Macromolecules Innovation Institute
At the intersection of science, engineering, and society

DEPARTMENT OF CHEMISTRY

HOMOGENEOUS NANODISCS OF NATIVE MEMBRANES FORMED BY STILBENE–MALEIC-ACID COPOLYMERS

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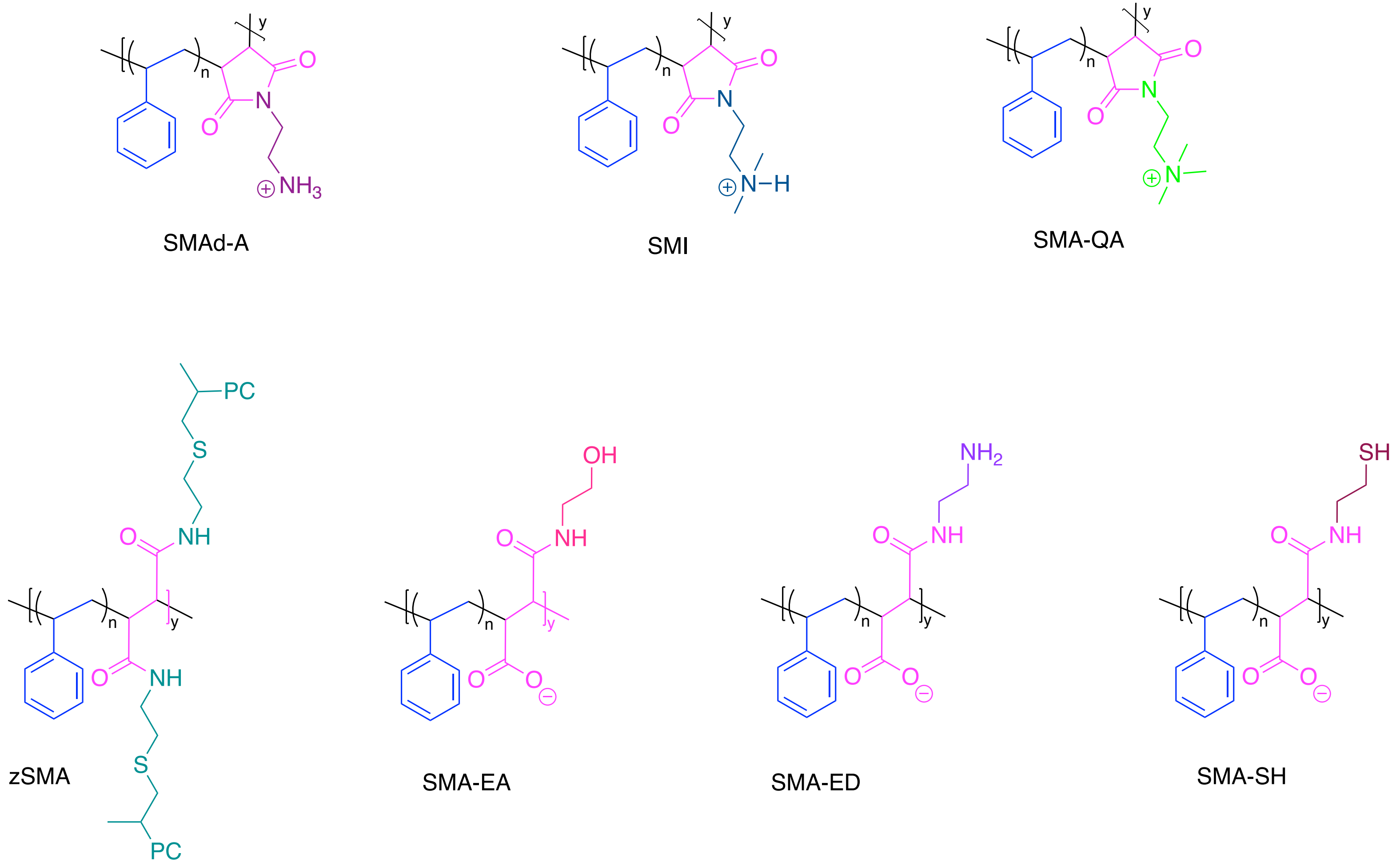
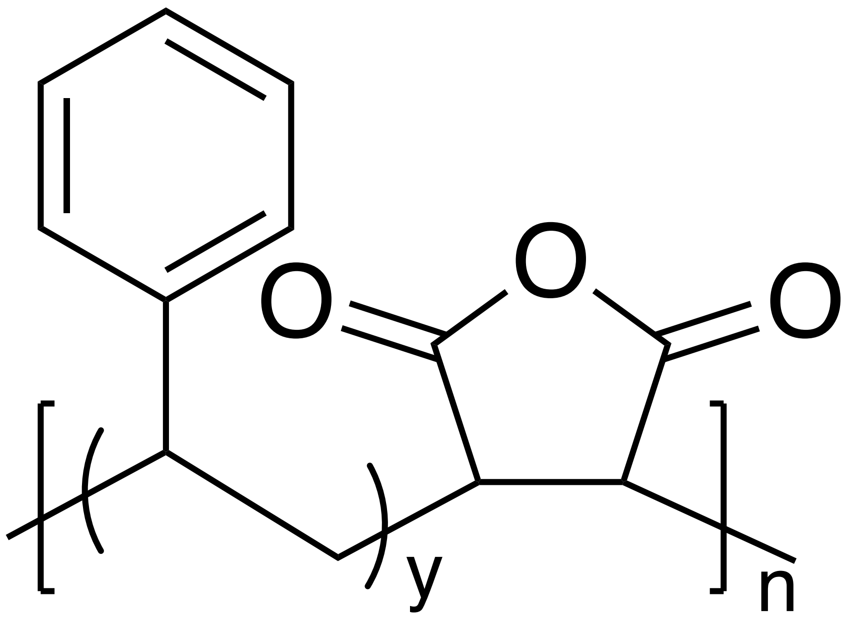
SMA ANALOGUES HAVE BEEN DESIGNED TO ADDRESS SHORTCOMINGS OF SMA



Ravula. T., et al., *Angew. Chem. Int. Ed.* **2018**, 57, 1342–1345.
Ravula. T., et al., *Angew. Chem. Int. Ed.* **2017**, 56, 11466–11470.
Lindhound, S., et al., *Biomacromolecules*. **2016**, 17, 1516–1522.
Hall, S. C. L., et al., *Nanoscale*. **2018**, 10, 10609.
Fiori, M.C., et al., *Sci. Rep.* **2017**, **7,** 7432.
Ravula. T., et al., *Langmuir.* **2017**, 33, 10655–10662.

