BioPolymer Statistics II
From ideal chains to real chains
(and shape and distributions)
**in the previous episode**

An ideal chain has **no net interactions** between two elements $A_i$ and $A_j$.  

**ideal chain**

[Diagram of ideal chain with notation $\phi$, $\theta$, $r_i$, and $r_j$.]
Mean Squared End-to-End Distance

- **Freely Jointed Chain**
  \[ \langle R^2 \rangle = m b^2 \]
  \[ \langle \cos \theta_{ij} \rangle = 0 \implies \langle R^2 \rangle = m b^2 \]

- **Real Polymer**
  \[ \langle \cos \theta_{ij} \rangle \neq 0 \]
  \[ \langle R^2 \rangle = C_m m b^2 \]
  \[ C_m = \sum_{i=1}^{m} \sum_{j=1}^{m} \langle \cos \theta_{ij} \rangle \]

- **Kuhn Segment**
  \[ \langle R^2 \rangle = C_\infty m b^2 = N_k b_k^2 \]
  \[ l_c = m b = N_k b_k \]
in the previous episode

**Mean Squared End-to-End Distance**

\[ \langle R^2 \rangle = m b^2 + b^2 \sum_{i=1}^{n} \sum_{j \neq i} \langle \cos \theta_{ij} \rangle \]

- **Freely Jointed Chain**
  \[ \langle \cos \theta_{ij} \rangle = 0 \Rightarrow \langle R^2 \rangle = m b^2 \]

- **Worm-Like Chain**
  \[ \langle \cos \theta_{ij} \rangle = \langle \cos \theta \rangle \left| r_{i} - r_{j} \right| \]
  \[ = e^{- \left| r_{i} - r_{j} \right| \log(\cos \theta)} = e^{- \frac{\left| r_{i} - r_{j} \right| b}{\left| r_{i} - r_{j} \right| \log(\cos \theta)}} \]

\[ \rightarrow \text{PERSISTENCE LENGTH} \]
\[ \langle R^2 \rangle = b^2 \sum_{i=1}^{m} \sum_{j=1}^{m} e^{-\frac{|i-j| b}{\ell_p}} \]

\[ \langle R^2 \rangle = 2 \ell_p \ell_c - 2 \ell_p^2 \left( 1 - e^{-\frac{\ell_c}{\ell_p}} \right) \]
Freely rotating chain

\[ \langle R^2 \rangle = 2l_pl_c - 2l_p^2 \left(1 - e^{-\frac{l_c}{l_p}}\right) \]

**Two limits:**

1. \(l_c \gg l_p\) - Flexible chain

\[ \langle R^2 \rangle = 2l_pl_c = N_k b_k = b_k N_k b_k \]

From Kuhn segment we can compute the persistence length and vice versa

\[ b_k = 2l_p \]

2. \(l_p \gg l_c\) - Rod-like

Taylor series of \(e^{-\frac{l_c}{l_p}}\)

\(e^{-x} = 1 - x + \frac{1}{2} x^2 - \frac{1}{6} x^3 + \cdots\)

\[ \langle R^2 \rangle = l_c^2 - \frac{l_c^3}{3l_p} + \cdots \]
radius of gyration

WHAT IS THE RADIUS OF GYRATION?
radius of gyration
TWO DEFINITIONS

\[ R_g^2 = \frac{1}{N_K} \sum_{i=1}^{N_K} \left( \mathbf{R}_i^0 - \mathbf{R}_c^0 \right)^2 \]

\[ R_g^2 = \frac{1}{2N_K^2} \sum_{i=1}^{N_K} \sum_{j=1}^{N_K} \left( \mathbf{R}_i^0 - \mathbf{R}_j^0 \right)^2 \]
\[ R_g^2 = \frac{1}{N_k} \sum_{i=1}^{N_k} (\vec{R}_i - \vec{R}_{cm})^2 \quad \rightarrow \quad R_{cm} = \frac{1}{N_k} \sum_{i=1}^{N_k} \vec{R}_i \]

Mean square distance of each element from the center of mass
\[ R_g^2 = \frac{1}{2N_k^2} \sum_{i=1}^{N_k} \sum_{j=1}^{N_k} (\vec{R}_i - \vec{R}_j)^2 \]

