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## Multivalent counterions-induced unusual stability of re-entrant protein against different denaturants

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Protein solution undergoes a re-entrant phase transition from one-phase to two-phase and then back to the one-phase in the presence of tri and tetravalent counterions [1]. Tri and tetravalent (unlike mono and divalent) counterions induce short-range attraction between the protein molecules, leading to the transformation from one-phase to two-phase system. The excess condensation of these higher-valent counterions in the double layer around the BSA causes the reversal of charge of the protein molecules resulting into re-entrant of the one-phase, at higher salt concentrations. Taking the benefit of charge condensation of multivalent ions around BSA protein, we have demonstrated the unusual stability of the protein against commonly used denaturants such as temperature and ionic surfactant using small-angle neutron scattering (SANS) [2]. Unlike monovalent counterions, which promote the denaturants-induced protein unfolding, the unfolding is restricted in the presence of multivalent ions. The observations are beyond the scope of general understanding of protein unfolding and are believed to be governed by the ion-ion correlations driven strong condensation of the multivalent ions.

### References

- [1] S Kumar, I Yadav, D Ray, S Abbas, D Saha, Vinod K Aswal, J Kohlbrecher. *Biomacromolecules*, 20, 2123-2134 (2019).
- [2] S Kumar, D Saha, D Ray, S Abbas, Vinod K Aswal, *Physical Review E*, 104, L012603 (2021).

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