University of BRISTOL

re:search

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The watchman's song

Dinosaur fact file

An inflamed response

re: search editorial

Science City Bristol

The Prime Minister, Gordon Brown, designated the Bristol city region a 'Science City' when he was Chancellor of the Exchequer. The region was chosen because of its world-class academic research, its potential to drive economic development through science and innovation, and the large number of small-to-medium scientific enterprises based in the area.

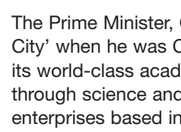
To celebrate its new status, Science City Bristol was officially launched in March this year as part of National Science and Engineering Week. The week kicked off with the University of Bristol's 'Science Alive!' event in Bristol's main shopping centre, and 'Bath Taps into Science' at the University of Bath. These hands-on events were designed to show the public some of the world-class research that's taking place on their doorstep.

The Bristol city region is known for its scientific heritage and its links with Brunel, but perhaps less well known is the fact that a whole range of iconic items – everything from plasticine to mobile phones, and from self-raising flour to self-healing aircraft wings – were also developed in the region. This cutting-edge research and development work continues today in the region's universities, businesses and large companies such as British Aerospace.

Working in collaboration with a wide range of partners across the region – and thanks to initial investment from the South West Regional Development Agency – Science City Bristol will play a key role in the sustainable economic and social development of the city region over the coming years. It aims to do this by:

- bringing business, academia and government together
- creating a more connected scientific community
- promoting the area's scientific achievements
- generating a culture that understands and celebrates science and technology

The University of Bristol is proud to be involved with Science City Bristol. It is a brilliant opportunity for academics, business people and the government to work together to develop and promote this area's excellence in science, engineering and technology. The benefits will be felt in everything from the strength of the economy to the pride that the people of the Bristol region take in their area.



Professor Eric Thomas
Vice-Chancellor, University of Bristol
Chair of Science City Bristol

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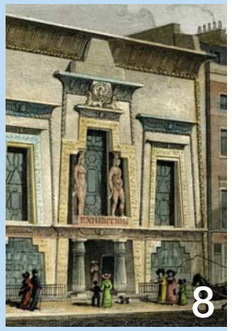
Cover image: The pied babbler acting as a sentinel. See article on page 4.



pre: view

Safer drinking water for millions

Over one billion people lack access to improved water sources; over two billion lack access to basic sanitation. The fight to combat this problem – one of the most serious threats to child health in developing countries – has received a grant for $13 million from the Bill & Melinda Gates Foundation. This will facilitate the development of *Aquatest*, the world's first low-cost, easy-to-use diagnostic tool that will give a clear, reliable indication of water quality. *Aquatest* is the result of groundbreaking work by an international consortium, led by Dr Stephen Gundry from the University's Department of Civil Engineering.

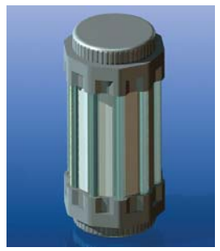
Aquatest involves a small, hand-held device that indicates whether the water is safe to drink or not by displaying the test results as coloured bands, indicating the degree of contamination. The kit could be used in many ways. Although water is provided in some areas by government or water utilities, it is still possible for it to become contaminated before being drunk. If a cheap test could produce reliable results without the need for a laboratory or special training, water engineers could arrange for their staff to test the water regularly. Even in remote areas, visiting health workers or community volunteers could undertake water testing to ensure safe water is arriving in villages.

Where no water is piped into a village, communities arrange their own water supply. This could be a naturally occurring source of water (a spring, river, lake or pond) or a well or borehole. These communities have a strong interest in ensuring water quality for their families, but at the moment they have no way of knowing that the water is free from *E. Coli*. They could make good use of *Aquatest* that would allow them to check the cleanliness of the water.

Stephen Gundry carrying water.

The project's vision is that low-cost water-testing devices will be in widespread use in 80 per cent of developing countries, within ten years. ■

www.bristol.ac.uk/aquatest



Above: Computer-generated image showing a possible design for the *Aquatest* device.

Left: Boys fetching water.

IMAGES COURTESY AQUATEST

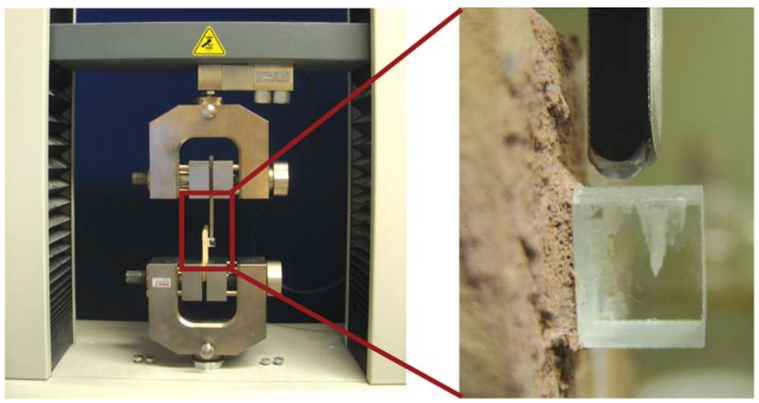
The conservation of medieval mosaics

The Interface Analysis Centre specialises in the analysis of surfaces and materials. Specific problems are dealt with by academics pursuing cutting-edge research who regularly apply their knowledge to solving commercial problems. The Centre's Director, Professor Geoff Allen, with one of his PhD students, Diana Edwards, has recently been investigating techniques that might help to restore the beautiful mosaics of the Basilica di San Marco in Venice.

The Basilica di San Marco – the cathedral of Venice – is the city's most famous church. It lies on St Mark's Square and is one of the best-known examples of Byzantine architecture in the world. The building was begun in 829 AD as an ecclesiastical structure to house and honour the remains of St Mark that had been brought from Alexandria. It now contains examples of some of the world's most beautiful mosaics dating from the 13th century. Unfortunately, the position of the Basilica adjacent to the Grand Canal creates damp conditions that have caused the mosaics to deteriorate so that today they require a long-term programme of restoration.

The location of the Basilica presents considerable challenges to the conservation of the mosaics. Piazza San Marco is the lowest-lying part of Venice and high tides flood the piazza with salt water twice a day. The salt water also floods the basement of the Basilica where it is absorbed by the stone in the Basilica walls. The water level in a normal stone wall is determined by the rate of absorption and evaporation, which in turn depends on the porosity of the stone.

The city's most famous church contains examples of some of the world's most beautiful mosaics



An innovative technique devised for testing the strength of modern-day mortars.

Example of a mosaic from the interior of the Basilica.

Usually this level does not exceed one metre; however, unlike a normal wall, the first five metres of the Basilica walls are coated in a layer of marble, which is impervious to water. Since the water is prevented from reaching the surface and evaporating, the water level in the wall increases and in some parts of the Basilica has reached a height of ten metres. The salt water penetrates the lime mortar of the mosaics causing detrimental effects such as salt explosions, which push the tesserae out of the mortar. As each tessera was individually positioned by the mosaicist so that any gold-leaf detail reflects light on to the observer, producing a golden sheen to the mosaics, it is important to be able to replace loosened tessera very precisely. Analysing the mortar that holds them in place is thus key to the restoration programme.

