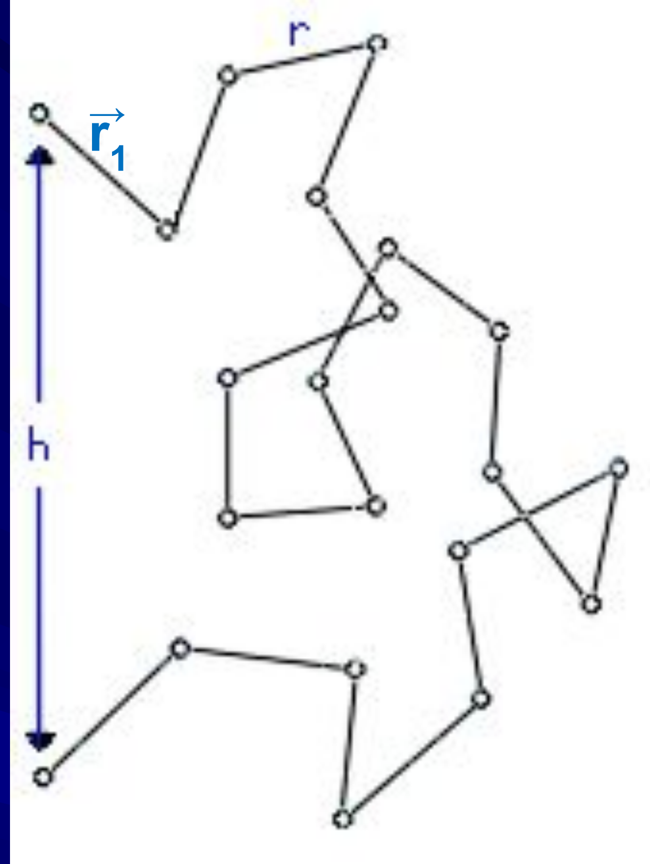
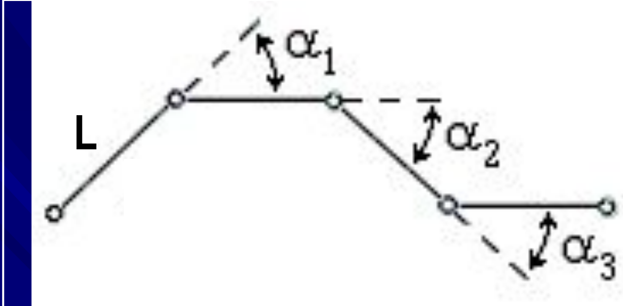
PROTEIN PHYSICS

LECTURES 9-10

Secondary structures

coil





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

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

$$<\mathbf{h}^2> = <(\sum_{i=1}^{M} \mathbf{r}_i)^2> = <\sum_{i=1}^{M} \mathbf{r}_i^2 + \sum_{i \neq j}^{M} \sum^{M} \mathbf{r}_i \mathbf{r}_j> = \sum_{i=1}^{M} <\mathbf{r}_i^2> + \sum_{i \neq j}^{M} \sum^{M} <\mathbf{r}_i \mathbf{r}_j> = Mr^2$$

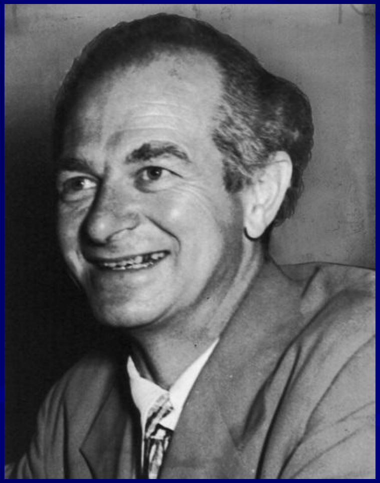
$$<h^2> = (Mr) \cdot r = L_M \cdot r \qquad |h| \sim M^{1/2}$$

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

Random coil:

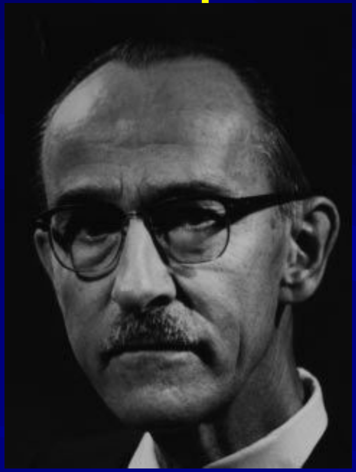
Werner Kuhn (1899 - 1963)

α-helices and **β-sheets**:



Linus Carl **Pauling** (1901-94)

— Nobel Prizes: 1954, 62



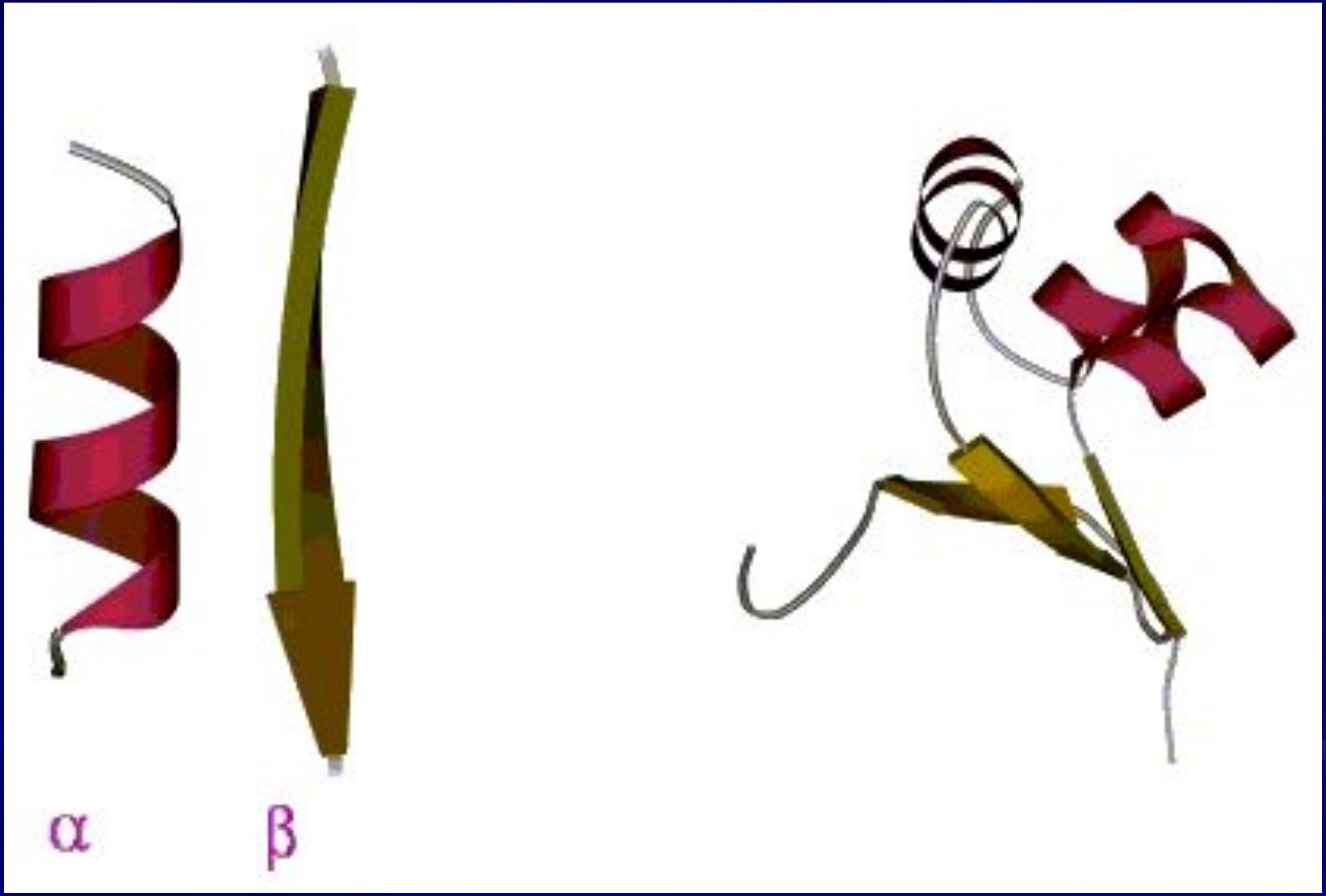
Robert Brainard **Corey**

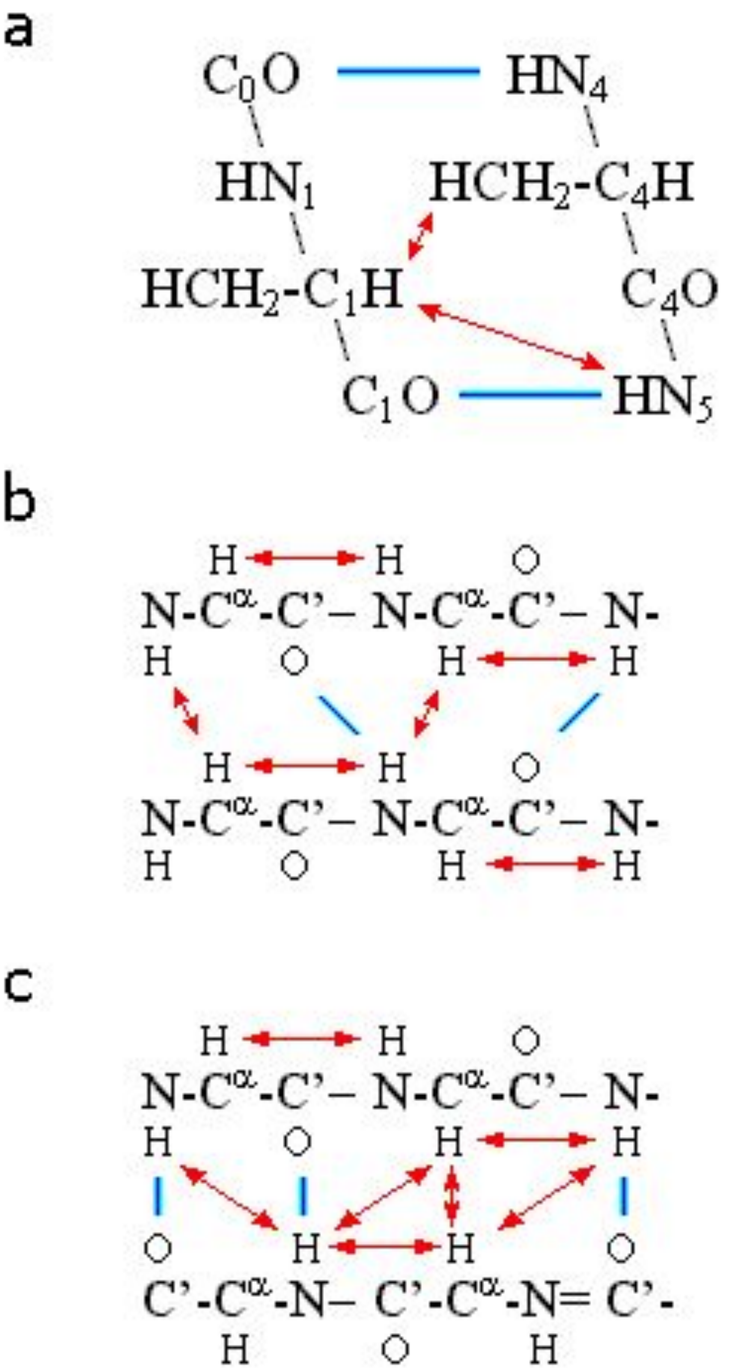
(1897 –1971)

