Perspectives on: Information coding in mammalian sensory physiology

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Our understanding of the physiological mechanisms allowing sensory signals to be processed in the brain is perhaps best understood in the visual system. There are several reasons for this, including that the eyes are relatively accessible to experimental manipulation, and the neural circuitry that processes visually evoked signals is well documented. The first article in this series, by Schwartz and Rieke, reflects the sophistication of our understanding of visual processing and deals with the integration of signals by ganglion cells, the output cells of the retina. Retinal ganglion cells receive excitatory input from bipolar cells and inhibitory inputs from amacrine cells. Schwartz and Rieke review, from a historical perspective, multiple models that describe the integration of photoreceptor signals by retinal ganglion cells. They begin by showing how early linear models fail to describe adequately the functional properties of ganglion cell responses, and proceed to demonstrate that combined linear–nonlinear models are more robust. What emerges is a functional framework that accounts better for known nonlinear steps in retinal processing. They further highlight that the best predictive models for ganglion cell activity also incorporate some form of feedback. The distinction between linear and nonlinear processing becomes important for a utilitarian understanding of the ganglion cell’s receptive field, because these models provide a guide for elucidating the physiological mechanisms contributing to visual function.

The accessibility of the retina, together with precise stimulus control, has allowed a detailed investigation of how visual signals are encoded. Such an analytical approach is more difficult when the mechanisms underlying stimulus transduction are not well understood, or when the stimulus space is more complex. For instance, the sense of touch is complicated by its multimodal nature; an area of skin can simultaneously encompasses numerous modalities, including touch, pressure, and vibration. In the second contribution to this Perspectives series, Bautista and Lumpkin focus on the cells and molecules that mediate light touch in the periphery.
Multiple subtypes of somatosensory neurons and end-organs innervate the skin and respond to tactile stimulation through the opening of mechanosensitive ion channels and the subsequent generation of action potentials. Genetic screens have identified several candidate molecules that may participate in the transduction of mechanical touch into these electrical signals, and in this article, the authors list several criteria that need to be met to establish these candidate molecules as essential components of the signal transduction mechanism. As an example, Bautista and Lumpkin discuss the recently described products of the FAM38A and FAM38B genes, Piezo1 and Piezo2, respectively, as promising new candidates for mediating mechanotransduction.

The sampling of a stimulus also has important consequences for sensory encoding. For example, in the olfactory system, the sampling of odorants follows a rhythmic pattern that depends on respiration. The third contribution to this Perspectives series by Reisert and Zhao focuses on how the properties of G protein signaling and adaptation influence how olfactory receptor cells encode the presence of odorants in the environment. Unlike retinal photoreceptors whose sensitivity is a result of the amplification of the input photon signals by G protein–coupled cascades, olfaction requires several odorant-binding events to generate an action potential in olfactory receptor cells. Furthermore, given the rhythmic pattern of odor presentation to olfactory receptor cells, the time course of the olfactory receptor cell’s response proves crucial to encoding. Reisert and Zhao discuss recent observations, which indicate that the mechanisms of adaptation in olfactory receptor cells that sharpen the temporal properties of transduction may differ from those previously thought to be important. They describe targeted genetic approaches that indicate Ca\(^{2+}\)-calmodulin feedback inhibition of the cyclic nucleotide–gated channel and phosphorylation of adenyl cyclase III may not be involved in adaptation, as had previously been suggested. Similarly, fast response termination may involve mechanisms that regulate ciliary Ca\(^{2+}\) concentrations. Recent experiments using knockout animals and electrophysiological measurements are discussed, as the authors identify important questions that need to be answered if we are to understand how olfactory signals are encoded.

Another key to understanding sensory encoding is the role played by the balance between synaptic inhibition and excitation in setting the properties of sensory signals. The final article in the Perspectives series, by Zhang et al., emphasizes the important and varied roles inhibitory synaptic mechanisms play in encoding auditory signals. Inhibition is important in all mammalian sensory systems. In the visual system, for example, inhibitory input from amacrine cells creates fundamental properties of the retinal ganglion cell output, including center-surround receptive fields and direction selectivity. Using in vivo whole cell patch-clamp recordings, the spectral and temporal properties of synaptic responses evoked by auditory stimuli can similarly be determined. Unlike intracellular or extracellular recordings, the high impedance of the microelectrodes does not compromise the whole cell clamp. Zhang et al. highlight the temporal relationships between excitatory and inhibitory inputs that have been revealed using this technique, and identify feedforward and feedback loops that are important in shaping the output action potential responses. They conclude with a brief discussion of questions about processing auditory signals that remain unanswered, but which appear experimentally accessible with newly developed measurement techniques.

It should be clear from the contributions to this Perspectives series that the cerebral interpretation of sensory input stimuli is a complicated process, which begins at the level of the transduction in sensory receptor cells, and involves the interplay of multiple types of neurons downstream in the circuitry. Although our understanding of the mechanisms whereby sensory stimuli are processed and integrated varies depending on the sensory system considered, a comparative approach across systems should provide insights about common strategies that might be used to encode information. Indeed, experimental methodologies have advanced significantly in recent years, allowing for the improved resolution of signals encoded by sensory receptor cells and their circuits. Although many questions remain, the articles in this Perspectives series suggest future experimental approaches to these questions, and hold out the tantalizing expectation that more exciting information will be available in the not too distant future.

Letters to the editor related to these Perspectives will be published in the December 2011 issue of the Journal. Letters to the editor should be received no later than Monday, October 17, 2011, to allow for editorial review. The letters may be no longer than two printed pages (approximately six double-spaced pages) and will be subject to editorial review. They may contain no more than one figure, no more than 15 references, and no significant references to unpublished work (and may not include supplemental material). Letters should be prepared according to the Journal’s instructions and can be submitted electronically at http://www.jgp.org, or as an e-mail attachment to jgp@mail.rockefeller.edu.