INTEGRATED SOLUTIONS AND CUTTING EDGE INSTRUMENTATION

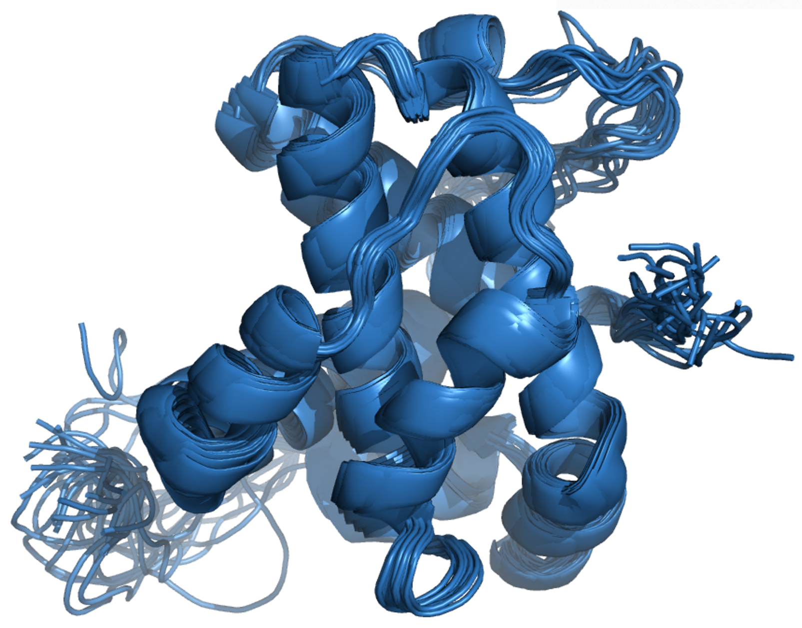
Magnetic Resonance in Structural Biology Research

Bruker is committed to bringing users the best possible performance and experience when working with biological molecules using NMR. These ongoing efforts include hardware developments, such as a wide variety of probes or pushing the boundaries with Ultra-High Field magnets, as well as tools for ease of use and convenience, such as DynamicsCenter, bioTop, or lately the NMRtist cloud platform.

The NMRtist Cloud Platform: Protein Assignment and Structure Determination

State of art machine learning tools such as the NMRtist[1] platform using the ARTINA[2] algorithm fully automate peak picking, assignment, and structure determination of proteins based on NMR data.

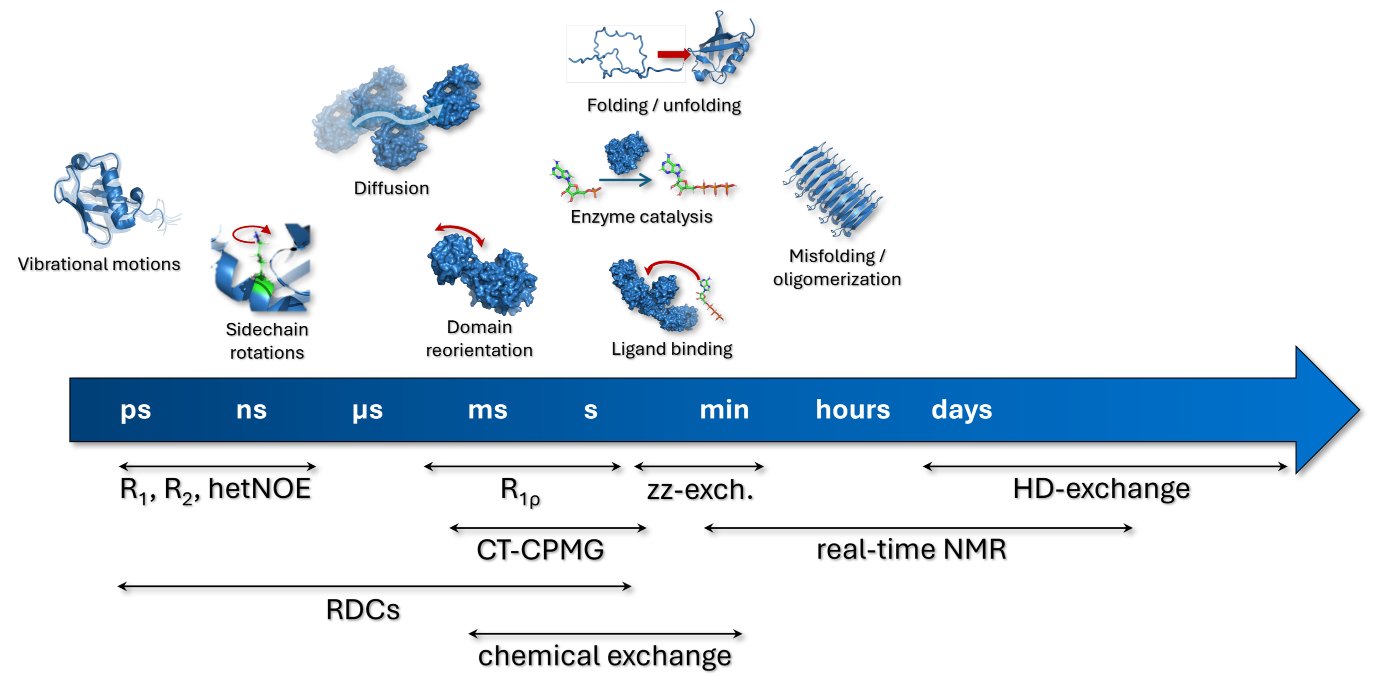
Taking the tedious tasks of peak picking and assignment off your hands, these tools not only simplify the task of protein structure determination but also reduce the time required from months to days or weeks.