Salt water penetrates the mortar of the mosaics causing detrimental effects such as salt explosions

Lime mortar is a complicated material to analyse. For example, polishing the surface to look at the structure will damage the sample and ruin the structure that requires analysis. So for these materials a more sophisticated technique is required involving the use of Focussed Ion Beam (FIB) technology, that can be used as a form of microsurgery to cut a section of the mortar without damaging the structure, allowing clear electron images to be obtained. Using this technique, unique evidence for organic matter in the mortar was discovered. While the inorganic regions have been identified as calcium carbonate, the precise identification of the organic matter is more difficult. However, work on mosaic mortars of a similar age in Hagia Sofia, Istanbul, has indicated the presence of egg white, which could have been incorporated to aid the positioning of the tesserae. In addition, X-ray Photoelectron Spectroscopy of the region between the glass tessera and the lime mortar shows a higher concentration of potassium and sodium salts, compared with the bulk mortar, indicating that the presence of these components may play a role in the deterioration of the mosaics.

As well as analysing the original mortar, innovative techniques and experimental design have tested the strength of modern-day mortars in 'simulated mosaic' experiments, with the aim of finding the best mortar with which to restore the mosaics to their original state. Using this technique, the lime mortar found to give the strongest bond with the glass tesserae was one prepared by mixing a Venetian dolomitic lime (a lime which contains magnesium) with Carrara Marble, in the ratio one of lime to three of marble. The next phase of the work will use all these results to create a lime mortar similar to the original, which will be tested to check whether it can withstand the harsh salt-water conditions of the Basilica. If it passes this final test, it will be used to sensitively restore the mosaics. ■

www.iac.bris.ac.uk

In the Young Persons' Lecture Competition, sponsored by the Institute of Materials, Minerals and Mining, Diana Edwards won the south west regional heat for her lecture about this work, and came second in the national finals.

Soldiers on sentry duty in hostile territory keep in regular radio contact with their colleagues to assure them that all is well and that they are safe to carry on their manoeuvres. New research by Dr Andy Radford of the School of Biological Sciences reveals that this is also a feature of the bird world.

THE WATCHMAN'S SONG

Pied babblers are small birds that live in groups of 3-15 individuals in the Kalahari Desert in Africa. They spend 95 per cent of their foraging time on the ground, probing beneath the sand for prey. In turn, they are preyed on by a variety of raptors, mammals and snakes.

The foraging groups have a sentinel perched above the ground, actively scanning for predators. The sentinel lets the others know of its presence by providing vocal cues, commonly called the 'watchman's song'.

The study population of babblers has been habituated to the presence of people, making it possible to observe them and make sound recordings from only a few feet away. This allows Radford to quantify an individual's foraging success by recording the capture rate of prey. Furthermore, the babblers have been trained to jump on to a scale, allowing weights to be gathered repeatedly during the day, thereby providing accurate and regular measures of the birds' condition.

About 30 per cent of the time, the foraging groups have a sentinel perched above the ground, actively scanning for predators (see cover image). The sentinel lets the others know of its presence by providing vocal cues, commonly called the 'watchman's song'. Because babblers often search for prey in holes, they are unable to check visually for the presence of a sentinel without suspending foraging; the watchman's song allows them to maximise their foraging time.

By playing back different recordings to the birds, Radford found that foragers capture more prey in response to the watchman's song. One reason for this is that the foragers spend less time looking out for predators themselves, and so have more time to search for food. However, the foragers also change their behaviour in three other important ways. First, by spreading out more widely, individuals may encounter fewer foraging patches already depleted by other group members. Second, by venturing into the open more, they may have a wider choice of foraging patches and thus access to those of better quality. Third, because individuals look up less often, foraging bouts are longer and less interrupted, which is likely to be beneficial when chasing mobile prey.

Natural selection suggests that individuals should act selfishly. The exciting implication from these results is that the watchman's song may represent truly cooperative behaviour. The presence of a sentinel results in increased survival rates of group-mates, which in turn leads to a larger group size, improving the group's chances of survival when under attack, or repelling rivals from the territory. Thus sentinels profit down the line from the increased foraging success of the others. Moreover, because group members tend to be close relatives, and therefore share a large number of genes, sentinels gain in reproductive terms from their increased survival. The next thing to test is whether sentinels differ in their reliability – so it's off to the Kalahari for another few weeks in the sun. ■

www.bio.bris.ac.uk

A pied babbler weighs itself.

IMAGES ANDY RADFORD

Dinosaur fact file

A rush of publications about dinosaurs meant that the Department of Earth Sciences hit the headlines three months running. But while most facts in the papers were correct, there isn't always room for the details …

The upper jaw of *Carcharodontosaurus saharicus* from Morocco, the closest relative to *Carcharodontosaurus iguidensis*.

The banana-sized tooth of *Carcharodontosaurus iguidensis*. Each box in the scale is one centimetre.

Student identifies new dinosaurs

Carcharodontosaurus iguidensis was probably 13-14 metres long, making it taller than a double-decker bus. It had a skull about 1.75 metres long and its teeth were the size of bananas. The newly-found fossils include several pieces of the skull – parts of the snout, lower jaw and braincase – as well as part of the neck. They were discovered in the Republic of Niger and showed a number of differences from previously identified Moroccan material, allowing Steve Brusatte, an MSc student in the department, to name the dinosaur as a new species.

Two other mega carnivores are known to have inhabited the same Saharan ecosystem during the Cenomanian, about 95 million years ago: *Spinosaurus*, a sail-backed creature which may have grown up to 18 metres in length, and a smaller abelisaurid theropod that only grew to about nine metres. But recognition of *C. iguidensis* reveals a diversity among these theropods that was previously unknown. The presence of distinct species in the Cenomanian of Niger and Morocco suggests localised faunal differentiation, possibly the result of shallow continental seas that may have acted as temporary barriers between these areas. Each of these large-bodied carnivores has very distinctive cranial and dental morphology, suggesting that their coexistence may have been enabled by dietary niche partitioning.

Two new meat-eating dinosaurs unearthed in the Sahara

A few months later, Brusatte was again in the news with more discoveries from the Niger, this time from a formation thought to be about 112 million years old (Mid-Cretaceous). The finds turned out to be the earliest records of two of the major carnivore groups that would go on to dominate Africa, South America and India during the next 50 million years. *Eocarcharia dinops*, an early relative of *C. iguidensis*, represents one of the oldest known carcharodontosaurids, and *Kryptops palaios* is the oldest African abelisaurid and the oldest confirmed abelisaurid on any continent.

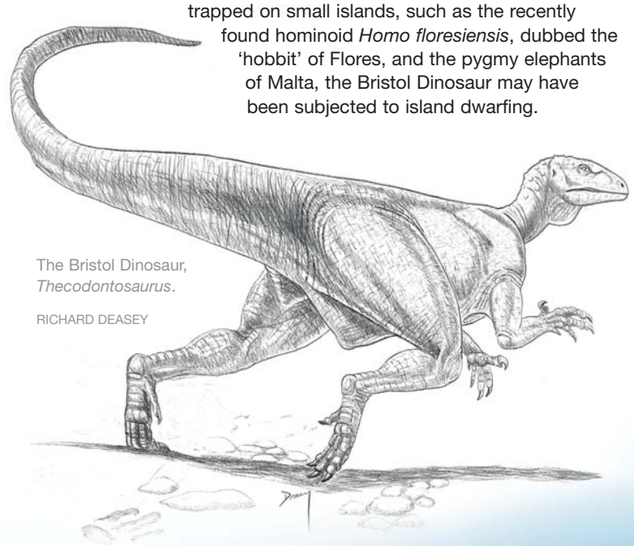
Abelisaurids have played a prominent role in helping to determine the time when Africa separated from Gondwanaland, a super-continent that formed in the southern hemisphere some 500 million years ago. Ten years ago it was suggested that the absence of abelisaurids in Africa and their presence in South America, India and Madagascar provided evidence of the separation of Africa from Gondwanaland about 120 million years ago. Their subsequent discovery in Africa, however, points to the final separation of South America and Africa being around 100 million years ago, significantly later than previously thought.