POLY(STYRENE-*co*-MALEIC ANHYDRIDE)



Yao, Z., et al., *J. Appl. Polym. Sci.* **2011,** 121, 1740−1746.

Conventional Solution Radical Polymerization

- Radical Initiators (e.g. AIBN)
- Solvents (e.g. THF)
- Dispersity ~1.5–2
- Compositional drift at high conversion

Commercial/Continuous Stirred Tank Reactor

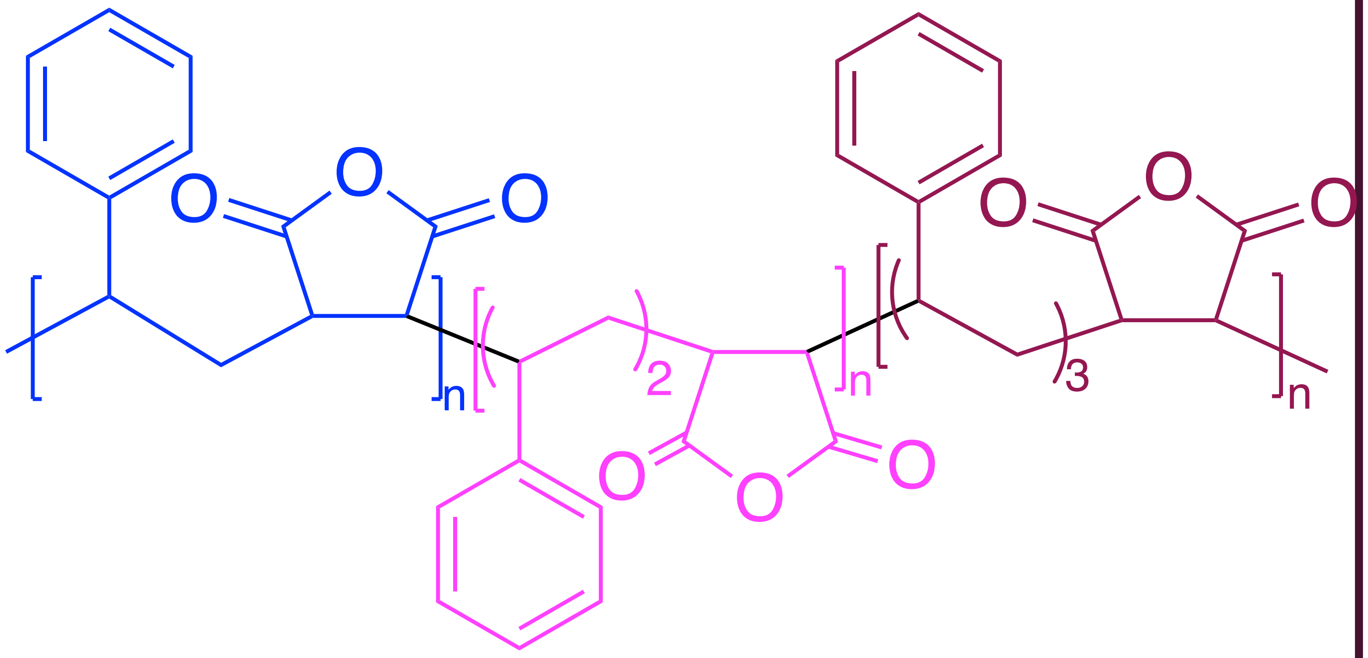
- High Temperatures
- Little/No Solvent
- Dispersity ~2–5
- Control of monomer composition via equilibrium

Montaudo, M. *Macromolecules*. **2001,** *34,* 2792-2797. Klumperman, B., *Polym. Chem*. **2010**, 1, 558–562.

POLY(STYRENE-*co*-MALEIC ANHYDRIDE)

RAFT Controlled Radical Polymerization

- Low Molecular Weight
- Narrow Dispersity
- Predictable Compositional Gradient
  - Variation of [S]:[MA] and [Total Monomer]:[RAFT]
  - Composition affects SMALP formation and protein extraction efficiency
- Styrene-rich Blocks
  - Consistent [Total Monomer]:[RAFT] while variation in [S]:[MA]
  - Composition affects nanodisc size

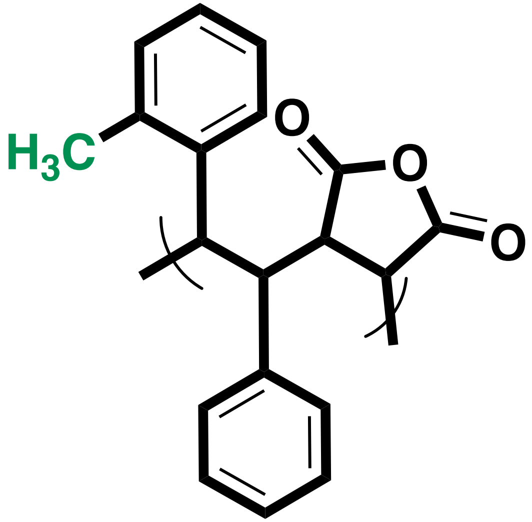


Yao, Z., et al., *J. Appl. Polym. Sci.* **2011,** 121, 1740–1746.

Smith, A. A., et al.; *Biomacromolecules*. **2017.** 18, 3706–3713.

