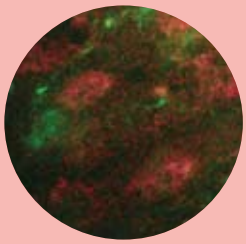

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Rhythms of the Neocortex: Where Do They Come From and What Are They Good For?

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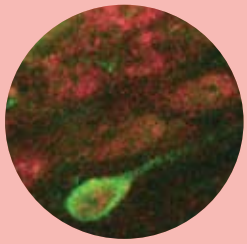

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Rhythms of the Neocortex: Where Do They Come From and What Are They Good For?

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Introduction

During the last 20 years, the study of neural rhythms has undergone a major renaissance: We now have far more information about how rhythms are produced, how they are associated with function, and how pathologies in rhythms relate to neurological diseases. However, the central question of what roles these rhythms play in sensory processing, cognitive activity and motor planning remains to be answered definitively. This short course summarizes the state of the art in the study of neocortical rhythms, touching on insights from *in vitro* and modeling work, and connecting the *in vivo* rhythms to the functional circumstances in which they are recorded. The work described comes from a variety of *in vitro* and *in vivo* technology, and one talk will address new techniques for investigating and engineering rhythms. In addition, there will be several breakout group discussions with the speakers, as well as an extra breakout session used for a tutorial on a variety of analysis methods for rhythmic data.

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New Techniques for Investigating Brain Rhythms: Optical Neural Control and Multielectrode Recording

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Giovanni Talei Franzesi, Stephanie Chan,
Jacob Bernstein, Xiaofeng Qian, PhD, and Mingjie Li

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Introduction

Progress in neuroscience commonly emerges from technological innovation. It can empower neuroscientists to answer old, much debated questions in a more conclusive fashion and often opens up the possibility of confronting entirely new questions about the brain. To understand how neural dynamics emerge from the action of coordinated ensembles of specific types of neurons in the brain, two core abilities are ever in need of innovation:

- The ability to perturb neural circuit elements in a temporally and spatially precise fashion throughout neural circuits *in vivo*; and
- The ability to record large ensembles of neurons in the brain of the awake behaving animal.

Rhythmic, synchronous neural activity within and between brain regions has been observed during, or associated with, many brain functions; these include timing-dependent plasticity, global stimulus feature processing, visuomotor integration, emotion, working memory, motor planning, and attention. These activities have been measured with multielectrode recording, electroencephalography (EEG), magnetoencephalography (MEG), and local field potential (LFP) analysis. Furthermore, abnormal patterns of neural synchrony have been associated with a variety of neurological and psychiatric disorders, such as Parkinson's disease, epilepsy, autism, and schizophrenia. Computationally, synchrony has been implicated in processes such as grouping neurons into cell assemblies that can more effectively represent information to downstream neural networks, acting as a clock for gating or multiplexing information, coordinating information flow within small neural networks, selecting stimuli for attention, and performing pattern recognition.

However, defining the causal role such synchronous patterns play in mediating neural computation and behavior has remained difficult. In recent years, we and others have developed novel technologies that support this agenda and are now finding wide use in neuroscience. In this chapter, we will focus on exploring the implications for neural rhythm analysis of two sets of technologies:

- Genetically encoded molecular sensitizers that enable neurons to be activated or silenced with light in a temporally and spatially precise fashion; and
- Hardware for perturbation and recording of neurons in complex (e.g., three-dimensional) geometries throughout the brain.

Optical Neural Control via Genetically Encoded Molecular Sensitizers: Application to Rhythms

The ability to activate or silence the neurons of a specific cell class allows one to explore the causal contribution it makes to generating a particular rhythm. For example, activating a set of neurons of a specific class at varying frequencies can reveal whether there is a frequency resonance in the circuit, mediated by that cell type (Cardin et al., 2009; Han et al., 2009). Activating different numbers of cells in a circuit, within a defined time window, can reveal whether neural dynamics undergo phase transitions in the kind of rhythm observed, as the number of cells recruited is increased (Boyden et al., 2009). Downmodulating the activity of a particular cell class enables one to test its necessity in contributing to a given oscillation (Sohal et al., 2009). Ideally, such studies are closely coupled with computational modeling (Boyden et al., 2009; Sohal et al., 2009; Talei Franzesi et al., 2009), since even with the use of precise optical manipulation, interpreting the effects of manipulating a cell type on a complex network can be a significant task.

