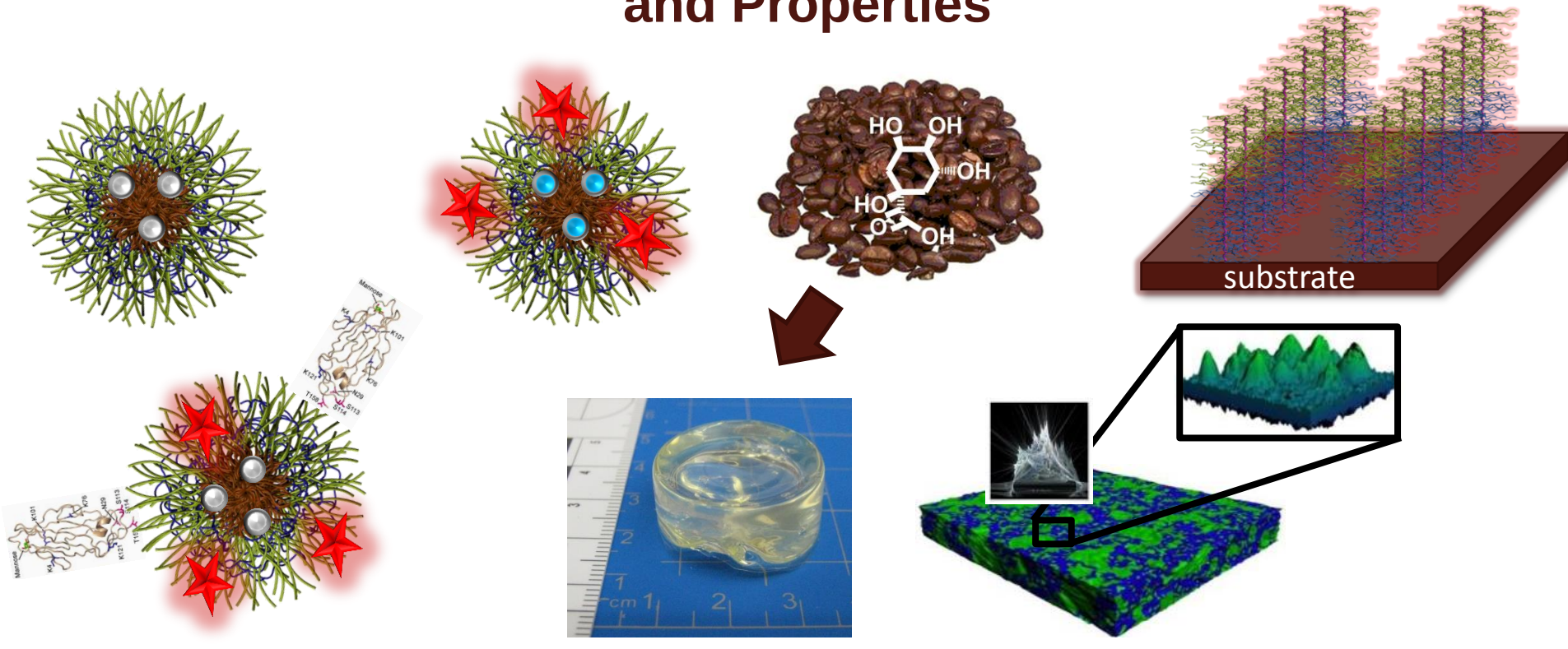
Targeted Applications as Inspirations to Develop Strategies toward Functionally-sophisticated Nanoscopic Macromolecules with Diverse Compositions, Structures, and Properties



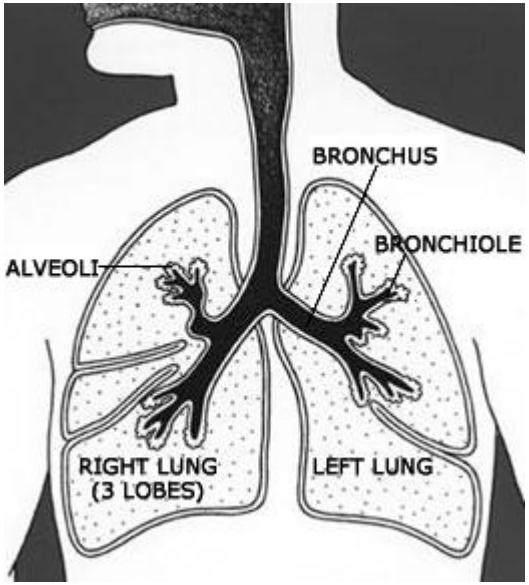
A few functional polymer chemistry goals:

- Antimicrobial nanoparticles for infectious disease treatment
- Chemotherapeutic nanoparticles for treatment of osteosarcoma lung metastases
- Engineering polymers derived from natural products
- Anti-biofouling and anti-icing coatings
- Advanced photoresist technologies

Silver-loaded Shell Crosslinked Nanoparticles for Antimicrobial Studies: Infectious disease treatments

Objective: To deliver anti-infective agents directly to the sites of origin of infectious diseases (lung and urinary tract) by using antimicrobial-bearing SCK nanoparticles—convenient routes of administration

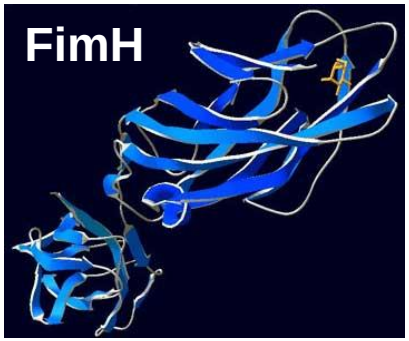
Lung Infections (*P. aeruginosa*)

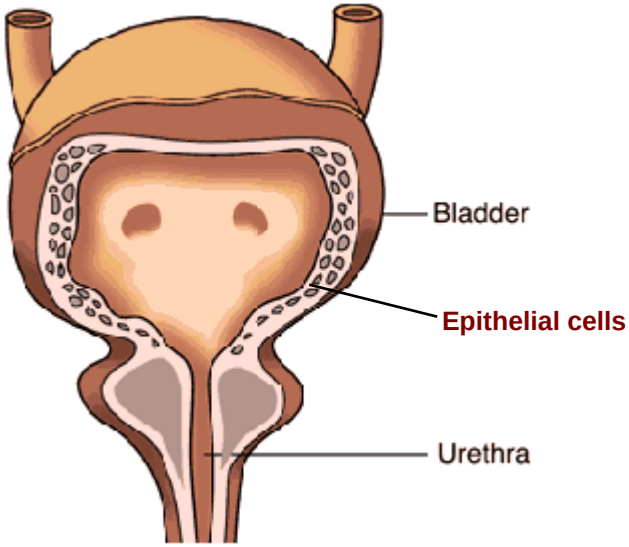


http://www.medinik.com/cancer/lung-cancer-symptoms

[Yali Li and Lily Yun Lin, w/Hunstad, Cannon, Youngs]

Urinary Tract Infections (*E. coli*)





FimH is the most common adhesin protein of *E. coli* and other enteric bacteria, which binds to mannose residues presented from epithelial cell surfaces

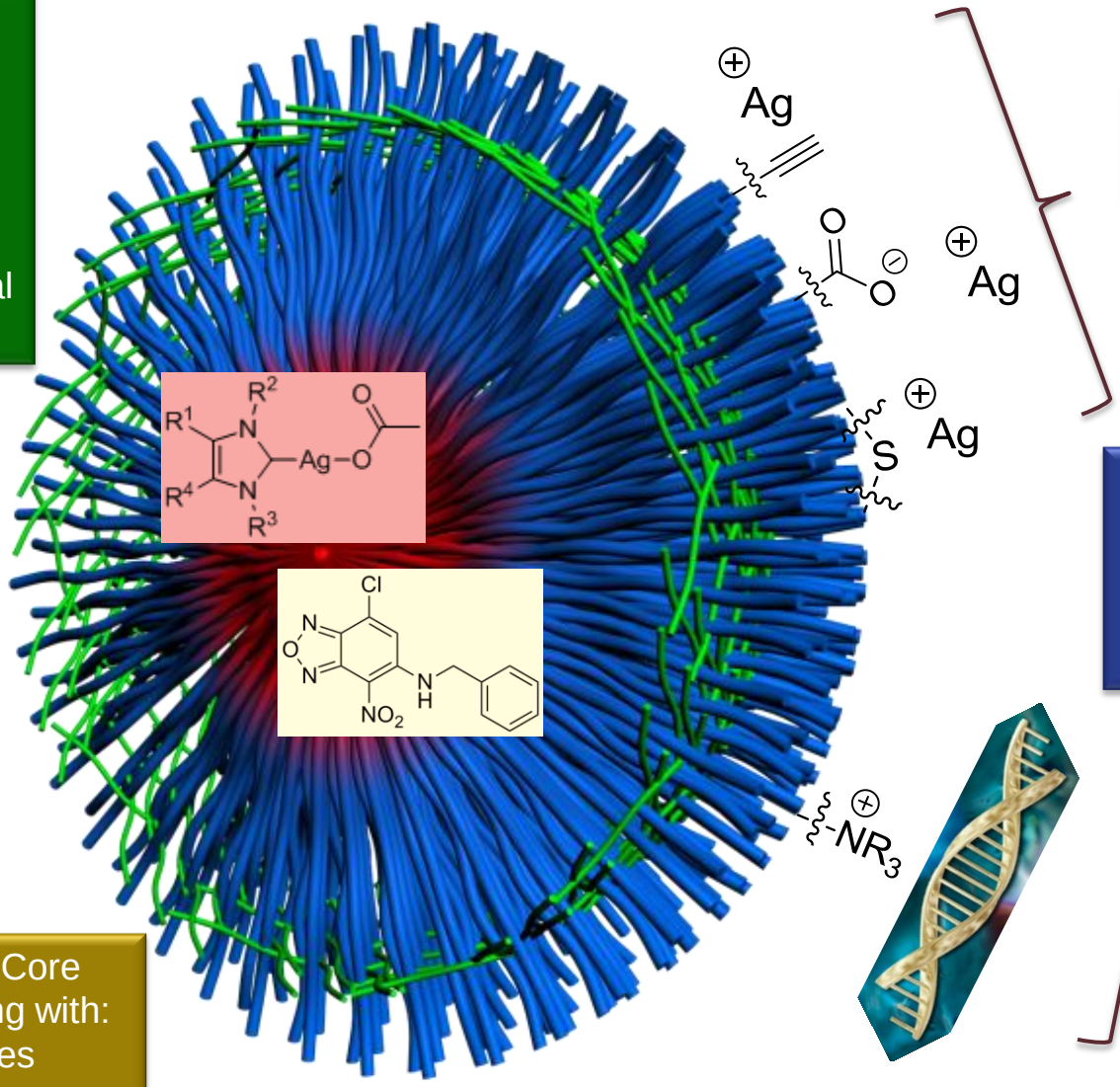
http://www.healthandage.com/html/res/primer/pics/k3bladder.gif
http://www.itb.uni-stuttgart.de/gfx/analytical/expec_3.jpg

SCK Nanomaterials Designed for Antimicrobial or Nucleic Acids Delivery to Treat Pulmonary Diseases

Shell Crosslinks for:
- Structural stability
- Gating of guest release
- Addition of functionality
- Alteration of biological properties

Hydrophobic Core For:
- Packaging of antimicrobials (or other therapeutics)
- Determination of particle shape, rigidity, *etc.*

Functionalities in the Core and/or Shell for Labeling with:
- Radiolabeling sites
- Fluorescent probes



