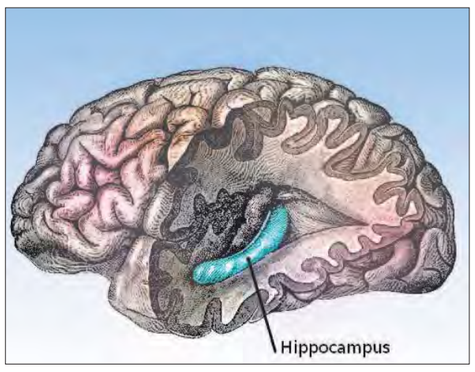
# Light on fading memory

A NEW STUDY MAY AFFORD MORE KNOWLEDGE ON THE WORKING OF THE HUMAN BRAIN, SAYS **S ANANTHANARAYAN**

Much of the brain's internal mechanism is hidden from view, as intense probing of a living brain is dangerous. What is known has been come about through tentative excisions, clinical records and animal studies. The functions of the major parts of the brain are, thus, only broadly known, including an organ called the *hippocampus*, located deep within the brain, which is associated with memory and spatial cognition. But studies of the hippocampus have been limited to findings derived from non-invasive imaging, like MRI, to supplement the symptoms that appeared in one classic case of brain surgery that affected the hippocampus.

Jacopo Annese, Natalie M Schenker-Ahmed, Hauke Bartsch, Paul Maechler, Colleen Sheh, Natasha Thomas, Junya Kayano, Alexander Ghatan, Noah Bresler, Matthew P Frosch, Ruth Klaming and Suzanne Corkin, working at San Diego and the Massachusetts Institute of Technology, USA, now report in *Nature Communications* the creation of a 3-D model derived from the post mortem examination of the brain of the same patient after his death in 2008.

The hippocampus is a short, tube-like structure, a major component of the brain of humans and other vertebrates. Mammals have a pair of hippocampi, one on each side of the brain. The name "hippocampus" is derived from the Greek for seahorse, which the organ resembles. It is known to play an important part in consolidating short term memory into



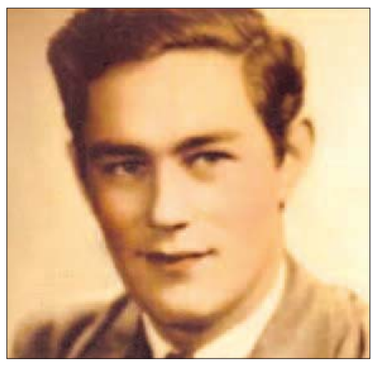

long term memory and in spatial navigation. In Alzheimer's disease, where there is loss of memory and disorientation, the hippocampus is one of the first parts of the brain that is damaged.

In respect of the "spatial" role, specific parts of the hippocampi of laboratory mice are known to become active when the rodents pass particular places. In monkeys, the activity is known to start when a monkey looks at particular places. Similar findings are reported in humans patients of epilepsy, who had implants in the hippocampus to identify the part that was involved in seizures. These findings indicate that the hippocampus has "place cells" or forms a cognitive map, or a representation of the physical environment that helps navigation.

In London, taxi drivers have to pass a strict examination of knowledge of the shortest route to different parts of the city. A study has shown that taxi drivers have larger hippocampi than others and also that the most experienced drivers have the largest of all.

In respect of the role in memory formation, it has been found that the hippocampus is involved in forming new memories. As there is a hippocampus in each hemisphere of the brain, it is found that damage to only one of them leaves memory formation almost unaffected. But damage to both affects formation of new memories and sometimes memories that were formed before the damage occurred. This could extend many years back but some older memories still remain.

The persistence of older memories indicates that, over time, memories are recorded in other parts of the brain, too. But damage to the hippocampus does not affect some kinds of memory. For


Henry Gustav Molaison.

instance, if a patient with hippocampus damage were to learn to play the violin, she would retain the new skill, although she would forget how she went about learning!


Jacopo Annese.

**Patient HM**

Much of the understanding of the functions of the hippocampus has come from the case of Henry Gustav Molaison (16 February 1926-2 December 2008), who came to be known as *Patient HM*. While there had long been a reluctance to perform surgical procedures on the brain to attempt cures of psychiatric or other conditions, these were tentatively attempted and after 1935, the procedure of lobotomy, or the scraping away of parts of the front of the brain had become popular. In 1953, a similar procedure was performed on Patient HM, in an attempt to cure him of severe epileptic seizures. At the age of 27, he was treated by William Beecher Scoville, a neurosurgeon, who localised the source of the seizures at parts of the brain and carried out surgical removal of the parts to control the seizures.

