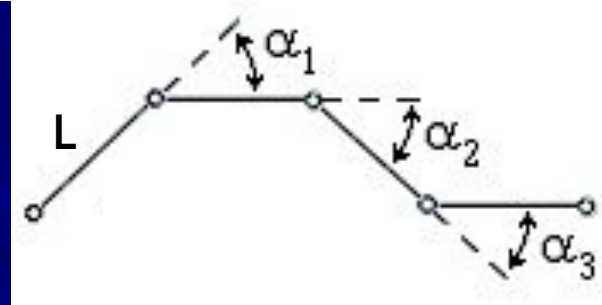
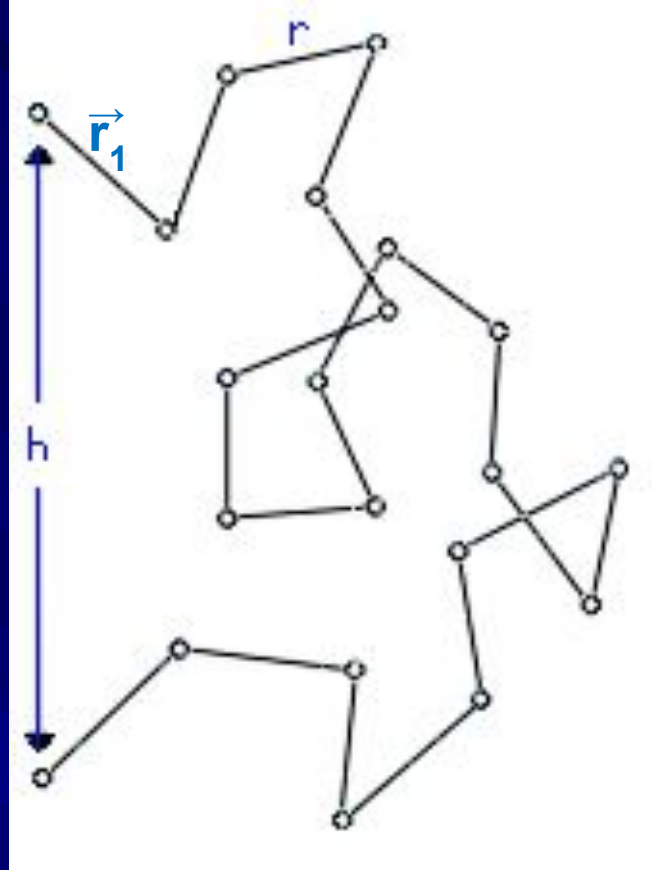


PROTEIN PHYSICS

LECTURES 9-10

Secondary structures

coil



$$r = \frac{1 + \cos \alpha}{1 - \cos \alpha} L$$

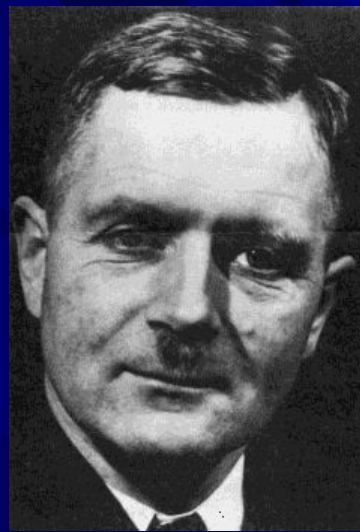
$$\mathbf{h} = \sum_{i=1}^M \mathbf{r}_i,$$

$$\langle h^2 \rangle = \langle \left(\sum_{i=1}^M \mathbf{r}_i \right)^2 \rangle = \langle \sum_{i=1}^M \mathbf{r}_i^2 + \sum_{i \neq j}^M \sum_{j=1}^M \mathbf{r}_i \mathbf{r}_j \rangle = \sum_{i=1}^M \langle \mathbf{r}_i^2 \rangle + \sum_{i \neq j}^M \sum_{j=1}^M \langle \mathbf{r}_i \mathbf{r}_j \rangle = M r^2$$

$$\langle h^2 \rangle = (M r) \cdot r = L_M \cdot r \quad |h| \sim M^{1/2}$$

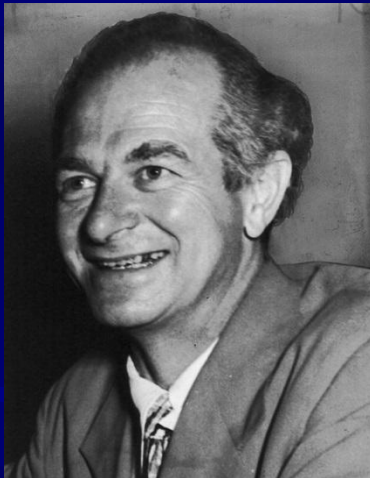
$$V \sim M^{3/2}$$

Random coil:



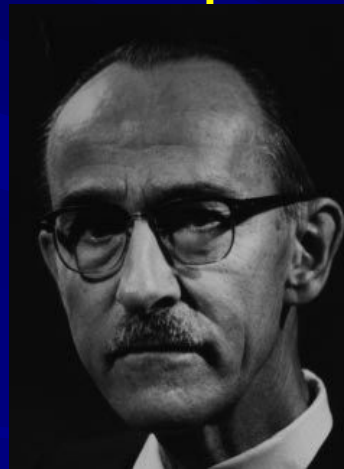
Werner Kuhn (1899 - 1963)

α -helices and β -sheets:



Linus Carl Pauling (1901-94)

— Nobel Prizes: 1954, 62



Robert Brainard Corey

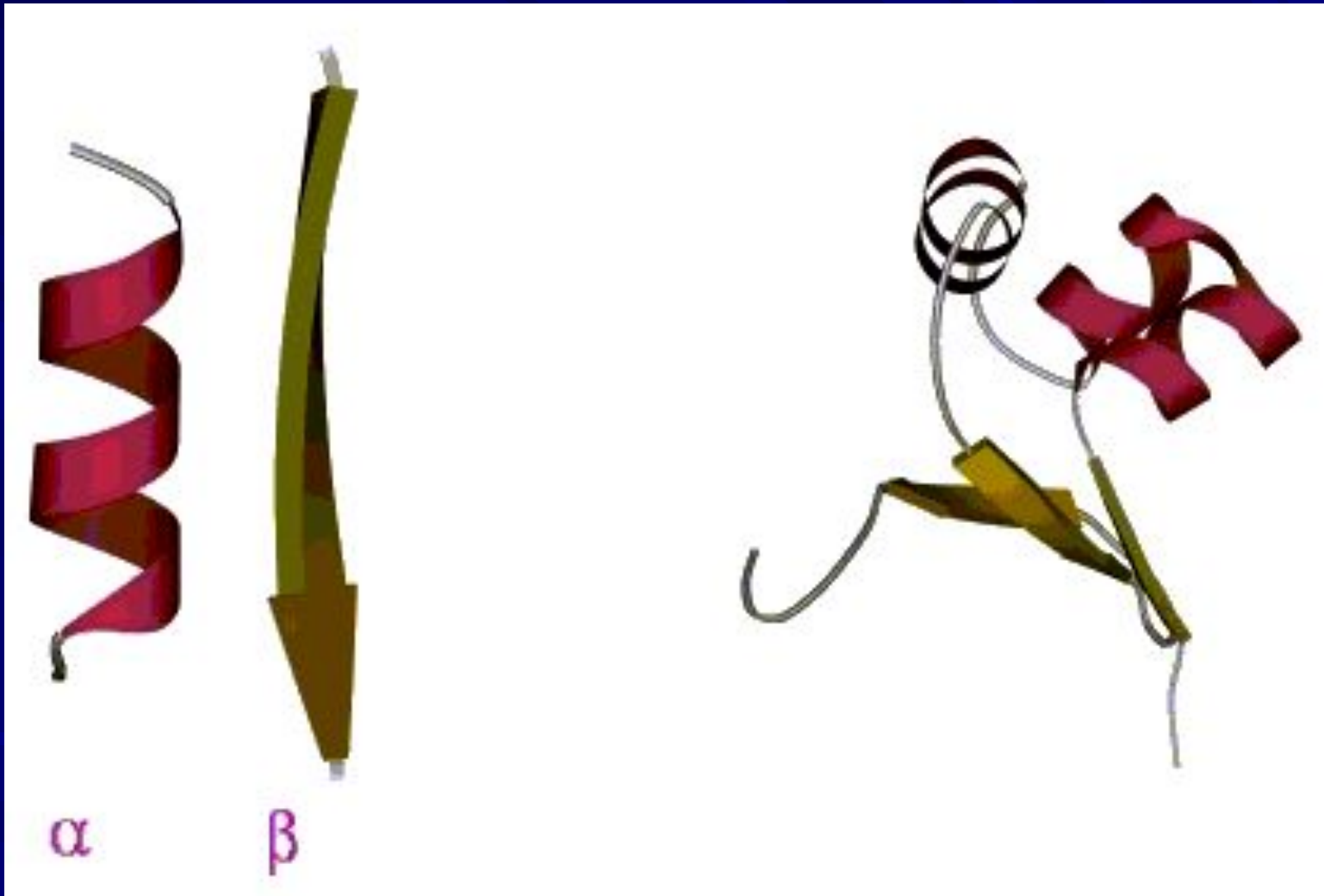
(1897 –1971)



Herman Russell Branson

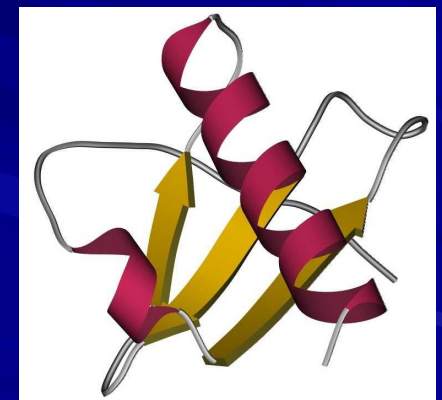
(1914 –1995)

Main secondary structures



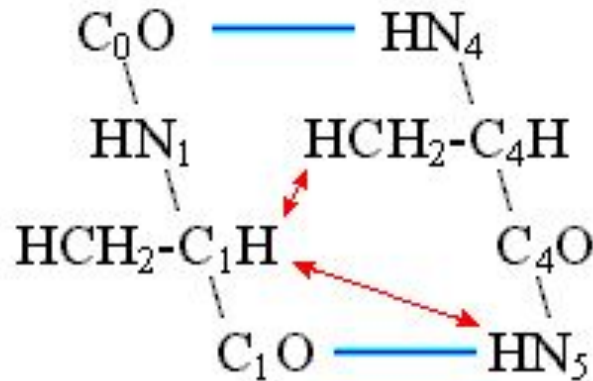
Experimental study of secondary structure

X-ray crystallography

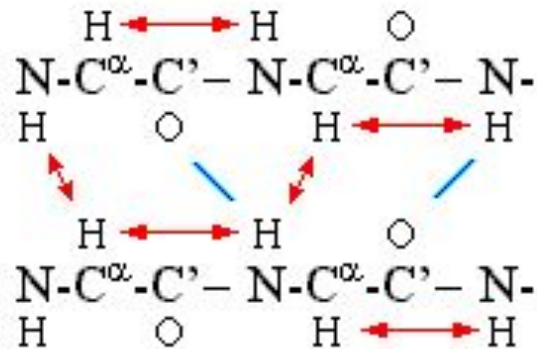


H^1 NMR spectroscopy (cross-peaks)

