# CINT

The Center for Integrated Nanotechnologies

*Nanomaterials*

*Integration*

*A U.S. DOE Nanoscale Science Research Center*

SAND2016-8633C

# Polymersomes:
# Dynamic Polymer Vesicle Membranes from Amphiphilic Block Co-Polymers

***Walter F. Paxton***

*Center for Integrated Nanotechnologies / Sandia National Laboratories*

Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company,
for the United States Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000

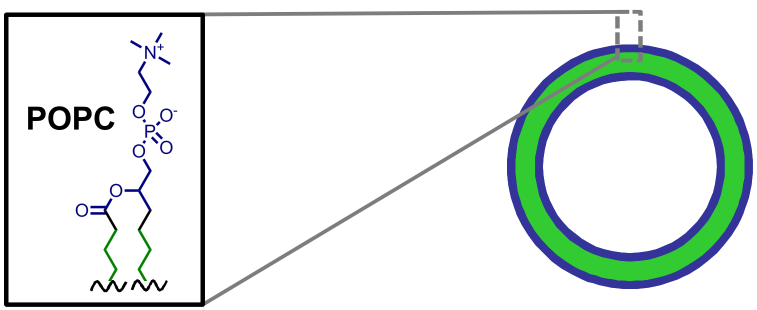
# Mimicking Biological Membranes

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

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

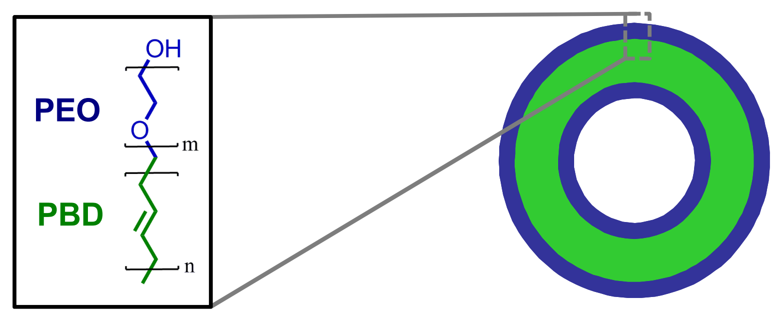
How can we incorporate or mimic **properties** and **functions** of biological cells to create robust **advanced materials**?

## Liposomes



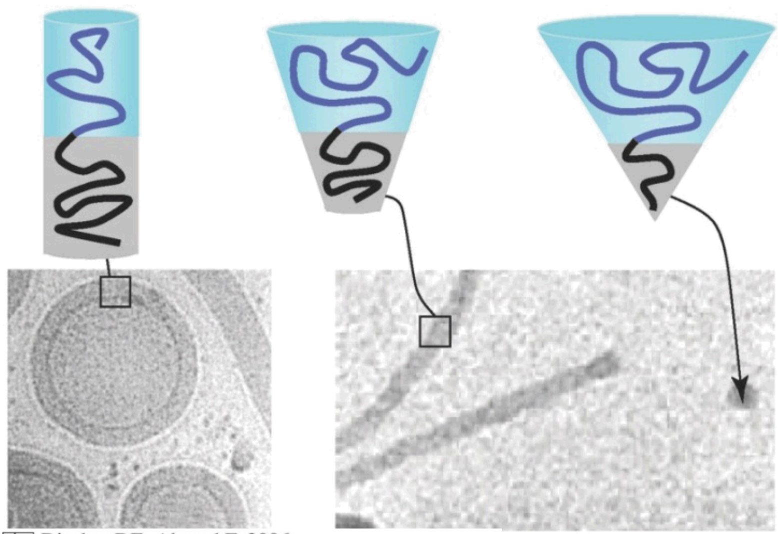

**2 Major Challenges:**
Limited Chemical and Mechanical Stability
Limited Modification Chemistries

## Polymersomes

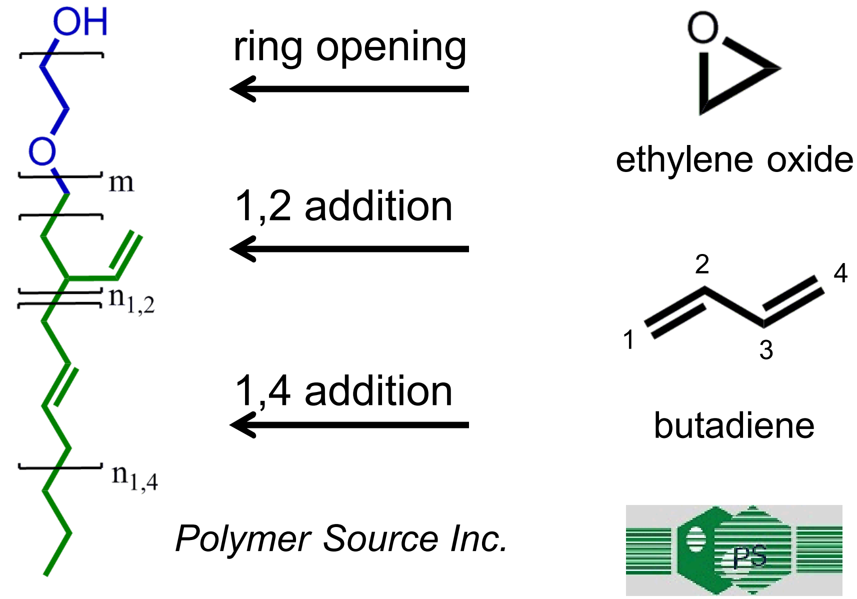


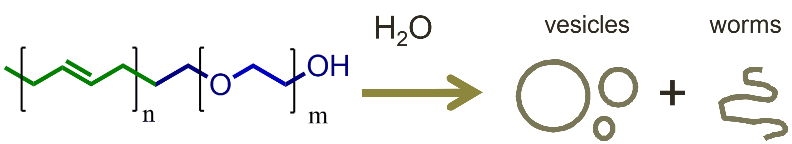

**Polymersomes Can Help**
*Enhanced* Chemical and Mechanical Stability
*Unlimited* Modification Chemistries

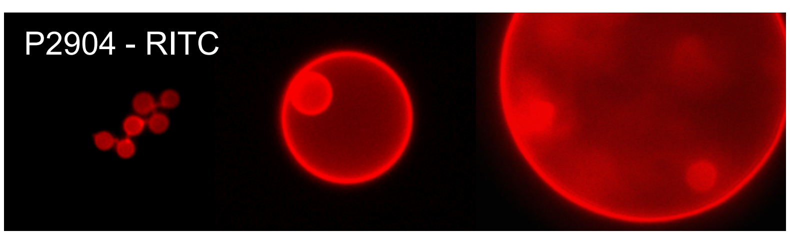
# PEO-PBd Polymer Vesicles

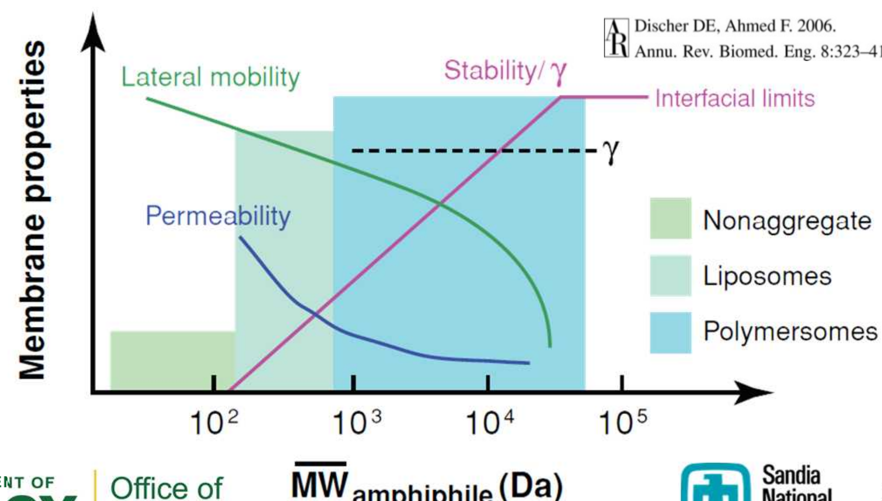


Discher DE, Ahmed F. 2006.
Annu. Rev. Biomed. Eng. 8:323–41



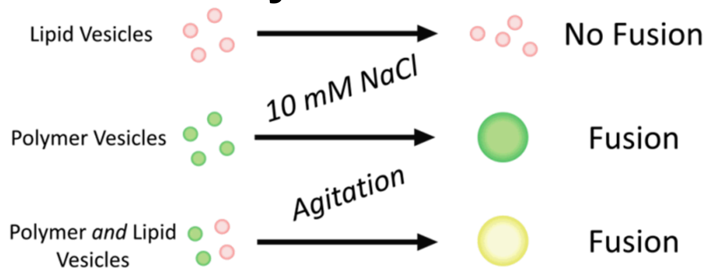



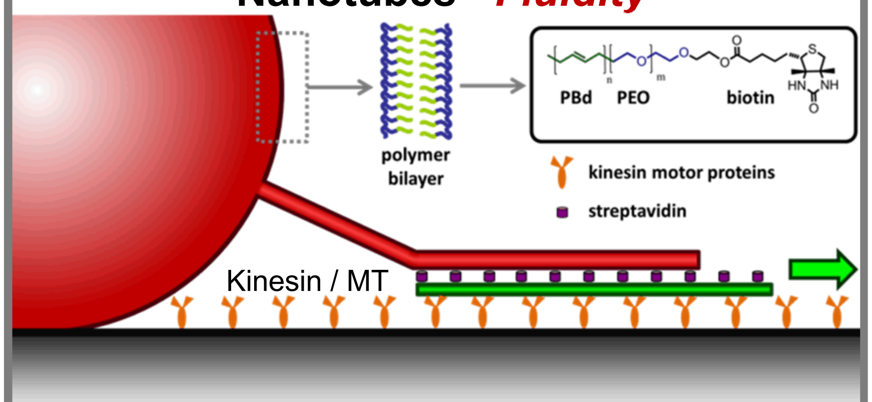
# *Dynamic* Polymer Vesicle Membranes

## Mechanically-Activated *Fusion*



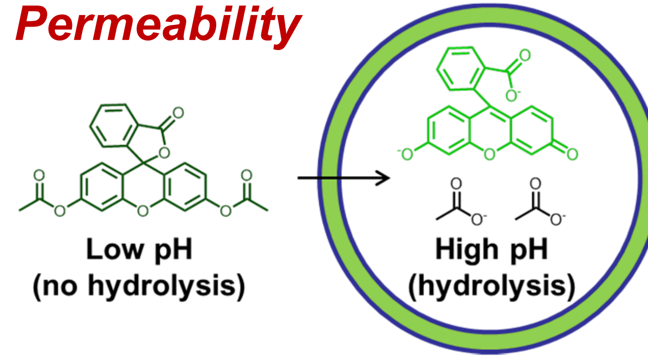

I. M. Henderson, W. F. Paxton, *Angew. Chem. – Int. Ed.* ***2014,*** *53,* 3372-3376; *J. Poly. Sci. B,* **2014,** *53,* 297–303

## Dynamic Assembly of Polymer Nanotubes - *Fluidity*



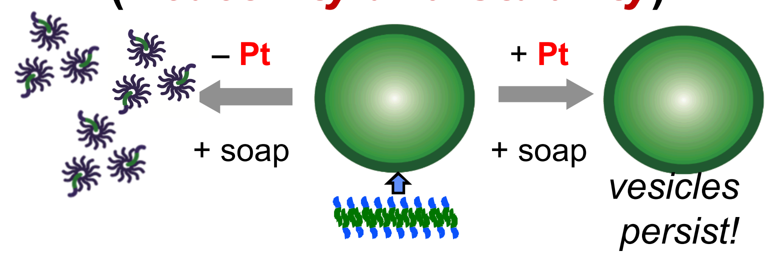

W. F. Paxton et al. *Nanoscale,* **2015,** *7,* 10998–11004

## Lysosome-Mimicking Vesicles *Permeability*




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

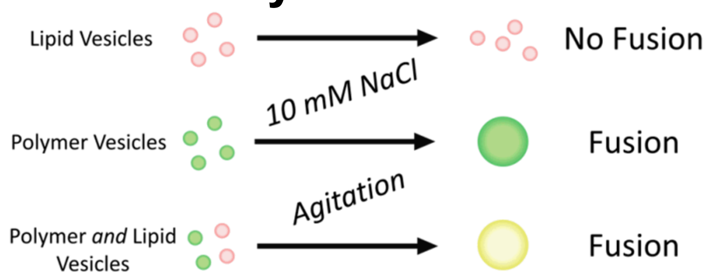
## Catalytically-Active Cross-Links (*Reactivity and Stability*)




