Harvard-MIT Division of Health Sciences and Technology
HST.508: Quantitative Genomics, Fall 2005
Instructors: Leonid Mirny, Robert Berwick, Alvin Kho, Isaac Kohane

Biomolecular Forces and Energies

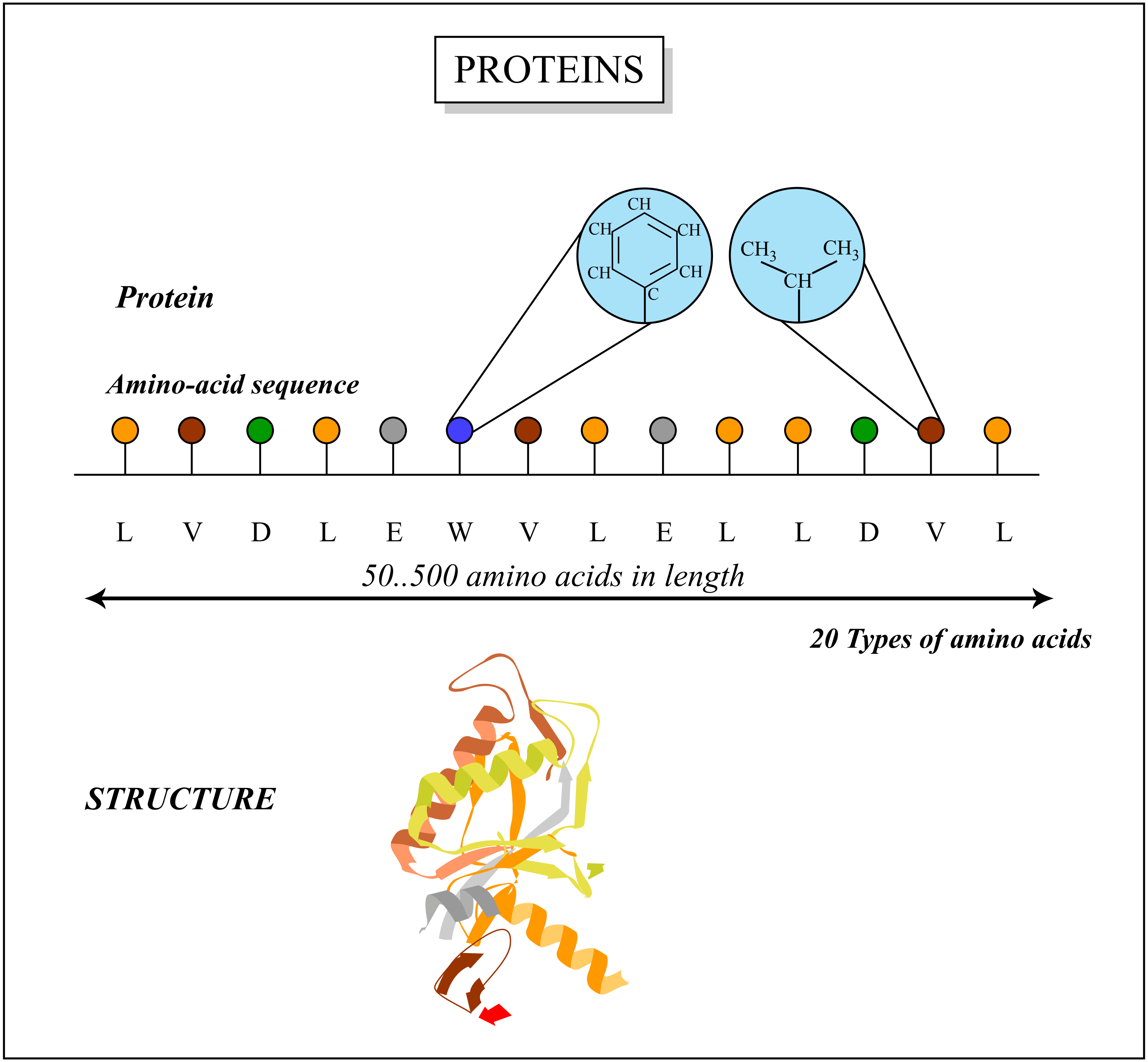
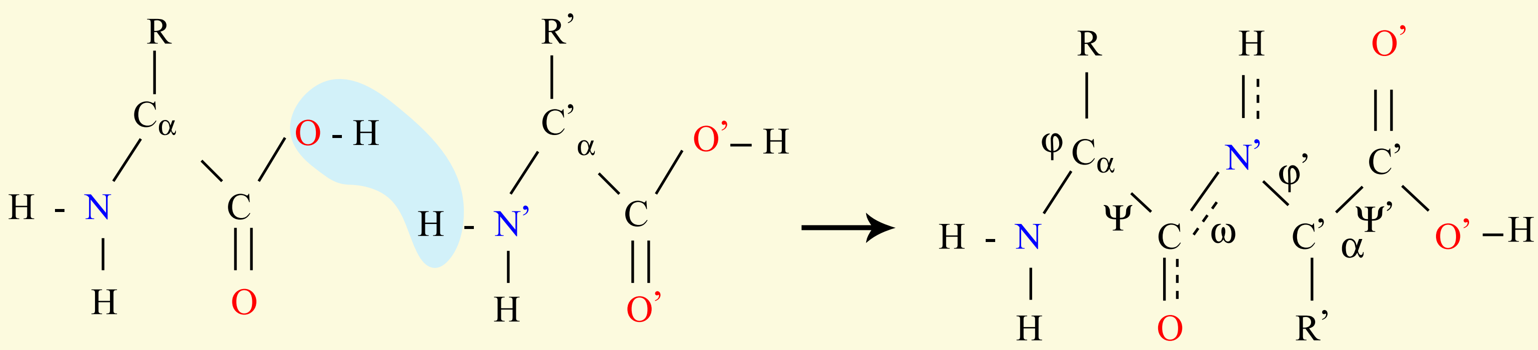


Figure by MIT OCW.

Amino Acids



GLY **ALA** **LEU** **TRP** **GLU** **LYS**

Hydrophobic Acidic Basic

Figure by MIT OCW.

Amino Acids

Name (Residue)	3-letter code	Single Code	Relative abundance (%) E.C.	MW	pK	VdW volume(Å^3)	Charged, Polar, Hydrophobic
Alanine	ALA	A	13.0	71		67	H
Arginine	ARG	R	5.3	157	12.5	148	C+
Asparagine	ASN	N	9.9	114		96	P
Aspartate	ASP	D	9.9	114	3.9	91	C -
Cysteine	CYS	C	1.8	103		86	P
Glutamate	GLU	E	10.8	128	4.3	109	C -
Glutamine	GLN	Q	10.8	128		114	P
Glycine	GLY	G	7.8	57		48	-
Histidine	HIS	H	0.7	137	6.0	118	P, C+
Isoleucine	ILE	I	4.4	113		124	H
Leucine	LEU	L	7.8	113		124	H
Lysine	LYS	K	7.0	129	10.5	135	C+
Methionine	MET	M	3.8	131		124	H
Phenylalanine	PHE	F	3.3	147		135	H
Proline	PRO	P	4.6	97		90	H
Serine	SER	S	6.0	87		73	P
Threonine	THR	T	4.6	101		93	P
Tryptophan	TRP	W	1.0	186		163	P
Tyrosine	TYR	Y	2.2	163	10.1	141	P
Valine	VAL	V	6.0	99		105	H

Figure by MIT OCW.

INTERACTIONS

Figure removed due to copyright considerations.

Review of Protein Structure

Secondary Structure: β-sheets

Figure removed due to copyright reasons.
Please see: Figure 6-9 in Voet, Donald, Judith G. Voet, and Charlotte W. Pratt. *Fundamentals of Biochemistry*. New York, NY: John Wiley & Sons, 2002, p. 130. ISBN: 0471417599.

Secondary Structure: β-sheets

Figure removed due to copyright reasons.

