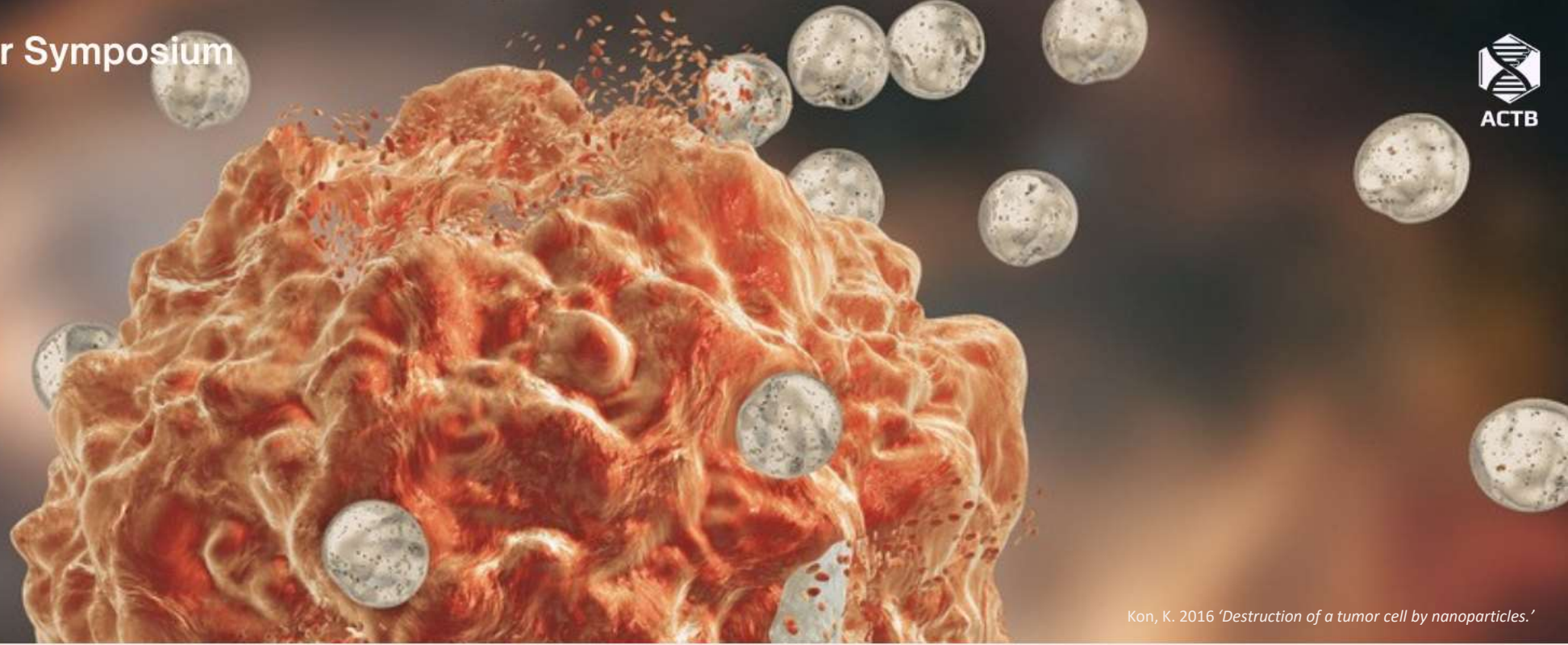


38th Australasian Polymer Symposium
Auckland, New Zealand
February 2024



ACTB

38APS



Kon, K. 2016 'Destruction of a tumor cell by nanoparticles.'

pH-Responsive polymer-homopeptide micelles: An investigation into morphology and pH- responsive behaviour of regioisomers

Cintya Dharmayanti | PhD Candidate

Primary supervisor: A/Prof. Anton Blencowe

Co-Supervisors: Dr Todd A. Gilliam, Dr Andrew J. Clulow, Dr Manuela Klingler-Hoffmann, Dr Hugo Albrecht

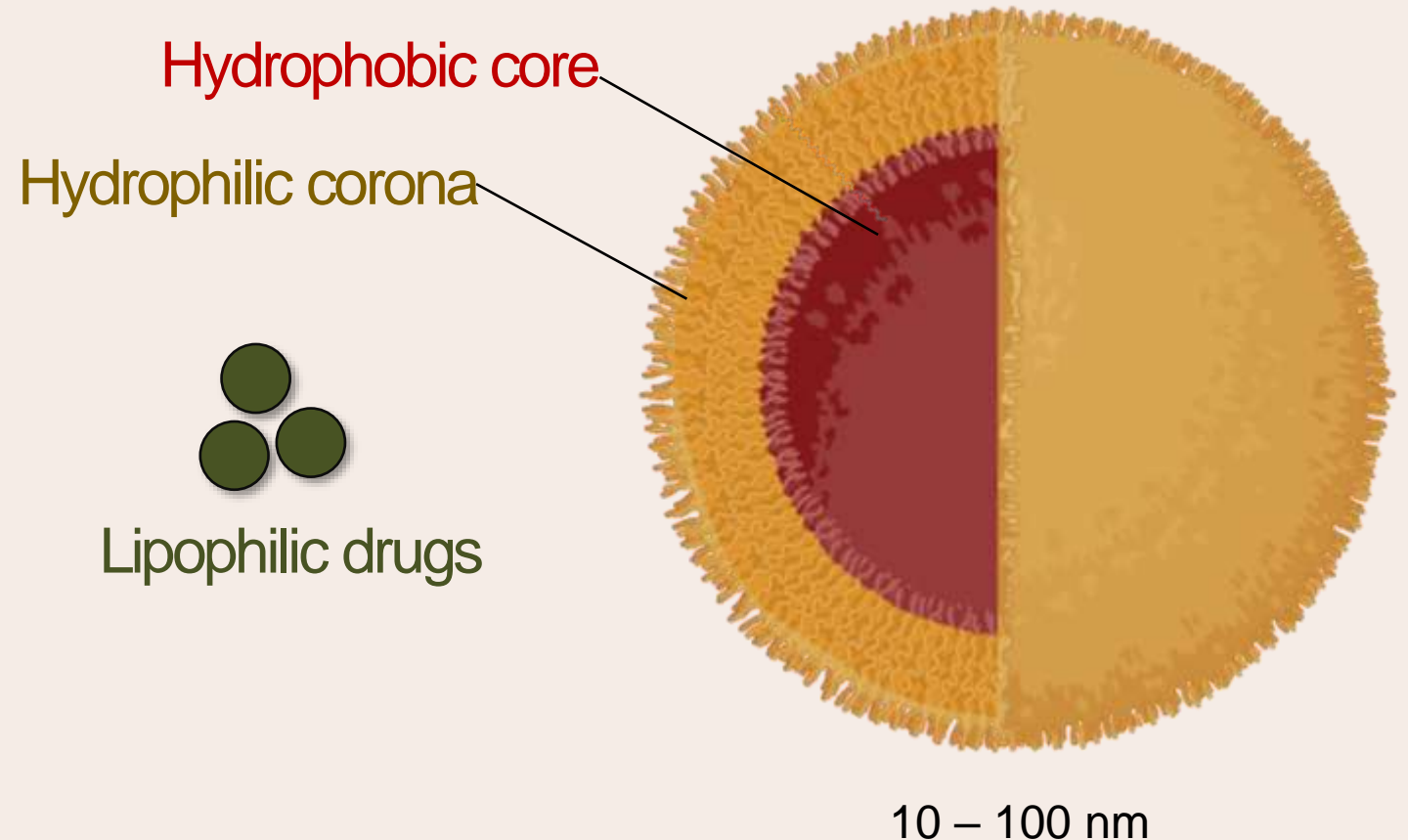


University of
South Australia

POLYMERIC MICELLES AS DRUG DELIVERY VEHICLES

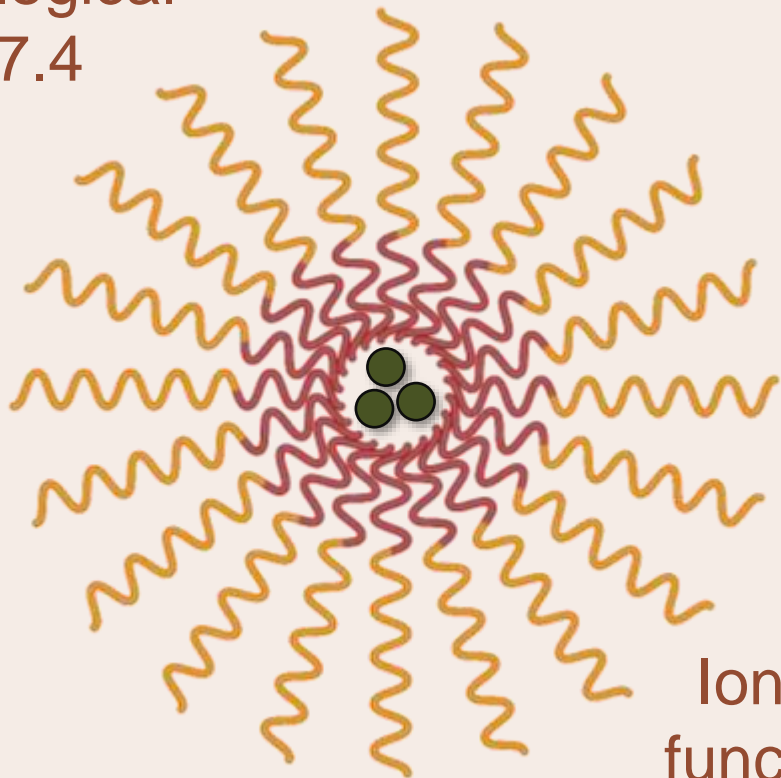
Advantages:

- ✓ Reduce drug toxicity
- ✓ Protect drugs from degradation
- ✓ Passively accumulate in tumour tissue based on enhanced permeation and retention (EPR) effect
- ✓ Prolong drug circulation
- ✓ Can be designed to respond to specific stimuli

