Journal of Physiology - Paris 104 (2010) 91–98

Contents lists available at ScienceDirect

Journal of Physiology - Paris

journal homepage: www.elsevier.com/locate/jphysparis

Spike timing-dependent plasticity is affected by the interplay of intrinsic and network oscillations

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ARTICLE INFO

Keywords:
STDP
Single-neuron dynamics
Intrinsic oscillations
Network oscillations
Learning
Self-organization

ABSTRACT

Spike timing-dependent plasticity (STDP) is a form of Hebbian learning which is thought to underlie structure formation during development, and learning and memory in later life. In this paper we show that the intrinsic properties of the postsynaptic neuron might have a deep influence on STDP dynamics by shaping the causal correlation between the pre- and the postsynaptic spike trains. The cell-specific effect of STDP is particularly evident in the presence of an oscillatory component in a cell input. In this case, the cell-specific phase response to an oscillatory modulation biases the oscillating afferents towards potentiation or depression, depending upon the intrinsic dynamics of the postsynaptic neuron and the period of the modulation.

1. Introduction

Experimental results have revealed a form of Hebbian learning which is extremely sensitive to the precise timing of pre- and postsynaptic firing patterns. In particular, in paired-pulse experiments (where brief suprathreshold current pulses are injected in the pre- and postsynaptic cell at a fixed temporal delay) LTP was observed when the evoked presynaptic spike led the postsynaptic spike (thus contributing to postsynaptic firing), while LTD was observed when the evoked presynaptic spike lagged behind the postsynaptic one (Markram et al., 1997; Bi and Poo, 1998; reviewed in Dan and Poo, 2004; Bi and Poo, 2001).

In the last few years, several theoretical works have stemmed from this experimental observations, predicting an important role for STDP in self-organization of neural microcircuits (Lubenov and Siapas, 2008; Kang et al., 2008; Kempter et al., 2001; Song and Abbott, 2001; Câteau et al., 2008), learning of input correlations (Song et al., 2000; Gütig et al., 2003; Meffin et al., 2006), and output firing rate normalization (Song et al., 2000; Tegnér and Kepecs, 2002; Rubin et al., 2001).

While the influence of different STDP rules upon the weight dynamics and the stationary weight distribution has been studied extensively (reviewed in Morrison et al., 2008; Kepecs et al., 2002), only recently there has been some attention drawn upon the influence of single-cell intrinsic properties in STDP dynamics (Câteau et al., 2008). The intrinsic dynamics of the postsynaptic cell determine the integration of subthreshold stimuli and the spike generation mechanism (see, for example, Richardson et al., 2003; Schreiber et al., 2004; Baroni and Varona, 2007; Gutkin et al., 2005), thus directly affect the cross-correlation between the input and the output spike trains. This consideration suggests that the intrinsic postsynaptic dynamics can potentially have a great impact upon the weight dynamics arising from a certain STDP rule.

In addition to shaping the input–output transformation performed, single-cell intrinsic properties determine the response to oscillatory stimuli. Oscillations of multiple, interacting frequencies are very common in the nervous system (Buzsáki, 2006; Buzsáki and Draguhn, 2004), and the phase of the response of a neuron embedded in an oscillating network is strongly biased by its intrinsic properties (Tateno and Robinson, 2007; Netoff et al., 2005; Narayanan and Johnston, 2008; Bland et al., 2005). In some neural structures, proteic and morphological characteristics of single cells seem to be precisely tuned in order to produce the observed network dynamics (Whittington and Traub, 2003; Gloveli et al., 2005). Since synaptic plasticity is highly sensitive to the precise timing of pre- and postsynaptic firing, the presence of an oscillatory component in a cell input is expected to reveal cell-specific biases in the STDP dynamics which would pass unnoticed in the absence of oscillations.

In this paper we consider a feedforward neuronal architecture where one postsynaptic cell receives a synaptic bombardment from several hundred presynaptic afferents, and compare the stationary weight distributions arising from the same STDP rule and presynaptic firing statistics, but different postsynaptic intrinsic

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doi:10.1016/j.jphysparis.2009.11.007

properties. In particular, we compare a purely passive Integrate and Fire (IF) model with an inductive Generalized Integrate and Fire (GIF) model with subthreshold oscillations.

Our results suggest that the intrinsic properties of the postsynaptic cell quantitatively affect the stationary weight distribution under different STDP rules when the input firing patterns are uncorrelated. More interestingly, a sinusoidal modulation of the firing rate of a subset of the presynaptic population reveals qualitative and important differences in the weight dynamics between the IF and the GIF model, which are the focus of this work.

2. Methods

2.1. Neuron models

The first neuron model we consider is the Integrate and Fire (IF), described by a single linear differential equation:

$$\frac{dv}{dt} = -gv + \boldsymbol{I}_{syn} \tag{1}$$

The model is endowed with an after-spike reset mechanism, so that when v crosses a threshold v_{thr} from below a spike is emitted and the membrane potential is reset to a value v_{reset}, and kept there for a refractory period t_{refr}. In its normal form (where time has been properly scaled) this model is described by a single parameter g, which is the rate of the exponential decay to the rest state in the absence of stimulation ($I_{syn} = 0$).

