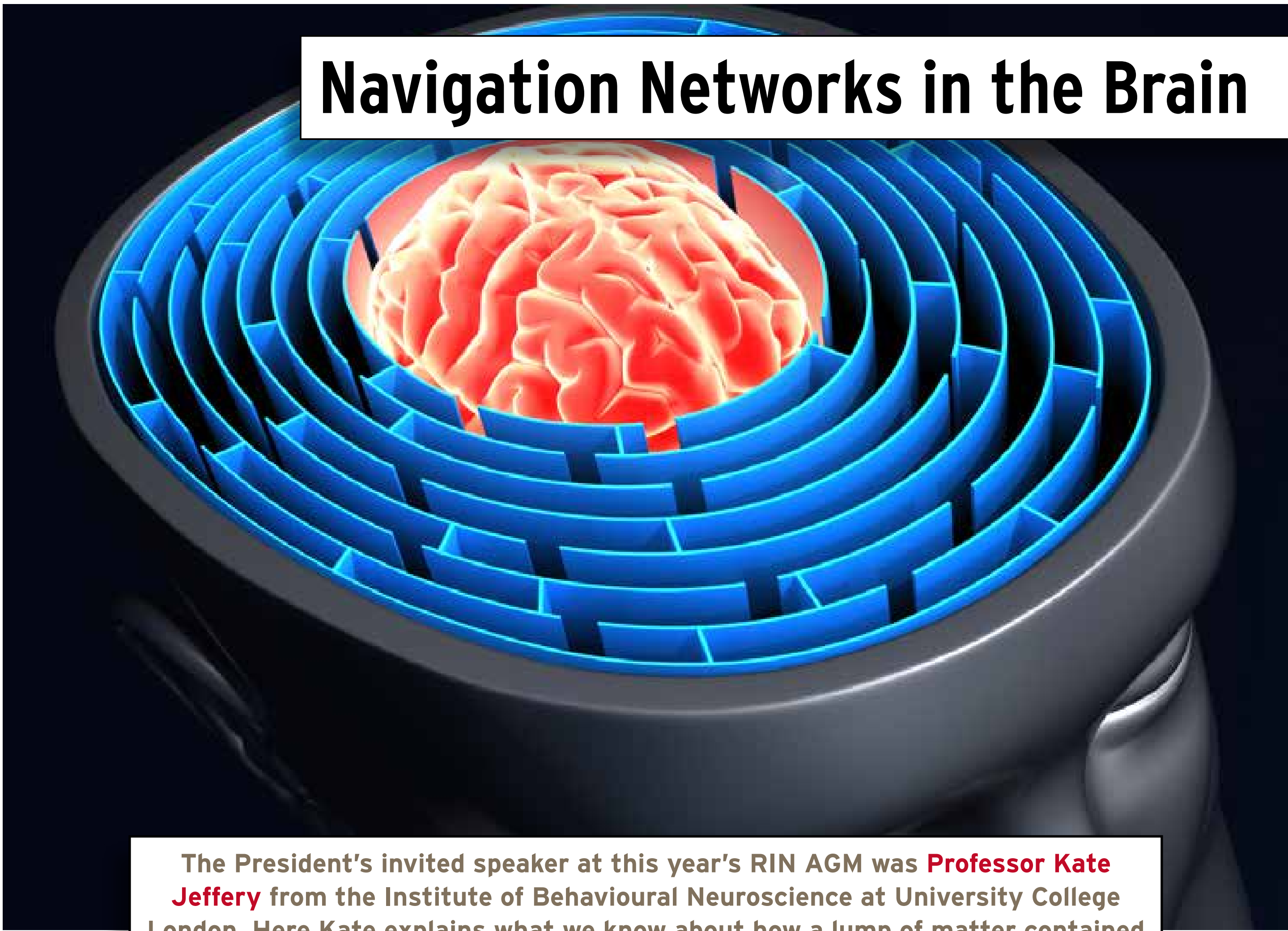

Navigation Networks in the Brain

The President's invited speaker at this year's RIN AGM was Professor Kate Jeffery from the Institute of Behavioural Neuroscience at University College London. Here Kate explains what we know about how a lump of matter contained in a bone safe can form complex and meaningful navigational networks. You'll never look at your head in quite the same way again.

