Volume 436 Number 7053 pp889-1064

In this issue (18 August 2005)

Editorials

Research Highlights

News

News Features

nature

www.nature.com/nature

Vol 436 | Issue no. 7053 | 18 August 2005

Science and religion in harmony

A spiritual leader with an interest in research has encountered opposition to his plans to speak at a scientific meeting. But he is perfectly entitled to do so.

The Dalai Lama is due to speak at the annual Society for Neuroscience meeting in Washington DC on 12 November, and some neuroscientists don't like it (see *Nature* **436,** 452; 2005). But the Buddhist leader's talk is part of a lecture series that the society is laudably conducting on the science and society — and it should go ahead as planned.

The invitation of the Dalai Lama to the meeting will be interpreted in some quarters as an insult to his nemesis, China. And, citing the oft-repeated refrain that science and religion should be kept separate, some neuroscientists are calling for the lecture to be cancelled.

The critics accuse the Dalai Lama of trying to use the meeting to sell science that they regard as substandard: research on the relationship between meditation and physiological changes in the brain. Even the researchers directly involved in these studies, many of whom are working with the encouragement and support of the Dalai Lama, say that the work is in its early stages.

But the society did not invite the Dalai Lama to speak as a scientist. He will be in Washington to kick off its lecture series on "Dialogues between Neuroscience and Society", in which non-scientists are expected to address "subjects of interest to neuroscientists". The second such lecture will be given by Frank Gehry, the architect who designed the Guggenheim Museum in Bilbao, Spain.

Since *Nature* first reported on this story three weeks ago, several neuroscientists have written to us criticizing efforts to stop the lecture (see page 912, for example). It seems reasonable to assume that a fair number of the 30,000 delegates expected to attend one of the world's largest scientific meetings will be interested to hear what the Dalai Lama has to say.

The Dalai Lama will not be a complete outsider at the meeting. Through the Colorado-based Mind & Life Institute, he has already interacted with many reputable neuroscientists. According to the society, he was invited, in part, because "he has already had an influence on the design of experiments of great interest to neuroscientists". As even one opponent of the talk admits: "He has views on controlling negative emotions, which is a legitimate area for neuroscience research in the future." But his lecture does not necessarily constitute an endorsement of his views by the society.

Critics counter that the talk threatens to "entangle the Society for Neuroscience with religious activities". The invitation for the Dalai Lama to speak will give him a chance to sell his religious beliefs in the guise of neuroscience, they claim. Their petition opposing the lecture even draws comparisons between the Dalai Lama, with his belief in reincarnation, and creationists.

But speakers at meetings — non-scientists or scientists — should not be barred on the basis of their religious beliefs. Well-known scientists including Newton have had religious beliefs that many people would disagree with, but these have no bearing on the credibility of their scientific ideas.

Furthermore, in stark contrast with the approach of most religious leaders, the Dalai Lama has tried for many years to encourage empirical research into the claims he makes for the value of meditation. He encourages monks to take part in such experiments. Resulting studies have appeared in respectable scientific journals.

"The Dalai Lama encourages monks to take part in experiments. Resulting studies have appeared in respectable scientific journals."

It is true that the invitation could be interpreted as an insult to China. But the manner in which it was issued — by a scientist who was attending a meeting on neuroplasticity at the Dalai Lama's home in India — implies that the neuroscience society harbours no such intent.

It is not unreasonable for the researchers who object to the invitation to protest against it, and to seek to draw attention to the limitations of the Dalai Lama's credentials as a speaker. But now that the point has been made, they should withdraw their threatened boycott of the meeting, and instead raise their issues in the open forum that will follow his talk. ■

Ratings games

Researchers have two rare opportunities to influence the ways in which they may be assessed in future.

How to judge the performance of researchers? Whether one is assessing individuals or their institutions, everyone knows that most citation measures, while alluring, are overly simplistic. Unsurprisingly, most researchers prefer an explicit peer assessment of their work. Yet those same researchers know how time-consuming peer assessment can be.