Mean square distance between each pair of elements
\[
\langle R_g^2 \rangle = \frac{1}{N_K^2} \cdot \sum_{i=1}^{N_K} \sum_{j=1}^{N_K} \langle (\mathbf{r}_i^D - \mathbf{r}_j^D)^2 \rangle
\]

From discrete to continuous variables:

\[
\frac{1}{N_K^2} \int_0^1 \int_0^1 \langle (\mathbf{r}_i^D - \mathbf{r}_j^D)^2 \rangle
\]

Internal distance:

\[
\frac{1}{N_K^2} \int_0^1 \int_0^1 \langle (\mathbf{r}_i^D - \mathbf{r}_j^D)^2 \rangle \cdot \delta^{(2)}(i-j) b_k^2
\]

\[
= \frac{N_K b_k^2}{6} \quad (*)
\]
\[ R_8^2 = \frac{1}{N} \sum_{i=1}^{N} \left( \overrightarrow{R}_i - \overrightarrow{n}_{\text{cm}} \right)^2 = \frac{1}{N^2} \sum_{i=1}^{N} \sum_{j=1}^{N} \left( \overrightarrow{R}_i - \overrightarrow{R}_j \right)^2 \]

**Demonstration:**

\[
\sum_{i=1}^{N} \left( R_i^2 + \left( \frac{1}{N} \sum_{i=1}^{N} \overrightarrow{R}_i \right)^2 \right) = \frac{2}{N} \sum_{i=1}^{N} R_i \overrightarrow{n} \]

\[
\frac{1}{N^2} \sum_{i=1}^{N} R_i \sum_{k=1}^{N} R_k = \frac{1}{N^2} \sum_{i=1}^{N} \sum_{k=1}^{N} R_i \overrightarrow{R}_k
\]

\[ N \text{ is the result of the sum over } k \]

\[
\sum_{i=1}^{N} R_i^2 + \frac{2}{N^2} \sum_{j=1}^{N} \sum_{k=1}^{N} \overrightarrow{R}_j \overrightarrow{R}_k = \frac{2}{N^2} \sum_{i=1}^{N} \sum_{j=1}^{N} R_i \overrightarrow{R}_j
\]

\[
\frac{1}{N} \sum_{i=1}^{N} \sum_{j=1}^{N} R_i^2 + \frac{1}{N} \sum_{i=1}^{N} \sum_{j=1}^{N} \overrightarrow{R}_i \overrightarrow{R}_j = \frac{1}{N} \sum_{i=1}^{N} \sum_{j=1}^{N} R_i \overrightarrow{R}_j
\]

*I have introduced a dummy index that sum N times \( R_i \)*
\[ \frac{1}{N} \left( \sum_{i=1}^{N} \sum_{j=1}^{N} \left( \vec{R}_i - \vec{R}_j \right) \cdot \left( \vec{R}_i - \vec{R}_j \right) \right) = \]
\[ \frac{1}{2N} \left( \sum_{i=1}^{N} \sum_{j=1}^{N} \left( \vec{R}_i - \vec{R}_j \right) + \sum_{j=1}^{N} \sum_{i=1}^{N} \left( \vec{R}_j - \vec{R}_i \right) \right) = \]
\[ \frac{1}{2N} \left( \sum_{i=1}^{N} \sum_{j=1}^{N} \left( \vec{R}_i - 2\vec{R}_i \vec{R}_j + \vec{R}_j \right) \right) = \frac{1}{2N} \left( \sum_{i=1}^{N} \sum_{j=1}^{N} \left( \vec{R}_i - \vec{R}_j \right) \right)^2 \]
\[ \vec{R}_j = \frac{1}{N} \sum_{i=1}^{N} \left( \vec{R}_i - \vec{R}_j \right) = \frac{1}{2N^2} \sum_{i=1}^{N} \sum_{j=1}^{N} \left( \vec{R}_i - \vec{R}_j \right)^2 \]
Asphericity and shape factor

How to describe the shape of a polymer?

\[ \mathbf{T}_{mm} = \frac{1}{N} \sum_{i=1}^{N} \mathbf{r}^{(i)} \cdot \mathbf{r}^{(i)} \]

\( \mathbf{r}^{(i)} \) referred to the center of mass \( \mathbf{r}^{(i)} = \mathbf{R}_i - \mathbf{R}_c \)
Asphericity and shape factor

$
\bar{T}
$ is a $3 \times 3$ **symmetric matrix**.

