

Non-random random mutations: a signature of evolution of evolution (EVOEVO).

Paulien Hogeweg¹

¹ Theoretical Biology and Bioinformatics group, Utrecht University, Utrecht, the Netherlands
P.Hogeweg@uu.nl

What has evolved in the ca 3.5 billion years of biological evolution on earth? A first answer which may spring to mind is your favorite organism, be it elephant, fly, slime mold, microbe or man. Other answers might be the stunning apparent diversity of lifeforms, or the greatly enhanced energy cycling at the earth surface. Or all this may be simplified to characterizing what has evolved as 'complexity'. The latter answer is often pursued within artificial life and is indeed possibly the easiest to study because the most abstract and least well defined, but certainly not trivial as the basic mechanism of Darwinian evolution leads to adaptation but not necessarily to complexity.

Beslon et al (evoevo-project <http://www.evoevo.eu/>) recently posed an other answer for the above question, namely that what has evolved is evolution itself, a perspective which is now pursued under the name EVOEVO. When we study in vivo or in vitro evolution of extant organisms, it is this evolved evolution that we observe. This in contrast to in silico evolution where we most often observe the course of evolution from random initial conditions.

The genomic revolution in biology allows a much closer look at evolution of evolved organisms than ever before. Some of the striking observation gained include:

- very fast adaptation (involving few mutations) to environmental changes or genome changes (knock-outs).
- adaptive mutations are often (further) deletions.
- Last common ancestors of lineages at multiple scales are surprisingly large.
- blow-up of single point mutation (SNP's) to expression changes of multiple genes.
- many processes which cause and regulate changes in DNA have been observed.

The last point has been stressed by Shapiro in his book 'Evolution: a view from the 21st century', in which he indeed tries to convince the reader with numerous examples that the premise "random mutations" is the basic fallacy of evolutionary theory. Despite the title of the book he does not discuss the evolution of such mutational mechanisms, which in my view is the basic fallacy of the book. Indeed elucidating how such non-random mutations evolved by the

basic process of Darwinian evolution by random mutations and selection is in my view the challenge we want to tackle in EVOEVO. We ¹ have made some progress in this direction, although we are only at the beginning of this pursuit.

Surprisingly some of these surprising features of evolution of evolved organisms turn out to be generic properties of Darwinian evolution. They had not before been recognized as such because both population genetics and in silico evolution protocols often restricts the degrees of freedom of the evolutionary process. For example, in multilevel evolutionary models, we have shown that early genome inflation, followed by fitness gain by deletion mutation is a generic pattern in the evolutionary history of *successful* lineages, (i.e. those lineages we should expect to encounter).

"Non-random mutations" in the broad sense involves both biased and/or regulated changes in the genome, as biased effect of mutations at the phenotypic level. We have shown that both these types of non-random mutations evolve in variable environments in a strict Darwinian setting. For example transposon dynamics can structure genomes such that beneficial mutations are overrepresented and very fast evolutionary adaptation to alternative environments evolve. Another example is the evolution of high HGT rates for particular types of genes. However non-random effect of random mutations seem to be an even stronger mechanism to enhance evolvability in evolved organisms. We have shown a bias to beneficial effects of random mutations of all types in simple models where the effect of random mutations is mediated by GRNs and/or metabolism. This is true to such an extend that such enhanced evolutionary potential seems to be a viable alternative to physiological (GRN based) adaptation to changing environments.

All these cases can be understood in terms of the evolution towards a very specific mutational neighborhood (and therewith the evolved quasi-species) through shaping the genome structure, the mutational processes and the genotype-phenotype mapping over long term evolution.

¹in particular Anton Crombach, Thomas Cuypers, Folkert de Boer, Nobuto Takeuchi, Sandro Colizzi and Bram van Dijk contributed to the results discussed here.