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Presentation Abstract

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Presentation Title: Automated exploration of intracellular mechanisms of *in vivo* neural computation

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Abstract: Many molecular, synaptic, and cellular mechanisms have been discovered and explored *in vitro* (e.g., in brain slices) or in anesthetized animals. Whether these mechanisms play a role in awake brain functions, however, often remains to be determined, in part because performing intracellular recordings in awake behaving animals - necessary for verifying the real-time contribution of a specific synaptic or ionic conductance to a specific network function, for example - is technically challenging. Accordingly, we recently developed an awake autopatching robot to perform whole cell patch clamp recordings in awake behaving animals. We are now working on strategies for automatically exploring whether specific types of cellular mechanisms observed *in vitro*, also contribute to neural computations in the awake behaving animal. To

achieve this, we are building informatics approaches to mine complex patterns of subthreshold and suprathreshold activity within single neurons undergoing whole cell patch clamp in vivo via our autopatcher robot. We can then mine the recordings that emerge for specific subthreshold patterns of synaptic activity or intrinsic conductance in an unbiased fashion, applying pharmacological (and even optogenetic) perturbation as needed to validate the findings. For example, one question amenable to this approach is the investigation of the fundamental timescales over which subthreshold activity patterns might be observed to repeat in a stereotyped fashion. By taking patch clamp recording traces, and cross-correlating each part of a trace with other parts, we can in an unbiased fashion survey whether specific patterns of activity repeat over time. These automated and unbiased methods of recording and analyzing intracellular activity in awake behaving animals may yield important insights into the computations that occur within neurons and neural networks. Moreover, combined with automated methods for feedback and causal hypothesis testing, as well as automated pharmacology and optogenetic approaches, this approach could enable rapid and systematic exploration in the awake brain of the specific roles played by the vast number of mechanisms identified in vitro. (Talei Franzesi, Singer, Kolb, and Sharma are co-first authors.)

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