Bornberglab
Molecular Evolution and Bioinformatics

MSc Thesis

neORFs Selection

Calculating positive selection on conserved neORFs

Background: Genomics changes can turn ancestrally non-genic sequence into new Open Reading Frames (neORFs). These represent an important source of novelty for species to adapt and evolve. Despite this importance, most neORFs experience a rapid birth-and-death lifecycle. It remains unclear what mechanisms help the small fraction of neORFs to escape their rapid life cycle to persist and become retained within their genome. One potential mechanism this project will explore is if neORFs persist by being under direct selection themselves.

Objectives: To test this hypothesis, the student will be given a list of pre-identified human neORFs. The student will then use a published whole genome alignment and extract alignments containing the neORFs. Then using PAML the students will calculate d_N/d_S to determine how many of the neORFs are under selection and compared with the neORFs relative age. If time remains, selection will also be determined using the McDonald-Kreitman test.

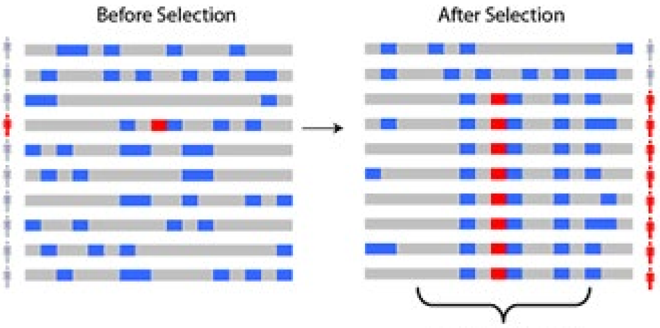

Figure from Schaffer & Sabeti 2008 illustrating the effect of positive selection on changing the frequency of genetic elements.

Requirements:

- Interest in genomics and bioinformatics
- Experience or willingness to learn coding

Methods: The student will learn some of the comparative genomic techniques including file manipulation, extraction of subregions from whole genome alignment, using PAML, and if time permitting, methods to characterize the new *de novo* genes.

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Selected Literature:

1. Zhao L, Svetec N, Begun DJ. De Novo Genes. Annu Rev Genet. 2024 Nov;58(1):211-232. doi: 10.1146/annurev-genet-111523-102413. Epub 2024 Nov 14. PMID: 39088850; PMCID: PMC12051474.
2. Schlötterer C. Genes from scratch--the evolutionary fate of de novo genes. Trends Genet. 2015 Apr;31(4):215-9. doi: 10.1016/j.tig.2015.02.007. Epub 2015 Mar 12. PMID: 25773713; PMCID: PMC4383367.
3. Schaffner S, Sabeti P. Evolutionary Adaptation in the Human Lineage. Nature Education. 2008; 1(1):14 https://www.nature.com/scitable/topicpage/evolutionary-adaptation-in-the-human-lineage-12397/
4. Álvarez-Carretero S, Kapli P, Yang Z. Beginner's Guide on the Use of PAML to Detect Positive Selection. Mol Biol Evol. 2023 Apr 4;40(4):msad041. doi: 10.1093/molbev/msad041. PMID: 37096789; PMCID: PMC10127084.