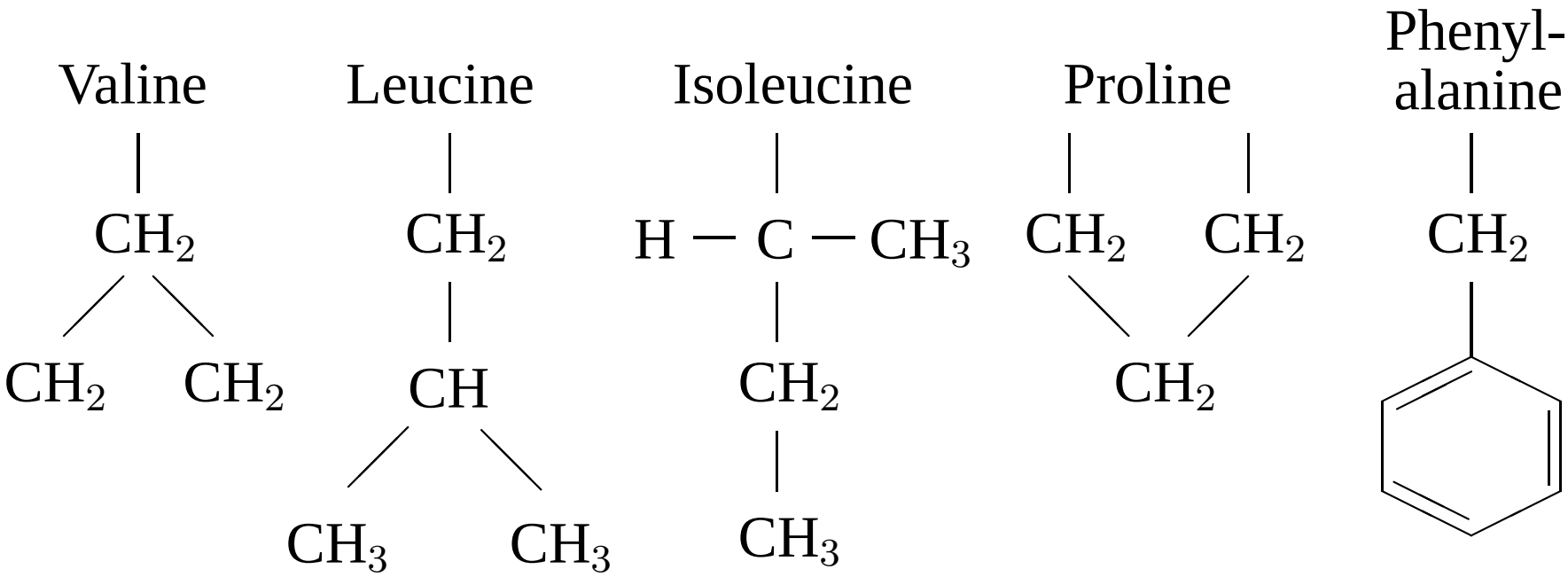
1 Tutorial on hydrophobic wrapping

Effect of modulation of dielectric by hydrophobic groups.

- Amino acid side chains have different properties
- Tutorial on hydrophobicity: carbonaceous groups
- Tutorial on dielectrics: more on this later
- Extent of wrapping changes nature of hydrogen bond
- Dehydrons: Under-wrapped hydrogen bonds
- A model for protein-protein interaction
- Extreme interaction: amyloid formation
- Stickiness of dehydrons

1.1 Amino acid side chains have different properties

Carbonaceous groups on certain side chains are hydrophobic:



Amino acids (side chains only shown) with carbonaceous groups.