Another simple model that linearly describes the subthreshold dynamics, with the addition of another dynamical variable w, is the Generalized Integrate and Fire (GIF) model, described by the following equations:

$$\begin{aligned} \frac{dv}{dt} &= -\alpha v - \beta w + I_{syn} \\ \frac{dw}{dt} &= v - w \end{aligned} \tag{2}$$

with the same after-spike resetting as in the IF model for the v variable, while no reset is applied to the additional dynamical variable w. The system (2) has proven particularly useful in studying neuronal intrinsic oscillations (Richardson et al., 2003; Verechtchaguina et al., 2007; Izhikevich, 2001; Schreiber et al., 2004). In a certain parameter range, the system (2) is mathematically equivalent to a dampened linear oscillator, and thus constitutes an analytically amenable model for the description of neuronal intrinsic oscillations, i.e., oscillations generated by intrinsic ionic mechanism as the activation of a resonant current or the inactivation of an amplifying current (Hutcheon and Yarom, 2000).

The numerical values of the parameters used here are: $v_{thr} = 20, v_{reset} = -4, t_{refr} = 0.3, g = 1, \alpha = 1$ and $\beta = 4$ (resulting in complex conjugate eigenvalues $-1 \pm 2i$, denoting subthreshold dampened oscillations with period π). Given the wide frequency range of intrinsic oscillations observed in mammalian brains, which spans at least two order of magnitude (from 0.5 Hz until 50 Hz Hutcheon and Yarom, 2000), we preferred to keep our models dimensionless.

2.2. Synaptic description

In general, synaptic dynamics interact with intrinsic neuronal dynamics (Muresan and Savin, 2007), both at the level of a single synaptic potential (in shaping the PSP profile), as during an intense synaptic bombardment from many afferents (in determining the output statistics). Calibration of the synaptic parameters in order to achieve similar PSP profile in different neurons is possible, but still involves a certain degree of subjectivity regarding which features of the synaptic response should be made equal. In order to guarantee equal postsynaptic effects in different neuron models, we modelled PSPs as instantaneous, voltage independent shifts in the voltage variable:

$$I_{syn} = \sum_{n=1}^{N} \sum_{t_n^s} g_n^{syn} \delta(t - t_n^s) \tag{3}$$

where $N = 250$ is the number of afferents, and g_n^{syn} is the synaptic strength of afferent number n. If the synaptic dynamics is fast with respect to the intrinsic neuronal dynamics, this approximation is reasonable (see, for example, Lubenov and Siapas, 2008). Furthermore, this choice guarantees a clear separation between the synaptic and the intrinsic dynamics, and assures that the observed differences between the GIF and IF neuron are due to their intrinsic dynamics only. We discretized the simulations in time steps of size $dt = 0.01$ u.t., and in each time step we generated a presynaptic input pattern in which each afferent which is not in its refractory period has a probability p_n of firing. Once an afferent fires, it will not be able to generate another spike for $t_{refr} = 0.3$ u.t.

We divided the afferent population in three subsets: $N_{exc} = 170$ Poisson excitatory afferents with a constant firing probability $p_{exc} = 0.0033$, corresponding to a mean ISI of 3 u.t.; $N_{osc} = 30$ Poisson excitatory afferents with a sinusoidally modulated firing probability $p_{osc} = p_{exc}(1 + A_{sin} \sin(\frac{2\pi}{T} t))$ with period $T = \pi$ (except in Figs. 3 and 5, where it has been varied in a range, and in Fig. 4, where $T = 1.2743$ or $T = 7.8476$) and modulation amplitude $A_{sin} = 0.5$; $N_{inh} = 50$ Poisson inhibitory afferents with a constant firing probability $p_{inh} = p_{exc} = 0.0033$. The synaptic strengths of the excitatory connections $g_n^{syn} = g_{syn}^{exc} w_n$ are obtained by multiplying the corresponding synaptic weights w_n (which are bounded in the interval [0,1] and subject to STDP) by a scaling factor $g_{syn}^{exc} = 4$. The synaptic strengths of the inhibitory connections are fixed at $g_{syn}^{inh} = 6$.

At the beginning of each simulation the synaptic weights w_n of the excitatory population are homogeneously initialized at their maximal value of 1. These values result in fast and regular postsynaptic firing at a frequency close to the maximal frequency allowed by the refractory period. In this regime the STDP weight dynamics strongly depress most synapses in a non-specific way due to the relative predominance of depression over potentiation (Fig. 1A and B), until the postsynaptic neuron sets in a lower frequency irregular firing regime. The regular and the irregular firing regimes display large differences not only in their firing statistics, but also in their response to a sinusoidal modulation (Richardson et al., 2003). Thus we disregarded the first 30×10^3 u.t. of simulation output and focused our analysis on the subsequent evolution of the synaptic weights through STDP in the low frequency, irregular firing regime, during which the mean and the standard deviation of the output ISIs (Inter Spike Intervals) can be considered stationary, as well as the phase of the response to the sinusoidal modulation. This irregular firing regime is more relevant for neuronal physiology, since neurons in many brain areas exhibit highly irregular firing patterns (Shadlen and Newsome, 1998).

All the simulations have been run for 5×10^6 u.t. Convergence has been assured by visual inspection of the output data and it has always been reached within 2×10^6 u.t. of simulation time.

The sinusoidal modulation in the input rate induces a modulation of the firing probability, which we fit to a sinusoidal function $r_{out}(1 + A_g \sin(\frac{2\pi}{T} t + \phi))$ to obtain the modulation gain A_g and phase ϕ plotted in Figs. 3–5.

