

Inter-molecular hydrogen bonds; from temperature-driven proton transfer in molecular crystals to DNA

Mark Johnson

Computation Lab & Computing for Science
Institut Laue Langevin, Grenoble, FRANCE

& Faculties of Science and Engineering,
University of Nottingham, UK

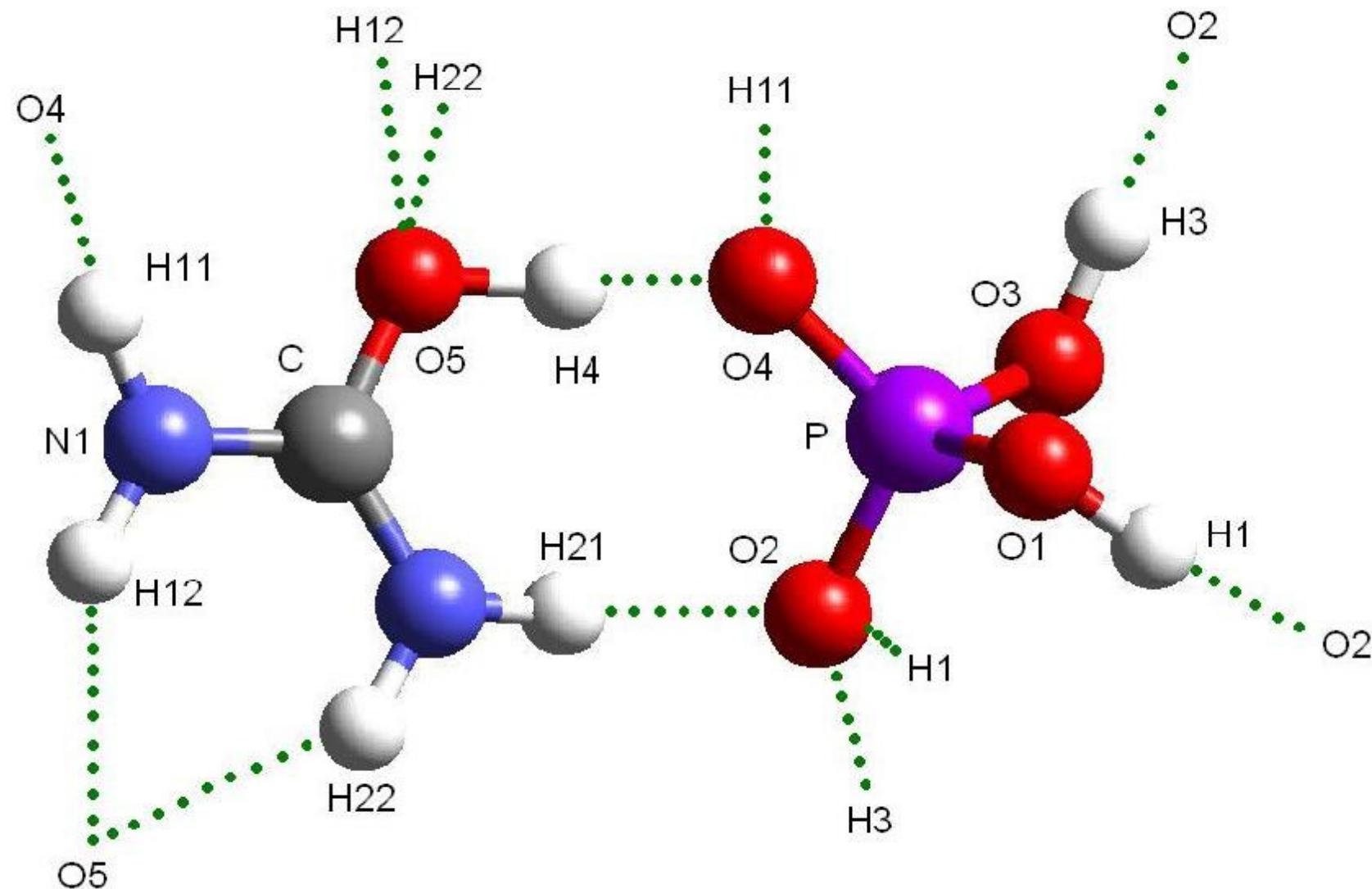
STRUCTURE, VIBRATIONS, DYNAMICS AND PROTON TRANSFER IN SHORT HYDROGEN BONDS

mobile proton links molecular entities, important
in enzyme catalysis e.g. HIV protease

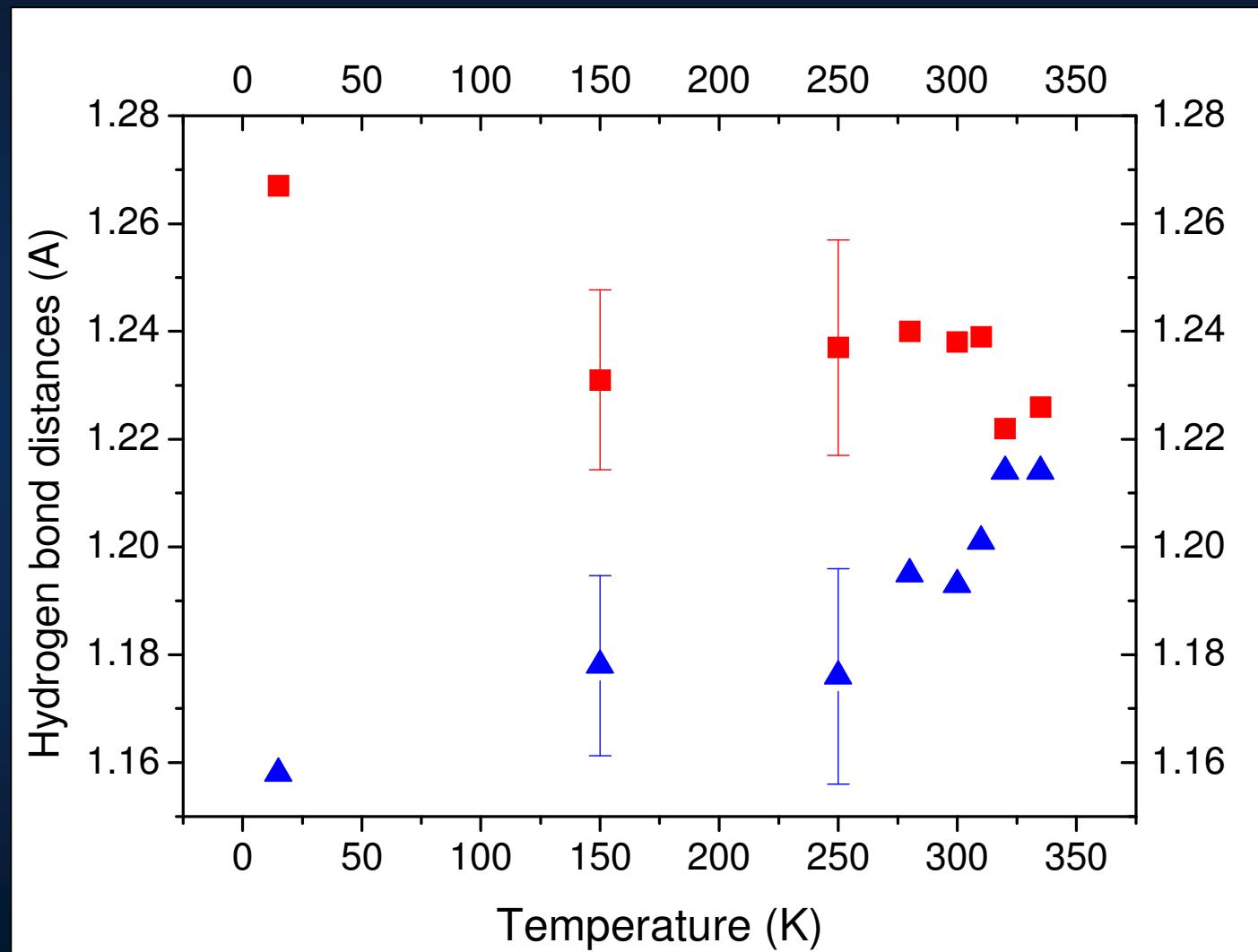
Fabien Fontaine-Vive, Judith Howard et al

JACS (2006), J. Chem. Phys. (2006)

