Chemistry 882

Lecture Notes 8

Welity

Chemical bonds make largest contribution to molecular energy (~350 kJ/mole for C-C single bond (≈ 10-100 × larger than intermolecular energy)

Steric energy is an important non-bonding interaction (electrostatic repulsion of e^- clouds between atoms not in the ^same functional group

trans - Peptide bond

cis - Peptide bond

Torsion angles
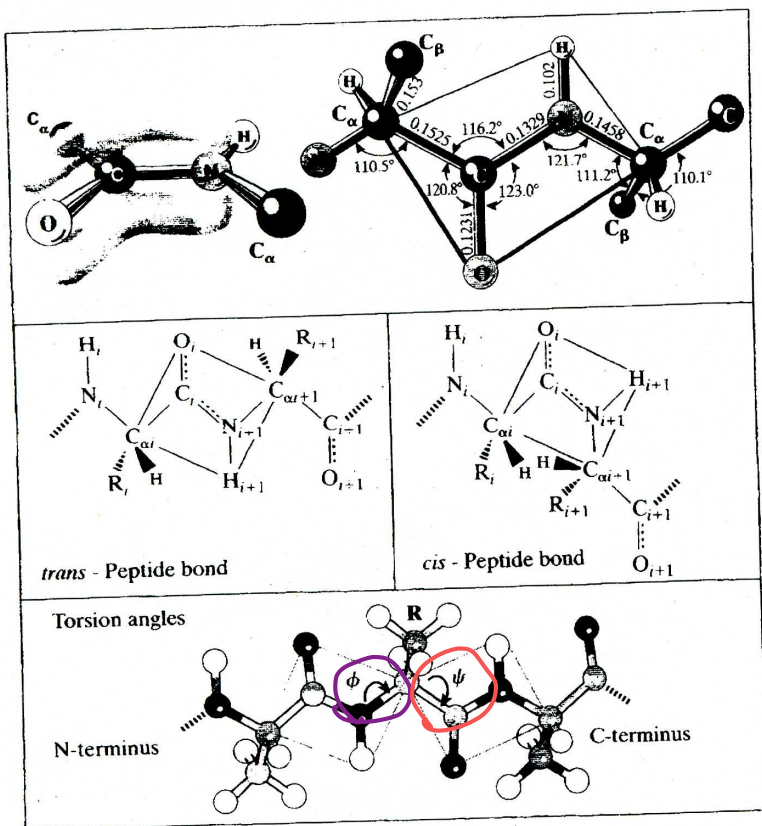
ϕ ψ

N-terminus   C-terminus

Figure 1.21 The peptide bond. The peptide bond that chemically links two amino acid residues along a polypeptide chain is a C—N bond of an amide linkage. The bond shows partial double-bond character, with the π-electrons distributed between the O—C—N atoms (top panel), and is not freely rotating [bond lengths and angles from Engh and Huber (1991), *Acta Crystallogr. A* **47**: 392–400]. The bond is found predominantly in the *trans*-configuration, but could also adopt the *cis*-form (middle panel). The two freely rotating bonds on either side of the C_α-carbon thus define the torsion angles ϕ (for rotation about the N—C_α bond) and ψ (for rotation about the Ca—C bond).
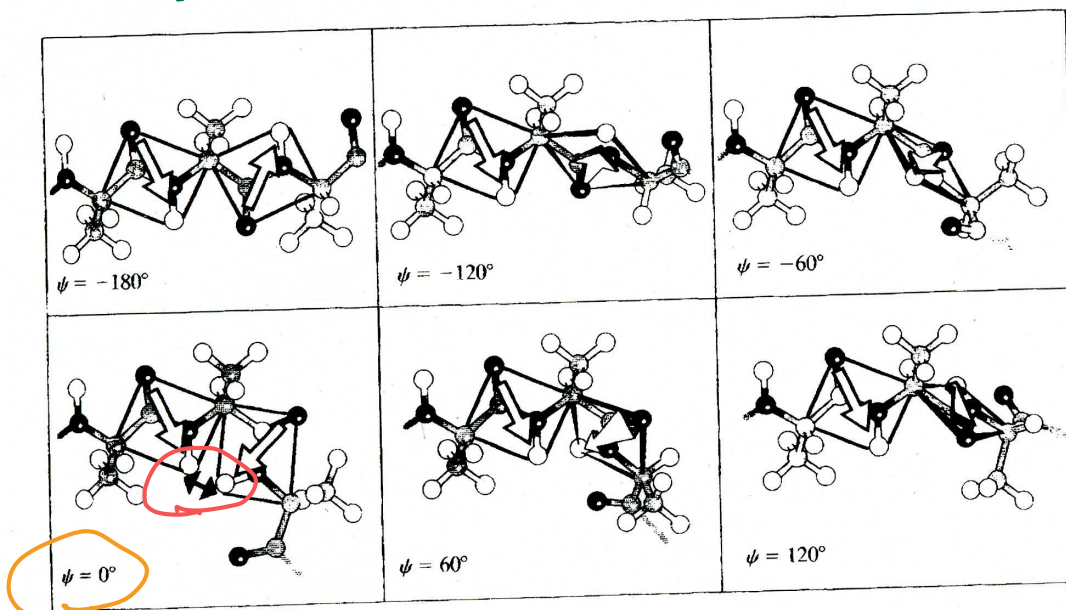
Protein backbone

