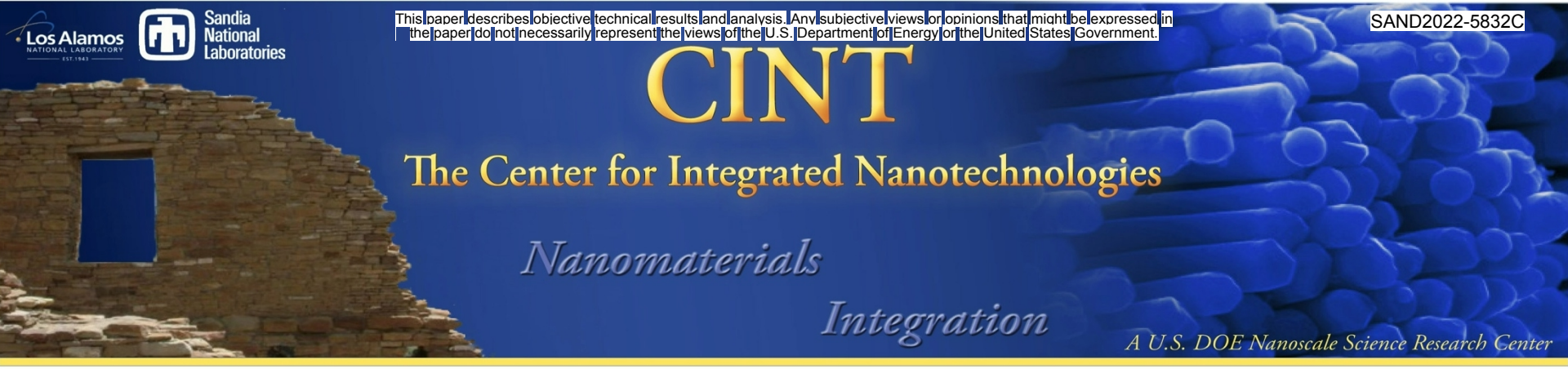
SAND2022-5832C



Double-Hydro*pH*ilic Polymersomes: Self-Assembly/Disassembly at Biologically-Relevant pH

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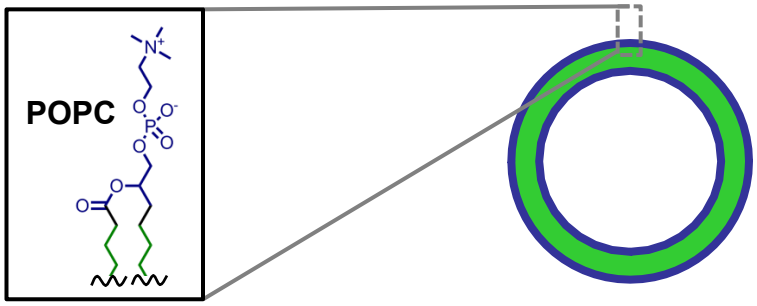
Mimicking Biological Membranes

Properties
- Radial/Axial Asymmetry
- Chemical Diversity
- Functional Components

Functions
- Mass transport
- Energy transduction
- Information flow
- Protection

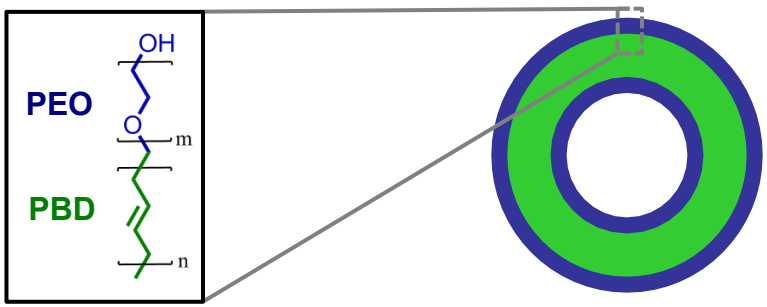
How can we incorporate or mimic **properties** and **functions** of biological cells to create robust **advanced materials**?

Liposomes



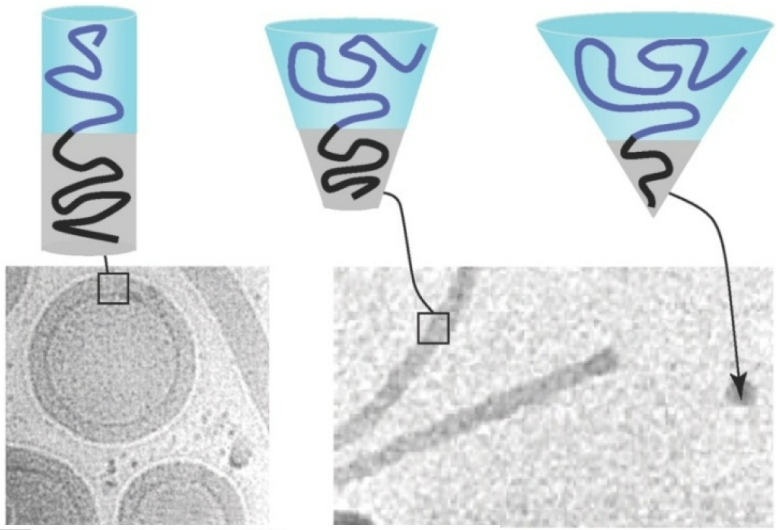
2 Major Challenges:
Limited Chemical and Mechanical Stability
Limited Modification Chemistries

Polymersomes

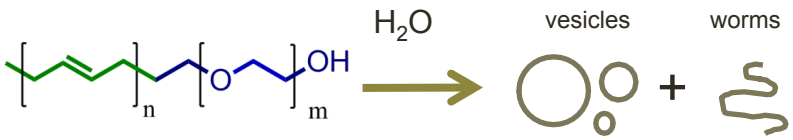


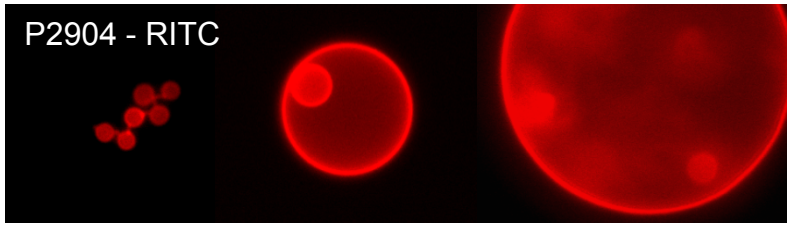
Polymersomes Can Help
Enhanced Chemical and Mechanical Stability
Unlimited Modification Chemistries