Craig, A. F., et al., *Biochim. Biophys. Acta, Biomembr.,* ***2016****, 1858, 2931–2939.*

POLY(STILBENE-*alt*-MALEIC ANHYDRIDE)



- Sequence and compositional regularity via strict alternation
- Semi-rigid polymer backbone
- Similar hydrophobicity to 2:1 SMA

Savage, A. M, et al., Appl. Petrochem. Res., 2015, 5(1), 27–33.
Huang, J., et al., Macromol. Rapid Commun., 2018, 39, 1700530.
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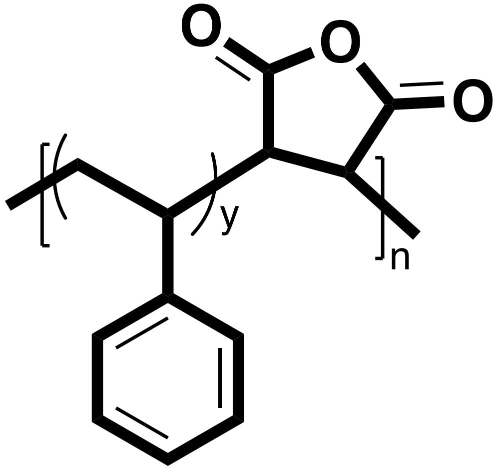
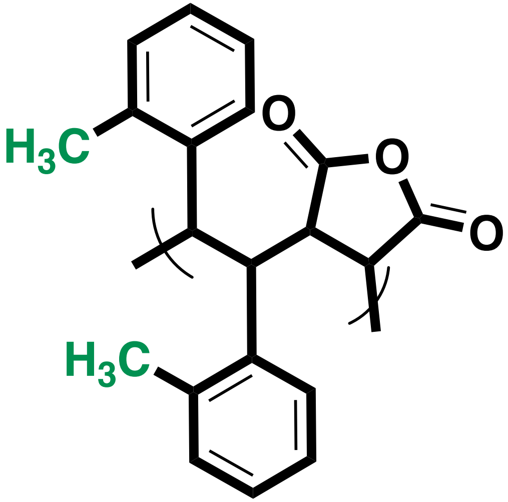


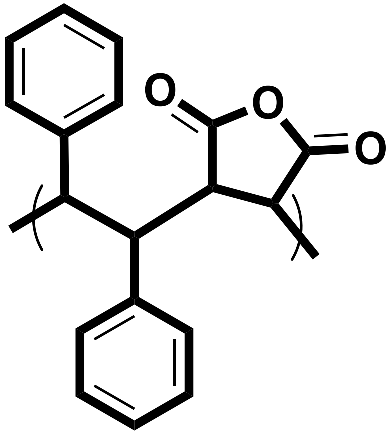
- Compositional regularity depends on method of polymerization
- The methylene group in each repeat unit decreases rigidity

Klumperman, B., *Polym. Chem.* **2010**, 1, 558–562.