W. F. Paxton et al. *Chem. Mater,* **2015,** *27, 4808–4813*

# *Dynamic* Polymer Vesicle Membranes

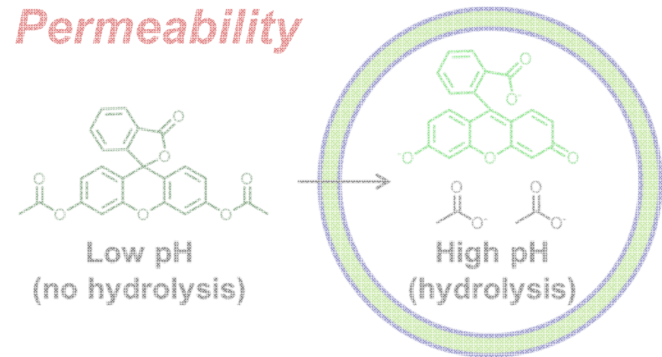
## Mechanically-Activated *Fusion*




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

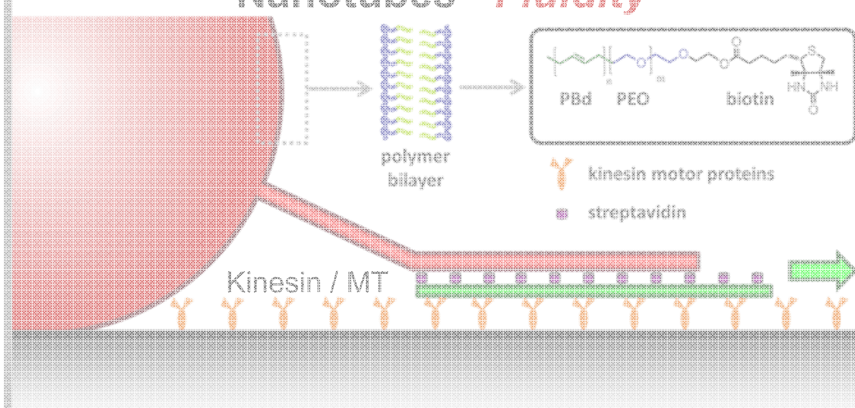
## Lysosome-Mimicking Vesicles

*Permeability*



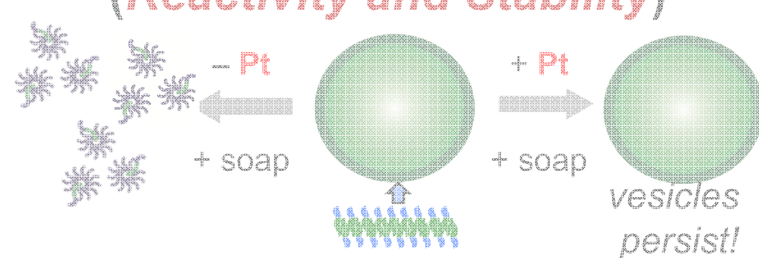

W. F. Paxton et al. *Soft Matter* **2013**, *9*, 11295–11302

## Dynamic Assembly of Polymer Nanotubes - *Fluidity*




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

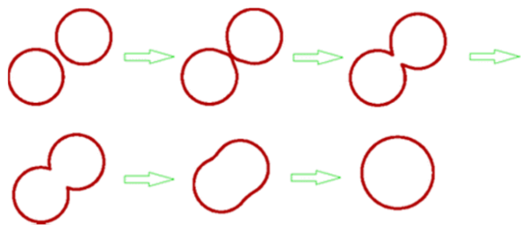
## Catalytically-Active Cross-Links (*Reactivity and Stability*)




W. F. Paxton et al. *Chem. Mater*, **2015**, *27, 4808–4813*

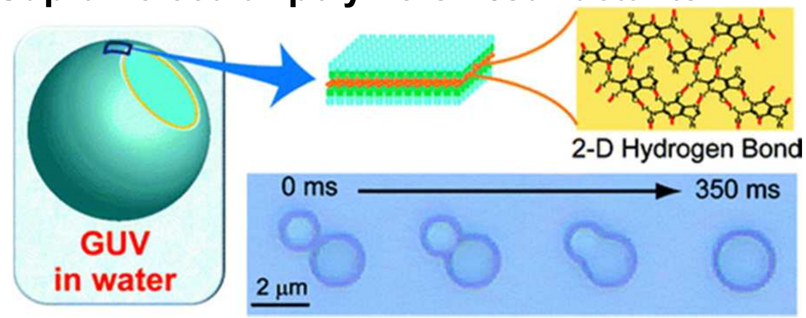
# Polymersomes Fuse…with Help

**Branched copolymer vesicles (w/sonication)**



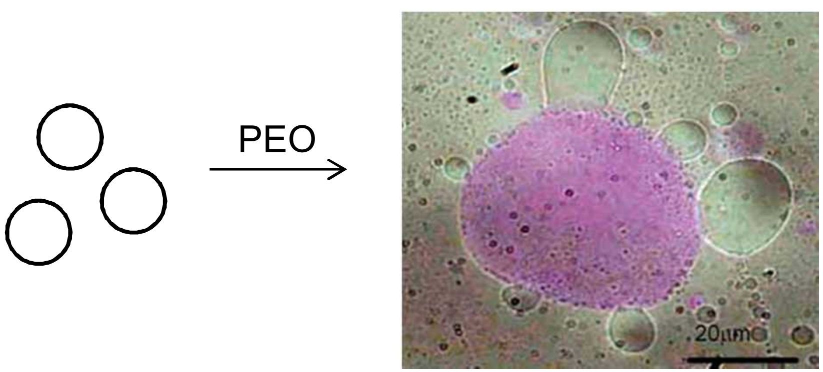
Zhou et al. *J. Am. Chem. Soc.* **2005**

**Supramolecular polymers w/surfactants**



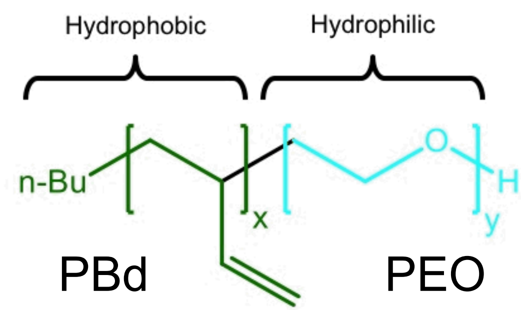

Sawayama et al. *Langmuir* **2011**

**Poloxamer (PEO-PPO) (w/PEO homopolymer)**



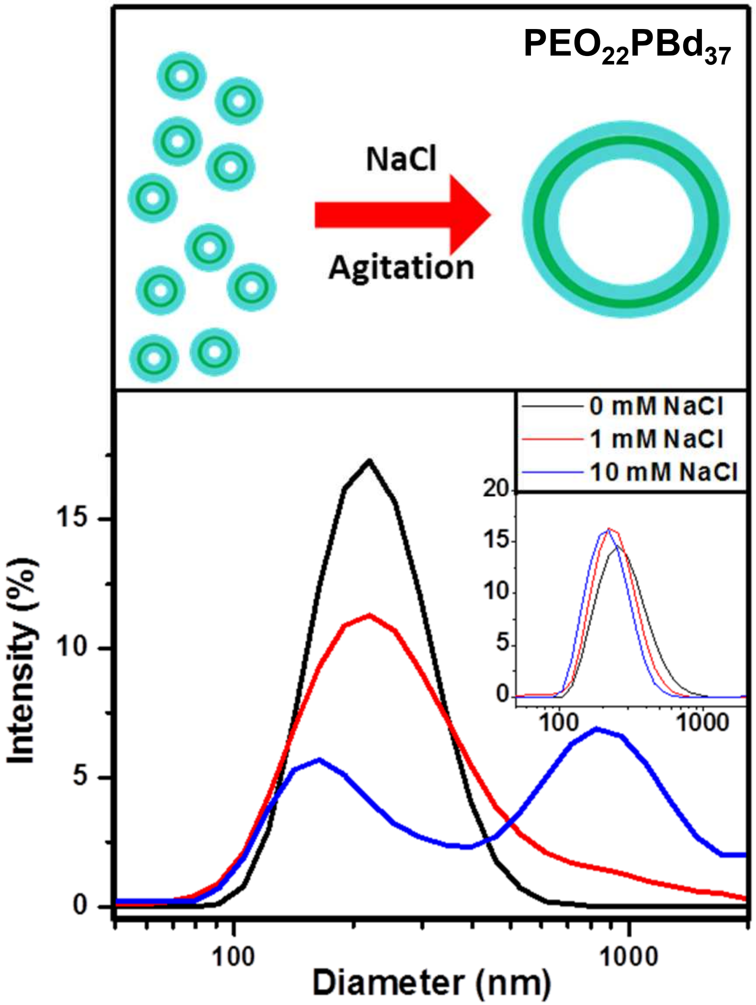

Smart et al. *Macromol. Rapid Comm.* **2008**

***General strategy for PEO-PBd polymers?***



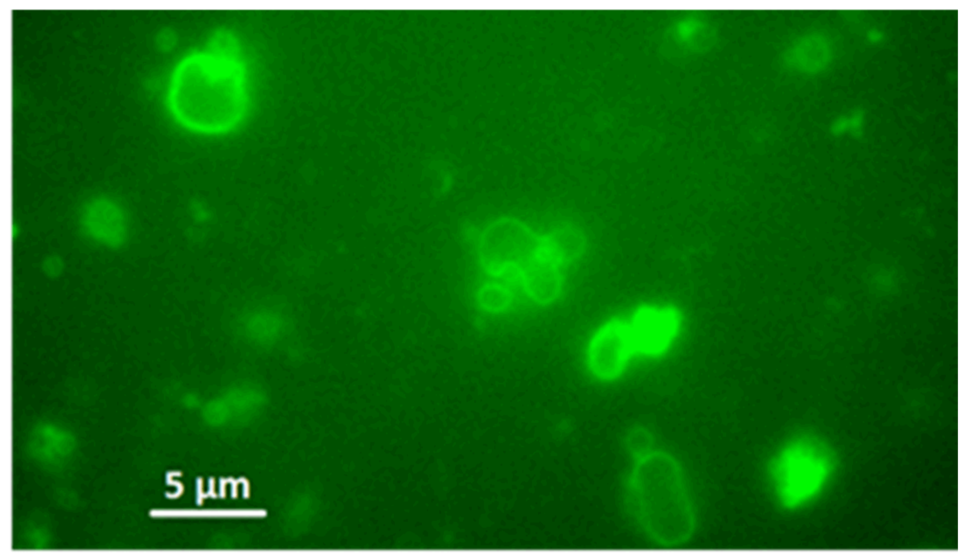

- **Commercially available (Polymer Source)**
- **>95% 1,2 addition**
- **Vesicle forming**
- **X = 32, Y = 22**

# Mechanically-Activated Fusion of Polymersomes

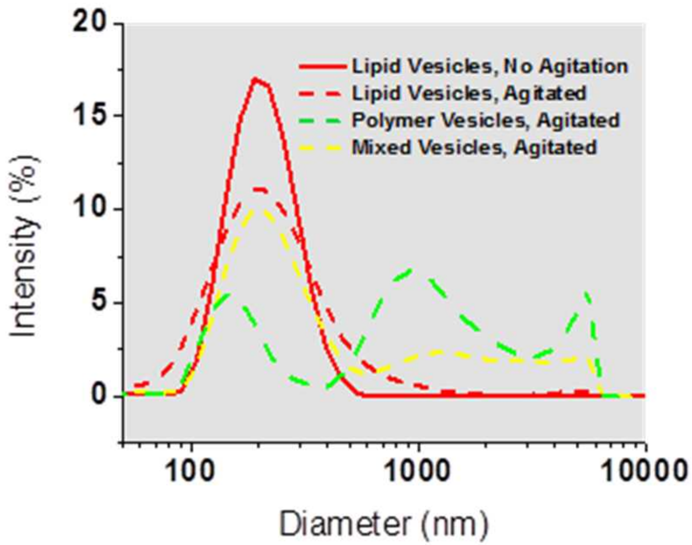



- 200 nm vesicles
- 10 mM NaCl
- Agitate 20 Hz for 60 Min.

