GENETICS: The Bacterial World Gets Smaller

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GENETICS

The Bacterial World Gets Smaller

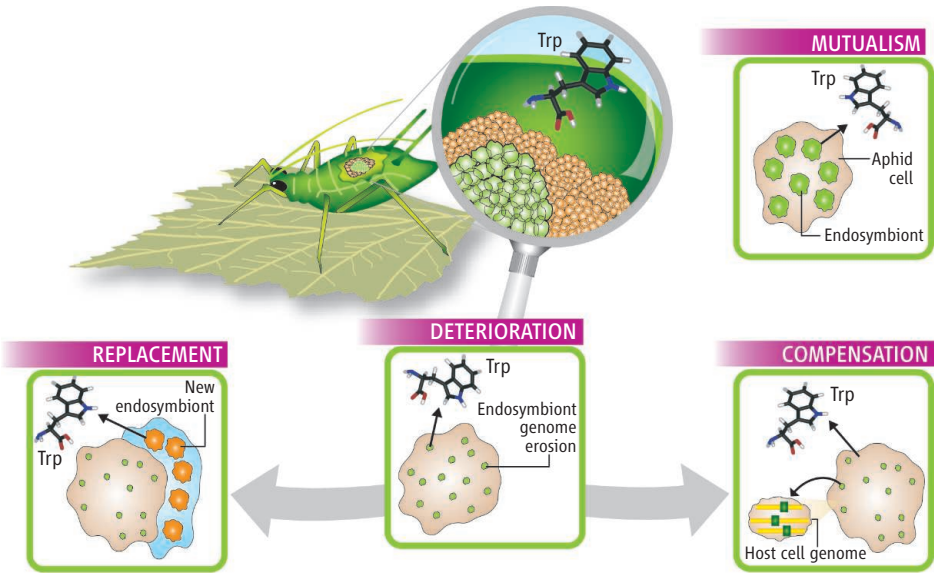
Bacterial symbionts with miniscule genomes can survive by relying on gene expression by host cells or other symbionts. This system may mimic the process of organelle genome evolution.

Siv G. E. Andersson

The race to find the smallest microbial genome has taken an amazing turn. On page 312 of this issue, Pérez-Brocal *et al*. (*1*) report the ~422-kb genome of an aphid endosymbiont, *Buchnera aphidicola*. Even smaller is the ~160-kb genome of a psyllid endosymbiont, *Carsonella ruddii*, reported by Nakabachi *et al.* on page 267 (*2*). These two bacterial genomes are the smallest sequenced to date. In addition to satisfying our desire to crown world-record holders, the genomes tickle our curiosity by approaching the sizes of terrestrial plant mitochondrial (<600 kb) and chloroplast (<220 kb) genomes.

Symbiotic relationships are widespread among invertebrates, including medically and agriculturally important pests. An estimated 10% of insect species house "farms" of bacterial endosymbionts that provide nutrients such as cofactors, amino acids, or other essential compounds that the host insects cannot obtain from their diet (*3*). The best-studied example is *B. aphidicola*. This bacterium, which produces all the essential amino acids except tryptophan, resides within a specialized group of aphid cells (see the figure). *B. aphidicola* has been directly inherited from insect mother to offspring for a few hundred million years. During the evolution of this host-symbiont relationship, approximately 75% of the ancestral *B. aphidicola* genome has been eliminated, resulting in genomes that are currently 600 to 700 kb in size (*4*–*6*). This small genome size is indicative of a closed ecosystem in which a bacterial genome encodes the near-minimal set of genes required for bacterial growth (*7*). Indeed, ~88% of the endosymbiont enzymes can be predicted by computer network analysis of minimal reaction sets stimulated under endosymbiont growth conditions (*8*).

