Chapter 1
Models of short-term synaptic plasticity

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Abstract We focus on dynamical descriptions of short-term synaptic plasticity. Instead of attending to the molecular machinery that has been reviewed recently by several authors, we concentrate on the dynamics and functional significance of synaptic plasticity and review some mathematical models that aim to reproduce dynamics of short term synaptic plasticity. The complexity and shortcomings of these models point to the need of simple, yet physiologically meaningful models. We propose a simplified model to be tested in different synapses.

Key words: synapse, synaptic facilitation, synaptic depression, short-term synaptic plasticity, synapses, GABA, striatum

1.1 Introduction

Synaptic efficacy is typically seen as the ability to evoke post-synaptic events upon the release of neurotransmitter by the presynaptic terminal. Synaptic plasticity is the capability of changing synaptic efficacy as result of previous activity in the synapse.

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Synaptic efficacy changes dynamically during the on-going function of the synapse. As a consequence, plasticity involves processes that occur at various time scales. Changes in synaptic efficacy that occur within a time scale of milliseconds to minutes are regarded as short-term synaptic plasticity (STSP Zucker and Regehr, 2002). That is, changes in efficacy that take place over tens of minutes to hours, or even longer, are regarded as long-term synaptic plasticity (LTSP, Morris, 2003) and tends to be maintained for long time. In the present work, we focus on short-term synaptic plasticity.

The arrival of an action potential at the presynaptic terminal opens voltage-dependent Ca2+ channels, raising intracellular calcium ($[Ca^{2+}]_i$) in the presynaptic terminal, triggering the activation of presynaptic machinery that results in the exocytosis of readily releasable vesicles containing transmitter molecules (Katz and Miledi, 1968). Transmitter released into the synaptic cleft diffuses and binds to postsynaptic receptors. The activation of receptors triggers an electrical response in the postsynaptic neuron that involves the activation of a postsynaptic current, which in turn causes a local change: the postsynaptic membrane potential. Several reviews deal with the chain of events that take place during synaptic activation, including, but not limited to, vesicle cycling, docking and priming due to the SNARE complex, exo- and endocytosis, synaptic receptor regulation (Dutta Roy et al, 2014; Neher, 2010; Gandhi and Stevens, 2003; Triller and Choquet, 2005). This review focuses on the dynamics of the short-term synaptic plasticity.

Postsynaptic events are seen as postsynaptic currents when recorded with the voltage-clamp technique. The postsynaptic current is excitatory if increases the probability of postsynaptic spiking and inhibitory if it decreases the probability of postsynaptic spiking. A postsynaptic current is regarded as excitatory (EPSC) if it causes a positive deflection in the postsynaptic membrane potential, called excitatory postsynaptic potentials (EPSPs). Similarly, inhibitory postsynaptic currents (IPSCs) are those that produce negative deflections of the postsynaptic membrane, called inhibitory postsynaptic potentials (IPSPs). The arrival of several action potentials at the presynaptic terminals triggers sequences of pulses in the intra-terminal $[Ca^{2+}]_i$ that may add sublinearly, supralinearly, or both. Depending on the type of synaptic terminal and on the context, neurotransmitter release may be enhanced or decreased as action potentials arrive (Bollmann and Sakmann, 2005; Dutta Roy et al, 2014; Tecuapetla et al, 2007). The postsynaptic currents triggered by the released neurotransmitter then change the postsynaptic potential in a way that often reflects on the sublinear or supralinear summation of the presynaptic $[Ca^{2+}]_i$ transients. Factors that affect the dynamics of such processes include the type of postsynaptic target; the presence of modulatory transmitters such as dopamine (DA) or acetylcholine (ACh), which modify presynaptic efficacy (Guzmán et al, 2003; Tecuapetla et al, 2007; Dehorter et al, 2009; Mansvelder et al, 2009) chelating proteins such as parvalbumin (PV) or calbindin (CB) that modify Ca^{2+} dynamics inside the terminal (Mochida et al, 2008); vesicle recycling including clathrin mediated endocytosis (Granseth et al, 2006; López-Murcia et al, 2014; Kavalali, 2007); and a variety of other factors that make synaptic plasticity highly dynamic.

