

Experimental evolution in Lisbon

Flexible Bugs

The rate at which beneficial mutations accumulate in genomes is difficult to quantify. However, Isabel Gordo's group has recently succeeded in doing so for *E. coli* and found a rate 1,000 times higher than previously estimated.

Genomics, proteomics, transcriptomics and many more strange 'omics'. Microarrays, real-time PCR, sequencing robots, databases and cooperative international projects. Do you think that modern biology has become an excessively technical and descriptive science? Do you miss the golden age of genetics, when a couple of boffins in a dusty lab required only the brains they were born with and some Petri dishes to tackle life's deepest mysteries? Have clever and elegant experiments, as pioneered by those classical geneticists that we all studied at university, disappeared forever?

Well, maybe. Or perhaps we should remove our rose-tinted spectacles and accept that hindsight is a wonderful, if sometimes deceptive, thing. Consider also that there are still diamonds to be found amongst



Old question, young researchers: Lilia Perfeito (l.) and Isabel Gordo.

the mediocrity of modern biology. Focus on the few cases of good back-to-basics science that rise to the surface of an otherwise murky pool.

Digging out a diamond

The work of Perfeito *et al.* (*Science* 317: 813) belongs to this last category of good back-to-basics scientific thinking, but also incorporates a good dash of modern technological expertise and descriptiveness. The introduction to their recent paper, *Adaptive mutations in bacteria: high rate and small effects*, states that, "the rate at which new

mutations arise in natural populations and their fitness effects are of key importance in evolutionary genetics". They go on to explain that, although beneficial mutation is considered the driving force of adaptation, theoretical models have always lacked good estimations of its actual significance in populations. The rate at which beneficial mutations accumulate is difficult to quantify. They are expected to be rare, with most of them exerting little effect upon fitness and experiencing a low probability of fixation because of stochastic loss and competition (clonal interference).

Persistence, will and group spirit

Trying to overcome these difficulties, Perfeito *et al.* designed an experiment to measure both the rate at which beneficial mutations are generated in the bacterial

genome and the effects that they have on bacterial fitness. As expected, they observed that clonal interference increases in populations with very large effective sizes. But by reducing a population's effective size, they got a surprising result: in *Escherichia coli*, the rate of ben-

eficial mutations was 1,000 times higher than previous estimates.

The research was done by four scientists working at the Instituto Gulbenkian de Ciência (IGC) in Lisbon (Portugal): Lilia Perfeito, Lisete Fernandes, Catarina Mota and Isabel Gordo. Isabel Gordo is a young group leader at only 34. She obtained a first degree in physics and then started on the Gulbenkian PhD programme in biology and medicine. After taking a year of advanced courses she wrote her thesis at the University of Edinburgh, under the supervision of Professor Brian Charlesworth, a well-



known evolutionary geneticist. In 2002, after a spell as an assistant researcher at Oxford University, she moved back to the Instituto Gulbenkian de Ciência, where she took a principal investigator (PI) position.

Gordo devised the project soon after finishing her thesis. Lisete Fernandes, a molecular geneticist leading another research group at the Instituto Gulbenkian, discussed the details and helped her to develop her ideas. In 2003, they obtained funding from the Portuguese Fundação para a Ciência e a Tecnologia. Lilia Perfeito joined the lab as a PhD student in 2004 and the project subsequently became the main focus of her thesis. In 2005, technician Catarina Mota joined the group to assist with experiments. "The initial period of the whole project was a bit hard" says Gordo, "since we had to carefully set up the conditions of the experiment to be able to collect and analyze the data. I was personally very excited, since in the beginning my experience in the field was not a huge one. But the persistence, the will and the group spirit that accompanied all the people in this work made it happen."

In need of data

The first stages of the project were a steep learning curve for Gordo, since she had little previous experience of experimental research. Until then, she had been doing theoretical research on evolutionary genetics. Together with Charlesworth, and with other collaborators later on, she produced analytical approximations, predictive models and calculations. These studies focused mainly on the evolution of asexual haploid populations and the processes by which they accumulate deleterious mutations in an irreversible manner (Muller's ratchet). But Gordo needed some accurate experimental data. "Since I started my PhD it became more and more evident for me the importance of estimating basic parameters that govern the strength of the different evolutionary forces, namely the rate and fitness effects of mutations. In 2001, a paper came out [Imhof and Schlotterer, 2001,