Figure 3.9 Intramolecular interactions between internal alanine residues in a polyalanine chain. The rotation along ϕ is fixed at $-180°$, and ψ rotated from $-180°$ to $+120°$. The dipole moment of the peptide bonds are shown as arrows in the plane of the bond. The close steric interaction between the hydrogen atoms of the amino groups at $\psi = 0°$ is highlighted by a double arrow.
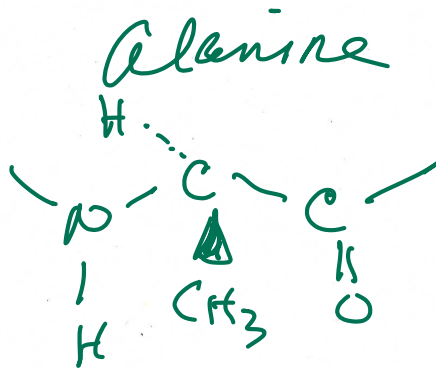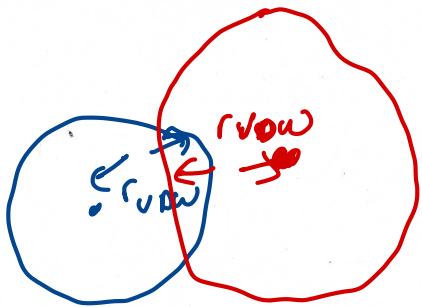
Alanine

Steric overlap/clash $\Rightarrow$ repulsive positive electrostatic energy
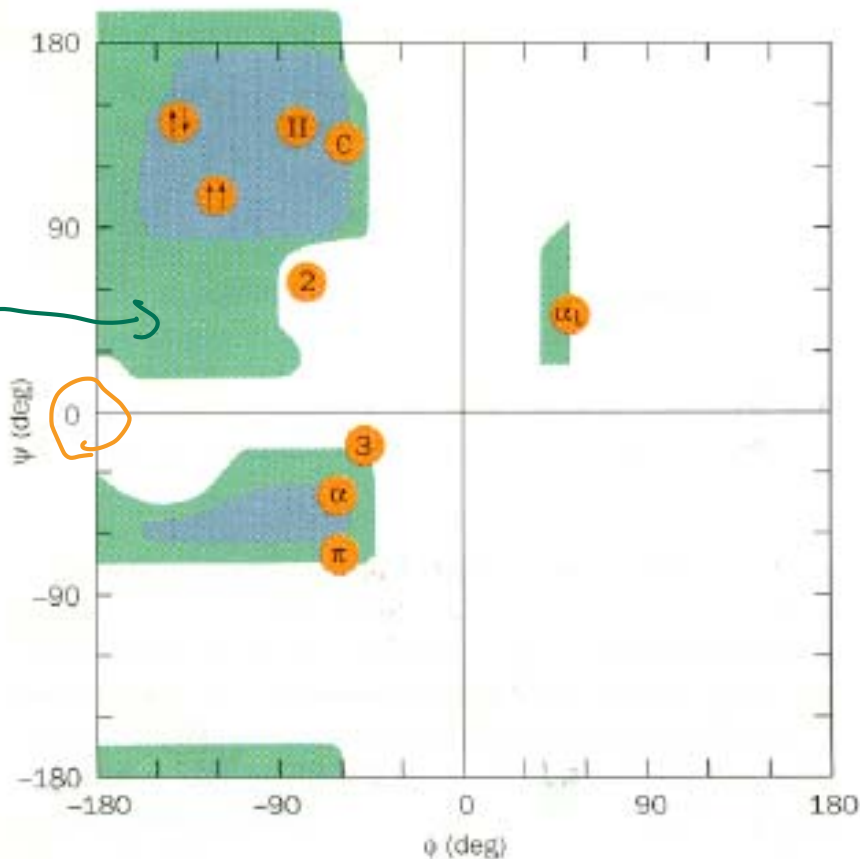
45

