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Neural Circuitry for Recognizing Interspike Interval Sequences

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Sensory systems present environmental information to central nervous system as sequences of action potentials or spikes. How do animals recognize these sequences carrying information about their world? We present a biologically inspired neural circuit designed to enable spike pattern recognition. This circuit is capable of training itself on a given interspike interval (ISI) sequence and is then able to respond to presentations of the same sequence. The essential ingredients of the recognition circuit are (a) a tunable time delay circuit, (b) a spike selection unit, and (c) a tuning mechanism using spike timing dependent plasticity of inhibitory synapses. We have investigated this circuit using Hodgkin-Huxley neuron models connected by realistic excitatory and inhibitory synapses. It is robust in the presence of noise represented as jitter in the spike times of the ISI sequence.

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Stimulus sensitive regions in central nervous systems are seen in several observations [1–3]. One striking example of this stimulus specific response is the auditory telencephalic nucleus high vocal center (HVC) in the songbird brain [4]. Projection neurons in HVC fire sparse bursts of spikes only in response to auditory feedback of bird's own song (BOS) and syllables of BOS played in reverse order.

If the stimulus produces spikes with indistinguishable waveforms, then all information about the stimulus is in the interspike intervals (ISIs). The presence of neural circuitry tuned to specific stimulus properties suggests a biological network capable of distinguishing among different ISI patterns generated by different stimuli.

We investigate a neural circuit constructed from biological components able to train itself on a given set of ISIs and then selectively respond to presentations of the same ISI sequence. This is of broad general interest as one explores how the outside world is represented and understood by nervous systems. The construction also gives insight about how nervous systems tell time [5–7].

The essential ingredients of the ISI recognition circuit are (1) a spike selection unit which dissects each spike in the input sequence and sends it out along its own neural process, (2) a tunable time delay circuit which receives an input spike at t_0 and produces an output spike at $t_0 + \tau(R)$; R is a dimensionless parameter characterizing an inhibitory synaptic strength, and (3) a strategy to tune $\tau(R)$ using an observed spike timing dependent plasticity rule for inhibitory synapses [8]. Our time delay circuit is based on observations in the anterior forebrain pathway of songbirds [9]. We abstract from that a simple three neuron circuit shown in Fig. 1(a). Each neuron in the time delay circuit is represented as a standard Hodgkin-Huxley (HH) neuron with Na and K voltage gated currents, a ''leak'' current, and an injected dc current. The forms of these equations are standard and are not repeated here [10]. We have used the kinetic functions and parameter values given in [11] (Section II and Appendix 1) for the model neurons. For these parameter values, increasing the dc input current to the HH neuron leads to stable limit cycle oscillations via a saddle node bifurcation. Each neuron has a well-defined spiking threshold [12].

We have also explored time delay circuits comprised of two neurons and a single synapse, and that, along with other details of our model ISI recognition circuit will appear in [13].

The input to the delay circuit [Fig. 1(a)] is a spike arriving at neurons A and B at t_0. In the absence of input neuron A is at rest near -65 mV. Neuron B oscillates at about 20 Hz and inhibits neuron C. Neuron C responds with subthreshold oscillations. In the presence of spiking input, neuron A produces a spike and this input to neuron B resets the phase of its oscillations. Neuron A then inhibits B resulting in removal of inhibition on neuron C. In response, neuron C produces a rebound spike at time $t_0 + \tau(R)$. $\tau(R)$ [Fig. 1(b)] is monotonic in R and $\frac{d\tau(R)}{dR} > 0$. If R is too small, neuron C fires spontaneously; if R is too large, neuron C never fires.

The spike selection unit (SSU) is shown in Fig. 2. Neural units β_n and γ_n are bistable having coexisting rest and spiking states. Each satisfies

$$\frac{dV(t)}{dt} = I_{\mathrm{dc}} + g_{\mathrm{Na}} m_\infty[V(t)][E_{\mathrm{Na}} - V(t)] + g_K n(t)[E_K - V(t)] + g_L[E_L - V(t)] + I_S(t)$$

