Numerical Simulations on reentrant condensation of proteins

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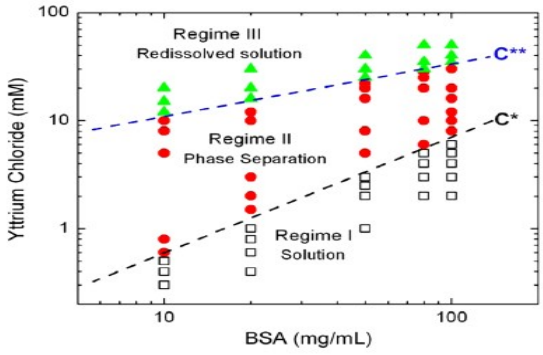
The highly interesting phenomenon of reentrant condensation of DNA and protein is imputed to correlations of multivalent ions. Reentrant condensation describes the phenomenon of the solution entering a condensed phase, which once again dissolves. This happens when adding multivalent ions to the solution, see left figure. While reentrant condensation has already been observed in systems like DNA or polyelectrolytes, it is a new and important but also to a large extent unknown field of research concerning proteins [1].



The whole phase diagram is shown on the right for the protein Bovine Serum Albumin with Y^{3+} as multivalent counter ions. The phase transitions, c* and c**, separate the different regions in the diagram. In [2] a set of proteins is studied and it turned out that the phase transition curves exhibit a linear dependence of counter ion and protein concentration. In addition, experimental measurements reveal that electrostatic interactions play a crucial role.

We developed a heuristic, general concept of metal ion-protein binding, where we assume a coordinative attachment of metal ions to the protein's surface: we combine the linear Poisson-Boltzmann theory with specific interactions between the strongly positive ions and local acidic sites to incorporate the correlation effect. This coordinative attachment is interpreted as an acid-base affinity. Thus, to elucidate the process a generalized titration model based on electrostatic interactions is developed. By introducing an affinity constant for the multivalent counter ions to bind to the acidic sites of the protein, the counter ions consecutively bind when increasing the counter ion concentration. By means of Monte Carlo Simulations we scanned the partition function to find the energetically optimal binding state of the ion-protein complex. From this we can deduce physical quantities such as the effective total charge and the effective dipole moment of the protein. Despite of the simplicity of our theoretical model the numerical results agree well with the experimental data.

[1] F. Zhang, A. Skoda, R. Jacobs, S. Zorn, R. Martin, C. Martin, G. Clark, S.Weggler, A. Hildebrandt, O. Kohlbacher, F.Schreiber, *PRL*, **2008**, *101*, 148101-1 - 148101-4.
[2] F. Zhang, S. Weggler, M. Ziller, L. Ianeselli, B. Heck, A. Hildebrandt, O. Kohlbacher, M. Skoda, R. Jacobs, F. Schreiber, submitted to PNAS, **2010**