1.2 Tutorial on hydrophobicity

Carbonaceous groups (CH, CH_2, CH_3) are hydrophobic because

- they are non-polar and thus do not attract water strongly
- they are polarizable and thus damp nearby water fluctations

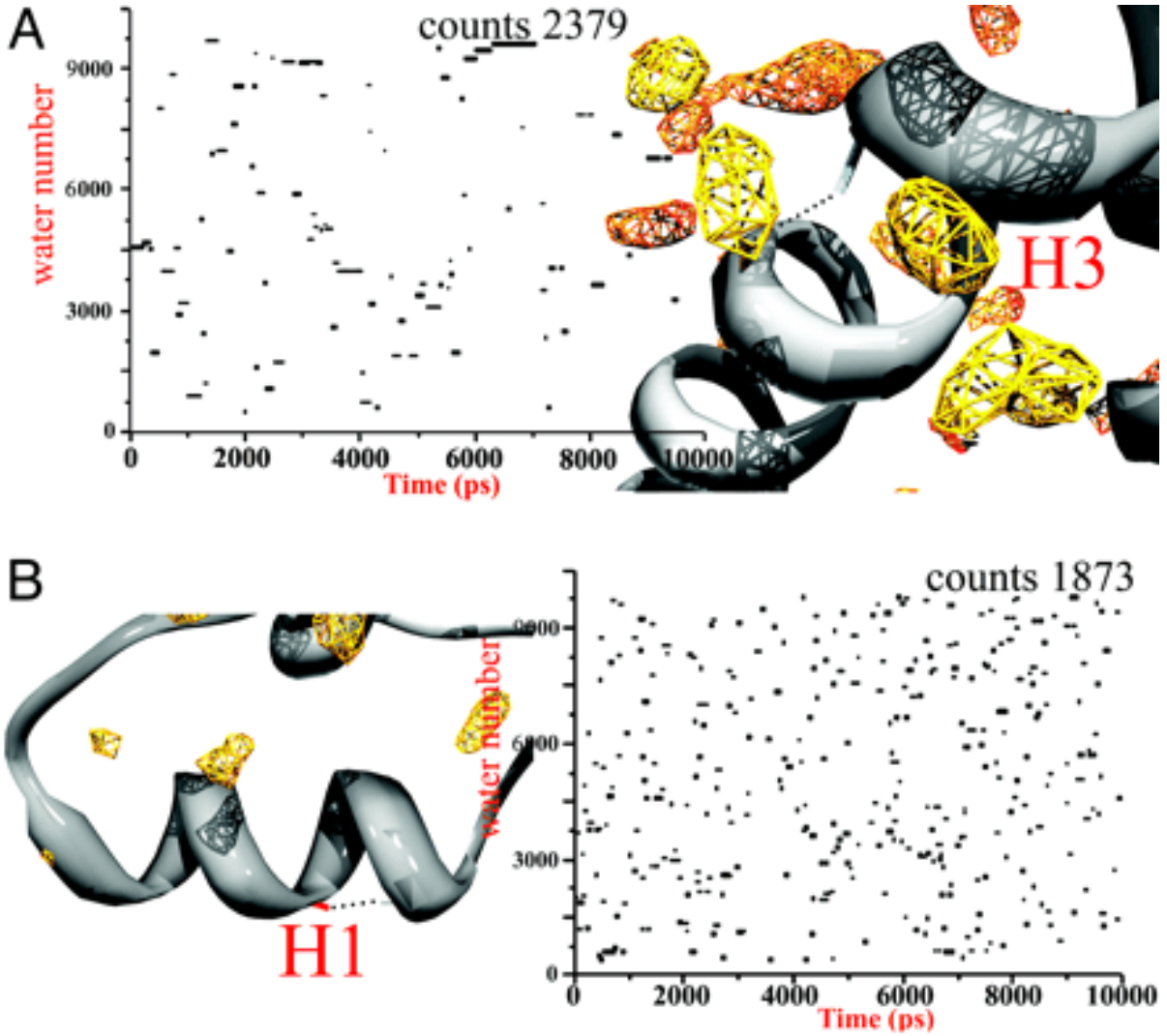
1.3 Tutorial on dielectrics

Water removal reduces the dielectric effect and makes electronic bonds stronger.

Number of carbonaceous groups in a region determine extent of water removal and strength of electronic bonds.