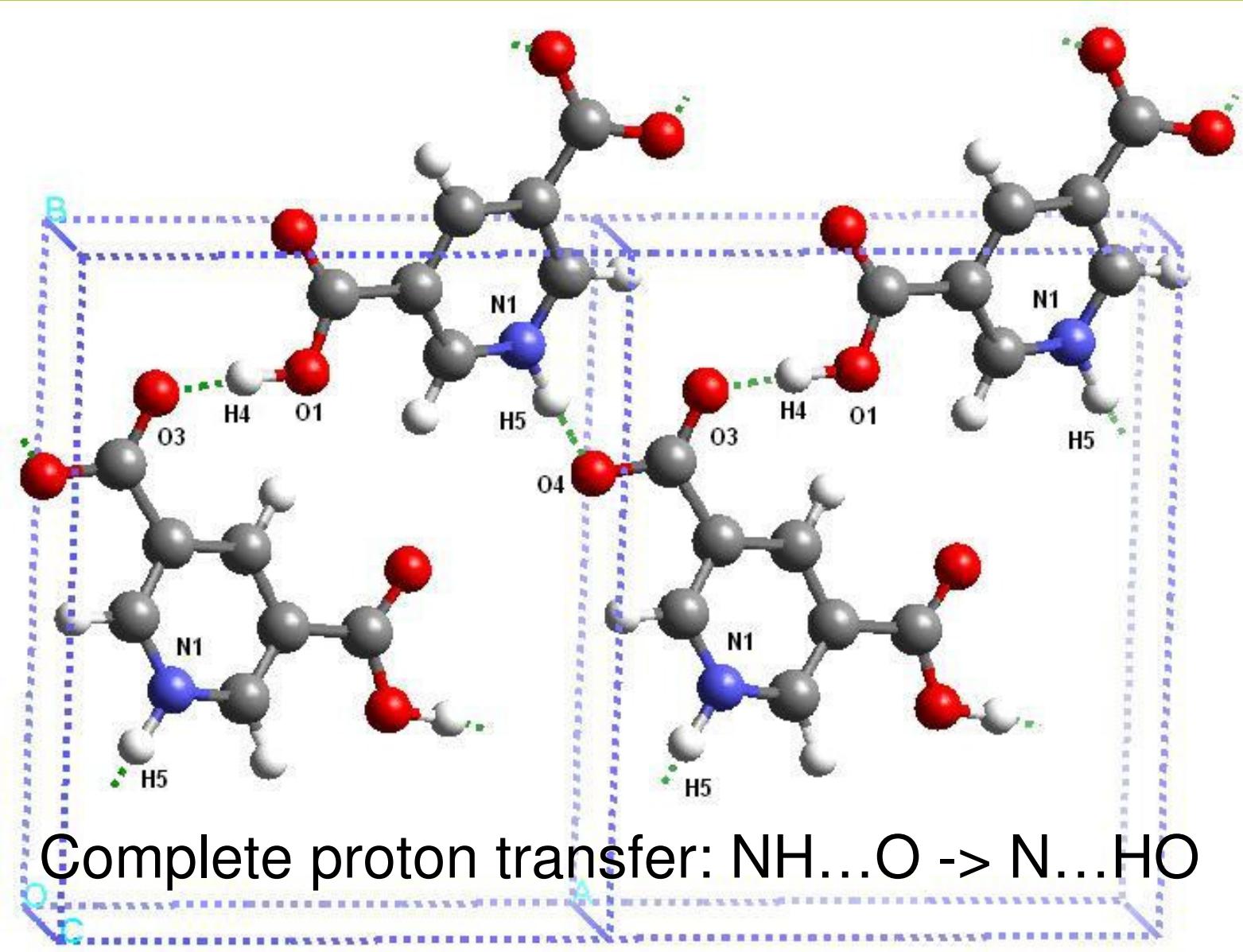
Urea - Phosphoric acid (Chick Wilson et al)



Proton migration in UPA by neutron diffraction



N-H...O bond in 3,5-Pyridine Dicarboxylic Acid



Why do protons transfer with increasing temperature?

1/ lattice expansion

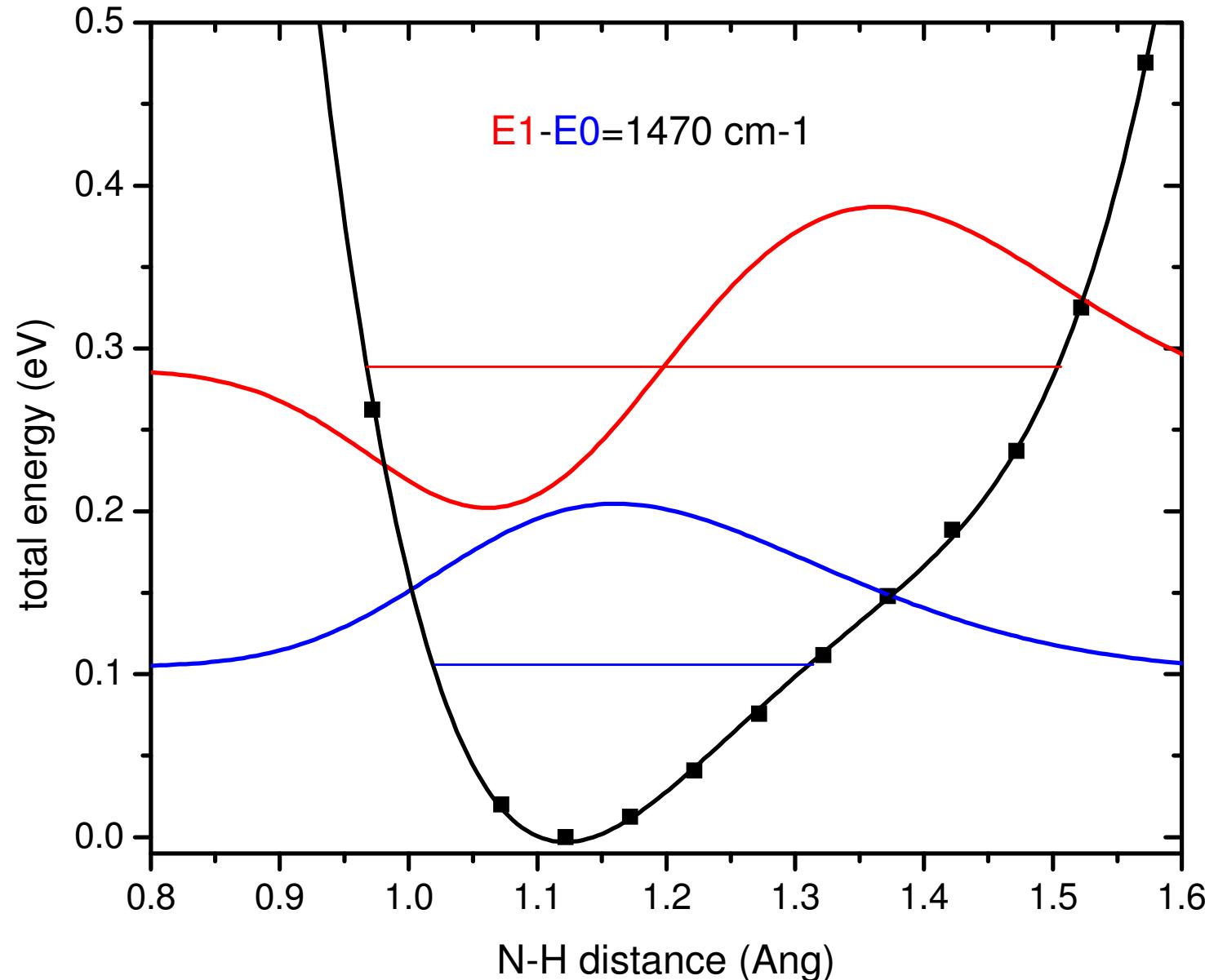
2/ population of excited vibrational levels

