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> ONE MONTH, ONE PROTEIN <

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paint my thoughts

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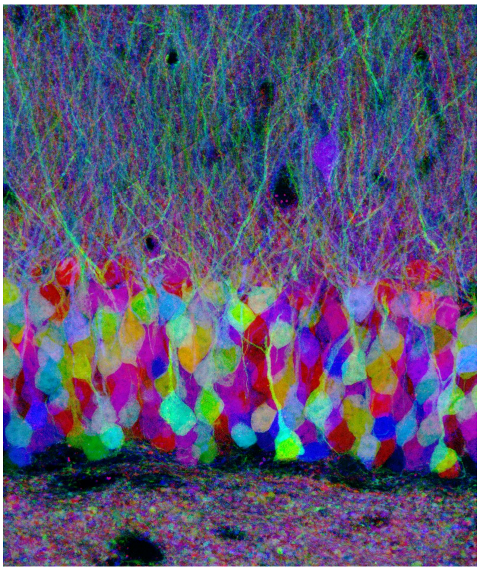
Drawing is probably not a talent the layman would normally associate with Science. Yet it has been an essential ingredient in the life of many scientists for the advancement of their field of research, among them, the Spanish neurobiologist Santiago Ramón y Cajal (1852-1934). Cajal contributed greatly to our understanding of the brain, not only in his writings but also by way of the fine drawings of his observations, which have always been heralded as a key element in conveying the evidence necessary to establish the neuron theory of the anatomy and physiology of the brain. Almost a century later, the world of brain research has gone one step further. Thanks to genetic recombination, scientists are getting proteins to draw for them. What is more, in colour and 3D… The artist's name is GFP – green fluorescent protein – a protein whose fluorescent properties have inspired many a researcher since its chance discovery in the 1960s.



A brainbow. Neurons are glowing all the colours of the rainbow by way of recombinant GFP.

Courtesy of J. Livet and J.W. Lichtman
Center for Brain Science, Harvard University

Not so long ago, the capacity to observe and translate an observation into a coherent drawing was a crucial component of a scientist's life – something on which he or she could base an emerging theory, or strengthen an existing one. In fact, the art of illustration is probably one of the qualities which built the very foundations of many fields of research today, until photography and computers took the relay. Natural philosophers have been drawing plants since the beginning of the first millennium, although the most popular illustrations date back to the 18th century when various classification systems were thought up in an attempt to identify specimens. Astronomers painstakingly recorded the movements of planets. Anatomists and embryologists documented the different stages of animal and plant development, and palaeontologists, like archaeologists, spent hours recording fossil remains and ancient sites with a pencil and a notebook. Today, however, scientists can count on progressive tools such as cameras, powerful microscopes, telescopes, and, surprisingly, biotechnology to help them record what they observe.

GFP has been one of the top ten proteins in laboratories for years now because of its capacity to glow. It was discovered in the 1960s in *Aequoria victoria*, the Pacific Northwest jellyfish. It took a further forty years before its 3D structure was solved, and researchers were able to admire its rounded barrel shape – known as the β-can – with a chromophore hidden in its centre, where it is protected from assaults such as photochemical damage. Scientists pounced on the opportunity: here was a protein which could be used as a biological beacon.

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Tagged to numerous molecules in many different creatures – from the slime mould to humans – its glow can signal a specific molecule's location and movement in an organism. And what if GFP shone different colours? Then scientists could follow the concomitant migrations of different molecules in a given tissue… It didn't take long before scientists learned how to modify GFP fluorescence the way you would tailor a suit, and variants can now beam all the colours of the rainbow. The exciting part is that, by the very nature of any tissue, GFP can brush a three-dimensional image.

There have been several successive developments in chemistry and molecular biology that made these achievements possible. Recently, Litchman and his team managed to combine different colour variants of GFP with a sophisticated system of genetic recombination – known as the Cre/Lox – which made it possible to paint, literally, inside the brain. The different recombination systems – suitably termed *Brainbows* – permit an exquisite recombination of the genetic elements and, by virtue of GFP, produce an amazing rainbow with a subtle palette of hues, colours and textures. And when such technology is applied to certain areas of the brain, it can create images of an amazing beauty and, what is more, scientific insight.

The variants of GFP created by molecular recombination, such as has been described above, illuminate with magnificent colours the images that Cajal could only painstakingly illustrate in black and white. But even more exciting is the fact that GFP will not only give a far clearer – and more colourful – idea of the progression of given brain molecules in space, but also in time…thereby flirting with the meanders of our mind, our memories, our feelings and our conscience. The GFP paintbrush will sketch, in a wide array of colours and patterns, the neuronal events that make us what we are and what we feel, what we crave and what we despise. There is no doubt that Cajal would be astonished by – but also very proud of – the foundations that he laid down in his makeshift laboratory in a corner of his kitchen, with only his ink drawings and his precious Zeiss microscope as tools for introspection.

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