Development of an Algorithm to Filter and Assign Signals in Protein NMR Spectroscopy to Accelerate Drug Discovery

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Given the importance of protein Nuclear Magnetic Resonance (NMR) spectroscopy, the goal was to develop an algorithm to filter and assign signals to accelerate drug discovery. From the 4D NOESY of spindle and kinetochore-associated protein 1 (Ska1), a linewidth ratio matrix was created for signal (SLWR) and non-signal (NLWR). 4,000 t-tests were conducted between the matrices to compute the accuracy of the signal filtering. To assign signals, a Structure Route Map Matrix (RMM) with angstromal distances between Alanine, Isoleucine, Leucine, and Valine and 3x3 matrix predictions of cross-peak type, strength, and quantity was matched with the 4D experimental data. The signal filtering component of the algorithm returned a 95.1% classification accuracy and the assignment component of the algorithm returned an index score, ΓProtein = ((Y•ξ)(ζ)) = 23.75, out of a maximum of 28, indicating successful signal filtering and assignment of the spectra. The results demonstrate the success of the algorithm in filtering and assigning protein NMR signals to accelerate drug discovery. Currently, spectroscopists need 15 3-day experiments to assign signals, but this algorithm reduces NMR time investment by requiring a 24-hour X-Ray Crystallography experiment, a 20-minute HSQC, and a 3 week 4D HMQC-NOESY-HMQC. The key matrices in the algorithm like the RMM, SLWR, and NLWR enable researchers to run and compute in less than 1 millisecond. This drastically reduces the time needed to assign signals from the NMR experiment to amino acids in the protein, leading to faster drug screening. In the future, this algorithm can be expanded to solve analogous problems in other disciplines such as flight radar analysis, seismic wave filtering, and energy efficiency analytics.

Awards Won:

Second Award of $2,000