reduces the amount of thermal energy available to the molecule to overcome its reaction barrier. But some remarkable reactions occur without the need for thermal excitation, through a process known as quantum tunnelling. Schreiner *et al.*[1] report that just such a process occurs for HCOH — when the molecule adopts a certain conformation, it decays to produce formaldehyde in a matter of minutes, even though the calculated barrier for the reaction is too high to be overcome at the temperatures used in the experiments. Instead, the hydrogen atom in the hydroxyl group (OH) of HCOH 'tunnels' through the barrier, in a process that relies on the wave–particle duality of the atom (Fig. 1). This unexpected reaction might explain why previous attempts to detect HCOH failed — the product decayed before it was found and analysed.

The authors[1] investigated the quantum tunnelling process by replacing the hydrogen atom of the hydroxyl group with deuterium (a heavy isotope of hydrogen). They found that the deuterated form of HCOH is essentially stable under their experimental conditions. This stabilizing effect occurs because the wave associated with the deuterium atom decays before reaching the exit of the barrier (unlike the wave for the hydrogen atom), and provides direct evidence of quantum-tunnelling. Turning again to theoretical predictions to validate their results, the authors modelled the tunnelling process computationally. The half-life for HCOH at close to zero kelvin was predicted to be 122 minutes, whereas that of deuterated HCOH was predicted to be more than 1,200 years, in good agreement with their experimental observations.

The data provided by this study[1] will be invaluable for those searching for HCOH under different conditions, for example in the gas phase, where it is expected to participate in many reactions. For such studies, it will be necessary to find out if the tunnelling process is similar in gases and solids — that is, does the matrix surrounding the HCOH molecules in Schreiner and colleagues' experiments have some role in the mechanism? The findings also provide a well-defined system of small molecules that will be a perfect model for studying the mechanisms of tunnelling reactions in solids. Far from being yesterday's news, small molecules still have much to teach us. ■

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ANIMAL BEHAVIOUR

Guardian caterpillars

Parasites are in the business of hijacking their hosts for their own purposes. A dramatic example is described by Amir Grosman and colleagues who studied behavioural changes induced in the Brazilian geometrid moth *Thyrinteina leucocerae* by a braconid parasitic wasp of the genus *Glyptapanteles* (A. H. Grosman *et al. PLoS ONE* **3,** e2276; 2008).

The wasp lays up to 80 eggs in a moth caterpillar, where they hatch, grow and then exit to form pupae on nearby leaves three weeks later. At this point the caterpillar ceases its previous activity, and instead stands guard over the wasp pupae (pictured). While 'guarding' the pupae, caterpillars make violent swings of their heads towards any passing insect or other potential threat.

Grosman *et al.* show that this behaviour is a direct result of parasite infestation and profits the wasp. Unlike the parasitized caterpillars, their unparasitized siblings failed to take up sentry duty when placed by wasp pupae, continuing to feed as normal. Also, the head butts of parasitized caterpillars proved effective protection for the pupae, repelling nearly half of the attacks by predatory stinkbugs (*Supputius cincticeps*) in the laboratory.

Such behaviour has no fitness advantage for the caterpillars, who die soon after the adult wasps emerge from the pupae. But the wasps profit hugely, the presence of a guarding caterpillar almost halving the mortality of pupae in field experiments.

J. LINO-NETO

Although the mechanism by which these parasites influence their hosts is not clear, live wasp larvae were found in the bodies of caterpillars even after their broodmates had departed. Such 'brain worms' have also been seen with trematode and liver fluke parasites that modify the behaviour of their ant hosts.

Christopher Surridge

HUNTINGTON'S DISEASE

Genetics lends a hand

Stéphane Palfi and Bechir Jarraya

A monkey model of Huntington's disease created by gene transfer is only a work in progress. But as a technological feat it offers great promise for fathoming this devastating condition.

Huntington's disease is a heritable disorder that affects more than 1 in 10,000 people. Its associated neurological symptoms are severe, and there is no therapy to halt or slow its progress. To understand its pathology, and with the ultimate hope of finding a treatment, researchers have generated several experimental models of this disease[1], in organisms such as flies and rodents. Although these models have led to tremendous progress in understanding the pathogenic mechanisms of Huntington's disease, none of them can replicate all the behavioural changes seen in the human disease or the changes that occur at the tissue level. The need for a primate model of the disease is thus clear.

On page 921 of this issue, Yang *et al.*[2] describe their attempt to generate a transgenic monkey model of Huntington's*. Although only a 'proof-of-principle', their achievement is a step forward, and will undoubtedly be welcomed by those involved in developing a cure for this distressing condition.

Initial symptoms of Huntington's disease, which generally appear between the ages of 30 and 40, include changes in personality, a progressive cognitive decline and a spectrum of motor disturbances ranging from abrupt to slow and sustained involuntary movements. At a cellular level, features of the human disease include severe neuronal loss in the striatum, a deep brain structure that regulates movement and the cognitive and emotional aspects of behaviour. At the molecular level, the disease is caused by mutation in the *HTT* gene, which encodes the huntingtin protein. This protein normally contains a chain of 6–35 glutamine amino-acid residues. But when *HTT* is mutated, the number of repeats of the CAG trinucleotide, which encodes glutamine, is greatly expanded, leading to extension of the glutamine chain in huntingtin by anything from 36 to 180 repeats[3].

The technique of transgenesis is used to generate organisms carrying a specific mutation, and involves the introduction of a foreign gene into an organism. The first transgenic primate,

*This News & Views article and the paper concerned[2] were published online on 18 May 2008.

a rhesus monkey[4], was generated in 2001. This animal carried a marker gene encoding green fluorescent protein (GFP). Yang *et al.*[2] faced a bigger challenge in trying to introduce a disease gene into rhesus macaques.

