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Optogenetics has allowed millisecond-precision bidirectional control of defined cell types in freely behaving mammals. ChR2 was the first microbial opsin brought to neurobiology, where we initially found that ChR2-expressing neurons can fire blue light-triggered action potentials with millisecond precision, without addition of chemical cofactors; this approach has since proven versatile across a variety of preparations. We next found that neurons targeted to express the light-activated chloride pump halorhodopsin from Natronomonas pharaonis (NpHR) can be inhibited from firing action potentials when exposed to yellow light in intact tissue and behaving animals; because of the excitation wavelength difference, the two optical gates can be simultaneously used in the same cells even in vivo. We then employed genomic strategies to discover and adapt for neuroscience a cation channel (VChR1) with action spectrum significantly redshifted relative to ChR2, to allow tests of the combinatorial interaction of cell types in circuit computation or behavior. Along the way we have developed genetic targeting tools for versatile use of microbial opsins including cell type-specific promoter fragments, transgenic animals, and AAV-based Cre-LoxP reagents, as well as developed fiberoptic approaches to allow specific cell types, even deep within the brain, to be controlled in freely behaving mammals. We are currently probing and quantifying measures of circuit performance during optogenetic control of defined neural elements to address longstanding questions about neural dynamics. For example, we have used this approach for depth targeting of 1) hypocretin/orexin cells in the lateral hypothalamus 2) subthalamic nucleus region circuit elements in animal models of Parkinson's Disease, and 3) neuronal subtypes relevant to neural reward, brain oscillations, and schizophrenia. In this work we have for the first time been able to establish causal relationships between frequency-dependent activity of genetically defined neurons important in neuropsychiatric disease, and complex orchestrated mammalian behaviors.