

What I do

(and what I want to do)

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Current projects

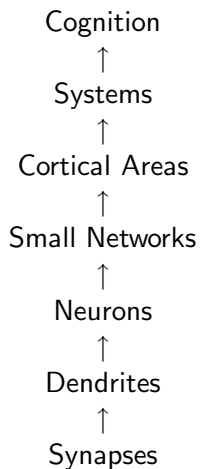
- What I do
 - AMPA receptor trafficking
 - Synaptic plasticity

Current projects

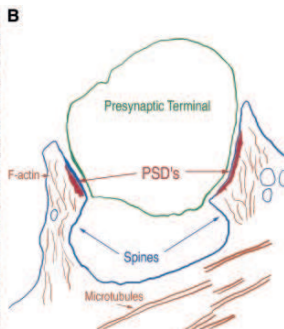
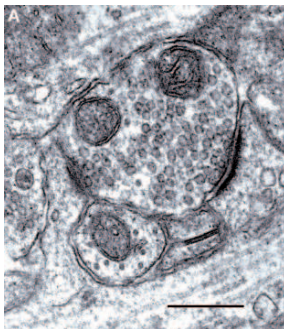
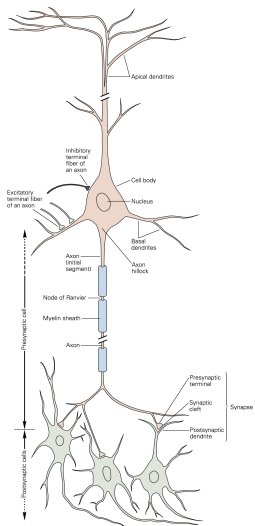
- What I do
 - AMPA receptor trafficking
 - Synaptic plasticity

- What I want to do
 - Just count things

Mathematical neuroscience at Utah

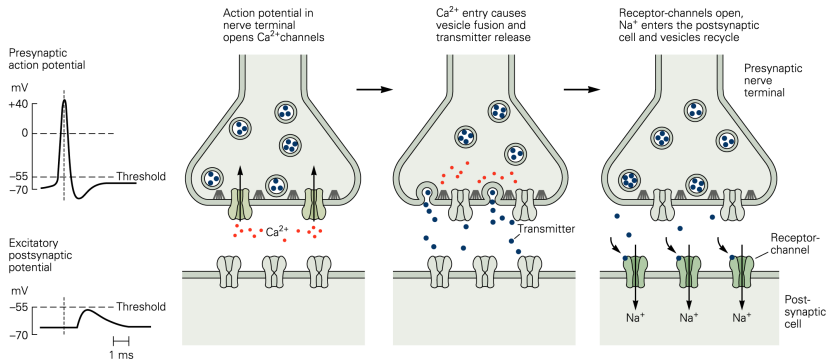


The synapse



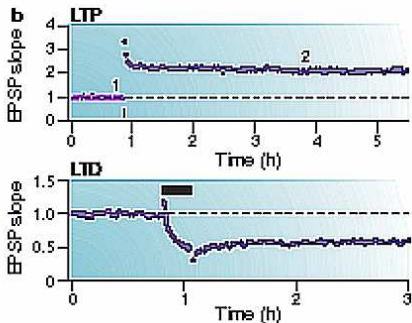
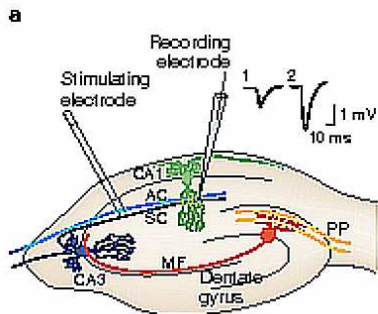
E.R. Kandel et al. *Principles of Neural Science* (2000)
M.B. Kennedy *Science* (2000)

Synaptic transmission



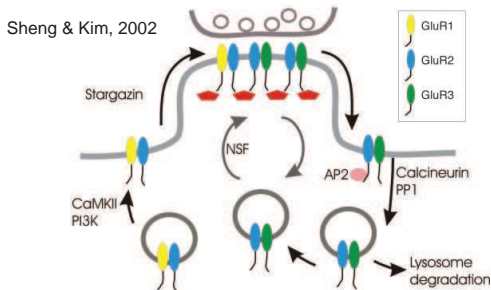
E.R. Kandel et al. *Principles of Neural Science* (2000)

