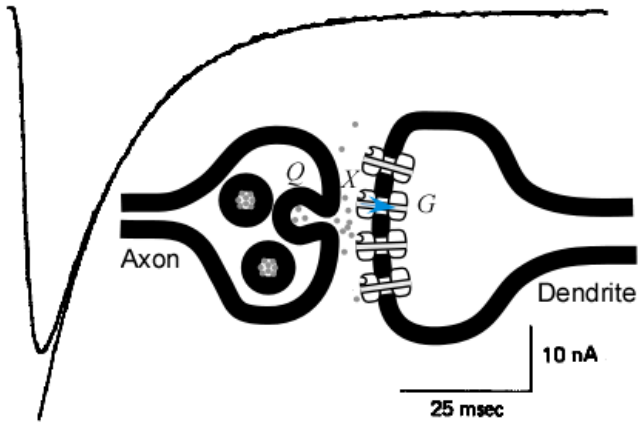
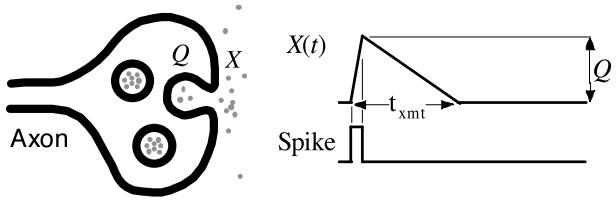
Synapse Model



Neurotransmitter is released into cleft between axonal button and dendritic spine

- **Binding and unbinding are modeled by first-order kinetics**
- **Concentration must exceed receptor affinity**

Dumping neurotransmitter



Neurotransmitter concentration in cleft increases rapidly and then decays slowly

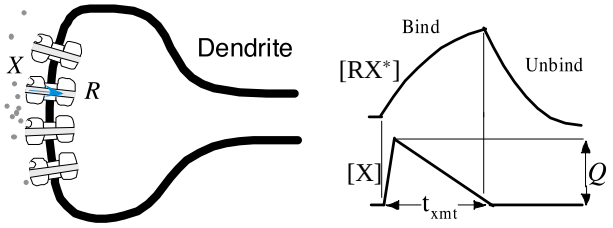
In[1]:= $\frac{dX}{dt} = -I_{leak}$ with $X[0] = Q$

In[1]:= $\Longrightarrow X[t] = Q - I_{leak}\, t$

Neurotransmitter remains in the cleft for some time:

In[1]:= $X[t_{xmt}] = 0 \Longrightarrow t_{xmt} = Q / I_{leak}$

Binding and unbinding rates



Channels do not open or close instantaneously; it takes time

Neurotransmitter (X) binds to receptors (R) at a rate α and unbinds from them at a rate β:

$$R + X \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} RX^*$$

The number of open channels changes at the rate:

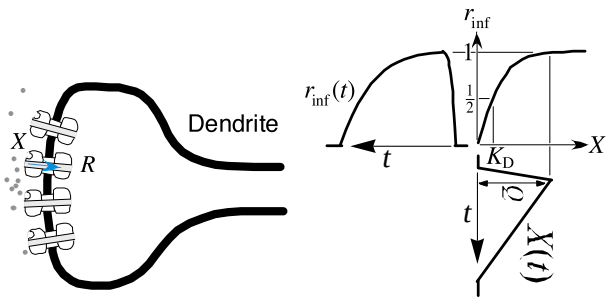
$$\frac{d[RX^*]}{dt} = \alpha [R][X] - \beta [RX^*]$$

Dividing both sides by [R] + [RX*], the total number of channels, which is constant, yields:

$$\frac{dr}{dt} = \alpha [X] (1 - r) - \beta r \Leftrightarrow \frac{dr}{dt} + (\alpha [X] + \beta) r = \alpha [X]$$

where $r = [RX^*]/([R] + [RX^*])$ is the fraction of channels that are open.