E_steric

< RT

FIGURE 7-7. A Ramachandran diagram (named in honor of its inventor, G.N. Ramachandran) shows the sterically allowed ϕ and ψ angles for poly-L-alanine. The diagram was calculated using the van der Waals distances in Table 7-1. Regions of "normally allowed" ϕ and ψ angles are shaded in blue, whereas green-shaded regions correspond to conformations having "outer limit" van der Waals distances. The conformation angles, ϕ and ψ, of several secondary structures are indicated below:

Secondary Structure	ϕ (deg)	ψ (deg)
Right-handed α helix (α)	−57	−47
Parallel β pleated sheet (↑↑)	−119	113
Antiparallel β pleated sheet (↑↓)	−139	135
Right-handed 3_{10} helix (3)	−49	−26
Right-handed π helix (π)	−57	−70
2.2₇ ribbon (2)	−78	59
Left-handed polyglycine II and poly-L-proline II helices (II)	−79	150
Collagen (C)	−51	153
Left-handed α helix (α_L)	57	47

[After Flory, P.J., *Statistical Mechanics of Chain Molecules*, p. 253, Interscience (1969); *and* IUPAC–IUB Commission on Biochemical Nomenclature, *Biochemistry* 9, 3475 (1970).]
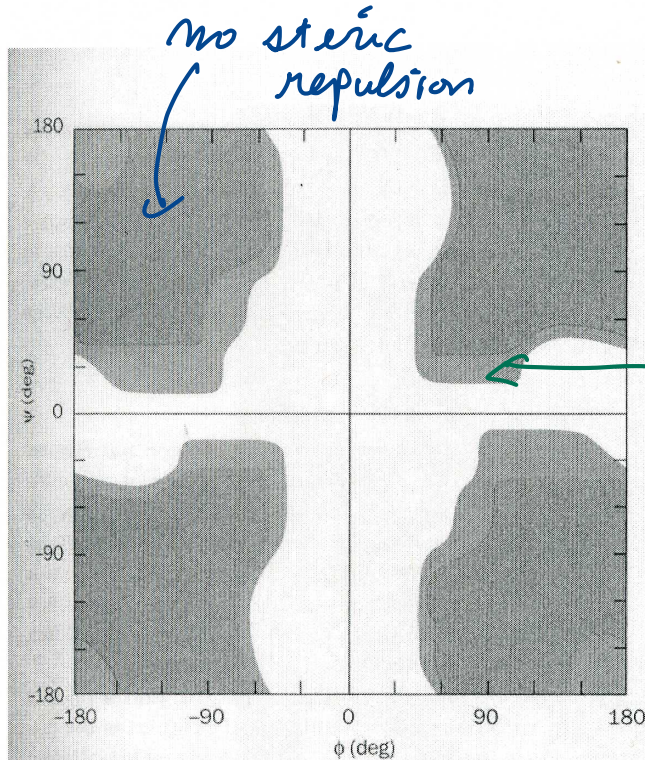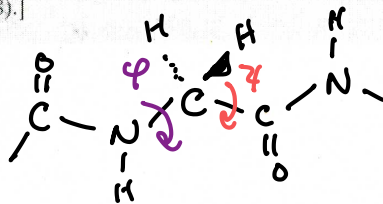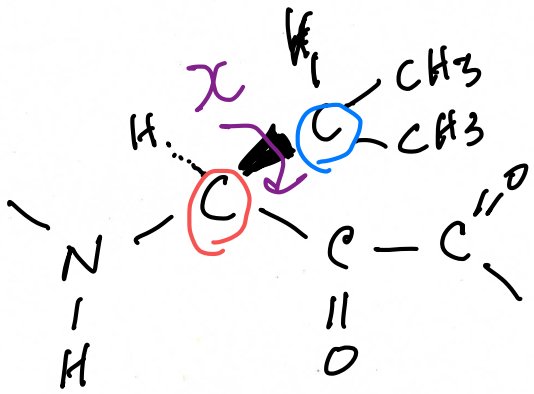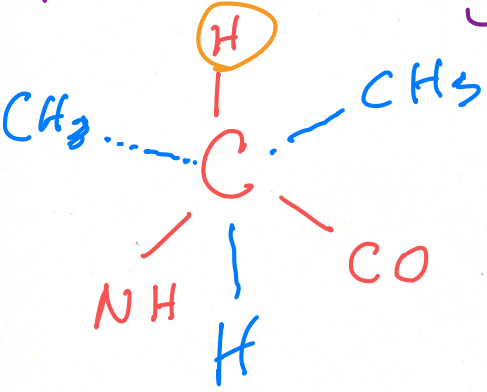
no steric
repulsion

