uplands by onshore winds. This benign contamination has been put to ingenious use by Kirchner *et al.* (page 524 of this issue[2]), who have examined the storage and flushing of solutes in Plynlimon (Fig. 1), a catchment in mid-Wales. Their aim was to use sea-salt chloride to probe the flushing rates of contaminants from rainfall to streams. They convincingly establish that this watershed exhibits a very clear fractal property: that the apparent travel times of unreactive solutes have a broad-tailed (power law) distribution. This means that some dissolved material will take a long time to be flushed out of the watershed. The general inference is that contaminated catchments may remain contaminated longer than we would expect[3].

Rainwater that is not lost through evaporation will eventually find its way to the stream that drains a watershed. But although rain showers or storms are reflected more or less immediately in increased stream discharge, variability in the chemistry of rainfall appears only as very subtle variability in stream chemistry. This has been attributed to the fact that, whereas the pressure of new rainwater (hydraulic head) can induce movement of older water into the stream as an immediate response to rain, the older water exhibits the integrated chemical signal of rainwater received over long periods of time.

Chloride is relatively non-reactive in groundwater, so it can be used as a conservative tracer for waters as it passes from rain to groundwater to the stream. By analysing time series of chloride concentration in rainfall and stream flow, Kirchner *et al.*[2] are therefore able to make some inferences about the time that a tracer takes to work its way through the system. In particular, they can deduce the distribution of apparent travel times of water in the catchment.

A typical simplifying trick in stochastic hydrology is to treat the catchment and its groundwater reservoir as a black box that acts as a simple spectral filter. Rainfall is fed into the system as a time series, and the catchment black box filters this into a time series that simulates stream flow. The same idea can also be applied to stream chemistry if the solute is unreactive.

This useful simplification lies at the heart of the time-series analysis of the Plynlimon study. The input (rainfall) chloride signal to this watershed has an approximately flat spectrum. The output chloride signal has a power-law spectrum, where the spectral energy is inversely proportional to frequency, which is diagnostic of what is technically termed a $1/f$ noise, or fractal signal. The black-box filter therefore appears to convert a flat input spectrum into a fractal output spectrum. This is one of the strong appeals of the Plynlimon case: it is very rare to find good examples in nature of systems which so clearly turn a non-fractal input into a fractal output.

If the fractal filtering property of conservative tracers can be demonstrated in catchments elsewhere, we may need to rethink our basic assumptions about the transit times of water and contaminants in shallow groundwater. A common black-box model assumes a simple, well-mixed reservoir, in which a single spike input of solute leads to an exponentially decaying yield of solute output. The equivalent distribution of travel times in this kind of reservoir has an exponential shape. The flushing of contaminants in such a system is more efficient than in a fractal reservoir — the yield of unreactive solutes is higher immediately after contamination, and diminishes relatively quickly. The inference to be made from the Plynlimon catchment is that something different occurs: a lower initial yield of tracer, and a more sustained yield over many subsequent years.

But the story is not quite as simple as that. A fundamental limitation of the spectral black-box approach is that it does not describe the response of the system to a point injection of contaminant, as would occur for example if a drum of benzene were spilt on a hillside. Nor does it directly describe the flux of contaminant over time during a single contamination episode. Rather, the spectral approach aggregates many such episodes, and assumes a reasonably spatially uniform input of contaminant. So how does the inferred fractal property of the catchment pertain to a single, point injection of contaminant? This remains to be seen.

On the other hand, this work will have wide application, despite its spatial imprecision. It is likely that its main use will be as a kind of baseline constraint for catchment-scale simulations of chemical transport. Modellers of solute flow will need to bear this fractal filtering in mind, regardless of whether the solute is reactive or not. Applications will no doubt emerge in models of the flushing of sulphates from acid rain, transport of dissolved organic carbon and nitrogen, and residence times of helium isotopes (helium-3).