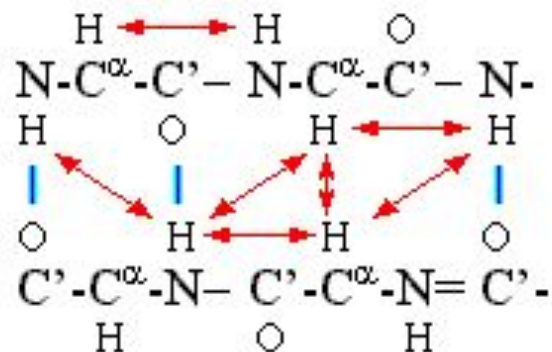
a



b

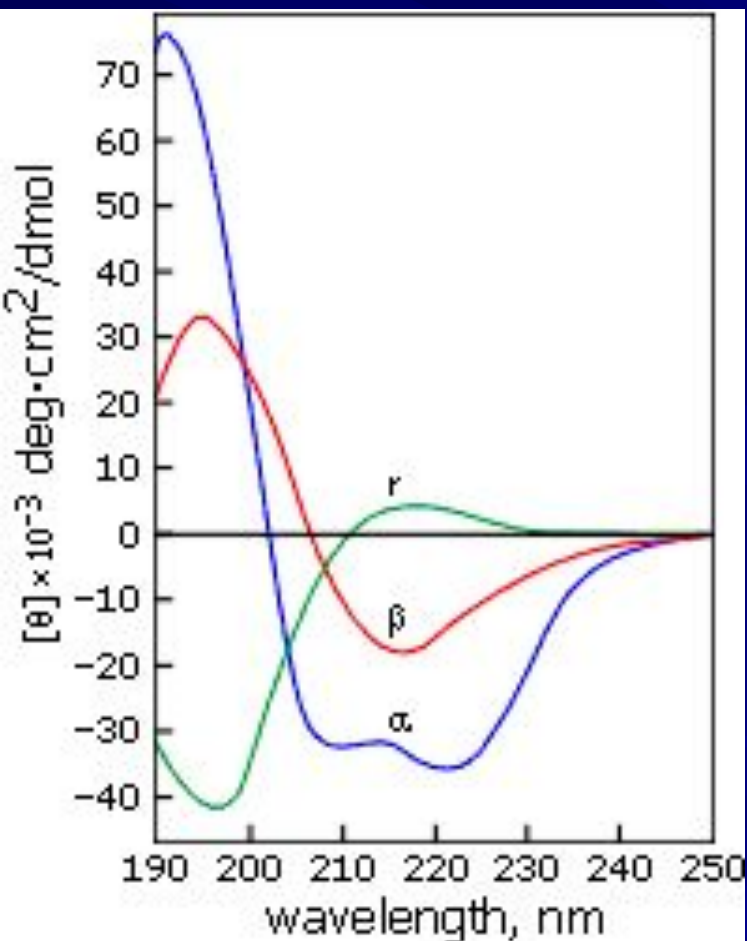


c

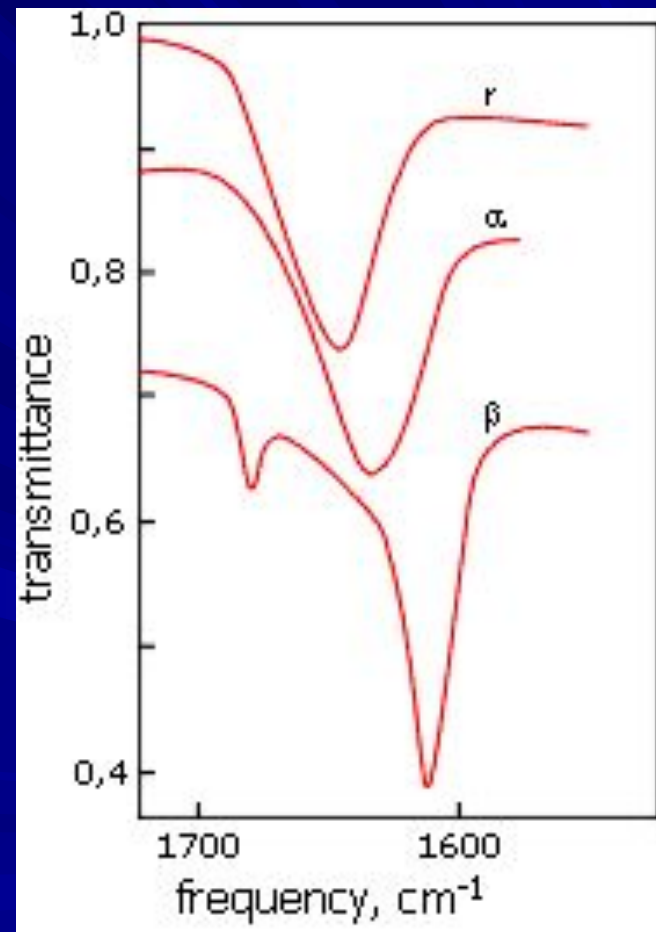


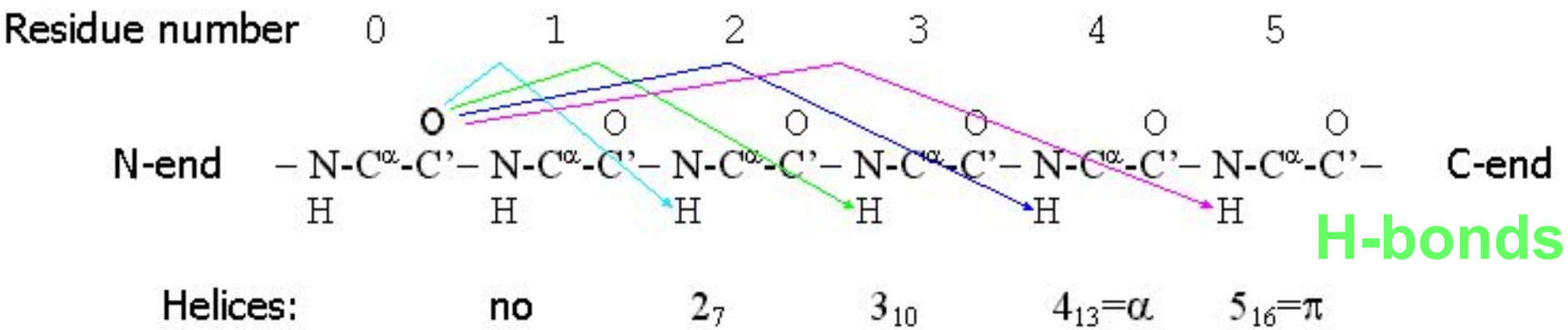
Experimental study of secondary structure

Far UV CD spectra
(peptide groups)

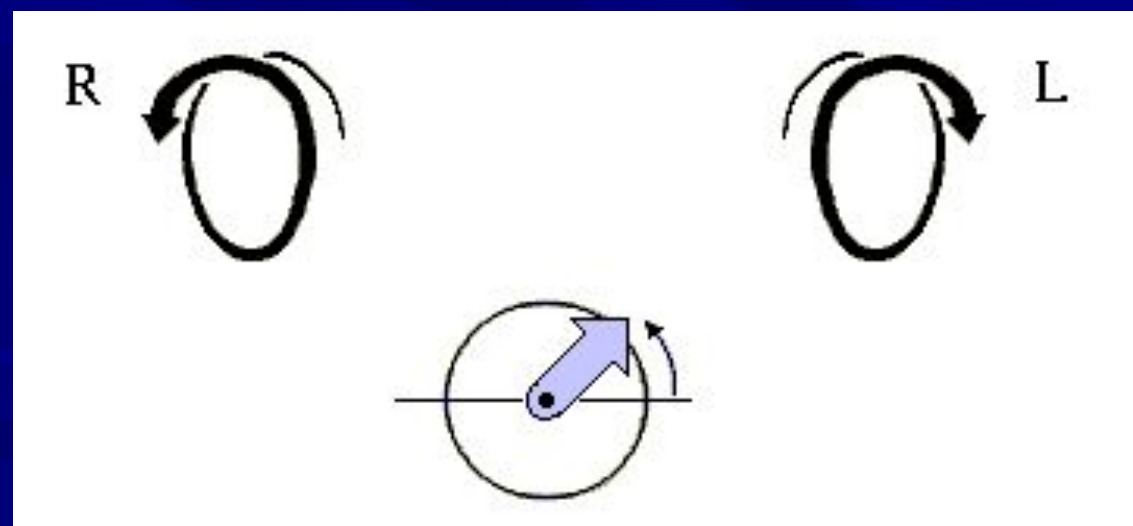


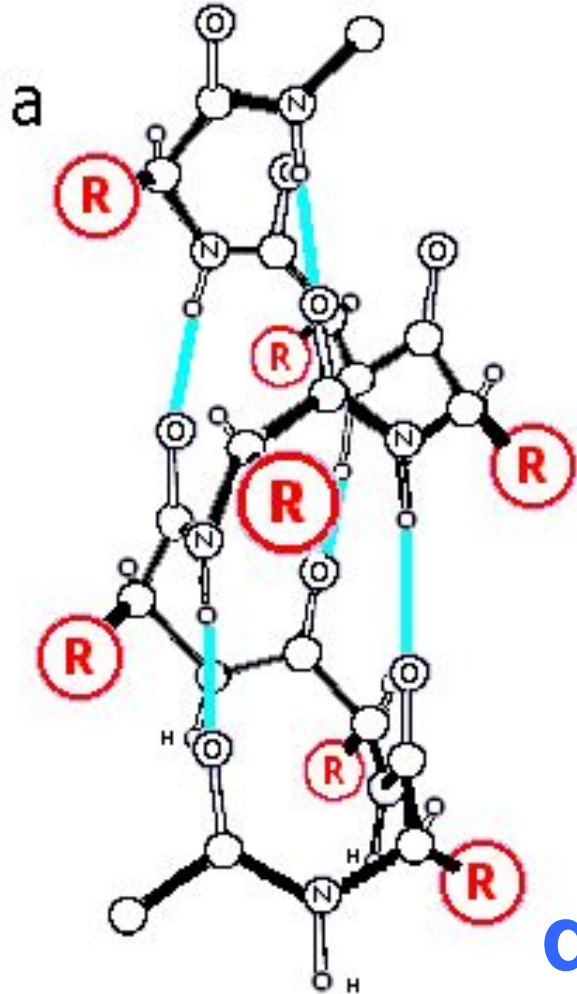
IR spectra
("amid I", C=O bond)