2.3. STDP model

The excitatory synaptic connections are plastic and evolve according to the STDP rule described in (Gütig et al., 2003). In brief, every pair of a presynaptic and a postsynaptic action potentials

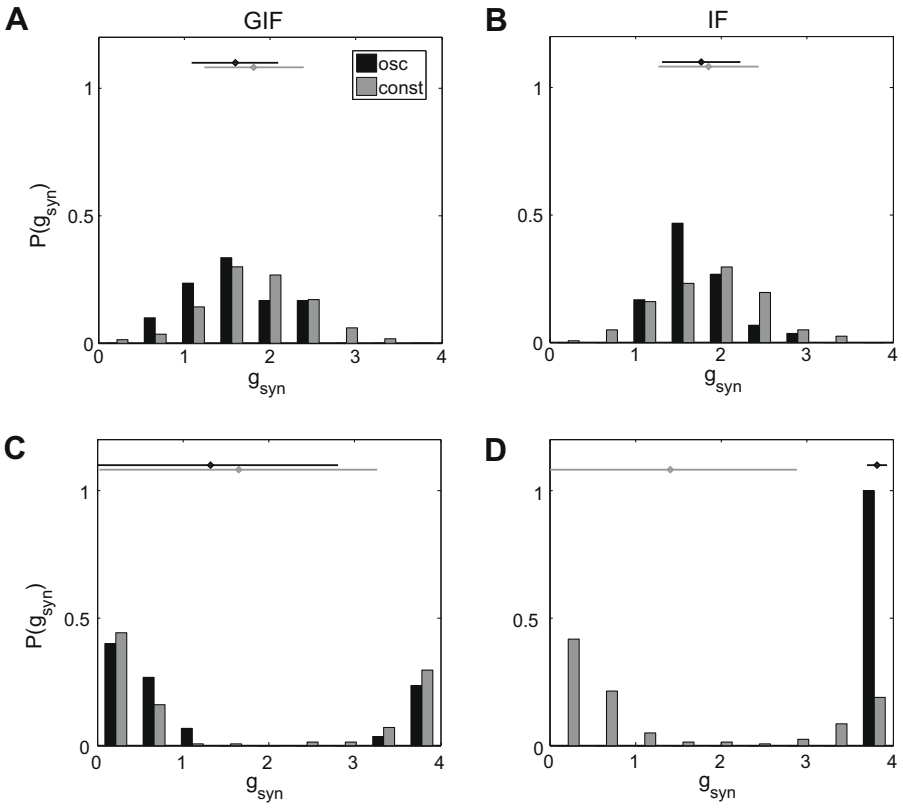

Fig. 1. Intrinsic neuronal properties determine the dynamics and the equilibrium distribution of the weights under STDP. Distributions of the synaptic weights for the GIF (left) and IF (right) neuron model at the beginning of the low frequency, irregular firing regime (top) and at equilibrium (bottom). For each afferent population, the diamond indicates the mean of the weight distribution and the horizontal line its standard deviation. In the initial high frequency, regular firing regime the synapses are depressed in a non-specific way and reach a unimodal distribution where the oscillatory and non-oscillatory populations overlap (A and B). After learning, the weight distributions are bimodal for both neuron types but while the two populations are still largely overlapping for the GIF neuron (C), the oscillatory population is significantly more potentiated for the IF neuron (D).

with time difference $\Delta t = t_{post} - t_{pre}$ induces a weight change given by

$$\Delta w = G(\Delta t|w) = \begin{cases} -\lambda f_-(w)K(\Delta t) & \text{if } \Delta t \leqslant 0 \\ \lambda f_+(w)K(\Delta t) & \text{if } \Delta t > 0 \end{cases} \quad (4)$$

where $K(\Delta t) = e^{-|\Delta t|/\tau}$ is the STDP window function, λ is a learning rate, and $f_\pm(w)$ describe the weight dependence of the STDP rule:

$$f_+ = (1-w)^\mu, \quad f_- = \alpha w^\mu \quad (5)$$

where μ is a parameter included in [0,1] which determines the weight dependence of the STDP rule. If $\mu = 0$, $G(\Delta t|w)$ results is the familiar weight independent (additive) STDP rule like in (Song et al., 2000); if $\mu = 1$ one recovers the multiplicative STDP rule like in (Rubin et al., 2001). Note that if $\mu > 0$ the effect of potentiation vanishes as w approaches 1, and so does the effect of depression as w approaches 0, preventing the synaptic efficacies from leaving the allowed range [0,1]. We chose $\mu = 0.02$, a weak weight dependence which corresponds to symmetry breaking in the absence of correlations in the inputs (not shown). The details of the STDP rule are not critical though: since our results depend on the phase response of the model neurons, we expect any temporally asymmetric STDP rule to yield similar results. The parameter α describes the asymmetry between depression and potentiation; we set it at a value slightly greater than 1 ($\alpha = 1.05$) to assure than uncorrelated pre- and postsynaptic firing yield synaptic depression. The numerical values for the other parameters are $\lambda = 0.002$ and $\tau = 0.8$. In most simulations a higher value of λ could be used, resulting in faster convergence to the steady state. Nevertheless, when the phase response is close to zero or positive, small random fluctuations could have a great effect upon the weight dynamics (see the next section). In this situation a small learning rate λ assures a time scale separation between the intrinsic neuronal dynamics, which determine the response to a sinusoidal modulation embedded in a random synaptic bombardment, and the weight dynamics.

