Paper Title: Network Hubs Buffer Environmental Variation in Saccharomyces cerevisiae

tags:

> genotype-phenotype relationship
> robustness to genetic and environmental Variation

Main question of the paper:
If biological systems are so robust, how do they diverge and adapt through evolutionary time?

My idea that relate to the paper:

Maybe Bem1 function as a phenotypic capacitor that after impairment of its function releases phenotypic diversity, highly dependent on the genetic background. However in this case this phenotypic variation is adaptive, because it can recover through experimental evolution.
Role of phenotypic capacitors on evolutionary trajectories.

Conceptual assumption of the paper:

The contradiction might be resolved if the robustness itself were to be modulated by particular mutations or environmental conditions. **The robust system would accumulate conditionally neutral, or "cryptic," genetic variation**. **A genetic or environmental perturbation that impaired the system's robustness would then reveal the cryptic variation in the form of greater phenotypic diversity**. The modulation of robustness would not only allow evolutionary divergence, but it might also accelerate it relative to the slow, step-wise fixation of fitness-increasing alleles that is normally considered within the Neodarwinian paradigm.

Experimental Model:

A model for the buffering and release of variation is provided by the **molecular chaperone Hsp90**, which targets a large set of signal transduction proteins.

In both Drosophila and Arabidopsis, compromised Hsp90 function results in diverse morphological changes that exhibit strong dependence on the genetic background. This implies that Hsp90 normally contributes to phenotypic robustness to genetic variation. Because **Hsp90 function allows stores of genetic variation to build up, and Hsp90 impairment releases this variation to have phenotypic effects, it is termed a "phenotypic capacitor"**.

Main issues in the topic:

- One issue is whether any fraction of the phenotypic variation revealed by an impaired capacitor is adaptive, or instead whether the variants consist entirely of hopeful, but ultimately unfit, monsters
- A second debate concerns the ultimate evolutionary reason that capacitance exists.
  - One view is that the ability to modulate evolvability is itself an adaptive trait, and that natural selection has therefore favored capacitor function. This view generally meets with great skepticism, as do similar views on the evolutionary benefits of mechanisms that alter mutation or recombination rates. Nonetheless, a population-genetic model has shown that an allele that modifies the rate of revelation of cryptic genetic variation can invade a population under a realistic range of parameter values.

- The buffering of genetic variation then results from a hypothesized mechanistic congruence between the impacts of allelic variation and environmental variation on regulatory networks

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Our working definition of a capacitor is a gene product that causes high variance in multiple nonredundant phenotypes when deleted.

To identify gene products that meet this criterion, three obstacles must be overcome:

(1) a measure of variance that is not dependent on the mean must be generated so as not to confound changes in variance with changes in mean phenotype;

(2) biologically or physically redundant phenotypes must be eliminated (dimensional reduction); and

(3) a robust score for the overall variance in multiple phenotypes must be generated.