3/ thermal modulation of the potential energy well

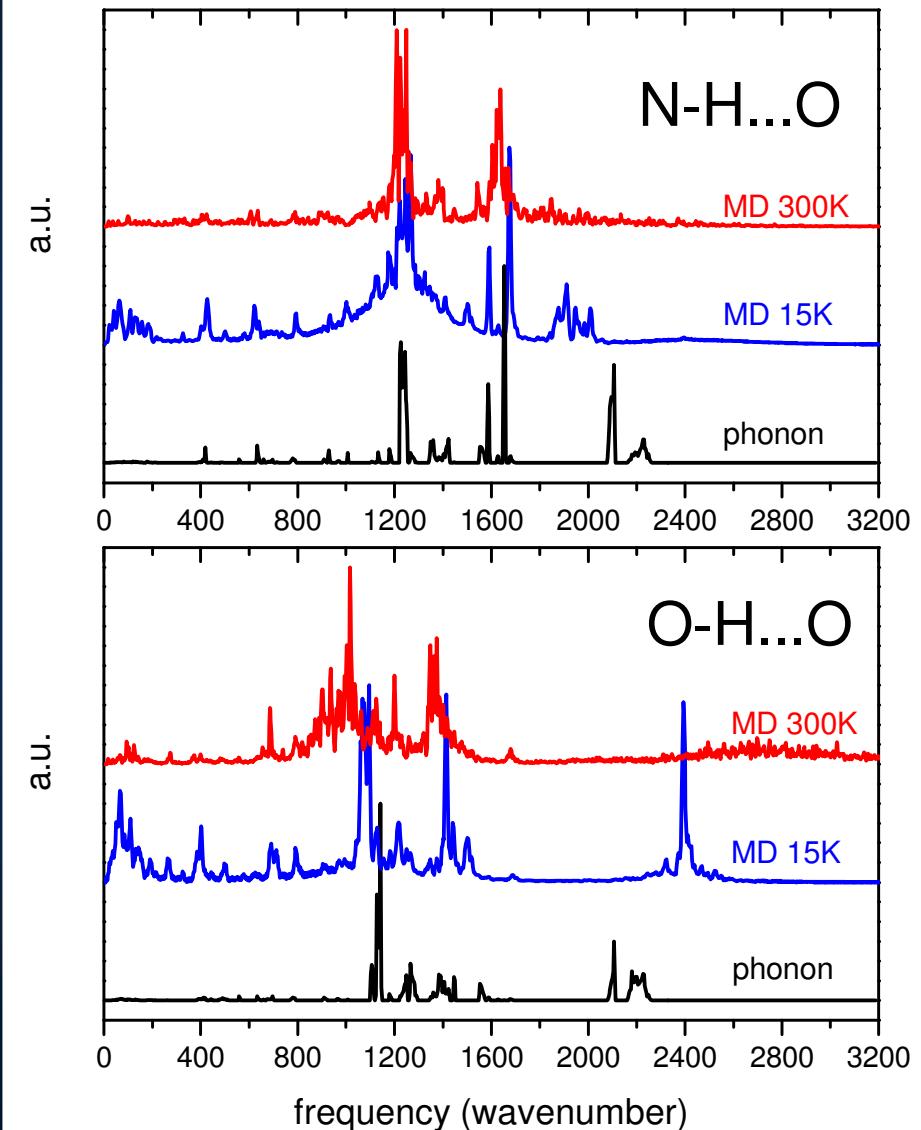
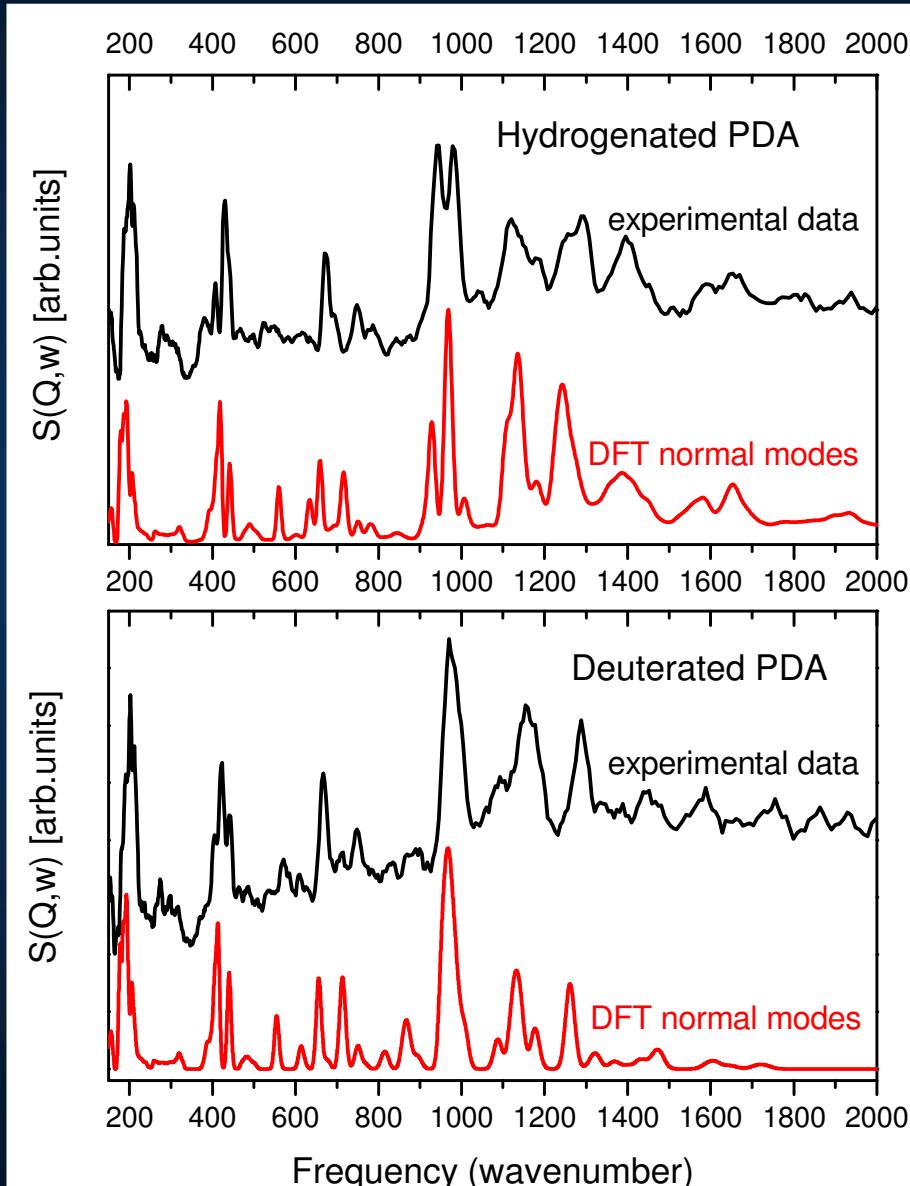
Computational Tools:

*Plane-wave, solid-state DFT (VASP)
phonons,
molecular dynamics*

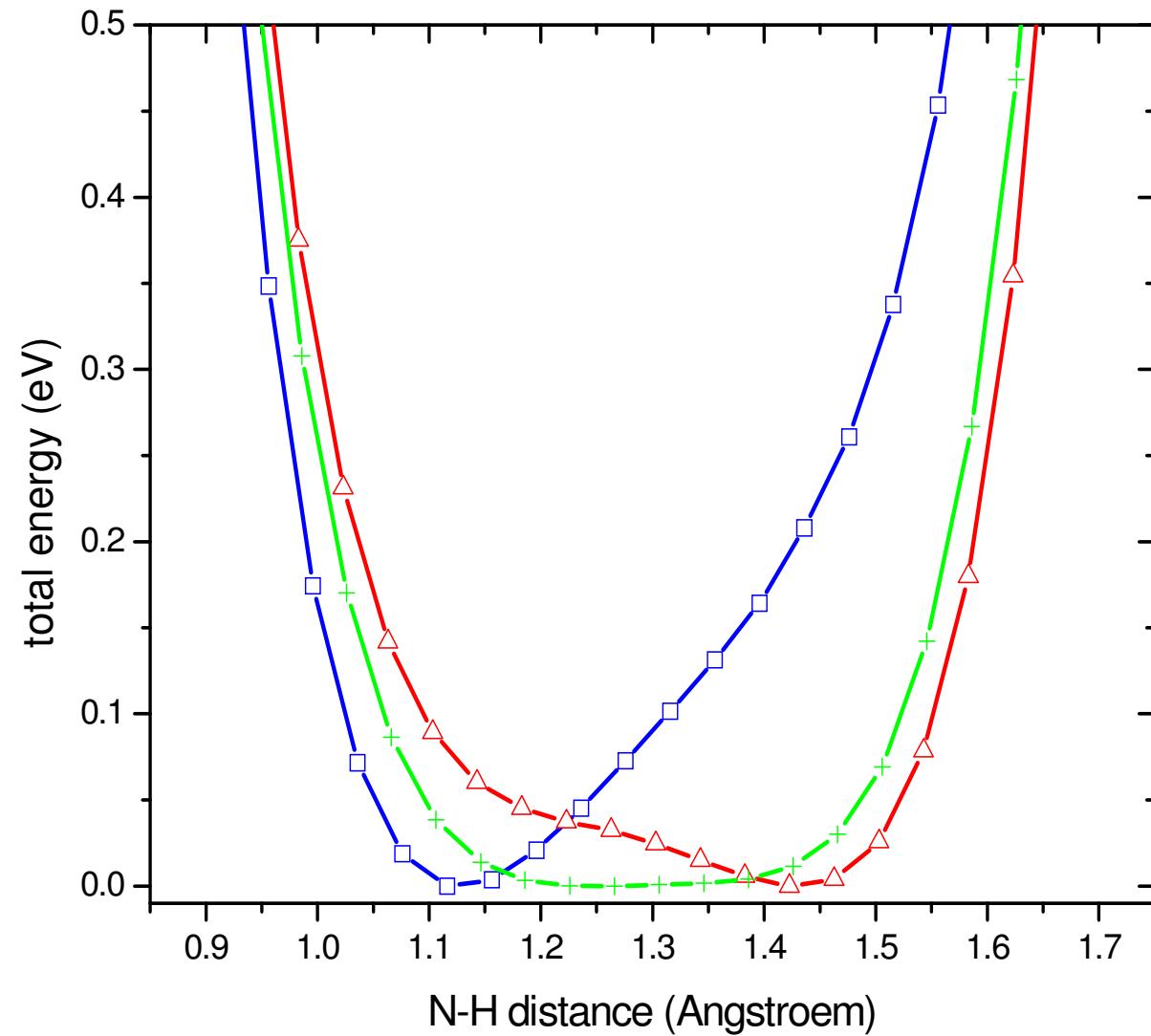
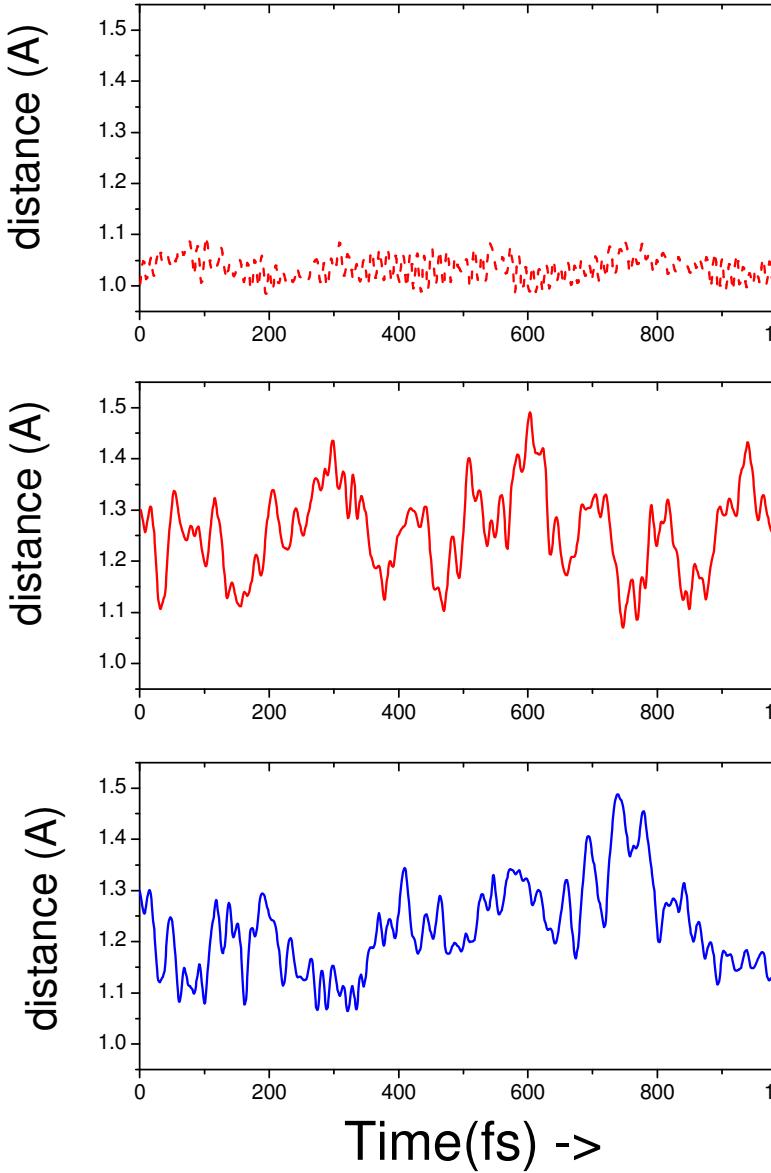
The potential energy well along the N-H...O bond



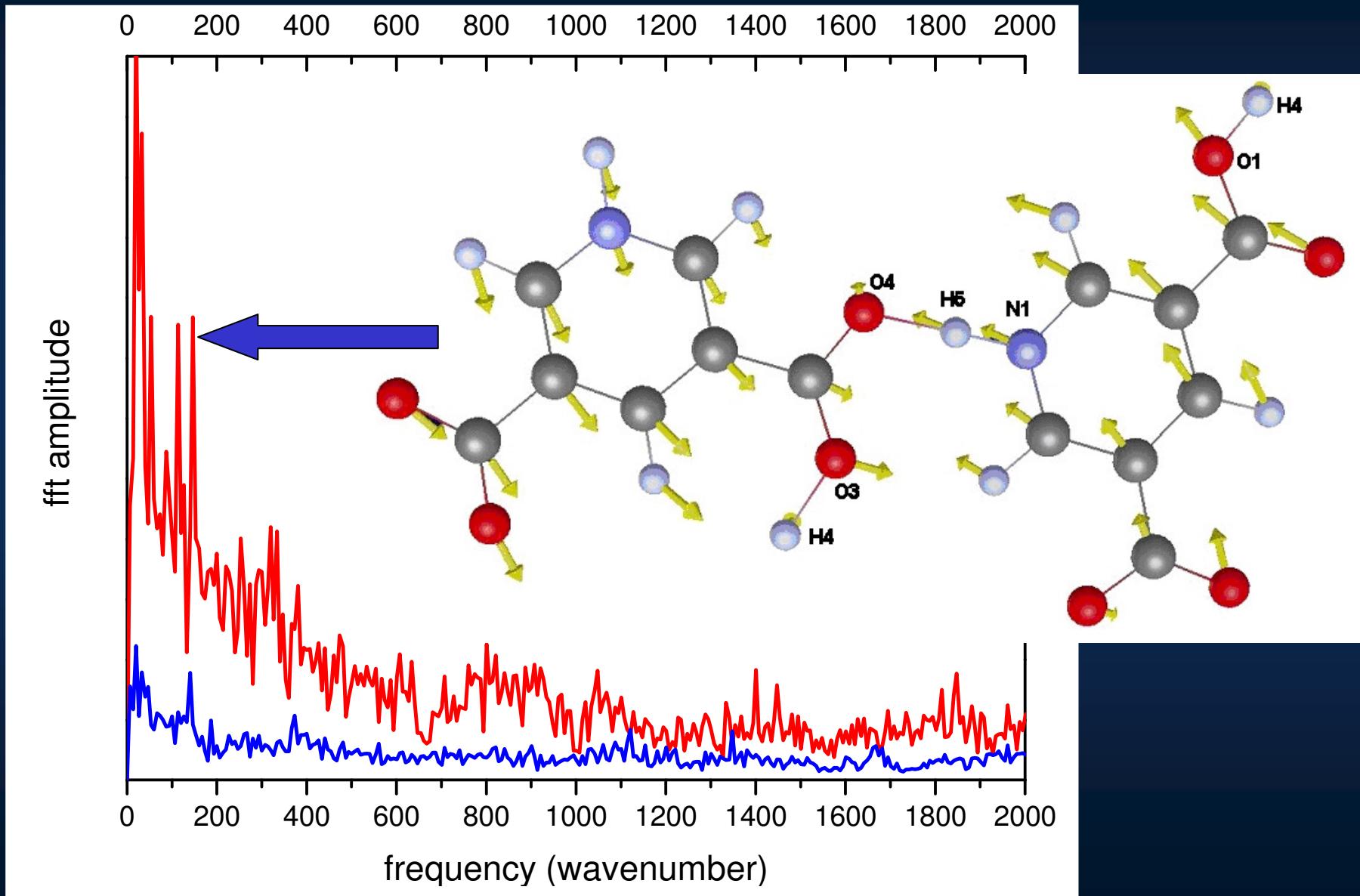
Molecular vibrations: short vs. normal H-bond



Proton transfer in N-H...O as a function of T



Which modes modulate the potential energy well ...