Giant Vesicles

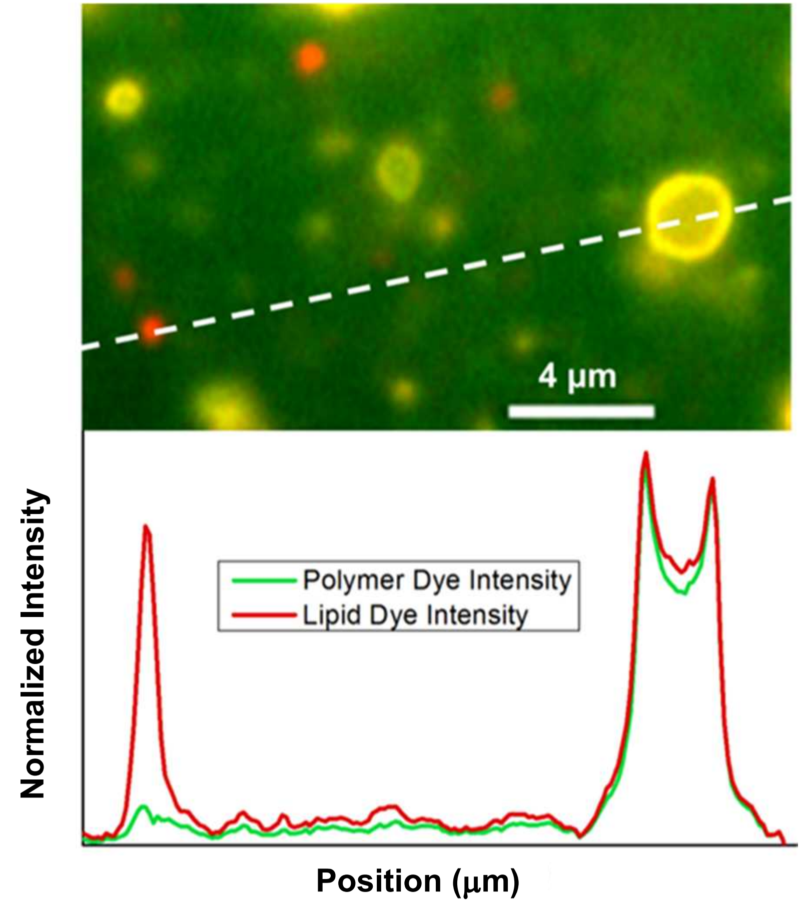


# Hybrid Polymer/Lipid Vesicles via Fusion



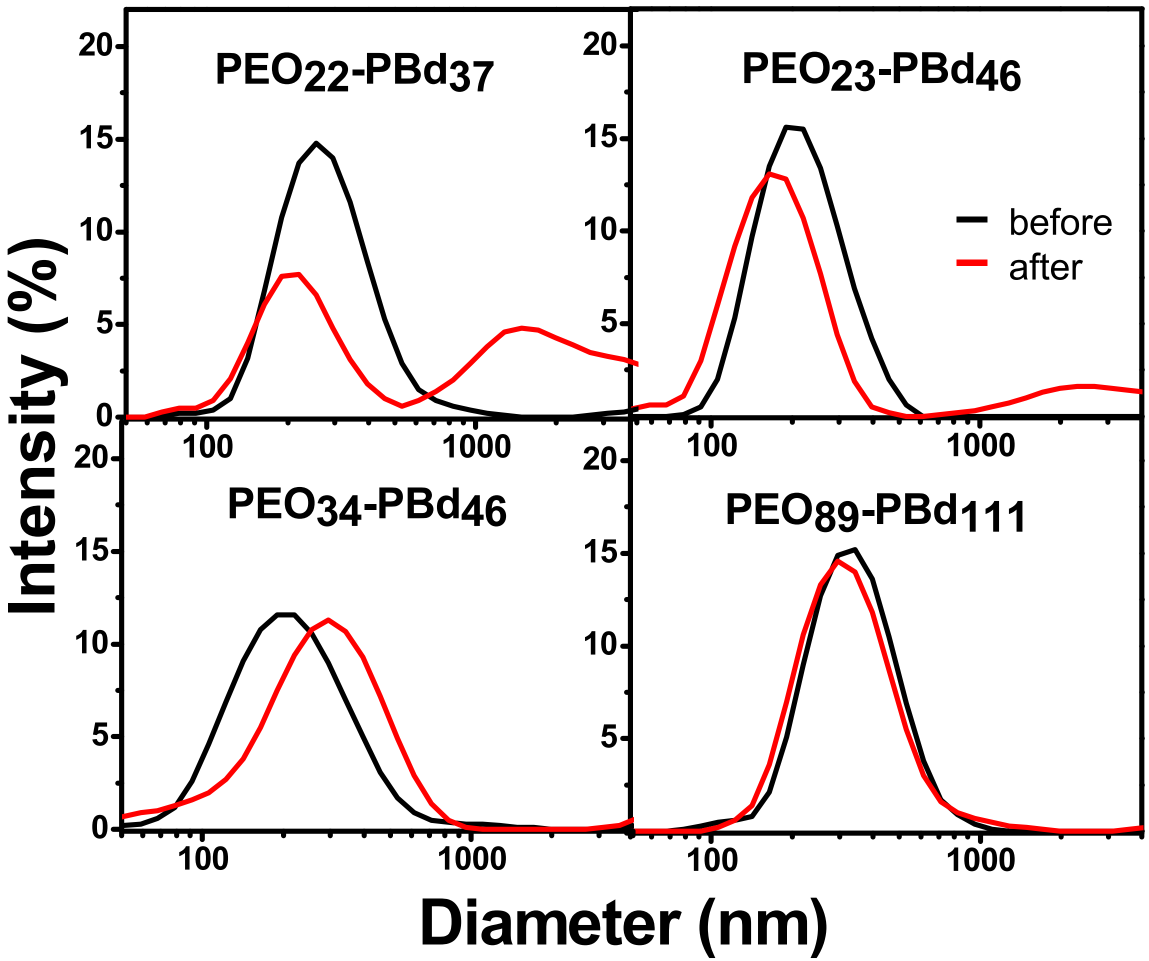

**Under these conditions:**

- Liposomes (DOPC) don't fuse…
- …Polymersomes DO!
- P-somes + L-somes DO!




*Deliver/Combine vesicles of different compositions (e.g. reagents, or membrane proteins)*