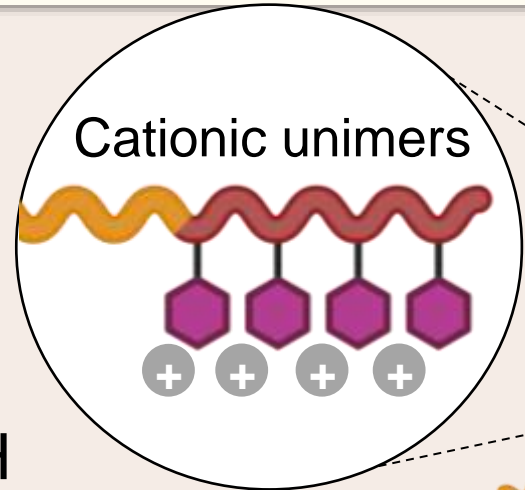


MICELLES CAN BE DESIGNED TO RESPOND TO pH

Physiological
pH 7.4



pH



Acidic pH
< 5.0

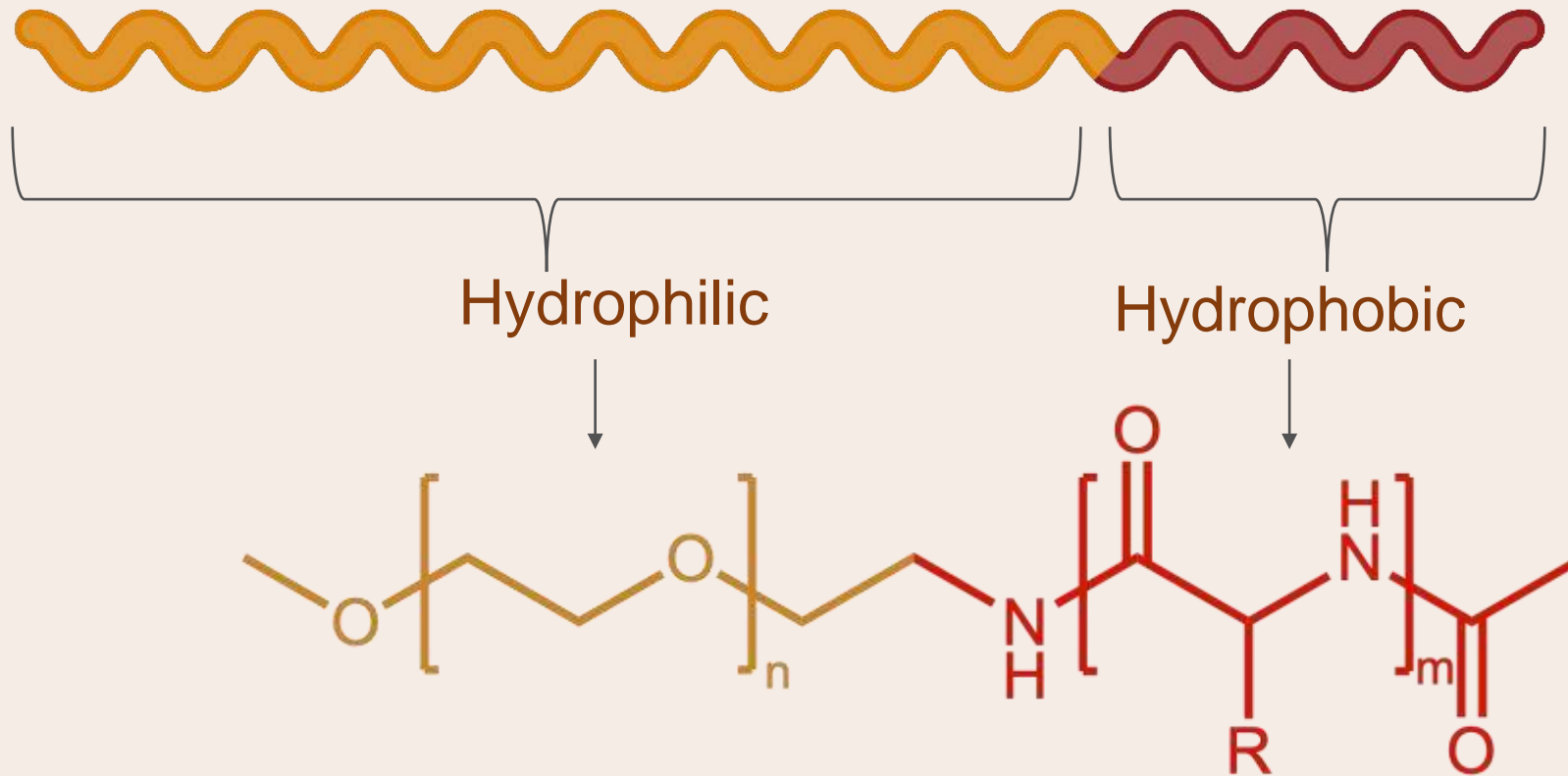


Ionisable basic
functional groups

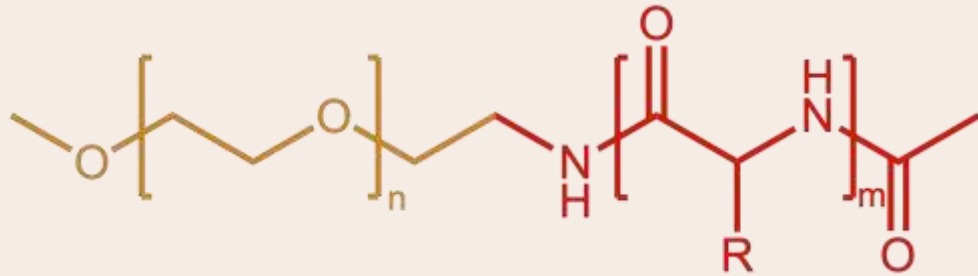
Drug release

POLYMER-HOMOPEPTIDE HYBRID MICELLES

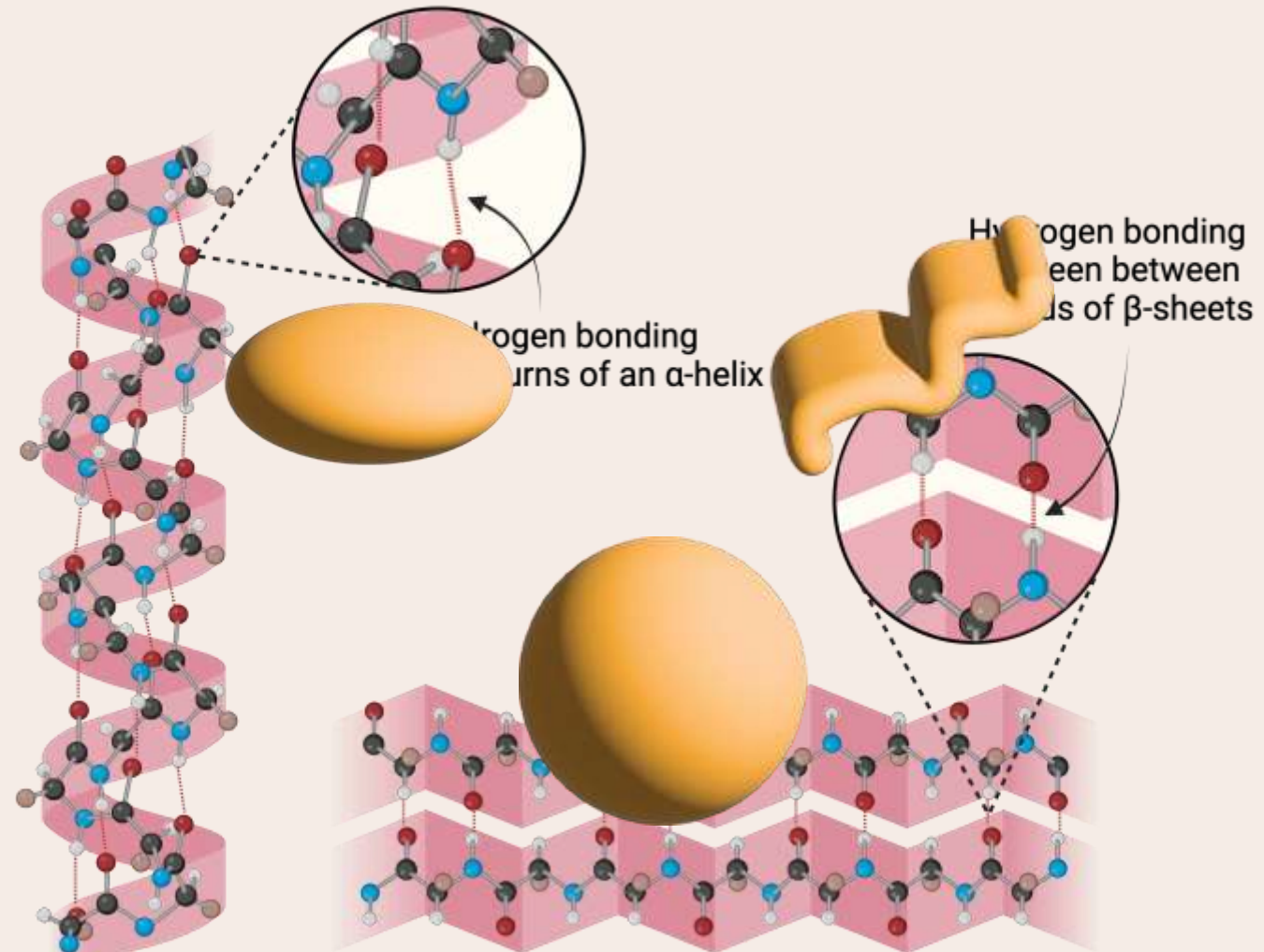
Amphiphilic di-block copolymer



POLYMER-HOMOPEPTIDE HYBRID MICELLES

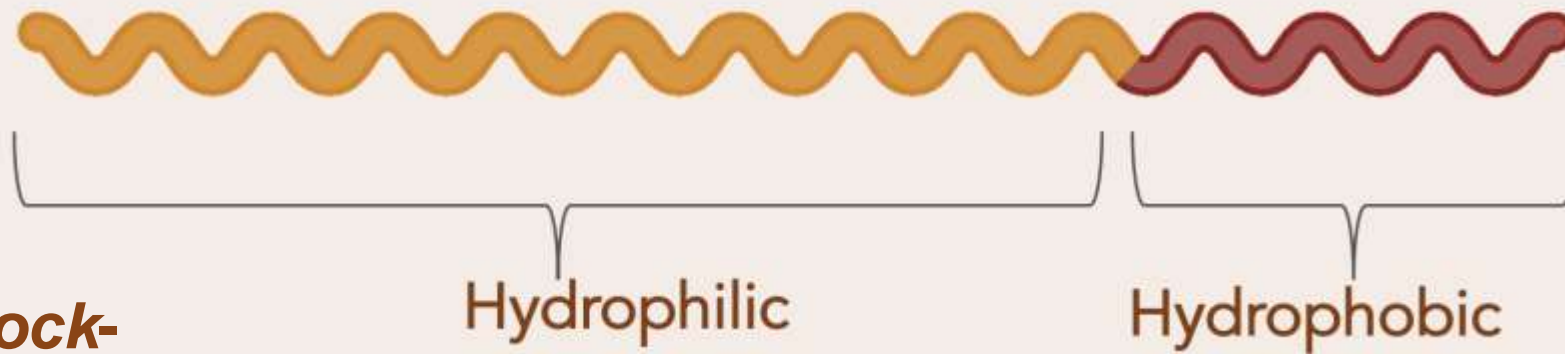


- Biocompatible
- Biodegradable
- Unique ability to form secondary structures
 - Spatially well-defined
 - Can influence micelle morphology

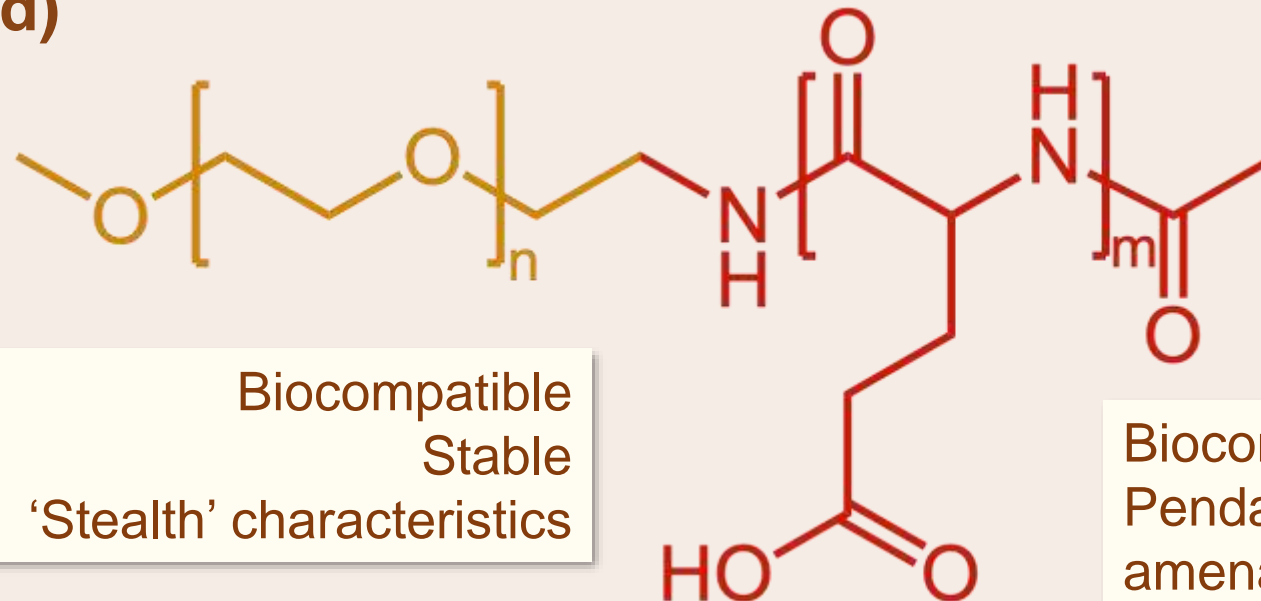


This project aimed to prepare **pH-responsive polymer-homopeptide micelles** and investigate their **morphology and pH-responsive behaviour.**