**Therefore there is a coordinate system in which can be diagonalized!**

$$
\bar{T} = \begin{pmatrix}
\lambda_x^2 & 0 & 0 \\
0 & \lambda_y^2 & 0 \\
0 & 0 & \lambda_z^2
\end{pmatrix}
$$

WHERE

$\lambda_x^2 \leq \lambda_y^2 \leq \lambda_z^2$

**principal tensors**
Asphericity and shape factor

The shape descriptors are then given by:

\[ T = \begin{pmatrix} \lambda_x^2 & 0 & 0 \\ 0 & \lambda_y^2 & 0 \\ 0 & 0 & \lambda_z^2 \end{pmatrix} \]

\[ R_g^2 = \text{Tr} \left( T \right) = \lambda_x^2 + \lambda_y^2 + \lambda_z^2 \]

Radius of gyration
Asphericity and shape factor

The shape descriptors are then given by:

$$
\mathbf{T} = \begin{pmatrix}
\lambda_x^2 & 0 & 0 \\
0 & \lambda_y^2 & 0 \\
0 & 0 & \lambda_z^2
\end{pmatrix}
$$

$$
\Delta = \frac{3}{2} \frac{\sum_{i=x,y,z} (\lambda_i - \overline{\lambda})^2}{\text{Tr} \ (\mathbf{T})^2} \\
\overline{\lambda} = \frac{\lambda_x + \lambda_y + \lambda_z}{3}
$$

"ASPHERICITY"
Asphericity and shape factor

The shape descriptors are then given by:

\[ \mathbf{T} = \begin{pmatrix} \lambda_x^2 & 0 & 0 \\ 0 & \lambda_y^2 & 0 \\ 0 & 0 & \lambda_z^2 \end{pmatrix} \]

\[ S = 27 \frac{\prod \left( \lambda_i - \bar{\lambda} \right)}{\text{Tr} \left( \mathbf{T} \right)^3} \]

"Shape Factor"
Asphericity and shape factor

$\Delta = \emptyset$  \hspace{1cm} PERFECT SPHERE

$S = \emptyset$  \hspace{1cm} OBLATE ELLIPSOID

$S < 0$  \hspace{1cm} OBLATE ELLIPSOID

$S > 0$  \hspace{1cm} PROLATE ELLIPSOID
Asphericity and shape factor

Even though we can always define a radius of gyration. This does not mean that the chain has spherical symmetry.

A freely jointed chain is not radial–symmetric and if one aligns all the conformation along their principal axis, one obtains a prolate (a cigar–shaped object).
probability distribution function

1D
$P_{1d}(N, x) = \left(\frac{1}{2\pi \langle x^2 \rangle}\right)^{1/2} \exp\left(-\frac{1}{2 \langle x^2 \rangle} x^2\right)$
probability distribution function

\[ P_{3d}(N, R) = P_{1d}(N, R_x) P_{1d}(N, R_y) P_{1d}(N, R_z) = \left( \frac{3}{2\pi \langle R^2 \rangle} \right)^{3/2} \exp\left( -\frac{3}{2} \frac{R^2}{\langle R^2 \rangle} \right) \]
\[ P_{1d}(N, R_x) = \left( \frac{1}{2\pi E_{R_x}^2} \right)^{1/2} \exp \left( -\frac{1}{2} \frac{R_x^2}{E_{R_x}^2} \right) \]

\[ P_{3d}(N, R) \, dR_x \, dR_y \, dR_z = P_{1d}(N, R_x) \, P_{1d}(N, R_y) \, P_{1d}(N, R_z) \]

\[ P_{3d}(N, R) = \left( \frac{1}{2\pi E_{R_x}^2} \right)^{1/2} \left( \frac{1}{2\pi E_{R_y}^2} \right)^{1/2} \left( \frac{1}{2\pi E_{R_z}^2} \right)^{1/2} \exp \left( -\frac{1}{2} \frac{R_x^2}{E_{R_x}^2} \right) \exp \left( -\frac{1}{2} \frac{R_y^2}{E_{R_y}^2} \right) \exp \left( -\frac{1}{2} \frac{R_z^2}{E_{R_z}^2} \right) \]

\[ \langle R^2 \rangle = \langle R_x^2 \rangle + \langle R_y^2 \rangle + \langle R_z^2 \rangle = N \, b_k^2 \]

