

Geometry and dynamics underlying the diversity of short term synaptic plasticities GABAergic and glutamatergic terminals in striatal neurons

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1. General rationale

Define a synaptic contact between two neurons A and B as the set of all synapses where the presynaptic membrane is part of A and the postsynaptic membrane is part of B. Each synapse is assumed to have a probability of release that depends on the amount of intracellular calcium c as

$$p(c; a, c_h) = \frac{c^a}{c^a + c_h^a} \quad (1)$$

where c_h is the half-maximal calcium concentration and g_c is a gain parameter.

The calcium dynamics for a single terminal can be described as

$$\partial_t c = \frac{c_\infty - c}{\tau_c} - k_c I_c(t) \quad (2)$$

where c_∞ is the steady state concentration of intracellular calcium, I_c is the calcium current at the terminal, and k_c is a conversion factor. The range for c_∞ can be assumed to be between 0.1 and 0.5 μM .

It is possible to derive an equation that describes the dynamics of the probability of release can then be derived taking into consideration equations (1) and (2). By the chain rule,

$$\begin{aligned} \partial_t p &= \partial_c p \cdot \partial_t c \\ &= \frac{a}{c} p(c) (1 - p(c)) \left(\frac{c_\infty - c}{\tau_c} - k_c I_c(t) \right) \end{aligned}$$

However, if the dynamics for p are fast enough, then it should be possible to assume $p = p_\infty$.

2. Peaks of the pre- and post-synaptic responses to trains of presynaptic action potentials

Assume that presynaptic action potentials occur at times $0 < t_1 < t_2 < \dots < t_n$. Let $x(t)$ and $p(t)$ represent the readily releasable neurotransmitter and the proportion of released neurotransmitter at time t , respectively. Recall that the dynamics for p and x can be written as

$$\begin{aligned} \partial_t p &= \frac{p_\infty - p}{\tau_p} + a(1 - p)\phi(t) \\ \partial_t x &= \frac{x_\infty - x}{\tau_x} - px\phi(t) \\ \phi(t) &= \sum_{k=1}^n \delta(t - t_k) \end{aligned}$$

In the absence of a pulse the dynamics of p and x are given by

$$\begin{aligned} p(t) &= p_\infty + (p_0 - p_\infty) \exp\left(\frac{t_0 - t}{\tau_p}\right) \\ x(t) &= x_\infty + (x_0 - x_\infty) \exp\left(\frac{t_0 - t}{\tau_x}\right) \end{aligned}$$

where $p(t_0) = p_0$ and $x(t_0) = x_0$ are initial conditions for p and x . At each pulse, p and x jump to new initial conditions. Specifically, at time $t = t_i$, p changes to $a(1 - p)$. As a consequence of the change in p , $x(t_i)$ changes to $x_i = x(t_i)(1 - p_i)$. The amount of neurotransmitter released at time $t = t_i$ is then $x(t_i) - x_i = x(t_i)p_i$.

Assuming that the initial condition $p_0 = p_\infty$, we have $p(t_1) = p_\infty$. We can now consider a new initial condition due to the effect of the term $a(1 - p)\phi(t)$ given by

$$p_1 = p(t_1) + a(1 - p(t_1)).$$

In general, the solution for p in each interval $[t_n, t_{n+1}]$ can be obtained by taking $p^* = p(t_n)$ and $t^* = t_n$ in (??).

The relation between $p(t_k)$ and the new initial condition at times $t = t_k$ is given by the non-autonomous difference equation

$$\begin{aligned} p(t_{k+1}) &= p_\infty + (p_k - p_\infty) \exp\left(\frac{t_k - t_{k+1}}{\tau_p}\right) \\ p_{k+1} &= p(t_{k+1}) + a(1 - p(t_{k+1})). \end{aligned} \quad (3)$$

It can be proved by induction that for $n \geq 2$

$$\begin{aligned} p(t_n) &= p_\infty + a(1 - p_\infty) \sum_{m=0}^{n-2} (1 - a)^m \exp\left(\frac{t_{n-m-1} - t_n}{\tau_p}\right) \\ p_n &= p_\infty + a(1 - p_\infty) \sum_{m=0}^{n-1} (1 - a)^m \exp\left(\frac{t_{n-m} - t_n}{\tau_p}\right) \end{aligned}$$