During the last few years, we and others have adapted a set of naturally occurring microbial opsins for neural expression. In this way, we have enabled specific, genetically defined neuron types expressing these opsins to be activated and silenced by pulses of light in a temporally precise fashion. These microbial opsins are 7-transmembrane proteins that bind the cofactor all-*trans*-retinal, which naturally occurs in the mammalian brain; thus, these single-component optogenetic reagents require no supplementation by exogenous chemicals in order to function in mammals. For example, when the gene for the naturally occurring light-gated cation channelrhodopsin-2 (ChR2) from the alga *Chlamydomonas reinhardtii* is expressed in hippocampal neurons by transfection or viral infection (Fig. 1*A*), neurons experience strong depolarizing currents in response to blue (~450–490 nm) light (Fig. 1*B*), allowing reliable spike firing in response to brief (1–10 ms duration) pulses of blue light at light powers of 1–10 mW/mm2 (Fig. 1C) (Boyden et al., 2005). When the gene for the naturally occurring light-driven chloride pump halorhodopsin (Halo/NpHR) from the archaebacterium *Natronomonas pharaonis* is expressed in hippocampal neurons by transfection or infection (Fig. 1*D*), neurons experience hyper-polarizing currents in response to yellow (~570–610 nm) light (Fig. 1*E*), allowing spike

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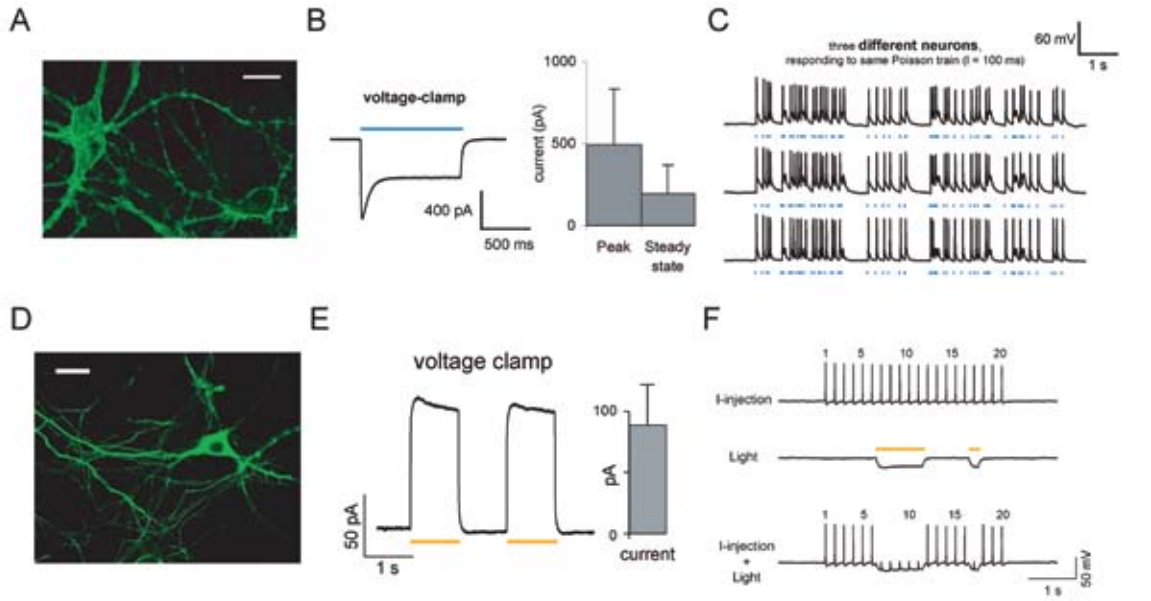

Figure 1. Channelrhodopsin-2 (ChR2) and halorhodopsin from *N. pharaonis* (Halo/NpHR): optical activation and silencing of neurons. ***A***, Hippocampal neurons *in vitro* expressing ChR2-YFP (scale bar, 30 μm). Adapted from Boyden et al., 2005, their Fig. 1, reprinted with permission. ***B***, *Left*, inward current in voltage-clamped neuron evoked by 1 s blue light (indicated by blue bar), with population data (right; mean + SD; $n = 18$). Adapted from Boyden et al., 2005, their Fig. 1, reprinted with permission. ***C***, Voltage traces showing spikes in three different hippocampal neurons, in response to the same temporally patterned light stimulus (blue dashes). Adapted from Boyden et al., 2005, their Fig. 2, reprinted with permission. ***D***, Hippocampal neuron *in vitro* expressing mammalian codon-optimized *N. pharaonis* halorhodopsin (abbreviated Halo/NpHR) fused to green fluorescent protein (GFP), under the CaMKII promoter. Scale bar, 20 μm. Adapted from Han and Boyden, 2007, their Fig. 1, used under open access license. ***E***, Neuronal currents elicited by optical activation of Halo. *Left*, representative currents elicited by two 1 s pulses of yellow (560 + 27.5 nm) light (~10 mW/mm^2) in a voltage-clamped neuron held at –70mV. *Right*, population data ($n = 22$ neurons). Adapted from Han and Boyden, 2007, their Fig. 1, used under open access license. ***F***, Light-driven spike blockade, demonstrated for a representative hippocampal neuron. *Top* ("I-injection"), neuronal firing of 20 spikes at 5 Hz, induced by pulsed somatic current injection (~300 pA, 4 ms). *Middle* ("Light"), membrane hyperpolarization induced by two periods of yellow light, timed so as to be capable of blocking spikes 7–11 and spike 17, out of the train of 20 spikes. *Bottom* ("I-injection + Light"), yellow light drives Halo to block neuron spiking (note absence of spikes 7–11 and of spike 17) while leaving spikes elicited during periods of darkness largely intact. Adapted from Han and Boyden, 2007, their Fig. 4, used under open access license.

silencing in response to pulses of yellow light (Fig. 1*F*) (Han and Boyden, 2007). Halorhodopsin currents increase by an additional ~75% from sequences that improve trafficking to the membrane (Gradinaru et al., 2008; Zhao et al., 2008).

