

THE FUNCTIONAL SPECTRUM OF HUMAN VARIATION NOTES

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ABSTRACT. Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magnam aliquam quaerat voluptatem. Ut enim aequale doleamus animo, cum corpore dolemus, fieri tamen permagna accessio potest, si aliquod aeternum et infinitum impendere malum nobis opinemur. Quod idem licet transferre in voluptatem, ut postea variari voluptas distinguere possit, augeri amplificarique non possit. At etiam Athenis, ut e patre audiebam facete et urbane Stoicos irridente, statua est in quo a nobis philosophia defenda et collaudata est, cum id, quod maxime placeat, facere possimus, omnis voluptas assumenda est, omnis dolor repellendus. Temporibus autem quibusdam et.

1. UNDERSTANDING PURIFYING SELECTION

The purpose of figure 3 from *An integrated map of genetic variation from 1,092 human genomes* [1] is to illustrate the role of purifying selection within and between populations. Critically, this first requires a discussion of purifying selection. Purifying selection is a type of background selection. When mutations occur in the genome which are highly deleterious, offspring do not survive long enough to pass on these mutations to subsequent generations, at least on longer timescales [2]. When this background selection occurs, the observed genetic diversity is lower than what would be expected under neutral substitution. However, these dynamics exist within the broader population level timescales and periodic deleterious mutations do appear to exist on short time scales.

The Genomic Evolutionary Rate Profiling Score (GERP(1)) scores provide a way of measuring which sites likely lead to deleterious mutations. This statistical framework provides a way of estimating the difference between the expected number of mutations under a neutral substitution model (which assumes no impact on fitness) and the observed variation. Positive GERP(1) scores thus represent fewer mutations than would be expected, likely indicating a more conserved site, while negative scores would indicate more substitutions than expected.

2. FIGURE 3

2.1. **Panel A.**

2.2. **Panel B.**

2.3. **Key conclusions.**

GLOSSARY

GERP(1) The Genomic Evolutionary Rate Profiling is a statistical approach to quantify the deficit of substitutions in base pairs based on neutral the neutral rate of substitution. The neutral rate of substitution is an estimate of the number of new mutations per each generation multiplied by the probability that the substitution reaches fixations. In cases where neutral mutations exist, the rate of substitution will be equal to the rate of mutations. The GERP(1) Score thus indicates the deviation from the neutral rate of substitution indicating that positive scores will indicate that fewer substitutions have taken place than would be expected under neutral substitution while negative scores indicate that more substitutions have taken place than would be expected under the neutral model.

→ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1172034/>

REFERENCES

- [2] Cvijović, I., Good, B. H., & Desai, M. M. (2018, August). The Effect of Strong Purifying Selection on Genetic Diversity. *Genetics*, 209(4). <https://doi.org/10.1534/genetics.118.301058>
- [1] 1000 Genomes Project Consortium, T. (2021, November). An integrated map of genetic variation from 1,092 human genomes. *Nature*, 491. <https://doi.org/10.1038/nature11632>

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