Pygmy dinosaur inhabited Bristol's tropical islands

Remains of the celebrated Bristol Dinosaur, *Thecodontosaurus*, were first excavated back in 1834 from the limestone quarries of Durdham Down, in Clifton, Bristol. In 1975, the remains of at least 11 other individuals were uncovered in a quarry at Tytherington, north of Bristol. Many people have subsequently worked on the specimens and *The Bristol Dinosaur Project* was set up four years ago to develop an interactive exhibit, displaying the dinosaur and the environment in which it lived.

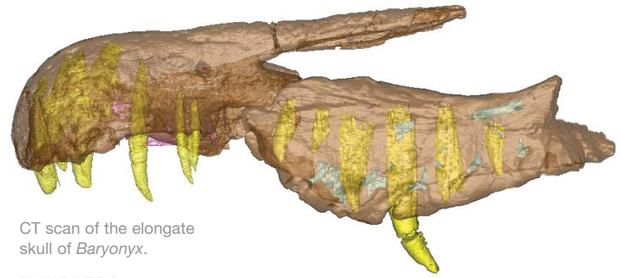
A collaboration between two palaeontologists – the University's Dr David Whiteside, an authority on extinct reptiles, and Professor John Marshall, an expert on fossil pollen from the University of Southampton – revealed that *Thecodontosaurus* lived more recently than was previously thought. The research involved a microscopic study of marine algae and fossil pollen. It shows that rather than inhabiting the arid uplands of the Late Triassic as previously thought, the dinosaurs lived just before the Jurassic on lushly vegetated islands around Bristol. The outlines of these islands can still be seen today in the shape of the land; for example, Bristol's famous Downs was one such island.

The discovery that the Bristol dinosaur lived on small islands is very important as it could explain the dinosaur's small size (two metres) in relation to its giant (ten metres) mainland equivalent, *Plateosaurus*. Geological mapping indicates that the islands were quite small in size. This suggests that, like other species trapped on small islands, such as the recently found hominoid *Homo floresiensis*, dubbed the 'hobbit' of Flores, and the pygmy elephants of Malta, the Bristol Dinosaur may have been subjected to island dwarfing.



The Bristol Dinosaur, *Thecodontosaurus*.

RICHARD DEASEY



CT scan of the elongate skull of *Baryonyx*.

EMILY RAYFIELD

Unusual British dinosaur had crocodile-like skull

Another British dinosaur, *Baryonyx walkeri*, was also the subject of a collaboration between experts at different institutions. Dr Angela Milner from the Natural History Museum, who first described the dinosaur, originally thought that the unusual skull of *Baryonyx* indicated that it might be a fish-eater, but it was the computer modelling techniques – more commonly used to discover how a car bonnet buckles during a crash – employed by Dr Emily Rayfield in the Department of Earth Sciences, which confirmed that to be the case.

Rayfield used an engineering technique called 'finite element analysis' that reconstructs stress and strain in a structure when a load is placed on it. The *Baryonyx* skull bones were CT-scanned by a colleague at Ohio University, USA, and digitally reconstructed so she could view the internal anatomy of the skull. She then analysed digital models of the snouts of four different animals – a theropod dinosaur, an alligator, an Indian gharial crocodile and *Baryonyx* – to see how each snout stressed during feeding.

The biomechanical data showed that the eating behaviour of *Baryonyx* was markedly different from that of a typical meat-eating theropod dinosaur or an alligator, and most similar to the gharial. Since the bulk of the gharial diet consists of fish, Rayfield's study suggests that this was also the case for *Baryonyx* back in the Cretaceous. This evidence was supported by the fact that on excavation, partially digested fish scales and teeth were found in the stomach region of the animal, demonstrating that at least some of the time this dinosaur ate fish. Through quirks in their evolutionary history, *Baryonyx* and the gharial have evolved independently to feed in a similar manner. This demonstrates that in some cases there is more than one evolutionary solution to the same problem. ■

www.gly.bris.ac.uk

William Bullock and Napoleon's carriage

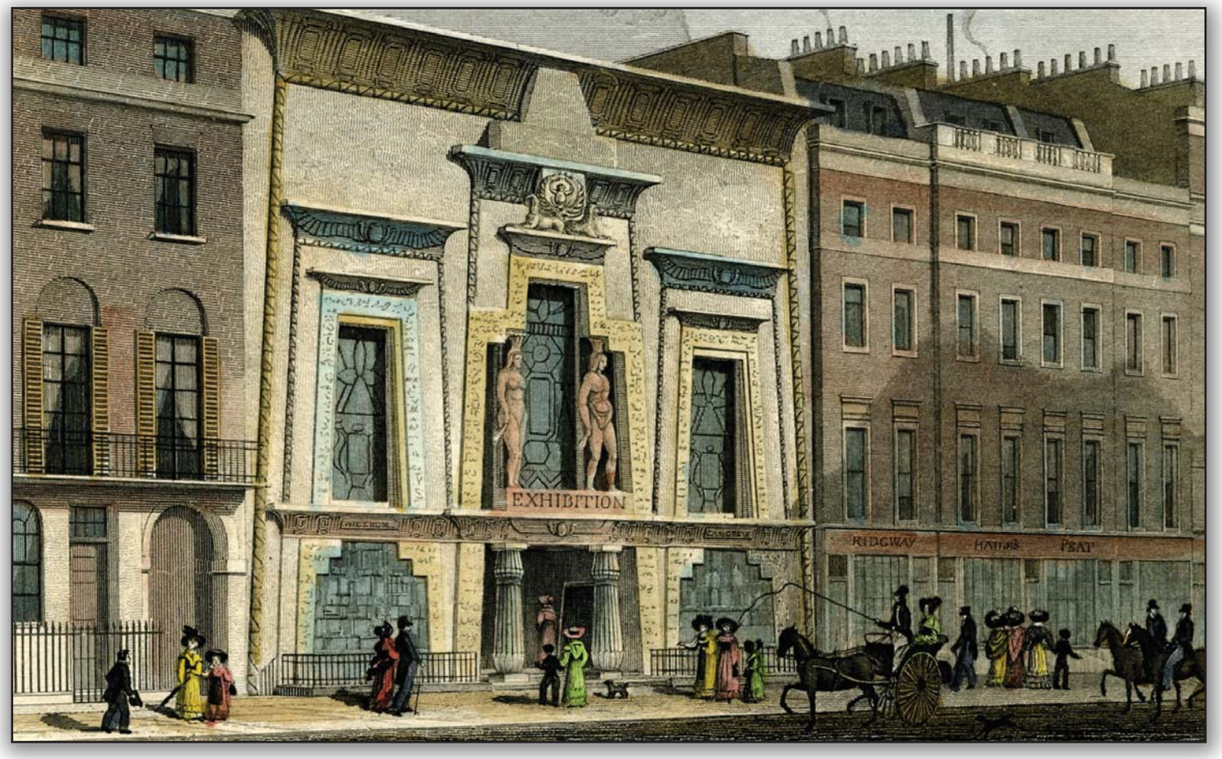
Professor Michael Costeloe, from the Department of Hispanic, Portuguese and Latin American Studies, worked on the history of Mexico for many years. His interest in William Bullock (c1773-1849) derives from an important book Bullock published about Mexico in 1824. In fact, Bullock's life turned out to be so interesting, Costeloe ended up writing his biography.

