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We have shown in the accompanying abstract that when stimulated with light, Channelrhodopsin-2 (ChR2) can control the spiking of neurons on the timescale of milliseconds. However, many applications of ChR2 will be realized only with precise regulation of ChR2 expression via modern genetic strategies, including the development of gene delivery systems appropriate to species and cell type, the use of cell-specific promoters that are highly selective within defined nervous system regions, and the creation of transgenic animals. We here highlight several principles governing effective tuning of ChR2 in these various scenarios. We first describe the creation of viral systems capable of targeting neurons of specific types either via their promoters or via the localization of dividing cells in the nervous system. Using promoters of varying strength and specificity, ChR2 can be expressed in a diversity of cell types, allowing focused perturbation of circuit computation and behavior. Second, we describe optical strategies for controlling ChR2 function in intact experimental systems. Together, these strategies will likely enable ChR2 to serve as a universal tool for understanding how specific neurons operate within important model systems.

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