For animals and machines that move around, the ability to navigate offers great advantages because it enables the planning of efficient and safe routes to goals. Biologists have long been fascinated by how this could be achieved by the grey flabby organ that constitutes the animal brain, and in recent decades have moved from simply documenting the often remarkable feats of animal navigation that occur in the wild, to bringing animals into the lab to study the action of brain cells (neurons) directly. Such research has, in the past few decades, revealed that brains seem to contain more or less the same components as human-made navigation systems. It has also revealed another surprising finding – that the navigation system also forms the scaffolding for our life memories.

The starting point for biologists was the understanding of navigation that we as humans have gained from engineering artificial navigation systems. This work, evolving over millennia, has uncovered a set of basic requirements for an effective navigation system (Fig. 1), central to which

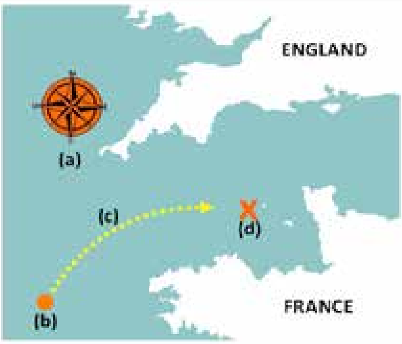

Figure 1 – Depiction of a simple map (in this case of the channel between England and France), showing the additional essential components of navigation: (a) A compass to indicate direction relative to the real world, (b) A position estimate, (c) An odometer to measure distance travelled, (d) A representation on the map of where the goal is located.

is a representation of the to-be-traversed space – a map. Use of a map also necessitates a compass (so as to know how the map should be oriented relative to the real world), an estimate of one's current position on the map, a representation of the goal, and some way of measuring the distance and direction of travel through space. If biological navigation uses similar tools then these must somehow be implemented by neurons, but how could neurons create a map, compass, odometer etc when they are just membrane-covered blobs of jelly?

A Map in the Brain

The answer to this question has to do with how space, distance, direction etc is represented. Representation in the brain takes place dynamically, by way of the electrical nerve impulses (also called action potentials or spikes) that are transmitted between neurons. This dynamism poses logistical challenges for researchers, because to understand how a representation such as a map or compass operates it is necessary to study this activity while the representation is in use – and for navigation, this means while its owner (usually a rodent, in scientific experiments) is actively moving around. This is technically difficult because a neuron is tiny (no wider than a hair) and the brain moves slightly during locomotion so it is hard for a traditional glass microelectrode to remain near enough to a neuron to detect its activity for long. It was only in the middle of last century that neuroscientists solved this problem, with the use of flexible wire electrodes that move along with the brain, enabling the monitoring of the electrical activity of a single neuron for hours or days – sometimes even weeks. Using this technology to record individual neurons in freely exploring rats, John O'Keefe, at University College London (UCL), made the astonishing discovery that neurons in a small region of the brain called the hippocampus become highly active when the rat enters a particular part of the environment, and fall silent when it leaves there again (Fig. 2), as if they are signalling the location of the animal. O'Keefe and his colleague Lynn Nadel proposed that the activity of these so-called place cells might be the equivalent of a 'you are here' signal relating to a map stored in the hippocampus. Of course, this finding produces many more questions than answers – for example how does a place cell 'know' where to fire, who or what 'reads' this map, and how is the information used? – but place cells certainly seem to provide an excellent starting point for investigating how the brain figures out where it is.

