NEUROSCIENCE

Attractors in Memory

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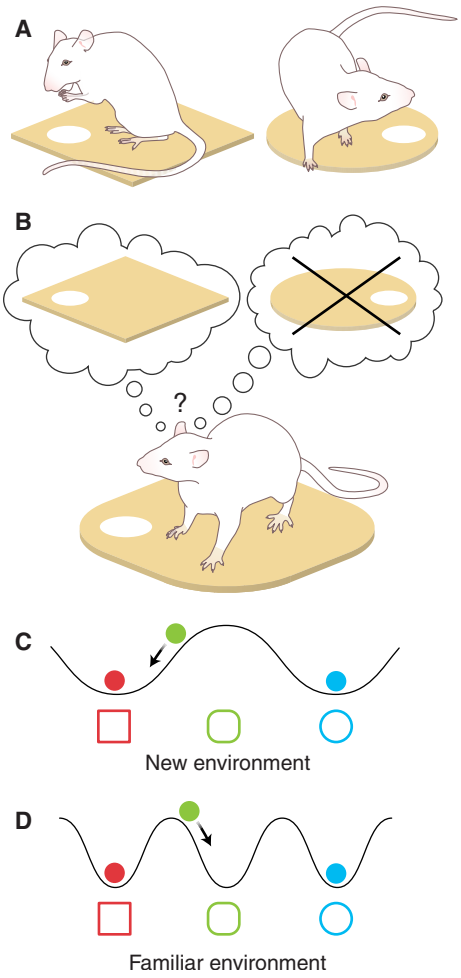
One of the most challenging questions facing contemporary neuroscience is how the brain encodes the memories of an individual's experiences. Within this broad question, the issue of how the brain makes a distinction between separate yet similar episodes is crucial. By recording the electrical discharges of neurons in the brains of animals performing different behavioral tasks, it is possible to decipher some of the rules governing this process. On page 873 of this issue, Wills *et al.* (*1*) suggest that memories are like attractor states in which all neurons abruptly and simultaneously change their electrical discharges in relation to the current experiences of the rats under study. To demonstrate this, Wills *et al.* recorded the firing activity of hippocampal place cells in the brains of freely moving rats exposed to a square or circular environment (see the figure).

The authors observed the neural activity of hippocampal place cells by recording spike activity from single hippocampal pyramidal neurons and simultaneously tracking the location of the rat in the environment. Each place cell discharges only when the animal is in a cell-specific stable region called its "place field." Place fields occur with about equal density over the entire surface of the environment, hence their ensemble firing can be decoded to determine the animal's location in space (*2*). Although place fields are stable across days and weeks in constant surroundings (*3*), they undergo great variation if large changes are made in the environment. Thus, changing the shape of the environment—for example, from a circle to a square—causes major modifications in the activity of all place cells (see the figure). Some place cells have fields in only one of the two environments and are silent in the other, whereas the fields of cells active in both environments are quite different in shape or location. Such changes, known as remappings, occur most reliably after modifying the shape of the environment, but also appear after more subtle changes (*4*, *5*). The remapping phenomenon suggests that the hippocampus learns and holds distinct maps for distinct contexts, with each specific map being reactivated as the rat commutes between the different contexts (*6*). Thus, place cells signal both the rat's current environment and its location within that environment.



Changing shapes. Rats exposed to a square or circular environment evoke distinct representations in "place" neurons of the hippocampus (*1*). (**A**) The place fields (white ellipses) are different for the circular and square environments. (**B**) When the rat is exposed to an intermediate shape (such as an octagon), all place cells simultaneously adopt one of the two learned activity patterns (the square in the example). (**C**) This observation reveals that the activity states of place cells are under the control of attractor-like mechanisms. (**D**) With experience, new attractors may develop so that intermediate shapes are represented.

Given that remapping reflects the learning process of a new environment, it is of interest to investigate its time course. Remapping may be very rapid, taking place in a matter of minutes when the rat moves freely from a familiar environment to a new one (*2*). In contrast, a slower variable rat-specific time course is observed when the rat is brought from a familiar environment (such as a square) to a new environment (such as a circle) (*7*). At first, the place fields are equivalent in both environments. With additional exposures to the circle, however, the fields of a progressively greater fraction of cells become distinct. Not only does this map differentiation occur at different rates in different rats, it also occurs at different rates for cells within a given rat. Gradual shifts in the place fields may be seen for individual place cells. Ultimately, however, discrimination of the square and circle appears to go to completion so that the fields of all cells become distinct.

What is the neural correlate of this discrimination once it is established? Wills *et al.* tackled this issue by using a series of "morph" boxes. Each morph box was made of a number of juxtaposed plastic elements that could be arranged in a variety of configurations. The overall geometry of the box could be varied from a circle to a square through four intermediate octagonal shapes, from more circular-like to more square-like. Rats were first extensively exposed to a wooden circle and to a square made of morph material. This ensured the rapid occurrence of remapping, which persisted when rats were exposed to circular and square boxes both made of morph material. Then Wills *et al.* exposed rats to a series of morph boxes in a pseudo-random order across successive recording sessions.

What became of the place fields when rats were exposed to morph boxes of intermediate shape? Wills *et al.* found that most cells adopted either the circle-like or square-like pattern in the morph boxes and almost never exhibited other patterns. The switch from one activity pattern to the other was abrupt, and the switch point was for the morph box whose shape was approximately at the midpoint between a circle and a square (see the figure). Not only was the switch point similar for all rats, it was also the same for all simultaneously recorded cells within a given rat. Because only the geometry of the recording box varied across successive exposures, such effects were unambiguously caused by changes in environmental shape. Interestingly, the same abrupt changes in place fields were seen on

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a second series of exposures to the morph boxes, although in some rats the shift point could vary from that displayed during the initial presentation. Moreover, the firing patterns within a session were established very rapidly, usually within the first 30 seconds.

