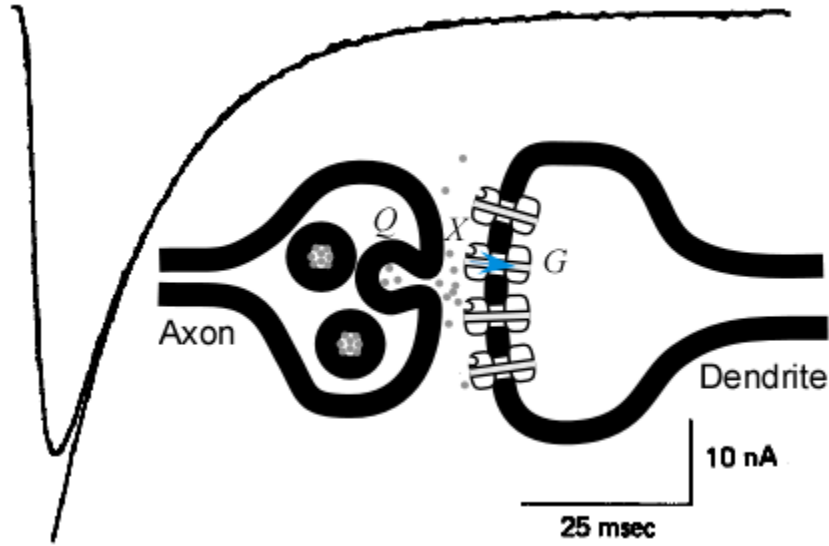


Synapse Model

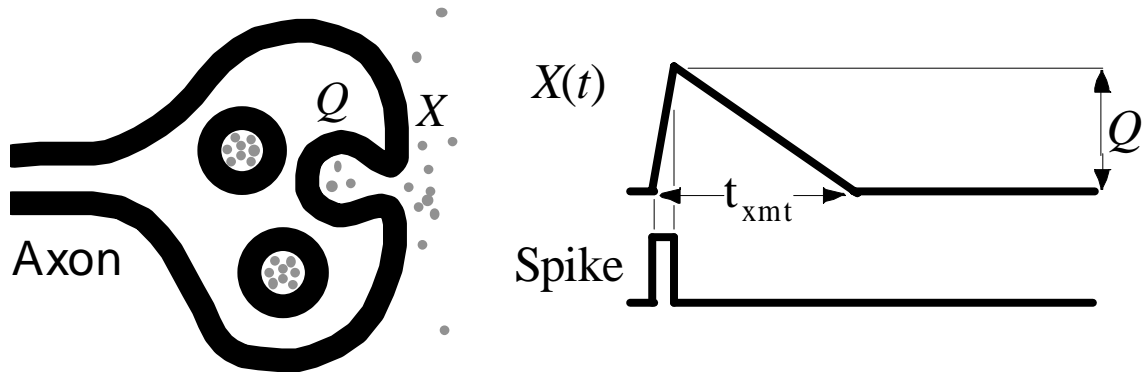


Neurotransmitter is released into cleft between axonal button and dendritic spine

