LETTER **Communicated by Ad Aertsen**

Synaptic Delay Learning in Pulse-Coupled Neurons

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We present rules for the unsupervised learning of coincidence between excitatory postsynaptic potentials (EPSPs) by the adjustment of postsynaptic delays between the transmitter binding and the opening of ion channels. Starting from a gradient descent scheme, we develop a robust and more biological threshold rule by which EPSPs from different synapses can be gradually pulled into coincidence. The synaptic delay changes are determined from the summed potential—at the site where the coincidence is to be established—and from postulated synaptic learning functions that accompany the individual EPSPs. According to our scheme, templates for the detection of spatiotemporal patterns of synaptic activation can be learned, which is demonstrated by computer simulation. Finally, we discuss possible relations to biological mechanisms.

1 Introduction and New Learning Scheme

The timing or coherence of a neuron's input signals determines whether the neuron behaves as an integrator or coincidence detector (Abeles, 1982). Regarding the number of impulses that are required to exceed a voltage threshold—for example, at the axon hillock or a dendritic site with voltage-dependent mechanisms—temporally incoherent signals are less effective than synchronized ones. However, if we take into account axonal and dendritic propagation times, significant coincidence cannot be expected for synchronous impulse emission (Glünder & Nischwitz, 1993). Consequently, and in contrast to the prevailing paradigm that learning manifests itself in the change of synaptic strengths, we took first steps toward a formalism for

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unsupervised learning of individual synaptic delays that aims to produce coincident excitatory postsynaptic potentials (EPSPs) at a defined site. If this site differs significantly from that of the synapses (of course, within the same postsynaptic neuron), we confront the well-known communication problem associated with any form of nonlocal synaptic coincidence learning, Hebbian learning included (see, e.g., Palm, 1982, and section 5 of this article). While other authors account for delay changes by synaptic selection from a multiplicity of axonal or dendritic pathways with different propagation times (e.g., Gerstner, Ritz, & van Hemmen, 1993; Hopfield, 1995; Miller, 1989; Tank & Hopfield, 1987), we propose postsynaptic processes. Promising candidates for adjustable delays between synaptic activation (transmitter binding) and the generation of a postsynaptic potential (opening of ion channels) are experimentally demonstrated molecular messenger cascades (Hille, 1994; Wickman and Clapham, 1995) that we consider as structurally less costly than the approach noted in the previous sentence (cf. section 5).

Aside from solving timing problems in neural circuits, delay learning can serve the evaluation of spatiotemporal patterns of synaptic activation (Carr, 1993; Eggermont, 1990; Wang, 1995). For such computational purposes, the idea of adjustable delays has been considered by several authors (Baldi & Atiya, 1994; Eckmiller & Napp-Zinn, 1993; Glünder & Nischwitz, 1993; Jansen, Bluhm, Napp-Zinn, & Eckmiller, 1991; Napp-Zinn, Jansen, & Eckmiller, 1996), and recently Hopfield (1995) has suggested a neural pulse position modulation with intensity-invariant demodulation by "coordinated time delays." For nonspiking networks, learning schemes have been formulated by Baldi and Atiya (1994), Bell and Sejnowski (1995), Bodenhausen and Waibel (1991), and Tank and Hopfield (1987), but to our knowledge, no mathematical framework for unsupervised delay learning in pulse-coupled neurons has yet been published.

This article relates our threshold rule (Glünder & Hüning, 1996) for unsupervised learning of synaptic delays to the gradient descent scheme. Figure 1 shows three synapses of a neuron that are activated at times $t_{\mathrm{act},i}$ and their EPSPs delayed by τ_i. The idea is to determine the delay changes $\Delta\tau_i$ during every time interval T where the somatic or a local dendritic depolarization $u(t)$, that is, summed EPSPs, is above a learning threshold θ (see Figure 2). For their computation we must assume a secondary process that accompanies each EPSP and determines the amount and direction of the changes. With this postulated learning function $\lambda(t)$, the delay change is

$$\Delta\tau_i \sim \int_T [u(t) - \theta] \cdot \lambda(t - t_{\mathrm{act},i} - \tau_i)\, \mathrm{d}t. \tag{1.1}$$

Thus we propose delay changes proportional to the temporal integral of the weighted learning function, where the weighting term is the suprathreshold depolarization $u(t) - \theta \geq 0$. A good choice for the learning function $\lambda(t)$ is the EPSP function's negative derivative (see section 3).

