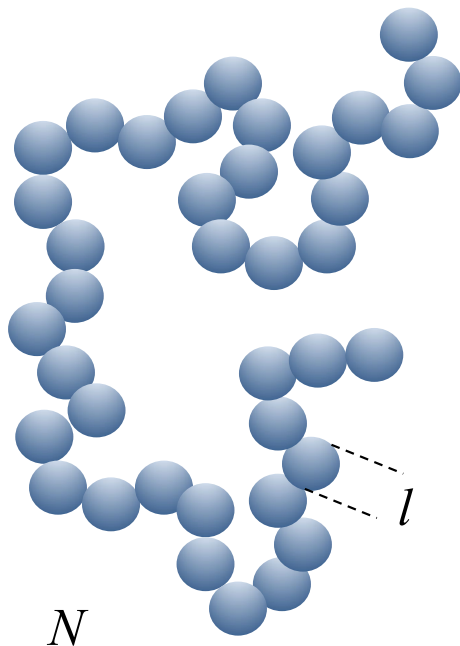


Conformations of macromolecules: Goal

polymer model



To understand **protein folding**, we require information about the **unfolded state** (that has an astronomical number of conformations)

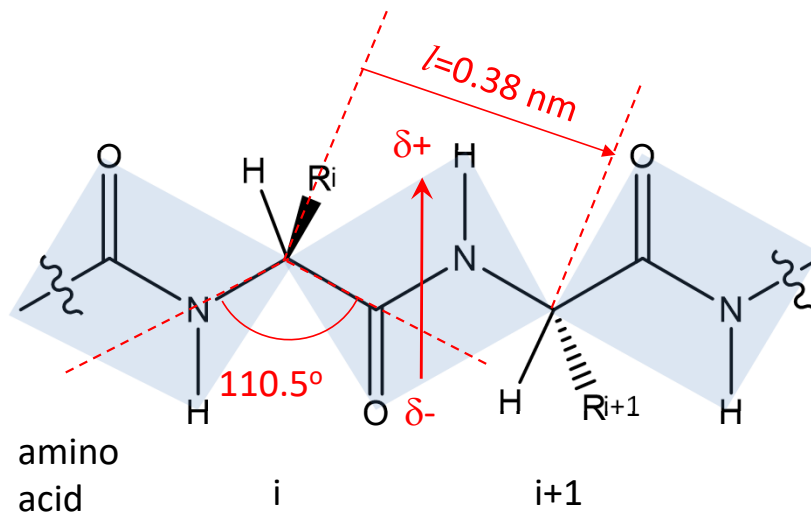
What can we know about such unstructured states? This includes **proteins** and other polymers such as **DNA**.

→ **Statistics**

Ignoring molecular details

- macromolecule consisting of N units of length l
- what are the allowed conformations?
- can we extract average properties (e.g. size)