In the last year or so, opsins have been developed or discovered that mediate improved optical activation at high frequencies (Lin et al., 2009; Wang et al., 2009), multicolor optical activation of neurons (Zhang et al., 2008), and enhanced optical neural silencing (Chow et al., 2009a,b). Thus, ongoing innovation will likely continuously improve the function of these molecular sensitizers. Using laser-coupled optical fibers, in conjunction with electrodes attached in parallel to them (Fig. 5*A*), allows for easily monitored control of neural computation or behavior in awake behaving mammals ranging from mice to primates (Aravanis et al., 2007; Bernstein et al., 2008b; Han et al., 2009); each fiber terminal typically illuminates a volume of a few cubic millimeters when laser power in the low tens of milliwatts is used. A detailed step-by-step protocol on building a multicolor laser-coupled optical fiber setup is available at http://edboyden.org/08.02.bernstein.html. The ability to target individual cells with two-photon photoactivation may, in the future, open up the ability to perform ChR2-mediated photoactivation at the single-cell level (Mohanty et al., 2008).

Strategies for Cell-Type-Specific Expression of Neural Control Opsins

Several strategies can be used for targeting opsin expression to a specific cell type in the brain. The development of transgenic mice has yielded two published ChR2-expressing lines to date, in which ChR2 is expressed under the Thy-1 promoter (Wang et al., 2007). These lines express ChR2 within excitatory neurons in layer 5 of cortex, excitatory neurons of hippocampus, and subsets of cells in other areas. Electroporation and gene-gunning are two strategies that have enabled plasmids containing ChR2 behind

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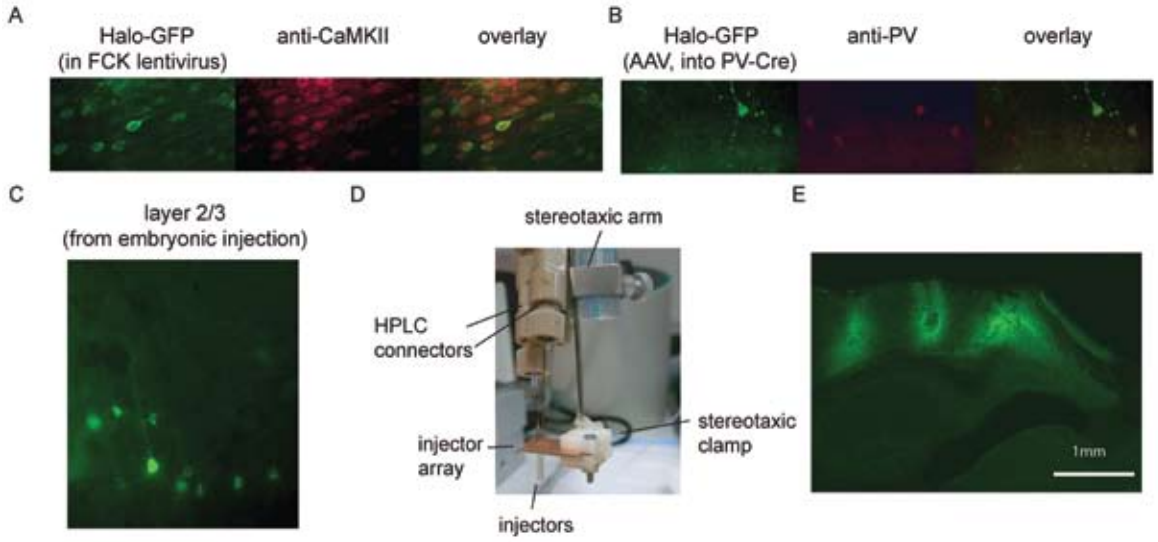

Figure 2. Methods of targeting optical control molecules to specific cell types. ***A***, Excitatory neurons specifically targeted via a lentivirus with CaMKII promoter. Figure shows targeted expression of Halo-GFP in excitatory neurons of the mouse cortex, as seen in 63× confocal image. From left to right: virally infected excitatory neurons expressing Halo-GFP under the CaMKII promoter (green); immunostaining with anti-CaMKII antibody (red); overlay. ***B***, Parvalbumin (PV)–positive inhibitory interneurons targeted via AAV containing lox-stop-lox-Halo-GFP, injected into the hippocampus of an adult PV–Cre mouse. From left to right: virally infected PV+ interneurons expressing Halo–GFP under the CaMKII promoter (green); immunostaining with anti-PV antibody (red); overlay. ***C***, Layer 2/3 pyramidal neurons expressing Halo-GFP under the CaMKII promoter, when lentivirus was injected into the ventricle of an E15.5 embryonic mouse. ***D***, Photograph of a parallel injector array system, showing a triple-injector configuration for three simultaneous injections. ***E***, Fluorescence image showing ChR2-GFP-labeled cells in three mouse cortical regions after lentiviruses encoding for ChR2-GFP were injected using the triple injector array shown in ***D***.