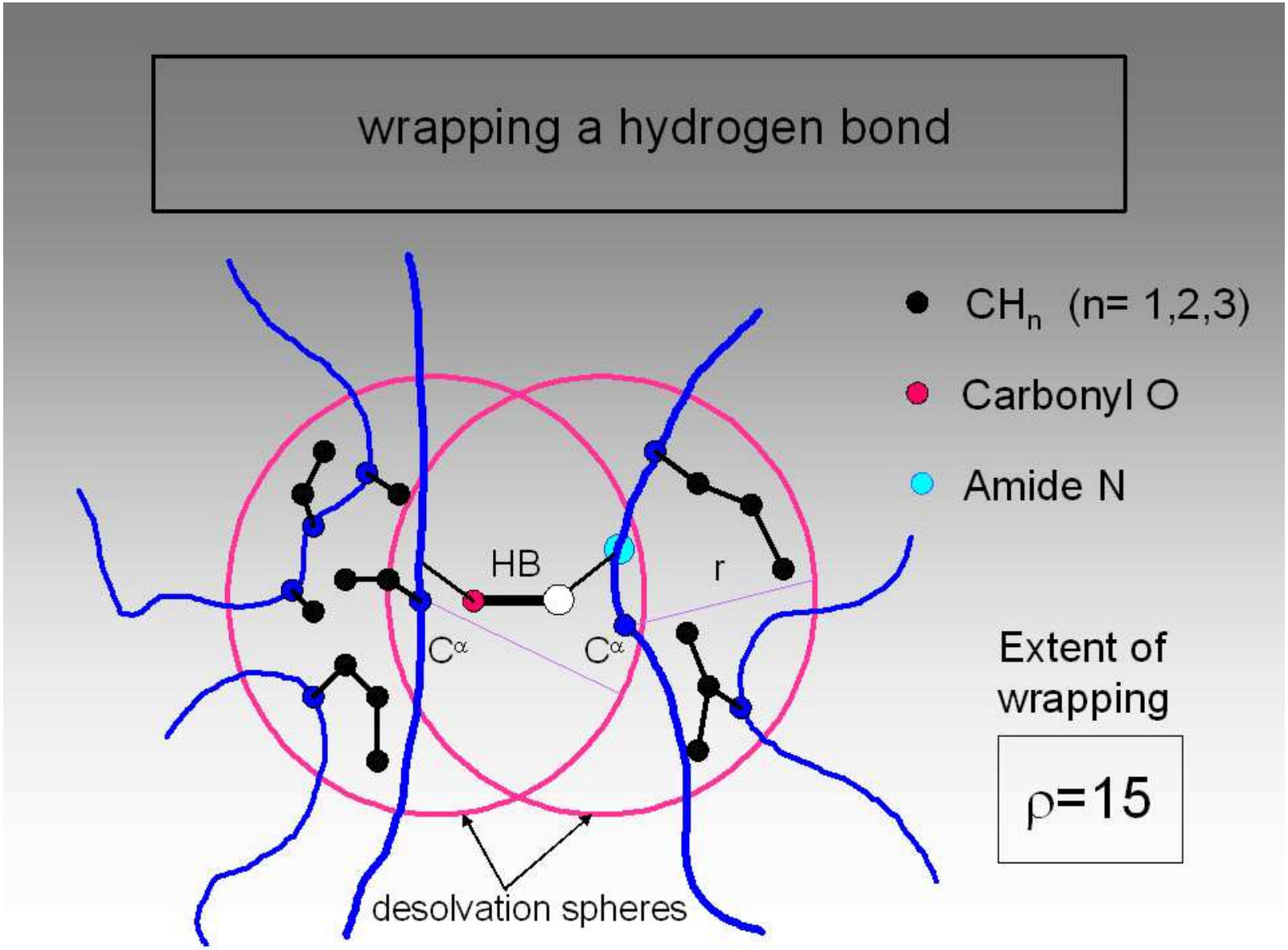
1.4 Extent of wrapping changes nature of hydrogen bond

Hydrogen bonds (B) that are not protected from water do not persist.