As for radioisotopes such as caesium-137, deposited in catchments following events such as the Chernobyl disaster, the complexities of fractal filtering are perhaps moot: caesium remains essentially fixed in the top few centimetres of the soil, bound to clays and other substrates. Another worry, perhaps, for those mud-soaked hikers in the Welsh hills. ■

Colin P. Stark and Marc Stieglitz are at the Lamont-Doherty Earth Observatory of Columbia University, Palisades, New York 10964, USA.
e-mail: cstark@ldeo.columbia.edu

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Huntington's disease

A predictor of pathology

John C. Rothwell

Like woodworm spreading through a ship's timbers, most slowly progressive diseases begin long before clinical symptoms appear. Although modern techniques can often detect preclinical changes — and, potentially, can identify how and where a disease begins — there is one main problem. Patients rarely complain of being ill before they experience symptoms, so it can be tricky to find a suitable population to test. Reporting in this issue, however, Smith and colleagues have neatly circumvented these difficulties in their study of the genetically inherited movement disorder Huntington's disease (Smith, M. A., Brandt, J. & Shadmehr, R. *Nature* **403,** 544–549; 2000).

Smith *et al.* have identified asymptomatic carriers of the Huntington's disease gene, and predict that these people will develop this movement disorder within the next five to ten years. The authors tested subjects for subtle deficits in the control of skilled arm movements, and, extraordinarily, found changes in their ability to point accurately at targets up to seven years before the predicted onset of clinical symptoms. Given that the pathology so early in the disease is probably

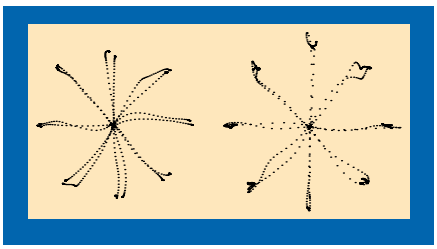

Figure 1 **Examples of arm movements made from a central starting position to eight peripheral targets in a healthy subject (left) and an asymptomatic carrier of the Huntington's disease gene (right). The tracks of two attempts at each movement are superimposed. Smith *et al.* have shown that asymptomatic carriers correct their trajectories much more than normal as they approach the targets, leading to greater jerkiness in the final stages of the movements. This is seen as much as seven years before the predicted onset of the disease.**

limited to a relatively small population of neurons within the basal ganglia (an area of the brain beneath the cerebral cortex that is involved in controlling movement), this observation gives an unexpected insight into the function of these neuronal structures in normal movement.

George Huntington of Pomeroy, Ohio, described his eponymous disease in 1872. The disease usually begins at between 30 and 40 years of age, with symptoms of clumsiness and subtle involuntary movements that gradually become more florid and are accompanied by a slow intellectual decline. It is an autosomal dominant inherited motor disorder, caused by repeated copies of the trinucleotide sequence CAG in the *IT15* gene on the short arm of chromosome 4. Pathologically, the initial neural damage is limited to the medium spiny neurons of the caudate and putamen within the basal ganglia. The pathology later spreads to involve the cerebral cortex and other structures.

In the years before the affected gene was identified, symptoms of the disease often had to be quite severe before a definite diagnosis could be made. At this late stage, it was never clear to what extent the movement disorder reflected the pathology within the basal ganglia or in other structures. Smith *et al.* have now circumvented this problem by studying carriers of the Huntington's disease gene before their symptoms begin.

The authors asked people carrying the affected gene and normal subjects to move a two-jointed object with their arm, from a central position to one of eight targets on a surrounding circle (Fig. 1). When asymptomatic gene carriers carried out the task, the initial trajectory of their arm movements seemed to be relatively normal. But as they approached the target, almost all movements failed to stop efficiently and smoothly. Smith *et al.* quantified how smooth each movement was by calculating the mean squared jerk along its course (jerk is the time derivative of acceleration). They found that the amount of extra jerk in the asymptomatic gene carriers was inversely proportional to the expected time of onset of clinical symptoms, as calculated from the length of the CAG trinucleotide repeat and the age of their parents when the carriers were born. In effect, the smoothness of the terminal error correction could be used to predict the approximate time at which symptoms of disease would begin.

