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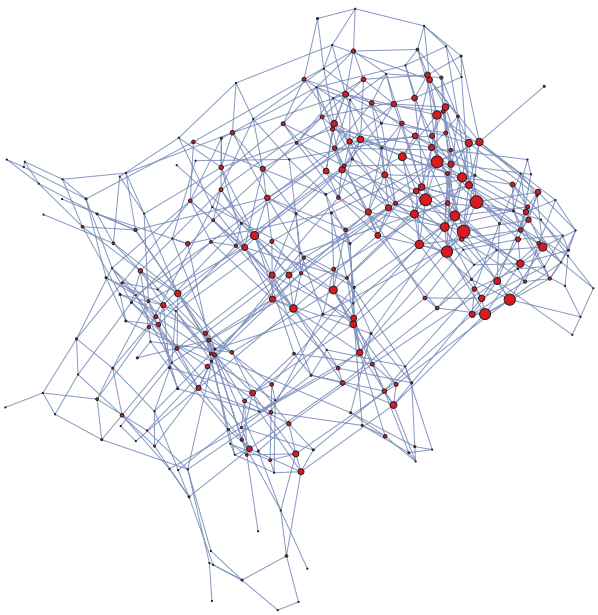
EVO–DEVO

Modelling the evolutionarily possible

The variety of forms seen in nature is remarkable, yet organisms display only a small fraction of all possible forms. Several factors influence this developmental constraint on phenotypic diversity, although their relative contribution has been difficult to quantify. A computational model based simply on regulatory interactions between epistatic genes has now succeeded in describing genotype–phenotype relationships in development and evolution.

The aim of studies in developmental dynamics is to explain how phenotypes are distributed in phenotypic space and, by extension, how a genotype is translated into one or many phenotypes during ontogeny or evolution. The model developed by the authors explores these issues by relating how a genetic input — a function of the number of genes and gene regulatory interactions — determines the phenotypic output, that is, the fraction of phenotypes that are actually visible out of all those that are theoretically possible. Genotypes are allowed to vary, and are mapped onto the resulting phenotypes via a fixed developmental plan.



Patchiness of the visible phenotypic subspace. The size of each node in this network of visible phenotypes is proportional to the logarithm of its frequency. Nodes that represent the most frequent phenotypes are, in most cases, separated by a single edge. Image reproduced from Borenstein, E. *et al. PLoS Comp. Biol.* **4**, e1000202 (2008)

Much as expected, the authors found that as the number of regulatory interactions grows, so does the number of phenotypes that can potentially be sampled. Surprisingly, this also leads to a reduction in the number of actual visible phenotypes — that is, an expansion in genotypic space makes the phenotypic space shrink owing to increased canalization (or genetic robustness), which itself is probably a result of a larger number of gene–gene interactions, or epistasis. So although increasing regulatory diversity allows a system to explore novel phenotypes, it also allows it to become more robust in specific areas of phenotypic space.

The phenotypes sampled by the model are not uniformly distributed across phenotypic space, but rather are clumped in a region of closely related phenotypes (see figure). Furthermore, the most frequent phenotypes occupy a smaller subspace than do all the other visible phenotypes, again invoking the action of canalization in compressing genotypes in phenotypic space. Adding complexity to the model by incorporating multiple layers of regulatory control gives qualitatively the same result — greater complexity leads to a smaller number of highly canalized phenotypes.

How does the model stand up when less-than-ideal parameters are used, that is, when the regulatory network is sparser? In this situation, a larger fraction of the phenotypic space is sampled — epistasis is lower and, therefore, frequent phenotypes are more diverged. This might correspond to the situation present during the early evolution of multicellular forms, which coincided with the radiation of many divergent phenotypes. By contrast, as developmental plans are allowed to evolve, they become more constrained by epistasis, so that the more frequent phenotypes become more similar. The model therefore describes not only the phenotypes generated during development but also the phenotypic diversity across phylogeny, which tends towards a deceleration of diversification over time.

Can developmental evolution be explained simply by the evolution of gene regulatory networks? To a large extent, yes, in that the model is an effective null hypothesis for the non-uniform distribution of phenotypes. It explains the basic features of ontogeny and phenotypic variation: that phenotypes occupy a small portion of phenotypic space; that the effect of mutation is canalized; and that morphological variation predominated early in the evolution of multicellular life.

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ORIGINAL RESEARCH PAPER Borenstein, E. & Krakauer, D. C. An end to endless forms: epistasis, phenotype distribution bias, and nonuniform evolution. *PLoS Comput. Biol.* **4**, e1000202 (2008)
FURTHER READING Raff, R. A. Written in stone: fossils, genes and evo–devo. *Nature Rev. Genet.* **8**, 911–920 (2007) | Pigliucci, M. Is evolvability evolvable? *Nature Rev. Genet.* **9**, 75–82 (2008)