Jupiter[8], Saturn and Uranus; in molecular clouds[9]; in the diffuse interstellar medium[10]; and possibly even in a supernova and an extragalactic object. The observations by Maillard *et al.*[8] of intense H_3^+ emission in the auroral regions of Jupiter show a spectacularly pure spectrum: all the spectral lines seen are due to the H_3^+ ion and the spectrum is practically free of background radiation[11]. The purity of the spectrum is such that it can be used to study plasma activities in the Jovian ionosphere from ground-based observatories simply by using an infrared camera with a proper filter.

So it seems natural to think of using the same spectrum to detect extra-solar giant planets, and indeed several projects are underway[12]. The detection by Brittain and Rettig of H_3^+ in the protoplanetary disk of HD 141569 is therefore big news. Although HD 141569 is so far away (320 light years) compared with Jupiter (40 light minutes), the dilution of the signal with distance (by a factor of around 10^{-13}) might be compensated for by the larger amount of gaseous H_2 available in a gas-giant protoplanet. (In Jupiter most of the H_2 molecules are locked up in its interior as a high-density metallic fluid, so the planet has a high magnetic field[11].) Nevertheless, questions remain as to how H_2 gas is ionized and how H_3^+ ions are excited to the higher energy state of the emission.

How convincing is Brittain and Rettig's claim to have detected H_3^+ emission? Frequency matching between astronomical and laboratory spectra has been the cornerstone of identifying molecules in space. The discriminative power of high-resolution spectroscopy is so great that the discoveries of important molecules such as H_2O, H_2CO, CO and HC_5N in space were all claimed on the strength of the detection of just one spectral line, and confirmed later by the observation of other lines. In view of this, Brittain and Rettig's observation of two spectral lines (shown in Fig. 2a and Fig. 2b on page 58), at the right frequencies, seems more than sufficient. The latter line is perhaps less convincing, but the authors' subsequent observations have confirmed this line with a higher signal-to-noise ratio (T. Rettig, personal communication).

However, a few enigmas remain. In particular, Brittain and Rettig note that another H_3^+ line is missing from their spectrum. This is in stark contrast to the data from Jupiter, in which that line was observed with an intensity comparable to that of one of the lines that Brittain and Rettig do see. There are also a few other details in the data that I find difficult to explain — more observations are needed to firmly establish H_3^+ emission in HD 141569.

Brittain and Rettig's findings will certainly stimulate interest in the formation of giant planets and H_3^+ spectroscopy. No doubt many of the world's infrared telescopes will be pointed towards HD 141569 and other young stars this year. It will be wonderful to see H_3^+ promoted as an essential probe for the studies of gas-giant protoplanets. ■

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Metabolism

Demand management in cells

Stephen Oliver

Many researchers have tried to increase the flux through metabolic pathways in cells by raising the supply of metabolic enzymes. Little attention has been paid to the demand side of the equation — until now.

Metabolic engineering is a frustrating occupation. The aim is to genetically manipulate a cell — usually a microorganism — so that it overproduces some desired product. The trouble is that it is the business of microbes to produce more microbes, not to divert resources into the wholesale generation of a protein or other metabolite that might be desirable to the metabolic engineer but whose overproduction is of no advantage to the organism itself. So, in trying to increase the flow of intermediates through a metabolic pathway, the metabolic engineer is working against the complex controls of the cell, which act to ensure that this flux remains constant. Writing in *Journal of Bacteriology*, however, Koebmann and colleagues[1] describe how they tricked *Escherichia coli* bacteria into doing what the authors wanted.

Cellular controls on metabolism are subtle and difficult to analyse. Until recently, metabolic engineers have worked on the premise that there is a single rate-determining step in any metabolic pathway. Increasing the flux through a pathway should then be a simple business of increasing the active concentration of the enzyme catalysing that step. This is easy to achieve with recombinant DNA technology. The number of copies of the gene encoding the rate-determining enzyme can be increased — for instance, by cloning onto multiple DNA molecules (plasmids) for insertion into the cell. Alternatively, the expression of the gene can be set to a higher level by cloning it behind a high-efficiency gene-control region. But, while conceptually and technically simple, this strategy seldom works.

The problem is that the concept is wrong. Single enzymatic steps rarely determine the flux through a pathway; instead, control is shared between many of the pathway's

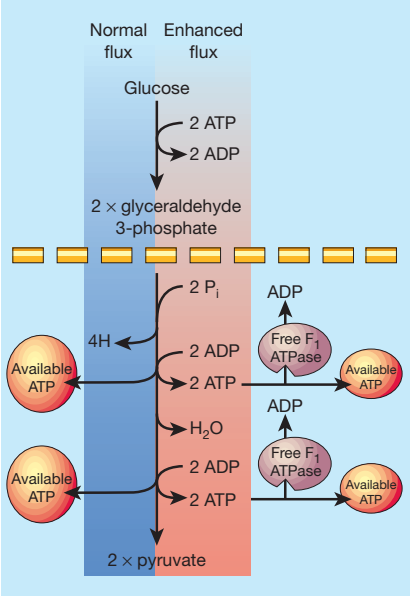

Figure 1 **A simplified view of glycolysis. Above the dashed bar, the pathway consumes two molecules of ATP. Below, it generates four molecules of ATP — making a net gain of two ATP molecules available to supply energy for cellular processes. In the normal *E. coli* strain (left), all of the ATP generated is available to the cell. In the genetically engineered strain described by Koebmann *et al.*[1] (right), some of this ATP is degraded by the free F_1-ATPase enzyme, making less available for use by the cell, but enhancing the flux through the glycolytic pathway.**

enzymes. This is a truth that was first realized by Kacser[2] when he proposed his method of 'metabolic control analysis' nearly 30 years ago. The idea has been gaining adherents (often called 'controlniks') ever since, and started to be noticed by metabolic engineers

when Kacser, Niederberger and colleagues[3] investigated the biosynthesis of the amino acid tryptophan in yeast. They found that a significant increase in flux, leading to the overproduction of tryptophan, required an increase in the copy number of all the genes encoding the necessary enzymes, not just one of them.

