Emergence of Connectivity Patterns from Long-Term and Short-Term Plasticities

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Abstract. Recent experimental evidence shows that cellular connectivity in the brain is *non-random*. More specifically, bidirectional connections between pairs of excitatory neurons are predominantly found when neurons connect by short-term facilitating synapses. For this type of synapses, excitatory postsynaptic potentials (EPSPs) transiently increase upon repeated presynaptic activation. On the contrary, unidirectional connections between pairs of excitatory neurons are predominantly found when neurons are connected by short-term depressing synapses. For these synapses, EPSPs transiently attenuate upon repeated activation. Here we present a simple model combining Short-Term Plasticity (STP) and Spike-Timing Dependent Plasticity (STDP) that might explain the correlation between specific synaptic dynamics and unidirectional or bidirectional connectivity patterns.

Keywords: Dynamical Synapses, Short-Term Plasticity, Spike-Timing Dependent Plasticity, Connectomics, Unsupervised Learning

1 Introduction

Recent evidences in rodent prefrontal cortex [1] and olfactory bulb [2] suggest that synaptic short-term facilitation and depression [3] may be correlated to specific cellular connectivity patterns. In particular, it was observed that two excitatory neurons with facilitating synapses form predominantly reciprocal connections, while two excitatory neurons with depressing synapses form unidirectional connections. Interestingly, the exact causes of these structural differences remain unknown.

We propose that connectivity patterns could emerge through the interaction of Short-Term Plasticity dynamics (STP) and long-term Spike-Timing Dependent Plasticity (STDP). While the influence of STDP on STP was shown experimentally *in vitro* [4], how STP and STDP mutually interact in active recurrent

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networks is largely unexplored. Our approach combines the Tsodyks-Markram STP phenomenological model [3] with the STDP triplet rule of Pfister & Gerstner [5, 6], which captures dependencies of long-term plasticity on both time and frequency. As proof of concept, we implement the STP-STDP rule on spiking networks with extreme initial topology (all bidirectional or all unidirectional connections) and expose them to identical external stimuli. Our simulations indicate that combining the STP and STDP models as we propose, could indeed account for the observed connectivity patterns.

2 Models and Methods

We simulate a model network of N excitatory integrate-and-fire neurons, with dynamical synapses that undergo facilitation or depression [3]. In either case, the network is exposed to the same stimulation protocol, and synaptic weights are evolving according an unsupervised STDP "triplet" learning rule, see [5–7]. The details of the model are given below and all parameters are reported in Table 1.

2.1 Neuron model

The network is composed by identical adaptive exponential Integrate-and-Fire neurons [8]. Each unit is described by a membrane potential $V_m(t)$ and by a spike-frequency adaptation variable $x(t)$. Below an upper voltage limit V_θ, $V_m(t)$ evolves as

$$C\,\dot{V_m} \;=\; g_{leak}\,(E_{leak} - V_m) + g_{leak}\;\Delta_T\;e^{(V_m - V_T)/\Delta_T} - x + I_{syn} + I_n + I_{ext} \quad (1)$$

where C is the membrane capacitance, g_{leak} the leak conductance, E_{leak} the resting potential, V_T is the threshold potential of the membrane voltage, Δ_T the slope factor, I_{syn} the synaptic input current (from other neurons), I_n the background noise and I_{ext} the external input (see below). When a spike occurs (as $V_m(t)$ crosses V_θ), $V_m(t)$ is reset to a hyperpolarized value E_{reset} and it remains clamped at such a value, in order to mimic neuronal absolute refractoriness, for a period of τ_{arp}. The spike-frequency adaptation variable $x(t)$ evolves as:

$$\tau_x\;\dot{x} \;=\; a\;\;(V_m - E_{leak}) - x \quad (2)$$

where is τ_x the time constant of the adaption of the neuron and a is the adaptation coupling parameter. When a spike occurs, x is increased by a fixed quantity $(x \;\rightarrow\; x \;+\; \Delta_x)$.

2.2 Synaptic Inputs and External Stimulation

The i-th neuron receives at any time a current $I_{syn\;i}$, evolving as

$$\dot{I}_{syn\;i} \;=\; -I_{syn\;i}\;/\;\tau_{syn} \;+\; \sum_{j=1}^{N}\sum_{k_j}^{\infty}\;C_{ij}\;G_{ij}\;\delta(t - t_j^f) \quad (3)$$

where t_j^f represents the occurrence time of the f-th spike emitted by the j-th presynaptic neuron, G_{ij} defines the amplitude of the postsynaptic current (PSC), corresponding to the activation of the synapse from (presynaptic) neuron j-th to (postsynaptic) neuron i-th and $\delta(t)$ indicates the Dirac's delta function. Neuron i receives also an external input $I_{ext\ i}$, whose amplitude is obtained from a gaussian profile, centred around neuron K, with standard deviation σ_{ext}:

$$I_{ext\ i} = c_1 e^{-\frac{(i-K)^2}{2\sigma_{ext}^2}} + c_2. \tag{4}$$

K changes in time from 1 to N, with N the network size, with period p_{ext}.

