# 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 2,108 variants with a higher fitness compared to the WT at 23 degrees, representing 26% of the options being better than the original.

We wanted to examine the role of fitness valleys in the evolution of this tRNA molecule. We tested whether there is a reasonable way to achieve each of these N2 neighbors, without suffering from fitness loss when acquiring the first mutation out of the two. We tested each of the single mutations to see if they exhibit fitness that is same or above of the fitness of the WT molecule. A variant was termed as "reachable" if the intermediate variant does not suffer fitness loss.

Out of the 2,108 N2 neighbors with a fitness advantage, 1,777 were reachable. This accounts for 84% of the N2 neighbors with a fitness advantage, which brought us to a conclusion that fitness valleys are not the main force that isolates the WT molecule from its better variants on the fitness landscape. Moreover, some of the non-reachable variants are composed of two mutations with fitness that is lower than 1 but not by much, for example 0.9917 and 0.9825. In cases like this, a single mutation could decrease the fitness of the individual carrying it but not cause its extinction, causing the gain of the 2nd mutation to be possible within a few generations, therefore allowing the existence of the N2 neighbor.

This trend repeats itself: in 30 degrees we see 1,569 reachable variants out of 1,848 N2 neighbors with fitness above 1 (84%), in DMSO we see 1,676 reachable variants out of 1,982 (84%), and in 37 degrees we see 1,611 reachable variants out of 1,798 (89%). Tables describing the 4 different conditions are attached.

Therefore, we propose that fitness valleys do not isolate the wild type from fitter genotypes. We would like to suggest that the underlying mechanism here is rather "survival of the flattest", where some genotypes are fixed not because they are the fittest but because they would suffer the least from gaining an accidental mutation. As shown in the paper, most N3 neighbors had very bad fitness in comparison to the wild type, which may explain why N2 neighbors are not fixed – they are too prone to gain another single mutation which would cause their extinction.