Near-optimal experimental design for sampling voltage on dendritic trees

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Understanding dendritic computation remains a key problem in cellular and computational neuroscience. The main challenge is in recording physiological signals (particularly voltage) with sufficient spatiotemporal resolution on dendrites, either via multiple-electrode recordings or imaging techniques. Statistical techniques can alleviate this difficulty, by de-noising the data and inferring the voltage in unobserved compartments.

Statistical optimal experimental design methods also offer a framework for maximizing the information provided by each measurement. These approaches require us to efficiently solve two challenging problems: first, we must evaluate the quality of any proposed design. Second, we must search over many candidate designs. This work proposes solutions to both of these problems.

To address the first problem, we take advantage of some particular features of the dendritic spatiotemporal filtering problem to efficiently calculate the optimal estimator error covariance (in $O(N)$ time and space, where N is the number of compartments on the tree). Using these computed covariance matrices we can easily calculate design metrics such as the expected weighted mean-squared error of the optimal voltage estimator. To efficiently search the space of possible designs, we utilized "lazy greedy" methods from the literature on submodular optimization, obtaining search speedups of multiple orders of magnitude. Combining these two techniques proved critical for tractable optimization.

We test our framework with simulations of real dendritic trees and compare the quality of both time-invariant and time-varying sampling schemes. Improvements ranged from 30-100% over some simpler methods (e.g., random sampling), with larger gains for fewer observations. The resulting near-optimal designs can be somewhat counterintuitive; for example, if an unweighted MSE design criterion is chosen, the optimal sampler spends most of its time observing the tips of highly-branched dendrites, not the soma or branch points of the tree. We are currently working to apply these methods to real dendritic imaging data.

References

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