Stochastic recruitment in parallel fiber activity patterns.

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Abstract: Random excitations granule cells are likely to overwhelm spatiotemporal sequences described as "tidal waves" in the target article. A mechanism is proposed involving the Golgi cells to reinforce tidal waves against noise. The recurrent inhibition by the Golgi calls can recruit random excitations of granule cells in phase with sequences of mossy fiber input.

Noisy Issues. The target article presents intriguing experimental support for the propagation of waves in parallel fibers, but the potential effects of the noise inherent in the nervous system has not been thoroughly addressed. Random excitations of granule cells can make a significant contribution to Purkinje cell activity. For each parallel fiber that contacts a Purkinje cell there is a 50% chance that a spike originated in a granule cell on a particular side. Let N be the number of parallel fiber spikes required to induce a simple spike from a Purkinje cell. The probability that of N spikes converging on the Purkinje cell, ℓ of them came from one side, $P(\ell; N-\ell)$, is equal to the number of combinations of N spikes taken ℓ at a time, divided by the total number of possibilities for spikes arriving from either side;

$$P(\ell; N-\ell) = \frac{N!}{\ell!(N-\ell)!} \cdot 2^{-N}. \tag{1}$$

The number of simultaneous parallel fiber spikes required to excite a single simple spike is found to be N = 50 (Barbour 1993). This would imply that the probability that all of the impulses come from one side is $P(0; 50) \approx 10^{-15}$. In contrast, the probability that the signals are equally distributed on either side is $P(25; 25) \approx 0.1$. The statistics implied by the function $P(\ell; 50-\ell)$ suggest that the amount of simple spike activity induced by noise would overwhelm the appearance of temporal sequences along the beams unless either the noise level is very low, or there is a mechanism that reinforces the temporal sequence in the presence of fluctuations.

Golgi inhibition. The Golgi cells have been implicated in temporal sharpening of granule cell activity (Eccles et al 1967). Although the authors of the target article state that the Golgi cells act mainly to "put a brake on" local activity, the recurrent inhibition induced on granule cell activity can lead to pattern formation. In species such as mammals where the Golgi dendrites reach deep into the molecular layer, a large portion of their input will arise from parallel fiber signals. Let $E(x,t)$ be the instantaneous firing frequency of granule cells at time t and point x along the beam (in the coordinates of the target article). In the molecular layer, signals split into two populations:"right movers" and "left movers," $M_{R,L}(x,t) = E(x \pm (vt + \Delta x_a), t - x/v)$, where Δx_a is the average length of the ascending fibers.

To study the consequences of granule-Golgi cell interactions, an activation-inhibition model (Ermentrout & Cowan 1979) will be used. The granule cells excite the Golgi cells which respond with a delayed inhibitory response. In the parallel fibers, this time delay is transformed into a spatial interval. If $I(x,t)$ represents the instantaneous firing frequency, then one is led to the equations,

$$\begin{aligned} \frac{\partial}{\partial t}E(x,t) &= f(E) - \int_{\mathcal{F}} \omega_I(x-x')I(x',t)dx' \\ \frac{\partial}{\partial t}I(x,t) &= g(I) - \int_{\mathcal{F}} \omega_E(x-x')[M_L(x',t)+M_R(x',t)]dx'. \end{aligned} \tag{2}$$

The functions f and g set the background firing level and possible thresholds of the corresponding cell population, and the integral is over the length of the folium ($\mathcal{F}$). The kernels, $\omega_i(x)$, $i = I, E$, denote the spatial extent of the interaction and can take the general form, $\omega_i(x) = A_i \exp[-b_i x^2]$, where b_E is a function of the spread of Golgi dendrites in the molecular layer along the beam, and b_I is related to the spread of Golgi axons in the granule layer. The constants, A_i, are determined by the interaction strength between the neuronal populations. These equations are presently under study and belong to a large class of models that can *spontaneously* generate spatiotemporal patterns.

Patterning of tidal waves. Qualitatively, under random excitation of the granule cells, there is a sinusoidal modulation of parallel fiber activity at a frequency that depends on the ascending fiber length (Δx_a). The amplitude of this modulation will depend on such factors as the spatial extent of Golgi dendrites and axons, the distribution of ascending fiber lengths, and the synaptic strength connecting the populations. These features have been checked using a cellular automata simulation of the parallel fiber system.

Our patterning results are relevant to the discussion of "tidal waves" under the combinatorical constraints mentioned above. If a temporal sequence of granule cell spikes make a moving wave in the right (left) movers $(M_{R(L)}(x,t))$, then there will be a right (left) moving trough following the wave. The trough will then silence the Golgi cells and allow a higher probability of granule cell activity in phase with the wave. Thus, the cerebellar circuitry allows for the *recruitment of noise* in phase with the stimulus while the noise is suppressed elsewhere. This effect can continue even *beyond the length of the parallel fibers* that carried the original tidal wave, thus propagating the signal across the folium. Although Golgi cells also receive inputs from both mossy and climbing fibers that will effect the propagation of activity waves, the mechanism proposed here can lead to significant consequences for cerebellar function.

References

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