

# Multistability Arising from Synaptic Dynamics

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## Definition

The strength of a synapse imparted by a presynaptic neuron onto its postsynaptic target can change as a function of the activity of the presynaptic neuron. This change is referred to as short-term synaptic plasticity. Networks of neurons connected with plastic synapses have the potential ability to display multiple stable solutions either at different parameter values or for the same set of parameters. This latter property is known as multistability. Self-consistency between the network frequency and the level of plasticity is needed to ensure multistability.

## Description

The central nervous system (CNS) controls a vast array of behaviors that include both basic functions such as processing of sensory input (Sharp et al. 1990), regulating circadian rhythms (Piggins and Guilding 2011), coordinating motor output (Marder and Calabrese 1996), and more complex functions such as spatial navigation (O'Keefe 1991), decision making, and memory formation (Treves and Rolls 1994). Although the CNS includes a large number of neurons and an even larger number of synaptic connections, these constitute a finite number of networks and few compared to the seemingly limitless number of behavioral tasks. This disparity strongly indicates that the networks of the CNS can reorganize to produce multiple outputs.

The output of a neuronal network can be quantified in a number of ways. The firing rate of the network neurons, for example, may encode information or, alternatively, the output may be coded in the pattern of activity of sub-networks of neurons. The specific timing of spikes or bursting events is also a way in which networks direct their output. In many contexts, to be useful to downstream targets, the neuronal output must be stable, resistant to perturbations or noise. From a mathematical viewpoint, this implies that the output is likely to be a stable periodic solution of a set of underlying equations that govern the network activity.

In order to have multiple functional roles, a network must have the ability to exhibit multiple stable outputs. There are two obvious ways in which this ability may arise. One is through neuromodulation, where different stable solutions exist for different parameter values or for different inputs to the network. The role of the modulator is to change parameter values between these states depending on the task to be completed. A second way is through multistability where more than one stable solution exists for the same set of parameter values. Which stable state ends up being the attracting solution depends on the initial conditions, i.e., the state at which the network becomes employed.

Short-term synaptic plasticity (STSP) refers to the ability of a synapse to change its synaptic strength depending on the frequency at which it is being activated by a presynaptic neuron.

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Facilitation refers to case where the strength is an increasing function of frequency and depression when it is a decreasing function. Significant research has been conducted to understand the mechanisms underlying plasticity. How STSP can shape the output of a neuronal network is also a central focus of investigation.

Just as there are synaptic rise and decay rates associated with different neurotransmitter receptor types, there are also different rates associated with facilitation or depression of a synapse. STSP acts at short timescales and, as a form of synaptic plasticity, is distinct from plasticity forms that act at long timescales: long-term potentiation and depression (LTP and LTD) and spike timing-dependent plasticity (STDP). LTP, LTD, and STDP last for very long time durations on the order of hours to weeks and are mainly associated with changes in synaptic strength due to the relative timing of firing in pre- and postsynaptic pairs. Timescales associated with STSP are on the order of several milliseconds to seconds, the same order as the rise and decay of excitatory, inhibitory, and typical voltage-gated ionic currents.

Below, we discuss a few basic models of STSP and provide some examples of how multiple stable solutions are created in small neuronal networks that involve STSP. Synapses that exhibit STSP have different steady-state amplitudes for different presynaptic firing rates. Multistability arises when the components of the network can be organized to access different values of these steady-state behaviors. This can occur through “fine-tuning” in predominantly feed-forward networks or through “self-consistency” in feedback settings. The role that STSP plays in creating these opportunities for multistability will be discussed below.

## Mathematical Models of Short-Term Synaptic Depression

Three phenomenological models of short-term synaptic plasticity are reviewed. The first two, the AVSN model of Abbott et al. (1997) and the TM model (Tsodyks and Markram 1997), are the most popular and are generally used in conjunction with networks of spiking neurons. The third model, BMN (Bose et al. 2001), is relevant to neurons, such as bursters, that display slow oscillations and has the added feature that it separates the dynamics of synaptic plasticity from those of synaptic rise and decay.

