Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Genomics. Author manuscript; available in PMC 2015 June 01.

Published in final edited form as:

Genomics. 2014 December ; 104(6 0 0): v–vi. doi:10.1016/j.ygeno.2014.11.008.

Editorial: Experimental Evolution: Prospects and Challenges

Frank Rosenzweig[1] and **Gavin Sherlock**[2,*]

[1]Division of Biological Sciences, University of Montana, Missoula, MT, United States of America

[2]Department of Genetics, Stanford University, Stanford, CA 94305-5120, United States of America

This issue of Genomics is devoted to the discipline of Experimental Evolution, with 8 diverse and complementary papers from prominent labs working in the field. Five of these papers are review articles, which survey the history of the field, its current state of knowledge, its applications, the state of the art, and provide insights into where the field is heading. The three remaining articles are original research articles, each using different organisms to study the evolutionary process.

Adams and Rosenzweig ([1]) begin the issue with a historical perspective, starting out not with Novick and Szilard where most such perspectives begin, but instead with Monod, who described the construction of the first continuous culture device wherein growth could be controlled by a single limiting nutrient. This device later became known as the chemostat, and has been a mainstay of experimental evolution studies for several decades. Only in the last ten years or so that it has become feasible to determine the population dynamics within evolving populations, and the molecular changes that occur during experimental evolution, which were previously inferred either from neutral markers, or assaying fitness as it increased. Adams and Rosenzweig coin the term “post-Mullerian” to refer to the complexity that such studies have so far revealed, though it is far from clear how much more complexity awaits, or what “post-post-Mullerian studies will reveal.

Dunham and Gresham ([2]) review the advantages that chemostats can offer in the field of Experimental Evolution, specifically how the environment can be kept constant even as the population within undergoes evolutionary change. They contrast chemostats’ constant resource limitation with serial batch culture, in which cells undergo boom and bust cycles with respect to available nutrients, as well as periodic population bottlenecks, then contrast these in turn with yet another continuous culture system, the turbidostat, in which cells are never resource limited. They suggest that the practical challenges of chemostat culture are outweighed by its advantages, though to some extent, this may depend on one’s goals. An environment that is predictably constant frequently selects for loss-of-function mutations ([3]) as cells dispense with unnecessary pathways that presumably carry a cost, because, even though they don’t know it, their next meal is guaranteed. Indeed, systems that might be essential for maintaining homeostasis in a fluctuating environment can often be dispensed with in a constant one, but such mutations may carry fitness costs in other environments. If,

*corresponding author: gsherloc@stanford.edu ; (650) 498 4012.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

for example, the goal is to generate robust strains for industrial applications, selective regimens that best capture the complexity of the intended environment may avoid fixing alleles that demonstrate antagonistic pleiotropy.

Winkler and Kao ([4]) describe advances in experimental evolution that have been made specifically with an eye on the industrial environment, in particular the use of adaptive evolution to create improved biocatalysts for a variety of industrial processes. These range from increasing diversity within populations by tuning mutation rates, to promoting recombination between lineages so that multiple beneficial alleles can accumulate in the same genetic background, speeding up the adaptive process. They also describe strategies by which researchers can aim to couple fitness to the production of a desired product (such as a biofuel). While it is straightforward to select for faster growth in just about any environment, the biological system being evolved often achieves increased fitness in unexpected ways that result in lower rather than higher product yield. This often results in a game of evolutionary "Whac-a-Mole", trying to re-engineer a strain to prevent that particular adaptive mode of failure, just to discover the next one. Experimentally coupling fitness to product output is one mechanism to avoid this time-consuming game.

Lang and Desai ([5]) review what has been learned from experimental evolutionary studies about the spectrum of beneficial mutations. The use of tiling microarrays allowed the first genome-wide determination of mutations in evolved strains ([6]), but this was rapidly supplanted by the use of whole genome sequencing. While sequencing is not a panacea, (there are regions of even the yeast genome that are not uniquely mappable with short reads, and it still remains challenging to find indels and structural variants with sufficiently low false positive rates to allow all candidates to be readily tested) it has resulted in the identification of thousands of mutations that have occurred in evolved clones and populations of microbial genomes, with *E. coli* and *S. cerevisiae* having the most available data. The challenge now is not to identify the mutations, but instead to distinguish the passengers from the drivers. We will likely never have enough mutations to use an approach such as that used in ([7]), but by exploiting parallelism, coupled with low mutation rates, such that the drivers are not greatly outnumbered by the passengers, we are likely to gain great insight into what types of mutation might be beneficial in which environments, which itself will shed light on how the cell is wired.

