

The Same One-Letter Typo Costs **15.75** Times More at One Position Than Another, and at the Second It Is Exactly **0**

— of the **183** single-base substitutions at each codon position, the number that change nothing is **8** at the first, **0** at the second and **126** at the third — **94.03** per cent of all silent errors are gathered at the third — [Paper 398]

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— *From thinking to syncing.* —

Abstract

The genetic code specifies 20 amino acids with 64 codons. This paper shows that the surplus is not distributed evenly — the same one-letter error costs 15.75 times more at one position than at another. No new theorem or law is claimed. First, over the 61 sense codons there are **183** single-base substitutions at each position (Section 2). Second, those that leave the amino acid unchanged number 8 at the first position and 126 at the third (Section 2). Third, and this is the core of the paper. At the second position it is exactly **0**: all 183 substitutions change the amino acid (Section 2). Fourth, the ratio is $126/8 = 15.75$, a fraction that divides exactly (Section 2). Fifth, of the 134 silent errors, **94.03** per cent are gathered at the third position (Section 3). Sixth, the separator is which position was hit, not how many bases changed (Section 5).

Scope of this paper (scope note): No new theorem or law is claimed—the standard codon table, degeneracy, the wobble hypothesis and robustness to error are all known in molecular biology. Origins are not discussed—why the code took this form (frozen accident, coevolution, optimisation) is not the subject. Only the numbers in the present table are counted. No optimality is claimed—it is not asserted that this code is the best. No comparison with random codes is made. Mutation rates are not treated—whether real mutations are equally likely at each position is not the subject. Only counts of possible substitutions. Only the standard code—variant codes such as the mitochondrial one are not the subject. Translation is not treated—tRNA, the ribosome and wobble base pairing are not entered. Relation to earlier papers: Paper 379 showed that “twice as hot” has three answers—here “a one-base error” has three weights. Paper 391 showed that the significant wave height is neither the mean nor the maximum—here a “mutation rate” quoted as a mean hides the positions. Paper 388 showed two different quantities going to one constant—here one operation becomes different quantities by position. Paper 300 showed that same-root and different-root can be decided—the three positions are different-root by that criterion. What is added is an exhaustive count of substitutions by position, showing that the second position is exactly zero, showing that the ratio $126/8 = 15.75$ divides exactly, obtaining the 94.03 per cent concentration at the third position, and placing the separator at “position”.

1. Notation and the Question

Setting: take the standard genetic code and the 61 codons that are not stop codons (UAA, UAG, UGA). At each position of each codon, count substitutions to the other three bases.

$$61 \times 3 = 183 \quad (\text{substitutions at each position}), \quad 183 \times 3 = 549 \quad (\text{in total})$$

Observation 1.1

64 codons specify 21 outcomes (20 amino acids plus stop). A surplus of 43—there is redundancy somewhere.

Observation 1.2

redundancy works as insurance. An error that leaves the amino acid unchanged leaves the protein unchanged—the question is where the insurance was bought.

Observation 1.3

it could have been spread evenly. A third at each position——whether it was is a matter of counting.

Question: how heavy is a one-letter error?

2. At the Second Position It Is Exactly Zero

Computation 2.1: single-base substitutions and synonymous rate by position (counted exhaustively in this paper).

Position	Substitutions	Synonymous (amino acid unchanged)	Rate
First	183	8	0.043716
Second	183	0	0.000000
Third	183	126	0.688525
Total	549	134	0.244080

Observation 2.2

this is the core of the paper. The synonymous count at the second position is exactly zero——all 183 substitutions change the amino acid; not one policy of insurance was bought here.

Observation 2.3

at the third position 68.85 per cent change nothing. 126 of them——more than two thirds pass in silence.

Observation 2.4

the ratio is $126/8 = 15.75$. It divides——cancel the common denominator 183 and an exact fraction remains.

Observation 2.5

the 8 at the first position is not zero but small.4.37 per cent—it comes from the six-fold degeneracy of leucine and arginine.

Observation 2.6

overall, 134 of 549 are synonymous, 24.41 per cent.A quarter—and this average describes none of the three positions.

3. Ninety-Four Per Cent of the Silent Errors Are in One Place

Computation 3.1: breakdown of synonymous substitutions by position (computed in this paper).

Position	Synonymous substitutions	Share of the 134
First	8	5.97 %
Second	0	0.00 %
Third	126	94.03 %

Observation 3.2

the redundancy is gathered in one place.94.03 per cent—an even spread would give 33.3 per cent each.

Observation 3.3

of the 61 sense codons, 32 are four-fold degenerate at the third position.Any of the four bases gives the same amino acid—with 24 two-fold, 3 three-fold and 2 not degenerate.

Observation 3.4

so for more than half the codons the third position carries no information.32 out of 61—one letter in three is frequently free.

Observation 3.5

the shape is that of Paper 391. There the mean of the “wave height” was not representative—here a “mutation rate of 24.41 per cent” fits none of the positions. An average conceals three.

Observation 3.6

they are different-root by the criterion of Paper 300. The three positions play different roles in tRNA recognition—one phrase, “a single-base substitution”, names three things with different roots.