Types of Short-term Synaptic Plasticity

Short-term depression

Following a train of presynaptic stimuli, the synaptic efficacy of some terminals tends to decrease in time scales of a few milliseconds to seconds. That is, postsynaptic events decrease in amplitude, possibly due to less transmitter release or less activation of postsynaptic receptors. This is called short-term depression (STD, Fig. 1.1A). Functionally, depression has been linked to habituation, sensory adaptation and an initial high probability of release (Zucker, 1989; Fisher et al, 1997; O'Donovan and Rinzel, 1997). Several mechanisms have been proposed to account for STD. One is the depletion of the readily releasable pool of synaptic vesicles (Del Castillo and Katz, 1954; Rosenmund and Stevens, 1996). If the frequency of action potentials is high enough, the fraction of vesicles in the readily releasable pool progressively declines after each action potential producing a decrease in synaptic efficacy over time. In such conditions, the stimulus has to stop to allow replenishment of the vesicles . High stimulus frequency can therefore contribute to depression, as high presynaptic release frequencies lead to more rapid vesicle depletion and saturation of the mechanisms that mediate recovery of the presynaptic machinery and vesicle refilling. Another possible explanation for synaptic depression is decreased Ca^{2+} entry due to inactivation of Ca^{2+} channels (Forsythe et al, 1998; Xu and Wu, 2005). Other mechanisms may depend on modulators, as for example endocannabinoids (Freund and Hájos, 2003; Freund et al, 2003) released by the presynaptic- (Straiker and Mackie, 2009) or postsynaptic elements (Fukudome et al, 2004; Uchigashima et al, 2007; Ohno-Shosaku and Kano, 2014). In the extreme, some synapses arising from the same presynaptic neuron may display synaptic facilitation in one target and synaptic depression in another target (Muller and Nicholls, 1974; Markram et al, 1998; Thomson et al, 2002a,b) depending on local $[Ca^{2+}]_i$ and modulatory messengers. Nevertheless, if the postsynaptic target, the extracellular conditions and the presynaptic stimulus remain constant, the short-term synaptic plasticity can be thought of as entirely dependent on the presynaptic element and the presynaptic dynamics becomes a reliable indicator for the dynamics of the whole synapse (Gupta et al, 2000; Tecuapetla et al, 2007; Savanthrapadian et al, 2014; Sedlacek and Brenowitz, 2014; Beierlein et al, 2003; Blackman et al, 2013; Wang et al, 2006). For instance, a common finding is that basket cells or neurons containing parvalbumin (PV-immunoreactive), especially the fast-spiking interneurons, exhibit short-term depression (Massi et al, 2012; Tecuapetla et al, 2007; Gittis et al, 2010; Planert et al, 2010), as well as the climbing fibers on Purkinje neurons (Dittman et al, 2000; **?**; **?**), the collateral projections between striatal projection neurons (Hoffman et al, 2003; Tecuapetla et al, 2007), and various synapses in the cochlear nucleus (MacLeod et al, 2007; Wang et al, 2011; MacLeod, 2011).

Short-term facilitation

Short-term facilitation or STF occurs when synaptic efficacy increases for brief periods and involves processes that are typically independent of protein expression (Fig. 1.1B). Besides STF there are different kinds of facilitation, which are distinguished by the time scales in which they occur, and represent different physiological processes. Sensitization is a process in which repeated trains of action potentials lead to a progressive increase of the response (Marinesco et al, 2004; Fulton et al, 2008; Nikolaev et al, 2013). Another kind of facilitation, called synaptic enhancement, occurs in two phases: the first one lasting tens of milliseconds, followed by a slower phase lasting hundreds of milliseconds (McNaughton et al, 1978). In a longer time scale, augmentation lasts several seconds and post-tetanic potentiation may last from 30 seconds to several minutes (Zucker and Regehr, 2002).