BASE-PAIR OPENING IN DNA

Fabien Fontaine-Vive, Franci Merzel et al

Comp. Phys. Comm. 177, 530 (2007)
DNA: Phys Rev E (2007)

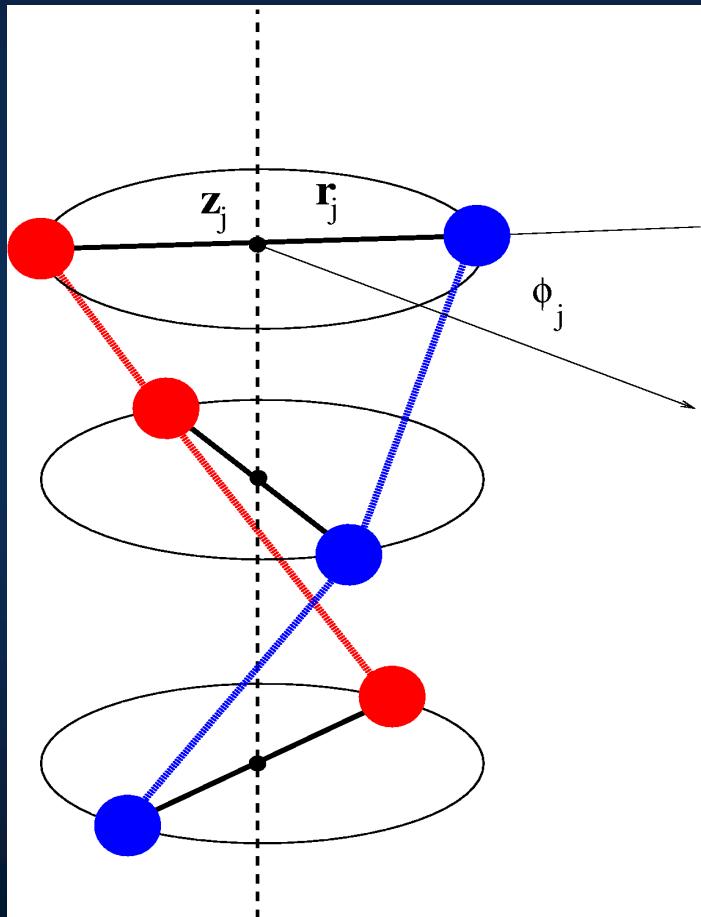
Motivation - I



Peyraud: Nature Physics 2007

Motivation - II

*BP opening has been addressed using simplified models e.g.
Peyrard-Bishop*

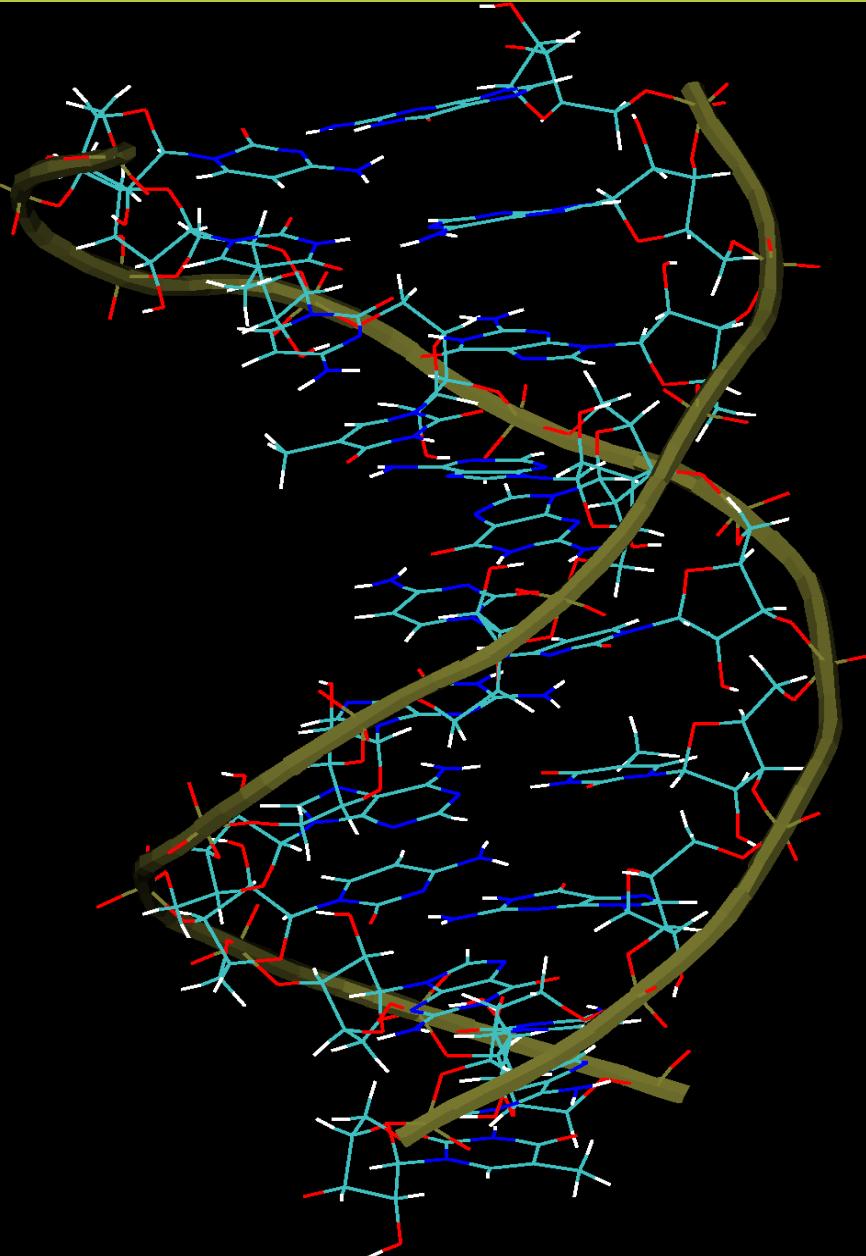


Accepted base pair
opening frequencies are
 $A-T: 60-90\text{cm}^{-1}$
 $G-C: 95-125\text{cm}^{-1}$

BUT DNA melting occurs
 $\sim 370 \text{ K} (> 250 \text{ cm}^{-1})$

-> "ENERGY GAP of 200 K"

The atomistic model



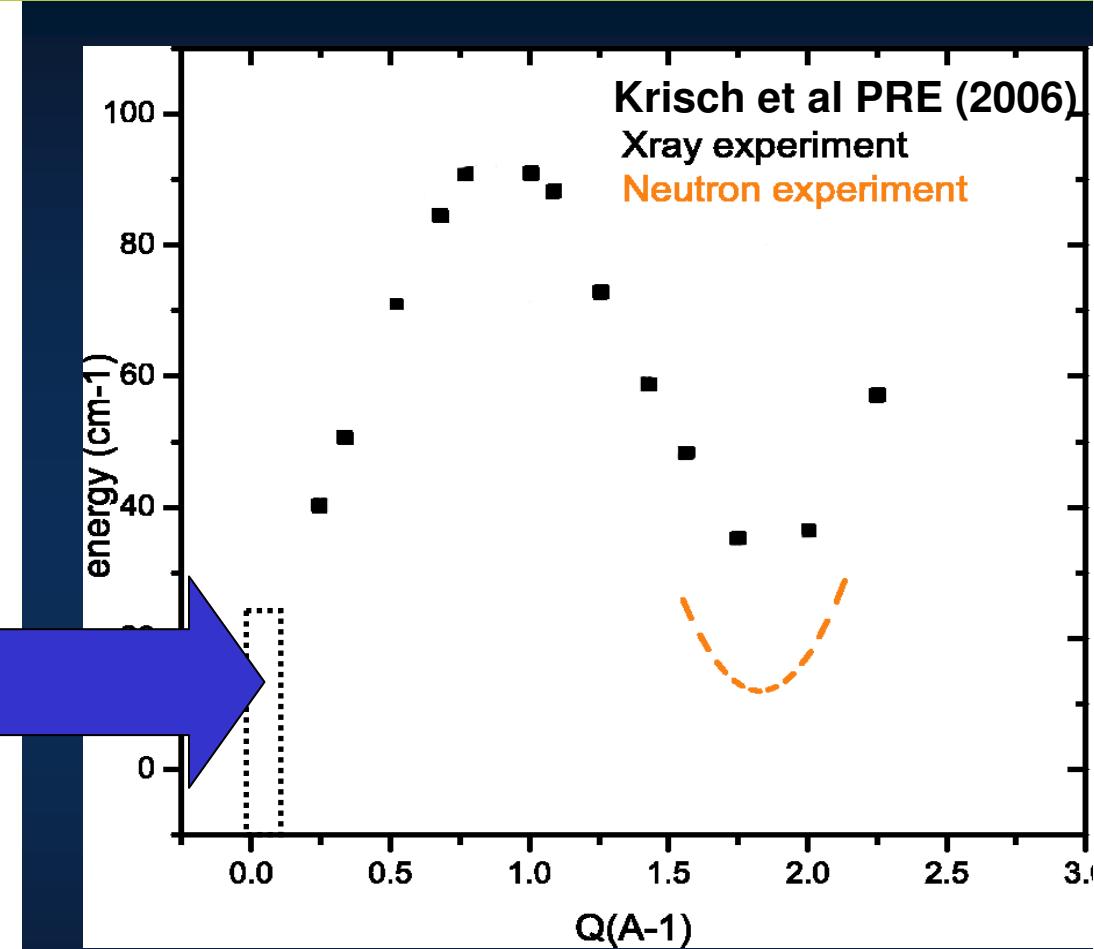
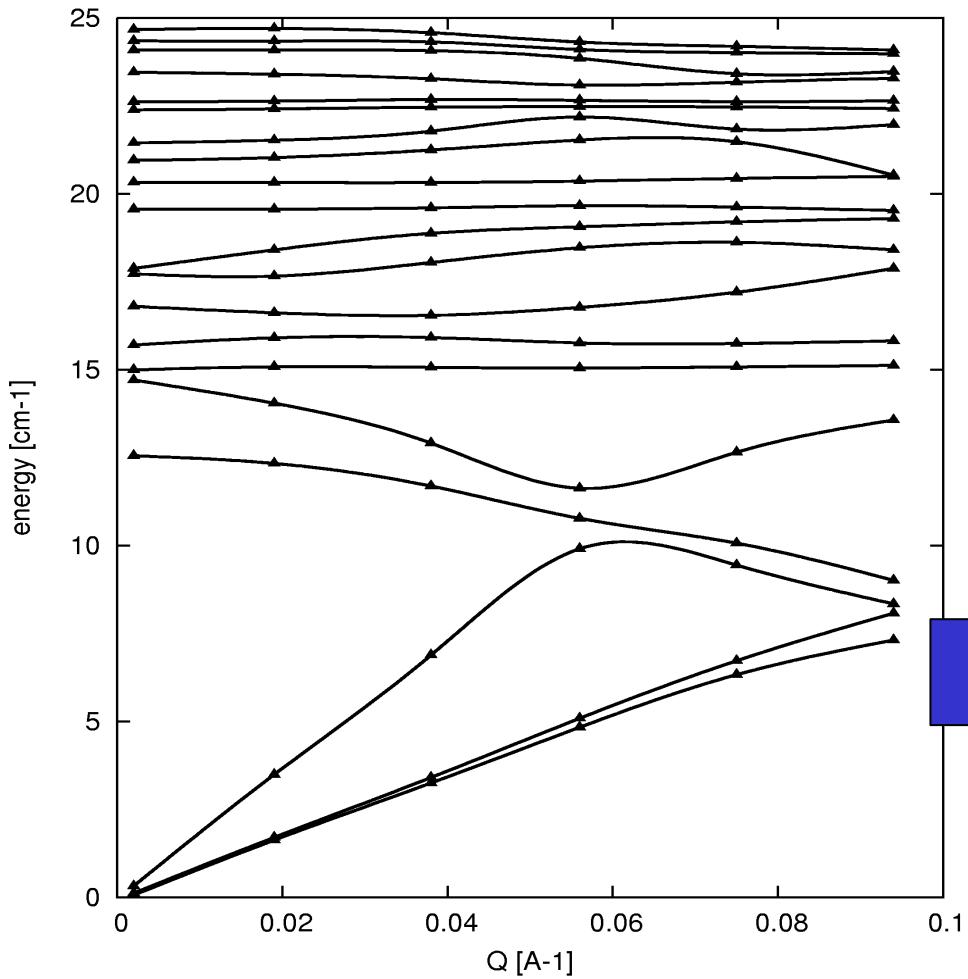
Sequence (10 base pairs):
AGCAGCAGAG