From De Simone, et al., PNAS 102 no 21 7535-7540 (2005)

Wrapping made quantitative by counting carbonaceous groups in the neighborhood of a hydrogen bond.



1.5 Under-wrapped hydrogen bonds

Hydrogen bonds with insufficient wrapping in one context can become well wrapped by a partner.

The hydrogen bond is much stronger when wrapped.

The change in energy makes these hydrogen bonds sticky.

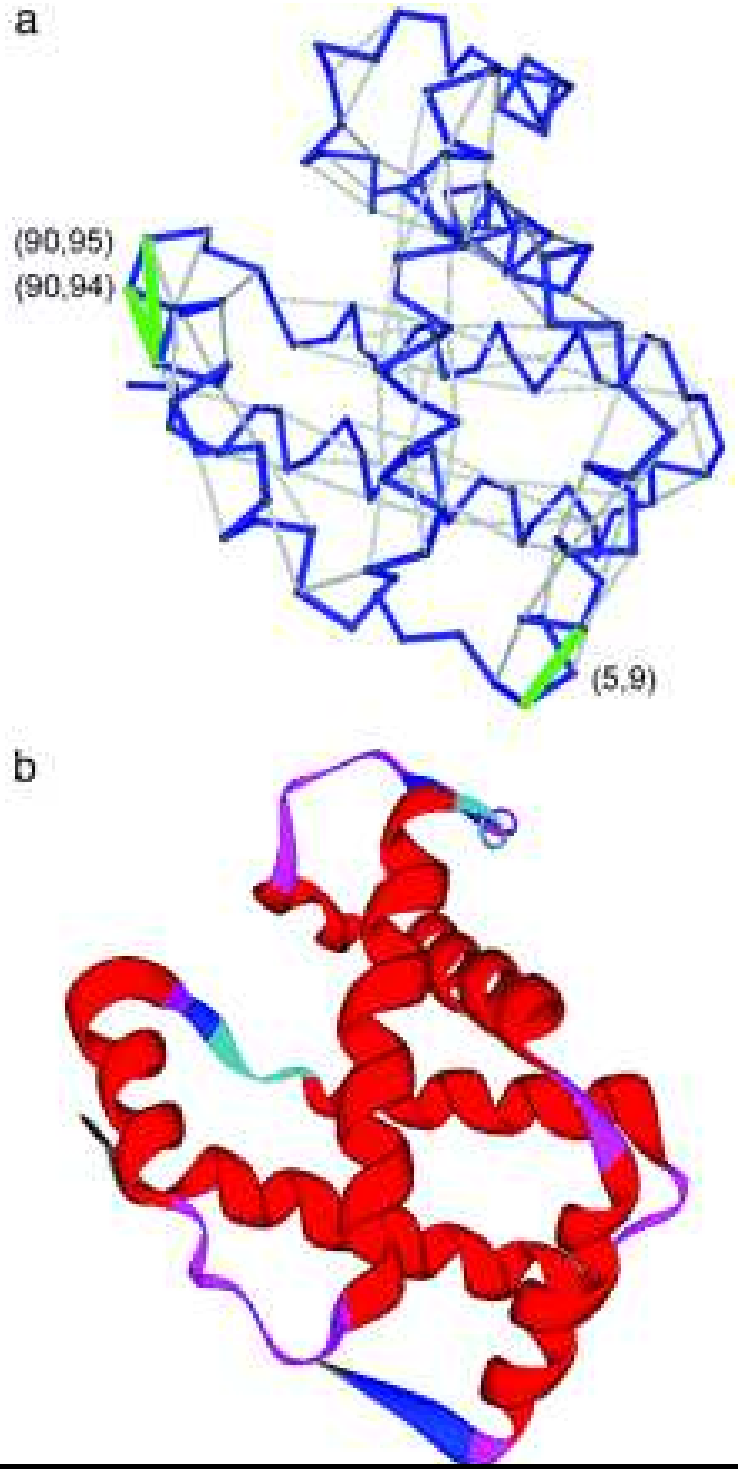
We call such under-wrapped hydrogen bonds

dehydrons

because they can benefit from becoming dehydrated.