# ↑ Molecular Weight ↓ Fusion




↑ Hydrophobic Block=
↑ Interchain attraction

↑ Hydrophilic Block=
↑ Steric Hindrance

***What other factors/polymers/ additives might facilitate fusion?***

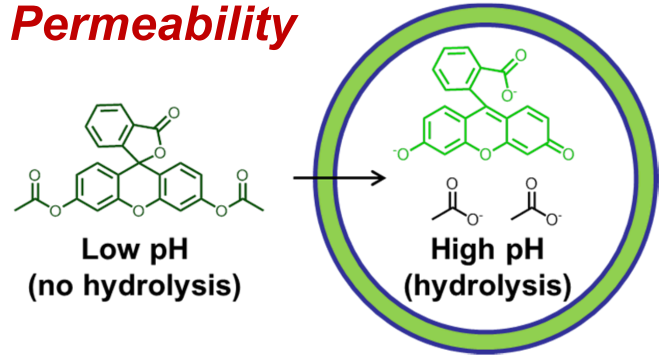
# *Dynamic* Polymer Vesicle Membranes

## Mechanically-Activated *Fusion*


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

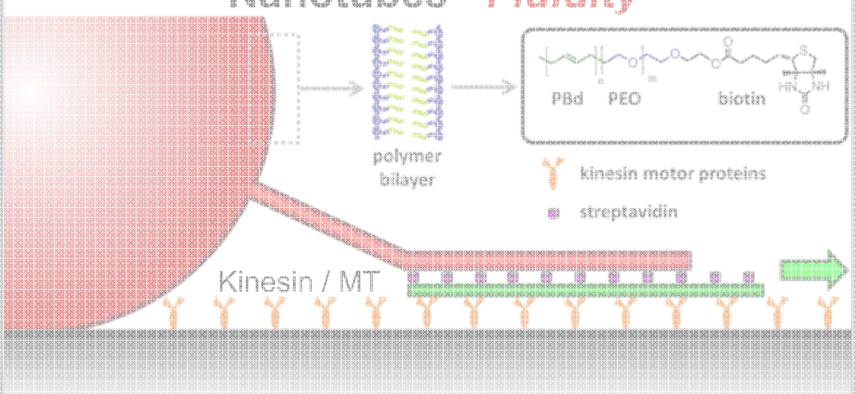
## Lysosome-Mimicking Vesicles

***Permeability***



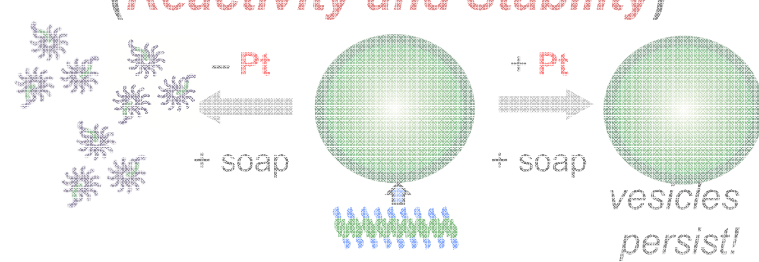

W. F. Paxton et al. *Soft Matter* **2013,** *9*, 11295–11302

## Dynamic Assembly of Polymer Nanotubes - *Fluidity*



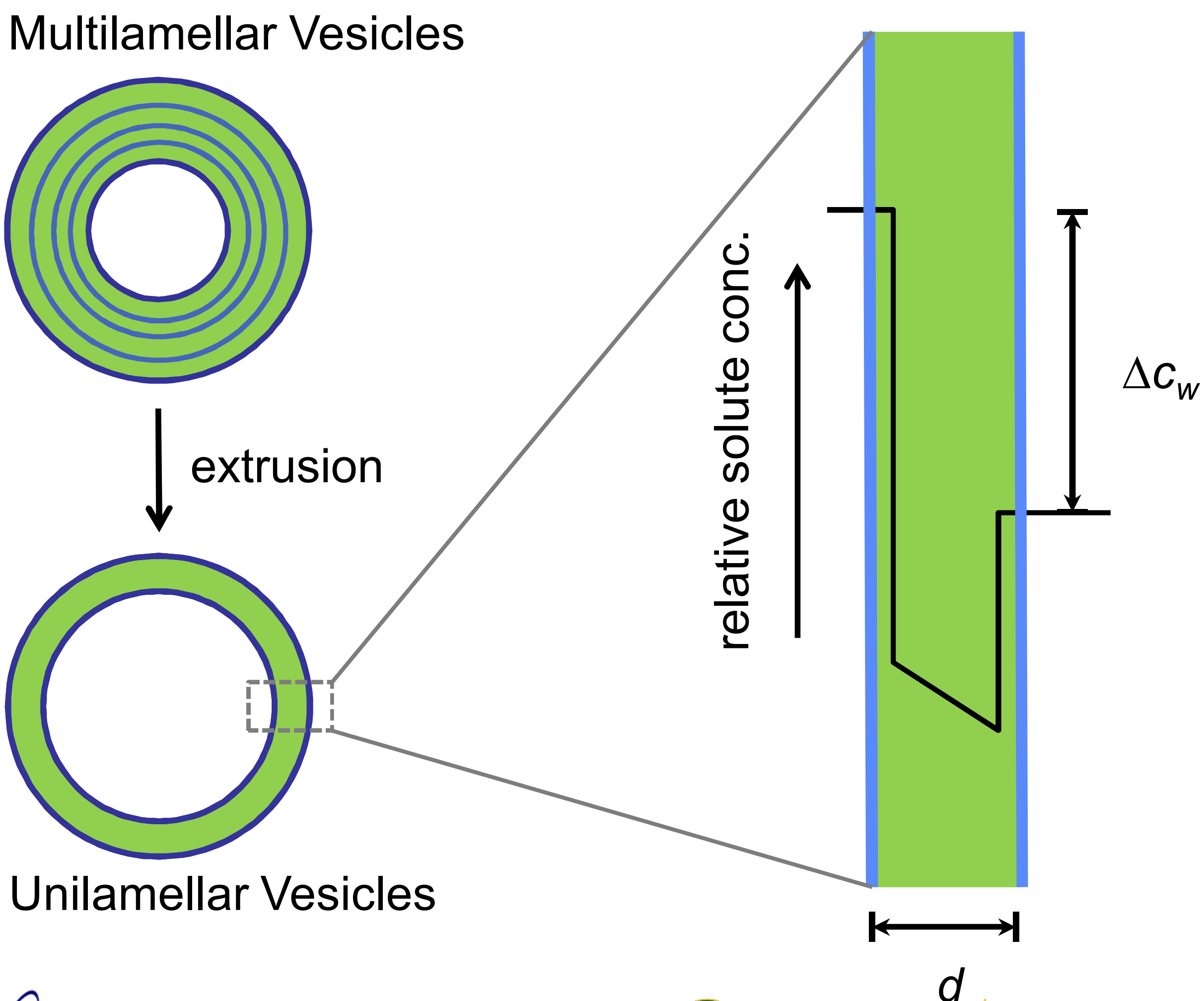

W. F. Paxton et al. *Nanoscale*, **2015**, *7*, 10998–11004

## Catalytically-Active Cross-Links (*Reactivity and Stability*)




W. F. Paxton et al. *Chem. Mater*, **2015**, *27*, *4808–4813*

# Permeability Across Vesicle Membranes

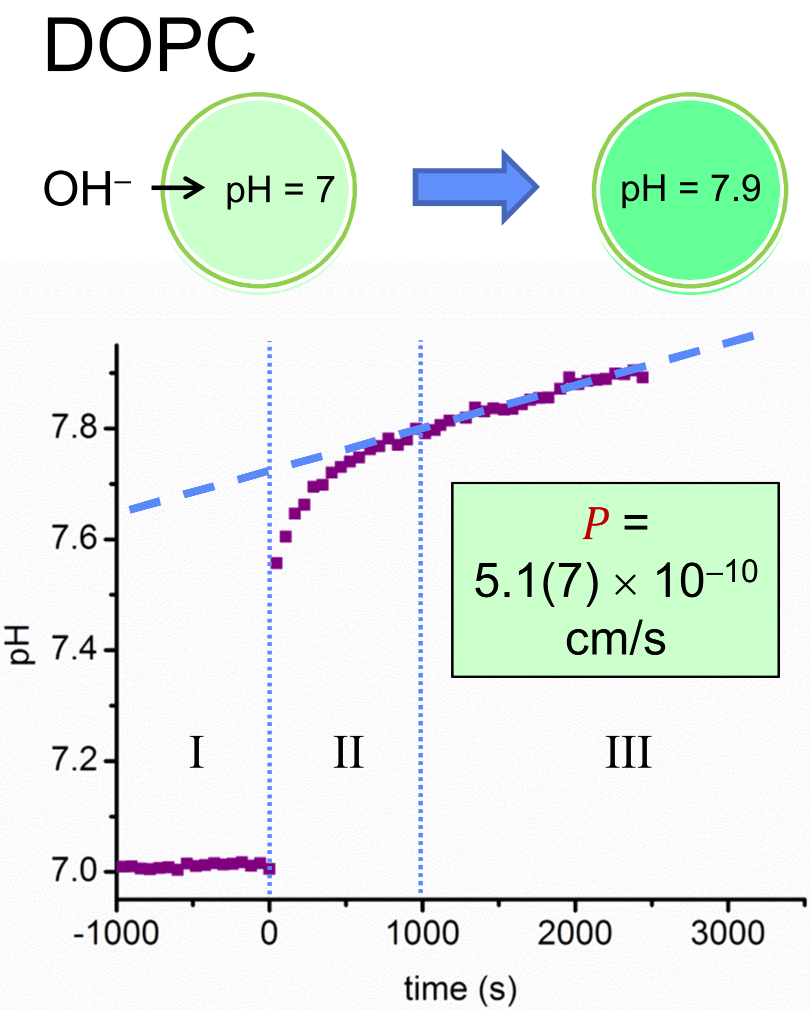



## Solubility-Diffusion Mechanism

$$\boldsymbol{P} = \frac{DK}{d} = \frac{J}{\Delta c_w}$$

***P*** **= permeability coeff.**
***D*** **= diffusion coeff.**
*K* = partition coeff.
*d* = bilayer thickness
*J* = solute flux
$\Delta c_w$ = solute gradient

# Measuring Permeability Across Lipid Membranes




$$\frac{\Delta n_{OH^-}}{\Delta t} = f([OH^-])$$

**via Henderson-Hasselbalch**

$$J_{OH^-} = \frac{\Delta n_{OH^-}}{\Delta t} \times \left(\frac{1}{S_{ave}}\right)$$

**$OH^-$ flux across a membrane**

$$\boldsymbol{P} = \frac{J}{\Delta c_w}$$

**Effective permeability coeff.**

$$\boldsymbol{D^*} = DK = \frac{J_{OH^-}}{\Delta c_w} d$$

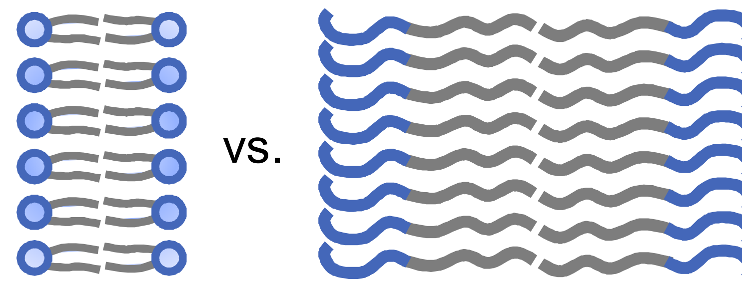
**Effective diffusion coeff.**

# Vesicle Permeability Summary

| Sample | Vesicle diameter (nm)[a] | Membrane Thickness (nm) | $P_{OH-}$ ($\times 10^{10}$ cm/s) | D* ($\times 10^{16}$ cm$^2$/s) |
|---|---|---|---|---|
| DOPS | 170(30) | 2.6[b] | 5.4(8) | 1.4(2) |
| DOPC | 190(30) | 2.7[c] | 5.1(7) | 1.4(2) |
| $EO_{20}BD_{33}$ | 200(40) | 6.8[d] | 1.5(3) | 1.0(2) |
| $EO_{89}BD_{120}$ | 260(70) | 22[d] | 0.4(1) | 0.9(2) |

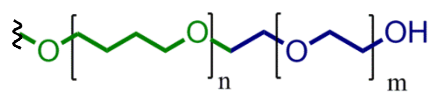
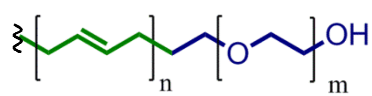
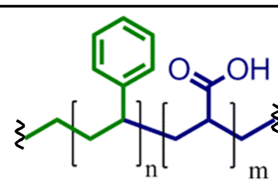
[a] DLS. [b,c] Literature values. [d] Estimated from published models.

Permeability ↔ Thickness



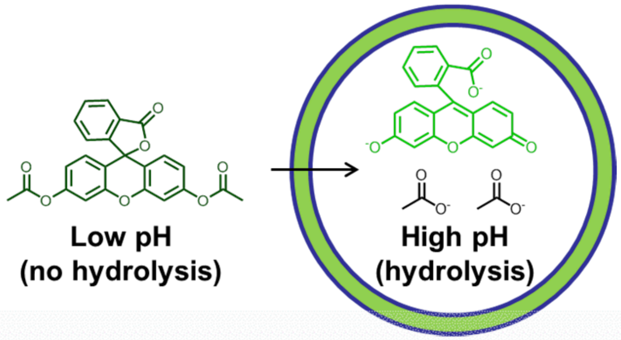

Permeability
↕
Chemical Composition

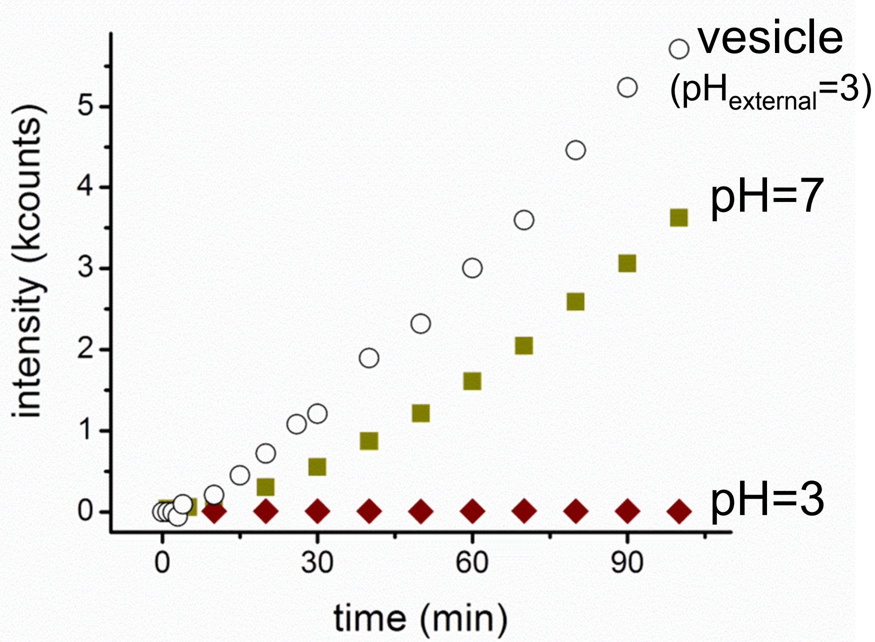
***Can this be PREDICTED?***

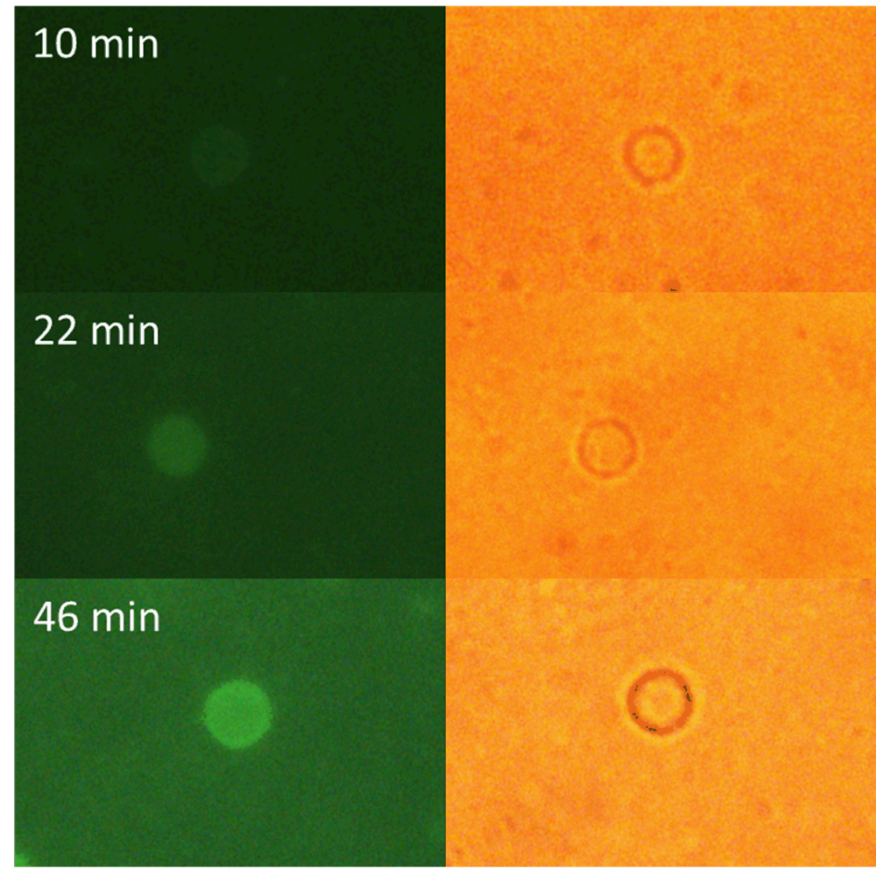
| Polymer | | Thickness (nm) | $P_{A-}$ (cm/s) | D* (cm$^2$/s) |
|---|---|---|---|---|
| PEO-PBO[a] |  | 2.4 | $10^{-7}$ | $10^{-14}$ |
| PEO-PBD |  | 6.8 | $10^{-9}$ | $10^{-16}$ |
| PS-PAA[b] |  | 33 | $10^{-13}$ | $10^{-18}$ |

[a] Battaglia et al. **2006**; [b] Eisenberg et al. **2006**

# A Nanoreactor for Ester Hydrolysis



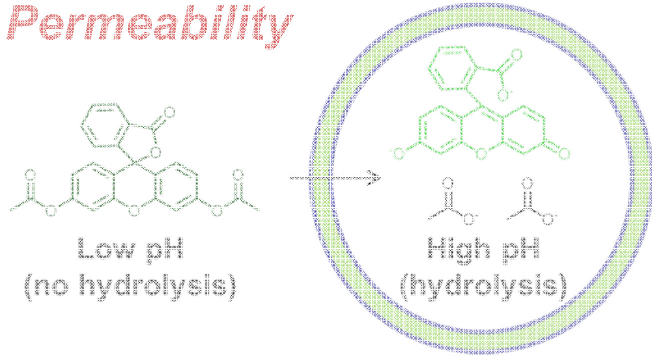

*Polymersomes act as an* ***artificial lysosome****, collecting and digesting hydrolysable materials*