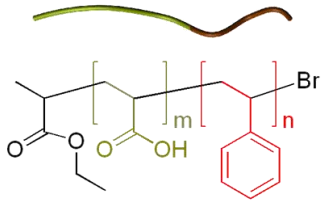
Lung Infections

Hydrophilic Shell for Packaging of:
- Ag^+
- DNA
- siRNA

Lung Injury

www.openbiosystems.com

1st Generation Non-degradable SCKs for Ag-based Antimicrobial Delivery for Treatment of Lung Infection



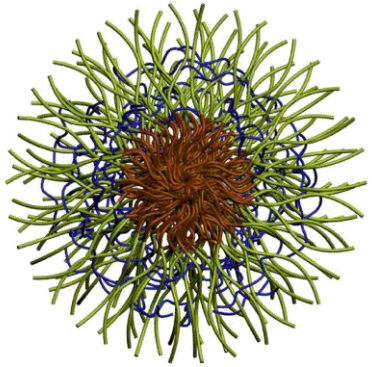
Amphiphilic diblock copolymer

Nanopure Water ⇌ THF

Micelle

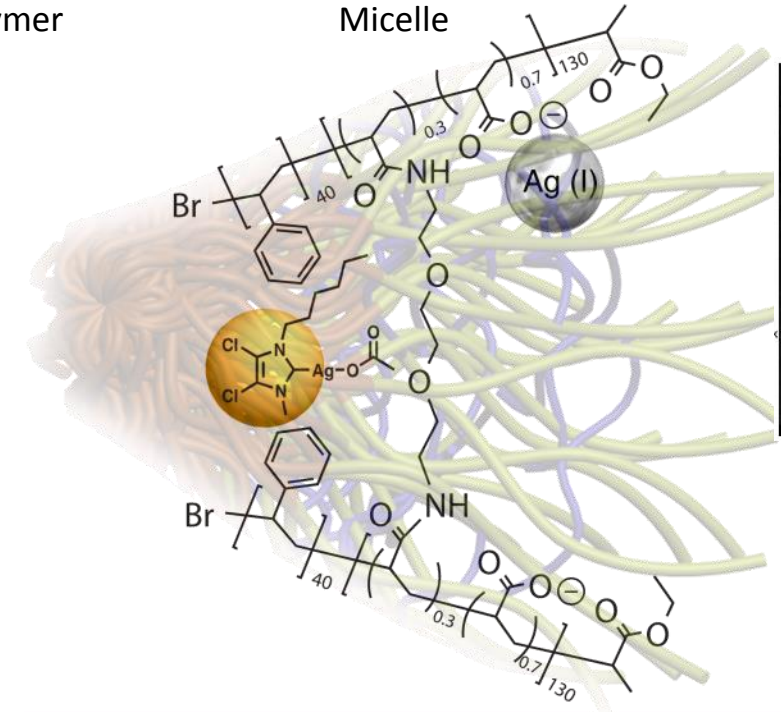
H_2N ~ O ~ O ~ NH_2

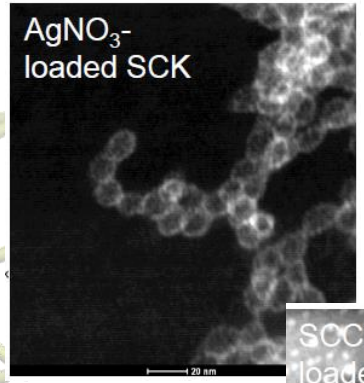
Shell Crosslinking →

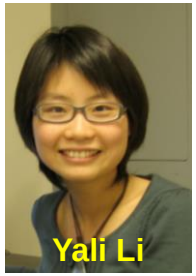


SCK

1) $AgNO_3$ in Nanopure water or/and SCC10 in $CHCl_3$
2) Stir over night →

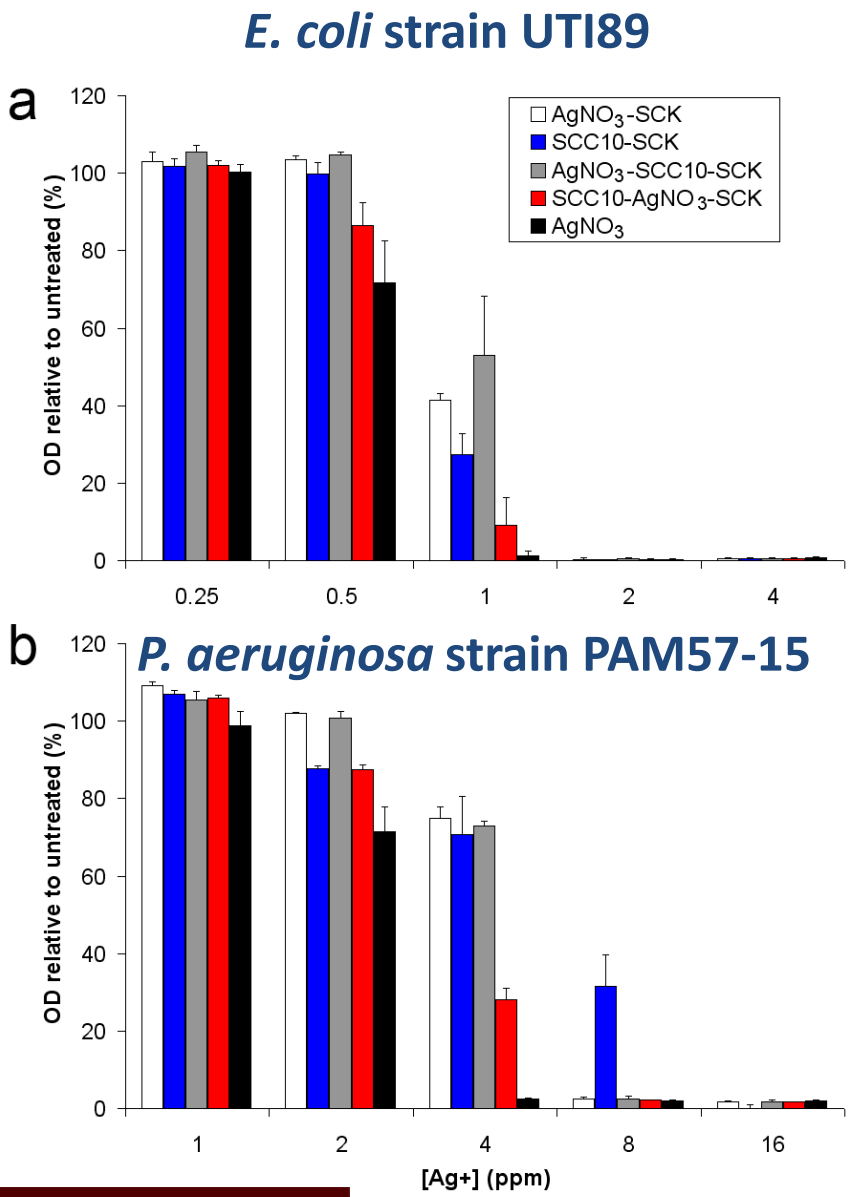






Li, Y.; Hindi, K.; Watts, K. M.; Taylor, J. B.; Zhang, K.; Li, Z.; Hunstad, D. A.; Cannon, C. L.; Youngs, W. J.; Wooley, K. L. *Chem. Commun.*, **2010**, *46*(1), 121-123.

In vitro Efficacy Reduced for Silver Loaded within SCKs

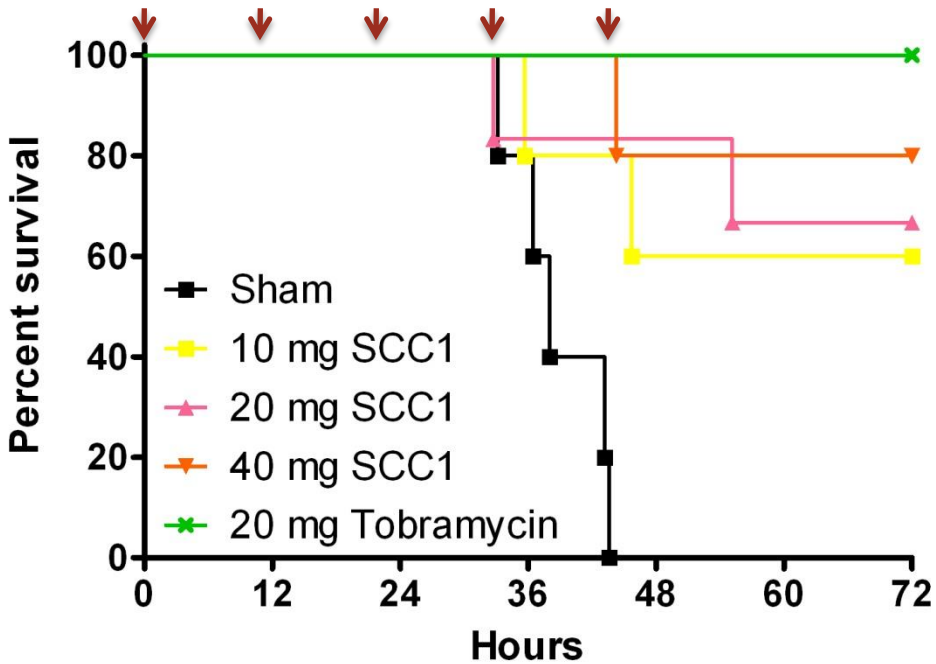


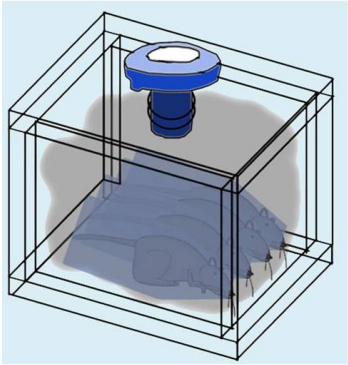
- Inhibition of growth of *E. coli* strain UTI89 (a) and *P. aeruginosa* strain PAM57-15 (b) by silver-bearing nanoparticles and $AgNO_3$.
- SCKs with no loaded silver had no antimicrobial activity.
- Activity of the silver-bearing nanoparticles was generally inferior to that of naked $AgNO_3$ by ≤1 two-fold dilution in inhibition of bacterial growth, suggesting near-equivalence in the availability of silver for antimicrobial action.

