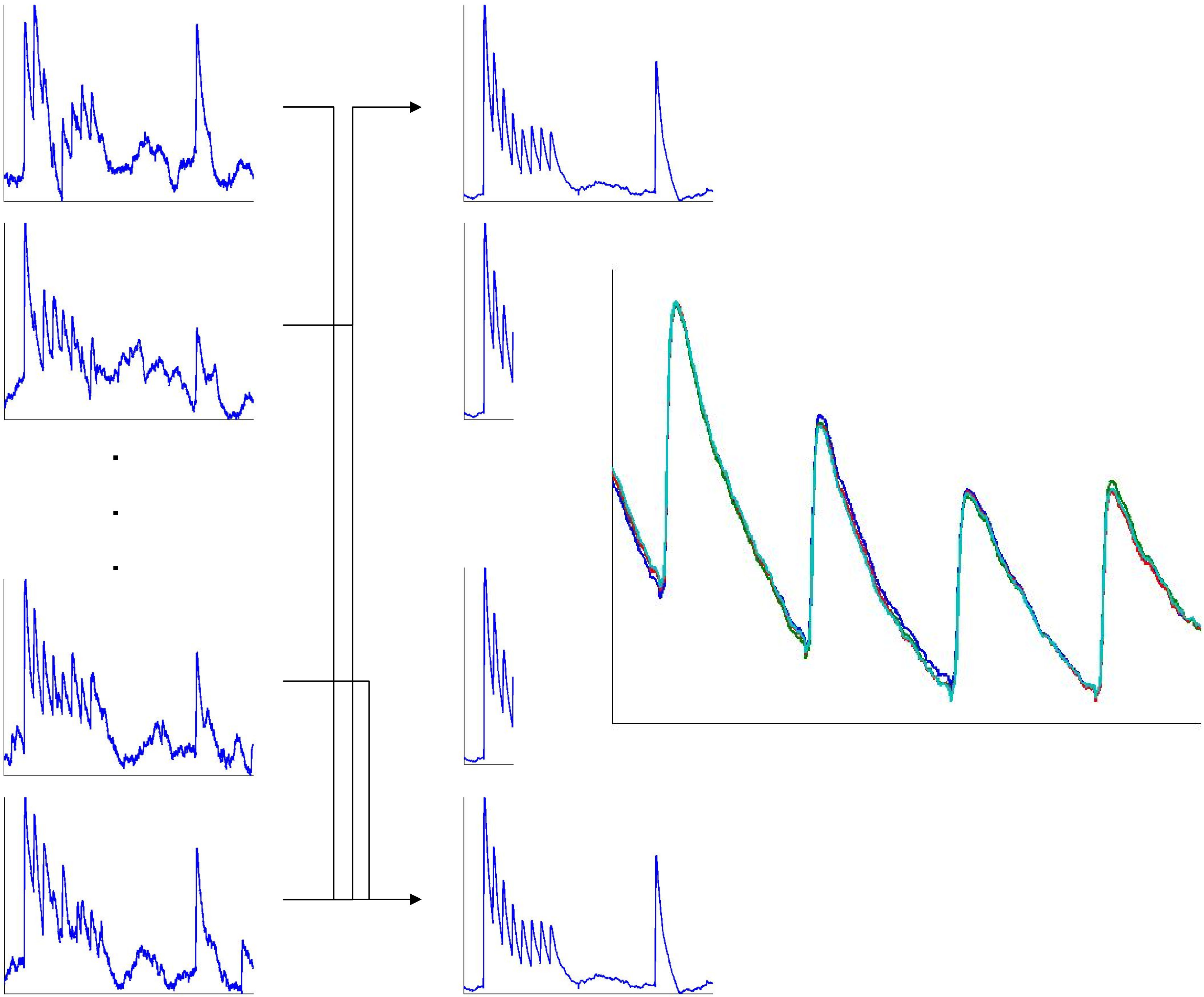
A quick rehearsal…





Jackknife method

- We have estimated the model parameters from an average of so many single traces.
- How do we know how accurate is our estimation?
- One way is to measure many sets of single traces from the same connection, produce an average from each set, estimate the parameters, and so on….
- Another way is the Jackknife method.



