7.S: Summary

7.1: Chapter Objectives and Preview of Correlation NMR Spectroscopy

- Complex molecules can be hard to elucidate solely with 1-D NMR because it doesn't quite solve the entire picture. This is where correlation NMR spectroscopy can be used.

7.2 Theory

- The splitting of resonances indicates that groups were "correlated" to each other due to the spins within each group.
- A simple 2-D experiment pulse sequence consists of a relaxation delay, a pulse, a variable time interval (t_1), a second pulse, and acquisition (t_2).
- In 2-D experiments, the signal detected during acquisition is a function of acquisition time (t_2), which has been modulated as a function of the time interval (t_1). This means that magnetization evolves around one frequency during t_1 and a different frequency during t_2.
- The output once Fourier transformed is a 2-D spectrum with two axes.
- One axis (v_2) represents the nucleus detected during acquisition (t_2), while the other axis (v1) can represent the same nucleus or a different nucleus.
- With two axes, it leads to cross peaks along a diagonal connecting coupled nuclei.

7.3 Two Dimensional Homonuclear NMR Spectroscopy

- Homonuclear 2-D NMR spectroscopy is looking at the correlation of the same nuclei in a molecule.
- COSY looks at ^{1}H coupling to ^{1}H through bonds typically 3 bonds away and relies on the J-coupling to provide spin-spin correlation to indicate which protons are close to each other.
- TOCSY obtains correlations between all protons within a given spin system and begin to chain together fragments of a molecule.
- A molecule can have just one spin system or hundreds in more complex systems.
- The goal in TOCSY is to transfer the magnetization beyond directly coupled spins.
- NOESY determines which signals arise from protons athar are close to each other in space, even if they are not bonded.

7.4 Two Dimensional Heteronuclear NMR Spectroscopy

- Heteronculear 2-D NMR is the correlation between different nuclei, such as a ^{1}H to ^{13}C.
- HSQC is used to determine the proton to carbon or heteroatom (often nitrogen) single bond correlations.
- The purpose of a HSQC is to determine which protons are coupled to what other specific carbon or heteroatom in the molecule through bonds.
- HMBC is used to determine long range ^{1}H to ^{13}C connectivity.
- HMBC gives the correlation between ^{1}H and ^{13}C when separated by two, three, and even four (if through a conjugated system) bonds away.

7.5 Uses of 2-DNMR Spectroscopy

- Complex structure elucidation often requires 2-D NMR spectroscopy.
- HSQC can be used to determine the profile of metabolites in low concentrations (microMolar) accurately.
- TOCSY has been utilized to show changes in tumor cells and identify biomarkers associated with these cells.
- Molecular dynamics can be studied using 2-D NMR spectroscopy to map the molecule's internal mobility patterns.

Skills to Master

- Skill 7.1 Distinguish between 1-D and 2-D techniques.
- Skill 7.2 Learn to read COSY, TOCSY, NOESY, HSQC, HMBC spectra.
- Skill 7.3 Know what type of experiment to use to gain the information needed.
- Skill 7.4 Understand applications of 2-D NMR spectroscopy.
- Skill 7.5 Solve unknown structure determination problems with 2-D spectroscopy.