We design **pH–responsive polypeptide–amphiphiles**

Structure and dynamics of intrinsically disordered polypeptide– amphiphiles

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INTRODUCTION

Motivated from disordered regions of neurofilament low protein, we conjugate disordered sequences to various hydrophobic domains and follow their mesophase structures in solution. We show that these intrinsically disordered polypeptide amphiphiles (IDPA) self–assembly is tunable by its disordered hydrophilic and hydrophobic domains. In particular, depending on the hydrocarbon tail geometry, we show a pH–dependent phase transition from repelling micelles to hexagonally packed elongated micelles or crystalline structures.

EXPERIMENTAL METHODS

- IDPAs are synthesized via solid phase and conjugated to either single or double hydrocarbon chains of different lengths (**Fig. 1**)
- pH dependent turbidity measurements are mapped to perception behavior of IDPA's overall charge **(Fig. 2, 3a, d)**
- Self–assembled nano–structures are determined using small angle X–ray scattering (in house apparatus and in Beamline I22 at Diamond Light Source)

RESULTS

Single–chained peptide amphiphiles transition from an uncorrelated micellar structure to a highly ordered micellar crystalline structure close to the PI (**Fig. 4a)**.

Double–chained peptide amphiphiles transition from an uncorrelated micellar structure to a more ordered condensed phase around to zero net charge (**Fig.4b)**.

Assuming spherical form factors for the micellar structure, $F \sim \sin(qr)/qr$, initial estimates for micellar radii can be made (**Fig. 5**). This analysis shows a strong correlation of tail length and sizing of micelles for all samples. The radii of double chained IPDA micelles decrease significantly for a net charge under –6.

Upon heating to 80°C this phase condenses to a highly ordered hexagonal phase (**Fig. 6a)** where hexagonal spacing increases with IDPAs hydrocarbon tail lengths (**Fig. 6b)** .

Increasing salinity at the condensed phase can suppress interaction of peptides amphiphiles due to electrostatic screening **(Fig. 7).**

Figure 1: Synthesized sequences

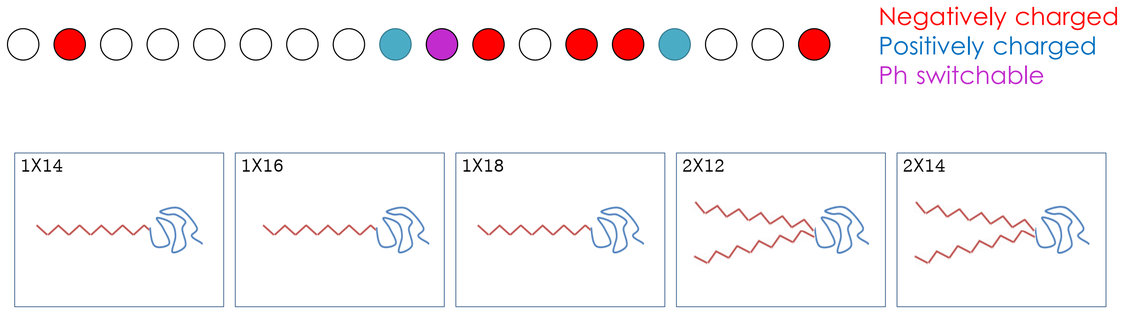


Figure 2: Net charge of peptide seuqence for different pHs

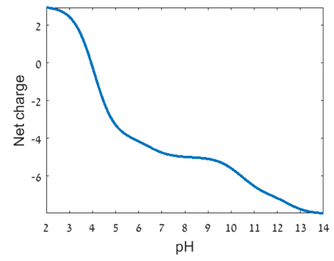
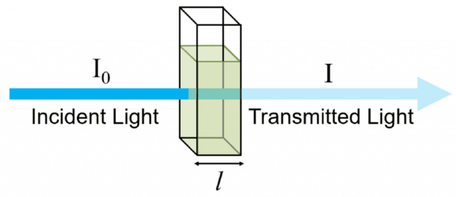
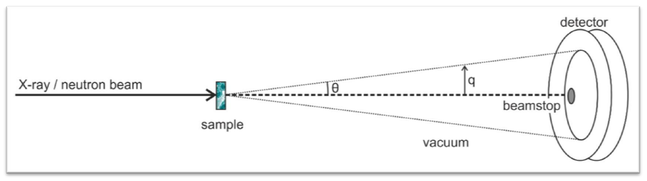