The surgery involved most of the hippocampus and also other parts of the brain and the relevant feature is the complete record, with sketches, that Scoville maintained. The surgery was successful in controlling the seizures but seriously affected HM's memory of new experiences. He also had moderate loss of older memories, entirely of events in the two years before surgery and partly till 11 years earlier. But he could learn new motor skills and, till his death at the age of 81, could solve crossword puzzles with clues that referred to pre-1953 knowledge. He could even form new memories, where the memory amounted to modifying a pre-1953 record.

The detailed record of the surgery and the long term observation of the patient have led to most of the new knowledge about the working of memory in humans. While the nature of memory loss and also the kind of memory that was retained helped refine theories of memory function, detailed imaging of HM's brain, using probes like MRI, in the 1990s revealed that there were more areas of the brain that had been damaged. But it was not clear if there were also recent age-related changes and the picture began to get cloudy as to what areas affected memory and what areas were not, in fact, responsible.

When HM died, his brain became available for anatomical study and in 2009 a team led by Dr Jacopo Annese, director of the Brain Observatory, San Diego, acquired a large number of brain slices for analysis. The paper now published in *Nature Communications* is the result of reconstructing a microscopic anatomical model of HM's brain, a procedure that was not possible while he was alive.

**Findings**

The objective of the exercise, Dr Annese and others say in the paper, was to reconstruct a 3-D model of HM's brain through high resolution images so that Scoville's original procedure could be revisited, through "virtual dissection". The procedure was a 53-hour collection of 2,401 digital images and corresponding sections, which were studied microscopically. The result was a 3-D model that enables computer-based study of HM's brain from any orientation. The whole procedure was also video recorded and broadcast for scientific scrutiny and public engagement.

The model so created found, the authors tentatively state, that HM's brain had a good portion of the hippocampus intact and also revealed the details to re-enact the surgery performed, at a level of clarity that was significantly higher than what was shown by MRI scans. "The findings constitute new evidence that may help elucidate the consequences of HM's operation in the context of the brain's overall pathology… During life, HM was the best-known and possibly the most studied patient in modern neuroscience; the availability of a large and organised collection of slices and digital anatomical images through the whole brain provides an unprecedented opportunity for collaborative and retrospective studies to continue," the authors say.

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## PLUS POINTS

### No longer secret

At least one enormous object of unknown origin has been visually verified as having landed on the moon. As a result, on 15 January three Terrier-Orion rockets blasted off within a span of 20 seconds from the national Aeronautic and Space Administration's Wallops Flight


Facility on hush-hush missions for the Department of Defence.

Turner Radio Network obtained photographs of the unknown spacecraft and had an audio interview with an outside consultant from Nasa's Meteoroid Environment Office who confirmed that for almost two years the US government used the MacDonald Observatory in Texas to track the approach of two of these enormous objects. A year ago, in January, the objects had gotten to within 200,000 miles of Mars when they suddenly vanished.

Realising these two craft were approaching earth and might not be visible to Nasa's Lunar Reconnaissance Orbital Camera depending upon where they went, the government reactivated the previously cancelled Lunar Atmosphere and Dust Environment Explorer to be launched to the moon on 6 September 2013. It took almost 100 days for Ladee to be placed into proper lunar orbit. By December last year, both Ladee and the LROC found at least one of the two enormous objects had landed on the moon, in a crater the size of Chicago.

All of this was kept secret until, quite by accident, the LROC images (which are generally made public) were uploaded to the publicly available GoogleMoon service, where intrepid users came upon the enormous object. Now, the whole world can see this "object" on the moon — the secret is out.

### Lone ranger

A flowering shrub found only on the mountainside of New Caledonia, a tiny island near?Australia, offers clue to evolution of flowering plants. The plant, *Amborella trichopoda*, is considered to be the lone species of one of two evolutionary lineages of flowering plants. The other lineage comprises more than 300,000 species.

Since Amborella is the direct descendent, scientists had long believed that understanding its genome would help understand the evolutionary process of flowering plants, which include most food crops.


