Bacterial genetics

A unicorn in the garden

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In 1943, Salvador Luria and Max Delbrück demonstrated (*Genetics* **28**, 491–511) that a strongly selective environment alters the genetic composition of a bacterial population by allowing the growth only of adapted mutants pre-existing in the population. Their experiment gave no support to the view that cells can mutate adaptively in response to a selective agent. Luria's and Delbrück's demonstration that bacterial evolution proceeds by natural selection of pre-existing mutants legitimized the genetics of these microorganisms. On page 142 of this issue, John Cairns, Julie Overbaugh and Stephan Miller challenge these credentials. They offer evidence that individual bacteria can, indeed, mutate adaptively in response to a selective agent.

Cairns *et al.* point out that Luria and Delbrück were unfair: they did not let *Escherichia coli* show us what it could do if given a decent chance. As a selective agent, Luria and Delbrück used bacteriophage T1, which instantly kills sensitive cells. By contrast, Cairns *et al.* challenge *E. coli* with an environment that simply fails to support the proliferation of the standard type in the culture, but does support growth of the mutant type. In the first of several examples, the standard type is a strain unable to use lactose as an energy source because of a chain-terminating codon in the structural gene for β-galactosidase.

Following the protocol of Luria and Delbrück, Cairns *et al.* grew parallel cultures of standard-type cells in the absence of the selective agent, lactose. They then plated the entire contents of each culture tube onto petri dishes in which the agar contains lactose as sole energy source. Mutation from Lac^- to Lac^+ was required for any given cell to give rise to a colony. If the Lac^+ mutants arose solely during growth in the culture tubes, lacking lactose, the plate-to-plate distribution of colonies would be clonal — mutations occurring in various generations in the different culture tubes would give rise to mutant clones containing widely divergent numbers of Lac^+ cells. On the other hand, colonies arising as a result of mutations to Lac^+ occurring after the cells were plated would be randomly distributed among the petri plates.

In the event, Cairns *et al.* report composite distributions, part clonal part random, indicating the occurrence of both classes of mutation to Lac^+. By various strategies, they then direct attention to the mutations that occur on the plates. They show that these mutations to Lac^+ happen only if lactose is present on the plates. Mutations to other phenotypes, which confer no selective advantage, do not occur. Additional experiments further the iconoclastic view that bacteria have mechanisms for making just those mutations that adapt the cell to an available energy source.

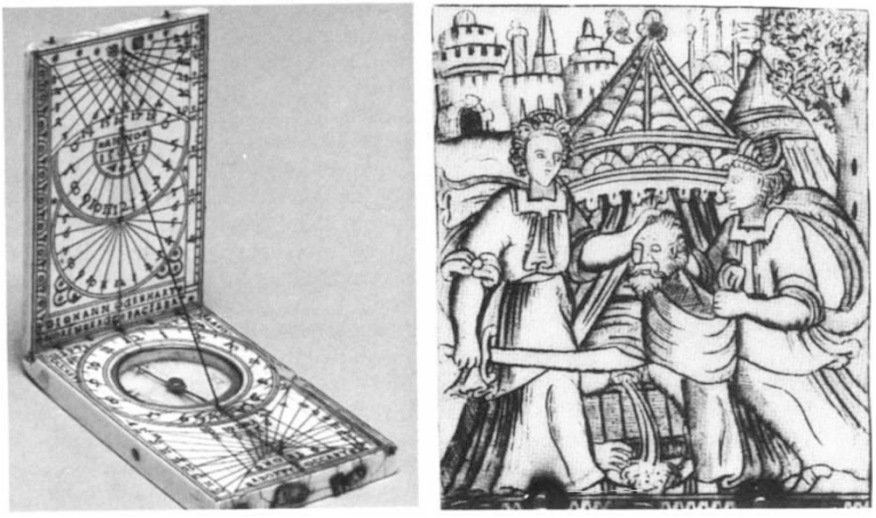
What's up? Can bacteria really direct their mutational processes? Did bacteria discover 'directed mutagenesis' before the genetic engineers did? Cairns *et al.* appear to eschew such an idea. (However, when I read ". . . bacteria are in the presence of lactose and under strong selection pressure *to become* Lac^+" (my italics), I wonder whether they may feel a bit drawn to the notion.)

More attractive, the authors suggest, is some sort of trial-and-error mechanism that allows the selection of serendipitous molecular misconceptions that have an adaptive phenotype, with the selection operating at the molecular level rather than at the level of the cell. How might we seek the mutable intracellular entities upon which selection can act to adapt an individual cell? Cairns *et al.* clearly indicate the sorts of models that might be considered. Readers will find it good exercise to try to build more highly specified schemes. Top marks will go to those who can build their model solely from familiar elements.

Here's one: my proposal is based on the post-Luria–Delbrück demonstration that mutation proceeds through a reversible intermediate. Polymerase-catalysed DNA synthesis has a mistake rate that is thousands of times higher than the observed mutation rate of freely growing cells. The fidelity normally observed is achieved by the action of post-replicative mismatch-correction enzymes. These enzymes remove stretches of newly synthesized chains whose sequences fail to be fully complementary to the templates on which they were made. To a good approximation, we can say that mutations result only when these correction systems fail.

I imagine that the Lac^- cells on lactose medium, starved by their inability to use the lactose, maintain some metabolism by cannibalizing macromolecules for energy

Exhibition of ivory-pocket sundials



In the sixteenth century, Nuremberg in south Germany became one of the most important centres in Europe for manufacturing ornamental goods and scientific instruments. This conjunction is strikingly illustrated by the numerous ivory pocket sundials produced by specialist craftsmen. Sixty of these beautiful objects can be seen in an exhibition at the Whipple Museum of the History of Science in Cambridge, UK, until 9 December 1988. Some of the sundials are small and merely functional but many are decorative objects that were proudly displayed by their owners. They tell the time by several systems, most of which were already obsolete when the dials were made, and provide astronomical and calendrical data of little practical use. Some carry extravagant tables of latitudes, used to adjust the dial for the various places the owner might imagine finding himself. A book and catalogue by Penelope Gouk explain in detail how the dials work and reconstruct their origins in the Nuremberg community of astronomers and craftsmen. The exhibition is open on Mondays to Fridays, and on Sundays during October, from 2–4 p.m. Left, a sundial by Johann Gebhart, made in 1561; right, detail from a sundial by Paul Reinmann, dated 1599, showing Judith beheading the Assyrian commander Holophernes. □