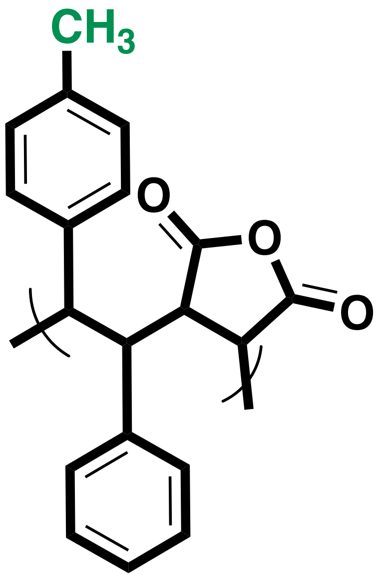
STRICTLY ALTERNATING STILBENE AND MALEIC ANHYDRIDE COPOLYMERS



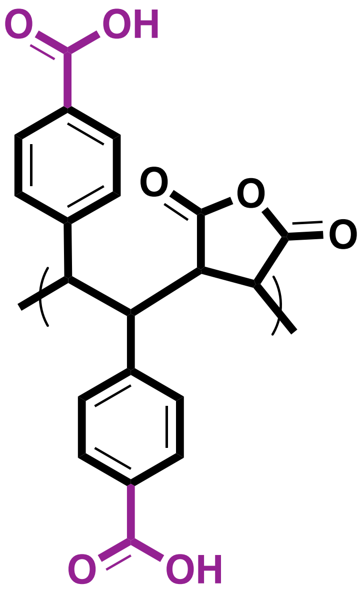
Mn = 5.1 kDa
Đ = 1.52



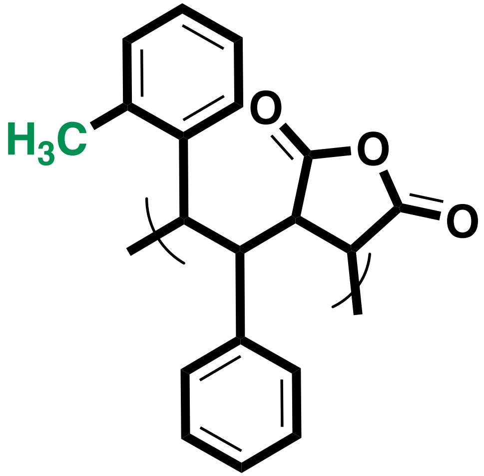
Mn = ND
Đ = ND



Mn = 5.8 kDa
Đ = 1.54



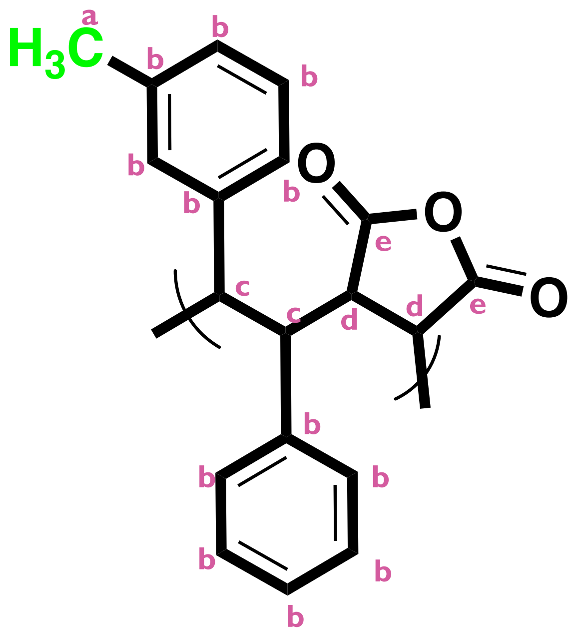
Mn = 40 kDa
Đ = 1.34



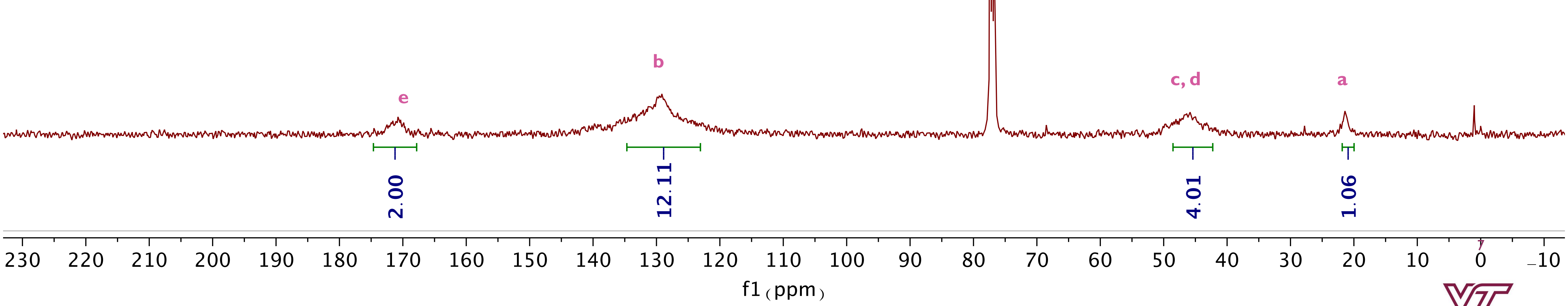
Mn = 4.4 kDa
Đ = 1.19

Esmaili, M., Brown, C.J., et al., *Nanoscale*, **2020**, 12, 16705–16709.

