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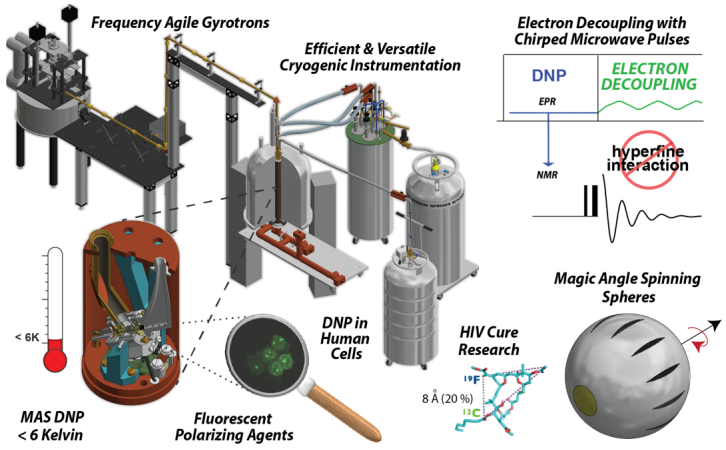
Magic Angle Spinning Spheres, Time Domain Electron Decoupling, and MAS DNP Below 6 Kelvin

Prof. Alexander Barnes
Laboratorium für Physikalische Chemie, ETH Zürich

NMR spectroscopy can elucidate atomic level structure and motion of chemical architectures ranging from the surface of materials to biomolecules within intact cells. Yet, NMR is plagued by poor sensitivity—solid state NMR signal averaging can last from minutes to months. In order to increase NMR sensitivity by more than factors of 50,000, our laboratory is inventing novel technology and developing new spin physics methodology. Critical to our efforts is the utilization of electron paramagnetic resonance (EPR) to transfer enhanced sensitivity from electrons to nuclei in a process known as dynamic nuclear polarization (DNP). Continuous wave (CW) DNP approaches at a sample temperature of 100 Kelvin can boost NMR signals by factors of 1000 in favorable samples.[1] To extend on this now commercially available technology, we are developing pulsed DNP spectrometers (analogous to pulsed EPR and NMR) and cooling spinning samples to 4.2 Kelvin.[2,3,4] Pulsed EPR control in conjunction with magic angle spinning (MAS) also enables us to remove detrimental electron-nuclear spin interactions by decoupling the electron spins.[5]
Utilizing the superb precision of solid state NMR structural measurements, we have resolved the conformational entropy present within an ensemble of (protein kinase C) PKC ligands.[6] PKC is a drug target of latency reversal agents important to HIV cure research.[7] The conformational entropy maps well onto the results of long (>500 microsecond) molecular dynamics trajectories.
Advancements in DNP instrumentation and methodology are being applied to study the ligand binding pocket of PKC regulatory domains in vesicles. Whereas site specific ^{13}C labeling of PKC domains affords resolution in cryogenic MAS DNP spectra *in vitro*, isotopic enrichment of ligands will extend these studies to binding characterization within intact human cells.[8] Novel fluorescent DNP polarizing agents are being developed to determine the sub-cellular localization of PKC ligands for in-cell NMR and show targeted DNP enhancements in HEK293 cells.
Lastly, in order to access magic angle spinning frequencies > 100 kHz , cool samples to temperatures <5 K with economical helium consumption rates, and improve microwave coupling, we have introduced spherical rotors for magic angle spinning.[9]



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