3. Results

Over time scales shorter than $1/\lambda$, the input–output correlation can be considered stationary and the mean weight drift can be obtained from (4) by integrating over the time difference Δt, weighted by its correspondent probability:

$$\langle \Delta w \rangle = \int_{-\infty}^{\infty} G(\Delta t|w) P_t(\Delta t|w) d\Delta t \quad (6)$$

The dependence upon the intrinsic neuronal properties of the postsynaptic cell is included in the input–output correlation term $P_t(\Delta t|w) = \langle \rho^{pre}(t)\rho^{post}(t+\Delta t, w)\rangle_t$, where $\rho^{pre}(t) = \sum_k \delta(t - t_k^{pre})$ and $\rho^{post}(t,w) = \sum_k \delta(t - t_k^{post})$ are the pre- and postsynaptic spike trains, and $\langle\cdot\rangle_t$ indicates averaging over time.

The postsynaptic intrinsic properties affect the integration of incoming stimuli, and determine the input–output transformation performed. For instance, an EPSP evoked on a regular spiking neuron at a certain point of its firing cycle can advance or delay its phase depending upon the intrinsic properties of the postsynaptic neuron (Gutkin et al., 2005; Galán et al., 2005; Oprisan and Canavier, 2002; Ermentrout, 1996). Furthermore, the stimulus features which most effectively result in a postsynaptic spike depend upon

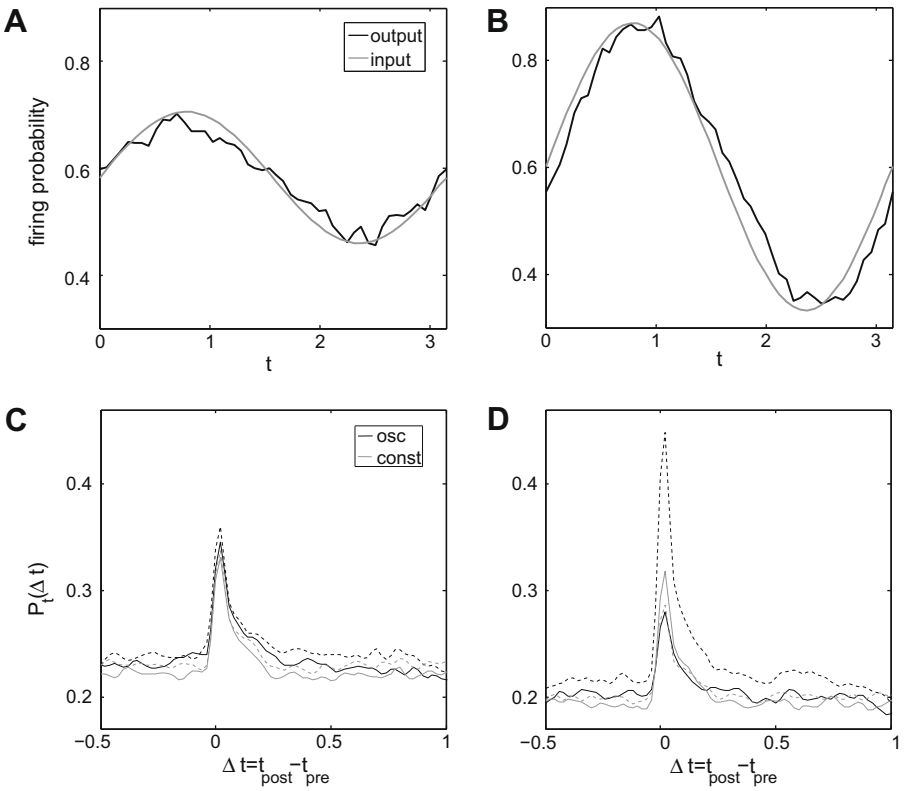

Fig. 2. Intrinsic neuronal properties determine the phase of the oscillating response, and hence the input–output cross-correlation. (A and B) The firing probability along the cycle at the end of the simulation (black line) is plotted together with the sinusoidal modulation of the input firing rate (gray). While the output is in phase with the input for the GIF neuron (left), there is a delay for the IF neuron (right). Moreover, the gain in the IF neuron is increased due to potentiation of the oscillating population. (C and D) $P_t(\Delta t)$ is plotted for the oscillatory (black) and non-oscillatory (gray) population for the GIF (solid line) and IF (dashed line) neuron at the beginning of the irregular firing regime (left) and at the end of the simulation (right). At the beginning of the irregular firing regime the oscillating afferents are slightly more efficient in firing the postsynaptic cell due to their common sinusoidal modulation. This can be deduced from the broader input–output correlation and the higher peak. Note that the broadening of the input–output correlation in the oscillating population has an important component for negative Δt pairs in the GIF neuron, while it mainly affects positive Δt pairs in the IF neuron, reflecting the different phase responses of the two neuron types. After learning the input–output correlation has clearly increased for the oscillating subgroup in the IF neuron.

the type of excitability and the dynamical mechanism of spike generation (Mato and Samengo, 2008).