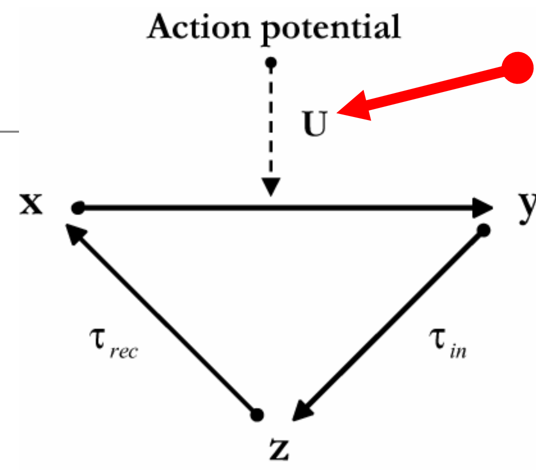
The Jackknife measures

$$\mathrm{Std} = \sqrt{\frac{\boxed{J-1}}{J}\sum_{i=1}^{J}\left(\mathrm{Par}_i - <\mathrm{Par}>\right)^2}$$

$$<\mathrm{Par}> = \frac{1}{J}\sum_{i=1}^{J}\mathrm{Par}_i$$

$$\mathrm{CV} = \frac{\mathrm{Std}}{<\mathrm{Par}>}$$

Short-term synaptic facilitation



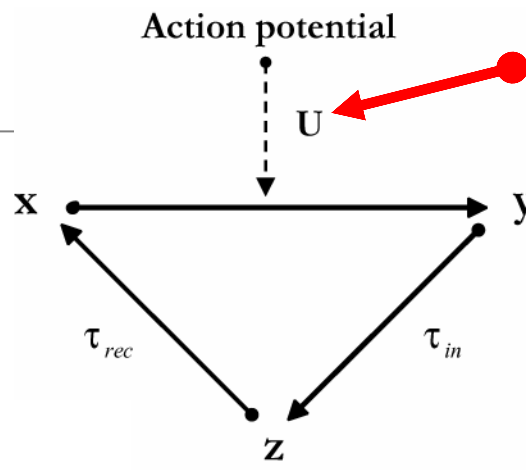
$$\dot{x} = \frac{1-x}{\tau_{rec}} - \boxed{u(t)} \cdot x \cdot \delta(t - \vec{t}_{sp})$$

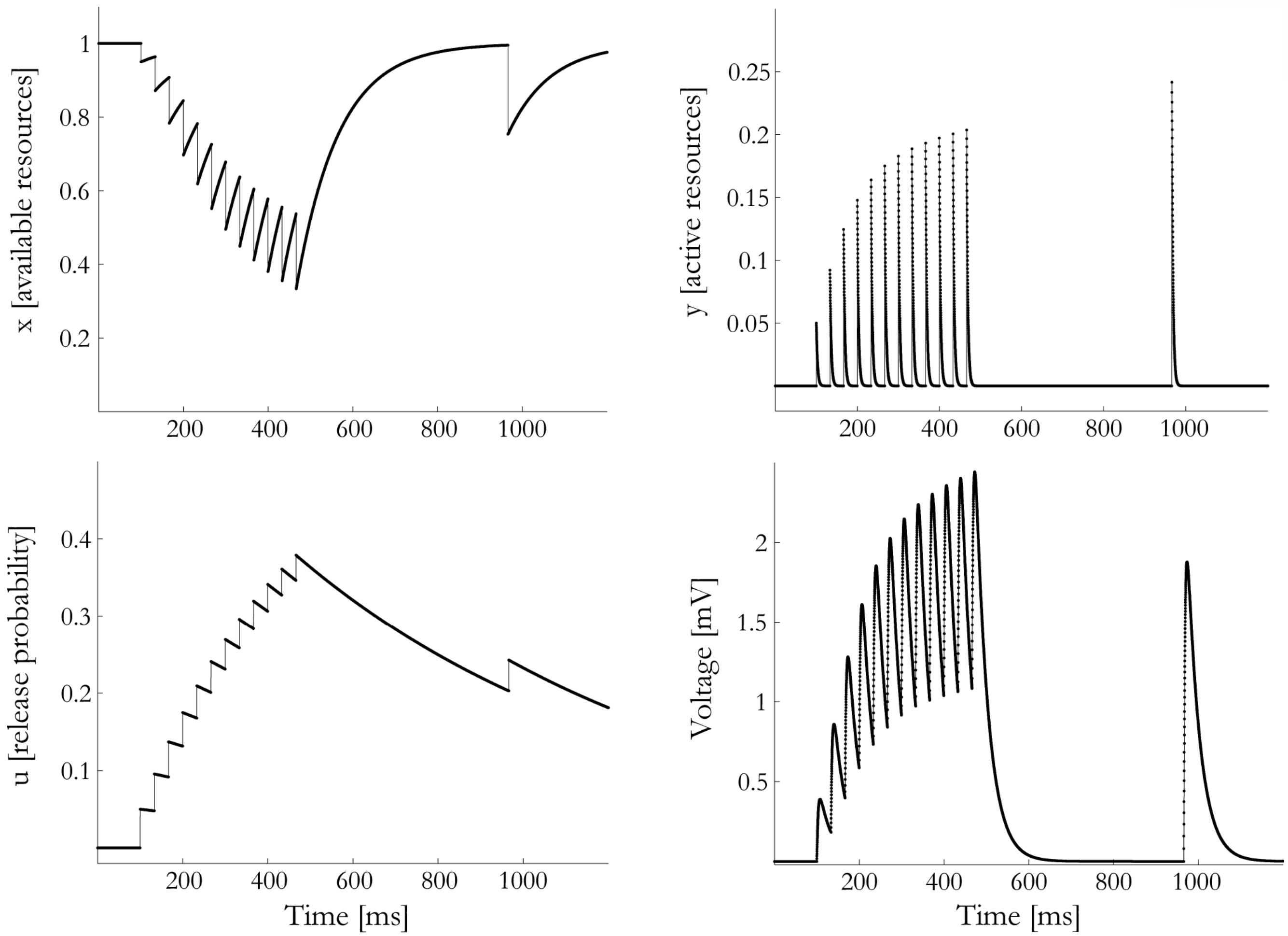
$$\dot{y} = -\frac{y}{\tau_{in}} + \boxed{u(t)} \cdot x \cdot \delta(t - \vec{t}_{sp})$$