a cell-specific promoter to be used to express ChR2 in specific cell types of the retina, hippocampus, and cortex (Petreanu et al., 2007; Zhang and Oertner, 2007; Lagali et al., 2008). Lentiviruses carrying an opsin under a cell-specific promoter also have been used to permanently integrate the opsin gene into the target cell's genome; this fairly general strategy works with a variety of different promoters, in species from mouse to nonhuman primate (Fig. 2*A*) (Boyden et al., 2005; Adamantidis et al., 2007; Han et al., 2009). These lentiviruses can also be injected into the ventricle of an embryonic mouse, resulting in cell-type-specific expression in layers 2/3 of the cortex (Fig. 2*C*). Adeno-associated viruses (AAVs) can also be used with a cell-type specific promoter (e.g., somatostatin, mGluR6), followed by an opsin, to deliver the opsin enduringly to a cell (Horsager et al., 2009).

Another strategy emerges from the fact that Cre recombinase will bind to pairs of lox sites and induce genetic recombination between the sites. Many mice exist that express Cre recombinase in specific cell types (e.g., serotonin-generating neurons, dopamine-generating neurons, parvalbumin-expressing neurons; many are available from Jackson Labs [Bar Harbor, ME] or other sources). Thus, using an AAV containing an opsin either behind a lox-flanked transcriptional stop sequence (Kuhlman and Huang, 2008) or embedded in an inverted fashion surrounded by different sets of lox sites (Atasoy et al., 2008) can be used to achieve cell-type-specific expression of opsins, simply by injecting the virus into the appropriate cell-type-specific Cre mouse (Fig. 2*B*). The viral injection strategy for targeting opsin expression to neurons of the mammalian brain has been successful. As a result, parallel injector hardware to facilitate the delivery of viruses encoding for opsins to complexly shaped circuits in the brain may be of great use (Fig. 2*D*), allowing "circuit-level" transgenic mice to be made (Fig. 2*E*). Plasmids from our lab can be obtained freely from Addgene (Cambridge, MA) (http://syntheticneurobiology.org/reagents.html). A detailed virus-making protocol can be obtained at http://edboyden.org/09.01.vir.html.

Informational Lesions: Perturbation of Synchrony Using Multiple Opsins or Opsin Fusion Proteins

The precise role that synchronous neural activity plays in neural computation has remained difficult to resolve using perturbative methods, because many of the technologies (e.g., pharmacological) that enable researchers to alter spike timing also alter other aspects of spike statistics, such as the spike rate. In some specific systems, in which pharmacological

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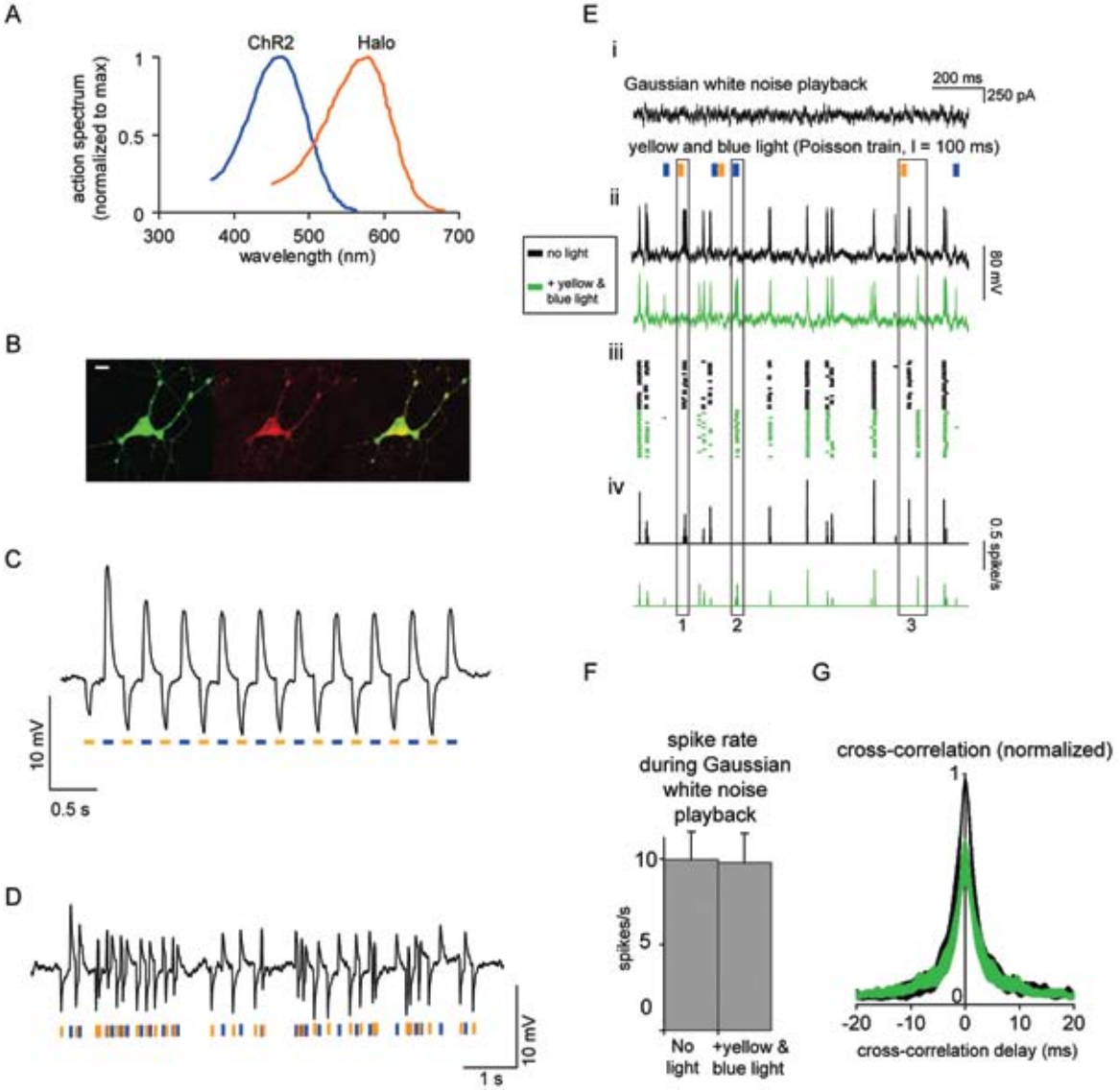