METHYL SUBSTITUTED STILBENE AND MALEIC ANHYDRIDE COPOLYMERS ARE STRICTLY ALTERNATING

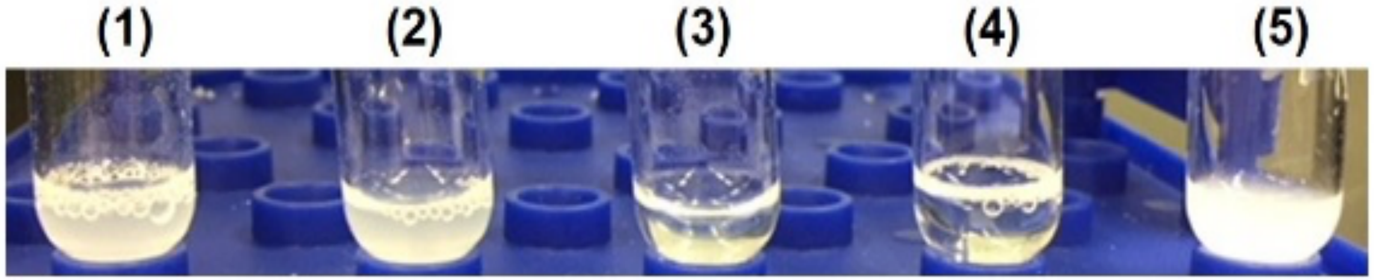


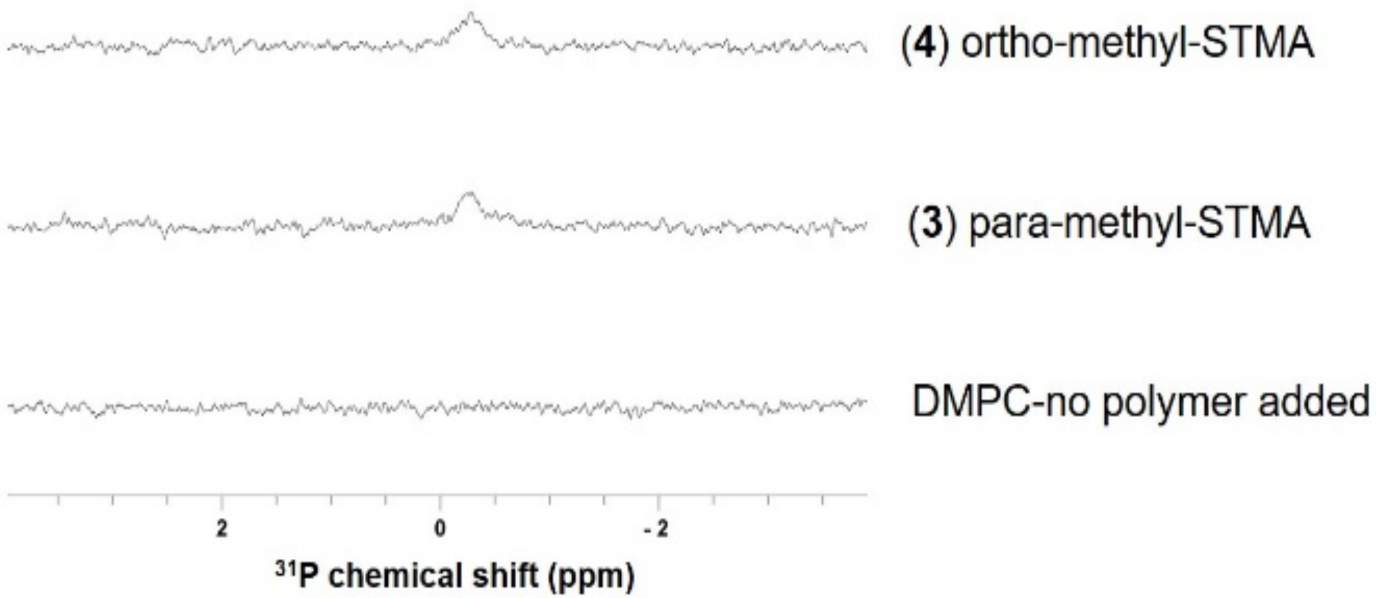
^{13}C NMR

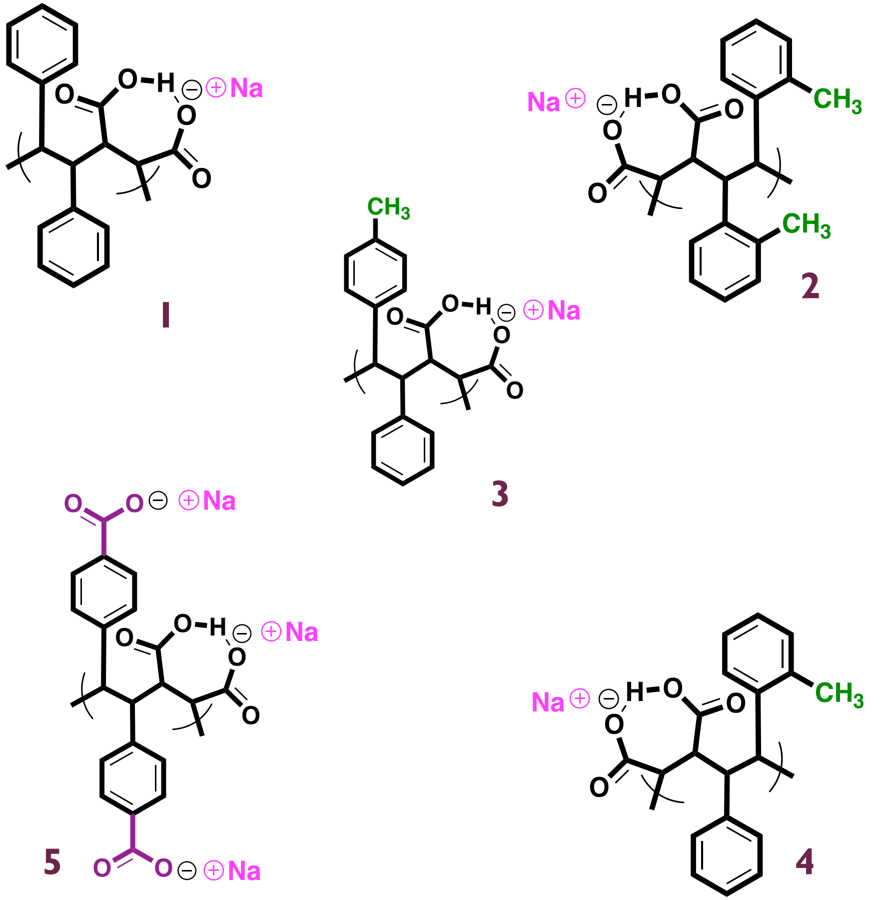


VIRGINIA TECH.

POLY(METHYL STILBENE-*alt*-MALEIC ACID) CAN SOLUBILIZE DIMYRISTOYLPHOSPHATIDYLCHOLINE (DMPC) VESICLES

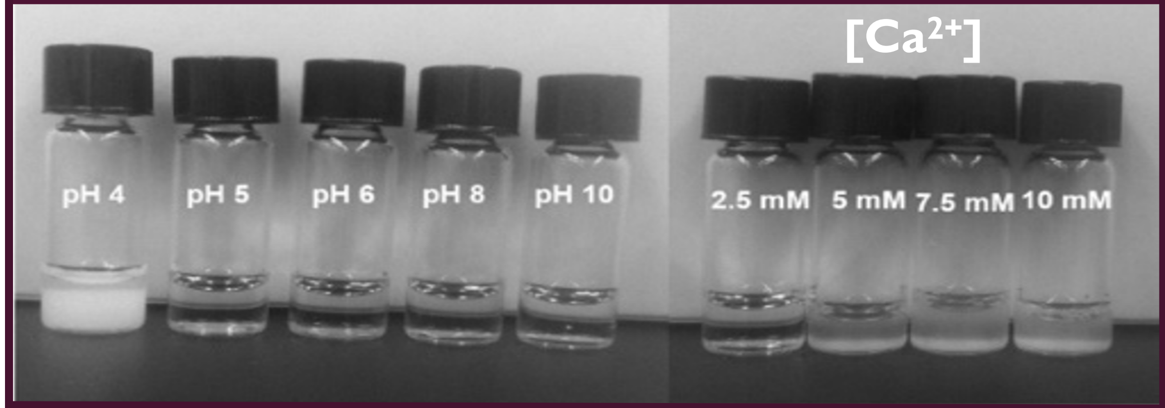


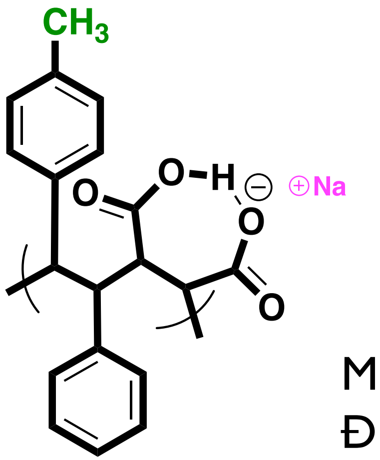




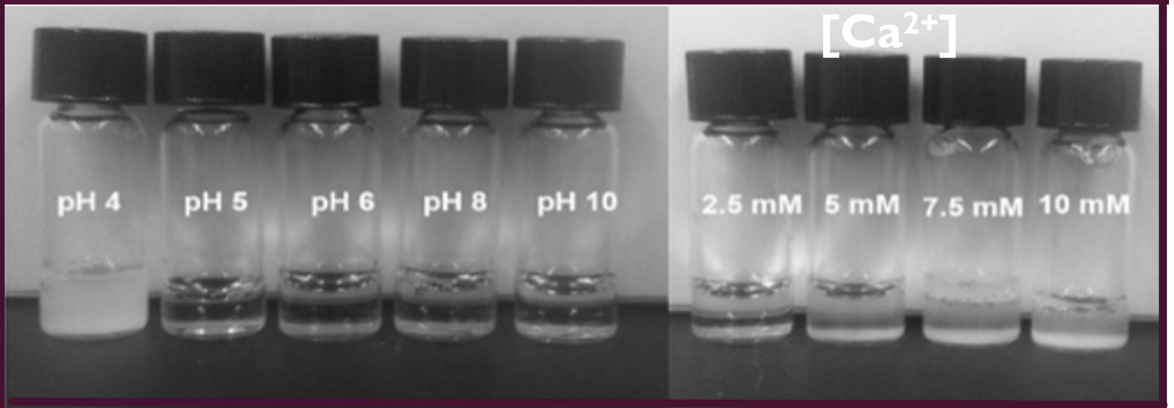
Esmaili, M., Brown, C.J., et al., *Nanoscale*, **2020**, 12, 16705–16709.

