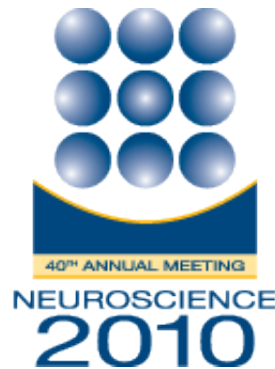


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## Presentation Abstract

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Title: An optogenetic toolbox designed for primates

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Abstract: Optogenetics is a cell type-specific approach to neural control in systems neuroscience that complements classical electrophysiology. To enable its broad applications, we have previously introduced a number of versatile optogenetics tools beyond the microbial opsins themselves (Boyden 2005; Zhang 2010), including fiberoptic neural interfaces (Aravanis et al., 2007) suitable for behaving mammals (Adamantidis et al., 2007; Gradinaru et al., 2007), optrodes that combine light delivery with electrical recording (Gradinaru et al., 2007, 2009), and specific targeting reagents (Zhang 2006; Zhang 2007; Aravanis et al., 2007). While these tools have since shown straightforward functionality in rats, mice, and monkeys, as expected, there are unique features of the large mammalian brain system that require more advanced and specialized technologies. We have therefore developed a panel of primate-focused tools, and report here the application of these tools to primate optogenetics in rhesus macaques. Specifically, we report 1) a novel fiber-based device for *in vivo* tracking of opsin expression level and localization in highly-trained or otherwise valuable animals that cannot be readily assessed for this measure histologically; 2) application to

macaques of excitatory and inhibitory opsins, channelrhodopsin-2 (ChR2) and enhanced halorhodopsin (eNpHR2.0) respectively, optimized for large tissue volume recruitment; and 3) AAV-based opsin delivery tools, the standard for safety in clinical work, coupled with two distinct human promoters, hSyn and hThy-1, that give rise to high expression levels and functionality at much lower light levels than previous efforts, assessed both with single-unit and local field potential readouts. Specifically, we showed that very low light levels (0.1-8 mW power through a 200 $\mu$ m optical fiber) were sufficient to robustly activate ChR2-expressing neurons: 50% (62/127) of all recorded hSyn-ChR2 neurons and 45% (24/53) of all recorded hThy-1-ChR2 neurons responded significantly to blue light ( $p < 0.01$ ,  $\chi^2$ -test). Moreover, these neurons were able to reliably follow stimulation frequencies from 20-50 Hz with latencies of approximately 3 ms. Similarly, we demonstrated that low intensities of green light (0.1- 8 mW through the same fiber) could shut down neural activity completely and rapidly in 38% (55/124) of all recorded eNpHR2.0 neurons. Lastly, we introduced mammalian codon-optimized step function opsins (SFO), which were functional in giving rise to bistable excitation at very low light powers as well. Together these results help define a panel of versatile primate-optimized optogenetic tools for systems neuroscience.

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