

and its descendants to proliferate more rapidly, that lineage will begin to increase in relative abundance in the population. By sequencing the cells' molecular barcodes at different time points throughout the experiment, beneficial lineages can be identified.

Levy and colleagues used their high-resolution lineage-tracking technique to quantify the fitness of each beneficial lineage, and to determine when the corresponding mutation occurred in the population's history. They found that, in evolving yeast populations containing 70 million cells, about 25,000 lineages showed fitness increases of more than 2% after just over 100 generations. Many of these lineages were present at frequencies lower than 0.001%. This means that there are initially many more competing lineages containing beneficial mutations in evolving populations than previously revealed by whole-population sequencing^{3–5}.

The aggregate effect of these thousands of beneficial lineages is to push the population fitness higher and higher. In doing so, a process of sequential purging occurs. First, the lineages that did not acquire a beneficial mutation are removed from the population. Then, as population fitness continues to increase, even lineages that contain beneficial mutations are purged once their individual fitness is less than that of the population as a whole.

Levy and colleagues' study shows that there are two distinct phases in the adaptive evolution of a large cell population (Fig. 1). In the first phase, population fitness increases in a predictable manner. This increase is attributable to the cohort of thousands of different lineages with beneficial mutations, and depends on the size of the population and the fitness associated with each mutation. The second phase is less predictable. The ultimate 'winners' must have higher fitness than the overall population and the mutations must have been introduced early enough in the population's history to establish themselves — this phase is unpredictable because such mutations are rare.

The ability to quantify the fitness of each beneficial mutation in a population enabled Levy and co-workers to measure the range of fitnesses conferred by beneficial mutations. Theory predicts^{6,7} that the distribution of fitness effects associated with new mutations has a particular mathematical shape, known as an exponential distribution. However, the authors find that this is not the case, at least not in this environment. Instead, they observe a complicated distribution of fitness effects that seems to be composed of a mixture of distributions, which may reflect beneficial mutations in different genes. The nature of the distribution of fitness effects of beneficial mutations is central to understanding and simulating adaptive evolution in future experiments. As such, the ability to empirically measure this distribution with precision

provides opportunities to reconcile theory and data.

Despite the power of Levy and co-workers technique, several limitations remain. First, the method does not actually identify the beneficial mutations, a key requirement for understanding the molecular basis of adaptation^{8,9}. Second, it tells us about the distribution of fitness effects for beneficial mutations, which are most relevant to the evolution of large asexual populations, but not those for neutral or deleterious mutations, which may be important in populations that are small, sexual or have high mutation rates. Last, and crucially, the method in its current form allows identification of only the earliest stages of adaptive evolution. Once a single lineage has swept to high frequency in the population, its barcode will be abundant. Loss of barcode diversity limits the ability to detect a second beneficial mutation within these lineages, a problem that could be overcome by somehow regenerating the diversity of barcodes during the course of the experiment.

The ability to track hundreds of thousands of individual lineages in a population is an exciting tool that allows us to address many questions in adaptive evolution. Levy *et al.* performed their experiment using enormous populations, ensuring an ample supply of mutations. However, studying the dynamics of adaptation in much smaller populations would also be informative, and will probably result in less-predictable outcomes in the early stages of adaptation. Furthermore, studying adaptation in different environments and different genetic backgrounds will be crucial for assessing the generality of the results. Application of high-resolution lineage tracking in other organisms may be useful for understanding the evolutionary dynamics of antibiotic resistance in pathogens and the evolution of human tumours. The ability to observe evolution in action with high resolution is certain to reveal unanticipated features of the universal force of adaptive evolution. ■

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50 Years Ago

The completion of the *Flora URSS* is a scientific event of great significance not only to botanists of the Soviet Union ... During the War work was almost entirely suspended as most of the authors were evacuated from Leningrad. However, incredible efforts were made to continue the work. Thus, late in the autumn of 1941 in the besieged city ... an attempt was made to print Volume 11. B. A. Tikhomirov ... obtained the necessary amount of paper and ... this volume was printed. N. F. Goncharov, already desperately weakened by starvation, proceeded with the account of the genus *Astragalus* which made up Volume 12. Later that winter this account was defended as his thesis for the degree of doctor of biology, and in February 1942 Goncharov died of hunger ... Thus, thirty-three years of work and the participation of about a hundred authors were required for the completion of ... a *Flora* of 30 volumes. We remember all our colleagues, many of them long dead, who contributed to its achievement. We have done what we could. We welcome the young botanists and wish them success.
From Nature 13 March 1965

100 Years Ago

Insects Injurious to the Household and Annoying to Man. By Prof. G. W. Herrick; *The House-Fly, Musca domestica, Linn. Its Structure, Habits, Development, Relation to Disease and Control.* By Dr. C. G. Hewitt — In addition to insects in the zoological sense of the term, spiders, mites, ticks, solpugids, scorpions, and centipedes are passed in review, and the British reader cannot but feel that some compensation for not being an American is afforded by the comparatively scanty house-fauna of his native land.
From Nature 11 March 1915