AMPA receptor trafficking and synaptic plasticity

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The brain: unparalled parallel computer

- 10^{11} neurons
- 10^{14} synapses
- network is plastic
- regulates behavior
- can **learn** and **remember**!

Mathematical Neuroscience at Utah

Cognition

↑

Systems

↑

Cortical Areas

↑

Small Networks

↑

Neurons

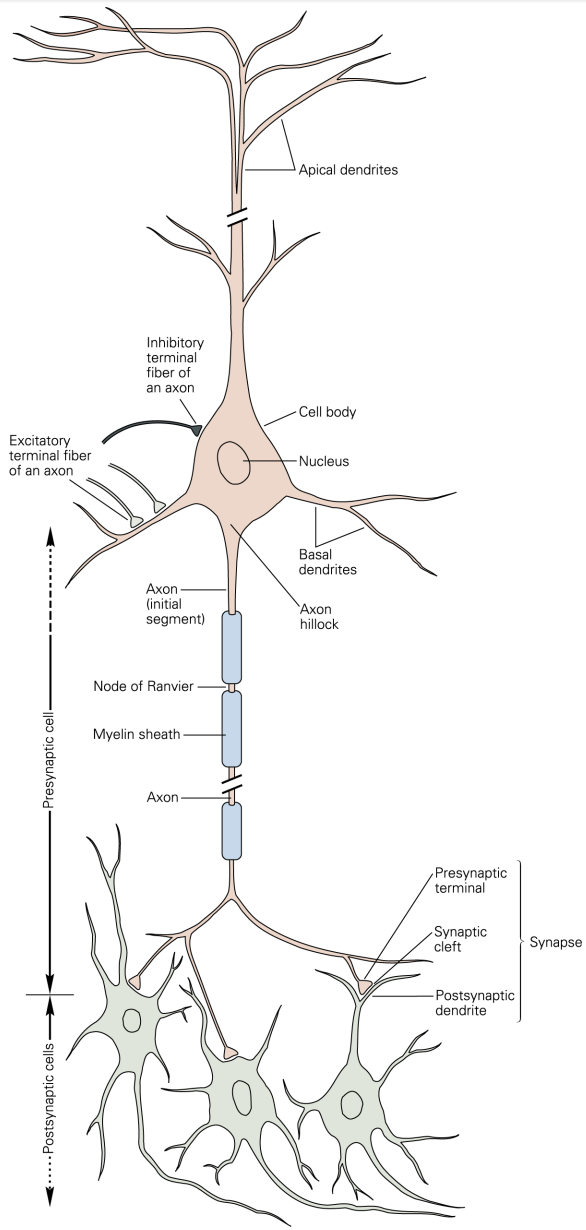
↑

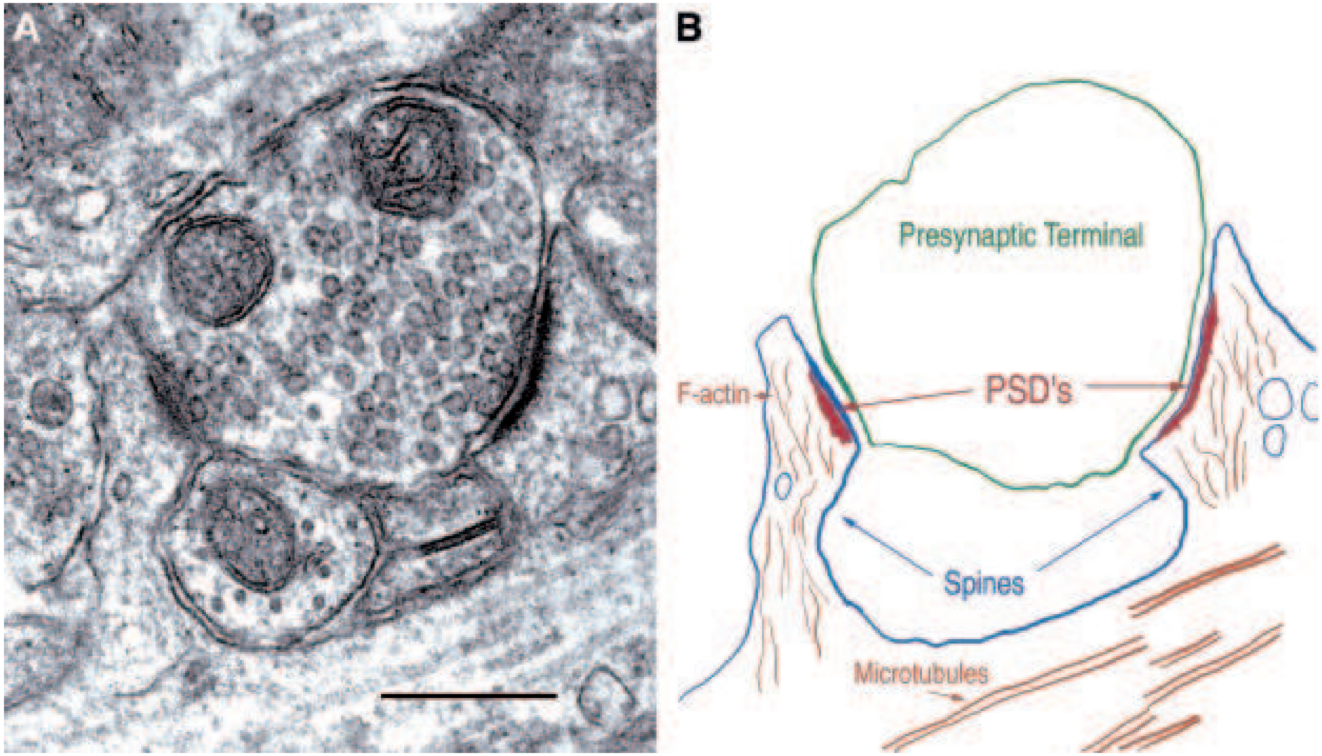
Dendrites

↑

Synapses

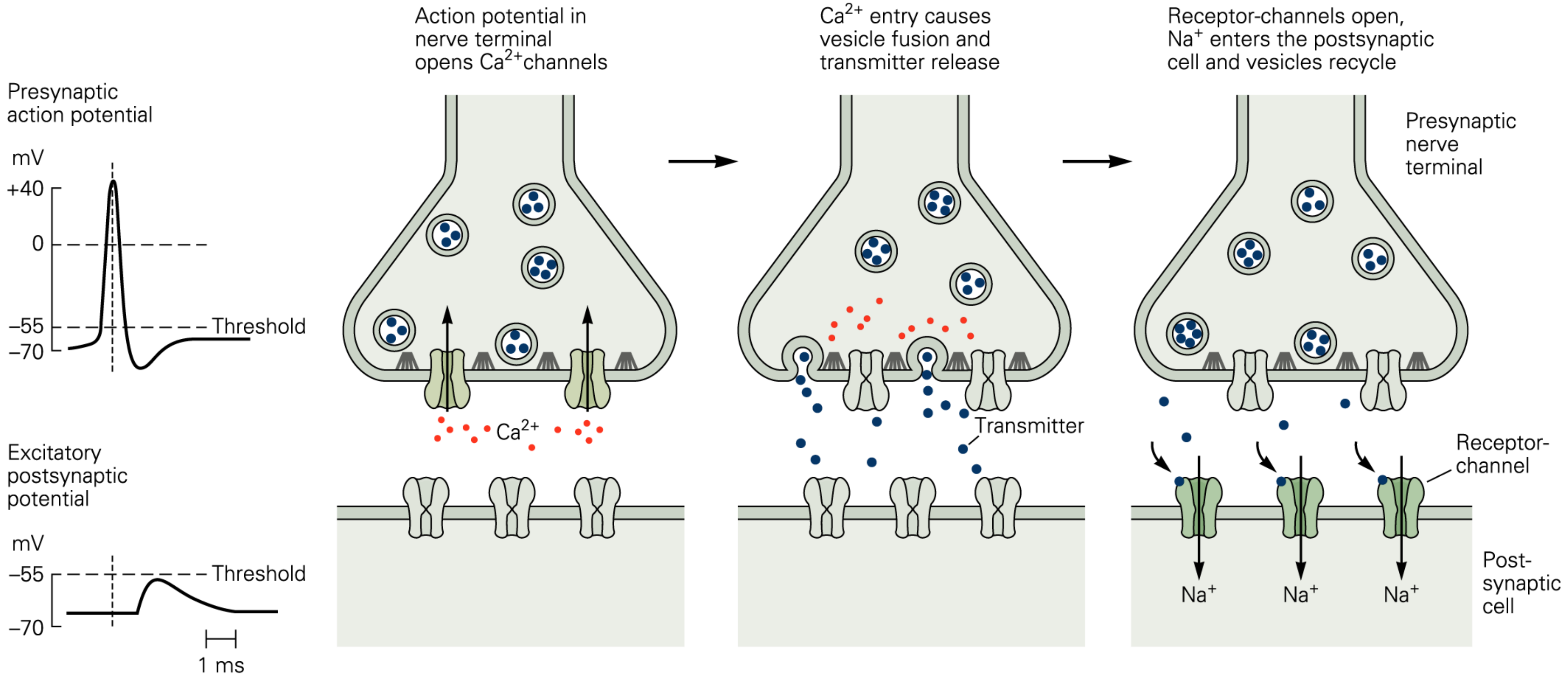
The Synapse





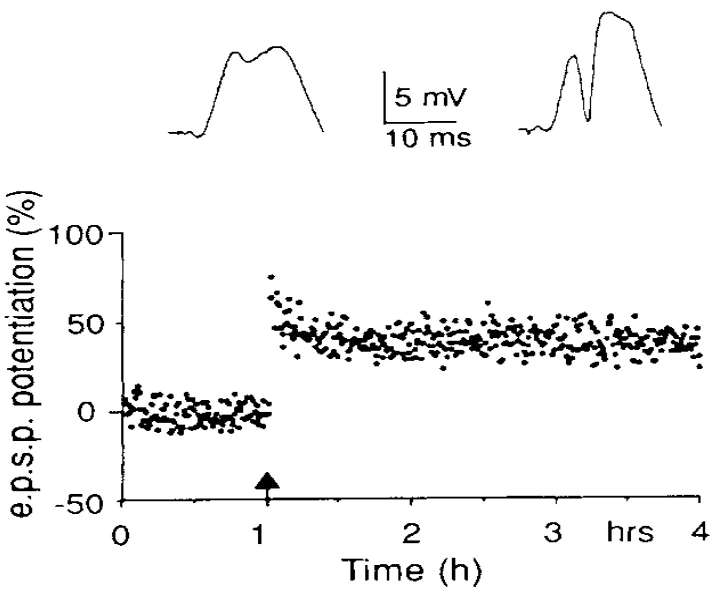
E.R. Kandel et al. Principles of Neural Science. 2000.
M.B. Kennedy. *Science* **290** 750–754 (2000).