Esteric
< RT

FIGURE 8-9 The Ramachandran diagram of Gly residues in a
polypeptide chain. "Normally allowed" regions are shaded in
blue, whereas green-shaded regions correspond to "outer
limit" van der Waals distances. Gly residues have far greater
conformational freedom than do other (bulkier) amino acid
residues, as the comparison of this figure with Fig. 8-7 indicates.
[After Ramachandran, G.N. and Sasisekharan, V., *Adv. Protein
Chem.* **23**, 332 (1968).]

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χ χ_1

CH3

H   C   CH3

C   C   O

N   C   C

H

H   O

Newman Projection

H

CH3   C   CH3

NH   CO

H

$\chi_1 = 0°$

CH3   NH

C   CH3

CO   H

H

-180   -120   -60   0   60   120   180
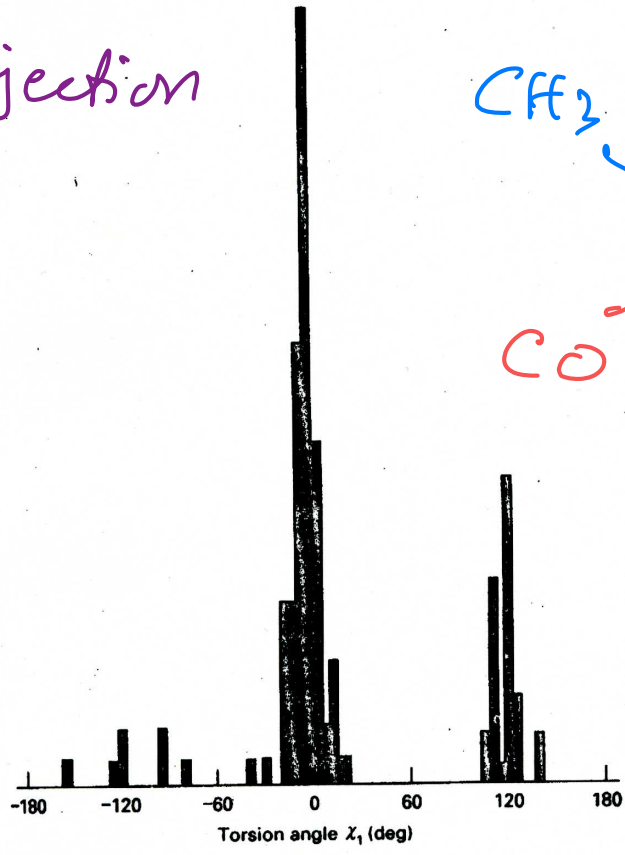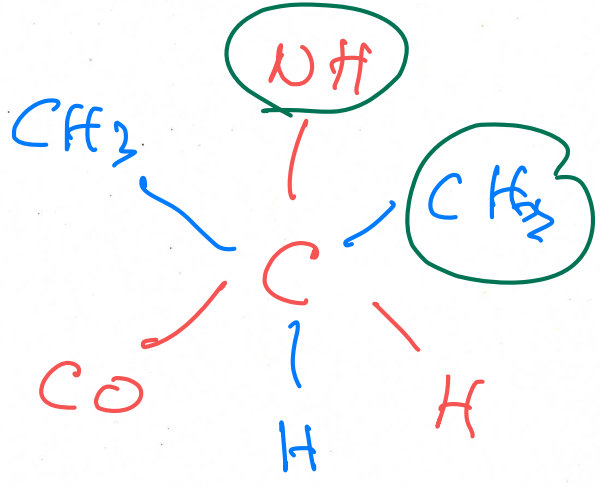
Torsion angle χ_1 (deg)

FIGURE 6.16
Histogram of the values of the $C^{\alpha}-C^{\beta}$ torsion angle χ_1 observed for 151 Val residues in highly refined protein structures. Similar sharp histograms of the three preferred rotamers are observed for other residues, but Val is special in having the greatest predominance of just one rotamer. (From J. W. Ponder and F. M. Richards, *J. Mol. Biol.* 193:775–791, 1987.)