\[ \langle R_x^2 \rangle = \langle R_y^2 \rangle = \langle R_z^2 \rangle = N \, b_k^2 / 3 \]

\[ P_{3d}(N, R) = \left( \frac{1}{2\pi E_{R_x}^2} \right)^{3/2} \exp \left( -\frac{1}{2} \frac{R^2}{E_{R_x}^2} \right) \]

\[ P_{3d}(N, R) = \left( \frac{3}{2\pi E_{R_x}^2} \right)^{3/2} \exp \left( -\frac{3}{2} \frac{R^2}{E_{R_x}^2} \right) \]
probability distribution function

distribution of end-to-end vectors

\[ P(R_{ee}) = \left( \frac{3}{2\pi \langle R_{ee}^2 \rangle} \right)^{3/2} \exp \left( -\frac{3}{2} \frac{R_{ee}^2}{\langle R_{ee}^2 \rangle} \right) \]

The probability density that the chain end is in a particular location between \((x,y,z)\) and \((x+dx,y+dy,z+dz)\). The most probable termination point is the origin.

distribution of end-to-end distance

\[ P(R_{ee}) = 4\pi R_{ee}^2 \left( \frac{3}{2\pi \langle R_{ee}^2 \rangle} \right)^{3/2} \exp \left( -\frac{3}{2} \frac{R_{ee}^2}{\langle R_{ee}^2 \rangle} \right) \]

The probability density that the chain end is anywhere in a radial shell between \(r\) and \(r+dr\).
probability distribution function

distribution of end-to-end distance

$P(R_e)$

$0 \quad R_{\infty} \quad l_e$

gaussian chain

F J C
There is no exact formula which describes the distribution of $R_g$. The Flory-Fisk (FF) distribution is an approximation that reproduces the first six moments of the distribution for a FJC correctly.

\[ P_{FF}(R_g) = Z^{-1} R_g^6 \exp \left( - \frac{7}{2} \frac{R_g^2}{\langle R_g^2 \rangle} \right) \]
The Worm-like chain (WLC) is the continuous limit (i.e. no discrete bonds) of the freely rotating chain. It is useful for relatively stiff chains.

The Worm-like chain (WLC) is the continuous limit (i.e. no discrete bonds) of the freely rotating chain. It is useful for relatively stiff chains.

\[
p_{WLC}(R_{ee}, l_p, l_c) = \frac{4\pi (R_{ee}/l_c)^2 f(l_p/l_c)}{l_c^2 \left(1 - \left(R_{ee}/l_c\right)^2\right)^{3/2}} \exp\left(-\frac{3l_c}{4l_p^2} \left(1 - \left(R_{ee}/l_c\right)^2\right)^2\right) 
\]

\[
f(l_p/l_c) = \frac{1}{\pi^{3/2} \alpha^{3/2}} \left(1 + 3/\alpha + 15/4\alpha^2\right)^{-1/2} \exp\left(-\frac{3l_c}{4l_p^2} \left(1 - \left(R_{ee}/l_c\right)^2\right)^2\right) 
\]

\[\alpha = \frac{3l_c}{4l_p^2}\]

one single fitting parameter

For small \(l_p\) the GC and the WLC are indistinguishable

Increasing \(l_p\) we start to see some small deviations from the GC

*from O’Brian et al. JCP 130, 124903 (2009)*
The Worm-like chain (WLC) is the continuous limit (i.e. no discrete bonds) of the freely rotating chain. It is useful for relatively stiff chains.

\[
p_{WLC}(R_{ee}, l_p, l_c) = \frac{4\pi(R_{ee}/l_c)^2 f(l_p, l_c)}{l_c^3 \left(1 - (R_{ee}/l_c)^2\right)^{3/2}} \exp\left(\frac{-3l_c}{4l_p\left(1 - (R_{ee}/l_c)^2\right)}\right)
\]

\[
f(l_p, l_c) = \frac{1}{\pi^{3/2} \alpha^{3/2} \alpha \left(1 + 3/\alpha + 15/(4\alpha^2)\right)}
\]

with \( \alpha = \frac{3l_c}{4l_p} \), one single fitting parameter

*from O’ Brian et al. JCP 130, 124903 (2009)

For small \( l_p \) the GC and the WLC are indistinguishable

Increasing \( l_p \) we start to see some small deviations from the GC
REAL CHAINS

In an ideal chain there are no "net interactions" between different components.