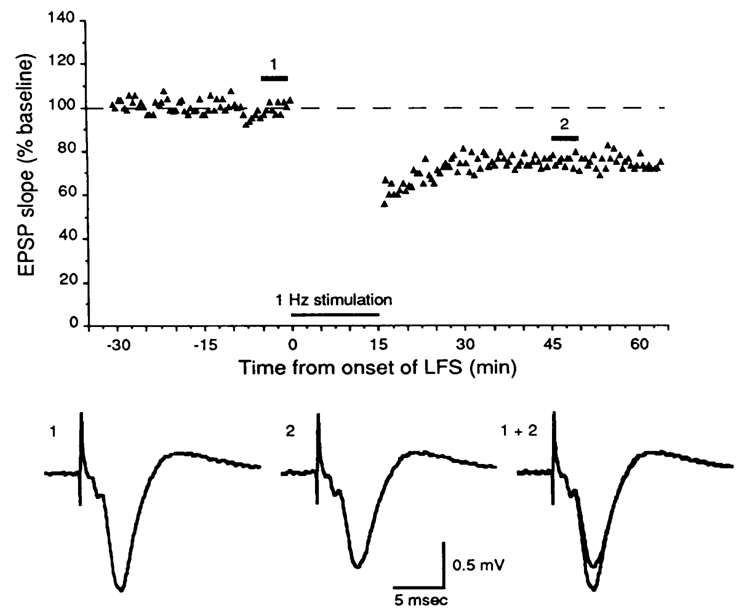
Synaptic transmission



E.R. Kandel et al. Principles of Neural Science. New York: McGraw-Hill. 2000.

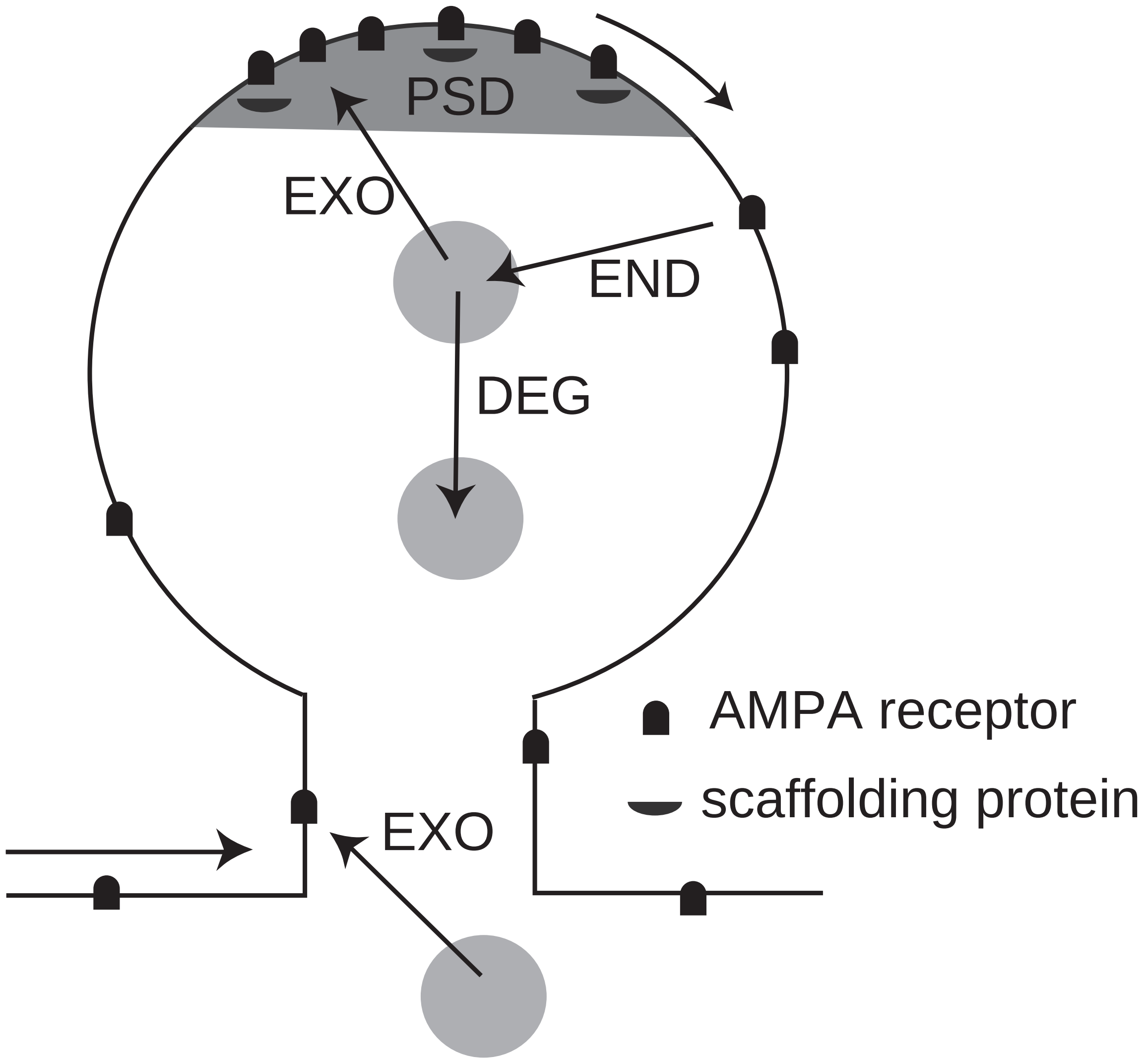
Long-term potentiation/depression





T.V.P. Bliss and G.L. Collingridge. *Nature* **361** 31–39 (1993).
S.M. Dudek and M.F. Bear. *PNAS* **89** 4363–4367 (1992).

AMPA receptor trafficking



B.A. Earnshaw & P.C. Bressloff. *J. Neurosci.* **26** 12362–12373 (2006).