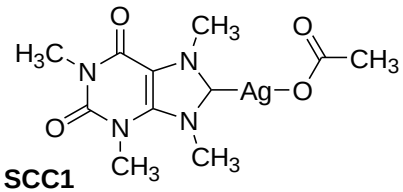
Li, Y.; Hindi, K.; Watts, K. M.; Taylor, J. B.; Zhang, K.; Li, Z.; Hunstad, D. A.; Cannon, C. L.; Youngs, W. J.; Wooley, K. L. *Chem. Commun.*, **2010**, 121-123

Efficacy of Novel Small Molecule Antimicrobial: SCC1

- *P. aeruginosa* inoculation:
  1.0 x 10^6 CFU PA M57-15 IN per mouse
- Five nebulized dose treatments, every 12 h







SCC1
Water solubility: 10 mg/mL
2.88 mg Ag per 10 mg SCC1

	Ag Conc. (mg)	Survival percentage
Tobramycin	40*	100%
40 mg SCC1	11.52	80%
20 mg SCC1	5.76	67%
10 mg SCC1	2.88	60%
Sham (water)	0	0%

***Tobramycin concentration**

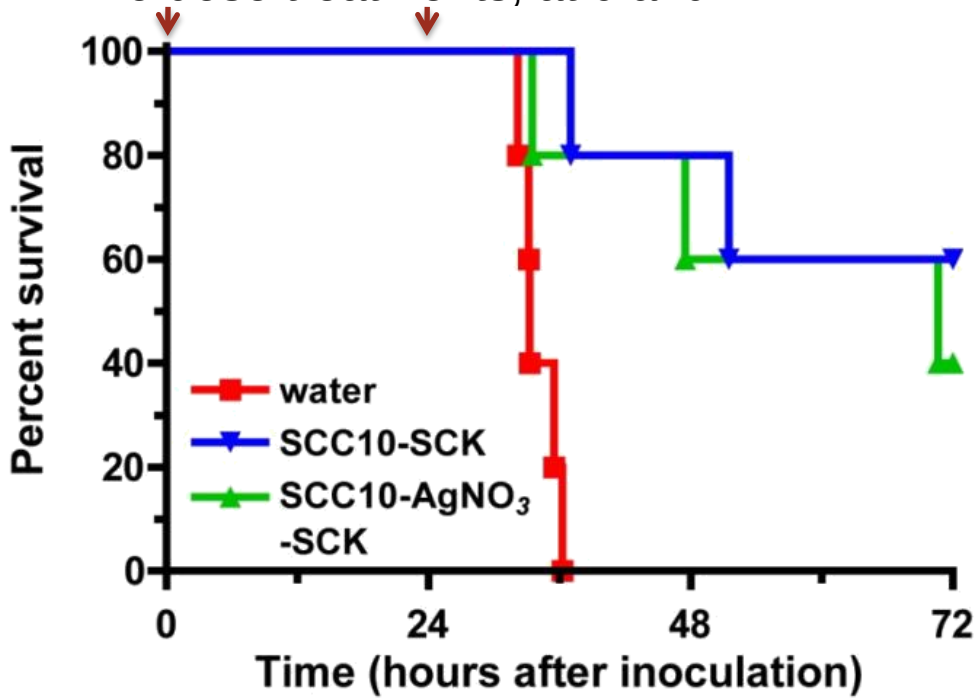
For a 60% survival advantage, 2.88 mg Ag^+ delivered 2x daily for 5 doses (14.4 mg Ag total) were required

Anticipated advantage of nanoparticles: redirect pharmacokinetics

[Carolyn Cannon, UTSW]

Silver-loaded SCKs Demonstrated Greater Therapeutic Effects than Small Molecule Silver Carbene Complexes Alone

- *P. aeruginosa* inoculation:
  1.5 x 10^6 CFU PA M57-15 IN per mouse
- Two dose treatments, at 0 and 24 h



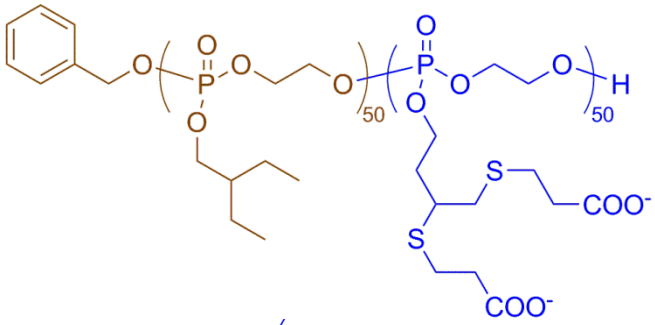
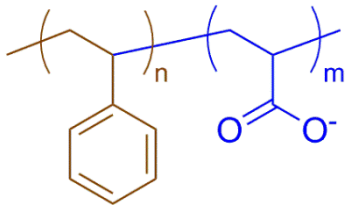
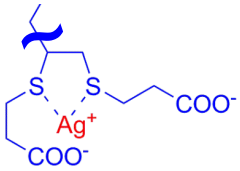
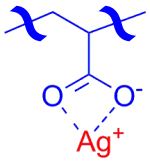
	Ag Conc. (mg)	Survival percentage
SCK-SCC10	0.88	60%
SCK-SCC10-$AgNO_3$	1.42	40%
Sham (water)	0	0%

SCC1: 14.4 mg Ag
SCC10-SCK: 0.88 mg Ag

***ca*. 16-fold less silver concentration** was needed to achieve the same survival rate when silver was incorporated into SCKs, compared with direct small molecule administration

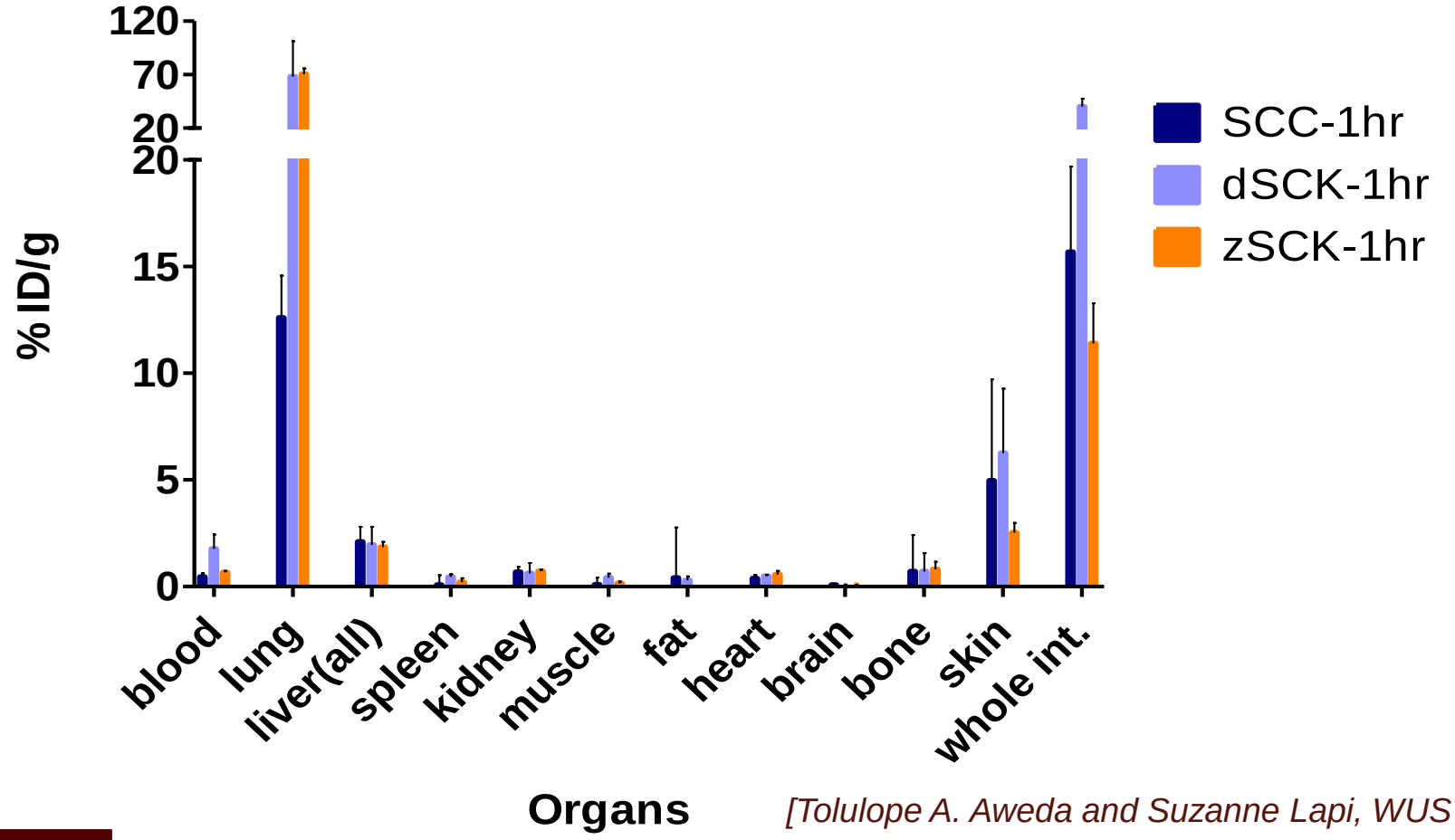
Shah, P. N.; Lin, L. Y.; Smolen, J. A.; Tagaev, J. A.; Gunsten, S. P.; Han, D. S.; Heo, G. S.; Li, Y.; Zhang, F.; Zhang, S.; Wright, B. D.; Panzner, M. J.; Youngs, W. J.; Brody, S. L.; Wooley, K. L.; Cannon, C. L. *ACS Nano*, **2013**, *7*(6), 4977-4987.

A Degradable Polyphosphoester-based System Gives Higher Ag^+ Loading and Greater Solution-state Stability *vs*. 1st Generation SCK System

	Degradable loading system	Non-degradable system
		
Interaction		
Stability in 150 mM PBS	up to 4 h w/no precipitation	precipitates form immediately
Polymer concentration	10 mg/mL	0.25 mg/mL
Silver Concentration	0.5 – 1.0 mg/mL (and even higher)	0.080 – 0.120 mg/mL

The Enhanced Therapeutic Efficacy may be due (in part) to Greater Lung Retention for the Nanoparticles

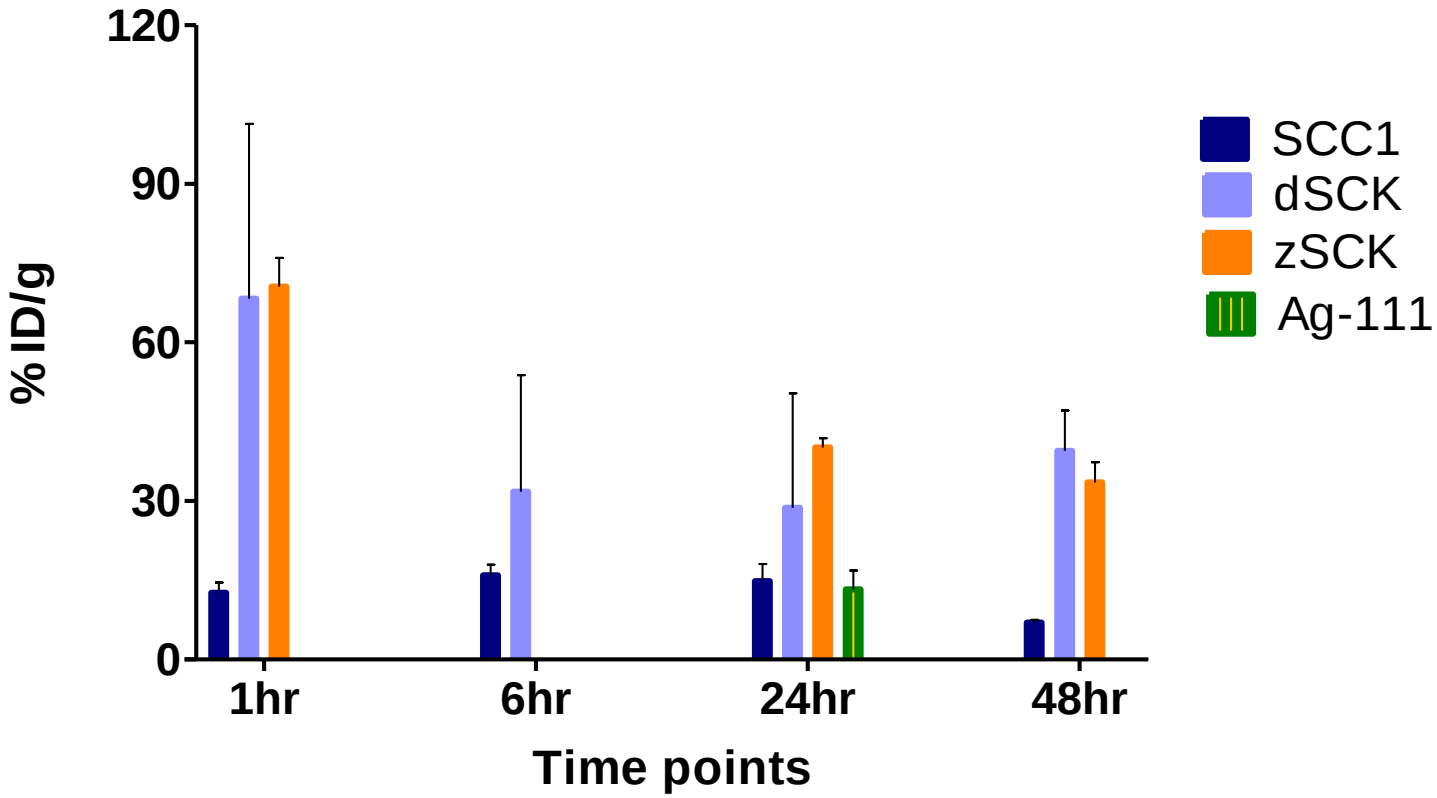
[^{111}Ag] Particles Biodistribution @ 1hr %ID/g-mice dose