Figure 3. Informational lesions: schema for how to alter neural spike timing using two-color illumination of neurons cotransfected with ChR2 and Halo in a 1:1 ratio. Adapted from Han and Boyden, 2007, their Figs. 5 and 7, used under open access license. ***A***, Action spectrum for ChR2 (blue), adapted from data presented in Nagel et al., 2003, their Fig. 4, overlaid with absorption spectrum for Halo (orange), adapted from data presented in Duschl et al., 1990, their Fig. 6. Each spectrum is normalized to its own peak, for ease of comparison. ***B***, Coexpression of Halo-GFP (left) and ChR2-mCherry (middle) in a single neuron expressing both (right, overlay). Scale bar, 20 µm. ***C***, Hyperpolarization and depolarization events elicited in a single representative neuron by two interleaved 2.5 Hz trains of yellow and blue light pulses (50 ms duration each), denoted by yellow and blue bars, respectively. ***D***, Hyperpolarization and depolarization events induced in a representative neuron by a Poisson train (mean interpulse interval λ = 100 ms) of alternating pulses of yellow and blue light (10 ms duration), denoted by yellow and blue bars, respectively. ***E***, Optical disruption of spike timing, without alteration of spike rate, for a representative current-clamped hippocampal neuron transfected simultaneously with ChR2 and Halo *in vitro*. Vertical boxes (labeled at bottom *1*, *2*, *3*) highlight features referred to in the text. ***i***, Stimulus trace showing a subsegment of the somatically injected filtered Gaussian white noise current used in all these experiments (top), as well as of the Poisson train (mean interpulse interval λ = 100 ms) of alternating yellow and blue light pulses (bottom). ***ii***, Twenty-trace overlays of voltage responses to the somatically injected white noise current, either with no light (top, black traces) or with delivery of a Poisson train of yellow and blue light pulses (bottom, green traces). ***iii***, Spike raster plots for the traces shown in ***Eii***. ***iv***, spike-timing histograms (bin size: 500 µs) for the rasters shown in ***Eiii***. ***F***, Spike rates of current-clamped hippocampal neurons transfected simultaneously with ChR2 and Halo *in vitro* (n = 7), injected with filtered Gaussian white noise current, either with no light (left) or with concurrent delivery of a Poisson train of yellow and blue light pulses (right). Plotted is mean + standard error. ***G***, Cross-correlation between spike trains elicited from the same filtered Gaussian white noise current injection, played twice, when either both current injections were performed in the dark (black curve), or when one of the current injections was performed with concurrent delivery of a Poisson train of yellow and blue light pulses (green trace). Data are plotted as mean + standard error (averaged across n = 7 neurons).

