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Population genetics inside a cell: Mutations and mitochondrial genome maintenance SIDHARTHA GOYAL, Kavli Institute for Theoretical Physics, University of California Santa Barbara, BORIS SHRAIMAN, University of California Santa Barbara, DAN GOTTSCHLING, Fred Hutchinson Cancer Research Center — In realistic ecological and evolutionary systems natural selection acts on multiple levels, i.e. it acts on individuals as well as on collection of individuals. An understanding of evolutionary dynamics of such systems is limited in large part due to the lack of experimental systems that can challenge theoretical models. Mitochondrial genomes (mtDNA) are subjected to selection acting on cellular as well as organelle levels. It is well accepted that mtDNA in yeast *Saccharomyces cerevisiae* is unstable and can degrade over time scales comparable to yeast cell division time. We utilize a recent technology designed in Gottschling lab to extract DNA from populations of aged yeast cells and deep sequencing to characterize mtDNA variation in a population of young and old cells. In tandem, we developed a stochastic model that includes the essential features of mitochondrial biology that provides a null model for expected mtDNA variation. Overall, we find approximately 2% of the polymorphic loci that show significant increase in frequency as cells age providing direct evidence for organelle level selection. Such quantitative study of mtDNA dynamics is absolutely essential to understand the propagation of mtDNA mutations linked to a spectrum of age-related diseases in humans.

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