Precipitation vs complex coacervation in proteins/polyelectrolyte lysozyme-based complexes of opposite charge: the influence of polyelectrolyte charge density and stiffness

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When proteins and polyelectrolyte of opposite charges are mixed, they form a solution of electrostatic complexes that may either precipitate or coacervate (i.e liquid-liquid phase separate). While it is of utmost importance for numerous applications purpose (proteins purification, food, drug release…) to determine which kind of phase transition would occur for given physico-chemical conditions, the mechanisms of complex coacervation are yet not fully understood. It is however now widely accepted that the first step of complex coacervation is the formation of soluble complexes formed by the oppositely charged individual species. The remaining questions for the understanding of complex coacervation concern thus the role of interactions between soluble complexes for the phase transition once they are formed.

This is in this framework that we will show how the charge density and stiffness of polyelectrolyte influences the surface charge density and shape of soluble complexes, which lead to either precipitation or coacervation. We will compare three proteins/polyelectrolyte systems based the same protein, lysozyme, a positively charged globular protein, and the following negatively charged different polyelectrolytes: Polystyrenesulfonate, a flexible highly charged PE, hyaluronan, a poorly charged rigid PE, and pectin, which behavior is intermediate from the two other ones. A refined SANS structural analysis has enabled us to obtain a perfect description of the soluble complexes [1,2,3].

For both PSS/lysozyme and pectin/lysozyme, globular complexes of a few hundreds of proteins are formed. The complexes are denser and more charged with PSS. In the PSS/lysozyme case, the soluble strongly charged complexes repel electrostatically and form aggregates via a Reaction Limited Aggregation process [1]. The metastable aggregates then unambiguously precipitate [4]. In the pectin/case, the less charged and more solvated complexes may undergo a coacervation process. The phase transitions of soluble complexes coacervation resemble thus to the ones occurring in suspensions of simple colloids [5]: depending on the shape of interparticular potential between objects, either a precipitation or a fluid-fluid phase separation (i.e ‘gas-liquid’) occurs. In the case of pectin, the soluble complexes are made of 1-D rigid chains decorated by proteins. Such highly solvated complexes can thus coacervate.