In a "real" chain we can have attractive and repulsive interactions.
FREE ENERGY OF AN IDEAL CHAIN

\[ F = U - T S \]

In an ideal chain, net interactions are equal to zero.

\[ S = k_B \log \Omega \]

\[ \frac{F}{k_B T} = \frac{3 R^2}{2 N b^2} - 2 \log R \]

Boltzmann constant

Number of states
\[ F = -TS \]

In an ideal chain, net interactions are equal to zero.

\[ \Omega = P_{\text{Gaussian}} (N, R_{\text{eq}}) = Z^{-1} \cdot 4\pi R^2 e^{-\frac{3}{2} \frac{R^2}{Nb^2}} \]

\[ S = k_B \log \Omega = k_B \left( -\log 2 + \log 4\pi + 2 \log R - \frac{3}{2} \frac{R^2}{Nb^2} \right) \]

\[ = k_B \left( \text{const} + 2 \log R - \frac{3}{2} \frac{R^2}{Nb^2} \right) \]

\[ F = -TS = k_B T \left( \frac{3}{2} \frac{R^2}{Nb^2} - 2 \log R \right) \]

\[ \frac{F}{k_B T} = \frac{3}{2} \frac{R^2}{Nb^2} - 2 \log R \]
ANALOGY WITH REAL GASES

\[ PV = N k_B T \left( 1 + \beta \frac{N}{V} + \gamma \frac{N^2}{V^2} + \ldots \right) \]

VIRIAL EXPANSION

\[ U = N k_B T \left( \beta \frac{N}{R^3} + \gamma \frac{N^2}{R^6} + \ldots \right) \]

THE TWO BODY INTERACTION FOR A POLYMER IS EQUAL TO \( \frac{V}{V} \) EXCLUDED VOLUME
TO COMPUTE THE CHANGE IN CHAIN
DIMENSIONS, THE FREE ENERGY OF THE
POLYMER IS MINIMIZED.

\[ \frac{2F}{2R} = 0 \]

\[ F = F_{\text{int}} + F_{\text{folded chain}} \]

\[ = k_B T \left[ \left( B \frac{N^2}{R^3} + \gamma \frac{N^3}{R^6} \right) + \left( \frac{3}{2} \frac{R^2}{N_b^2} - 2 \log R \right) \right] \]
\[ \frac{\partial F}{\partial R} = 0 \]

\[ \left( \frac{R}{R_\theta} \right)^5 - \frac{2}{3} \left( \frac{R}{R_\theta} \right)^3 = \beta^1 N^{1/2} + \gamma^1 \left( \frac{R_\theta}{R} \right)^3 \]

with \( R_\theta = N^2 b^2 \)

**Often**

\[ \frac{R}{R_\theta} = \alpha \]

\[ \alpha^5 - \left( \frac{2}{3} \right) \alpha^3 = \beta^1 N^{1/2} + \gamma^1 \alpha^{-3} \]

**Two Body**

\[ \downarrow \]

**Three Body**

\[ \downarrow \]
TO QUANTIFY THE CHANGE IN CHAIN
DIMENSIONS WE CAN USE THE FREE
ENERGY OF THE CHAIN

\[ F = U - TS \]

\[ \frac{\partial F}{\partial R} = k_B T \left[ -3 \beta N^2 \frac{1}{R^3} + 6 \gamma N^3 \frac{R}{R^7} + 3 \frac{R}{N B^2} - 2 \frac{1}{R} \right] = 0 \]

\[ = \frac{R}{N B^2} - 2 \frac{1}{3} \frac{1}{R} - \frac{3}{8} \beta N^2 - \frac{6 \gamma N^3}{R^5} = 0 \]

\[ = \frac{R^5}{N B^2} - \frac{2}{3} \frac{R^4}{R} - \beta N^2 - 2 \gamma \frac{N^3 R^4}{R^7} = 0 \]

\[ = \frac{R^5}{N B^2} - \frac{2}{3} \frac{R^3}{R} - \beta N^2 - 2 \gamma \frac{N^3}{R^3} = 0 \]
\[ \frac{R^5}{N^{5/2} b^5} - \frac{2}{3} \frac{R^3}{N^{3/2} b^3} = B \frac{N^{1/2}}{b^3} + 2 \chi \frac{N^{3/2}}{R^3} \]

\[ \left( \frac{R}{R_0} \right)^5 - \frac{2}{3} \left( \frac{R}{R_0} \right)^3 = B' N^{1/2} + \chi' \left( \frac{R}{R_3} \right)^3 \]

\[ \left( \frac{R}{R_0} \right) = \lambda \]

\[ \lambda^5 - \frac{2}{3} \lambda^3 = B' N^{1/2} + \chi' \lambda^{-3} \]
Let's focus on the effect of two-body interactions.