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or genetic strategies for selectively disrupting synchrony turned out to be compatible with local cellular and network properties, pioneering attempts have been made to perturb spike timing without altering other aspects of neural coding such as spike rate (MacLeod and Laurent, 1996; Bao et al., 2002; Robbe et al., 2006). However, no generalized method for doing so exists. Thus, we have developed a prototype strategy for perturbing spike timing without altering spike rate (Han and Boyden, 2007). Our strategy takes advantage of the fact that the spectral peaks for ChR2 activation and Halo activation are separated by more than 100 nm (Fig. 3*A*). This makes it possible to express both molecules in the same neuron (Fig. 3*B*), thus conferring upon that neuron bidirectional control of its voltage by pulses of blue and yellow light (Fig. 3*C*,*D*). As a consequence of this two-color bidirectional voltage control, precisely timed blue and yellow light pulse trains, delivered to a neuron expressing both ChR2 and Halo, can be used to insert spikes into, and delete spikes from, the ongoing activity experienced by that neuron (Fig. 3*E*). This selectivity results in precise perturbations of spike timing without changing overall spike rate (Fig. 3*F*,*G*).

The mechanism of this perturbation is clear: Close inspection of Figure 3*E* shows that optically driving Halo and ChR2 could sometimes abolish previously reliable spikes (highlighted in box 1, spanning Fig. 3*Ei–iv*), create new spikes (box 2, spanning Fig. 3*Ei–iv*), or advance or delay the timing of specific spikes (box 3, spanning Fig. 3*Ei–iv*). In the case shown, for every spike deleted, another is inserted, enabling alteration of spike timing without alteration of overall spike rate. To make this and other synchrony-disrupting and rhythm-disrupting experimental protocols more practical, we have recently begun to develop gene fusions between ChR2 and Halo, resulting in ChR2-2A-Halo (Han et al., 2008). These fusions allow ChR2 and Halo to be expressed in a predictable proportion to one another within a single-expression cassette. However, other strategies, such as delivery of ChR2 and Halo via separate plasmids or viruses, or the transgenic expression of ChR2 and Halo from a bidirectional promoter, could also potentially work to accomplish these computational neuroscience goals.

Prototype synchrony-disruption protocols

What kinds of experiments are enabled by the use of ChR2 and Halo (or improved versions of these opsins) for bidirectional control of voltage of neurons? Figure 4 outlines four protocols appropriate for perturbing spike timing and neural synchrony, in schematic form. In all these protocols, appropriately timed blue and yellow light pulses are used to disrupt the timing of spikes in a region containing neurons sensitized to light with both ChR2 and Halo, thus enabling experimenters to alter the spike statistics. It is important to recognize one caveat: Because light will scatter throughout a given region, and since all optically sensitized neurons in the region will be exposed to the same pattern of blue and yellow light, they will experience a common input driven by the blue and yellow light. This input may alter (e.g., increase) the synchrony of optically sensitized neurons within the illuminated region, thus complicating later analysis of data obtained using protocols that focus only on synchrony within a region (Fig. 4*A*, 3*E*) (unless synchronizing the neurons within the region is part of the experimental goal).

The first of the four protocols is a direct generalization of the strategy outlined in Figure 3: the delivery of a light-pulse train to a brain region to increase interspike interval (ISI) variability, turning highly rhythmic neurons into irregularly firing ones (Fig. 4*A*). This "informational lesion" might enable the deletion of the information carried by the cells of interest without allowing downstream cells to leave their normal dynamic range of activity (which might otherwise occur with a gross disruption of the inputs, as with a conventional lesion). A slightly more complex version of this protocol is illustrated in Figure 4*B*, in which light pulses are precisely triggered in a closed-loop fashion upon the occurrence of particular recorded spikes so that the neuronal firing rate becomes more bursty. Testing the role of bursting in neural signaling may be of great importance to understanding how the temporal integration properties of neural circuit elements contribute to neural computations.

A third strategy of using both ChR2 and Halo (or, ChR2-2A-Halo) to mediate bidirectional control can also be used to disrupt correlations between regions that exhibit synchrony (Fig. 4*C*). This strategy makes spiking more variable in timing in one region in order to disrupt its correlation with activity in a second region, or in order to assess the effect such disruption has on activity within that second region. In this way, it might be possible to understand how regions communicate and process information together in a coordinated fashion.

As a fourth example, the multisite experiment can be performed in a closed-loop fashion (Fig. 4*D*), triggering a specific light-pulse train delivered to a region off the LFP in a second region reaching a particular phase, thereby phase-shifting the spikes in the first