Herman Russell **Branson**

(1914 –1995)

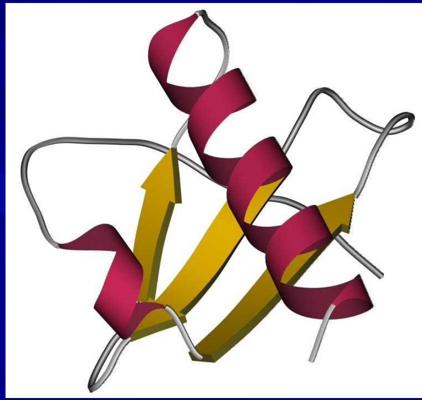
Main secondary structures





Experimental study of secondary structure

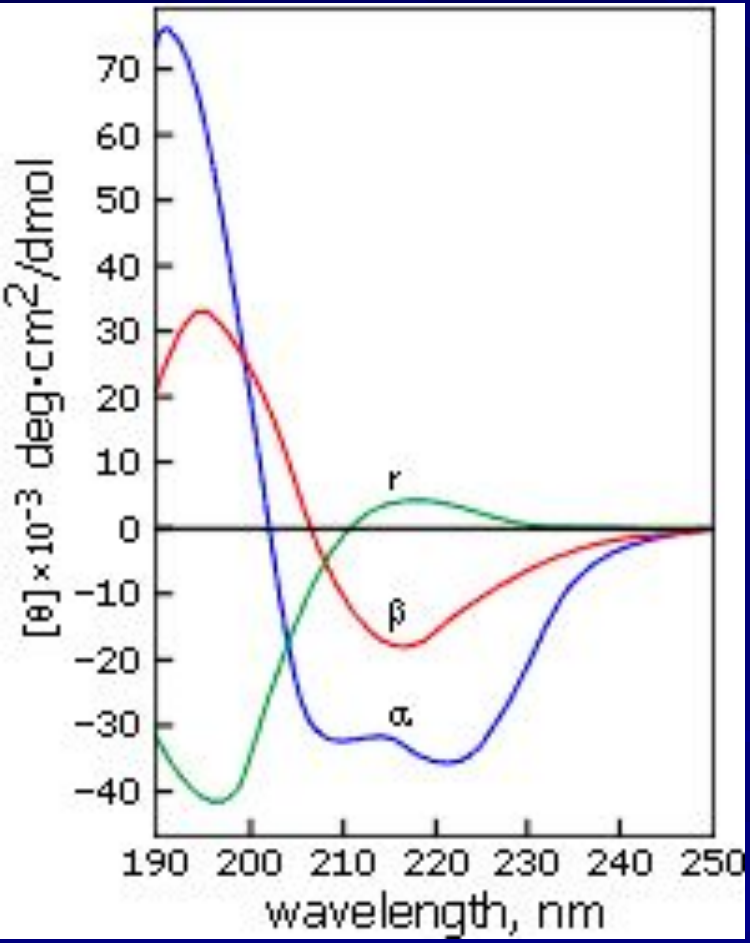
X-ray crystallography



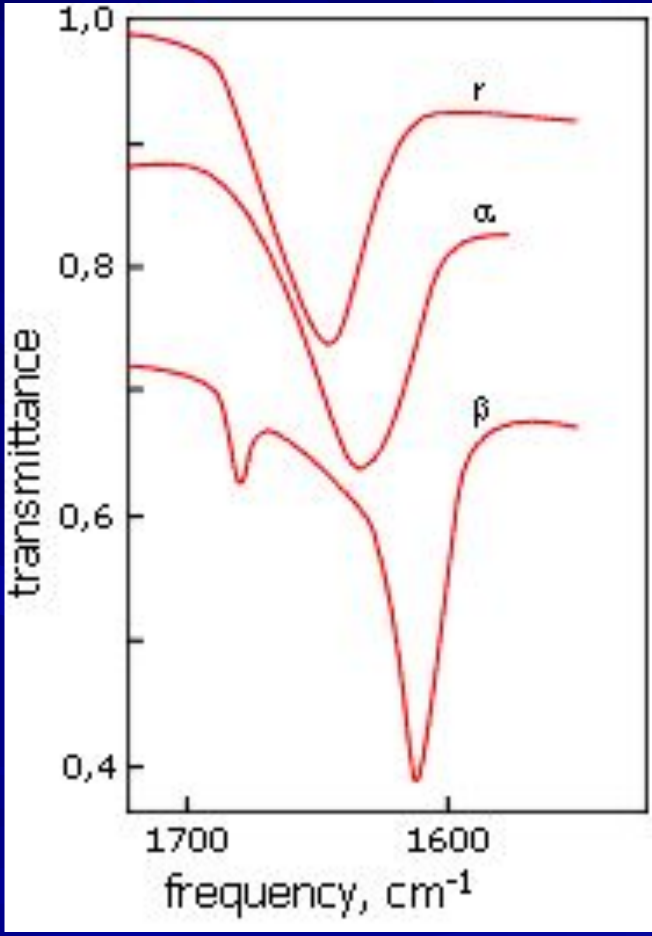
H^1 NMR spectroscopy (cross-peaks)

Experimental study of secondary structure

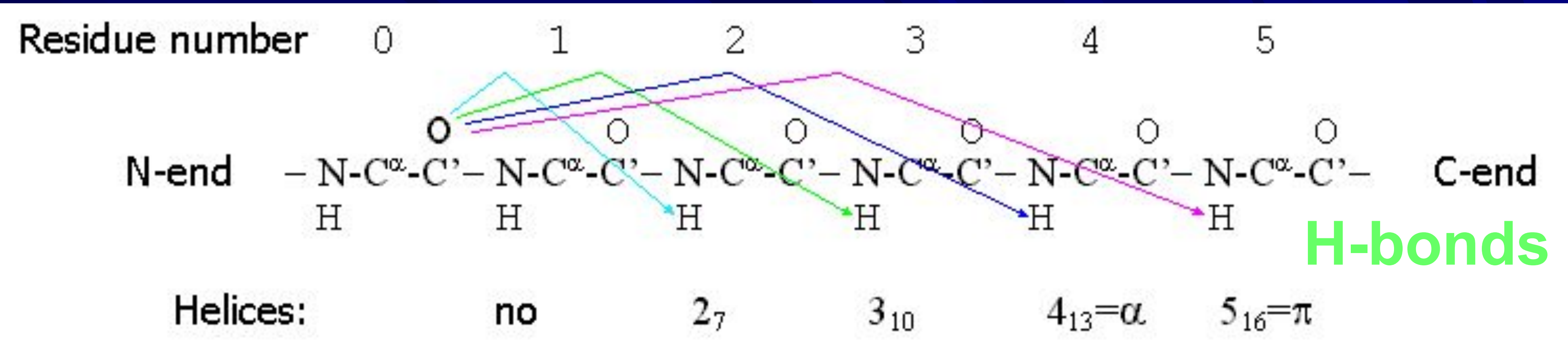
Far UV CD spectra
(peptide groups)