# *Dynamic* Polymer Vesicle Membranes

## Mechanically-Activated *Fusion*

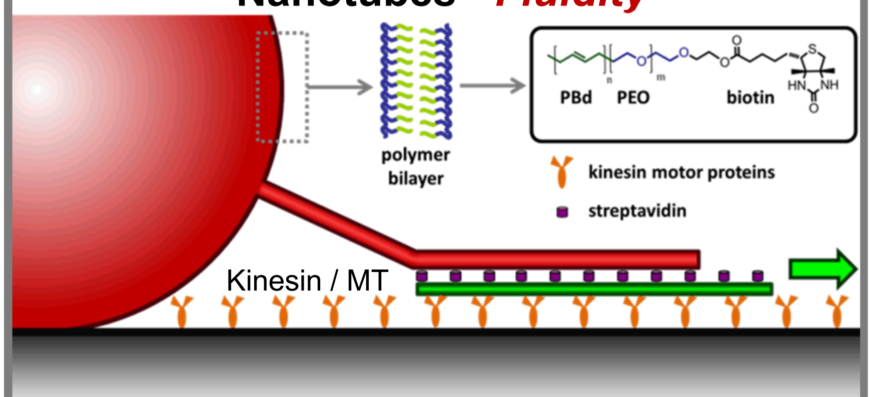

I. M. Henderson, W. F. Paxton, *Angew. Chem. – Int. Ed.* **2014**, *53*, 3372-3376; *J. Poly. Sci. B*, **2014**, *53*, 297–303

## Lysosome-Mimicking Vesicles *Permeability*



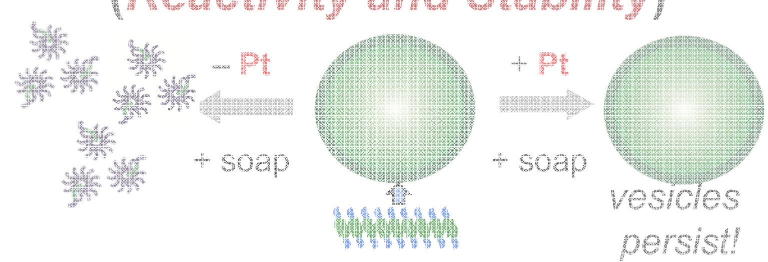

W. F. Paxton et al. *Soft Matter* **2013**, *9*, 11295–11302

## Dynamic Assembly of Polymer Nanotubes - *Fluidity*



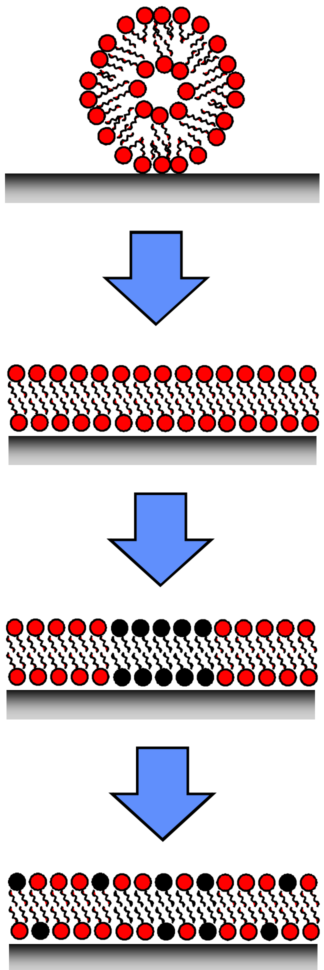

W. F. Paxton et al. *Nanoscale,* **2015,** *7,* 10998–11004

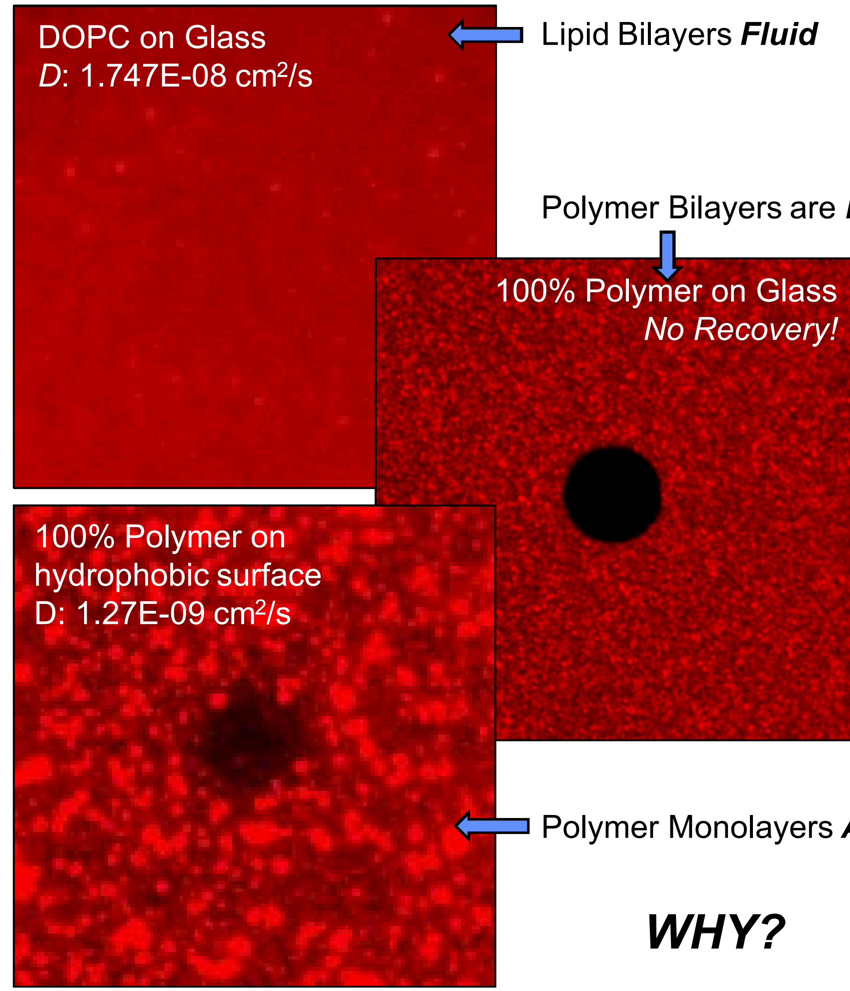
## Catalytically-Active Cross-Links (*Reactivity and Stability*)




W. F. Paxton et al. *Chem. Mater,* **2015**, *27*, *4808–4813*

# Polymer Membrane Fluidity via FRAP




Lipid Bilayers ***Fluid***

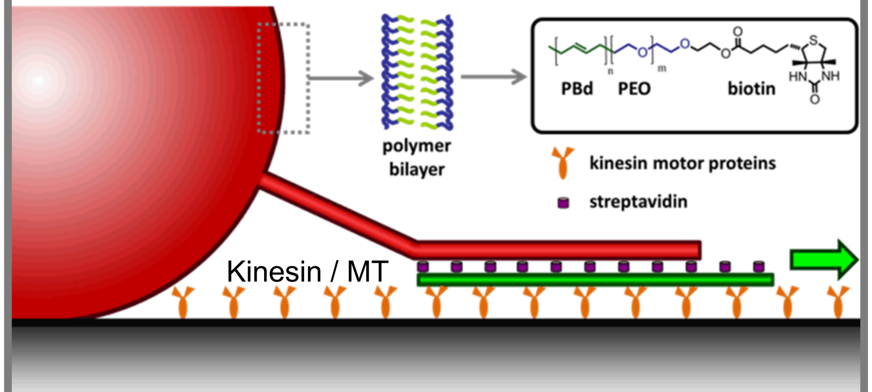
Polymer Bilayers are ***NOT!***

Polymer Monolayers ***ARE!***

***WHY?***

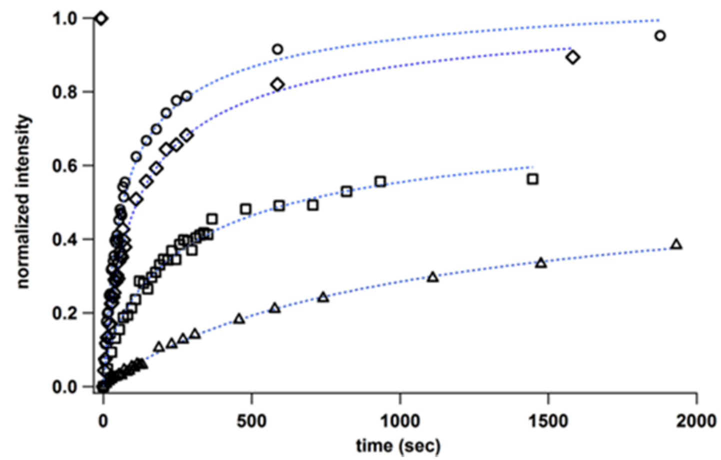
# Fluidity in Polymer Membrane Nanotubes

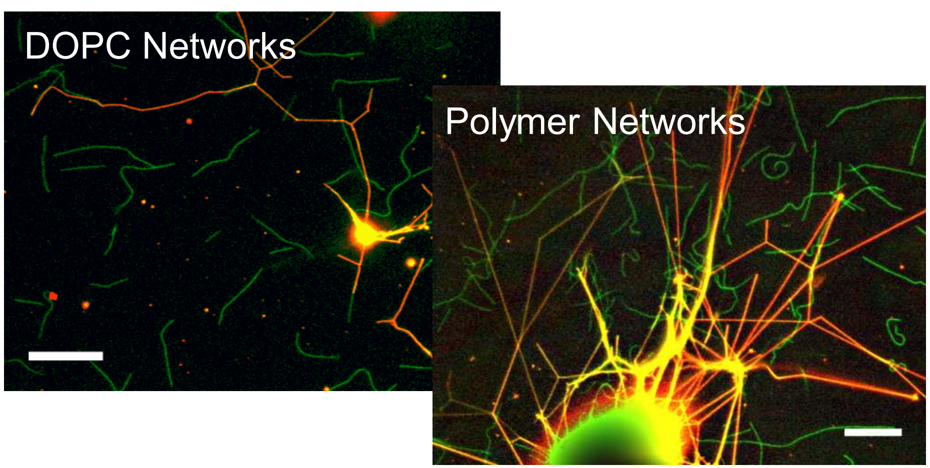
## Dynamic Assembly of Polymer Nanotubes