Receptor affinity (K_D)



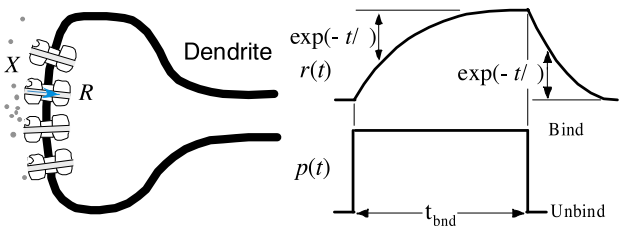
To open over half the channels, the neurotransmitter concentration must exceed K_D

Setting dr/dt = 0, and replacing [X] with X, yields this steady-state solution to the ODE:

$$r_\infty[X] = \frac{\alpha X}{\alpha X + \beta} = \frac{X}{X + K_D}$$

where $K_D \equiv \beta/\alpha$ is the receptors' affinity. Half the channels open when $X = K_D$ and most of them open when $X \gg K_D$.

Response to rectangular pulse ($p(t)$)



The difference between the initial and steady-state levels decreases exponentially with time

We can solve the ODE if X is constant, making $\tau[X]$ constant, which yields:

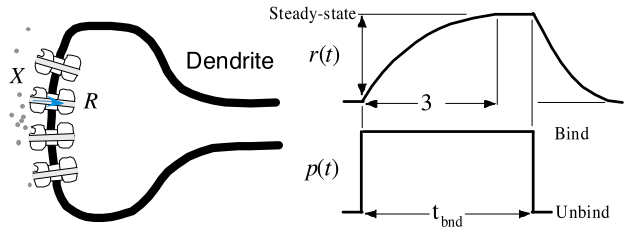
$$r[t] = r_\infty + (r[t_0] - r_\infty)\, e^{-(t-t_0)/\tau[X]}$$

where the time-constant is given by:

$$\tau[X] = \frac{1}{\alpha X + \beta} = \frac{1}{\alpha}\,\frac{1}{X + K_D}$$

Its dependence on the neurotransmitter concentration introduces an asymmetry: Because τ increases as X decreases, the channels take longer to close ($X \ll K_D$) than they take to open ($X \gg K_D$).

Reaching steady-state ($t_{bnd} > 3\,\tau$)



It takes three time-constants to reach steady-state

How long does $p(t)$ have to be for $r(t)$ to reach steady-state (r_∞)? In fact, when $t = 3\,\tau$, starting with $r[0] = 0$ at $t_0 = 0$, we have:

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r[3 τ] = r∞ (1 - e^-3) = (1 - 0.0498) r∞
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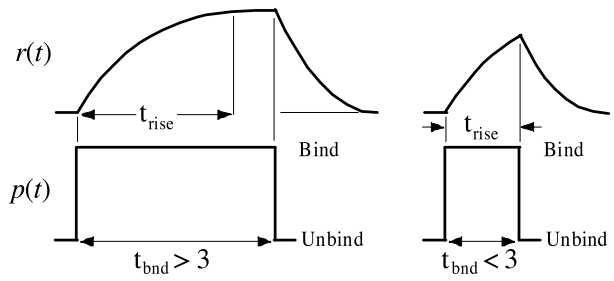
Thus, only 5% of the channels that are going to open remain unopened when the pulse's duration is 3τ. So steady-state is essentially reached within three time-constants.

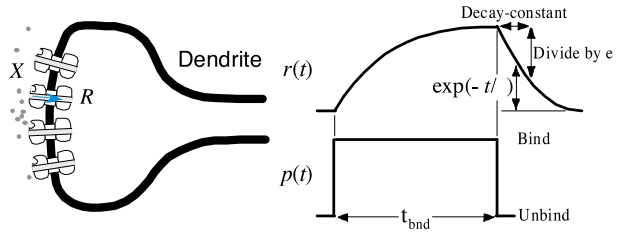
Rise-Time



Rise-time equals the time-to-steady-state (3τ) or the pulse length, whichever is shortest.

For long pulses, $r(t)$ stops rising once steady-state is reached, which essentially occurs at 3τ. Hence, the rise-time is 3τ.
For short pulses, $r(t)$ stops rising when the pulse ends, failing to reach steady-state. Hence, the rise-time is t_{bnd}.