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Coulomb Energy

$$u = C \frac{q_1 q_2}{D r}$$
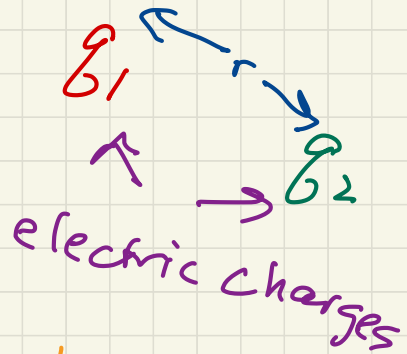
electric charges

$$C = 9.0 \times 10^9 \; \frac{J \text{-} m}{C^2} \equiv \text{Coulomb constant}$$
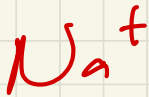
Coulomb unit

$D \equiv$ dielectric constant $\Rightarrow$ describes shielding (reduction) of coulomb energy by intervening matter

vacuum $D = 1$

water $D \approx 80$

hydrocarbon $D \approx 2$

protein interior $D \approx 4$

Na^+ H_2O H_2O Cl^-

H_2O H_2O H_2O

δ^- $\delta+$

O H H $\delta+$

Na^+ δ^- $\delta+$

O $\delta+$ H $\delta-O$ H Cl^- H $\delta+$

H $\delta+$ H

$\delta+$ $\delta+$ $\delta-$

H

$\delta+$

Na^+

$+e$

Cl^-

$-e$
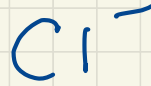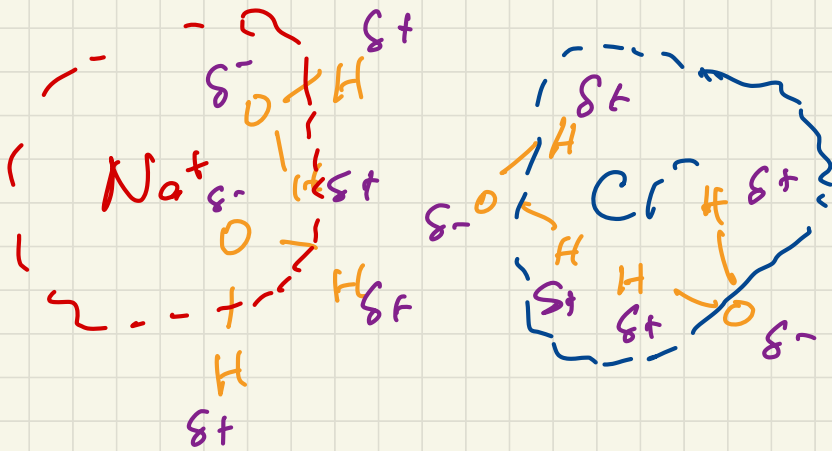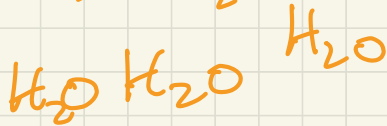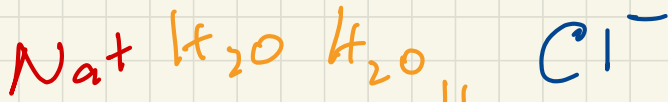
Often consider the energy of a single charge
q with the surrounding charges
$\equiv$ electrostatic potential / voltage
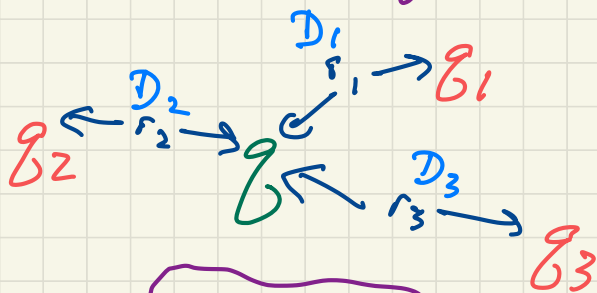
$$u = q \left[\sum_{j=1}^{N} C \frac{q_j'}{D_j r_j} \right]$$

$\Phi \equiv$ electrostatic potential
$\equiv$ voltage $\left(\dfrac{energy}{charge} \right)$