Molecular details: The peptide unit revisited



Dipole moment of 3.5 Debye

bond length and angles
are described by
harmonic potentials

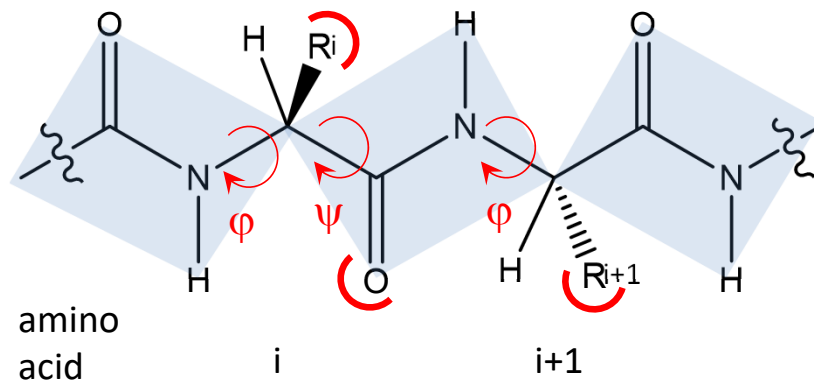
$$U(x) = \frac{1}{2} \phi (x - x_0)^2$$

force constant for bond
flexing (C-C):
2761 kJ / Å² / mol

displacement of 0.05 Å more
than $kT \rightarrow$ bond lengths are
constant

For bond angles: 10x smaller

Molecular details: The peptide unit revisited



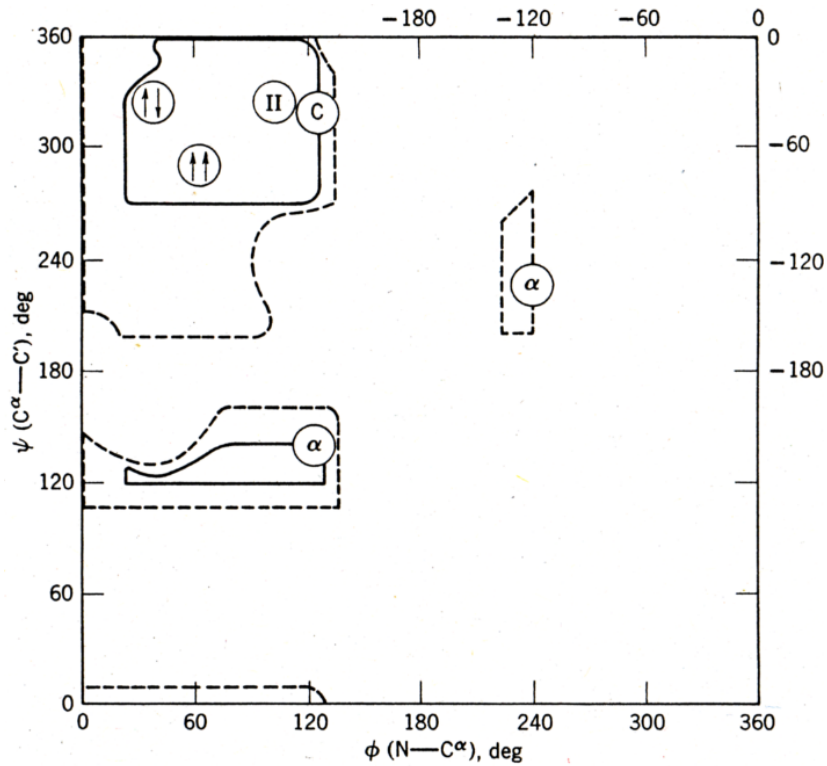
Torsion angles

Per amino acid, two rotatable bond in backbone

Complex potential

Rotation leads rapidly to steric interactions → restrictions in the allowed angles