Normal subjects make small corrections to their initial arm trajectories as they approach the target, meaning that jerkiness occurs towards the end of a movement. The authors found that asymptomatic gene carriers seem to have no problem in calculating the initial trajectory of the movement. Instead, these people appear to have trouble implementing the appropriate corrections that are needed towards the end point. So, in a second experiment, Smith and colleagues deliberately perturbed the initial trajectory of the arm movements. Again, the corrective movements of asymptomatic gene carriers were disturbed far more dramatically than expected. This result was quite different from that seen in a separate group of patients with disease of the cerebellum, who also had clumsy movements. When these patients were analysed in the pointing task, the initial trajectory was more irregular than usual but the reaction to the external perturbation was normal.

Because the pathology in asymptomatic carriers of the Huntington's disease gene is probably limited to the basal ganglia, the implication is that these neuronal structures might be involved in implementing error corrections during arm movement. Indeed, Smith *et al.* propose that pathology of the basal ganglia may affect how the cortex processes sensory signals relating to the magnitude of the error. However, as in all studies of chronic disease processes, there is an alternative possibility. The observed movement deficit may not itself be caused by the primary pathology in the basal ganglia. As the disease develops, other parts of the brain may increase their function to compensate. So any deficit might actually reflect a secondary side effect of compensation, rather than being a result of the initial pathology. To decide between the two possibilities we need further evidence in healthy people for activity in the basal ganglia during this type of task.

As the human genome is slowly revealed, the approach of identifying subtle subclinical deficits in asymptomatic gene carriers can be used in more and more neurological diseases. It may allow us to develop simple predictive tests of symptom onset, and to study the physiological effects of pathological processes that are confined to a relatively small part of the central nervous system. But a classic ethical dilemma remains. Until we have a treatment for these diseases — and Huntington's disease, with its relentless downward clinical course, is currently untreatable — we, and the people who participated in this experiment, are no better than the blind prophet Tiresias, who commented: "It is but sorrow to be wise when wisdom profits not". ■

John C. Rothwell is at the MRC HMBU, Institute of Neurology, Queen Square, London WC1N 3BG, UK.
e-mail: j.rothwell@ion.ucl.ac.uk

Molecular dynamics

Optical control of reactions

Stuart A. Rice

Active control of the internal motions of a molecule, by use of a tailored optical field (such as a laser pulse), can be achieved by exploiting a variety of interference effects associated with the quantum mechanics of molecular motion. For example, the population of a specified vibrational state, which may be a precursor to the end-product of a chemical reaction, can be controlled using a timed sequence of laser pulses, as was first suggested 15 years ago[1,2]. The theories behind several other control methods were worked out at about the same time[3–5] and are still being actively developed[6–10].

A few years ago the first experimental confirmations of the proposed control methods began to appear[11,12], and the art of optical control of molecular dynamics is now advancing rapidly[13]. An example of the state of the art in pulse-timing control of molecular dynamics is provided by a report in *Chemical Physics Letters* by Frohnmeyer *et al.*[14], in which they directly map the atomic separation of sodium atoms in a sodium dimer by using intense femtosecond laser pulses.

The fundamental time scale of chemical reactions is set by the internal vibrations of

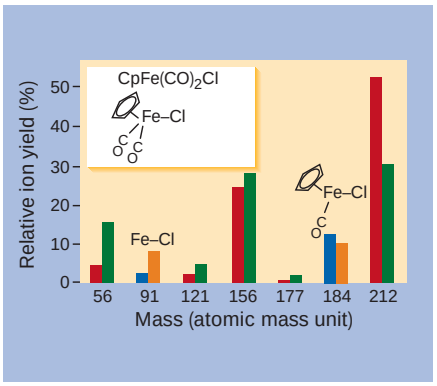

Figure 1 **Selection of bond-breaking in a polyatomic molecule using femtosecond laser pulses. Starting from the parent molecule ($CpFe(CO)_2Cl$), two different bond-breaking reactions are chosen that lead to chemically different final products ($FeCl^+$ and $CpFeCOCl^+$). In the experiment, the ratio of competing products ($CpFeCOCl^+$ / $FeCl^+$) is maximized (blue) or minimized (orange) by an algorithm that sends a feedback signal to control the laser pulses. In each case, the relative yield of $CpFeCOCl^+$ and $FeCl^+$ is significantly different. The abundances of the parent molecule (red) and any other fragments (green) are not included in the feedback signal.**