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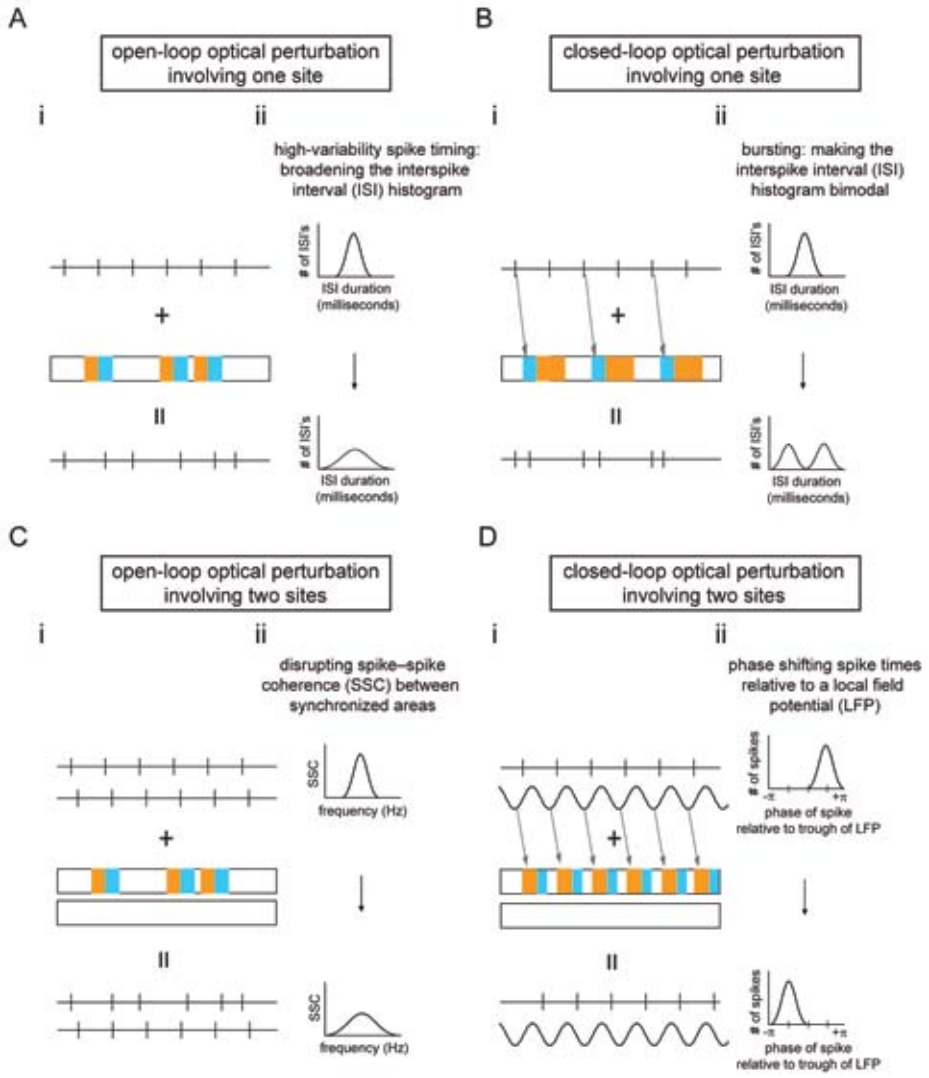

Figure 4. Synchrony-perturbation and spike timing–perturbation protocols, enabled by use of ChR2 and Halo in concert. Each of the four panels (*A–D*) displays a schematic experimental protocol (*i*) along with the anticipated effect of the protocol on the neural circuit dynamics (*ii*). An example is given of each of four kinds of experiment: *A*, open-loop/one site, *B*, closed-loop/one site, *C*, open-loop/two sites, and *D*, closed-loop/two sites. Detailed descriptions of each panel follow. *A* shows the use of Poisson train light-pulse delivery to a site in which rhythmically firing neurons express both ChR2 and Halo (or ChR2-2A-Halo). This results in the interspike interval (ISI) becoming more variable than in the unilluminated state. *i*, From top to bottom: spike train trace (for one example neuron) in dark; timeline of when yellow or blue light is delivered; spike train trace (for one example neuron) in light (e.g., the result of combining the original case, shown at top, with the delivery of light, shown in the middle). *ii*, From top to bottom: ISI histogram in dark; ISI histogram in light. *B* shows the use of optical perturbation in a closed-loop fashion, triggering blue-yellow pairs of light pulses off recorded spikes in order to make the spike train more bursty. *i*, From top to bottom: spike train trace in dark; timeline of when yellow or blue light is delivered (in this case, each blue-yellow pair is triggered by a spike; each trigger is indicated by an arrow); spike train trace under the closed-loop protocol. *ii*, From top to bottom: ISI histogram in dark; ISI histogram under the closed-loop protocol. *C* shows the use of optical perturbation in the style of *Ai*, with light delivered to one site to disrupt the timing of activity at that site, relative to another site, which is left unilluminated. *i*, From top to bottom: spike train traces recorded at two sites in the dark; timeline of when yellow or blue light is delivered to one of the sites while the other is kept in the dark; spike train traces in light. *ii*, From top to bottom: spike-spike coherence (Fries et al., 2008) across the two areas plotted versus spike frequency, measured in dark; spike-spike coherence across the two areas plotted versus spike frequency, measured when one site is illuminated. *D* shows the use of optical perturbation in a closed-loop fashion, triggering yellow-blue pairs of light pulses at one site, off a feature of the LFP recorded at another site, which is left unilluminated. In this case, the trough of the LFP (bandpass filtered to yield a set of frequencies) at the second site serves as the trigger for delaying spikes at the first site. *i*, From top to bottom: spike train trace and LFP trace recorded at two separate sites; timeline of when yellow or blue light is delivered to the site from which spikes are recorded (in this case, each yellow-blue pair is triggered by the trough of the LFP at the second site; each trigger is indicated by an arrow); spike train trace and LFP trace under the closed-loop protocol. *ii*, From top to bottom: phase relationship between spikes recorded at the first site and LFP troughs recorded at the second site, in the dark (Pesaran et al., 2002; Gregoriou et al., 2009); phase relationship between spikes recorded at the first site and LFP troughs recorded at the second site, under the closed-loop protocol.