For simplicity, we focus on models that only involve synaptic depression. In the Abbott et al. model, synaptic depression is based on the assumption that when a presynaptic spike results in transmission, the synaptic strength is decremented by some fraction  $f$ . Between spikes, the synapse recovers from depression. If  $A(t)$  denotes the synaptic strength at time  $t$  and  $t_i$  denotes a sequence of spike times, then at each spike time

$$A(t_i^+) = fA(t_i^-),$$

where the superscript  $+$  denotes limit from above and  $-$  from below. Between spikes, the variable is allowed to recover according to

$$A' = (1 - A)/\tau_A$$

for time constant  $\tau_A$ . If a set of presynaptic spikes arrives periodically with rate  $r$ , then the steady-state synaptic amplitude  $A(r)$  can be calculated as

$$A(r) = \frac{1 - e^{-1/r\tau_A}}{1 - f e^{-1/r\tau_A}}. \quad (1)$$

In this model, the dynamics of depression and those of synaptic efficacy are both modeled by a single variable  $A$ .

The TM model describes synaptic plasticity by partitioning synaptic resources into three states: effective ( $E$ ), inactive ( $I$ ), and recovered ( $R$ ), with  $E + R + I = 1$ . Each presynaptic spike at  $t = t_{AP}$  utilizes a fraction  $U_{SE}$  of recovered resources transferring them to the effective pool. Resources in this group decay with time constant  $\tau_{inact}$  to the inactive pool. From here, resources reenter the recovered pool with time constant  $\tau_{rec}$ .

$$\begin{aligned} R' &= \frac{I}{\tau_{rec}} - U_{SE}R\delta(t - t_{AP}) \\ E' &= -\frac{E}{\tau_{inact}} + U_{SE}R\delta(t - t_{AP}). \end{aligned}$$

If action potentials arrive with interval  $\Delta t$  and if this time is large compared to  $\tau_{inact}$ , then the postsynaptic current at each action potential can be calculated from

$$PSC_{n+1} = PSC_n(1 - U_{SE})e^{-\Delta t/\tau_{rec}} + A_{SE}U_{SE}\left(1 - e^{-\Delta t/\tau_{rec}}\right), \quad (2)$$

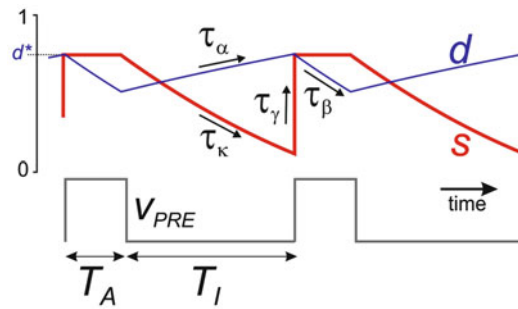
where  $A_{SE}$  is the maximal  $PSC$  that can be produced if all resources immediately go from  $R$  to  $E$ . As with the AVSN model, the efficacy and timescales associated with the synaptic current are modeled by the same set of variables that describe depression.

The BMN model is different than the above models in two ways. First, it dissociates the dynamics of plasticity from those of synaptic efficacy. Second, it is designed to model the effect of slow wave or bursting oscillations, not just spiking neurons. A variable  $d$  keeps track of the level of depression of the synapse, while the variable  $s$  transmits the synaptic efficacy. These variables are linked at  $t = t_{sp}$  defined by the moment when the presynaptic voltage  $v$  increases through a threshold  $v_\theta$ . Both are governed by first-order equations:

$$d' = \frac{1 - d}{\tau_\alpha} H(v_\theta - v) - \frac{d}{\tau_\beta} H(v - v_\theta) \quad (3)$$

$$s' = \frac{d(t_{sp}) - s}{\tau_\gamma} H(v - v_\theta) - \frac{s}{\tau_\kappa} H(v_\theta - v), \quad (4)$$

where  $H(x)$  is the Heaviside function equal to one when  $x \geq 0$  and zero otherwise. The postsynaptic current generated by this model is simply  $I_{syn} = \bar{g}_{syn}s(v - E_{syn})$  where  $\bar{g}_{syn}$  and  $E_{syn}$  are the maximal conductance and reversal potential of the synapse. Figure 1 shows an example of how the  $s$  and  $d$  variables interact in the BMN model. Equations 3 and 4 are coupled only when the presynaptic neuron crosses  $v_\theta$  at which point the value of  $s$  is allowed to evolve towards the value  $d(t_{sp})$ . If  $\tau_\gamma$  is small, then this effectively serves as an instantaneous reset. Note that the dynamics of  $s$  then remains uncoupled from those of  $d$  until the next moment that  $v$  increases through threshold. In particular, when the presynaptic neuron is below threshold, the synaptic current decays with time constant  $\tau_\kappa$  that is independent of the recovery of synaptic resources which is dependent on  $\tau_\alpha$ . If  $A(t)$  from the