Model Equations

Dendrite:

$$\frac{\partial U}{\partial t} = D\frac{\partial^2 U}{\partial x^2} - \rho\Omega(U - R)$$

$$J(0) = \sigma,\ J(L) = 0,\ J(x) = -DU'(x)$$

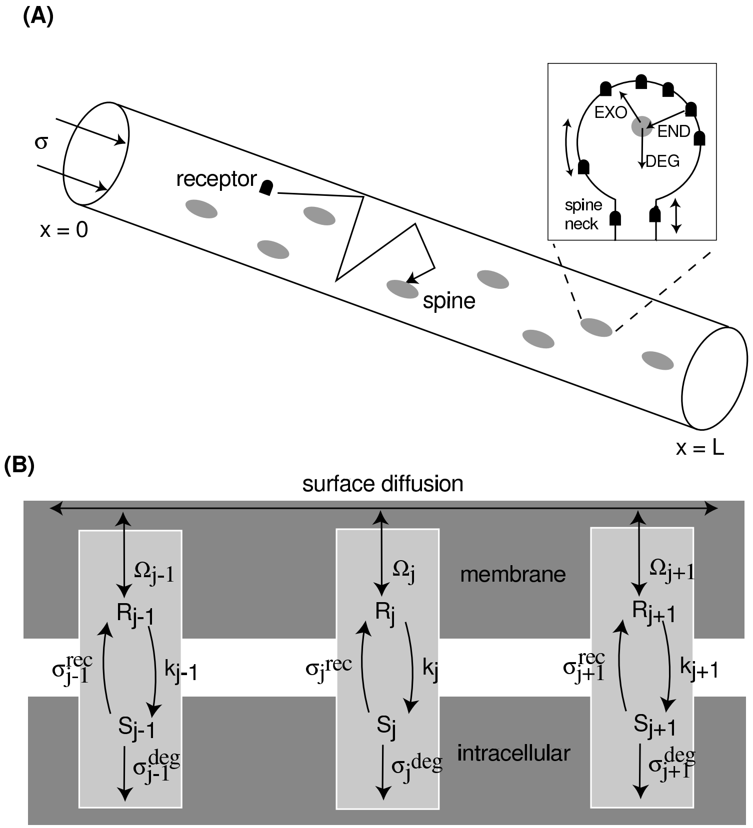
Spine:

$$\frac{dR}{dt} = \frac{\Omega}{A}(U - R) - \frac{k}{A}R - \frac{h}{A}(R - P)$$

$$\frac{dC}{dt} = -\sigma^{rec}C - \sigma^{deg}C + kR + \delta$$

$$\frac{dP}{dt} = \frac{h}{a}(R - P) + \frac{\sigma^{rec}}{a}C - \alpha(Z - Q)P + \beta Q$$

$$\frac{dQ}{dt} = \alpha(Z - Q)P - \beta Q$$



Steady-state solution

In steady-state, U satisfies

$$\rho\widehat{\Omega}U - D\frac{\partial^2 U}{\partial x^2} = \rho\widehat{\Omega}r$$

$$\widehat{\Omega} = \frac{\Omega k(1-\lambda)}{\Omega + k(1-\lambda)}, \quad r = \frac{\lambda\delta}{k(1-\lambda)}, \quad \lambda = \frac{\sigma^{rec}(1-f)}{\sigma^{rec}(1-f) + \sigma^{deg} f}$$