DESIGNING THE POLYMER



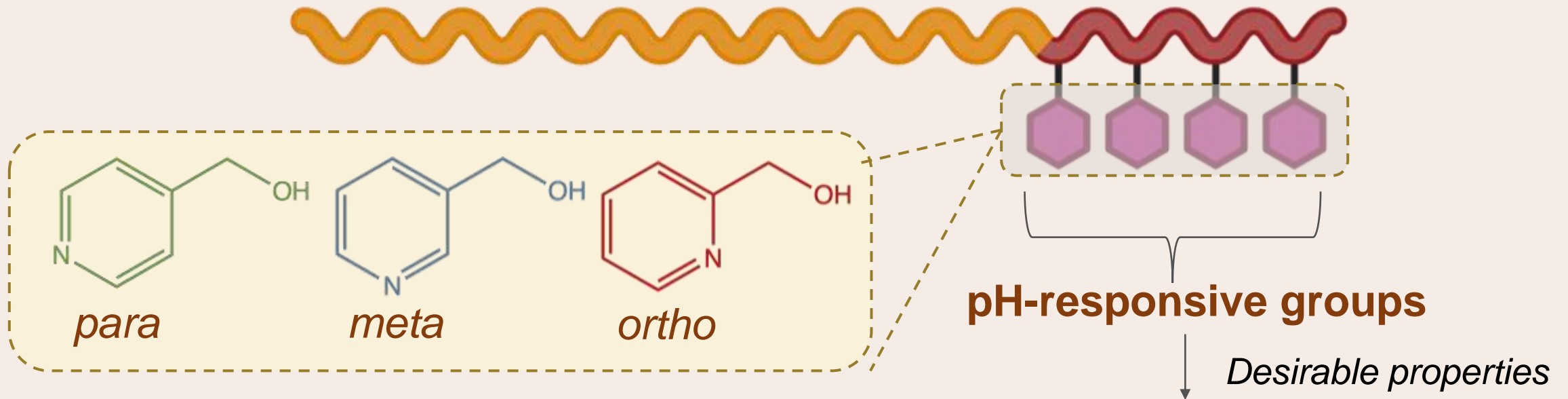
**PEG-*block*-
poly(glutamic acid)
(PEG-*b*-PGA)**



Biocompatible
Stable
'Stealth' characteristics

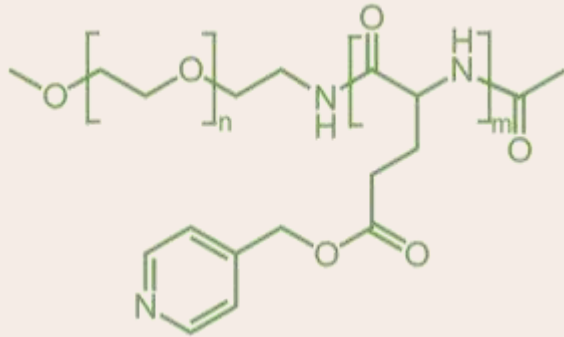
Biocompatible/biodegradable
Pendant functional groups
amenable to modification

DESIGNING THE POLYMER



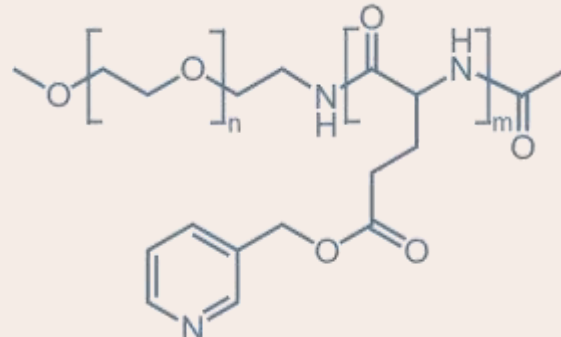
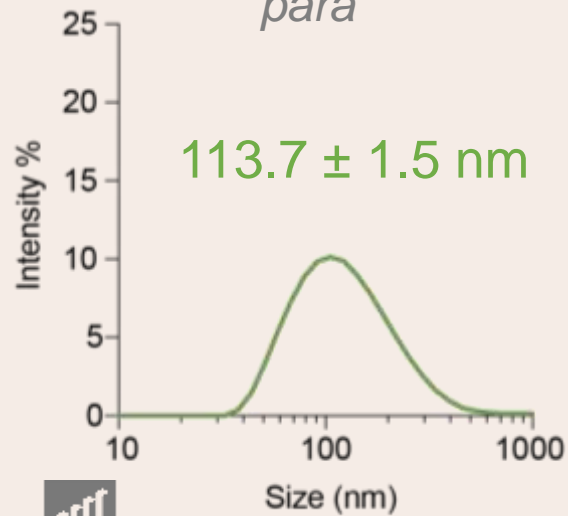
Pyridine Can be conjugated as pendant group on the hydrophobic block
 Basic functional group to facilitate acid-mediated disassembly
 Commercially available (simplifies synthesis)
 Low cost

LIBRARY OF PEG-*b*-PMG MICELLES



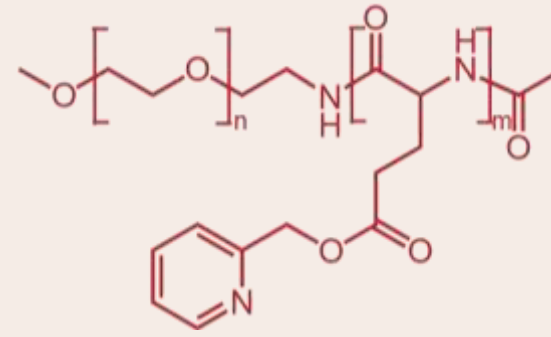
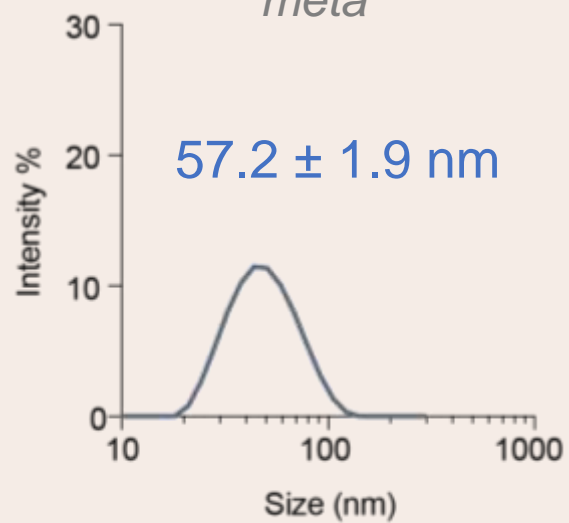
PEG-*b*-4PMG

para



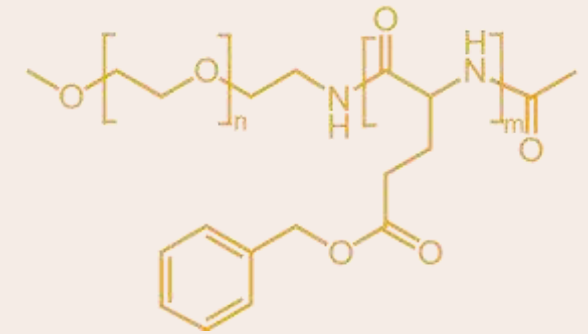
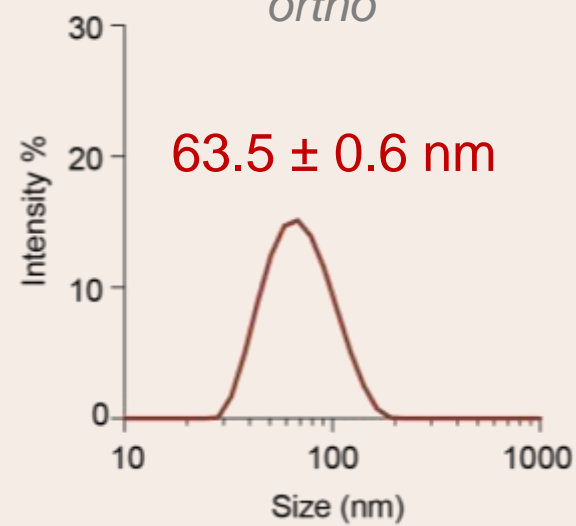
PEG-*b*-3PMG