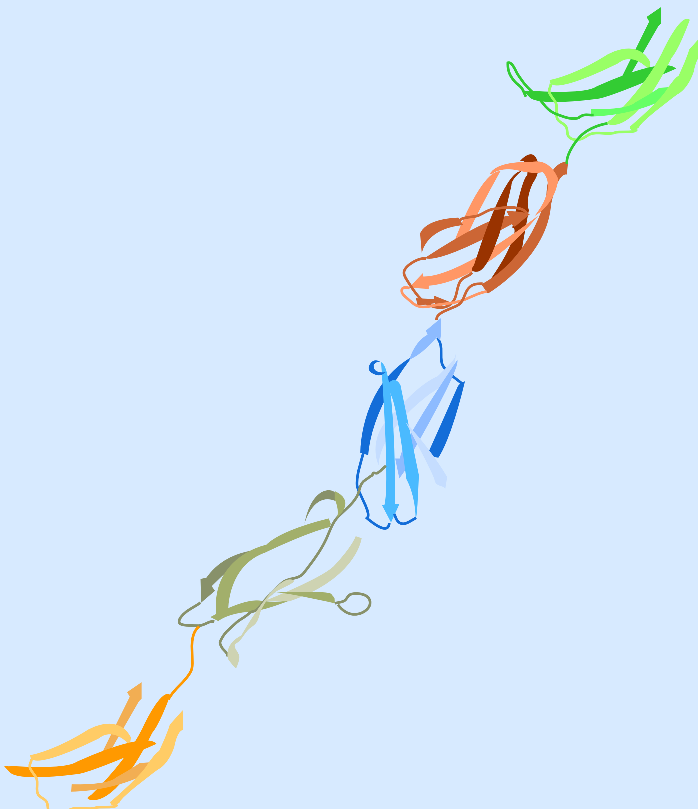
Secondary Structure:
α-helices

Figure removed due to copyright reasons.
Please see: Figure 6-7 in Voet, Donald, Judith G. Voet, and Charlotte W. Pratt. *Fundamentals of Biochemistry*. New York, NY: John Wiley & Sons, 2002, p. 129. ISBN: 0471417599.

Secondary Structure: α-helices

Figure removed due to copyright reasons.

DOMAIN STRUCTURE

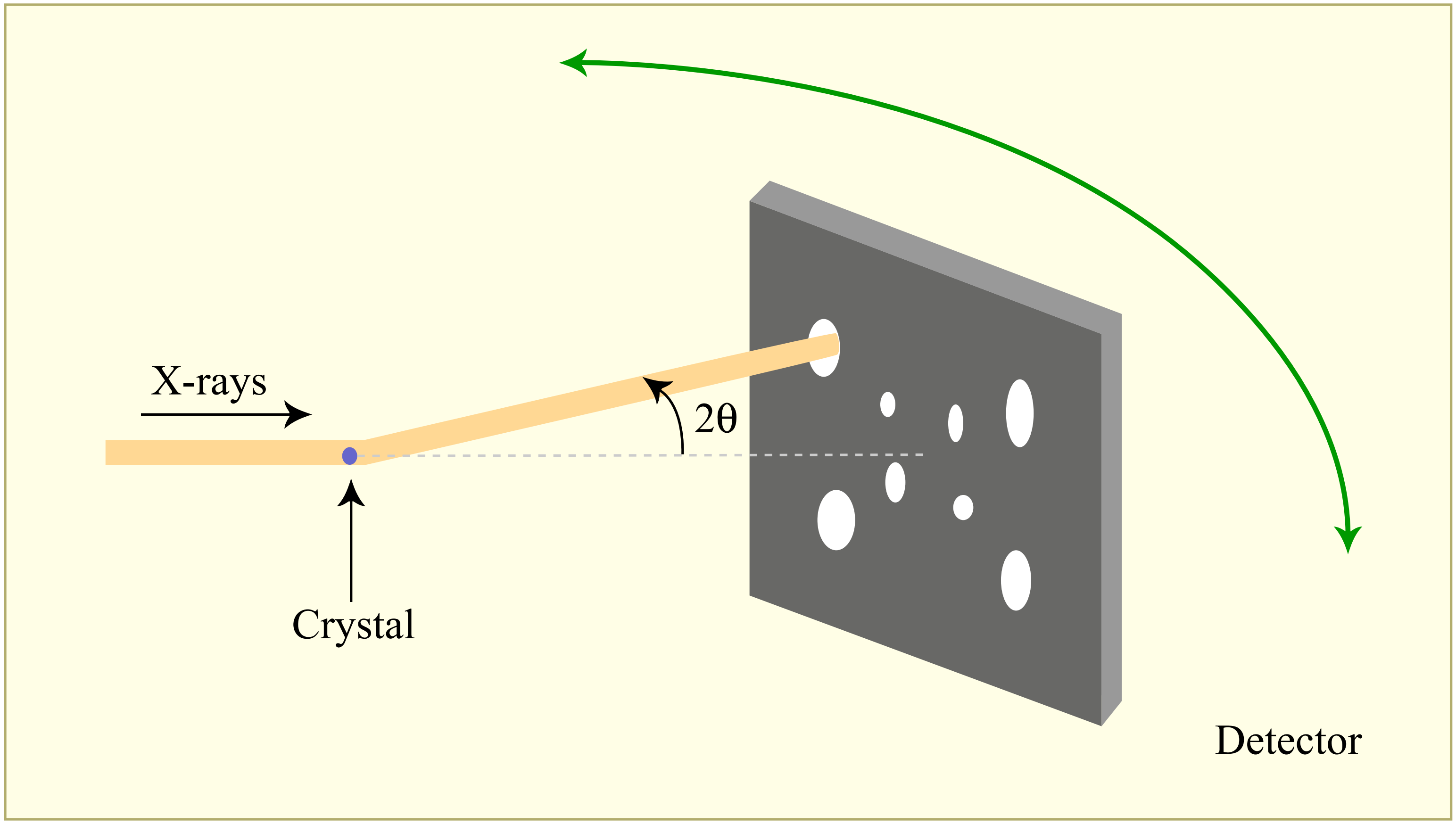


Many proteins consists of several domains

Many proteins are dimers or oligomers which consist of several polypeptide chains.

Figure by MIT OCW.