**Fig. 1** The time trace of the  $d$  and  $s$  variables for the BMN model plotted in response to the presynaptic activity  $V_{pre}$ . The time constants that control depression ( $\tau_\beta$ ), recovery ( $\tau_\alpha$ ) and decay ( $\tau_\kappa$ ) of the synapse are shown.  $s$  approaches the value of  $d$  at the onset of activity ( $d^*$  at steady state) with a fast time constant ( $\tau_\gamma$ )

AVSN model and the  $R$  variable from the TM model were plotted, they would qualitatively resemble the  $d$  variable of the BMN model (Fig. 1), except that, in the former two models, the variables would instantaneously be decremented at the time of a spike and recover between spikes, as opposed to the gradual decline over the time  $T_A$  in the BMN model. If a periodic train of presynaptic spikes or bursts with active time given by  $T_A$  and inactive time given by  $T_I$  drives Eqs. 3 and 4, then the steady-state amplitude for the synaptic resources, called  $d^*$ , measured at the time that  $v$  increases through  $v_\theta$  is

$$d^* = \frac{1 - e^{-T_I/\tau_\alpha}}{1 - e^{-T_A/\tau_\beta} e^{-T_I/\tau_\alpha}}. \quad (5)$$

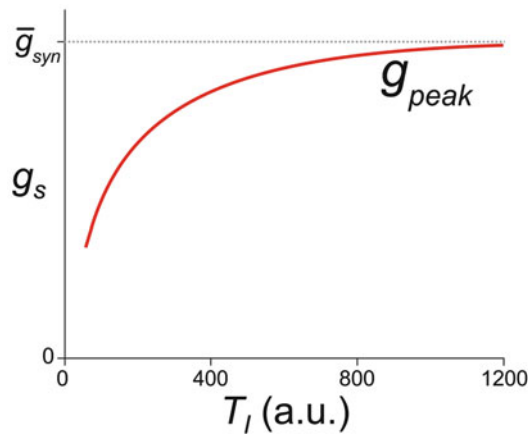
The peak synaptic strength  $g_{peak}$  can be calculated as the product of  $d^*$  with the maximal synaptic conductance

$$g_{peak} = \bar{g}_{syn} d^* \quad (6)$$

Note that for fixed  $T_A$  the expression for  $d^*$  is equivalent to that of  $A(r)$  given in Eq. 1 in the AVSN model. Further,  $T_I \rightarrow \infty$ ,  $d^* \rightarrow 1$ , monotonically showing that the level of available synaptic resources recovers back to a maximal value as the inactive time increases (equivalently as the frequency tends to 0).

All three models describe the short-term dynamics of a synapse when the presynaptic neuron is intrinsically rhythmic. In this case, the parameters  $r$  in the AVSN model,  $T_{AP}$  in the TM model, and  $T_I$  and  $T_A$  in the BMN model can be adjusted to achieve a specific synaptic strength. In particular, in a feed-forward or driven network, the level of plasticity can be finely tuned by controlling the frequency of the drive. In the case of a depressing synapse, strong drive leads to higher frequencies of synaptic usage, leading to weaker synapses. The opposite is true for lower-frequency driving. Figure 2 shows how the peak synaptic strength  $g_{peak}$  increases as a function of increasing  $T_I$  ( $T_A$  is kept fixed) for the BMN model. A qualitatively equivalent graph arises using Eq. 1 by plotting  $A(r)$  versus  $1/r$  or by using Eq. 2 to plot the steady-state PSC versus  $\Delta t$ . As the period increases (frequency decreases), the peak synaptic strength increases to the maximal level  $\bar{g}_{syn}$ .

In a feedback network containing many synapses with STSP, the quantities  $r$ ,  $T_{AP}$ ,  $T_I$ , and  $T_A$  do not necessarily remain parameters. Instead they can be affected by the synaptic inputs that the neuron receives. Thus to obtain periodic solutions, the plasticity variables must satisfy a consistency condition. Namely, network period is a function of synaptic strength and, alternatively, peak synaptic strength is a function of network period. When these two are self-consistent, a periodic



**Fig. 2** For a depressing synapse, the peak synaptic strength is an increasing function of the presynaptic silent duration  $T_I$  as derived from Eqs. 5 and 6

solution can occur. Multistability results when this consistency condition can be satisfied in different ways at different network periods.

