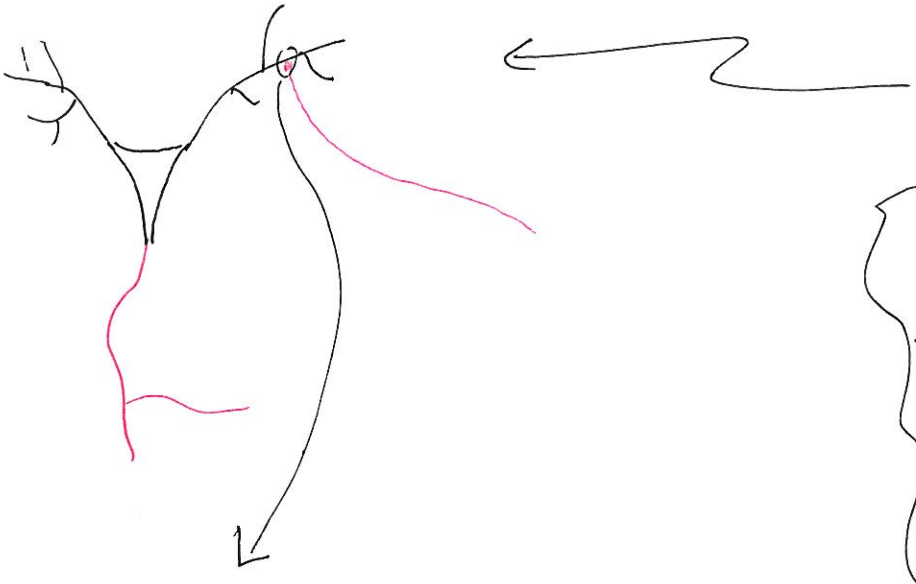
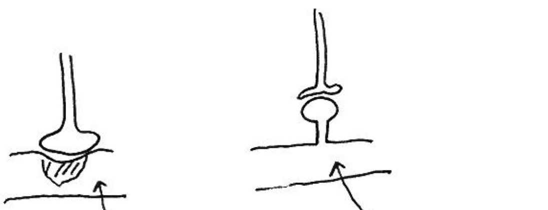
① 10/15/04

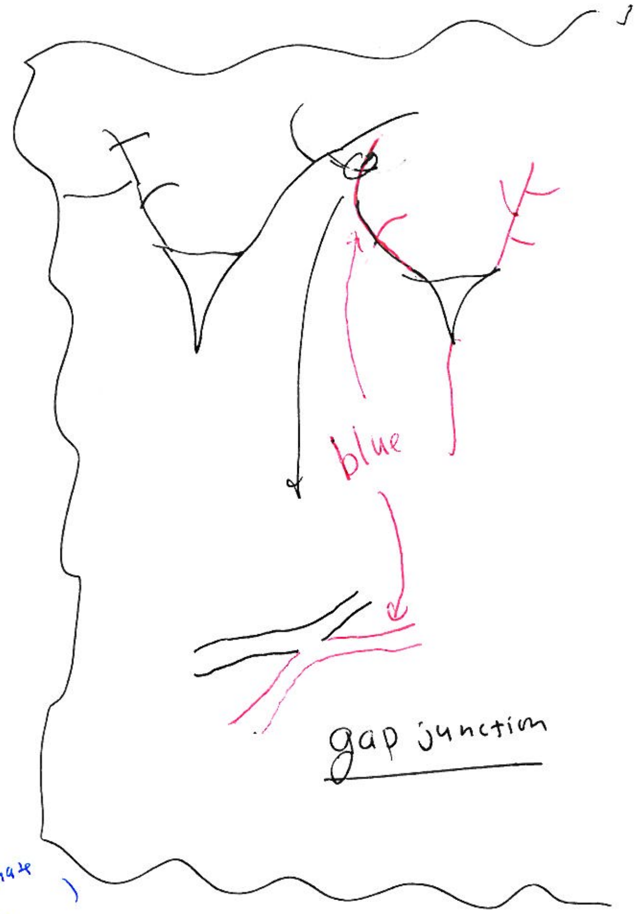
replaced by 10-16!! (except for page 2)