Intrinsic neuronal properties (in particular, intrinsic oscillations) affect the neuron's behavior in response to a sinusoidal modulation (Richardson et al., 2003). In the irregular firing regime, a purely passive neuron like an IF always follows a sinusoidal modulation with some delay, while a GIF neuron with intrinsic oscillations can synchronize to an input modulation or even lead ahead of it, depending upon its intrinsic frequency and the frequency of the modulation (Richardson et al., 2003, see also Fig. 3A).

When the synaptic afferents to a neuron are composed of two different populations, one with a constant firing frequency and another with a sinusoidally modulated firing frequency, the phase with which the postsynaptic neuron follows the sinusoidal modulation determines if the oscillating population will differentiate from the non-oscillating population, and in which direction, through the STDP dynamics. Indeed, an IF neuron which follows a sinusoidal modulation with a phase delay will on average fire after most of the neurons in the oscillating population (Fig. 2B), leading to a selective strengthening of the synapses belonging to this group (Fig. 1D). Conversely, the GIF neuron follows the same sinusoidal modulation without any significant phase difference (Fig. 2A), hence its spikes will be symmetrically distributed with respect to the oscillating population (see also Fig. 2C and D), leading to no net potentiation nor depression with respect to the non-oscillating population (Fig. 1C).

To quantify the degree of separation between the oscillating and the non-oscillating populations, we computed the ratio between the mean conductance in the two subgroups $R = \langle g_{osc} \rangle / \langle g_{const} \rangle$. Fig. 3 shows the relationship between R and the phase of the sinusoidal response: as expected from our theoretical considerations, the sign of the phase lag determines if the oscillating subgroup will be potentiated or depressed. A negative phase (the postsynaptic neuron lags behind the sinusoidal modulation) results in relative potentiation of the oscillating subgroup of afferents ($R > 1$), while a positive phase leads to relative depression of the oscillatory population ($R < 1$). This general relationship does not hold for very short input periods T, for which a very negative phase results in no differentiation or only slight potentiation of the oscillating subgroup: at very high input frequencies a postsynaptic spike lagging behind a given cycle can also be considered as leading ahead the next cycle, so that as soon as the STDP window becomes comparable in width with the input oscillation period the effects of potentiation and depression tend to cancel out. Measures of the separation between the two different populations which also take into account the standard deviation of the two distributions yielded similar results. In spite of this general tendency, there are some additional differences between the GIF and the IF models which cannot be explained solely on the basis of the phase of the sinusoidal response. For example, for a certain range of negative phase lags there is a stronger potentiation of the oscillating subgroup in the GIF neuron (Fig. 3B).

The cell-specific potentiation or depression of the oscillating population affects in turn the postsynaptic firing statistics, and in particular the gain of the oscillatory component of the postsynaptic response (Figs. 4 and 5). In particular, a sinusoidal modulation

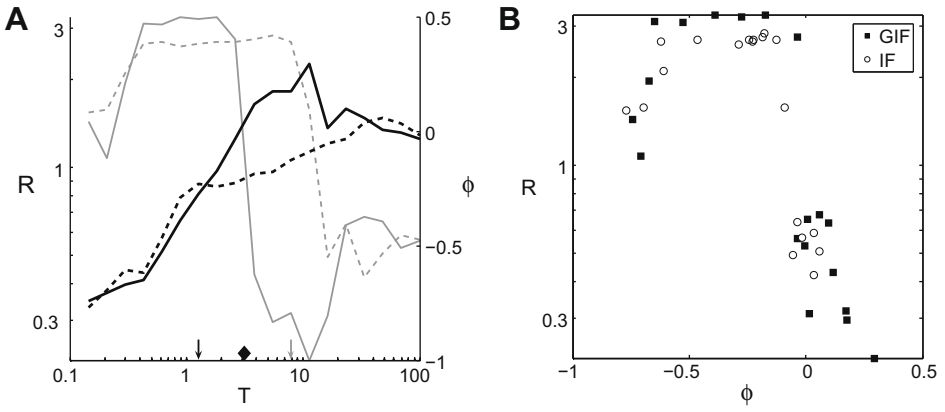

Fig. 3. The phase of the sinusoidal response determines the mean drift of the oscillating population. (A) Ratio between the mean oscillatory conductance and the mean non-oscillatory conductance $R = \langle g_{osc} \rangle / \langle g_{const} \rangle$ and phase of the sinusoidal response ϕ for the GIF (solid line) and IF (dashed line) models as a function of the period of the sinusoidal modulation. While the IF neuron always lags behind, the GIF neuron can synchronize with or even lead ahead of the sinusoidal input modulation. The sign of the phase determines the potentiation ($R > 1$) or depression ($R < 1$) of the oscillating population with respect to the other afferents. The black diamond indicates the intrinsic period for the GIF neuron considered, and the input period used in the simulations plotted in Fig. 1. The black and the gray arrows indicate the input periods used in the simulations plotted in Fig. 4. (B) R ratio for the GIF (filled squares) and IF (empty circles) models after learning is plotted versus the correspondent phase.