In the last of the review articles, Blundell and Levy ([8]) discuss the use of lineage tracking. This idea is a satisfying echo of the pioneering efforts in the field, where a poor man's lineage tracking was achieved by assaying a neutral marker, providing a resolution of a single subpopulation within the overall population. While this idea has been improved upon by the use of fluorescently marked subpopulations (e.g. [9]), the lineage tracking idea discussed by Blundell and Levy is a quantum leap beyond these previous efforts, and may allow us to answer some of the outstanding questions in the field.

Prospects

We leave it to the reader to discover the content of the very different original research papers (though unified by a common theme), and instead discuss the prospects for the field

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

going forward. While in some sense, it always seems that biology is entering a new golden age of discovery (which is what makes it so exciting to be a research scientist) we are at a point in time when it seems that the answers to multiple longstanding questions in evolutionary genetics are at last within reach. Moreover, to the extent that these questions are answerable by sequencing, it is clear that over time we will generate answers that have finer and finer resolution, as the quality and throughput of sequencing will only increase, while cost decreases. Such questions include – what is the beneficial mutation rate, U_b? What is the distribution of fitness effects (DFE) for those beneficial mutations, and what are the identities of the mutations themselves? How do beneficial mutations selected in one environment fare in another environment (antagonistic pleiotropy), or on another genetic background (epistasis)? How do the answers to all these questions vary as a function of ploidy, environment and founding genotype? Is it ever possible to achieve the (or a) fitness optimum in an experimental evolution, or is the situation akin to Zeno's dichotomy paradox, whereby each step is always a fraction of the remaining distance to go? (Even after 50,000 generations, the *E. coli* in the long term evolution experiments founded by Richard Lenski are still becoming ever more fit, even though the rate at which their fitness is increasing is slowing down ([10])). The papers in this special issue make clear how far experimental evolution has come in the past decade and how far it is likely to advance in the decade to come.

References

1. Adams JP, Rosenzweig F. Experimental Microbial Evolution: History and Conceptual underpinnings. Genomics. 2014
2. Gresham D, Dunham MJ. The enduring utility of continuous culturing in experimental evolution. Genomics. 2014
3. Kvitek DJ, Sherlock G. Whole genome, whole population sequencing reveals that loss of signaling networks is the major adaptive strategy in a constant environment. PLoS genetics. 2013; 9:e1003972. [PubMed: 24278038]
4. Winkler JD, Kao KC. Recent advances in the evolutionary engineering of industrial biocatalysts. Genomics. 2014
5. Lang GI, Desai MM. The spectrum of adaptive mutations in experimental evolution. Genomics. 2014
6. Gresham D, Ruderfer DM, Pratt SC, Schacherer J, Dunham MJ, Botstein D, Kruglyak L. Genome-wide detection of polymorphisms at nucleotide resolution with a single DNA microarray. Science. 2006; 311:1932–1936. [PubMed: 16527929]
7. Davoli T, Xu AW, Mengwasser KE, Sack LM, Yoon JC, Park PJ, Elledge SJ. Cumulative haploinsufficiency and triplosensitivity drive aneuploidy patterns and shape the cancer genome. Cell. 2013; 155:948–962. [PubMed: 24183448]
8. Blundell JR, Levy SF. Beyond genome sequencing: Lineage tracking with barcodes to study the dynamics of evolution, infection, and cancer. Genomics. 2014
9. Kao KC, Sherlock G. Molecular characterization of clonal interference during adaptive evolution in asexual populations of *Saccharomyces cerevisiae*. Nature genetics. 2008; 40:1499–1504. [PubMed: 19029899]
10. Wiser MJ, Ribeck N, Lenski RE. Long-term dynamics of adaptation in asexual populations. Science. 2013; 342:1364–1367. [PubMed: 24231808]