In a similar way, assuming that the initial condition for $x(t)$ lies in the stationary state x_∞ one has that $x(t_1) = x_\infty$. The jump due to $\phi(t)$ can be measured as $x_1 = x(t_1)(1 - p_1)$, and in general the quantities $x(t_n)$ and x_n satisfy the non-autonomous difference equation

$$\begin{aligned} x(t_{n+1}) &= x_\infty - (x_k - x_\infty) \exp\left(\frac{t_k - t_{k+1}}{\tau_x}\right) \\ x_{k+1} &= x(t_{n+1}) - p_{n+1}x(t_{n+1}) \end{aligned}$$

After some cumbersome algebra, an inductive argument yields for $n \geq 2$

$$\begin{aligned} x_n &= x_\infty (1 - p_n) \left[1 - p_{n-1} \exp\left(\frac{t_{n-1} - t_n}{\tau_x}\right) - \sum_{k=2}^{n-1} p_{n-k} \prod_{j=k+1}^{n-1} (1 - p_j) \exp\left(\frac{t_{n-k} - t_n}{\tau_x}\right) \right] \\ &= x_\infty \left[(1 - p_n) - \sum_{k=1}^{n-1} p_{n-k} \prod_{j=k+1}^n (1 - p_j) \exp\left(\frac{t_{n-k} - t_n}{\tau_x}\right) \right] \end{aligned}$$

The dynamics of the proportion of activated postsynaptic channels, as proposed by Destexhe et al. (1998)

$$\partial_t y = y[\alpha\eta(t)(1 - y) - \beta y]$$

where $\eta(t) = \delta(t - t_i)x(t_i)p_i$.

In the absence of a complete model that generates action potentials, the time course of the calcium current at the terminal can be assumed to be a sum of pulses, each of which behaving like α -functions ():

$$\alpha(t; \tau) = 1_{\{t \geq 0\}} \frac{t}{\tau} e^{1 - \frac{t}{\tau}} \quad (4)$$

2.1. Pulses of intracellular calcium concentration

$$\partial_t c = \frac{c_\infty - c}{\tau_c} + \phi(t) \quad (5)$$

$$\phi(t) = a \sum_{i=1}^n \delta(t - t_i) \quad (6)$$

The dynamics in the absence of pulses are given by

$$c(t) = c_\infty + (c_0 - c_\infty) \exp\left(-\frac{t}{\tau_c}\right) \quad (7)$$

If a pulse occurs at time t , then $c(t)$ jumps to $c(t) + a$. Let $c_0 = c_\infty$. If a pulse occurs at time $t = t_1$, then let

$$c_1 = c(t_1) + a = c_\infty + a \quad (8)$$

For $t_1 \leq t$:

$$c(t) = c_\infty + (c_1 - c_\infty) \exp\left(\frac{t_1 - t}{\tau_c}\right) \quad (9)$$

$$= c_\infty + a \exp\left(\frac{t_1 - t}{\tau_c}\right) \quad (10)$$

$$\begin{aligned} c_2 &= c(t_2) + a \\ &= c_\infty + a \left(1 + \exp\left(\frac{t_1 - t_2}{\tau_c}\right)\right) \end{aligned}$$

For $t_2 \leq t$:

$$\begin{aligned} c(t) &= c_\infty + (c_2 - c_\infty) \exp\left(\frac{t_2 - t}{\tau_c}\right) \\ &= c_\infty + a \left(1 + \exp\left(\frac{t_1 - t_2}{\tau_c}\right)\right) \exp\left(\frac{t_2 - t}{\tau_c}\right) \\ &= c_\infty + a \left[\exp\left(\frac{t_2 - t}{\tau_c}\right) + \exp\left(\frac{t_1 - t}{\tau_c}\right)\right] \end{aligned}$$

At $t = t_3$,

$$\begin{aligned} c_3 &= c(t_3) + a \\ &= c_\infty + a \left(1 + \exp\left(\frac{t_2 - t_3}{\tau_c}\right) + \exp\left(\frac{t_1 - t_3}{\tau_c}\right)\right) \end{aligned}$$

In general, for $t \geq t_n$,

$$\begin{aligned} c(t) &= c_\infty + (c_n - c_\infty) \exp\left(\frac{t_n - t}{\tau_c}\right) \\ &= c_\infty + a \sum_{k=1}^n \exp\left(\frac{t_k - t}{\tau_c}\right) \\ &= c_\infty + a \exp\left(\frac{-t}{\tau_c}\right) \sum_{k=1}^n \exp\left(\frac{t_k}{\tau_c}\right) \end{aligned}$$

Assume that a neuron receives M synaptic contacts of the same type (e.g. AMPA, GABA-A).

