Mutation limitation and the genetic mechanisms of adaptation

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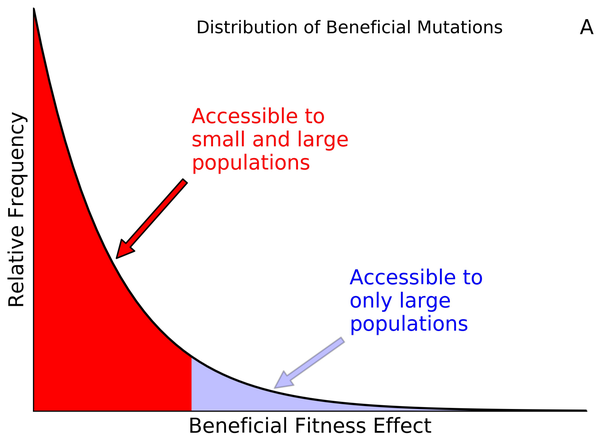
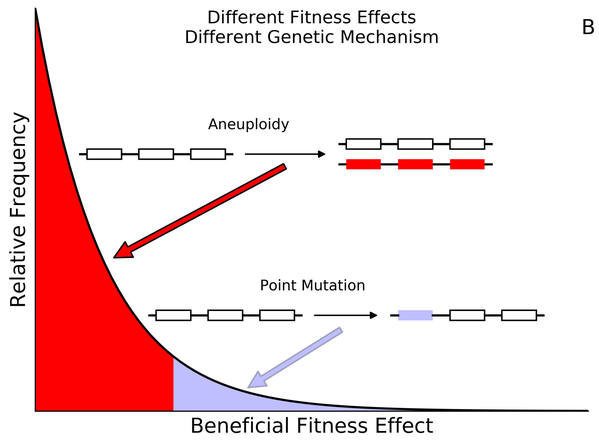
DAMON RUNYON CANCER RESEARCH FOUNDATION

What alters the genetic mechanisms underlying adaptation?

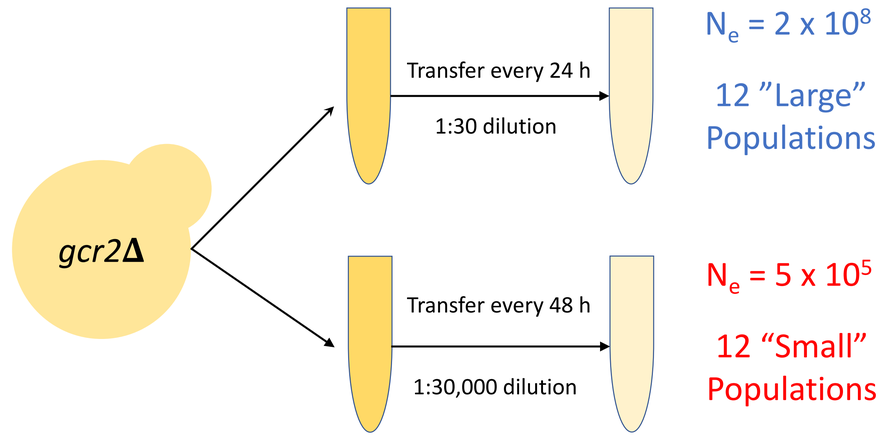
Evolutionary Theory





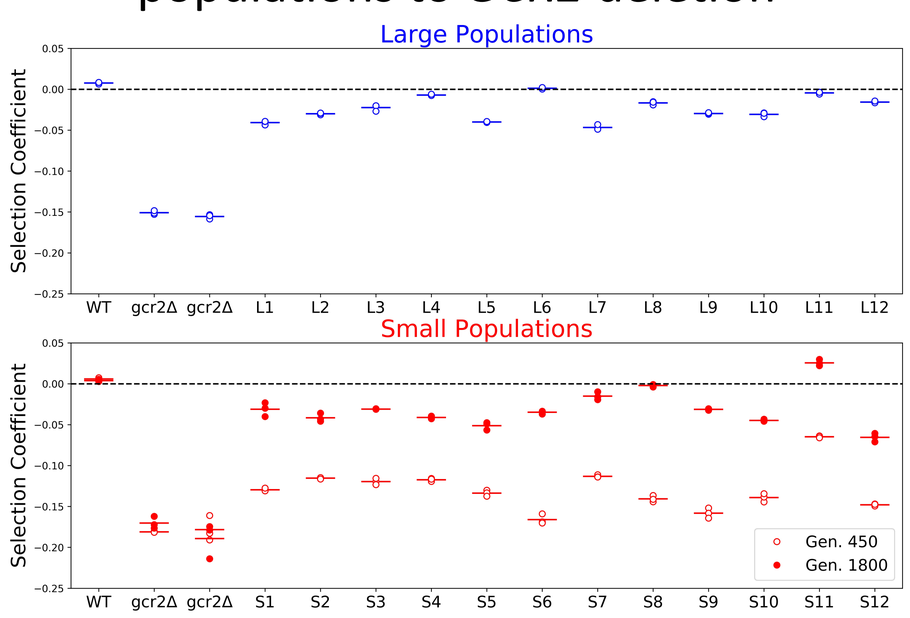
If differences in fitness effect and frequency between mutations result from different genetic mechanisms, then one should expect mutationally-limited small populations to adapt using different genetic mechanisms than large populations with access to larger-effect beneficial mutations.

