(Fig. 1). Attempts to understand how this system works focused first on trying to find a protein that binds to the SECIS region, on the assumption that such a protein might work in a similar way to the bacterial SelB protein. Nevertheless, despite numerous false alarms, the mammalian counterpart(s) of the bacterial SelB remained elusive. These ‘scarlet pimpernel’ properties can be explained by the discovery that, in mammals, the functions of SelB are divided into two proteins.

One protein, called SBP2 (SECIS-binding protein 2), binds the SECIS element. The binding specificity of this protein depends on a key feature of the SECIS — a quartet of non-Watson–Crick base pairs. But this protein does not have the task of binding to the selenocysteine-carrying tRNA, and it does not have the sequence features that would be expected of a protein that brings tRNAs to the ribosome. The discovery of the mammalian protein that does this — called eEFsec1,2 — was helped by the finding of a specialized elongation factor in Methanococcus jannaschii, a microorganism from the Archaea. This elongation factor from M. jannaschii does not bind to the SECIS element, but does bind to the selenocysteine tRNA.

Tujebajeva et al.1 and Fagegaltier et al.2 have now discovered the mammalian counterpart of this archaeal protein, by searching through databases using the amino acid sequence of the archaeal protein as a starting point. Like its archaeal counterpart, the mammalian protein does not bind the SECIS element but does interact directly with both tRNAs bearing selenocysteine1,2 and SBP2 (ref. 1). So the SECIS element — through a two-protein complex containing SBP2 and eEFsec — can recruit selenocysteine-carrying tRNAs (Fig. 1).

But this protein complex, when bound to the stem-loop structure, is a long way from the UGA codon. How does the distant complex find the waiting ribosome and deliver selenocysteine? This is especially perplexing in the case of a protein called SelP, whose mRNA has between 10 and 17 UGA codons depending on the species3,4, each coding for selenocysteine. For such cases, one could imagine a processive model based on the known proximity of the two ends of an mRNA strand. In this model the SECIS element would deliver the SBP2 complex to a ribosome that is just starting translation. When the ribosome reaches the first UGA codon, the required selenocysteine is already with the ribosome, ready to be inserted into the growing protein. Afterwards, the ribosome-bound tRNA might be able to pick up a second tRNA-bound selenocysteine, and so on. But, if operative, this or other processivity models must have sophisticated aspects that are not yet apparent.

The obvious model, by analogy with the situation in E. coli, is that the protein complex, bound to the tRNA and to the SECIS element, reaches back and delivers the tRNA (plus selenocysteine) directly to the ribosome5 (Fig. 1). But how the loaded SECIS finds the waiting ribosome remains a mystery. With the new proteins identified, one hopes that answers to these questions will not be long in coming. Help will no doubt come from studies of the supramolecular-translation complexes6,7 that may coordinate interactions central to the decoding of genetic text.

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**Following the crowd**

David J. Low

When we are at a major sporting event or travelling on public transport, our safety and comfort depend crucially on our fellow crowd members and on the design and operation of the facility we are in. So it is unnerving to realize that the modelling currently used to design and operate these venues has more in common with the assumption that such a protein might work in a similar way to the bacterial SelB design of water-pipe networks than anything currently used to design and operate the facility we are in. Such a processive model indicates how quickly the crowd will move. However, this traditional approach assumes that the crowd is made up of identi-
news and views

cal, unthinking elements. A fluid particle cannot experience fear or pain, cannot have a preferred direction of motion, cannot make decisions, and cannot stumble or fall. The diverse behaviour of individual crowd members can drastically change the way in which the crowd as a whole behaves. Injuries to crowd members are related less to average pressure within the crowd than to point pressures at individual localities, and an injured pedestrian can fall and become an obstacle to the movement of others.