## Fine-Tuning Synaptic Strength in Feed-Forward Networks

In many central pattern-generating networks, the constituent neurons maintain a constant relative phase with respect to the network cycle even as the period of oscillations varies. To examine the role of STSP in such phase constancy, consider a network of two neurons  $O$  and  $F$  in which  $O$  is an oscillatory pacemaker neuron (with period  $P$ ) which inhibits  $F$  and  $F$  rebounds from this inhibition to fire. After each inhibitory input to  $F$ , the time  $\Delta t$  that  $F$  takes to reach threshold can be determined. This defines a phase  $\phi = \Delta t/P$  as the phase at which  $F$  fires. Manor et al. (2003) showed how synaptic depression could help the  $O$ – $F$  network maintain phase. Namely, if  $O$  has small period, its synapse to  $F$  is depressed and thus weak. There is little effect on the timing  $\Delta t$  of  $F$  firing. In this case, there is a periodic solution in which the time to  $F$  firing is basically constant and controlled by parameters that are intrinsic to  $F$ . Alternatively, when the period of  $O$  is increased by increasing  $T_I$ , then its synapse to  $F$  has a chance to recover and become stronger. Now the firing time  $\Delta t$  depends more strongly on  $g_{\text{peak}}$  and the decay rate of inhibition  $\tau_\kappa$ . This represents another stable solution where the phase of firing is controlled by the interplay of parameters associated with the  $O$  synapse and those intrinsic to  $F$ . In Manor et al. 2003, it is shown that  $\Delta t$  satisfies an equation of the form

$$c_1 e^{-\Delta t/\tau_w} + c_2 g_{\text{peak}} e^{-\Delta t/\tau_\kappa} = c_3, \quad (7)$$

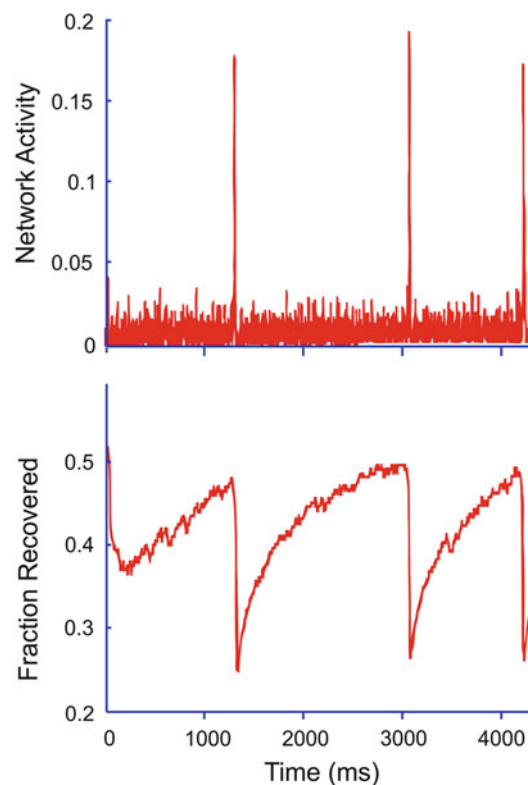
for  $c_1, c_2 > c_3 > 0$  and  $\tau_w$  being a time constant associated with a potassium current in  $F$ . At small periods,  $g_{\text{peak}}$  is small and the first term in Eq. 7 dominates. As can be seen,  $\Delta t$  is independent of  $T_I$ , and therefore,  $\phi = \Delta t/P \sim 1/P$ . At larger periods,  $g_{\text{peak}}$  given in Eq. 6 increases with  $T_I$  and the second term dominates. In this case  $\Delta t$  changes with  $P$  leading to a complicated dependence of phase with  $P$  [see (Manor et al. 2003) for the full details].

The main point to convey here is that, in a feed-forward network, if the peak synaptic strength is controlled by the pacemaker, then it can be effectively treated as a parameter. In particular, by controlling the period of the pacemaker,  $g_{\text{peak}}$  can be fine-tuned to any desired value leading to

different kinds of solutions. Also see Carver et al. (2008) and Lewis and Maler (2002) where similar ideas are employed in a feed-forward context.