$$\frac{dn(t)}{dt} = [n_\infty(V) - n(t)]/\tau_n,$$

where $V(t)$ is the membrane potential, I_{dc}, a dc current,

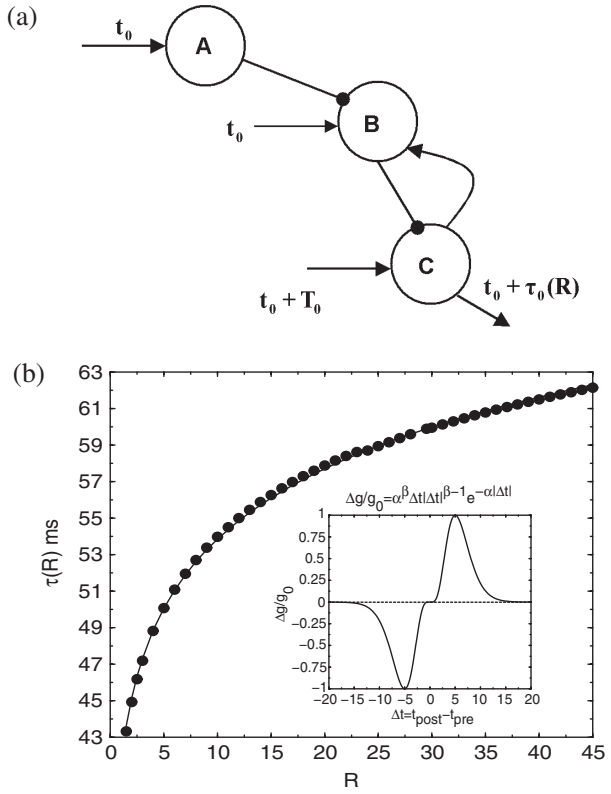

FIG. 1. (a) Time delay circuit. Input to the circuit is a spike arriving simultaneously at units A and B at time t_0. The output of the circuit is a single spike at time $t_0 + \tau(R)$. The excitatory connection $C \rightarrow B$ is used for learning as explained in the text. (b) The time delay $\tau(R)$ as a function of R. The time delays resulting from the use of standard HH neurons can range from tens of ms to about 100 ms, depending on the parameters of the model neuron. Here the range is about 40–65 ms. Empirical fit to the inhibitory synaptic plasticity rule with the function of the form $\Delta g(\Delta t)/g_{I0} = \alpha^{\beta}\Delta t|\Delta t|^{\beta-1}\exp(-\alpha|\Delta t|)$, used for learning is shown in the inset of Fig. 1(b).

$I_S(t)$, the synaptic current. E_r are reversal potentials. The gating variables $m_\infty(V)$ and $n_\infty(V)$ satisfy $X_\infty(V) = 1/[1 + \exp((V_X - V)/k_X)]$. The parameters of the model are (in $\frac{\text{mS}}{\text{cm}^2}$) $g_r = (20, 10, 8)$ and (in mV) $E_r = (60, -90, -80)$ for $r = \text{Na, K, L}$. In mV we have $V_m = -20$, $V_n = -25$, $k_m = 15$, $k_n = 5$, and in ms $\tau_n = 0.16$. $I_{\text{dc}} = 4.0\,\frac{\mu\text{A}}{\text{cm}^2}$. The membrane capacitance is $1\ \frac{\mu\text{F}}{\text{cm}^2}$. Absent any ISI input, neurons γ_n are in the stable oscillating state (with $I_{\text{dc}} = 6.0\frac{\mu\text{A}}{\text{cm}^2}$), and neurons β_n are at rest. Neurons α_n are HH neurons described earlier; they are at rest.

The input to the SSU in Fig. 2 is shown as a sequence S of three spikes at times $\{t_0, t_1, t_2\}$. When the spike at t_0 arrives at neuron α_0, that neuron is excited into its spiking state. It then excites neuron β_0, and it produces an output spike at t_0. When excited, neuron β_0 begins oscillating and inhibiting neuron α_0; no further spikes from S excite α_0. β_0 also inhibits neuron γ_1 moving it from oscillation to

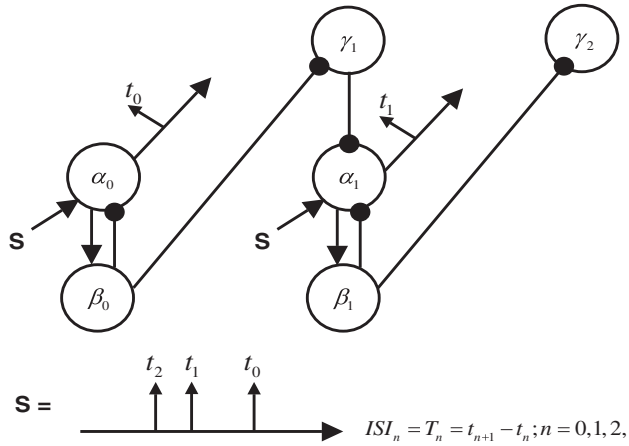

FIG. 2. Spike selection unit. This receives the spike train S at neurons α_n and each neuron α_n produces only one spike at t_n.

