



## Presentation Abstract

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Presentation Title: Multiple-color optical excitation of distinct neural populations using sets of novel channelrhodopsins derived from algal genomic diversity

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Abstract: The ability to independently excite two distinct populations of neurons using different wavelengths of light would enable researchers to assess the causal contribution of different types of neurons to emergent neural circuit dynamics. Thus far only a handful of algal channelrhodopsins have been reported to date, and only channelrhodopsin-2 (ChR2) and its mutants have been shown to function well in a variety of neural circuit analysis scenarios. As part of the 1KP consortium, we systematically sequenced the transcriptomes of diverse genera of algae, from which we mined the sequences encoding for dozens of new channelrhodopsins with novel spectral sensitivity patterns, current amplitude, and channel kinetics. We are exploring this “channelrhodopsinome” to find systematic amino acid residues that predict opsin features and performance, aiming to discover broad principles of channelrhodopsin operation.

The prospects for contributing new tools to neuroscience is significant. For example, we found a new channelrhodopsin, here nicknamed ChR66, to have an action spectrum 30nm blue-shifted relative to that of ChR2, and can reliably mediate high frequency spike trains in neurons in response to 406nm light. ChR66 also has improved tau-off kinetics of 6.5ms and it does not desensitize appreciably (<10%). In addition, we found another novel channelrhodopsin, here nicknamed ChR65, to have improved high-speed expression and membrane trafficking, and can generate

large currents in response to 543nm (green) light in neurons.

We engineered a yellow light drivable mutant of ChR65, here nicknamed Chello, in order to attain significantly reduced light sensitivity at 406nm; indeed, Chello does not elicit spikes at 406nm at irradiances up to 10mW/mm<sup>2</sup>. Chello can be reliably driven at 543nm and has tau-off kinetics of 32ms. We show that by expressing ChR66 and Chello in two distinct populations of neurons, we can independently drive the two populations using 406nm and 543nm light respectively. We believe these new reagents will enable researchers to optically interrogate distinct neural circuits in a fast temporally-precise manner that has previously not been possible, and the diversity of new channelrhodopsins we report, may provide platforms for engineering a variety of new kinds of optical neural activator in the future.

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