# Solid-state NMR, synchrotron-radiation CD and oriented CD: a complementary toolbox for structural investigations of transmembrane proteins

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Membrane proteins and polypeptides are key players in many biological processes, as they control the flow of information and material between cells and their environment, and they are prime drug targets. Membrane proteins have been studied for decades, and many biochemical and biophysical aspects of lipid-protein interactions and function are well characterized. Detailed structural investigations of membrane proteins, on the other hand, still pose a great challenge for structural biology. Low expression yields, challenging purification procedures, difficult sample purification and stability, protein misfolding and aggregation are some of the drawbacks of membrane protein research. Moreover, conventional techniques for high-resolution structural determination such as NMR and X-ray crystallography have severe limitations when it comes to the hydrophobic world of the lipid bilayer, resulting in an astonishing low number of solved structures of membrane proteins. Membrane protein research is an aspiring and challenging task driven by the hope to gain insights and knowledge of how membrane proteins insert into the lipid bilayer, how they fold into their three-dimensional conformation how they align into their specific orientation, how they interact with other molecules, and what is going wrong in diseases.

Here we describe three complementary methods which are ideally suitable for membrane protein structure analysis: state-of-the-art synchrotron radiation circular dichroism (SRCD), oriented circular dichroism (OCD), and solid-state NMR. The key advantage of these methods is that they can be used to characterize the conformation, alignment and dynamics of membrane-bound peptides and proteins in the quasi-native environment of a lipid bilayer. A structural analysis of two interacting proteins is presented: the PDGF-receptor β is a receptor tyrosine kinase that gets activated by the oncogenic E5 protein via transmembrane helix-helix interactions [1,2]. A complementary PISEMA-NMR, SRCD and OCD analysis was used to resolve the structures and orientations of both proteins in their native lipid environment [3,4,5,6].

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