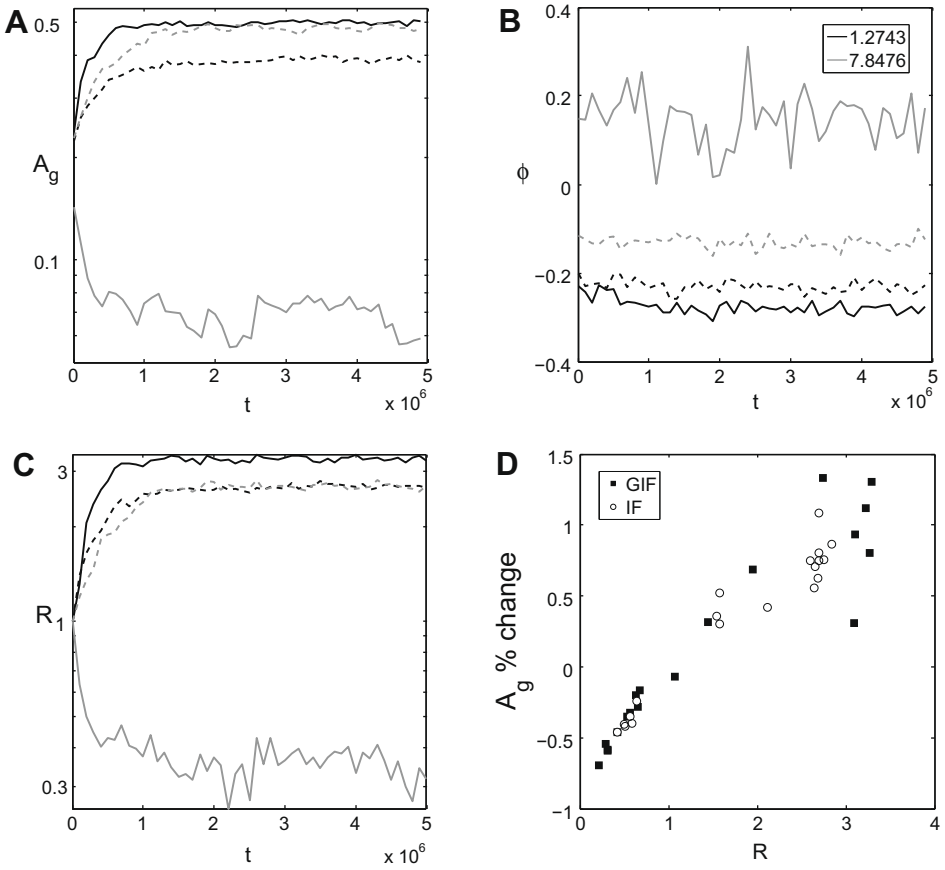

Fig. 4. Evolution of some relevant quantities along a typical simulation for the GIF (solid line) and IF (dashed line) model, for two different values of the input modulation period. (A) Sinusoidal gain A_g. (B) Sinusoidal phase ϕ. (C) R ratio. (D) The relative potentiation of the oscillating population is the main determinant of the change in the sinusoidal gain due to STDP.

which results in negative phase lag (the postsynaptic cell lags behind the sinusoidal modulation) leads to a selective strengthening of the oscillatory population, which in turn produces an increase in the sinusoidal gain. The opposite trend is observed for modulation periods and postsynaptic intrinsic properties which result in positive phase lag (the postsynaptic cell leads ahead of the sinusoidal modulation). This dynamics is shown in Fig. 4, where the amplitude gain A_g and the separation index R are plotted for the GIF and IF neurons along a typical simulation for two representative values of the modulation period T. For short modulation periods ($T = 1.2743$ in the plotted example, the non-integer values are due to the logarithmically spaced values for T) both GIF and IF neurons lag behind the sinusoidal modulation, their oscillating afferents are potentiated and their sinusoidal gain is consequently

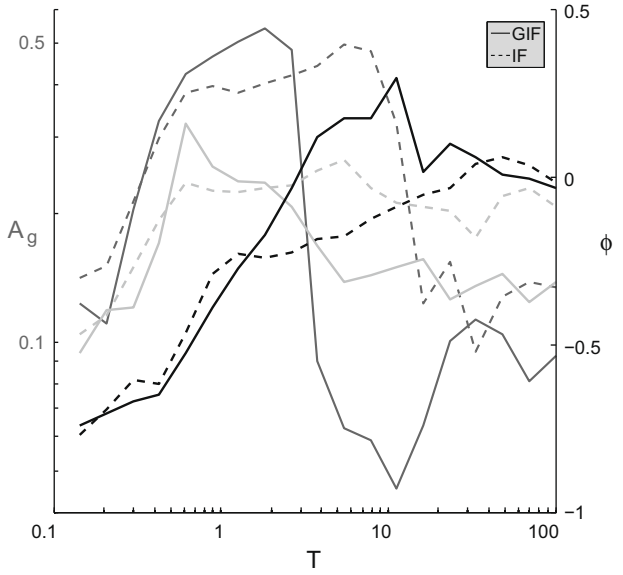

Fig. 5. Gain and phase of the sinusoidal modulation as a function of the period T of the modulation. The gain is plotted at the beginning of the irregular firing regime (light gray) and at the end of the simulation (dark gray).

increased (Fig. 4A and C). For modulation periods slightly greater than the intrinsic period π, the GIF and the IF neurons behave in a qualitative different way: the IF neuron still lags behind the sinusoidal modulation, while the GIF neuron leads ahead of it, resulting in an opposite trend in their separation index R and consequently in their gain A_g (compare panels A and C). This cell-specific regulation of the sinusoidal gain through STDP is also apparent in Fig. 5, where the gain for the GIF (solid) and IF models (dashed) is plotted at the beginning (light gray) and at the end (dark gray) of the simulations, for input periods T spanning three orders of magnitude. For all tested input periods, the difference in gain at the beginning of the simulations is rather small, but it increases dramatically through the action of STDP for those input periods which result in qualitatively different behavior in the GIF and IF neuron (with T in the interval (3,10) approximately, the phase is positive for the GIF neuron and negative for the IF neuron). Conversely, the difference in gain between the two neuron models remains small for very short or very long modulation periods, for which the two models display similar phase shifts. Note the negative peak in A_g for the GIF neuron, which corresponds to maximal phase advance and consequently maximal relative depression of the oscillating subgroup (compare Fig. 5 with Fig. 3A).