The force associated with dehyrdons is not huge, but they can act as a guide in protein-protein association.

In our pictures, our new lens colors dehyrdons GREEN to distinguish from ordinary hydrogen bonds.



Dehydrons

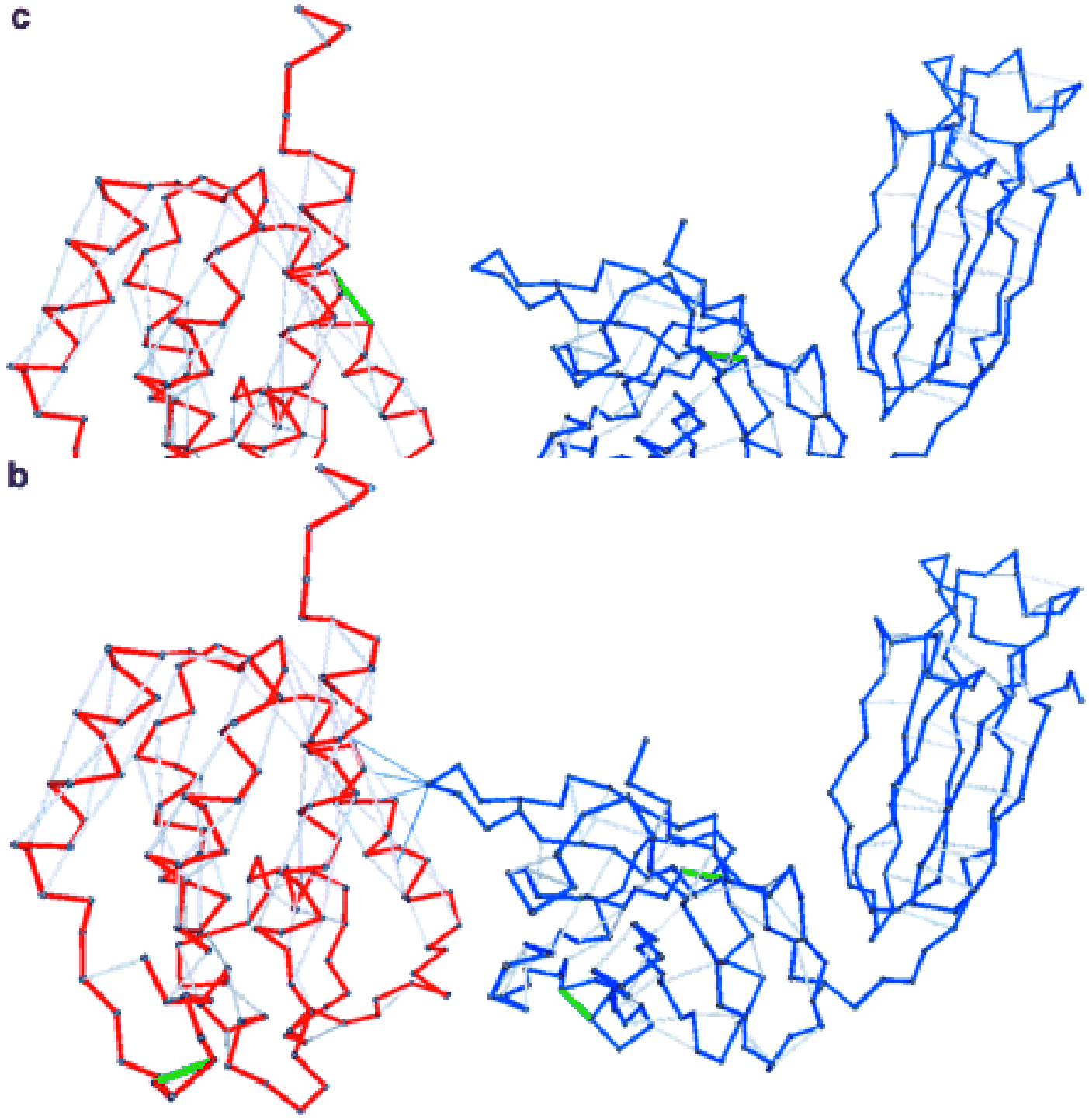
in human hemoglobin, From PNAS 100: 6446-6451 (2003) Ariel Fernandez, Jozsef Kardos, L. Ridgway Scott, Yuji Goto, and R. Stephen Berry. Structural defects and the diagnosis of amyloidogenic propensity.