\[ U(r) \]

\text{Hard-core repulsion} \quad \text{Attracting well} \quad \text{\( U(r) \) is the interaction potential between the two monomers.}
Let's focus on the effect of two body interactions.

\[
e^{-\frac{U(r)}{k_B T}} \quad \text{Probability of the two monomers of being at distance (r)}
\]

\[ U(r) \text{ is the interaction potential between the two monomers.} \]
Let's focus on the effect of two body interactions.

$U(r)$ is the interaction potential between the two monomers.

$e^{-U(r)/k_B T}$ \[ \text{probability of the two monomers of being at distance (r)} \]

$1 - e^{-U(r)/k_B T}$ \[ \text{probability of the two monomers of not being at distance (r)} \]
Let's focus on the effect of two-body interactions.

\[ U(r) \] is the interaction potential between the two monomers.

\[ e^{-U(r)/k_BT} \] probability of the two monomers of being at distance \( r \).

\[ 1 - e^{-U(r)/k_BT} \] probability of the two monomers of not being at distance \( r \).

Excluded volume:

\[ V = \int (1 - e^{-U(r)/k_BT}) \, d^3r \]
We can split the potential between the two contributes for the hard-core repulsion and the attractive well.

\[
V = 4\pi \left[ \int_0^b r^2 \left( 1 - e^{-\frac{u(r)}{k_B T}} \right) dr \right] \approx 0 + 4\pi \int_b^\infty r^2 \left( 1 - e^{-\frac{u(r)}{k_B T}} \right) dr
\]
We can split the potential between the two contributes for the hard-core repulsion and the attractive well.

\[ V = 4\pi \int_0^b r^2 \left( 1 - e^{-u(r)/k_B T} \right) dr + 4\pi \int_b^\infty r^2 \left( 1 - e^{-u(r)/k_B T} \right) dr \]

\[ V = \frac{1}{3} \pi b^3 \quad \text{positive} = \text{repulsive} \]

\[ -\frac{4}{3} \pi b^3 \frac{\theta}{T} \quad \text{negative} = \text{attractive} \]
We can split the potential between
the two contributions for the
hard-core repulsion and the attractive
well.

\[ V = 4\pi \int_0^b r^2 \left(1 - e^{-U(r)/k_BT}\right) dr + \int_0^\infty r^2 \left(1 - e^{-U(r)/k_BT}\right) dr \]

\[ V = + \frac{4}{3} \pi b^3 \frac{1}{\theta} \]

Positive = repulsive

Negative = attractive

\[ V = \frac{4}{3} \pi b^3 \left(1 - \frac{\theta}{\Theta}\right) \]

For a given potential \( U(r) \)
\( \Theta \) is fixed.

What happens when we tune the temperature?
WHAT HAPPENS IF WE TUNE THE TEMPERATURE?

\[ V = \frac{4}{3} \pi b^3 \left( 1 - \frac{\Theta}{T} \right) \]

. AT \( T >> \Theta \), \( V = \frac{4}{3} \pi b^3 \) HARD-ONCE REPULSION DOMINATES

THE SOLVENT IS A THERMAL
What happens if we tune the temperature?

\[ V = \frac{4}{3} \pi b^3 \left( 1 - \frac{\Theta}{T} \right) \]

1. At \( T \gg \Theta \), \( V = \frac{4}{3} \pi b^3 \) Hard-core repulsion dominates. The solvent is athermal.

2. At \( T = \Theta \), \( V = 0 \) Net interactions are equal to zero. The solvent is \textit{"theta" solvent} and the chain is behaving as an ideal chain.
WHAT HAPPENS IF WE TUNE THE TEMPERATURE?

\[ V = \frac{4}{3} \pi b^3 \left( 1 - \frac{\Theta}{T} \right) \]

- AT \( T \gg \Theta \), \( V = \frac{4}{3} \pi b^3 \) and the solvent is athermal.