meta



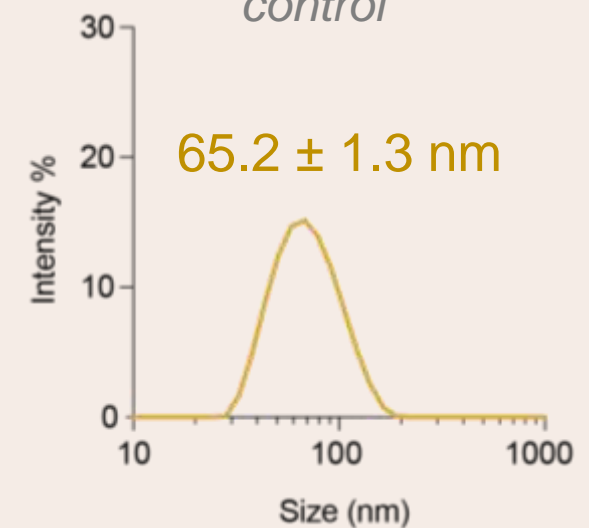
PEG-*b*-2PMG

ortho

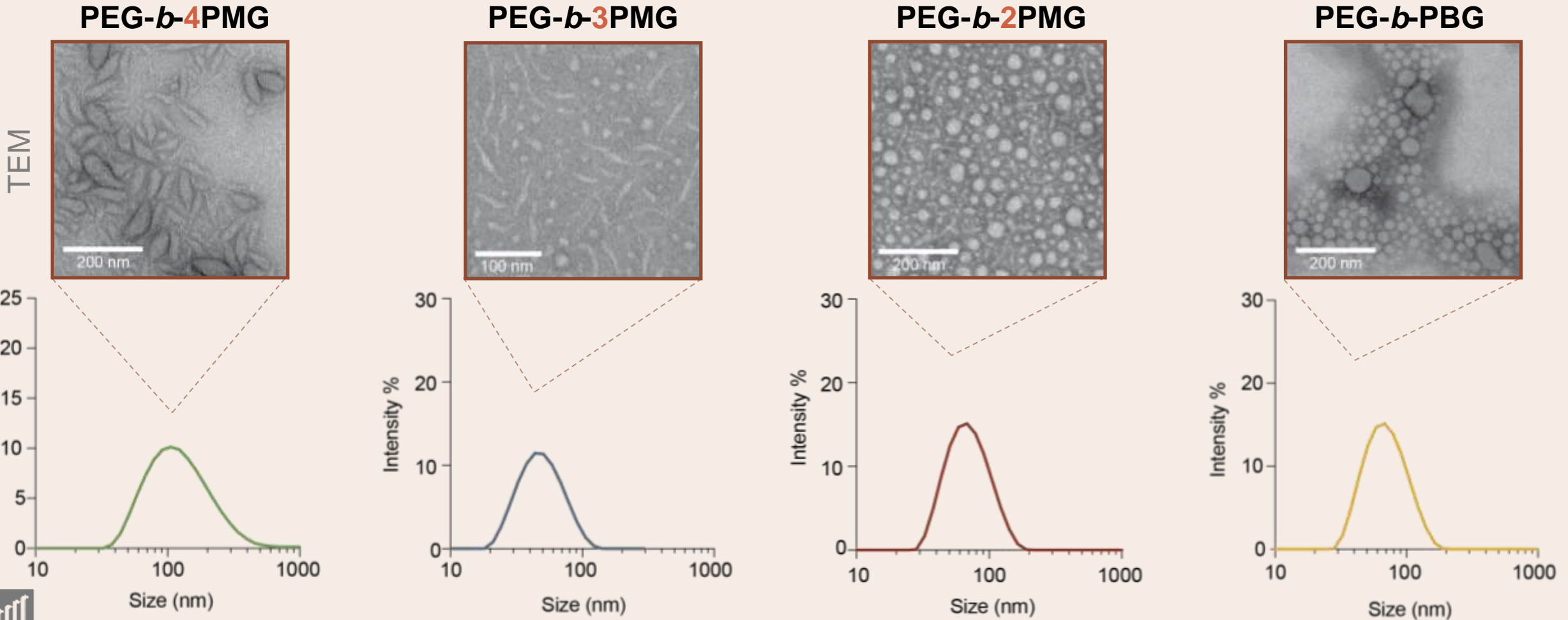


PEG-*b*-PBG

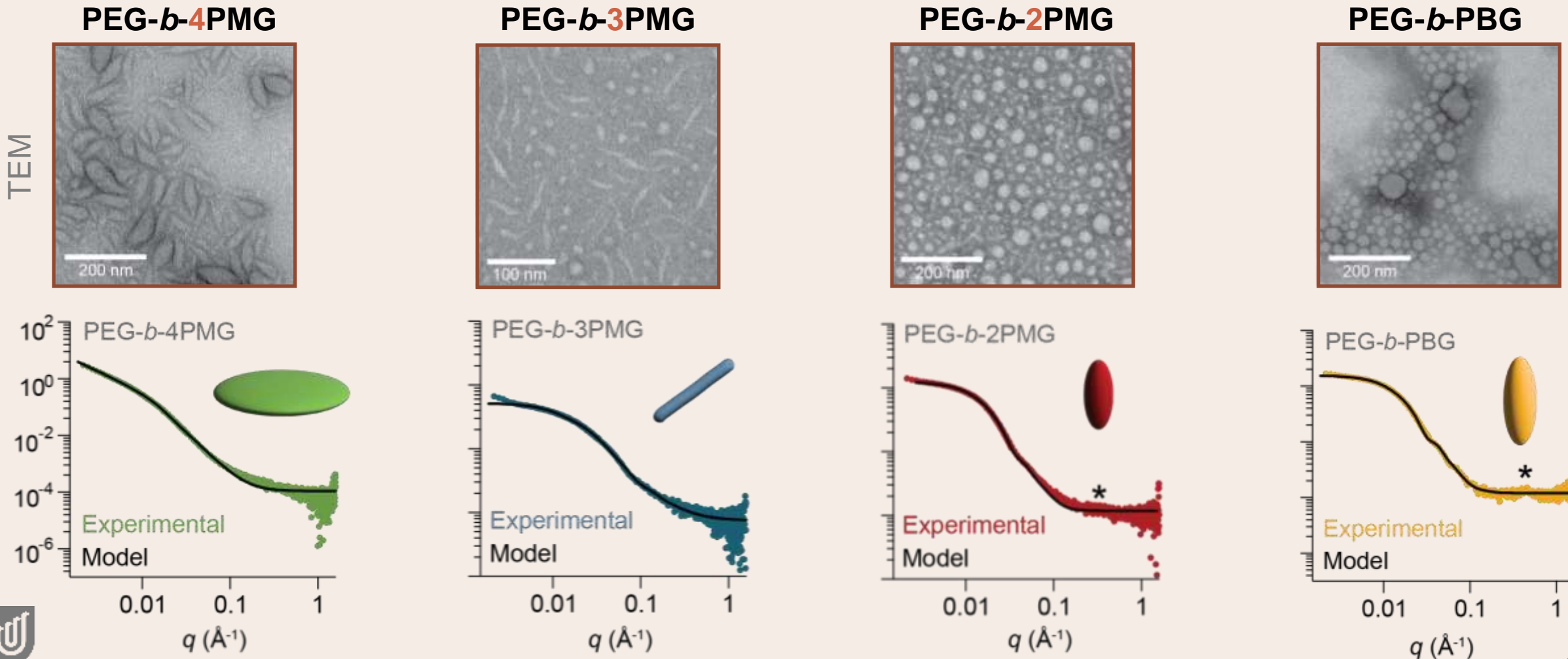
control



REGIOISOMER DICTATES MICELLE MORPHOLOGY



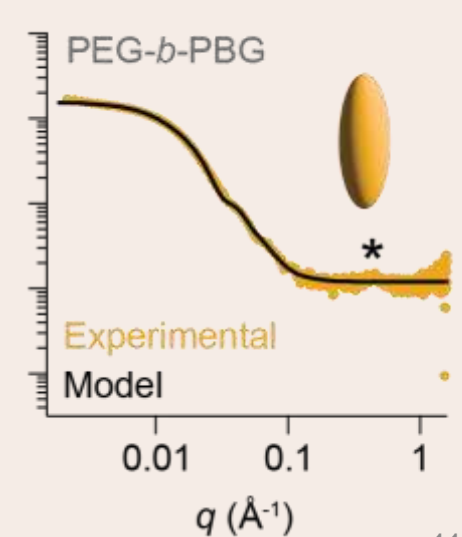
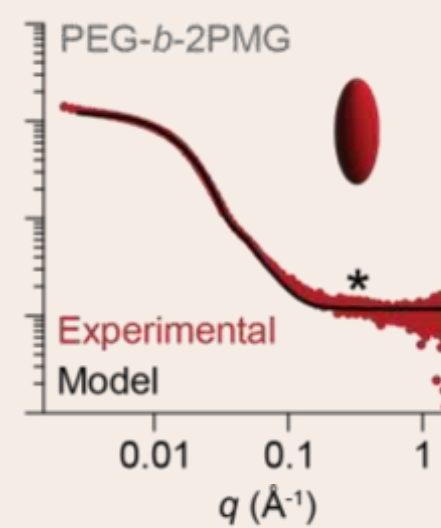
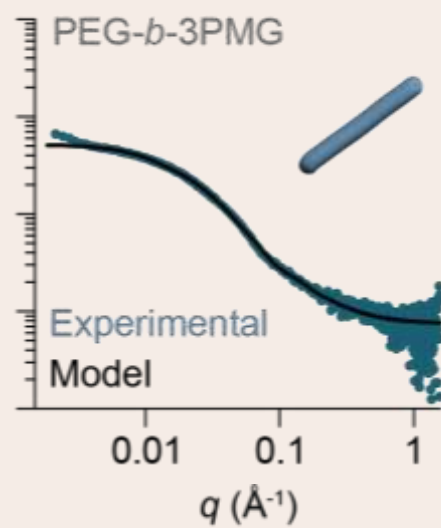
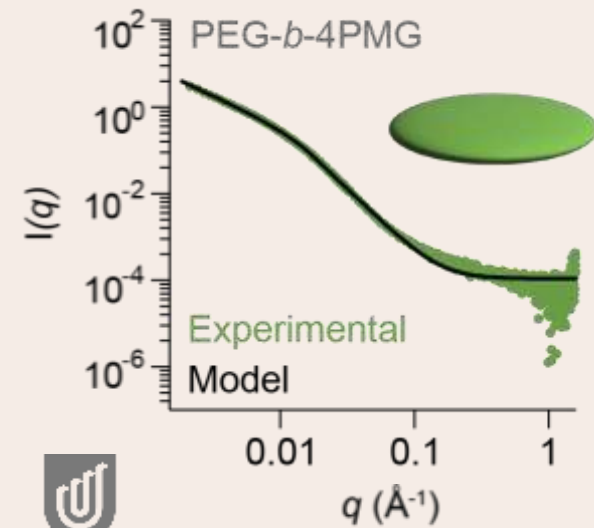
REGIOISOMER DICTATES MICELLE MORPHOLOGY



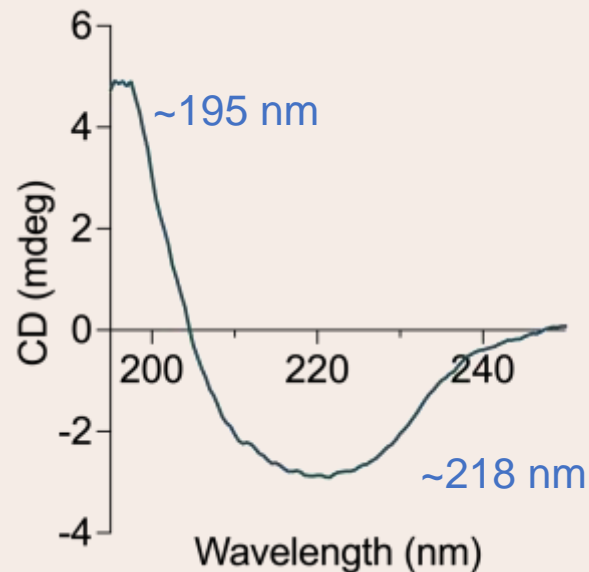
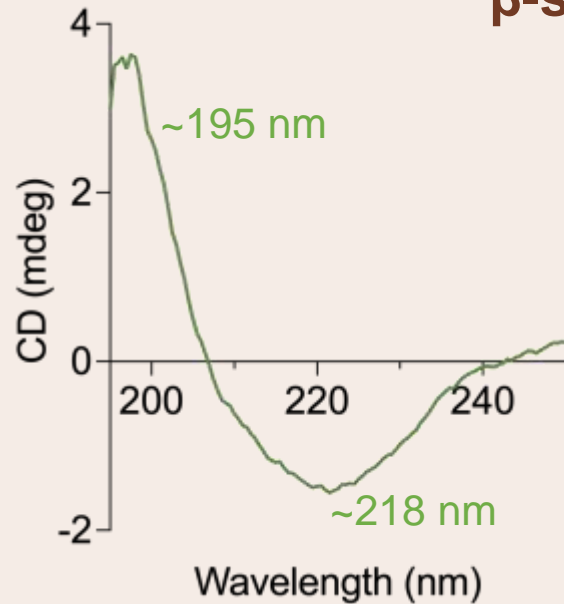
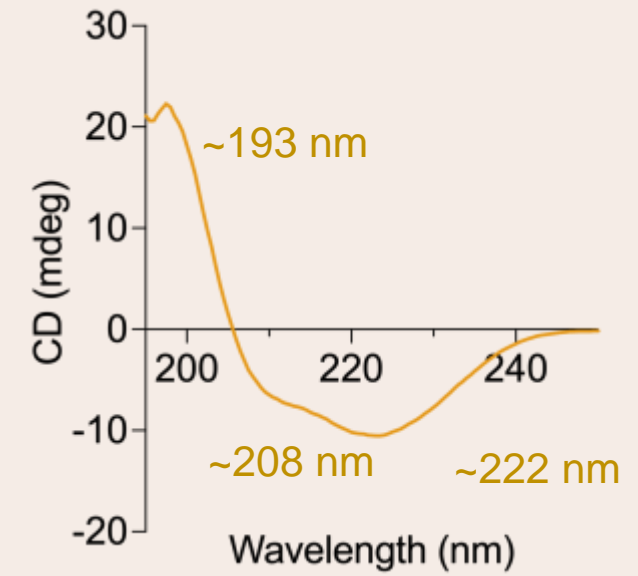
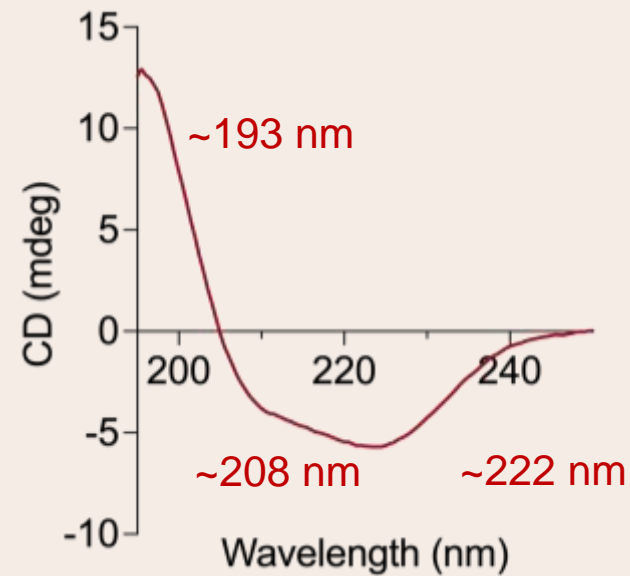
REGIOISOMER DICTATES MICELLE MORPHOLOGY

