The navigator protein

THE NATURE OF THE BIO-COMPASS MAY HAVE FALLEN TO RESEARCH, WRITES **S ANANTHANARAYANAN**

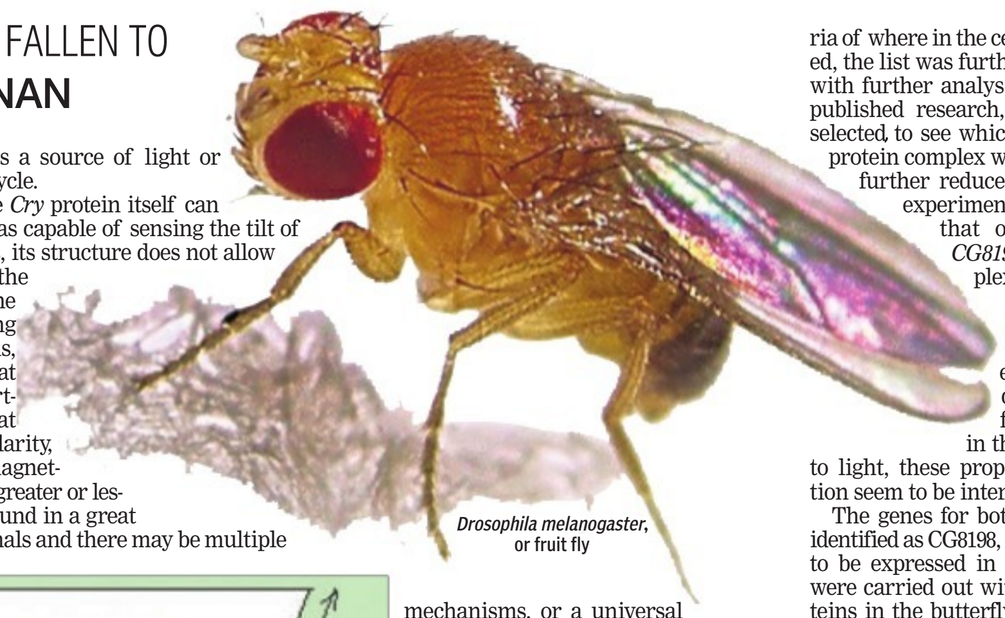
That birds and insects can sense the earth's magnetic field and use its direction to navigate was long proposed, sometimes doubted and now firmly established. But the mechanism by which the perception actually comes about has remained unclear. Certain substances on whose presence the ability seems to depend have been identified, but not their role in enabling response to magnetism.

Siying Qin, Hang Yin, Celi Yang, Yunfeng Dou, Zhongmin Liu, Peng Zhang, He Yu, Yulong Huang, Jing Feng, Junfeng Hao, Jia Hao, Lizong Deng, Xiyun Yan, Xiaoli Dong, Zhongxian Zhao, Taijiao Jiang, Hong-Wei Wang, Shu-Jin Luo and Can Xie, from the Chinese Academy of Sciences and the Tsinghua and Peking Universities in Beijing, report in the journal *Nature Materials* that they have isolated a protein complex that aligns itself along magnetic fields, like a magnetic needle, and could, hence, be the medium for their detection by animals and also the means for new applications.

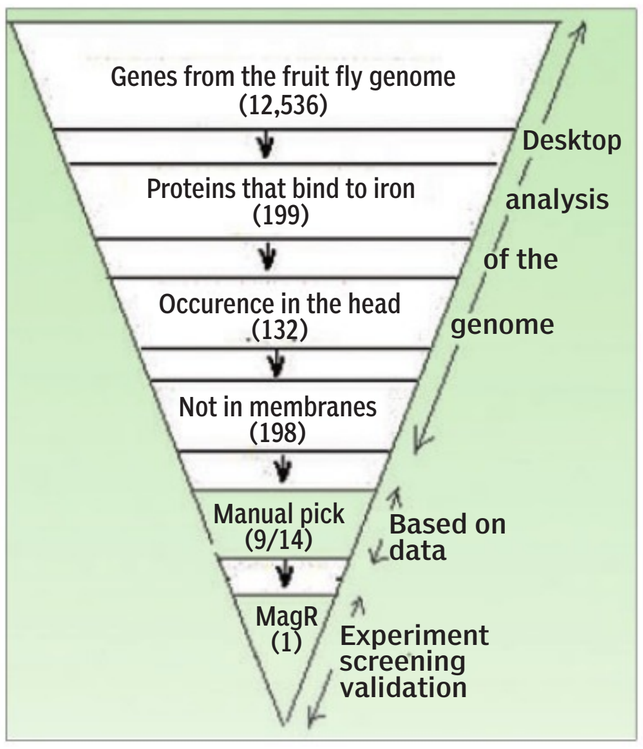
That animals use the earth's magnetic field for navigation has been established by trials where birds and insects are seen to flounder if the field were cut off or to follow the lead of artificial magnetic fields. A group in Virginia Tech, USA, reported in 2007 that fruit fly larvae that were exposed to UV light and magnetic fields immediately on hatching later moved along the magnetic sense opposite that of the direction of the UV light used during training. The homing pigeon has been found to respond to the direction of a magnetic filed in an experimental enclosure and even that they lose the capacity if their beaks are anaesthetised.