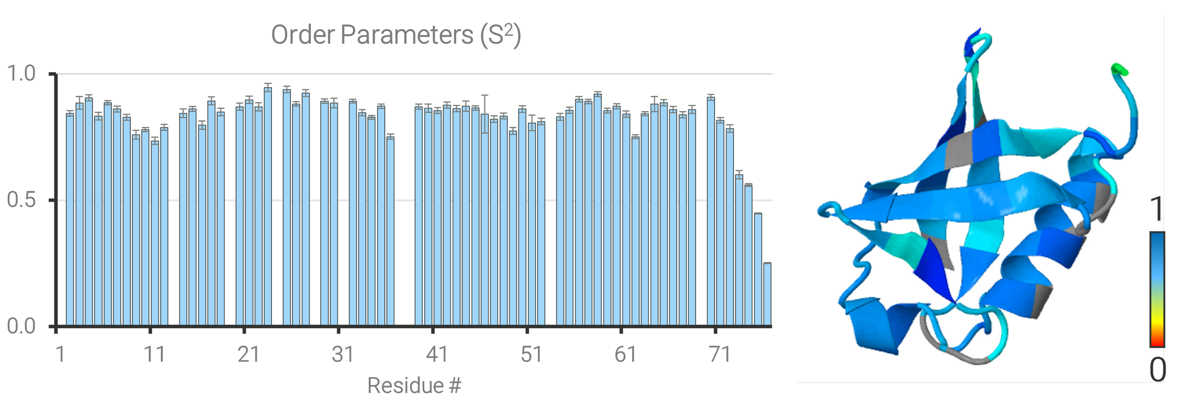
Example of a protein structure, determined using NMRtist. The structure of this fully labeled 19.5 kDa cancer related protein has been determined in full automation. Total measurement time was 2 weeks followed by a 24 hour NMRtist run.

Dynamics at Atomic Resolution

Dynamic information is often crucial for understanding the biological function of biomolecules, such as proteins or RNA. The combination of bioTop for acquisition and processing, NMRtist for automated assignments, and DynamicsCenter for analyzing acquired relaxation experiments makes obtaining this type of information easier and quicker than ever before.



Motion timescales with associated NMR experiments and biological processes.



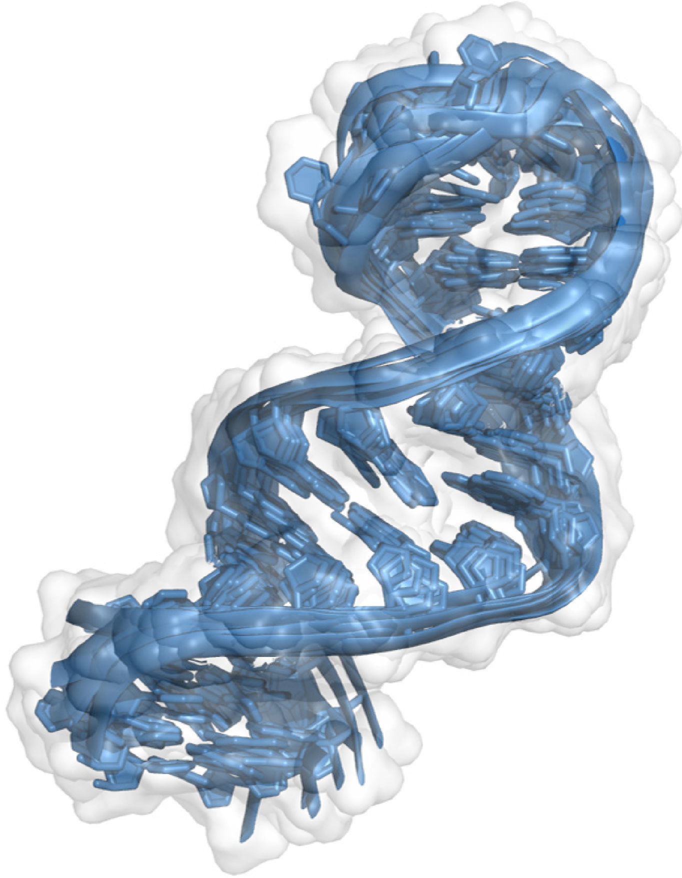
Order parameters (~rigidity) for ubiquitine, determined using bioTop, DynamicsCenter and assignments from NMRtist.