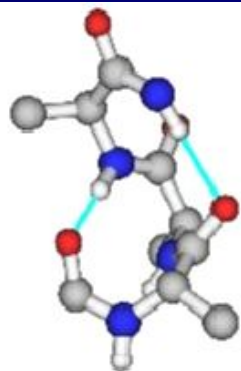
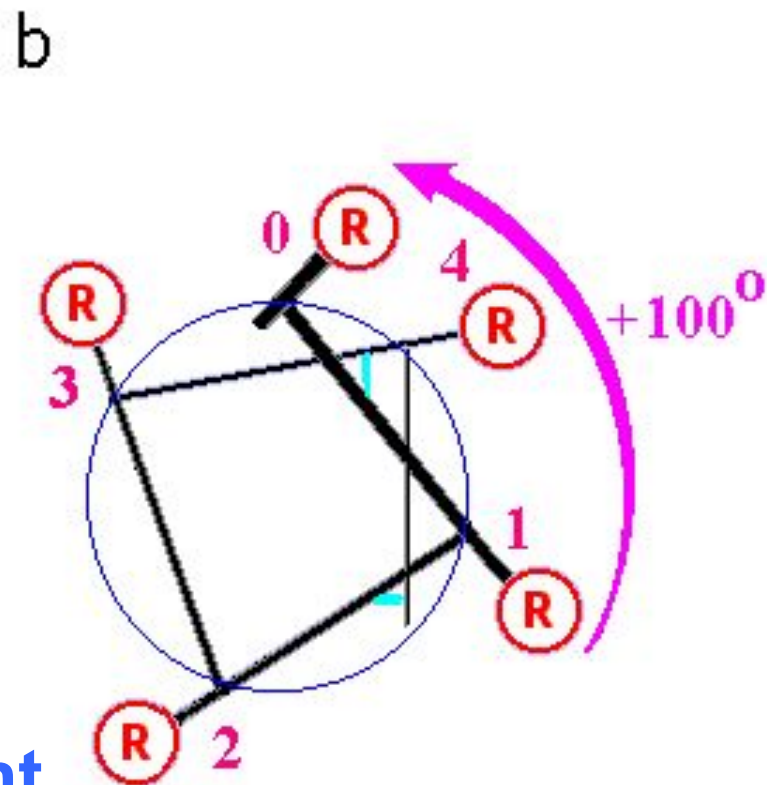


Helices: Right and Left

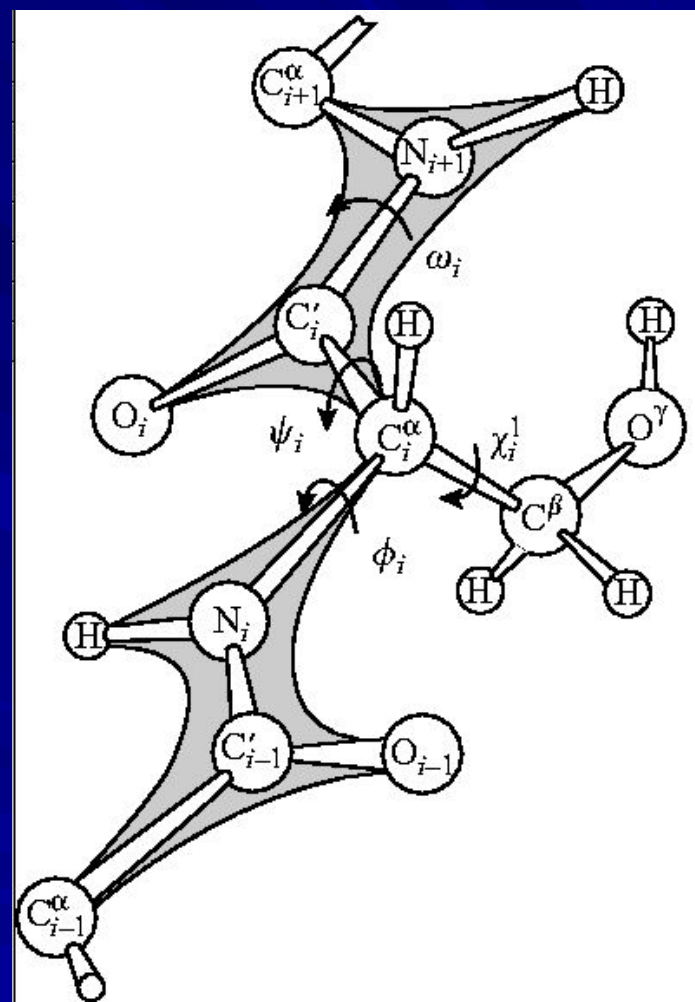
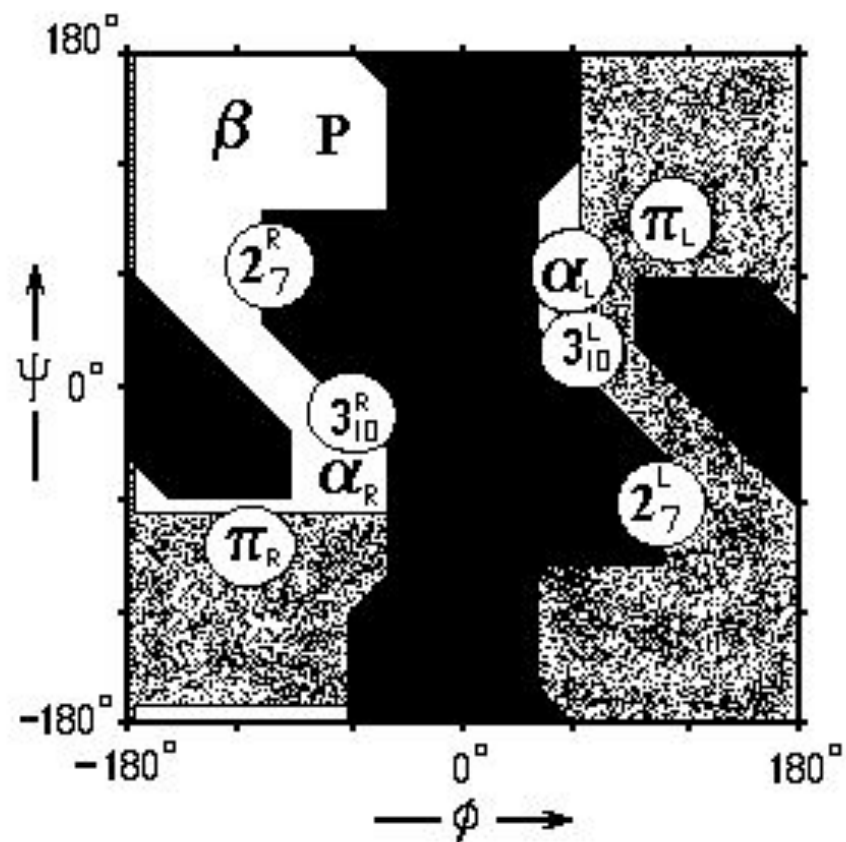
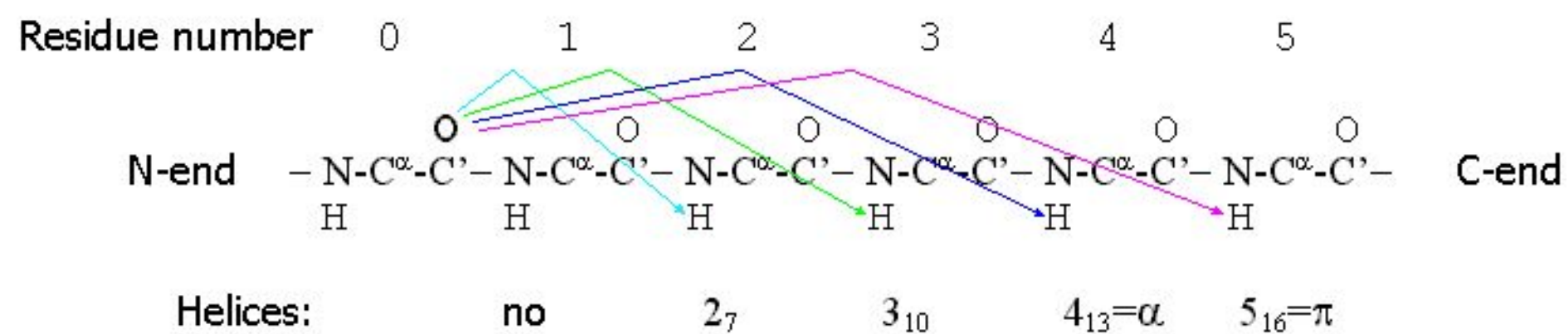


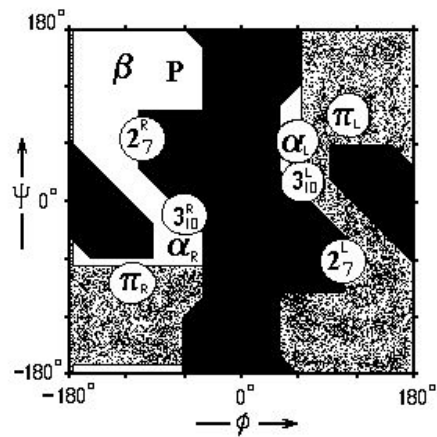


Right
 α -helix



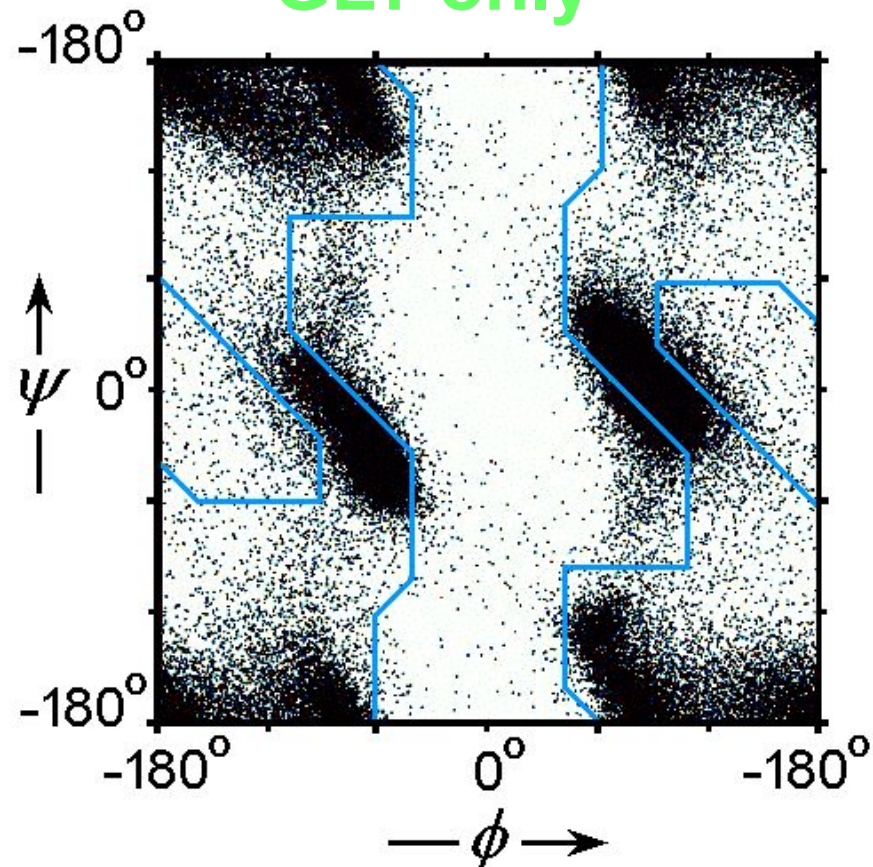
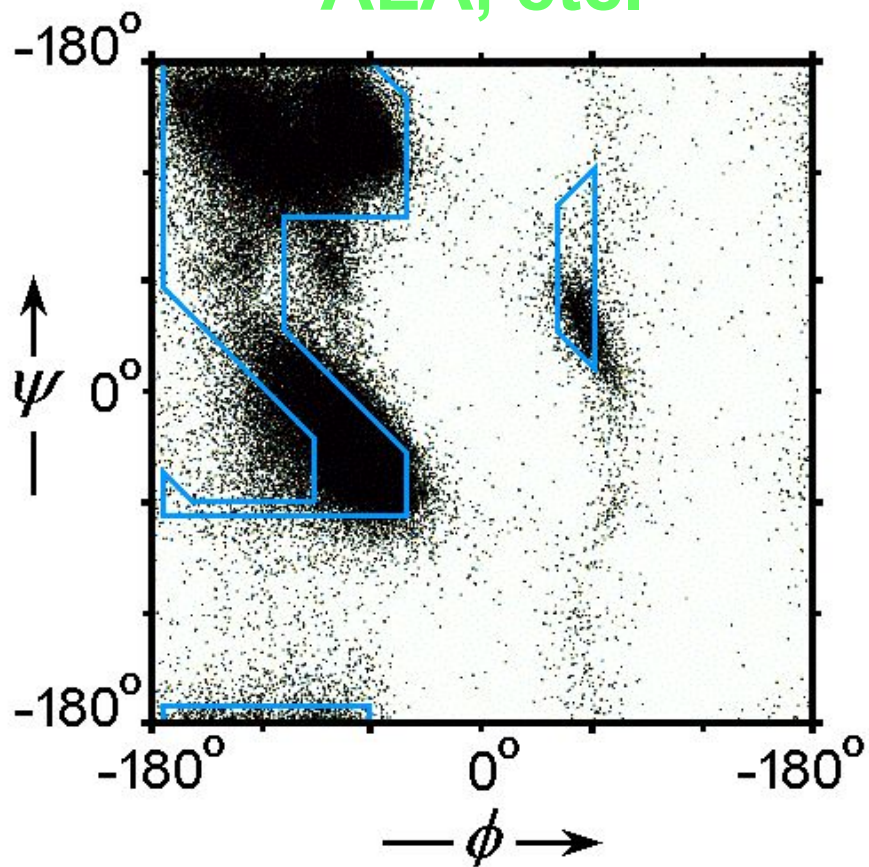
Right
 3_{10} -helix