Synaptic plasticity



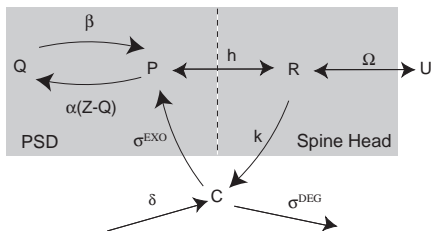
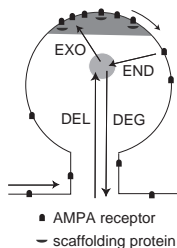
Collingridge et al., *Nat. Rev. Neurosci.* (2004)

AMPA receptor trafficking at a single spine



- Surface AMPARs constitutively recycle with intracellular stores
- Laterally diffuse within postsynaptic membrane
- Crosslink to scaffolding proteins in PSD

Model of trafficking at a single spine



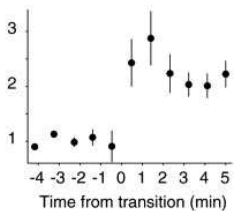
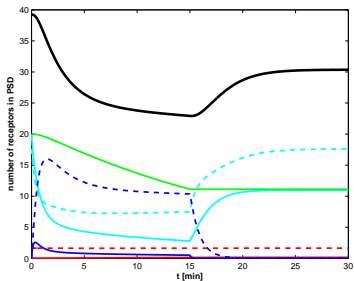
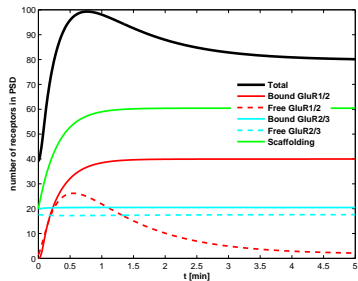
Spine head:
$$\frac{dR}{dt} = \frac{1}{A} (\Omega[U - R] - kR - h[R - P])$$

PSD unbound:
$$\frac{dP}{dt} = \frac{h}{a} [R - P] - \alpha[Z - Q]P + \beta Q + \frac{\sigma^{\text{EXO}} C}{a}$$

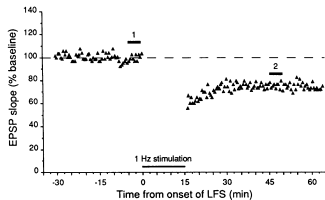
PSD bound:
$$\frac{dQ}{dt} = \alpha[Z - Q]P - \beta Q$$

Intracellular:
$$\frac{dC}{dt} = -\sigma^{\text{EXO}} C - \sigma^{\text{DEG}} C + kR + \delta,$$

Trafficking during LTP/LTD



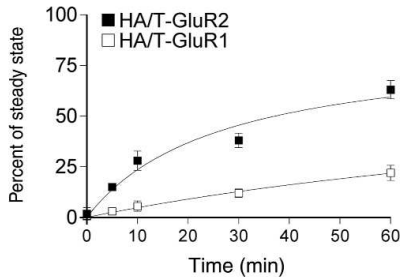
O'Connor et al. *PNAS* (2005)



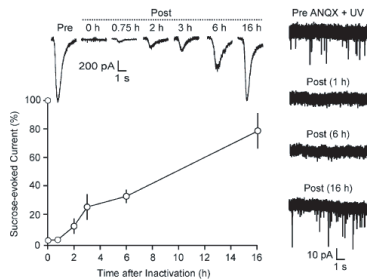
Dudek & Bear *PNAS* (1992)

Fast or slow recycling?