## Self-Consistency in Feedback Networks

In Tsodyks et al. (2000), Tsodyks et al. showed how synaptic depression can be used to obtain population bursts in cortical excitatory-inhibitory ( $E-I$ ) networks. Tabak et al. (2000) showed a similar result in a model of development of the chick spinal cord using a rate model that only involved excitation. Both models operate using similar principals. In the Tsodyks et al. study, a network of 400  $E$  cells was mutually and randomly coupled to a set of 100  $I$  cells. All synapses display both synaptic facilitation and depression of varying degrees. The effect of synaptic depression was more relevant, as facilitation plays less of a role in creating the population burst. Focusing solely on synaptic depression, if the  $E$  cells have a high firing rate, then their synapses weaken and have less effect on their postsynaptic targets. At lower frequencies, their synapses have a chance to recover so that, when they fire, they can strongly recruit other  $E$  and  $I$  cells into the population activity. In effect, the model utilizes the two distinct stable states (strong versus weak synapses) that are present in the feed-forward network described in the previous section, but now finds a way to internally toggle between the two. Figure 3 is from Tsodyks et al. (2000) in which the top panel shows the fraction of neurons that are active in a specified time bin and the bottom panel the time course of synaptic resource recovery from depression, averaged over all  $E$  cells. As the top panel shows, there are bursts of network activity where larger numbers of neurons are coactive.



**Fig. 3** Population bursts in a network model of  $E$  and  $I$  neurons coupled with dynamic synapses. *Top panel* shows network population activity. *Bottom panel* depicts the average synaptic resources for each  $E$  cell (Modified from Tsodyks et al. (2000))



Correspondingly, associated with each burst is a rapid drop in the average synaptic resources, followed by recovery on a longer timescale. Note that the recovery dynamics shown in the bottom panel corresponds to the trace of the  $d$  variable in Fig. 2 of the BMN model for the case where  $T_A$  is very short.

A critical reason that population bursts exist in the Tsodyks et al. model is the heterogeneity in the basal firing rates of the individual  $E$  cells. The network is tuned so that some fractions of  $E$  cells have high spontaneous firing rates. It is the firing of this group that initiates recruitment of other  $E$  cells that form the burst. Self-consistency then dictates that the level of available synaptic resources is sufficient to continue the recruitment of enough cells to form the burst. This will occur only if the recruitment occurs after a suitably (and self-consistently) long inter-burst interval. See Tsodyks et al. (2000) for further details including how the existence of the burst depends on the maximal synaptic conductance.

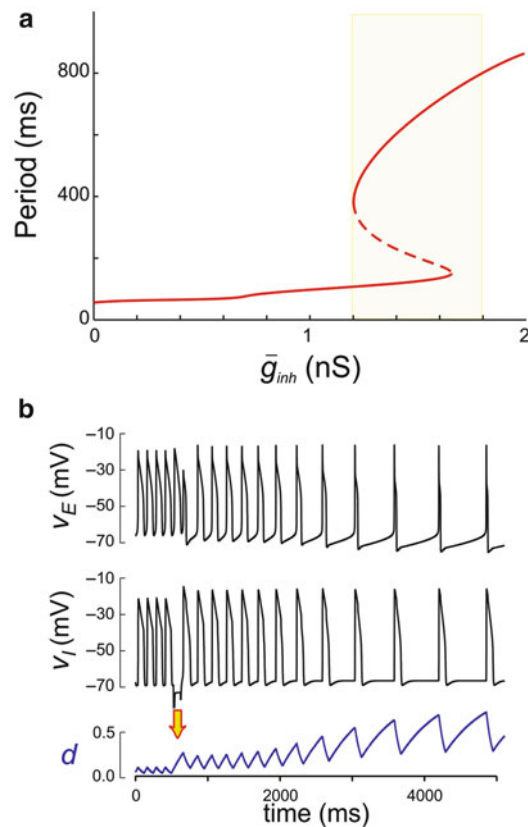
In Bose et al. (2001), a simpler deterministic system consisting of just one  $E-I$  pair with depression in the  $I$  to  $E$  synapse is considered. Here, it is possible to mathematically analyze the self-consistency condition. In this model, the activity of  $I$  is slaved to that of  $E$ . A map  $\Pi(d)$  is derived that measures the value of the depression variable each time  $E$  fires. This map is easily obtained by solving Eq. 3 over one complete cycle of a typically  $E$  oscillation. Namely, solve  $d' = -d/\tau_\beta$  with initial condition  $d(0)$  for a time  $T_A$  corresponding to how long  $E$  is active. Then solve  $d' = (1 - d)/\tau_\alpha$  with initial condition  $d(T_A)$  for a time  $T_I$  to find  $d_{n+1} = \Pi(d_n)$  given by

$$d_{n+1} = 1 - \left(1 - d_n e^{-T_A/\tau_\beta}\right) e^{-T_I/\tau_\alpha}. \quad (8)$$