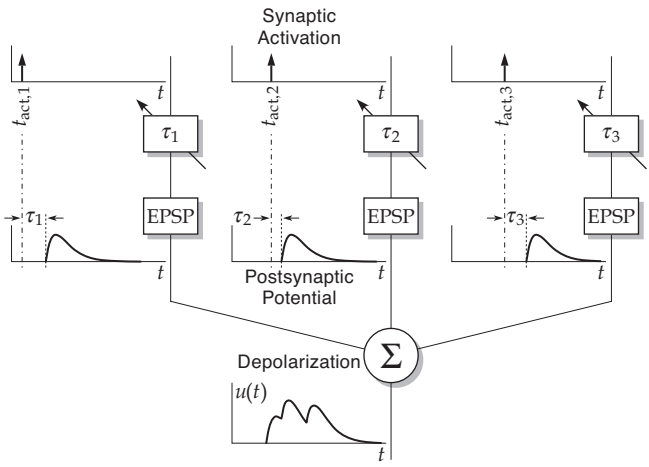

Figure 1: Differently timed ($t_{\mathrm{act},i}$) activation of three synapses at a cell or cell patch evokes delayed (τ_i) EPSPs that result in the net depolarization $u(t)$. The continuously adjustable delays are to be learned for coincident EPSPs.

In the next section we present a gradient descent approach to synaptic delay learning, from which a first learning function is derived, and we introduce the computation of the delay changes at the time of maximum depolarization. In section 3, we further develop this scheme to our threshold rule and generalize the concept of the learning function. We proceed with the simulated formation of a detector that becomes tuned to a spatiotemporal pattern of synaptic activation, and we consider the issue of stability. In the conclusion, we briefly relate our theoretical investigations to known and expected biophysical and neurobiological mechanisms.

2 Relation to Unsupervised Gradient Descent Learning

We relate the unsupervised learning of synaptic delays to schemes of error minimization by using the mathematically convenient parabolic EPSP function (see Figure 2A),

$$h_p(t) = \begin{cases} 1 - t^2 & \text{for } -1 \le t \le 1 \\ 0 & \text{else} \end{cases} .$$

For reasons that will soon become evident, we define the activation onset (beginning of the transmitter binding) of synapse i as $t_{\mathrm{act},i} = t_{\mathrm{ref}} - t_i$. With a relative activation time $t_i > 0$, it then precedes the reference time t_{ref} at which the delay changes are computed. We assume that N excitatory and

linearly transmitting synapses contribute—each with a single EPSP—to a neuron's depolarization $u(t = t_{\mathrm{ref}})$. For this to happen, the synaptic delays τ_i must obey the relation $|t_i - \tau_i| < 1$. Then the summed potential is

$$u(t = t_{\mathrm{ref}}) = N - \sum_i (t_i - \tau_i)^2.$$

Clearly, $u(t = t_{\mathrm{ref}})$ becomes maximum for N coincident EPSPs, which can be achieved by minimizing—through gradient descent—the squared Euclidean distance between the relative activation times t_i and the associated delays τ_i. This leads to the well-known learning rule, here for synaptic delays $\Delta\tau_i \sim t_i - \tau_i$. Unfortunately, the relative activation times t_i are unknown to the neuron. However, formally $t_i - \tau_i$ can be expressed by the derivative of the EPSP function as $-\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t} h_p(t + t_i - \tau_i)|_{t=0}$, using $t_{\mathrm{ref}} = 0$ for simplicity. An essential point of this article is that such a secondary and clearly hypothetical signal is indispensable. It accompanies each EPSP (see similar ideas in Gerstner et al., 1993), and we refer to it as a synaptic learning function $\lambda(t)$. For the parabolic EPSP $h_p(t)$, the learning function resulting from gradient descent is $\lambda_p(t) \sim -\frac{\mathrm{d}}{\mathrm{d}t} h_p(t) = 2t$ for $-1 \le t \le 1$ and zero where the EPSP is zero as well. At the reference time, all EPSPs' learning functions are sampled to give the delay changes (learning increments) of the corresponding synapses.

Although specific signals may exist that define a reference time, we now propose to consider the time at which the depolarization $u(t)$ is maximum. If the sum of N parabolic EPSPs exhibits a single maximum, then the hereby defined reference time becomes $t_{\max} = \frac{1}{N}\sum_i (\tau_i - t_i)$ and the maximum potential is $u(t_{\max}) = N - \|\vec{e}\|^2$, with the components of the error vector

$$e_i = (t_i - \tau_i) - \frac{1}{N}\sum_j (t_j - \tau_j).$$

Hence, if we keep to the learning function $\lambda_p(t)$, we arrive at the learning rule $\Delta\tau_i \sim e_i$ (Hüning, 1995). Here, the sampling of the learning function takes place at the maximum of the depolarization. Although this signal-defined reference time is less ad hoc, maximum detection is difficult to implement, highly sensitive to noise, and thus biologically quite implausible.

