

Part 2: "How neuron networks store and retrieve memories."



WonderQuest
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Our senses pick up information, and pass it to sensory memory, where it lasts a fraction of a second. Interesting stuff goes into short-term memory, but just a few items at a time, maybe seven. The info lasts for less than a minute. Finally information that may help us in the future (for instance, the smell of a saber-tooth tiger) goes into long-term memory, where it can last a lifetime.

A new short-term memory, for example, 'Delicious apple', gets into long-term memory by associating the concept with many key descriptive ideas: red color, tastes sweet, looks round, the sound of the crisp apple as I snap off a bite — and then such contextual items as 'I'm feeling good because it's a happy fall day and I'm picking apples.'

We use the hippocampus, an ancient evolutionary part of the cortex, to consolidate a new memory. An event creates temporary links among cortex neurons. For example, 'red' gets stored in the visual area of the cortex, and the sound of a bitten apple gets stored in the auditory area. When I remember the new fact, 'Delicious apple', the new memory data converge on the hippocampus, which sends them along a path (called the Papez circuit) several times to strengthen the links, and to pick up any emotional associations like 'happy fall day', and spatial connections like 'apple orchard'.

Neuron networks

That's the big picture. Now let's examine how neuron networks store and retrieve memories.

Special neuron networks exist that are pre-wired to link cortical neurons into a new network memory. One such network is the Papez circuit in the hippocampus we discussed earlier. The Delicious apple example illustrates how the Papez circuit entrenches temporary connections existing between visual (RED), hearing (BITE-SOUND) and limbic neurons (a HAPPY fall day) to form a new lasting memory: Delicious apple.

Consider, first, the RED part of the Delicious apple memory. It's a network in the visual area of the cortex that contains the sensation of the particular red color of a Delicious apple. This network (depicted in the drawing by solid dots) forms a path defined by its synapses. The RED neurons' synapses changed so their cellular membranes maintain a resting potential difference close to the outgoing neurons' firing threshold voltage. This makes it easy for the neurons along this path to fire, establishing a potentially conducting

circuit. The path is the firing path for nerve impulses that stores and invokes the sensation RED in the Delicious apple memory.

Click here for an illuminating animation showing [how a neuron fires](#), courtesy of Bruno Dubuc and here for a lucid look at the [firing mechanism](#), including threshold voltages, courtesy of Eric Chudler.

A similar situation exists for a network in the auditory area for the sound of the apple bite and in the limbic area for the memory of a happy fall day. Moreover, an OVERALL network (green lines in the figure) exists that connects each of these memory parts: RED, BITE-SOUND and HAPPY. The synapses of the OVERALL network changed in the same way to establish a preferred path linking each memory part. The structure of favored connections (OVERALL, RED, BITE-SOUND and HAPPY) all link to form the total DELICIOUS-APPLE MEMORY.

The brain retrieves the information by firing the DELICIOUS-APPLE MEMORY network, causing electrical signals to travel through the network that connects Delicious apple sensory data.

http://www.usatoday.com/tech/columnist/aprilholladay/2007-03-19-hazel-eye-memory_N.htm

Part III: "How synapse molecules change to define a network path and, hence, a pattern and a memory."

Two weeks ago we considered how information flows through the brain, and how the brain places a new short-term memory into long-term memory. Last week we described how neuron networks store and retrieve memories. This week concludes our memory series by seeing how hippocampus synapse molecules change to define a network path and, hence, a pattern and memory.

The action takes place in the border region (called a synapse) between two neurons. A synapse is a small molecular-size gap (20 to 40 nanometers across) between two neuron cells and the cell membranes of both neurons at the gap. A nanometer is one billionth of a meter (or yard). This tiny region between neurons in the hippocampus is where a memory-defining path is born.

Neurons carry information across the brain in the form of electrical pulses. One neuron fires a signal, which propagates down its tail-like axon to the synapse. Chemical messengers at the synapse carry the disturbance across the synapse, and change the potential difference across the cell membrane of the second neuron. If the change is great enough (about 15 mV), the second neuron fires an outgoing signal (peak of +30 mV). So far, so good. That's how signals go down a neuron network. But there's more to establishing a long-term pattern.

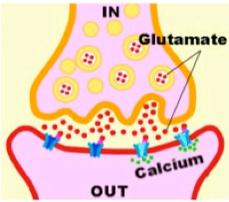
For a preferred path, we need frequent-firings. If the incoming neuron fires frequently enough so that the outgoing neuron's cell membrane receives many jolts in a short period of time, the jolts excite the outgoing neuron's membrane long enough to elevate the

voltage across the cell membrane for a sustained time. That's the ticket: To jack up the voltage for a time. Five thousand or more molecules and ions drift and bop their way across the gap to the outgoing neuron. Molecules bond with molecules on the outgoing side. Each bonding releases energy. Activity avalanches into a frenzy of catalytic-induced growth. New proteins are born, which create new synapses, which define a new network.