Well-wrapped

hydrogen bonds are

grey, and dehydrons are green.

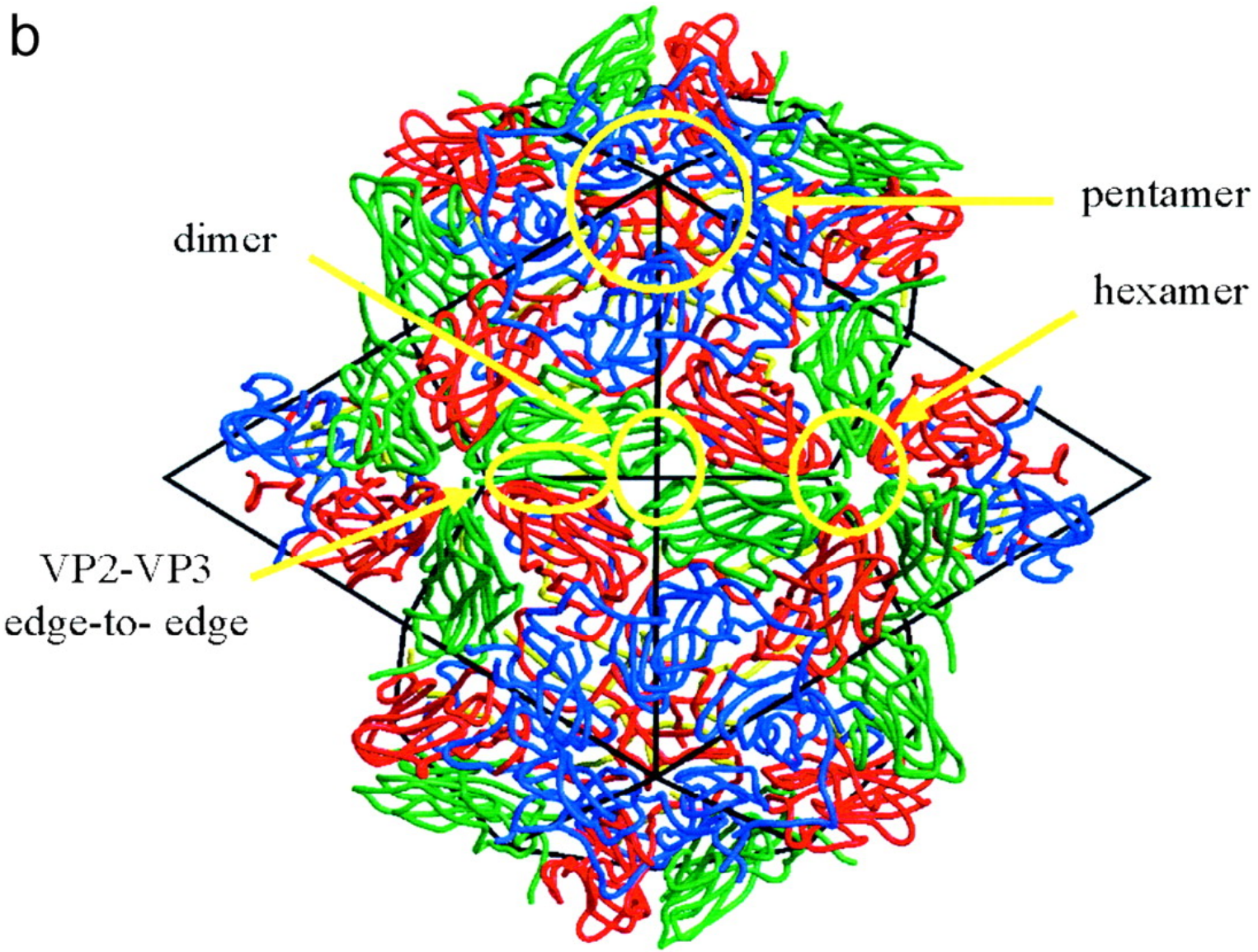
The standard ribbon model of “structure” lacks indicators of electronic environment.



