Peptide Self-Assembled Polymers

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Questions

● Why and when do peptides self-assemble?
● What is a good coarse-grained model for the energies of interaction?
● What limits fibre/bundle diameters?
● What are the slow kinetics?
● Do they constitute and example of tightly entangled stiff polymers?
● .....

Self-Assembled Peptide Tapes as Stiff Biopolymers
Peptide 1: K24 - organic solvent

Lys-Leu-Glu-Ala-Leu-Tyr-Val-Leu-Gly-Phe-Phe-Gly-Phe-Phe-Thr-Leu-Gly-Ile-Met-Leu-Ser-Tyr-Ile-Arg

Hydrophobic

did this at only 1% in water

Peptides 2 and 3: P_{11}-I and P_{11}-II; aqueous

I CH 3 CO-Gln-Gln-Arg-Phe-Gln-Trp-Gln-Phe-Glu-Gln-Gln-NH 2

… the same plus a hydrophobic side..

II CH 3 CO-Gln-Gln-Arg-Phe-Gln-Trp-Phe-Glu-Gln-Gln-NH 2
Self-Assembled Peptide Tapes as Stiff Biopolymers

They must have formed polymers...

Flexible β-sheet ribbons

Hydrogen bonding modified by electrostatics
Self-Assembled Peptide Tapes as Stiff Biopolymers

A standard biological motif

Lac-repressor

AFM:

Alastair Smith
Check with spectroscopy

Surely an example of 1-d self-assembly:

\[
\frac{F}{k_B T} = \sum_m N_m \ln \left( \frac{N_m v_0}{eV} \right) + \sum_m N_m \epsilon_m
\]

with \( \sum_m N_m m = N \)

So we need a model for
Famous example: wormlike micelles

\[ \varepsilon_m = 2 \varepsilon_{cap} \]

\[ \Rightarrow \langle m \rangle = c^{1/2} \varepsilon_{cap} \]

But the Spectroscopic self-assembly curves are S-shaped:

Not \( \sim c^{1/2} \)!
So modify the picture with a transition state...

**Flexible β-sheet ribbons**

**Pseudo-helix free state**

Now this gives:

\[
\langle m_{tape} \rangle = \left( \frac{c - c_{tape}^*}{c_{tape}} \right)^{1/2} e^{E_{trans}/2} \quad \text{with} \quad c_{tape}^* \equiv e^{-E_{tape} + E_{trans}}
\]

With increased concentration they go on self-assembling..
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So that, \( \epsilon \), e.g.

\[
\langle m_{\text{ribbon}} \rangle = \left( \frac{c - c_{\text{ribbon}}^*}{c_{\text{ribbon}}^*} \right)^{1/2} \epsilon^{(\epsilon_{\text{trans}} + \epsilon_{\text{tape}})/2}
\]

with

\[
c_{\text{ribbon}}^* \equiv c_{\text{tape}}^* + \epsilon_{\text{ribbon}}^{-2} \epsilon_{\text{tape}}^{-1}
\]

\( P_{11} \) looks like curly tapes
**Self-Assembled Peptide Tapes as Stiff Biopolymers**

**P$_{11}$-II must be ribbons, then fibrils**

- No isochroic point
- Single tapes too short
- Persistence ⁴₀~500nm

**But what stabilises the fibrils?**

$$\varepsilon_{\text{elast}} = \frac{1}{2} k_{\text{bend}} (\nu - \nu_0)^2 + \frac{1}{2} k_{\text{twist}} (\theta - \theta_0)^2$$

**Twist-Stack Model**

$$\nu = \gamma^2 \frac{\rho}{(1 + \gamma^2 \rho^2)}; \quad \theta = \gamma \frac{1}{(1 + \gamma^2 \rho^2)}$$

$$\varepsilon_{\text{fibril}} = \frac{p - 1}{2p} \varepsilon_{\text{fibril}}^{\text{attr}} - \varepsilon_{\text{elast}}$$
A structural phase diagram:

We can predict their formation quantitatively..

..and observe a nematic phase..
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P_{11-II} the story...

Parameter Summary

Dr. Tom McLeish, ITP & Leeds (ITP Complex Fluids Program 3/14/02)
Self-Assembled Peptide Tapes as Stiff Biopolymers

Dynamics and Rheology: K24 in 2chloroethanol

Plateau Modulus looks like stiff-entangled:

Estimate of $L_c \sim 100\text{nm}$ gives

$$G_{\text{curve}} \approx \frac{\rho k_B T}{L_c} \equiv 4\text{Pa}$$

at

$$\varphi = 5 \times 10^{-3}$$

so

$$\rho = 10^{14}\text{m}^{-2}$$
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Additional evidence from stiffness from DE-like spectrum

By fitting: \( L_p/L_e \sim 10 \)

More from Morse, Maggs and more….

Useful relation:

\[
\ln \left( \frac{\omega_{\text{min}}}{\tau_d} \right) = \frac{2}{3} \left[ 1 + \ln \left( \frac{L^2}{L_p L_e} \right) \right] \Rightarrow \frac{L}{L_e} \equiv 250 \equiv 100 \mu
\]
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Depolarised Light Scattering

$\mathbf{I_{VH}}$

... looks like rods locally

... $D(q) \sim q^0$

Relaxation rate with concentration

But $L$ should only be at most 100nm down here

Strange slowing down

Anomalous semi-dilute exponent with $c$
Application: these structures resemble “amyloids”

C. Dobson and A. Hill (Oxford)

- Next step is to understand kinetics (months!)
- We may have a cleanish model system
- Physics may have more to say about biology when it goes