NMR on RNA

Because of its very dynamic nature, RNA is ideally suited to be studied by NMR, while also very challenging for a lot of other biophysical techniques.

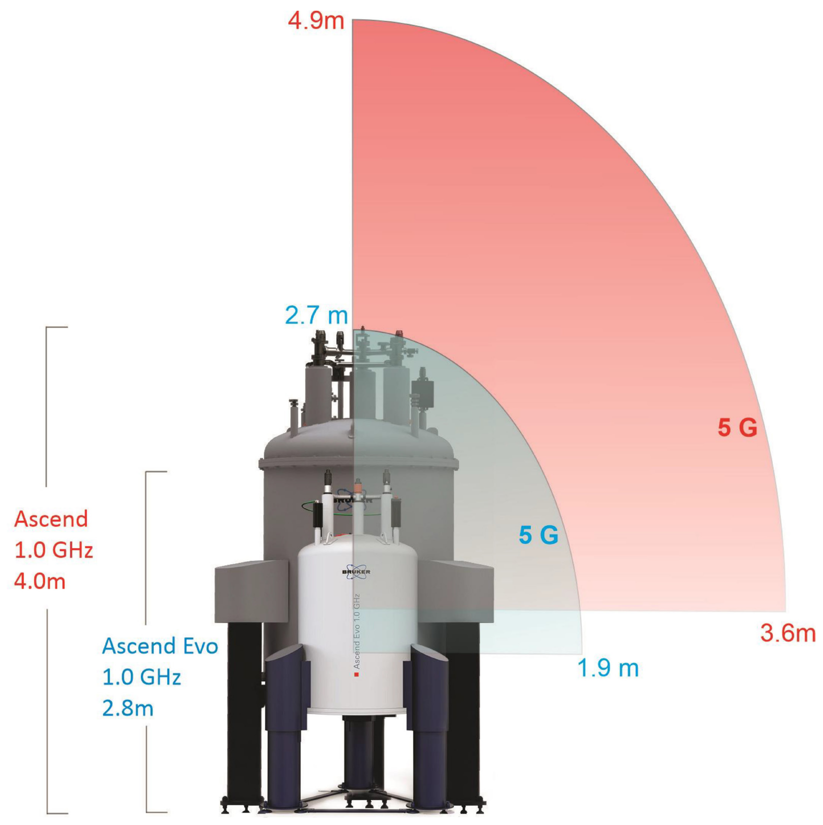
Recent advancements in the field of NMR, such as easy to site high-field magnets, like the Ascend EVO 1 GHz, benefit RNA research to a large extent.

5'-terminal stem loop RNA from SARS-CoV-2 studied by NMR[3].



Cutting Edge Instrumentation for Biomolecular NMR

Ultra-High Field magnets benefit biomolecular NMR by providing both increased resolution as well as enhanced sensitivity. Further field dependent effects, such as the TROSY[4] effect make use of increasing field strengths. While systems such as 1.2 GHz push the boundaries of what can be accessed by NMR, only slightly smaller systems such as the Ascend EVO 1 GHz system, make it easier than ever to site a high field instrument.



Modern CryoProbes offer an increased sensitivity, which is much needed for the often concentration- or quantity-limited samples in the area of biomolecular NMR. At the same time, CryoProbes have become extremely robust, especially when utilizing high RF duty cycles. This makes them the ideal tool when carrying out demanding experiments such as ^{15}N CPMG relaxation dispersion to study exchange processes or transiently low populated states.

Conclusion

- The fully automated NMRtist cloud platform provides easy access to assignment and structure.
- Challenging molecules such as flexible nucleic acids can be studied in a native-like environment.
- Dynamics at atomic resolution provide detailed insights into molecular function.
- CryoProbes deliver increased sensitivity while also being extremely robust, allowing the most demanding experiments.
- Ultra-High Field magnets are pushing the limits in terms of the size and complexity of biomolecules being accessible.

Integrated Solutions for Structural Biology

Literature References

1. P. Klukowski, R. Riek, & P. Güntert, NMRtist: an online platform for automated biomolecular NMR spectra analysis, Bioinformatics (2023)

2. P. Klukowski, R. Riek, & P. Güntert, Rapid protein assignments and structures from raw NMR spectra with the deep learning technique ARTINA. Nature Communications 13, 6151 (2022)

3. A. Wacker, H. Schwalbe et. al., The 5'-terminal stem–loop RNA element of SARS-CoV-2 features highly dynamic structural elements that are sensitive to differences in cellular pH. Nucleic Acids Research, gkae477 (2024)

4. L. Pervushin, R. Riek, G. Wider & K. Wüthrich, Attenuated T2 relaxation by mutual cancellation of dipole–dipole coupling and chemical shift anisotropy indicates an avenue to NMR structures of very large biological macromolecules in solution, Proc. Natl. Acad. Sci. 94 (23) 12366-12371 (1997)