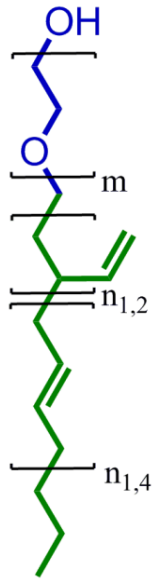
PEO-PBd Polymer Vesicles



Discher DE, Ahmed F. 2006.
Annu. Rev. Biomed. Eng. 8:323–41





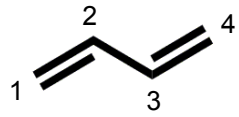


ring opening

1,2 addition

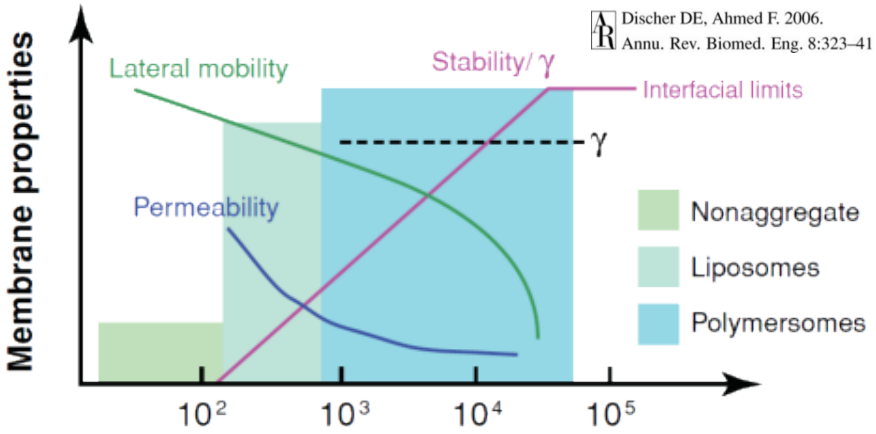
1,4 addition

ethylene oxide



butadiene

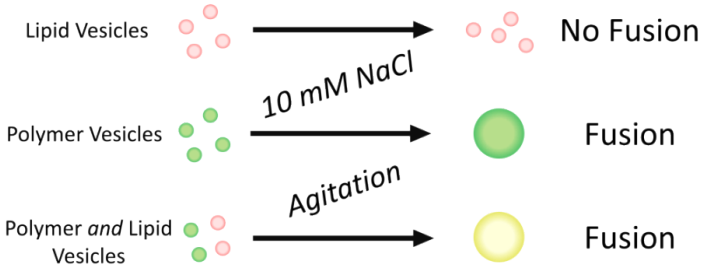
Polymer Source Inc.

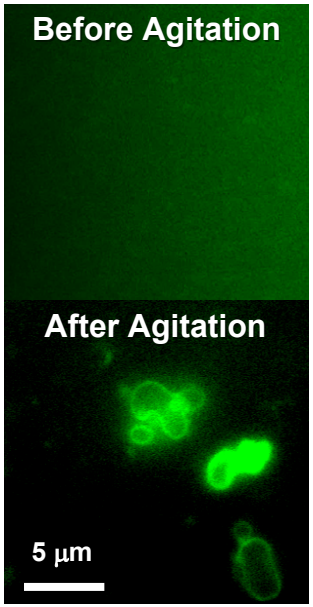


Discher DE, Ahmed F. 2006.
Annu. Rev. Biomed. Eng. 8:323–41

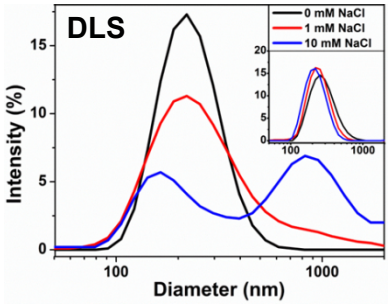
Dynamic Polymer Vesicle Membranes

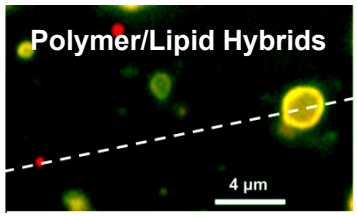
Mechanically-Activated Fusion





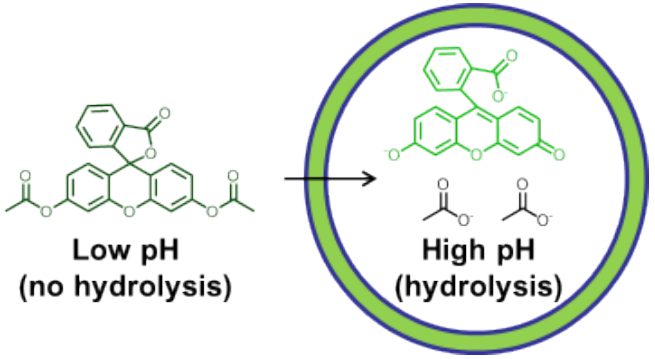
Vesicle Sizes After Agitation





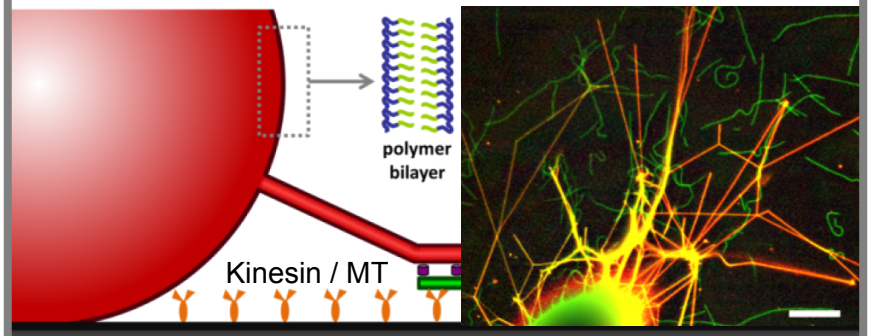
I. M. Henderson, W. F. Paxton, *Angew. Chem. – Int. Ed.* ***2014,*** *53,* 3372-3376; *J. Poly. Sci. B,* **2014,** *53,* 297–303

Lysosome-Mimicking Vesicles



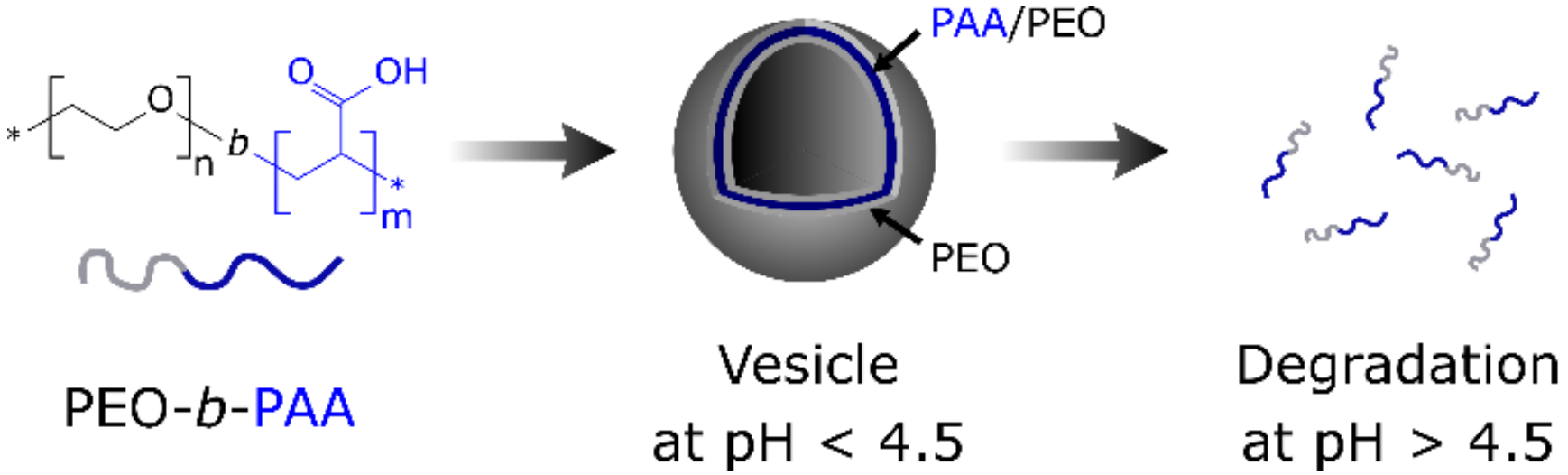
W. F. Paxton et al. *Soft Matter* **2013,** *9,* 11295–11302