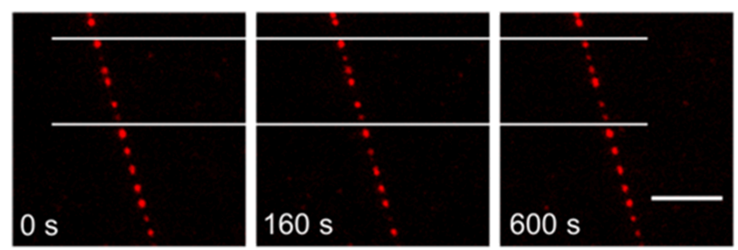

W. F. Paxton et al. *Nanoscale,* **2015,** *7,* 10998–11004

## FRAP in Polymer Nanotubes



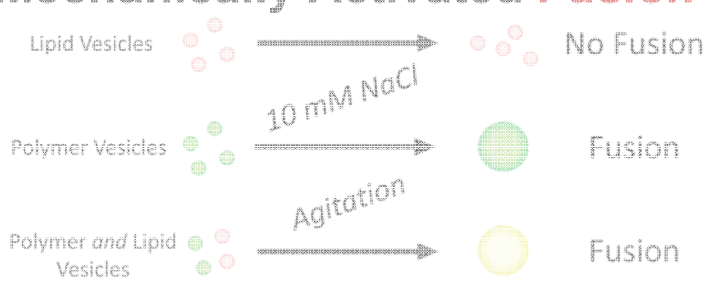

## Fluidity of Adsorbed Quantum Dots




*No fluidity in polymer nanotubes either…**WHY?***

# *Dynamic* Polymer Vesicle Membranes

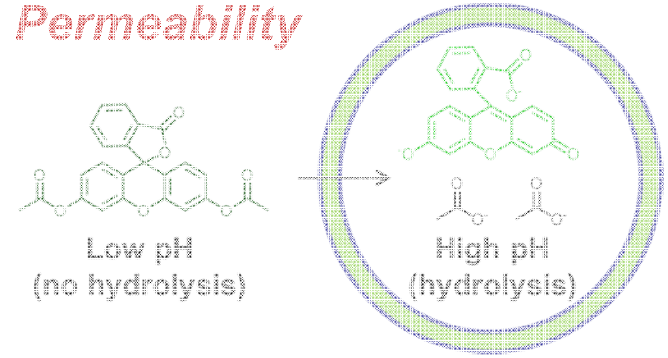
## Mechanically-Activated *Fusion*




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

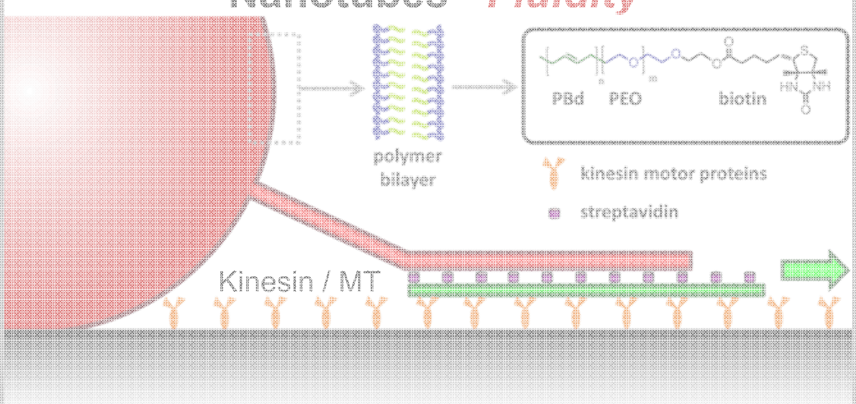
## Lysosome-Mimicking Vesicles

*Permeability*



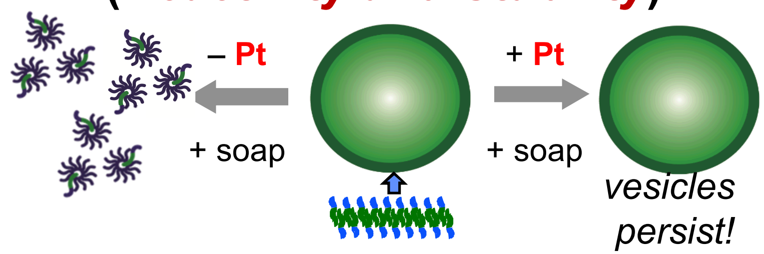

W. F. Paxton et al. *Soft Matter* **2013**, *9*, 11295–11302

## Dynamic Assembly of Polymer Nanotubes - *Fluidity*




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

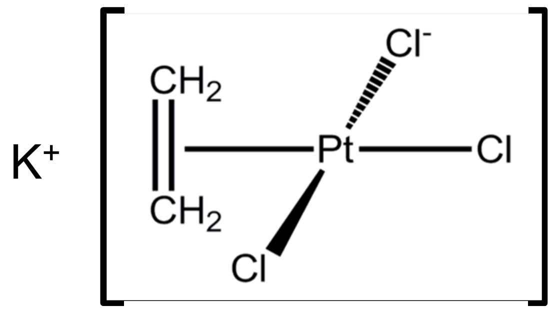
## Catalytically-Active Cross-Links (*Reactivity and Stability*)




W. F. Paxton et al. *Chem. Mater*, **2015**, *27*, *4808–4813*

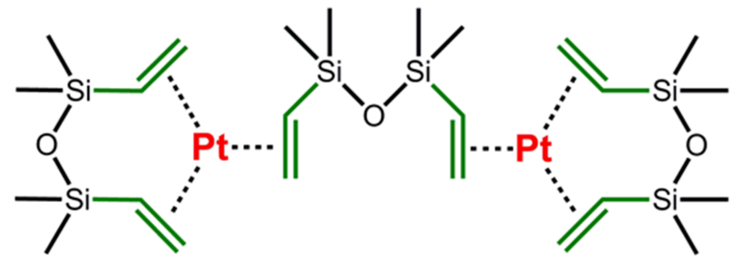
# Platinum-Alkene Complexes

## Zeise's Salt



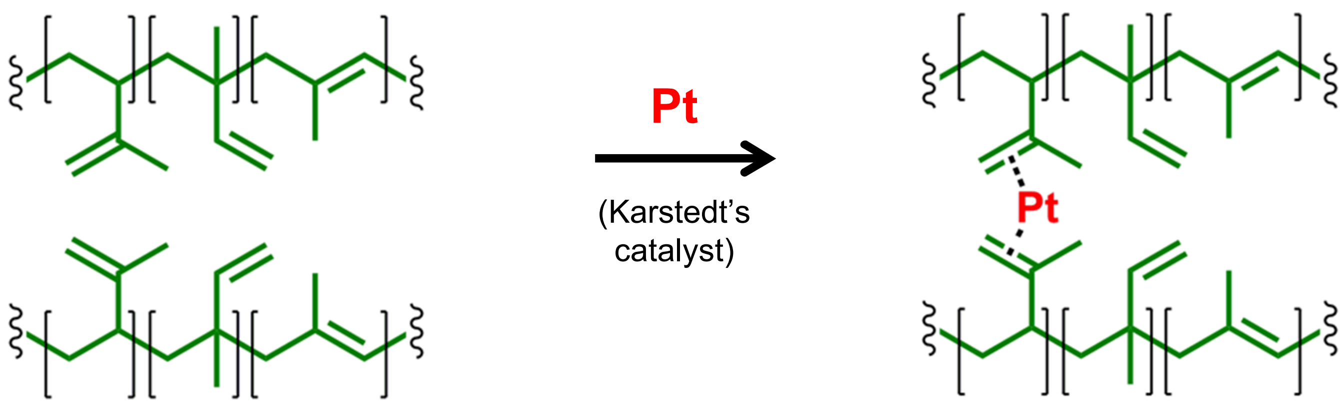

$\eta^2$-alkene compound (1831)

## Karstedt's Catalyst

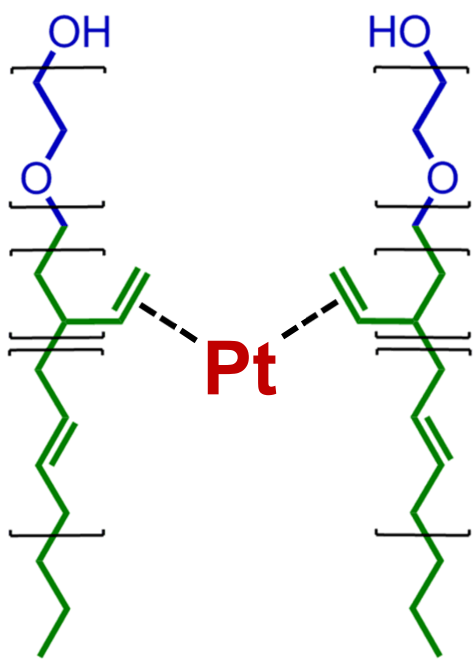



$\eta^2$-alkene compound (1973)
hydrosilylation catalyst

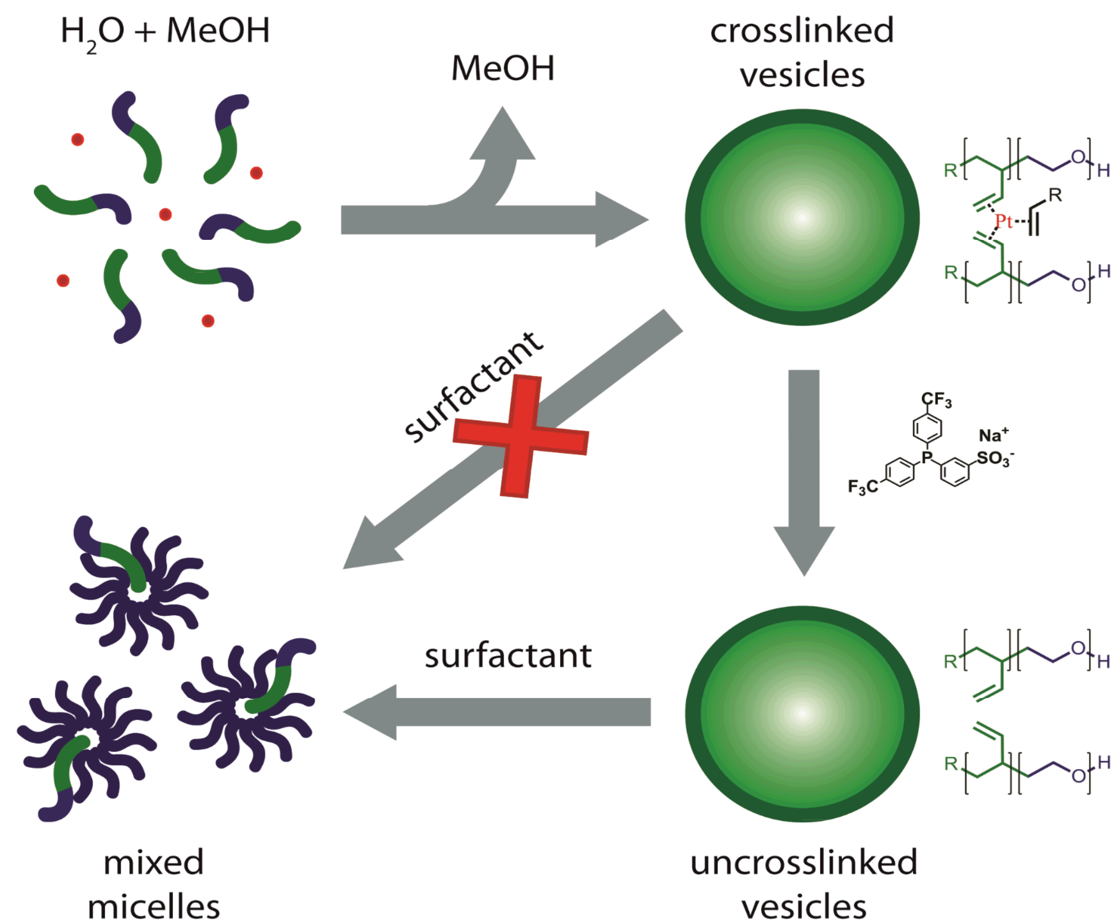
## Isoprene–Pt(0) Coordination (Rupar et al. *JACS*, **2011**)



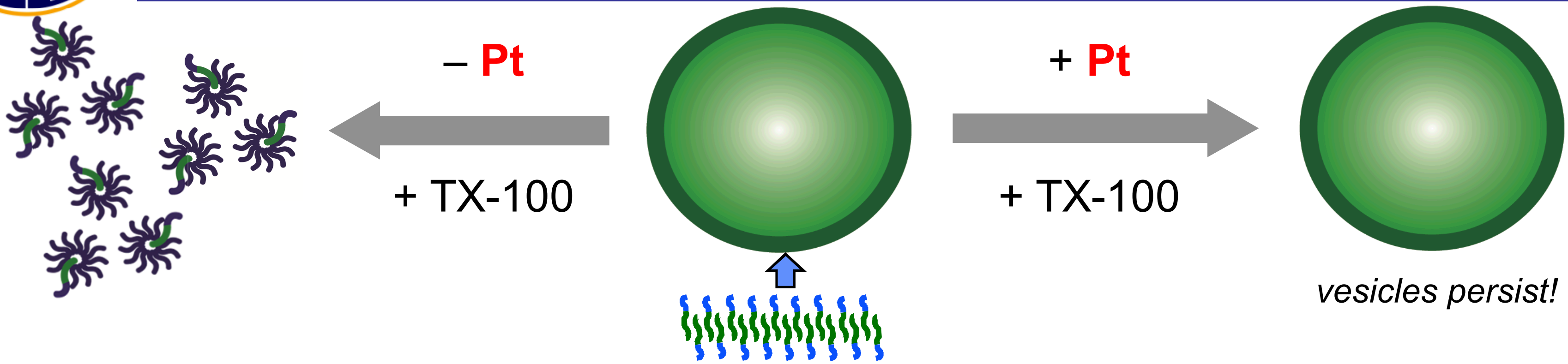
# Capable Crosslinks: Polymersomes Reinforced with Catalytically Active Metal-Ligand Bonds

