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## The brain: Milestones of neuroscience

03 April 2013 by **Michael O'Shea**
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*We now have a detailed understanding of the brain's building block – the neuron. But it's taken us 2500 years to get here, and it has not been a smooth journey*

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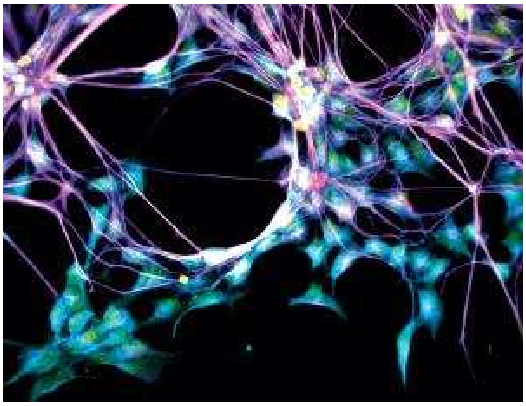

Smart wiring *(Image: SPL)*

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About 250,000 years ago, something quite extraordinary happened. Animals with an unprecedented capacity for thought appeared on the savannahs of Africa. These creatures were conscious and had minds. Eventually, they were smart enough to start questioning the origins of their own intelligence. We are finally close to getting some answers, with a particularly detailed understanding of the brain's building block – the neuron. But it has not been a smooth journey.

### The beginnings

The birth of neuroscience began with Hippocrates some 2500 years ago. While his contemporaries, including Aristotle, believed that the mind resided in the heart, Hippocrates argued that the brain is the seat of thought, sensation, emotion and cognition.

It was a monumental step, but a deeper understanding of the brain's anatomy and function took a long time to follow, with many early theories ignoring the solid brain tissue in favour of the brain's fluid filled cavities, or ventricles. The influential 2nd-century physician Galen was perhaps the most notable proponent of this idea. He believed the human brain had three ventricles, and that each one was responsible for a different mental faculty: imagination, reason and memory. According to his theory, the brain controlled our body's activities by pumping fluid from the ventricles through the nerves to other organs.

Such was Galen's authority that the idea cast a long shadow over our understanding of the brain, and fluid theories of the brain continued to dominate until well into the 17th century. Even such luminaries as the French philosopher René Descartes compared the brain to a hydraulic-powered machine. Yet the idea had a major flaw: a fluid could not move quickly enough to explain the speed of our reactions.

A more enlightened approach came when a new generation of anatomists began depicting the structure of the brain with increasing accuracy. Prominent among them was the 17th-century English doctor Thomas Willis, who argued that the key to how the brain worked lay in the solid cerebral tissues, not the ventricles. Then, 100 years later, Luigi Galvani and Alessandro Volta showed that an external source of electricity could activate nerves and muscle. This was a crucial development, since it finally suggested why we respond so rapidly to events. But it was not until the 19th century that German physiologist Emil Du Bois-Reymond confirmed that nerves and muscles themselves generate electrical impulses.

All of which paved the way for the modern era of neuroscience, beginning with the work of the Spanish anatomist Santiago Ramón y Cajal (pictured) at the dawn of the 20th century. His spectacular observations identified the neuron as the building block of the brain. He found them to have a diversity of forms that is not found in the cells of other organs. Most surprisingly, he noted that insect neurons matched and sometimes exceeded the complexity of human brain cells. This suggested that our abilities depend on the way neurons are connected, not on any special features of the cells themselves.

Cajal's "connectionist" view opened the door to a new way of thinking about information processing in the brain, and it still dominates today.

## Wired to think

While investigating the anatomy of neurons in the 19th century, Santiago Ramón y Cajal proposed that signals flow through neurons in one direction. The cell body and its branched projections, known as dendrites, gather incoming information from other cells. Processed information is then transmitted along the neuron's long nerve fibre, called the axon, to the synapse, where the message is passed to the next neuron (see diagram).

It took until the 1940s and 50s for neuroscientists to get to grips with the finer details of this electrical signalling. We now know that the messages are transmitted as brief pulses called action potentials. They carry a small voltage – just 0.1 volts – and last only a few thousandths of a second, but they can travel great distances during that time, reaching speeds of 120 metres per second.

The nerve impulse's journey comes to an end when it hits a synapse, triggering the release of molecules called neurotransmitters, which carry the signal across the gap between neurons. Once they reach the other side, these molecules briefly flip electrical switches on the surface of the receiving neuron. This can either excite the neuron into sending its own signal, or it can temporarily inhibit its activity, making it less likely to fire in response to other incoming signals. Each is important for directing the flow of information that ultimately makes up our thoughts and feelings.

The complexity of the resulting network is staggering. We have around 100 billion neurons in our brains, each with 1000 synapses. The result is 100 trillion inter-connections. If you started to count them at one per second you would still be counting 30 million years from now.

## The plastic brain

Unlike the electronic components of a computer, our networks of neurons are flexible thanks to a special class of neurotransmitter. These "neuromodulators" act a bit like a volume control, altering the amount of other neurotransmitters released at the synapse and the degree to which neurons respond to incoming signals. Some of these changes help to fine-tune brain activity in response to immediate events, while others rewire the brain in the long term, which is thought to explain how memories are stored.

Many neuromodulators act on just a few neurons, but some can penetrate through large swathes of brain tissue creating sweeping changes. Nitric oxide, for example, is so small (the 10th smallest molecule in the known universe, in fact) that it can easily spread away from the neuron at its source. It alters receptive neurons by changing the amount of neurotransmitter released with each nerve impulse, kicking off the changes that are necessary for memory formation in the hippocampus.

Through the actions of a multitude of chemical transmitters and modulators, the brain is constantly changing, allowing us to adapt to the world around us.

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***Michael O'Shea** is a professor of neuroscience in the school of life sciences and co-director of the Centre for Computational Neuroscience and Robotics at the University of Sussex in the UK. He is the author of The Brain: A very short introduction (Oxford University Press, 2005).*

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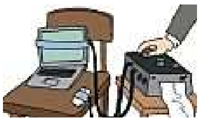

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