

Minimal genome should be twice the size, study shows

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The simplest bacteria need almost twice as many genes to survive than scientists first believed, according to new research published in *Nature* (30 March 2006). Bacteria are some of the simplest forms of life and have been studied by scientists trying to identify the smallest collection of genes – or minimal genome – that is needed for maintaining life.

Traditionally scientists have done this by removing, or ‘knocking out’, a series of individual genes from a bacterial genome to see what effect this has on its ability to survive.

They can then infer which genes are essential to the organism, and which are not, to work out which are needed for the minimal genome.

However this knock out approach wrongly removes many of the genes that are essential to the survival of bacteria, according to researchers from Heidelberg (Germany), Manchester (UK), Budapest (Hungary) and Bath (UK).

The researchers made this discovery after developing a new approach to genome modelling which, given the organism’s evolutionary history and knowledge of its surrounding environment, allows them to predict which genes a bacterium’s genome should contain.

“Previous attempts to work out the minimal genome have relied on deleting individual genes in order to infer which genes are essential for maintaining life,” said Professor Laurence Hurst from the Department of

Biology and Biochemistry at the University of Bath.

“This knock out approach misses the fact that there are alternative genetic routes, or pathways, to the production of the same cellular product.

“When you knock out one gene, the genome can compensate by using an alternative gene.

“But when you repeat the knock out experiment by deleting the alternative, the genome can revert to the original gene instead.

“Using the knock-out approach you could infer that both genes are expendable from the genome because there appears to be no deleterious effect in both experiments.

“In fact, because there are alternative pathways to the same product, by removing either of the genes you make the other essential for survival; each gene deletion reduces the available space for further reduction of the genome.

”Including these alternative pathways into the minimal genome almost doubles its size.”

The researchers have developed a way of predicting bacterial genome content using two bacteria that have evolved from E.coli.

Buchnera and Wigglesworthia live inside insects in a symbiotic relationship where they provide essential molecules for their hosts in return for essential basic foods.

Since evolving from E.coli, the Buchnera and Wigglesworthia genomes have lost some of the genes that they would otherwise need for survival.

Using computer modelling and knowledge of the present day ecology of the bacteria the researchers were able to model this process of gene loss.

They accurately predicted about 80 per cent of the gene content of the two bacteria, including some of the non-obvious features of their genomes.

“Far from being a cause for disease, the insects need these bacteria to supply them with essential nutrients,” said Professor Hurst.

“In these relatively cosy conditions, *Buchnera* and *Wigglesworthia* have lost some of the genes they would otherwise need to produce some of the basic molecules they need to survive.

“Being able to predict the content of a genome based on the ecology of an organism is useful because we could potentially use it to predict gene content at different stages of an organism’s evolution.

“This will help us understand more about how the genome of different organisms have evolved over long periods of time and should also inform attempts by experimentalists to construct minimal genomes by gradual evolution in the laboratory.”

Similar methods might also be used to build a blueprint of a bacterium with desired metabolic properties, for example identifying which genes would a bacterium need to efficiently digest specific waste chemicals.

The research has been supported by the Hungarian Scientific Research Fund, EMBO, the Human Frontier Science Program, DFG and the Biotechnology and Biological Sciences Research Council.

'Chance and necessity in the evolution of minimal metabolic networks' will be published in *Nature* on 30 March 2006.

Source: University of Bath

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