PEG-*b*-4PMGPEG-*b*-3PMGPEG-*b*-2PMGPEG-*b*-PBG

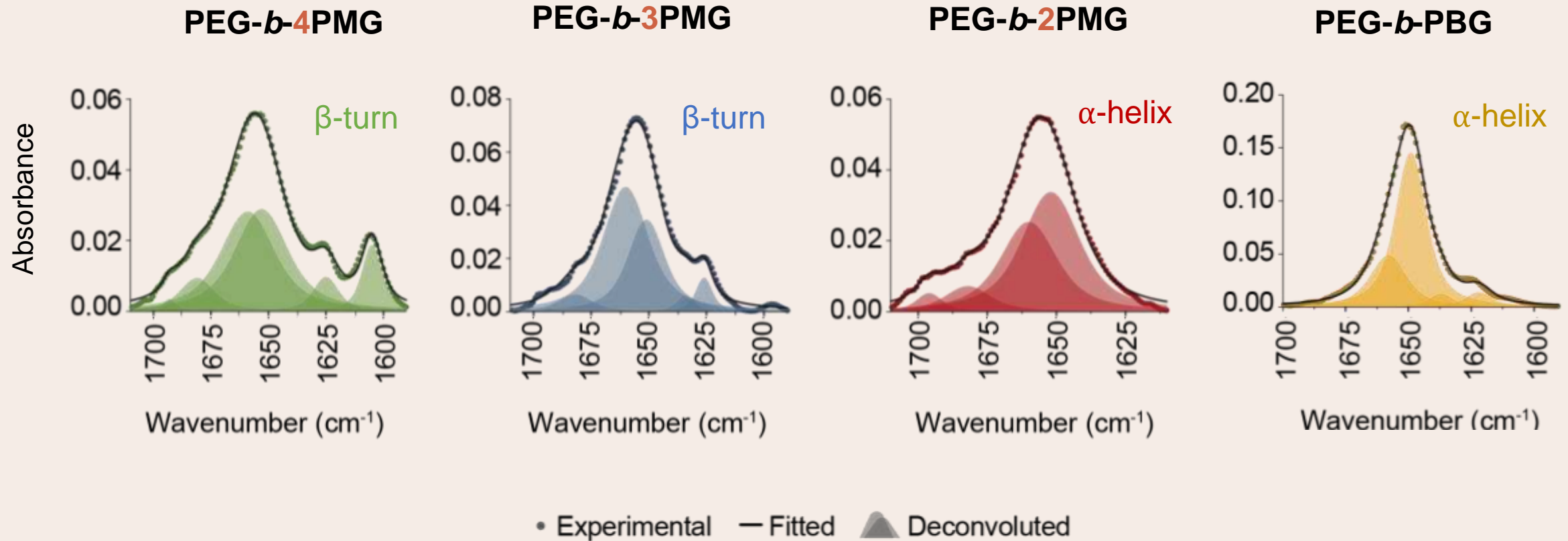
?



REGIOISOMER DICTATES SECONDARY STRUCTURE

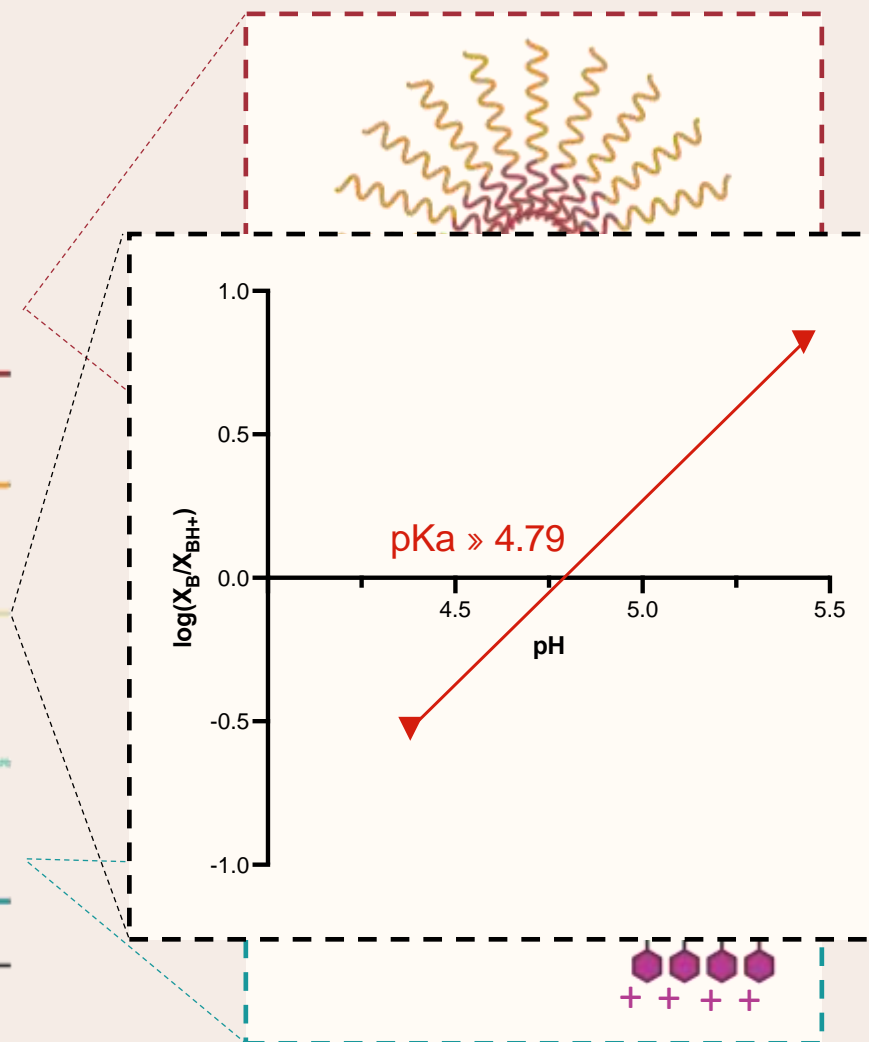
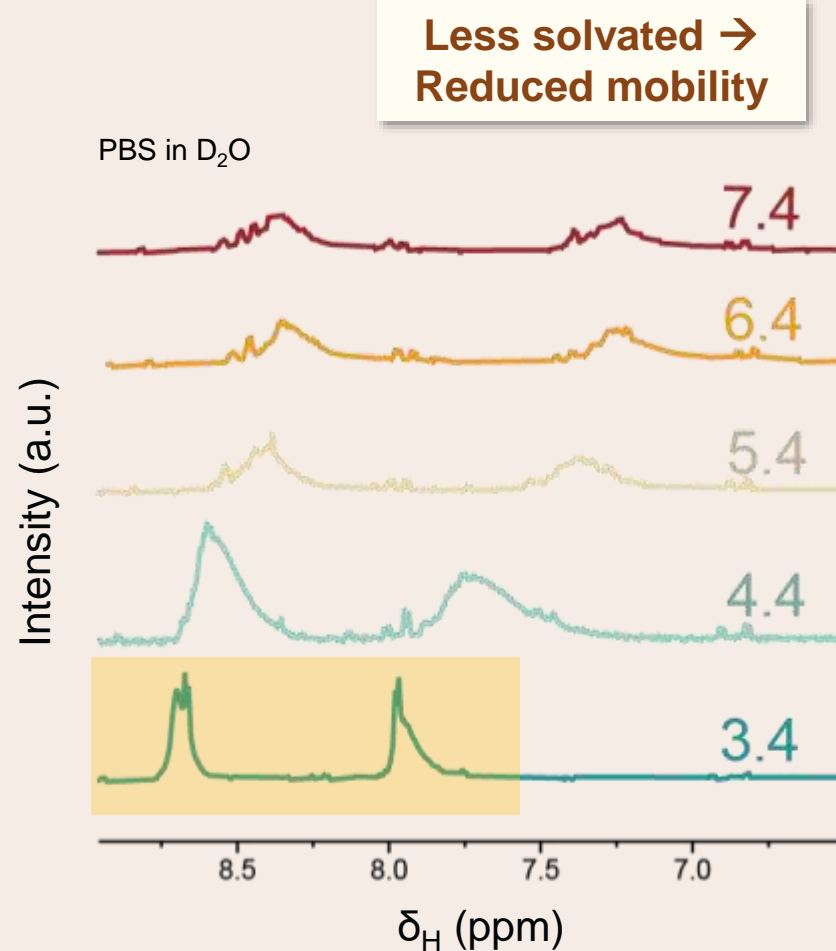
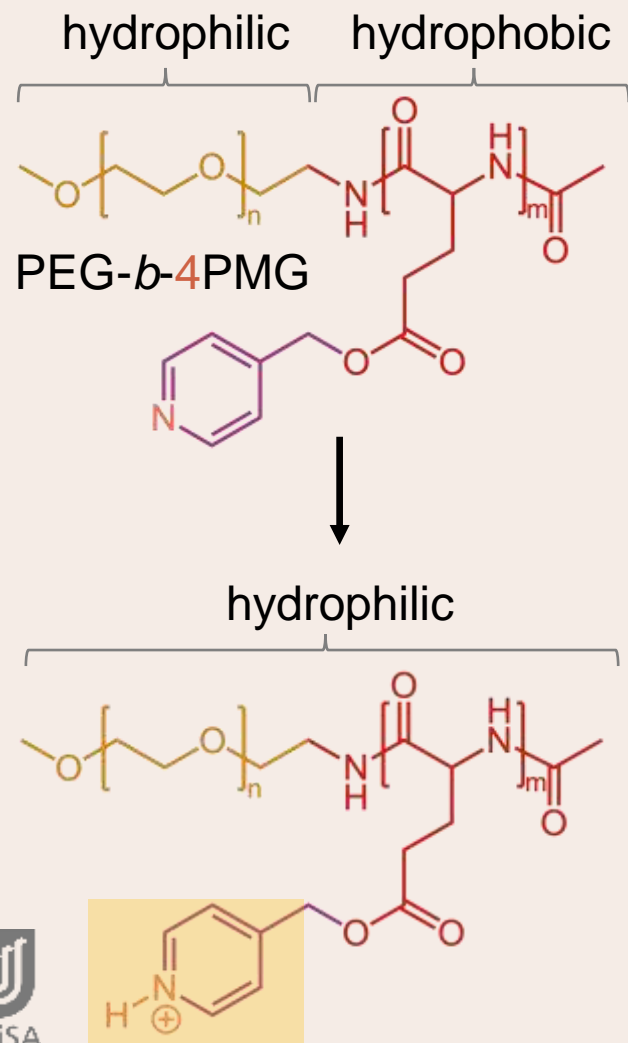
PEG-*b*-4PMGPEG-*b*-3PMGPEG-*b*-2PMGPEG-*b*-PBG β -sheets α -helices

REGIOISOMER DICTATES SECONDARY STRUCTURE

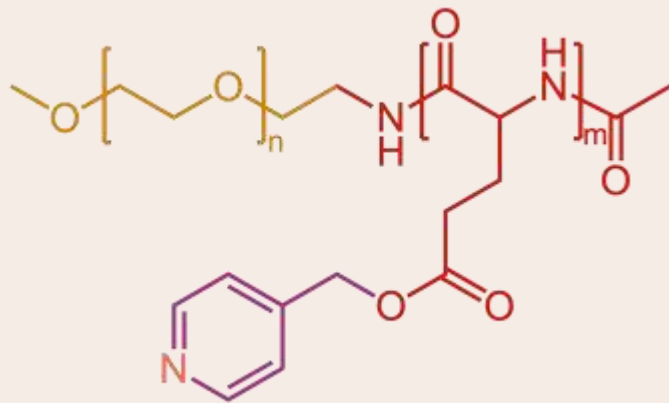


What about the pH-responsive behaviour?