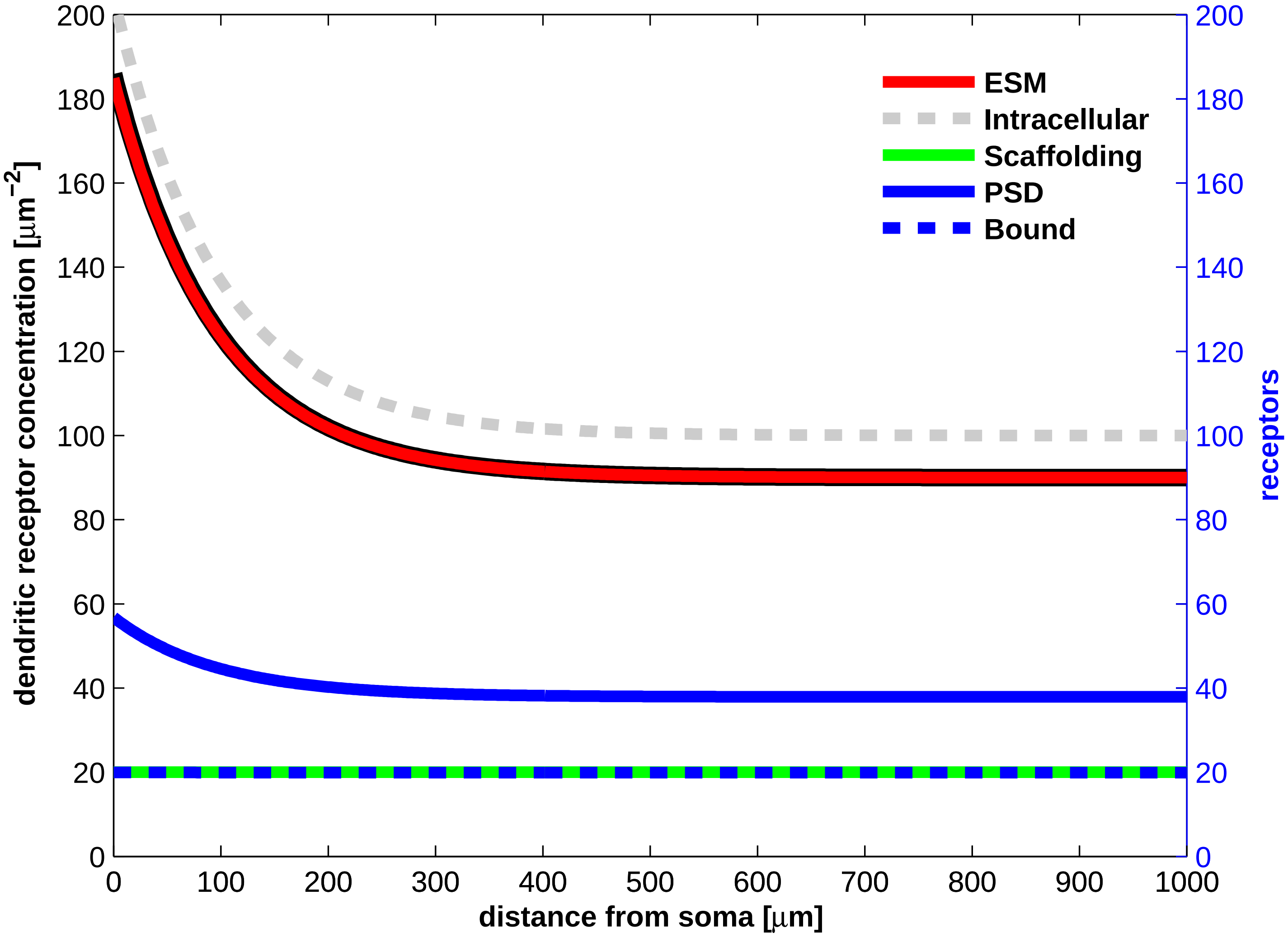
If $\rho\widehat{\Omega}$ is constant,

$$U(x) = \frac{\sigma}{D}G(x,0) + \Lambda^2 \int_0^L G(x,x')r(x')dx', \qquad \Lambda = \sqrt{\frac{\rho\widehat{\Omega}}{D}}$$

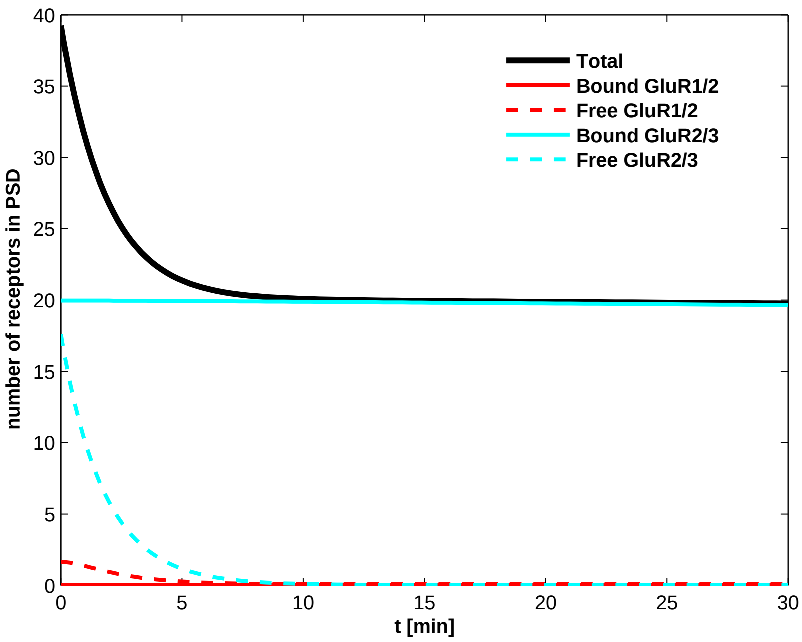
where

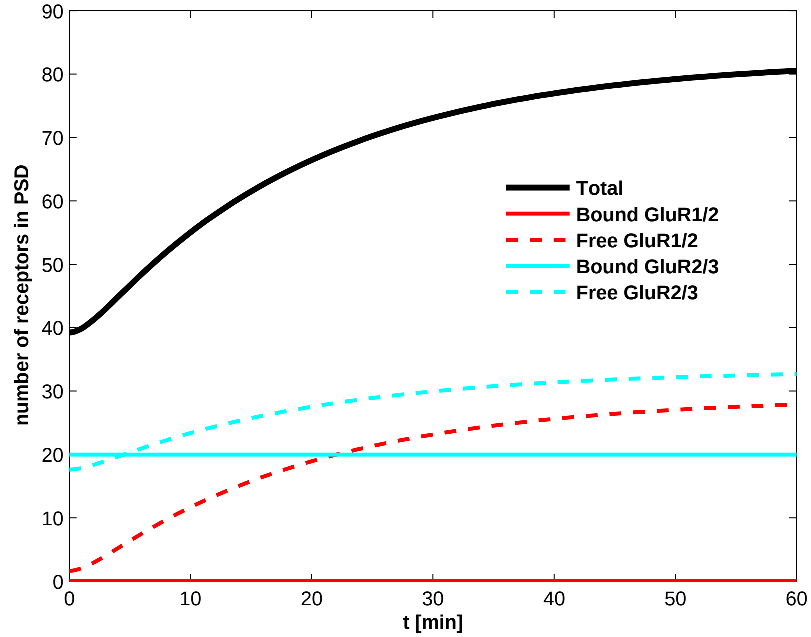
$$G(x,x') = \frac{\cosh\left(\Lambda[|x-x'|-L]\right) + \cosh\left(\Lambda[x+x'-L]\right)}{2\Lambda\sinh(\Lambda L)}$$