Consider the case where  $T_A$  is fixed, but  $T_I$  varies as a function of the synaptic strength of the  $I$  to  $E$  synapse. Because this synapse is frequency dependent,  $T_I$  is an unknown in Eq. 8. However,  $T_I$  can be determined at each cycle using an equation similar to Eq. 7 given by

$$c_1 e^{-T_I/\tau_w} + c_2 \bar{g}_{\text{inh}} d_n e^{-T_I/\tau_\kappa} = c_3, \quad (9)$$

where  $\bar{g}_{\text{inh}}$  is the maximal inhibitory conductance. A fixed point of the map  $\Pi$  corresponds to a periodic solution of the  $E-I$  network. The value of  $d$  at the fixed point, denoted  $d^*$ , determines the overall level of depression associated with that solution and correspondingly determines the network period. Note that  $d^*$  is still given by Eq. 5 and it represents the situation where there is a self-consistency between the network period ( $T_I + T_A$ ) and synaptic strength ( $g_{\text{peak}}$ ). As  $\bar{g}_{\text{inh}}$  changes the fixed points of  $\Pi$  undergo two different saddle-node bifurcations leading to range of values over which there are two stable solutions shown in Fig. 4a. Along the lower stable branch of fixed points, the maximal synaptic strength is small and the ensuing  $I$  to  $E$  synapse never becomes strong enough to slow the high-frequency intrinsic oscillations of  $E$ . Here,  $T_I$  is small and the value of the fixed point is small. On the upper branch,  $\bar{g}_{\text{inh}}$  is large enough so that when  $I$  fires, it forces  $E$  to remain inactive for a longer time. This makes  $T_I$  become larger through Eq. 9, which through Eq. 5 forces  $d^*$  to become large. This leads to a low-frequency solution. In Bose et al. (2001), it is shown that both solutions can coexist leading to bistability. Figure 4b illustrates the bistability showing a voltage trace of an  $E-I$  pair along with the corresponding trace for  $d$ . At the beginning of the trace,  $E-I$  oscillates at a high frequency in which the  $I$  to  $E$  synapse is depressed. Transient hyperpolarization of  $I$  allows its synapse to recover so that when it again fires, it can strongly inhibit  $E$ . The transition to longer periods then ensues. The transition back to high-frequency oscillations could occur, for

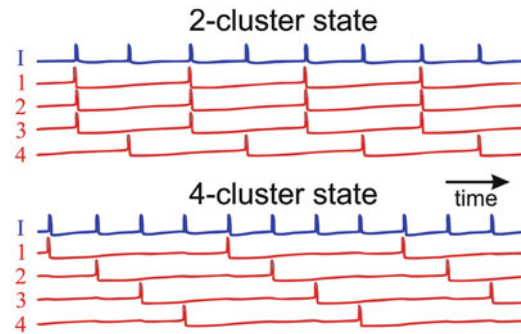


**Fig. 4** Bistability of a two-cell  $E$ – $I$  network where the  $I$  to  $E$  synapse is depressing. **(a)** The bifurcation diagram of network period versus the maximal conductance of the depressing synapse. *Shaded region* shows the bistable range. *Solid lines* are stable, *dashed lines* unstable. **(b)** Voltage traces of the two cells and the depression variable shown for a value of  $\bar{g}_{inh}$  in the bistable range. A brief hyperpolarizing pulse in the  $I$  cell (*arrow*) results in a transition from the fast period oscillations [lower solid branch of **(a)**] to slow period oscillations [higher solid branch of **(a)**] (Modified from Bose et al. (2001))

example, by transiently driving  $E$  to higher frequencies (not shown). Thus, there are two coexistent stable solutions, and transient inputs can make the network transition between them.