STF may be explained by diverse presynaptic phenomena. Quantal analysis has revealed that synaptic enhancement may be due to an increment in the probability of release (p) or to an increase in the number of release sites (n) (Clements, 2003; Clements and Silver, 2000). Residual Ca^{2+} has been proposed repeatedly to account for these changes, the hypothesis being that Ca^{2+} accumulation in the presynaptic terminal after an action potential increases the amount of released neurotransmitter if subsequent action potentials occur close enough in time (Katz and Miledi, 1968; Ravin et al, 1999; Van der Kloot and Molgo, 1993). Importantly, buffering presynaptic Ca^{2+} reduces both facilitation and augmentation (Magleby, 1979; Regehr et al, 1994; Stevens and Wesseling, 1999; Salin et al, 1996). Nevertheless, some synapses are remarkably fast in replenishing the readily releasable pool (Trommershäuser et al, 2003; Neher, 2010; Watanabe et al, 2013), as is the case for parallel fibers synapsing onto Purkinje cells (Dittman et al, 2000), terminals of cholecystokinin (CCK) containing and somatostatin (SOM) containing interneurons (Blackman et al, 2013; Savanthrapadian et al, 2014), regular spiking pyramidal neurons synapsing onto somatostatin-expressing low threshold-spiking (LTS) neurons in the neocortex (Thomson et al, 1993; Markram et al, 1998; Reyes et al, 1998; Beierlein et al, 2003; Hayut et al, 2011), Schaffer collaterals onto SOM interneurons (Sun et al, 2009), and striatal projection neurons onto target cells in other basal ganglia nuclei (Sims et al, 2008; Miguelez et al, 2012; Hernández-Martínez et al, 2015), among others.

Short-term biphasic plasticity

During a train of presynaptic action potentials, some synapses may undergo a combination of facilitation followed by depression, a phenomenon called short-term biphasic plasticity or STB (Markram et al, 1998; Wang et al, 2006; Savanthrapadian et al, 2014) (Fig. 1.1C). This is the case for the terminals from SOM containing interneurons of the hippocampus (Savanthrapadian et al, 2014). The mechanisms behind this type of plasticity have not been studied in depth, but basic ex-

planations have been proposed through the use of mathematical models (Tsodyks and Markram, 1997; Hennig, 2013). A diverse collection of microcircuits capable of displaying multiple states, arguably fulfilling different functions, has been revealed (Traub et al, 2004; Klausberger and Somogyi, 2008; Carrillo-Reid et al, 2009; Kopell et al, 2011). Such a multifunctional capability can be explained by combining the dynamics of synaptic plasticity mentioned above with the intrinsic properties of neurons, all subject to neuromodulation. We now concentrate on explaining how these synaptic dynamics combine from a functional perspective

Short-term synaptic plasticity as a temporal filter in brain microcircuits

As already pointed out, different classes of synapses behave in diverse ways with respect to time. The classic role of synapses is to mediate the induction of postsynaptic responses by presynaptic action potentials. Therefore, a most invoked hypothesis has been that they act as temporal filters for incoming input (Fortune and Rose, 2000; Buonomano, 2000; Zucker and Regehr, 2002; George et al, 2011; Dittman et al, 2000; Wang et al, 2006; Abbott and Regehr, 2004).