[Tolulope A. Aweda and Suzanne Lapi, WUSTL]

The Enhanced Therapeutic Efficacy may be due (in part) to Greater Lung Retention for the Nanoparticles

[^{111}Ag] Particles Lung Biodistribution @ different time points

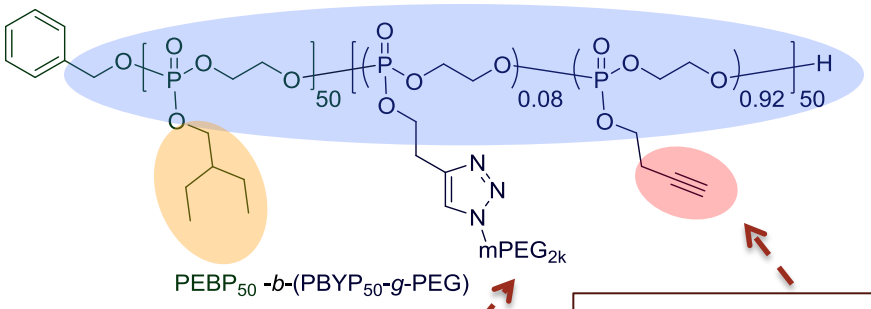


[Tolulope Aweda and Suzanne Lapi, WUSTL]

Two New Generation Degradable, Functional Polymers for Construction of Silver-loaded Nanoparticle Therapeutics

Polyphosphoester-based backbone

[Fuwu Zhang and Richen Li]

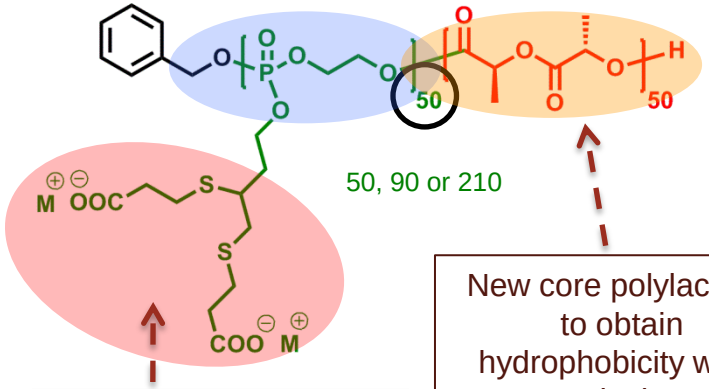


PEG to increase hydrophilicity and mucosal transport

New interaction for silver loading and post-modification by alkyne-azide or thiol-yne reactions

Poly(phosphoester-b-lactide) system

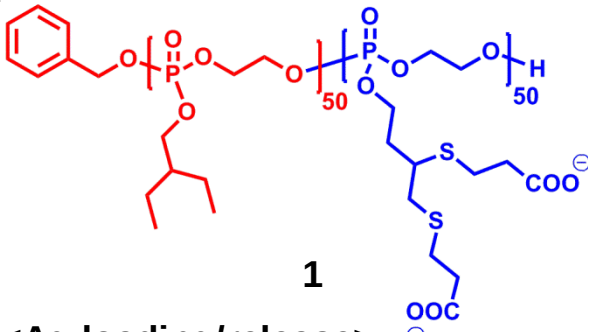
[Young Lim and Gyu Seong Heo]



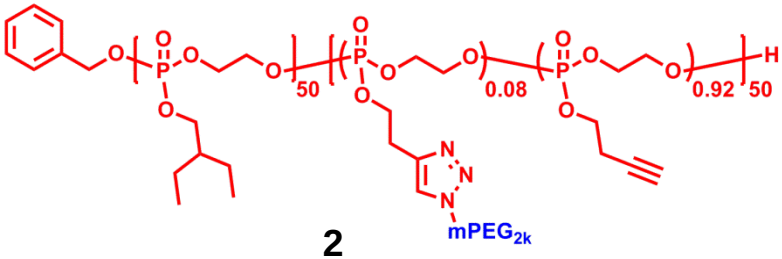
Established interaction for loading silver cations

New core polylactides to obtain hydrophobicity while reducing polyphosphoester content

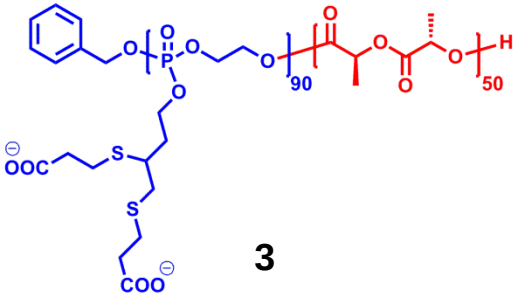
A Series of Degradable Particles That Exhibit Different Antimicrobial Agent Loading/Release Characteristics, Designed for Treatment of Lung Infections



1



2

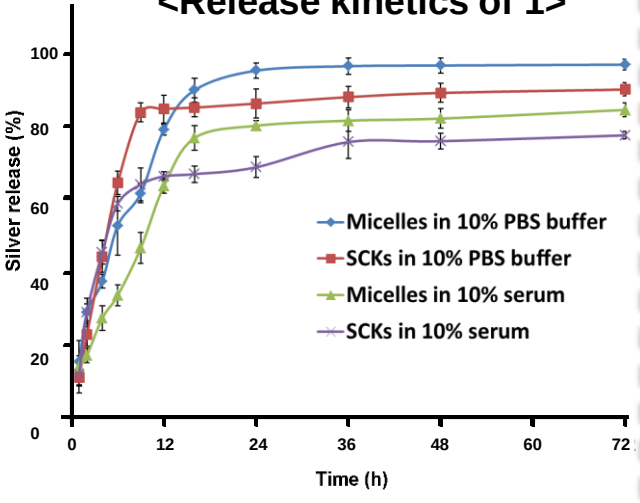


3

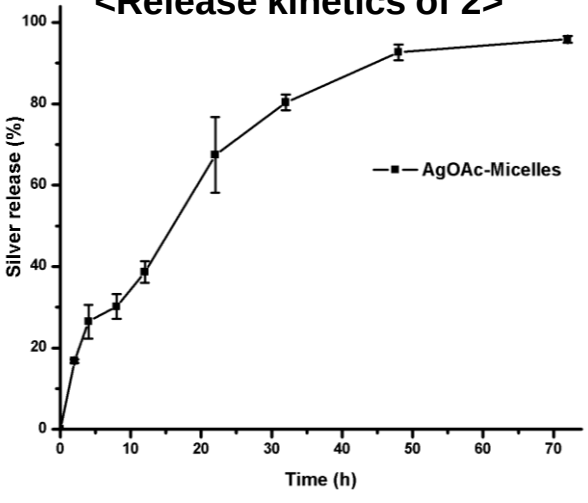
<Ag loading/release>

Polymers	1	2	3
Max. loading capacity	*ca.* 10 wt.%	*ca.* 16 wt.%	*ca.* 12 wt.%
Release rate (50%)	4-10 h	16 h	2.5–5.5 h
$D_{h,\ number}$ (DLS)	*ca.* 16 nm	*ca.* 11 nm	*ca.* 17 nm

<Release kinetics of 1>

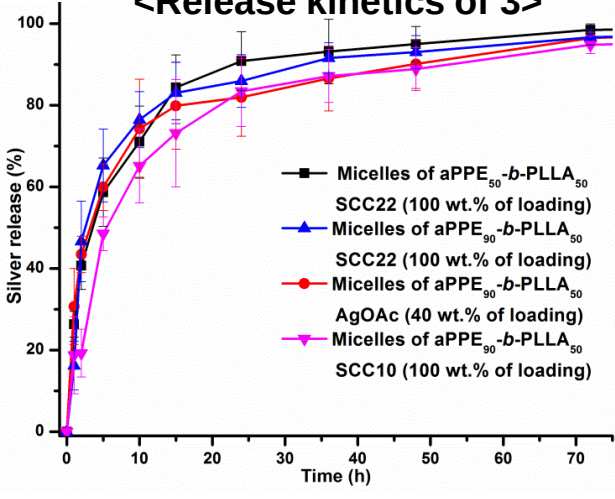


<Release kinetics of 2>



10 mM phosphate buffer (pH 7.4) with 10 mM NaCl at 37 °C

<Release kinetics of 3>



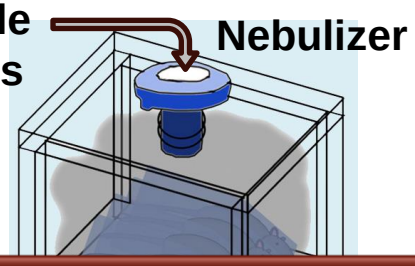
Nanopure water at 37 °C

Efficacy of Ag^+-loaded SCK *in vivo*

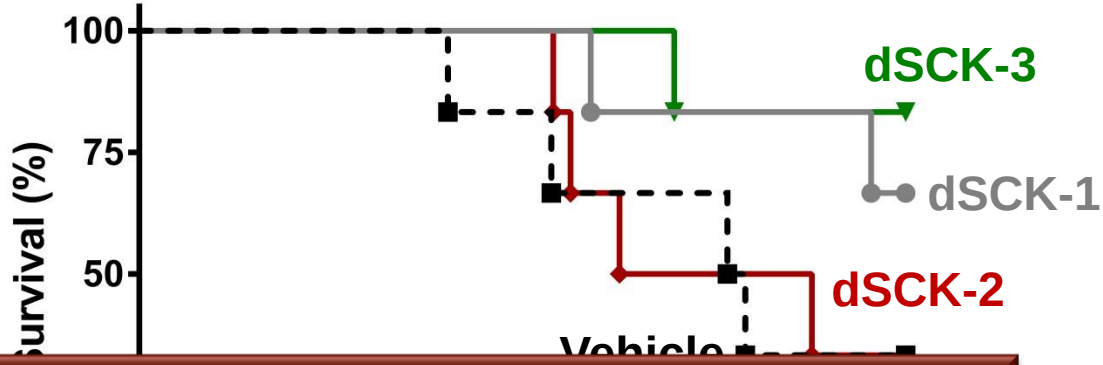
- **C57BL/6 mice**
- **~10^6 CFU Pseudomonas (M57-15 strain, intranasal)**

24h

- **Vehicle**
- **dSCKs**



dSCK-1 loaded with Ag-acetate
dSCK-2 loaded with Ag-acetate
dSCK-3 loaded with SCC22