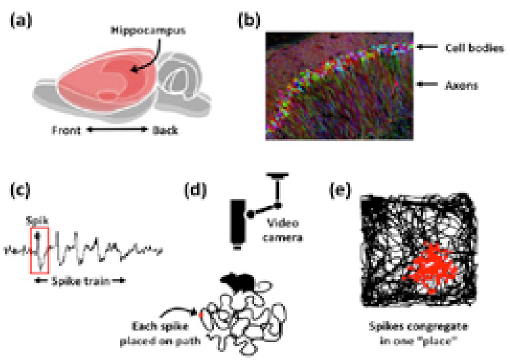

Figure 2 – Recording of place cells. (a) Schematic of the rat brain, with the two cerebral hemispheres in pink, and within these, the hippocampus in dark pink. (b) High-magnification view of a section of hippocampus showing the neuronal cell bodies and the axons – tendrils that emanate from the cell bodies and reach out to contact other neurons. The cells have been tagged with fluorescent proteins so that they appear as different colours, to enable them to be distinguished more easily. From http://cbs.fas.harvard.edu/science/ connectome-project/brainbow. (c) The pattern of spikes emanating from a single hippocampal neuron as seen on an oscilloscope, recorded from a walking rat. (d) Schematic of a typical recording situation with an overhead camera logging the path of the rat (squiggly line). The red spot shows one of the neuron's spikes, superimposed on the place where the rat was at the time the spike occurred. (e) By the end of a recording trial, the rat has covered the square recording box extensively, and it can be seen that all the spikes from this particular neuron are concentrated in one place, in this case the South-East corner of the box.

The finding of place cells was a landmark discovery not only in the biology of spatial cognition but also in psychology generally, because it comprised the first-discovered example of a high-level, complex and abstract representation in the brain. The idea that place cells might be part of a map was met with scepticism at first by the scientific community, but studies in both rats and humans subsequently confirmed that indeed, damage to the hippocampus (experimentally inflicted in rats, or following disease or surgery in humans) abolishes the ability to navigate, and other animals that navigate using a map, such as homing pigeons, also use their hippocampus, as do animals that have to remember the location of food they have stored. Thus, the hippocampus seems to be required in all cases where a 'mental map' is needed for way-finding. Interestingly, experimenters also found that the hippocampus is not necessary if the journey can be worked out by simply heading towards a landmark, or remembering a sequence of landmarks and their associated actions (turn left, turn right etc). This exception immediately suggests that there may be more than one navigation system in the brain, a point that we shall come back to.

A mental map is something we all have and all use from time to time, but some people make constant, sustained use of theirs – one such group are London's taxi drivers, who are required to memorize the layout of the city's roads so that they can navigate from any place to any other place without having to stop and look at a map. The mental map that they form is known as 'The Knowledge' and takes months or years to acquire; this knowledge is then used all day long, every day, and should in theory (if O'Keefe and Nadel were correct) keep the hippocampus almost constantly busy. Inspired by the findings in animals, Eleanor Maguire, also at UCL, decided to investigate whether such sustained use of a mental map by London's taxi drivers has any effects on either the structure or the function of the hippocampus. She found that when the taxi drivers were asked to plan a journey across town then their hippocampus became active – this was observed by using a brain scanning technique called functional magnetic resonance imaging (fMRI), which is able to reveal which brain areas are busy when a subject is thinking. She also found, remarkably, that taxi drivers of many years' service have physical enlargement of the posterior (rear) part of the hippocampus, suggesting that such 'brain training' can actually change the brain's physical structure. (She furthermore found, alas, a shrinking of the anterior, or front, part,

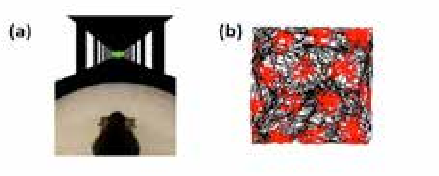

Figure 3 – (a) A mouse in a virtual reality corridor (image by F. Collman, http://news.bbc.co.uk/1/hi/ sci/tech/8308537.stm). (b) The firing pattern of a grid cell, shown in the same format as for the place cell in Fig. 1(e), showing multiple evenly spaced activity "hotspots" reflecting the cell's distance-measuring capability.

together with a reduction in the ability to draw a visually complex abstract figure from memory, suggesting that a gain in one area is accompanied by a loss in another).