Against that background, two new efforts to tackle the challenge deserve readers' attention and feedback. One, a citations metric, has the virtue of focusing explicitly on a researcher's cumulative citation achievements. The other, the next UK Research Assessment Exercise, is rooted in a deeper, more qualitative assessment, but feeds into a numerical rating of university departments, the results of which hang around the necks of the less successful for years.

Can there be a fair numerical measure of a researcher's achievements? Jorge Hirsch, a physicist at the University of California, San Diego, believes there can. He has thought about the weaknesses of current attempts to use citations — total counts of citations, averaged or peak citations, or counts of papers above certain citation

thresholds — and has come up with the 'h-index'. This is the highest number of papers that a scientist has written that have each received at least that number of citations; an h-index of 50, for example, means someone has written 50 papers that have each had at least 50 citations. The citations are counted using the tables of citations-to-date provided by Thomson ISI of Philadelphia. Within a discipline, the approach generates a scale of comparison that does seem to reflect an individual's achievement thus far, and has already attracted favourable comment (see page 900). The top ten physicists on this scale have h values exceeding 70, and the top ten biologists have h values of 120 or more, the difference reflecting the citation characteristics of the two fields.

The author placed his proposal on a preprint server last week (www.arxiv.org/abs/physics/0508025), thereby inviting comment before publication. Given the potential for indicators to be seized upon by administrators, readers should examine the suggestion and provide the author with peer assessment.

Whatever its virtues, any citation analysis raises as many questions as it answers and also tracks just one dimension of scientific outputs. *Nature* has consistently advocated caution in the deployment of the impact factor in particular as a criterion of achievement (an index that Hirsch's h indicator happily ignores). Wisely, the UK Research Assessment Exercise (RAE) has long committed itself to a broader view and the organizers of the next RAE, to take place in 2008, have prohibited assessment panels from judging papers by the impact factors of the journals in which they appeared. What the costs of that will be in panel members' time remains to be seen.

The common approach of the RAE's disciplinary panels is to assess up to four submitted outputs (typically research papers or patents) per researcher, of which a proportion will be assessed in some detail (25% for the biologists, 50% for the physicists). There will no doubt be something of a challenge in taking into account the fact that a typical publication has several co-authors.

"Given the potential for such indicators to be seized upon by administrators, readers should examine the suggestion and provide the author with some peer assessment."

These outputs will sit alongside indicators of the research environment such as funds and infrastructure, and of esteem, such as personal awards and prestige lectures. The specific indicators to be considered and the weightings applied are now open for public consultation (see www.rae.ac.uk/pubs/2005/04/docs/consult.doc). Given that the RAE is so influential both nationally and, as a technique, internationally, there is a lot at stake. Stakeholders should express any concerns they may have by the deadline of 19 September. ■

Climate for progress

The painstaking US approach to the assessment of climate-change science yields some useful results.

The US Climate Change Science Program, which is seeking to produce a comprehensive set of reports on climate change, has been widely criticized as a stalling exercise whose work duplicates that of the Intergovernmental Panel on Climate Change, and whose findings may be prone to political manipulation.

However, the programme yielded some promising outcomes last week, when several participants of a panel it convened published some findings on the apparent discrepancy between the record of warming on the Earth's surface and the change experienced in the troposphere, the lowest level of the atmosphere (see page 896).

The climate-change programme had brought together 22 experts to look into the problem. In the course of five meetings and countless e-mail exchanges, the participants conceded flaws in some of the their earlier analyses and produced new data sets, some of which were published online in *Science* (doi:10.1126./science1114772; doi:10.1126./science1114867; doi:10.1126./science1115640; 2005).

The release of the draft report summarizing the panel's conclusions for public review, which was due in June, is being delayed, however. The delay may reflect the intrinsic difficulty of getting a large committee containing disparate views to agree on a final form of wording. But it seems to fit in with a pattern at the climate-change programme, which was criticized by the Government Accountability Office in April for failing to meet a 2004 deadline for issuing a new national climate-change assessment. Critics also point out that since the programme issued a strategic plan just two years ago, some of the completion dates for the 21 reports that it plans to produce have slipped by several years.