Even so, these enzymes were together responsible for only 26% of the control of flux through the pathway. So the manipulation of this pathway in yeast was a successful demonstration of the power of metabolic control analysis, but only a modest increase in the rate of synthesis of the amino acid was achieved. Kacser and colleagues had worked to increase the supply side of the equation. They did not, however, consider the demand for tryptophan — they never measured the flux due to the consumption of the amino acid in protein synthesis. What if, in the management of the cellular economy, it is demand, not supply, that dominates?

Koebmann *et al.*[1] have now tested this idea by looking at glycolysis — the basic pathway that derives useful energy, in the form of adenosine triphosphate (ATP), from the breakdown of glucose in all organisms. As with tryptophan biosynthesis, attempts to manipulate the control of glycolysis have looked at the supply side of the cell's economic equation. Various ways have been tried to speed up glycolysis by increasing the activity of the enzymes that degrade glucose, and they have all failed.

Instead, Koebmann *et al.* decided to increase the demand for ATP in *E. coli*. They achieved this by lowering the concentration of ATP in the bacterium through overproduction of the enzyme F_1-ATPase. This enzyme is normally anchored to the bacterial cell membrane, where its role is to synthesize ATP in the respiratory pathway that follows on from glycolysis. But Koebmann *et al.* engineered *E. coli* to make F_1-ATPase free from its membrane anchor. Now, instead of synthesizing ATP, the enzyme degrades it. From the cell's viewpoint, all of its energy-requiring metabolic reactions seem to have been stepped up — there appears to be an increased demand for ATP. And what the authors found was that the greater the activity of the ATP-degrading enzyme (that is, the higher the cell's demand for ATP), the greater was the flux through glycolysis. The cells also generated more of another end-product of glycolysis — pyruvate (or rather acetate, which is derived directly from it).

Demand management is a model of metabolism that is much loved by one group of controlniks[4], and for which Koebmann *et al.*[1] have now provided compelling experimental evidence. The full story might be a little more complex because, as Fig. 1 shows, the first part of the glycolytic pathway creates its own demand for ATP, and it is unclear how enough ATP is channelled in this direction to sustain the increase in flux. Nevertheless, these results have implications for understanding the control of glycolysis in all organisms. They might enable us to brew beer faster and to generate more alcohol, and might also suggest new treatments for diseases, such as diabetes, in which the control of sugar metabolism goes wrong. Moreover, they could mean that biologists in the twenty-first century need a rethink of their view of cellular economy that is every bit as radical as that initiated for political economy by John Stuart Mill and William Stanley Jevons in the nineteenth century. ■

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Relativity

Special treatment

Giovanni Amelino-Camelia

The detection of cosmic rays with unexpectedly high energies has prompted a rethink of Einstein's theory of special relativity. A new formulation, called 'doubly special relativity', might be the answer.

At the turn of the twentieth century, the theory of space and time that had originated with Galileo and Newton was abandoned — it was incompatible with the mathematical structure of Maxwell's equations for electromagnetism and in conflict with the results of the Michelson–Morley experiments that had disproved the existence of the aether. Galileo–Newton theory was superseded by Einstein's theory of special relativity, but, after a century of success, that too is now being questioned. The observation of ultra-high-energy cosmic rays[1] seems to be in conflict with a key prediction of special relativity, and some approaches to the construction of 'quantum gravity' — a theory that would unite quantum mechanics and general relativity — seem to require[2] the introduction of a new absolute scale in the theory of special relativity. Writing in *Physical Review Letters*, Magueijo and Smolin[3] propose a scheme for the modification of special relativity, in which a new absolute scale sets simultaneously the maximum energy and maximum momentum of fundamental particles.

Special relativity has only one absolute scale: the speed of light is the same for all

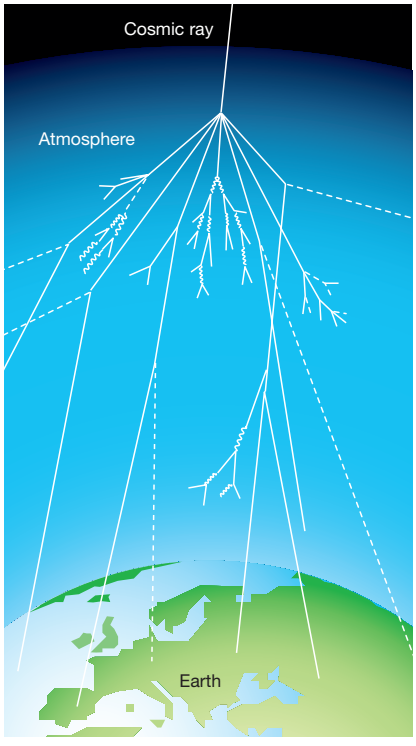

Figure 1 **Cosmic-ray shower. High-energy particles from distant galaxies impinge on the Earth's atmosphere, generating showers of secondary particles, including electrons, protons, muons and neutrinos. By detecting these secondary particles, the energy of the original cosmic ray can be reconstructed — but it seems that some cosmic rays have energies higher than is theoretically allowed[1]. Modifying Einstein's theory of special relativity could account for this anomaly: Magueijo and Smolin[3] present a new theory based on the idea[2] of 'doubly special relativity', in which the Planck energy scale is introduced as a second absolute scale, alongside the speed of light.**