In molecules, charges are often delocalized over functional groups
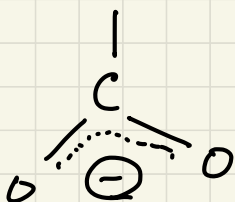
Born (Self) energy of delocalized charges
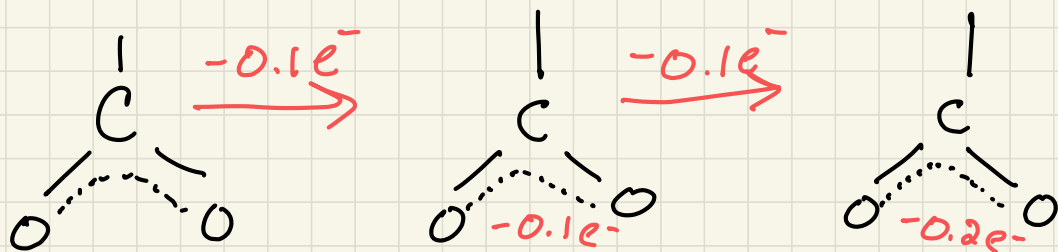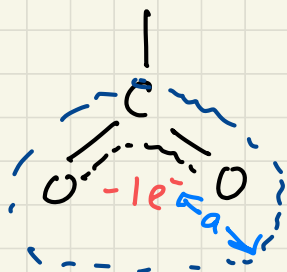
$$G_{born} = \frac{C q^2}{2Da}$$

Difference in Born energies provides basis for single charges to be in region with larger D

$$\Delta u = \frac{C q^2}{2\,a}\left(\frac{1}{D_1} - \frac{1}{D_2}\right)$$

$9 \times 10^9 \ \dfrac{J \cdot m}{c^2}$ (over C)

$3 \times 10^{-38} \ c^2$ (charge of $1e$) (over q^2)

$3 \times 10^{-10} \ m$ (under a)

4 — protein interior (under D_1)

80 — water (under D_2)

$$\approx 1 \times 10^{-19} \ J$$

$$\times \frac{6 \times 10^{23}}{mole} \approx 60 \ \frac{kJ}{mole}$$

Electrostatic energy can be
calculated using charges,
partial charges, charge geometry
and dielectric constants

In chemical bonds and
functional groups, there is
often net absence of charge
but asymmetric distribution
of charge $\Rightarrow$ electric dipole

It's often convenient to consider
dipoles

Table 3.2 Examples of Partial Charges of Atoms in
Proteins Calculated from Quantum Mechanics

Amino Acid	Atom Type	Charge
Backbone	N	−0.36
	H_N	+0.18
	C_α	+0.06
	H_α	+0.02
	C	+0.45
	O	−0.38
Ser	C_β	+0.13
	H_β	+0.02
	O_γ	−0.31
	H_γ	+0.17
Tyr	O_η	−0.33
	H_η	+0.17
Cys	S_γ	+0.01
	H_γ	+0.01

Source: From Momany et al. (1975), *J. Phys. Chem.* **79**, 2361–2381.

Dipole is represented as two
charges of equal magnitude
and opposite sign separated
by a distance a
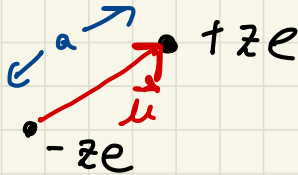
Dipole moment $\vec{\mu}$ is a vector
pointing from negative to
positive charge with
magnitude charge × distance =
zea

For two dipoles separated

by distance r,

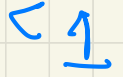$$\boxed{u} \approx C \frac{\mu_1 \mu_2}{D r^3} = \frac{C}{D}\left(\frac{z_1 z_2 e^2}{r}\right)\left(\frac{a_1 a_2}{r^2}\right)$$
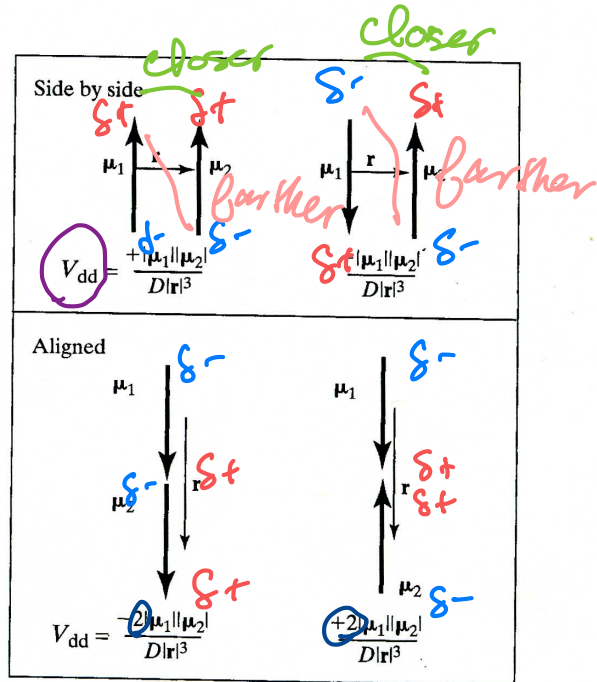
approximate
magnitude

