acoustic-phonetic information is processed in the superior temporal gyrus. For example, a hierarchy of processing has been proposed in which neural responses running lateral and anterior from primary auditory cortex become more selective to linguistic information in the speech signal and are therefore less driven by acoustic properties[15]. With these more sensitive techniques, will we start to refine this into a more comprehensive perspective on the (presumably massively parallel) processes that underlie the mapping of sound to meaning[14]?

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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"Yes! We're all individuals!": redundancy in neuronal circuits

Timothy E Holy

In the mouse olfactory bulb, cells with common input respond to odors with similar firing rates but with different timing. This suggests that such 'sister' cells make independent and unique connections with local interneurons.

In small organisms such as *Caenorhabditis elegans*, each neuron in a circuit often serves a distinct functional role; in mammals, with far more neurons, it is sometimes presumed that individual cells are more or less redundant, acting as members of a sizable pool of functionally equivalent neurons. However, the true extent of cellular redundancy in neuronal circuits is generally unknown; only in rare circumstances has it been possible to compare neurons that share common excitatory input. In this issue, Dhawale and colleagues[1] describe experiments examining this issue in the mouse olfactory bulb. Using the light-activated channel channelrhodopsin-2 to identify downstream pairs of neurons ('sister' mitral or tufted cells) excited by the same pool of sensory inputs, they compared the responses of these pairs to a large collection of odorants. In average firing rate, sister cells showed high redundancy, mostly consistent with a view of coding by large pools of interchangeable cells. But the results also contained a twist: substantial differences between sister cells were revealed by examining how their firing was timed relative to the inhalation–exhalation cycle of sniffing. The outcome is consistent with a model in which sister cells make nearly independent connections with local interneurons, and it provides new evidence for parallel streams of representation in olfaction.

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Electronic computers are good examples of processing systems that are largely non-redundant. For example, a single bit in physical memory is most commonly implemented as a single transistor/capacitor pair; failure in a single bit is grounds for replacing an entire memory chip containing billions of transistors. Memory chips intended for more demanding environments frequently implement error-correcting codes, which require a certain amount of redundancy: to detect and correct an error, there has to be some way to check whether a value is unexpected, and this check requires that some extra bits be stored. Such chips can continue to function accurately even if a single bit is damaged. Nevertheless, to pack the most storage into the least space, the degree of redundancy and therefore the capacity to correct errors is typically modest; even in high-end systems, memory corruption is one of the most common modes of failure[2].

In some organisms, of which the nematode *C. elegans* is a prime example, killing individual neurons—or pairs of neurons, because of bilateral symmetry—often results in obvious behavioral deficits. Like computers, such nervous systems would be considered to have relatively little redundancy. In contrast, mammalian nervous systems are frequently suspected of having high redundancy, containing pools of neurons that are essentially 'doing the same thing', and coding is thought to involve averaging the activity of such pools. Even a system such as the retina, which is thought to engage in efficient coding[3], shows significant redundancy in its information transmission[4]. However, estimates of the degree of redundancy more broadly throughout the brain are fraught with large uncertainties[5]. One reason is that, in most brain regions, defining the distinct cell types—each of which could, in principle, encode different information—is still a work in progress; another is our uncertainty over whether two neighboring neurons of the same type make essentially the same connections with other neurons.

A good opportunity to examine this question of redundancy in the nervous system can be found in the olfactory system. Sensory neurons express individual odorant receptor types, and cells expressing the same receptor type project their axons to a common region of neuropil, called a glomerulus. In addition to pooling the outputs of many sensory neurons, a single glomerulus is also the principal source of excitatory input for downstream neurons called projection neurons (in insects) or mitral and tufted cells (in vertebrates, including mice). Although the number of mitral cells receiving input from the same glomerulus varies (with differences between species and even developmental stages[6]), in the mouse there is a pool of several tens of 'sister' mitral cells receiving input from a single glomerulus (**Fig. 1**). Are these sister cells interchangeable? Or might they differ substantially—for example,

in their connections with interneuron populations?

To identify sister cells, Dhawale and colleagues[1] generated mice in which channelrhodopsin-2 is expressed in all olfactory sensory neurons. These mice were used for tetrode recordings of spike activity in the mitral cell layer of the olfactory bulb. Using a digital micromirror device to control the light used to drive channelrhodopsin, the authors were able to map the surface of the bulb to identify the glomerulus providing input to a given mitral cell. This apparently straightforward task faced an important technical hurdle: channelrhodopsin is activated not only in the terminals inside a glomerulus, but also in fibers of passage, potentially causing significant confusion about glomerular location. However, the authors discovered that the glomeruli themselves were particularly sensitive to the lowest intensities of light stimulation, presumably because of the high density of terminals extending over a thick volume within a given glomerulus. Thus, by mapping at several different light intensities, the authors could identify the glomerulus providing input to a recorded mitral cell.