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

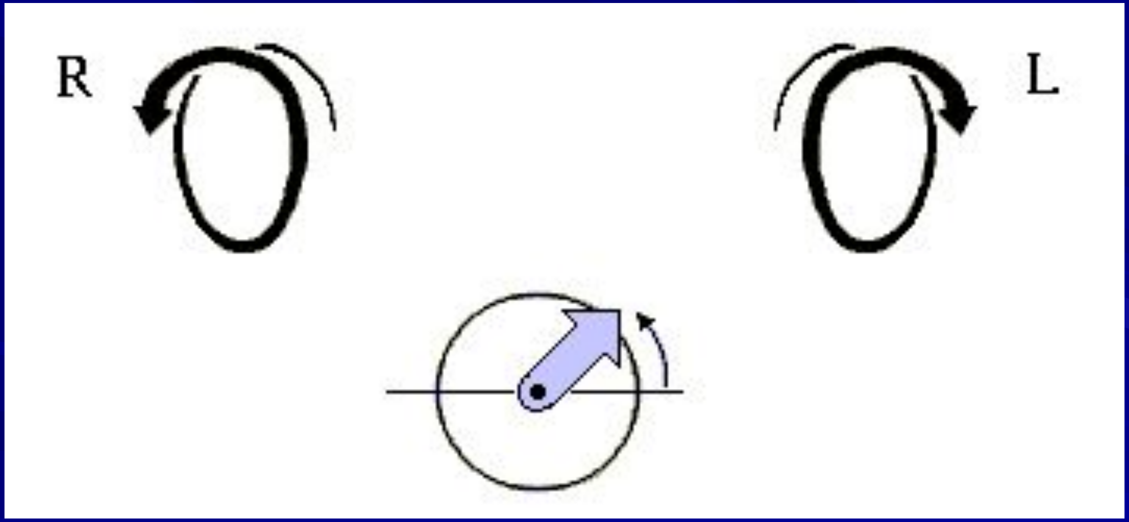


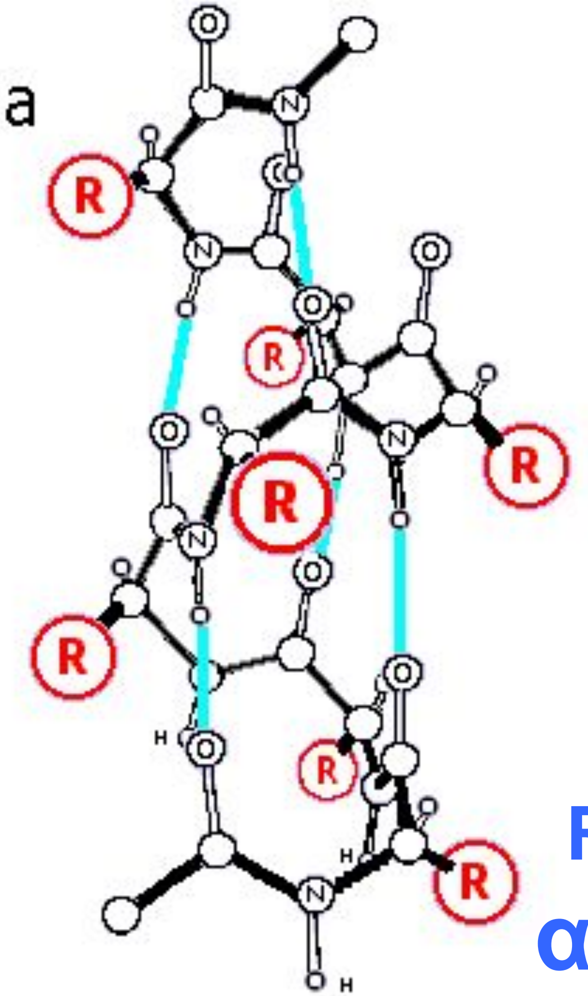
H-bonds

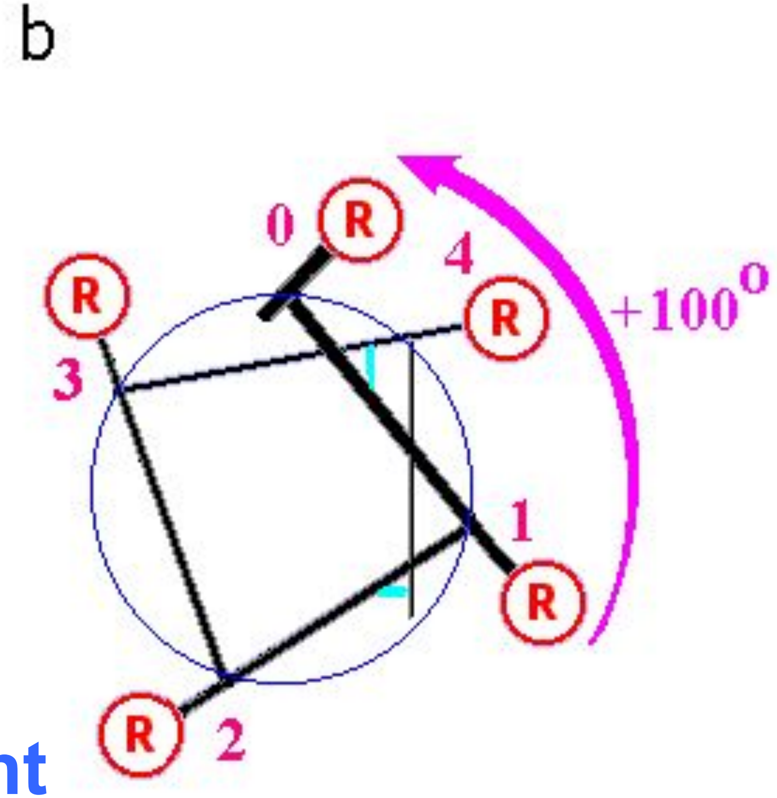


Helices:

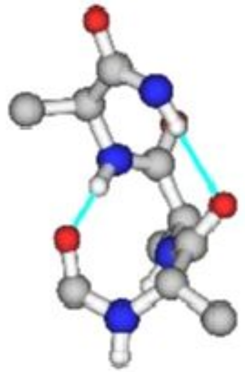
Right and Left



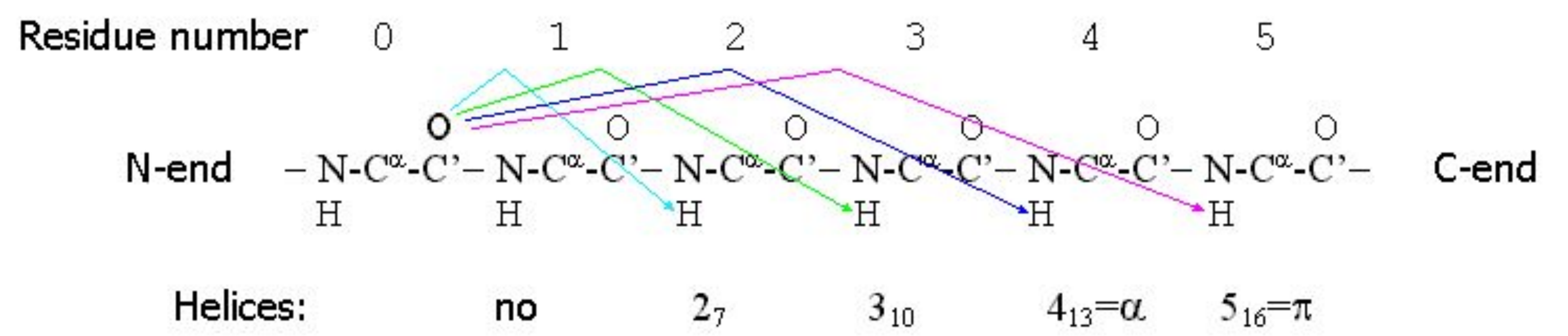


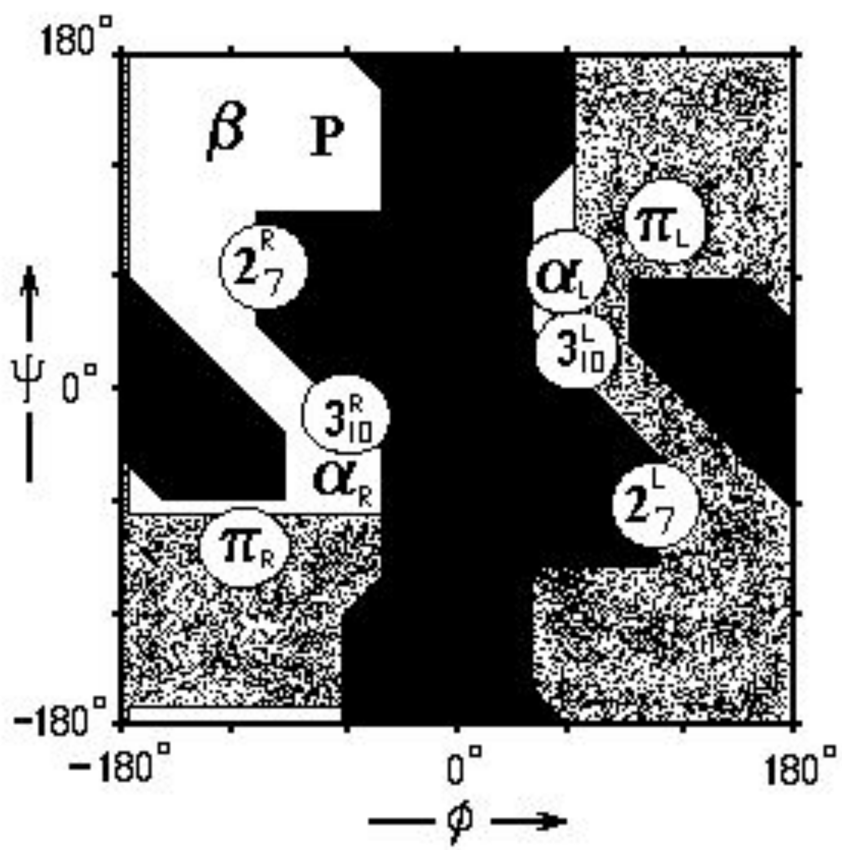


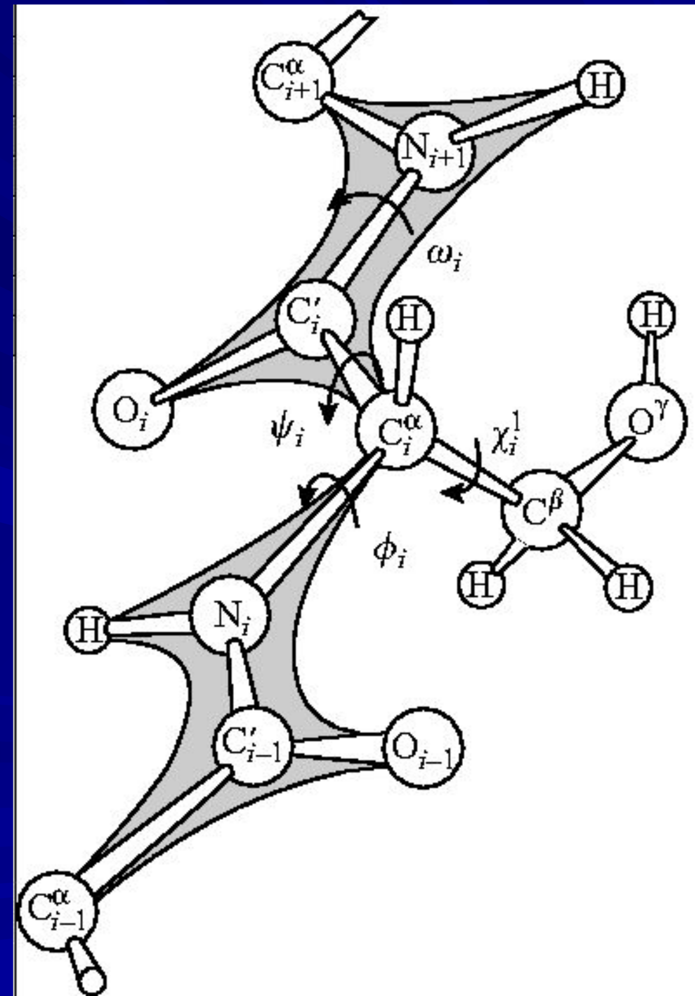
Right
α-helix

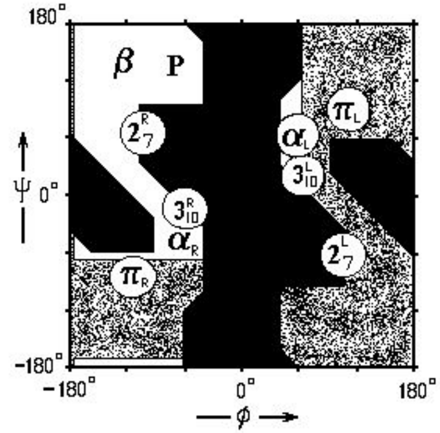


Right
3_{10}-helix

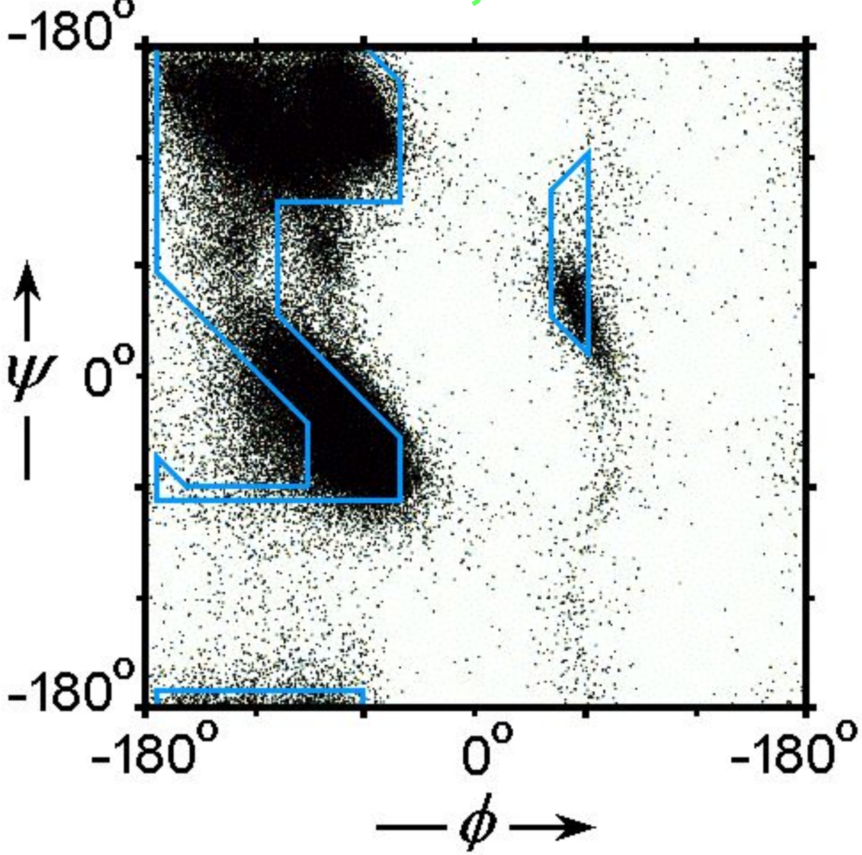

Residue number 0 1 2 3 4 5
N-end
– N-Cα-C'– N-Cα-C'– N-Cα-C'– N-Cα-C'– N-Cα-C'– N-Cα-C'–
C-end
Helices: no 2_7 3_{10} 4_{13}=α 5_{16}=π


