

## The sounds of silence in the genetic code

*New data shows that DNA sequence changes that do not alter the protein they code for can have a wide range of fitness effects. Genetics may never be the same.*

The genetic code – how a DNA sequence is translated into amino acids, the building blocks of proteins – carries redundancies. The same amino acid can be produced by different DNA sequences. When a mutation changes the DNA sequence but not the amino acid it codes for, we call these ‘synonymous’ or ‘silent’ mutations.

Because synonymous mutations do not change the protein, geneticists assumed these changes would be hidden from natural selection. But there have been hints that this assumption might be wrong. Many organisms preferentially use some synonymous sequences over others, suggesting that natural selection has played a role in curating which sequences are used in a species. Synonymous mutations have also been linked to at least 50 genetic diseases in humans, demonstrating that they can have major effects on protein function and fitness.

How often synonymous mutations have measurable effects on fitness, the ability of an organism to grow and reproduce, remains a mystery. We aimed to find out.

We had previously found a gene in *Pseudomonas fluorescens*, a common plant-associated bacterium, that had adapted to life in a limited glucose environment through two synonymous changes in a gene involved in glucose transport. We wondered how many synonymous mutations in this gene might have similar beneficial effects.

It turns out, surprisingly, that many do! Some also decreased fitness. In fact, the range of fitness values we measured matched almost exactly that of nonsynonymous mutations (those that do change the amino acid). And the most beneficial synonymous mutations in our experiments are also present in related strains and species. This means that our results are not just an idiosyncratic effect of life in the lab; they seem to matter in the real world as well.

How does this happen? The answer lies in quantity, rather than quality. Beneficial synonymous mutations create better landing sites for the enzyme complex that converts DNA sequences into proteins. The result is that more protein is produced, both in this gene and those just downstream who are also involved in glucose transport. More proteins mean more glucose inside the cell, which in turn provides more energy and so higher fitness.

What this means is that we might have to rethink some of the foundational assumptions of genetics. Synonymous mutations are not always hidden from natural selection, as we have thought. They can have a range of fitness effects, sometimes beneficial and sometimes deleterious. Just how common they are in other species remains to be seen.

**Read the paper:** Lebeuf-Taylor *et al.* (2019) The distribution of fitness effects among synonymous mutations in a gene under directional selection. *eLife* 8:e45952; doi: [10.7554/eLife.45952](https://doi.org/10.7554/eLife.45952)

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