The Bullock family's main occupation was a wax-modelling business in Birmingham, but when they moved to Liverpool in 1801 young William Bullock's interest increasingly turned towards natural history. He had acquired a small 'cabinet of curiosities' with 200-300 artefacts, but once in Liverpool, then a thriving port, he was able to obtain a vast range of novelties from many countries, brought back by sailors.

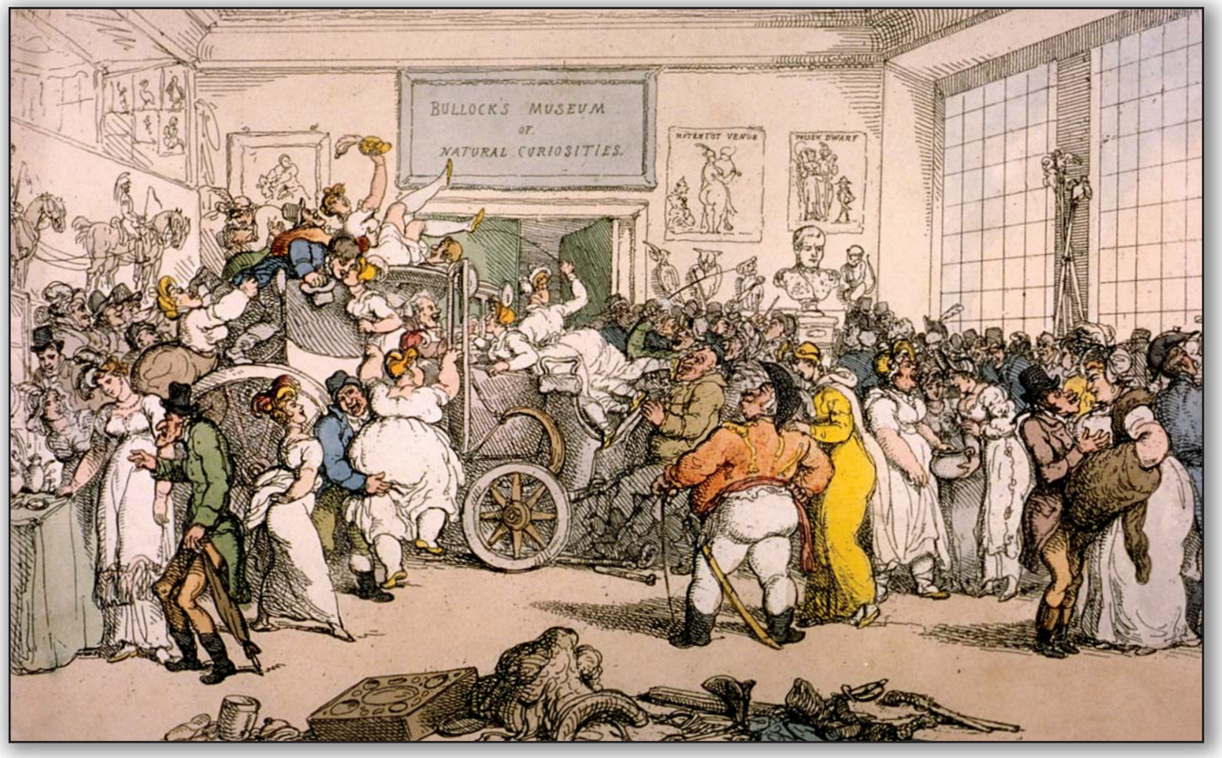
The museum was being hailed in *The Times* as the most interesting ever seen in the capital

His collection rapidly expanded and what he called his Liverpool Museum quickly became the largest of its kind in Britain, and possibly in the world. Thousands of exhibits were on display including myriad specimens of the natural world, prepared by William who was an expert taxidermist. His ambition, he said, was to have an example of every known creature on Earth.

In 1809, William decided to capitalise on his growing reputation by moving his museum to London, opening at 22 Piccadilly in October that year. The London exhibition was an instant success and within weeks the museum was being hailed in *The Times* as the most interesting ever seen in the capital. William continued to buy and collect new exhibits such that within a year of his arrival in the metropolis, he needed larger premises. Noting vacant land at the south end of Piccadilly, he arranged for the construction of a purpose-built museum that for almost a hundred years was to be among the most instantly recognisable buildings in Britain. Soon known as the Egyptian Hall, reflecting its architectural style, the museum became the most fashionable place of entertainment and instruction in the capital. Everybody from Dorothy Wordsworth and Jane Austen to British and European royalty paid the one shilling entry charge and wandered round the galleries.



The Egyptian Hall, Piccadilly, 1828.



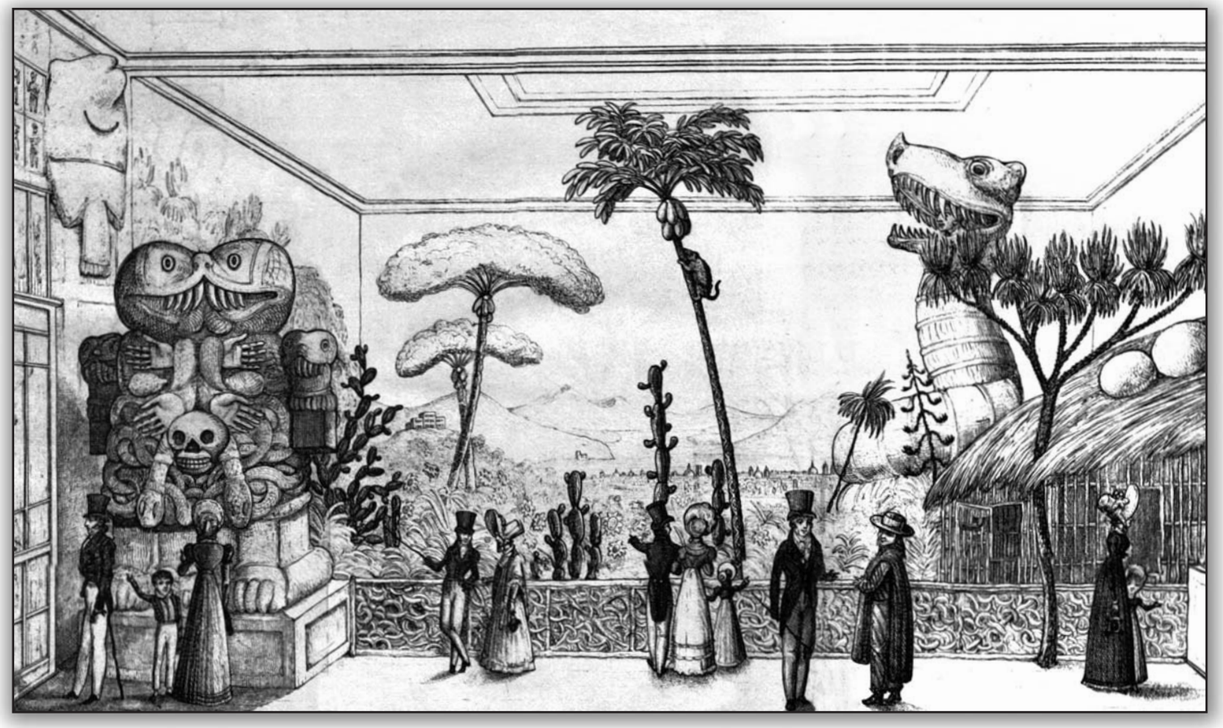
The exhibition of Bonaparte's carriage.