X-ray Crystallography

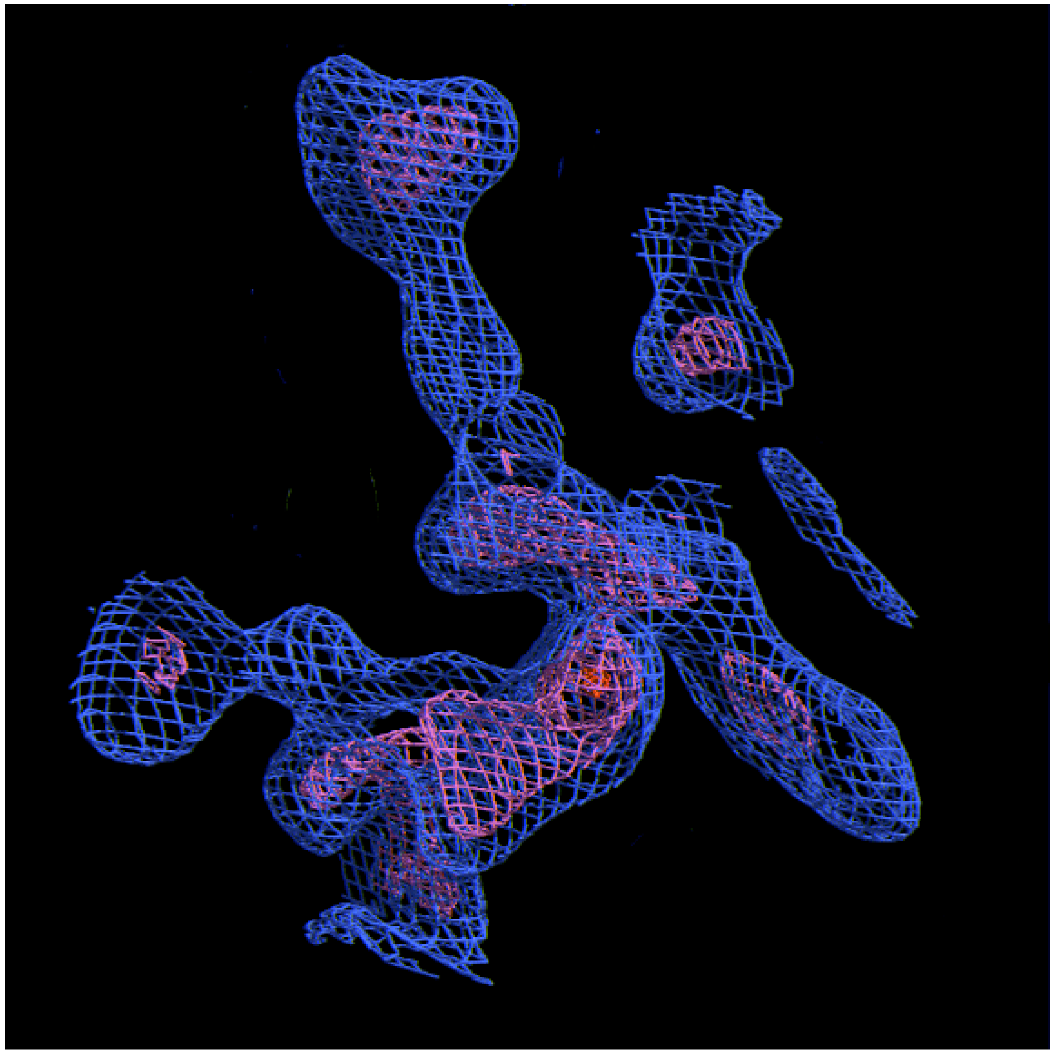


Protein ⟶ Crystal ⟶ Diffraction ⟶ Electron Density ⟶ Protein Structure

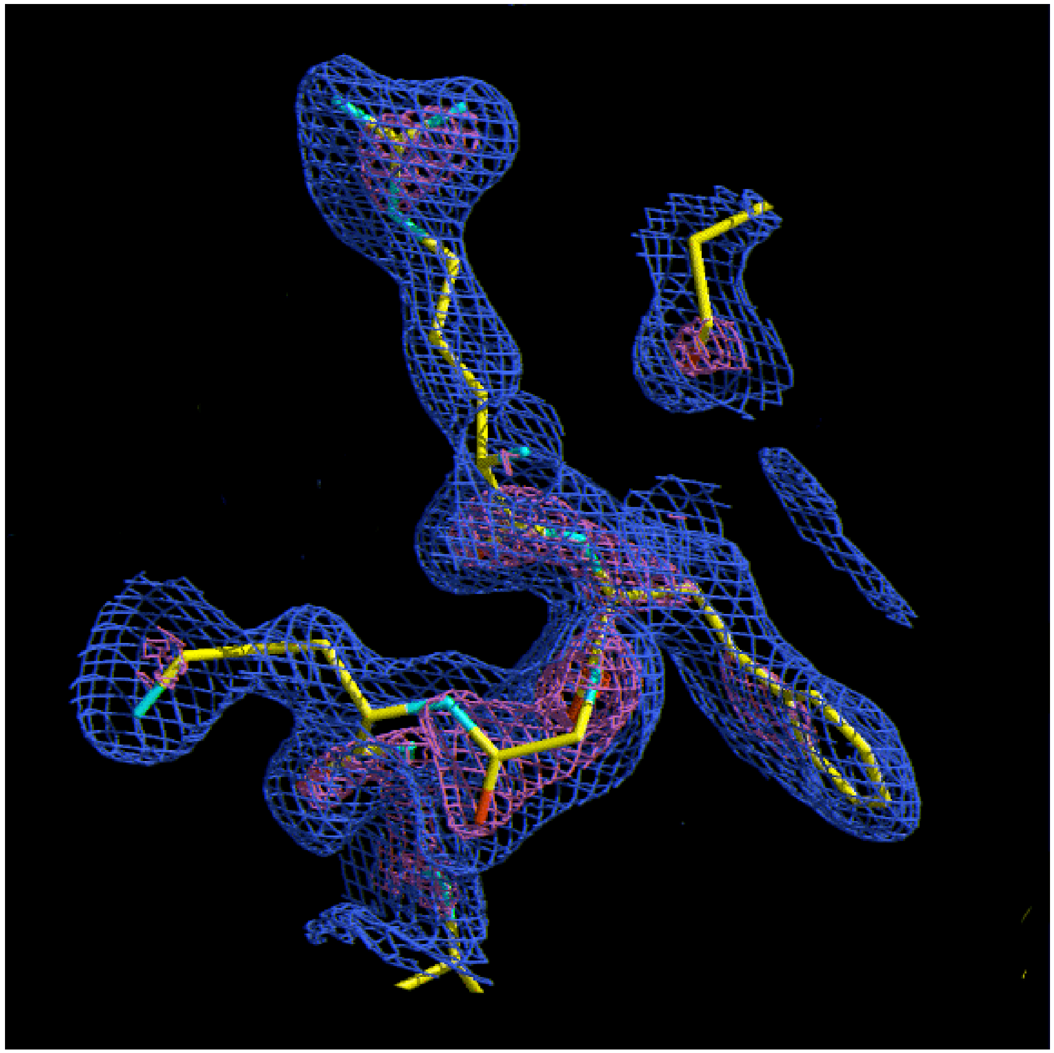
MOLECULAR DYNAMICS used to: 1) Fit structure into density
2) Refine the structure

Figure by MIT OCW.