To further clarify the relation between the R index and the sinusoidal gain, we lumped all the data obtained with different T for the same neuron model, and plotted the percentual change in sinusoidal gain A_g during learning versus R for the GIF (filled squares) and IF models (empty circles) (Fig. 4D). This figure shows that the relationship between the sinusoidal gain change and the oscillating/non-oscillating ratio R is almost linear, with a R value of 1 (indifferentiation between the two subgroup of afferents) resulting in no gain change. This suggests that the evolution of the sinusoidal gain along a simulation is mainly driven by the relative potentiation or depression of the oscillating subgroup.

The effect of STDP on the phase lag of the different model neurons is somewhat subtler. When the postsynaptic neuron lags behind the sinusoidal modulation, the oscillating afferents are potentiated with respect to the other afferents, and keep the postsynaptic cell at a constant, negative phase. Conversely, when the postsynaptic neuron leads ahead of the sinusoidal modulation, the oscillating afferents are depressed and their entrainment of the postsynaptic cell is less efficient, resulting in low sinusoidal gain and variable, positive phase (Fig. 4C).

4. Discussion

In this work we considered a simplified framework, in which a single postsynaptic cell receives a synaptic bombardment from several hundred presynaptic afferents in a purely feedforward configuration. While the adoption of a simplified model is useful in dissecting the minimal dynamical mechanisms required for the observed behavior, the introduction of additional biological details might significantly alter, or extend, our results. In this section we discuss the main assumptions of our model which are not expected to hold in biological neural networks, discuss how they might affect our results, and suggest future work which will further unravel the complex interplay between neuronal properties and synaptic plasticity.

In our approach we did not take into account propagation delays along neurites. However, the effects of linear, frequency-independent propagation delays can easily be predicted in the current framework. If we consider an axonal conductance delay τ_a from the soma of the presynaptic neuron until the synaptic contact, and a dendritic conductance delay τ_d from the synaptic contact until the soma of the postsynaptic cell (equal among afferents for simplicity), we expect the phase response to be delayed by $(\tau_a + \tau_d)/T$, where T is the period of the sinusoidal modulation. This will result in a shrinking of the frequency range with positive phase response, suggesting a bias towards potentiation of the oscillating population. However, this latter effect depends upon the relative magnitude of the axonal and dendritic conductance delays. Given that synaptic modifications depends upon the relative timing of the pre- and postsynaptic activity as observed at the synaptic site (more precisely, upon the time difference between the calcium influx through synaptically gated postsynaptic channels and the postsynaptic depolarization due to a backpropagating action potential (Markram et al., 1997)), we could substitute Δt in Eq. (4) with $\Delta t_{syn} = t^{syn}_{post} - t^{syn}_{pre} = \Delta t + (\tau_d - \tau_a)$. Since in most cases the propagation delay along the axon is greater than along the dendrite, we would expect a rightward shift of the temporal dependence of STDP, with zero phase lag observed at the somae resulting in synaptic depression, thus partially compensating for the downward shift in the phase response.

The adoption of a more realistic synaptic description, i.e. exponentially decaying synaptic conductances or alpha functions, is also expected to increase the phase lag, because the synaptic current will peak a certain time after its onset. We performed some exploratory simulations with exponential synapses, and indeed observed a general downward shift in the phase response and consequently a bias towards potentiation of the oscillating population (not shown). As the synaptic dynamics interacts with the intrinsic dynamics, the differences between the IF and GIF neuron which could not be attributed to the phase response are bigger than in the present case, and deserve further study which will be addressed in the future. The adoption of linear neuron models might also seem unrealistically simple. However, these simple models with parameters obtained from linearization around the steady state of realistic, conductance-based model neurons are known to replicate faithfully the response to a weak sinusoidal modulation of their realistic counterparts, even when embedded in strong background noise (Richardson et al., 2003). Still, it is possible that a more realistic spike generation mechanism might affect the neuronal response to a sinusoidal modulation, especially at high input rates (Fourcaud-Trocmé et al., 2003). This possibility will be addressed in future work.

In our model, the oscillating population follows a sinusoidally modulated Poisson statistics, without any additional temporal structure. Hence, if the postsynaptic cell is in phase with the input modulation, one particular presynaptic neuron will sometimes lead, sometimes lag the postsynaptic response so that the mean synaptic drift it will experience is zero. Conversely, if the oscillating population activity were temporally structured, a differentiation of the oscillating population from the rest of the afferents could still be observed. For instance, if a subset of the oscillating population were imposed to fire earlier on average than the other afferents of the oscillating population, this subset would be expected to undergo potentiation.

