1 Reduced models of short term synaptic plasticity

Let c, p, and x represent the intracellular concentration of Ca^{2+} at the presynaptic terminal, the proportion of released vesicles per unit time, and the normalized readily releasable vesicles. Assume that the dynamics are given by

$$\partial_t c = \frac{c_b - c}{\tau_b} - k_r \alpha_r (1-r) c + f(t) \quad (1)$$

$$\partial_t r = \alpha_r \, c \, (1-r) - \beta_r r \quad (2)$$

$$\partial_t q = \frac{q_\infty - q}{\tau_q} - \delta \, q \, r \quad (3)$$

where c_b and τ_b represent the steady state and time constant for presynaptic calcium due to buffering in the absence of any other perturbation. The term $f(c)$ represents the flux of Ca^{2+}into the terminal via voltage-dependent channels. The term $k_c \alpha_r \, c \, (1-r)$ represents the decrease in the calcium concentration due to binding to the release machinery.

Table 1: Parameters and values

c_b	μM	steady state constant for presynaptic Ca^{2+} due to buffering
α_r	ms^{-1} μM^{-1}	Activation rate of the release machinery in the presence of Ca^{2+}
β_r	ms^{-1}	Deactivation rate of the release machinery
k_r	μM	Impact of the Ca^{2+} activating the release machinery on the intracellular Ca^{2+} concentration in the terminal
q_∞		Steady state for que normalized quanta in the readily releasable pool
τ_b	ms	time constant for presynaptic Ca^{2+} due to buffering
τ_q	ms	Time constant for the recovery of the readily releasable pool
δ	ms^{-1}	Conversion rate

1.1 Ca^{2+} dynamics

It is worth noticing that the dynamics for c are linear when $f(t) = 0$. To see this, equation (1) can be transformed to

$$\partial_t c = f(t) + \frac{c_\infty - c}{\tau_c}$$

where

$$\tau_c = \frac{\tau_b}{1 + k_r \alpha_r \, (1-r) \tau_b}, \quad (4)$$

$$c_\infty = \frac{c_b}{1 + k_r \alpha_r \, (1-r) \tau_b}. \quad (5)$$

That is, if $f(t) = 0$, then the dynamics for c from an initial condition $c_o = c(t_o)$ behave like

$$c(t) = c_\infty - (c_\infty - c_0) \exp\left(\frac{t_o - t}{\tau_c}\right).$$

which means that in the absence of any Ca^{2+} influx, the concentration of Ca^{2+} in the presynaptic terminal goes to a steady state c_∞ that becomes the steady state for buffering only for fast buffering (small τ_b), or if the rate of binding to the activation machinery is slow enough (small α_r).

Calcium influx. To better understand the Ca^{2+} dynamics, this time in the presence of calcium influx, assume $f(t)$ is a Dirac comb given by

$$f(t) = h \sum_{k=1}^{n} \delta\left(t - t_k\right) \tag{6}$$

where t_0, ..., t_n represent stimulus times (e.g. presynaptic action potential-driven fluxes). Also, suppose that there has been a long enough interval of time so that before the first pulse, presynaptic terminal Ca^{2+} concentration is at steady state; that is, that $c(t) = c_\infty$ for $t \leq t_0$. Also, suppose that, at the kth pulse time, the value of $c(t)$ changes to $c_k = c(t_k) + h$, for $k \in \{0, ..., n\}$. Then, at $t = t_0$, let $c_0 = c_\infty + h$ be the new value of c after the jump. The dynamics for c before the next pulse are given by,

$$c(t) \quad = \quad c_\infty + h \exp\left(\frac{t_0 - t}{\tau_c}\right)$$

for $t \in (t_0, t_1)$. At $t = t_1$ the calcium concentration changes again, to $c_1 = c(t_1) + h$, which becomes a new initial condition. Then, for $t \in (t_1, t_2)$,

$$\begin{aligned} c(t) &= c_\infty - (c_\infty - c_1) \exp\left(\frac{t_1 - t}{\tau_c}\right), \\ &= c_\infty + h\left(\exp\left(\frac{t_1 - t}{\tau_c}\right) + \exp\left(\frac{t_0 - t}{\tau_c}\right)\right). \end{aligned}$$

In general, for $t \in (t_{n-1}, t_n)$,

$$c(t) \quad = \quad c_\infty + h \sum_{k=0}^{n-1} \exp\left(\frac{t_k - t}{\tau_c}\right)$$