US government officials say that they were too ambitious in setting the original deadlines. But they also admit that some of the panels' work is being delayed by two other factors: the need to comply with recent legislation that makes it extremely difficult to incorporate fresh scientific information into government reports, and the requirement that the climate-change work is approved at the political, as well as the scientific, level.

"The handling of the lower-atmosphere report over the next few months will help to clarify whether the programme really is a serious attempt to grapple with uncertainty in climate-change science."

The programme's director, James Mahoney, argues that the latter process will be managed in a way that will preclude political interference. Once the scientific authors have agreed their final draft, the report will be posted online for a 45-day period of public comment. Once that closes, the report will be revised again. Only then, in the final step before publication, will it be reviewed by administration officials.

This process will make it hard for the Bush administration to put its own spin on the report's scientific findings — provided that the drafts are published promptly, without political interference, and that the final documents adhere to the spirit of the drafts. The handling of the lower-atmosphere report — the first from the programme's strategic plan — in the next few months will help clarify whether the programme is a serious attempt to grapple with uncertainty in climate-change science, or is merely an exercise in obfuscation. ■

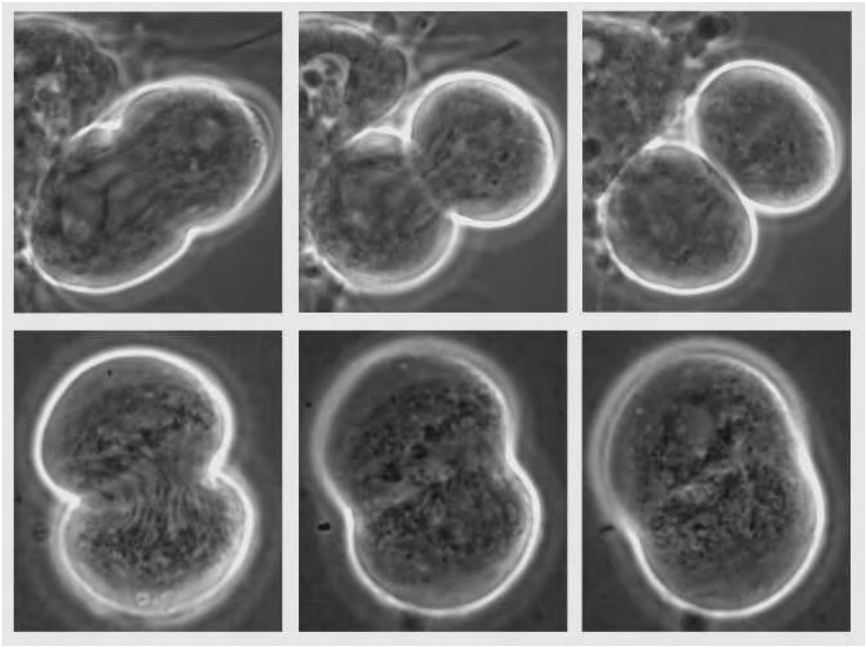
RESEARCH HIGHLIGHTS

Getting good cleavage

Curr. Biol. **15,** 1401–1406 and 1407–1412 (2005)
The composition of the cell membrane and signalling via calcium ions are key to controlling the final step of cell division, according to two independent studies.

Julie Brill and her colleagues at the Hospital for Sick Children in Toronto, Canada, found an important component of the calcium signalling pathway, the phosphoinositide PIP2, in the dividing cell's membrane. Sperm cells from the fruitfly *Drosophila* deprived of either calcium or PIP2 (pictured bottom right, compared with control, top right) can begin cytokinesis, but not complete it, the researchers found.

Meanwhile, a group of researchers led by Seth Field of Harvard Medical School in Boston has shown that PIP2 accumulates at the cleavage furrow in mammalian cells, where the molecule helps the cell membrane to stick to the contracting ring of proteins that divides the cell.