180°
−180°
0°
ψ
φ
β
P
2_7^R
3_{10}^R
α_R
π_R
π_L
α_L
3_{10}^L
2_7^L

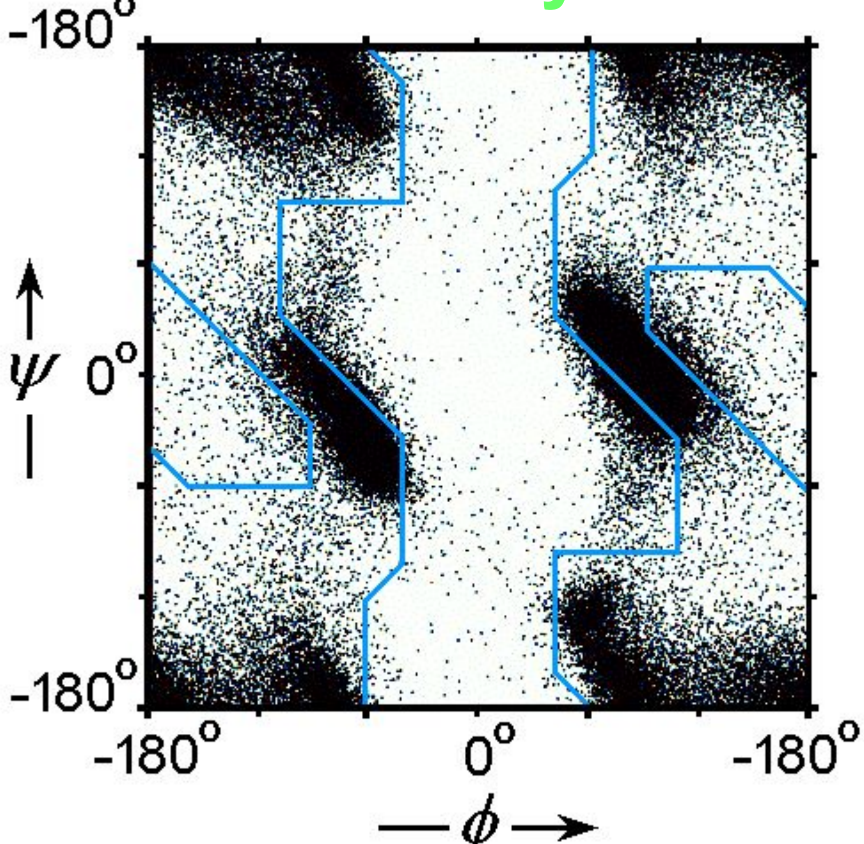

C^α_{i+1}
H
N_{i+1}
ω_i
C'_i
O_i
ψ_i
C^α_i
χ^1_i
O^γ
C^β
ϕ_i
N_i
C'_{i-1}
O_{i-1}
C^α_{i-1}



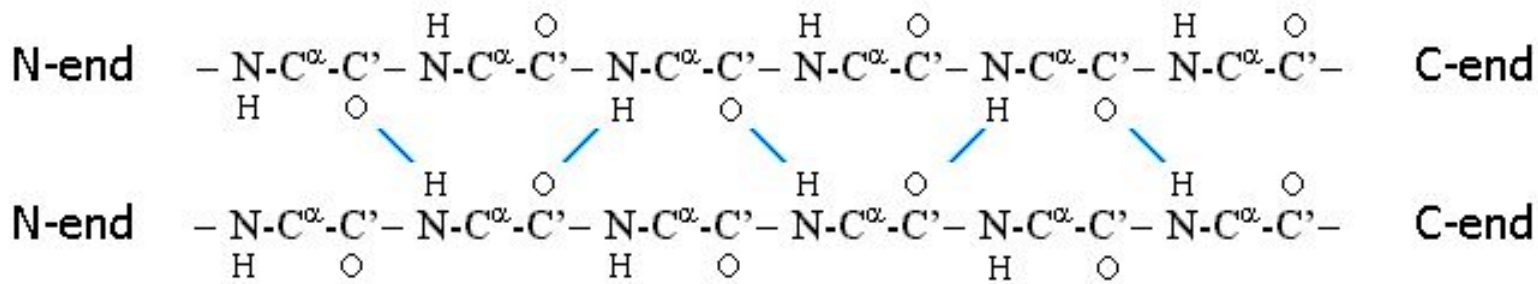
ALA, etc.