Each type of short-term synaptic plasticity mentioned above works as an electrical frequency filter, as revealed by experiments exploring the functional relationship between the magnitude of postsynaptic responses induced by a stimulus train at given stimulus frequencies (bode-plots) (Markram et al, 1998; Dittman et al, 2000; Izhikevich et al, 2003). In general, synapses displaying short-term depression (STD) show progressively decreased responses to high frequency inputs and tend to conserve low frequency inputs intact. In contrast, synapses that exhibit short-term facilitation (STF) amplify high frequency inputs and tend to produce responses of constant amplitude for low-enough input frequencies. For these reasons, synapses exhibiting STD, STF, and STB profiles have been described as equivalent to low, high, and band pass filters, respectively (Markram et al, 1998; Dittman et al, 2000; Fortune and Rose, 2000; Wu et al, 2001; Izhikevich et al, 2003; Abbott and Regehr, 2004; Lange-Asschenfeldt et al, 2007). However, it is worth remarking that synapses that display STF are not quite analogous to a high-pass filter because they tend to amplify high-frequency inputs. By extension, the commonly accepted analogy between band-pass filters and synapses exhibiting STB profiles is also not quite correct. Nevertheless, an important consequence of the observations above is that, synaptic function is not limited to excitation and inhibition and includes temporal filtering as an important function that has been proposed to play a role in adaptation, gain control, spatial detection, and rhythm generation (Wang and Buzsáki, 1996; Whittington and Traub, 2003; Sirota et al, 2008; Cardin et al, 2009). For instance, STF has been postulated as a mechanism for the generation of low frequency oscillations in the θ-range (Whittington and Traub, 2003; Sirota et al, 2008; **?**). STB could be playing a role in synchronizing neuronal ensembles in the β-band frequency, a main oscillatory behavior observed in Parkinson disease (Hammond

et al, 2007; te Woerd et al, 2014). STD helps in determining sensory habituation; responses showing a greater efficacy at the onset of an input and at low frequencies (Abbott and Regehr, 2004). Depressing synapses have been proposed to produce more reliable transmission in response to new stimuli and may contribute to the removal of redundant correlated inputs, allowing information to flow more efficiently (**??**). Because of the multiple functions mentioned above, there is an increasing interest in incorporating the models of short-term synaptic plasticity into larger circuit models.

Some mathematical models of short-term synaptic plasticity

Although the postsynaptic terminal also contributes to STSP (e.g. receptor desensitization and retrograde messengers), the presynaptic processes involving the dynamics of transmitter release and the replenishment of the vesicle pool are arguably among the most important determinants of short-term synaptic plasticity (Körber and Kuner, 2016). Each of these processes depends on ion channels, pumps, enzymes, vesicle recycling and other factors (Trommershäuser et al, 2003; Neher, 2010; Dutta Roy et al, 2014). Ideally, models try to lump all these pieces into the least possible number of variables and parameters while capturing the essence of the biophysical processes involved. The existing mathematical models of neurotransmitter release based on experimental data try to support and predict biophysical and behavioral aspects of synaptic transmission at different levels of detail (Trommershäuser et al, 2003; Pan and Zucker, 2009; Neher, 2010), including priming, vesicle-fusion (Magleby and Zengel, 1982; Blank et al, 2001; Millar et al, 2005; Taschenberger et al, 2005) and endocytosis (Balaji and Ryan, 2007; Granseth et al, 2006). We next review three of the most widely used models of short-term synaptic plasticity, and later we propose a new generalized model capable of reproducing a vast repertoire of synaptic plasticity dynamics that can be tested for different synapses. The main variables in models of synaptic plasticity typically include the amount of neurotransmitter being released, $NT(t)$, detected by passive postsynaptic receptors of the membrane. Let $N(t)$ be the number of vesicles available for release, each vesicle assumed to contain the same amount of neurotransmitter and let $p(t)$ the release probability. Assuming that any two vesicles are released independently of each other, the average release can then be thought of as

$$NT \propto N(t)p(t). \tag{1.1}$$

Assuming that the released neurotransmitter is instantly detected, the postsynaptic conductance $g(t)$, can be assumed to be proportional to the amount of neurotransmitter released

$$g(t) = \bar{g}NT(t). \tag{1.2}$$

Where $\bar{g}$ is the maximal conductance of the postsynaptic element. For simplicity, gis assumed to be a constant. However, to model synaptic desensitization, $\bar{g}$ can

