The signal enhancement provided by dynamic nuclear polarization based on the cross-effect enables to address molecular questions by solid-state NMR, which are difficult to approach otherwise. Especially for mechanistic studies of membrane proteins, DNP-enhanced MAS-NMR offers unique possibilities. On our experimental setup, enhancements between 40- and 100-fold are routinely achieved for membrane proteins within lipid bilayers (400 MHz/263 GHz, biradicals as polarizing agent, MAS at 8-10 kHz, T=100K), which enabled a range of novel applications:

(a) **Trapping intermediate states**: Channelrhodopsin-2 (ChR2) is a light-gated ion channel, which has attracted considerable interest because of its unparalleled role in optogenetic applications. The link between photocycle and channel gating is still unclear and the chromophore conformation has been disputed. We have established a DNP setup for *in situ* sample illumination. Important functional intermediate states could be trapped in thin ChR2 films. Using $^{15}$C-labelled retinal within $^{15}$N-ChR2, we were able to show unambiguously an all-trans conformation for the retinal co-factor in the groundstate. The retinal conformation was characterized by bond-length and torsion angle measurements. DNP enabled the first NMR studies on ChR2 groundstate and intermediates.

(b) **Visualizing cross-protomer contacts in membrane protein complexes**: Membrane proteins often form oligomeric complexes within the lipid bilayer, but factors controlling their assembly are difficult to determine. Here, we demonstrate for the pentameric proteorhodopsin, how such interactions could be visualized. The oligomeric complex has been has been re-assembled in the membrane from differently labeled protomers. Cross-protomer contacts can be detected e.g. by applying e.g. $(^{15}$N)$^{15}$C-TEDOR experiments. The low number of unique spin pairs in these mixed complexes makes the use of DNP mandatory. The presented approach is universally applicable and opens the door toward analyzing membrane protein interactions within homo-oligomers directly in the membrane.

(c) **Structural analysis of substrates in complex with membrane proteins**: The DNP enhancement has also allowed us to approach challenging cases such a mammalian G-protein coupled receptors and ABC transporters for which first data will be presented. In addition, precise structural rearrangements responsible for color tuning within proteorhodopsin could be detected.

From the technical point of view, novel concepts for optimizing polarizing agents based on host-guest chemistry will be presented and practical aspects such as sample handling and doping will be discussed. In addition, novel experiments at the interface between solid- and liquid state NMR towards high temperature DNP utilizing aligned lipid bilayers will be introduced.