rest. The quieting of γ_1 allows neuron α_1 to respond to the spike in S at t_1 producing an output spike at t_1. Neuron β_1 now is excited to oscillation and inhibits α_1 and γ_2. α_1 does not respond to any other spikes in the sequence S. This series of events continues as long as there are spikes in S. Not shown in this schematic is the final step whereby all neurons β_n are returned to rest, and all neurons γ_n are returned to their oscillating state. This is accomplished by global inhibition of the β_n and excitation of the γ_n after S has stimulated output spikes from all neurons α_n, which can be done through a signal sent back to the spike separation unit after the detection unit has triggered a spike after adjusting $\tau(R)$ through learning which indicates the detection of input ISI.

The third ingredient for the ISI recognition unit (IRU) is the mechanism adjusting the time delays to be equal to the input ISIs $T_k = t_{k+1} - t_k$; $k = 0, 1, \ldots$. A spike timing dependent plasticity (STDP) window for inhibitory synapses has been reported in [8] and has the form $\Delta g(\Delta t)/g_{I0} = \alpha^{\beta}\Delta t|\Delta t|^{\beta-1}\exp(-\alpha|\Delta t|)$, where $\Delta t = t_{\text{post}} - t_{\text{pre}}$. t_{pre} is the time of presynaptic spike stimulation, i.e., the spike produced by neuron B in the time delay unit. t_{post} is the time of the postsynaptic spike, i.e., the spike produced by neuron C in the time delay unit and g_{I0} is the scaling factor chosen to be 1 in all the calculations presented here. We utilize this to tune R and the time delay $\tau(R)$. The STDP [8] rule is obtained for a single prepost spike pair, and a key feature of the rule is the zero around $\Delta t = 0$. This rule provides a biologically feasible mechanism for modifying R and setting $\tau(R)$.

The IRU comes from putting together an SSU able to separate the spikes in $S = \{t_0, t_1, \ldots, t_N\}$ and a set of time delay units with one $\tau_k(R_k)$ for each ISI $T_k = t_{k+1} - t_k$; $k = 0, 1, \ldots, N-1$. The output of the neurons α_n; $n = 0, 1, \ldots, N$ are sent in pairs to the time delay units. In Fig. 1 the output of neurons α_0 and α_1 at t_0 and $t_1 = t_0 + T_0$ are

sent, respectively, to neurons A and B and to neuron C. The output unit of the IRU is a ''detection unit'' which receives outputs from each of the ''C'' neurons of the time delay units in the IRU. The detection unit is composed of neurons which fire when two spikes arrive within a time resolution δ ms of each other. This means that when $\delta t_k = |\tau_k(R_k) - T_k| < \delta$ as a result of the adjustments to $\tau_k(R_k)$, the detection unit fires.

When $\delta t_k > \delta$, we must invoke the learning rule to decrease δt_k. To explain how this is accomplished, we focus on a generic time delay unit receiving input at t_0 to neurons A and B and input at $t_0 + T$ to neuron C. Neuron C would fire at $t_0 + \tau(R)$. Note there is an excitatory feedback from neuron C to neuron B. Consider the situation when $\delta t > \delta$, and $T > \tau(R)$. Neuron C produces a spike at time $t_0 + \tau(R)$ resulting in a spike response in neuron B at time $t_0 + \tau(R) + \epsilon$ where ϵ corresponds to the synaptic delay. This excitation of neuron B is presynaptic to the $B \rightarrow C$ inhibitory coupling and is identified with t_{pre} in the STDP rule. Neuron C again receives excitatory input at time $t_0 + T$. This is postsynaptic to the $B \rightarrow C$ inhibitory coupling and we set $t_{\text{post}} = t_0 + T$. $\Delta t = T - \tau(R)$.

This combination of spiking activity in neurons B and C results in an increase in the $B \rightarrow C$ inhibitory synaptic connection. Since $\frac{d\tau(R)}{R} > 0$, $\tau(R)$ increases, approaching T from below. This learning process continues until $T - \tau(R) < \delta$ when the detection unit fires.