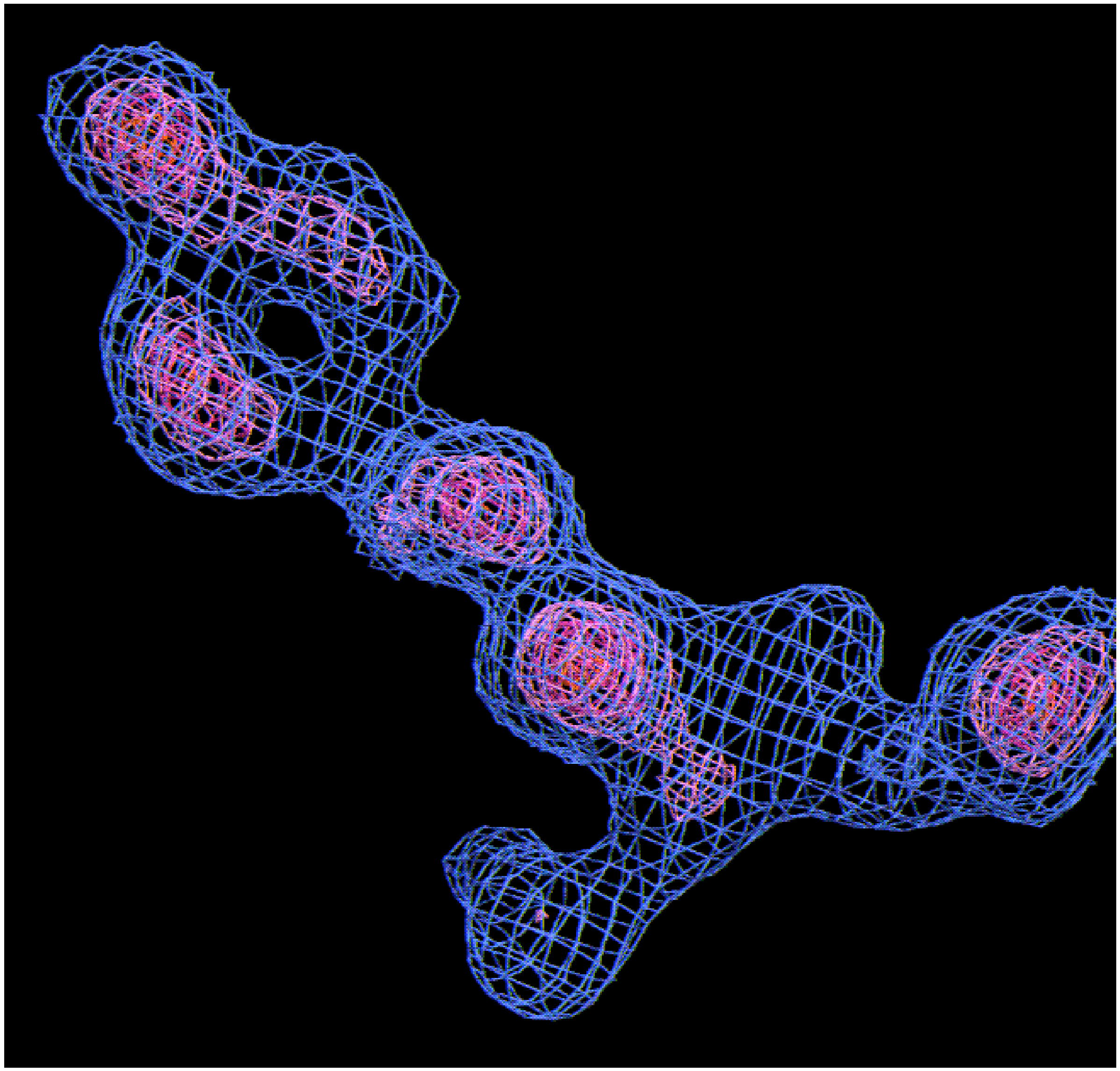
X-ray Crystallography



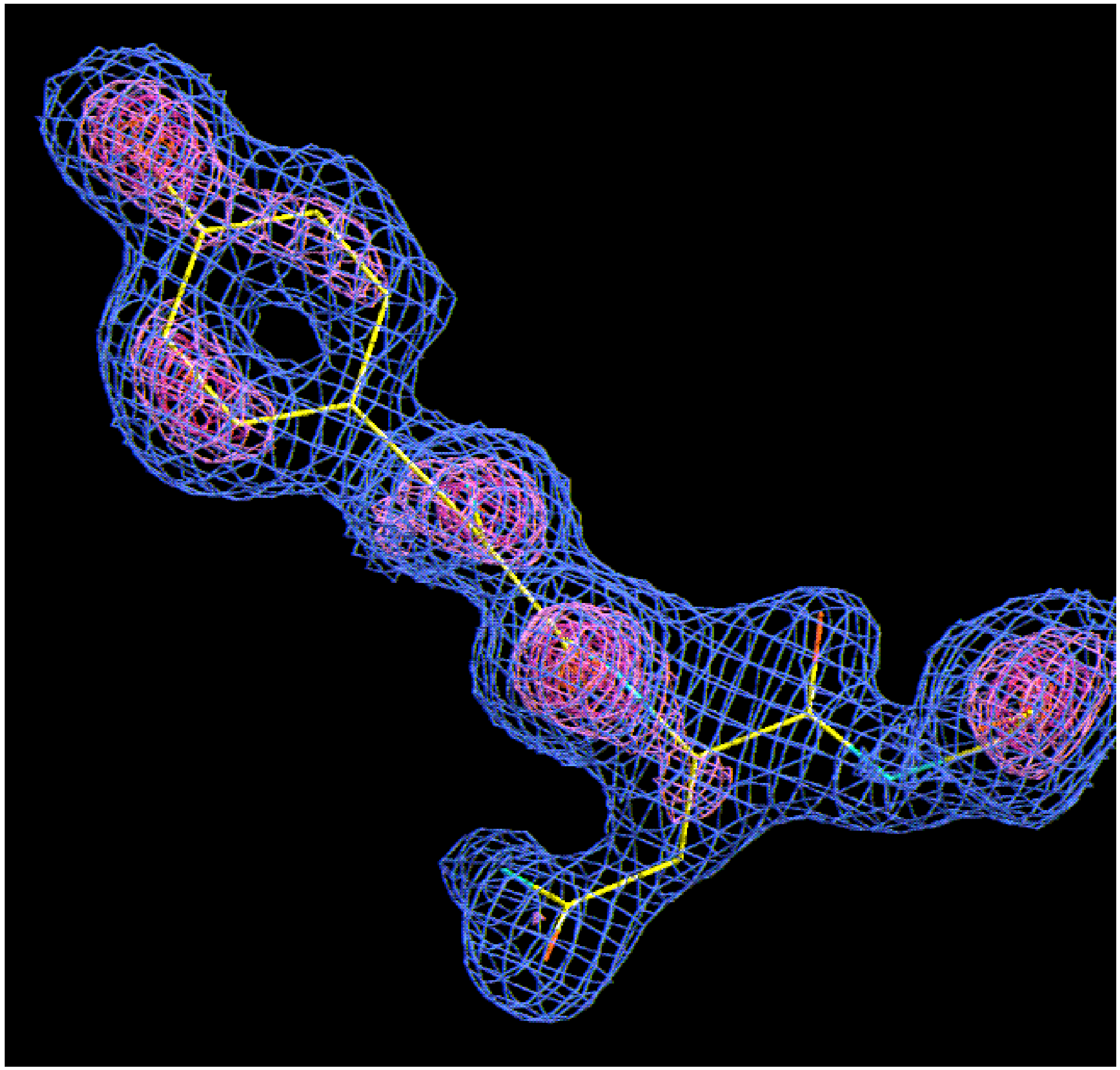
X-ray Crystallography



X-ray Crystallography



X-ray Crystallography



Protein Strcutures

- Protein Data Bank
  http://www.rcsb.org/pdb/
- Structural Classification of Proteins (SCOP)
  http://scop.mrc-lmb.cam.ac.uk/scop/

Forces

BONDED INTERACTIONS

NON-BONDED INTERACTIONS

- van der Waals
- Hydrogen bonds
- Hydrophobic
- Electrostatic (with screening)