By 1814, William and his Egyptian Hall had achieved an international reputation

By 1814, William and his Egyptian Hall had achieved an international reputation, but it was an incident following Napoleon's escape from Elba and the battle of Waterloo that was to really make his fortune. In 1815, the French emperor's travelling carriage, used by him in campaigns across Europe and filled with hundreds of his personal possessions, was captured by a Prussian army unit. Having removed items of immediate value – Napoleon had diamonds hidden in the tea caddy – the Prussian commanding officer took the carriage to London in October 1815 and presented it to the British government.

A few weeks later the carriage, with its contents and four of Napoleon's horses to pull it, were bought from the government by William for something between £2,500 and £3,000. The carriage and contents were exhibited in the Egyptian Hall in January 1816. The show caused a sensation and thousands of people poured into Piccadilly to see it. Six months later William decided to take it to the provinces and after stopping off at Windsor to show it to the royal family, he brought it to the West Country. Large crowds lined the route wherever it went and on Friday, 30 August, it entered Bristol. Driven by two of Napoleon's own coachmen and decorated with the flags of the Allied Powers, and the British standard in the centre above the French banner, the arrival strongly impressed Bristolians and the editor of *The Bristol Mercury* who said:

What a lesson to unbridled ambition does this equipage afford; lately it appeared as a harbinger of subjugation to most of the Crowned Heads of Europe; now a public exhibition to the powerless object of idle curiosity of the British populace.



View of the exhibition of ancient and modern Mexico.

The exhibition was staged in a specially constructed building in Wellington Street, near St Mary Redcliffe. In the same building there was a separate exhibition of paintings depicting stages in the fallen emperor's career, busts and figures of him in marble and bronze, and several cases of weapons that William had acquired from the palaces of Malmaison and St Cloud. Entry to each exhibition cost a shilling and in the first week it was reported that 1,700 people a day bought tickets. Within a couple of weeks, 16,000 had paid and, after a tour of Bath and other towns across Britain, William estimated that some 800,000 people had bought tickets, making him a profit of many thousands of pounds.

Within a couple of years, public interest in Napoleonic memorabilia waned and William sold the carriage and it contents. Years later, in 1842, it was bought by Madame Tussaud and remained on show in her exhibition until it was destroyed by fire in 1925. But the immense success of his Napoleonic venture encouraged William to look for other popular shows. He sold the entire contents of his museum of natural history in 1819 and used the vacant space in the Egyptian Hall to show other exhibits, including the first exhibition to be seen in Britain of ancient and modern Mexico, complete with what was said to be the first Mexican Indian seen in Europe since the Spanish Conquest. William and his son were among the first Britons to travel to Mexico after its emancipation from Spain in 1821. They spent six months there in 1823 travelling and collecting exhibits, several of which are still on display in the British Museum.

William and his son were among the first Britons to travel to Mexico after its emancipation from Spain

William acquired a silver mine during his first visit to Mexico and in 1825 he took all his family to live there. However, for his many adventures there and later in the United States, you will have to read the full biography. In the words of a New York newspaper in 1839, William was one of the greatest virtuosos and connoisseurs of his age. He died in London in March 1849. ■

www.bristol.ac.uk/hispanic

Professor Costeloe's book *William Bullock, connoisseur and virtuoso of the Egyptian Hall: Piccadilly to Mexico (1773-1849)* is to be published in the Bristol monograph series, HiPLAM. Copies will be available from the general editor, Professor David Hook, Department of Hispanic, Portuguese and Latin American Studies, University of Bristol.

WHY CAN'T I LEARN A NEW LANGUAGE?

Adults, even the brightest ones, often struggle with learning new languages. Dr Nina Kazanina in the Department of Psychology explains why.

People comprehend their native language with great speed and accuracy, and without visible effort. Indeed, our ability to perform linguistic computations is remarkable, especially when compared with other cognitive domains in which our computational abilities may be rather modest. For example, an average person is infinitely slower than a computer when it comes to adding up numbers or remembering facts. On the other hand, most humans surpass computers when it comes to language-related tasks such as recognising sounds and words, and comprehending sentences.

My work deals with one aspect of language processing, namely, the identification of sounds, which is needed for subsequent word recognition. Sound recognition is a complex task, because the same sounds may be spoken differently depending on the speaker's sex, age, pitch of the voice or mood. In addition, people may whisper or shout, be in a quiet room or a noisy street. All of these, and many other factors, lead to huge variation in individual acoustic instances of the same sound. It is precisely this acoustic variation that for decades has caused problems for computational linguists and speech engineers building automatic speech recognition systems. Humans, however, even five-year-olds, can successfully recognise sounds and words and understand what other people say almost instantly.

So what allows humans to be so efficient at sound recognition and how does that impact on our ability to learn a new language? In order to answer this question, we used non-invasive techniques called electroencephalography and magneto-encephalography, which record electromagnetic signals from the brain while people listen to different speech sounds. We focused on activity in the auditory cortex, a region in the temporal lobe of the brain that is responsible for processing sound information. The results show that the auditory cortex of an adult speaker selectively preserves variation in speech that is meaningful in the listener's language and disregards variation that is irrelevant for word meaning.

For example, in English the difference between the sounds 'r' and 'l' is meaningful and serves as a basis for distinguishing words like rice and lice or rack and lack; consequently, this difference is highlighted by the auditory cortex of an English speaker. On the other hand, a Japanese speaker's brain will not notice the difference between 'r' and 'l' right away, because in Japanese these two sounds are used interchangeably. This strategy, which highlights only conceptually important variation in sounds, ensures the quickest way to interpret a word's meaning.

Hence, what the brain perceives is not fully determined by the physical input to the ear but rather is filtered through the listener's native language. Such selective – if not biased – perceptual abilities of adult listeners develop through their language experience during early years of life. As a result, the brain is wired optimally for the first (native) language communication. Unfortunately, this wiring may be less than ideal for learning a foreign language. The learner may find themselves a prisoner of their native language 'regulations' and be unable to perceive additional sound contrasts that are important for the new language. We are now trying to identify whether representations in the auditory cortex change as a result of continued exposure to a foreign language. ■

The learner may find themselves a prisoner of their native language

http://psychology.psy.bris.ac.uk

An inflamed response

Paul Martin, Professor of Cell Biology in the Departments of Physiology and Pharmacology, and Biochemistry, talked to Cherry Lewis about the discovery made in his lab that speeds up wound healing and reduces the size of the wound scar. She was interested not only in the discovery itself, but also in the processes and years of research that led up to it.