be assumed to change in time. For instance, $\bar{g}$ can be a function of the amount of neurotransmitter concentration ($\bar{g} \to 0$). One model originally developed by (Liley and North, 1953) for the neuromuscular junction explains synaptic depression by vesicle depletion during thetanic stimulation of the rat neuromuscular junction. This process was described by a first order, non-autonomous differential equation of the form

$$\partial_t n = \frac{1-n(t)}{\tau_n} - \sum_{i=1}^{n} \delta\,(t-t_i) \cdot p \cdot n(t), \tag{1.3}$$

where $n(t)$ is the proportion of occupancy of the readily releasable pool and p is a parameter representing the probability of release. The first part of Eq. (1.3) corresponds to the total replenishment of the release pool with a time constant τ_n. The second part corresponds to instantaneous release of neurotransmitter assuming action potentials arriving at times t_i, with function $\delta(s)$=1 for s=0 and 0 otherwise. This model accurately fits the behavior of a number of depressing synapses with a variety of time constants (Liley and North, 1953; Tsodyks and Markram, 1997). Note that replenishment and probability of release are part of the same equation. A more detailed model (Tsodyks and Markram, 1997) characterized synaptic connections by describing the proportion of vesicles in three active states, effective (E), inactive (I), and recovered (R), respectively, with dynamics given by

$$\partial_t R = \frac{I}{\tau_{rec}} - U_{SE} \cdot R \cdot \delta(t-t_i), \tag{1.4}$$

$$\partial_t E = -\frac{E}{\tau_{inac}} + U_{SE} \cdot R \cdot \delta(t-t_i), \tag{1.5}$$

$$I \propto 1-R-E. \tag{1.6}$$

An action potential arrives at the terminal at time t_i, instantaneously activating a fraction of resources. This is controlled by a parameter U_{SE} that controls the utilization of synaptic efficacy. The recovery process begins as soon as the utilization of resources does. The net postsynaptic current is assumed to be proportional to the fraction of resources in the effective state, which inactivates with a time constant τ_{inact} and recovers with a time constant τ_{rec}. However, synaptic facilitation could not be fitted until the model included a facilitating mechanism (Markram et al, 1998). Thus, short-term depression and facilitation had to be approximated with two independent variables, R and u, respectively, and time-dependent changes given by

$$\partial_t R = \frac{1-R}{D} - u \cdot R \cdot \delta(t-t_i), \tag{1.7}$$

$$\partial_t u = \frac{U-u}{\tau_{inac}} + U_{SE} \cdot (1-u) \cdot \delta(t-t_i). \tag{1.8}$$

The first equation models the exponential recovery (or replenishment) to the value $R=1$ with a rate constant D^{-1}, minus the instantaneous release of neurotransmitter assuming action potentials arriving at times t_i. Notice the similarity with the Liley and North (1953) model. The second equation describes the time-dependent evo-

lution of release after the ith stimulus. Again, there is an exponential recovery of u to its resting value U in the absence of inputs (synaptic efficacy during the first action potential), and an increase proportional to $U(1-u)$ when inputs arrive. This model explains the kinetics of a variety of synapses (Markram et al, 1998; Izhikevich et al, 2003; Gupta et al, 2000) and reproduces the bode-plots of facilitating and depressing synapses. However, the biphasic synapse, at least in the striatum, is not reproduced. Thus, a more detailed model of STSP was proposed (Dittman et al, 2000) with very different synaptic dynamics depending on the contributions of various calcium-dependent mechanisms. The two main dynamic variables in this model are facilitation and refractory depression, emphasizing the role of residual calcium (Ca_{res}). An end-plate synaptic current

$$EPC = \alpha \cdot N_T \cdot F \cdot D \tag{1.9}$$

where NT is the number of release sites and the fraction of released sites is divided into two parts, facilitation (F) and depression (D), respectively, and α is a scaling factor for the averaged miniature end plate postsynaptic current EPC (mESC) amplitude. Enhancement of release was assumed to be a calcium dependent increase from an initial value F_1 dependent on a calcium-bound molecule $CaXF$ with dissociation constant K_F .