Amino acids

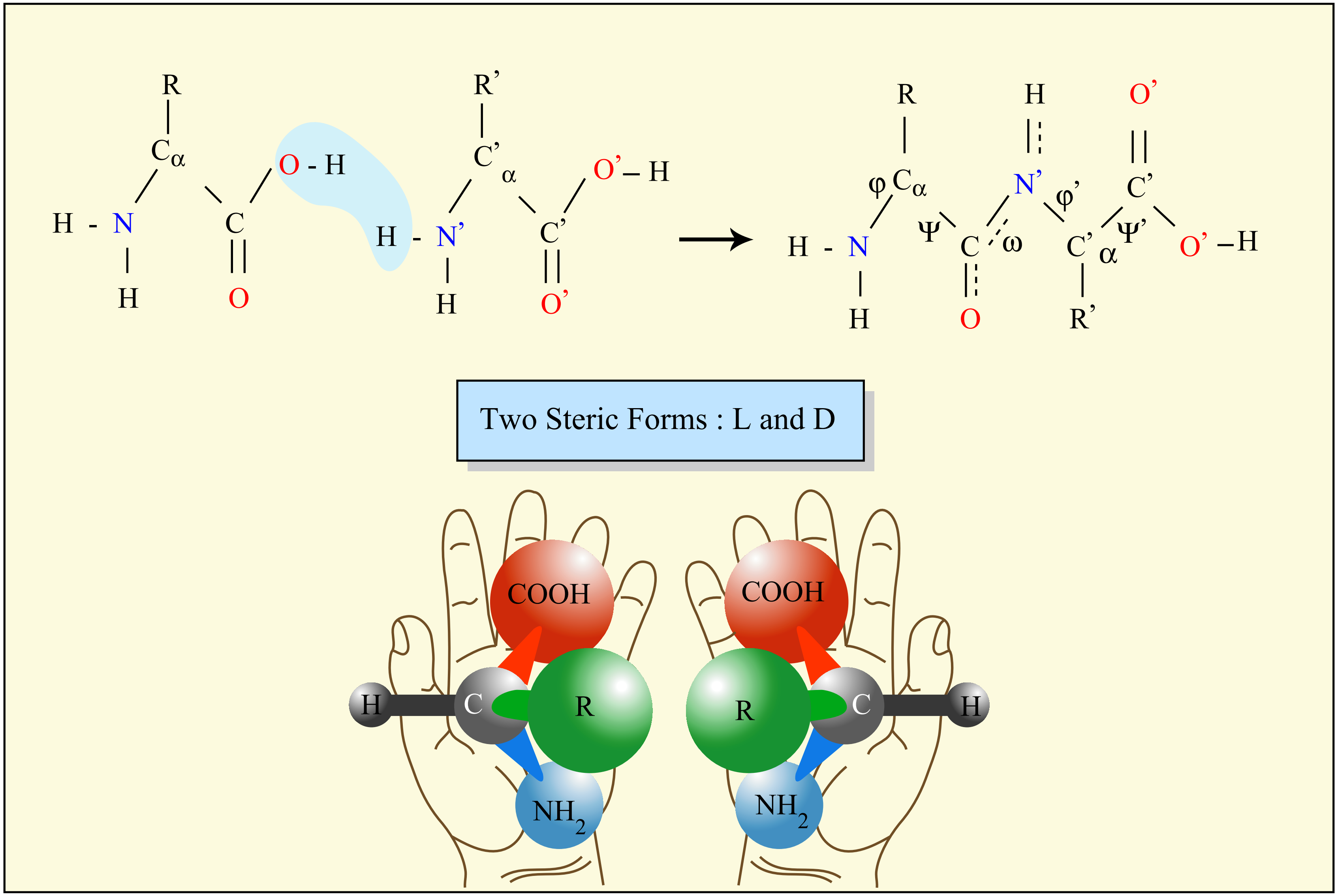
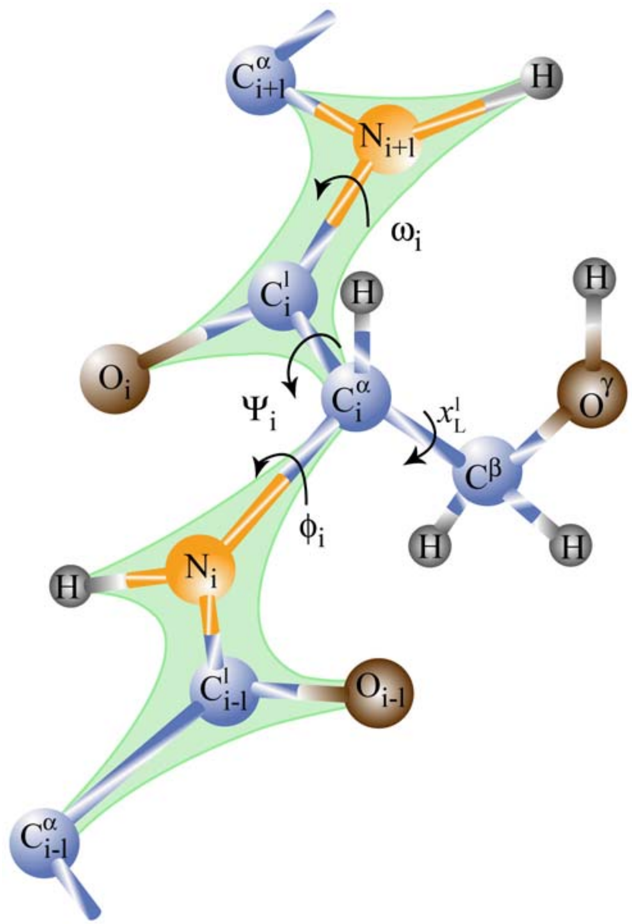
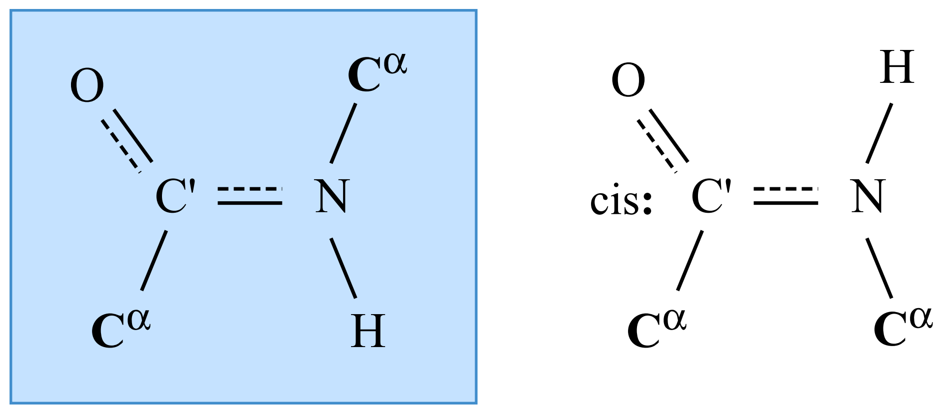


Figure by MIT OCW.

POLYPEPTIDE UNIT





All but PROLINE

Figure by MIT OCW.

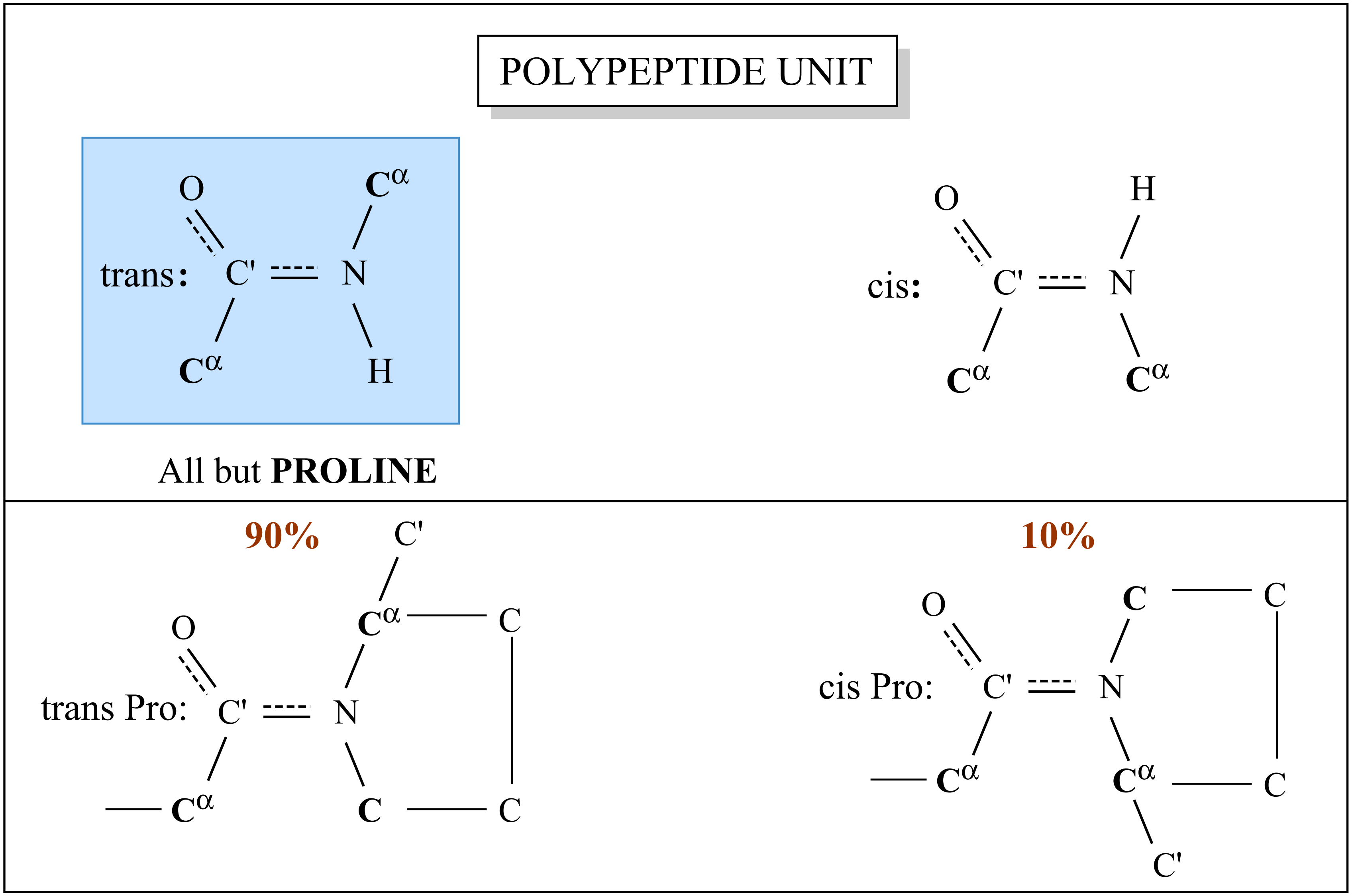
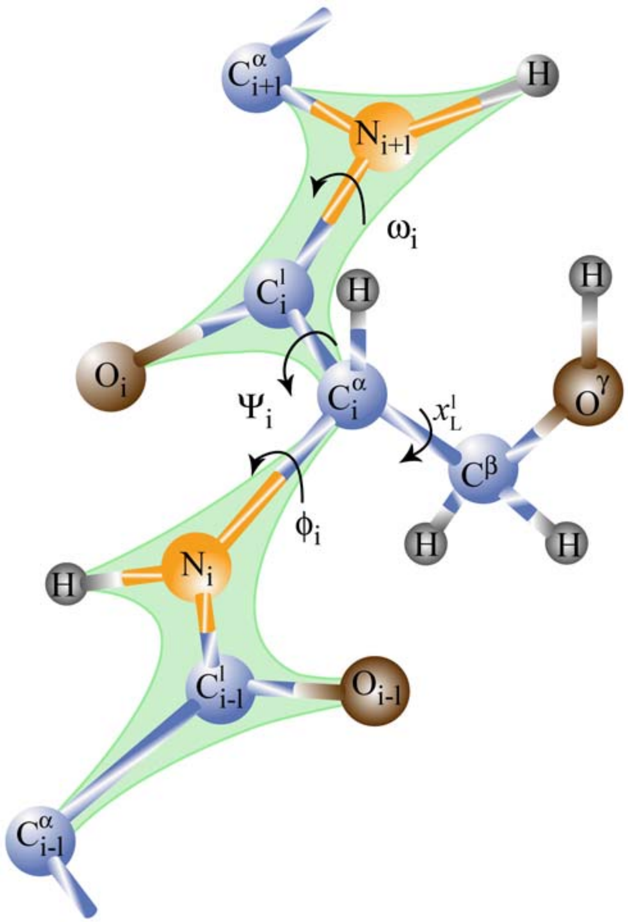
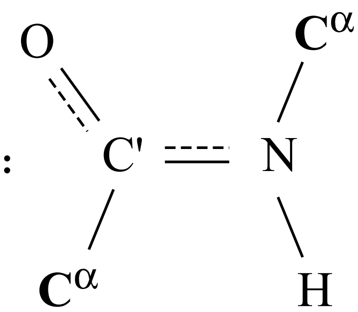