CL: Given that scarring is a natural process, what made you think you could improve on it?

PM: Well, we know that the natural process isn't perfect because wounds don't heal very rapidly and they often leave a nasty scar. However, we also know that in an embryo you get tissue repair that is perfect. I'm a developmental biologist and we often do what we call cut-and-paste surgery on mice and chick embryos. What we see is that within an hour of making a cut, you can't see any evidence of having done so. The repair and regenerative capacities of an embryo are amazing, and what it tells you is that perfection is achievable. Indeed, human foetal surgeons take advantage of this. If they go in early enough, they can do major corrective surgery in the womb without leaving any sign of a scar.

CL: At what point does scarring start, then?

PM: It has been known for some time that there is a transition moment during development – embryogenesis – when you start to scar. Some 15 years ago, in my lab in Oxford, I discovered that you get scarring from the first time in development when inflammatory cells are drawn to the wound – that is, the first time an inflammatory response was activated upon wounding. So it seemed very likely that inflammation was causing scarring.

CL: But isn't it important to our survival to have an inflammatory response?

PM: Indeed, it's been evolutionarily selected for in order to kill microbes wherever there's a breach in your skin. The key thing is to not die of septicaemia because bugs get into a cut. So as soon as the embryo starts generating inflammatory cells, it's practising raising an inflammatory response.

CL: So what is it about the inflammatory response that causes scarring?

PM: Scarring is rather like laying down a rushed, slightly excessive and poorly organised collagen matrix. Collagen is a protein that is rich in all connective tissues, but in normal skin it's laid down in a special way. What happens when tissue repairs is that it's laid down badly in dense bundles, which is why scars feel hard and matted. So we set about wondering how you might stop them forming in the first place.

As I explained, there seemed to be evidence that it was inflammatory cells rushing into the wound and releasing signals that somehow told the local wound fibroblasts to make a scar. To test this theory, we scratched a mouse that had a gene 'knocked out' that it needs in order to make the white blood cell types that are the inflammatory response. If you scratch mice that are missing this PU.1 gene much later than the transition moment in embryogenesis when you should start getting scars, it doesn't scar. This demonstrates that inflammation leads to scars.

CL: And you were able to identify which gene was responsible for scarring?

PM: Well, not exactly. There are hundreds of genes that are switched on when you wound skin and many of them are needed to close the wound hole. But by subtracting the genes that are switched on in the PU.1 knockout mouse where there's no inflammation when you wound it, from the larger pool of genes that are switched on in a normal mouse we were able to identify the extra ones that were present due to inflammation. One of these was a gene called osteopontin.

CL: How did you know it was the culprit?

PM: We didn't. The next step took ages to design. We could have just made a knock-out mouse that didn't have the osteopontin gene, but while that might have told us osteopontin was the culprit, it wouldn't have said anything about how to counter its scarring effects. Instead, what we decided to do was allow the inflammatory response to happen and osteopontin to be switched on, but then to dampen down its effect and see what happened.

We already knew of a Pluronic gel that acted as a delivery system. The great thing about this gel is that it is liquid at low temperatures so you can squirt it into a wound, but as soon as it reaches body temperature it goes hard. So it moulds itself into the wound and then slowly releases whatever is in the gel.

CL: And what is in the gel?

PM: When the genetic sequence of a particular gene is known to cause a disease, or, as in this case, an inflammation, it is possible to synthesise a strand of DNA that will bind to the MRNA encoded by that gene and inactivate it, effectively turning that gene off. This synthesised nucleic acid is termed an 'anti-sense oligonucleotide'. So what we put in to the gel was an anti-sense oligonucleotide against osteopontin. What happens is that the inflammatory cells are still rushing in to the wound, they're still telling the fibroblasts to make osteopontin but all the osteopontin is being shut down by the anti-sense oligonucleotide. And sure enough, what we found is that if you block osteopontin, the wound heals faster and you block scarring. We don't fully understand yet how and why osteopontin causes scarring, but what we do know is that if you reduce osteopontin, you reduce scarring.

CL: And there are no indications of side effects?

PM: Good question and one I can't answer yet. However, my guess is that there's no benefit to having osteopontin switched on in the wound and therefore switching it off shouldn't cause side effects, but I might be wrong. And it's important to realise that it's not only external scarring of the skin that will be improved. Any kind of surgery – heart operations and caesarean sections, for example – will benefit from reduced scarring.

CL: So might we eventually see this as a treatment?

PM: Hopefully, but it is at an early stage in development and will require further research, followed by human clinical trials. This takes considerable funding and particular skills, so we have to have an industrial partner. We therefore worked closely with the University's Technology Transfer team who have been invaluable in helping us patent our findings. Furthermore, we have just granted an exclusive licence to an established pharmaceutical company who will take the development forward. So watch this space! ■

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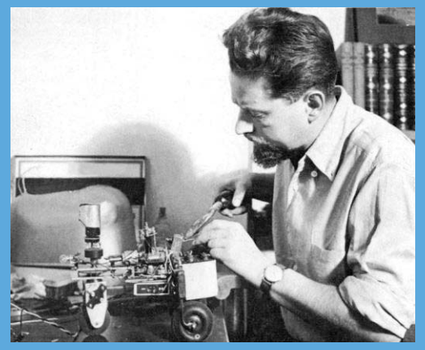

Grey Walter in the 1950s.

Grey Walter and his tortoises

From the first autonomous robots to stem cells for treating multiple sclerosis.

The Burden Neurological Institute (BNI) has an international reputation for its work in clinical and experimental neuroscience. Based in the Burden Centre at Frenchay Hospital in Bristol, the BNI is a research unit specialising in the human nervous system and human neurological disorders. But as well as playing a significant role in today's neuroscientific research, the BNI holds an important position in the history of neuroscience. For it was there that (William) Grey Walter, who was in charge for more than 30 years, created the first autonomous robots. His 'tortoises', complete with primitive neural pathways, led to new insights into the function of the nervous system, and to Grey Walter becoming recognised as a founding father of cybernetics.

The first autonomous robots were built at the Burden Neurological Institute in Bristol, in the 1940s.

In 1939 Walter moved to Bristol to open the BNI as a research centre in neuropsychiatry. He believed that the secret of how the brain worked lay in how it was wired up and wanted to prove that connections between a small number of brain cells could give rise to very complex behaviours. His first robots, Elmer and Elsie, constructed between 1948 and 1949, were mobile with a plastic shell that was phototropic – it could follow light – and acted as a bump sensor. The robots were designed to show the interaction between two sensory systems: light-sensitive and touch-sensitive control mechanisms (in effect, two nerve cells with visual and tactile inputs). These systems interacted with the motor drive in such a way that the tortoises exhibited 'behaviour'; finding their way around obstacles, for example. They were described as tortoises due to their shape and slow rate of movement – and because they 'taught us' about the secrets of organisation and life.