$$\dot{u} = -\frac{u}{\boxed{\tau_{facil}}} + U \cdot (1-u) \cdot \delta(t - \vec{t}_{sp})$$

Exc. 6

Short-term synaptic facilitation





Underlying physiology

N → Number of vesicles

p → probability of release

q → post-synaptic quantal contribution

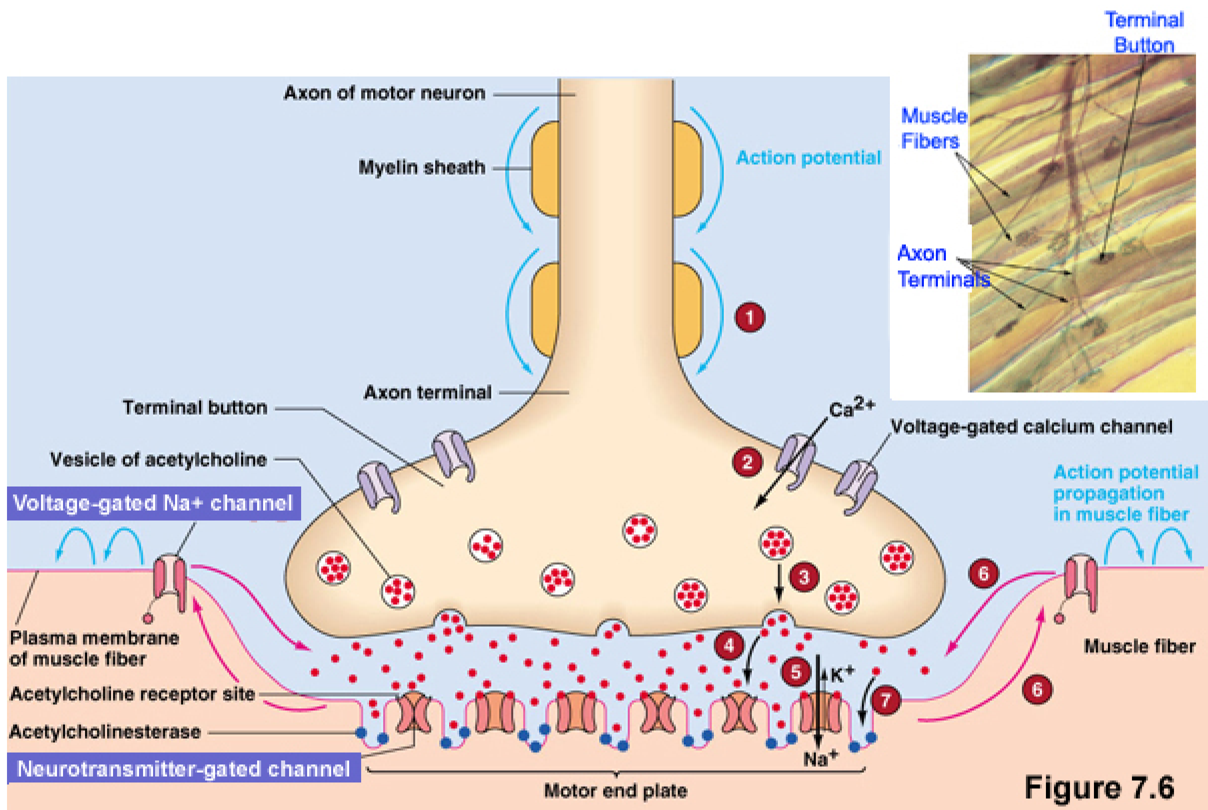


Figure 7.6

(del Castillo and Katz, 1954)

And now, it is your turn! ☺