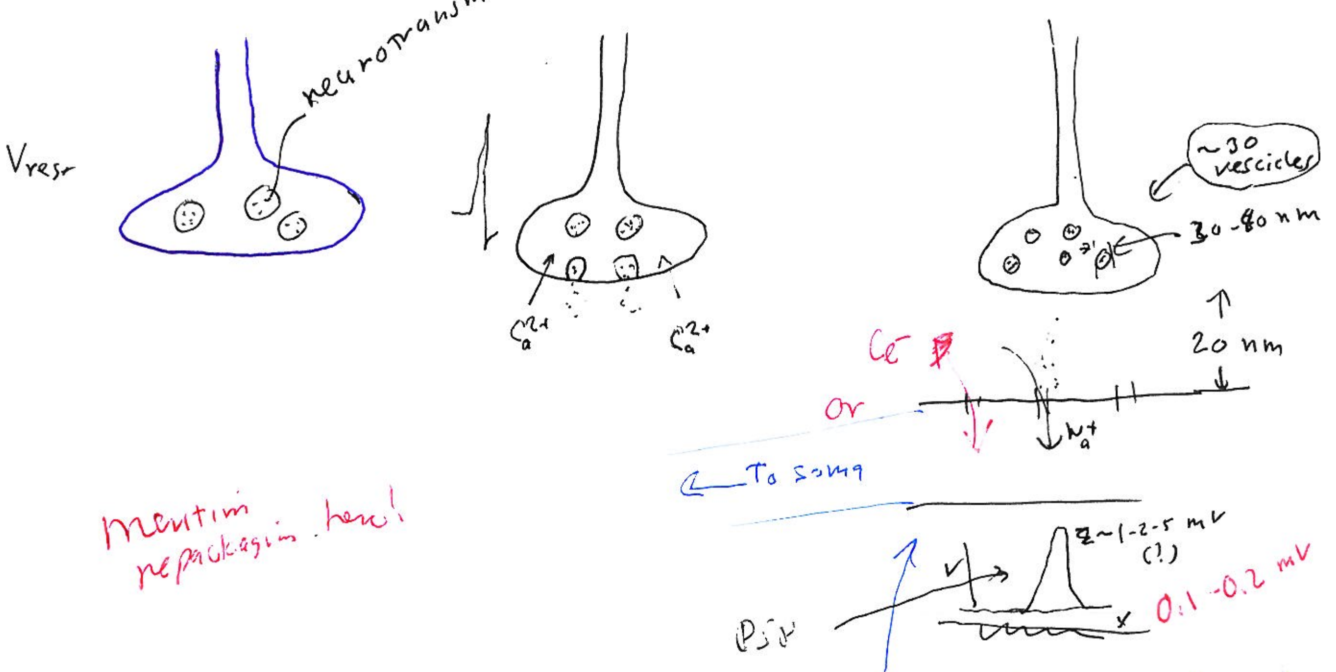
Synapses



~ 5-10,000 connections







mention repackaging here!

Several mV, can even cause spikes (& co-operative effects). 0.1-0.2 mV at soma

Questions

1a) How many packets released /spike?

1b) How are the repackaged?

1c) What ~~kind of~~ neurotransmitters are released? ← glutamate

→ What channels are opened?

} presynaptic: facts

2a) What is the time course of release?

2b) How does ~~it~~ ~~release prob.~~ depend on history ← OK

} presynaptic: facts/math

3a) How does PSP size depend on parameters?

~~3b)~~ How do we put synaptic release into models

3b) How " " " " " history?

} postsynaptic: facts/math

2006 What do we want to know! - write down full set of eqns.

~~1) What kind o~~

1) What happens when AP arrives at a presyn term?

a) quantum model. (AMPA, GABA_A,B, NMDA) pg. 10

2) What determines synaptic strength?

a) # packets

b) prob of release

} binomial pg. 3, 4

c) postsynaptic channel density

3) history dependence ~~pg. 6~~

Short term: pg. 6

long term: pg.