Dynamic Assembly of Polymer Nanotubes



W. F. Paxton et al. *Nanoscale,* **2015,** *7,* 10998–11004

pH-Switchable Polymers

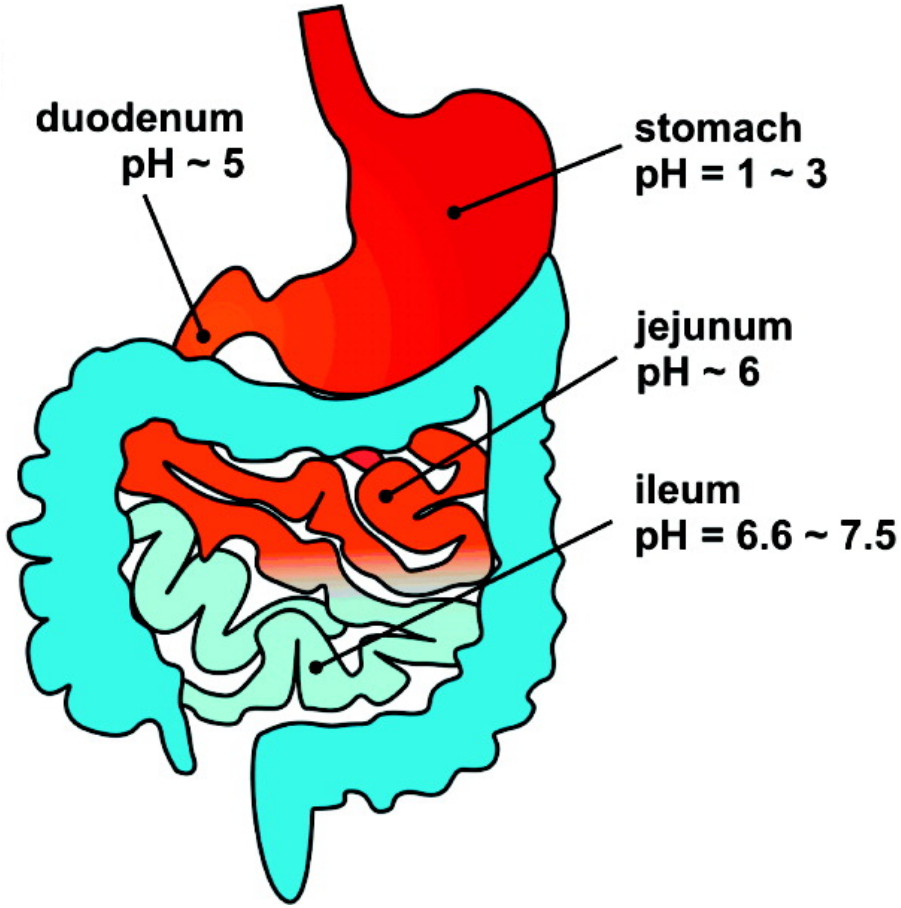


PEO-*b*-PAA

Vesicle
at pH < 4.5

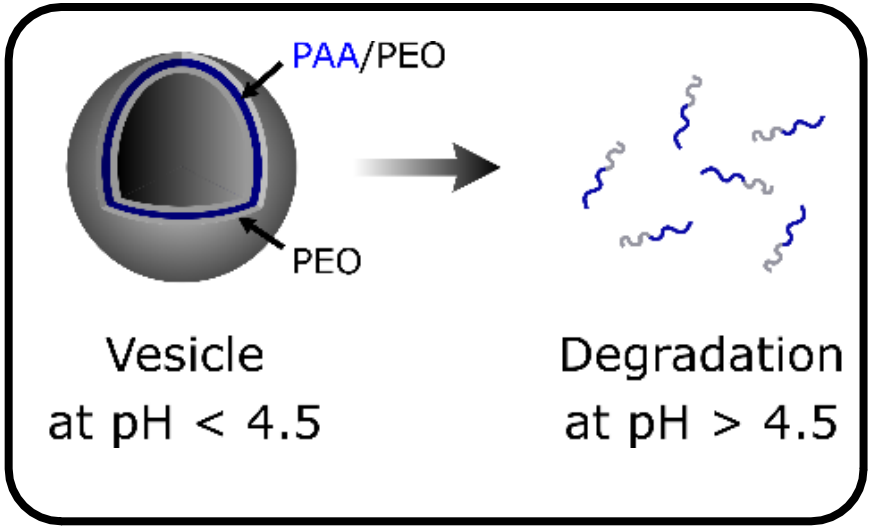
Degradation
at pH > 4.5

Drug Delivery and pH



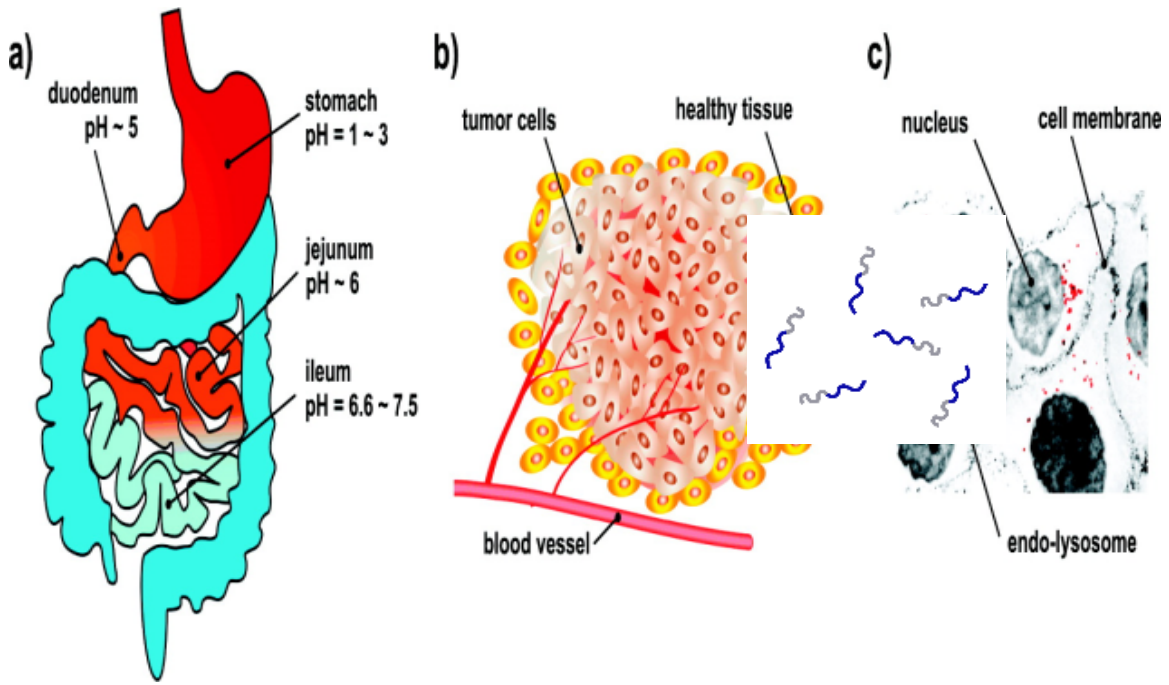
Oral Delivery is easy, convenient, and cheap…

…BUT strong acid and enzymatic degradation reduces bioavailability of some drugs and proteins (e.g. insulin) .