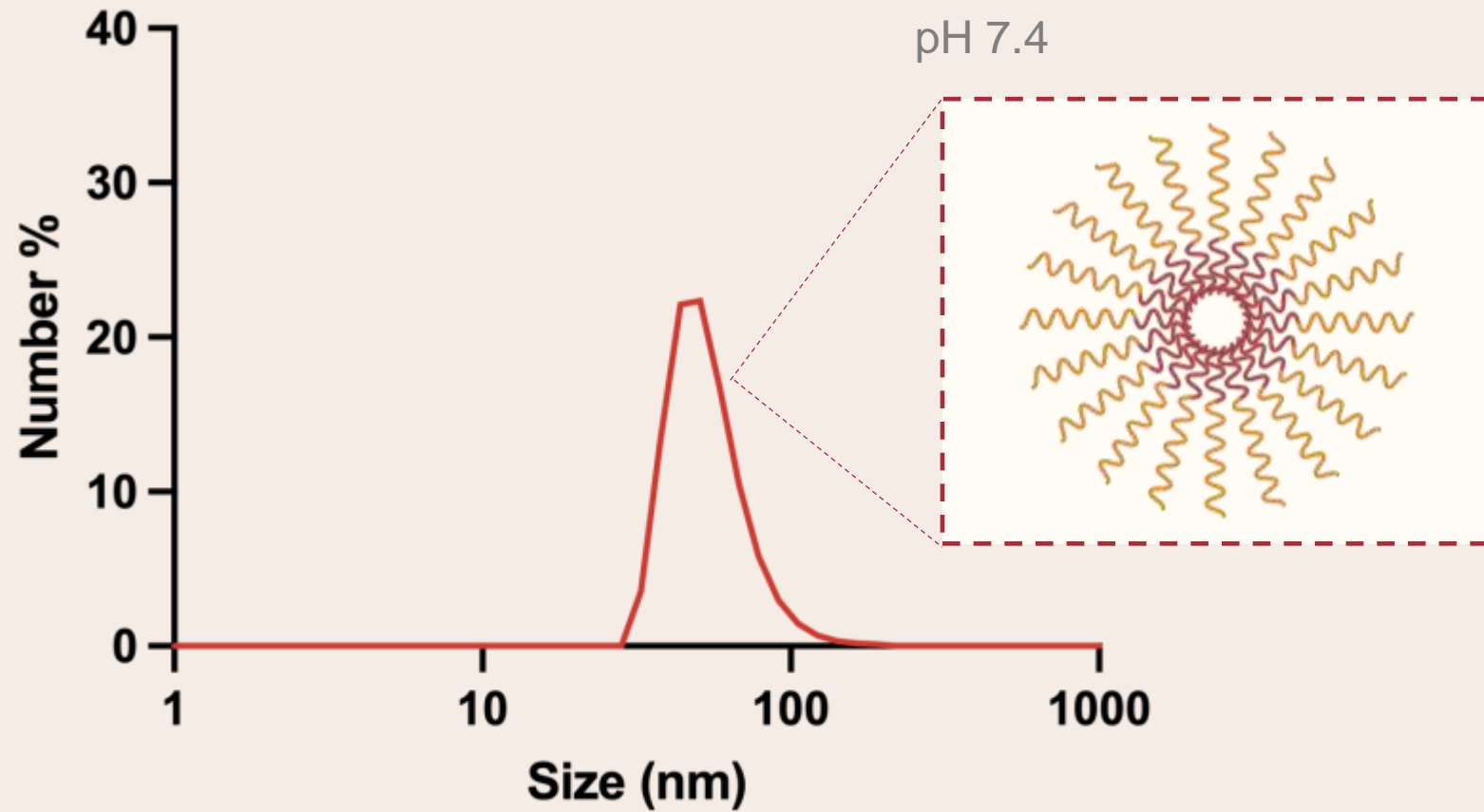
PEG-*b*-PMGs ARE pH-RESPONSIVE



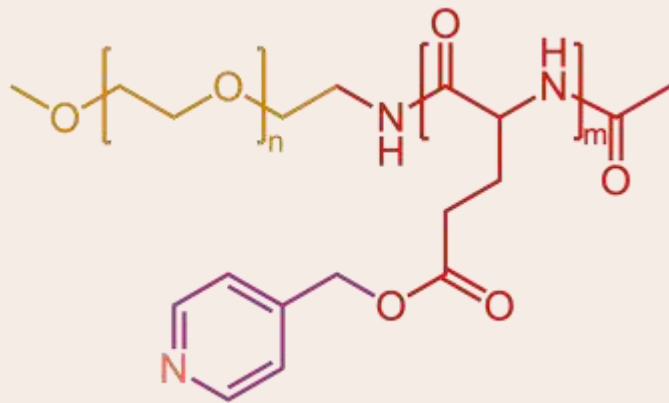
DECREASE IN DLS PARTICLE SIZE DUE TO DISASSEMBLY



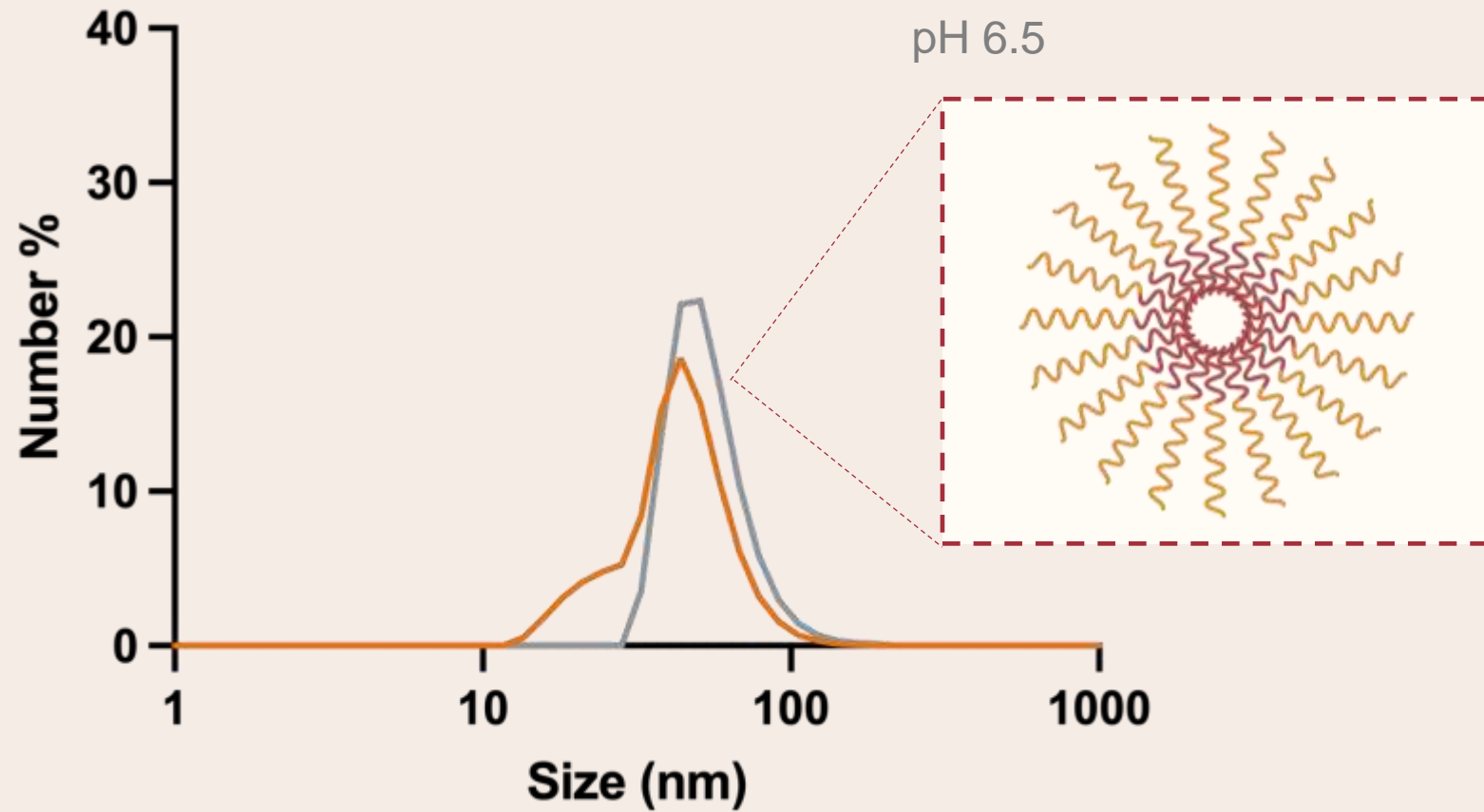
PEG-*b*-4PMG
para



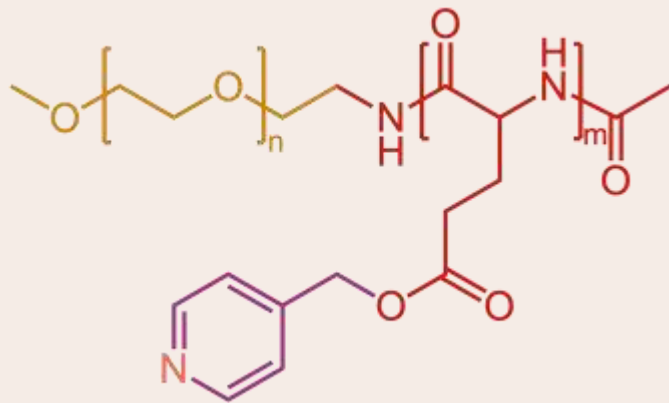
DECREASE IN DLS PARTICLE SIZE DUE TO DISASSEMBLY



