Rethinking the taxonomy of visual neurons

L.F. Abbott and Frances S. Chance

Neurons in primary visual cortex have long been classified into simple and complex cells, but a new paper notes that different firing patterns need not imply different underlying circuitry.

Most of what we know about neuronal responses to sensory stimuli comes from extracellular recordings of action potentials. Extracellular recordings provide insight into a neuron's function within a circuit by describing the information passed from one neuron to another. However, if we want to go beyond functional descriptions to explore the mechanisms that generate neuronal responses, we need the information about underlying membrane potentials, currents and conductances provided by intracellular recordings. Unfortunately, recording intra-cellularly from intact brains is difficult, so this information is hard—though not impossible—to come by. As a result, much of our knowledge concerning the synaptic, cellular and circuit mechanisms that generate neuronal responses must be inferred from extracellular data. A recent paper in *Vision Research* by Mechler and Ringach[1] reminds us that, in doing this, we must be careful.

The authors address one of the best-known functional classifications in neuroscience, the division of neurons in mammalian primary visual cortex into simple and complex cell types[2] on the basis of their extracellularly recorded responses to patterns of light and dark. A simple-cell response can be predicted by determining how well a visual stimulus matches a template defined by the receptive field of the cell. Complex-cell responses, on the other hand, do not correspond to simple template matching. Although complex cells are selective for a number of features related to the spatial pattern of illumination in an image, they are not sensitive to the precise location of the image within their receptive fields (known as spatial phase).

L. F. Abbott is at the Volen Center and Department of Biology, Brandeis University, Waltham, Massachusetts 02454, USA.
Frances S. Chance is at the Center for Neural Science, New York University, New York, New York 10003, USA.
e-mail: abbott@brandeis.edu;
e-mail: chance@cns.nyu.edu

Mechler and Ringach[1] make the important point that classifying neurons by the mechanisms underlying their responses may produce different groupings from classifying them according to the responses themselves. Specifically, they point out that simple and complex cells might be grouped together into a single category, despite their distinct response characteristics, if they were classified using intracellular (that is, mechanistic) rather than extracellular (functional) criteria. This is an important qualification for anyone thinking about the circuitry that makes simple and complex cells respond the way they do.

To illustrate their basic point in a simpler, though hypothetical, context, imagine that the firing rates recorded from a group of neurons were distributed as in **Fig. 1a**. The bimodal distribution shown suggests that, at the functional level, these neurons fall into two classes that we might call weakly and highly responsive. If we extended this classification to the mechanistic level, we might suppose that these two groups correspond to neurons receiving two distinct levels of afferent drive, or having two different degrees of intrinsic excitability. However, in this particular example, the distribution in **Fig. 1a** was generated by assuming that all the neurons had identical intrinsic properties, and that they received synaptic input currents drawn from a unimodal distribution (**Fig. 1b**). The bimodal firing-rate histogram (**Fig. 1a**) arises from a nonlinear relationship between synaptic current and firing rate (**Fig. 1c**). The dip in the firing-rate histogram is caused by the kink in the firing-rate curve (**Fig. 1c**), not by a bimodal distribution of input currents or intrinsic firing properties. Thus, in this example, the functional classification of neurons into two groups does not imply that distinct classes exist at the circuit level. Mechler and Ringach[1] go on to illustrate that similar effects can occur for a wide variety of nonlinear firing-rate relationships and that these can affect distributions of other quantities besides firing rates.

Neurons are often classified as simple or complex according to the degree of modulation in their responses to a grating, consisting of alternating light and dark stripes, moved steadily across their receptive fields[3]. Simple cells respond to a moving grating with an oscillating firing rate that is high when the grating is in register with their receptive-field template and low (or zero) when the alignment is poor. The response of a complex cell to a moving grating tends to be sustained, rather than oscillatory, because the complex cell is not sensitive to the positioning of the grating as it moves. The degree of modulation is quantified by the ratio *F1/F0*, which is the amplitude of the best sine wave fit to the firing rate at the frequency defined by the motion of the grating divided by the average firing rate. Cells are traditionally classified as simple if the ratio *F1/F0* is greater than one and complex if it is less than one. Although neurons in primary visual cortex display a range of *F1/F0* values, these fall into a bimodal distribution[3] (**Fig. 2a**). Such data provide the evidence for two functional classes.

Mechler and Ringach[1] point out that nonlinearities inherent in the relationship between *F1/F0* and the synaptic input to a

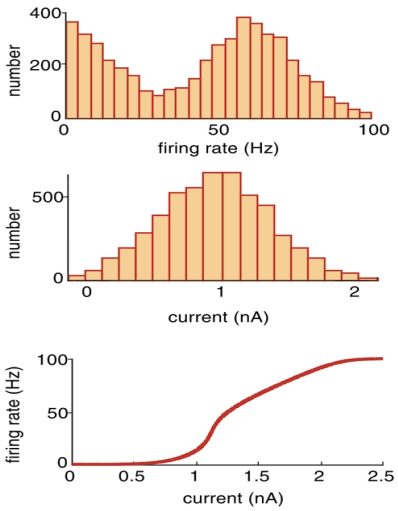

Fig. 1. A bimodal firing-rate distribution arising from a unimodal distribution of input currents. This example is analogous to Fig. 1 of Mechler and Ringach[1]. (**a**) Bimodal distribution of firing rates for a hypothetical population of neurons. (**b**) The distribution of synaptic input currents underlying the firing-rate distribution in (**a**). (**c**) The nonlinear relationship between input current and firing rate that produced the bimodal firing-rate distribution in (**a**) from the current distribution in (**b**). The kink in the firing rate curve around 30 Hz produces the dip between the two peaks of the firing-rate distribution in (**a**).