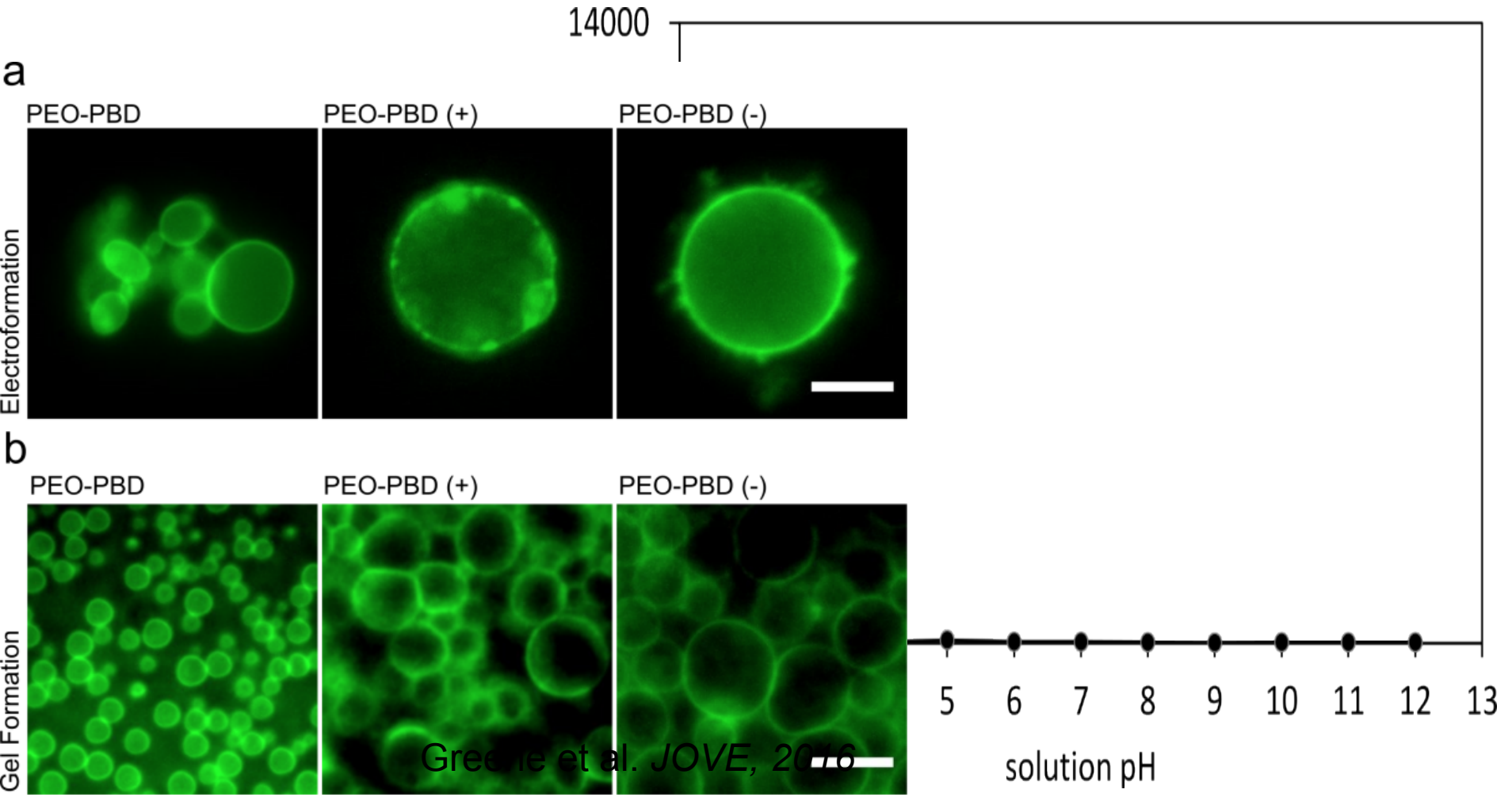
Gao et al. *Molecular Pharmaceutics,* **2010,** *7,* 1913

DLS of EO-AA



Hydrodynamic diameter of aggregates formed by PEO-PAA polymer in aqueous solution at various pH and (b) count rate of same solution.