R. WONG/J. BRILL/ELSEVIER

BIOTECHNOLOGY

Made to order

Nature Biotechnol. doi:10.1038/nbt1128 (2005)
Escherichia coli bacteria have been engineered to make novel polyketides — molecules that can kill bacteria and inhibit cancer cells — using a modular approach.

Typically, soil microorganisms make polyketides using hefty enzymes encoded in genetic sequences up to 50,000 bases long. To make these genes more wieldy, researchers headed by Daniel Santi from Kosan Biosciences in Hayward, California, divided the sequences into modules about 5,000 base pairs long. They then engineered modules from different enzymes to combine inside *E. coli*, allowing the bacterium to synthesize polyketides not found naturally. Such compounds could help fight drug-resistant pathogens.

PROSTATE CANCER

RNA interference delivers

Proc. Natl Acad. Sci. USA doi:10.1073/pnas.0501753102 (2005)
Small interfering RNA molecules have been shown to shut down disease-causing genes in many animal models, but an obstacle has been delivering the RNA to where it is needed. Takahiro Ochiya at the National Cancer Center Research Institute in Tokyo and his colleagues have pioneered one possible solution by combining small interfering RNAs with a modified form of the natural protein collagen.

The group used such a mixture, injected into mice's bloodstreams, to shut down the genes implicated in the spread of prostate cancer to bone. This inhibited the cancer's spread, without the side-effects or inflammation that have plagued other approaches — providing the first hints that small RNAs could treat advanced prostate cancer.

COMPUTER SIMULATION

Cracked it

Phys. Rev. Lett. **95,** 060202 (2005)
Warming news for materials scientists: a way to simulate the behaviour of solids that previously worked only when the temperature of the material was set to absolute zero has been adapted to work at higher, more realistic temperatures.

Laurent Dupuy of the Lawrence Livermore National Laboratory in California and his colleagues have made this improvement to the quasicontinuum method, which combines atomic-scale simulations of crucial regions with cruder treatment of the rest. This technique speeds the simulation of phenomena such as fracture, which involve processes at scales from the atomic to the macroscopic. The team showcases its work by simulating the formation of dislocations in a flat nickel crystal at different temperatures.

METABOLISM

Melting fat

Dev. Cell **9,** 271–281 (2005)
The insulin signalling pathway controls whether the body burns or stores fat. Stephen Cohen's group at the European Molecular Biology Laboratory in Heidelberg, Germany, have now found that a protein called Melted is involved in regulating this pathway

The researchers found that Melted, which resides in the cell membrane, binds to proteins from two different branches of the insulin pathway. Mutating the gene for Melted in the fruitfly *Drosophila* reduced the activity of the TOR pathway but activated FOXO, producing flies with 40% less body fat than normal. Giving the mutants the human version of the gene restored their fat, suggesting that Melted is involved in human fat metabolism, too.

ELECTRONICS

Y NOT?

Nature Mater. doi:10.1038/nmat1450 (2005)
The first electrical switch made entirely from carbon nanotubes has been unveiled by Prabhakar Bandaru of the University of California, San Diego, and his colleagues. They report that a current

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

flowing across two branches of a Y-shaped nanotube can be switched on and off by applying a voltage to the third branch. Although the details of the switching process are not yet well understood, it should be possible to use the Y-shaped nanotube to create a NOT gate, which inverts its input, and to implement other logic operations.

ANTIBIOTIC RESISTANCE

TB's second secret

Proc. Natl Acad. Sci. USA
doi:10.1073_pnas.0505446102 (2005)
One reason for the spread of tuberculosis is the remarkable ability of its causative agent, *Mycobacterium tuberculosis*, to resist antibiotics. This stems, in part, from the low permeability of the cell envelope, a membrane inside the organism's cell wall. Now a gene that coordinates a second line of defence within the cell's cytoplasm has been discovered.

Charles Thompson from the University of British Columbia in Vancouver and his team spotted that a mutation in the gene whiB7 made the bacterium *Streptomyces lividans* more vulnerable to antibiotics. *Mycobacterium* also carries this gene, and mutating it had the same effect. The researchers analysed gene activity to study the protection mechanism.