We humans may use our hippocampi for navigating, but do we also have place cells? Recording actual place cells in humans is obviously tricky, since few human subjects are willing to have holes drilled in their skulls just to satisfy scientific curiosity, but neurosurgeons have found a way around this difficulty by using the fact that some epilepsy patients already have electrodes implanted into the hippocampus and surrounding regions, in order to try and localise the source of their seizures (the hippocampus being very seizure-prone). Such patients, who are often bored in hospital for days or weeks while undergoing diagnostic monitoring, have graciously allowed neuroscientists to eavesdrop on the neuronal activity detected by these implanted electrodes. By recording neurons as the subjects navigate around virtual environments, researchers have found that human hippocampal neurons are, just as in rats, very active in particular (virtual) places. Thus, place cells seem not to be simply a rat-specific oddity, but rather a more fundamental phenomenon possessed at least by (we assume) all mammals, and possibly other taxa as well.

A Neural Compass

If the hippocampus constructs a map, and a you-are-here signal, what about a compass? There is no point in having a map if you don't know which way you are facing when you set out on your journey. The neural compass in rats was discovered about 20 years after the place cells – it appears in fact to be a compass *system*, located in a network of structures strewn throughout the brain; neurons in these areas fire whenever the animal faces in a particular direction and so are called head direction cells. Quite why the brain needs so many head direction cells in so many brain areas remains puzzling, but it may be that the different regions contribute different kinds of processing. For example, some of the areas communicate with deeply buried and ancient sub-cortical parts of the brain and probably process sensory and motor information to do with movements such as head-turns, while others are located in the more recently-evolved surface-located neocortex and receive information from visual and other brain areas about landmarks, extracted using higher-order complex cognitive processes such as object recognition, learning and memory. This last observation suggests a connection between the navigation system and the memory system in the brain, a point we shall return to at the end.

Updating a Positional Calculation

The moment a navigator starts moving, their position changes and the 'you are here' marker on the map needs to be moved. How is this accomplished? In human-made navigation systems there are two ways of doing this. One is to use the available landmarks to re-calculate position (ie take a fix) at each time-step; this requires that the landmarks be continuously perceptible. An alternative method, which is robust to losing sight of landmarks but prone to accumulating errors, is to track distances and directions of movement since the last known positional fix. This process, known to sailors and pilots as dead reckoning and to biologists also as path integration, operates continuously, and works hand-in-hand with the landmark system, with the path integrator filling in the gaps between positional fixes and the landmarks correcting the errors accumulated by the path integrator. It is natural to wonder whether biological navigation systems are similarly organised, and indeed there is much evidence to support this. For example, place cells can use landmarks to calculate their position but if the landmarks are removed or if the lights are turned off then the cells can still fire in the correct places, using information about the rat's movements alone. This has been demonstrated by recent intriguing experiments in virtual reality in which a rat is induced to believe it is moving through space by having it run on a treadmill while the visual panorama, projected onto a screen, is moved past its eyes at the appropriate speed (Fig. 3a). In such situations, place cells are able to fire in stable, virtual 'places' that could only be computed by processing the apparent speed of movement through the environment. By disconnecting the speed of the treadmill from the speed of the visual display it has been possible to show that some neurons use vision, some use running speed and some use both, suggesting that all these sources of information combine in the hippocampus. Virtual reality, which is a new technology for biologists, promises to be an enormously useful tool for navigation researchers because it enables them to subject the rat to physically impossible experiences such as being teleported instantly from one place to another, or exploring four-dimensional environments.

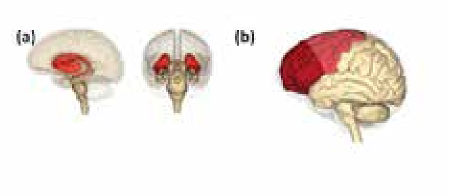

Figure 4 – (a) Transparent schematic of the human brain showing the location of the striatum in red (image under Creative Commons license from http://nl.wikipedia.org/wiki/Corpus_striatum). (b) A similar schematic showing the frontal lobe (red) with the prefrontal part highlighted (dark red). (image under Creative Commons license from http://commons.wikimedia.org/wiki/File:Frontal_lobe_-_lateral_view.png).