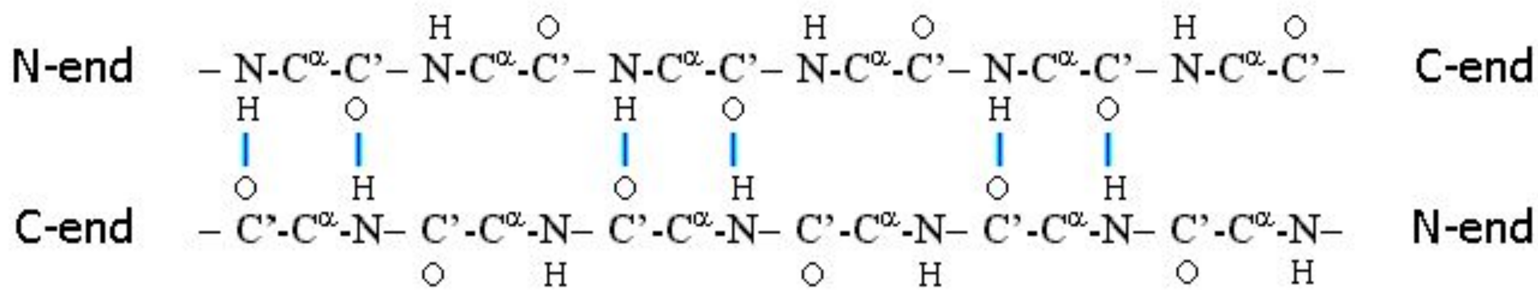
GLY only



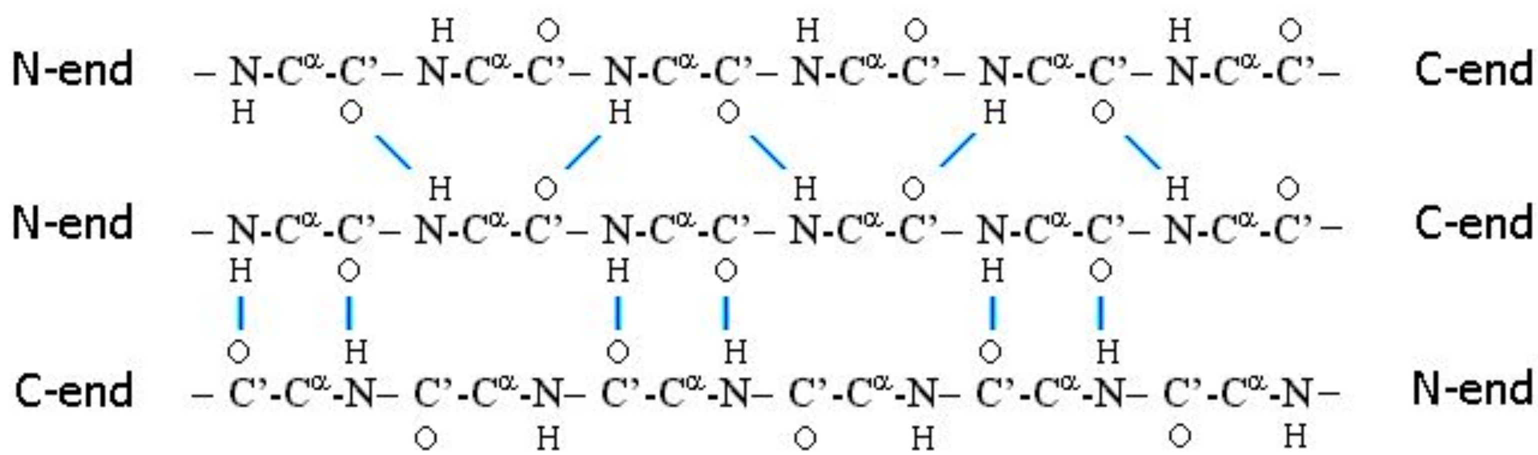
β↑↑

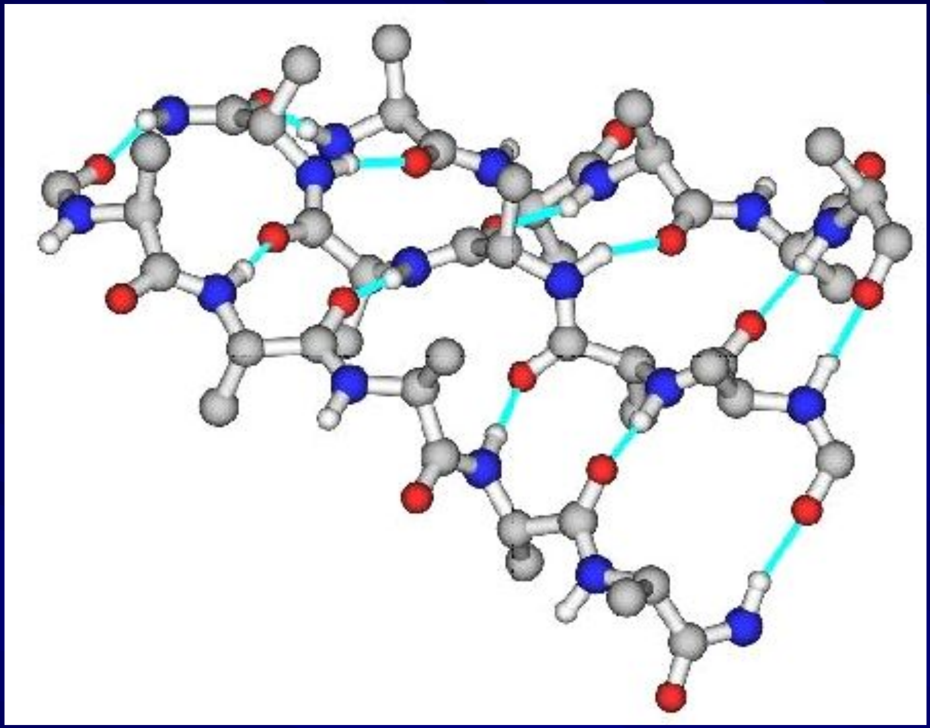

N-end
C-end
N-end
C-end

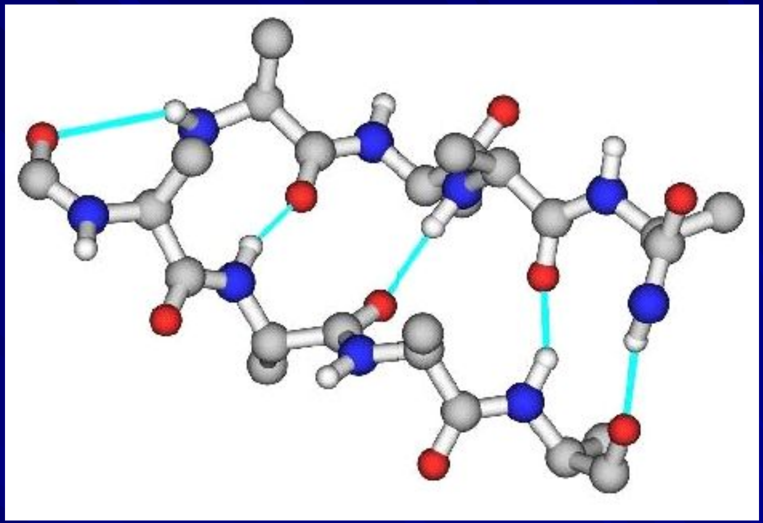
β↓↑

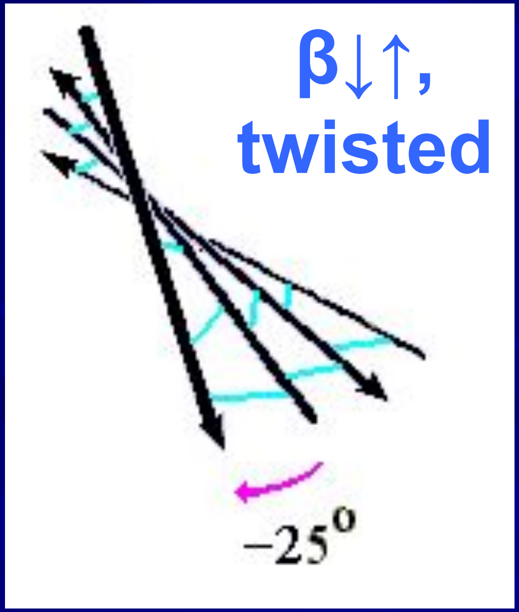

N-end
C-end
C-end
N-end

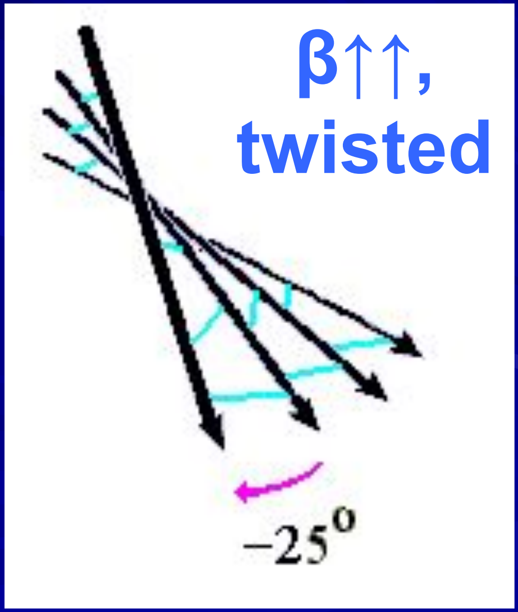
β↑↑↓

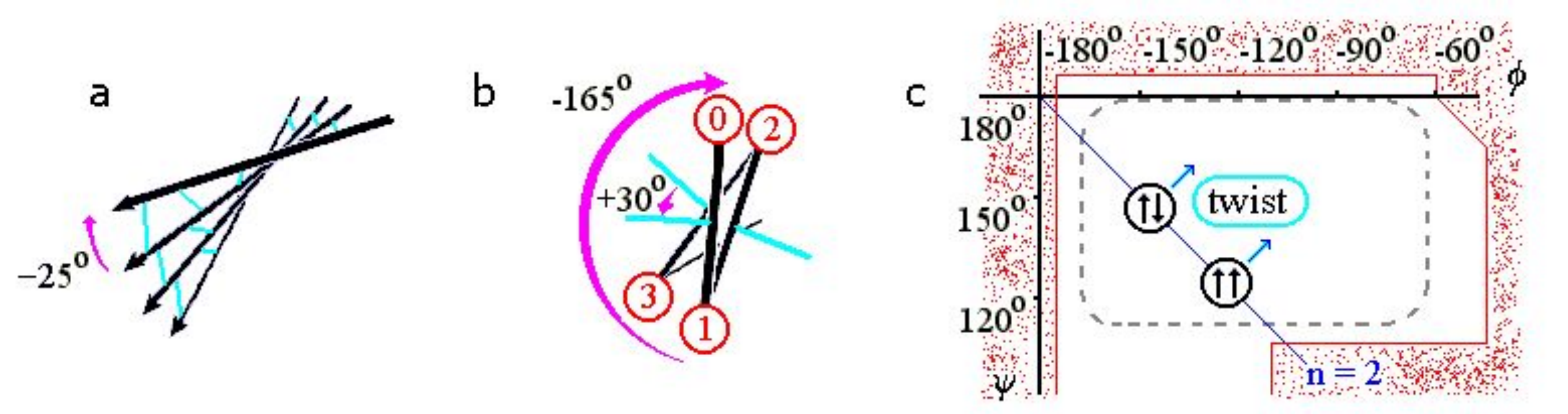

N-end
C-end
N-end
C-end
C-end
N-end

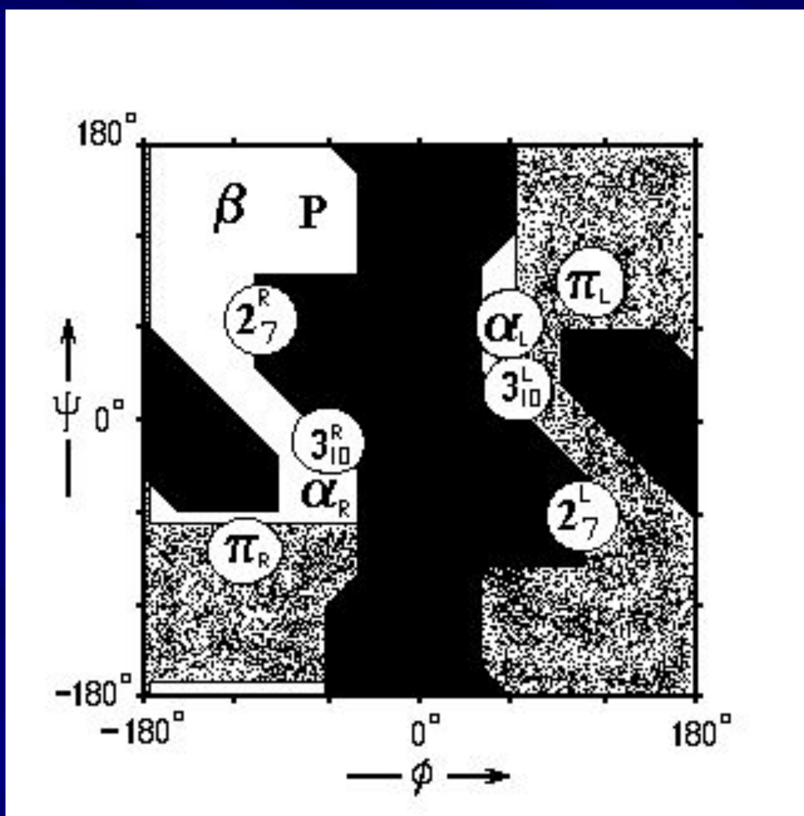


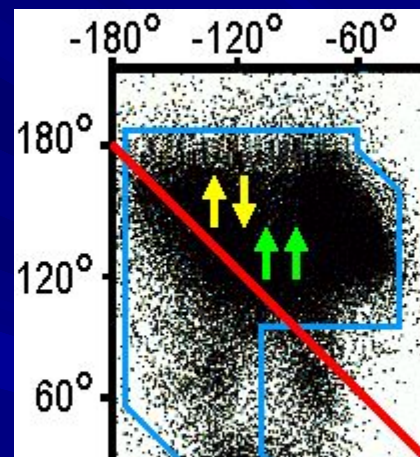



β↓↑,
twisted
−25°

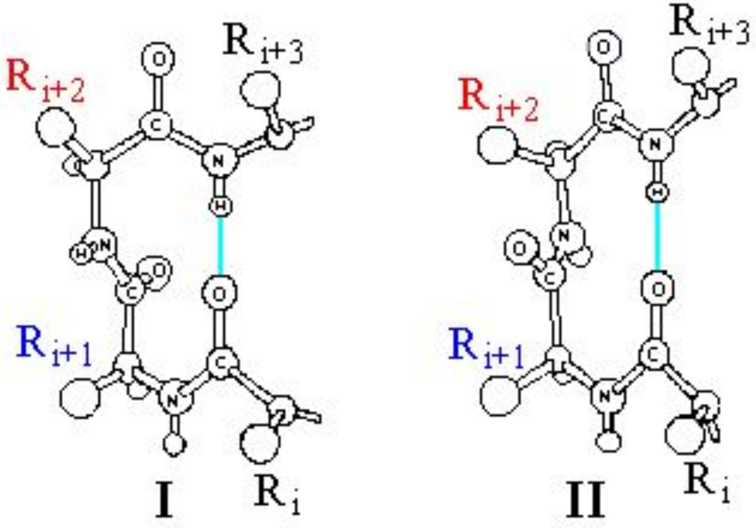

β↑↑,
twisted
−25°

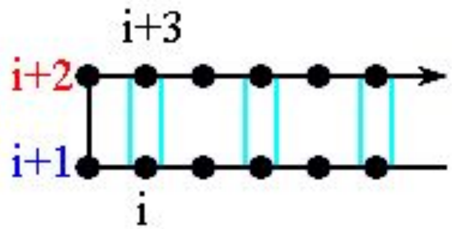


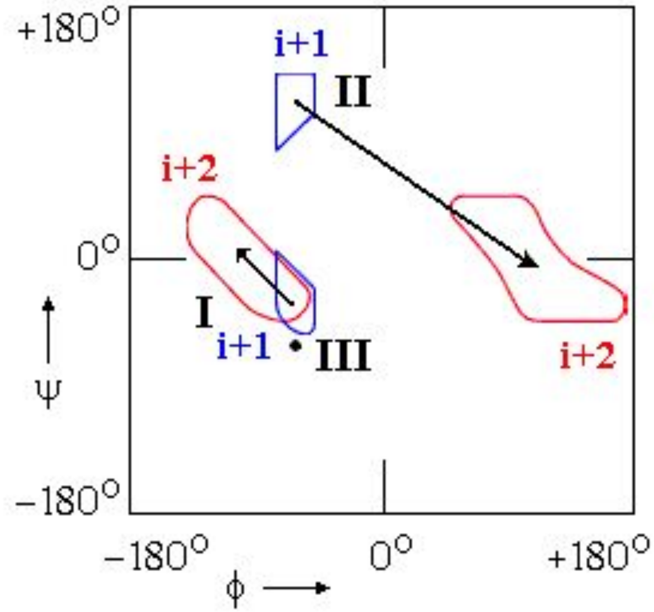




Mirror-asymmetric amino acids – mirror-asymmetric twist of β-sheets

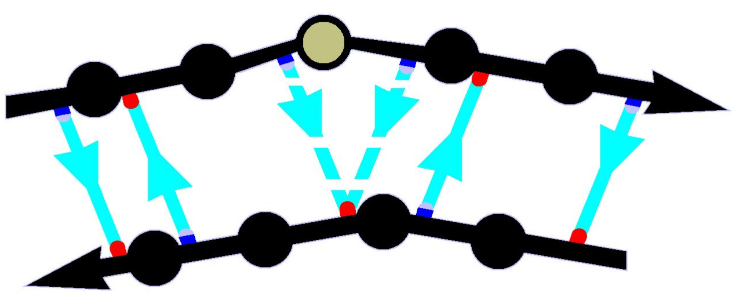


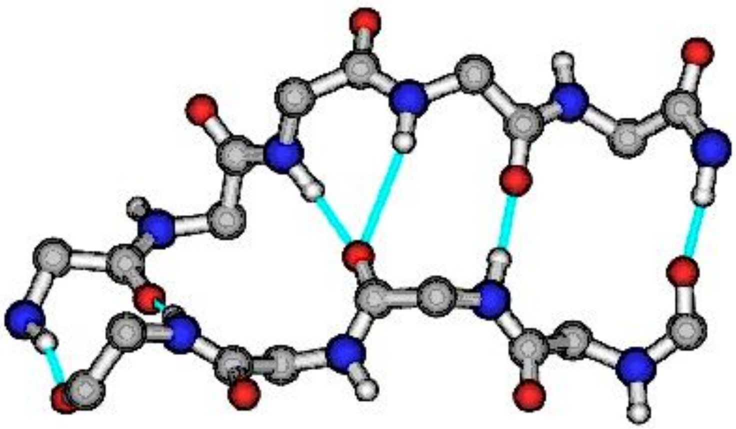




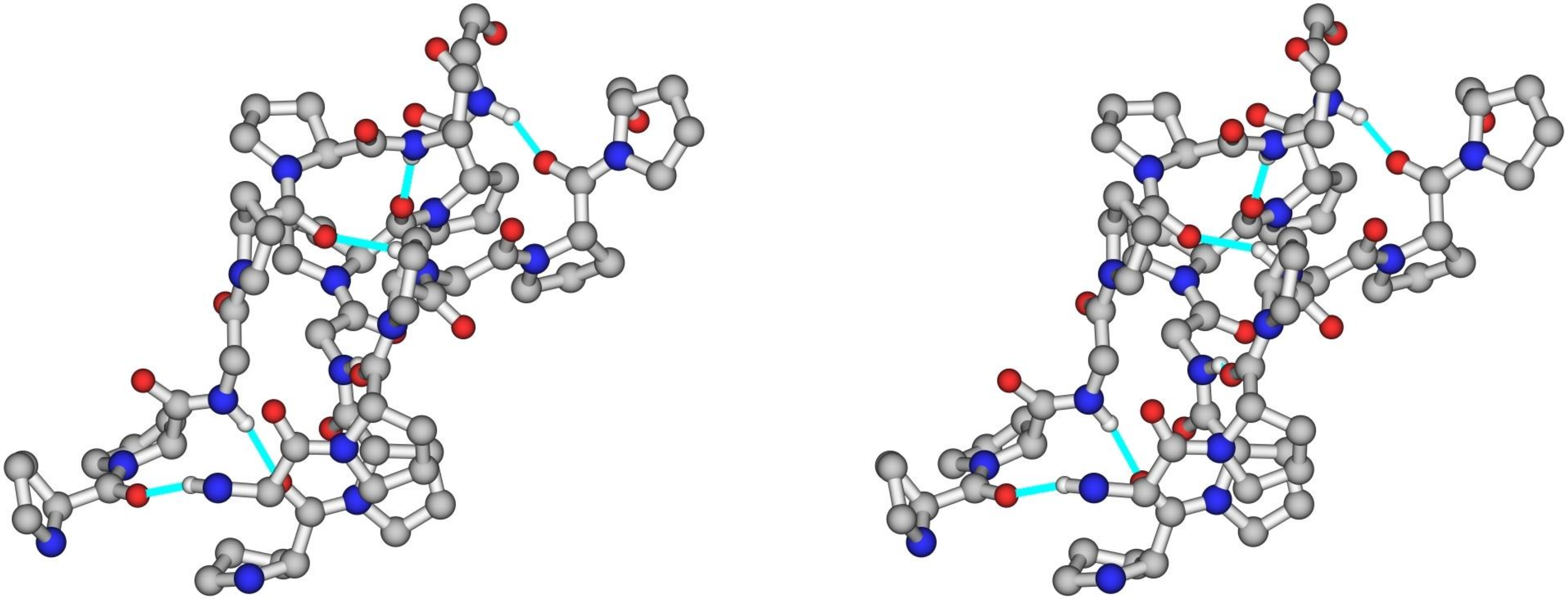