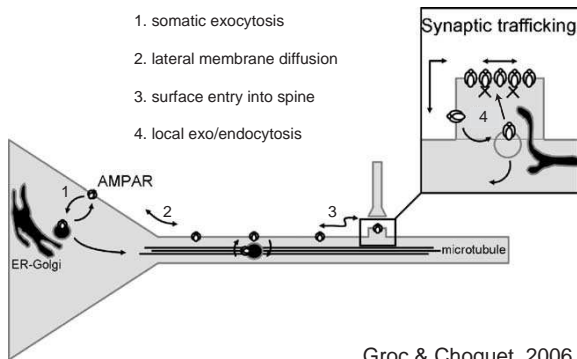
Passafaro et al., 2001



Adesnik et al., 2005



AMPA receptor trafficking along a spiny dendrite

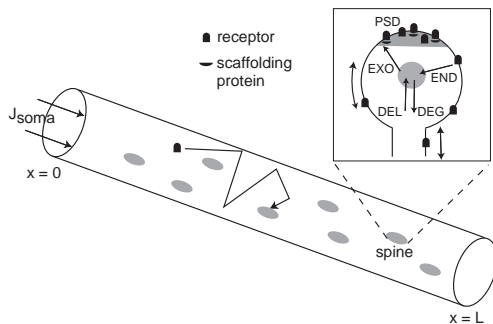


- AMPARs trafficked in vesicles along microtubules?
- AMPARs diffuse from soma to synapse?

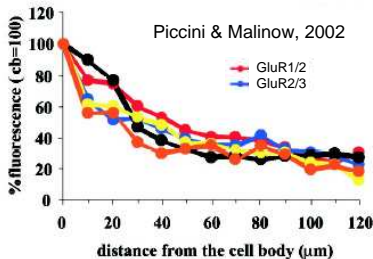
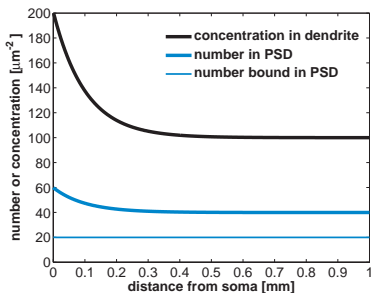
Model of trafficking along a spiny dendrite

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

$\rho(x)$ = spine density at x

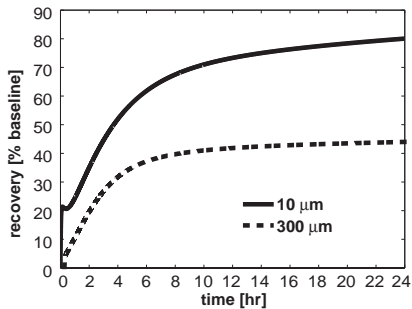


Steady-state receptor concentrations



- 1,000 identical spines distributed uniformly
- Two sources of AMPARs
 - at soma
 - local intracellular delivery

Recovery rate depends on distance from soma

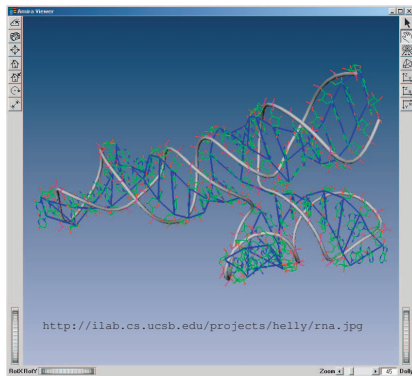


- Recovery exhibits many time-scales!

Now that we're done with that...

...let's count something!

A single strand of RNA



- Primary structure: sequence of bases (A,G,U,C)
- Secondary structure: pairing of bases
 - Watson-Crick pairs: A-U, G-C (less often U-G)
- Tertiary structure: resulting 3D molecule
 - Different tertiary structures \Rightarrow different enzymatic properties

A single strand of RNA: An example

- Primary structure:

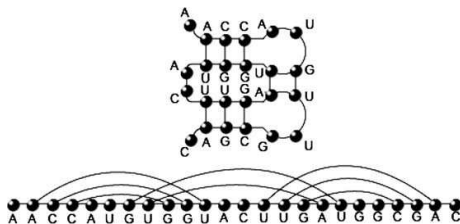
AACCAUGUGGUACUUGAUGGCGAC

A single strand of RNA: An example

- Primary structure:

AACCAUGUGGUACUUGAUGGCGAC

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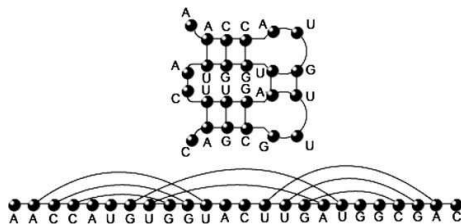