1a) Quantal release

- n vescicles
- each released independently w/ probability p
- amount released = q_0

$$p(k) = \frac{n!}{k!(n-k)!} p^k (1-p)^{n-k}$$

average release = $q_0 \langle k \rangle$

Standard deviation = $q_0 \left[\langle k^2 \rangle - \langle k \rangle^2 \right]$

↑ facts
↓ math

$$\langle k^\ell \rangle = \sum_{k=0}^{n} \frac{n!}{k!(n-k)!} k^\ell p^k (1-p)^{n-k}$$

$$= \sum_{k=0}^{n} \frac{n!}{k!(n-k)!} k^\ell p^k q^{n-k} \Big|_{q=1-p}$$

$$p \frac{d}{dp} p^k = k p^k$$

$$p \frac{d}{dp} \left[p \frac{d}{dp} \right] p^k = k^2 p^k$$

$$k^\ell = \left(p \frac{d}{dp} \right)^\ell p^k$$

$$\Rightarrow \langle k^\ell \rangle = \left(p \frac{d}{dp} \right)^\ell \underbrace{\sum_{k=0}^{n} \frac{n!}{k!(n-k)!} p^k q^{n-k}}_{(p+q)^n} \Big|_{q=1-p}$$

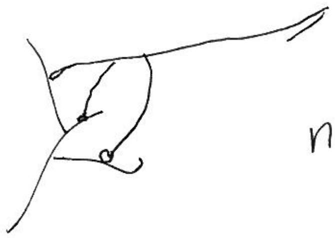
$$\langle k^\ell \rangle = \left(p \frac{d}{dp} \right)^\ell (p+q)^n \Big|_{p+q=1}$$

$$\left.\begin{aligned} \langle k \rangle &= np \\ \langle k^2 \rangle &= n(n-1)p^2 + np \end{aligned}\right\} \Rightarrow \langle k^2 \rangle - \langle k \rangle^2 = np(1-p)$$

NMJ : Katz

$n = 100-1000$

central synapses: $n = 1$ per synapse (hypothesis)



$n = 3$

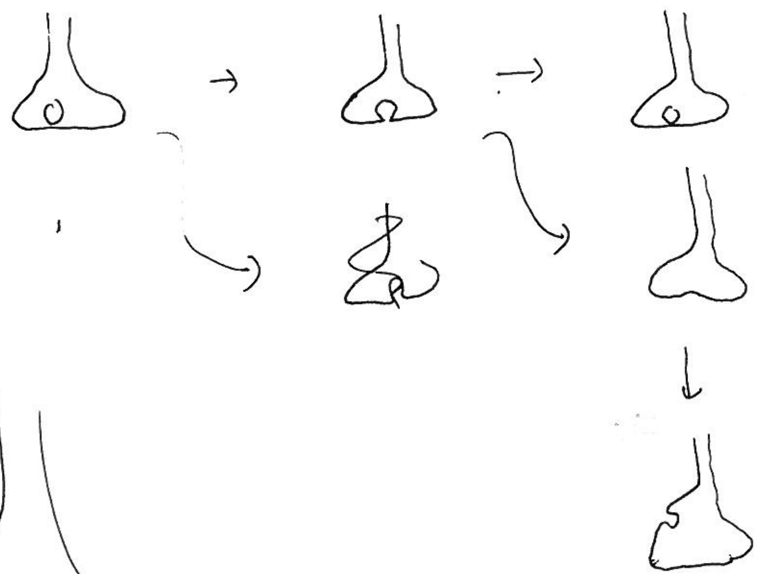
$\boxed{p : 0.1 - 0.9}$ total mystery!!!!

$$\langle \text{release} \rangle = q_0 \, np$$
$$\text{Var}[\quad] = q_0^2 \, np(1-p)$$