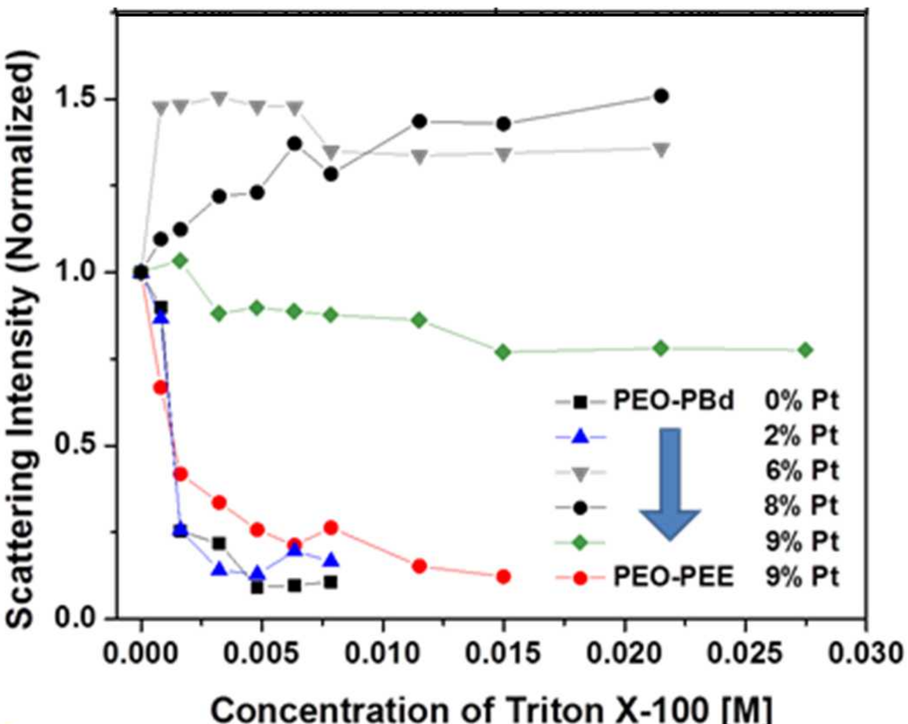


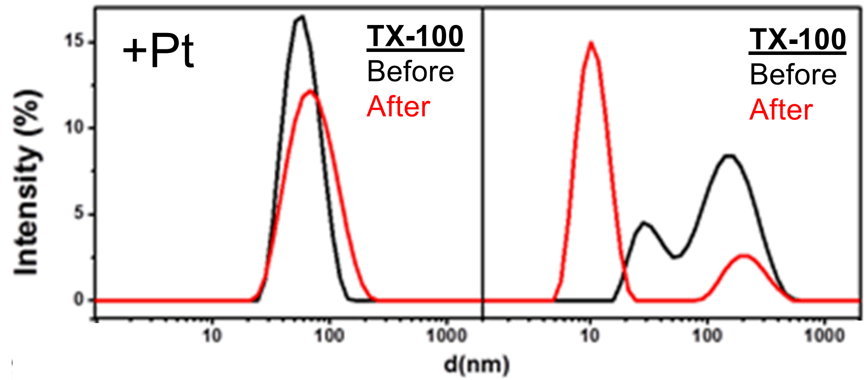

Exploit organometallic interactions to create membranes that are both ***robust*** and ***dynamic***.



# Surfactant-Resistant Cross-linked Polymersomes



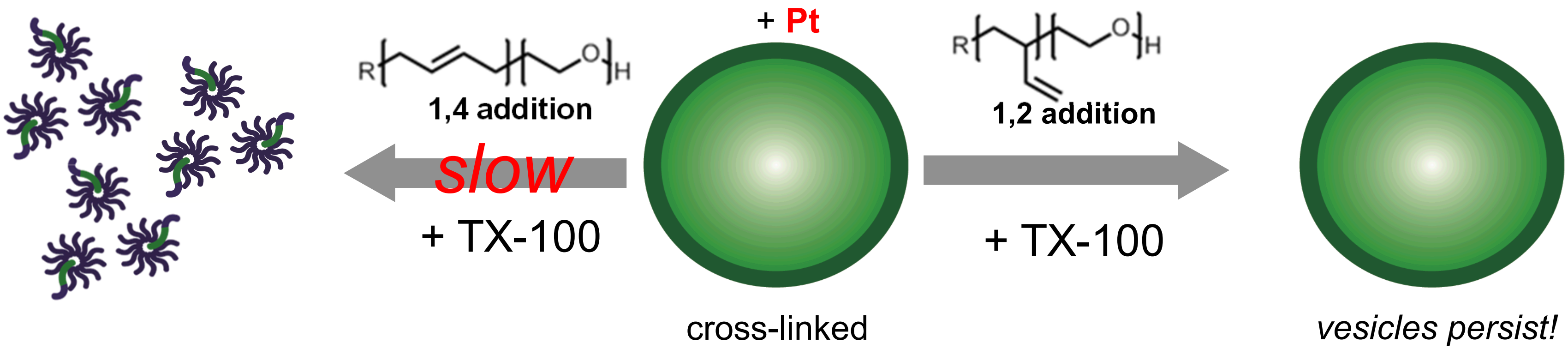



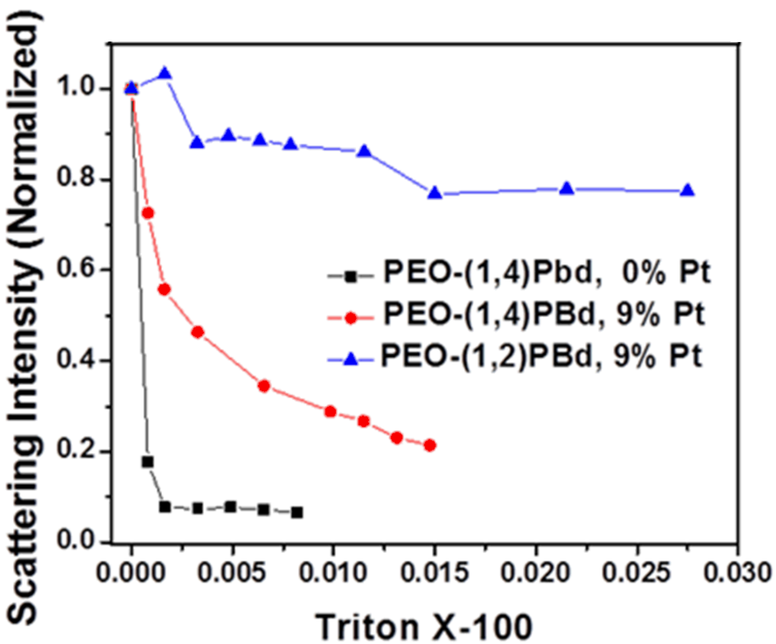




Uncross-linked vesicles → mixed micelles

***Cross-linked vesicles resist surfactant***

# Stability of PEO-PBd--Pt: 1,2 vs. 1,4 addition



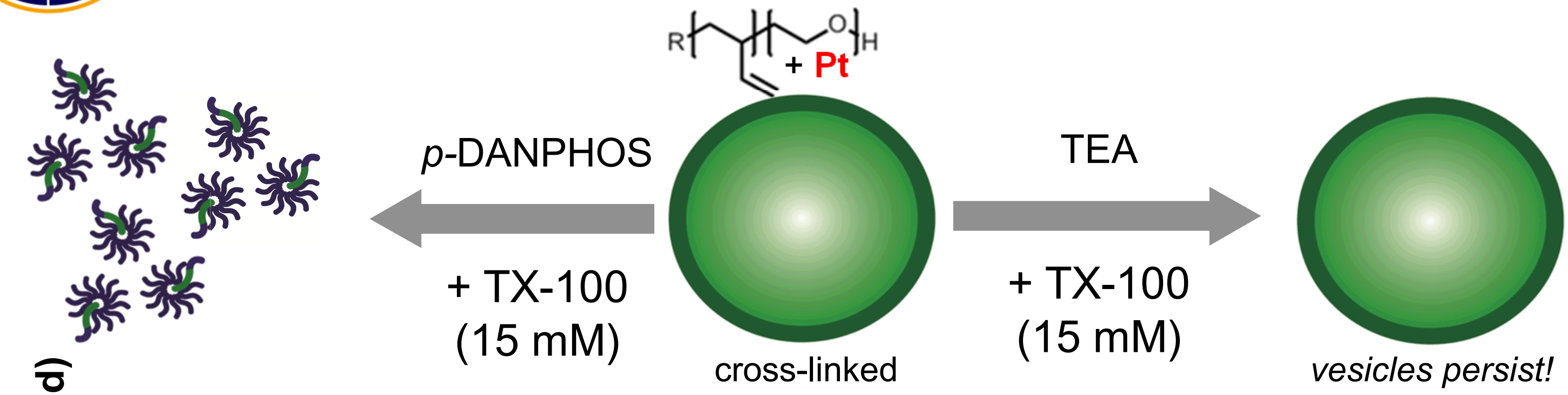

1,4 PBd is *MORE* resistant with **Pt**…

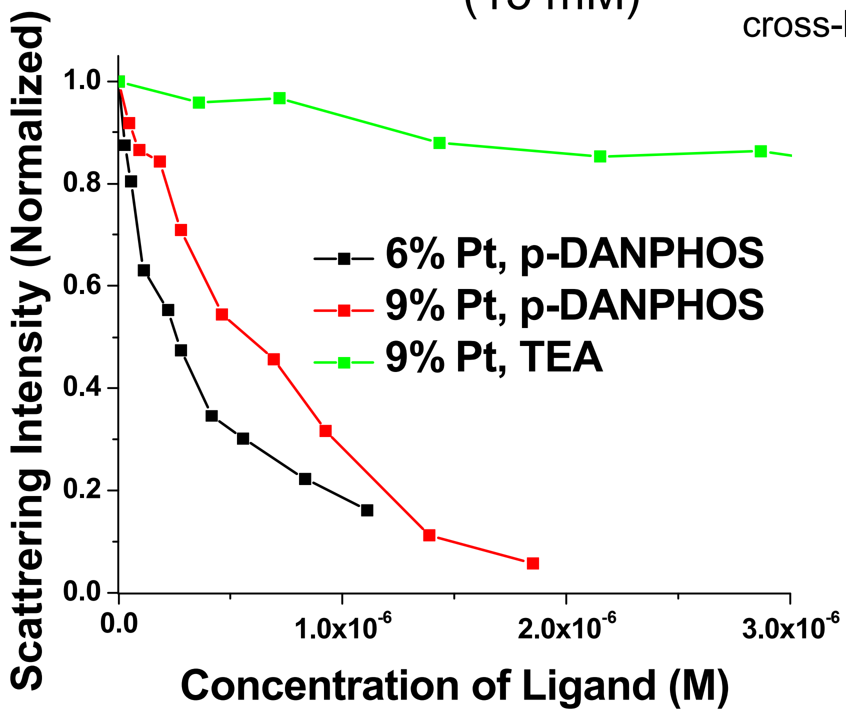
…but *LESS* resistant than 1,2 PBd

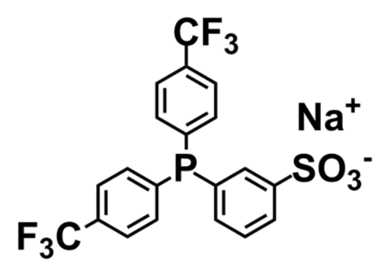
**Two effects:**

- Sterics: Pendant vs. main-chain
- Electronics: bond energies
  (1,2--**Pt** > 1,4--**Pt**)

