In Retrospect

A spotlight on bacterial mutations for 75 years

In the debate about how bacterial mutations arise, an experiment in 1943 showed that they can occur spontaneously and independently of a selection pressure. This study also popularized the use of maths–driven analysis of biological data.

MANOSHI S. DATTA & ROY KISHONY

D o bacteria acquire mutations randomly, or do mutations arise adaptively as a direct response to environmental pressures? This question has wide implications in areas ranging from evolution to the treatment of bacterial infections. In 1943, writing in *Genetics*, Luria and Delbrück[1] revealed, by a combination of experimental analysis and profound mathematical insight, that bacteria evolve through random mutations that arise independently of an environmental stress, and that occur even before bacteria encounter such selective conditions. Their study was a milestone in a debate about the nature and causes of bacterial evolution that is still ongoing. Moreover, this work has inspired the fields of microbial evolution and quantitative biology.

Luria and Delbrück worked at a time when scientists disagreed on the fundamental nature of bacterial evolution[2], despite tremendous advances in molecular biology and microbiology. For plants and animals, there was a general consensus that, consistent with Charles Darwin's theory of evolution, natural selection acted on mutations that arose randomly, regardless of their benefit to the organism. However, the unusual nature of bacterial genetics — such as the absence of sexual reproduction — sparked a vigorous debate about whether the principles that drive animal evolution also apply to bacteria (see go.nature. com/2brojqp). The main alternative hypothesis was Lamarckian evolution, named after the French biologist Jean-Baptiste Lamarck. In this model, the specific mutations that provide an advantage to an organism are acquired directly in response to the organism's environment[3].

For present-day microbiologists, this debate might seem strangely contrived — after all, if other organisms evolve in a manner consistent with the Darwinian principles of randomly occurring organismal variation that selection can act on, why should bacteria be an exception? Yet, it's worth having sympathy for our scientific predecessors. Even though we now accept that bacteria evolve through Darwinian mechanisms, 'quasi-Lamarckian' processes of bacterial evolution are still being discovered and debated[4–6].

Luria and Delbrück themselves encountered some difficulties when they entered the debate about how bacterial evolution occurs. To establish an approach to study mutations in bacteria, they allowed individual *Escherichia coli* cells to grow into large populations in individual test tubes, and added the cells from each of these tubes to Petri dishes containing agar coated with viruses known to kill the bacteria. Luria and Delbrück monitored the number of visible bacterial colonies on each of the plates. Each of these virus-resistant colonies arises from a cell and its descendants that had a mutation enabling the cells to survive the viral attack. Yet, for a simple experiment, their results were initially confusing: the number of colonies was highly variable between the different plates, a result that the authors initially attributed to an experimental error (see go.nature.com/2brojqp). But in a moment of clarity, Luria realized[7] that the high variability in the number of bacterial colonies might be an important clue, not an error.

Let's consider the experimental variance in the number of virus-resistant colonies per Petri dish expected under the process of either adaptive or random mutation. If mutations arise by an adaptive process, each bacterial cell would have a chance of acquiring a resistance mutation only on encountering the virus. Assuming each cell's chance of becoming resistant is small, the prediction would be that the number of virus-resistant colonies per Petri dish would vary according to a Poisson distribution (a standard probability distribution for random events, in which the standard deviation of the data equals the square root of the mean).

But, if evolution is driven by random mutations, mutations that confer viral resistance would arise during the growth of the bacterial population before viral exposure. In this case, the experimental variance in the number of virus-resistant bacterial colonies between different Petri dishes would be much higher than in the adaptive-mutation scenario, because the number of virus-resistant bacteria in a given test tube would depend on the random timing of when mutations occurred. A single virus-resistance mutation that occurred early in the growth of the bacterial population would result in a large number of virus-resistant bacterial descendants of the original mutated cell, whereas mutations that arose much later during the growth of the bacterial culture, just

50 Years Ago

After the wreck of the Torrey Canyon in March 1967, some 8,000 seabirds were taken to cleansing stations in Britain — but well under ten per cent … of these birds were rehabilitated and returned to the sea. Even this figure gives too optimistic a picture of the cleansing operation, for a large proportion of the so-called rehabilitated birds were recovered dead within a few days. Although exact figures are hard to come by, the Torrey Canyon episode revealed the complete inadequacy of the current methods of rehabilitating oiled birds … Legislation can never totally eliminate accidental pollution and it is estimated that even the much vaunted "load on top" system of washing tankers, although a great improvement on previous practice, produces pollution at a rate of 400,000 tons a year.
From *Nature* 30 November 1968

100 Years Ago

[U]ndoubtedly the war has been responsible for an enormous amount of destruction of capital; but when estimates are given … of the percentage of loss in Belgium, France, Italy, Serbia and other countries, it is not usually borne in mind that capital does not merely consist of gold and silver, of bricks and mortar … or even of railways, steamships and machinery … but of scientific knowledge … When, therefore, we compile estimates of the losses due to the war, let us not forget that our greatest asset, the vast store of knowledge that Science has gathered together for us … is still intact. It is a store that has slowly been accumulating ever since the beginning of the world — a store which enables man more and more to triumph over Nature, and one that for ever remains practically indestructible as the real permanent capital of the race, and by far its most precious heritage.
From *Nature* 28 November 1918