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

\[
\frac{dX}{dt} = -I_{\text{leak}} \quad \text{with} \quad X[0] = Q
\]

\[
X[t] = Q - I_{\text{leak}} t
\]

Neurotransmitter remains in the cleft for some time:

\[
X[t_{\text{xmt}}] = 0 \implies t_{\text{xmt}} = Q / I_{\text{leak}}
\]

### Binding and unbinding rates

Channels do not open or close instantaneously; it takes time

Neurotransmitter \((X)\) binds to receptors \((R)\) at a rate \(\alpha\) and unbinds from them at a rate \(\beta\):

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

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

\[
\frac{dr}{dt} = \alpha X (1 - r) - \beta r \iff \frac{dr}{dt} + (\alpha X + \beta) r = \alpha X
\]
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 $X \gg K_D$. 

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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:

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

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

\[
\tau[X] \frac{dr}{dt} + r = p(t) \quad \text{where} \quad \tau[X] = \frac{1}{\alpha X + \beta}
\]
The difference between the initial and steady-state levels decreases exponentially with time.

Setting $X = a$ constant yields this solution to the ODE:

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

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

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

Setting $X = a$ constant yields this solution to the ODE:

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

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Its dependence on the neurotransmitter concentration introduces an asymmetry: Because $\tau$ increases as $X$ decreases, the channels take longer to close ($X \ll K_D$) than they take to open ($X \gg K_D$).
It takes three time-constants to reach steady-state

How long does $p(t)$ have to be for $r(t)$ to reach steady-state ($r_\infty$)? 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 $3\tau$. So steady-state is essentially reached within three time-constants.

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### Rise-Time

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

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

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 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:

$$r(t) = r_{\text{peak}} e^{-(t-t_{\text{peak}})/\tau}$$

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 $\tau_\beta$ — it is entirely determined by the unbinding rate $\beta$.

Overlapping Pulses

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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.

**Pulse Extension**
Temporal Integration

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:

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

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

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

This requires two assumptions to be true:

1. $\tau$ 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

Experiment 2.2: Linearity of colliding pulses

\[ V_{q1} = 0.1956V, \ V_{p1} = 0.079V \]

Pulse Extender Pulse Length = 8.5ms
Integrate-and-Fire Neuron