

## BCH 258 lecture notes Wed. Sept 07, 2011 Structure stabilizing interactions

Hydrogens: all-atom contacts, H-bonds, and waters

- Handouts:
- Assignment: [WrkSht6-H-bonds2011.pdf](#)
- Kinemages: [HbondPractice-KiNG.kin](#)

In class: N-caps: [Top5200\\_Ncaps\\_i+3\\_phipsiSubset.kin](#)

How things fit together: 2v2p helix contacts: [2v2pFH-multi.kin.gz](#) & [2v2p.omap.gz](#)

Hydrogens: all-atom contacts, H-bonds, & waters

0) Water – a few internal; at active site may mimic substrate

<= one layer well-ordered on outside, esp. around polar groups  
crystal or domain contacts often through 1 layer of ordered water

1) Hydrogen atoms : half of atoms; make most intra- & inter-molecular contacts,

both H-bonds and van der Waals

Just edge “decoration” on 1D, but central to 3D

Imagine (visualize) polypeptide chain white with red O, blue N, add H’s as green

e.g. [c2Motifs.kin](#) [kin5 RNase](#) with H (& H-bonds)

fuzz on the outside of the sticks, but are what makes contacts!

Hydrogens are usually omitted (for very good but not adequate reasons)

make images fuzzy and calculations slow | so only used for H-bonds

not seen well by x-ray data |

Can be handled now, and give big payoffs

We’ll usually show either all or none, but other programs may add just polars, for H-bonds

2) All-atom contacts : using std. vdW radii, see which atoms touch (or within 0.5Å)

to directly visualize the non-covalent 3D interactions

[howdotswork3KiNG.kin](#) : overview sticks; vdW; dots; → closeup,

small probe generating dots

3 terms: vdW, clashes, H-bonds; color-coding by gap or by atom

[1mjhHdot-KiNG.kin](#) : good packing, at Leu, at Arg

H atoms interdigitate; even methyls fit staggered

H-bonds on Arg: significant overlap, but favorable

H-bonds to waters at interface; water really part of structure

(technique also finds occasional mistakes:

impossible overlap at Lys 74,

His flips (in active site!)

(Note: All-atom contact analysis empowers evaluation of proposed mutations: to be continued...)

(<http://molprobit.biochem.duke.edu> evaluates model by many criteria.)

7RSA: **STRUCTURE OF PHOSPHATE-FREE RIBONUCLEASE A REFINED AT 1.26 Å**

Explicit hydrogens are present (Continue) ...

[Analyze all-atom contacts and geometry](#) ... check ribbons: (Run programs to perform these analyses > )

(Admire scores) click on: Multi-criterion kinemage ... (admire structure model and graphics analyses)

3) Hydrogen bonds : much weaker than covalent, but very significant to 3D structure

close, oriented interaction of H donor and H acceptor , e.g. (mc) NH --- OC

H donors: -NH, -NH<sub>2</sub>, -NH<sub>3</sub>, water, -OH, (-SH) ...

H acceptors: O, N, water, (S)

obligate donors: mc & other NH, Lys, Arg, ...

obligate acceptors: mc & other CO, COO<sup>-</sup>, PO<sub>4</sub><sup>=</sup>

ambiguous: -OH, water, His, ...

distance: N & O < 3.5Å approx;

H & O < 2.5Å (i.e. < vdW touch) good H-bond has H & O ~ 2Å

angles: N → H vector should point at O position (good ± 30°) N—H—O angle 180° ± 30

C—O—H angle OK ± 90° : N—H - - - O (not: H - - - O—C )  
C ( N )

electrostatic dipoles: H partial +, O <sup>-</sup>, so attractive

some bonding, or orbital-sharing, character: H partly “shared”

overlap of H & acceptor vdW directly shows H-bonding

e.g. c2Motifs.kin kin5 for RNase mc H-bonds

4) Model: how well do we know the Model? 1US0-aldolase model-in-map

Segue:

The Model is NOT the molecule, how well do we know the Molecule?

(How consistent is the model with measurable properties of the molecule?)

Worksheet: addition to worksheet 6: H-bonds, Use Web services to assemble a kinemage to investigate: Catalytically important H-bonds in Ribonuclease proposed to stabilize transition state as seen with a bound nucleotide, a possible product of the reaction.

**<http://MolProbity.biochem.duke.edu>**: fetch 1W4P, **BINDING OF NONNATURAL 3'-NUCLEOTIDES TO RIBONUCLEASE A**, (continue>) [Add hydrogens](#), use default flips, (start adding H >) accept flips by clicking (Regenerate H, applying only selected flips >) (continue >) [Analyze all-atom contacts and geometry](#) : add “Ribbons” to default check boxes (Run programs to perform these analyses >) scores show many defects in the model, but we can look for particular features. Download the Multi-criterion kinemage to your own computer to look at it in KiNG. While in MolProbity, can download original 1W4P.pdb, or go yourself to Protein Data Bank: <http://www.rcsb.org/> enter 1W4P and (Search). On its page select in upper right Download Files/PDB File (Text) and put it in the directory with the kinemage.

**KiNG**: Center on the P of the inhibitor and zoom in, (search for “p” works to do this) turn on mainchain, sidechain, H’s, turn off Calphas. Note the 2 hisidines pointing hydrogens at the phosphate group. Turn on H-bonds to help you see these interctions. Also turning on vdw contact and small overlap gives an additional (rather overwhelming) view of more interactions which clipping will help make sense of. Turning on ribbons helps give context but more effective zoomed out to see more of the molecule. (scroll in button panel to turn on “ribbons” as well as “coil”, ”alpha”, ”beta”.

**Electron Density server**: <http://eds.bmc.uu.se>: enter 1W4P (Submit) then select Download/Maps and use default O format and Type 2mFo-DFc (Generate map) click on [1w4p.omap.gz](http://1w4p.omap.gz) to download the gzipped map.

From KiNG menu Tools/Structural Biology/Electron density maps navigate to and select [1w4p.omap.gz](http://1w4p.omap.gz) accept O format map and zoom in on the phosphate group to see how well the model fits the electron density.

Drag 1W4P.pdb file to the open kinemage in KiNG: scroll choices to “Open the file in Molikin” (OK) then add mainchian, sidechain, disulfides to default choices for Ball & Stick, and check “balls on N,O,P etc. and “balls on C atoms too”. Also select “Ribbons” keep default Color by secondary structure and then at bottom right of dialog box select (Append to current). Now it is easy to see both the \_\_\_\_\_ nitrogen of his \_\_\_\_\_ and the \_\_\_\_\_ nitrogen of his \_\_\_\_\_ each points a hydrogen at oxygen atoms of the phosphate.