β-turns

β-bulge





collagen triple helix



Secondary structure transitions

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

$E = E_{COORD} + E_{KIN}$; $E_{KIN} = \Sigma mv^2/2$ - does not depend on coordinates

$S = S_{COORD} + S_{KIN}$

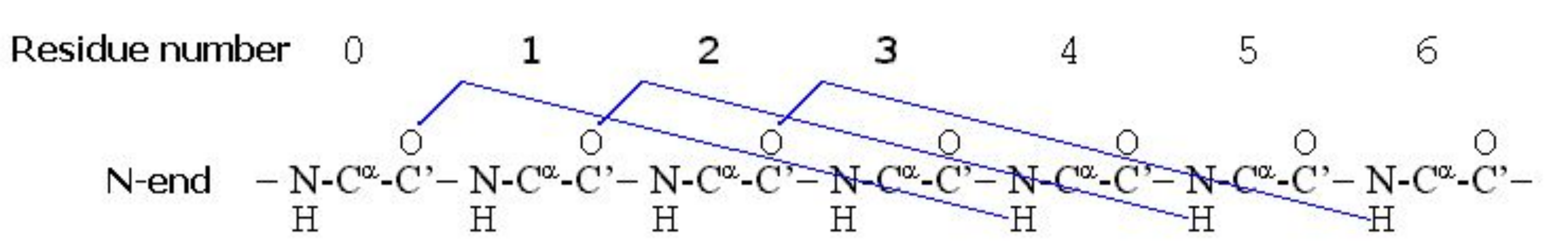
We may consider only potential energy, etc.:

$E \Rightarrow E_{COORD}$

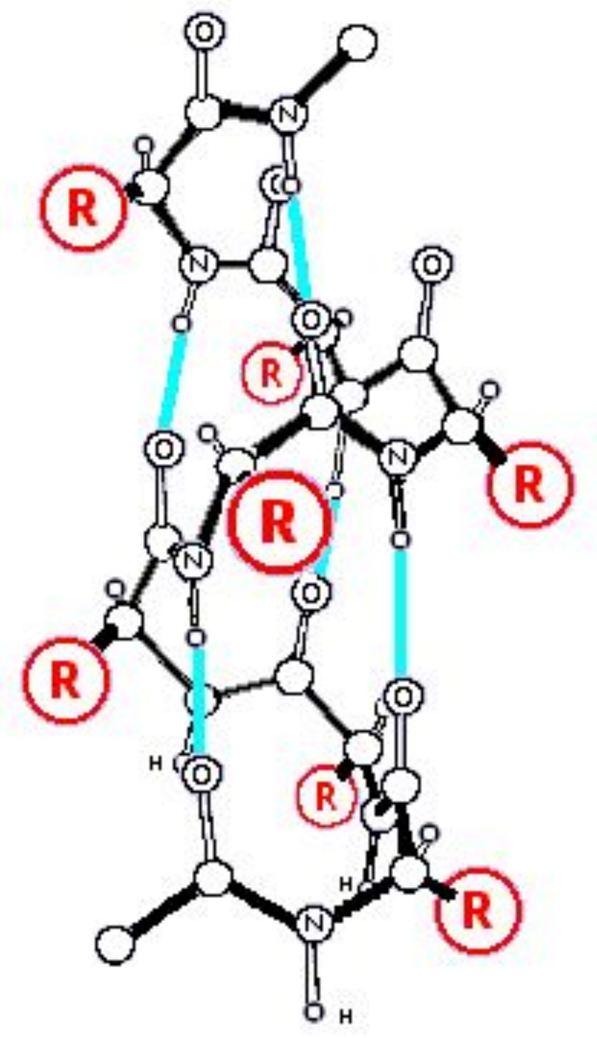
$M \Rightarrow M_{COORD}$

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

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



α-helix



homo-polypeptide:

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

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

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

f_{INIT} f_{EL}

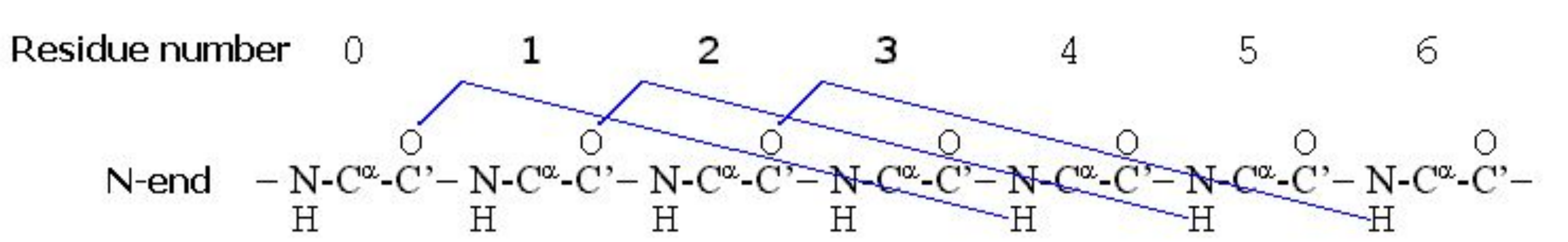
f_{EL}: elongation (≈ 0) :

