From the crystal to the structure using « Molecular Glues »

Sylvain Engilberge

sylvain.engilberge@psi.ch

X-ray crystallography is the most common method used to solve protein structures leading to many discoveries with benefits ranging from drug design to bio-inspired nanomaterials. Crystallography is crucially dependent on protein crystallization which remains one of the major bottlenecks of the technique with the phase problem. « Molecular glues » such lanthanide complexes,[1] calixarenes[2,3] and cucurbiturils[4] can target residues on protein surfaces *via* supramolecular interactions, promote protein self-assembly[2] and crystallization.[1-4] The first part of my presentation will be focus on the development and the application of « molecular glues » in order to facilitate protein crystallization[1] and to achieve protein crystal engineering.[3,4] In a second part, I'll present how the phase problem in bio crystallography can be addressed *de novo* using either the anomalous signal of a lanthanide complex[5,6,7] or more simply the anomalous signal of sulfur atoms intrinsically present in biological macromolecules.[8]

1. **Engilberge, S.**; Riobe, F.; Di Pietro, S.; Lassalle, L.; Coquelle, N.; Arnaud, C.A.; Pitrat, D.; Mulatier, J.C.; Madern, D.; Breyton, C.; Maury, O.; Girard, E. *Chem. Sci.* 2017, 8, 5909-591
2. Rennie, M.L.; Fox G.C.; Pérez, J.; Crowley. P.B. *Angew. Chem.* 2018, *42*, 13960-13965.
3. **Engilberge**, **S**.; Rennie, M.L ; Dumont, E. Crowley, PB. *ACS nano* 13 (9), 10343-10350
4. Guagnini, F.; **Engilberge**, **S**.; Ramberg, KO; Pérez, J; Crowley, PB. *Chem. Comm*. 56 (3), 360-363.
5. **Engilberge, S**.; Riobé, F.; Wagner, T.; Di Pietri, S.; Breyton, C.; Franzetti, B.; Shima, S.; Girard, E.; Dumont, E.; Maury, O. *Chemistry.* 2018, 39, 9739-9746.
6. Vögeli, B.; **Engilberge, S.**; Girard, E.; Riobé, F.; Maury, O.; Erb, T.J.; Shima, S.; Wagner, T. *PNAS* 2018, 13, 3380-3385.
7. Bernhardsgrütter, I.; Vögeli, B.; Wagner, T.; Peter, D.M.; Cortina, N. S.; Kahnt, J.; Bange, G.; **Engilberge, S.**; Girard, E.; Riobé, F.; Maury, O.; Shima, S.; Zarzycki, J.; Erb, T.J. *Nat. Chem. Biol.* 2018, 14, 1127.
8. Basu, S.; Finke, A.; Vera, L.; Wang, M.; Olieric, V. *Acta Crystallogr D*. 2019, 75, 262–271.