Unit cell (fiber DNA):
 $32.2\text{\AA} \times 32.2\text{\AA} \times 33.5\text{\AA}$
explicit water
~3600 atoms (including ions and water)

MD simulation 1ns at 300K NPT, NVE
using CHARMM program:

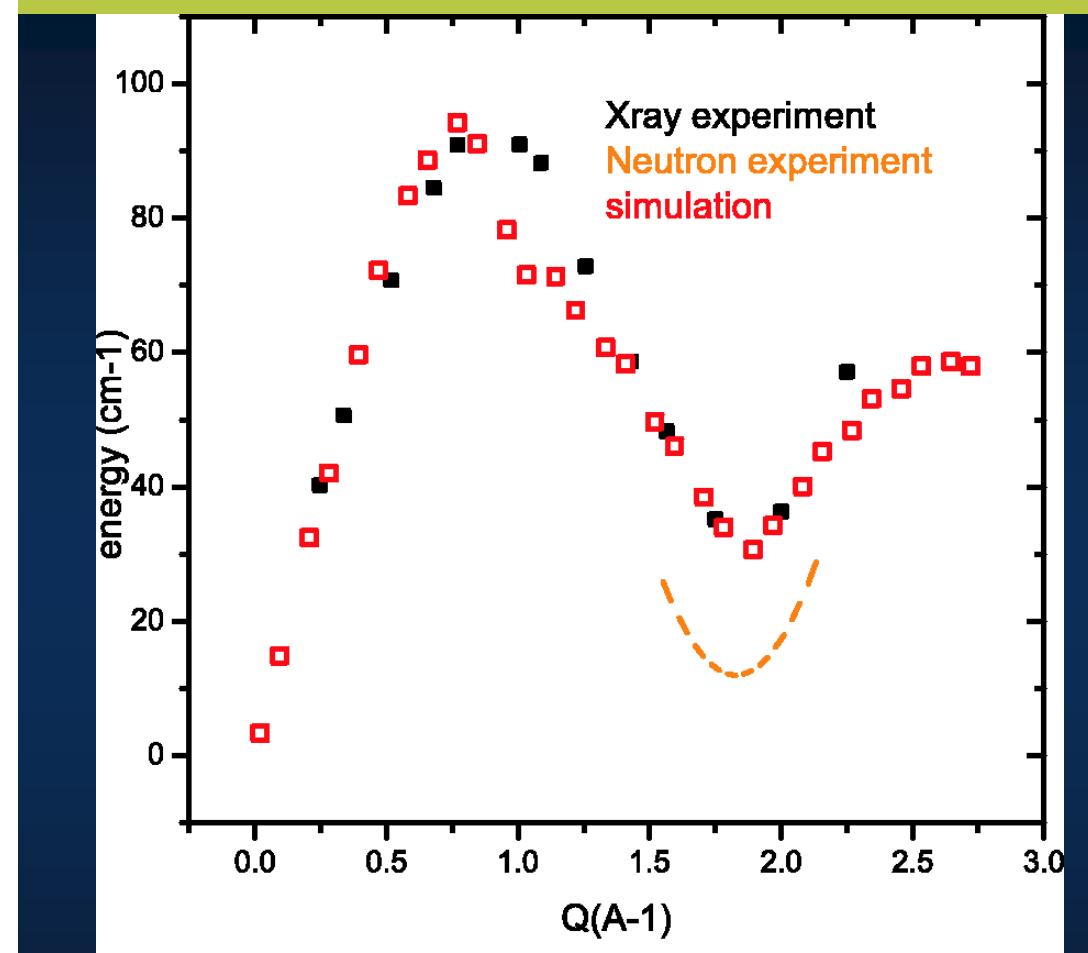
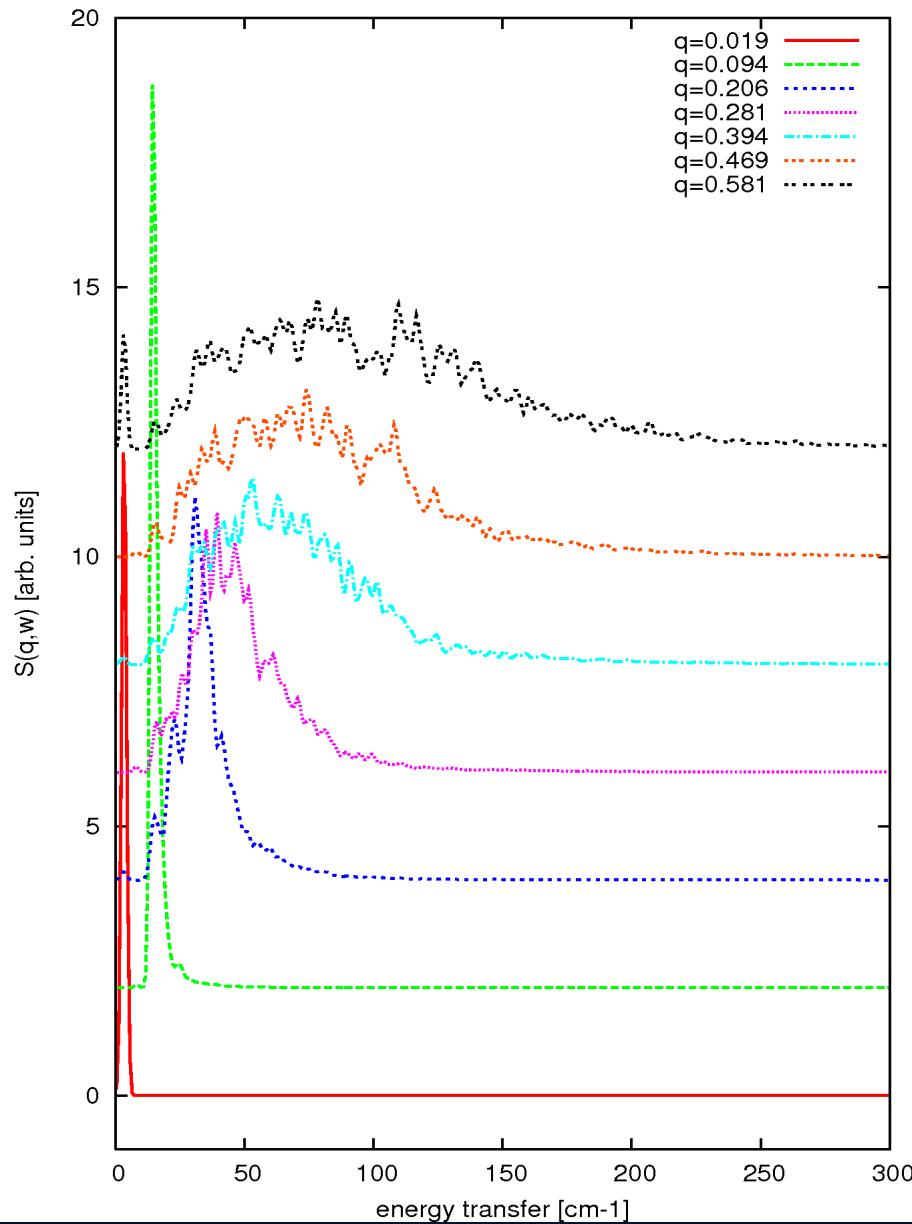
- > equilibrated structure
- > minimized structure
- > Hessian matrix