Finally, each neuron receives uncorrelated background inputs $I_{n\ i}$, modeled as an Ornstein-Uhlenbeck process [9], with variance σ_n^2 and correlation time τ_n, according to the following equation:

$$\tau_n\ \dot{I}_{n\ i} = -I_{n\ i} + \sigma_n \sqrt{2\tau_n}\ \xi_i(t), \tag{5}$$

where $\xi_i(t)$ is a Gauss-distributed continuous-time process, characterised by zero mean and covariance given by a Dirac's delta function.

2.3 Short-Term Facilitating and Depressing Synapses

The running value of G_{ij} changes on the short-term time scale as a function of the firing activity history of the presynaptic neuron (homosynaptic plasticity), leading to transient and reversible synaptic efficacy depression or facilitation [3]. G_{ij} is related to the absolute amount of "resources" available for neurotransmission (r_{ij}). If all the resources were activated by a presynaptic spike, they would lead to the largest $G_{ij} = A_{ij}\ W_{ij}$, where A_{ij} is a scaling factor and W_{ij} is the "synaptic factor". Each presynaptic spike however utilises only a fraction of the available resources ($u_{ij}\ r_{ij}$), which first becomes instantaneously inactive and then exponentially recovers to its maximal value with a time constant $\tau_{rec\ ij}$. A single PSC is then proportional to the used resources,

$$G_{ij}\ =\ A_{ij}\ W_{ij}\ u_{ij}\ r_{ij} \tag{6}$$

where W_{ij} is referring to the connection from neuron j to neuron i, and it is modified by the STDP learning rule (see the relevant section below). Both short-term depression and facilitation are captured by the same set of equations (depending on the parameters used) [3, 10, 11]:

$$\begin{aligned} \dot{r}_{ij}\ &=\ (1 - r_{ij})/\tau_{rec}\ -\ \textstyle\sum_{k_j}^{\infty}\ u_{ij}\ r_{ij}\ \delta(t - t_{k_j}) \\ \dot{u}_{ij}\ &=\ -u_{ij}/\tau_{facil}\ -\ \textstyle\sum_{k_j}^{\infty}\ U_{ij}\ (1 - u_{ij})\ \delta(t - t_{k_j}) \end{aligned} \tag{7}$$

For simplicity, we drop indices ij from the time constants in (7), although in general each synapse may have its own parameters (see Table 1).

2.4 Triplet Spike-Timing Dependent Long-Term Plasticity

The synaptic factor W_{ij} changes on time scales longer than τ_{rec} and τ_{facil} and according to the correlated activity of pre- and postsynaptic neurons, by the model proposed in [5]. For each neuron of the network, the variables (r_1, r_2, o_1, o_2) act as running averages of the neuron firing rate over distinct time scales (τ_{r_1}, τ_{r_2}, τ_{o_1}, τ_{o_2}). In the lack of any spikes they exponentially relax to zero:

$$\tau_{r_1}\,\dot{r_1} \;=\; -r_1 \qquad \tau_{r_2}\,\dot{r_2} \;=\; -r_2 \qquad \tau_{o_1}\,\dot{o_1} \;=\; -o_1 \qquad \tau_{o_2}\,\dot{o_2} \;=\; -o_2 \quad (8)$$

while as the j-th neuron fires, its corresponding variables are instantaneously increased by a unit. When the j-th neuron fires, for all i

$$\begin{array}{l} W_{ij} \;\rightarrow\; W_{ij} \;-\; o_{1_i}(t)\;\left(A_2^- \;+\; A_3^-\;r_{2_j}(t-\epsilon)\right) \\ W_{ji} \;\rightarrow\; W_{ji} \;+\; r_{1_i}(t)\;\left(A_2^+ \;+\; A_3^+\;o_{2_j}(t-\epsilon)\right) \end{array} \quad (9)$$

The synaptic factor W_{ij} is bounded in the range $[0\;;\;W_{max}]$. When no spike occurs at the i-th and j-th neurons, W_{ij} maintains indefinitely its value. The rule falls under the category of "Unsupervised Learning", as synaptic changes are passively driven by correlations between pre- and postsynaptic signals in the absence of a supervisor. More specifically, the rule captures spike-triplet effects, see also [5–7]. Of particular interest for our work, taking into account firing-rate averages over different time scales allows this model to reproduce the firing-rate dependence of STDP described experimentally in [12]: at low rates Spike-Timing dependency prevails, but at high rates conventional Hebbian plasticity prevails.