At t_n the value of c jumps to

$$c(t_n) \quad = \quad c_\infty + h \sum_{k=0}^{n} \exp\left(\frac{t_k - t_n}{\tau_c}\right)$$

If pulses are periodic, with $d = t_{k+1} - t_k$, for all $k \in \{1, ..., n\}$ then $t_n - t_k = (n - k)d$. In this case, the calcium concentration becomes

$$\begin{aligned} c(t_n) &= c_\infty + h \sum_{k=0}^{n} u^{(n-k)} = c_\infty + h \sum_{l=0}^{n} u^l, \\ &= c_\infty + h\left(\frac{1 - u^{n+1}}{1 - u}\right), \end{aligned}$$

where

$$u = \exp\left(-\frac{d}{\tau_c}\right). \tag{7}$$

Explicitly,

$$c(t_n) \quad = \quad c_\infty + h\left[\frac{1 - \exp\left(-(n+1)\frac{d}{\tau_c}\right)}{1 - \exp\left(-\frac{d}{\tau_c}\right)}\right]. \tag{8}$$

The asymptotic behavior as $n \to \infty$ is then

$$c_* = c_\infty + h\left(\frac{1}{1-\exp\left(-\frac{d}{\tau_c}\right)}\right). \tag{9}$$

which written explicitly in terms of the parameters for Ca^{2+} buffering and activation of the release machinery, becomes

$$c_* = c_\infty + h\left(\frac{1}{1-\exp\left(-d\frac{1+k_r\alpha_r\,(1-r)\tau_b}{\tau_b}\right)}\right). \tag{10}$$

1.2 p dynamics and the subsystem $c-p$

The dynamics of the subsystem c, p are given by

$$\partial_t c = \frac{c_\infty - c}{\tau_c} + f(t) \tag{11}$$

$$\partial_t p = \alpha\, c\,(1-p) - \beta p \tag{12}$$

The time constant and steady state for the p are

$$\tau_p(c) = \frac{1}{\alpha\, c + \beta} \tag{13}$$

$$p_\infty(c) = \frac{\alpha\, c}{\alpha\, c + \beta} = \frac{c}{c + \frac{\beta}{\alpha}} \tag{14}$$

c increases as action potentials arrive, then $\tau_p(c)$ decreases and $p_\infty(c)$ increases. So p increases with c, but the dynamics for p become faster as that happens.

if $\tau_c >> \tau_p$, then the dynamics for p are fast enough to substitute p with $p_\infty(c)$. Explicitly, it would be required that

$$\tau_c > \frac{1}{\alpha\, c + \beta}.$$

2 Binary classification trains of pulses.

$a_0, ..., a_n$ pulse amplitudes. The change in amplitude during the kth interval is $s_k = \frac{a_k - a_{k-1}}{\delta_k}$, for $k \in \{1, ..., n\}$. Similarly, the change in amplitude relative to the first pulse in a train is given by $r_k = \frac{a_k - a_0}{\sum_{i=1}^{k} \delta_i}$, for $k \in \{1, ..., n\}$

The heavy side function defined by $H(x) = 1$ if $x > 0$, 0 if$x \leq 0$ can be used to determine whether there was an increase in the amplitudes between any two pulses. In particular,

One way to describe the history of changes during a train of postsynaptic responses is to record whether there was an increase or decrease in the amplitudes for each pair of responses using a binary code, and add all the results. To do so, let

$$b_{pp}(s_1, ..., s_n) = \sum_{k=1}^{n} \frac{H(s_k)}{2^k} \tag{15}$$

for the slopes of pulses taken by pairs. Similarly, for the slopes relative to the first pulse, let

$$b_{fp}(r_1, ..., r_n) = \sum_{k=1}^{n} \frac{H(r_k)}{2^k} \tag{16}$$

3 Short term synaptic plasticity from a whole cell approach

The model can be thought of in terms of 3 main components. First, a system capable of producing spiking dynamics, which can be 2- or 3-dimensional in case bursting or spike frequency adaptation are required. Second, a 2- or 3-dimensional system that describes the dynamics of presynaptic release, and third, at least one more equation that describes the dynamics of postsynaptic activation upon release.

$$\partial_t c = \frac{c_\infty - c}{\tau_c} + f(t) \tag{17}$$

$$\partial_t p = \alpha\, c\, (1-p) - \beta p \tag{18}$$

$$\partial_t x = x\left(\frac{x_\infty - x}{\tau_x}\right) - x\, p \tag{19}$$

where $f(c)$ represents the flux of Ca^{2+}into the terminal.