Phonons: simulation vs. experiment (I)



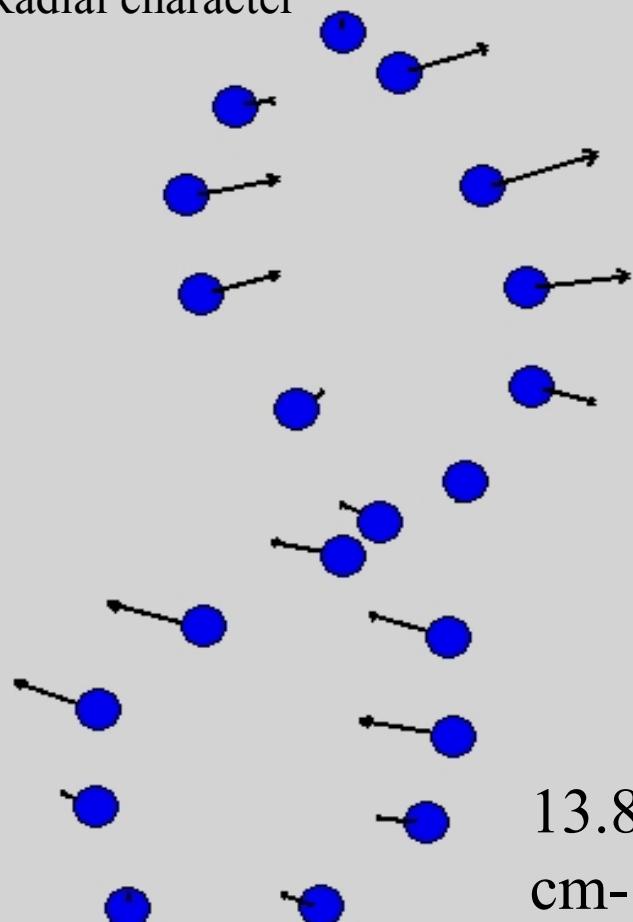
Experimental signal is not a direct measurement of acoustic phonons but is a projection of spectral intensity over opt. modes.

Phonons: simulation vs. experiment (II)

