

## Seminar

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### How epistatic interactions shape the fitness landscape on a macroevolutionary scale

The fitness landscape has been one of the most useful conceptual tools used to understand micro- and macroevolution. In other words, we often think about what the fitness landscape looks like to understand how the genotypes in populations and between species change over time. Unfortunately, large-scale and unbiased experimental assays of fitness landscapes have only recently become possible. In my talk I will focus on developing a general intuition of what the fitness landscape of specific proteins likely looks like based on some recent experiments. Specifically, I will talk about our recent and yet unpublished work on the evolutionary-relevant section of the fitness landscape of His3 in yeasts. His3, a gene coding for an enzyme in the histidine synthesis pathway that likely functions without significant interactions with other proteins, allowing us to focus on the landscape of the protein itself without the interference of trans effects. Across 12 independent sections of the His3 protein we identified all amino acid substitutions between dozens of His3 yeast orthologues. For each segment we then created the vast majority of all possible combinations of amino acid substitutions, which represent all of the possible direct evolutionary trajectories between the extant orthologous regions. An intuitive understanding of protein evolution dictates that, with the exception of adaptive substitutions, amino acid states should be freely exchangeable between the same gene from different species. Thus, all of the combinations of amino acid states from extant species should confer high fitness and all of the evolutionary trajectories between orthologues should be traversable. Our results show that in many cases, combining amino acid states leads to very low fitness due to the epistatic interactions between the extant amino acid state. The nature of these interactions can mostly be described by a threshold fitness function, however, more complex interactions of an unknown character also likely play a role. Time permitting I will present an attempt of a formal model evolution in a complex, epistatic fitness landscape.

**Monday, February 25, 2019**

**2:30 PM**

**Laufer Center lecture hall 101**

**Host: Josh Rest**

*Refreshments following the lecture  
Laufer Hub 110*