Not only are these two bacterial genomes among the smallest, they are also among the most stable, with no acquisition of external DNA, no repeated sequences greater than 25 bp, and no chromosome rearrangements over the past 50 to 100 million years (*5*). This would represent a biological system of heavenly bliss, were it not for the slow erosion of endosymbiont genomes. This deterioration accounts for an estimated loss of about one gene per 5 to 10 million years (*5*). This is as expected from Muller's ratchet (*9*), which proposes that deleterious mutations accumulate in small asexual populations with no incorporation of new genes. In effect, such organisms may decrease in fitness over time until they become extinct. It is debated whether sequence erosion will eventually come to a halt, or whether endosymbiont genomes will continue to deteriorate, causing the demise of these microbes and the collapse of their hosts.



Endosymbiont evolution. Many insects contain bacterial endosymbionts (green) that produce essential compounds, such as tryptophan (Trp), for the host (mutualism). As the endosymbiont's genome diminishes (deterioration), lost gene functions can be rescued (replacement) by the gain of a secondary endosymbiont (orange). Alternatively, endosymbiont genes can be transferred to the host nuclear genome (compensation).

The two genomes presented in this issue have surpassed the previous lower limit for sequenced genomes of *B. aphidicola*, which range in size from 615 to 641 kb. The genome of *B. aphidicola* from the aphid *Cinara cedri* (the *B. aphidicola* strain BCc) consists of a ~416-kb chromosome with 362 protein-coding genes and a 6-kb circular plasmid (*1*). The ~160-kb chromosome of *C. ruddii* encodes no more than 182 proteins (*2*). Absent from both organisms are genes encoding most membrane and transport functions, a finding indicative of freely diffusible systems with a passive exchange of metabolites. Surprisingly, no genes for the biosynthesis of tryptophan were identified in the BCc genome, although it has been shown experimentally that the aphid host is dependent on the bacterial provision of tryptophan (*10*). Intuitively, we would expect such extensive gene loss in an endosymbiont genome to be lethal for the insect.

Pérez-Brocal *et al.* suggest a possible way out of this conundrum—replacement of the BCc strain with a secondary endosymbiont to supply tryptophan. Indeed, it has been shown experimentally that it is possible to force secondary symbionts to take over the functions of primary endosymbionts if infected into aphids that have been cured of their primary endosymbionts (*11*). This offers a solution to the dreaded "collapse" scenario; although the ancestral endosymbiont may become extinct, the aphid population will be saved by fresh endosymbionts that gradually replace the deteriorating ones. This is consistent with mathematical modeling, which predicts that strong host-level selection will usually protect the endosymbiont genomes from extinction, but that deleterious mutations will rapidly proceed through the process of Muller's ratchet if host fitness is preserved by compensatory changes elsewhere (*12*).

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Nakabachi *et al.* suggest a different scenario to explain the loss of genes in the *C. ruddii* genome—the transfer of endosymbiont genes to the host nuclear genome for expression. Parallels can be drawn to organelles such as mitochondria in that most genes encoding mitochondrial proteins are located in the cell's nuclear genome. Some of the genes may have been transferred from an ancestral endosymbiont, whereas others represent modified cytosolic cellular proteins recruited for service in the mitochondrion (*13*). Deterioration and gene loss are evident in both organelle and endosymbiont genomes despite strong host-level selection. This is because the balance between the two opposing forces—deleterious mutations and host-level selection—shifts toward mutational erosion when the destroyed functions are compensated by genes from other endosymbionts or by a cell's nuclear genes.

The endosymbionts of insects are an excellent model system to test theoretical predictions about the evolution of genome size in small, nonrecombining bacterial populations. As we continue to study these systems, we are likely to discover even more extreme examples of miniscule bacterial genomes. A stronger focus is needed on the compensatory changes that have taken place in the secondary endosymbionts and the nuclear genomes of the hosts. The results will provide hints about the processes shaping the development of organelles and the various routes taken to minimal gene-sets in nature. Potential applications include new weapons in the fight to eliminate agricultural pests and vector-borne diseases. However, for the smallest of small endosymbionts (*1*, *2*), the future seems gloomy. It is a dead end from which there is no escape.