In 1951 three new tortoises were displayed at the Festival of Britain and caused great interest, but after the Festival they were auctioned off and, it is believed, Elmer and Elsie were scrapped. In 1970 Walter suffered severe brain damage in a road accident which effectively ended his career. Only one tortoise remained which passed to Grey Walter's son Nicolas, following his death in 1977. Nicholas stored the tortoise in his basement in Islington until 1995 where it was finally located after months of searching by Owen Holland, then Professor of Computer Science in the Intelligent Autonomous Systems laboratory (IAS) at the University of the West of England (UWE), in Bristol.

Holland carefully restored the tortoise to working order, but it was fragile and could not really be used for any extended experiments. The solution was to build replicas. The project commenced in 1995 and was greatly assisted by Bunny Warren, the designer of the 1951 batch, who still worked at the Burden Institute. He was able to produce many original records and spare parts, including some of the transparent perspex (Plexiglas) shells that he had been using as cloches in his garden. In a satisfactory repeat of history, the two replicas, Ninja and Amy, were demonstrated at the Millennium Dome, almost 50 years after the Festival of Britain. Today, Professor Alan Winfield at UWE looks after the surviving original; a replica is in the Science Museum. ■

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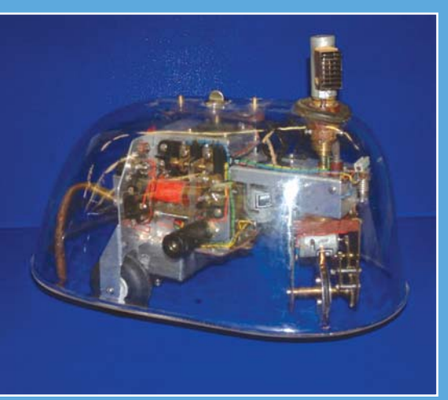
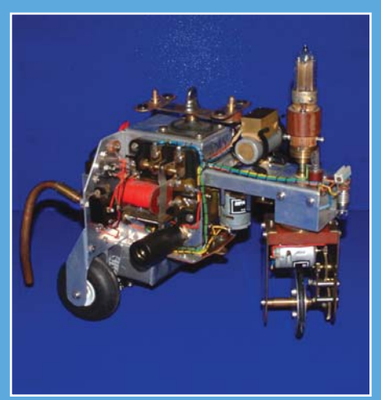




Modern replicas of Grey Walter's tortoises, with and without the perspex shell.

Walter's legacy

In partnership with the University of Bristol, the IAS has now been renamed the *Bristol Robotics Laboratory*. Research there aims to further the understanding of systems that operate autonomously and exhibit intelligent behaviour; ie, make appropriate decisions without reference to any human assistance. At the Burden Neurological Institute, current projects include investigating movement disorders such as Parkinson's disease and, most recently, the use of stem cells for treating multiple sclerosis. Grey Walter's legacy to Bristol science has been comprehensive and wide-ranging.

Dr Kazem Alemzadeh in the Bio-engineering research group of the Department of Mechanical Engineering has invented a Dental Robotic Testing Simulator called 'Dento-Munch' that can replicate human chewing, in order to test dental materials. The design inspiration was based on a human skull (structure), a spider (general look) and an aircraft simulator (dynamics and control of chewing).

The skull, the spider and the aircraft simulator

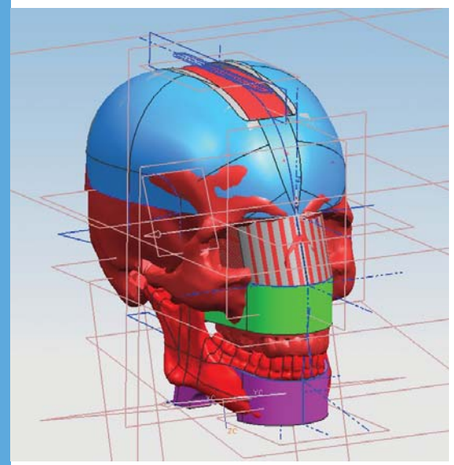
The UK spends £2.5 billion each year on dental materials to replace or strengthen teeth, but despite the frequent use of metals, polymers and ceramics for tooth replacement or restoration, their properties – strength, hardness, wear and fatigue – are often poorly understood. Without this knowledge, the likely long-term performance of such materials cannot be assessed. While randomised clinical trials can test such materials, they are time-consuming and expensive, and by the time a new material has been evaluated, the market has often moved on. Laboratory simulators do exist, but they too have their problems in that they do not truly represent human chewing, so results from different simulators are often inconsistent. This lack of an adequate method of testing is hindering the development of dental materials.

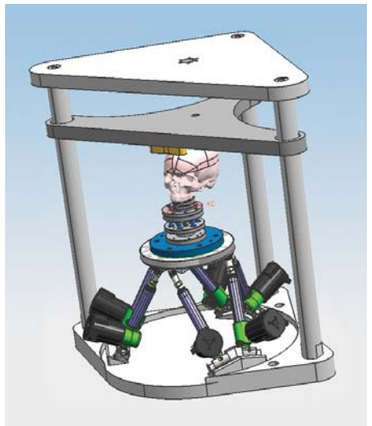
The temporomandibular joint, more fondly known as 'TMJ', is arguably the most complex set of joints in the human body. It connects the lower jaw – the mandible – to the temporal bone at the side of the head. If you place your fingers just in front of your ears and open your mouth, you can feel the joint move on each side of your head. Because these joints are flexible, the jaw can move smoothly up and down and side to side, enabling us to chew our food, talk and yawn. In humans, the TMJ joint and the high versatility of our muscles enables the jaw to move with 'six degrees of freedom'. It is therefore important that simulators can reproduce this same amount of 'freedom'.

Given the space constraints of Dento-Munch, the muscles of the TMJ had to be placed outside the skull and are represented by mechanisms that introduce motion. This is similar to the design of an aircraft simulator. However, despite looking nothing like a human jaw, the lower platform on Dento-Munch plays the part of the lower jaw and is capable of moving in six degrees of freedom, due to the platform's sophisticated controls. It therefore accurately mimics the chewing motion and forces in human jaws. It will soon be loaded with copies of real human teeth in order to test how implants, replacement or restored teeth might wear during use.

Using nothing more sophisticated than an office projector, a digital camera and some customised software, Alemzadeh has adapted a cheap way of imaging 3D objects. The Dental Optical Scanner, 'Dento-OS', as he calls it, will allow him to scan standard plaster casts of teeth made by dentists. The detailed 3D digital images that result will be used to machine replicas that will be loaded into the jaw. The potential of Dento-Munch and Dento-OS to improve the testing of dental materials was quickly recognised and the systems have now been patented in the US and the UK respectively. Ormco and Renishaw, specialists in orthodontics, have already shown great interest. ■

