- 2018/31/D/ST5/01866 [2019-2022] Od pojedynczej cząsteczki do inteligentnego materiału - zrozumienie tworzenia się i właściwości kompleksów polipeptydów - dr. inż. P. Batys

1. Research project objectives/Research hypothesis

The molecular level understanding of thermal and mechanical properties in hydrated polyelectrolyte complexes (PECs) is limited and the lack of relevant information in the literature can be observed. Our recent findings, reveal that PECs properties are related with the number of the intrinsic polycation-polyanion pairs and water molecules around them. The number of intrinsic pairs, on the other hand, strongly depends on the polyelectrolyte physicochemical properties, such as effective charge or conformation and, therefore, on the assembly conditions. Understanding how these factors contribute and linking the assembly conditions with the properties of the final material in a quantitative manner will serves as an extremely useful predictive tool for the designing the PECs with well-defined and tuneable properties. To achieve this goal, the following research objectives are proposed:

✓ *Objective 1: Explore and determine the role of pH and ionic strength on the single polypeptide molecule physicochemical properties in solution.*

How does the pH and ionic strength affect the effective charge and molecule conformation of polypeptide? The changes in pH close to the polypeptide isoelectric point are expected to strongly influence the ionization degree of the molecules and, therefore, its conformation and secondary structure.

✓ *Objective 2: Examine and understand the mechanism and thermodynamics of the polypeptide complex formation.*

What is the mechanism of the polypeptide complex formation and how the energetic and entropic factors contribute at various pH and ionic strength? Polypeptide association is expected to change from entropy driven to enthalpy driven when the molecule effective charge decreases.

✓ *Objective 3: Determine the polypeptide complexes structure and their properties dependence on the assembly process conditions.*

To what extent we are able to control mechanical or thermal properties of PEC, just by the assembly conditio modification? The solution pH, ionic strength determine polypeptide's conformation and effective charge in solution. These, in turn, implicate the number of intrinsic and extrinsic ion pairs formed in PEC. The PI and co-workers will complete these objectives via molecular modelling and experimental studies. The work is enhanced by the collaboration with Prof. Markus Linder and Dr. Maria Sammalkorpi (Aalto University, Finland) as well as Prof. Jodie Lutkenhaus (Texas A&M University, USA)

2. Research project methodology

The primary methodological approach for this research is atomistic molecular dynamics (MD) simulations, conducted using the latest GROMACS software suite. We will use a standard computational chemistry MD setup, an explicit water model, ions, and PME electrostatics. To improve conformational sampling and initial relaxation, replica exchange and coarse-grained MD methods will be applied, respectively.

Experimental investigations will primarily encompass the characterization of polypeptides in solution at different conditions (pH and ionic strength) via density and viscosity measurements, light scattering methods, i.e., dynamic light scattering and laser Doppler velocimetry, as well as the sedimentation velocity experiments using analytical ultracentrifuge. To gain insight in thermodynamics of polypeptide complex formation, the isothermal calorimetry method will be used. The dynamic mechanical analysis and differential scanning calorimetry measurements, will determine respectively the mechanical response and the states of the water molecules in PECs assembled at different conditions.

3. Expected impact of the research project on the development of science

Completing the above mentioned objectives will:

✓ Provide quantitative relationship between the polypeptide properties and the assembly conditions, i.e., solution pH and ionic strength

✓ Reveal the mechanism and thermodynamics of polypeptide complexation

✓ Provide molecular level understanding of the PECs properties and link them with single molecule physicochemical properties. These, enable for a better assembly process control and quantitative connection between its conditions and the final PEC structure. This could be a breakthrough in the designing the PECs with well-defined and tuneable properties. Additionally, as the PECs still remain an extremely interesting and undiscovered research direction, the results of this project are expected to increase our general knowledge in the field of polypeptides, their complexes and its applications. Specifically, the project outcome will be beneficial for the development of new smart materials for the medical and biotechnological application, which requires non-toxic polyelectrolytes, such as polypeptides.