SOMATOSENSORY CORTEX

Maps of time and space

Mriganka Sur

CRUCIAL to our perception of the world are orderly maps of the body's sensory surfaces in the brain. For most sensory pathways, such as those involved with sight, touch or hearing, an important principle is the maintenance of this topography, whereby adjacent sites on the receptor surface project to adjacent sites in brain centres. How does the brain create and maintain these maps, and what do they signify?

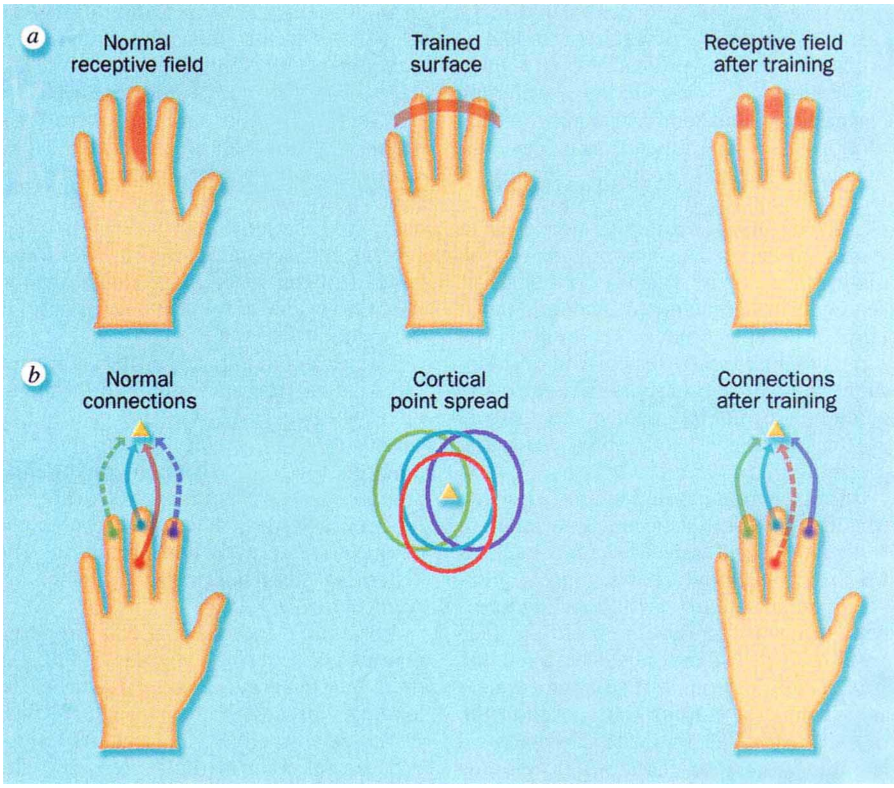
On page 71 of this issue[1], Merzenich and co-workers provide compelling evidence that maps in somatosensory cortex are spatial memory-traces of the timing of tactile stimuli. The cortex uses the temporal coincidence of arriving inputs to maintain and even create spatial representations — inputs that are synchronously active are represented together and integrated right down to the level of single neurons, while asynchronous inputs are actively segregated.

It has been known for some time that space is not the only parameter that comes to be mapped in orderly fashion in the cortex. In the primary visual cortex, for example, neurons respond (depending on the species) to various stimulus attributes such as line orientation, direction of movement, eye dominance, spatial frequency, colour and stimulus contrast. There are systematic and partially continuous maps of these attributes horizontally across the visual cortex, grouping together neurons that prefer a particular value of one attribute and representing them next to neurons that prefer an adjacent value[2]. Although these representations are created during development, a great deal of evidence (derived mainly from studying maps of the body in somatosensory cortex) indicates that they are maintained dynamically and can be altered by changes in inputs[3].

The experiment reported by Wang and colleagues[1] is simple in principle and elegant in practice. Normally, the representation of the hand in somatosensory cortex of monkeys contains neurons with receptive fields confined to a single finger (shown in part *a* of the figure). Wang *et al.* reasoned that such receptive fields, and the accompanying discrete representation of each finger in cortex, occur because normal use of the hand by monkeys (and humans) causes synchronous stimulation of skin mainly on one finger and asynchronous stimulation of adjacent fingers. They trained adult owl monkeys on a task that involved stimulation in a direction orthogonal to normal use, using a bar that stimulated either the distal or proximal segments of three fingers simultaneously. They found that many neurons now had receptive fields that spanned the stimulated surfaces, including several fingers. Furthermore, there was a discontinuity in the map between the distal and proximal digit representations, rather than between individual fingers. In other words, the spatial properties of neuronal receptive fields and the spatial features of the map came to reflect the temporal synchrony of stimulation during training.