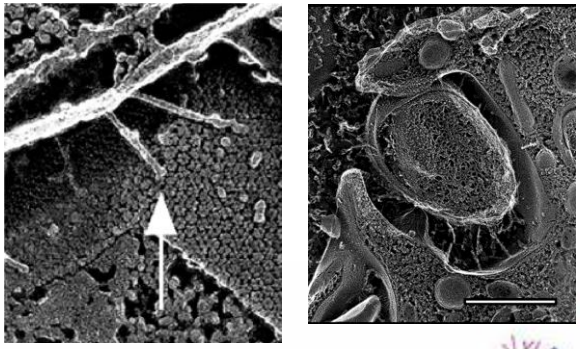


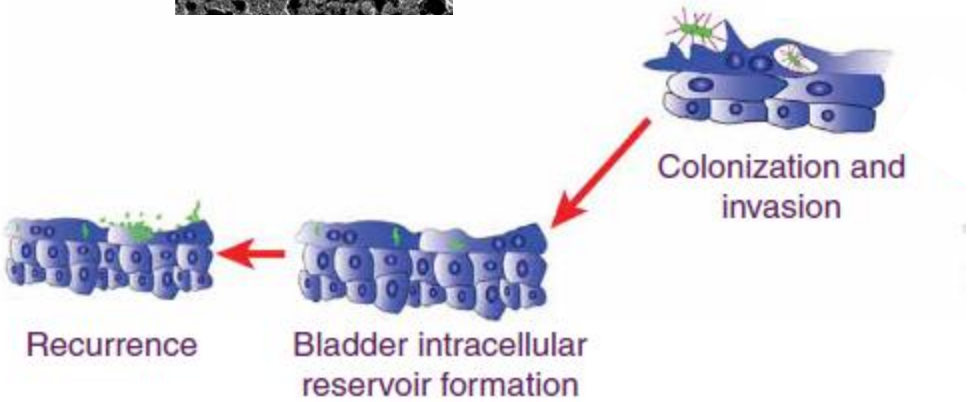
Based upon *in vivo* efficacy,
1 or **3** is likely the next candidate
for scale-up by the PEN PROD Core (C. J. Hawker, UCSB)

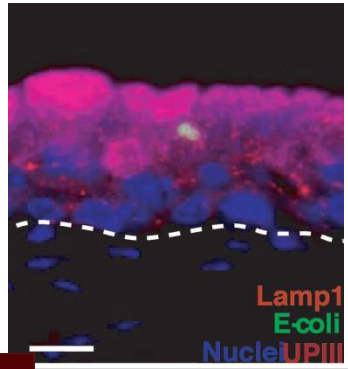
Synthetic versatility, reproducibility and scalability, formulation stability, and nanoparticle degradability are also key factors to be considered in the final PROD candidate selection

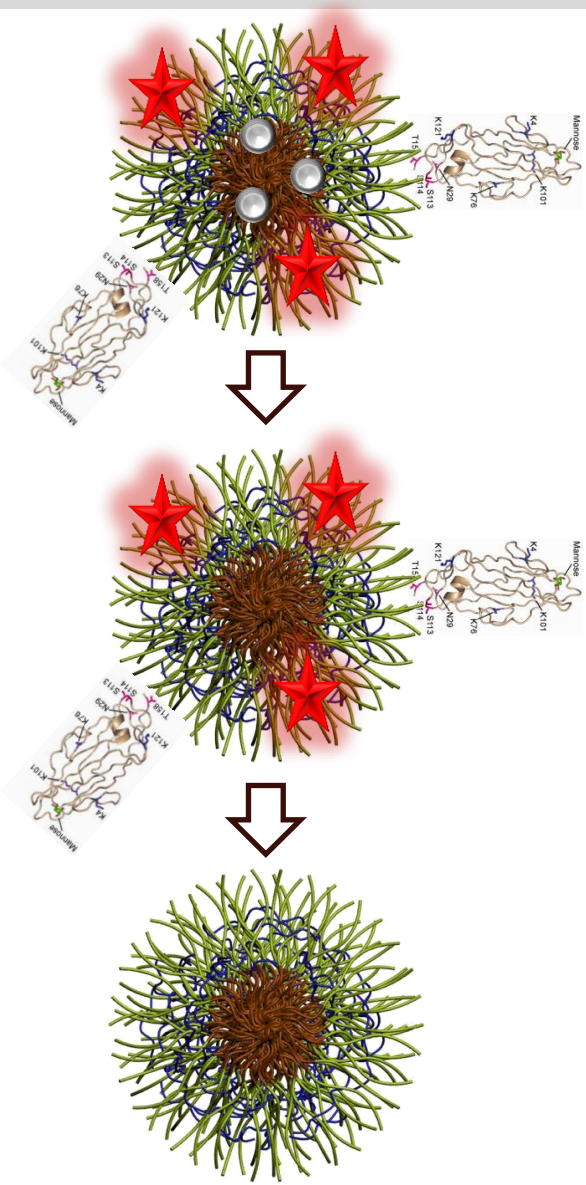
Strategy to Treat Recurrent Urinary Tract Infections (UTI) by Hijacking Biological Aspects Involved in the Pathogenesis

Mysorekar *et al*., **2006**; Hung *et al*., **2009**; Hunstad *et al*., **2010**



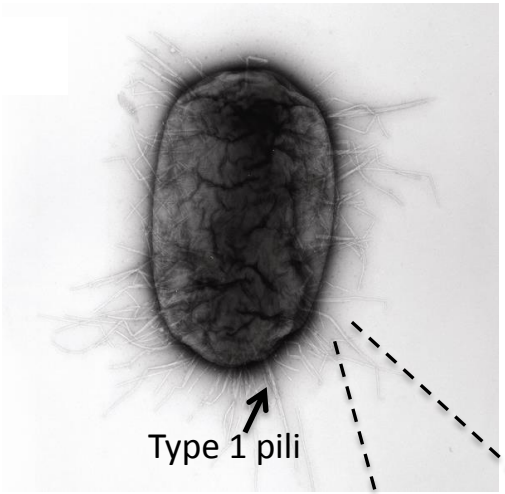




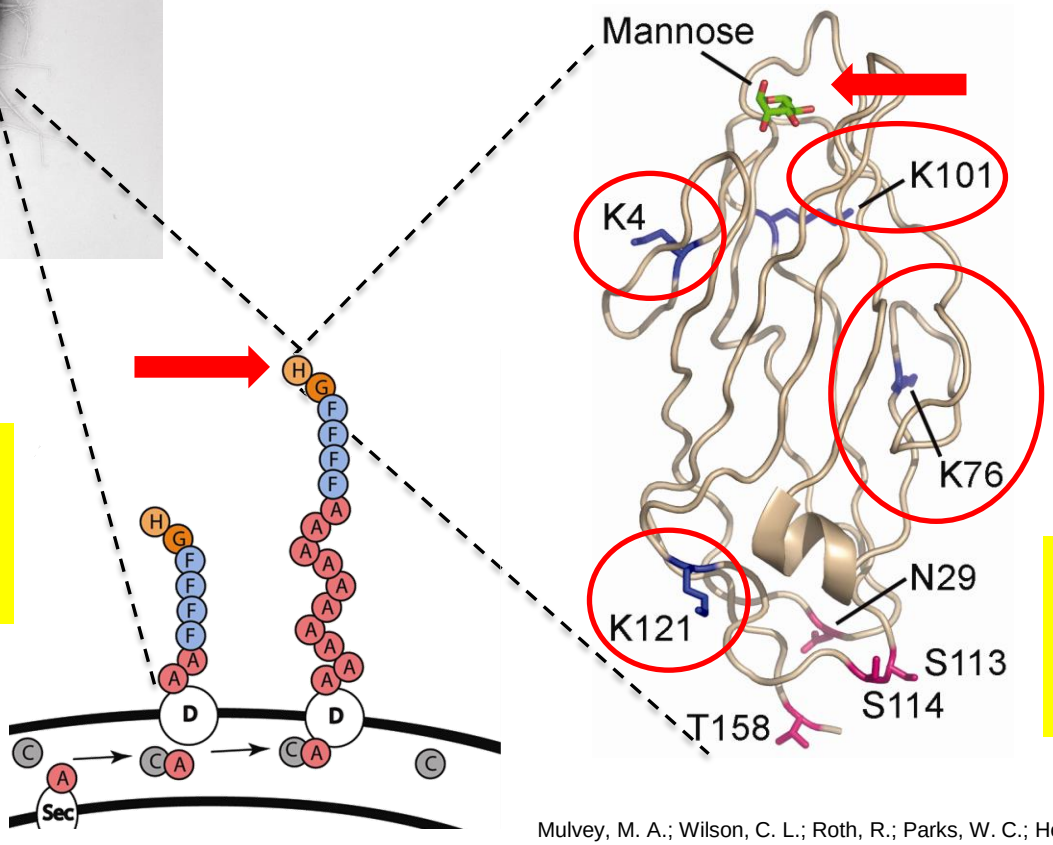


UTI: $FimH_A$ bacterial adhesin-facilitated invasion of bladder epithelial cells

UPEC



- Binding and invasion of bladder epithelial cells through type 1 pili



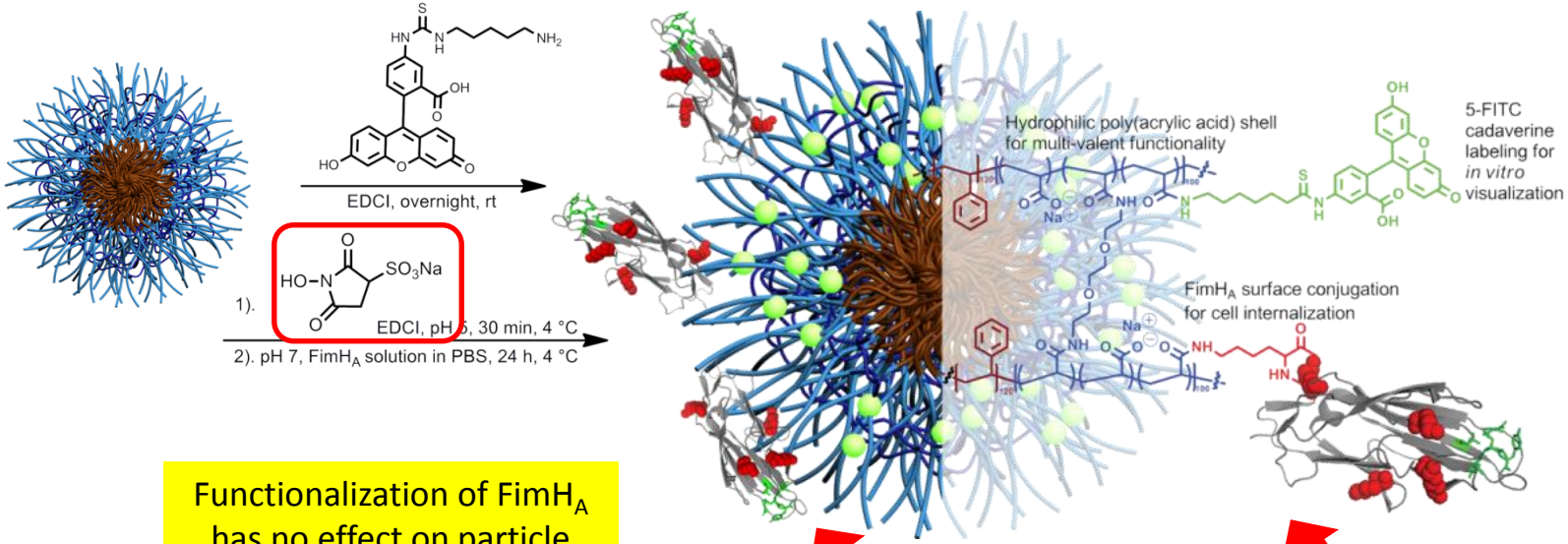
The tip adhesin protein $FimH_A$ mediates bacterial binding

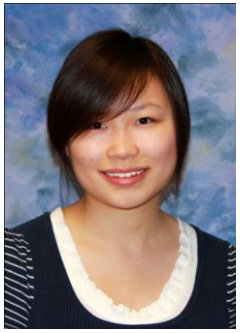
$FimH_A$ has a binding pocket that binds **mannose moieties** of uroplakin expressed on epithelial cells (w/~16 nm spacings between mannose sites across 50-100 µm epithelial cell)

$FimH_A$ has four **lysine groups for functionalization** onto the SCK to **emulate** the bacterial mode of invasion

Mulvey, M. A.; Wilson, C. L.; Roth, R.; Parks, W. C.; Heuser, J.; Hultgren, S. J. *Science* **1998**, *282*, 1494.
Hung, C. S.; Bouckaert, J.; Hung, D.; Pinkner, J.; Widberg, C.; DeFusco, A.; Auguste, C. G.; Strouse, R.; Langermann, S.; Waksman, G.; Hultgren, S. J. *Mol. Microbiol.* **2002**, *44*, 903.