A single strand of RNA: An example

- Primary structure:

AACCAUGUGGUACUUGAUGGCGAC

- Secondary structure:



- Tertiary structure: extremely difficult to predict (probably NP-hard)

RNA secondary structure as k -noncrossing arch diagram

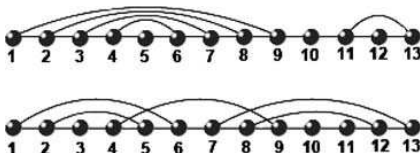
- k -noncrossing arch diagram of order n
 - graph on vertex set $\{1, \dots, n\}$
 - all vertices have degree ≤ 1
 - there do not exist k arches $\{i_1, j_1\}, \dots, \{i_k, j_k\}$ such that

$$i_1 < \dots < i_k < j_1 < \dots < j_k$$

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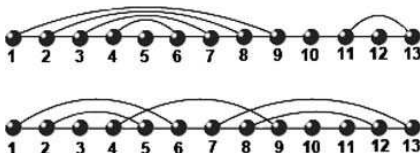
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- RNA secondary structure of n bases, pseudoknot type $k - 2$
 - k -noncrossing (but not $k - 1$) arch diagram of order n
 - no 1-arches $\{i, i + 1\}$
 - “abstract” secondary structure (no primary structure)

k -noncrossing arch diagrams and walks in Weyl chamber

- Walk in \mathbb{Z}^m of length n
 - sequence of vectors $\mathbf{x}_0, \mathbf{x}_1, \dots, \mathbf{x}_n \in \mathbb{Z}^m$ s.t. $|\mathbf{x}_{i+1} - \mathbf{x}_i| = 0$ or 1

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- Weyl chamber
 - subset of vectors $\mathbf{x} = (x_1, \dots, x_m) \in \mathbb{Z}^m$ s.t. $x_1 > \dots > x_m > 0$

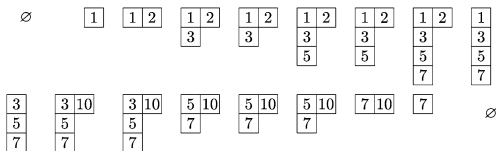
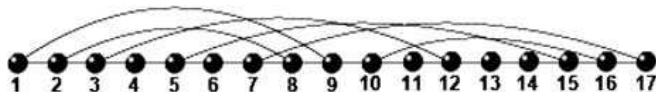
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Theorem (Chen et al. (2007) *Trans. Am. Math. Soc.* 359)

There exists a bijection between k -noncrossing arch diagrams of order n and walks of length n in \mathbb{Z}^{k-1} which start and end at $\mathbf{a} = (k-1, k-2, \dots, 1)$ and remain in the Weyl chamber.

Idea of proof: The bijection



$(4,3,2,1), (5,3,2,1), (6,3,2,1), (6,4,2,1), (6,4,2,1), (6,4,2,1)$
 $(6,4,3,1), (6,4,3,1), (5,4,3,1), (5,4,3,2), (6,4,3,2), (6,4,3,1)$
 $(6,4,3,1), (6,4,2,1), (6,4,2,1), (6,3,2,1), (5,3,2,1), (4,3,2,1)$

Counting k -noncrossing RNA secondary structures

- Set

$A_k(n, l) = \#$ k -nc arch diagrams of order n , l isolated nodes

$B_k(n, l) = \#$ k -nc RNA structures of n bases, l isolated bases

Counting k -noncrossing RNA secondary structures

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Theorem (Jin, Qin & Reidys, 2008)

$$B_k(n, l) = \sum_{b=0}^{(n-l)/2} (-1)^b \binom{n-b}{b} A_k(n-2b, l)$$

where $A_k(n, l)$ is given by the generating function

$$\sum_{n=1}^{\infty} \sum_{l=0}^n A_k(n, l) \frac{x^n}{n!} = e^x \det[l_{i-j}(2x) - l_{i+j}(2x)] \Big|_{i,j=1}^{k-1}$$

and $l_r(2x) = \sum_{j=0}^{\infty} x^{2r+j} / (j!(r+j)!)$ is hyperbolic Bessel function of 1st kind of order r .

The end

Thank you!