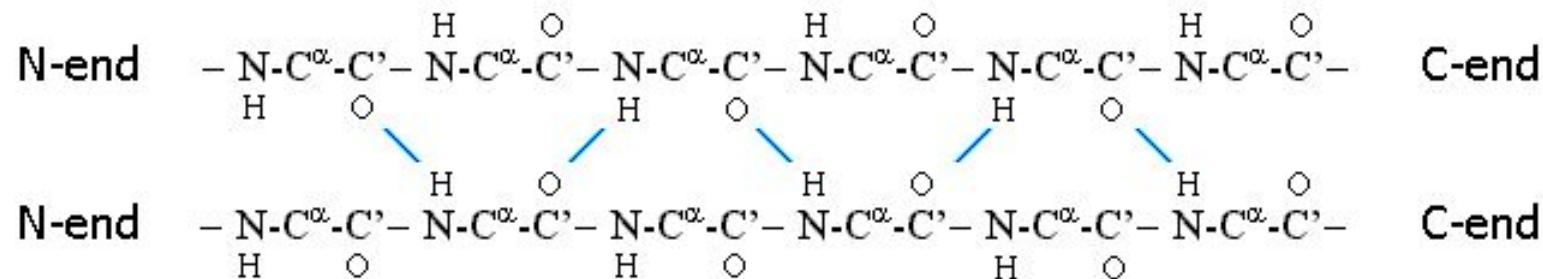
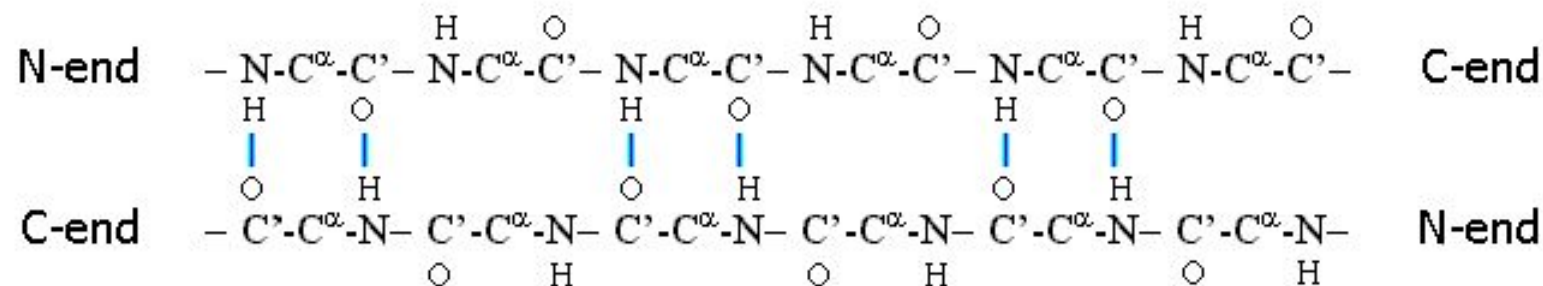
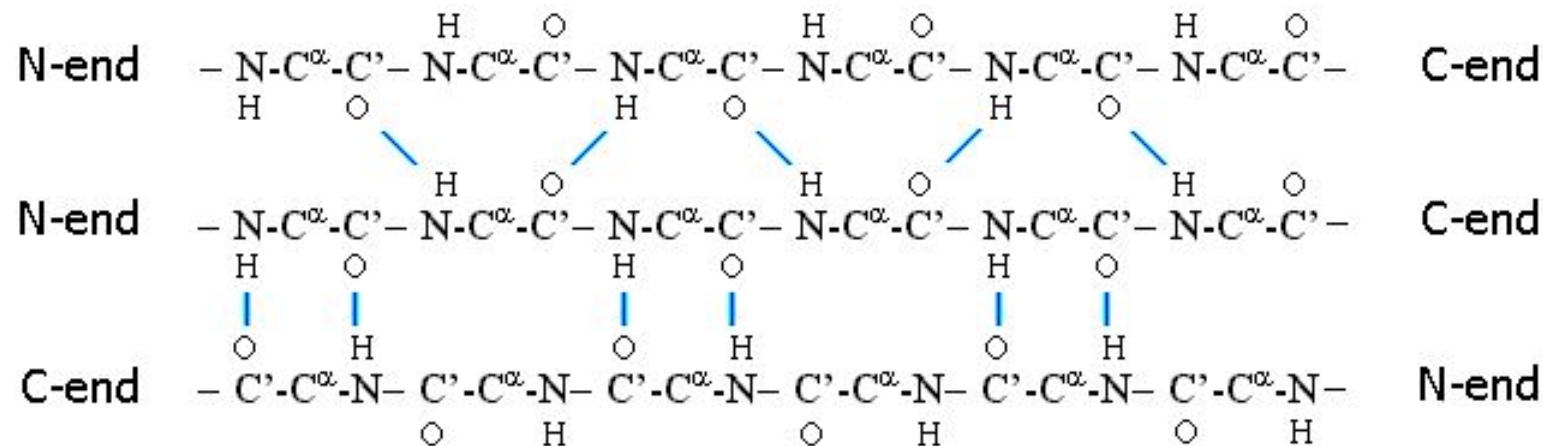


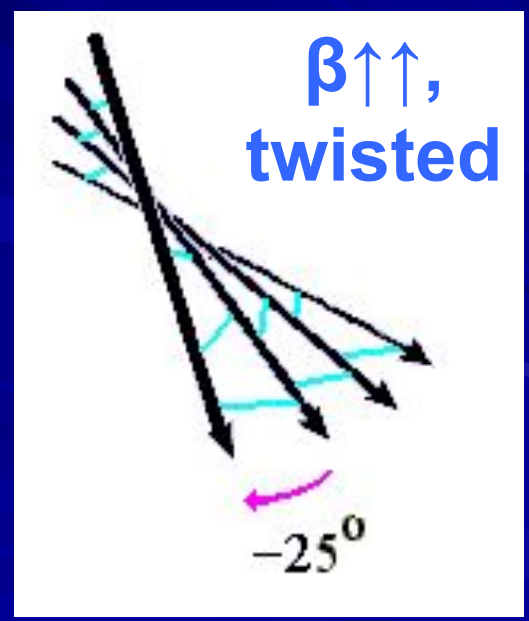
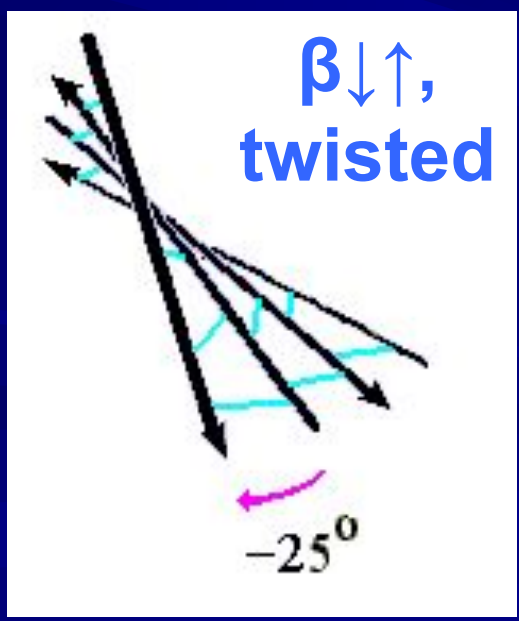
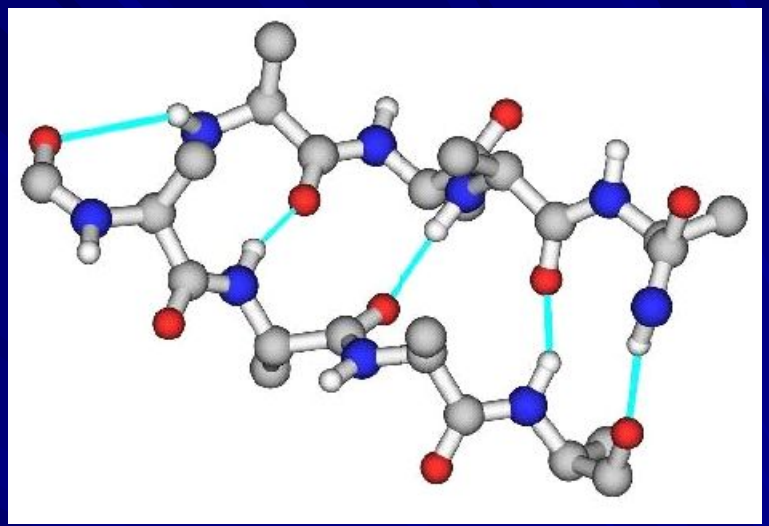
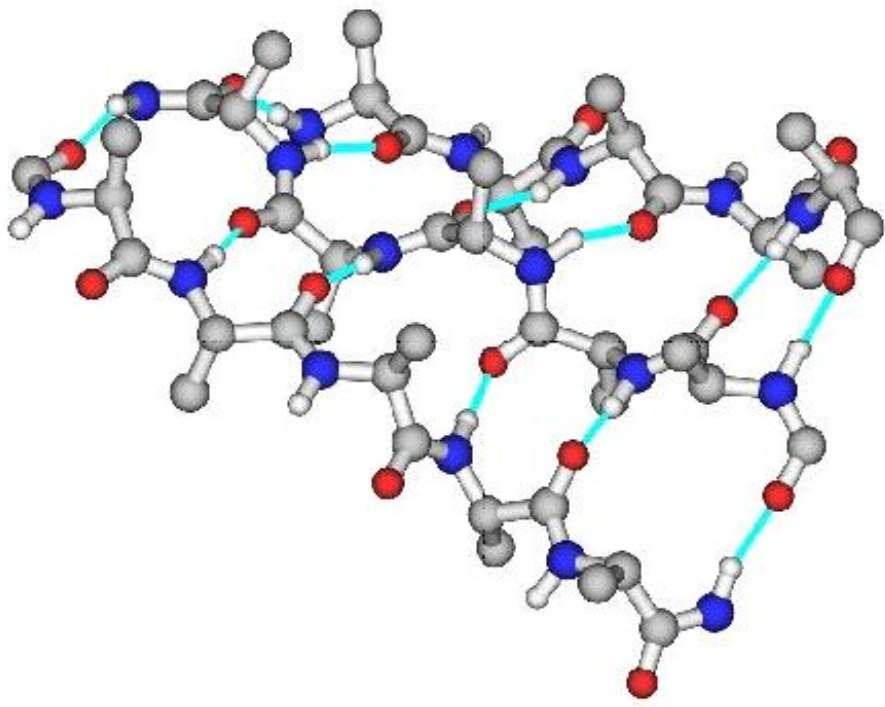