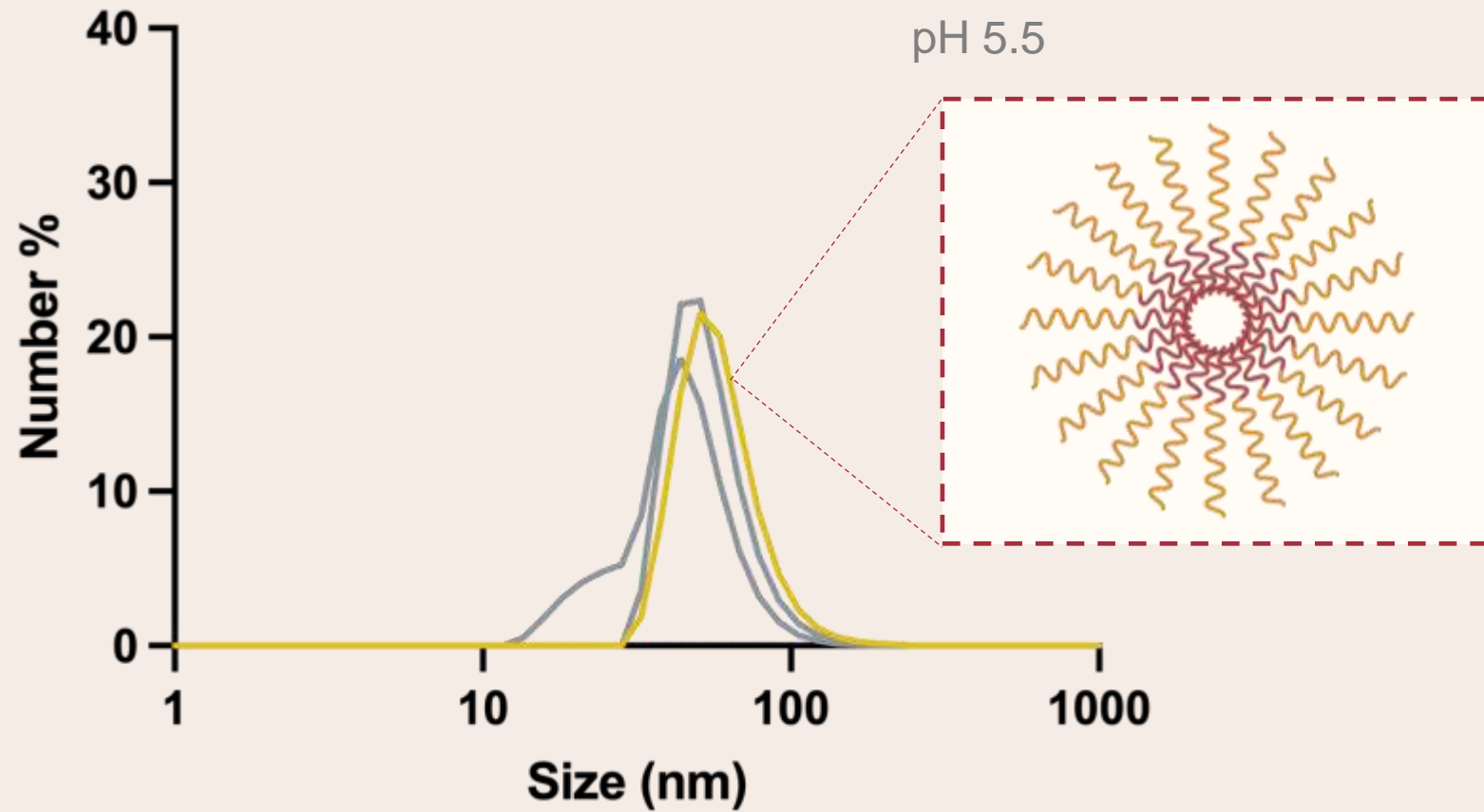
PEG-*b*-4PMG
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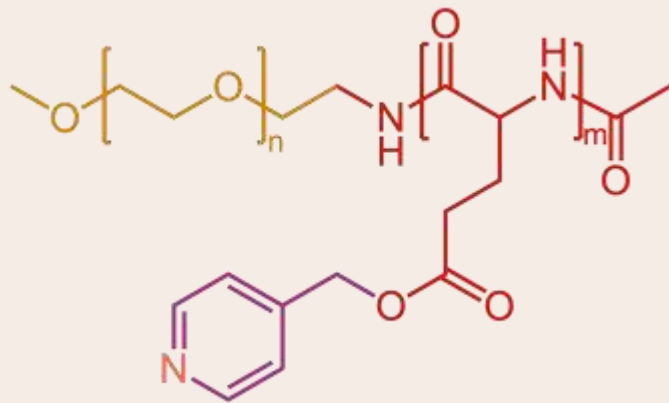
DECREASE IN DLS PARTICLE SIZE DUE TO DISASSEMBLY



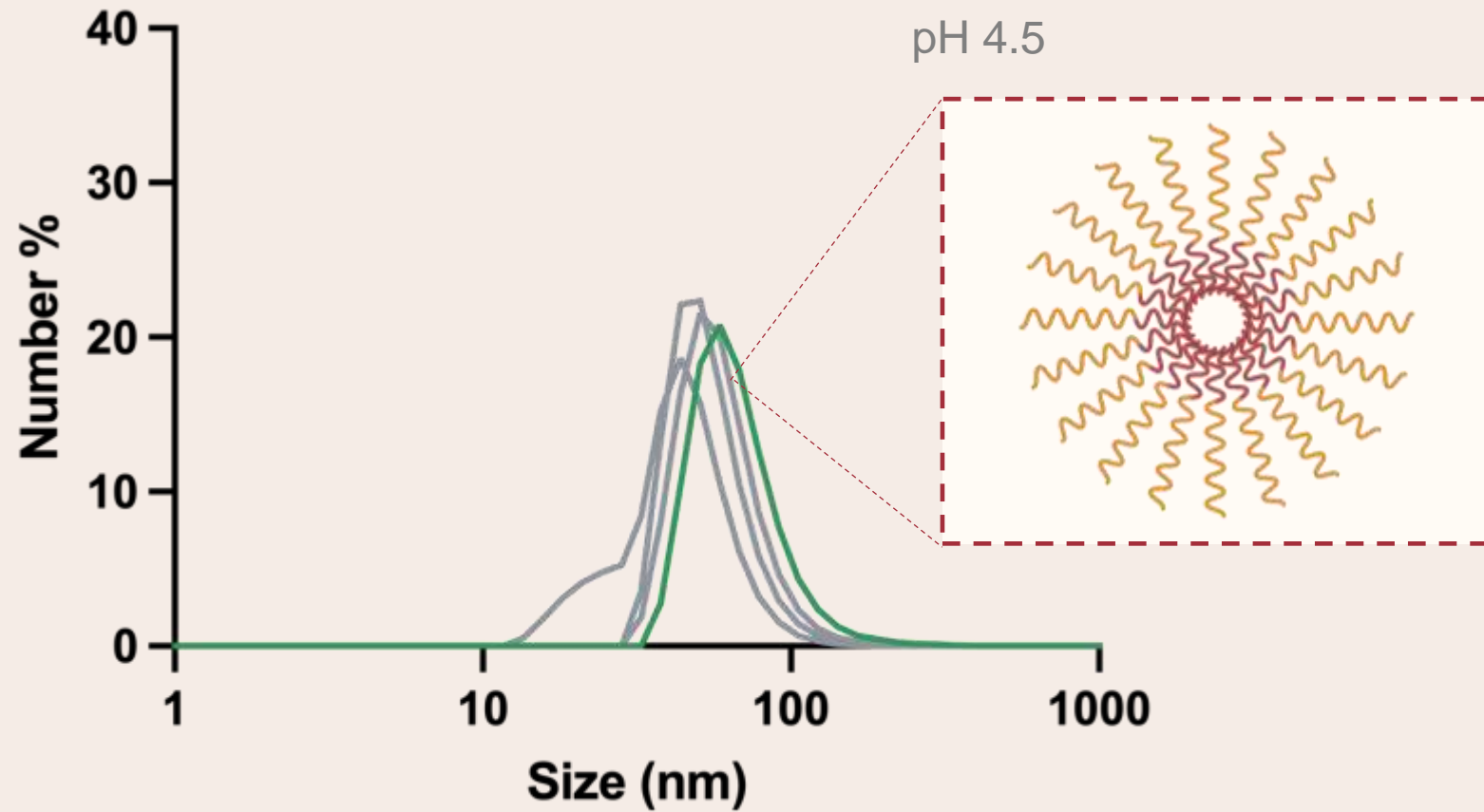
PEG-*b*-4PMG
para



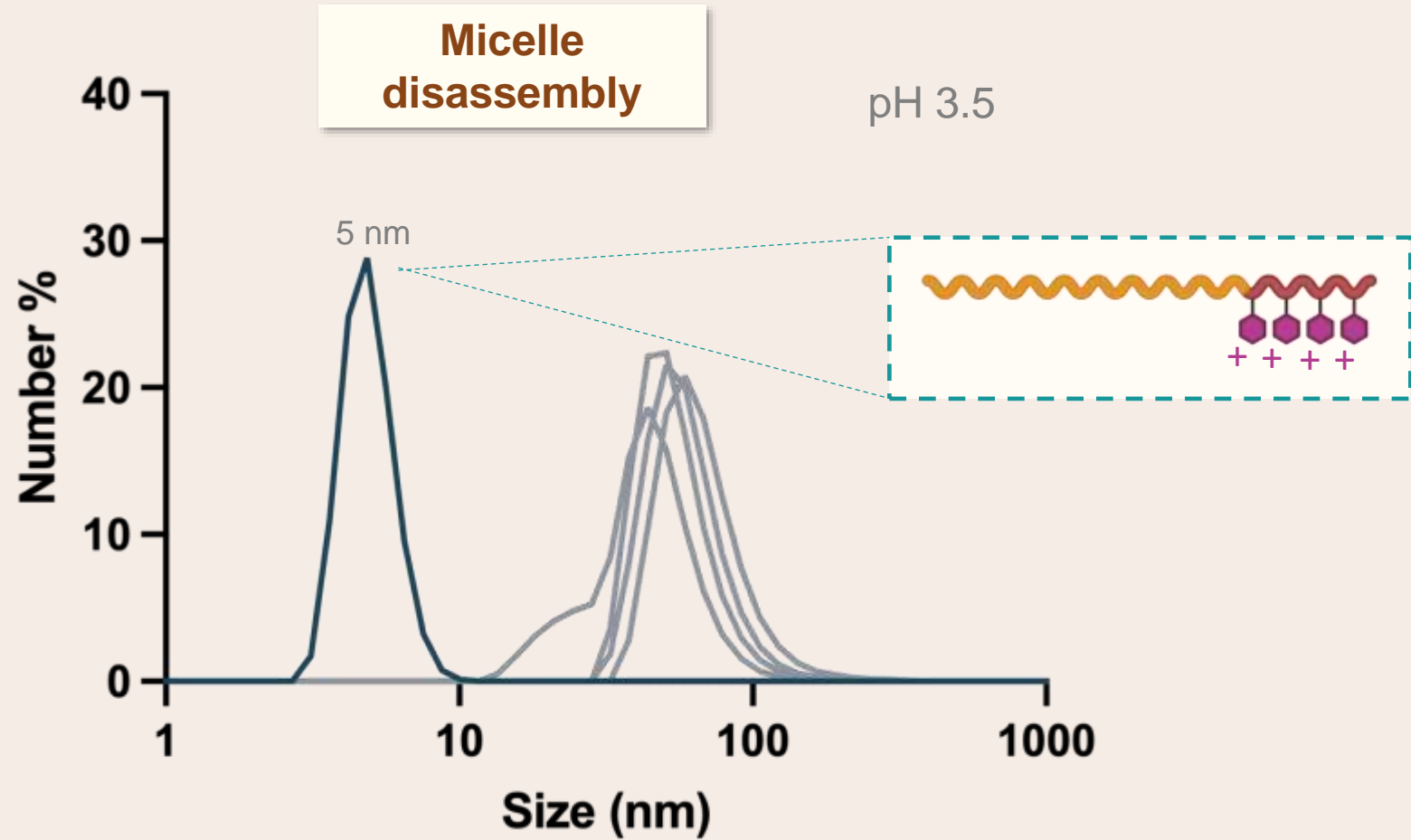
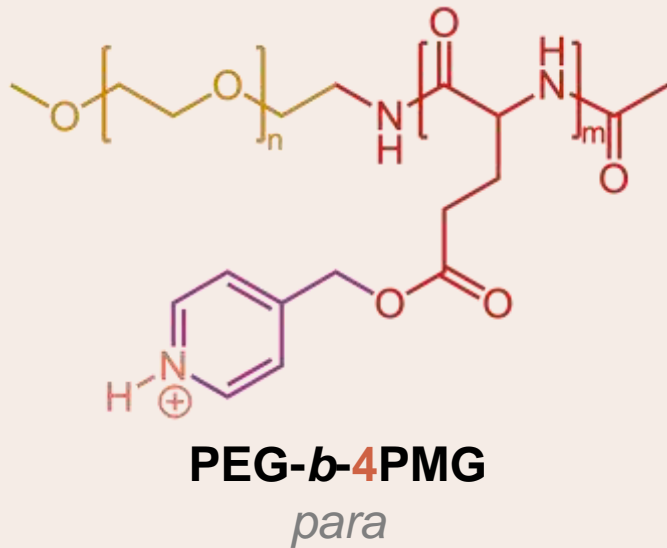
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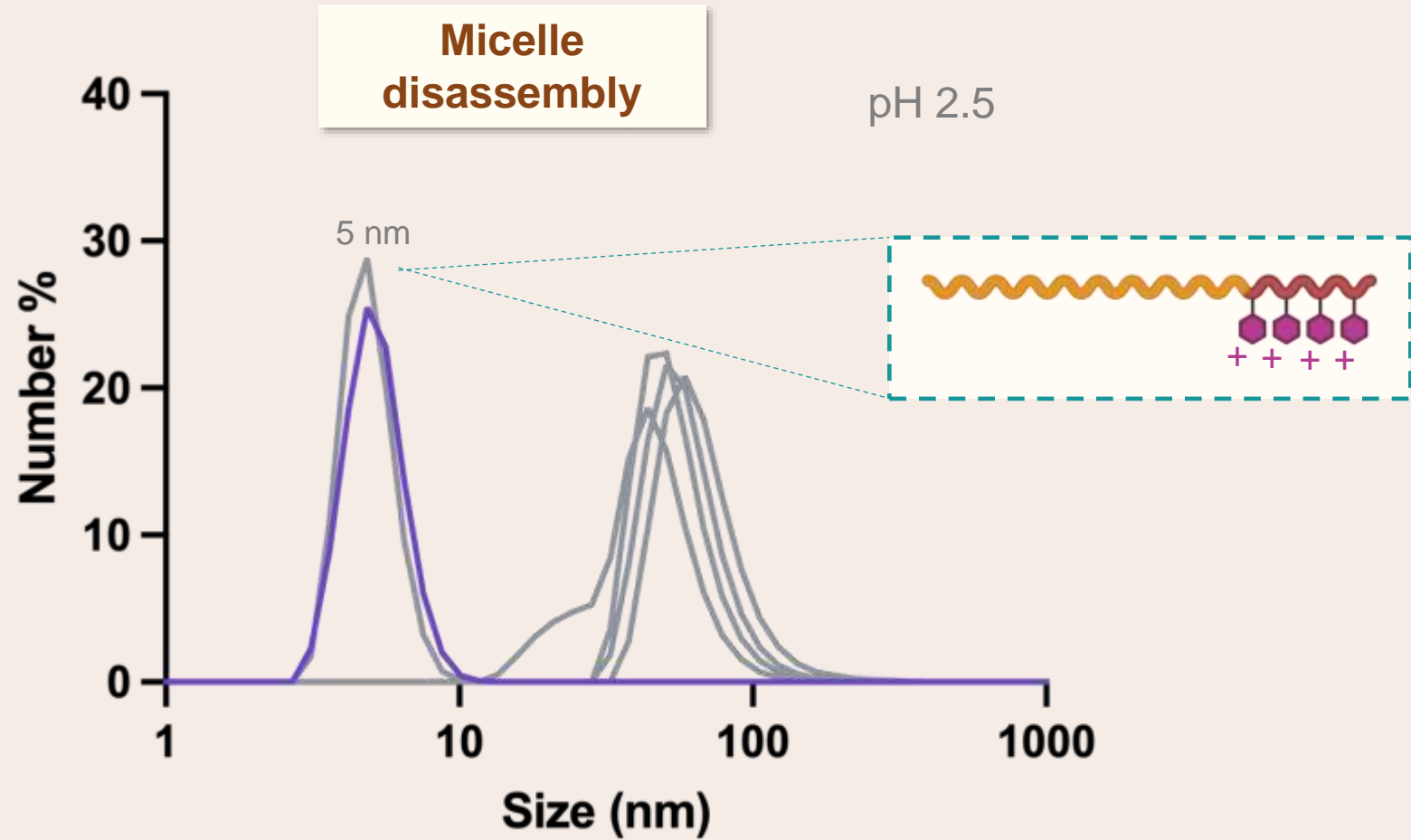
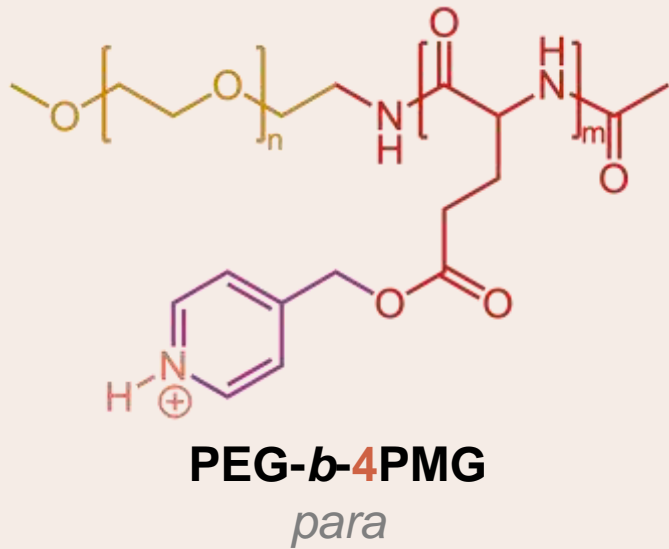
PEG-*b*-4PMG
para