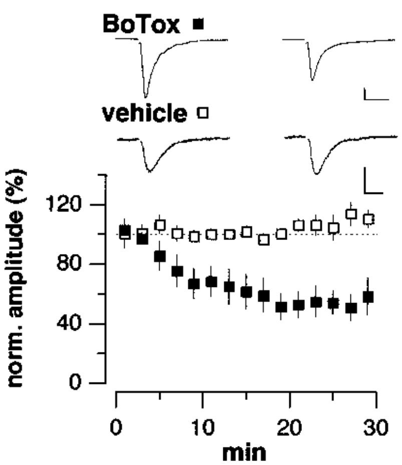
Steady-state distribution of receptors

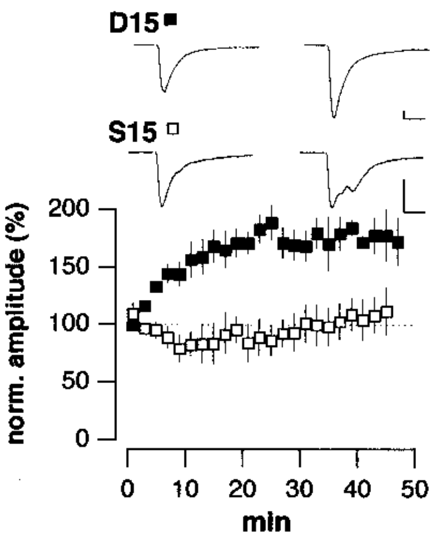


Blocking exo/endocytosis



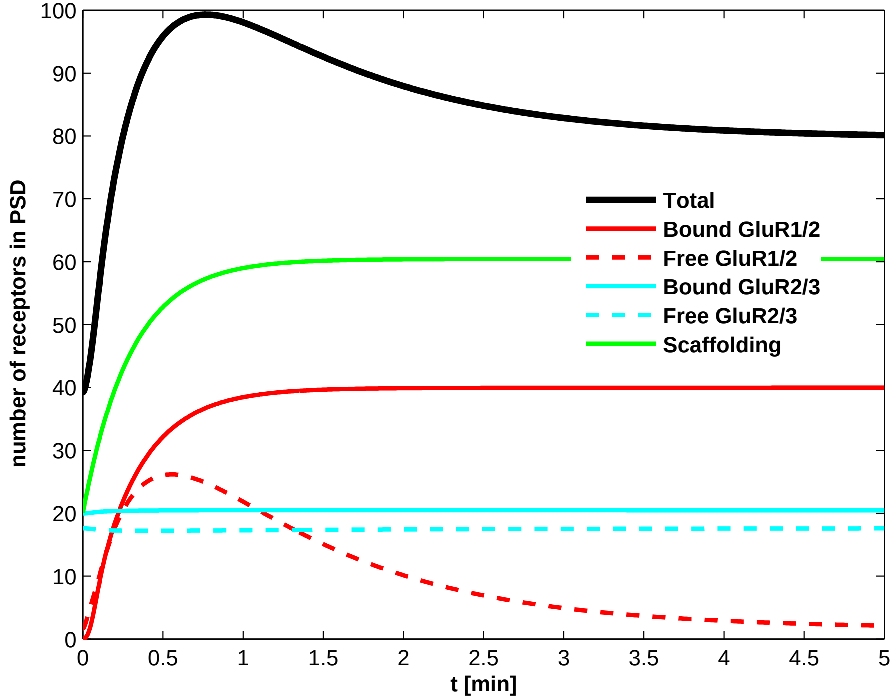


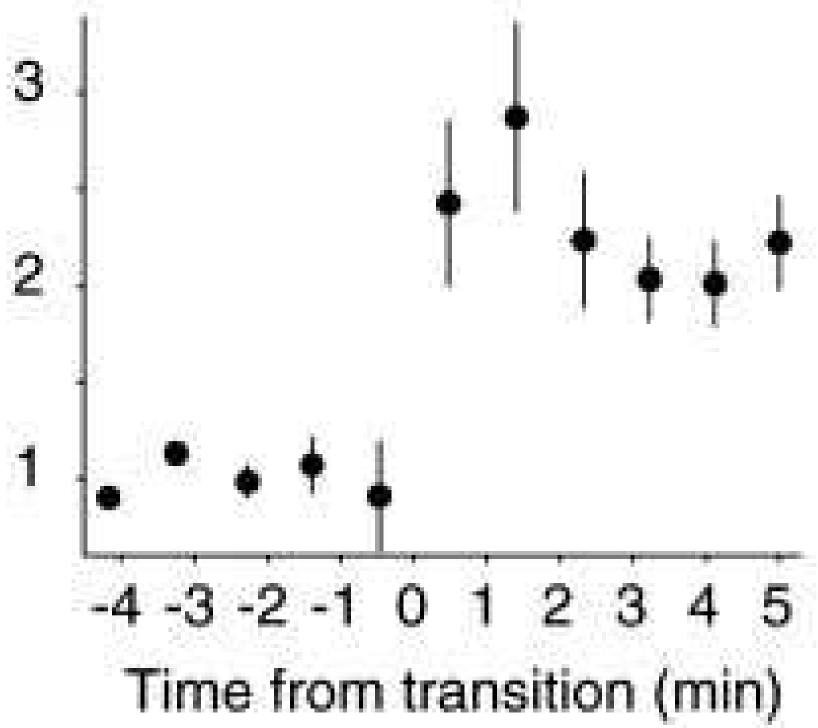




C. Luscher et al. *Neuron* **24** 649–658 (1999).

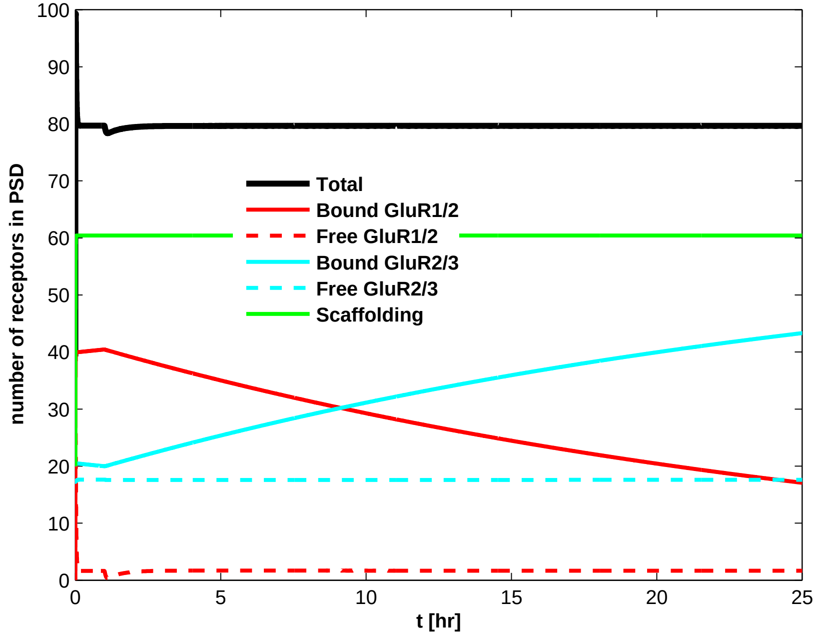