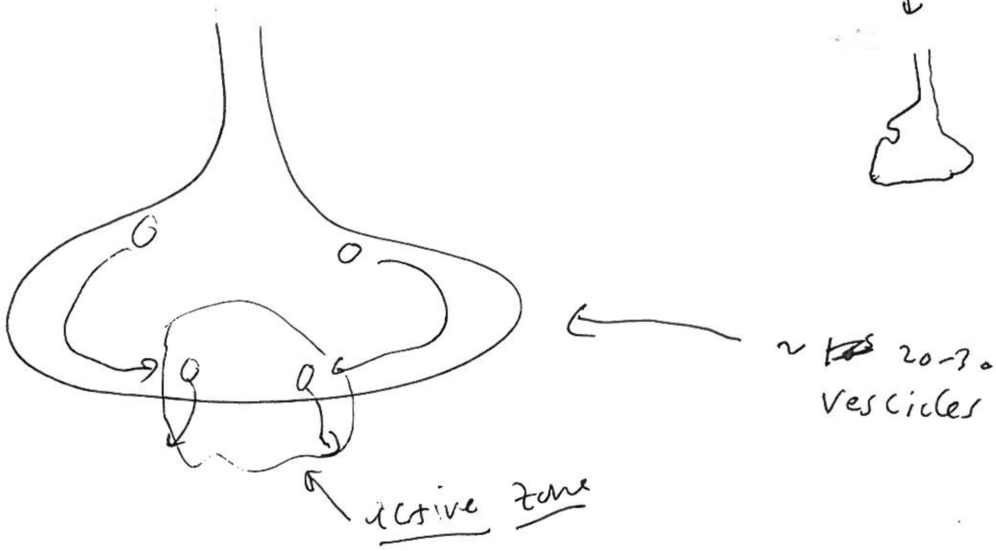
$$\left[\frac{sd}{mean}\right]^{-1} = \frac{np}{\sqrt{np(1-p)}} = \sqrt{\frac{np}{1-p}} = \text{big!!!}$$

$$\frac{\sqrt{np(1-p)}}{np} = \sqrt{\frac{1-p}{np}}$$

1b) · Kiss + run



- standard model



Later

1C) Excitatory: AMPA → mix of Na^+, K^+, Ca^{++}

NMDA $\mathcal{E} \sim 0$ mV

Inhibitory: $GABA_A$

$GABA_B$ → Cl^- $\mathcal{E} \sim -70$ mV

-100 mV

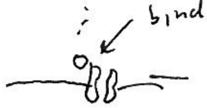
AMPA ~~Ampa~~ + $GABA_A$: ~~fast~~ ionotropic (fast) 2 - 10 ms

NMDA + $GABA_B$: metabotropic (slow) 50 - 200 ms

the only metabotropic one, according to Koch

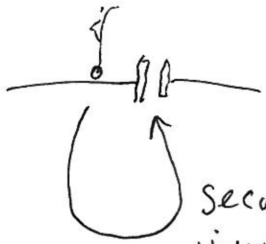
binding causes opening

fast



in beginning

slow



Second messenger cascade, G-protein mediated

~~involving G-coupled~~

Start w/ new Fig - tell them about Ca^{++} + active zones, mention ionotropic vs metabotropic

2a) Working hypothesis: only Prelease changes as a function of history.

- Facilitation (A.K.A. augmentation or potentiation) probably result from a buildup of Ca^{++} ← remember, Ca^{++} triggers release

- Depression probably results from a depletion of resources (meaning everybody in the readily releasible pool is gone)

- We'll look at the two separately

$$\tau \frac{dP_{rel}}{dt} = P_0 - P_{rel} + \left[\sum_i \delta(t-t_i)\right] \begin{cases} -\tau(1-f_D)P_{rel} \\ +\tau f_F(1-P_{rel}) \end{cases}$$

between spikes:

do this first →

$$P_{rel}(t) = P_0 + [P_{rel}(0) - P_0]\, e^{-t/\tau}$$ [check this!!]

