NEWS AND COMMENTARY

Genome evolution
. . . .

Micro(be)-economics

JAG Ranea

. . . .

The recent sequencing of the genomes of two of the most abundant (comprising up to 25% of their local populations) pelagic bacteria, *Pelagibacter ubique* and *Prochlorococcus marinus*, have revealed that they have two of the smallest genomes of any known free-living bacteria (Dufresne *et al*, 2005; Giovannoni *et al*, 2005). In general, bacterial genomes are under strong positive selection for economy of size: typified by the almost total absence of nonfunctional DNA, around 85–90% of their genomes being dedicated to encoding proteins. These two newly described genomes appear to have undergone strong purifying selection for a small genomic size. This discovery demonstrates that the drive towards reduction, as with other complex biological processes, can be caused by entirely opposing environmental circumstances. It can derive from the relaxation of selection in small populations of subsidised host-dependent bacteria (Mira *et al*, 2001), or from intense competition among the most abundant marine bacteria. They also provide some valuable insights into what conditions are necessary to allow genome reduction.

P. marinus and *P. ubique* occupy very different environmental niches and are phylogenetically very distant – the former being a photosynthetic Cyanobacteria and the latter a heterotrophic Proteobacterium. This leads us to discard the notion that the loss of a specific gene complement is the common feature shared by the two genome reduction processes. Rather, what these studies indicate is that there is strong selection for the economical use of DNA in highly competitive populations. DNA reduction can directly provide five inherent economic advantages (Cavalier-Smith, 2005): reducing nutrient use, particularly phosphate, which is scarce in the biosphere; reduction of energy consumed in replicating and maintaining the DNA; creating spare space for other cellular components; reducing the cell's susceptibility to lethal or disadvantageous mutations; and reducing the time needed to duplicate the cell. These two genomes have provided some remarkable insights into how much each of these factors influence genome reduction.

P. ubique, in particular, takes the deletion of nonfunctional DNA to the extreme, with a median intergenic space of three bases and a complete absence of pseudogenes or phage genes. Its genetic redundancy is almost completely zero with no detectable recent gene duplications and the lowest proportion of paralogous genes (belonging to the same gene family) observed among free-living organisms. This extreme genome reduction process drove *P. ubique* to have a genome of just 1.3 megabases (Mb), the smallest known for any free-living bacteria. The *P. marinus* genome exhibits similar features and almost all its genes are single copies in a tightly packed genome of 1.7 Mb. As a comparison, free-living *Escherichia coli* have genomes of around 4.5–5.5 Mb.

A genomic feature shared by these bacteria with the endosymbiotes is a low G:C to A:T ratio. However, in *P. ubique*, it is likely that the poor oceanic environment drives this ratio; adenine and thymine DNA bases require less nitrogen in their synthesis. *P. ubique* contains genes coding a broad variety of transporters specific for nitrogenous compounds, and two out of the four two-component regulatory systems found in this bacteria are dedicated to controlling responses to nitrogen and phosphate limitations.

In addition to the significant savings in nutrients, energy and space released by genome reduction in these species, reducing the number of potentially deleterious mutations per cell division also seems to be of significant benefit. The amino-acid substitution rate for protein-coding genes in *P. marinus* indicates that genome reduction has been accompanied by an increased rate of protein evolution for all functional categories.

Somewhat surprisingly, genome reduction has apparently not led to a faster duplication time in *P. ubique*, which shows slower growth rates (0.40–0.58 cell divisions per day) than many other heterotrophic bacteria with larger genomes. So, contrary to what is often assumed, DNA replication speed does not seem to constitute a bottleneck in the whole reproduction process of this species; rather, its strategic priorities seem to lie with reducing energy and nutrient use.

Genome reduction explains an important proportion of a cell's economic savings. However, the current formulation of this streamlining theory has the problem of being highly focussed on DNA metabolism and replication, perhaps due to the ease of DNA sequencing in comparison to other forms of investigation. For future advances in this field it could be necessary to extend our vision beyond the genome. For example, the protein biosynthesis machinery alone comprises about half of the dry weight of a bacterial cell and consumes up to 80% of all cellular energy. Clearly, any improvement in protein synthesis efficiency could produce significant economies and competitive advantages.

Adoption of biological network concepts could help further genome size research. In bacteria, genome length is a direct indicator of how many different pieces make up the cell and hence how complex the cell is. In any integrated system, as the bacterial cell is, increasing its complexity is not free of cost; the more complex a cell becomes the more difficult it is to regulate (Bird, 1995). We can consider bacterial genes to form the nodes of an *accelerating network* (Mattick and Gagen, 2005). In this type of network, connectivity increases quadratically as the network grows, since each new node must be integrated with all the previous nodes. In genetic terms, this means that for each new gene the regulatory burden increases at a faster than linear rate. Indeed, we can hold this statement to be true in reverse: a linear reduction in metabolic genes leads to a greater than linear reduction in regulatory genes (Ranea *et al*, 2005), although with a corresponding decrease in metabolic diversity.

This implies that extreme genome reduction will mostly take place in environments where the bacteria are able to draw on stable resource types – for example, dissolved organic carbon (DOC) in oceans or the nutrient stores of a host cell. This type of environment also allows the stable expression of metabolic genes, further reducing the regulatory burden. This effect can be seen in *P. ubique*, which shows a constant growth rate when exposed to pulses of higher nutrient concentrations; other heterotrophic marine bacteria

with larger genomes vary their duplication rate in response to nutrient availability.

Selection for economy is a universal principle that applies equally to bacteria and eukaryotes. The efficient use of nutrients, energy, space and time, in order to maximise the production of progeny cells from limited resources affects all organisms. These new genomic studies on some of the smallest oceanic bacteria have given us some of our greatest insights into the governing rules of bioeconomic evolution.

JAG Ranea is at the Biomolecular Structure and Modelling Group, Department of Biochemistry and Molecular Biology, University College London, London WC1E 6BT, UK.

E-mail: ranea@biochemistry.ucl.ac.uk

Bird AP (1995). *Trends Genet* **11**: 94–100.
Cavalier-Smith T (2005). *Ann Bot (London)* **95**: 147–175.
Dufresne A, Garczarek L, Partensky F (2005). *Genome Biol* **6**: R14.
Giovannoni SJ *et al* (2005). *Science* **309**: 1242–1245.
Mattick JS, Gagen MJ (2005). *Science* **307**: 856–858.
Mira A, Ochman H, Moran NA (2001). *Trends Genet* **17**: 589–596.
Ranea JA, Grant A, Thornton JM, Orengo CA (2005). *Trends Genet* **21**: 21–25.