

# Chem590N1 Jan. 30, 2008

Palmer's Chapter 6.4-6.6 MQ, TOCSY, NOESY, ROESY

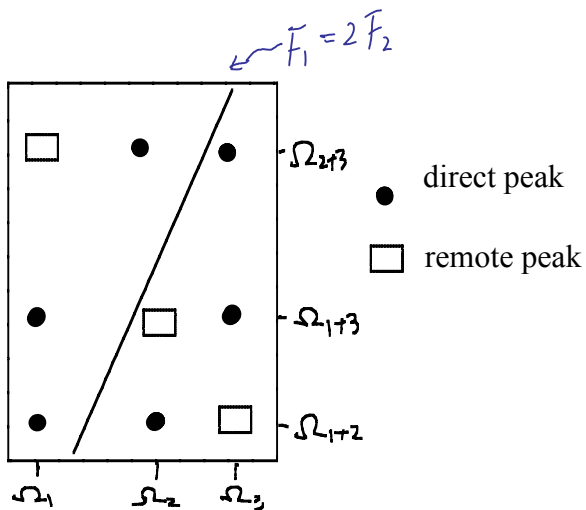
## 1. Multiple-quantum spectroscopy

The receiver coil detects only single-quantum coherence, multiple-quantum coherence is however allowed to evolve in an indirect dimension. MQ spectra provides complementary information to COSY.

Notice the difference between MQ filtered COSY and MQ spectroscopy.



2Q spectrum from a 3 spin system



### Pros of 2Q spectroscopy over COSY

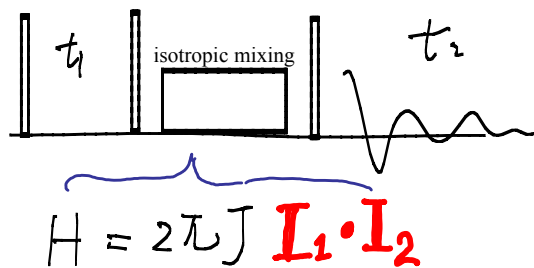
- 1) free of diagonal peaks: reveal correlation peaks with similar chemical shifts.
- 2) no self-cancellation (peaks are either absorptive in-phase or dispersive antiphase in F1): reveal peaks of small J-coupling or large linewidth.
- 3) attenuation by solvent presaturation no longer a problem:  $H^N-H^a$  peaks occur even when  $H^a$ 's resonate at the water chemical shift.
- 4) remote peaks provide additional information to help resolve degeneracy.

### 3Q spectroscopy

- 1) spectral simplification
- 2) uniquely useful information from remote peaks: for glycine alpha protons, aromatic ring protons, long side chain (arginine, lysine, proline)

## 2. TOCSY total correlation spectroscopy

Motivation: to connect the "fingerprint regions" identified in the COSY-type experiments



The Hamiltonian and the "total correlation"

1) chemical shift is suppressed to meet the HOHAHA condition (homonuclear Hartman-Hahn) that facilitates polarization transfer among all protons in an amino acid (or  $^{13}\text{C}$  spins in enriched samples, e.g. in HCCH-TOCSY to be introduced later).

2) strong J-coupling enables faster transfer than in COSY-type experiments (weak coupling  $I_{1z}I_{2z}$ )

Figure 6.49: example TOCSY spectra with short to long mixing times.

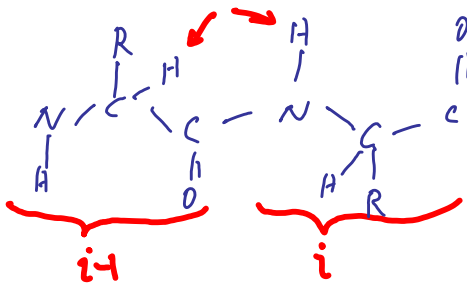
50 ms:  $\text{H}^{\text{N}} \rightarrow$  as far as  $\text{H}^{\text{e}}$

100 ms:  $\text{H}^{\text{N}} \rightarrow$  as far as  $\text{H}^{\text{e}}$

## 2. NOESY and ROESY

Motivation: to build sequential or long-range connectivities using through-space NOE/ROE cross-relaxation. COSY and TOCSY, which are based on through-bond J-coupling interactions, only connect protons in the same amino acid.

very weak  $^4J$ , but close in space ( $\sim 2.5$  Å in b-strand and  $\sim 3.5$  Å in a-helix)



NOE can probe distances up to 5 Å. NOE distance restraints are indispensable in solution NMR structural determination. However, NOE distances are only semi-quantitative because the peak intensities are complicated by the multi-step relay (aka the "spin-diffusion" phenomenon). Therefore, the distances are usually categorized into short, medium, and long groups according to peak intensities of strong, medium, and weak, respectively.

NOE: nuclear Overhauser effect (Chapter 5.5)

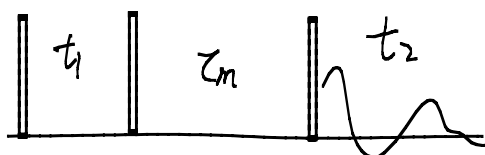
principle: dipolar-coupled spins do not relax independently.

practically: Decrease of polarization (for example by saturation) for spin I induces polarization change for coupled spin S. The change depends on molecular tumbling rate and could be an **increase** for **small molecules** (the positive NOE effect), but a decrease for **large** molecules (the negative NOE effect). For medium size molecules (like short peptides) the NOE effect diminishes.

ROE: rotating-frame NOE

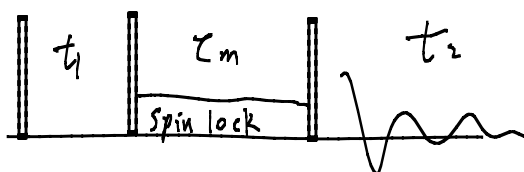
The effect is always positive; it complements NOESY.

NOESY



Spec. see Fig 6.53

ROESY



Spec. see Fig 6.60