$\dot{x} = f(x) + g(x)\delta(t)$

$x(t+dt) = x(t+dt) + \int \dot{x}\,dt$

$\int f(x)\,dt \sim dt$

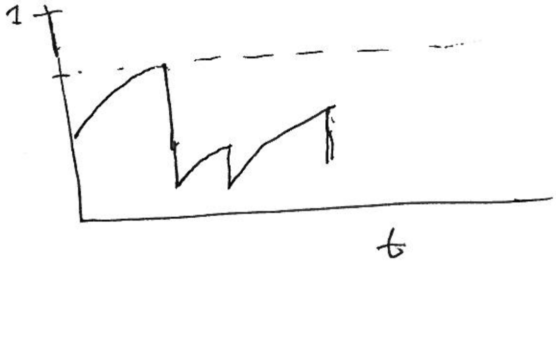
$\int g(x)\delta(t)\,dt \sim g(x)$ — we'll use better

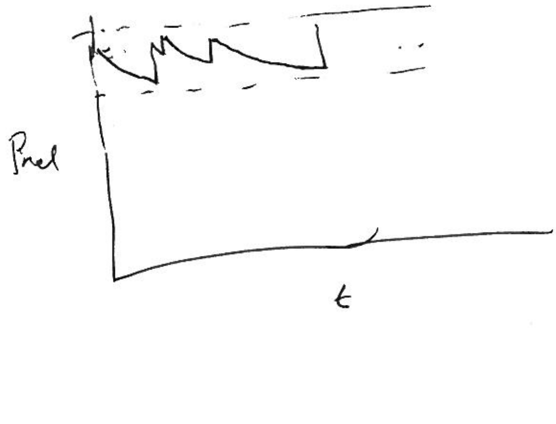
$x \to x + g(x)$

$P_{rel} \to P_{rel} + \begin{cases} -P_{rel} + f_D P_{rel} \\ +f_F(1-P_{rel}) \end{cases}$

at spikes:

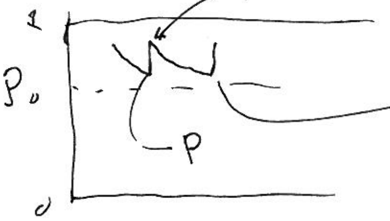
$$P_{rel} \to \begin{cases} +f_D P_{rel} \\ +f_F(1-P_{rel}) \end{cases}$$ [Check this]





Skip ~~[illegible]~~ : facilitation
— HWK

2b) Implications



$$P_0 + \left(p + f_F(1-p) - P_0\right) e^{-\Delta t/\tau}$$

$$P(t_{n+1}) = P_0 + \left(p(t_n)(1-f_F) + f_F - P_0\right) e^{-\frac{\Delta t}{\tau}}$$

$$\langle p(t_{n+1}) \rangle = P_0 + (f_F - P_0)\left\langle e^{-\frac{\Delta t}{\tau}} \right\rangle + (1-f_F)\left\langle p(t_n)\, e^{-\frac{\Delta t}{\tau}} \right\rangle$$

$$\bar{p} = P_0 + (f_F - P_0)\left\langle e^{-\frac{\Delta t}{\tau}} \right\rangle + (1-f_F)\underbrace{\underset{\bar{p}}{\langle p(t_n)\rangle} \left\langle e^{-\frac{\Delta t}{\tau}} \right\rangle}_{\text{approx!!!}}$$

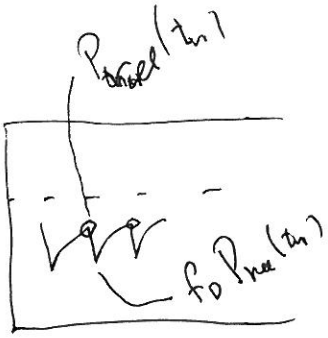
Poisson at rate r:

$$p(\Delta t) = r\, e^{-\Delta t\, r}$$

$$\left\langle e^{-\frac{\Delta t}{\tau}} \right\rangle = \int_0^\infty d(\Delta t)\, r\, e^{-\Delta t\left(r + \frac{1}{\tau}\right)}$$

$$= \frac{r}{r + 1/\tau} = \frac{r\tau}{1 + r\tau}$$

(8)



depression:
$P_{rel}(t_{i+1}) = P_0 + [P_{rel}(t_i) - P_0]\, e^{-\frac{\Delta t_i}{\tau}}$

$$P(t_{n+1}) = P_0 + (f_D P(t_n) - P_0)\, e^{-\frac{\Delta t}{\tau}}$$

$$\Rightarrow \langle P \rangle \approx \frac{P_0}{1 + (1 - f_D) r \tau}$$

← do averaging here because we skipped facilitation

average drive to the cell:

$$r \langle P \rangle \approx \frac{P_0 r}{1 + (1 - f_D) r \tau} \rightarrow \frac{P_0}{\tau (1 - f_D)} \quad \text{as } r \to \infty$$