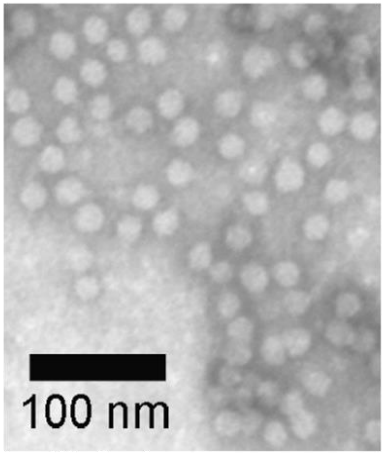
Synthetic polymer nanoparticles functionalized with $FimH_A$ emulate the bacterial mode of epithelial internalization



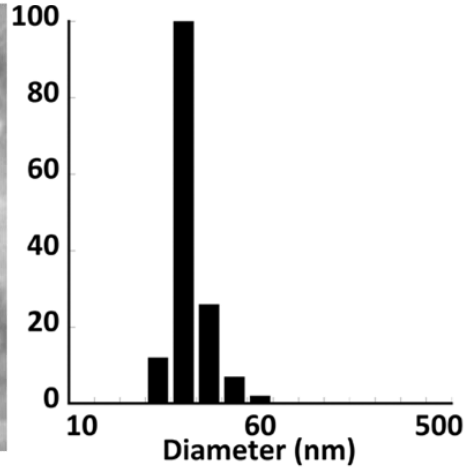


Lily Lin

Functionalization of $FimH_A$ has no effect on particle size and morphology



Diameter = 20 ± 3 nm



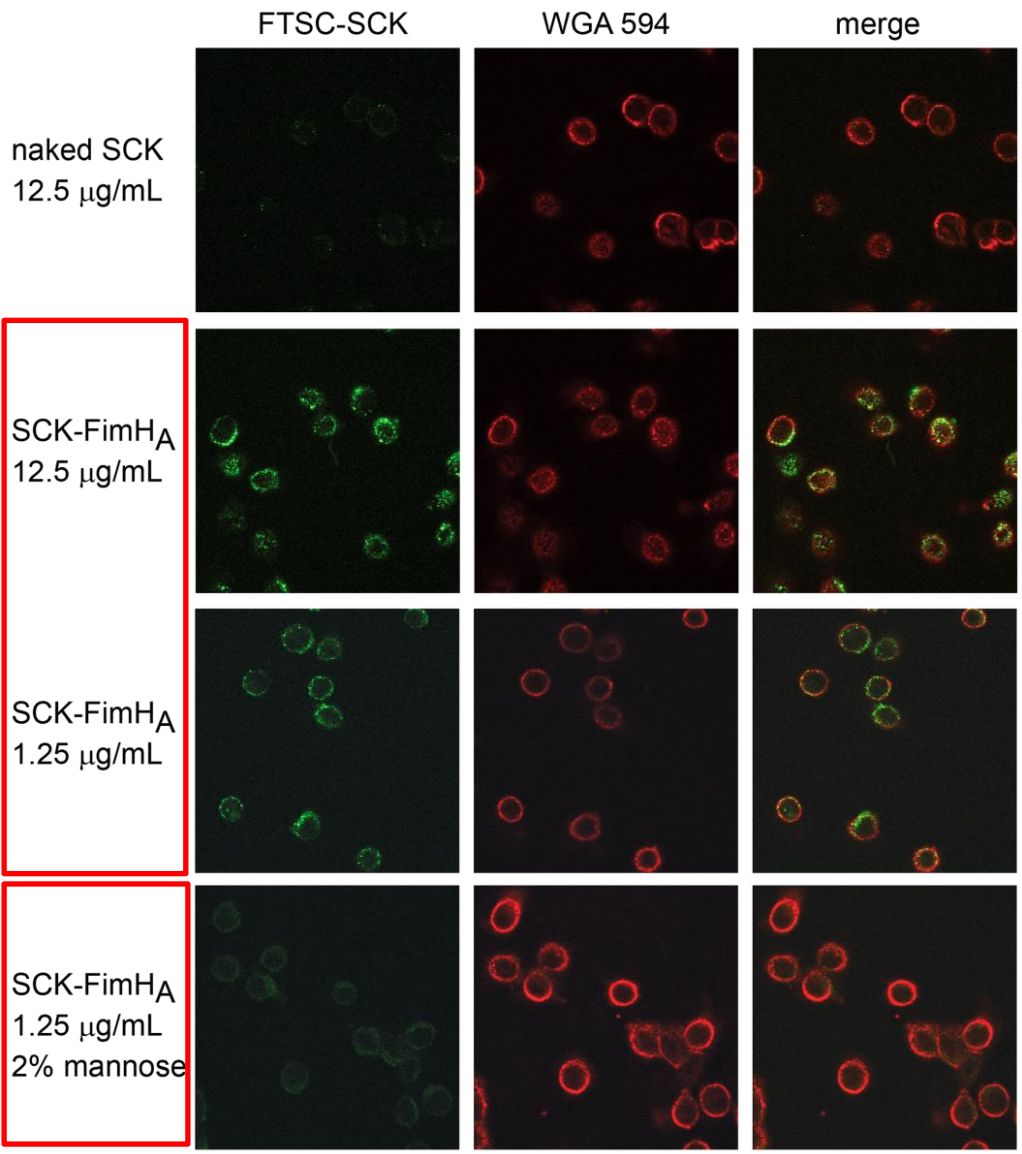
$D_{h(number)}$ = 40 ± 10 nm

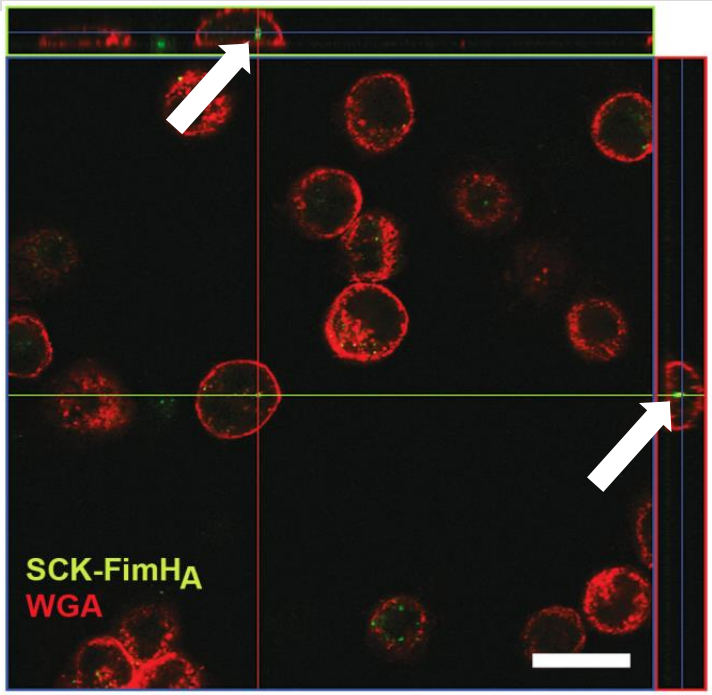
Physical association *vs.* Covalent conjugation

- Absence *vs*. presence of the amidation coupling agents
- No coupling agents: more free protein was observed
- With coupling agents: minor amount of free protein, and physically associated protein with the SCKs
- Final purified product existed as a mixture of physically- and covalently-associated proteins and nanoparticles

Lin, L. Y.; Tiemann, K. M.; Li, Y.; Pinkner, J. S.; Walker, J. N.; Hultgren, S. J.; Hunstad, D. A.; and Wooley, K. L., *J. Am. Soc. Chem.*, ***2012***, *134*(9), 3938-3941.

Confocal fluorescence microscopy demonstrated binding and internalization of bladder epithelial cells





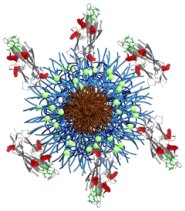
Scale bar, 20 μm

- By fluorescence microscopy, the association of SCKs with the cell surfaces was shown to be **dose dependent**, **FimH$_A$ specific**, and **inhibited by addition of mannose**
- Ongoing studies are investigating SCK size and shape effects, including therapeutically-loaded, degradable nanoparticles

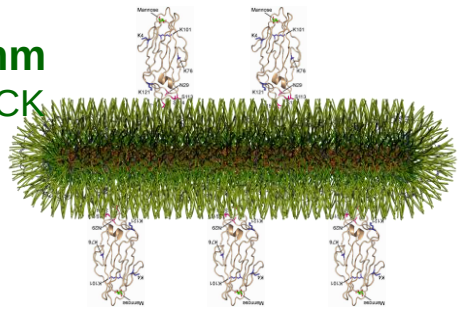
Lin, L. Y.; Tiemann, K. M.; Li, Y.; Pinkner, J. S.; Walker, J. N.; Hultgren, S. J.; Hunstad, D. A.; and Wooley, K. L., *J. Am. Soc. Chem.*, ***2012***, *134*(9), 3938-3941.

Future Nanostructures for UTI Treatment Studies

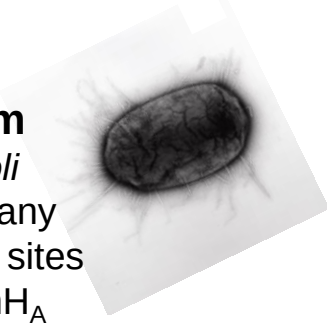
~30 nm
Spherical $FimH_A$-SCK
(may bind only 1 or 2 mannose sites)

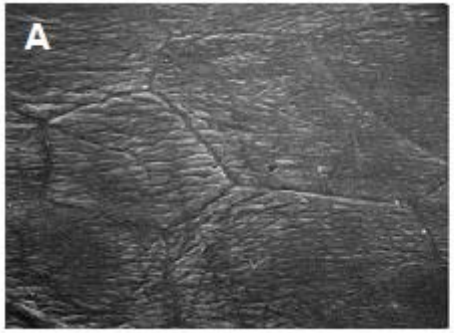


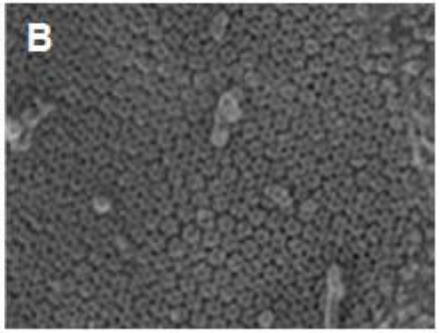
~30 nm x > 100 nm
Cylindrical $FimH_A$-SCK
(may bind many mannose sites)



~5 μm
E. Coli
(bind many mannose sites *via* $FimH_A$ at pili termini)

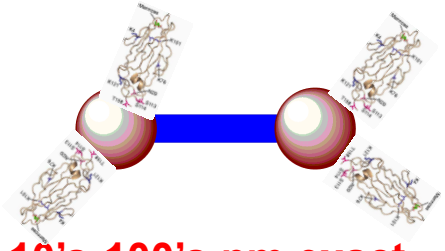






50-100 μm
superficial facet cells lining the bladder

16 nm
hexagonal uroplakin plaques w/a terminal mannose at the center of each



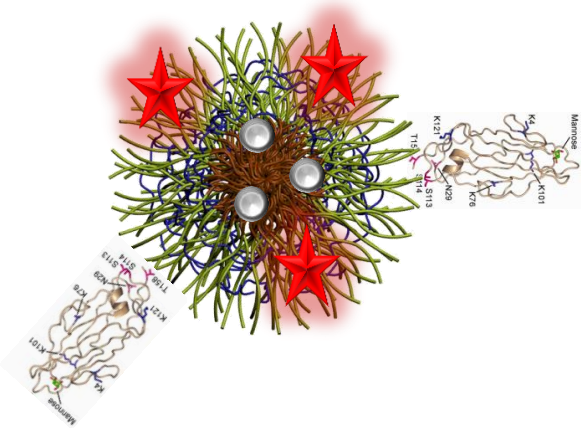
10's-100's nm exact dimensions and compositions
$FimH_A$-Dumbbells
(may bind many mannose sites, with defined tuning)

Spherical *vs*. cylindrical *vs*. dumbbell dimensions and selective chemistry are to be used with $FimH_A$ conjugation to optimize the effects of size, shape and $FimH_A$ spacing to emulate bacterial cell internalization by binding to mannose moieties of uroplakin expressed on epithelial cells

Lin, L. Y.; Tiemann, K. M.; Li, Y.; Pinkner, J. S.; Walker, J. N.; Hultgren, S. J.; Hunstad, D. A.; and Wooley, K. L., *J. Am. Soc. Chem.*, ***2012***, *134*(9), 3938-3941.