- AT \( T = \Theta \), \( V = 0 \) and the solvent is a "theta" solvent.

- AT \( T \leq -\frac{\Theta}{2} \), \( V \leq -\frac{4}{3} \pi b^3 \) and the solvent is a non-solvent.

HARD-CORE REPULSION DOMINATES

NET INTERACTIONS ARE EQUAL TO ZERO

ATTRACTION INTERACTIONS DOMINATE CHAIN CONFORMATIONS
\[ V = \frac{4}{3} \pi b^3 \]

| \(0 < V < \frac{4}{3} \pi b^3\) | A-THERAL \ SOLVENT |
| \(V = 0\) | GOOD \ SOLVENT |
| \(-\frac{4}{3} \pi b^3 < V < 0\) | THETA \ SOLVENT |
| \(V \leq -\frac{4}{3} \pi b^3\) | POOR \ SOLVENT |
| \(V \leq -\frac{4}{3} \pi b^3\) | NON \ SOLVENT |
\[ V = \frac{4}{3} \pi b^3 \]

\[ 0 < V < \frac{4}{3} \pi b^3 \]

\[ V = 0 \]

\[ -\frac{4}{3} \pi b^3 < V < 0 \]

\[ V \leq -\frac{4}{3} \pi b^3 \]

- **ATHERAL SOLVENT**
- **GOOD SOLVENT**
- **THETA SOLVENT**
- **POOR SOLVENT**
- **NON SOLVENT**
Coil-to-globule transition

POLYSTYRENE/CYCLOHEXANE

$$\Theta = 308.6 \text{ K} \quad \langle S^2 \rangle_0^{1/2} = 217 \text{ nm}$$

$$M_W = 4.4 \times 10^7$$

$$r = 4.2 \times 10^5$$

Expansion Factor, $$a^2$$

$$T/\Theta$$

0.95 - 1.075
Coil-to-globule transition

**Polystyrene/Cyclohexane**

\[ \Theta = 308.6 \text{ K} \quad \langle S^2 \rangle_0^{1/2} = 217 \text{ nm} \]

\[ M_W = 4.4 \times 10^7 \]

\[ \alpha^2 = \frac{\langle R^2 \rangle}{\langle R^2_\theta \rangle} = \frac{\langle R^2 \rangle}{Nb^2} \]

**Graph**:
- **Expansion Factor** vs **T/\Theta**
- **Points** along the curve with \[ r = 4.2 \times 10^5 \]
Dependence on chain length

![Graph showing the dependence of expansion factor $\alpha^2$ on $T/\Theta$ for different values of $N$.]
Coil-to-globule transition in simulations of disordered peptides

\[ \xi = \frac{\langle R_g \rangle}{\sqrt{N}} \]

\( T \) (K)

Andreas Vitalis, Xiaoling Wang, Rohit V. Pappu
Atomistic Simulations of the Effects of Polyglutamine Chain Length and Solvent Quality on Conformational Equilibria and Spontaneous Homodimerization, JMB, 2008
Temperature can induce collapse of IDPs in the experimental accessible range.
Coil–globule transition in the denatured state of a small protein

Eilon Sherman and Gilad Haran
PNAS 103, 2006
Scaling exponents

\[ \langle R_g^2 \rangle \propto N \]
\[ \langle R^2 \rangle \propto N \]
\[ \langle R_{ij}^2 \rangle \propto (i - j) \]

scaling with the number of monomers
Scaling exponents

\[ \langle R_g^2 \rangle \propto N^{2\nu} \]

\[ \langle R^2 \rangle \propto N^{2\nu} \]

\[ \langle R_{ij}^2 \rangle \propto (i - j)^{2\nu} \]

Scaling exponent

\[ \nu = 1/2 \]

THETA SOLVENT
Scaling exponents

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What is the scaling exponent for other solvent conditions?
Scaling exponents

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What is the scaling exponent for other solvent conditions?

\[ \nu = 1/2 \]
Scaling exponents

| Athermal Solvent | \( \nu = \frac{3}{5} \) |
| Good Solvent     | \( \nu = \frac{1}{2} \) |