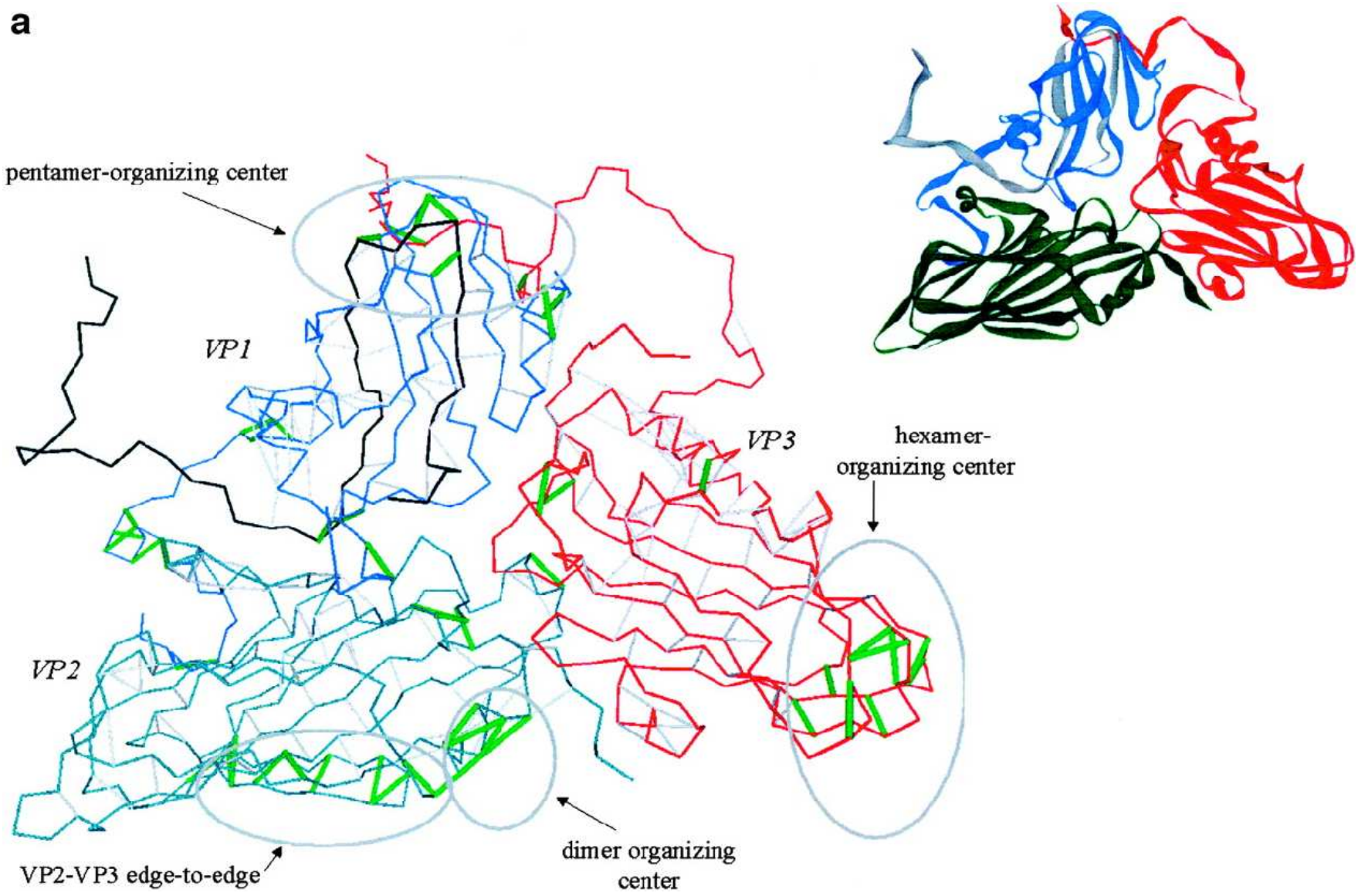
The HIV protease has a dehydron at an antibody binding site.

