Nuclear magnetic resonance (NMR)

Some concepts

- different kinds of experiment
- spectrum interpretation:
  peak assignment, spin systems, chemical shifts
- distance restraints
- model quality

Some issues for structural bioinformatics

- structure calculation
- under- and over-constrained distance restraints
- ensembles of structures
- conformational flexibility
- identifying structural cores

Protein NMR

Samples of purified protein in solution.

Exploits magnetic properties of certain atomic nuclei: ^{1}H, ^{13}C, ^{15}N.

Can think of “spinning spheres”.

Net excess of nuclei aligned with magnetic field.

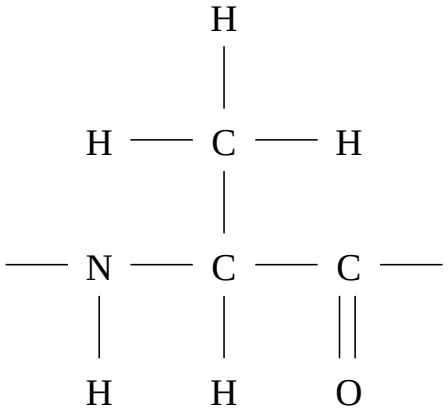
Radio frequency pulse tilts nuclear spin.

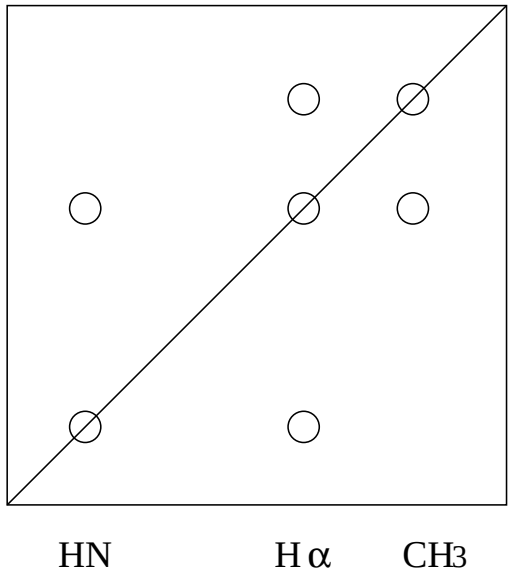
2D Proton NMR (^{1}H):
correration spectroscopy (COSY), total correlation spectroscopy (TOCSY), nuclear Overhauser effect spectroscopy (NOESY), ...

Other nuclei and higher dimensions.

COSY

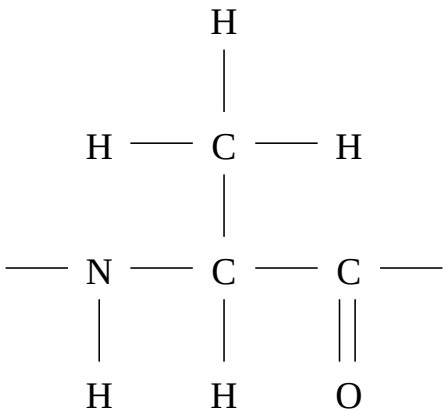
- correlation spectroscopy
- magnetization can be transferred between protons on adjacent atoms