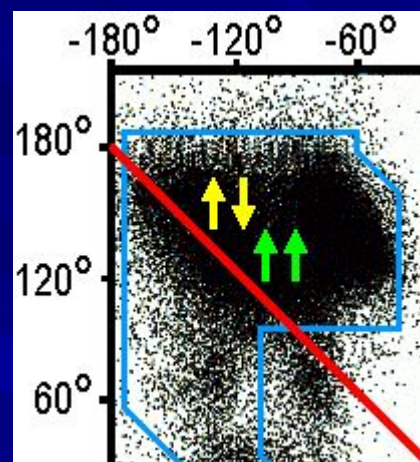
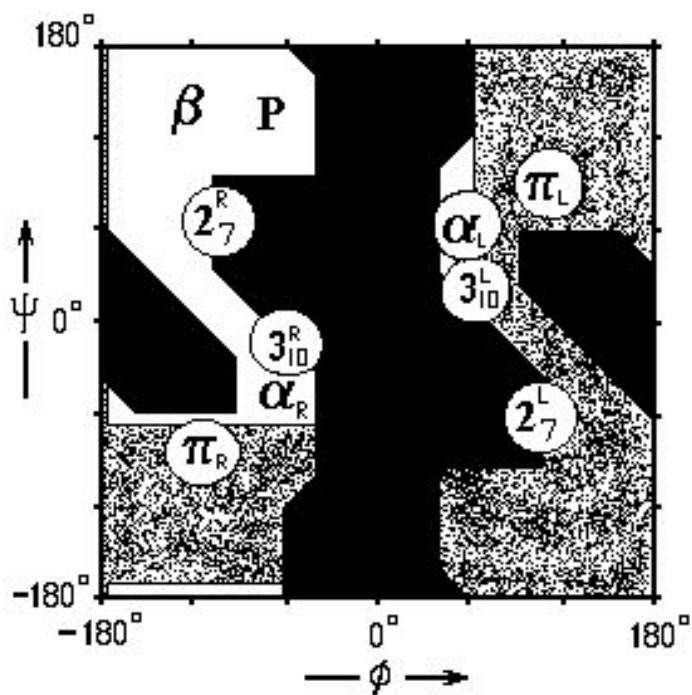
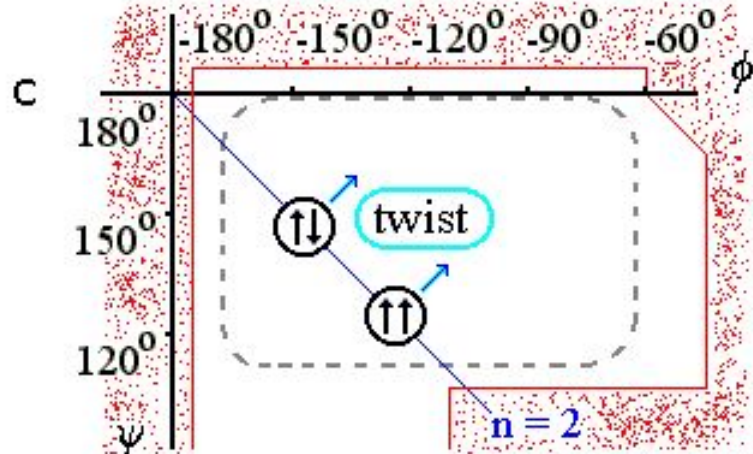
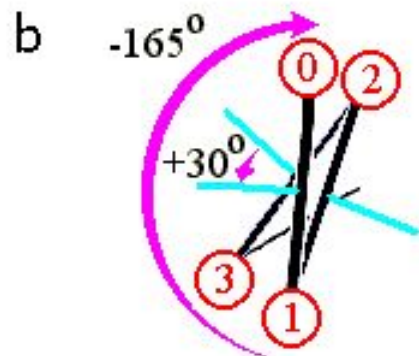
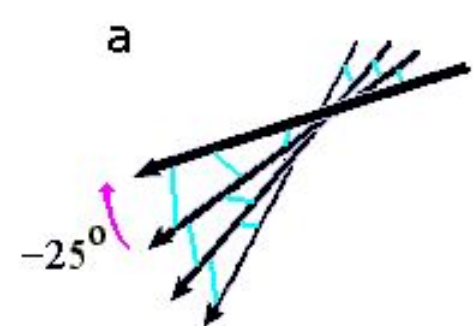
ALA, etc.

GLY only

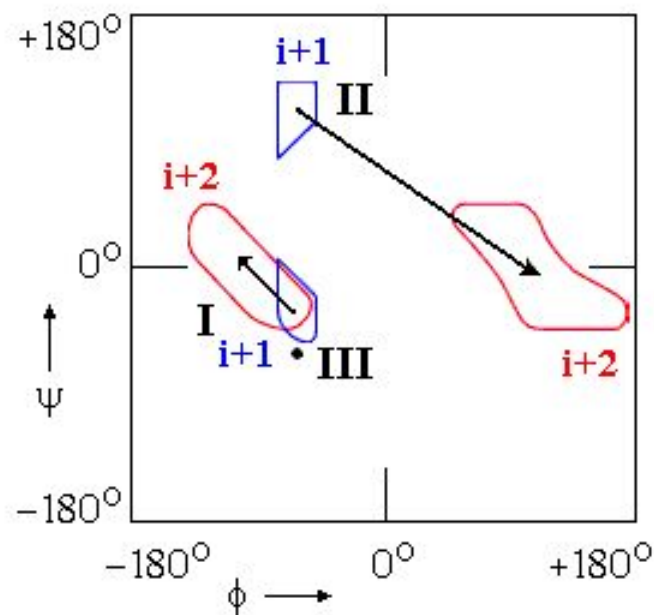
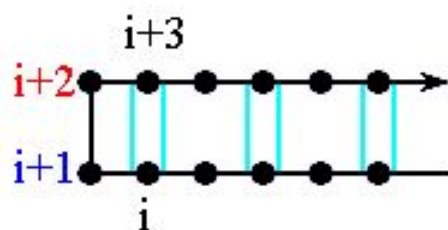
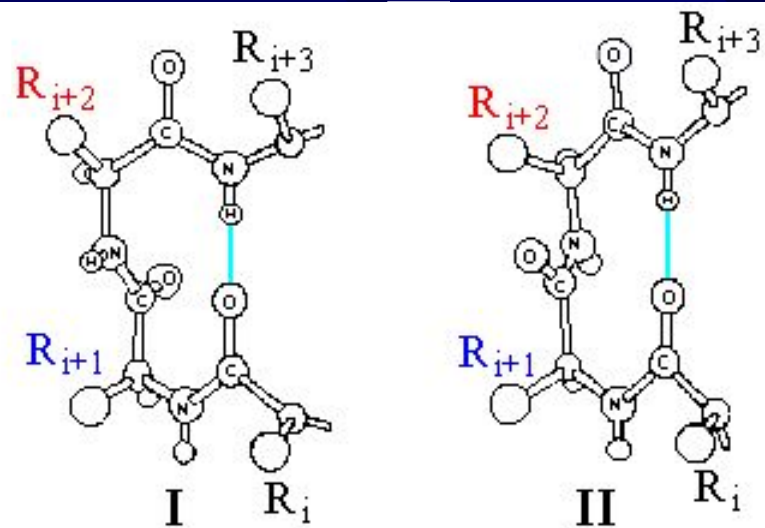


$\beta \uparrow \uparrow$  $\beta \downarrow \uparrow$  $\beta \uparrow \uparrow \downarrow$ 



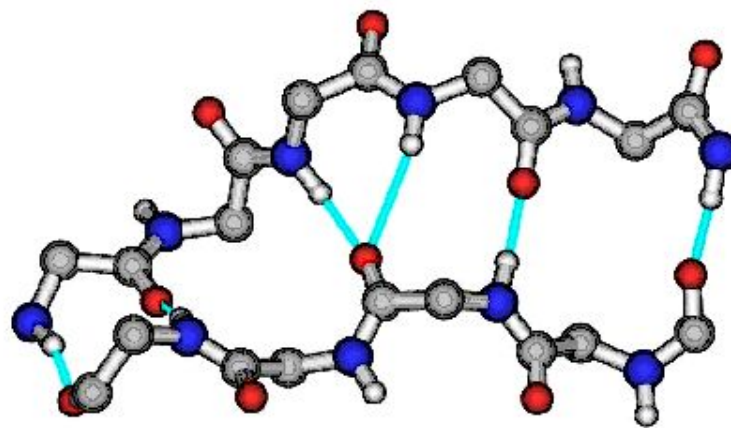
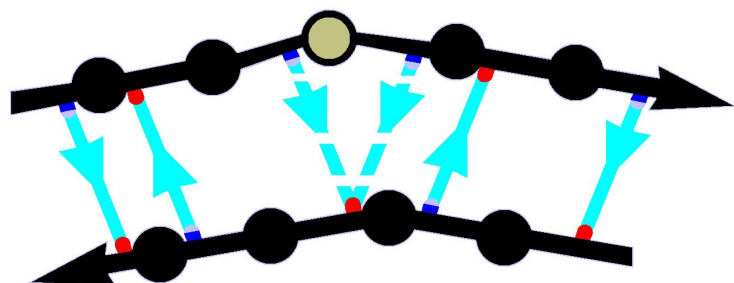