While the iron-rich substances found in pigeon beaks have subsequently been shown not to be related to this ability, the sensing has been found to depend on certain shades of light being present and also a light-sensing protein known as *Cryptochrome* or *Cry*, which is known to regulate plant growth towards a source of light or the day-night cycle.

Although the *Cry* protein itself can be understood as capable of sensing the tilt of magnetic fields, its structure does not allow it to identify the direction of the field, the Beijing team notes. It is, hence, likely that there is a partner protein that helps sense polarity, they say. But magnetic sensing, to a greater or lesser extent, is found in a great variety of animals and there may be multiple mechanisms, or a universal detector that is used differently by different animals, they say.



Drosophila melanogaster, or fruit fly



The approach of the Beijing team was to carry out a desktop survey of a suitable genetic landscape to see what possible factors could lead to a functional companion, that could be called *MagR*, of the *Cry* protein. As the genetic make-up of *D.Melanogaster*, or the fruit fly, which shows magnetic sensing, with the presence of the *Cry* protein as a crucial factor, is well documented, this was the genome that was studied. The survey was aimed at finding proteins that would: first bind to magnetic materials like iron or iron-sulphur clusters, second, be found in the retina or the brain, as that was where the crucial *Cry* protein was expressed and, third, that the protein tended to form a long chain complex with the *Cry* protein,to be sensitive to weak magnetic fields.

Identifying MagR

The survey resulted in 199 iron-binding proteins and, of these, 132 were found to be expressed in the head, including the brain and the eyes. Applying criteria of where in the cells the *Cry* protein is located, the list was further reduced to 98 and then, with further analysis that made use of other published research, just 14 candidates were selected, to see which ones may form a stable protein complex with *Cry*. This list of 14 was further reduced to nine and, finally, on experimental screening, it was found that only one protein, called *CG8198*, formed a stable complex with *Cry*.

Interestingly, the Beijing paper says, this is the protein that has been reported to be essential for the day-night rhythm of the fruit fly. As *Cry* is involved in this rhythm and sensitivity to light, these properties and magnetoreception seem to be inter-related, the paper says.

The genes for both *MagR*, which has been identified as CG8198, and *Cry* were further found to be expressed in almost all animals. Tests were carried out with the *MagR* and *Cry* proteins in the butterfly, pigeon, mole rat, minke whale and humans and it was seen that the *MagR-Cry* complex occurred in all. Some species have several forms of *Cry* for different purposes, and in these species only one of them forms the complex with *MagR*. Tests with the *MagR-Cry* complex isolated also show the complex had inherent magnetic property to help it align itself with a magnetic field.

What has been done is, hence, to clearly prove that there is an iron-sulphur cluster protein that interacts with the known magnetoreception-related protein *Cry* to form a nanoscale complex that seems to be the same across species and is able to align along magnetic fields. The interaction of the protein with *Cry* and its structure, of a long, iron-containing protein, surrounded by *Cry* proteins, suggests a relationship between magnetic sensing and light sensing or day-night timing.

Apart from being a step forward in understanding a mechanism that seems to be of great antiquity, as it is found in the same form in many species, magnetic features of a protein complex suggest methods to isolate and manipulate macromolecules using magnetic fields, which could have wider applications, the paper says.