- independent of r!!
- synaptic depression democratizes ~~synaptic~~ presynaptic spikes
- why??? – change detector!!

mention minis!!

3a) 4 main kinds of channels:

AMPA, NMDA } glutamate receptors / excitation $\quad E \sim 0$ mV

$GABA_A$, $GABA_B$ } GABA receptors / inhibition, $E = \begin{matrix} -70 \text{ mV} \\ -100 \text{ mV} \end{matrix}$

model:

$$\tau_m \frac{\partial V}{\partial t} = \lambda^2 \frac{\partial^2 V}{\partial x^2} - I_m + r_m i_e$$

$$g(V - E)$$

this we know

$$\cancel{\bar{g}\, x}$$

~~(Transmitter)~~

$$\cancel{\dot{x} = \alpha(1-x) - \beta x}$$

$$\cancel{\tau \dot{x} = x_\infty - x} \qquad \cancel{\tau = \frac{1}{\alpha+\beta}}$$

$$\cancel{x_\infty = \frac{\alpha}{\alpha+\beta}}$$

} AMPA, $GABA_A$

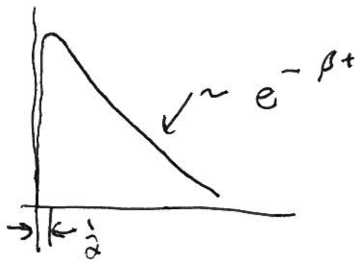
AMPA

GABA$_A$: $I_m = \bar{g}x(V - \Sigma)$ 0, -70

GABA$_B$

constant

$$\dot{x} = \alpha(\text{transmitter})(1-x) - \beta x$$

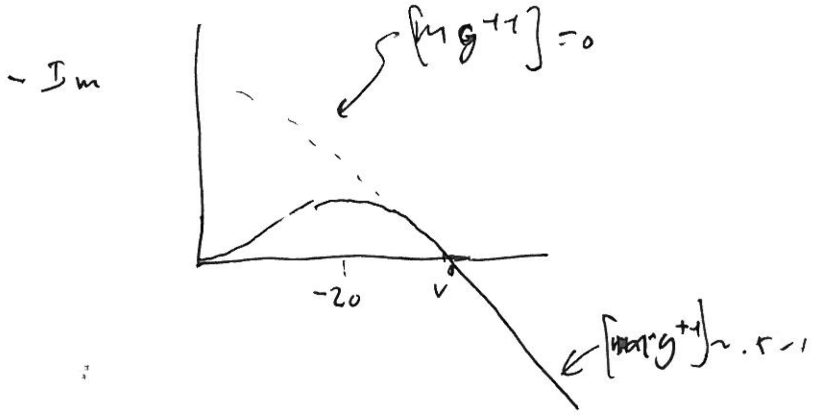


NMDA:

$$I_m = \frac{\bar{g} \quad x\,(V - \Sigma)}{\left(1 + \frac{[Mg^{++}]}{3.57\,mM}\exp(-V/16.2\,mV)\right)}$$

0

16.1



NMDA only opens when postsynaptic cell is ~~activated~~ depolarized: coincidence detector

~~Ampa~~

	τ_{rise} ($1/\alpha$)	τ_{decay} ($1/\beta$)
AMPA	~0	5
NMDA	1.5	~150
GABA$_A$	0.3	5
GABA$_B$	~10	~200

full model - single compartm

$$C_m \frac{dV_i}{dt} = -\bar{g}_L(V_i - \mathcal{E}_L) - \bar{g}_{Na} m^3 h (V_i - \mathcal{E}_{Na}) - \bar{g}_K n^4 (V_i - \mathcal{E}_K) - \sum_j \bar{g}_{ij} x_{ij} (V_i - \mathcal{E}_x)$$

$$\dot{x}_{ij} = \alpha_x (1 - x_{ij}) \sum_e \delta(t - t_j^e) - \beta x_{ij}$$

instantan rise

(can replace w/ a square pulse)