3 Temporally Distributed Delay Learning (Threshold Rule)

As a scheme for the unsupervised learning of synaptic delays that is more robust with respect to noisy potentials we finally propose the depolarization-dependent threshold rule (see equation 1.1). With this scheme, delay changes are executed either continuously during or at the end of learning intervals T_μ for which the net depolarization remains above a learning threshold θ (see Figures 2A and 2B, bottom). Although learning defined by equation 1.1 appears functional also without the suprathreshold function

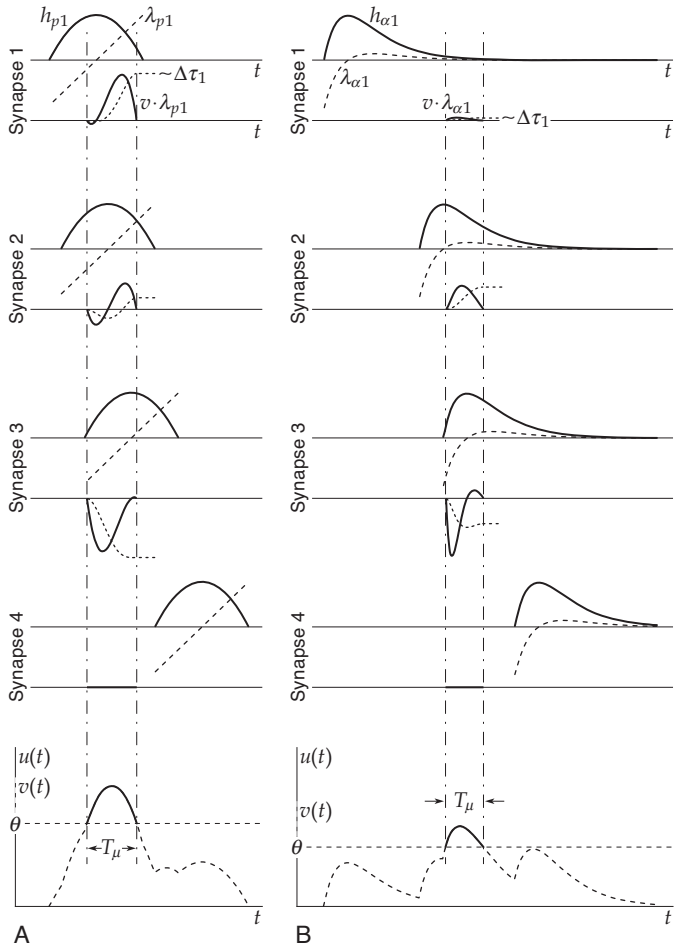

Figure 2: Evaluation of individual synaptic delay changes $\Delta\tau_i$ from the net depolarization $u(t)$ (bottom) of a cell patch with four active synapses. For every synapse, we show an EPSP, its learning function λ (dashed line, except bottom), the weighted learning function $v \cdot \lambda$ (with $v(t) = u(t) - \theta \geq 0$), and its integral (dotted line) that is proportional to the delay change. EPSP shape $h(t)$: (A) parabolic, $h_p(t) = 1 - t^2$ for $-1 \leq t \leq 1$; (B) α-function, $h_\alpha(t) = \alpha^2 t \cdot e^{-\alpha t}$ for $t \geq 0$.

$v(t) = u(t) - \theta \geq 0$, we include this weighting to avoid conflicting and sometimes stable oscillatory delay changes that otherwise can result from concurring activation patterns at successive learning intervals (see section 4).

If every parabolic EPSP and therefore the associated synaptic learning function $\lambda_p(t) \sim -\frac{\mathrm{d}}{\mathrm{d}t} h_p(t)$ entirely cover the learning interval, we obtain from equation 1.1 the learning rule $\Delta\tau_i \sim V_\mu \cdot e_i$ with the suprathreshold area $V_\mu = \int_{T_\mu} [u(t) - \theta]\, \mathrm{d}t$. Figure 2A depicts a situation where three parabolic EPSPs cover the learning interval, while a fourth EPSP comes later and is not captured. In contrast to schemes relying on reference times, where EPSPs are not captured if they do not contribute to the sampled depolarization, our threshold rule shows a gradual coupling of EPSPs that only partly reach into the learning interval. In the latter case, the delay changes increase with every presentation of a spatiotemporal activation pattern until an EPSP's maximum enters the learning interval. This behavior becomes pronounced with more realistic EPSPs—that is, with unimodal functions that steeply rise and slowly decay. (For asymptotically decaying EPSPs, we reasonably assume learning functions of finite duration $\lambda(t > t_\varepsilon) = 0$, with $h(t > t_\varepsilon) < \varepsilon$, where ε may depend on the noise level.) With this kind of asymmetric EPSP function and $\lambda(t) \sim -\frac{\mathrm{d}}{\mathrm{d}t} h(t)$, early EPSPs will be captured long before their maxima enter the learning interval, whereas late EPSPs, which rise after the interval, either fail to be captured (the fourth synapse in Figure 2B) or create a separate learning interval (for a lower threshold than in Figure 2B).