3. Linear dynamics

Let us assume that a neuron receives N synapses, with n_j readily releasable vesicles and p_j the probability of release at the j th synapse. Assume that all the synapses are all GABAergic or all glutamatergic, let $p = N^{-1} \sum_{i=1}^N p_i$ and $x = N^{-1} \sum_{i=1}^N x_i$ represent the average of the

$$\partial_t p = \frac{p_\infty - p}{\tau_p} + h(1 - p) \sum \delta(t - t_i) \quad (11)$$

$$\partial_t x = \frac{x_\infty - x}{\tau_x} - px \sum \delta(t - t_i) \quad (12)$$

3.1. Analysis for p

$$p(t) = \frac{p_\infty p_0}{p_0 + (p_\infty - p_0) \exp\left(\frac{-tp_\infty}{\tau_p}\right)} \quad (13)$$

$$= p_\infty \left[1 + \left(\frac{p_\infty}{p_0} - 1 \right) \exp\left(\frac{-tp_\infty}{\tau_p}\right) \right]^{-1} \quad (14)$$

$$= p_\infty \left[1 - \left(1 - \frac{p_\infty}{p_0} \right) \exp\left(\frac{-tp_\infty}{\tau_p}\right) \right]^{-1} \quad (15)$$

If $p(0) = p_\infty$ and there is a pulse at time $t = t_0$, then $p(t_0) = p_\infty + h(1 - p_\infty) = p_\infty(1 - h) + h$. Before the next pulse at time $t_0 < t < t_1$,

$$p(t) = p_\infty \left[1 + \left(\frac{p_\infty}{p_\infty - 1} (1 - h) + h \right) \exp\left(\frac{-tp_\infty}{\tau_p}\right) \right]^{-1} \quad (16)$$

4. Logistic dynamics

$$\partial_t p = p \frac{p_\infty - p}{\tau_p} + h(1 - p) \sum \delta(t - t_i) \quad (17)$$

$$\partial_t x = x \frac{x_\infty - x}{\tau_x} - px \sum \delta(t - t_i) \quad (18)$$

Analysis for p .

$$p(t) = \frac{p_\infty p_0}{p_0 + (p_\infty - p_0) \exp\left(\frac{-tp_\infty}{\tau_p}\right)} \quad (19)$$

$$= p_\infty \left[1 + \left(\frac{p_\infty}{p_0} - 1 \right) \exp\left(\frac{-tp_\infty}{\tau_p}\right) \right]^{-1} \quad (20)$$

$$= p_\infty \left[1 - \left(1 - \frac{p_\infty}{p_0} \right) \exp\left(\frac{-tp_\infty}{\tau_p}\right) \right]^{-1} \quad (21)$$

If $p(0) = p_\infty$ and there is a pulse at time $t = t_0$, then $p(t_0) = p_\infty + h(1 - p_\infty) = p_\infty(1 - h) + h$. Before the next pulse at time $t_0 < t < t_1$,

$$p(t) = p_\infty \left[1 + \left(\frac{p_\infty}{p_\infty - 1} (1 - h) + h \right) \exp\left(\frac{-tp_\infty}{\tau_p}\right) \right]^{-1} \quad (22)$$

5. Log relationship between Ca^{2+} and probability of release

Usually concentrations of $[Ca]_i$ are expressed in \log_{10} units. The relationship between $[Ca]_i$ and the probability of release in a presynaptic terminal is usually described by

$$p(c; c_0, b) = \frac{\exp[b(l - l_0)]}{1 + \exp[b(l - l_0)]}$$

$$l = \log_{10} c = (\log_{10} e) (\ln c)$$

Then

$$e^l = (e^{\ln c})^{\log_{10} e} = c^{\log_{10} e}$$

so

$$\begin{aligned} p(c; c_h, b) &= \frac{c^{b \log_{10} e}}{c^{b \log_{10} e} + c_h^{b \log_{10} e}} \\ &= \frac{c^a}{c^a + c_h^a} \end{aligned}$$

with $a = b \log_{10} e$.

Referencias

Alain Destexhe, Zachary F Mainen, and Terrence J Sejnowski. Kinetic models of synaptic transmission. *Methods in neuronal modeling*, 2:1–25, 1998.