Another assumption of our feedforward model which is not expected to hold in generic neuronal networks is the independence between inhibition and excitation. Inhibition if often correlated with excitation, either because of excitatory–inhibitory loops in the same brain area, or because of common inputs from other brain areas which target both interneurons and principal cells (Buzsáki, 1984; Pouille and Scanziani, 2001; Wang et al., 2007). This interdependence might bias synapse strengthening in a cell-specific way. For example, inhibition which shortly precedes excitation increases the responsiveness and reliability of neurons with subthreshold oscillations, but not of purely passive neurons (Mato and Samengo, 2008).

In our model inhibitory connections are fixed, and plasticity of excitatory synaptic weights is the only mechanism responsible for adjusting the spiking statistics of the postsynaptic cell from the initial high frequency, regular spiking regime to the low frequency, irregular firing regime which is commonly observed in the brain. This results in a dependence of the output firing statistics after learning upon the initial values of the synaptic weights. Even if most experimental and theoretical studies have focused on synaptic plasticity of excitatory (typically glutamatergic) synapses, inhibitory connections are also known to undergo activity-dependent plasticity (Gaiarsa et al., 2002), which, at least in some systems, exhibits a high sensitivity to the relative timing of pre- and postsynaptic spiking (Haas et al., 2006). Contrary to the anti-homeostatic effect of excitatory STDP, which tends to strenghten the stronger synapses, the effect of inhibitory STDP is homeostatic, increasing the inhibitory effect if it was not sufficient to prevent the postsynaptic cell from firing. It will be worth exploring whether the interaction of these complementary mechanisms might result in robust self-organization of network dynamics and, in a feedforward network like the one presented here, in convergence to a given output statistics from a broad range of initial synaptic weights.

5. Conclusions

Intrinsic neuronal properties may affect the integration of incoming stimuli in a nontrivial way. For instance, an EPSP evoked on a regular spiking neuron can advance or delay the occurrence of the next spike, depending upon the intrinsic properties of the postsynaptic neuron and the exact time in which it is delivered.

Intrinsic neuronal properties (in particular, intrinsic oscillations) affect the neuron behavior in response to a sinusoidal modulation embedded in a random synaptic bombardment (Richardson et al., 2003). In the irregular firing regime, a purely passive neuron like an IF always follows a sinusoidal modulation with some delay, while a GIF neuron with intrinsic oscillations can synchronize to an input modulation or even lead ahead of it, depending upon its intrinsic frequency and the frequency of the sinusoidal modulation.

The phase of the sinusoidal response determines the net drift that will affect the weights of the oscillating population: if the phase is positive (the postsynaptic neuron leads ahead of the presynaptic sinusoidal modulation) the oscillating population will experience a net depressing effect (most postsynaptic spikes will lead the presynaptic spikes originating from this population), while if the phase is negative (the postsynaptic neuron follows the sinusoidal modulation with some delay) the oscillating population will be potentiated.

The net weight drift experienced by the oscillating population affects in turn the postsynaptic firing statistics, and in particular the sinusoidal gain response. If the postsynaptic neuron follows the sinusoidal modulation with some delay, as in the case of the passive IF neuron, the oscillating population will undergo potentiation and will increase the gain of the sinusoidal modulation. Conversely, if the postsynaptic neuron is synchronized with the sinusoidal modulation, the net weight drift on the oscillating population will be the same as the one experienced by the other afferents, hence the sinusoidal gain will stay constant. Thus, it seems that STDP might have a regulatory effect upon the sinusoidal gain in the presence of oscillatory inputs, by increasing the oscillatory input to target cells which follow the modulation with some delay, while not affecting or even decreasing the oscillatory inputs to target cells which display intrinsic oscillations in resonance with the frequency of the oscillatory modulation.

Since both network oscillations and intrinsic resonant neurons are widespread in many brain areas, we believe that this mechanism might be highly relevant for structure formation during both development and mature life. For example, we could hypothesize that the distribution of intrinsic neuronal properties in a certain brain area might impose some restrictions upon the possible wiring schemes, thus contributing to the specification of network connectivity and possibly decreasing the amount of information about wiring which needs to be genetically encoded. This effect is expected to be especially relevant in higher and evolutionarily more recent neural structures, where the heterogeneity of intrinsic properties is higher (Freund and Buzsáki, 1996; Markram et al., 2004; Somogyi and Klausberger, 2005). Intrinsic single-cell properties might tune incoming connections in order to enhance responsiveness to neuronal assemblies which tend to fire at a certain phase of network oscillations, thus fostering specialization and multiplexing in network processing (Friedrich et al., 2004). According to our numerical results, we expect passive neurons to be driven mostly by synchronized presynaptic assemblies which fire at the peak of the oscillatory input component, while neurons with subthreshold oscillations might more often develop strong connections from neurons which tend to fire earlier than their other afferents.

Finally, single-cell processing is a distributed phenomenon. Single domains along the neuronal morphology can be characterized by specific intrinsic properties (Johnston and Narayanan, 2008), interneuron innervation (Klausberger and Somogyi, 2008) and local plasticity rules (Froemke et al., 2005; Letzkus et al., 2006; Saudargiene et al., 2005). The investigation about the complex interplay between network oscillations, the heterogeneity of intrinsic neuronal dynamics, and the local nature of synaptic plasticity is likely to be of key importance for understanding information processing in the nervous system.

Acknowledgements

This work was supported by MICINN BFU2009-08473 and CAM S-SEM-0255-2006.

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