What do these results suggest about the neural processes of memory in the brain? First, all place cells were seen to switch abruptly between two distinct states across successive sessions, which seems to indicate the operation of attractors. Such attractors induce the hippocampal system to adopt one of the two possible activity states triggered by the two well-learned box shapes. This major property of hippocampal representation is akin to pattern separation, which allows slightly different inputs to result in distinct output representations. Such a process reduces interference between similar experiences and complements another process necessary for memory retrieval; pattern completion, in which an autoassociative network recalls stored patterns based on incomplete information (*8*). Second, the results reveal that the hippocampal place cell system can build categories within which the representation of each intermediate box shape is nested. Although these properties of pattern separation and categorization are useful for initial encoding of new experiences within familiar contexts, they must also be accompanied by additional mechanisms that allow incremental storage of new contexts. Thus, with repeated exposure, the geometry of a new environment could ultimately lead to a new activity state that may permit the encoding of new memories (*7*).

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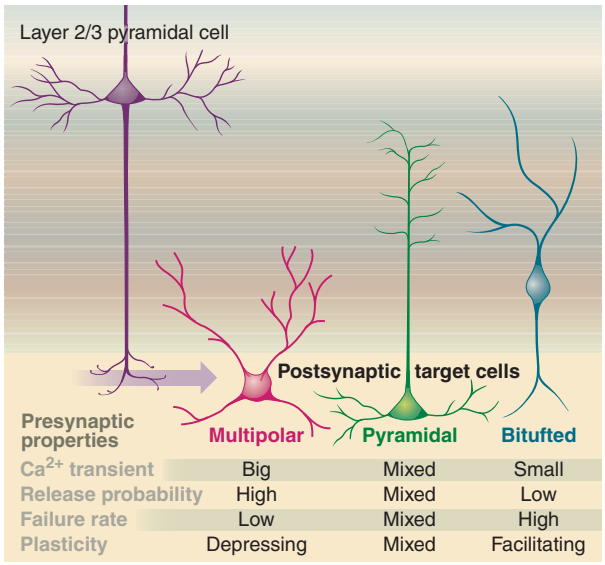
Matching at the Synapse

Scott M. Thompson

One of the wonders of the brain is how its neurons organize themselves into complex synaptic networks. There are more cells in the mammalian brain than there are stars in the Milky Way. In the brain's cortex, each neuron forms synaptic contacts with as many as 10,000 target cells (*1*) that belong to five or more different cell types. The details of how these synaptic connections are constructed are important as synaptic strength governs the reliability of information transfer (through release of neurotransmitter) from the presynaptic to the postsynaptic neuron. On page 863 of this issue, Koester and Johnston (*2*) offer unexpected observations about just how precisely these synaptic connections are formed.

The strength of a synaptic connection depends on several key factors: the number of synaptic contacts formed between the two neurons (<10 in neocortex) (*3*), the number of neurotransmitter receptors expressed by the postsynaptic neuron, and the probability that an action potential will trigger the release (exocytosis) of neurotransmitter from the presynaptic nerve terminal into the synapse. The release probability of a given synaptic contact depends on the concentration of calcium ions (Ca^{2+}) in the presynaptic nerve terminal after arrival of an action potential and the sensitivity of the exocytotic machinery to the Ca^{2+} ion concentration.



Making connections. Dependence of presynaptic terminal properties on the type of postsynaptic target cell. Presynaptic boutons formed by the axons of layer 2/3 pyramidal cells of the rat somatosensory cortex form connections with three different classes of postsynaptic target cell (*2*). The three postsynaptic cell types include two classes of inhibitory interneurons, multipolar and bitufted, and pyramidal cells.

But what determines the probability of neurotransmitter release for each particular nerve terminal? Because of their small size, there are few synapses where release probability can even be measured. Working on the nerve terminals of rat neocortical pyramidal cells, Koester and Johnston now succeed in correlating the size of the transient increase in Ca^{2+} concentration evoked by the action potential with the probability of neurotransmitter release. They show that the properties of the presynaptic terminal responsible for neurotransmitter release differ depending on the type of postsynaptic target cell (see the figure).

To perform their technically superb studies, the authors made whole-cell recordings from 63 pairs of monosynaptically coupled neurons in ex vivo slices from the rat somatosensory cortex, maintained on the stage of a two-photon microscope. Presynaptic layer 2/3 pyramidal cells were loaded with the green Ca^{2+} indicator dye, OGB-1, and three different classes of postsynaptic target cells were visualized with the red dye Alexa-594. The authors then searched for and identified the small sites of synaptic contact between the two neurons. Measurements of the transient change in emission of the Ca^{2+} indicator dye provided an assay of the action potential–induced Ca^{2+} concentration in the nerve terminal.

The simplest outcome one might expect from such an experiment is that all of the presynaptic boutons (enlargements of the presynaptic nerve terminal from which neurotransmitter is released) of a given pyramidal cell would be essentially identical. The size of their Ca^{2+} transients would be dependent primarily on the level of voltage-dependent Ca^{2+} channel expression in that cell. There is, in fact, a 10-fold variation in the amplitudes of Ca^{2+} signals in the boutons from a single pyramidal cell (*4*). The surprising observation made by Koester and Johnston is that the size of the Ca^{2+} signal in a given bouton is not random, but rather is determined by the target cell with which that bouton forms a synapse. Ca^{2+} transients in pyramidal cell boutons apposed to one class of inhibitory interneuron that releases the

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