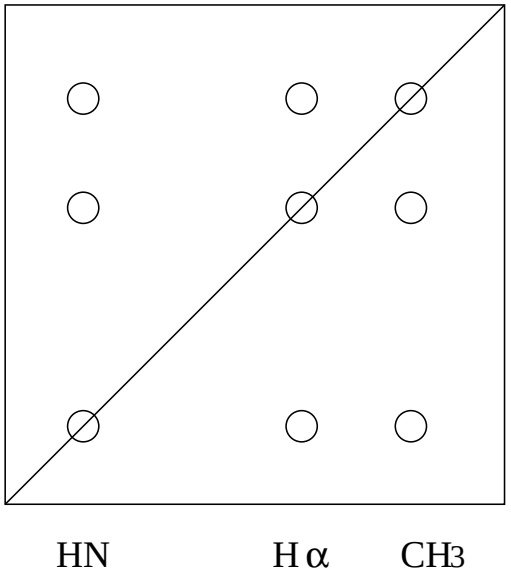




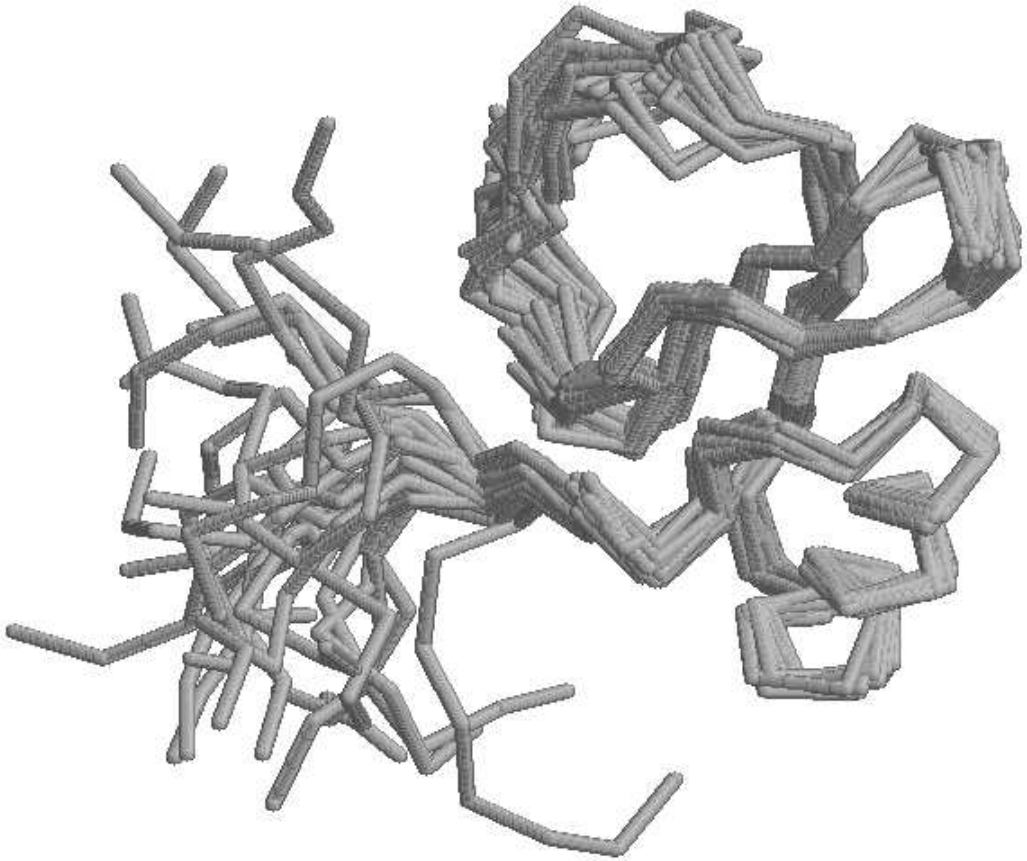
TOCSY

- total correlation spectroscopy
- magnetization can be transferred from alpha proton to beta protons, from beta protons to gamma protons, and so on, through several bonds