How is movement through the environment calculated? Are there neurons that encode distance travelled? Indeed it seems that there are – in 2005, a team headed by Norwegian researchers May-Britt and Edvard Moser discovered that in the entorhinal cortex, which communicates directly with the place cells in the hippocampus, single neurons display patches of high firing, like place cells do, but there are several of these patches instead of just one or two, and they are evenly spaced in a close-packed hexagonal array (Fig. 3b). These activity patches are so regularly ordered that their discoverers named the cells grid cells. Because the 'grids' of grid cells are observable even in a new environment which the animal has never encountered before, the implication is that the cells must use an internally generated estimate of distance travelled (which can be computed even in a completely unfamiliar place) in order to determine where to lay down these patches – once this is done, the grid becomes, we now know, aligned using the now-learned-about local landmarks, so that if the animal is replaced in that environment subsequently then the cell will still fire in the same places. Thus, the grid cells offer a method for calculating distance travelled (although exactly how this information is used by place cells is still debated) and of relating this to learned environmental features.

Reaching a Goal

With a map, a compass and an odometer in its brain, an animal is well placed to figure out where it is and how it is moving. But there is a remaining important ingredient for navigation, which is some kind of representation of a goal – where is the animal going to, and which part of its brain holds this information? We saw earlier that animals and humans with hippocampal damage can still solve some kinds of navigational problems, so there are at least two brain systems, one dependent on the hippocampus and another that must be independent of it. Loosely speaking, these correspond to navigation requiring 'thought' using a mental map (the hippocampal-dependent version), and automatic navigation that can be executed mindlessly, using familiar landmarks and without stopping to think. Most drivers are familiar with the experience of arriving at a destination but not really remembering how they got there – this is the automatic variety of navigation, often called route-based. Route-based navigation depends on a brain system called the striatum (Fig. 4A), which has the job of orchestrating movements in response to environmental cues – these movements can be simple, like stepping over an obstacle or typing in a PIN number, or complex, like driving a familiar rat-run. Striatal damage leads to movement impairment syndromes, of which Parkinson's disease is by far the best-known, but animal studies have revealed that it also impairs landmark-based navigation. Map-based navigation, on the other hand, requires some kind of explicit representation of a goal to be held in mind, and we still do not know exactly where this goal information is located. Studies of place cells have seen only glimpses of goal-related activity, and many researchers believe that detailed goal information is more likely to be held in the frontal part of the brain, particularly the prefrontal cortex (the front of the frontal lobe, behind the forehead, Fig. 4B) which houses the executive control systems responsible for making plans, deciding between alternative options and so on. Evidence suggests that the hippocampus and prefrontal cortex interact closely when navigating to a goal. One intriguing phenomenon arising during such interactions is that the oscillatory activity of neurons in the two brain areas becomes synchronised, suggesting that information is actively being transmitted during this time. The question of whether and how brain oscillations might encode and transmit information is currently a hot topic in neuroscience, and many researchers believe that oscillatory activity is critical for navigational computations.

Biological research over the last several decades has thus revealed that the brain has the same essential navigational components as our own, human-made navigation systems – this seems hardly surprising in some ways, because the basic problems to be solved – recognising landmarks, computing self-motion – are the same in both cases. There is one final twist to the biological story, however, which is that the hippocampal system does not just do navigation. In fact, navigation may be the smaller part of what it does – its primary role may in fact be to form and retrieve memories.

The link between place and memory in human cognition has been understood by intellectuals for millennia – in classical times, orators used to memorize their speeches using the method of loci, by imagining traversing a route through a familiar landscape and mentally attaching the key components of their speech to waypoints along the route. When O'Keefe made his seminal discovery of place cells he was actually looking for memory cells, because of recent clinical findings implicating the hippocampus in some kinds of amnesia. We now know that damage to the hippocampus, such as occurs to devastating effect in Alzheimer's disease, impairs navigation and memory together. Indeed, an uncharacteristic navigational failure such as getting lost on the way home from the local shops is often the first sign of incipient Alzheimer's disease.