2.5 Symmetry Measure for Network Connectivity

Similar to [6], we define as "strong" a connection whose corresponding STDP factor W_{ij} is above the 2/3 of its upper bound W_{max}. All other connections are considered "weak" connections that are not considered when evaluating the connectivity patterns in the network. With such a definition, we introduce the following quantity to quantify and describe concisely the emergence of reciprocal or unidirectional connections in the network:

$$s(W) \;=\; 1 \;-\; (0.5\;N\,(N-1) \;-\; M)^{-1}\;\sum_{i=1}^{N}\sum_{j=i+1}^{N}\,|W_{ij}^* \;-\; W_{ji}^*| \quad (10)$$

where N is the size of the matrix (the number of neurons in the network) and $W_{ij}^* \;=\; W_{ij}\;/\;W_{max}$ if $W_{ij} \;>\; 2/3\;W_{max}$, and otherwise $W_{ij}^* \;=\; 0$. In (10), M represents the number of null pairs $\{W_{ij}^*,\;W_{ji}^*\} \;=\; \{0,\;0\}$. By these definitions, two neurons (i and j) are said to be connected by a *unidirectional* connection when $W_{ij}^* \;\neq\; 0$ and $W_{ji}^* \;=\; 0$, or viceversa. When both $W_{ij}^* \;\neq\; 0$ and $W_{ji}^* \;\neq\; 0$, the connection is said to be *reciprocal*. The evaluation of $s(W)$ on networks with a majority of unidirectional connections results in values close to 0, while on networks with a majority of bidirectional connections its value is close to 1.

Symbol	Description	Value
dt	Forward Euler method integration time step	0.1 $msec$
N	Number of simulated neurons	7
C	Membrane capacitance	281 pF
g_{leak}	Membrane leak conductance	30 nS
E_{leak}	Resting membrane potential	-70.6 mV
E_{reset}	After-spike reset potential	-70.6 mV
Δ_T	Spike steepness of the exponential IF model	2 mV
V_θ	Spike emission threshold of the exponential IF model	20 mV
V_T	Threshold voltage parameter of the exponential IF model	-50.4 mV
τ_{arp}	Absolute refractory period	2 $msec$
a	Voltage dependence coefficient of the spike frequency adaptation	4 nS
Δ_x	Spike-timing dependence parameter of the spike frequency adaptation	0.0805 nA
τ_x	Time constant of the spike frequency adaptation	144 $msec$
τ_{syn}	Excitatory postsynaptic currents decay time constant	5 $msec$
U_D	Release probability, for depressing synapses	0.8
U_F	Release probability, for facilitatory synapses	0.1
$\tau_{rec\ D}$	Time constant of recovery from depression, for *depressing* synapses	900 $msec$
$\tau_{rec\ F}$	Time constant of recovery from depression, for *facilitating* synapses	100 $msec$
$\tau_{facil\ D}$	Time constant of recovery from facilitation, for *depressing* synapses	100 $msec$
$\tau_{facil\ F}$	Time constant of recovery from facilitation, for *facilitating* synapses	900 $msec$
A_2^-	STDP model LTD amplitude for post-pre event	7.1 10^{-3}
A_3^-	STDP model LTD amplitude for post-pre event (triplet-term)	0
A_2^+	STDP model LTP amplitude for pre-post event	0
A_3^+	STDP model LTP amplitude for pre-post event (triplet-term)	6.5 10^{-3}
τ_{r_1}	STDP model decay time of presynaptic indicator r_1	16.8 $msec$
τ_{r_2}	STDP model decay time of presynaptic indicator r_2	101 $msec$
τ_{o_1}	STDP model decay time of postsynaptic indicator o_1	33.7 $msec$
τ_{o_2}	STDP model decay time of postsynaptic indicator o_2	114 $msec$
W_{max}	Upper boundary for STDP scaling factor W_{ij}	5
σ_n	Standard deviation for the noise	250
τ_n	Correlation time for the noise	1 ms
σ_{ext}	Standard deviation for the gaussian-shaped external stimulation	0.5
p_{ext}	Period for the gaussian-shaped external stimulation	5 ms
c_1	Parameter of the gaussian-shaped external stimulation	1000 mA
c_2	Parameter fof the gaussian-shaped external stimulation	500 mA

Table 1. Model parameters: STDP parameters are as in [5]; short-term depression / facilitation parameters as in [1]; neuron parameters as in [6].

