

On Stress Induced Hyper-Mutators in Bacteria

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The phenomenon of hyper-mutation in bacteria is common in nature, as several studies show that hyper mutating strains represent a few percent (>1%) of natural isolates. This was surprising, as mutations are deleterious more often than not and therefore mutator alleles are subject to selection as their genetic backgrounds become poorer with time.

In this project it is suggested that hyper-mutation can be better understood if it is induced by stress. We refer to such mutator alleles as SIM alleles - Stress Induced Mutators. When a SIM allele is surrounded by an advantageous genetic background, it will be repressed. But when surrounded by a poor genetic background, it will induce a higher mutation rate and effectively change the clone's genetic background. Although in most cases the clone will suffer even more deleterious mutations, in some cases advantageous mutations will emerge and spread, carrying the SIM allele with them.

At the gene level, SIM alleles can spread by association to generated advantageous mutations, just like uniform mutator alleles. But differently from uniform mutators, SIM alleles would not change an advantageous genetic background by generating deleterious mutations. At the population level, SIM alleles increase variability, allowing the population to handle environmental changes, such as introduction of novel antibiotics.

As classical models of the evolution of antibiotic resistance usually assume a constant mutation rate, introduction of stress induced hyper-mutators to these models can alter their predictions.

In this project we investigate the evolution of Stress Induced Mutators and their effect on adaptation in bacterial populations using simulations.

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