Functional constraints do not cause observed correlations between maximal conductances in an identified neuron

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Neurons typically express many different types of voltage-gated channels. The density of these channels, their kinetics, and their spatial distribution determine how the neuron behaves. While the density of channels in a particular identified neuron can vary widely, the behavior of that cell in a network is often tightly conserved [1]. Naively, this seems paradoxical. However, if different conductances are correlated, this could resolve the apparent paradox. In the stomatogastric ganglion (STG) of the crab, *Cancer borealis*, recent work has shown that the expression levels of many voltage-gated channels are correlated [1,2,3]. While it is tempting to conclude that these correlations are necessary for the cell's behavior to be tightly constrained, it is not at all clear that this is the case. We wanted to understand whether the observed correlations are necessary for these neurons to function properly.

We investigated this question by constructing a population of multicompartment models of the LP neuron. Each member of this population had maximal conductances drawn randomly, independently, and uniformly from a range that roughly matched the observed biological range. We generated, simulated, and automatically classified the behavior of ~240,000 model neurons. We then filtered this population, selecting only those neurons whose behavior was consistent with the behavior of the LP cell. This was done by measuring six different properties in each model cell and comparing their values to those in biological LP cells. The six measurements were: resting membrane potential, tonic firing rate, input resistance, phase of spike onset, spike-frequency within the burst, and slow-wave oscillation amplitude. These quantities have all been measured in biological LP cells, and model LPs were considered "admissible" if they were within two standard deviations of the mean value of these measurements. Of the original ~240,000 models, 131 qualified as admissible LP models.

The data on mRNA expression levels show strong positive correlations between the levels of four channel genes: shab (Kd), shaw (Kd), shal (A) and IH (h). (All pairs were correlated.) We looked for correlations between the corresponding channels in the model population of 131 cells, but failed to find any such correlations. The lack of correlations in the model suggests that the observed correlations are not *necessary* for a neuron to function as a proper LP neuron. This implies that the correlations found in the data may be present for reasons not related to electrophysiological function per se. For instance, they could reflect constraints imposed by the architecture of channel expression regulation.

Acknowledgments
We thank J.M. Goaillard and D.J. Schulz for helpful discussions. This work was supported by NIH NS50928 (ALT), and NIH MH46742 and the McDonnell Foundation (EM).

References
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