Because various synaptic learning functions are feasible for a given unimodal EPSP function $h(t)$, we have investigated general requirements. Evidently learning functions must change sign from minus to plus in order to give the direction of the delay changes. Formally, we have found that all learning functions $\lambda(t) \sim -\frac{\mathrm{d}}{\mathrm{d}t} f\{h(t)\}$ with any monotone increasing function f comply with the demand that learning must stop, that is, the integral (see equation 1.1) must vanish, if coincidence of the EPSPs is reached (Hüning, 1995). This holds for all threshold settings. Function f permits one to tailor the properties of the learning process. For instance, it may serve the smoothing of a learning function's otherwise discontinuous onset and the restriction of its duration. Furthermore, we can conclude that coincidence learning still works with EPSPs of various amplitudes.

4 Simulation of Spatiotemporal Template Learning

We demonstrate unsupervised synaptic delay learning by the simulated formation of detectors for spatiotemporal patterns of synaptic activation. As an example, we consider the time courses of activation at 10 synapses of a formal neuron (see Figure 3A). Each of the two distinct patterns lasts longer than a single EPSP. Before the repeated presentations of the pattern pair, the 10 synaptic delays are randomly distributed in the interval $0.5\Delta \leq \tau_i \leq 3\Delta$, where Δ is the duration of the parabolic EPSP. Therefore, and because both patterns are well separated in time, the neuron, at best, will be tuned to one of them. A steady time course of the neuron's depolarization (see Figure 3B) is reached after 21 presentations of the pattern pair. Owing to the greater

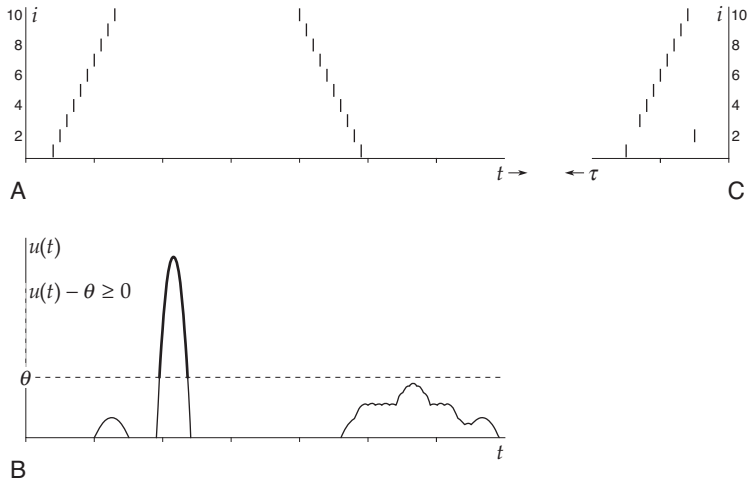

Figure 3: Formation of templates for spatiotemporal patterns. (A) Sample of the stimulation patterns at 10 synapses of a neuron. (B) Steady time course of the net depolarization after delay learning. (C) Final delay configuration $\tau(i)$.

similarity of the first pattern to the specific random initialization, the threshold rule has produced a detector for this pattern which is obvious from the final synaptic delay configuration (slightly imperfect template) depicted in Figure 3C.

Apart from the functionality of delay learning with the threshold rule, our simulation illustrates the effect of temporally limited EPSPs and learning functions, as well as the competition of different patterns. As long as an EPSP contributes to the suprathreshold depolarization, the corresponding synaptic delay becomes adjusted, which in our example is not fulfilled for the second synapse. Furthermore, if both patterns produce suprathreshold depolarizations, we then obtain opposing delay changes. However, oscillations are avoided by the weighting term of equation 1.1, which drives the learning process toward the pattern that evoked the largest initial suprathreshold voltage.