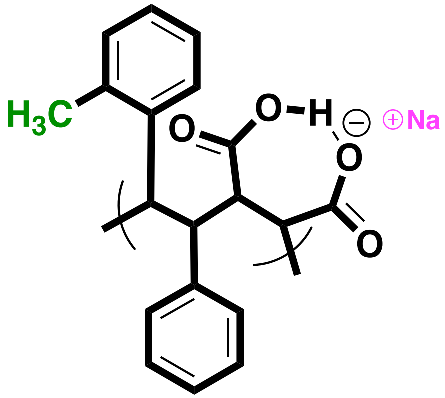
Ph & DIVALENT CATION TOLERANCE OF POLY(METHYL STILBENE-*alt*-MALEIC ACID)





Mn = 5.8 kDa
Đ = 1.54



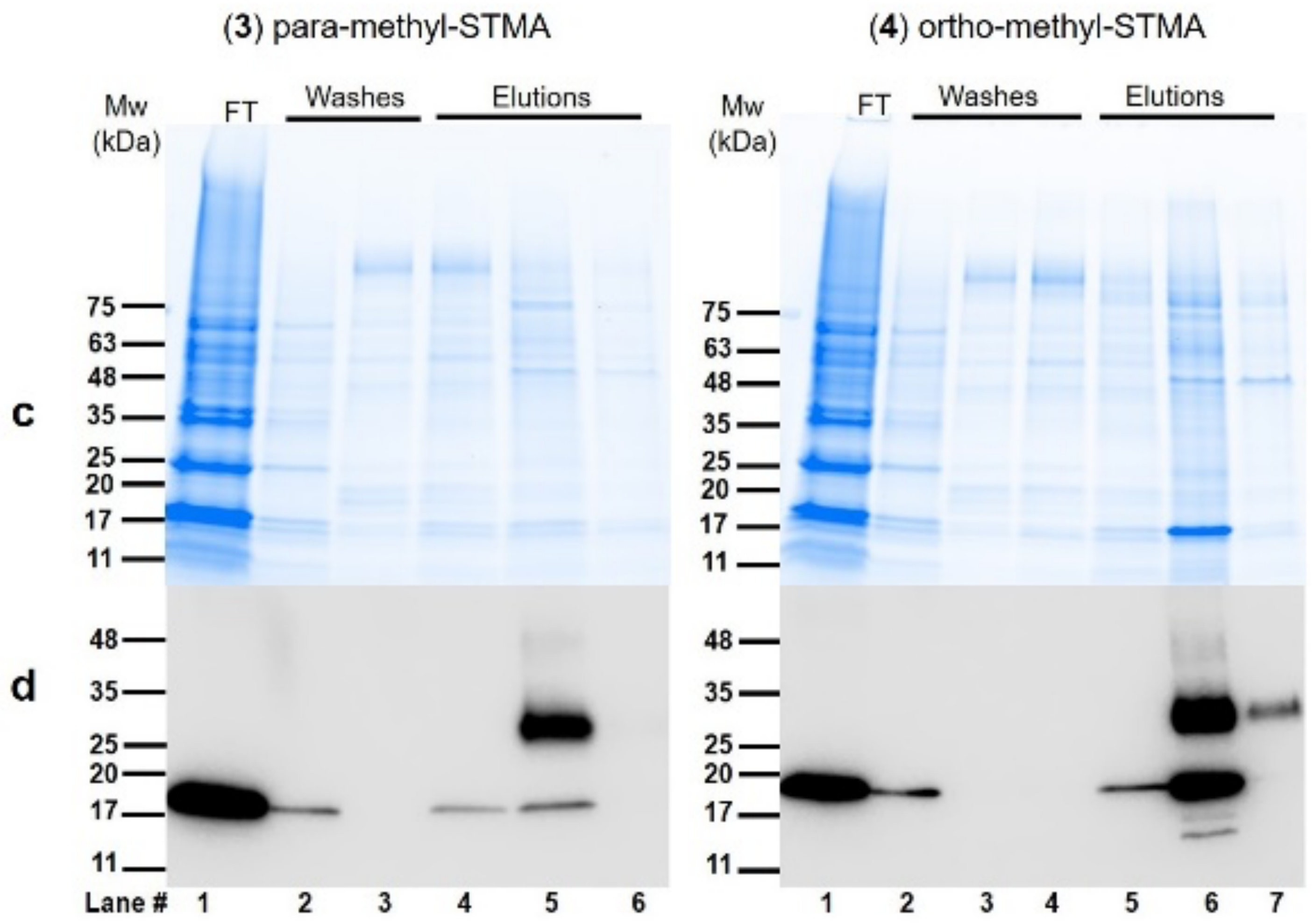


Mn = 4.4 kDa
Đ = 1.19

Esmaili, M., Brown, C.J., et al., *Nanoscale*, **2020**, 12, 16705–16709.