3b) ~~Hebb rule~~

LTP - memory stored in synaptic strength

Long Term Potentiation - learning changes strength (weight)

give example

randomly connected network:
- output doesn't tell you much about input

after learning:
- output says "yes, that's a black dog in my visual field"

- what is synaptic strength?

- p can increase
- n can increase
- q_0 probably not
- $\bar{g}_{postsynaptic}$

long argument over which one changes
- final answer: both.

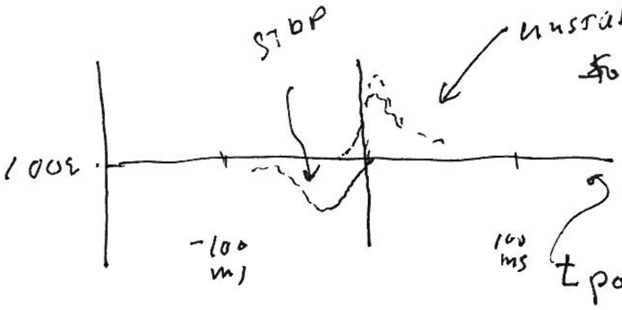
- ~~how does~~ what causes it change?

history dependent

both pre-synaptic activity + post-synaptic activity.

- ~~how~~ does

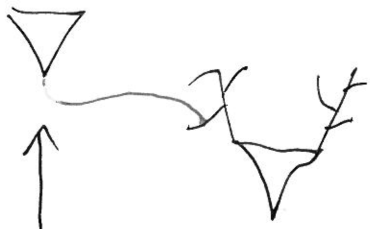
near-simultaneous pre + post-synaptic spikes produce either a decrease or increase in strength.



unstable unless a normalization rule is applied

$\sum$ weights = const.
neuron

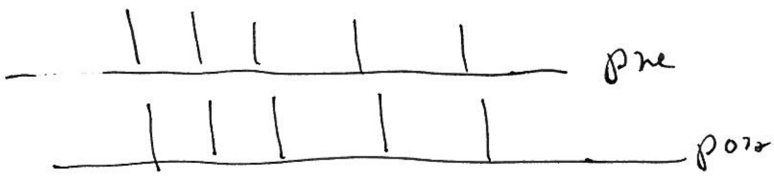
Important because it gives you a factor of 5000 more parameters to play with.



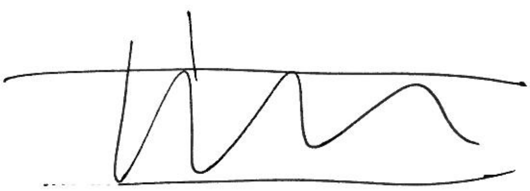
Spike occurs at time t_{post}

Spike occurs at time t_{pre}

- Situation is more complicated:



← 10 ms → pot.
← 10 s → depression

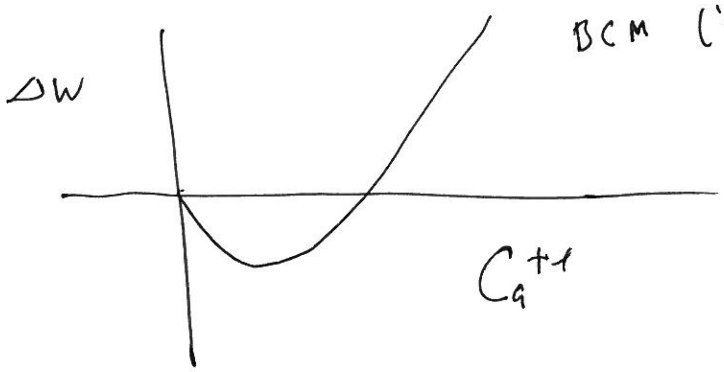


- nobody really know how all of this works in network
- Peter Dayan will provide more info.

