

Project 4.5. Protein folding and aggregation on the ribosome (theoretical)

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Background:

Ribosome is a molecular machine for protein synthesis which consists of four phases of translation - initiation, elongation, termination and ribosome recycling. This process is an area of intense research due to the essential role of proteins to life. For many decades, protein folding research has been dominated by the assumption that thermodynamics determines protein structure and function. However, recently accumulated evidence has supported the emerging paradigm of non-equilibrium control of protein behavior. Namely, speed of synthesis of proteins in the ribosome greatly influences their properties, mRNA sequence evolution, and protein aggregation in bulk related to diseases.

Aim:

Changes in codon translation rates have recently been shown to alter a protein's function but not necessarily its solubility, suggesting that structural changes in the nascent protein must be modest because otherwise aggregation would likely occur. One of the main goals is explore how extensive these structural rearrangements may be by simulating the synthesis of proteins that dimerize and calculating how their binding affinity changes as codon translation rates are altered.

Formation of disulfide bonds is very important for the folding of the protein and its functions. Recent experiments suggested that the speed of synthesis of proteins in the ribosome influences the formation of disulfide bonds in bulk. Therefore, this project is aimed at understanding this interesting phenomenon by using computational modeling.

Requirements:

The project will involve a lot of numerical simulations, and hence good programming skills are needed. A master's degree in physics, chemistry or computer science is required. Knowledge of biophysics, biology or biochemistry will be beneficial. Fluent command of spoken and written English is required.

Funding:

Scholarship: NCN grant funding of 5000 PLN per month, before subtracting obligatory employer and employee social security contributions, for 36 months. Afterwards, standard Polish PhD scholarship.

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