

Master's Thesis

MSLS: Applied Computational Life Sciences

Title of project / Master's thesis	How does an ancient protein expression regulation mechanism affect how the choice of codons in DNA?
Track	Digital Life Sciences
Topic / Key words	population genetics, codon usage bias, mathematical modeling, programming
Supervisor	Victor Garcia, ZHAW / IAS
Co-Supervisor	Maria Anisimova, ZHAW / IAS
External partners	
Place(s) of work	Wädenswil
Abstract	<p>The discovery of synonymous codon usage bias (CUB) –the unequal use of codons that code for the same amino-acid– has strengthened the notion that synonymous mutations can alter the fitness of organisms, and with it, their evolution. Synonymous or silent mutations are mutations in DNA that do not alter the encoded amino acid sequence. Since CUB cannot be explained by neutral mutational biases alone, it has been concluded that it arises from the fitness effects of silent mutations. However, the target of the selection pressure giving rise to CUB remains debated. The translation efficiency hypothesis states that CUB emerges from selection for codons that match the most abundant iso-accepting tRNA, whose use improves translational efficiency and accuracy. In this way, protein expression may be fine-tuned by appropriate codon choice. Other mechanisms also alter translation to regulate protein expression, such as -1 programmed ribosomal frameshifting (-1 PRF). -1 PRF is an evolutionarily ancient mechanism found across all domains of the tree of life, in which ribosomes are induced to 'slip' or frameshift at particular slippery sites. Such slipping leads to the discarding of the protein product and mRNA, thereby diminishing protein expression. In this project, the successful student applicant will aim to study how -1 PRF signals in mRNA affect CUB, and what these modifications of CUB reveal about the nature of translational selection.</p>
Requirements	Knowledge of R, python, basic algebra and optimization techniques
Comments	
Date of document	20.7.2020
Contact	Victor Garica, gara@zhaw.ch