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APPLIED PHYSICS

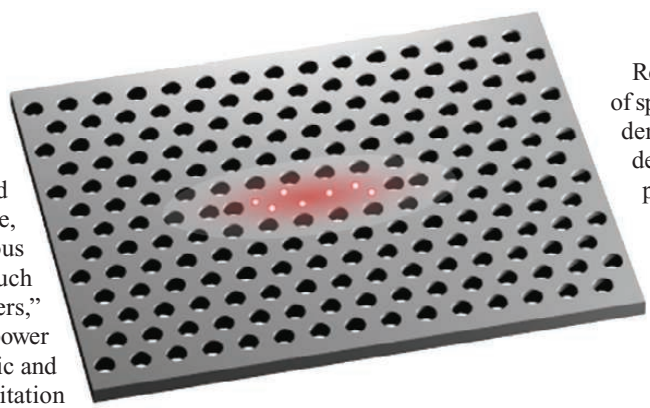
Seeking the Ultimate Nanolaser

Combining photonic nanostructures with quantum dots may lead to semiconductor lasers having much higher efficiency and performance.

Susumu Noda

Semiconductor lasers generally emit a large amount of undesired spontaneous emission before starting lasing oscillation, which degrades their efficiency and performance substantially. Therefore, lasers that emit almost no spontaneous emission have long been sought. Such devices are called "thresholdless lasers," where light output versus excitation power has no obvious threshold characteristic and lasing occurs at extremely low excitation powers. These lasers should have the maximum allowable performance and thus be very useful for optical applications. One promising approach has been to construct lasers with a nanocavity in a photonic crystal, in which the optical properties are structurally designed rather than intrinsic to the material. The photonic crystals and nanocavities can then be tailored to control spontaneous emission to achieve thresholdless operation. Recent progress in the engineering of photonic crystal nanocavities and their combination with quantum dots has accelerated this effort (*1*–*4*).

Several key issues (*5*) must be addressed before thresholdless lasers can be realized. The threshold behavior of semiconductor lasers arises from spontaneous emission coupled to the many optical modes inherent to the laser cavity. Only one of these can be the lasing mode. The undesired spontaneous emission into other modes dissipates the excited carriers in the semiconductor and, consequently, the laser efficiency is degraded. Before the ultimate laser can be realized, the following issues must be addressed: (i) Optical modes that induce undesired spontaneous emission should be suppressed where possible; (ii) a single-cavity mode with a sufficiently high Q factor (the so-called quality factor of the cavity) and a small modal volume is essential; and (iii) excited carriers should be concentrated to emit light coupled to the single-cavity mode.



Connecting the dots. A high-Q nanocavity (red) is formed in a 2D photonic-crystal slab that inhibits spontaneous emission. Quantum dots embedded in the nanocavity confine electrons (and holes) three-dimensionally and have sharp gain functions. Such a configuration may allow thresholdless laser operation.

Regarding the issue (i), the suppression of spontaneous emission has recently been demonstrated (*2*, *3*). Progress in the development of two-dimensional (2D) photonic-crystal slabs (see the figure) has been integral to this achievement. The 2D slab structure facilitates a quasi–three-dimensional (3D) confinement of photons as a result of the large refractive-index contrast perpendicular to the slab. Although spontaneous emission from light emitters inside the 2D slab structure can be coupled to confined or leaky optical modes, it is possible to couple ~94% of the spontaneous emission to the confined mode. Therefore, the use of a 2D photonic-bandgap structure can inhibit ~94% of the spontaneous emission (*3*). Recent experiments have suppressed the spontaneous-emission rate of this system by roughly the theoretical limit (~15 times) (*6*).

As for the fabrication of appropriate cavity modes, a single mode can be introduced by forming an artificial defect in a 2D photonic-crystal slab (see the figure) (*1*). The modal volume (V) of this defect (nanocavity) can be on the order of a cubic wavelength. When the Q factor of the cavity is sufficiently large, the emission coupled to the single-cavity mode can be substantially enhanced by a factor of Q/V, which is called the Purcell

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