In the situation when $T < \tau(R)$ neuron C fires at time $t_0 + T$ which is earlier than the rebound spike time for C. Since firing of C excites B, which in turn inhibits C, neuron C is prevented from producing any further spikes. The detection unit receives just one spike output from neuron C and does not fire. In this case the presynaptic time to be paired with the firing of neuron C is the next action potential generated by neuron B as it resumes its oscillations. This occurs at a time $t_0 + T + t_B$, with $t_B > 0$, and this is greater than $t_0 + \tau(R)$ when neuron C would have fired if there were no input spike at $t_0 + T < t_0 + \tau(R)$. The STDP rule then sees $\Delta t = t_0 + T - (t_0 + T + t_B) < 0$. This leads to a decrease in R and a decrease in $\tau(R)$. The decrease in $\tau(R)$ continues until $\tau(R) \approx T$, when the time delay unit has completed its learning. $\tau(R)$ does not decrease beyond T for then we would have the first situation where $T > \tau(R)$, and we have seen that STDP operates to send $\tau(R) \rightarrow T$ in that case. Of course, when $|\tau(R) - T| < \delta$, the detection unit fires, and learning is completed.

The overall IRU is comprised of an SSU and as many time delay units as there are ISI in the sequence S. Once the SSU has separated the spikes from the input sequence, each time delay unit is trained in precisely the same way, namely, to the nth time delay unit spikes at times t_n and $T_{n+1} = t_n + T_n$ are delivered. The time delay $\tau_n(R_n)$ is adjusted to correspond to T_n within a resolution δ. Since each unit is trained in precisely the same way, we present here results on the training of just one time delay unit. The training consists of N presentations of the spike sequence S to the time delay unit. To illustrate the two training scenarios just described, we choose the synaptic strength $g_{BC}(N = 0)$ first to correspond to $\tau_n(R_n) < T_n$ and second, to $\tau_n(R_n) > T_n$.

In Fig. 3 we show results from training two IRU units tuned to detect an ISI of $T = 55$ ms. The first IRU has $g_{BC}(N = 0) = 2$, corresponding to $\tau(R) \approx 43$ ms, so $T > \tau(R)$. The second has $g_{BC}(N = 0) = 30$ leading to $\tau(R) \approx 60$ ms, so $T < \tau(R)$. Each IRU trains itself on the given ISI input presented $N = 1, 2, \ldots$ times. In the detection unit we set $\delta = 4$ ms. This resolution represents the widths of realistic neural spikes.

The training is completed when the detection unit responds with a spike output. The contribution of multiple spike pairs in the STDP learning is considered additively [14]. We have also trained an IRU using a simple STDP rule wherein only the contribution from the nearest spike pairs are considered. The convergence persists though the number of steps to convergence in the training differ. The additive rule for spike pairs is also considered in number of earlier works [15,16]. IRUs are trained by invoking the inhibitory STDP rule as $\Delta g_{BC} = \frac{1.0}{g_{\text{norm}}} \sum_j \alpha^\beta \Delta t_j |\Delta t_j|^{\beta-1} \exp(-\alpha|\Delta t_j|)$, with $g_{\text{norm}} = \beta^\beta e^{-\beta}$, where $\Delta t_j = T_C - T_{B_j}$ when we have one postsynaptic spike in neuron C at time T_C and T_{B_j} represents the presynaptic spike times of neuron B. In the situation when there are two postsynaptic spikes in neuron C at times T_{C_1} and T_{C_2}, such that $T_{C_1} < T_{C_2}$ as in the case

