

The phenomenon of secondary structure and codon usage of mRNAs

Markus Fricke¹⁻³, Ruman Gerst¹, Michael Niepmann⁴,
Manja Marz^{1-3,5,6}

¹*Faculty of Mathematics and Computer Science, Friedrich Schiller University Jena, Germany;* ²*German Centre for Integrative Biodiversity Research (iDiv), Halle-Jena-Leipzig, Germany;* ³*European Virus Bioinformatics Center (EVBC), Jena, Germany;*
⁴*Justus-Liebig-University, Giessen, Germany;* ⁵*FLI Leibniz Institute for Age Research, Jena, Germany;* ⁶*Michael Stifel Center Jena, Germany;*
markus.fricke2@uni-jena.de, manja@uni-jena.de

The discovery of non-coding RNAs shaped our knowledge of RNA secondary structures regulating most molecular biological processes. However, the secondary structure of mRNAs has been described only for very few cases. It remains an open question how secondary structure and amino acid sequence influence each other. Generally, three possibilities have been considered for the relationship between amino acid sequences and mRNA secondary structure (1) codon sequence and secondary structure are independent. That would mean that only the codon sequence is under selection pressure and the most stable RNA secondary structure is determined by the codon sequence; (2) natural selection between synonymous codons could permit the optimization of RNA secondary structure; and (3) selection pressure for specific RNA secondary structures could influence the choice of triplets at both synonymous and non-synonymous positions in the mRNA. We systematically describe the influence of RNA secondary structures to protein-coding RNAs of all major life forms, including viruses, bacteria, archaea, protozoa, plants, fungi, invertebrates and mammals. We found a strong base-pair bias of mRNA secondary structures at both synonymous and non-synonymous codon positions. We show this bias does not occur by chance, is not triggered by single specific base-pairs and is not affected by folding algorithms. The observed bias is an indicator for a co-evolution between RNA secondary and the underlying codon distribution. We propose, that the RNA secondary structure increases the mRNA lifetime and also ribosomal density. Both factors positively influence the ribosomal translation elongation. Based on the strong base-pair bias and the proposed dual function, the mRNA secondary structure could be one of the major factors influencing the codon bias and the ribosomal translation elongation.