The new approach requires a recognition that the crowd is made up of individuals who possess the ability to think and react to events around them. One of the most dramatic cases in which human behaviour influences events is in a panic situation. Helbing et al. address this particular problem with a computer model of pedestrian behaviour that includes realistic reactions to crushing, panic and reduced visibility. They also simulate the tendency of people to do what others do and ‘follow the crowd’, but also allow for individuals to adopt personal strategies. Helbing et al. demonstrate that, because of their increased speed, panicking individuals will block up an exit that they could pass through safely at normal walking speed. They also show that a widening in a corridor actually slows down the movement of pedestrians, rather than allowing them to move faster, as one would assume. This surprising result is explained by those pedestrians who might have tried to move away from or overtake each other having to squeeze back into the mainstream flow at the end of the widening.

Modelling a crowd composed of discrete individuals rather than a continuous fluid clearly brings added complications. Helbing et al. model ‘non-fluid’ crowd properties, such as the ‘faster-is-slower’ phenomenon in which people in a rush end up going slower. They also investigate the best evacuation strategy for people in a smoke-filled room (Fig. 1). Such information can then be used to work out low-risk designs for the width of corridors, the number and position of doors, and the size of areas where people may gather. But these types of study can also provide us with a wider range of possible solutions to crowd problems. The crowd composed of individual people can respond to information directed towards them, to help them choose the most appropriate direction to take or the most appropriate exit to use.

In the past, one of the main barriers to adopting this approach was the enormous number of calculations that are required to solve separate equations of motion for each crowd member. Modern computing power has dramatically changed that situation. Indeed, individual-centred approaches are now widely used in the modelling of road traffic networks15, which also used to be dominated by fluid-flow models. Similar individual-centred traffic models6 have produced excellent results and have led to effective new traffic management strategies. There has been extremely strong financial motivation to produce such improved traffic models. Traffic management strategies and road-building projects cost enormous sums of money, as do the delays caused by road congestion, and improved traffic modelling techniques can produce considerable savings. But the potential benefit of improved pedestrian models is even more valuable — a reduction in personal injury.

The model presented by Helbing et al. is just one of many possible models. To decide whether a particular model is an accurate description of real life, or to determine which model is the ‘best’ for the situation under consideration, requires real data to compare with each model’s predictions. But such data are scarce or non-existent and may be extremely difficult to collect. With any type of mathematical modelling we always have to be careful to distinguish between ‘real life’ and our attempt to model it. Failing to recognize this difference can have serious consequences. But provided we are aware of when it is appropriate to use a particular model, it can provide valuable information to guide the planning process, for construction and for dealing with emergencies. Perhaps perfect safety is unattainable, but improved models of crowd dynamics can help to increase our safety in crowded situations.

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References


Genomics

Use your neighbour’s genes

Don Cowan

On page 508 of this issue, Ruepp and colleagues describe the complete genome sequence of the acid- and heat-loving microorganism Thermoplasma acidophilum. This hardy organism, which lacks a cell wall, grows best on organic substrates at pH 2 and 59 °C. It was first isolated, in the late 1960s, from a self-heating ore pile2; such ore piles generate heat through internal microbial activity.

Microbial physiologists and structural biologists have long been fascinated by the ability of this microorganism to grow at high temperatures and low pH without the structural protection of a conventional cell wall. T. acidophilum is also interesting from an evolutionary perspective. Its cellular morphology seems primitive, and it contains complexes involved in protein folding, degradation and turnover that look like simple versions of related structures in eukaryotic cells (loosely, those cells with a nucleus — the type of cell that makes up higher organisms such as you and me). These facts intrigue evolutionary biologists, who have speculated that T. acidophilum is an ancestor of the eukaryotic cell.

Initially, T. acidophilum was classified as a thermophilic mycoplast — a heat-loving example of a group of primitive, gliding bacteria, which lack cell walls3. But following analysis of its lipid composition and ribosomal RNA sequences, it was reassigned to the new ‘third domain of life’ — the Archaea’ (Fig. 1). T. acidophilum is the ninth member of the Archaea for which the genome has been completely sequenced1–10. All except one of these microorganisms are heat-loving. Why is there this focus on the thermoacetococcus? Methanopyrus thermoacetococcus and the other microorganisms in the new ‘third domain of life’ — the Archaea’ (Fig. 1). T. acidophilum is the ninth member of the Archaea for which the genome has been completely sequenced1–10. All except one of these microorganisms are heat-loving. Why is there this focus on the...