**Mirror-asymmetric
amino acids –
mirror-asymmetric
twist of β -sheets**

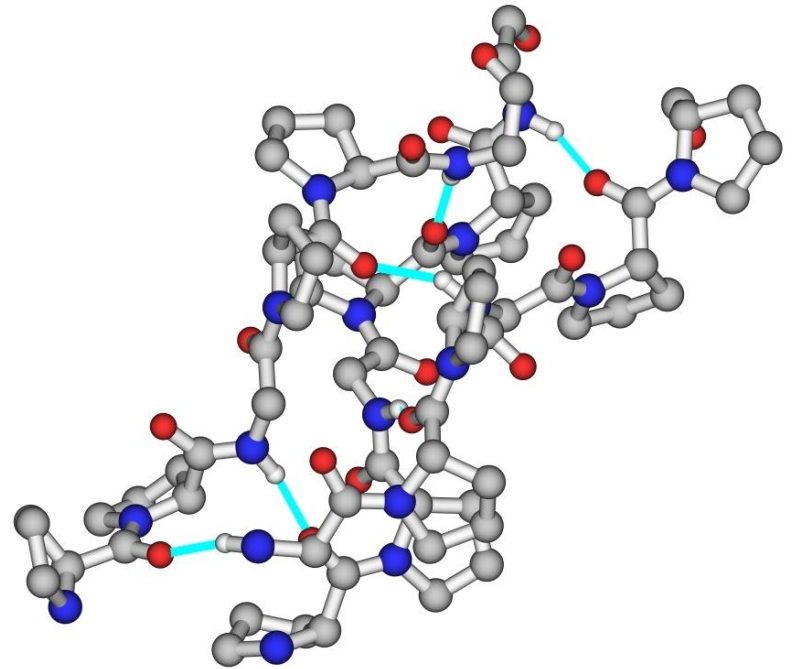
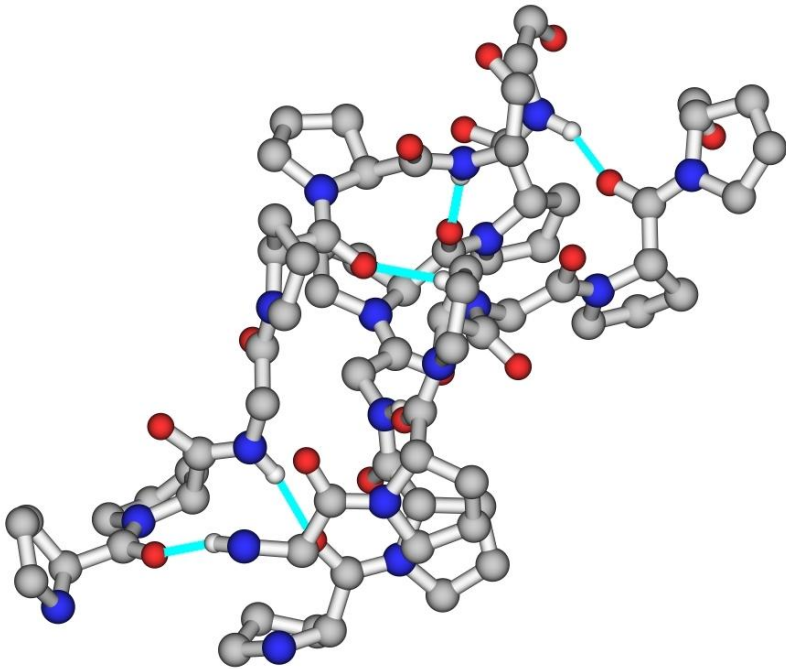


β -turns

β -bulge



collagen triple helix



Secondary structure transitions

Separation of potential energy
in classic (non-quantum) mechanics:

$$E = E_{\text{COORD}} + E_{\text{KIN}}; \quad E_{\text{KIN}} = \sum mv^2/2 - \text{does not depend on coordinates}$$
$$S = S_{\text{COORD}} + S_{\text{KIN}}$$

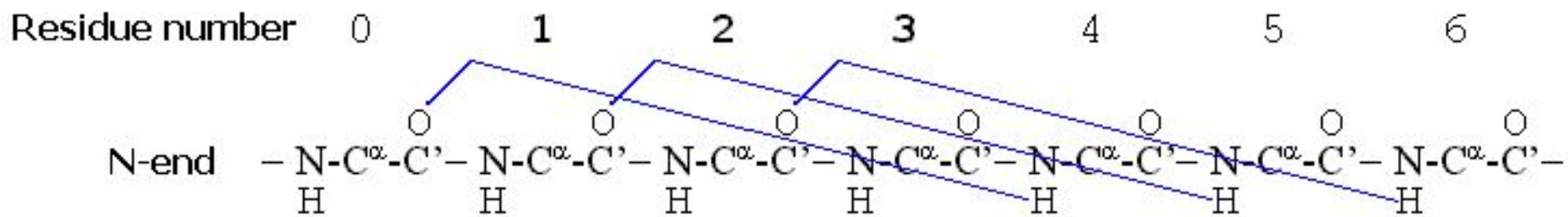
**We may consider
only potential energy, etc.:**

$$E \Rightarrow E_{\text{COORD}}$$

$$M \Rightarrow M_{\text{COORD}}$$

$$S(E) \Rightarrow S_{\text{COORD}}(E_{\text{COORD}})$$

$$F(E) \Rightarrow F_{\text{COORD}}, \quad \text{etc.}$$



α -helix

homo-polypeptide:

$$\Delta F_{\alpha} = F_{\alpha} - F_{\text{coil}} = (n-2)f_H - nTS_{\alpha} =$$

$$= -2f_H + n \times (f_H - TS_{\alpha})$$

||=====|| ||=====||

f_{INIT}

f_{EL}

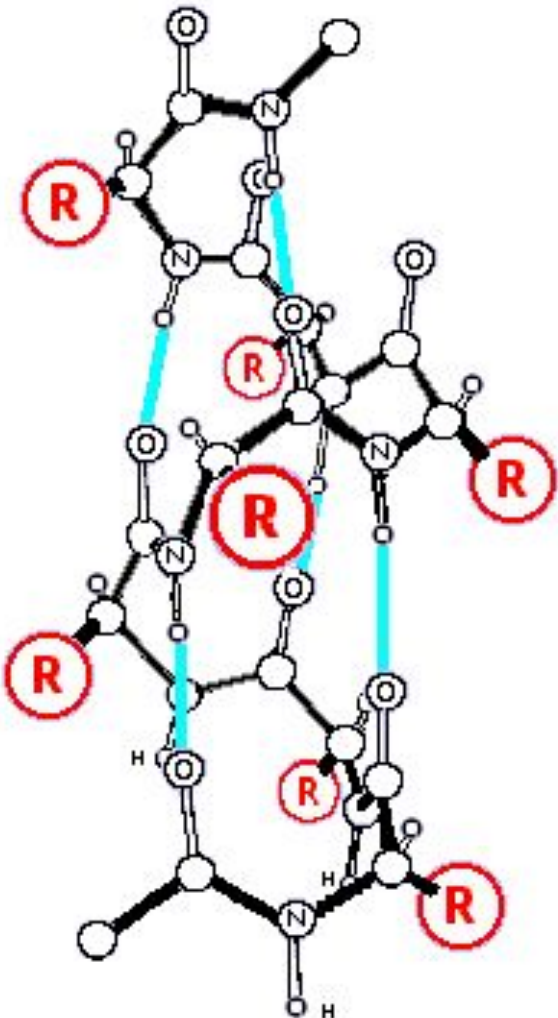
f_{EL} : elongation (≈ 0):

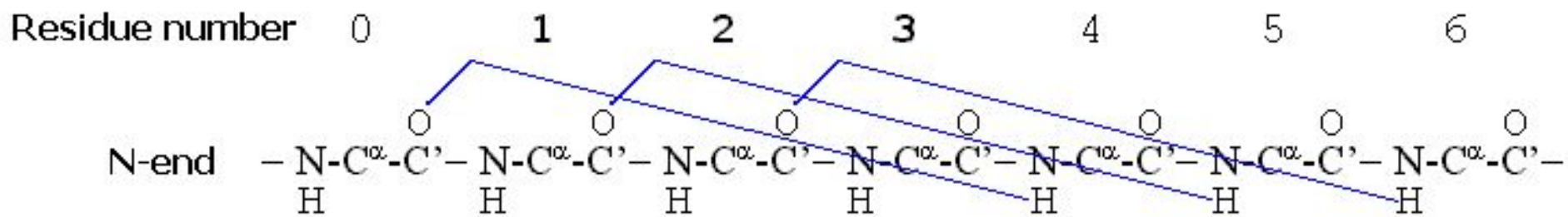
$\approx -0.5 \cdot k_B T$ Ala --- $\approx +1.5 \cdot k_B T$ Gly

$S = \exp(-f_{\text{EL}}/k_B T)$: $S = 2 - 0.2$

$f_{\text{INIT}} = -2f_H$: initiation ($\gg k_B T$)

$\sigma = \exp(-f_{\text{INIT}}/k_B T)$: $\sigma \ll 1$ (~ 0.001)





α -helix

homo-polypeptide:

$$\Delta F_{\alpha} = F_{\alpha} - F_{coil} = (n-2)fH - nTS_{\alpha} =$$

$$= \underbrace{-2fH}_{\text{FINIT}} + \underbrace{n \times (fH - TS_{\alpha})}_{\text{fEL}}$$

FINIT

fEL

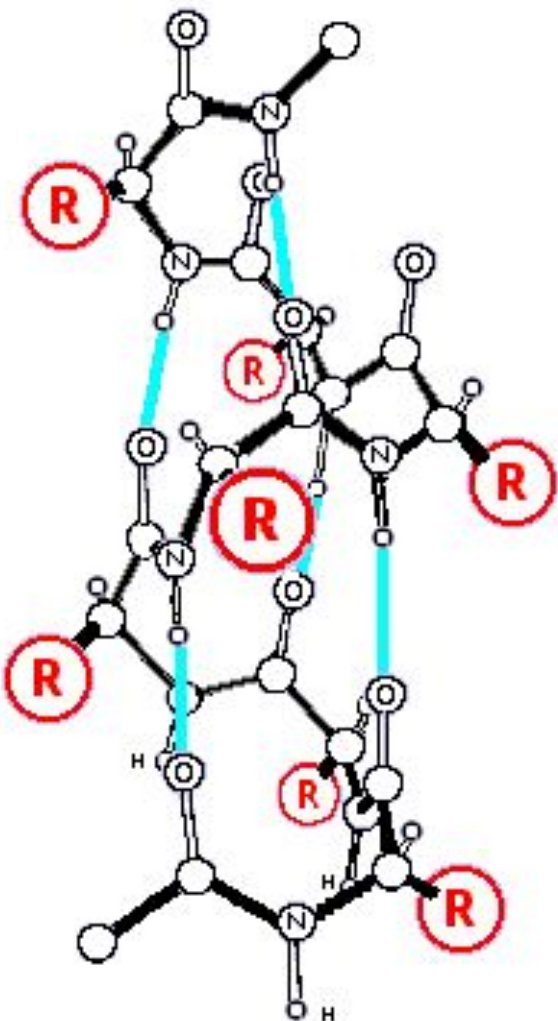
fEL: elongation (≈ 0):

$$\approx -0.5 \cdot kBT \text{ Ala} \quad \text{---} \quad \approx +1.5 \cdot kBT \text{ Gly}$$