≈ $-0.5 \cdot k_BT$ Ala --- ≈ $+1.5 \cdot k_BT$ Gly

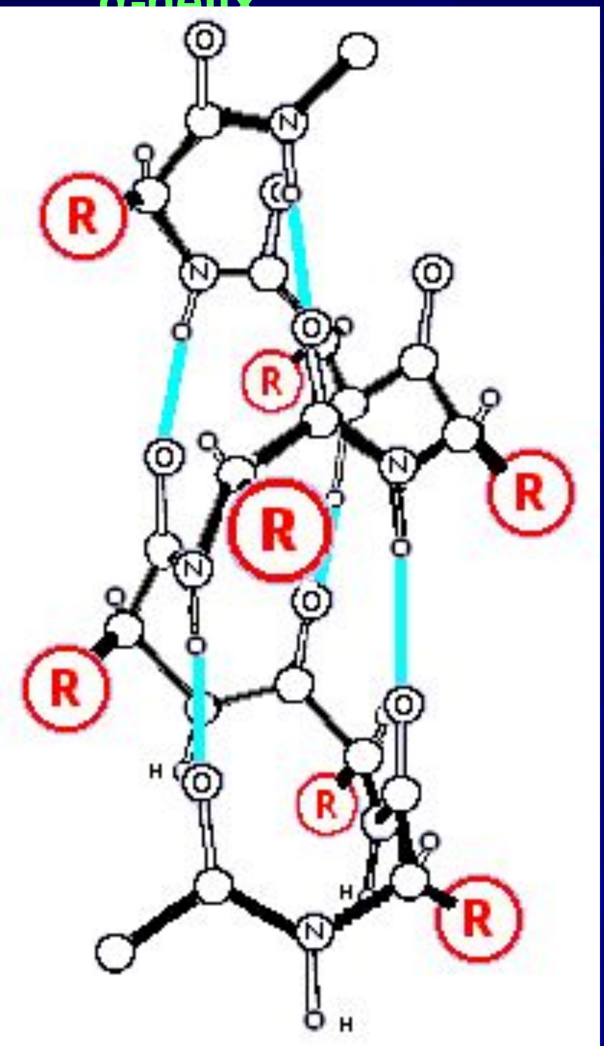
$s = \exp(-f_{EL}/k_BT)$: $s = 2 – 0.2$

$f_{INIT} = -2f_H$: initiation ($>>k_BT$)

$\sigma = \exp(-f_{INIT}/k_BT)$: $\sigma<<1$ (~0.001)



α-helix



~~homo-polypeptide:~~

$\Delta F\alpha = F\alpha - F_{coil} = (n-2)f_H - nTS\alpha =$

$= -2f_H + n\times(f_H - TS\alpha)$

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

fINIT **fEL**

fEL: elongation (≈ 0) :

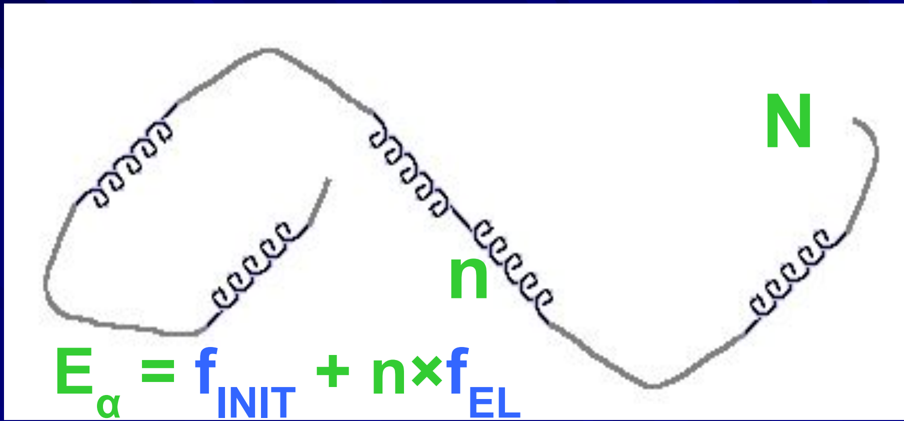
≈ -0.5·kBT Ala --- ≈ +1.5·kBT Gly

$s = \exp(-f_{EL}/k_BT)$: $s = 2 – 0.2$

$f_{INIT} = -2f_H$: initiation (>>kBT)

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

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



positional entropy

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

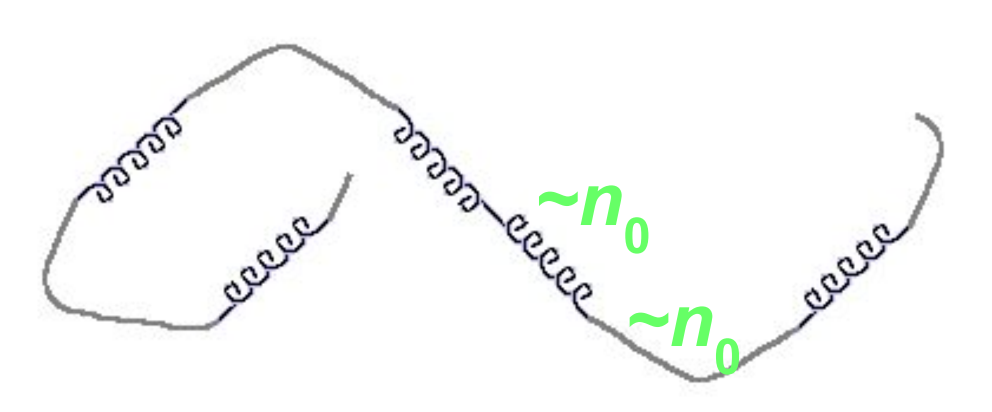
n is large: $f_{INIT} - T \cdot k_B \ln[\mathbf{n \times n}] < 0$: insertion of coil is favorable

EQUILIBRIUM: ΔG = 0:

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

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

Width of helix-coil transition

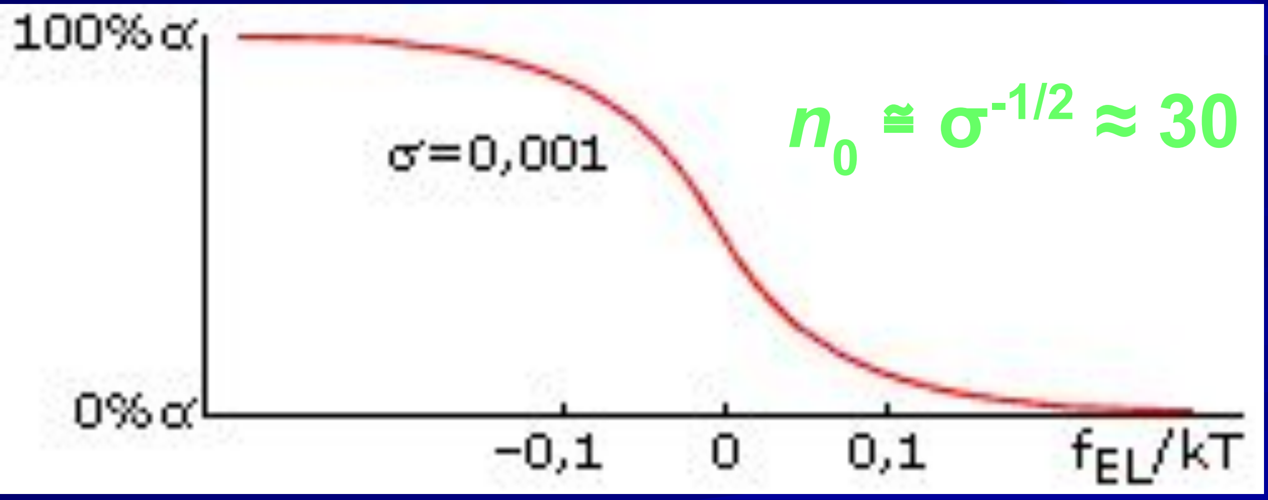


When f_{EL} changes:

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

IF $n_0 \times f_{EL} >> +k_BT$; i.e., $f_{EL}/k_BT >> +1/n_0$: ***un**stable helix, stable coil*

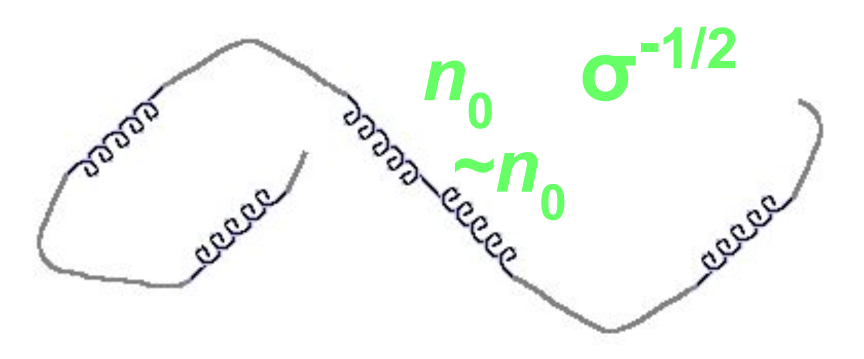
Transition width: $\Delta[f_{EL}/k_BT] \sim 4/n_0 = 4\sigma^{1/2}$



$f_{EL}=0$ *if %α = 50% for very long chain*

n_0: *%α → 0 when chain is shorter than* n_0

TIME of coil-helix transition



Barrier for initiation:

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

Time to initiate helix in given place:

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

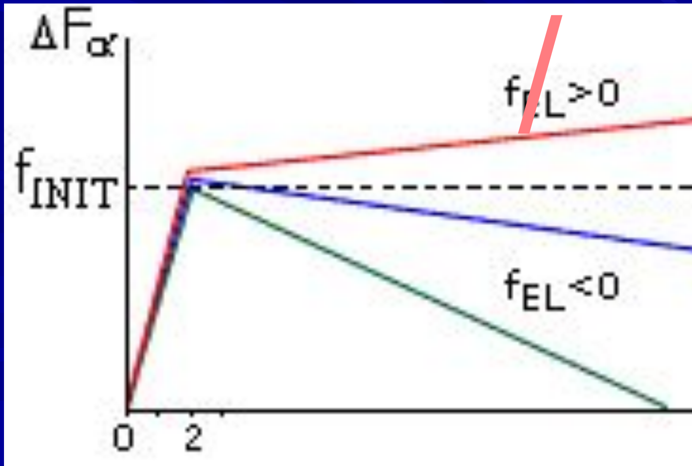
Time to initiate helix in any of n_0 places:

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

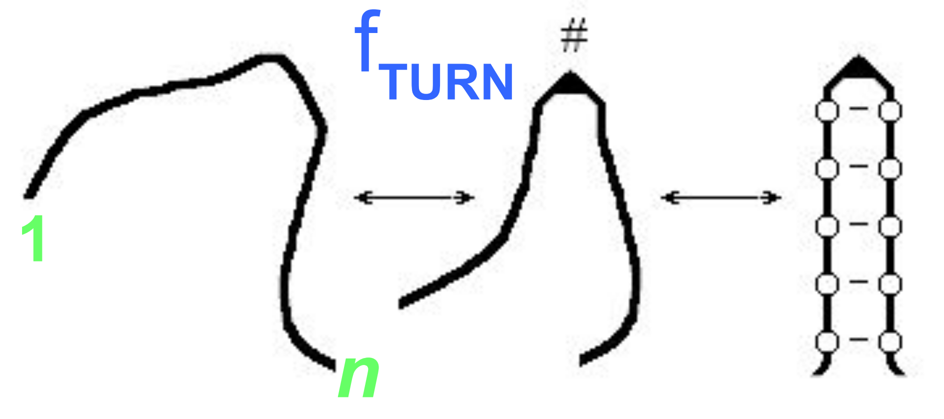
To extend helix to n_0 residues:

$t_{EL\_H} = n_0 \times \tau \equiv \tau \times \sigma^{-1/2}$ ~100 ns

t_{HELIX} ~ 200 ns



TIME of coil – *stable* β-hairpin transition



Barrier for initiation:

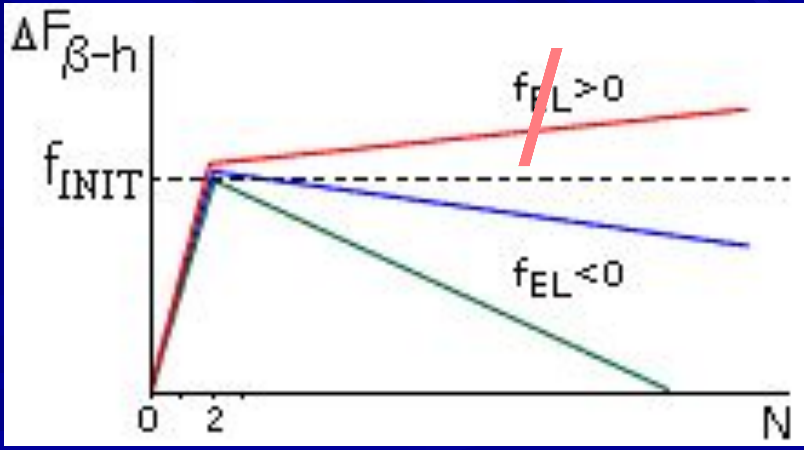
$\Delta F^{\#} = f_{TURN} \approx f_{INIT\_\alpha}$;

Time to initiate β-hairpin with turn in the middle of the chain:

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

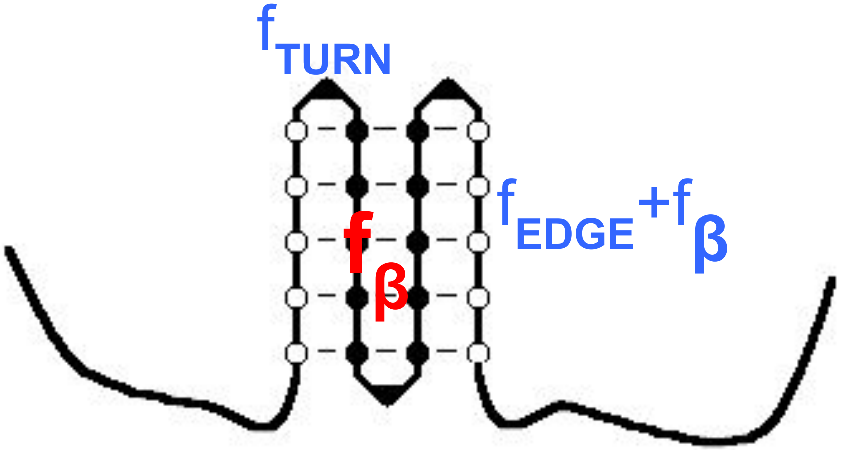
Time to extend β-hairpin to *n* residues:

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



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

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

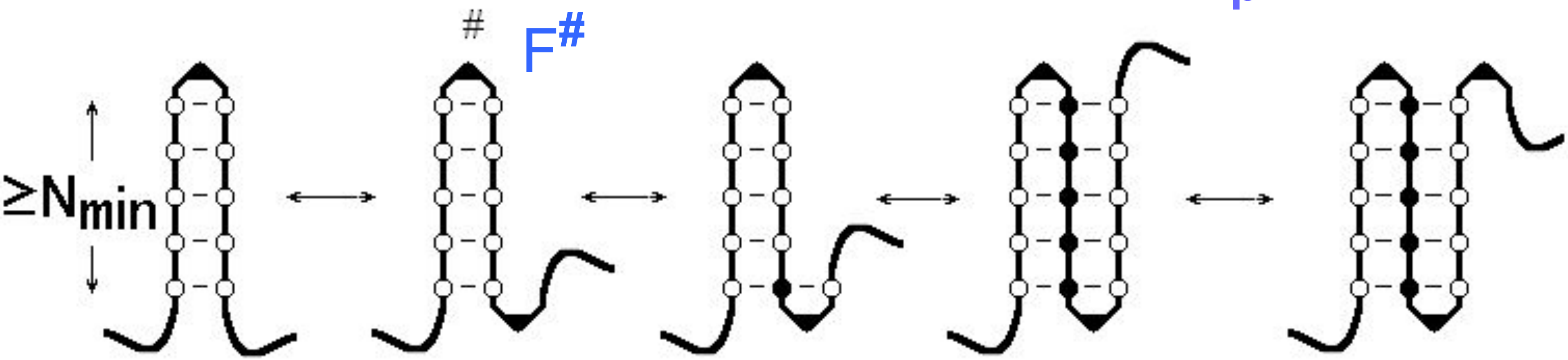


$f_{\beta} < 0$

H-phil.: $f_{\beta} = -0.3 – +0.3\ k_BT$;

$f_{EDGE}+f_{\beta} > 0$

H-phob.: $f_{\beta} \approx -1 – -0.5\ k_BT$



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

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

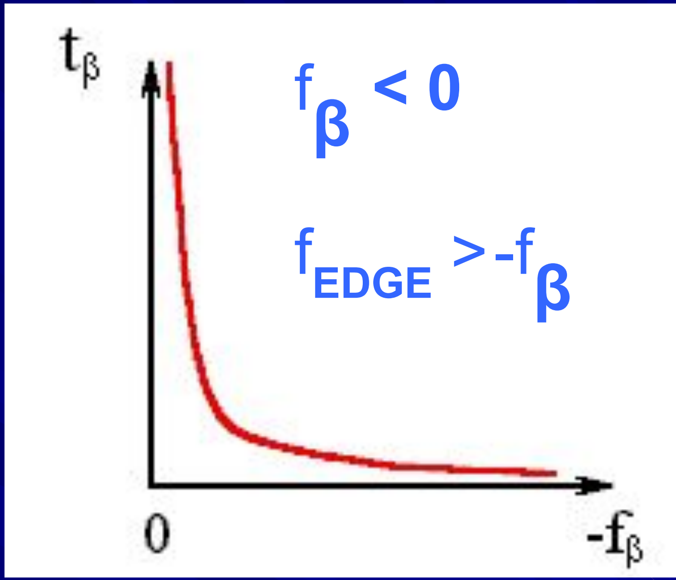
TIME of coil – β-sheet transition

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

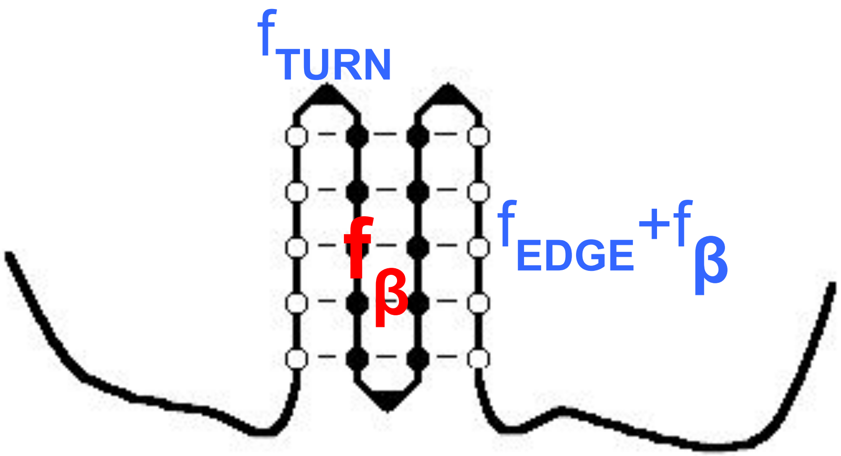
Time to initiate β-sheet folding:

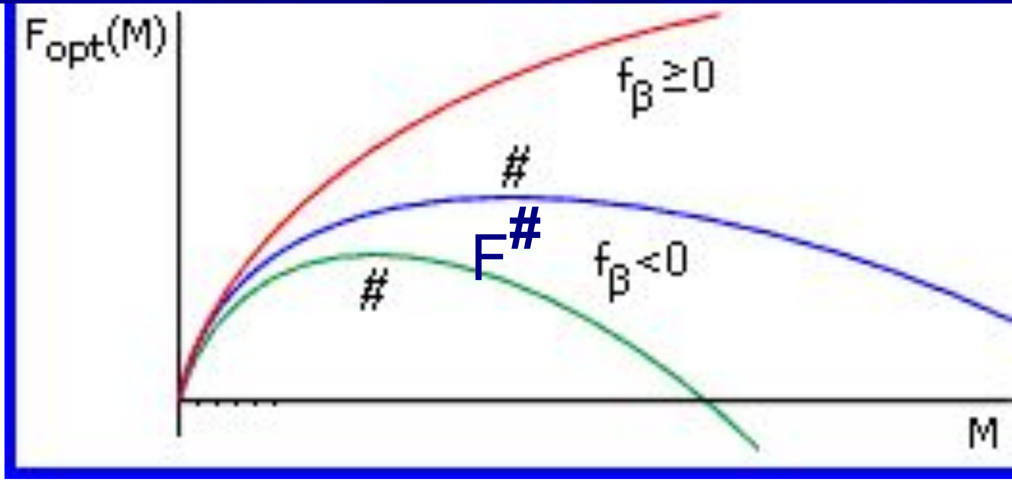
$t_1 = T \times \exp(+\Delta F^{\#}/k_B T)$

$\rightarrow \infty$ **when** $(-f_\beta) \rightarrow 0$



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

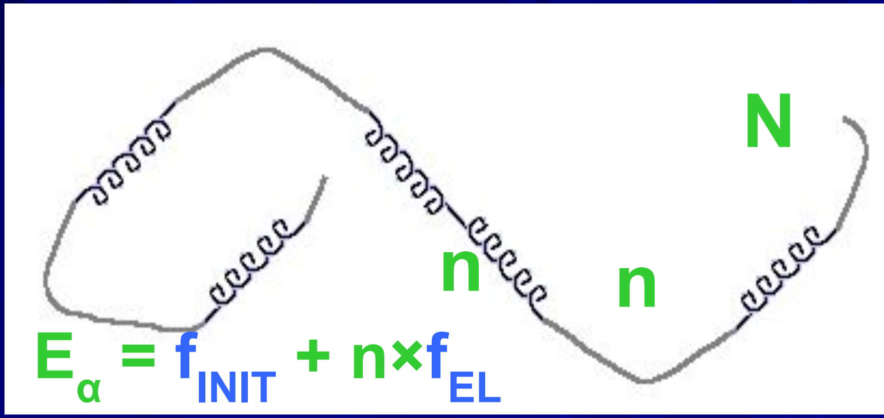




The End

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

of ends: ν; region's n ≅ N/ν
: ν/2 helices, 1+ν/2 coils



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

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

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

EQUILIBRIUM: ΔG = ΔE-TΔS=0:

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

(when σ<<1)