Ensemble of models from an NMR experiment



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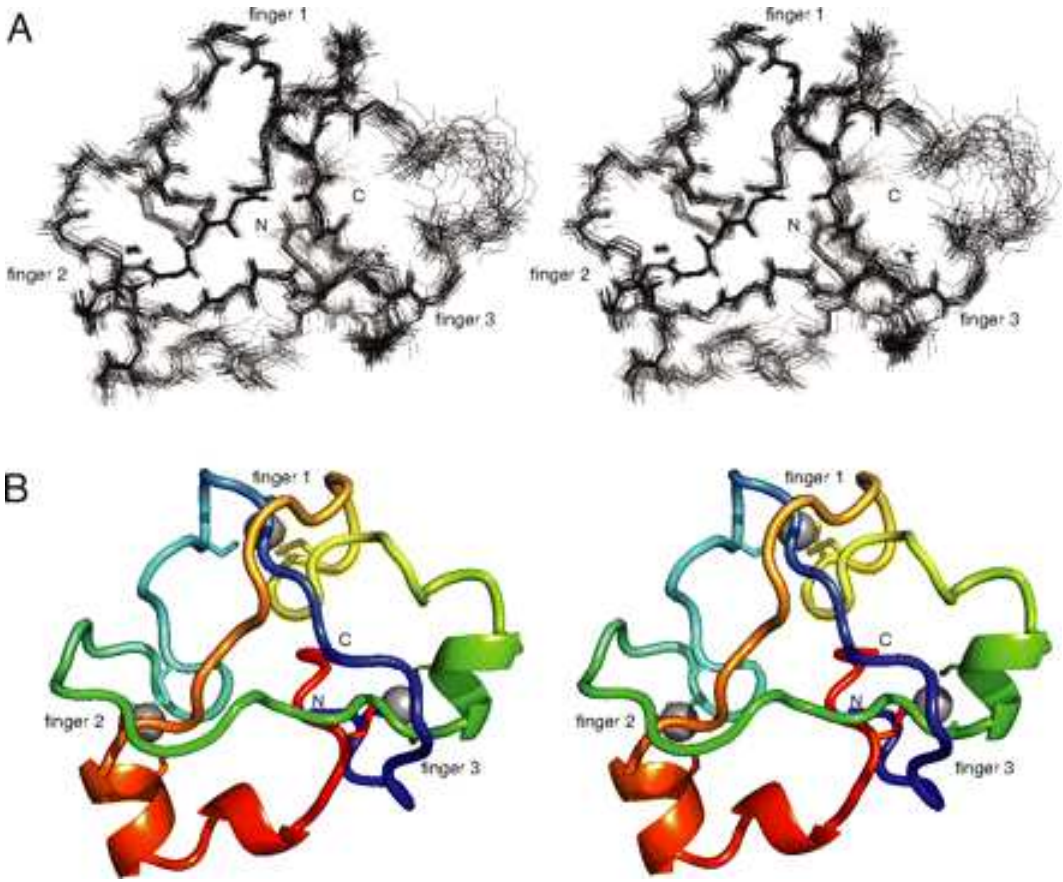
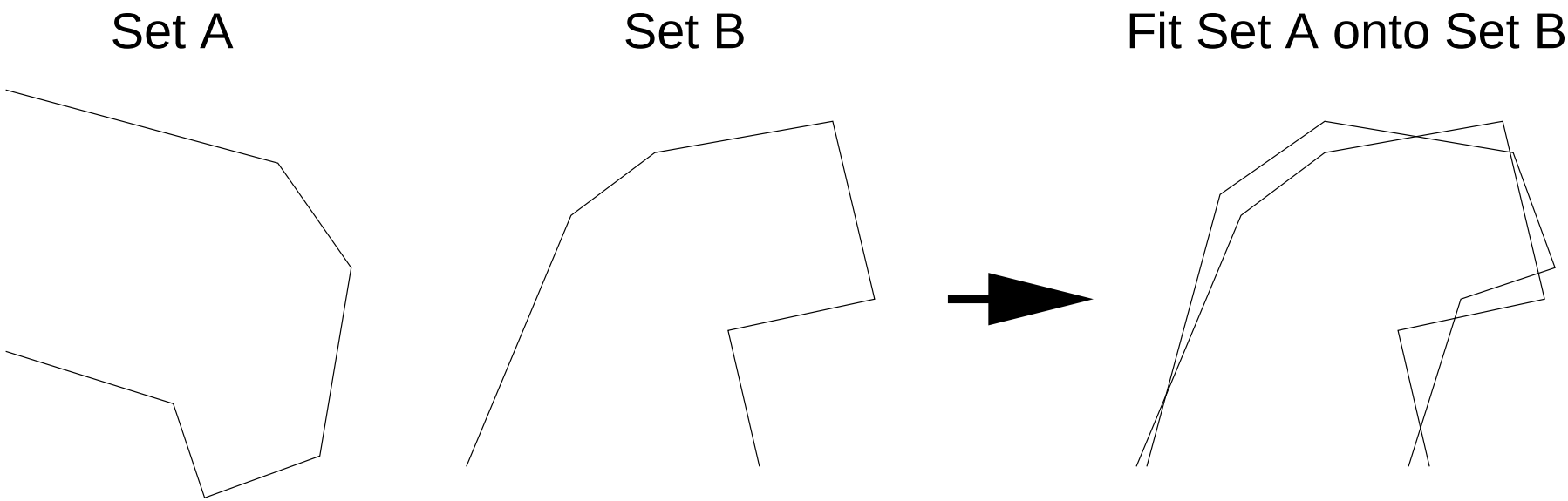


van Roon et al., PNAS USA, 2008, 105(28):9621-6

Comparing molecular fragments



- 3-D transformation to map Set A onto Set B
- Root Mean Square (RMS) distance

KBB057/KEM360 — Structure and dynamics of biomolecules

Course TDA507/DIT741 includes only a very light introduction to experimental methods for determining macromolecular structures, with emphasis on some of the issues that structural bioinformaticians should be aware of when using structures from the Protein Data Bank.

Course KBB057/KEM360 describes these experimental methods more thoroughly:

> “This course aims to provide an understanding of the methods that can be used the determination of protein structure and dynamics. The course will cover how X-ray crystallography and Nuclear Magnetic Resonance Spectroscopy, Electron Paramagnetic Resonance and Electron Microscopy can be used for structure determination. Students will be expected to understand the steps required to solve a protein structure, and the physical concepts which underpin these methods. They will get introduced to spectroscopic methods (based on NMR and vibrational spectroscopy) that can be used for studying protein dynamics at different timescales.”