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

$$\text{In}[1] := \frac{dx}{dt} = -I_{\text{leak}} \quad \text{with } x[0] = Q$$

$$\text{In}[1] := \Rightarrow x[t] = Q - I_{\text{leak}} t$$

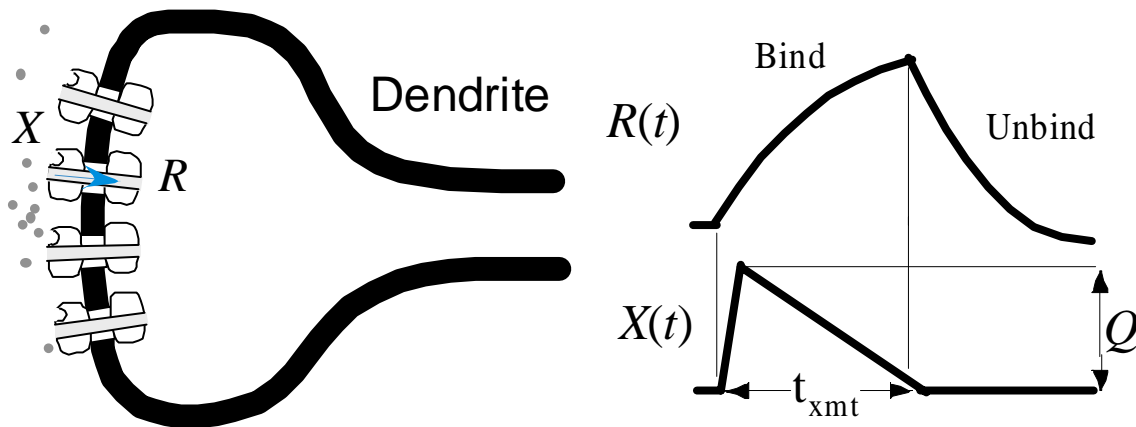
Neurotransmitter remains in the cleft for some time:

$$\text{In}[1] := x[t_{\text{xmt}}] = 0 \Rightarrow t_{\text{xmt}} = Q / I_{\text{leak}}$$



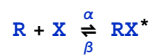
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Binding and unbinding rates



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 :



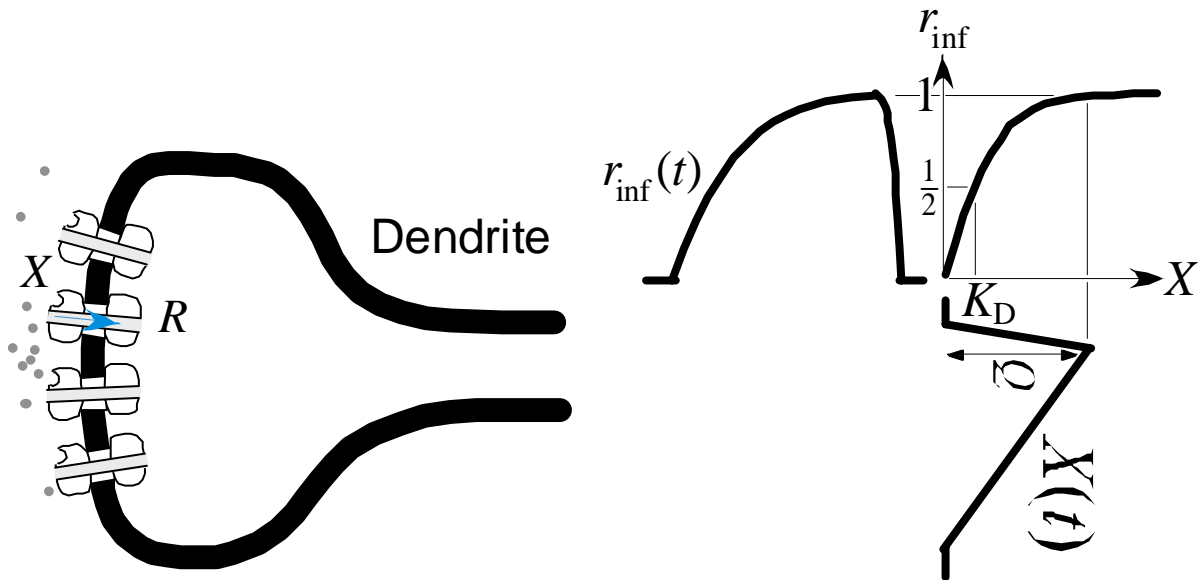
The fraction of channels that are open $r = [RX^*]/([R] + [RX^*])$ changes at the rate:

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



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Receptor affinity (K_D)