Scaling exponent

\[
\langle R_g^2 \rangle \propto N^{2\nu}
\]

\[
\langle R^2 \rangle \propto N^{2\nu}
\]

\[
\langle R_{ij}^2 \rangle \propto (i - j)^{2\nu}
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What is the scaling exponent for other solvent conditions?
### Scaling exponents

<table>
<thead>
<tr>
<th>THRESHOLD</th>
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<tbody>
<tr>
<td>A THERMAL SOLVENT</td>
<td>$\nu = 3/5$</td>
</tr>
<tr>
<td>GOOD SOLVENT</td>
<td>$\nu = 1/2$</td>
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<td>THETA SOLVENT</td>
<td>$\nu = 1/3$</td>
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<td>POOR SOLVENT</td>
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<tr>
<td>NON SOLVENT</td>
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</table>

- $\langle R_g^2 \rangle \propto N^{2\nu}$
- $\langle R^2 \rangle \propto N^{2\nu}$
- $\langle R_{ij}^2 \rangle \propto (i-j)^{2\nu}$

**SCALING EXPONENT**
Scaling exponents of denatured proteins

Fig. 1. The $R_g$ of the large majority of chemically denatured proteins scale with polymer length, $N$, by means of the power-law relationship $R_g = R_0 N^\nu$. Two statistically significant outliers, creatine kinase and angiotensin II, are indicated. The solid line, which is the least-squares fit ignoring the two potential outliers, produces an exponent, $\nu = 0.598 \pm 0.028$ (95% confidence interval), that is indistinguishable from the 0.588 predicted for an excluded-volume random coil. The shaded region represents the 95% confidence intervals for future measurements, assuming that the errors about $(\log)R_g$ are normally distributed around the fitted relationship. Only the measurements for creatine kinase and angiotensin II fall outside this predictive interval, and, thus, only these measurements can be said to represent unambiguously significant deviations. Error bars indicate the reported experimental (i.e., standard) deviations of the sample. These were derived by using a variety of approaches and widely varying numbers of observations and therefore provide only an approximate indication of experimental precision.
Scaling exponents of denatured proteins

FIGURE 6 Scaling of internal distances as a function of sequence separation. Internal correlations are shown for four representative protein sequences. In each of the log-log plots, the solid line has a slope of 0.59 and intercept of 2.0 and the dashed line has a slope of 1.0 and intercept of 1.33. Average internal distances obey the universal power law scaling for sequence separations that go beyond five to nine residues.
Scaling exponents of denatured and unfolded proteins

Polymer scaling laws of unfolded and intrinsically disordered proteins quantified with single-molecule spectroscopy
Hofmann et al, PNAS, 2012
Scaling exponents of denatured and unfolded proteins

Innovative scattering analysis shows that hydrophobic disordered proteins are expanded in water

Ryback et al, Science, 2017
ELECTROSTATICS

POLY ELECTROLYTE

POLYAMPHOLYTE
\[ V^* = V + \frac{4 \pi l_B (f-g)^2}{K^2 b^3} - \frac{\pi l_B (f+g)^2}{K b^3} \]

\[ f = \text{fraction of positive charges} \]
\[ g = \text{fraction of negative charges} \]

\( l_B = \text{BJERRUM length} \)

Distance at which the electrostatic interaction between two elementary charges is equal to \( k_B T \)

\[ \frac{1}{4 \pi \varepsilon_0 e^2} = k_B T \]

At 25°C, \( l_B \approx 7.0 \text{ Å} \).
\[ V^* = V + \frac{4\pi l_B (f-g)^2}{K^2 b^3} - \frac{\pi l_B (f+g)^2}{K b^3} \]

\[ K^{-1} : \text{Debye screening length} \]

At distance closer than \( \frac{1}{K} \) two charges "see" each other and interact. At longer distances their interaction is shielded by salt.

\[ K^{-1} = \sqrt{\frac{E_r E_0 K_B T}{2 N_A e^2 I}} \]

\[ I = \left( \frac{Ze^2_+ + Z_- e^2_-}{2} \right) \]

\( l_B \) is the ionic strength.
IDPs and unfolded proteins

In a polyampholyte sequence, charge patterning can alter conformational properties and impact function of IDPs.
IDPs and unfolded proteins

Salt screens electrostatic interactions

CSP (unfolded)

ProTα-N

ProTα-C

Denaturant concentration (M)

R_g (nm)
single-stranded DNA