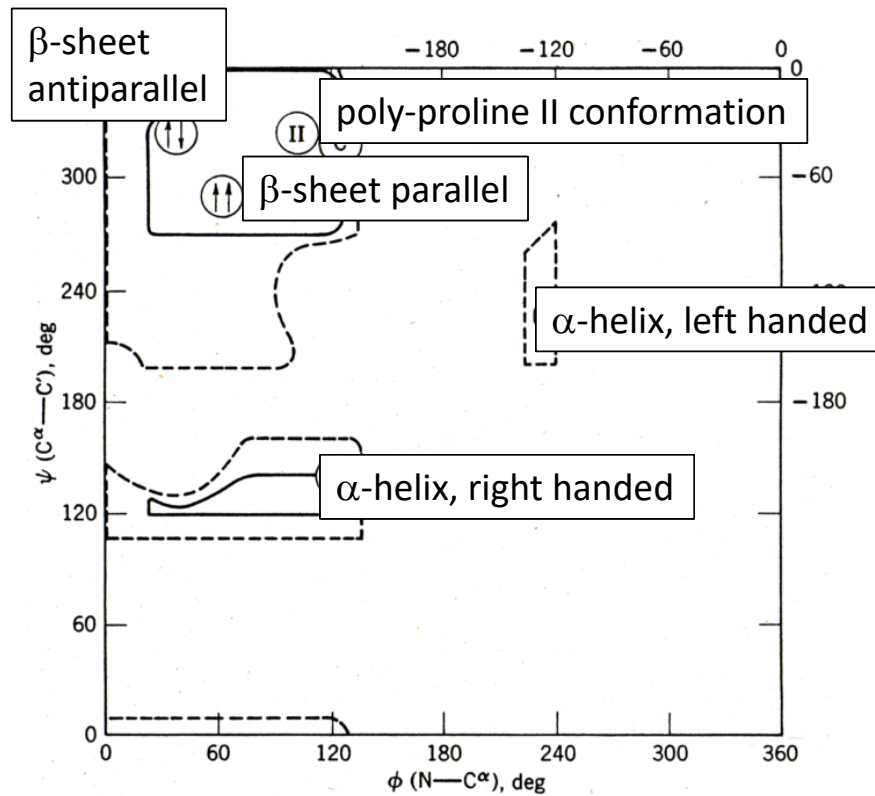
The Ramachandran steric map



G. N. Ramachandran
1922-2001

Mapped allowed angles based
solely on **steric** grounds

The Ramachandran steric map



G. N. Ramachandran
1922-2001

Mapped allowed angles based
solely on **steric** grounds

Conformational energy maps

What are the configurational distributions of **real peptide chains**?

Recalculation of the φ, ψ -maps using an energy function:

torsion angle potential

$$V(\varphi, \psi) = \frac{V^0_\varphi}{2}(1 - \cos 3\varphi) + \frac{V^0_\psi}{2}(1 - \cos 3\psi)$$

+ $\sum_{k,l} E_{k,l}(\varphi, \psi)$ + E_C Coulomb interactions (charges and dipoles)