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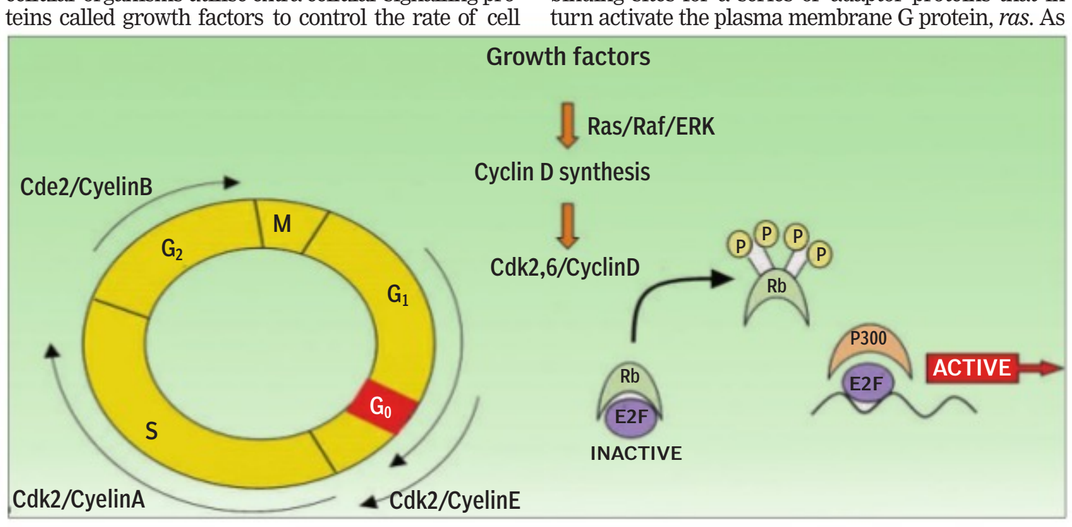
PROTEIN PATHWAYS

TAPAN KUMAR MAITRA EXPLAINS THE MECHANISM BY WHICH CELLS PROFILERATE IN MAMMALS AFTER BEING STIMULATED BY GROWTH FACTORS

Simple unicellular organisms, such as bacteria and yeast, live under conditions where the presence of sufficient nutrients in the external environment is the primary factor that determines whether cells grow and divide. In multi-cellular organisms, the situation is usually reversed — cells are typically surrounded by nutrient-rich extra-cellular fluids but the organism as a whole would be quickly destroyed if every cell were to continually grow and divide just because it had access to adequate nutrients.

Cancer is a potentially lethal reminder of what happens when cell proliferation continues unabated without being coordinated with the needs of the organism as a whole. To overcome this potential problem, multicellular organisms utilise extra cellular signalling proteins called growth factors to control the rate of cell growth and division. Most growth factors are mitogens — they stimulate cells to enter the S phase of the cell cycle, followed by G2 and then mitosis.



Cyclins/Cdk complexes control entry and exit through the four phases of the cell cycle. Growth factors through the action of Ras, Raf and ERK trigger the synthesis of D-type cyclins which complex with Cdk4 or Cdk6 to regulate cell cycle progression through Go. The phosphorylation of pRb by G1 cyclins (D1, D2, D3, and E)/Cdk complexes promotes the release of E2F-1 from Rb. Through its association with p300, E2F-1 activates the transcription of genes important for the G1 transition to S phase.

If mammalian cells are placed in a culture medium containing nutrients and vitamins but lacking growth factors, they normally become arrested in Gl despite the presence of adequate nutrients. Growth and division can be triggered by adding small amounts of blood serum, which contains several stimulatory growth factors. Among them is platelet-derived growth factor, a protein produced by blood platelets that stimulates the proliferation of connective tissue cells and smooth muscle cells. Another important one called epidermal growth factor is widely distributed in many tissues and body fluids.

PDGF and EGF act by binding to plasma membrane receptors located on the surface of target cells. Different kinds of cells have different receptors and hence differ in the growth factors to which they respond. Growth factor receptors exhibit tyrosine kinase activity. The binding of a growth factor to its receptor activates this tyrosine kinase activity, leading to phosphorylation of tyrosine residues located in the portion of the receptor molecule protruding into the cytosol. Phosphorylation of these tyrosines in turn triggers a complex cascade of events that culminates in the cell passing through the restriction point and entering into S phase. The *ras* pathway plays a central role in these events, as shown by studies involving cells that have stopped dividing because growth factor is not present.