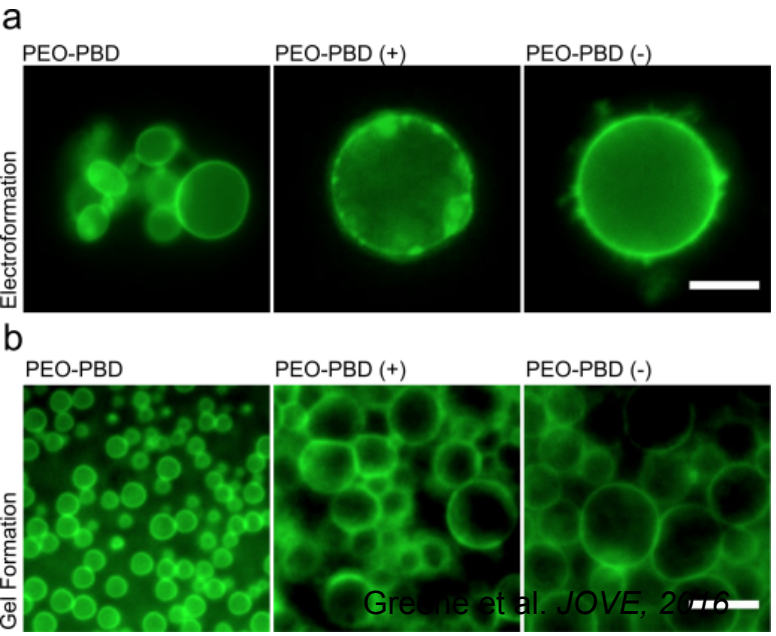
Gel Assisted Rehydration



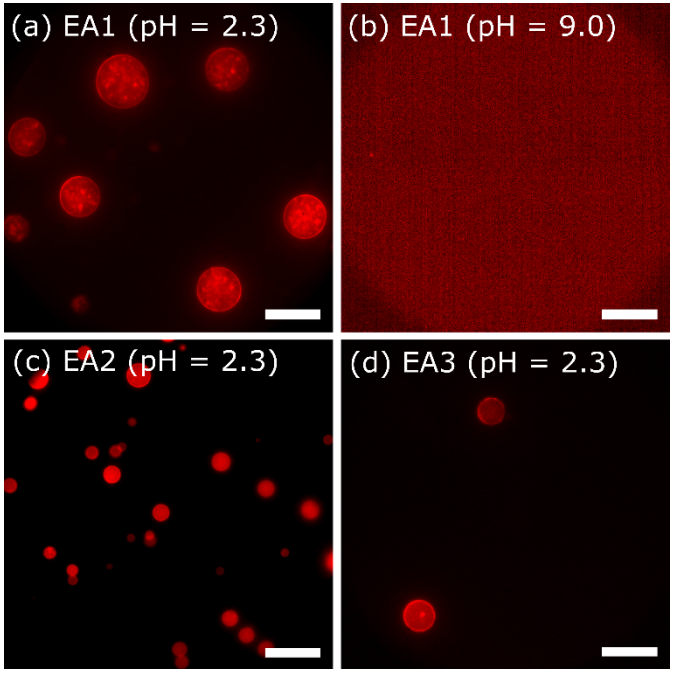
Greene et al. *JOVE, 2016*

Greene et al. *PLOS One, 2016*

EO-AA Vesicles at Low pH



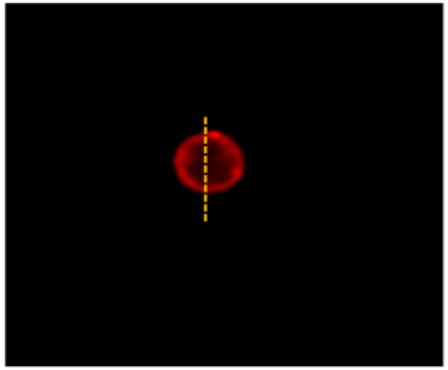
Greene et al. *JOVE, 2016*

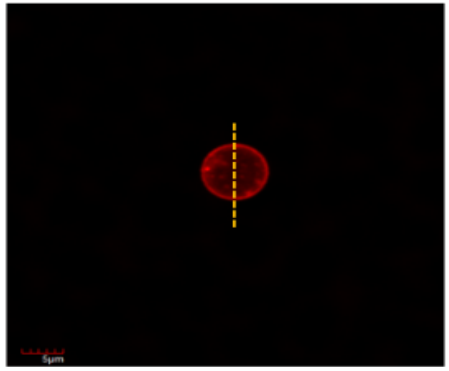


Designated name	Formula[a]	f_{EO}[b]
EA1	EO_{45}-AA_{56}	0.33
EA2	EO_{45}-AA_{21}	0.57
EA3	EO_{68}-AA_{18}	0.70

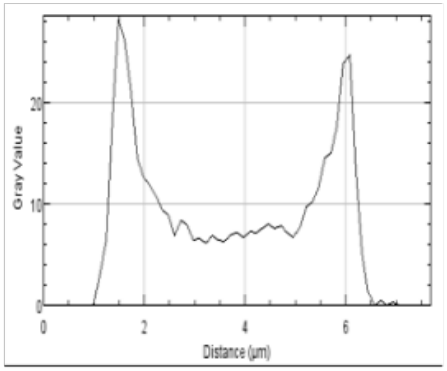
But are they *REALLY* vesicles?