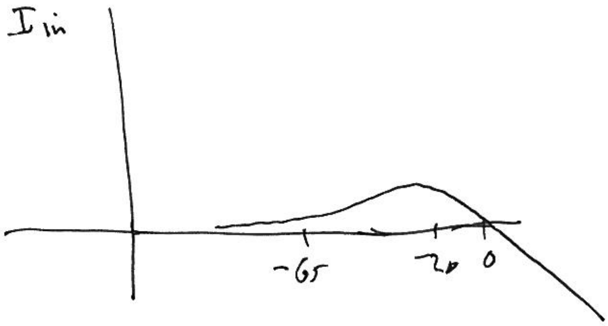
Mechanism

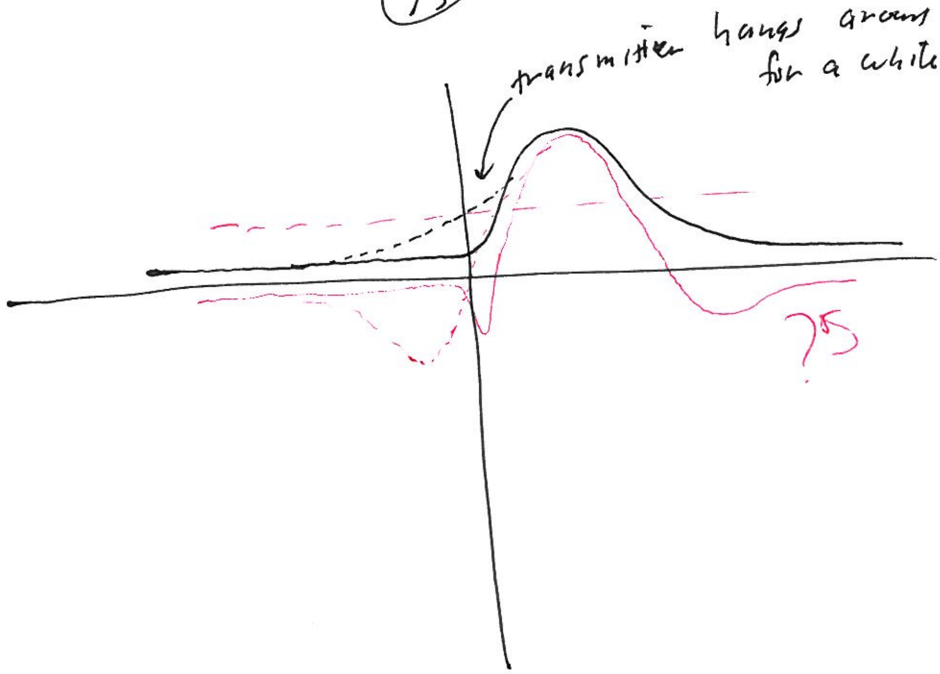
~~high Ca^{++} in pre~~

BCM ('82)

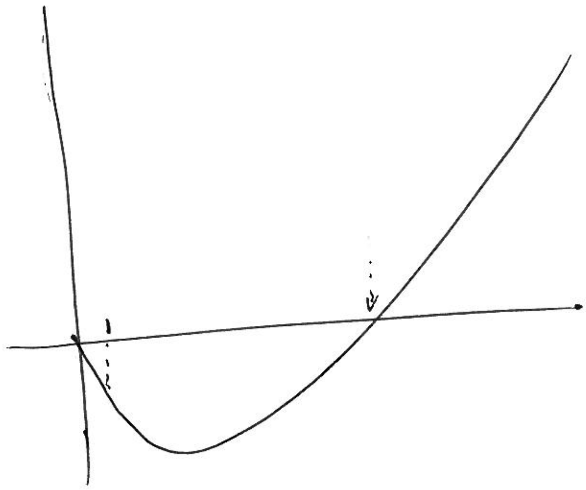


NMDA
lets in
Ca^{++}!





unsolved problem!



Be sure to do ML!!