

## T-15. Processing properties of medulla neurons define neural substrates of motion detection in *Drosophila*

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The brain processes spatiotemporal changes in luminance to extract visual motion cues. The algorithms employed in this task and the neural circuits that implement them have been the focus of intense research for more than 50 years. An influential correlation-based model, the Hassenstein-Reichardt correlator (HRC) relies on the differential filtering of two spatial input channels, delaying one input signal with respect to the other. This delay allows selective amplification of the output only when the delayed and non-delayed signals coincide in time, signaling motion. Recent work in flies has identified two parallel motion channels specialized for detecting either moving light or dark edges. Each of these pathways requires two critical processing steps to be applied to incoming signals: differential delay between the spatial input channels in each pathway, and asymmetric treatment of light and dark contrast signals. While the neural substrates that define the input and output channels of the light and dark edge circuits have been identified, the neural substrates that implement these two critical processing steps remain elusive. Using *in vivo* patch-clamp recordings, we show that four medulla interneurons exhibit these processing properties. The interneurons Mi1 and Tm3 respond selectively to brightness increments, with the response of Mi1 delayed relative to Tm3. Conversely, Tm1 and Tm2 respond selectively to brightness decrements, with the response of Tm1 delayed compared to Tm2. HRC models that are constrained by these measurements produce outputs consistent with previously measured tuning properties of motion detectors in flies. We therefore propose that Mi1 and Tm3 perform critical processing of the delayed and non-delayed input arms of the correlator responsible for the detection of light edges, while Tm1 and Tm2 play analogous roles in the detection of moving dark edges.

## T-16. A theory of neural dimensionality and measurement

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In many experiments, neuroscientists tightly control behavior, record many trials, and obtain trial-averaged firing rates from hundreds of neurons in circuits containing millions of behaviorally relevant neurons. Dimensionality reduction has often shown that such datasets are strikingly simple; they can be described using a much smaller number of dimensions (principal components (PCs)) than the number of recorded neurons, and the resulting projections onto these components yield a remarkably insightful dynamical portrait of circuit computation. This ubiquitous simplicity raises several profound and timely conceptual questions. What is the origin of this simplicity and its implications for the complexity of brain dynamics? Would neuronal datasets become more complex if we recorded more neurons? How and when can we trust dynamical portraits obtained from only hundreds of neurons

in circuits containing millions of neurons? We present a theory that answers these questions, and test it using data from reaching monkeys. We derive a theoretical upper bound on the dimensionality of data. Our bound has a natural interpretation as a quantitative measure of task complexity. Interestingly, the dimensionality of motor cortical data is close to this bound, indicating neural activity is as complex as possible, given task constraints. Our theory provides a general analytic framework to ascertain whether neural dimensionality is constrained by task complexity or intrinsic brain dynamics, furthering our ability to interpret large-scale datasets. We also describe sufficient conditions on PCs underlying neural activity so that low dimensional dynamical portraits remain unchanged as we record more neurons, and show that they are satisfied by motor cortical data. This theory yields a picture of the neural measurement process as a random projection of neural dynamics, conceptual insights into how we can reliably recover dynamical portraits in such under-sampled measurement regimes, and quantitative guidelines for the design of future experiments.

## T-17. Mapping the brain at scale

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The behavior of an animal reflects computations across its entire nervous system, involving the coordinated activity of thousands of neurons within and across multiple brain areas. New imaging technologies [1] allow us to monitor neural function during naturalistic behavior at unprecedented scales. But the data are quickly outpacing the capabilities of ordinary analytical approaches: a half hour experiment can yield a terabyte or more. These data are complex and high-dimensional, and we want to understand how their structure evolves over both space and time. Recent developments in distributed computing on clusters are making rich data analytics at the terabyte or petabyte scale tractable. By adapting a novel, open-source platform for distributed computing, Spark [2], we have developed a library of analyses and interactive visualizations for revealing spatiotemporal structure in large-scale calcium imaging data. With Spark, we leverage both the computing power of a distributed environment and its distributed memory, performing in seconds complex, iterative computations that would be intractable or impossibly slow with existing methods. We apply these tools to the larval zebrafish. Calcium responses from nearly all neurons ( $\sim 10^9$  voxels reflecting the activity of  $\sim 10^5$  neurons) are recorded in a fish expressing GCaMP5 pan-neuronally using light-sheet microscopy. For the first time, whole-brain imaging is performed while the animal is behaving in response to visual stimuli. Our analyses yield computational brain maps at single-cell resolution. Anatomically structured populations of neurons are found to play distinct roles in stimulus encoding and the generation of motor behavior. The evolution of whole-brain activity through a low dimensional space can be monitored on a trial-by-trial basis and linked directly to behavior. The open-source analytical framework we offer thus holds promise for turning brain activity mapping efforts into interpretable results.