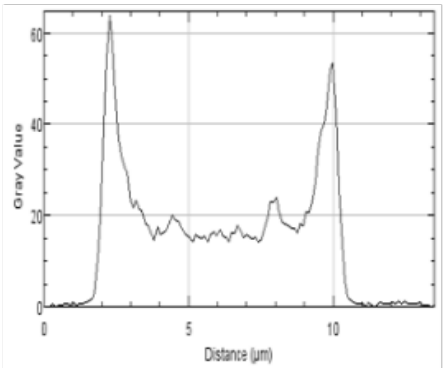
confocal



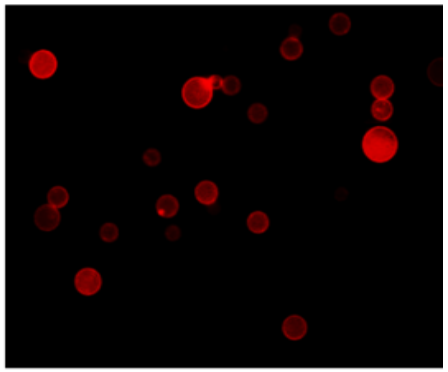


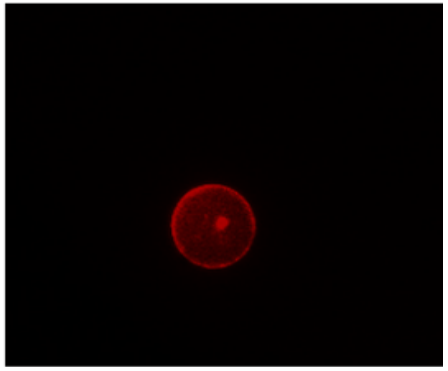
confocal





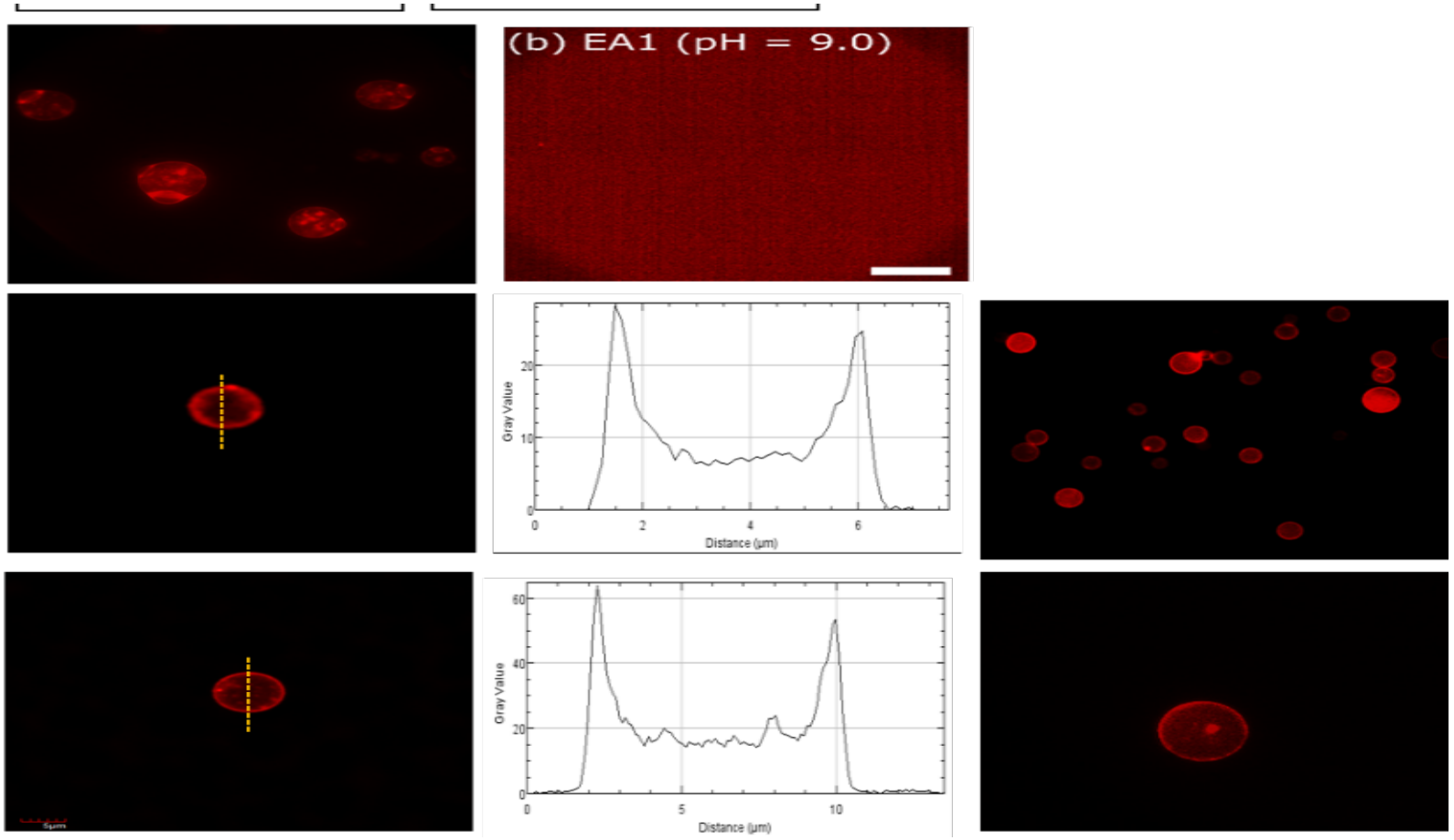
epifluorescence



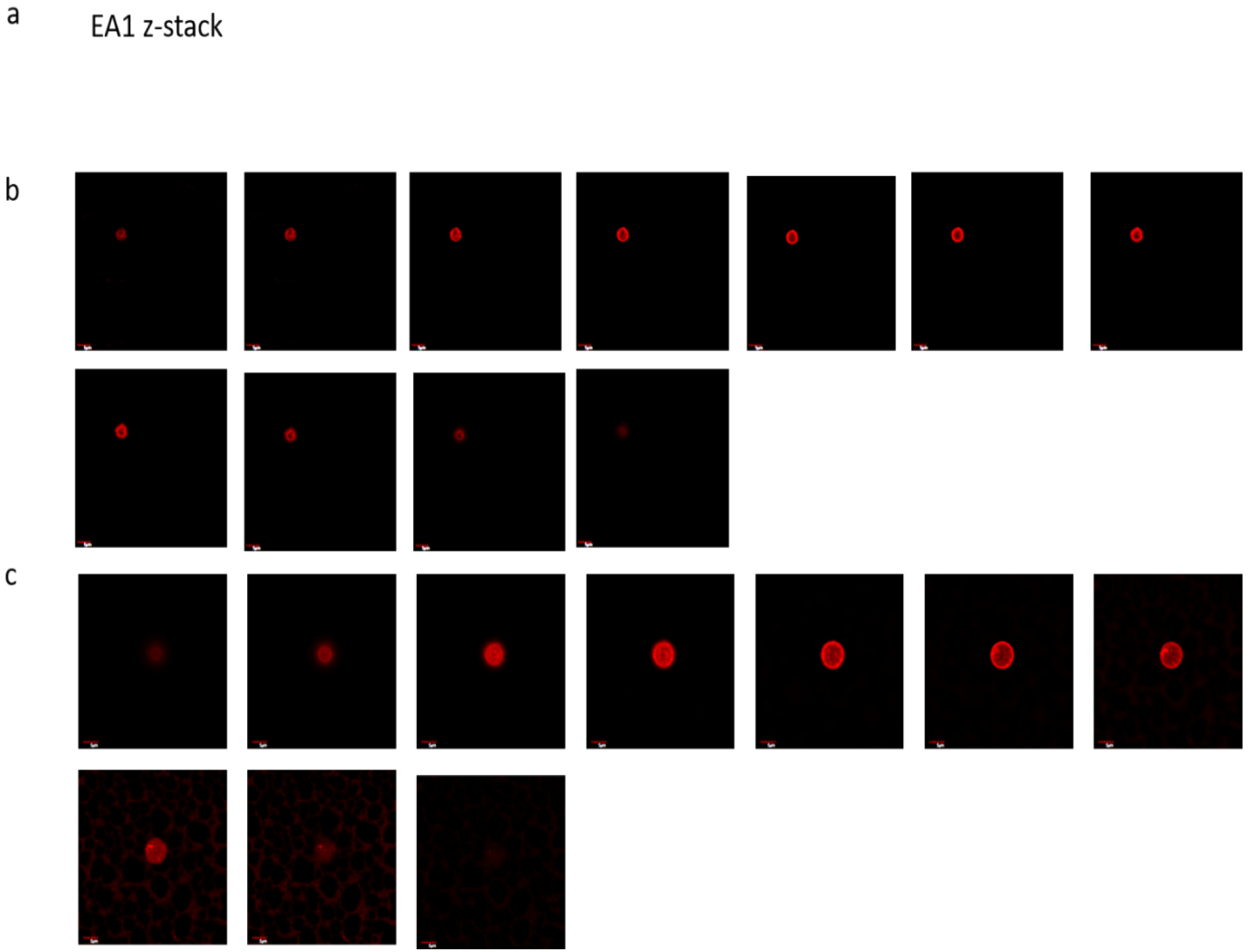


YES!