Because a neuron's delay tuning is not changed by patterns that remain subthreshold, a sufficiently high learning threshold retains a tuning even without any further occurrences of the pattern that gave rise to it. Therefore, a threshold that adapts toward the peaks of the depolarization provides a stable delay tuning. Intermediate thresholds cause an adaptive averaging behavior. Accordingly, the delay tuning can follow a slowly changing and repeatedly presented pattern of synaptic activation (Napp-Zinn et al., 1996),

provided the threshold is crossed at every occurrence. For small, random fluctuations of a pattern, the delays are expected to be tuned to the temporal mean, because the integral (see equation 1.1) behaves approximately linear around the zero crossing for realistic EPSP functions.

5 Conclusion

In summarizing our results, in particular concerning their neurobiological implications, we have to speculate about possible biological mechanisms, not an easy task for theoreticians. However, our general impression of the recent progress in the investigation of synaptic mechanisms gives us a good confidence that suitable biological mechanisms for anything that is logically possible will be found eventually. So one should not worry too much about the concrete mechanisms proposed below.

We have presented a systems view of unsupervised and robust coincidence learning in pulse-coupled neurons that essentially relies on three assumptions.

1. **Only a sum of EPSPs is accessible at a defined measuring site at which the EPSP coincidence is to be established.** Similar to long-term changes of synaptic strengths (Brown, Kairiss, & Keenan, 1990), synaptic delay changes also are assumed to depend on pre- and postsynaptic potentials. With respect to postsynaptic potentials, local dendritic learning is based on dendritic depolarization, whereas more global neural learning relies on the potential at a neuron's axon hillock. The process of delay learning will lead to coinciding EPSPs at these sites.

2. **The time course of the voltage above a learning threshold at the measuring site is available to the individual synapses.** Voltage thresholds are biologically plausible (Artola & Singer, 1993), and their adaptation according to the long-term mean of the depolarization was proposed earlier (Bienenstock, Cooper, & Munro, 1982). In the case of local dendritic learning schemes, the suprathreshold depolarization can easily be sensed by synapse-related molecular mechanisms. Rules that are nonlocal within the postsynaptic cell require the suprathreshold depolarization to be instantaneously signaled, for example, from a neuron's axon hillock, back to all its synapses, which appears more involved. This well-known and indeed fundamental communication problem exists with any form of nonlocal synaptic coincidence learning, Hebbian learning of synaptic strengths included. Except for the work reported by Stuart and Sakmann (1994), to date we have to rely more on speculations than on direct experimental evidence for possible communication mechanisms. Interestingly, Hebbian learning today generally is assumed local (Brown et al., 1990), although Hebb (1958) described a global scheme: "When an axon of a neuron x is near enough to fire a neuron y and does so, some change takes place such that x becomes more effective at exciting y. What is this change and how does it work? This is a question to which we have no final answer." In case of passive or active dendritic

propagation of action potentials (e.g., back from the soma to the synapses), these potentials will act in the same way as the dendritic depolarizations do in our scheme; they will define the learning intervals and the weighting of the learning function.

3. **A uniform learning function is attributed to every synapse and is triggered at the opening of its ion channels (EPSP onset).** Delay learning, as proposed in this article, requires that the synapse contributes to the postsynaptic depolarization and that a postulated differentiating (biochemical) process parallels its individual contribution. This kind of process could be realized by the interaction of an intracellular messenger, such as an activated G protein, and channel proteins (Destexhe, Mainen, & Sejnowski, 1995).

Under these circumstances, we have shown how to compute the delay change of an active synapse from the values of its learning function in conjunction with its suprathreshold depolarization. Biologically speaking, we assume the suprathreshold depolarization to have a nonlinear influence on the differentiating (biochemical) process. During the periods of suprathreshold depolarization, this process could, for example, modify the temporal behavior of intracellular messengers that determine the delay between the transmitter binding to a transmembrane receptor and the intracellular opening of ion channels. This modification could be similar to changes of presynaptic messenger cascades, as initiated by retrograde diffusion of nitric oxide (Montague, 1993), that are hypothesized to cause long-term changes of synaptic strengths. In this respect, we do not rule out alternative mechanisms for delay changes, such as modifications of the temporal behavior of presynaptic molecular processes. Currently there is increasing interest in membrane-delimited mechanisms of rather direct and thus comparatively fast (within a second) interaction between activated G proteins and ion channels (Hille, 1994; Wickman & Clapham, 1995), but to our knowledge, on a millisecond time scale, the properties and their modifiability of these interactions have not been investigated yet.

Although the concrete biophysical or biochemical realization of delay learning is still unclear, we have demonstrated that this simple learning mechanism is well within the possibilities of our current neurobiological knowledge and would provide a useful addition to the commonly accepted plasticity of synaptic efficacy.

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