The net result is to raise the resting potential in the outgoing neuron's membrane for a long period. The elevated resting potential makes it easier for an incoming signal to exceed the neuron's firing threshold voltage and, therefore, to fire the outgoing neuron. The synapse is strengthened, can fire more efficiently and a new preferred path is created.

How molecules drifting across the gap strengthen the synapse and, therefore, create a preferred path

A close-up of the synapse between an incoming and outgoing neuron. The outer curves (orange for incoming neuron, red for outgoing) represent the cell membranes. The voltage potential difference across the membrane (from inside the cell to outside) changes when the synapse receives an incoming signal. Those changes across both cells eventually may cause the outgoing cell to fire. Drawing courtesy of Bruno Dubuc and <http://thebrain.mcgill.ca/>, modified by the author.



It's a four step process that's unbelievably complicated. I shall simplify to describe the main ideas.

- The incoming signal perturbs the potential across the incoming cell's membrane at the synapse. This stimulates little sacs at the synapse to release the neurotransmitter, for example, glutamate (an amino acid, shown as red balls in the figure).
- The glutamate molecules drift over to the outgoing side, and bond to big proteins there (blue in the figure), called receptors. The chemical bonding causes an electrical disturbance that raises the potential difference (making it more positive) across the outgoing neuron's cell membrane. If the potential increase is high enough, cell channels (proteins) open, and allow a flood of positive sodium ions into the outgoing neuron cell from outside the membrane, which creates an electrical pulse.
- If the increase in membrane potential is bigger than the neuron's threshold voltage, the neuron fires an outgoing signal spike. This achieves typical firing.
- For a preferred path, we need frequent firings. If the incoming neuron fires frequently so that the outgoing neuron's membrane receives many bonding jolts in a short period of time, the jolts excite the outgoing neuron's membrane long enough to elevate the voltage across the cell membrane for a sustained time, which activates yet another kind of receptor proteins (aqua in the figure), called NMDA (N-methyl d-aspartate) receptors.
- The NMDA receptors clear channels of blocking magnesium ions, allowing a small number of calcium ions (green balls in the figure) to move into the outgoing neuron.

The calcium ions trigger a frenzy of catalytic activity. Enzymes change the arrangement of the atoms within their molecules, usually by adding a phosphate ion to them. This catalytic activity stimulates growth of new proteins, which create new receptors and even new synapses. The net result of this action is to raise the resting potential in the

outgoing neuron's membrane for a long period. The elevated resting potential makes it easier for an incoming signal to exceed the neuron's firing threshold voltage and, therefore, to fire the outgoing neuron. The synapse is strengthened, can fire more efficiently and a new preferred path is created.

We've known for some time neurons make new proteins to trigger long-term storage and strengthen synapses. But we haven't known how the proteins do it. In 2004, Nobel laureate [Susumu Tonegawa](#) and his team at Picower Institute for Learning and Memory at MIT discovered how the neurons make the needed proteins. "There is a direct activational signal from the synapse to the protein synthesis machinery," says Tonegawa. An enzyme called mitogen-activated protein kinase (MAPK) provides a molecular switch that turns on increased synthesis of a large number of proteins.

So, in summary, the brain stores information chemically by making proteins that strengthen certain synapses, which establishes new patterns of neural networks, and thereby a memory.

The brain retrieves a memory by firing those networks, perhaps across different areas of the brain, to get the information. "Very limited cues are sufficient to trigger a chain reaction that permits us to become aware of the rich and detailed content of a memory," Tonegawa says. "This phenomenon is called pattern completion because it reflects cellular processes accompanying memory retrieval in which activation of a pattern of cellular connections harboring memory is completed by very limited input."

(Answered March 26, 2007)

Note: The content of the site "The Brain from Top to Bottom" is under copyleft, which allows free access to the material. I am in debt to Bruno Dubuc and his excellent primer.

http://www.usatoday.com/tech/columnist/aprilholladay/2007-03-26-memory-part-three_N.htm

and

wonderquest.com/details-memory3.htm

Questions and Vocabulary

I. Underline the words in the text used to structure the facts.

II. Underline the irregular verbs used in the text and then write out the missing forms: root word / past (preterit) / past participle / a synonym (you can probably remember the French translation)

III. Define the following words or expressions as they are used in the text.

Sweet	a border
snap off	a gap
a happy fall day	so far so good
a path	a jolt
an orchard	That's the ticket
to retrieve	To jack up
to entrench	To drift
to last (a lasting memory)	To bop
to depict	To bond
a dot	A threshold
overall	To drift
hence	An outgoing signal spike

IV. Can you sum up the process of creating a new memory in your own words? You can leave out some of the technical and molecular details.