Confocal z-Stacks reveal Spherical Vesicles



Cryo Electron Microscopy

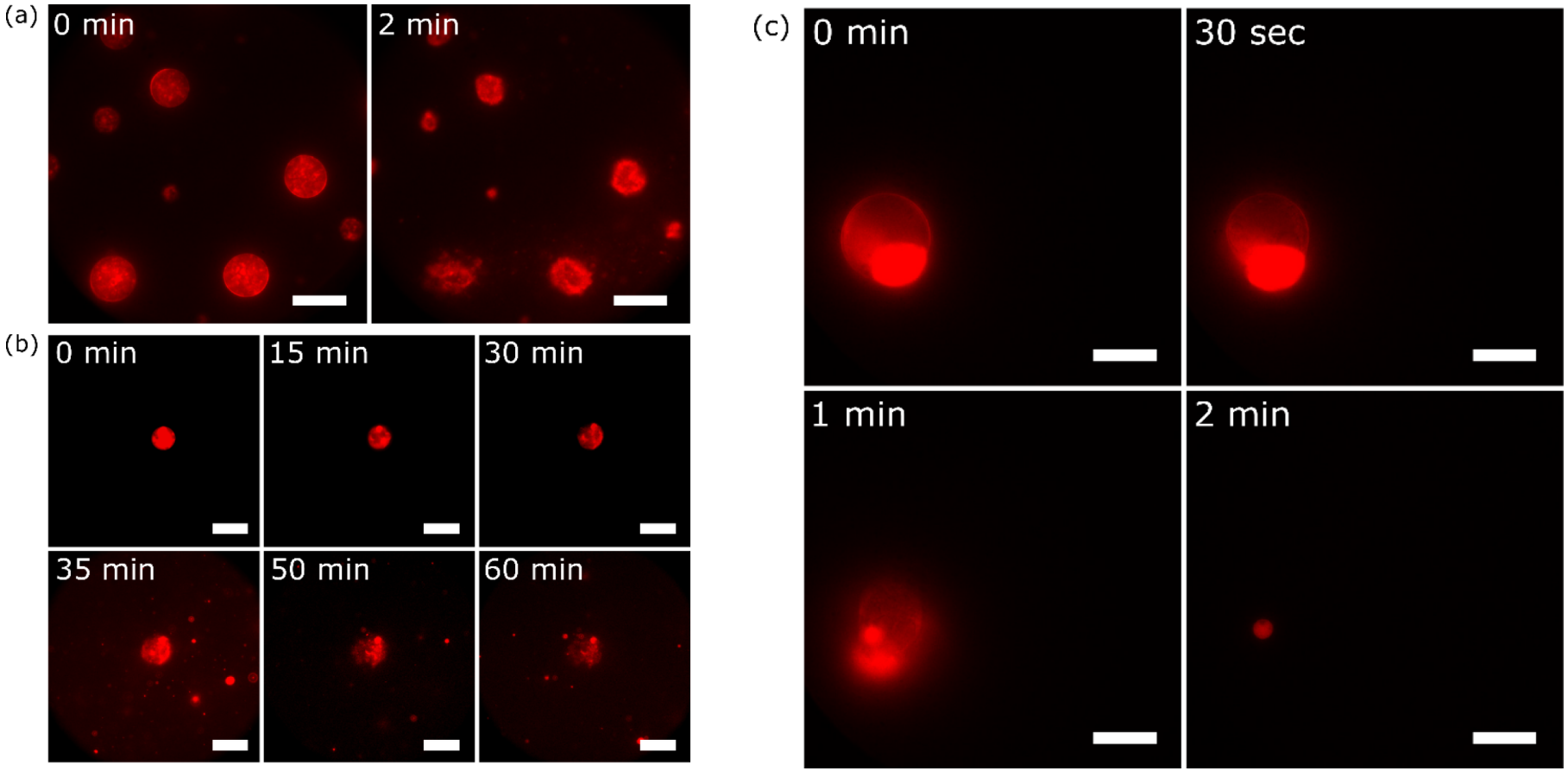


Small vesicles transposed to cryoEM grid

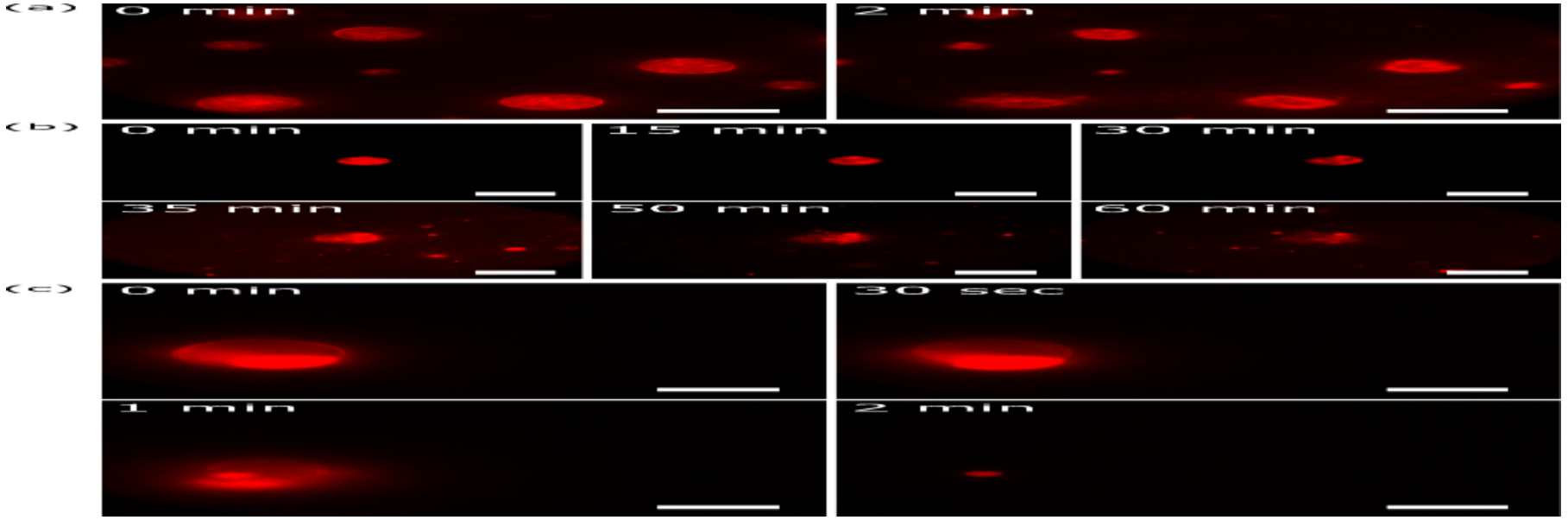
Membrane thickness 27 +/- 6 nm

pH Sensitivity of EO-AA Vesicles

pH-sensitive PEO-PAA vesicles. Epifluorescence microscopy images of (a) **EA1**, (b) **EA2**, and (c) **EA3** vesicles after addition of NaOH (iso-osmolar solution) showing degradation of PEO-PAA vesicles at pH 10.2 (scale bar = 20 µm).



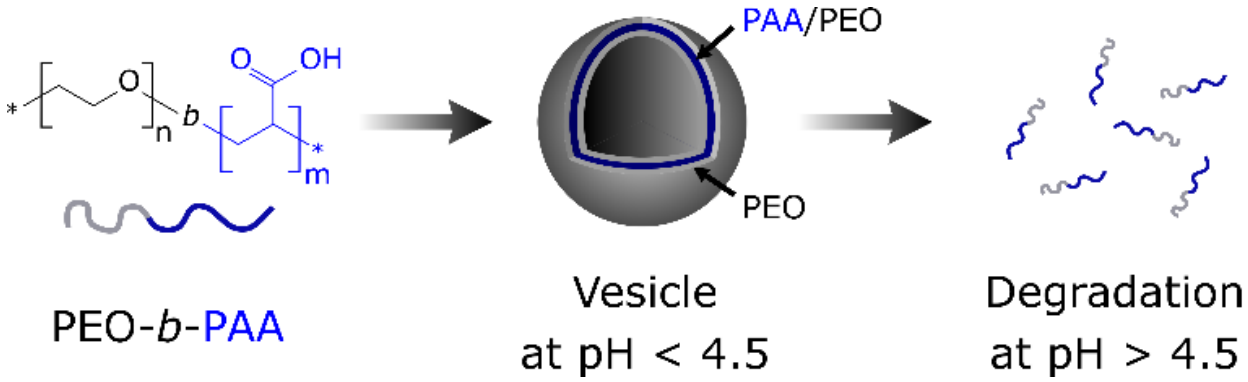
Encapsulation of Cargo



Epifluorescence microscopy images of PEO-PAA (**EA1**) vesicle with Texas Red filter and Alexa Fluor 488 filter, and merged image showing encapsulation of hydrophilic dye (green) within giant polymer vesicle (red) (scale bar = 20 µm).