*Amborella trichopoda.*

Researchers from Penn State University, the University at Buffalo, the University of Florida, the University of Georgia and the University of California-Riverside in the USA recently sequenced the complete genetic material (present in both nucleus and mitochondria) of Amborella. They found that the ancestor of all flowering plants evolved following a genome doubling event that occurred some 200 million years before the lineage diversification. While some of the duplicated genes were lost over time, others took on new functions, such as controlling the development of floral organs.

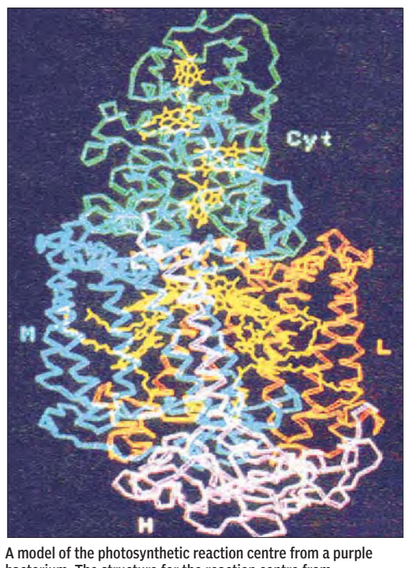
Amborella seems to have acquired some unique characteristics since it branched off. Unlike in other flowering plants, DNA sequences that can change locations or multiply within the genome seem to have stabilised in Amborella, affecting the expression of genes and resulting in a slowed rate of evolution. The researchers also found its mitochondrial genome containing genes from a number of other plant species, including three green algae and one moss. This is believed to be the largest example of horizontal gene transfer — the acquisition of foreign genes from other species — in any organism. It could be that these organisms lived in close association with Amborella millions of years ago, the researchers note in two papers published in the 20 December 2013 issue of *Science*.

CSE/DOWN TO EARTH FEATURE SERVICE

# PHOTOSYNTHETIC BACTERIA

**TAPAN KUMAR MAITRA** EXPLAINS THE REACTION CENTRE COMPLEX OF A PURPLE BACTERIUM

Much of our knowledge of photosynthetic reaction centres and the chemistry of capturing light energy has come from studies of reaction centre complexes isolated from photosynthetic bacteria. In the late 1960s, Roderick Clayton and co-workers successfully purified the reaction centre complex of a purple bacterium, *Rhodo-*



A model of the photosynthetic reaction centre from a purple bacterium. The structure for the reaction centre from *Rhodopseudomonas viridis* was deduced from X-ray diffraction measurements. The cytochrome (blue-green) with four heme groups (yellow) is attached to the outer surface of the bacterial plasma membrane. Sub-units L and M span the membrane and bind components for light harvesting and electron transfer. Sub-unit H lies mostly on the cytoplasmic side of the membrane.

*pseudomonas sphaeroides* (now called *Rhodobacter sphaeroides*).

More recently, Hartmut Michel, Johann Deisenhofer and Robert Huber crystallised a reaction centre complex from a different purple bacterium, *Rhodopseudomonas viridis* (now called *Blastochloris viridis*), and determined its molecular structure by X-ray crystallography. Michel and his colleagues not only provided the first detailed look at how pigment molecules are arranged to capture light energy, they were also the first group to crystallise any membrane protein complex at all. For their exciting and groundbreaking contributions, the three shared a Nobel Prize in 1988.

The reaction centre of *R. viridis* includes four protein sub-units. The first is a *cytochrome c* molecule bound to the outer surface of the bacterial membrane. The second and third sub-units, called *L* and M, span the membrane and stabilise a total of four *bacteriochlorophyll b* molecules, two *bacteriopheo-phytin* molecules and two *quinones*. Sub-units L and M are homologous to proteins Dl and D2, respectively, of PSII in oxygenic phototrophs. A fourth sub-unit, called *H*, is bound to the cytoplasmic surface of the membrane and is homologous to a PSII protein-called CP43. Electron flow through this bacterial photosystem and a second membrane protein complex, the *cytochrome blcx* complex, resembles the flow of electrons through PSII and the cytochrome $b_6/f$ complex of oxygenic phototrophs, with one major difference – the bacterial photosystem does not include an oxygen-evolving complex.

Two of the bacteriochlorophyll b molecules, designated P960 to indicate their absorption maxima at 960 nm, have a direct role in catalysing the light-dependent transfer of an electron to an ETS. Absorption of a photon, either directly or by accessory pigments, lowers the reduction potential of P960 from about +0.5 to -0.7 V. The photo-excited electron is immediately transferred to bacteriopheophytin, thereby stabilising the charge separation. From bacteriopheophytin, the electron flows exergonically through two quinones and a cytochrome $b/c_1$ complex to cytochrome c. This electron flow is coupled to unidirectional proton pumping across the bacterial membrane.