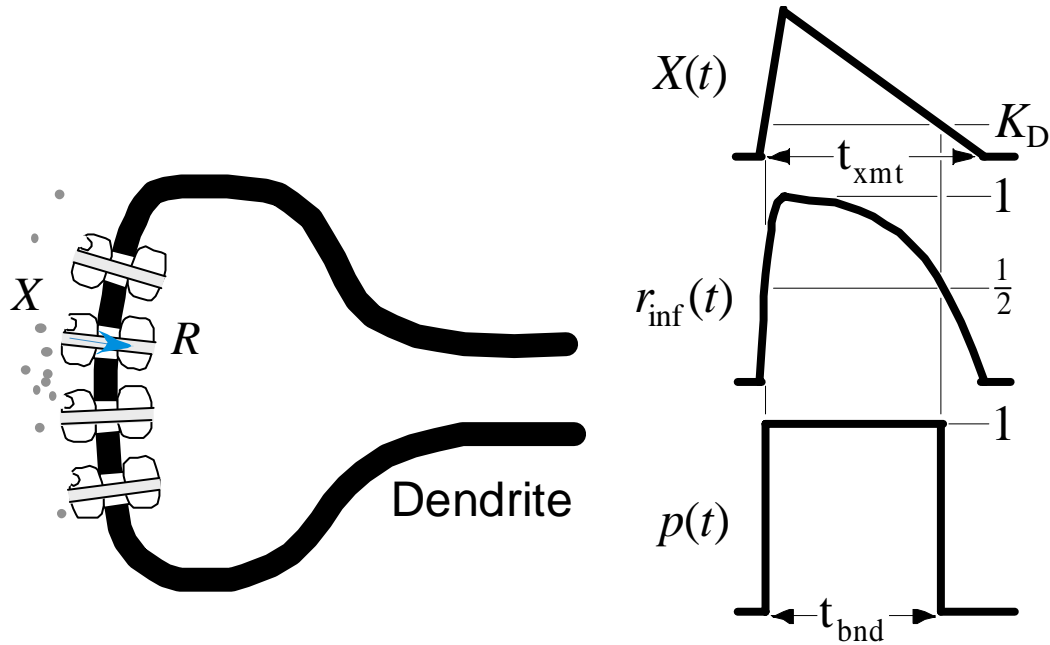
To open most of the channels, the neurotransmitter concentration must exceed the receptors' K_D

Setting $dr/dt = 0$ yields this steady-state solution to the ODE:

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

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

Rectangular pulse approximation ($p(t)$)



The steady-state level ($r_{\infty}(t)$) may be approximated by a rectangular pulse ($p(t)$)

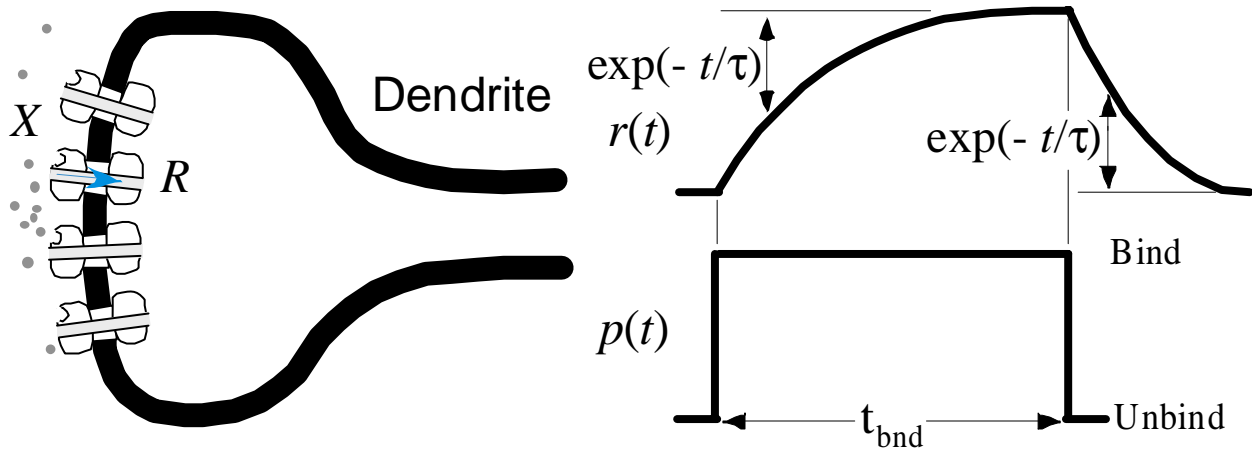
We assume $r_{\infty}[t] \approx 1$ when $X(t) > K_D$ and $r_{\infty}[t] \approx 0$ otherwise, which gives us the approximation $p(t)$, a rectangular pulse. Note that, pulse's durations is given by:

$$X[t_{bnd}] = K_D \implies t_{bnd} = (Q - K_D) / I_{leak} = t_{xmt} - K_D / I_{leak}$$

With this approximation for $r_{\infty}[t]$, the ODE becomes

$$\tau[X] \frac{dr}{dt} + r = p[t] \quad \text{where} \quad \tau[X] = \frac{1}{\alpha X + \beta}$$

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



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

Setting $X = \text{a constant}$ yields this solution to the ODE:

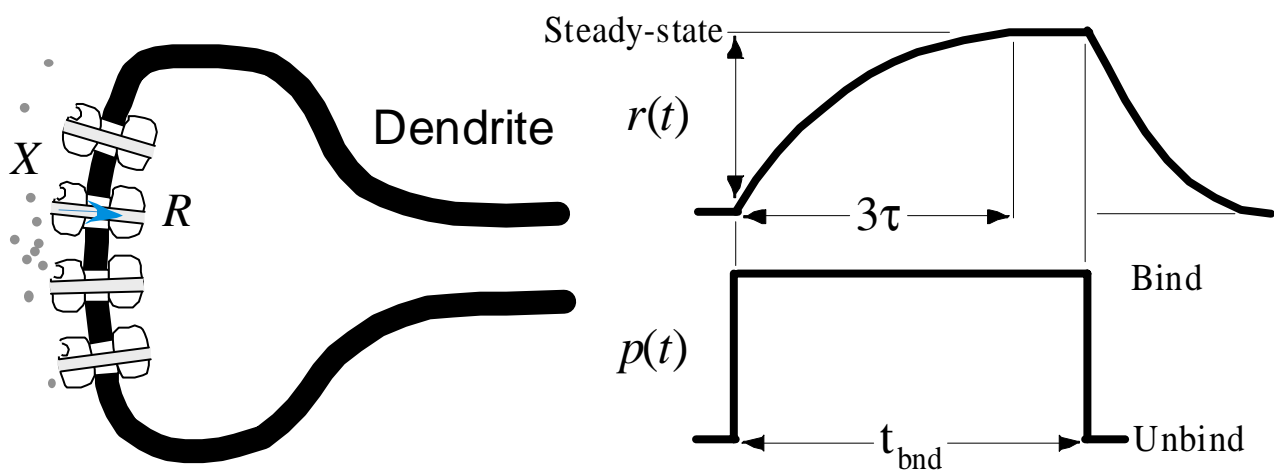
$$r[t] = r_{\infty} + (r[t_0] - r_{\infty}) e^{-(t-t_0)/\tau[X]}$$

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 ($t_{\text{bnd}} > 3\tau$)



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:

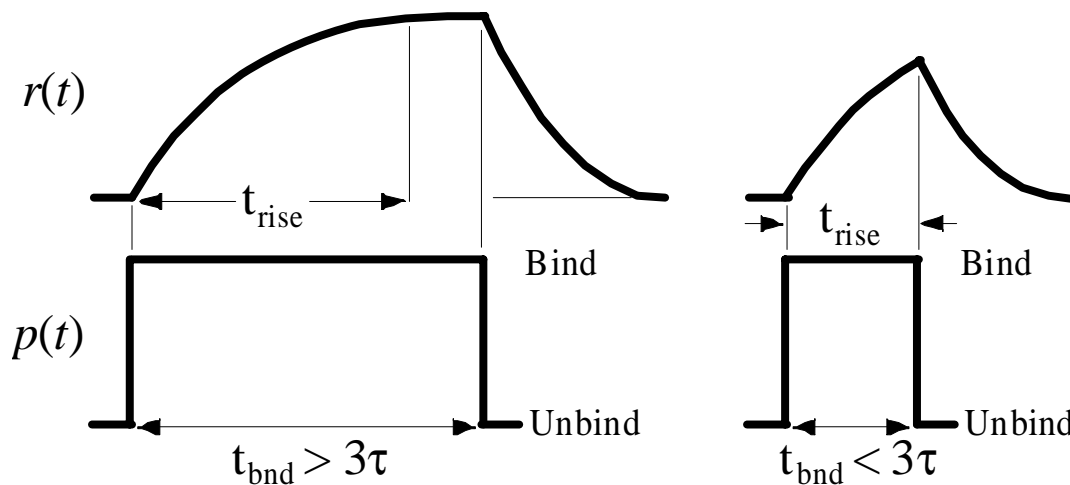
$$r[3\tau] = r_\infty (1 - e^{-3}) = (1 - 0.0498) r_\infty$$

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.



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Rise-Time



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

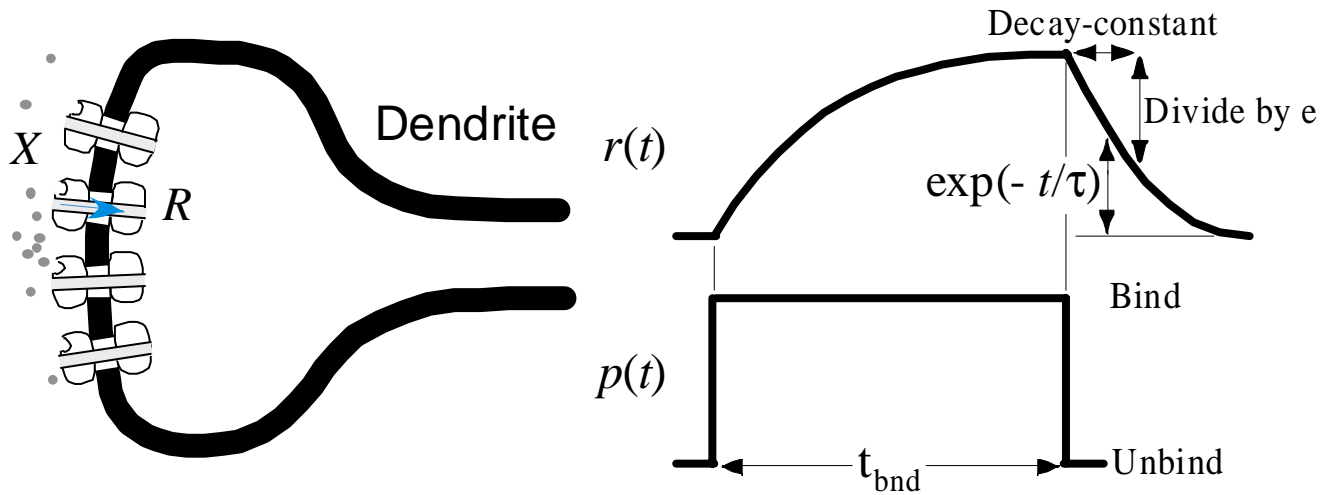
For long pulses, $r(t)$ stops rising once steady-state is reached, which essentially occurs at 3τ . Hence, the rise-time is 3τ .