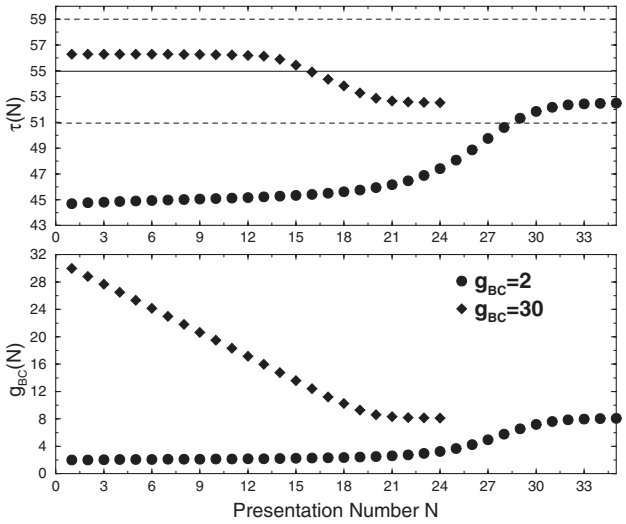

FIG. 3. Training an IRU to learn an ISI of $T = 55$ ms. The initial values of $g_{BC}(N = 0)$ are set to explore the two scenarios described in the text. $\tau(R)$ (top panel) and g_{BC} (bottom panel) are plotted as function of the number of presentations of the training sequence N. The resolution limit $\delta = 4$ ms is shown in dotted lines for $\tau(R)$ and $T = 55$ ms is shown as a solid line.

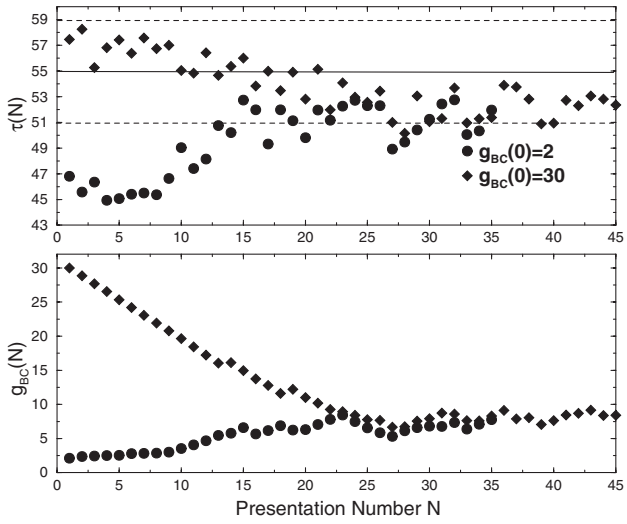

FIG. 4. Training an IRU to learn an ISI of $T = 55$ ms in a noisy environment. The input ISI has a uniform jitter of 2 ms. The initial values of $g_{BC}(N = 0)$ are set to explore the two scenarios described in the text. $\tau(R)$ (top panel) and g_{BC} (bottom panel) are plotted as function of the number of presentations of the training sequence N. The resolution limit $\delta = 4$ ms is shown in dotted lines for $\tau(R)$ and $T = 55$ ms is shown as a solid line.

when $T > \tau(R)$, we compute Δt_j as

$$\begin{aligned}\Delta t_j &= T_{C_1} - T_{B_j}, \qquad T_{B_j} \le T_{C_1} \\ &= T_{C_2} - T_{B_j}, \qquad T_{B_j} > T_{C_2} \\ &= (T_{C_1} - T_{B_j}) + (T_{C_2} - T_{B_j}), \qquad T_{C_1} < T_{B_j} \le T_{C_2}.\end{aligned}$$

The parameters for the empirical learning rule were taken as $\alpha = 0.54$, $\beta = 3$ for $\Delta t > 0$ and $\alpha = 0.24$, $\beta = 5$ for $\Delta t \le 0$.

In Fig. 3, top panel, we show $\tau(R)$ as function of presentation number N, and in Fig. 3, bottom panel, $g_{BC}(R)$ as a function of N. We see that in each case both IRUs train themselves to the same values of $\tau(R)$ and g_{BC}. The former is within the resolution $\delta = 4$ ms.

To explore the robustness of the training procedure in the presence of noise we show in Fig. 4 the training of the same two IRUs but now with a uniform jitter of 2 ms.

Using a time delay circuit suggested by a birdsong control loop [9], implemented in Hodgkin-Huxley model neurons, and an observed spike time dependent plasticity rule for inhibitory plasticity, we have constructed an answer to the interesting general question: how is timing in the range of tens to hundreds of milliseconds implemented and learned in biological neural circuits. This also informs the broad question of how nervous systems tell time with a focus on time intervals important to many neural processing tasks.

Biological circuits similar to the IRU are capable of recognizing specific sensory input as it is delivered, presumably segmented into useful patterns in space and time, for higher order neural recognition and processing. We have examined the robustness of this circuit to noise in the form of ISI jitter in the input ISI sequence. There are many other formulations of noise in spike recognition one may consider, and we examine them in the context of a collection of ISI sequences and associated IRUs which follow the segmentation of a neural response to a complex input [13]. The importance of IRUs as biological recognition units will depend on their ability to sort desired sequences from the complex array associated with actual input signals.

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