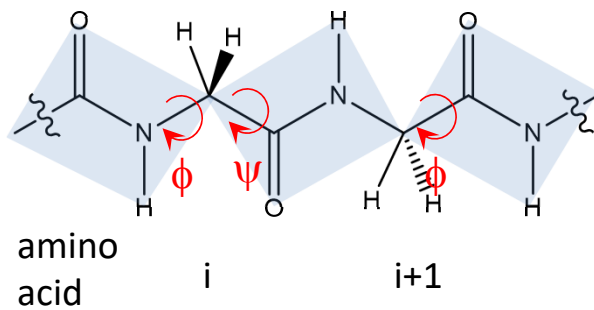
sterics and
VdW interactions

$$E_{kl} = A_{kl} / r_{kl}^{12} - B_{kl} / r_{kl}^6$$



Paul John Flory
1910-1985
1974 Nobel Prize

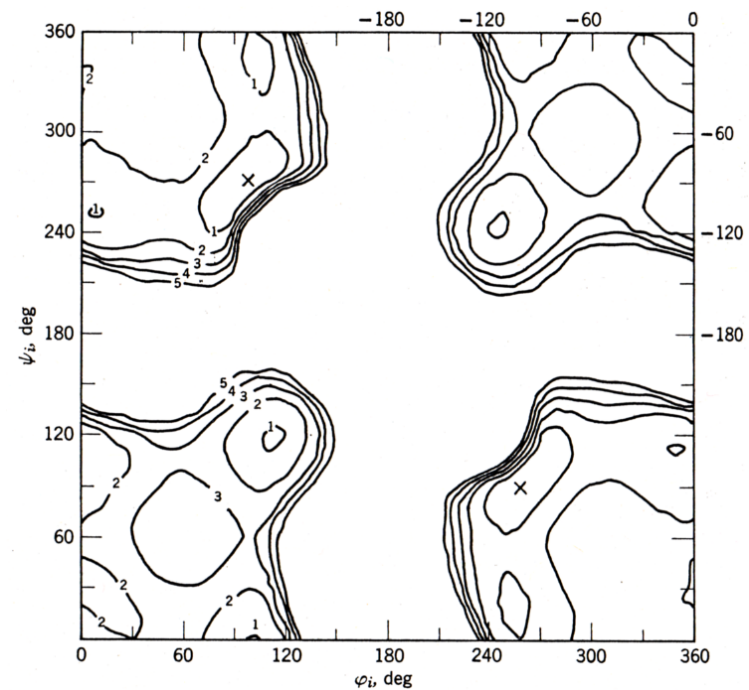
The glycine-glycine dipeptide



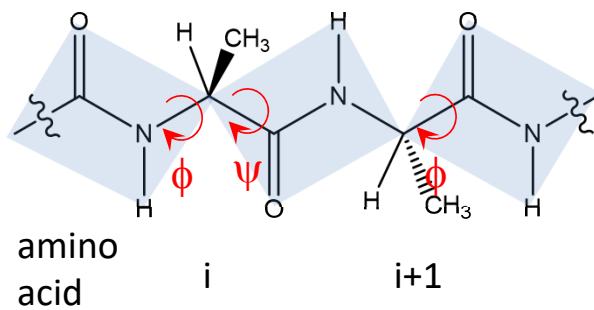
Glycine has **no sidechain**

large accessible conformational space, closest to ideal chain

high chain entropy



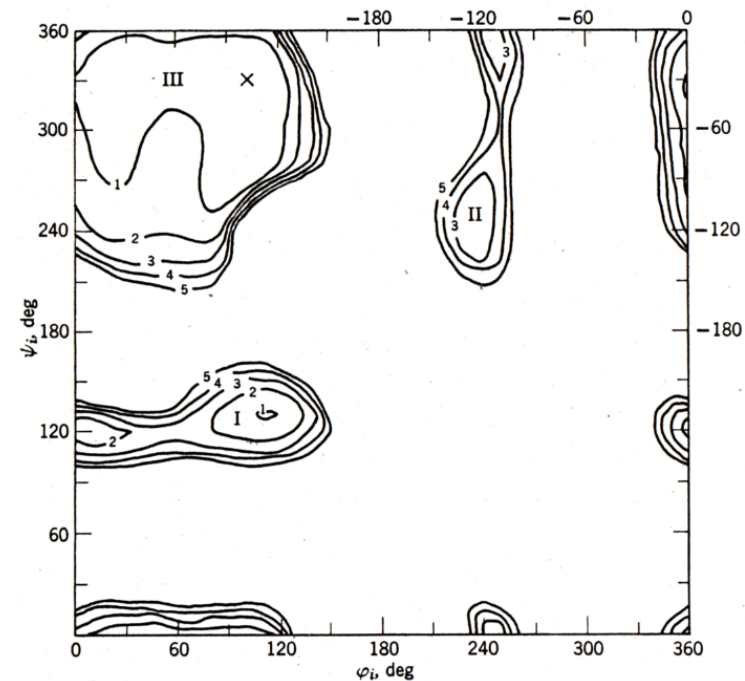
The alanine-alanine dipeptide



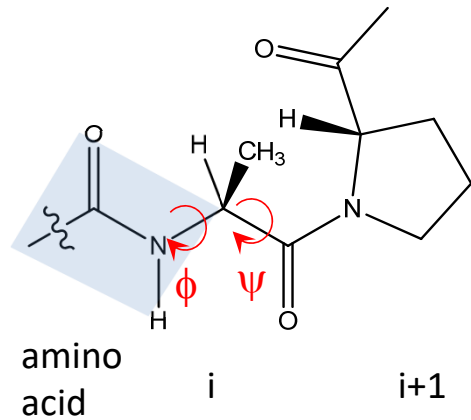
Alanine has a **small sidechain**

similar to Ramachandran map

β-branched amino acids are more restricted

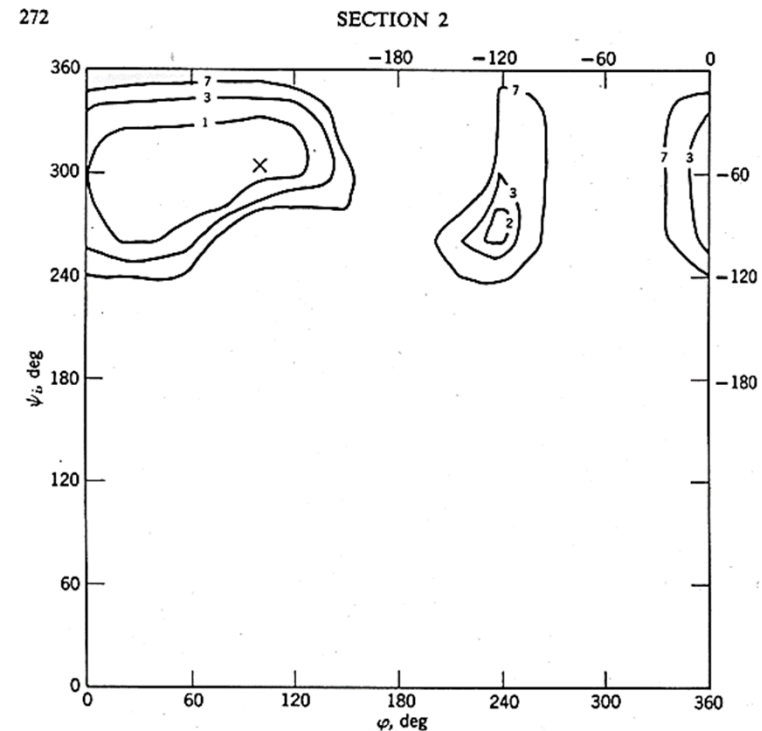


The alanine-proline dipeptide



Proline has a **seriously restricted** conformational space

