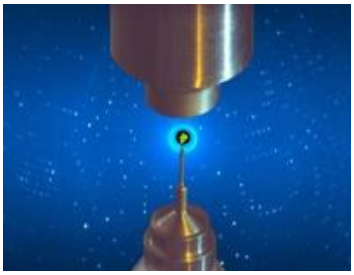

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Structural dynamics of substrate processing by the PAN-proteasome complex studied by TR-SANS

Wednesday, 9 June 2021 11:30 (20 minutes)

Crystallography and cryo-EM have provided new and exciting insight into protein substrate degradation by AAA+ ATPases and the PAN-proteasome system. However, direct structural information on the conformational changes of the working complex, as well as the respective substrate states and populations during the active unfolding and degradation process remain scarce.
Here, we apply time-resolved small angle neutron scattering (TR-SANS) to obtain structural insight into the respective components during the active process in solution. By combining solvent contrast variation and selective macromolecular deuteration with online fluorescence, we were able to obtain separate structural information on the conformational states of the protein unfoldase PAN and the GFP substrate during the active reaction on the sub-minute timescale [1, 2].
While PAN undergoes a reversible conformational contraction during the substrate unfolding process, GFP aggregates rapidly in the presence of PAN alone, but is being hydrolyzed very efficiently once the proteasome partner is added to the reaction.
TR-SANS is thus a very promising technique that can provide structural kinetics from individual partners in complex solution ensembles, impossible to separate by SAXS [3], and complementary to “static snapshots” from crystallography and cryo-EM.

[1] Ibrahim et al. (2017) Sci. Rep. 7, 40948
[2] Mahieu et al. (2020) Biophys. J. 119(2), 375
[3] Mahieu et al. (2020) EPJ Web of Conferences 236, 03002

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