$$F(t) = \frac{CaX_F}{CaX_F + K_F} \tag{1.10}$$

where CaX_F was modeled with first order kinetics and a time constant τ_F after a jump of size ΔF during the action potential arriving at time t_i

$$\partial_t CaX_F = -\frac{CaX_F}{\tau_F} + \Delta_F \cdot \delta(t - t_i) \tag{1.11}$$

If CaX_F is allowed to decay to 0, a correction to Eq. (1.10) has to be made with the addition of a baseline release probability F_1 when $CaX_F = 0$

$$F(t) = F_1 + (1 - F_1)\frac{CaX_F}{CaX_F + K_F}. \tag{1.12}$$

Now, $F(t)$ ranges from F_1 to 1 as CaX_F increases from 0. After the arrival of an action potential, CaX_F increases to ΔF and $F(t)$ increases to

$$F_2 = F_1 + (1 - F_1)\frac{\Delta_F}{\Delta_F + K_F}. \tag{1.13}$$

If a second stimulus arrives when no recovery from the refractory state has occurred, then the second EPC will be determined by the increased release probability F_2 and the remaining number of release sites as follows:

$$EPC_2 = \alpha \cdot N_T \cdot (1 - D_1 \cdot F_1) \cdot F_2. \tag{1.14}$$

Since $F_2 \leq 1$, the initial probability of release has as upper bound

$$F_1 = \frac{1}{1+\rho}, \tag{1.15}$$

where

$$\rho = \frac{EPC_2}{EPC_1} = \frac{(1-F_1)F_2}{F_1}$$

is the facilitation ratio. The depression mechanism assumes three active states: R is a refractory state, T is a transitional state and N the readily releasable sites. A total of release sites NT is determined as:

$$N_T = R + T + N.$$

Similar to the dynamics of facilitation, recovery rate was assumed to be depend on the concentration of a Ca-bound molecule CaX_D with unbinding time constant τ_D defining the dynamics

$$\partial_t CaX_D = -\frac{CaX_D}{\tau_F} + \Delta_D \cdot \delta(t - t_i), \tag{1.16}$$

in which bound Ca is assumed to jump which instantaneously rises by ΔD units after an action potential arrives at time t_i . The release probability is described by a depression variable $D = N/N_T$ (number available sites / total number of sites) with

$$\partial_t D = (1-D) \cdot k_{recov} CaX_D - D \cdot F \cdot \delta(t - t_i), \tag{1.17}$$

where

$$k_{recov}(CaX_D) = (k_{max} - k_i)\frac{CaX_D}{CaX_D - K_D} + k_i.$$

After the first action potential, NT, F_1, and D_1 sites have released transmitter and pass to a refractory state, leaving $NT(1 - F_1 D_1)$ sites available to release. Then

$$D_2 = 1 - F_1 \cdot D_1. \tag{1.18}$$

For simplicity, $D_1 = 1$ if all sites are available to release. Thus, Eq. (1.18) can be written as $D_2 = 1 - F_1$. This model also captures a spectrum of synaptic dynamics of STSP, including the dynamics during irregular stimulus trains (Dittman et al, 2000). Nevertheless, the ideal to lump the various physiological phenomena into a minimal, simple and intuitive set of variables is partially lost, in particular, because extra assumptions about calcium management have to be made. In the next section we propose a simplified model that generalizes some of the ideas previously mentioned, which we have been testing in a set of GABAergic striatal synapses. The proposed model aims to recover the ideal of using the least number of variables and assumptions. This does not mean that more detailed models with experimentally testable variables are not needed.