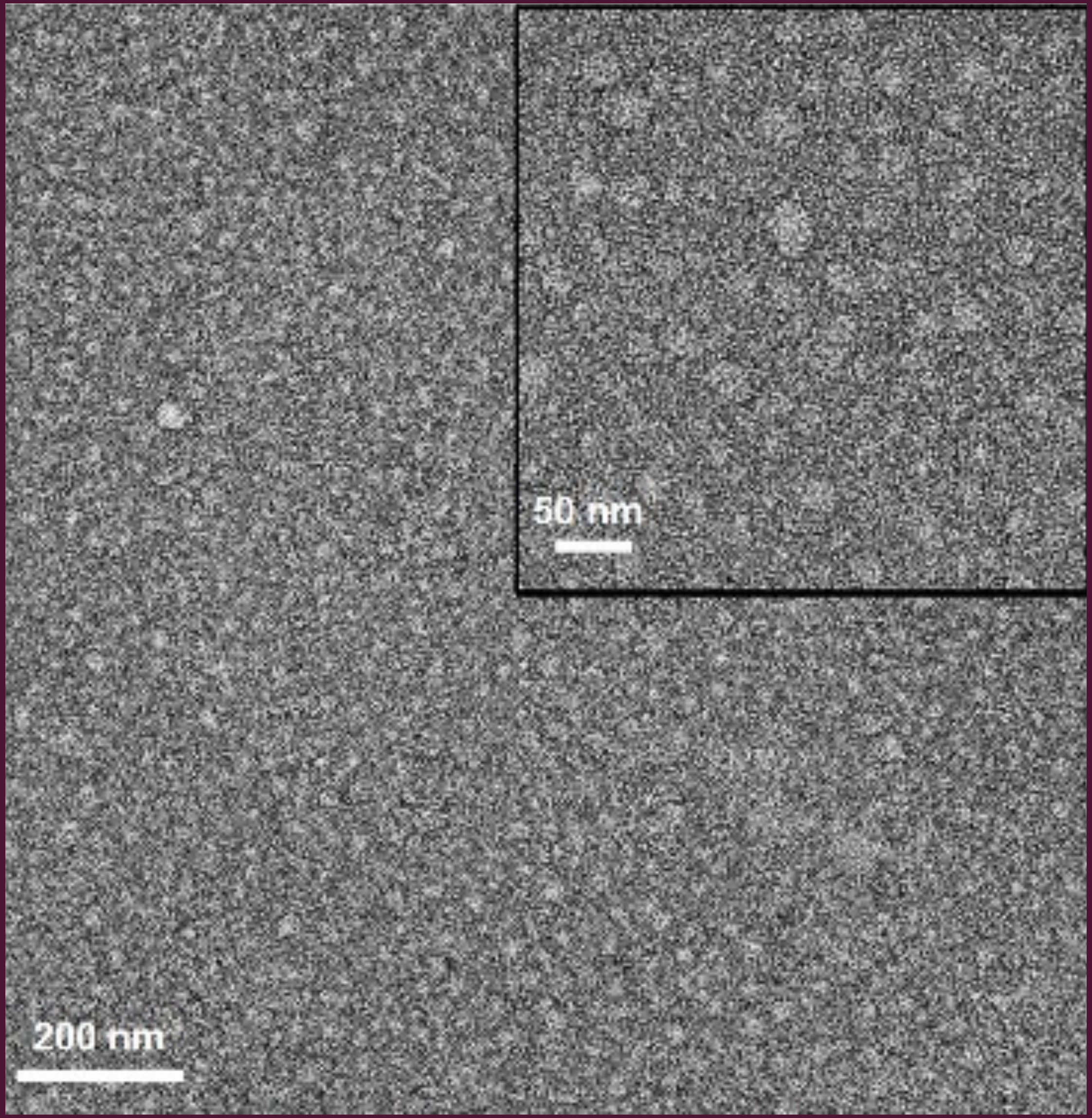
POLY(METHYL STILBENE-*ALT*-MALEIC ACID) CAN EXTRACT PAG-P PROTEIN FROM *E. COLI* OUTER MEMBRANE

- Pag-P–STMA nanodiscs are compatible with common metal affinity tags.
- 2-methyl-STMA appears to generate a higher yield of purified protein.



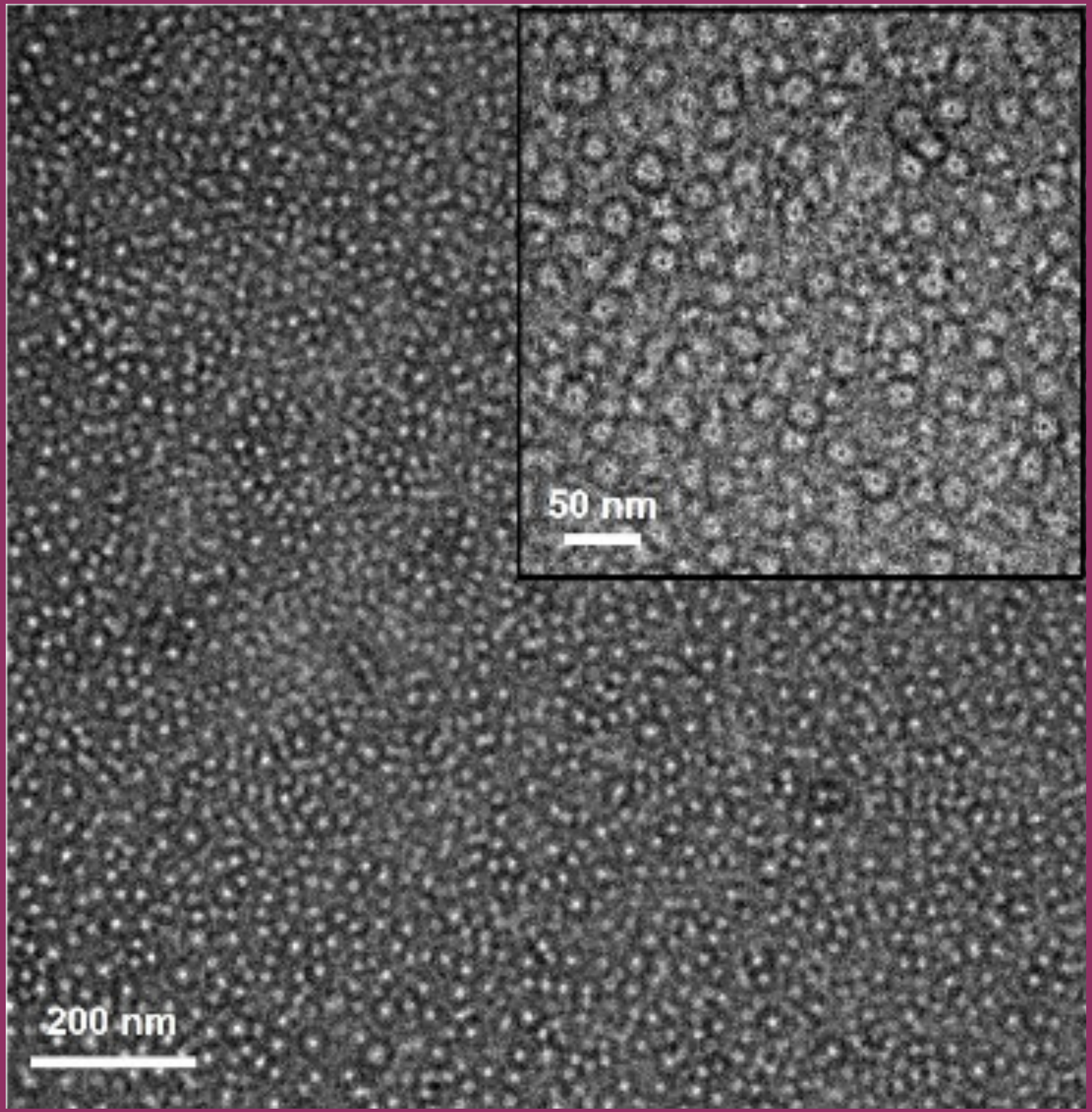
Esmaili, M., Brown, C.J., et al., *Nanoscale*, **2020**, 12, 16705–16709.

