NMRtist - A Cloud Based All-in-One Solution for Protein Assignment and Structure

NMRtist[1] is a cloud based, AI supported software platform which has been developed by the group of Roland Riek at the ETH Zurich. It utilizes the underlying ARTINA[2,3] algorithm to perform protein spectra analysis including peak picking and assignment in full automation.

Bruker and the group at the ETH in Zurich have entered a collaboration to provide an even easier to use platform to perform these traditionally very time-consuming tasks, executed by a trained expert.

Peak Picking

The ARTINA algorithm consists of the three individual steps which can be executed separately or in consecutive order.

The ARTINA peak picking application uses a deep convolutional neural network to detect positions of signals in the selected NMR spectra. For each spectrum, the method returns peak lists in various formats. Additionally, the application performs a spectrum referencing check, verifying relative shifts between pairs of spectra that record frequencies of the same atoms.

ARTINA
peak picking

Fig. 1: Examples of automatically calculated structures using NMRtist (yellow) versus original PDB deposited structures in blue.

Resonance Assignment

The second step is resonance assignment. What usually is a days- or weeks-long undertaking can be automated and executed in a matter of minutes or hours.

The ARTINA shift assignment application first uses a deep convolutional neural network to detect positions of signals in the selected NMR spectra (see ARTINA peak picking application above). Afterwards, the detected signals undergo FLYA[4] automated chemical shift assignment. The method returns protein chemical, together with assigned peak lists for the individual NMR spectra.

ARTINA
shift
assignment

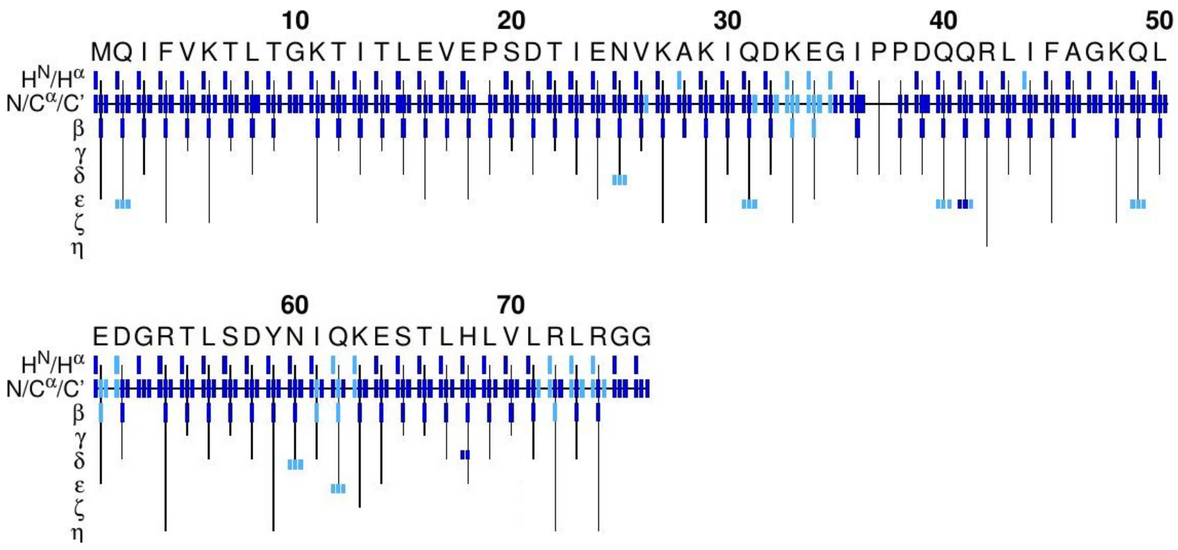

Fig. 2: Example of an automated assignment result succeeding fully automated peak picking

3D Structure Calculation

3D Structure determination using NMR is very often turned towards when proteins or other biomolecules cannot be crystallized or, more likely nowadays, AI based predictions are questioned and have to be verified or refined. The task however is time-consuming and often requires an expert with experience in the required software packages.
The ARTINA structure determination application implements end-to-end protein structure solving. Given a set of spectra and a protein sequence as input, the application generates the abovementioned peak lists and assignments, followed by a fully automated structure calculation using CYANA[5].

ARTINA
structure
determination

Next Steps

Working together with the developers at the ETH in Zurich, Bruker will provide the users with a high performance, secure platform to run ARTINA jobs. Security will be provided using state of the art cloud infrastructure as well as regular security audits by 3rd parties.

In addition, Bruker will provide and interface from within TopSpin and bioTop to integrate the NMRTist platform seamlessly into other workflows, for example using automated assignment results to determine protein dynamics.

References

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

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

3. Klukowski, P., Riek, R. & Güntert, P. Time-optimized protein NMR assignment with an integrative deep learning approach using AlphaFold and chemical shift prediction, Science Advances, 2023.

4. Schmidt, E., & Güntert, P. (2012). A new algorithm for reliable and general NMR resonance assignment. Journal of the American Chemical Society, 134, 12817-12829.

5. Güntert, P. & Buchner, L. (2015). Combined automated NOE assignment and structure calculation with CYANA. J. Biomol. NMR 62, 453-471.

From spectra to assignment and structures

- Cloud based, AI supported software platform
- Fully automated peak picking of multidimensional NMR spectra
- Performs resonance assignment, thereby simplifying the most time-consuming task in biomolecular NMR
- Fully automated structure determination
- High performance, secure cloud architecture
- Upcoming integration of automated assignments into other workflows