QUANTUM PHYSICS

It must be glove

Phys. Rev. A **72,** 022304 (2005).
Information about handedness can be transmitted by a physical object such as a glove, because the left hand is different from the right. But what would a pair of 'quantum gloves' look like?

Daniel Collins, formerly of the University of Geneva, Switzerland, and his colleagues point out that four entangled particles can assume one of two configurations that are, like gloves, mirror images of each other.

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

But these gloves are much more economical than a classical glove, they argue, because they are burdened with less of the extra information that comes from knowing the position of every part of a classical glove with certainty.

In contrast, the absolute positions of the particles in their quantum glove are unknown, so they only carry information about handedness.

CELL BIOLOGY

Nuclear escape

Cell **122,** 379–391 (2005)
The editing of messenger RNA, or splicing, was assumed to occur only in a cell's nucleus. But now splicing has been seen in human platelets, which have no nucleus.

Mature mRNA molecules, which are used to synthesize proteins, are made by splicing of pre-mRNA. Andrew Weyrich's group at the University of Utah in Salt Lake City identified components of the splicing apparatus in platelets (pictured below, surrounded by red blood cells), and showed that external signals could set the machinery going. This prompted them to examine bone-marrow cells called megakaryocytes, which spawn platelets. Parts of the splicing complex were also found in these cells' cytoplasm.

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

D. SCHARF/SPL

GENETICS

Surprise connection

Mol. Cell **19,** 381–391 (2005)
Inside the cell nucleus, DNA wraps around proteins called histones. Chemical modifications of these proteins are thought to switch genes on and off. A study of the histone H3 provides clues to how sophisticated this control may be.

Adding methyl groups to the ninth amino acid in this protein's chain had been thought to deactivate genes. Gerd Blobel of the Children's Hospital of Philadelphia and his colleagues were therefore surprised to find di- and tri-methylation of this region in active genes. These modifications disappear when the gene is repressed. Other histone modifications must also be influencing the gene's status.

DORLING KINDERSLEY/GETTY IMAGES

JOURNAL CLUB

Douglas Hamilton
University of Maryland

Now you see them, now you don't, but at least this researcher knows why his favourite features of Saturn's rings have gone missing.

Images from the Voyager spacecraft in the 1980s revealed dark streaks across Saturn's rings, dubbed spokes. They grew rapidly to span thousands of kilometres, sheared apart, and then faded over a few hours.

These unusual structures are known to be composed of micrometre-sized dust grains, made by meteoroid impacts on large ring particles, but their evolution is not well understood. I had been working on this problem, and had come up with some very promising leads, based on models of the motions of charged dust grains. However, the late 1990s brought data that threatened to make my theory redundant.

Colleen McGhee from Wellesley College in Massachusetts and her colleagues were using the Hubble Space Telescope to monitor Saturn's rings. They found, mysteriously, that spokes lessened in number and intensity over several years, then disappeared altogether in late 1998. I learnt about these observations at meetings, and was left wondering what had happened to the spokes.

McGhee *et al.* now offer an elegant explanation for the spokes' remarkable disappearing act (*Icarus* **173,** 508–521; 2005). They suggest the spokes form a dusty scattering layer above the thin main rings. Until the mid-1990s, Saturn's rings were seen edge-on, so sunlight had to travel a long distance through the dusty layer before reflecting from the rings, making the spokes look dark.

Now, Saturn's rings are tilted towards the Sun. This geometry makes the spokes invisible to Earth-based telescopes, and even to the Cassini spacecraft currently orbiting Saturn. But the dusty spokes still exist, and so my budding theory survives.

NEWS

Synthetic biologists face up to security issues

WASHINGTON DC

Concerns about safety and security in the young field of synthetic biology are developing almost as rapidly as the research itself.

With scientists now able to create complete genomes from scratch and to introduce new characteristics into viruses and bacteria, there are fears that accidental — or worse, intentional — release of such creatures could occur.

As a result, the US government, academics and the field's first private companies are now working together to address the potential problems before they become a reality.