A new model for short-term synaptic plasticity

The present computational model was generated by characterizing short-term synaptic plasticity with two main dynamic variables: occupancy of vesicles in the readily releasable pool $x(t)$ (between 0 and 1) and the probability of release $p(t)$. Assume a presynaptic neuron firing a train of action potentials at times t_k, $k = 0, 1, .., n$. The release dynamics in the presynaptic terminal can be described by the product xp with rules of evolution given by

$$\partial_t x = x^{\alpha} \frac{x_{\infty} - x}{\tau_x} - px \sum_{k=1}^{n} \phi(t - t_k) \tag{1.19}$$

$$\partial_t p = p^{\beta} \frac{p_{\infty} - p}{\tau_p} - (1 - p)x \sum_{k=1}^{n} q(h_k)\phi(t - t_k) \tag{1.20}$$

where,

$$\phi(t; t_k, \tau_{\phi}) = (t - t_k) \exp\left[1 - \left(\frac{t - t_k}{\tau_{\phi}}\right)\right]$$

represents the time course of activation of the presynaptic release machinery and

$$q(h; \bar{q}, \tau_q) = \bar{q} h \exp\left(1 - \frac{h}{\tau_q}\right)$$

is a function that models the dependence of the increase in the probability of release on the inter-spike interval h, caused by a presynaptic action potential. The parameter τ_q is a time constant after which the increase in p starts to decay. The parameters α and β that allow better adjustment of experimental data. For instance, $(\alpha, \beta) = (1, 0)$ describe logistic and linear dynamics for x and p, respectively, in the absence of inputs. The parameters and represent the steady state occupancy of the readily releasable pool and the probability of release, respectively. τ_x and τ_p are time constants for the recovery of the releasable pool from depression and the recovery from facilitation, respectively. The function $\phi(t)$ represents the shape of the input (e.g. the shape of the Ca^{2+} transients resulting from an afferent volley). Increase in $p(t)$, denoted by $q(h)$ can be assumed to depend on the presynaptic interspike intervals (h) with as the maximum increase $\bar{q}$ in the probability of release, reached at a time τ_q. In most experiments we have used trains of 20 Hz with regular interspike intervals. Up to now, this model has been able to reproduce, within reasonable approximation, the dynamics of a variety of inhibitory inputs onto striatal projection neurons (Körber and Kuner, 2016) (Fig. 1.2). The present contribution was published in its present form in order to be tested by other researchers and be able to receive feed-back.

Conclusion

The anatomical connections of neuronal networks, the intrinsic properties of neurons and the nature of their synapses, excitatory or inhibitory, are not sufficient when making considerations to model a microcircuit. One reason is STSP , in which synapses change as a function of time in different ways. STSP plays several roles that are important for information processing and coding within circuits. The various synaptic dynamics supply the circuit with a variety of frequency filters that modulate the computational and the informational transfer capabilities of the network. Although existing models that approximate experimentally recorded short-term synaptic plasticity can be very complex there is still a need for simple models based on only a few variables that can be used as a first probe to explore the variety of synapses found in many circuits. The general and yet simple model proposed here approximates all the various short-term synaptic plasticity found in the literature. In addition, synapses do not work in "voltage-clamp" mode. When recorded in current clamp, the decay of synaptic events has to include the membrane time constant which induces different kinds of temporal and spatial summations which will modify the class of filtering the synapses can make. In turn, the membrane time constant can change due to postsynaptic intrinsic currents that can be open or close depending on, for example, modulatory transmitters that activate G-protein coupled receptors. These last phenomena increases the richness and possibilities of neuronal circuits dynamics.

