# Evolution through Programming

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## Assignment 4 –

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### Question 3 - Exploring Fitness Valleys in the tRNAArgCCU Landscape

Out of 8,101 N2 neighbors of the original tRNA that were tested and reported, there were

#### Background

You have been provided with:

1. The published article by Li et al. (Science 352:837–840, 2016) describing the fitness landscape of the yeast tRNAArgCCU gene under high-temperature challenge (37°C).
2. The full table of measured genotype fitness values for all single and double mutants relative to the wild type (fitness = 1.0000).

The article reports that some N2 mutants (genotypes differing from wild type by exactly two point mutations) exhibit fitness values greater than the wild type.

#### Conceptual Focus

A fitness valley exists when a genotype with higher fitness cannot be reached by a series of single‐mutation steps that never decrease fitness (i.e., there is no non‐decreasing path). Such valleys impede adaptive evolution.

#### Tasks

1. Identify all N2 neighbors of the wild type whose fitness (fN2) exceeds 1.0000.

out of 42k

1. For each of these high‐fitness N2 mutants, determine whether it is reachable from the wild type by a two‐step path in which each intermediate N1 mutant has fitness ≥ 1.0000.
   1. Decompose each double mutant into its two-constituent single‐point mutations (A→B at position i, and C→D at position j).
   2. Check the fitness of both single mutants (i: A→B; j: C→D).
   3. Note: You may choose the order of the two single steps; if either order yields non‐decreasing steps, the double mutant is reachable.
2. Count the number of high‐fitness N2 mutants that are reachable by a non‐decreasing two‐step path.
3. Count the number of high‐fitness N2 mutants that are not reachable (i.e., both single mutants have fitness < 1.0000 in at least one order, creating a fitness valley).
4. Interpretation and Conclusion:
   1. Based on your counts, discuss whether the concept of a fitness valley explains why the wild type is not the highest‐fitness variant.
   2. Consider the implications for adaptive evolution: Do fitness valleys isolate the wild type from fitter genotypes?

#### Deliverables

* A table summarizing each high‐fitness N2 mutant, its two constituent N1 steps, their fitness, and reachability status.
* A brief explanation presenting your counts and your conclusion on the role of fitness valleys in this landscape.

Good luck!