For short pulses, $r(t)$ stops rising when the pulse ends, failing to reach steady-state. Hence, the rise-time is t_{bnd} .



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Decay-Constant



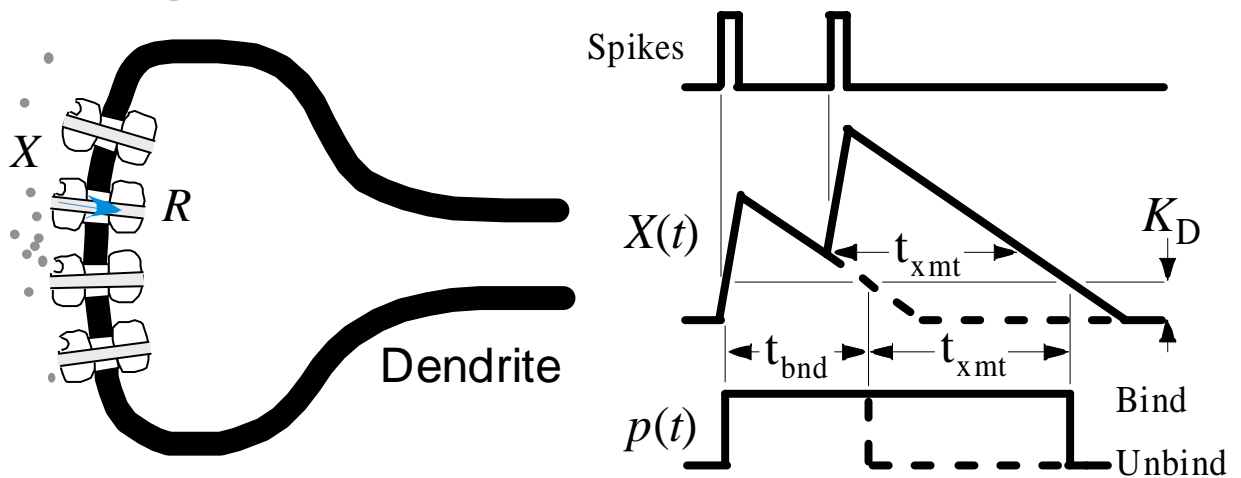
In a time equal to the decay-constant, the number of open channels drops by a factor of e .