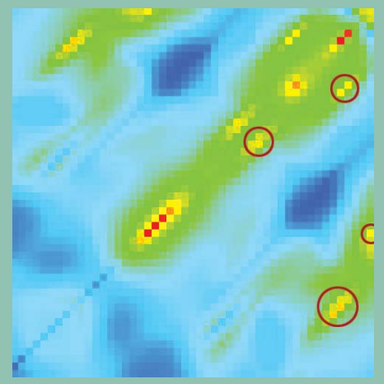
www.bristol.ac.uk/mecheng

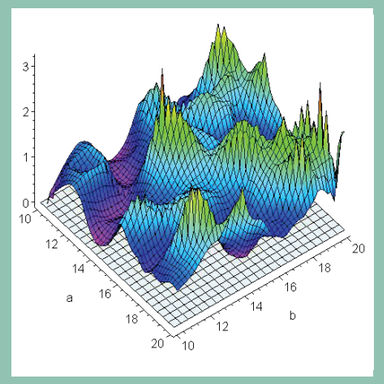




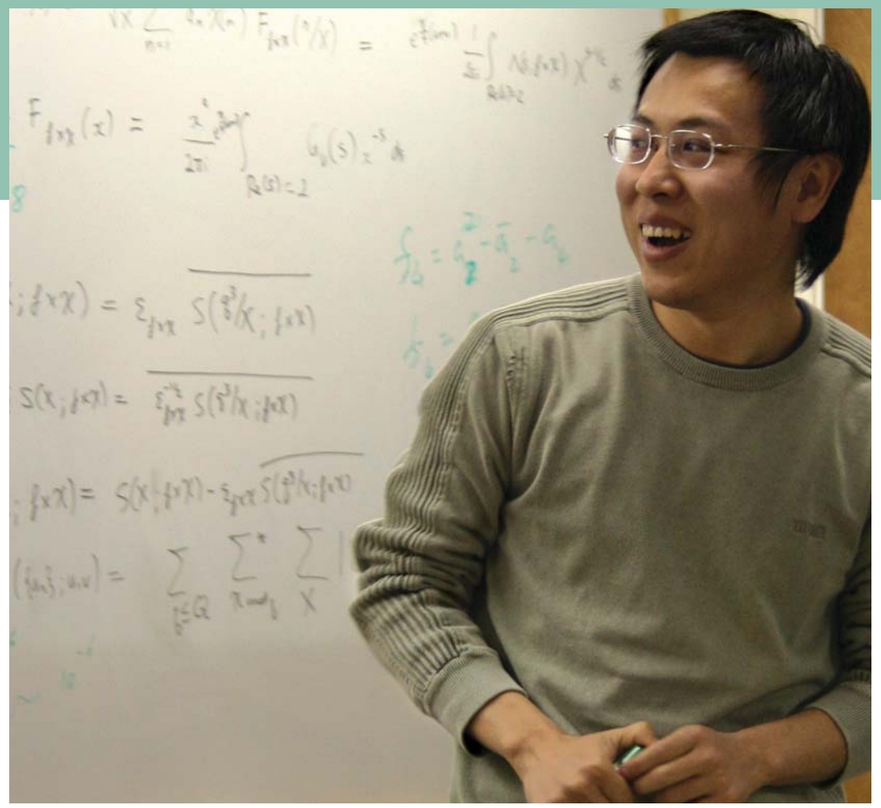
The Dento-Munch concept.

HUNTING THE ELUSIVE L-FUNCTION





Left: Andrew Booker. Middle: The 'hot' areas in this image suggest the presence of 3rd degree transcendental L-functions. Bian zoomed in on the four off-the-line examples (circled) before the workshop. Right: A 3D representation of the hot areas.



Ce Bian demonstrating his discovery of the new L-functions.

There was a lot of excitement last month about 'L-functions'. A PhD student in the Department of Mathematics, Ce Bian, in collaboration with his supervisor, Dr Andrew Booker, had discovered some new ones …

Ce Bian revealed his discovery at a workshop organised by the American Institute of Mathematics where teams of researchers from Europe and America, all competing for the same result, planned to announce their findings. Despite 'only' being a postgraduate student (the others were more senior), Bian was the only one to succeed before the workshop. After months of preliminary work and testing, he finally got everything working just before flying out to California – the computers were still crunching while he was in the air.

like. It gives us a glimpse of new worlds," he said. Clearly something important had been discovered, but what was it? "Unfortunately, L-functions are rather like fundamental particles in physics, in the sense that they are very important to the universe in which they exist, but hard to relate directly to everyday experience," explained Booker.

There are two types of L-functions – algebraic and transcendental – but in the same way that there are billions

L-functions are rather like particles in physics, they are very important to the universe in which they exist, but hard to relate directly to everyday experience

Bian's discovery caused considerable excitement among the world's leading mathematicians who were attending the workshop. Dorian Goldfeld, Professor of Mathematics at Columbia University, USA, likened it to finding new planets in remote solar systems: "We know they are out there, but the problem is how to detect them and determine what they look

of electrons in the universe, there are billions of each type of L-function, which are classified according to their degree. For example, the Riemann zeta-function – the granddaddy of all L-functions – is a first-degree algebraic L-function which holds the secret to how the prime numbers are distributed. What Bian has found is a new class of L-function – a 'third degree

Prime numbers – numbers that are only divisible by themselves or one – have been the subject of intense research since the Ancient Greeks

transcendental L-function' – and he has demonstrated four examples of that class. The last L-function to be discovered was more than 30 years ago when the second degree transcendental L-function was found by Harold Stark from the University of California, San Diego.

Prime numbers – numbers that are only divisible by themselves or one – have been the subject of intense research, probably since the Egyptians, and certainly since the Ancient Greeks. The problem of modelling their distribution is a tantalising one for mathematicians working on number theory because when one looks at individual numbers, the primes seem to be randomly distributed, but the 'global' distribution of primes follows well-defined laws. It's rather like the way that physics follows well-defined laws at the macro scale, which then completely change at the quantum scale. So some fundamental questions about prime numbers, such as the Riemann Hypothesis, have remained unresolved for more than a century.

The Riemann Hypothesis, announced in 1859 and today the most important of all unsolved mathematical problems, seeks to understand the connection between addition and multiplication. There is an unclaimed million-dollar prize for a valid proof of the hypothesis. But despite not being able to prove it, most mathematicians believe it to be true; if it isn't true, the world is a very different place from what we imagine. Bian's discovery of his new L-functions is a small step toward a greater understanding of these elusive objects, and many mathematicians believe that the route to a proof of the Riemann Hypothesis will go through families of L-functions.

In order to check that Bian really had found something new, and that his discovery had all the properties it was expected to have, Michael Rubinstein from the University of Waterloo in Canada, who was attending the workshop, immediately tested the Riemann Hypothesis for this newly-minted L-function. Rubenstein enthused: "Being able to explore this new L-function gives me the excitement that a biologist must feel when discovering a new mammal. The techniques developed by Bian and Booker open up whole new possibilities for experimenting with these powerful and mysterious functions."

To achieve his results, Bian's computer programme needed to solve systems of equations in roughly 10,000 unknowns, which took nearly 10,000 hours of computer time. Ten years ago this work would have required a supercomputer; today it's feasible using a PC on your desk. One day, with sufficient advances in number theory and computing power, someone will succeed in proving the Riemann Hypothesis and win that million-dollar prize, but Bian freely admits that their results are just a small step along the way. ■

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Prize for work on Riemann Hypothesis

The University's Maths Department is one of the leading research centres in the world for the study of random matrix theory and its applications to number theory, including the modelling of L-functions and the Riemann Hypothesis. Earlier this year, Professor Brian Conrey, also from the department, was awarded the 2008 Conant Prize by the American Mathematical Society for his article entitled *The Riemann Hypothesis*. Conrey is also Executive Director of the American Institute of Mathematics and was present at the AIM workshop when Bian and Booker presented their findings. He too was impressed: *"It's a big step towards our understanding the 'world of L', which is where most of the secrets of number theory are kept".*

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