increases chain stiffness, but
decreases chain entropy, as lower
number of conformations are
allowed



Chain stiffness & the characteristic ratio

To account for the **increased chain stiffness** due to torsion angle restriction

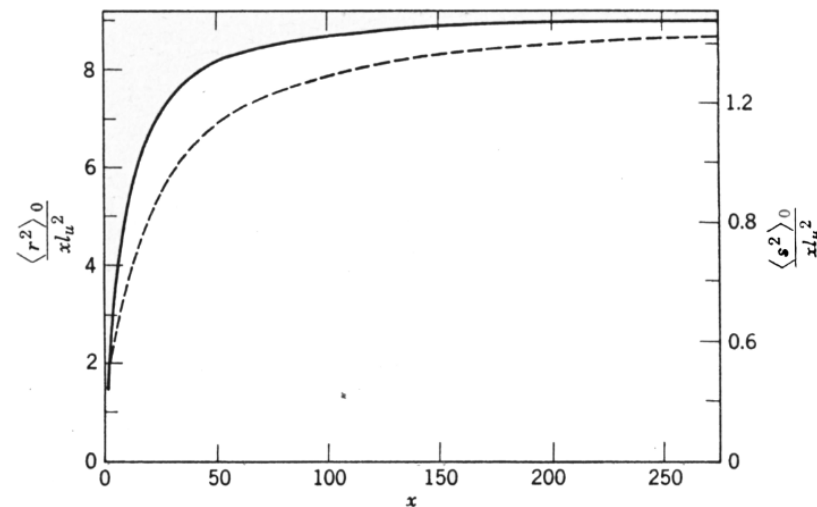
Flory introduced the **characteristic ratio**: $\langle R^2 \rangle = CNl^2$

$$C = \frac{\langle R^2 \rangle}{Nl^2}$$

C is dependent on the length of the polymer

for long polymers, C adopts a **limiting value**:

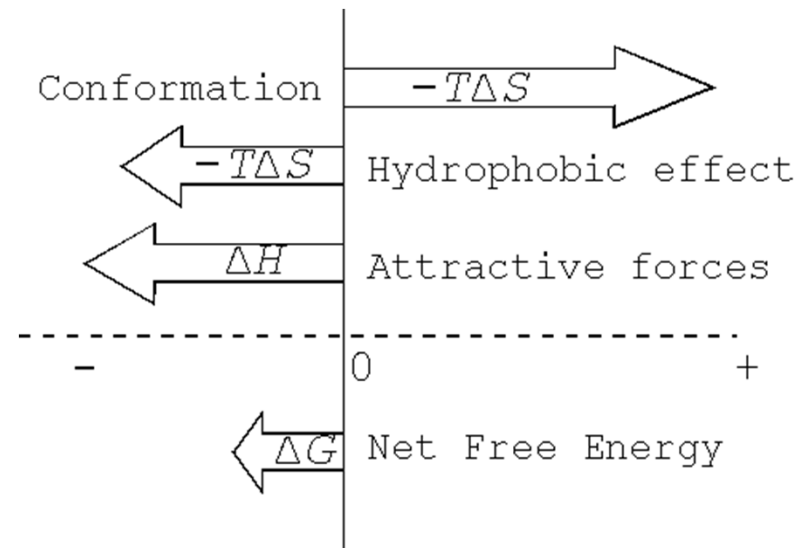
	C_∞
Gly	2.16
Ala	9.27
Pro	116



Summary - Energies

We have investigated all **energetic contributions to protein stability**

We have tried to characterize a ground state for protein folding – **the unfolded state**



What about protein structure?