The authors inserted a virus vector carrying part of the mutated human *HTT* gene, with 84 CAG repeats, into unfertilized monkey egg cells. The virus, which became integrated into the egg's genome, also contained a gene for GFP, the fluorescent properties of which served as a marker for the success of the transgenic procedure. Of the six resulting pregnancies, five were born at full term. Of these, three newborns carried between two and four copies of mutated *HTT*. They all developed severe symptoms of Huntington's disease and died within the first month. Of the two surviving monkeys, each of which carries a single copy of the mutated gene, one has only 29 CAG repeats and so shows no disease symptoms, and the other has 83 CAG repeats and has developed mild symptoms, which began within 1 week of birth. The authors suggest that the discrepancy in the number of CAG repeats is due to their instability during integration into the viral vector. These two macaques are still under detailed investigation for disease progression as they get older.

Previous studies[5,6] of patients with Huntington's disease have shown that the expanded stretch of glutamine residues forms aggregates in the nucleus and cytoplasm of affected neurons. Yang *et al.* found that only monkeys expressing mutated *HTT* show the anatomical changes (aggregates in neurons in both the striatum and cortex) and movement abnormalities characteristic of the disease. But the authors' transgenic monkeys show only modest signs of neurodegeneration at the tissue level, suggesting that the neuronal degeneration they observed is at a very early stage.

Researchers working on other experimental models of Huntington's disease are divided over both the exact effect of the *HTT* mutation and the temporal relationship between protein aggregation and neuronal death. Current hypotheses predict that abnormalities may occur in neurotransmission, the regulation of gene transcription, the function of mitochondria (the cell's powerhouses), and transport within axons (neuronal extensions)[7,8]. So far, the features of Yang and colleagues' transgenic primates do not favour any one hypothesis. But because of the fundamental physiological and genetic similarities between monkeys and humans (including lifespan, cellular metabolism, and endocrine and reproductive function), a primate model is more likely than other animal models to provide insights into the mechanisms of cell death associated with Huntington's disease.

In contrast to rodents, non-human primates show neuroanatomical and behavioural characteristics, both motor and cognitive, that closely resemble those of humans. For instance, primate models of Parkinson's and Huntington's diseases[9] that were generated chemically have improved our understanding of the behavioural characteristics of these diseases. But the role of genetic factors in the development of neurodegenerative diseases cannot be determined in such models. Thus, transgenic approaches (for example, local transfer of mutated *HTT* into the monkey striatum[10] or gene introduction into oocytes, as Yang *et al.* have done) seem to be the way forward in addressing the remaining crucial questions.

The primate model generated by Yang *et al.*[2] takes us another step on the long road towards developing a treatment for Huntington's disease. The history of translational (bench-to-bedside) research in neuroscience has shown a strong correlation between the availability of relevant primate models for a given disease and the development of new treatments[11]. But we must retain a healthy caution, as there is a need to determine how closely the characteristics of these authors' transgenic monkeys[2] match the spectrum of symptoms of Huntington's disease.

Yang and colleagues' approach to generating transgenic monkeys should also facilitate the development of a more elaborate model for the common form of Huntington's disease, which is characterized by a delayed clinical onset of motor and cognitive dysfunction. What's more, it opens the way to generating non-human primate models for other neurodegenerative diseases that are caused by single-gene mutations, such as familial forms of Parkinson's disease, Alzheimer's disease and amyotrophic lateral sclerosis. ■

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NUCLEAR PHYSICS

A neutrino's wobble?

Philip M. Walker

Periodic oscillations have been observed in what should be straightforward exponential decay curves of two radioactive isotopes. An entirely mysterious phenomenon, its proposed cause seems equally exotic.

It is a well-established fact that the rate at which a collection of radioactive atoms decays itself decays exponentially over time. It's easy to see why: the number of decays is directly proportional to the number of radioactive atoms remaining in the sample; so the fewer active atoms there are left, the fewer decays will occur. That makes observations from Litvinov *et al.*[1], in a paper in *Physics Letters B*, all the more surprising. Investigating β-decays of highly positive ions of heavy elements, these authors see a decay rate whose decline is not purely exponential, but which seems to be modulated up and down over time. They propose that the modulation arises from the 'mixing' of different types of neutrino — chargeless and almost massless particles produced in β-decays. That explanation would itself raise a host of further questions.

The observations were made at the Experimental Storage Ring (ESR) of the GSI nuclear physics laboratory in Darmstadt, Germany. The 108-metre-circumference ESR has been the scene of many experiments with highly charged radioactive ions since the early 1990s. Most of these have been precise measurements of ion masses made possible by fastidious determinations of the time ions take to circumnavigate the ring — half a microsecond, give or take. Individual ion decays have also been monitored, and their half-lives deduced. This has yielded a crop of new decay processes: an example is bound-state β-decay[2], in which the β-particle (electron) produced by the ion in its decay is captured in one of its many vacant electron orbitals.

Litvinov *et al.*[1] studied the decay of two heavy radioactive nuclides: praesodymium-140 (^{140}Pr) and promethium-142 (^{142}Pm), both from the lanthanide series of the periodic table. The nuclides, with half-lives of 3 minutes 23 seconds and 40.5 seconds respectively, were produced by smashing stable samarium (^{152}Sm) atoms into a beryllium target at more than two-thirds the speed of light. The violence of this impact strips the samarium atoms not only of almost all of their electrons, but also of several protons and neutrons — knocking off a proton and nine neutrons makes ^{142}Pm, and the loss of three protons and nine neutrons creates ^{140}Pr. With the help of magnets, the isotopes can be selected from others produced. Injected into the ESR, the precise revolution frequency for each individual ion can be obtained, so that the