When mutant, hyper active forms of the *ras* protein are injected into such cells, they enter S phase and begin dividing, even in the absence of a growth factor. Con-versely, injecting cells with antibodies that inactivate the *ras* protein prevents cells from entering S phase and dividing in response to growth factor stimulation.

The mechanism by which the *ras* pathway induces cells to pass through the restriction point and enter S phase involves six steps.

First, the stimulating growth factor binds to its plasma membrane receptor. Then, the binding causes two receptor molecules to cluster together, forming a dimer in which the tyrosine kinase associated with each receptor phosphory-lates tyrosines of the neighbouring receptor. The phos-phorylated tyrosines serve as binding sites for a series of adaptor proteins that in turn activate the plasma membrane G protein, *ras*. As is generally the case for G proteins, activation of the *ras* protein is accompanied by GTP binding and the release of GDP.

The activated *ras* molecule then triggers a cascade of protein phosphorylation reactions, beginning with phosphorylation of a protein kinase called *raf.*

Activated raf phosphorylates serine and threonine residues in a protein kinase called *MEK,* which in turn phosphorylates threonine and tyrosine residues in a group of protein kinases called *Map* (mitogen-activated protein). Thereafter, the activated MAP kinases enter the nucleus and phosphorylate several regulatory transcription factors, which are proteins that activate the transcription of specific genes.

As part of the last step, in the delayed genes, there are several coding for either Cdk or cyclin molecules, whose production leads to the formation of Cdk-cyclin complexes that phosphorylate Rb and hence trigger passage from Gl into S phase.

Thus in essence, the *ras* pathway is a multi-step signalling cascade in which the binding of a growth factor to a receptor on the cell surface ultimately causes the cell to pass through the restriction point and into S phase, thereby starting the cell on the road to cell division.

The importance of this pathway for the control of cell proliferation has been highlighted by the discovery that mutations impacting the *ras* pathway appear frequently in cancer cells.

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Mysterious 'heat spots'

OFFICIALS ARE UNSURE ABOUT WHERE THE 'THERMAL ANOMALIES' IN EGYPT'S ANCIENT PYRAMIDS ARE COMING FROM, BUT IT COULD INDICATE A SO FAR UNKNOWN CHAMBER, SAYS **ANDREW GRIFFIN**

Mysterious heat patches have been found at the bottom of the Egyptian pyramids and experts are puzzled as to how they got there. A team of architects and scientists has found strange heat patterns in three stones at the bottom of the Great Pyramid at Giza. They were searching for hidden chambers when they came across the mysterious thermal activity and aren't sure where the heat energy is coming from. But it could be that it is emanating from previously unknown parts of the pyramid, or a sign of internal air currents.

The Great Pyramid was built around 2600 BC and is the oldest and biggest of three pyramids in Giza. It takes its name from Egyptian Pharaoh Khufu.

As part of Operation Scan Pyramids, the team said it had "concluded the existence of several thermal anomalies that were observed on all monuments during the heating up or the cooling down phases". It said in particular that it had found an "impressive" heat spot "on the eastern side of the Khufu pyramid at ground level". It also found the anomalies in the upper half of the pyramid.

It said the area should be "the subject of further investigation" through the rest of the project, which will last until the end of 2016. The team began scanning the pyramids around two weeks ago. The project is using infrared thermal cameras to take pictures of the pyramids at sunrise, when they start to heat up, and again at sunset as they cool down again.

Egypt is hoping to uncover the secrets of the only remaining Wonder of the Ancient World — and save its struggling tourism industry in the process. Throughout 2016, a team of scientists, engineers and architects from Egypt, France and Japan will survey the famous Pyramids of Giza in search of hidden chambers inside the ancient structures. The Scan Pyramids Project is also looking to answer a question that has puzzled Egyptologists and engineers for centuries: how these huge structures were built without the aid of modern technology.

The team will use non-invasive technologies such as radiography, drone-mounted scanners and thermal imaging to survey the pyramid complex, both to create three-dimensional models of the exterior and to examine the internal structures. The Japanese KEK particle physics institute and the University of Nagoya will use muon radiography, a technique employed to scan active volcanoes in Japan, to search for undiscovered voids.

