removed by vaporization, cannot be used as building blocks of the planets. So these papers provide no support for popular planetary building models[5–7].

Incidentally, they also dispose of the old idea[8] that the depletion of sodium and potassium in lunar basalts was due to evaporation as the basaltic lavas were extruded on to the hard vacuum and low temperatures of the Moon's surface. The low abundance of the alkali elements in the Moon (less than 20% of the Earth's already depleted budget) is now shown to be an inherent property of the material that formed the Moon. Evaporative loss of potassium during the formation of chondrules and refractory inclusions is also ruled out, so that the depletion of volatile elements in chondrules can no longer be ascribed to loss during the flash-melting episode that melted the precursor silicate dust balls.

Chondrules are major components of the chondrites, dated at 4,563 million years old[9]; the refractory inclusions give slightly earlier ages of 4,566 million years[9]. So it seems that the depletion of volatile elements occurred before the formation of the chondrules, or the refractory inclusions, and thus before 4,566 million years ago. Because these are the earliest available samples of the Solar System that we can measure, we must retreat to a remoter epoch in our search for the mechanism for depletion.

Although Humayun and Clayton[2] incline to condensation from an initially hot nebula as the cause, considerable problems remain. The observed oxygen isotopic heterogeneity in meteorites seems unlikely to have survived in such a high-temperature environment, while condensation might be expected to affect the isotopic ratios. It is tempting to ascribe the depletion to early violent solar activity that swept water and other volatiles out to a 'snow line' at five astronomical units from the Sun, where condensation enabled the rapid, early growth of Jupiter. All of these problems provide rich pickings for further investigation.

About 20 years ago, oxygen isotope data from Clayton's laboratory[10] clarified the relationships among the meteorite groups, indicating that they mostly came from distinct reservoirs, and swept away models that produced the various classes by derivation from primitive meteorites. The new data will likewise enable cosmochemists to concentrate on early solar nebular processes, and to assemble everything from meteorites to planets from materials that have already been depleted in volatile elements, without having to invoke evaporation and vaporization. The work is a nice example of progress in science by the erection of testable hypotheses, while the small number of samples used in this decisive experiment recalls the comment of Charles Darwin that "six samples are enough for a scientist". □

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PATTERN RECOGNITION

Time for a new neural code?

Terrence J. Sejnowski

THE relative timing between spikes from neurons in your two ears conveys information to your brain about the locations of sound sources in space. On page 33 of this issue, John Hopfield[1] suggests that the relative timing of spikes between cortical neurons conveys information about the location of individual components in the multidimensional space of a sensory stimulus such as a smell: recognition of patterns occurs when each spike arrives simultaneously at a 'recognition cell'.

Temporal codes are not new, and one of the simplest — synchronous firing — has already been suggested as a candidate for binding sensory features together in the cortex[2]. What is new is Hopfield's observation that if the logarithm of the analogue strength of a sensory cue is encoded by the time advance of a spike, then the information contained in the relative timing of spikes in a population of neurons can be transmitted rapidly, in a scale-invariant form, and decoded into a computationally versatile radial basis function representation[3,4] (see figure). However, this time-advance code requires a precision of spike initiation and a sensitivity to the temporal coincidence of spikes from different neurons that until recently was considered beyond the capability of cortical neurons[5].

Sensory neurons in cerebral cortex respond vigorously when the right combination of sensory cues is present, but there is great variability in the timing of spikes from trial to trial. As a consequence, the average firing rate, which ignores spike timing, is believed to be the primary cortical information code. The apparently noisy properties of electrical signals in cortical neurons would seem to preclude a temporal code that depends on the timing of spikes[6]. But even if the firing rate is the primary information code, there is danger in ignoring spike timing entirely, because one man's noise can be another man's signal.

Indirect evidence that cortical circuits are capable of processing with high temporal precision has been lurking for many years in the psychophysical and physiological background. When images are flashed on the retinae, onset-time differences in the range of a few tenths of a millisecond between the two eyes are interpreted as differences in depth[7]. As the primary visual cortex is the first area in the brain where information from the two eyes converges onto a single neuron, this suggests that timing information is preserved at least up to that point, and that precise temporal differences can influence perception. Measurements of orientation-tuned neurons in visual cortex indicate that the first few spikes in a response are as tuned as the average firing rate[8]: evidently, cortical circuits only need a few spikes to form a judgement about their preference. Finally, experiments on cortical neurons in a slice preparation have shown that the precision of spike timing in response to the repeated injection of the same 'noisy' current, meant to mimic synaptic bombardment *in vivo*, is less than a millisecond[9]. Although spike initiation in cortical neurons can be quite precise, cortical synapses do not appear to be as reliable, at least under conditions studied in slice preparations.