LTP trafficking

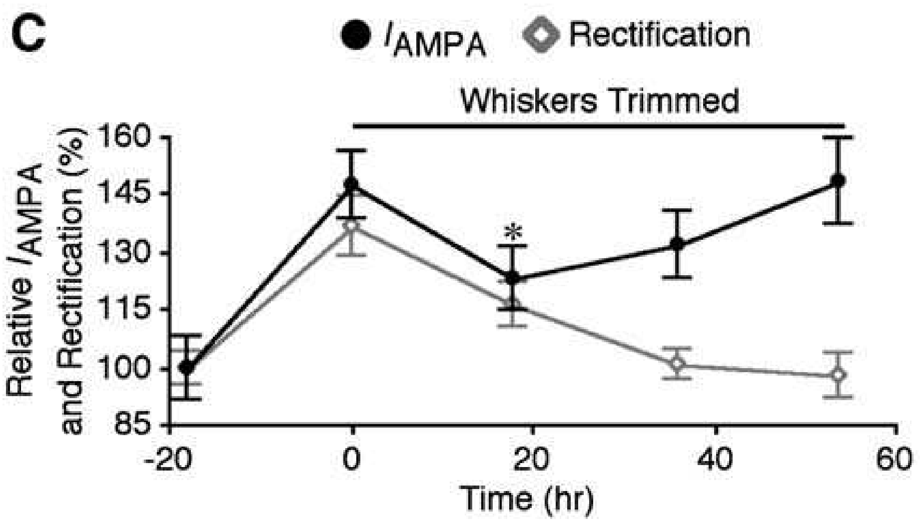




D.H. O'Connor et al. *PNAS* **102** 9679–9684 (2005).

Exchange of GluR1/2 with GluR2/3

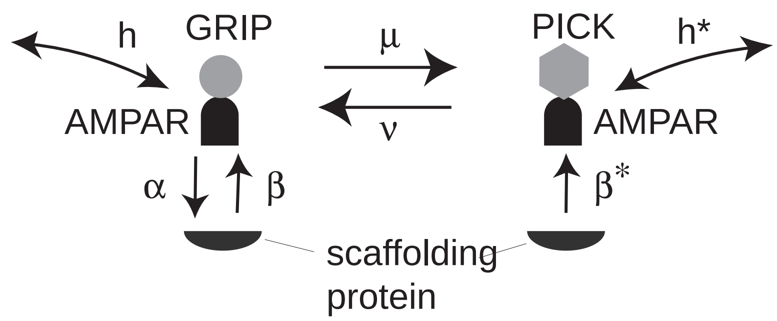


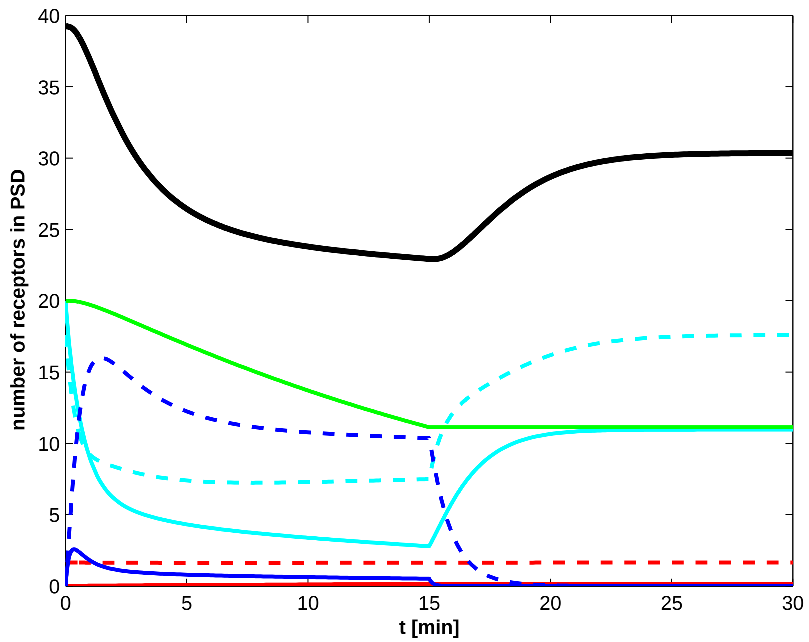


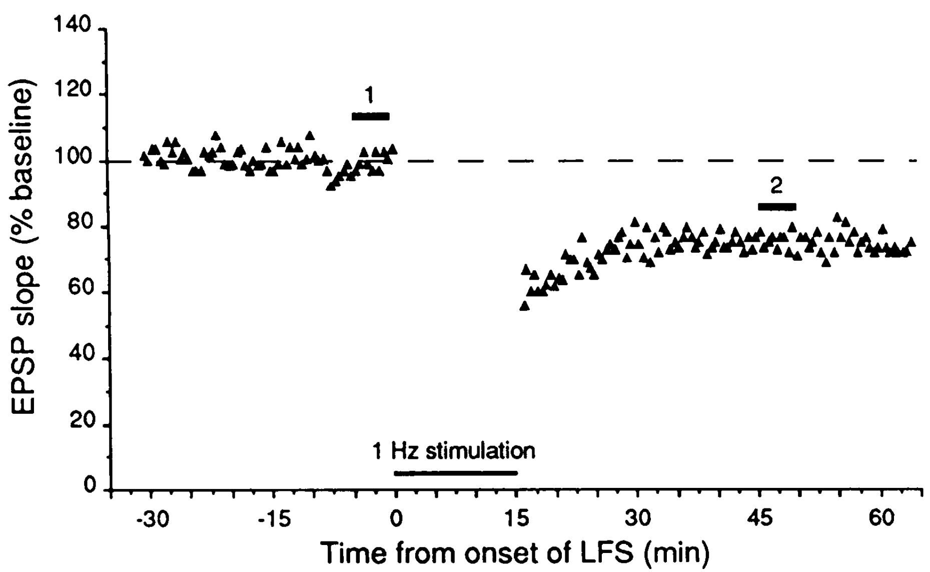
S.G. McCormack et al. *Neuron* **50** 75–88 (2006).