Experimental Design



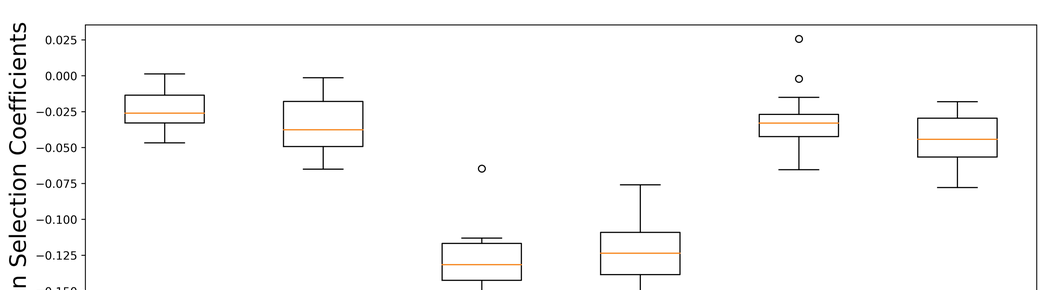
I evolved a *gcr2Δ* yeast strain at a large and small population size for 450 and 1800 generations, respectively. This strain is deficient in transcriptional activation of glycolysis and evolving this strain in a glucose environment is hypothesized to select for increased glycolytic expression.

Large populations adapt faster than small populations to *GCR2* deletion



Selection coefficients from competition experiments for all populations. Three biological replicates were performed. Circles are individual measurements and dashed lines are their means. **Small populations require four times as many generations to reach approximately the same fitness as large populations.**

Differences in adaptation rate is not due to differences in the dilution environment



Mean selection coefficients from competition experiments for all evolved populations across evolved population sizes (Large or Small), generations (450 or 1800), and competition-experiment dilutions (1:30 or 1:30000). **Large populations are fitter than small populations at generation 450 in both dilution environments, which is consistent with small populations fixing mutations of lesser beneficial effect.**

Putatively-adaptive mutations suggest large and small populations initially adapt through different genetic mechanisms

Large Populations	
GAL11 (9)	Subunit of Mediator Complex
GCR1 (3)	Transcriptional activator of glycolysis
RPP2B (3)	Component of ribosomal stalk
TRA1 (1)	Subunit of SAGA and NuA4 histone acetyltransferase complexes
Small Populations	
**IES1* (3)	Subunit of the INO80 chromatin remodeling complex
**IES5* (1)	Subunit of the INO80 chromatin remodeling complex
INO80 (1)	Subunit of the INO80 chromatin remodeling complex
TUP1 (2)	General repressor of transcription
**CTI6* (2)	Component of the Rpd3L histone deacetylase complex
**RXT3* (1)	Component of the Rpd3L histone deacetylase complex
TOD6 (1)	Component of the Rpd3L histone deacetylase complex
GCR1 (1)	Transcriptional activator of glycolysis
RPP2B (1)	Component of ribosomal stalk

Non-exhaustive list of mutations from whole-population sequencing at generation 450. Number of populations in which a given gene is mutated in parenthesize. * genes indicate nonsense mutations. **Large populations adapted primarily through non-synonymous mutations in the Mediator complex, while small populations initially fixed more *hypothesized* loss-of-function mutations in multiple transcriptional modules. This result suggests that large populations did fix rarer mutations than the those fixed in small populations if one assumes loss-of-function mutations are more abundant than gain-of-function mutations.**

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