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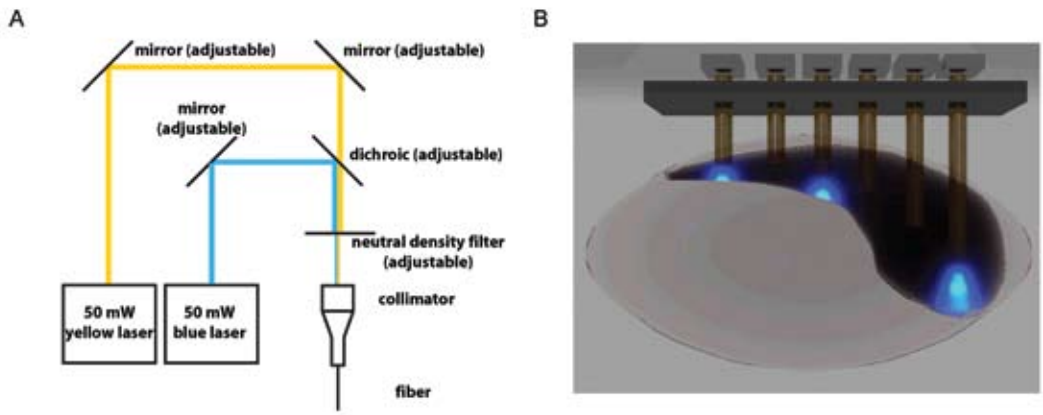

Figure 5. Hardware for delivery of light into the brain. *A*, Schematic of a setup that allows blue and yellow light to be focused down a fiber whose tip is inserted into the brain, for bidirectional control of a single kind of neuron at a single site within the brain, or for activation and silencing of two different kinds of neuron at a single site within the brain (Bernstein et al., 2008b). *B*, Schematic model of an array of LEDs coupled to optical fibers, for delivery of light to complex three-dimensional brain structures (Bernstein et al., 2008a). One or more fiber sites can be replaced by a tetrode bundle or a "Michigan-style" probe.

region with respect to the LFP of the second. Many other possibilities exist; for all of them, however, the key advance enabled by the use of both ChR2 and Halo (or, ChR2-2A-Halo) is the ability to lesion (or alter) the information without grossly disrupting the spike rate, as happens with conventional lesions, electrical stimulation, or pharmacology.

Multielectrode recording

Ideally, we would be able to record from, and perturb, neurons across as much of the brain as possible, and analyze the data in real time, perhaps using inexpensive parallel supercomputers such as NVIDIA (Santa Clara, CA) CUDA GPU cards. Multielectrode recording strategies that employ "Michigan probes" (linear silicon probes with multiple electrodes along the length of the probe) and "Utah arrays" (rectangular arrays of probes that emerge in a two-dimensional array), as well as high-density microwire and tetrode arrays, are having an increasingly broad impact on neuroscience. These technologies are allowing neuroscientists to analyze not only the temporal properties of synchrony and oscillations in the brain, but also the spatial properties. For example, they are revealing how oscillations that were once considered to take place in a spatially static fashion may actually be traveling waves. Such technologies are enabling experiments that forge a solid link between anatomy and neural dynamics.

Within-brain data acquired at a large number of sites can reveal fundamentally higher order correlations than could ever be revealed by single or pairwise recordings, even collected from many animals. For example, no amount of pairwise recording could easily prove that dynamics at a site in the brain is contingent upon joint activation at two other sites, whereas a triple recording can easily do so. We are currently pursuing the integration of three-dimensional recording strategies with three-dimensional light delivery strategies (Fig. 5*B*), aiming towards the goal of being able to perform multipoint recording and multipoint perturbation in the same brain (Zorzos et al., 2009a). The use of functional magnetic resonance imaging (fMRI) in conjunction with optical perturbation may also open up the possibility of surveying large regions of the brain to optimize electrode placement for analysis of cross-region synchrony (Desai et al., 2009).

Photoelectrochemical artifacts

An important caveat for optical neuromodulation and multielectrode recording must be highlighted. Currently, LFPs are prominently used to characterize oscillatory activity in the brain. A photoelectrochemical artifact is observed on metal electrodes when, immersed in saline, they are illuminated with light of power appropriate to cause optical activation or silencing using the above-described tools (Ayling et al., 2009; Han et al., 2009). Using glass micropipette-style electrodes can prevent this artifact, but most multielectrode strategies utilize metal or solid-state materials, which may be subject to such artifacts; thus, careful controls are essential for interpreting these data. In future, the development of novel electrode architectures (Zorzos et al., 2009b) may make it possible to perform chronic multielectrode recording without any photoelectrochemical artifacts.

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