LTD trafficking

During induction of LTD, AMPAR+GRIP → AMPAR+PICK



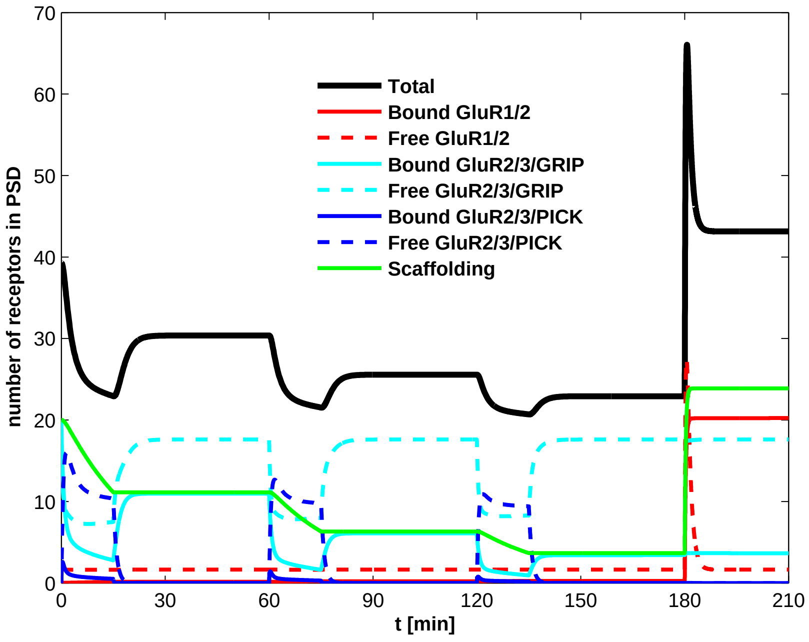


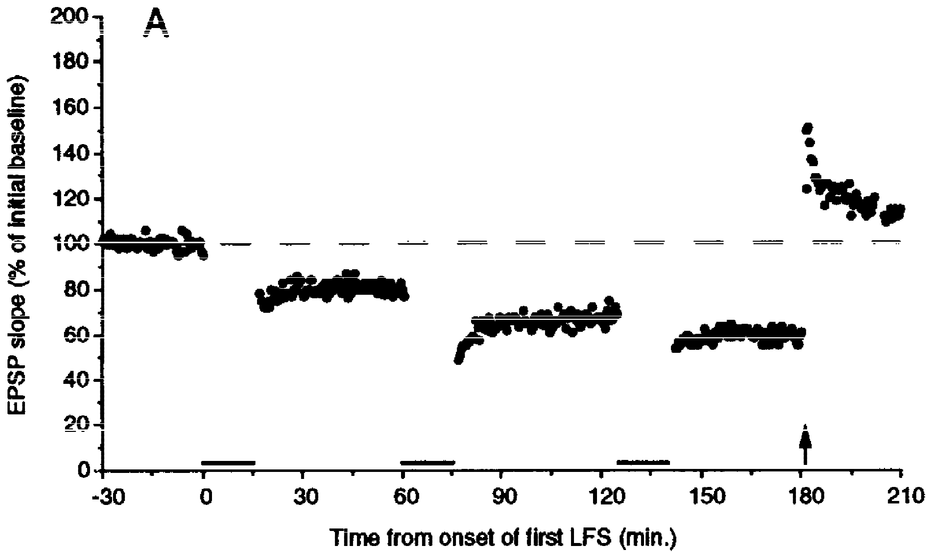


S.M. Dudek and M.F. Bear. *PNAS* **89** 4363–4367 (1992).

Saturation of LTD

Induce LTD 3 times, then LTP

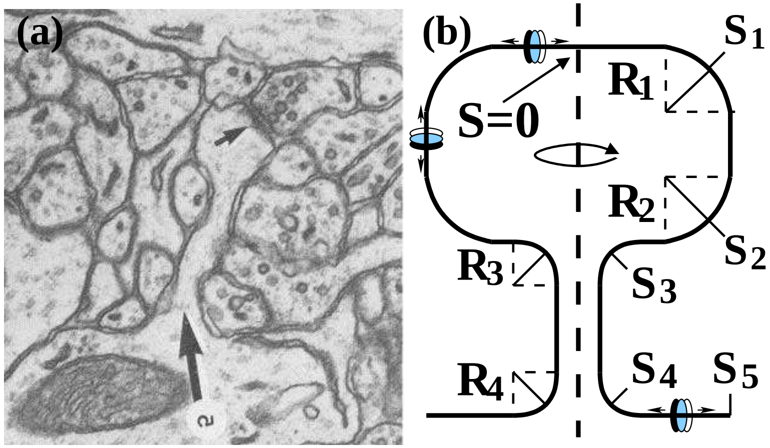




S.M. Dudek and M.F. Bear. *J. Neurosci.* **13** 2910–2918 (1993).

Current work

- **Effects of membrane curvature**
  - Curvature may affect receptor diffusion
  - $\Omega = D\left[\int_{s_3}^{s_4} \frac{ds}{r(s)}\right]^{-1} \approx \frac{Dd}{2l}$



- **Stochastic model**
  - Estimate variance in EPSP recordings