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

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

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

Overlapping Pulses

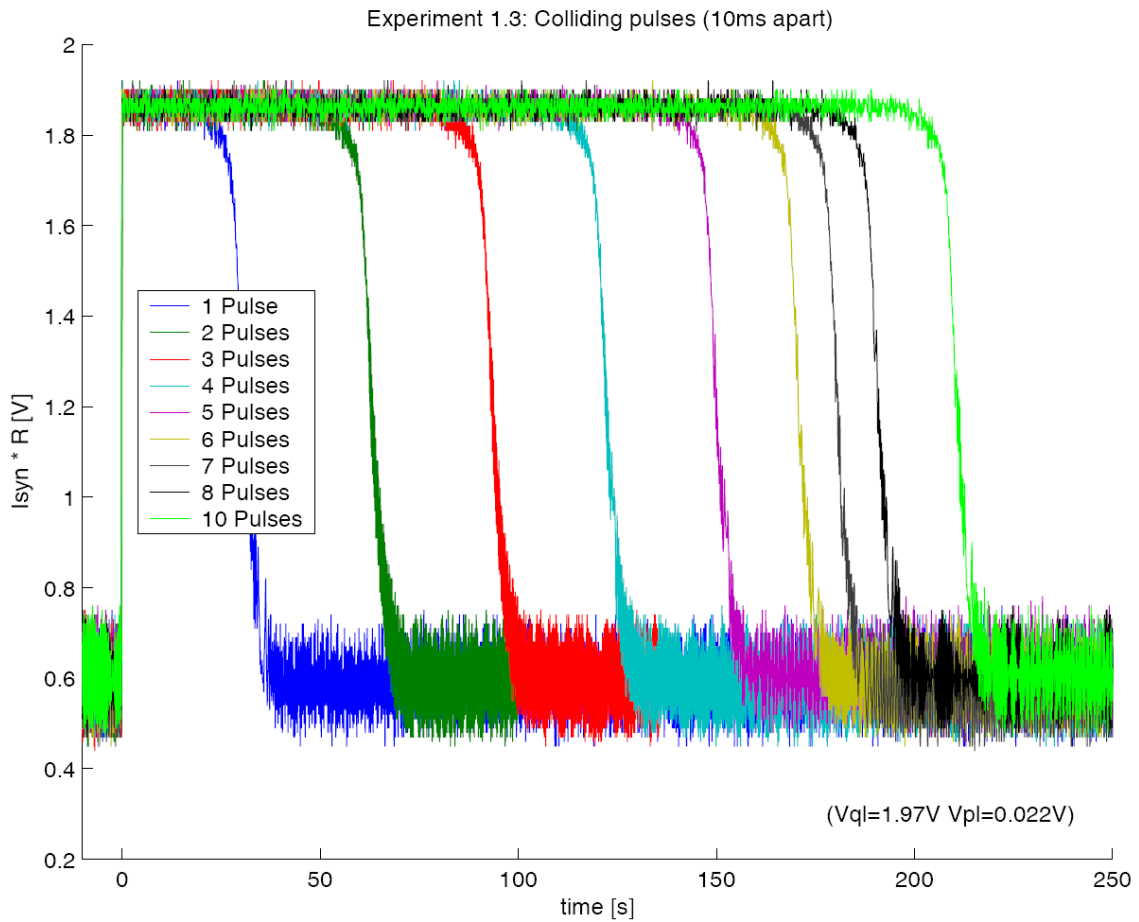


A second spike builds up neurotransmitter concentration and extends $p(t)$.

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

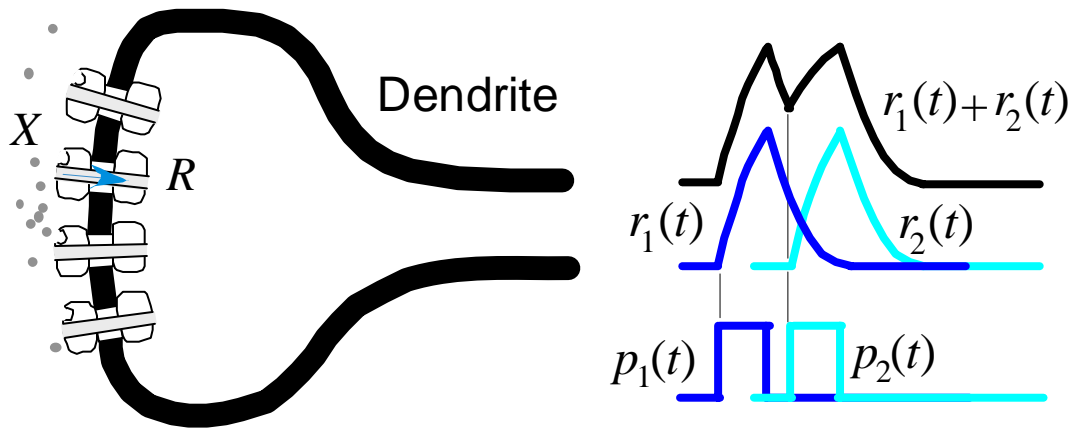
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Pulse Extension