Wang *et al.* demonstrate that the changes they describe are due to cortical mechanisms, although others have described changes at subcortical levels of the somatosensory pathway following manipulations of afferent input[4]. Dynamic changes in maps are likely to accompany the learning of spatiotemporal skills by humans as well, but how are such dramatic changes possible in the adult brain? The answer lies in the tremendous convergence and divergence of inputs to cortex (part *b* in the figure).

A single cortical neuron receives several thousand synapses, very few of which are from any one presynaptic axon[5]. Similarly, single thalamocortical axons have broad arborizations and contact many hundreds of cortical cells[6]. If the convergence and divergence of intracortical connections is added to the thalamocortical spread, the potential cortical area over which a point of skin can be represented (the anatomical point spread in cortex) can be very large indeed. Conversely, the potential area of skin surface that provides input to a cortical cell is extremely large.



Role of coincident inputs in creating cortical neuron receptive fields. *a*, Normal receptive fields and receptive fields recorded after training. Normally, the receptive field of a neuron in area 3b of primate somatosensory cortex is limited to a single finger (left). Training monkeys in a protocol that caused synchronous stimulation of either the distal or proximal segments of three fingers (middle) caused single neuron receptive fields to span several fingers (right). Not only were skin surfaces that were stimulated together represented together through multiple-finger receptive fields, skin surfaces that were not stimulated in coincident fashion (distal as opposed to proximal segments) were segregated in the cortical representation. *b*, A possible explanation for how coincident inputs create receptive fields. A neuron in cortex (triangle) receives input from a large region of skin; focal regions of skin project anatomically to extensive regions of cortex (middle). The spatiotemporal pattern of skin stimulation determines which connections have greater efficacy (unbroken arrows). Normally, skin regions on a single finger are stimulated together, leading to single-finger receptive fields (left). When monkeys are trained so that several fingers are stimulated together, receptive fields are reorganized orthogonally (right).

A cell's 'receptive field', measured as the region of receptor surface which causes a spike response when stimulated, is a subset of this large skin area. The role of input timing could then be physiologically to increase the effectiveness of a subset of synapses (those that are repetitively coactive), and possibly decrease the effectiveness of others, from the broad set available anatomically. Thus, a cell's receptive field could change, often in dynamic fashion based on the history of stimulation, without changing the anatomical connections that provide input to the cell.

These patterns of anatomical connections to cortical neurons are set up during development and would appear to define the limits of the kind of adult physiological plasticity demonstrated here (though long-term reorganization in the adult cortex following removal or ablation of peripheral input can also involve sprouting of axons into denervated territory[7]). The timing of afferent inputs is crucial for shaping projections not only in the adult cortex, but in the developing cortex as well, as demonstrated by manipulations of visual input during development. Artificially induced strabismus (squint), which alters the temporal synchrony of inputs from the two eyes to visual cortex without altering the overall quantity of input, enhances eye-specific segregation of thalamocortical[8] and intracortical connections[9]. Routing visual inputs to auditory cortex early in development changes the temporal structure and spatial pattern of input activity to auditory cortex, creating visual receptive fields and maps there[10].

Input correlation-dependent plasticity in cortical responses occurs on a range of timescales[11], and some of the mechanisms underlying adaptive changes in the adult brain might share significant features with those in the developing brain. Perhaps the critical difference between the role of input timing in regulating connections in the developing as opposed to the mature cortex is that the physiological changes in synaptic efficacy in developing cortex lead to subsequent anatomical changes, whereas the anatomical substrate remains relatively unaltered in the mature cortex. □

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1. Wang, X., Merzenich, M. M., Sameshima, K. & Jenkins, W. M. *Nature* **378**, 71–75 (1995).
2. Bonhoeffer, T. & Grinvald, A. *J. Neurosci.* **13**, 4157–4180 (1993).
3. Merzenich, M. M. *et al. Neuroscience* **8**, 33–55 (1983).
4. Nicolelis, M. A. L., Lin, C. S., Woodward, D. J. & Chapin, J. S. *Nature* **361**, 533–536 (1993).
5. Peters, A., Payne, B. R. & Budd, J. *Cerebral Cortex* **4**, 215–229 (1994).
6. Rausell, E. & Jones, E. G. *J. Neurosci.* **15**, 4270–4288 (1995).
7. Darian-Smith, C. & Gilbert, C. D. *Nature* **368**, 737–740 (1994).
8. Shatz, C. J., Lindstrom, S. & Wiesel, T. N. *Brain Res.* **131**, 103–116 (1977).
9. Lowel, S. & Singer, W. *Science* **255**, 209–212 (1992).
10. Sur, M., Pallas, S. S. & Roe, A. W. *Trends Neurosci.* **13**, 227–233 (1990).
11. Armstrong-James, M., Diamond, M. E. & Ebner, F. F. *J. Neurosci.* **14**, 6978–6991 (1994).