Figure by MIT OCW.

POLYPEPTIDE UNIT IS FLAT



trans: 

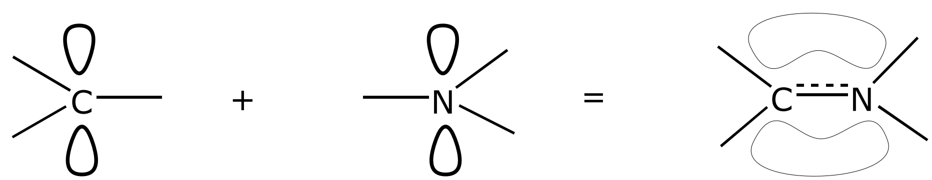
Sp2 Hybridization LI 

Figure by MIT OCW.

Vibration of covalent bonds

- IR spectra of C-H : $\nu \sim 7 \times 10^{13}\ s^{-1}$
  wave length $\lambda = c/\nu = 5\ \mu m$
- IR spectra of CH3 - CH3 : $\nu \sim 2 \times 10^{13}\ s^{-1}$
  wave length $\lambda = c/\nu = 15\ \mu m$
- Thermal fluctuations:

  $\nu \sim 7 \times 10^{12}\ s^{-1}$

  <u>insufficient to excite</u>

  <u>covalent bonds</u>

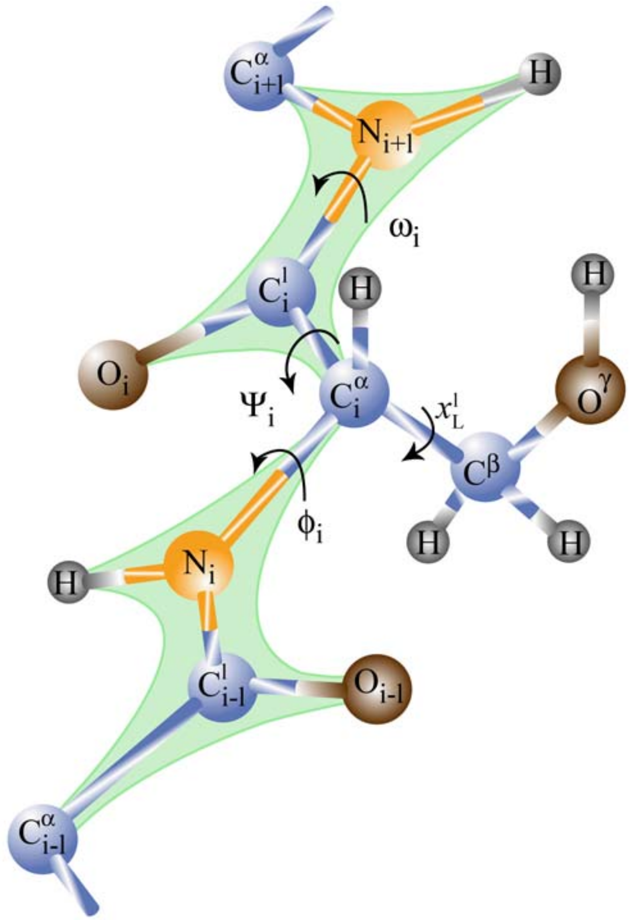
Vibration of covalent angles

- IR spectra of X-Y-Z angle :
  $\nu \sim 10^{12} - 10^{13}\ s^{-1}$
  Thermal fluctuations:

  $\nu \sim 7x10^{12}\ s^{-1}$

  Sufficient to excite covalent angles,
  but fluctuations are small $\sim 5^{o}$

ROTATION AROUND BONDS



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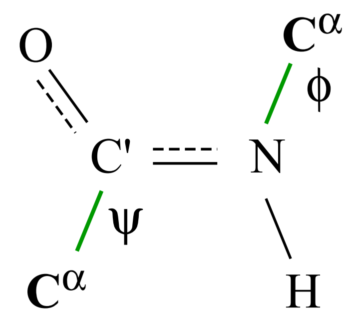
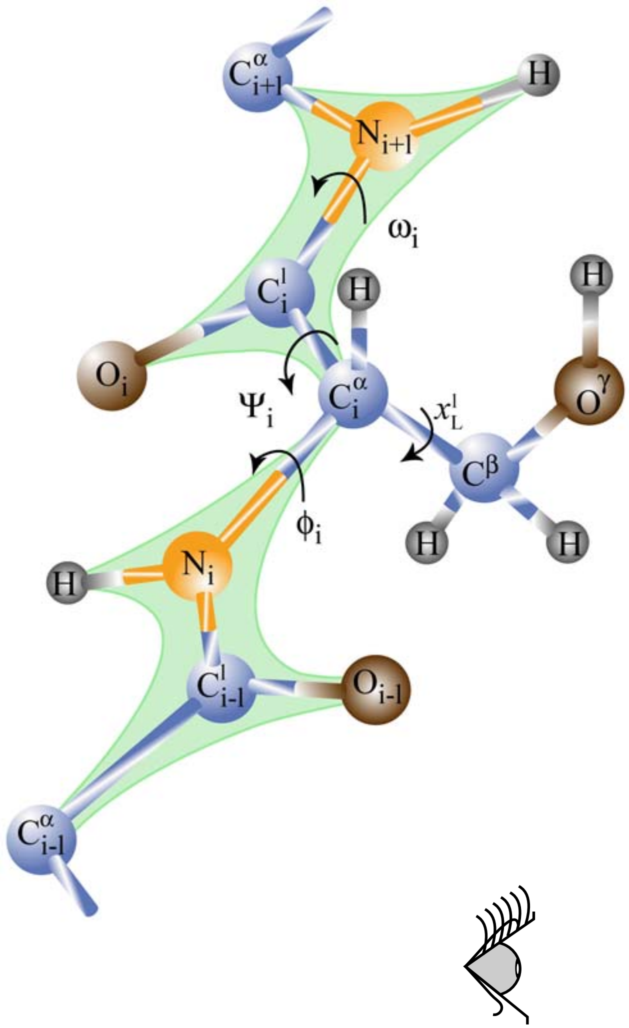
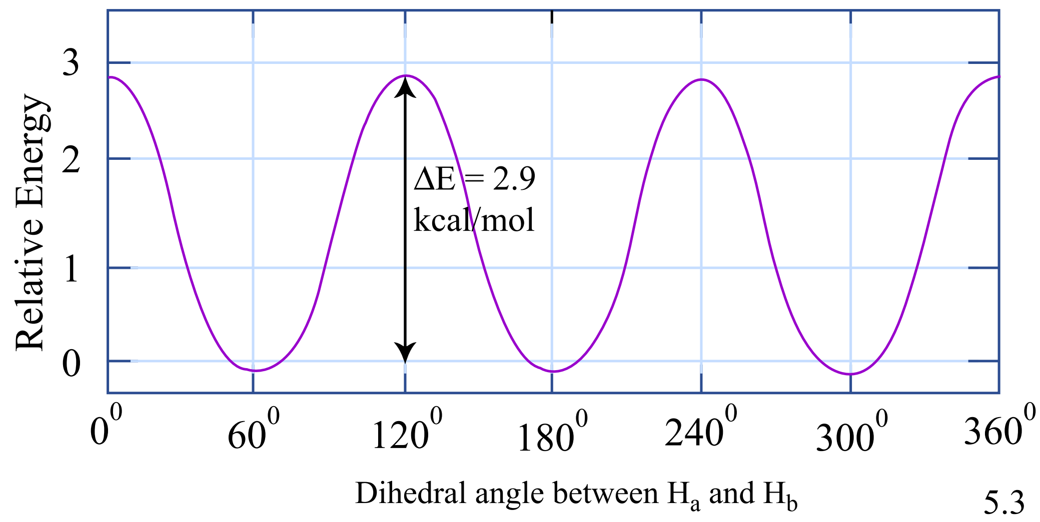
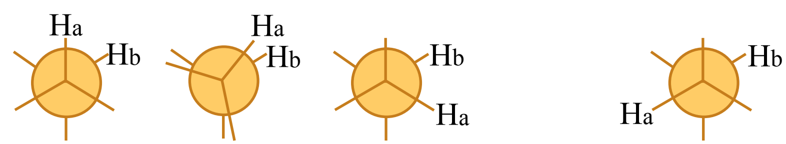


Figure by MIT OCW.

ROTATION AROUND BONDS







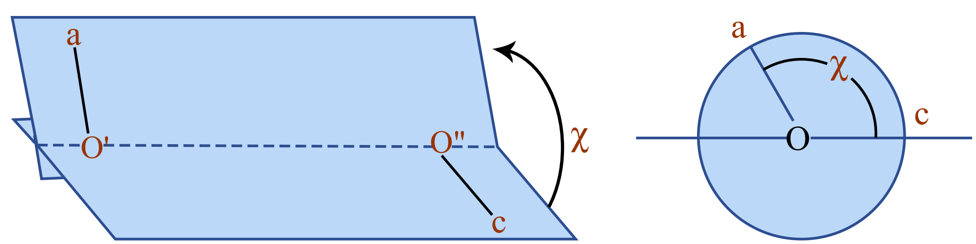


Figure by MIT OCW.

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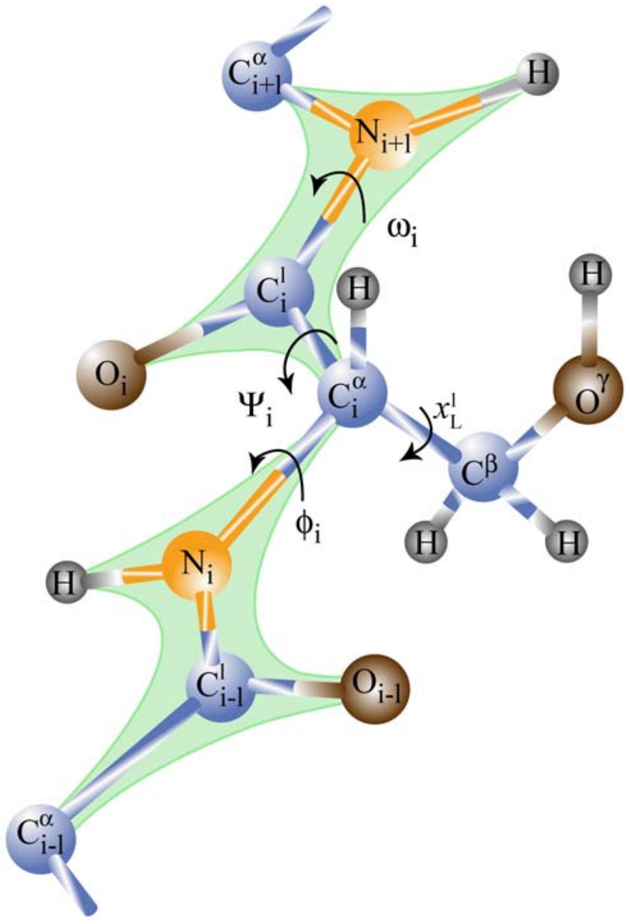

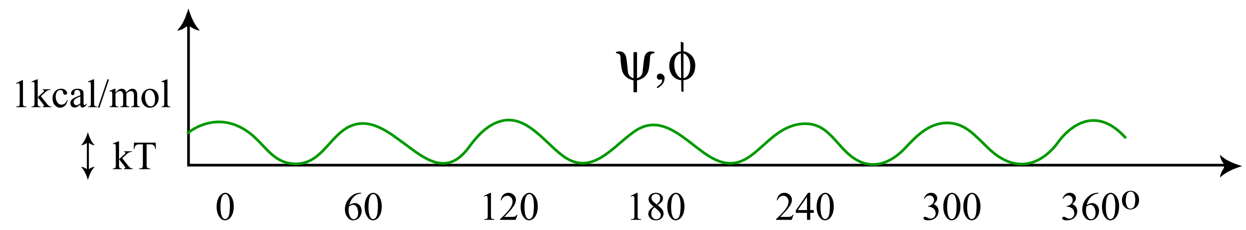

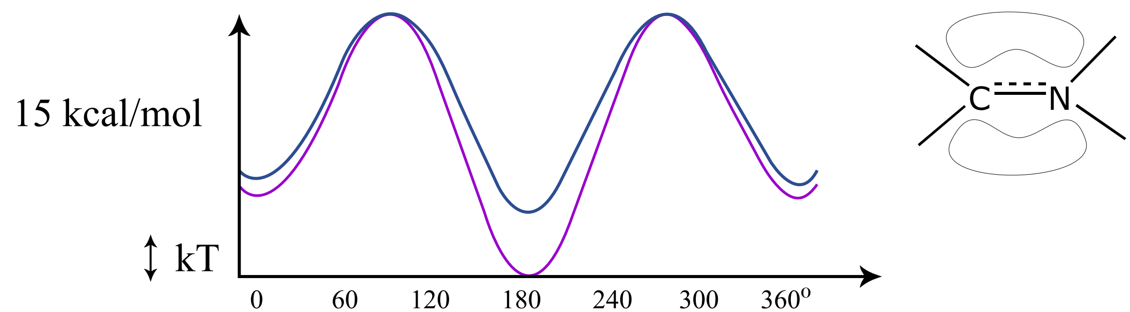

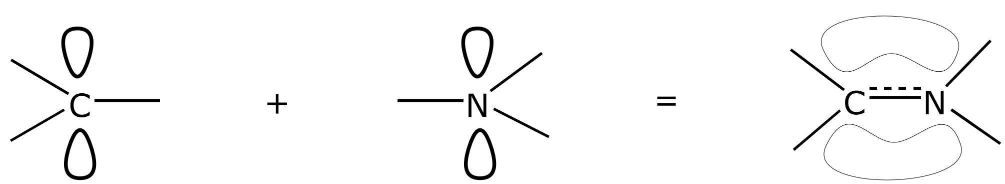

Figure by MIT OCW.