Summary and Conclusions

- **Giant Polymer Vesicles from PEO-PAA.**
- **Vesicles are pH-sensitive over biologically-relevant pH.**
- **Vesicles capable of loading small-molecule cargo.**



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(NMSU)


Sergei Ivanov
(CINT)

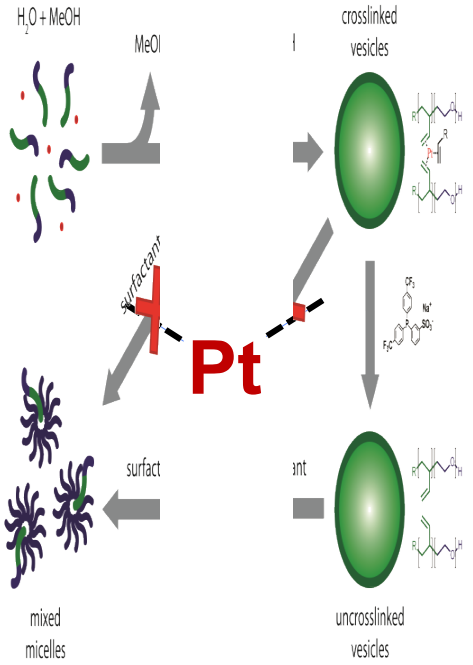
Center for Integrated Nanotechnologies

Helping you understand, create, and characterize nanomaterials

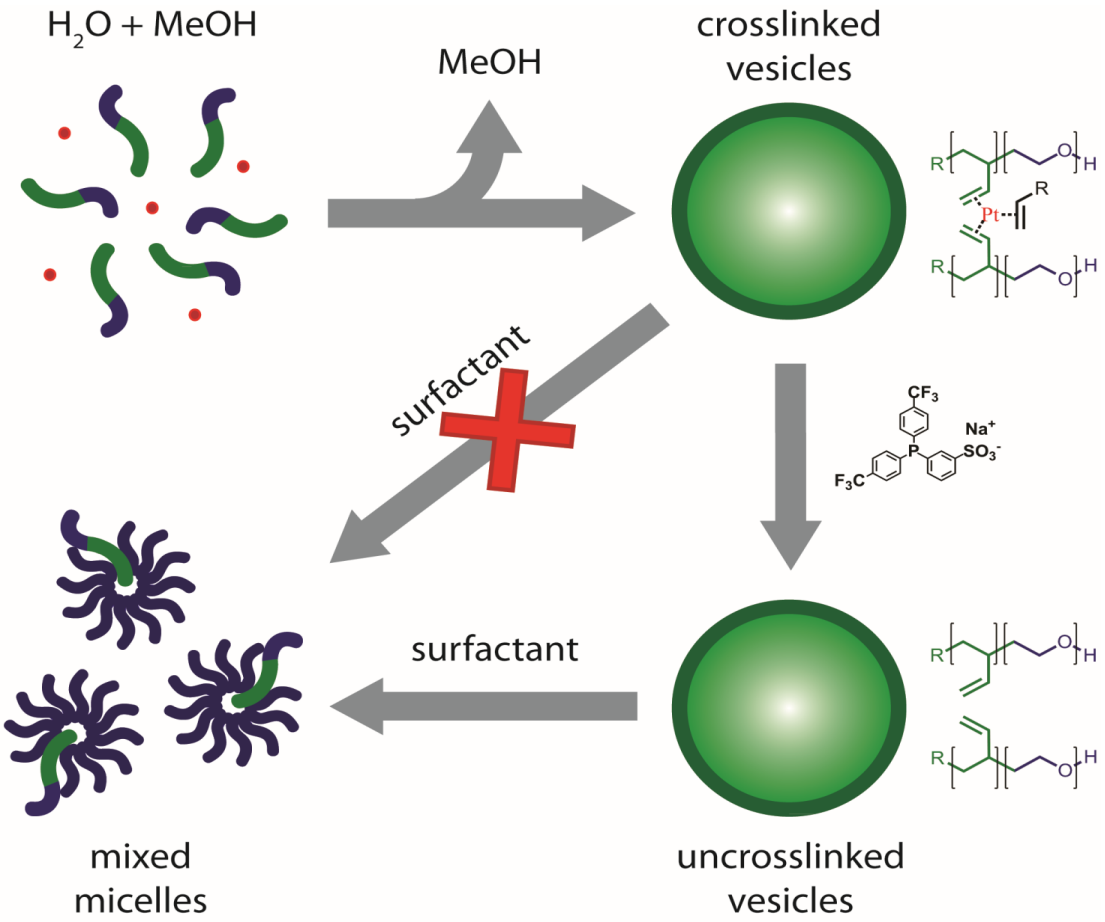
The DOE/SC nanoscience centers:

- Are defined by a scientific field, not specific instrumentation.
- NSRC staff support user projects and conduct original research.
- Capabilities involve expertise, hardware and software.
- Users access Synthesis, Fabrication, Characterization and Theory capabilities.

Capable Crosslinks: Polymersomes Reinforced with Catalytically Active Metal-Ligand Bonds



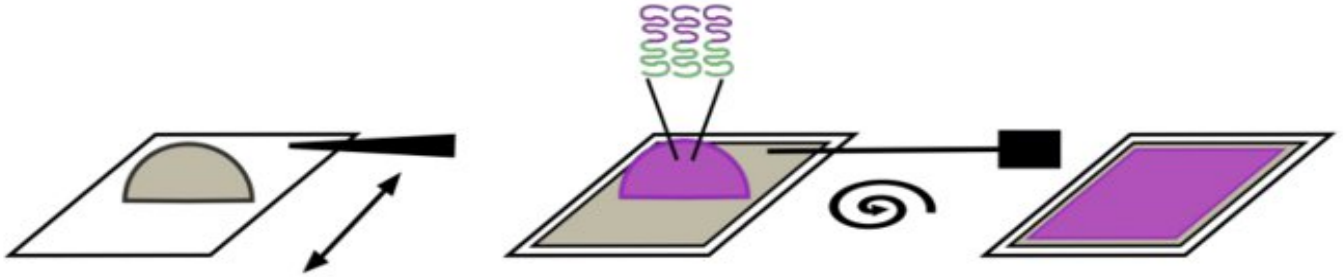
Exploit organometallic interactions to create membranes that are both ***robust*** and ***dynamic***.



1. Spread dissolved agarose on coverslip with a pipette tip

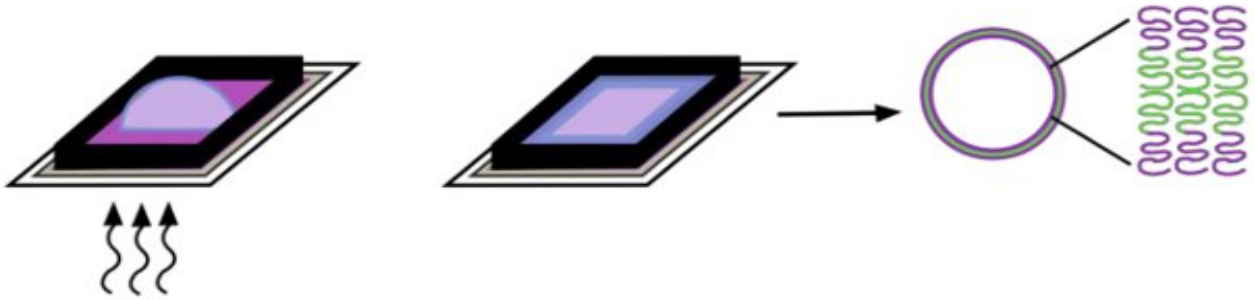
2. Spread polymer solution in circular motion on agarose films with needle

3. Dehydrate polymers on agarose films



4. Adhere a coverwell and rehydrate polymers with desired solution and heat

5. Image directly on an inverted microscope



EO-AA interactions