# Evolution through Programming

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## Assignment 4 –

This is the extension of Assignment 4, introducing question 3. **CHOOSE 1** question to answer from all 3 options.

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

#### 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.

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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!