< 1

sign of u depends on relative

orientation of $\vec{\mu}_1$ and $\vec{\mu}_2$

Figure 3.6 Potential energy functions for dipole-dipole interactions. Dipoles that are arranged side by side in parallel and antiparallel directions have dipole moments that are perpendicular to the distance vector **r**. The potential energy is calculated by Eq. 3.14. The potential energies of the head-to-tail and head-to-head alignments of dipoles, however, must be evaluated using the more general relationship in Eq. 3.13.

Dipolar Energy

Side by side

$$V_{dd} = \frac{+|\mu_1||\mu_2|}{D|r|^3}$$

$$V_{dd} = \frac{|\mu_1||\mu_2|}{D|r|^3}$$

Aligned

$$V_{dd} = \frac{-2|\mu_1||\mu_2|}{D|r|^3}$$

$$\frac{+2|\mu_1||\mu_2|}{D|r|^3}$$

van der Waals (dispersion) energy
is between two functional
                or atoms
groups, ⟹ always attractive ⟹
e^- locations (densities) in one
functional group change
slightly in response to Coulomb
energies with nuclei and e^-'s of
the other functional group
            and nuclei
The e^-'s, still have repulsive
(positive) Coulomb energy
with other e^-'s and nuclei
(steric repulsion)

e^- e^- $+$ e^-
e^- $+$ $+$ $+$
e^- $+$ $+$
e^- e^-

e^- e^- e^-
e^- e^- $+$ $+$ e^-
$+$ $+$ e^-
$+$ $+$ $+$
e^- e^- e^- e^-

$\longleftrightarrow$ r $\longrightarrow$
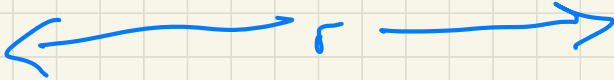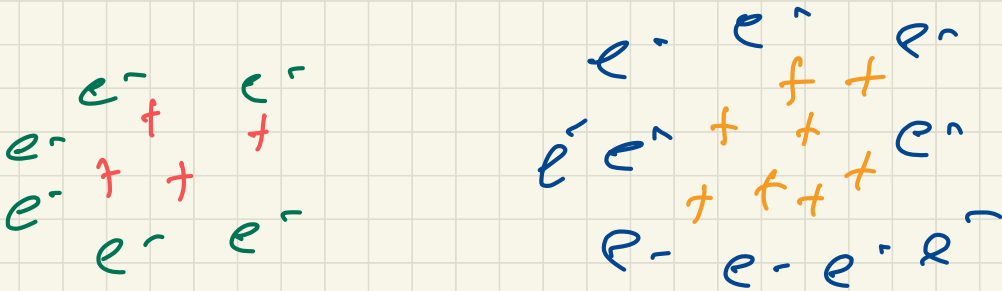
Lennard-Jones potential

$$u = \boxed{\frac{A}{r^{12}}} - \left(\boxed{\frac{B}{r^{6}}}\right)$$

functional
group
dependent
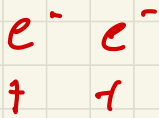
dispersion
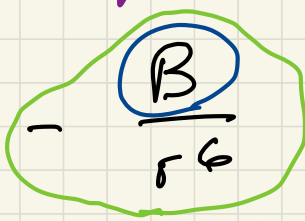
e^- e^-
$+$ $+$
steric
repulsion