3 Results

We run 1000 instances of each of four networks (1: all facilitating synapses, bidirectional initial connections 2: all depressing synapses, bidirectional initial connections, 3: all facilitating synapses, unidirectional initial connections 4: all depressing synapses, unidirectional initial connections). In each case, the results are conclusive: facilitating networks evolve to a bidirectional configuration, while depressing networks to a unidirectional configuration, see Fig. 1 (A-B,D-E). This

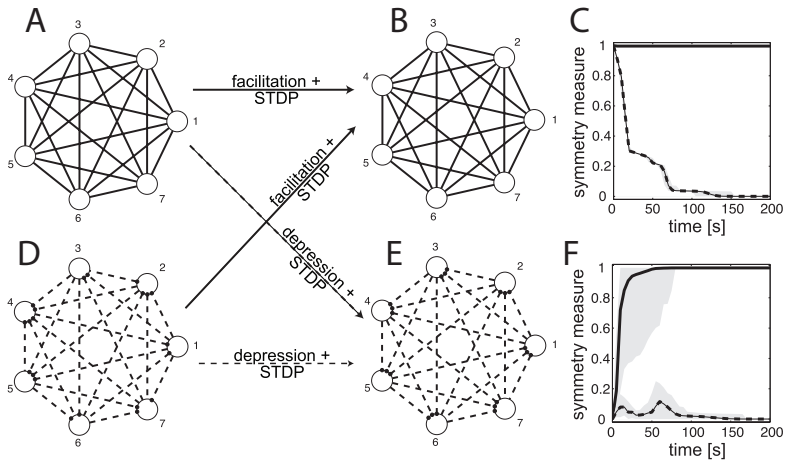

Fig. 1. Evolution of symmetry patterns in the network. Starting from all bidirectional connections (A), the topology of the network with all facilitating synapses remain in the same state (B), while with depressing synapses it develops unidirectional connections (E). In (C) we depict the corresponding evolution of the symmetry measure for facilitating (solid line) and depressing connections (dashed line). Starting from all unidirectional connections (D), the topology of the network with all facilitating synapses goes to a new state of all bidirectional connections (B), while with depressing synapses, it goes to a new state of again unidirectional connections (E), as directed by the timing of the external stimuli. In (F) we depict the corresponding evolution of the symmetry measure for facilitating (solid line) and depressing connections (dashed line). Symmetry measures have been averaged over 1000 simulations, with grey shading indicating maximal and minimal symmetry measures, across all simulations.

is confirmed by the symmetry measure, Fig. 1 (C,F). In Fig. 1 (F), we note that the symmetry measure initially increases prior to resting to zero. This is due to the initialisation of unidirectional conditions, where direction of each synapse is randomly set. During the simulation, the connectivity is shaped by the simulation protocol, i.e. neuron 1 fires first, then neuron 2, etc, which is designed to induce pre- post- correlations. Hence neuron 1 projects to neurons 2-4, neuron 2 to neurons 3-5 etc, see Fig. 1 (E).

The explanation behind this emergent connectivity profiles is intuitively simple, and is based on the frequency dependence of the STDP (see [12]). Facilitating synapses require time to "charge" to their full capacity, and as a consequence, if receiving input from a spike train, they would respond weakly to the first spike and progressively stronger to the next ones (depending on the recovery time of their "resources"). Depressing synapses, contrary to this, they respond

the strongest to the first spike, and they progressively get fatigued. In our simulations, facilitating synapses, result in higher firing rates ($\sim 58Hz$) than the depressing synapses ($\sim 29Hz$). The firing rate of the network for facilitating synapses falls in the regime where Spike-Timing doesn't matter, and the traditional hebbian rules are revealed: if neurons fire together, they wire together. Depressing synapses however, exhibit a low frequency in a domain where Spike-Timing matters. The triplet rule of [5] is designed to capture precisely this effect. In our model, we proposed to combine the triplet rule in a multiplicative way with short-term dynamics (eq. 6). Hence the "facilitating network" activity is further enhanced by learning on the longer scale, as more projections per neurons are established in comparison to the "depressing network". As long as the firing frequency of the facilitating network is above $40Hz$ ([12]), no long-term depression is observed and bidirectional connections are formed. On the contrary, as long as the firing frequency of the depressing network is below $40Hz$, Spike-Timing Dependent Plasticity prevails and only unidirectional connections are formed.

4 Conclusions

It has been experimentally shown that short-term plastic facilitating synapses are involved in bidirectional connectivity patterns while depressing synapses in unidirectional patterns. We hypothesise that short-term and long term plasticity interactions might lead to these configurations. By combining a "triplet" Spike-Timing Dependent Plasticity (STDP) rule with well established models of Short-Term Plasticity (STP), we demonstrate in simulations that starting from extreme initial topologies (all bidirectional or all unidirectional connections), and upon identical external stimuli, networks with depressing synapses evolve unidirectional connections, while networks with facilitating synapses evolve bidirectional connections. To systematically characterise these "proof of concept" simulations, we have introduced an appropriate symmetry measure. According to our results, STP and STDP interactions, combined in the specific way that we propose, lead to experimentally observed connectivity patterns.

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