

THE BENEFITS OF BEING DIFFERENT

How variation in our DNA helps us function

BY HAROLD EYSTER

Mark Twain once said, “I don’t see any use in having a uniform and arbitrary way of spelling words. We might as well make all clothes alike and cook all dishes alike. Sameness is tiresome,” (1). Researchers at Harvard University and the University of Chicago recently agreed with Twain by showing that it’s useful to have multiple “spellings” for amino acids (2).

Our DNA is written using only four ‘letters’ in the form of nucleotides. Three of these nucleotides together form a codon, and each codon translates to an amino acid, from which we form a protein. Probability tells us that four letters combined into a three-letter long string can be arranged in $4^3 = 64$ different ways. However, there are only 20 different amino acids, which leaves a lot of ‘spellings’ left over. In English, there are multiple ways to spell the same word: for example, the color midway between black and white

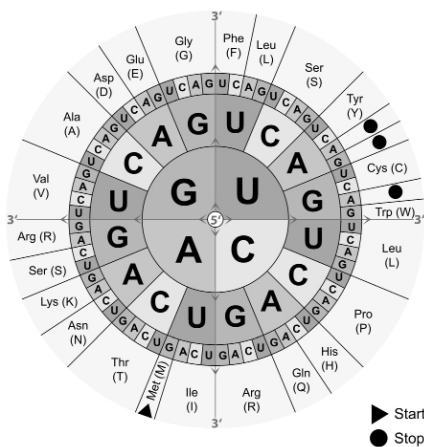


Figure 1: Universal genetic code, with codon translations.
Photo courtesy of Wikimedia Commons.

can be written either ‘gray’ or ‘grey.’ Likewise, there are also multiple ways to describe most amino acids: for example, the amino acid serine (a major component of silk) can be encoded by six different nucleotide combinations. This redundancy, where unique codons encode for the same protein, is called degeneracy.

But is each unique codon equally able to encode for a particular amino acid? Are they true synonyms? Arvind R. Subramaniam and Philippe Cluzel of Harvard and Tao Pan of the University of Chicago sought to answer this question in a recent paper published in the (*Proceedings of the National Academy of Sciences*, 2). The researchers made multiple copies of the gene for a fluorescent protein, each copy containing several different codons for one of seven amino acids. They then inserted these genes into the bacterium *Escherichia coli*, tracked the fluorescent genes and found that protein growth was very similar for all of the different ‘spellings’ of the genes. In other words, the codons were truly degenerate. This was consistent with current knowledge and was what they expected to find. This finding also provided a valuable control for the second part of their experiment.

But then when they starved the *E. coli* of amino acids, things got interesting. They found that some codons were more robust, i.e. better at forming the protein under a wide variety of conditions, than others: one codon was 100 times more successful in synthesizing the fluorescent protein. From this, they were able to tell that the codons are not true synonyms because they had lifted the degeneracy

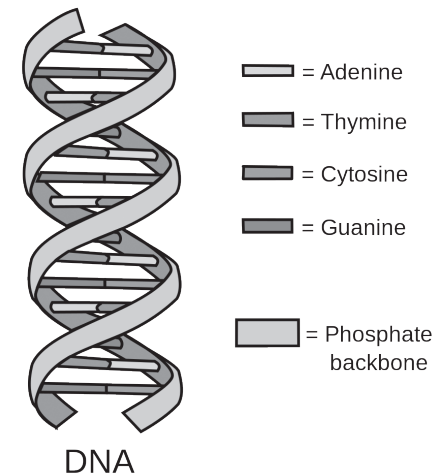


Figure 2: The individual nucleotides of adenosine, guanine, cytosine, and thymine compose the genetic code.
Photo courtesy of Wikimedia Commons.

of the genetic code. The variation in ‘spellings’ of the amino acids may help the organism function when stressed, so that an organism can synthesize only the most important proteins when amino acids are scarce. The authors also suggest that perhaps these findings can be extrapolated to eukaryotes, such as humans, and used to mitigate amino acid shortages caused by some medications. The beautiful efficiency of nature shows that sameness truly is tiresome.

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References

1. J. P. Wickersham, *The Pennsylvania School Journal*. (Pearsol & Geist, Lancaster, PA, 1875), vol. 24.
2. A. R. Subramaniam, T. Pan, P. Cluzel, Environmental perturbations lift the degeneracy of the genetic code to regulate protein levels in bacteria. *Proc Natl Acad Sci U S A* **110**, 2419 (Feb 5, 2013).