Once pairs of cells were identified as either sisters or non-sisters, the authors recorded their spiking responses to a collection of odorants. By all measures, sisters proved on average to be far more similar in their responses than non-sisters. This is not surprising, because they share the same dominant excitatory drive, whereas non-sisters receive excitation from distinct odorant receptors that may prefer different ligands. However, given recent findings on the diversity of intrinsic membrane properties among mitral cells of the olfactory bulb[7], the extent of similarity between sisters was more surprising: when responses were measured in terms of the change in mean firing rate, on average two sisters were as similar as were separate trials from the same cell. Therefore, the evidence from mean firing rates is consistent with a model in which sister cells are mutually redundant. Similar results were obtained in a recent study of fluorescently tagged sister projection neurons in *Drosophila*[8].

As it turns out, these mean firing rates do not tell the whole story: a large body of evidence indicates that olfactory coding also exploits relationships in the detailed timing of spikes[9]. Therefore, the authors also examined the phase of firing relative to the sniffing cycle. When sniffing clean air, sisters were once again just as similar to each other as were separate trials from a single cell. However, this picture changed once odorants were considered: the 'phase similarity' (a measure of timing correlation) between sisters was cut nearly in half in the presence of odors. Because the changes were odorant specific, the authors suggest that these differences arise owing to local circuit connections, particularly with inhibitory interneurons in the bulb. The authors measured the percentage of odors that triggered responses with statistically significant differences in timing; surprisingly, by this measure, sisters and non-sisters were indistinguishable.

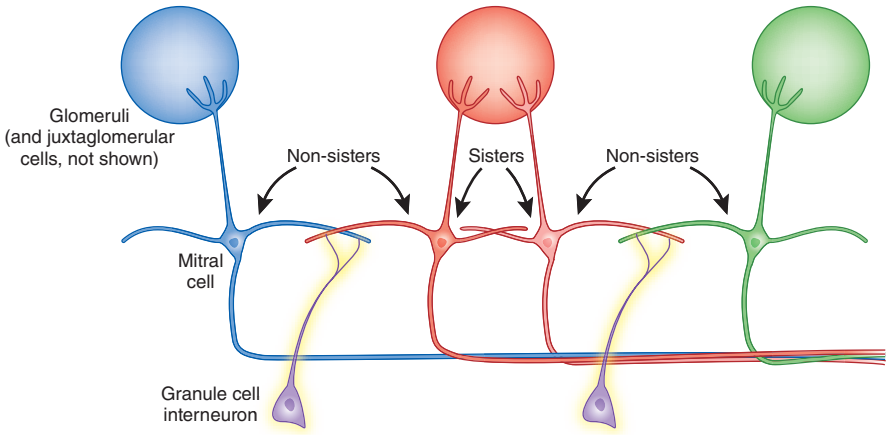

Figure 1 Redundancy in the circuits of the olfactory bulb. Sister mitral cells receive input from the same glomerulus. Sister cells would be redundant if they also made synapses with a common set of interneurons. If instead they contact interneurons that bridge distinct sets of glomeruli (as shown here), then the processing of outputs is non-redundant.

This careful comparison of sisters and non-sisters led the authors to suggest a simple and remarkable picture of wiring in the bulb: even though sisters receive the same glomerular input, their interneuron connections are typically as unique as one would find between non-sister pairs. So although the sensory inputs are redundant, any processing performed in the bulb is not. All neurons, therefore, are individuals.

The anatomical interpretation of these physiological measurements relies on two associations: the association of mean firing rate with glomerular input, and the association of phase shifts with interneuron input. The data—particularly the lack of correlation between odorants' effects on firing rate and phase response among sister neurons—provide substantial support for these associations. Nevertheless, one would expect that these two variables must, at least under some conditions, be related. Another recent study in the mouse[10] found noteworthy differences among 'sister' tufted cells (in this case, recorded in separate mice). In contrast with the Dhawale *et al.* study[1], these differences were found in the mean firing rates in response to odorants; the differences were strongest at the highest odorant concentrations. It seems likely that there is no contradiction here: inhibitory input sufficient to shift timing at lower odorant concentration might well suffice to alter firing rates at higher concentration.

At this stage, it is not known whether the individuality of sister cells is exploited by downstream processing. The circuitry and biophysical properties of olfactory cortex[11,12] make this plausible, but this will clearly be an important area for future studies. Overall, these studies by Dhawale *et al.*[1] and others provide compelling examples of the advantages of combining new molecular tools with the quantitative traditions of systems neurophysiology. This union seems poised to delight for many years to come.

COMPETING FINANCIAL INTERESTS
The author declares no competing financial interests.

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