Hopfield provides strong theoretical arguments of why the cortex might use a time-advance code. Nearly all models of

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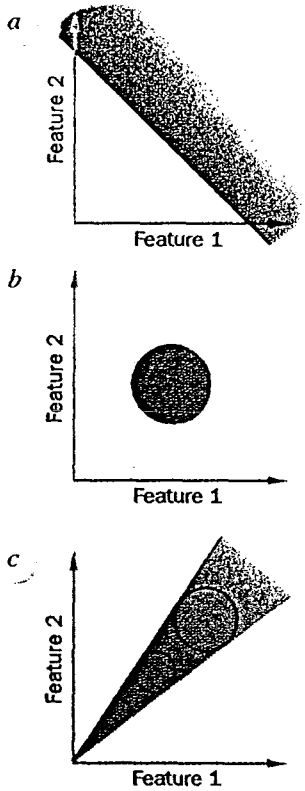

Comparison of different ways that cortical neurons could represent sensory features. A neuron achieves its peak firing rate when the value of two features (vertical and horizontal axes) are located in the shaded region. The neuron in *a* fires best when the values fall above the line; the neuron in *b* only responds well when the values lie within the circle. If the response is only sensitive to the ratio of the two values, as in *c*, then the region of maximal firing is a wedge. The time-advance coding scheme[4] provides a direct way to compute the receptive fields in *c*.

neural networks start with the assumption that the firing rate is a sigmoidal function of the summed inputs. This allows single neurons to make linear discriminations in the space of input features, as shown in *a* in the figure. A radial basis function, in contrast, only responds to inputs in compact regions of a feature space, as in *b* in the figure. The time advance coding scheme suggested by Hopfield can naturally compute such radial basis functions, if the inputs to the neuron have the appropriate time delays. In addition, the neuron would also respond vigorously if the values of all of its inputs were multiplicatively scaled by a constant factor (*c* in the figure), which would produce a constant time advance in the logarithmic coding scheme.

It would be impossible to determine by recording from a single neuron alone whether it was computing with time advances; only simultaneous recordings from several neurons could reveal how the information was propagated and decoded. In recordings from pairs of cortical neurons, reliable differences in spiking times ranging from a fraction of a millisecond to over 100 milliseconds have been reported[10,11]. There is also evidence for time advances in the rat hippocampus, where single hippocampal neurons respond to spatial location: as a rat moves through the preferred place, the timing of the spikes relative to a background of 4–6 Hz theta rhythm changes from phase lag to phase lead[12]. Thus, the relative timing of spikes in the population could carry information about relative location.

The timing of spikes is already well established as a means for conveying information in the electrosensory system of electric fish[13], in the auditory system of echolocating bats[14], and in the visual system in flies[15]. Does the timing of spikes mean anything in cerebral cortex? If so, then there must be a sophisticated system in the cortex to adjust the time delays of spikes. We need to design new experiments that manipulate spike timing in cortical neurons, perhaps by selectively interfering with specific timing mechanisms. Although the time-advance code is indeed a clever scheme, we must not forget that nature, which has been in the coding business for a long time, is cleverer than we are. □

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CELL SIGNALLING

A taste of things to come

Charles S. Zuker

TASTE transduction is one of the most sophisticated forms of chemotransduction[1,2], operating throughout the animal kingdom from simple metazoans to the most complex of vertebrates. Its purpose is to provide a signalling response to non-volatile ligands (olfaction provides a highly specific, extremely sensitive response to volatile ligands). Higher organisms have four basic types of taste modality: salty, sour, sweet and bitter. Each of these is thought to be mediated by distinct signalling pathways that lead to receptor cell depolarization, release of neurotransmitter and synaptic activity[3]. Although much is known about the psychophysics and physiology of taste cell function[4], very little is known about the molecules and pathways that mediate these sensory signalling responses. To complicate matters, some taste-receptor cells respond to more than one taste modality, raising important mechanistic questions about signal cross-talk and information encoding and decoding. Now, on pages 80 and 85 of this issue[5,6], Margolskee and colleagues offer us some surprising insights into these signalling cascades.

Sour and salty tastants are believed to modulate taste cell function by direct entry of H^+ and Na^+ ions through specialized membrane channels localized on the apical surface of the cell (reviewed in ref. 7). In the case of sour compounds, taste-cell depolarization is thought to result from H^+ blockage of K^+ channels, and salt transduction from the entry of Na^+ through amiloride-sensitive Na^+ channels. None of the molecular components of the sour or salty pathway has been identified.

Sweet and bitter transduction are believed to be G-protein-coupled transduction pathways. However, nothing is known about the membrane receptors activated by bitter and sweet compounds — this is surprising, given the tremendous biotechnological and pharmaceutical applications for bitter antagonists and sweet agonists. The transduction to sweet tastants appears to involve cyclic AMP as a second messenger[8–10]. The current view is that a seven-helix-transmembrane sweet receptor activates a G_s type G protein, which in turn activates adenylate cyclase. Increased cAMP leads to the activation of protein kinase A and the phosphorylation and blockage of a family of potassium channels. In this regard, cAMP has been shown to mimic the effect of sweeteners, leading to receptor-cell depolarization via a blockade of a potassium conductance. Interestingly, there is also evidence for an amiloride-sensitive conductance in sweet transduction[11].

Bitter transduction appears to make use of a number of intracellular pathways relying on different signalling strategies. For instance, denatonium, one of the most bitter substances known to humans, leads to release of calcium from intracellular stores in some taste-receptor neurons[12]. This suggests an involvement for phosphoinositide–phospholipase C (PLC) signalling in this pathway. But cyclic nucleotide phosphodiesterases (PDE) have also been implicated in bitter transduction. The PLC pathway probably involves the modulation of Ca^{2+}-activated conductances, whereas the PDE pathway may alter the gating of cyclic-nucleotide-modulated ion channels.

The only molecule to be identified so far in the bitter signalling cascade is gustducin[13], a Gα subunit that is highly specific to taste neurons and very similar