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Tracking solution structures by scattering and modeling

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Small-angle neutron scattering (SANS), combined with ab initio modeling or coarse-grain simulations, has proven to be an essential technique for obtaining structural information on proteins when classical high-resolution methods (e.g. NMR, radiocrystallography) are not possible. SANS is a low resolution technique but has the advantage of being used in solution. Above all, the "contrast matching"method, only possible with SANS, is often the only one capable of removing certain obstacles and answer relevant questions in structural biology.

SANS is particularly suited to the study of membrane proteins by literally "turning off"the signal from the membrane and thus specifically probing the structure of the protein. I will illustrate this feature in two studies of membrane proteins:

(i) Structural changes of dystrophin, a filamentous peripheral membrane protein supporting the plasma membrane of muscle cells. Its absence due to genetic mutations leads to the severe Duchenne muscular dystrophy. Most of dystrophin consists of a central domain, made of 24 coiled-coil repeats. We probed by SANS, using stealth phospholipid bicelles, the solution structure of the R1-3 fragment, which is known to interact with membrane lipids.

(ii) The structural investigation of TSPO translocator protein, a ubiquitous and functionally important membrane protein of about 18 kDa, used as a marker in many brain diseases in humans. For mammalian TSPO, no crystals have yet been obtained and high-resolution structure determination remains challenging. We study the structure of mouse TSPO (mTSPO) in different amphiphilic environments, from detergents and lipid/detergent mixtures to more biomimetic environments such as nanodiscs.

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