Cytochrome c then returns the electron to oxidised P960. As in chloroplasts and mitochondria, the electrochemical proton gradient across the membrane drives ATP synthesis by a $CF_0CF_1$ complex. The flow of electrons described is cyclic, with no net gain of reducing power.

However, in *R. viridis*, the cytochrome $b/c_1$ complex and cytochrome c accept electrons from donors such as hydrogen sulfide, thiosulfate or succinate. The ATP generated by cyclic photophosphorylation is then used to push electrons energetically uphill from the cytochrome $b/c_1$ complex or cytochrome c to $NAD^+$. The cyclic flow of electrons described is very different than the cyclic flow through PSI in oxygenic phototrophs. Thus, the bacterial photosystem is most accurately described as a somewhat simplified version of PSII in plants, green algae and cyanobacteria.

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# Sherlock-style forensics

A UNIVERSITY OF TEXAS TEAM HAS BEEN ABLE TO WORK OUT THE EXACT DATE WHEN MONET PAINTED HIS SUNSET MASTERPIECE. **JAMES VINCENT** REPORTS

In the finale of the first series of *Sherlock*, the high-functioning sociopath-cum-detective is being forced to decipher a series of puzzles in exchange for the lives of four hostages. Given just 10 seconds to prove why a painting — supposedly a lost masterpiece by Vermeer — is a fake, Holmes scrutinises the depicted night sky before turning from the frame with a snort of triumph. "The Van Buren supernova!" he declares. "Exploding star. Only appeared in 1858."

"So how," asks Watson, the penny dropping with an audible clang, "could it have been painted in the 1640s?"

This bit of razzle-dazzle deduction may be fictional (the Van Buren supernova doesn't actually exist) but the technique that Holmes used to date the painting is most definitely real. This sort of artistic forensics is known as "astronomical chronology" and it has just helped scientists from Texas State University date a series of paintings by the


The Manneport, Cliff at Etretat, Sunset, by Claude Monet (1883), and Benedict Cumberbatch as Sherlock Holmes.

Impressionist master Claude Monet.

Using astronomical and geophysical clues from Monet's paintings, astrophysicist Donald Olson and his team were able to piece together the date of a series of works painted by the Frenchman during a trip to Normandy in 1883. In fact, their calculations were so detailed that they were able to narrow down the timestamp of one painting to the exact minute. The painting that proved fruitful was *Étretat: Sunset*, as it contains both a distinctive rock formation and a sunset — clues for both the geography and the chronology of the piece. Once Olson and his team had found an area of coast depicted (a landmark to the locals) they took a series of angular "declination" measurements to calculate the path that the sun must have taken to appear as it does in the painting.

They then fed this information into a piece of software capable of winding back the clock, astronomically speaking, by reversing the motion of the stars and working out how the night sky would have appeared on any given day in the past. However, this only gave them a rough date around 3-7 February.

To finesse this further, they looked at letters written by Monet during his trip to the area and, after picking out some further clues (the painter was particularly careful in his observations of the tides), they arrived at a final time and date — 5 February, 1883, 16:53 pm. Sherlock Holmes, eat your heart out.

Unfortunately, despite the romanticism of these findings — to be published in the February issue of *Sky & Telescope* — it has to be said that they do have an air of triviality to them. Like the date of Creation worked out by 17th century clergyman Bishop Ussher (Sunday, 23 October 4004 BC, apparently) there comes a point where too much precision can look ridiculous.

This sort of criticism is well established in scholarly circles. Writing in a 2003 paper titled "The Use and Abuse of Astronomy in Establishing Absolute Chronologies", historian John Steele admits that while astronomical chronology can be "a powerful tool", it can also be misleading, "easily (producing) precise and impressive looking results based on invalid assumptions — results so precise and impressive they may not be questioned by scholars in other fields".

But although the artistic sleuthing by Olson and his team might unfortunately have more in common than we'd like to believe with the fictional deductions of Sherlock Holmes, the idea that we can know exactly when Monet sat down to put paintbrush to canvas is undeniably enticing. And, unlike Holmes and his Vermeer, the end result of this bit of "astronomical chronology" is to make the painting seem more real, not less.

THE INDEPENDENT