Forces

- Van der Waals

  "London forces" (after Fritz London)

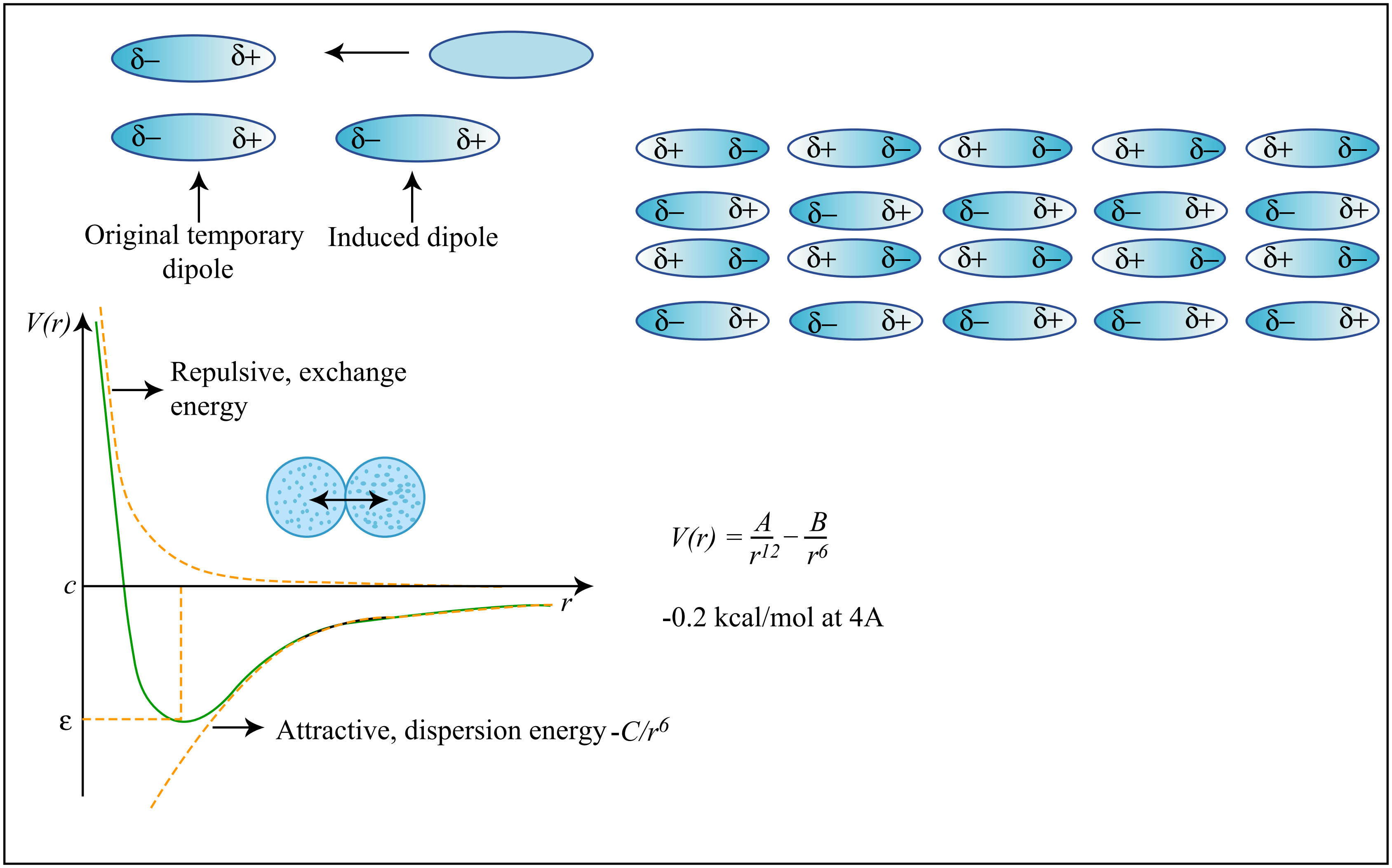

Figure by MIT OCW.

Van der Waals interactions

Interaction	E_0 kcal/mol	r_0,A	r_{min},A	Atomic radii (A)	
H . . . . H	0.12	2.4	2.0	H:	1.0
H C	0.11	2.9	2.4		
C C	0.12	3.4	3.0	C:	1.5
O . . . . O	0.23	3.0	2.7	O:	1.35
N . . . . N	0.20	3.1	2.7	N:	1.35
CH_2 . . . CH_2	~ 0.5	~ 4.0	~ 3.0	CH_2:	~ 1.5

$$V(r) = \frac{A}{r^{12}} - \frac{B}{r^6} = E_0\left(\left(\frac{r_0}{r}\right)^{12} - \left(\frac{r_0}{r}\right)^{6}\right)$$

Forces

Hydrogen Bonds

-Anisotropic

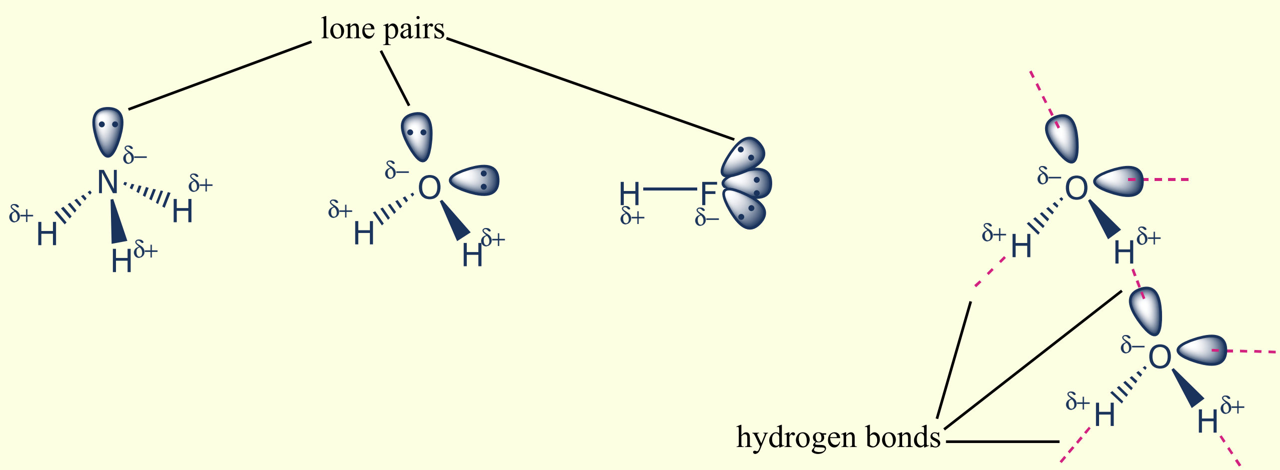

Figure by MIT OCW.

SOLVENT: Hydrogen bonds

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Forces

- Hydrophobic interactions
  Walter Kauzmann
  energetic (<1nm) and
  entopic (>1nm)

Substitution	Number of examples	$\Delta\Delta G$ (kcal/mol) Low	High	Average	ΔG_{tr} (kcal/mol)
Ile $\longrightarrow$ Val	9	0.5	1.8	1.3 ± 0.4	0.80
Ile $\longrightarrow$ Ala	9	1.1	5.1	3.8 ± 0.7	2.04
Leu $\longrightarrow$ Ala	17	1.7	6.2	3.5 ± 1.1	1.90
Val $\longrightarrow$ Ala	11	0.0	4.7	2.5 ± 0.9	1.24
$-CH_2-$	46	0.0	2.3	1.2 ± 0.4	0.68
Met $\longrightarrow$ Ala	4	2.1	4.6	3.0 ± 0.9	1.26
Phe $\longrightarrow$ Ala	4	3.5	4.4	3.8 ± 0.3	2.02

Figure by MIT OCW.

~10 cal/mol/A^2