Chemical Control is Critical to Any Strategy That Intends to Construct Sophisticated Functional Materials

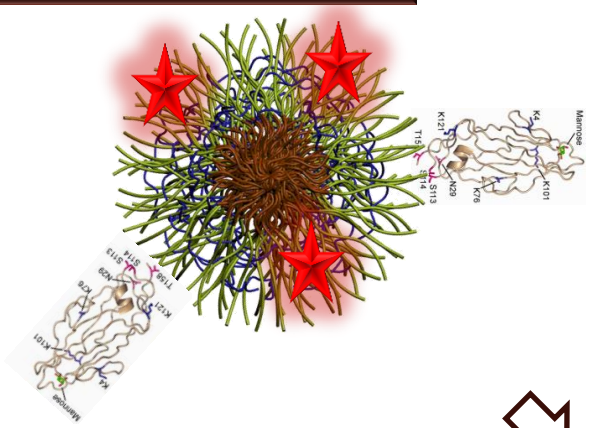
Iterative processes build up increasingly-complex and functional materials



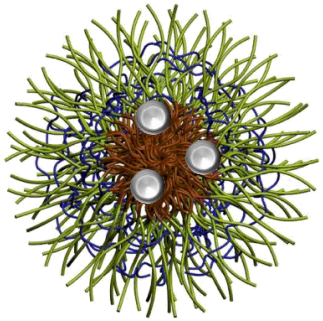
Ultimate target

Any serendipitous therapeutic benefit?

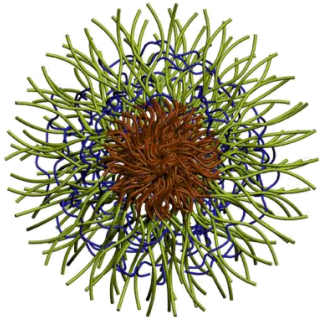
Level of efficacy without targeting?



Intermediate materials are also of interest, *e.g.*…



…as a targeted diagnostic



…as a non-targeted therapeutic for this and other applications

A few functional polymer chemistry goals:

- Antimicrobial nanoparticles for infectious disease treatment
- Chemotherapeutic nanoparticles for treatment of osteosarcoma lung metastases
- Engineering polymers derived from natural products
- Anti-biofouling and anti-icing coatings
- Advanced photoresist technologies

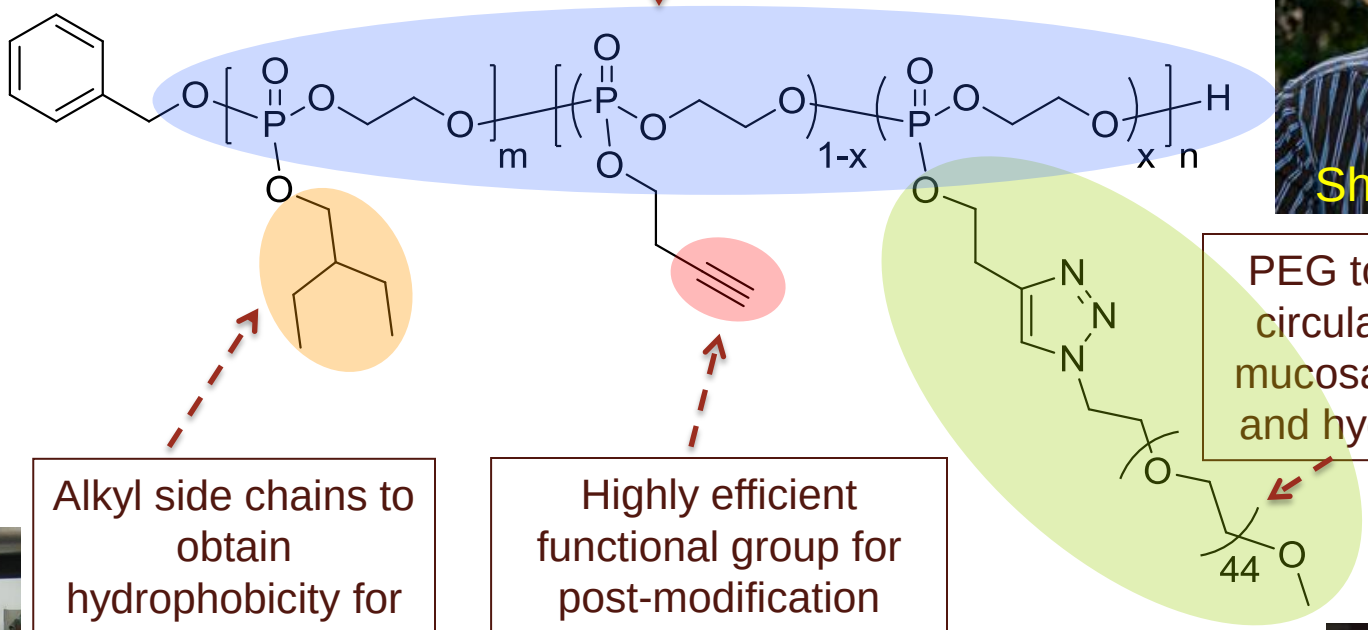
Koshkina, N. V.; Kleinerman, E. S.; Waldrep, C.; Jia, S.-F.; Worth, L. L.; Gilbert, B. D.; Knight, V. *Clin. Cancer Res.* **2000**, *6*, 2876-2880.

"…drugs delivered to the respiratory tract in liposomal formulation resulted in high pulmonary drug concentration, reduced systemic toxicity, and reduced dosage requirements compared with parenteral and oral administration."

And, "…L-9NC (liposomal 9-nitrocamptothecin) aerosol therapy is effective in the treatment of melanoma and osteosarcoma pulmonary metastases in mice."

Physically- or Covalently-loaded PTX Micelles and SCKs: Degradable polyphosphoester (PPE) block copolymer design

Water soluble and degradable backbone

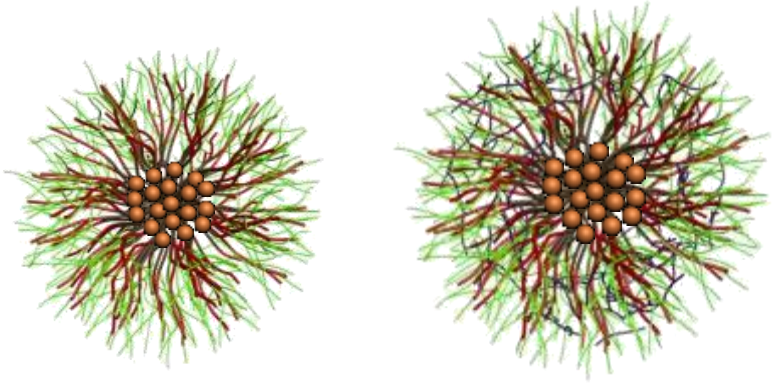


PEG to increase circulation time, mucosal transport and hydrophilicity

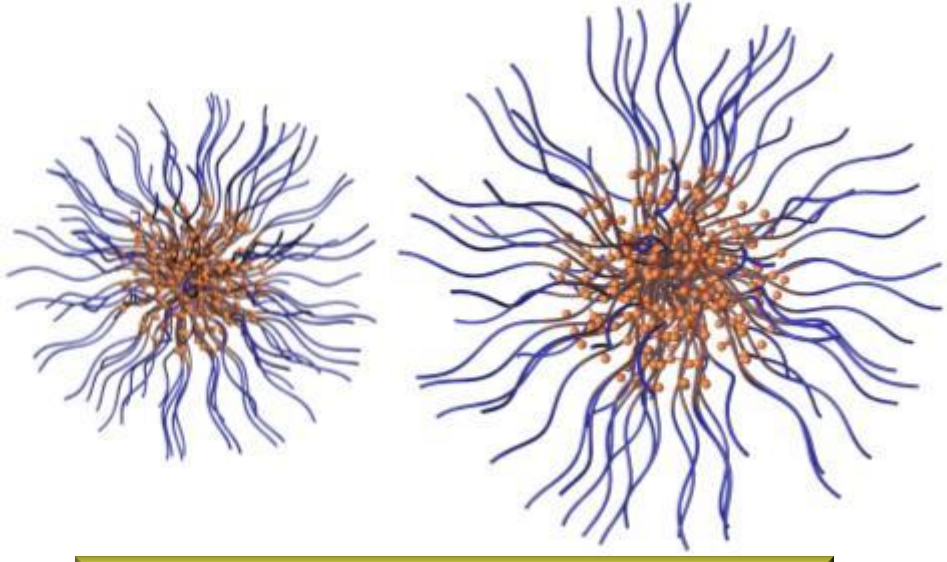
Alkyl side chains to obtain hydrophobicity for micellization and for PTX incorporation

Highly efficient functional group for post-modification by alkyne-azide or thiol-yne reactions

Design and Synthesis of Polymeric Nanoparticles for the Treatment of Osteosarcoma Lung Metastases



Physically-loaded PTX Nanosystems
Micelles SCKs
$(D_h)_n$ = 14 ± 4 nm and 24 ± 6 nm
PTX conc. *ca*. 5 mg/mL
PTX release $t_{½}$ = 6.5 h and 12 h

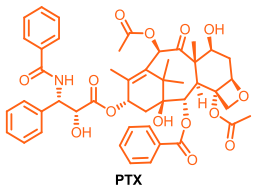


Covalently-conjugated PTX Nanosystems
G1 Micelles G2 Micelles
$(D_h)_n$ = 26 ± 7 nm and 114 ± 31 nm
PTX conc. >6 mg/mL and >0.7 mg/mL
PTX release $t_{½}$ = unknown and >100 h

Zou, J.; Zhang, F.; Zhang, S.; Pollack, S. F.; Elsabahy, M.; Fan, J.; Wooley, K. L. *Adv. Healthcare Mater.*, **2014**, *3*(3), 441-448

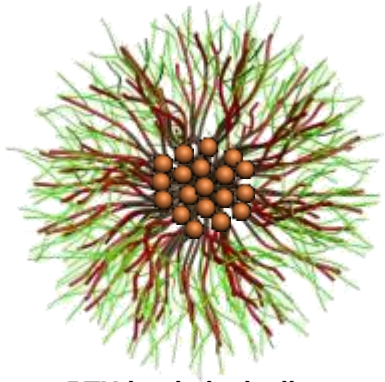
Zhang, S.; Zou, J.; Elsabahy, M.; Karwa, A.; Li, A.; Moore, D. A.; Dorshow, R. B.; Wooley, K. L. *Chem. Sci.*, **2013**, *4*, 2122-2126