Figure 3: Experimental methods

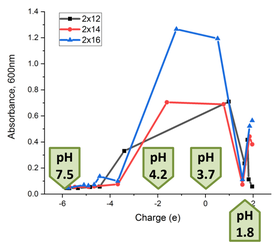
a) Turbidity measurements



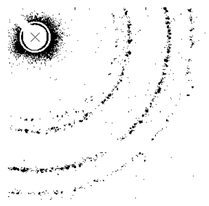
b) SAXS measurements



double tail IDPAs



1x 16, crystalline SAXS scattering



1x 16, integrated SAXS data

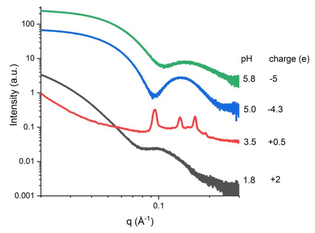
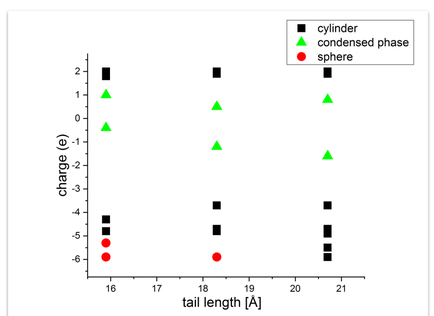


Figure 4: pH dependent phase diagrams

a) Single tailed IDPAs



b) Double tailed IDPAs

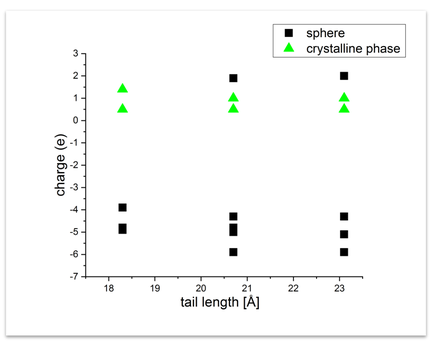
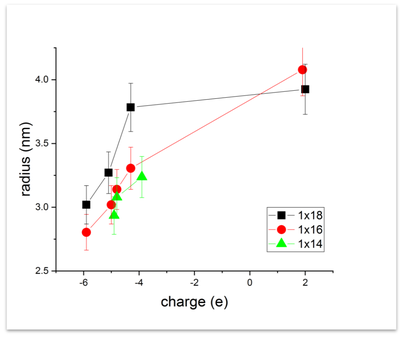


Figure 5: pH dependent radii using minima of SAXS pattern

b) Single tailed IDPAs



b) Double tailed IDPAs

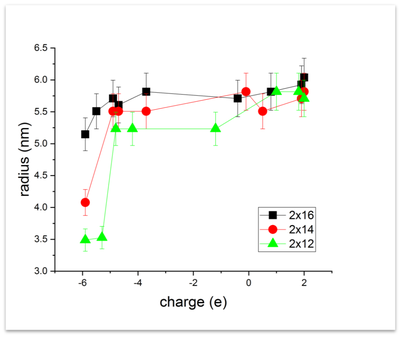
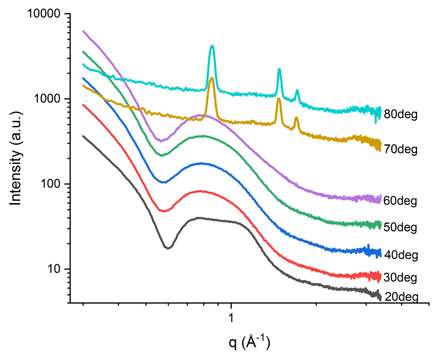
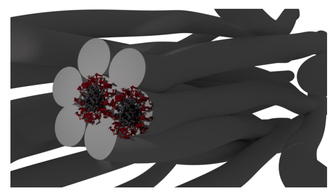


Figure 6: Hexagonal phase upon heating

Exemplary data (2x12)



a) Schematics for hexagonal packing



b) Hexagonal spacing at >70deg for double tails with different lengths

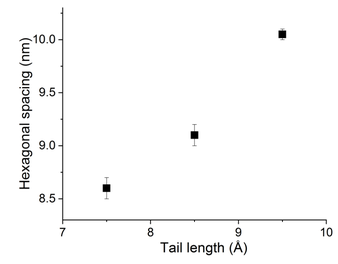
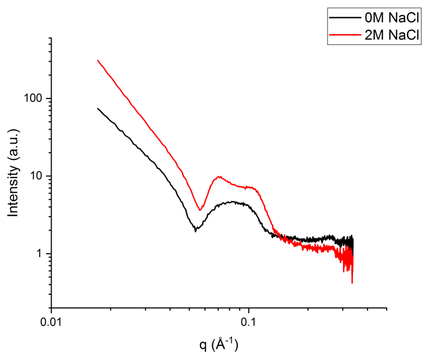


Figure 7: Surpression of structure factor by high salinity



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