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Temporal Integration



Responses summate over time

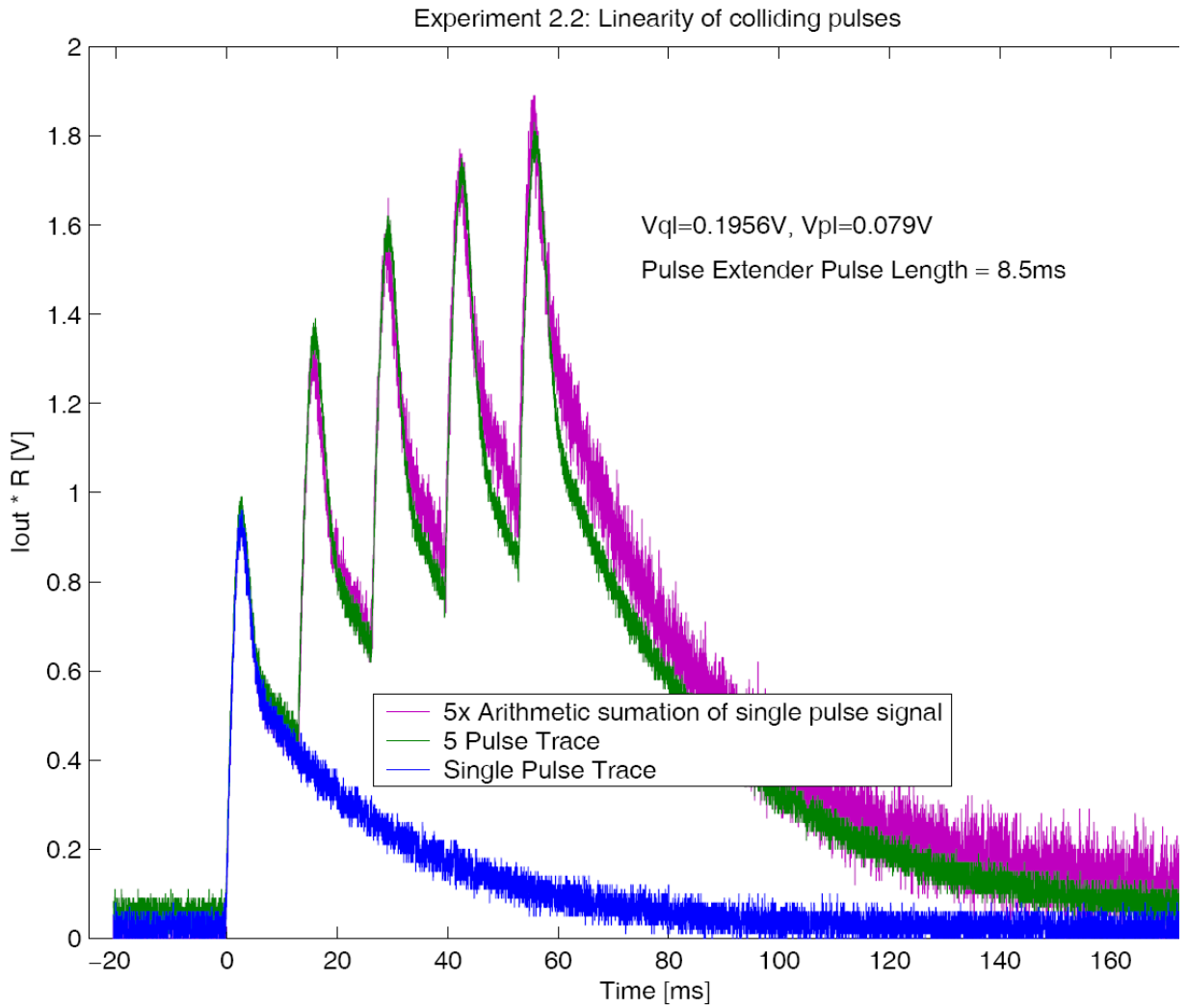
The responses to the pulses $p_1(t)$ and $p_2(t)$, evoked by the first and second spike, are $r_1(t)$ and $r_2(t)$, respectively, when they are presented separately. Will the response be $r_1(t) + r_2(t)$ when the spikes are presented together (this is called linear behavior)? For this to be the case,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

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

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



Integrate-and-Fire Neuron