# Selective Reversibility w/ a Competing Ligand

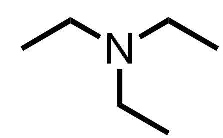



*p*-DANPHOS

bis(4-trifluoromethylphenyl)(3-sulfonatophenyl)phosphine

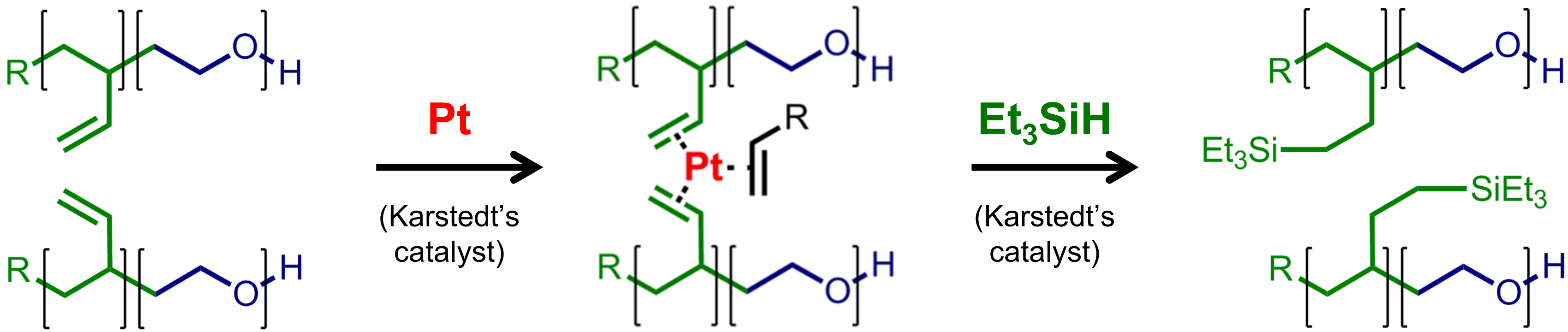


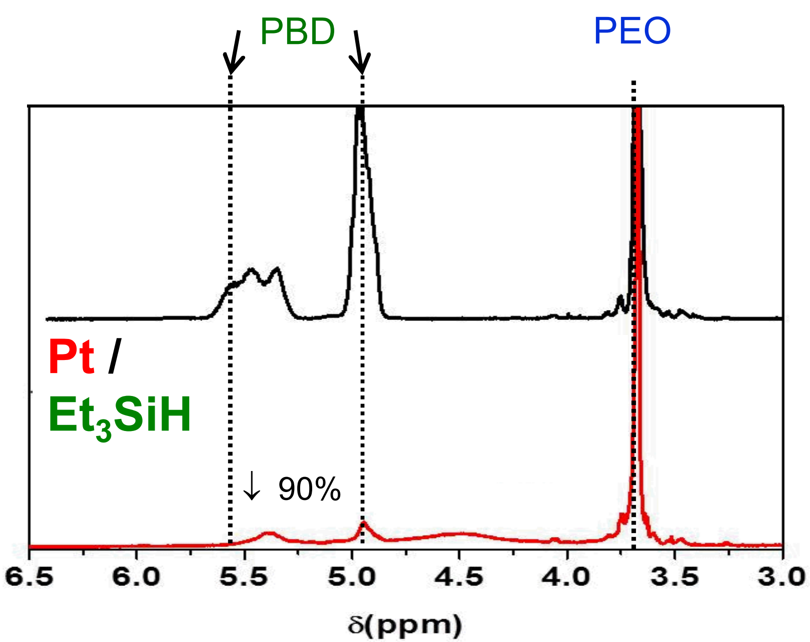

TEA

triethylamine

***Reversible/Dynamic Cross-links via Competitive ligands***

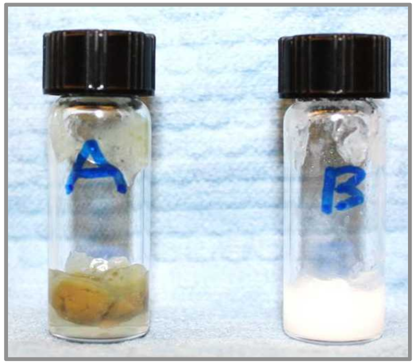
# Pt in Cross-linked Polymersomes Are Catalytically Active




**1 h Agitation:**

- 90% hydrosilylation
- emulsion (both)
- color = Pt(0)↓




***Catalytically-Active Cross-links***

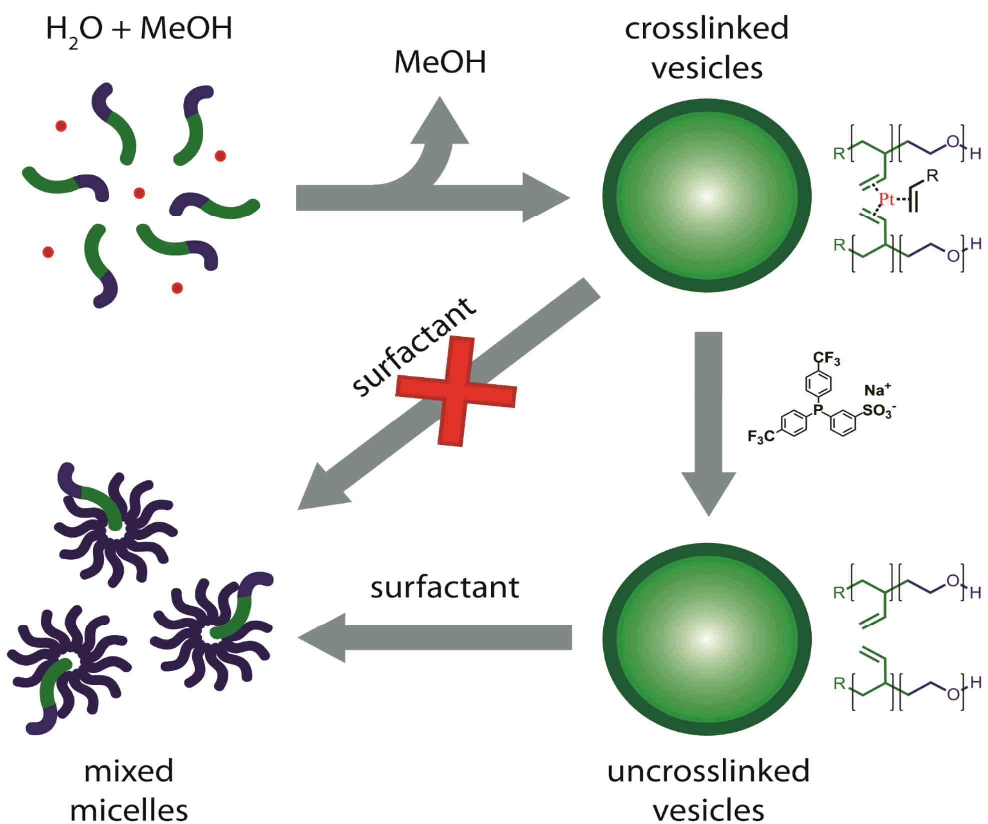
# Conclusions

Used organometallic interactions to modulate the properties of "normal" polymersomes:

1. Enhanced Stability:
   - Pt--‖ → Organometallic cross-links
   - Resistant to destabilization
   - Crosslinking can be selectively reversed w/ phosphine ligands

2. Catalytic Activity:
   - Pt centers still active
   - Enable hydrosilation reactions

To produce soft self-assembling material that is both ***robust*** and ***dynamic***.



# Acknowledgements

Ian Henderson (SNL) | Hope Quintana (NMSU/LANL) | Julio Martinez (NMSU) | Sergei Ivanov (CINT) | Nathan Bouxsein (SNL) | Gabe Montaño (CINT) | Aaron Collins (S. New Hampshire) | Patrick McAninch (UNM)

## Center for Integrated Nanotechnologies

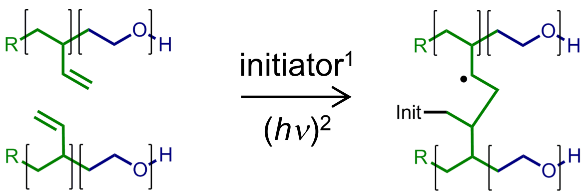
*Helping you understand, create, and characterize nanomaterials*

The DOE/SC nanoscience centers:

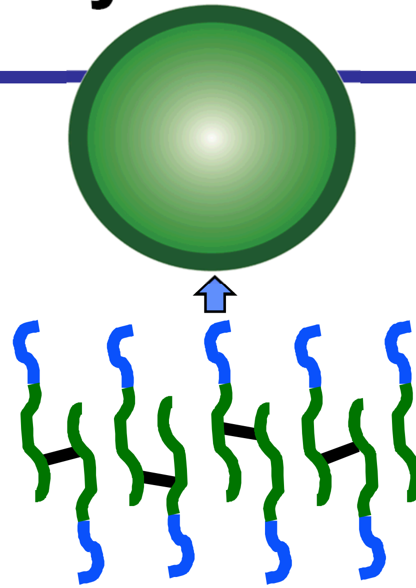
- Are defined by a scientific field, not specific instrumentation.
- NSRC staff support user projects and conduct original research.
- Capabilities involve expertise, hardware and software.
- Users access Synthesis, Fabrication, Characterization and Theory capabilities.

# *ROBUST* Polymer Vesicles Membranes

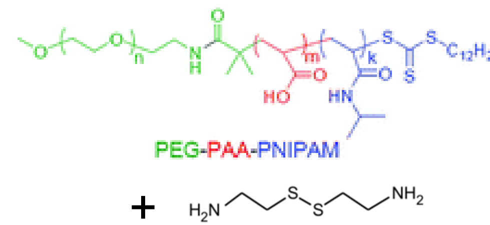
## Radical cross-linking




1. Discher et al. *JPCB* **2002,** *106,* 2848.
2. Jofre et al. *JPCB* **2007,** *111,* 5162.

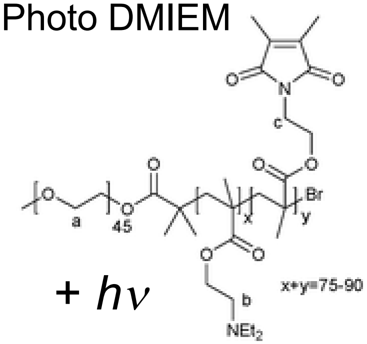


## Amide coupling…




Zhiyuan Zhong et al. *J. Mater. Chem.*, **2011,** *21,* 19013.

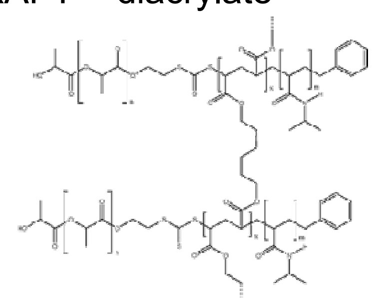
## Photo DMIEM




+ $h\nu$

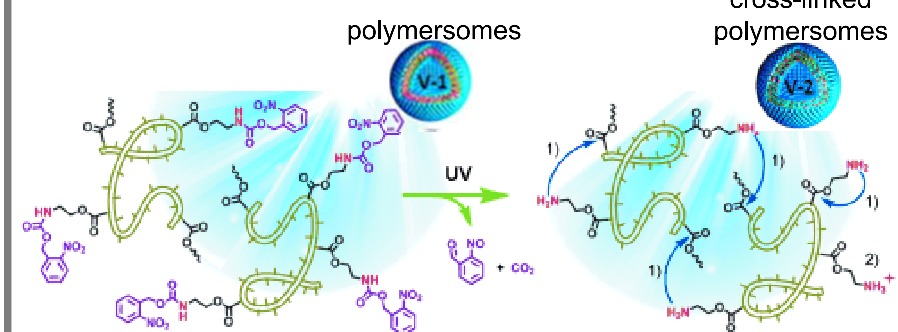
Voit et al. *Chem. Commun.* **2011,** *47,* 3466-3468.

## RAFT + diacrylate



Stenzel et al. *Langmuir* **2004,** *20,* 10809-10817

## …and from photocaged amines

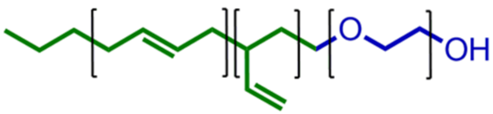



***photocaged amine***

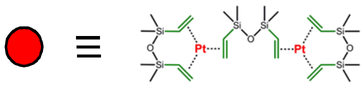
Shiyong Liu et al. *Angew. Chem.* **2014,** *53,* 3138.

***Covalent X-links are ROBUST but, limited control over DYNAMICS***

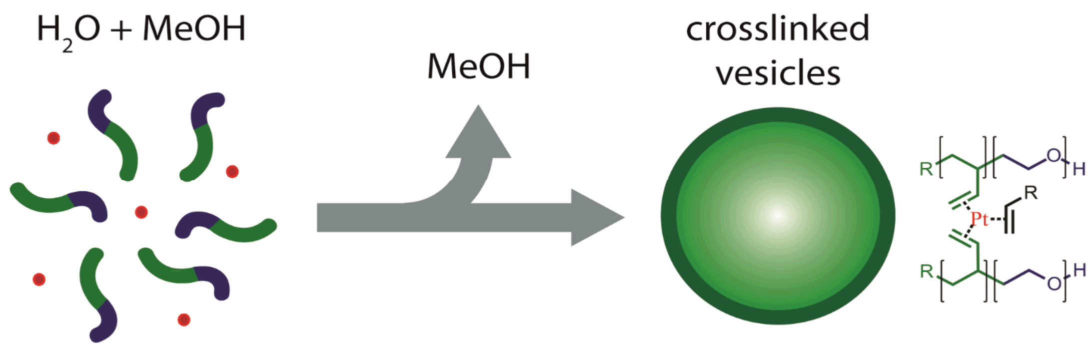
# Forming Cross-linked Vesicles with Pt and PEO-PBd



$EO_{21} - Bd_{32}$ (1,2 addition)



Karstedt's catalyst




Karstedt's / PEO-PBd in MeOH

↓

Add $H_2O$ / Remove MeOH

↓

***60-100 nm vesicles***