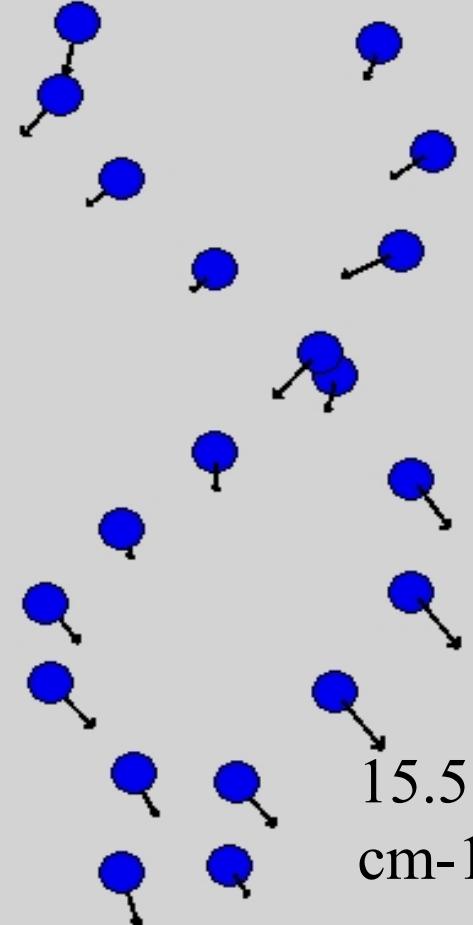


Analysis: nucleotides as beads

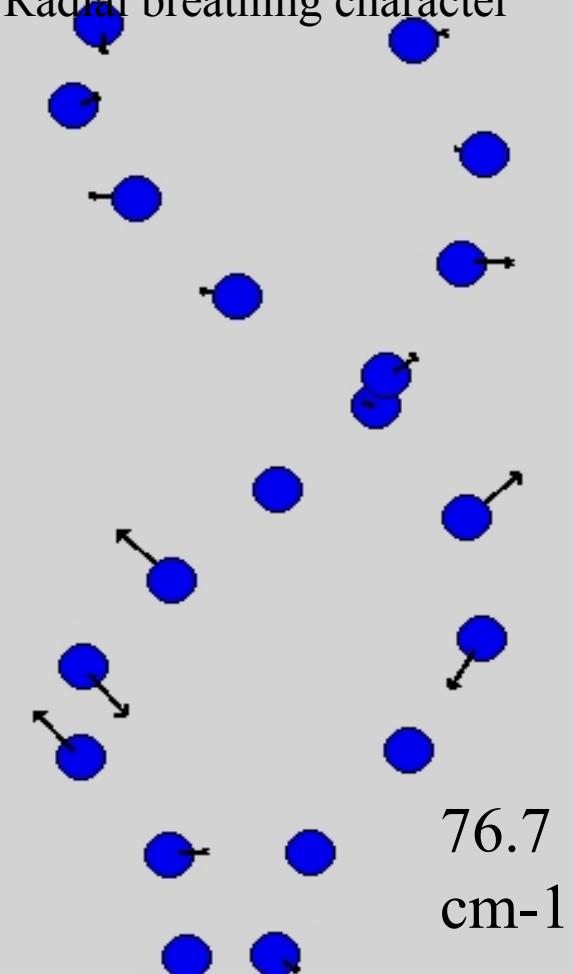
Radial character



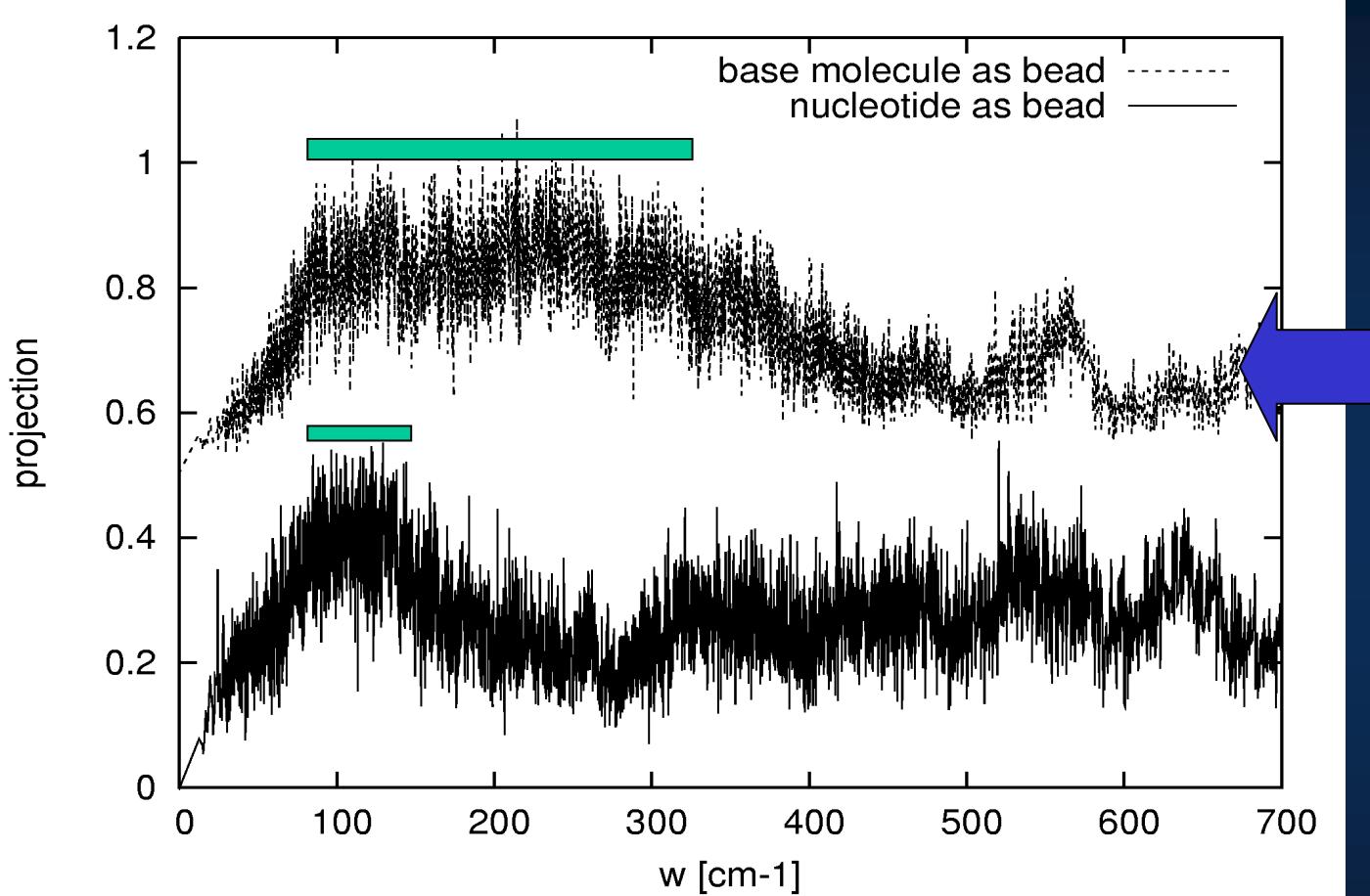
Axial character



Radial breathing character

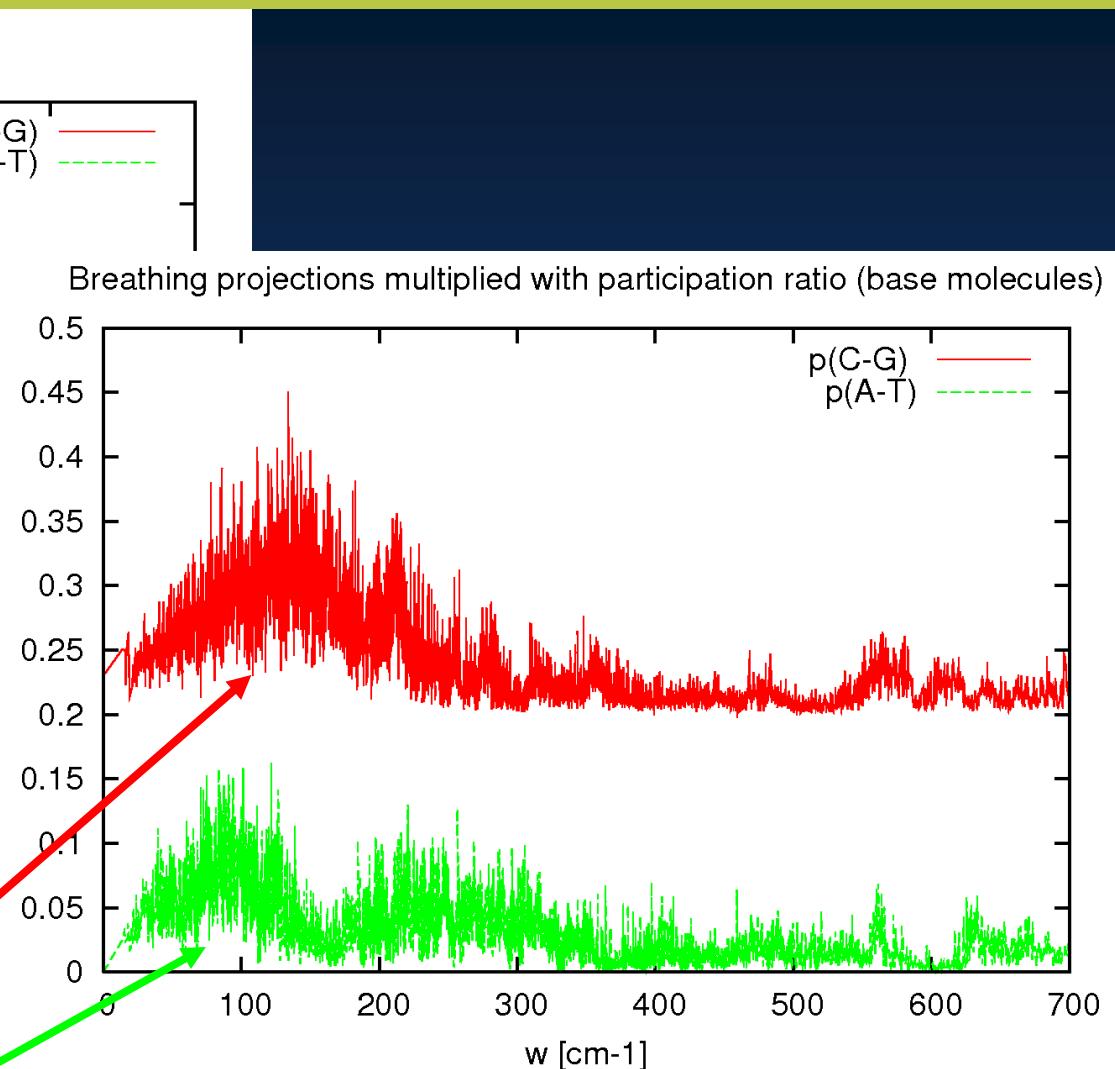
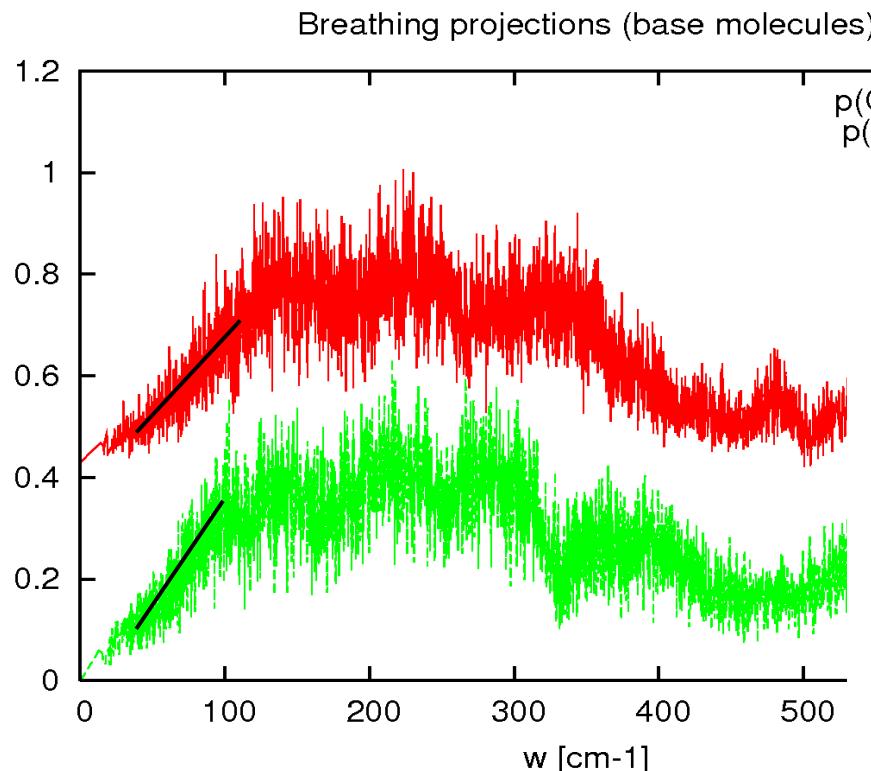


Analysis: breathing projection of displacement vectors



wider range of modes
with base pair
opening
character up to
 300cm^{-1} ($\sim 400\text{ K}$)
when using base and
sugar molecules as
beads.

Analysis: 'breathing' for different base pairs



Agreement with
 mesoscale or 'fitted'
 theoretical models:
 G-C: 95-125cm⁻¹
 A-T: 60-90cm⁻¹

CONCLUSION & PERSPECTIVES

Experiment + simulation (theory) to understand
H-bonds

*Why don't all short H-bonds transfer the
proton?*

Can we improve the force field for DNA using
DFT?

OUTLINE



Neutrons and hydrogen bonds

Strongest 'incoherent' scattering for H

*Good for dynamics (relaxation, ps - ns)
& spectroscopy (no selection rules)*

'coherent' scattering for D like C, N, O ... Fe ...

Good for structure determination

Sample quantity: >10 mg for diffraction, >100 mg
for dynamics & spectroscopy