## Accuracy of codon reading by transfer RNAs and termination factors

Translation of the genetic code on ribosomes requires recognition of 61 sense codons by amino acid carrying transfer RNAs and recognition of 3 stop codons by termination factors, two in *bacteria* and one in *eukarya*. mRNA translation and termination of protein synthesis have evolved to high speed and high accuracy. The accuracy of sense codon reading relies on Watson-Crick base pairing between the three codon bases of mRNA and the three anticodon bases of tRNAs cognate to the codons, but also on ribosome aided stereo-selection of the codon-anticodon helix. The accuracy of tRNA recognition is greatly enhanced by a two-step mechanism consisting of initial selection and proofreading selection, where the two steps are separated by GTP-hydrolysis on elongation factor Tu in ternary complex with tRNA and GTP. The accuracy of termination of protein synthesis relies on specific interactions between the amino acid residues of termination factors and stop codons, in a one-step mechanism lacking proofreading.

We will discuss structural elements of codon-anticodon interactions and codon-release factor interactions of importance for the accuracy genetic code translation and define the intrinsic single step selectivity of codon reading (*d*-value), the actual (current) selectivity of single step reading (*I*-value for initial and *F*-value for proofreading). We will discuss the speed-accuracy trade-off of single step codon reading: when the *I*- or *F*-value approaches the *d*-value the rate of codon translation necessarily goes to zero. The working principle of proofreading and its manifestation in codon translation will be discussed along with biochemical experiments to estimate *I*- and *F*-values as well as intrinsic *d*-values. Calibration of biochemical systems to the accuracy of codon reading in the living cell will be discussed along with criteria for optimal translation accuracy for maximal fitness of growing cells. Finally, some subversive experimental data, relating to combinations of ribosomal accuracy mutants, which apparently contradict current ideas of how ribosomes modulate the accuracy of codon reading will be mentioned.