Decay-Constant



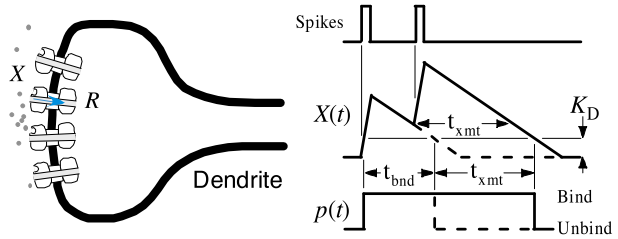
In a time equal to the decay-constant, the number of open channels to drops by a factor of e.

Starting with $r[t_0] = r_{peak}$ at $t_0 = t_{bnd}$, and setting $r_\infty = 0$ for $t > t_{bnd}$, we have:

$$r[t] = r_{peak}\, e^{-(t-t_{bnd})/\tau_\beta} \quad \text{where } \tau_\beta = \tau[0] = 1/\beta$$

Thus, the open fraction decays by a factor of e (63% decrease) when $t = t_{bnd} + \tau_\beta$. Hence, the decay-constant is τ_β — it is entirely determined by the unbinding rate β.

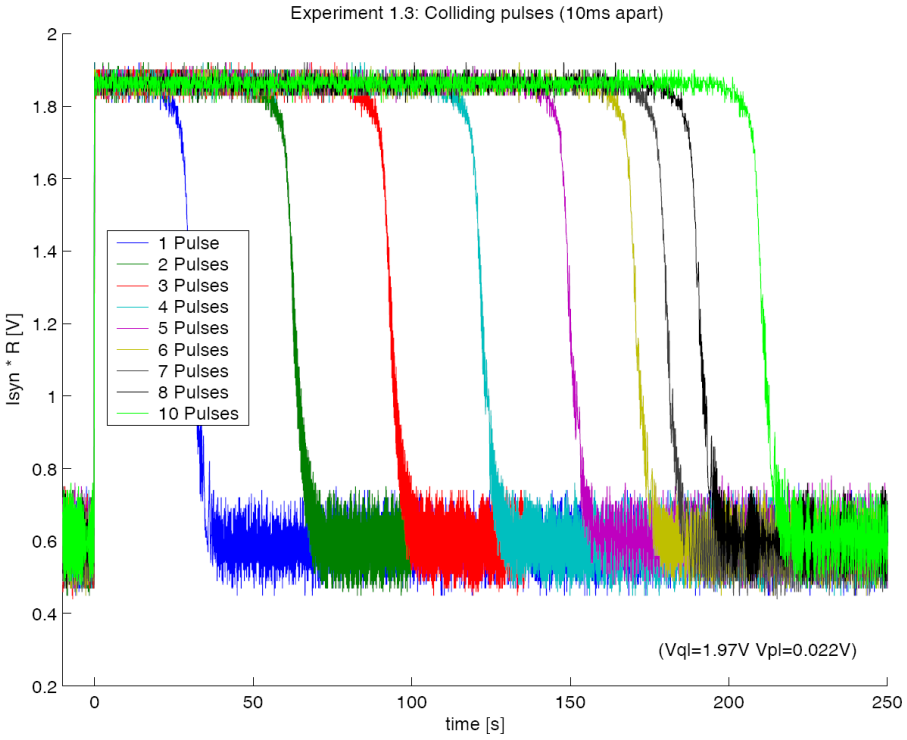
Overlapping Pulses



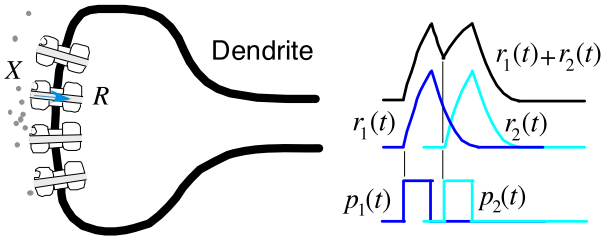
A second spike builds up neurotransmitter concentration and extends $p(t)$.

The second spike extends the time neurotransmitter is in the cleft from t_{xmt} to $2t_{\text{xmt}}$ and the time its concentration is above K_D from t_{bnd} to $t_{\text{bnd}} + t_{\text{xmt}}$ — more than $2\, t_{\text{bnd}}$. It acheives this higher efficacy (facilitation) by riding atop the dollop of neurotransmitter the first spike evoked.