POLY(4-METHYLSTILBENE-*ALT*-MALEIC ACID) CAN EXTRACT PAG-P PROTEIN FROM *E. COLI* OUTER MEMBRANE



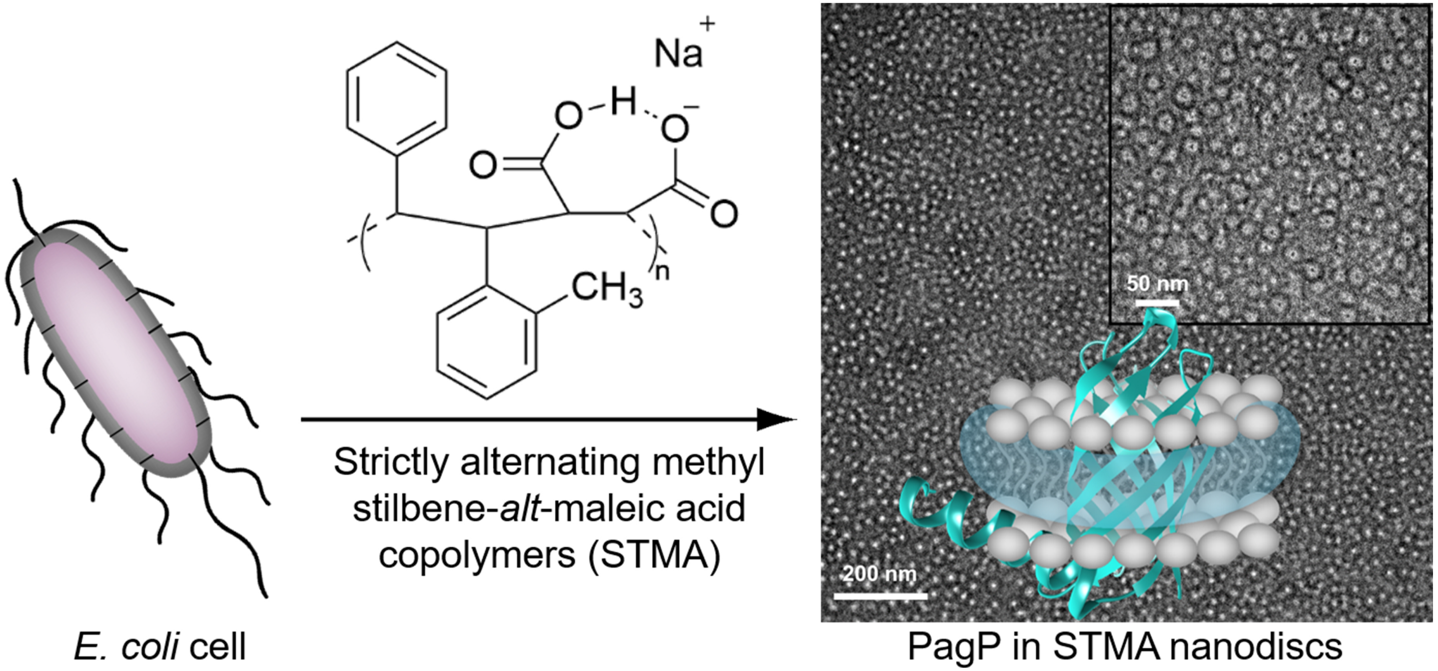
Esmaili, M., Brown, C.J., et al., *Nanoscale*, **2020**, 12, 16705–16709.

POLY(2-METHYLSTILBENE-*ALT*-MALEIC ACID) CAN EXTRACT PAG-P PROTEIN FROM *E. COLI* OUTER MEMBRANE



Esmaili, M., Brown, C.J., et al., *Nanoscale*, **2020**, 12, 16705–16709.

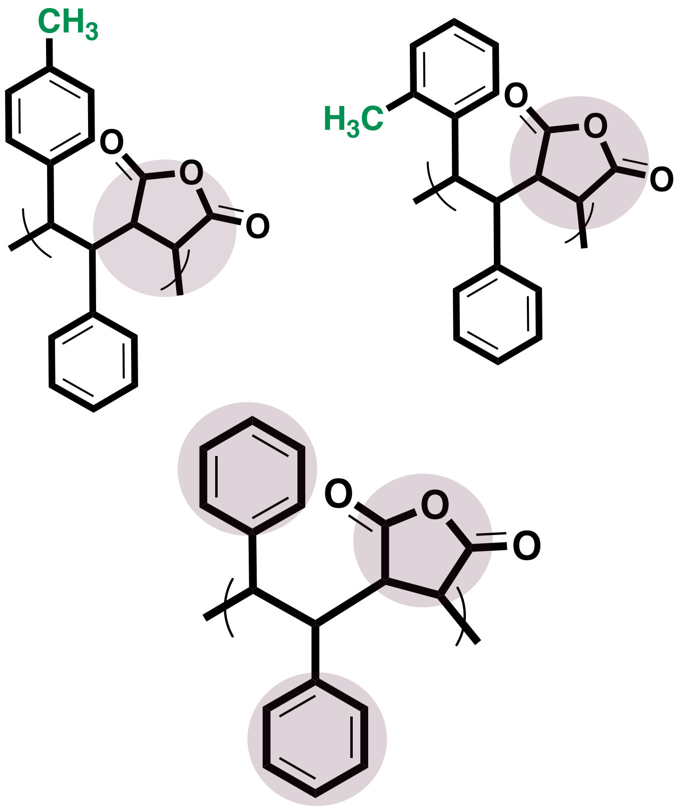
CONCLUSIONS



- Poly(4-methylstilbene-*alt*-maleic acid) and poly(2-methylstilbene-*alt*-maleic acid) are a class of amphiphilic copolymers that offer several advantages when compared to poly(styrene-*alt*-maleic acid):
  - Increased rigidity of the copolymer backbone
  - Sequence and Compositional regularity
  - Size of nanodiscs

Esmaili, M., Brown, C.J., et al., *Nanoscale*, **2020**, 12, 16705–16709.

FUTURE RESEARCH



Polymerization Methods and Processing

- Low Molecular Weight
- Narrow Dispersity
- Facile Purification

Post-polymerization Modifications

- Maleimide Functionalization
- Thiol Functionalization

Phenyl ring(s) Functionalization

- Use of other substituted/functionalized stilbenes (Wittig)

ACKNOWLEDGEMENTS

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