Synthetic biology is one of the priorities for the newly formed US National Science Advisory Board for Biosecurity (NSABB), which met for the first time in June. A working group on the topic, set up by the board, will begin its discussions later this month. Its members have already consulted synthetic biologists who have set up their own governance project, funded by the Alfred P. Sloan Foundation in New York, which will have its first meeting in September.

And one of the first public discussions of the issue comes this week, at a synthetic-biology meeting in San Francisco on 19–20 August. As well as looking at the field's potential in areas such as drug development, cellular reprogramming and biological robotics, participants will tackle ethical and legal issues.

The discussion will echo an event in 1975, when pioneers of genetic engineering retreated to the Asilomar Conference Center in California to set safety and ethical principles to guide their field. The fear was that modified microorganisms might escape into the environment with unpredictable effects, perhaps causing disease or out-competing wild strains.

Now synthetic biologists have much more powerful techniques at their disposal. Improved DNA synthesis means, for example, that microbial genomes can be built from scratch, bypassing the need to get hold of the actual organism. A dramatic demonstration of the potential consequences came in July 2002, when researchers at the University of New York at Stony Brook reported that they had synthesized an infectious poliovirus using mail-order DNA (see *Nature* **418,** 265; 2005). Genome sequencer Craig Venter followed that by announcing plans to build a bacterium from lab synthesized DNA and by taking just three weeks to synthesize a virus that infects bacteria (H. O. Smith *et al. Proc. Natl Acad. Sci. USA* **100,** 15440–15445; 2003).

Others are using made-to-order components to re-engineer the genomes of bacteria or viruses — either to investigate how they work or to try to give them abilities that they would not have naturally, such as producing drug molecules or generating hydrogen for use as an energy source. In theory, these techniques could be used to create deadly organisms in the lab, such as Ebola or anthrax, or to make bacteria more dangerous by giving them antibiotic resistance, for example, or the ability to make additional toxins.

Does this increased sophistication mean that the field needs radically new rules? Drew Endy, a synthetic biologist at Massachusetts Institute of Technology and one of the leaders of the Sloan Foundation project, is not sure. "There hasn't been a clear conversation about whether *de novo* synthesis poses a different threat from genetic engineering," he says.

Wendell Lim at the University of California, San Francisco, who uses synthetic biology to study basic processes such as how cells grow and move, says that there is nothing special about the field that requires blanket restrictions and that each type of study should be judged on its own risks and merits. "To broadly raise alarms about all such approaches is akin to saying we should worry about all uses of semiconductors because one of their uses could be in launch systems for nuclear weapons," he says. "We need to distinguish the sub-areas of the field and specific biological components that truly pose a hazard, and figure out how to regulate them."

Taking care

But there are some general precautions that most synthetic biologists support. Many think it would make sense to monitor products ordered from companies that generate synthetic genes on demand, such as Codon Devices in Cambridge, Massachusetts, and Blue Heron Biotechnology in Bothell, Washington.

George Church, who co-founded Codon Devices this spring, wants to go further, arguing that strict regulation is a key to heading off the public-relations problems that have plagued other areas of biotechnology. As well as monitoring orders for components such as synthetic genes, he says the government should screen certain raw materials that scientists could use to brew up their own DNA. "Basically you want a series of licences to cover almost every step where there's a reasonable bottleneck you can regulate," he says.

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

The ability to build genomes in the lab has raised fears that the technology could be abused.

But many argue that the openness of the field offers a built-in safety mechanism against unintentionally creating something harmful. For instance, Endy's lab hosts an online library of parts that can be built into genomes. The library is open source, meaning that all scientists in the field can test them. "There's an element of safety in using well characterized components," says Christopher Voigt, a synthetic biologist at the University of California, San Francisco.

Other synthetic biologists point out the success of initiatives to encourage young scientists to think about safety and ethical issues relating to their work. "It's important to talk about ways to minimize risk, and one of the most important ways to do that is to train responsible scientists and engineers," says Christina Smolke, a chemical engineer at the California Institute of Technology in Pasadena.