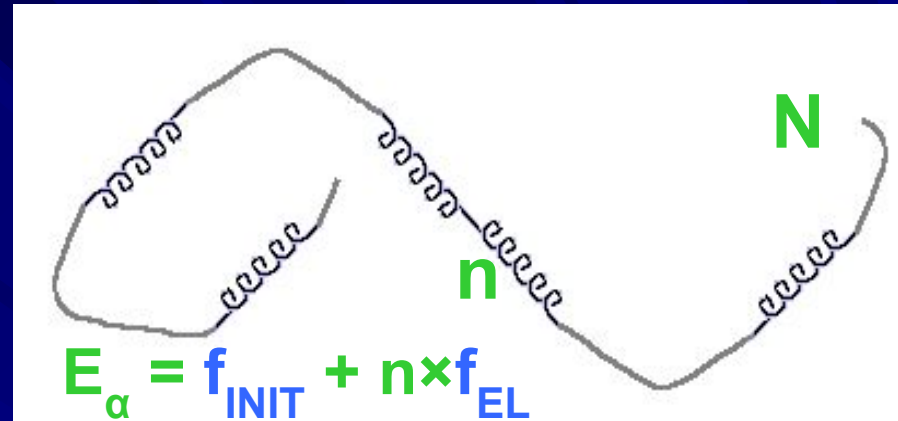
$$s = \exp(-fEL/kBT): \quad s = 2 - 0.2$$

FINIT = $-2fH$: initiation ($\gg kBT$)

$$\sigma = \exp(-\text{FINIT} / kBT): \quad \sigma \ll 1 \quad (\sim 0.001)$$



Average lengths n_0 of helix and coil regions at mid-transition (when $f_{EL} = 0$, $f_{INIT} \gg k_B T$):



positional entropy

n is small: $f_{INIT} - T \cdot k_B \ln[n \times n] > 0$: insertion of coil is unfavorable

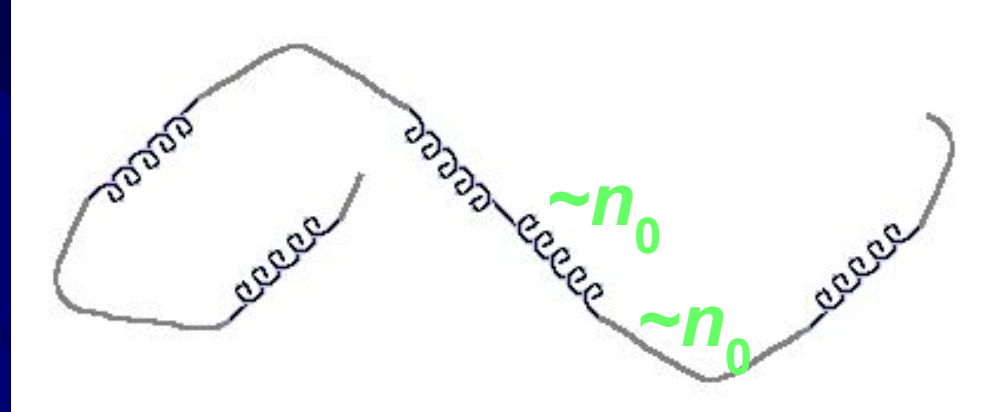
n is large: $f_{INIT} - T \cdot k_B \ln[n \times n] < 0$: insertion of coil is favorable

EQUILIBRIUM: $\Delta G = 0$:

$$f_{INIT} - T \cdot 2k_B \ln[n_0] = 0 \Rightarrow n_0 \approx \exp(+f_{INIT}/2k_B T) = \sigma^{-1/2} \gg 1$$

$$\sigma = \exp(-f_{INIT}/k_B T) \ll 1$$

Width of helix-coil transition

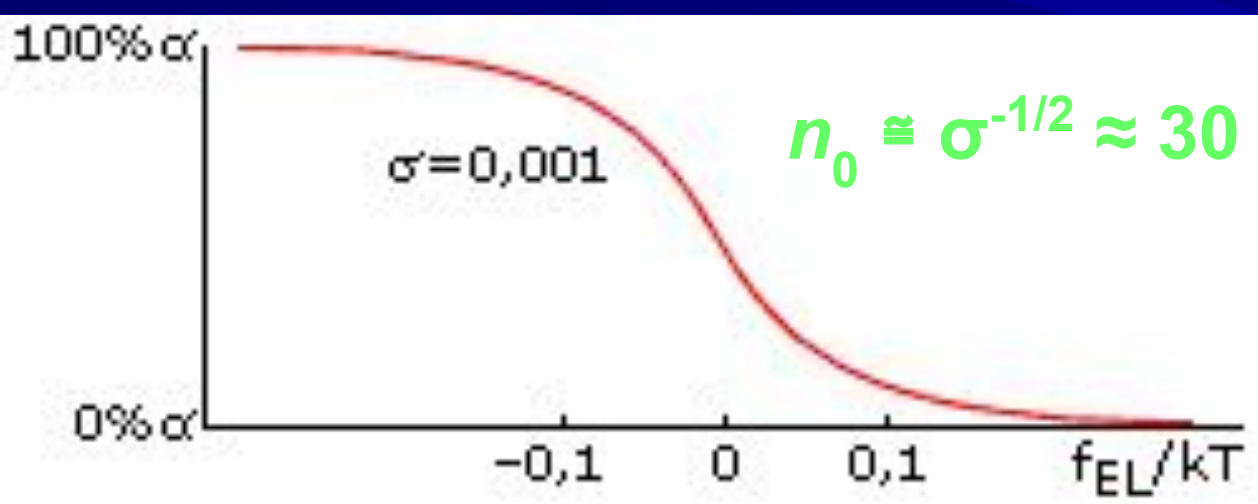


When f_{EL} changes:

IF $n_0 \times f_{EL} \ll -k_B T$, i.e., $f_{EL}/k_B T \ll -1/n_0$: *stable helix*

IF $n_0 \times f_{EL} \gg +k_B T$; i.e., $f_{EL}/k_B T \gg +1/n_0$: *unstable helix, stable coil*

Transition width: $\Delta[f_{EL}/k_B T] \sim 4/n_0 = 4\sigma^{1/2}$



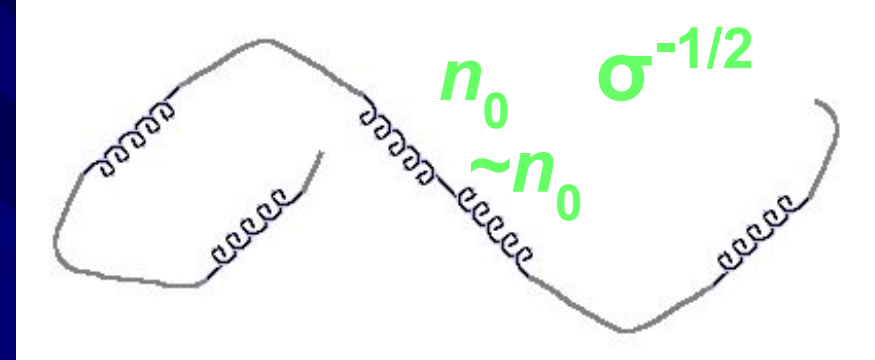
$f_{EL} = 0$ if $\% \alpha = 50\%$
for very long chain

n_0 : $\% \alpha \rightarrow 0$
when chain is
shorter than n_0

TIME of coil-helix transition

Barrier for initiation:

$$\Delta F^\# = f_{\text{INIT}};$$



Time to initiate helix in given place:

$$t_1 = T \times \exp(+\Delta F^\# / k_B T) = T \times \sigma^{-1} = T n_0^2 \quad T \sim 1-10 \text{ ns}$$

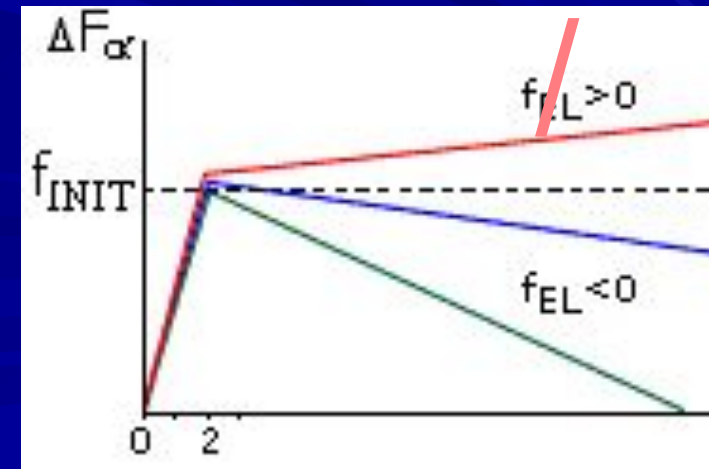
Time to initiate helix in any of n_0 places:

$$t_{\text{INIT}_H} = n_0^{-1} \times t_1 = T n_0 \equiv T \times \sigma^{-1/2} \sim 100 \text{ ns}$$

To extend helix to n_0 residues:

$$t_{\text{EL}_H} = n_0 \times T \equiv T \times \sigma^{-1/2} \sim 100 \text{ ns}$$

$$t_{\text{HELIX}} \sim 200 \text{ ns}$$



TIME of coil – *stable* β -hairpin transition

Barrier for initiation:

$$\Delta F^\# = f_{\text{TURN}} \approx f_{\text{INIT}_\alpha};$$

Time to initiate β -hairpin

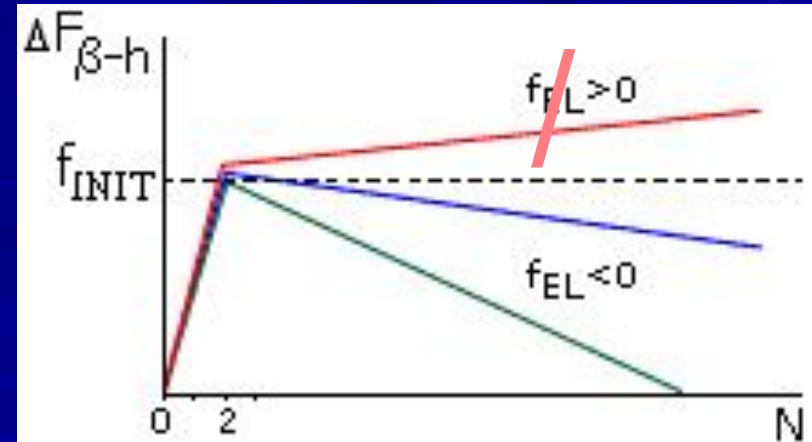
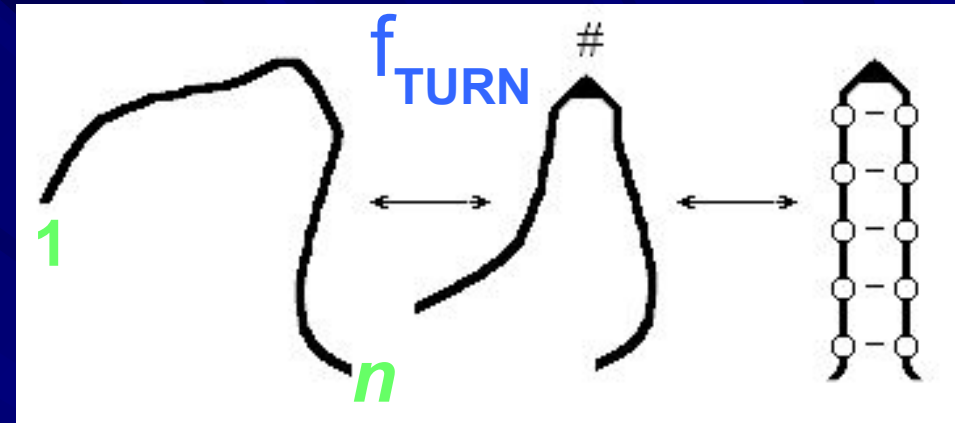
with turn in the middle of the chain:

$$t_1 \approx T \times \exp(+\Delta F^\# / k_B T) = T \times n_0^2 \sim 3000 \text{ ns}$$