Of particular interest is the Khufu or Cheops Pyramid, the only remaining Wonder of the Ancient World. "I think it's a noble endeavour," said Professor Salima Ikram, of the American University in Cairo. "With the effects of climate change (on the pyramids), it's good to have a record of the current state."

The initiative is not the first in recent times to try to unlock the secrets of the ancient structures: in 1985, French architects Gilles Dormion and Jean-Patrice Godin led a failed investigation to prove the existence of a hidden network of passages within the Khufu Pyramid."Previous expeditions in the 1980s didn't have the technology we have today," said Hisham Zazou, Egypt's minister of tourism.

He was also frank that the project could entice tourists back to Egypt, after years of political instability decimated a once-thriving industry. With tourism representing more than 10 per cent of Egypt's GDP, Zazou "swore an oath" to the Egyptian people that the project would drum up business.

THE INDEPENDENT

Tourists at the Giza pyramids, on the southern outskirts of the Egyptian capital, Cairo.

PLUS POINTS

'Wrongly named'

In an embarrassing finding for a profession that is allegedly based on fact, more than half the world's natural history specimens may be wrongly named, according to British scientists. The sheer amount of samples being collected is outpacing the number of experts who can accurately record them, according to researchers at the University of Oxford and the Royal Botanic Garden Edinburgh.

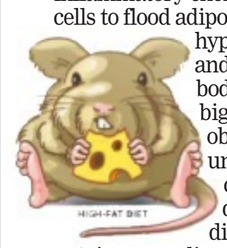
They examined 4,500 specimens of the African ginger genus *Aframomum*, from 40 collections in 21 countries, using a monographic study completed last year as a reference. "The team were surprised to find that prior to this monograph at least 58 per cent of specimens were either misidentified, given an outdated or redundant name, or only identified to the genus or family," according to the research, published in *Current Biology Magazine*. "As few plant groups have been recently monographed, the team suggests that a similar percentage of wrong names might be expected in many other groups," it adds.

Researchers also discovered that two specimens from the same plant were often recorded differently. An analysis of 21,075 samples of *Dipterocarpaceae*, a family of rainforest trees from Asia, found that a third (29 per cent) had different names in different collections. Mistakes were also found within records kept online.

JONATHAN OWEN/THE INDEPENDENT

Fanning the flames

Obesity often comes with a side of chronic inflammation, causing inflammatory chemicals and immune cells to flood adipose tissue, the hypothalamus, the liver and other areas of the body. Inflammation is a big part of what makes obesity such an unhealthy condition, contributing to Type 2 diabetes, heart disease, cancers, autoimmune disorders and, possibly, even neurodegenerative diseases.



To better understand the relationship between obesity and inflammation, Toshinori Nakayama, Yusuke Endo and their colleagues at Chiba University in Japan started with what often leads to obesity: a high-fat diet. They fed mice rich meals for a couple of months and looked at how gene expression in the animals' T cells compared to gene expression in the T cells of mice fed a normal diet. Most notably, they found increased expression of *Acaca*, a gene that codes for a fatty acid synthesis enzyme called acetyl coA carboxylase 1 (ACC1). They went on to show that the resulting increase in fatty acid levels pushed CD4 T cells to differentiate into inflammatory T helper 17 (Th17) cells.

KATE YANDELL/THE SCIENTIST

Low-tech alerts

Five people were killed and thousands lost their homes in a fire that tore through Khayelitsha, a township home to around a million people on the fringes of Cape Town in South Africa on New Year's Day 2013. Such fires are common in South Africa's informal settlements, what with houses being built cheek-by-jowl from reclaimed, easily flammable materials.

When fires break out, emergency services have difficulty locating and reaching houses and the impact can be devastating.

After the 2013 fire, a group of Cape Town students set out to design a fire alarm system for townships. Using a "mesh network" of radio and cellular alarms, the resulting Lumkani system identifies and alerts people to dangerous fires at a fraction of the cost of smoke detectors.

Fire detectors are now in place in 3,000 homes across the Western Cape. "This is a social, cultural and psychological as well as a technological intervention," James Boonzaier, Lumkani design engineer said in a recent audio interview. The goal is to enable local people to defend their lives and livelihoods from fire. The Lumkani team hopes it can expand the low-cost system for use in informal settlements across Africa, where 200 million people — or 60 per cent of the urban population — live in slums, the highest rate in the world.

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