50

Non-bonded atoms
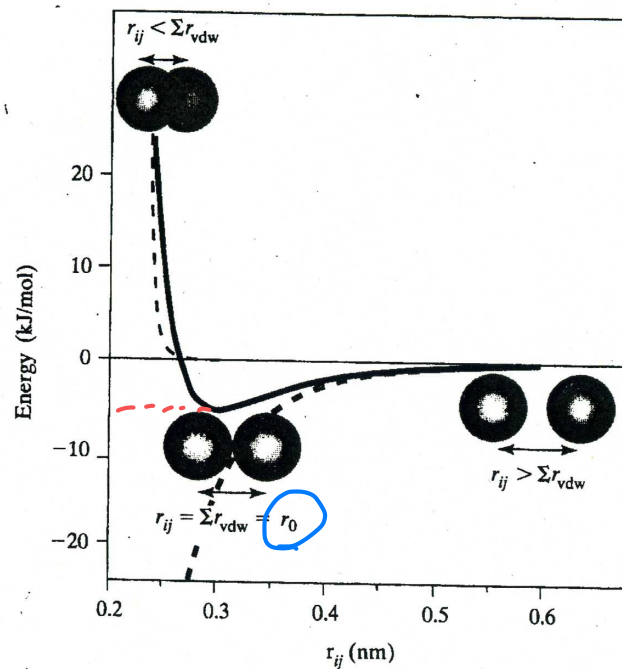
Figure 3.7 The van der Waals potential is a sum of the very short-range attraction between atoms (London dispersion forces) and the extremely short-range steric repulsion between atoms. Together, the two functions define an optimal distance r_0, which is sum of the van der Waals radii r_{vdw} of the two atoms.

Table 3.4 Coefficients for the Repulsive (A) and Attractive (B) Terms of the 6-12 van der Waals Potential in Eq. 3.17

Atomic Interaction	A (kJ-nm^{12}/mol)	B (kJ-nm^6/mol)	r_0 (nm)
H$\cdots$H	1.84×10^{-8}	1.92×10^{-4}	0.240
H$\cdots$C	1.57×10^{-7}	5.27×10^{-4}	0.290
H$\cdots$N	1.11×10^{-7}	5.15×10^{-4}	0.275
H$\cdots$O	1.03×10^{-7}	5.11×10^{-4}	0.272
H$\cdots$P	6.35×10^{-7}	1.43×10^{-3}	0.310
C$\cdots$C	1.18×10^{-6}	1.52×10^{-3}	0.340
C$\cdots$N	8.90×10^{-7}	1.51×10^{-3}	0.325
C$\cdots$O	8.49×10^{-7}	1.51×10^{-3}	0.322
C$\cdots$P	4.49×10^{-6}	4.12×10^{-3}	0.360
N$\cdots$N	6.63×10^{-7}	1.50×10^{-3}	0.310
N$\cdots$O	6.30×10^{-7}	1.50×10^{-3}	0.307
N$\cdots$P	3.44×10^{-6}	4.08×10^{-3}	0.345
O$\cdots$O	5.97×10^{-7}	1.51×10^{-3}	0.304
O$\cdots$P	3.28×10^{-6}	4.10×10^{-3}	0.342
P$\cdots$P	1.68×10^{-5}	1.12×10^{-2}	0.380

The equilibrium distance r_0 is the sum of the van der Waals radii of the two interacting atoms.

Hydrogen bonds are

an energy between H and non-bonded other atoms (commonly C, N, O, F)

Evidence for H-bonds is distance between H and non-bonded other atom

$\leftarrow 1.9\overset{o}{A} \rightarrow$

$N-H \cdots O = C$

$\vec{\mu}_{NH}$

$z = 0.3$
$a = 1.0 \overset{o}{A}$

$\vec{\mu}_{CO}$

$z = 0.4$
$a = 1.2 \overset{o}{A}$
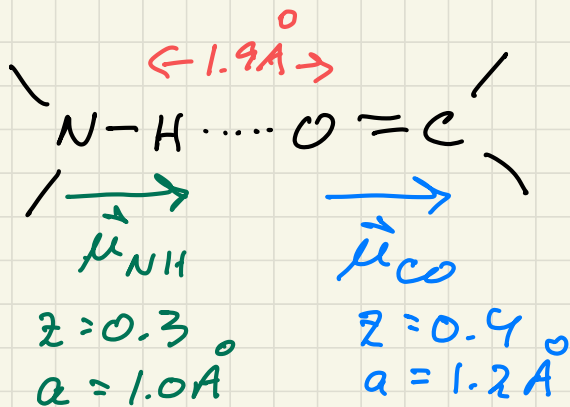
H-bond energies are typically 4 - 50 $\dfrac{kJ}{mole}$