When the antibody binds at the dehydron, it wraps it with hydrophobic groups.

1.6 A model for protein-protein interaction



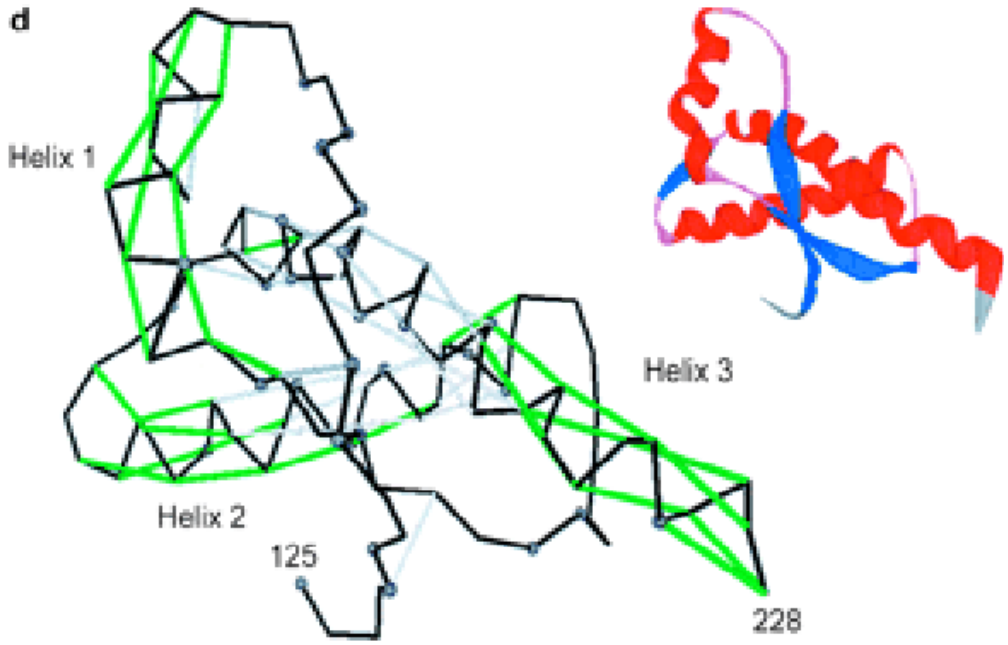
Foot-and-mouth disease virus assembly from small proteins.



Dehydrons guide binding of component proteins VP1, VP2 and VP3 of foot-and-mouth disease virus.

1.7 Extreme interaction: amyloid formation

If some is good, more may be better, but too many may be bad.



Too many dehydrons signals trouble: the human prion.

From PNAS 100: 6446-6451 (2003) Ariel Fernandez, Jozsef Kardos, L. Ridgway Scott, Yuji Goto, and R. Stephen Berry. Structural defects and the diagnosis of amyloidogenic propensity.

1.8 Stickiness of dehydrons

Attractive force of dehydrons predicted and measured in

Ariel Fernandez and L. Ridgway Scott.

Adherence of packing defects in soluble proteins.

Phys. Rev. Lett. 2003 91:18102(4)

by considering rates of adhesion to phospholipid (DLPC) bilayer.

Deformation of phospholipid bilayer by dehydrons measured in

Ariel Fernandez and L. Ridgway Scott.

Under-wrapped soluble proteins as signals triggering membrane morphology.

Journal of Chemical Physics 119(13), 6911-6915 (2003).

Fine print: careful definition of dehydron requires assessing modification of dielectric enviroment by test hydrophobe. That is, geometry of carbon groups matters, although counting gets it right 90% of the time.