In Chandrasekaran et al. (2009), the two-cell network is generalized to a globally inhibitory network consisting of a single  $I$  cell that is reciprocally coupled to a network of  $E$  cells. The  $E$  cells have no direct synaptic connections to one another. Each of the  $I$  cell synapses exhibits short-term depression. Similar to the previous example,  $I$  fires whenever any  $E$  cell fires. If the  $E$  cells are all synchronized, the  $I$  cell's firing rate will be low in comparison to when the  $E$  cells are clustered into different groups. As a result, the firing rate of  $I$  can be used as a proxy for determining how many clusters the  $E$  cells have broken into; see Fig. 5. The different firing rates of  $I$  yield different levels of depression which in turn can only exist if there is self-consistency with the exact number of clusters needed to produce the specific amount of depression. The generalization of equations and Eq. 9 to handle this case led to a 2-dimensional map for which there are multiple coexistent fixed points. Each fixed point corresponds to a solution with a different number of clusters of  $E$  cells. Full details are in Chandrasekaran et al. (2009), where it is shown that the firing rate of  $I$  has a one-to-one increasing relationship with the number of clusters. See also Bose and Booth (2011), which considers the role of synaptic depression in phase locking of two heterogeneous  $I$  cells.





**Fig. 5** Two of multiple stable solutions in a network of one *I* neuron reciprocally coupled to four *E* neurons. The *I* to *E* synapse is depressing (Modified from Chandrasekaran et al. (2009))

## General Observations Regarding Networks and Short-Term Synaptic Plasticity

Short-term synaptic plasticity has been suggested to be of importance for many functions in the nervous system. It has been proposed to play a role in cortical gain control (Abbott et al. 1997), population rhythm generation (Tabak et al. 2000; Tsodyks et al. 2000), and direction selectivity (Carver et al. 2008). In addition, temporal coding in cortical processing such as novelty detection, coincidence detection (Thomson 2000), sound localization (Cook et al. 2003), and phase maintenance (Manor et al. 2003) may be attributed to depression. In experimental (Manor and Nadim 2001) studies of invertebrate central pattern generators, synaptic depression has been shown to introduce bistability of firing patterns. In Izhikevich et al. (2003), it is proposed that STSP creates a synaptic resonance whereby networks align themselves to operate at frequencies where there is a balance between synaptic facilitation and depression. That work suggests that by operating at resonant frequencies, networks increase the reliability of synaptic transmission and provide a novel mechanism for selective communication between neurons.

A specific proposed role of synaptic plasticity is that it gives rise to multistability or the existence of multiple different stable states. Multistability is defined as the coexistence of different stable states for the same parameter values. Alternatively, networks can have different stable states as a result of changing of parameter values due to neuromodulation or external drives to the network. These two situations give rise to distinct types of networks, predominantly feedback versus feed-forward. Furthermore, they lead to different kinds of mathematical questions and challenges.

In studying networks involving STSP, the underlying intrinsic dynamics of individual neurons are relevant, but often only in how they affect the synapses. Indeed, an important point to note is that there are effects of plasticity that are independent of the properties of the postsynaptic cell. This is especially true in feed-forward networks where the level of plasticity, as argued above, can be fine-tuned. One can then assess how the level of fine-tuning affects different kinds of model cells. The fine-tuning itself is just a synaptic property. Where the interplay between synapse and cell model can become important is in feedback networks, where the postsynaptic cell has to transform the synaptic input it receives into a synaptic output. If the outgoing synapse itself exhibits plasticity, then how the intrinsic properties of the cell interact with the incoming synaptic properties would quantitatively affect the output of the system. However, the qualitative behavior of the network, including the existence of multistability, would be less affected by these intrinsic properties.

There are several mathematical challenges that arise in assessing whether multistability arises due to synaptic plasticity. In the absence of plasticity, when the synaptic coupling is not frequency dependent, then it is often possible to derive a 1-dimensional map to assess the existence and

stability of solutions. Further, when the coupling between neurons is weak, then averaging can be used to derive a simplified 1-dimensional equation based on phase differences to assess these questions (Ermentrout and Kopell 1991). Synaptic plasticity, by its nature, does not lead to weak coupling. The maps in this case are typically 2 dimensional or higher. While the analysis of these higher-dimensional maps poses significant mathematical challenges, it also affords the opportunity to derive new mathematical techniques for their analysis that can be generalized to other scenarios.

## Acknowledgments

This work was supported in part by NSF DMS 1122291 (AB, FN) and NIH MH-60605 (FN).

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