Pulse Extension



Temporal Integration



Responses summate over time

The responses to the pulses $p_1(t)$ and $p_2(t)$, evoked by the first and second spike, are $r_1(t)$ and $r_2(t)$, respectively, when they are presented separately. Will the response be $r_1(t) + r_2(t)$ when the spikes are presented together (this is called linear behavior)? For this to be the case, $p_1(t) + p_2(t)$ and $r_1(t) + r_2(t)$ should satisfy the ODE, just like the individual pairs do:

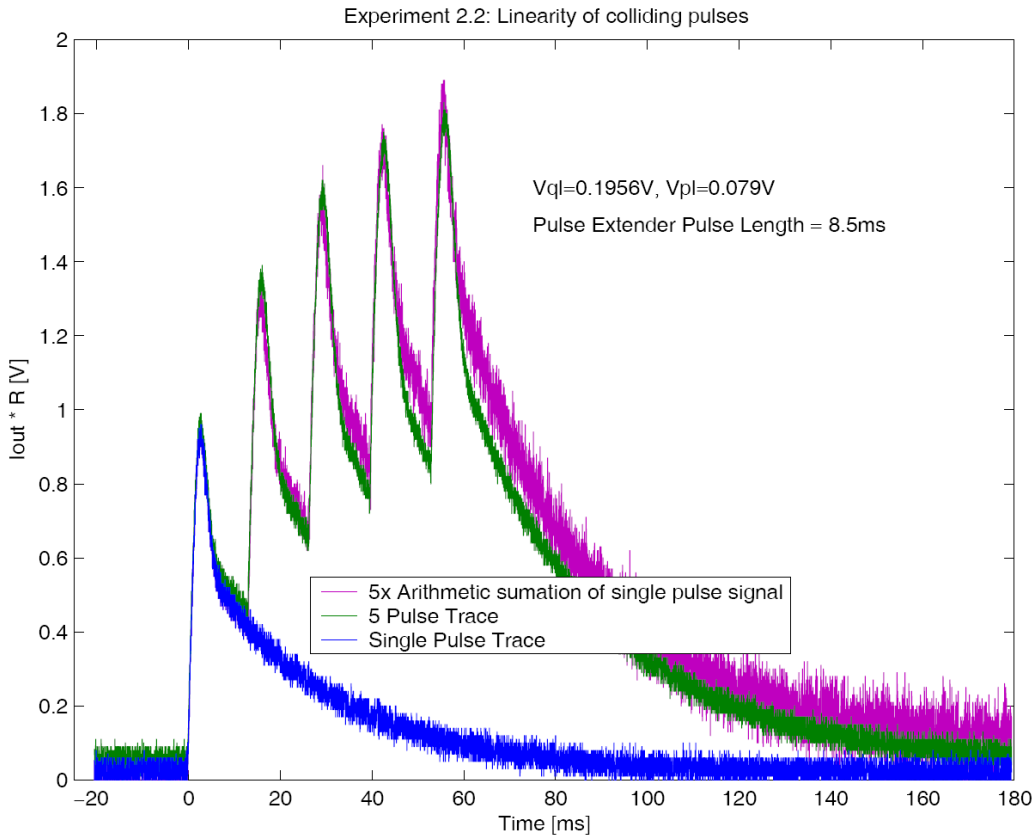
$$\frac{1}{\tau}\frac{d}{dt}(r_1[t] + r_2[t]) + (r_1[t] + r_2[t]) = p_1[t] + p_2[t]$$

$$\Leftrightarrow \left(\frac{1}{\tau}\frac{d}{dt} r_1[t] + r_1[t]\right) + \left(\frac{1}{\tau}\frac{d}{dt} r_2[t] + r_2[t]\right) = p_1[t] + p_2[t]$$

$$\Leftrightarrow p_1[t] + p_2[t] = p_1[t] + p_2[t]$$

This requires two assumptions to be true:
1. τ is the same in all three cases ($p_1(t)$, $p_2(t)$ and $p_1(t) + p_2(t)$) — true if neurotransmitter levels are the same.
2. Summing does indeed yield the third case's steady-state — true if pulses don't overlap.

Linear Behavior



Question: If the amount of neurotransmitter released increased but the number of receptors remained the same, how could I tell from the measured postsynaptic current trace?

Integrate-and-Fire Neuron