4. And When It Does Change, the Manner of the Change Also Differs

Computation 4.1: among non-synonymous substitutions, the fraction that preserves the polarity class (non-polar, polar, charged) (computed in this paper).

Position	Non-synonymous	Fraction preserving the class
First	166	0.469880
Second	176	0.375000
Third	50	0.440000

Observation 4.2

the second position not only changes things but changes them most crudely.0.375000, the lowest of the three—zero synonymous substitutions, and the lowest preservation of character as well.

Observation 4.3

even so, 37.5 per cent preserve the class. Not wholly defenceless——with no first line of insurance, a second line remains.

Observation 4.4

the third position has only 50 non-synonymous substitutions. Out of 183——it rarely changes anything in the first place.

Observation 4.5

the defence is two-tiered. First “do not change it”, then “change it to something close”——and which tier acts differs by position.

5. Separator: Which Position Was Hit

Observation 5.1

separator——not how many bases changed, but which position changed.

Position	Synonymous rate	Class preserved	Overall weight
First	0.0437	0.4699	middle
Second	0.0000	0.3750	heaviest
Third	0.6885	0.4400	lightest

Observation 5.2

the two middle columns point the same way. The position with the lowest synonymous rate also preserves polarity least——by chance they could have pointed opposite ways.

Observation 5.3

so “one mutation occurred” is not enough information. Without the position the weight is undetermined—a range of 15.75.

Observation 5.4

this separator can be tested. Whether real sequences accumulate substitutions preferentially at the third position between species—counting synonymous and non-synonymous rates separately settles it.

Observation 5.5

to be honest—both 15.75 and 94.03 per cent are counts of possibilities under an assumption of equally likely substitutions. Real mutations are biased by base type—what does not move is that the second position has exactly zero synonymous substitutions, and that $126/8$ divides exactly.

Observation 5.6

one last thing—three letters is one letter more than 20 outcomes require. $4^2 = 16 < 20 \leq 64 = 4^3$ —the surplus was not discarded; it was placed, all in one position, as margin against error.

6. Roll Call and Closing

1. **183 per position, 549 in total** (Section 1): **over the 61 sense codons.**
2. **8 at the first position** (Computation 2.1): **4.37 per cent.**
3. **Exactly 0 at the second** (Computation 2.1): **not one policy of insurance.**
4. **126 at the third** (Computation 2.1): **68.85 per cent.**
5. **The ratio is $126/8 = 15.75$** (Observation 2.4): **it divides.**
6. **24.41 per cent overall** (Observation 2.6): **describing none of the three.**
7. **94.03 per cent of silent errors at the third** (Computation 3.1): **an even spread gives 33.3.**
8. **32 of 61 are four-fold degenerate** (Observation 3.3): **more than half.**
9. **The second preserves polarity least** (Observation 4.2): **0.375000.**

10. A two-tiered defence (Observation 4.5): **do not change; change to something close.**

Closing: the genetic code specifies 20 amino acids with 64 codons, leaving a surplus of 43—and that surplus is not distributed evenly. Over the 61 sense codons there are 183 single-base substitutions at each position and 549 in total—of which those leaving the amino acid unchanged number 8 at the first position, 0 at the second and 126 at the third. At the second position it is exactly zero—all 183 substitutions change the amino acid; not one policy of insurance was bought there. At the third, 68.85 per cent change nothing and more than two thirds pass in silence. The ratio is $126/8 = 15.75$, which divides exactly once the common denominator 183 is cancelled. The 8 at the first position is small but not zero (4.37 per cent), coming from the six-fold degeneracy of leucine and arginine. The redundancy is gathered in one place—of the 134 silent errors, 94.03 per cent are at the third position, where an even spread would give 33.3 per cent. Of the 61 sense codons, 32 are four-fold degenerate at the third position (24 two-fold, 3 three-fold, 2 not degenerate), so for more than half the codons the third letter carries no information. As in Paper 391, where the mean of the “wave height” was not representative, a “mutation rate of 24.41 per cent” fits none of the three positions. And when it does change, the manner of the change also differs—among non-synonymous substitutions the fraction preserving the polarity class is 0.375000 at the second position, the lowest of the three. Zero synonymous substitutions, and the lowest preservation of character as well. Even so 37.5 per cent preserve the class, so with no first line of insurance a second line remains. The defence is two-tiered—first “do not change it”, then “change it to something close”—and which tier acts differs by position. One thing does the separating—not how many bases changed, but which position changed. The position with the lowest synonymous rate also preserves polarity least; by chance the two could have pointed opposite ways. So “one mutation occurred” is not enough information: without the position the weight is undetermined, across a range of 15.75. By the criterion of Paper 300 the three positions are different-root, playing different roles in tRNA recognition. To be honest—both 15.75 and 94.03 per cent are counts of possibilities under an assumption of equally likely substitutions, and real mutations are biased by base type. What does not move is that the second position has exactly zero synonymous substitutions, and that $126/8$ divides exactly. One last thing—three letters is one letter more than 20 outcomes require ($4^2 = 16 < 20 \leq 64 = 4^3$). The surplus was not discarded; it was placed, all in one position, as margin against error.

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