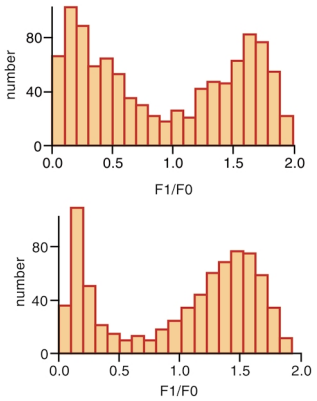

Fig. 2. Bimodal distributions of *F1/F0* indicating distinct populations of simple and complex cells. (**a**) Data collected from 1061 neurons in cat striate cortex (redrawn from ref. 3). (**b**) Distribution of *F1/F0* values generated by a model[4] in which simple and complex cells correspond to weakly and strongly coupled elements in a single interconnected network. In this example, the firing rate in response to a synaptic input current I was proportional to $I_r^2/(C + I_r^2)$, where C is a constant and I_r is the half-wave rectified input current given by I if $I > 0$ and zero otherwise. The distribution of network coupling strengths was Gaussian with mean 0.82 g_{max} and standard deviation 0.16 g_{max}, where g_{max} is the coupling strength above which the network shows sustained activity in the absence of sensory input.

neuron can lead to a phenomenon similar to that shown in **Fig. 1**, in which a group of neurons with inputs drawn from a unimodal distribution and with identical firing properties can nevertheless generate a bimodal distribution for *F1/F0* similar to **Fig. 2a**. Rather than attempting to review their very thorough and extensive analysis, we illustrate this phenomenon in a model of simple and complex cells[4]. In this model, neurons are connected by excitatory synapses in a manner that is independent of their spatial-phase tuning. Neurons that are strongly coupled to other neurons in such a scheme show complex-cell responses, whereas weakly coupled neurons respond as simple cells. There is no distinction between simple and complex cells in the construction of such a model as there would be in a hierarchical model[2]. To produce **Fig. 2b**, we gave all the neurons identical intrinsic properties, and selected their network coupling strengths (total excitatory input from other neurons) from a unimodal distribution (**Fig. 2**, legend). The critical feature, as Mechler and Ringach[1] point out, is that the relationship between input current and firing rate is nonlinear. We used a form proposed to account for a number of features of neuronal responses in primary visual cortex[5] (**Fig. 2**, legend). Although simple and complex cells are not divided into separate classes by the circuitry of the model, the distribution of *F1/F0* values evoked by a drifting grating is bimodal (**Fig. 2b**). This provides an example of precisely what Ringach and Mechler suggest; the functional division between simple and complex cells need not reflect distinct classes of neurons at the circuit level.

Ultimately, the question of whether simple and complex cells are mechanistically distinct is an experimental one. What is needed are histograms of *F1/F0* ratios computed not from firing rates recorded extracellularly, but from either membrane potentials or membrane currents recorded intracellularly (see ref. 6, for example). It will be extremely interesting to see whether the resulting view of simple and complex cells supports a hierarchical model in which they arise from distinct cortical circuitry, or a more egalitarian picture in which they do not.

1. Mechler, F. & Ringach, D. L. *Vision Res.* **42**, 1017–1033 (2002).
2. Hubel, D. H. & Wiesel, T. N. *J. Physiol. (Lond.)* **160**, 106–154 (1962).
3. Skottun, B. C. *et al. Vision Res.* **31**, 1079–1086 (1991).
4. Chance, F. S., Nelson, S. B. & Abbott, L. F. *Nat. Neurosci.* **2**, 277–282 (1999).
5. Heeger, D. J. *Vis. Neurosci.* **9**, 181–198 (1992).
6. Carandini, M. & Ferster, D. *J. Neurosci.* **20**, 470–484 (2000).

Neural stem cells: form and function

Thomas A. Reh

Two reports demonstrate more convincingly than ever that progeny of adult hippocampal stem cells become functional neurons *in vitro* and integrate into existing circuitry *in vivo*.

During central nervous system development, neurons and glia are derived from cells of the neural tube ventricular zone. These mitotically active cells (variously known as neural progenitors, precursors or stem cells) are a heterogeneous population, showing complex patterns of gene expression in both space and time[1]. After birth, few mitotic figures are found in the brain, which led early investigators to conclude that neurogenesis was absent in adult mammals. However, the advent of a method for specifically labeling mitotically active cells with [^{3}H]thymidine allowed several investigators to discover that a few zones of persistent proliferation continue to exist into adulthood: the subventricular zone and the hippocampal dentate gyrus. In 1965, Altman and Das[2] described the progeny of the proliferating cells in the hippocampus as granule neurons or microneurons, to contrast them with the larger projection neurons that were generated in these structures prenatally. Over the next five years, Altman carried out a variety of experiments to uncover the function of these cells, but in the end was unable to prove that they were functionally integrated into brain circuitry. Indeed, by the late 1970s, the leading text on developmental neurobiology claimed that the cells Altman had been studying were glia, not neurons[3].

Now, nearly 40 years later, new studies published recently in *Nature*[4] and in this issue of *Nature Neuroscience*[5] show the clearest evidence yet that these adult-generated neurons are functional and integrate into the brain circuitry. In doing so, the studies define several criteria that are necessary to determine whether a cell has generated a functional neuron. The cell should be (1) postmitotic, (2) polarized, with a single axon and multiple dendrites, (3) capable of firing voltage-gated action potentials and (4) able to communicate with other neurons through synapses, requiring both neurotransmitter release and neurotransmitter receptors. Because most

The author is in the Department of Biological Structure, Box 357420, Health Sciences Center, I-500, University of Washington, Seattle, Washington 98195, USA
e-mail: tomreh@u.washington.edu