Why should this deep connection between navigation and memory exist? Perhaps it is just chance – nature is often parsimonious in her use of resources, and many body organs do more than one job (bones both support the body and make blood cells, for example). But another possibility is that space and memory have been bound together for adaptive reasons. We saw earlier that memory for landmarks is required for self-localization, and a mental map is obviously a memory of sorts. Furthermore, when an animal remembers an event, such as being nearly eaten by a predator, then remembering where that event took place is critical for survival. Similarly, if the animal makes a navigational decision, then accurately remembering the consequences of that decision will adaptively inform a decision at that same place next time it is there (assuming of course that it made a good decision and there is a next time!). As the brain evolved and memory storage became more complex and abstract, it seems plausible that this expansion could simply entail elaboration of the basic navigational memory systems that were already in place. Thus, space and memory may be stored together because they belong together in life.

Mailbox

Does The RIN Need an Astro-Van?

Dear Sir

Astro Van!

In writing this letter I'm prompted by two thoughts. First, Channel 4's recent programme with Tristan Gooley shows that since its demise and the introduction of GNSS, which is only a build-your-own star system, astronavigation, which was always considered a black art by the uninitiated, is achieving renewed fame as being absolute magic. Secondly, it's difficult for the East Midlands Branch to find items which might attract the general public, and youngsters in particular, to practical navigation. It's not so bad near the south coast and around the major seaports which have nautical institutes, because they have companies producing on-board navigation equipment, ship simulators and similar which can be borrowed. Although the East Midlands and Nottingham in particular is a centre of excellence for GNSS research, the output is invariably to a computer screen, which is great for the computer buff but doesn't always suit the more 'rule of thumb,' 'hands-on' sort of person.

My aim is to give our visitors something to handle and try out while at the same time demystifying astro. The problem is, while a nautical sextant might be ideal for a south facing promenade on the south coast, we don't have many of those in the East Midlands. An aircraft bubble or pendulous reference sextant would be better, but the WWII handheld sextants like the ubiquitous Mark IX are now so dirty inside you can barely see the sun, let alone the stars. They are also getting very stiff to operate, so we are left with the Kollsman and the Smiths periscopic sextants, of which I have working examples. However, to use them properly you really need a mounting - of which I have only one, rescued from a Dominie.

Smiths Periscopic Sextant Mk2B

The next problem is setting up the facility. The sextant stands which once graced RAF training establishments have all mysteriously disappeared, and they wouldn't fit into a car in any case, so I started to think about a tall trailer or horsebox. Unfortunately, the longest, clearest nights for astro occur between November and March, and neither of the above would be very warm or inviting. Then I thought 'What about a caravan?' You can buy a tired 12 ft caravan for less than £500. Often the price is lower, because the roof lights need replacing. That wouldn't worry us, because we're going to remove them to fit the sextant mountings. The crew could sit inside in the warm, brewing up if necessary, while working out astro with AP3270 at a desk inside. If a long way from home, you could also sleep in the caravan, saving hotel fees. The addition of an astrodome, if we could find one, would also allow demonstration of the use of an astro compass for taking heading checks and bearings on distant features. If we couldn't run to such sophistication, a circular hatch and a hand-bearing compass would have to suffice.

Astro Compass Mk II

Once set up, the caravan could be towed to any venue which offered the opportunity to make good use of her (Do you call astro-vans her?). We might even persuade the current companies to display examples of their latest gear inside (suitably bolted down). My shopping list is: Essential: an old 12 ft caravan, and a current decade *AP3270* Vol 1 Red Band, Desirable: a mounting for a Kollsman periscopic sextant, an astrodome, and a mounting for an Astro Compass Mk II. What do people think?

Steady for Astro

Dave Pike FRIN
Secretary RIN East Midlands Branch
emidlands@rin.org.uk