DECREASE IN DLS PARTICLE SIZE DUE TO DISASSEMBLY

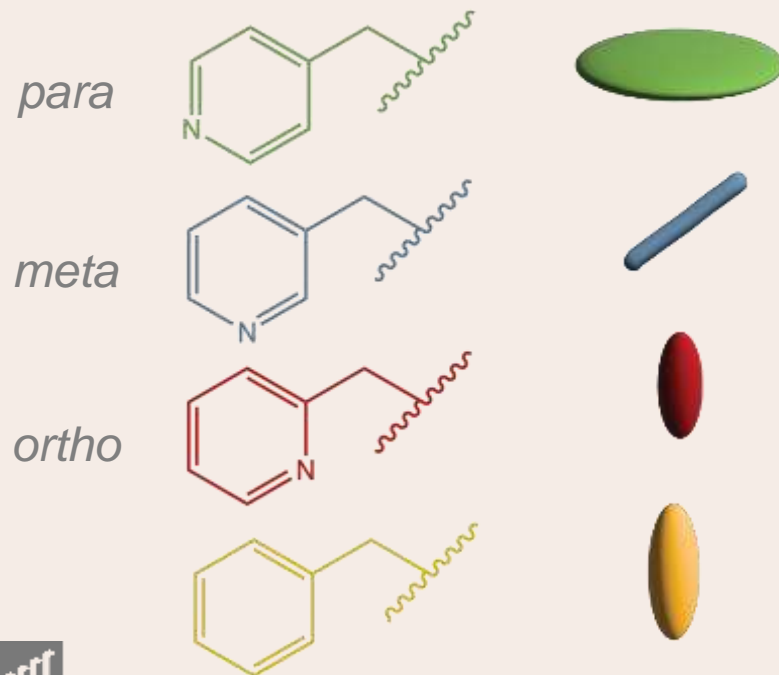


DECREASE IN DLS PARTICLE SIZE DUE TO DISASSEMBLY

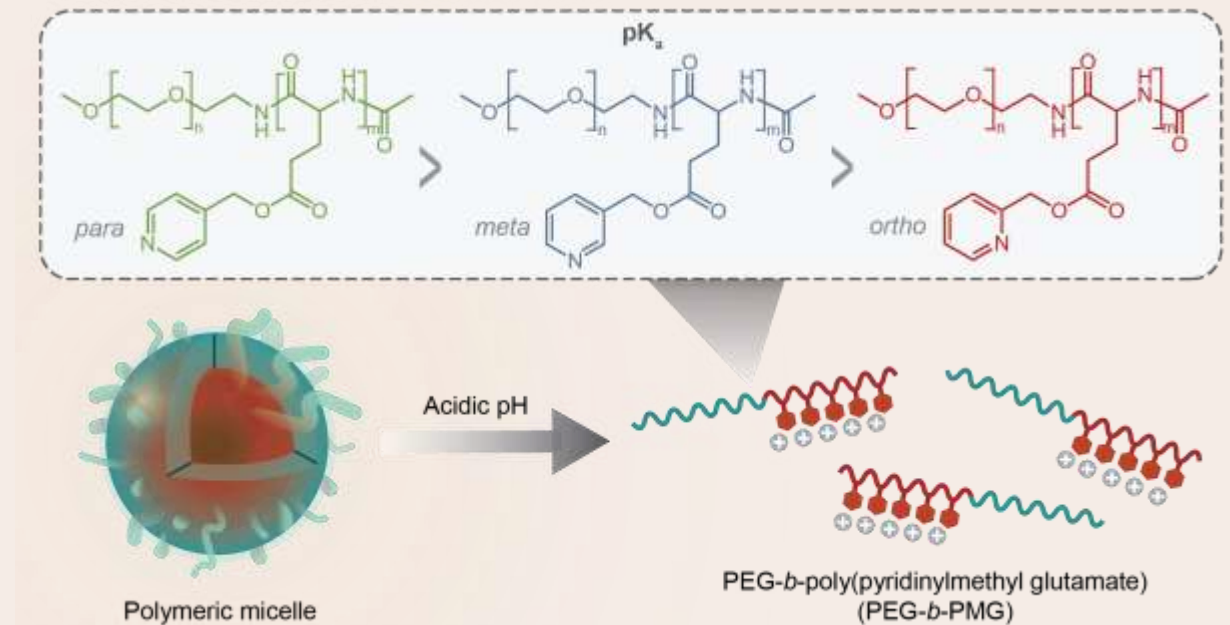


SUMMARY

1. Position of regioisomers in PEG-*b*-PMG micelles governs dominant secondary structure and micelle morphology



2. Modification of PEG-*b*-PGA with pyridine groups leads to pH-sensitive micelle disassembly



ACKNOWLEDGEMENTS

Supervisory Panel


A/Prof. Anton Blencowe

Dr Todd Gillam

Dr Manuela Klingler-Hoffmann

Dr Hugo Albrecht

Dr Andrew J. Clulow (ANSTO co-supervisor)

Thank you to:  **raci**
Royal Australian Chemical Institute

- Royal Australian Chemical Institute Polymer Division O'Donnell Travel Bursary
- AINSE Postgraduate Research Award
- Australian Government RTP PhD Scholarship
- Gould Experimental Science Grant Commendation



Australian Government



Get in touch!



@Cintya_D_



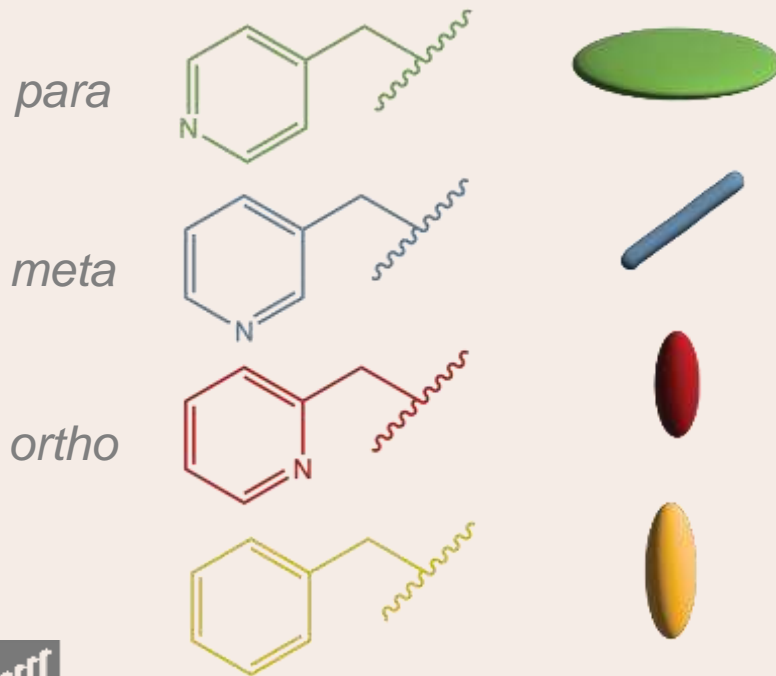
Figures created with



Applied Chemistry and Translational Biomaterials (ACTB) Group Members

QUESTIONS?

1. Position of regioisomers in PEG-*b*-PMG micelles governs dominant secondary structure and micelle morphology



2. Modification of PEG-*b*-PGA with pyridine groups leads to pH-sensitive micelle disassembly