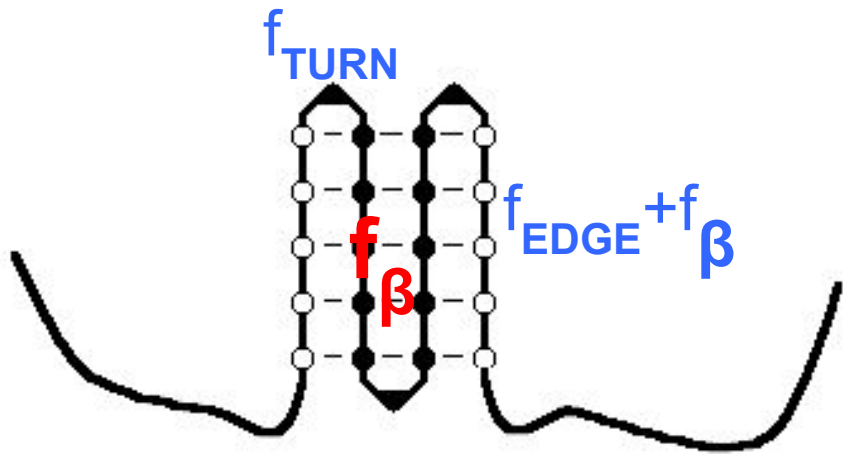
Time to extend β -hairpin to n residues:

$$t_{\text{EL}_\beta\text{-HAIRPIN}} \approx n \times T \sim 100 \text{ ns}$$

$$t_{\beta\text{-HAIRPIN}} \sim 3000 \text{ ns}$$

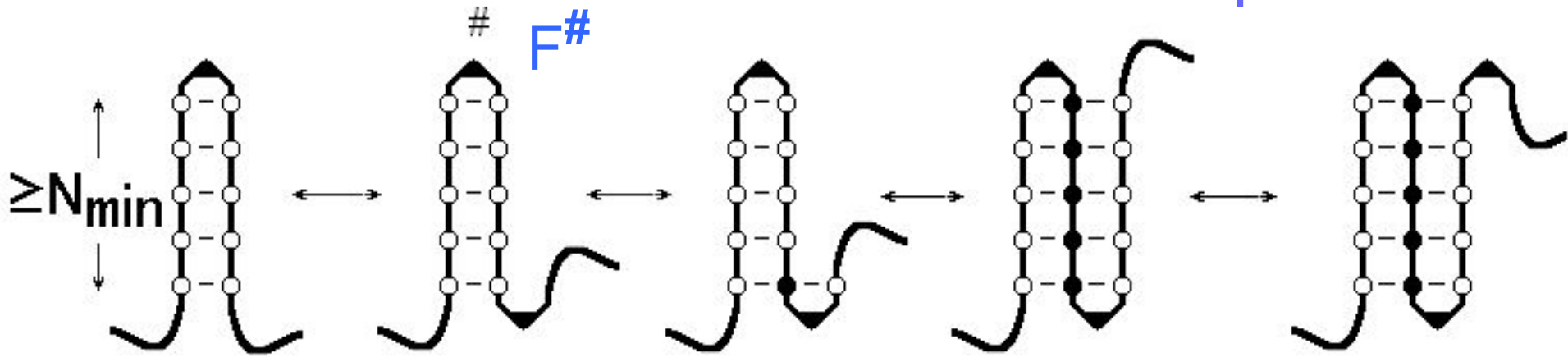


TIME of coil – β -sheet transition (when hairpin is unstable)



$f_{\beta} < 0$
 H-phil.: $f_{\beta} = -0.3 - +0.3 k_B T$;

$f_{\text{EDGE}} + f_{\beta} > 0$
 H-phob.: $f_{\beta} \approx -1 - -0.5 k_B T$



$$f_{\beta} N + f_{\text{TURN}} < 0 \quad \Rightarrow \quad N_{\text{min}} = f_{\text{TURN}} / (-f_{\beta})$$

$$F\# = f_{\text{TURN}} + 2N_{\text{min}}(f_{\text{EDGE}} + f_{\beta}) + f_{\text{TURN}} = 2 f_{\text{TURN}} f_{\text{EDGE}} / (-f_{\beta})$$

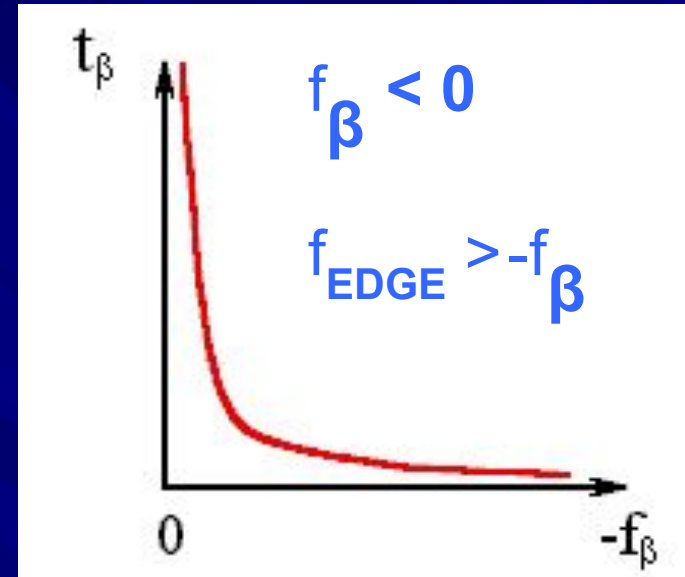
TIME of coil – β -sheet transition

$$F^\# = 2 f_{\text{TURN}} f_{\text{EDGE}} / (-f_\beta) \rightarrow \infty \text{ when } (-f_\beta) \rightarrow 0$$

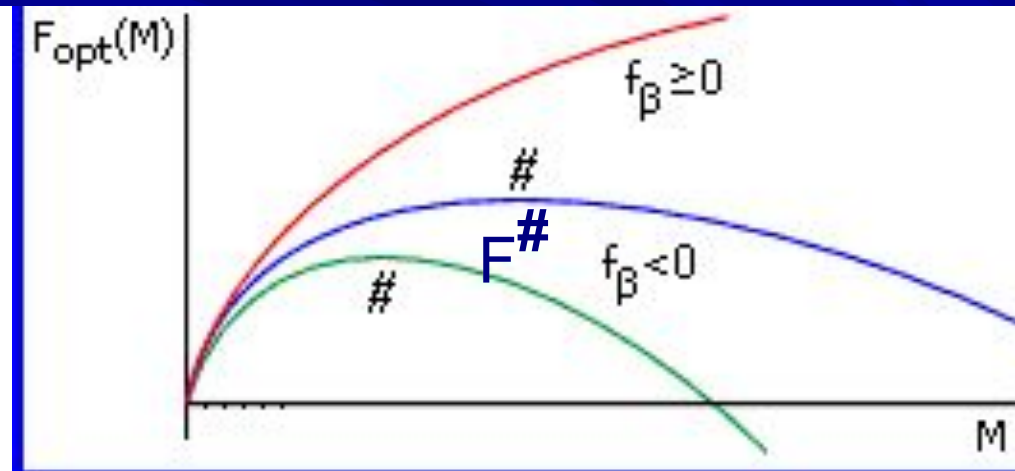
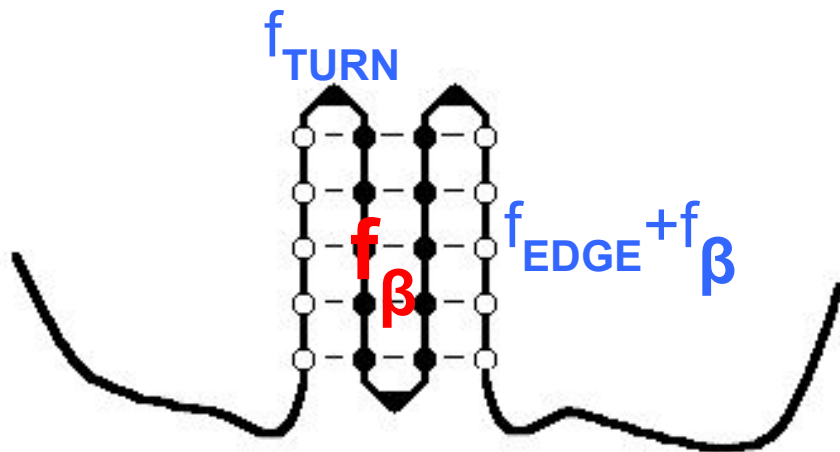
Time to initiate β -sheet folding:

$$t_1 = T \times \exp(+\Delta F^\# / k_B T)$$

$$\rightarrow \infty \text{ when } (-f_\beta) \rightarrow 0$$



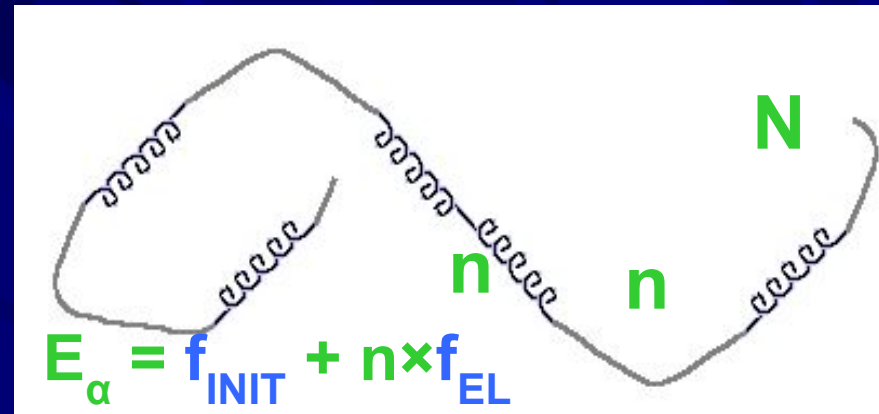
$$!! F_{\text{opt}}(M^\#) = 2 f_{\text{TURN}} f_{\text{EDGE}} / (-f_\beta) - f_{\text{TURN}}$$



The End

Average lengths n_0 of helix and coil regions at mid-transition (when $f_{EL}=0$):

of ends: v ; region's $n \approx N/v$
 : $v/2$ helices, $1+v/2$ coils



when $f_{EL}=0$: $\Delta E = E(v+2) - E(v) = f_{INIT}$

$$S(v)/k_B = \ln[N \cdot \dots \cdot (N-v+1) / v \cdot \dots \cdot 1];$$

$$\Delta S/k_B = [S(v+2) - S(v)]/k_B \approx 2\ln[N/v] = 2\ln(n) \quad (\text{when } N \gg v)$$

EQUILIBRIUM: $\Delta G = \Delta E - T\Delta S = 0$:

$$f_{INIT} - T \cdot 2k_B \ln[n_0] = 0 \Rightarrow n_0 \approx \exp(+f_{INIT}/2k_B T) = \sigma^{-1/2}$$

(when $\sigma \ll 1$)