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1.2 Abbreviations

ACh	acetylcholine
DA	dopamine
$[Ca^{2+}]_i$	intracellular Ca^{2+} concentration
CB	calbindin
CCK	cholecystokinin
EPSC	Excitatory postsynaptic current
EPSP	Excitatory postsynaptic potential
GABA	Gamma-aminobutyric acid
IPSC	Inhibitory postsynaptic current
IPSP	Inhibitory postsynaptic potential
LTS	Low threshold spiking
LTSP	Long terms synaptic plasticity
PV	parvalbumin
SOM	somatostatin
STD	short term depression
STF	short term facilitation
STB	Short term biphasic plasticity
STSP	Short term synaptic plasticity

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Figures

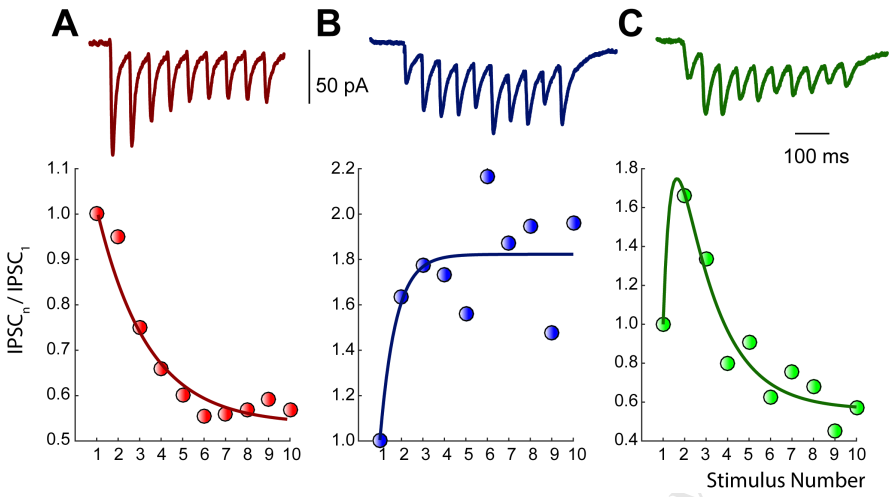

Fig. 1.1 Examples of inhibitory inputs onto striatal projection neurons with different short-term synaptic plasticity profiles. A) Synapse with depression. B) Facilitating synapse. C) Biphasic plasticity.

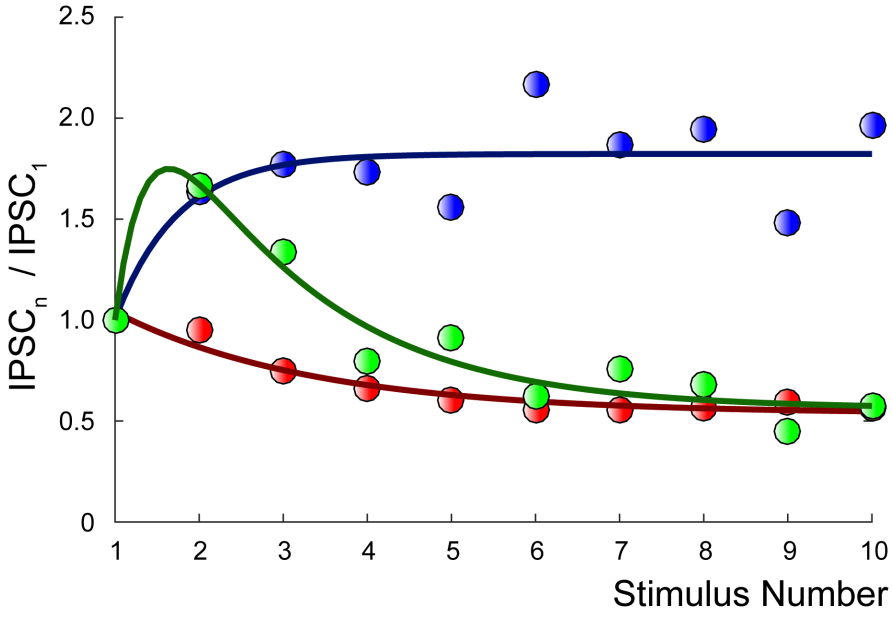

Fig. 1.2 Fitting of the proposed model to different types of short-term synaptic plasticity recorded from spiny neurons in the rat striatum. Dots represent IPSCs amplitudes in Figure 1.1 and lines represent fitted curves of the computed normalized response by the proposed model.