HIGH-PRESSURE CHEMISTRY

Turning off the water

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THAT the chemistry of materials can be radically different under pressure is one of the essential results of high-pressure research in recent years. Pressure can turn on new chemical reactions, alter kinetics and make possible new materials. Investigations of simple molecular materials have been particularly informative as a result of their simple electronic structure and high compressibility, and the variety of their metastable transformations. And of these systems, those involving water continue to present new surprises. On page 44 of this issue, a study by Loubeyre and LeToullec[1] adds another twist to this theme. They find that the normally explosive reaction between hydrogen and oxygen, surely one of the best studied of chemical reactions, is shut down by pressure at ambient temperature. Moreover, instead of the reaction producing water, they find evidence for a new compound in the system.

The simple combustion of H_2/O_2 mixtures under pressure has been exhaustively studied since the earliest days of chemistry, but details of the reaction kinetics have always been enigmatic. The reaction of interest today is the ideal clean fuel source. Also, the cosmic abundance of these elements is high, rendering the system of great importance to planetary science.

Loubeyre and LeToullec[1] prepared mixtures of these simple gases and loaded them into diamond-anvil cells. During the loading process, the pressure was increased carefully in several steps because at intermediate densities the combustion process occurs readily. (In one inauspicious loading, the pressure was increased too quickly and the mixture ignited.) They used visual observations to determine the phase diagram, together with Raman spectroscopy which provides an ideal means to characterize molecular bonding and can be used to determine the relative concentration of each molecular species within a given phase. Thus, the authors could measure directly the persistence of H_2 and O_2 and the appearance of H_2O, the expected reaction product.

What they found was remarkable: the diatomic molecules persisted to very high pressures and no water formed. The effect of pressure is to slow down the rate of reaction to an astonishing degree. This is unexpected because studies of the gases at lower densities indicate that the reaction rate should increase with pressure. So there must be an unexpected turn-around in the previously documented rate–density relation[2].

Instead of water, there is evidence for a new, kinetically stable compound in the system — a phase consisting of intact diatomic molecules with a stoichiometry near $(H_2)_4(O_2)_3$. Such high-pressure 'van der Waals' compounds, or ordered alloys, were first documented in He–N_2 mixtures[3] and have been found in a growing number of binary mixtures, but never before in a system as reactive as hydrogen–oxygen. What generally drives the formation of such compounds is packing effects; that is, the molecules fit together more efficiently in the compound than separately as pure phases, so the higher density gives a lower free energy. Such compounds can in principle have rather unusual stoichiometries — for instance, a helium–nitrogen compound where the phase had a formula of $He(N_2)_{11}$. Indeed, surprisingly complex structures have been predicted from simulations of binary mixtures in which the particles are treated as hard spheres[4]. It must be said, however, that identification of the compound in the H_2–O_2 system remains tentative. Spectroscopic properties of the reported compound are very similar to those of the pure phases, and crucial diffraction data are not yet in hand.

The results could have important implications in several areas. First, the newfound pressure control of the $H_2 + O_2$ combustion reaction may be useful for energy technology. Dense, quiescent mixtures of these otherwise reactive molecules might provide a convenient means for fuel storage. Moreover, the shift in the stability of the reported compound to lower densities with decreasing temperature suggests that this (or related) compounds could be exploited as fuel sources.

Beyond this, the results may be relevant to the outer planets, where hydrogen is in abundance. The outer layers of the large gaseous planets are believed to contain clouds of solid condensates at different depths. Could metastable H_2–O_2 compounds form within these layers? It is likely that the effects of increasing temperature with depth and heterogeneous reaction kinetics would drive combustion to completion, but this remains to be determined by quantitative measurement of the reaction kinetics. Loubeyre and LeToullec did unexpectedly obtain some information on the kinetics during an attempt to determine the structure by X-ray diffraction with an intense synchrotron beam. This resulted in decomposition and the formation of H_2O, confirming that water is still the stable phase and, furthermore, that the reaction is not completely shut down by pressure: heating, as yet unquantified, can drive the reaction towards the stable product.

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