Comparable *in vitro* Cytotoxicities to Taxol

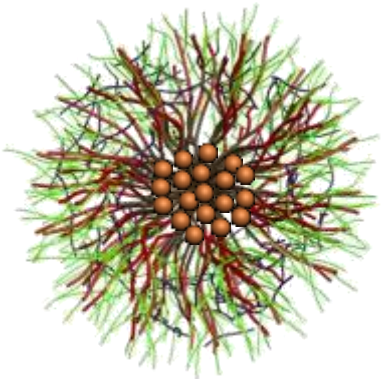


+
Cremophor EL

Taxol

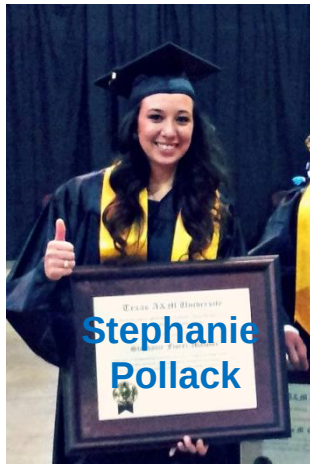


PTX-loaded micelles



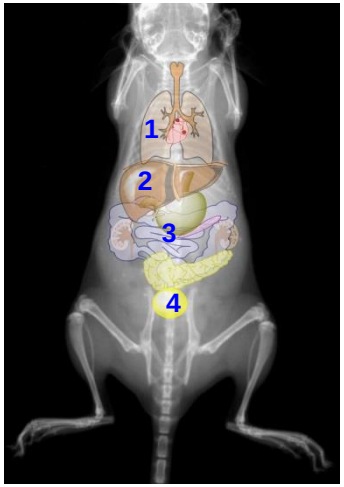
PTX-loaded SCKs

Formulation	IC_{50} (μM) CCH-OS-O	CCH-OS-D	OVCAR-3	RAW 264.7
Taxol	0.0281 ± 0.001	0.1291 ± 0.004	0.005 ± 0.002	0.04 ± 0.01
PTX-Micelles	0.0283 ± 0.001	0.0598 ± 0.02	0.015 ± 0.010	0.10 ± 0.04
PTX-SCKs	0.0141 ± 0.001	NA	0.010 ± 0.008	0.08 ± 0.02

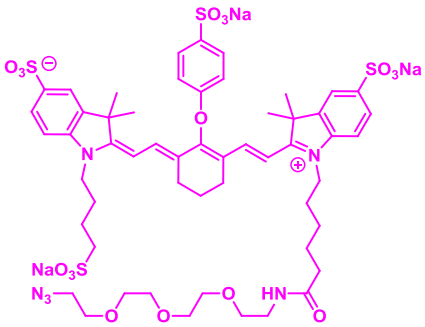


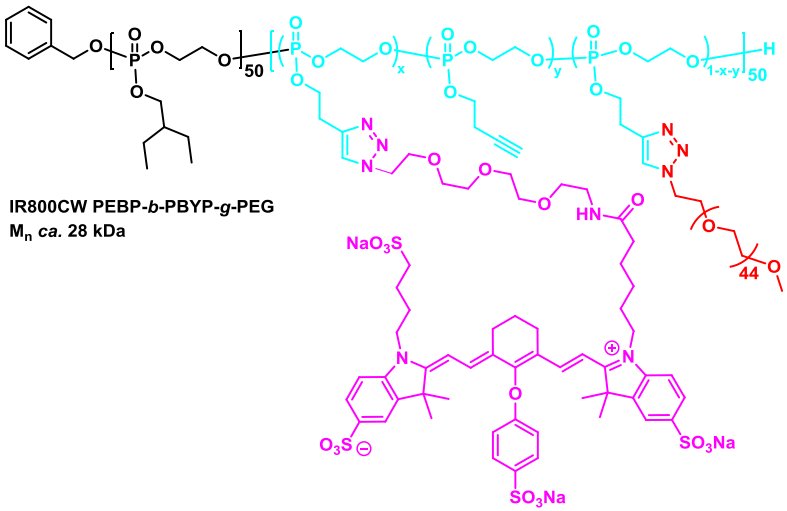
NPs without PTX did not induce any toxicity at the tested concentrations

Conjugation of IR800CW Azide to PEBP-*b*-PBYP-*g*-PEG Allows for Observation of Polymer Retention and Biodistribution

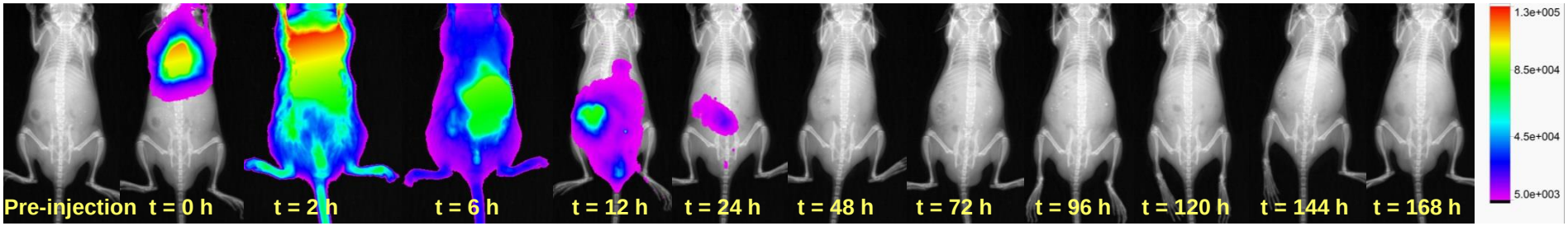


1. Lung
2. Liver
3. GI Track
4. Bladder

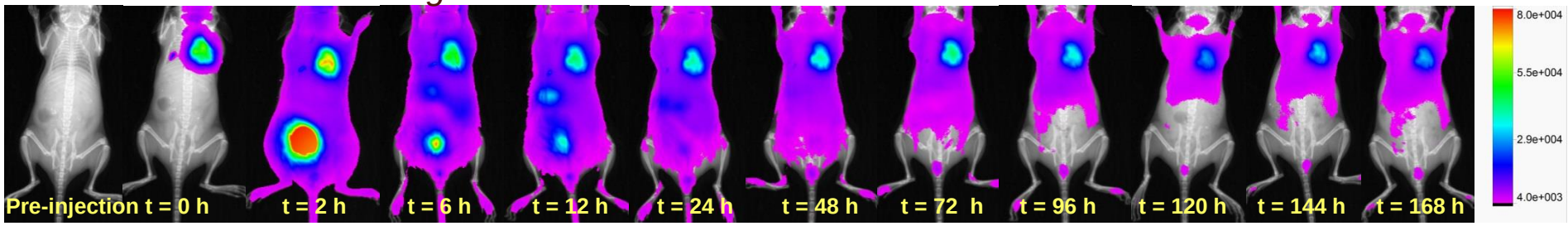




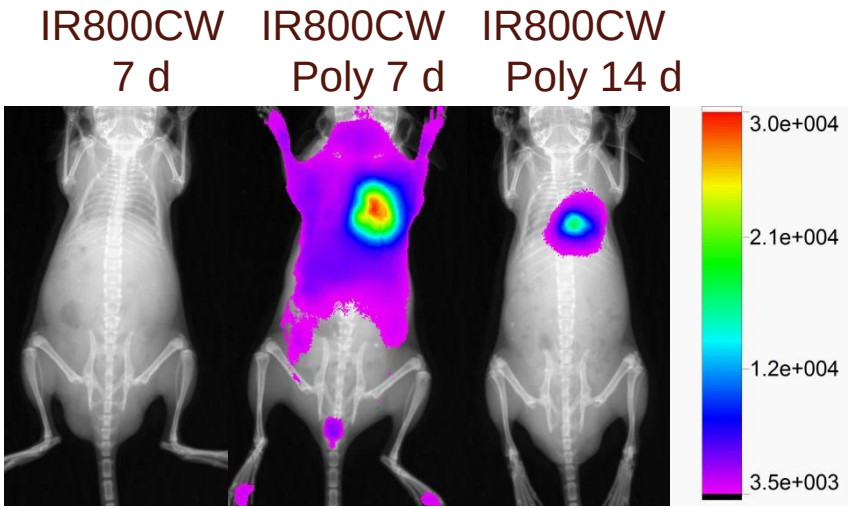
IR800CW Azide

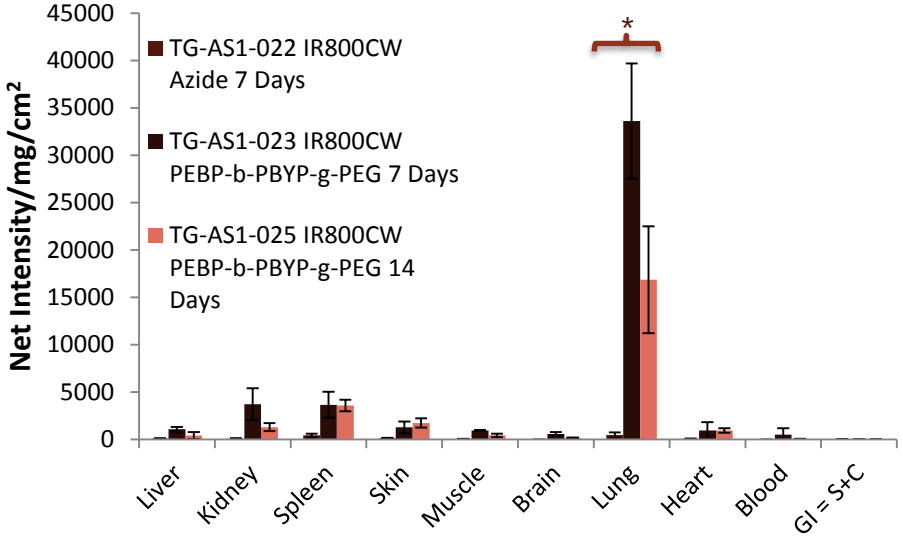


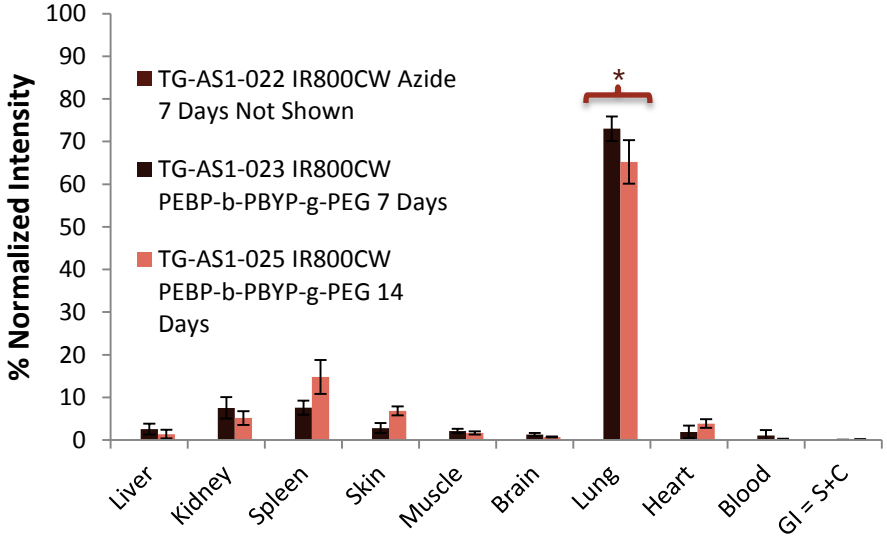
IR800CW PEBP-*b*-PBYP-*g*-PEG



NIR Optical Imaging Studies *in vivo* Confirm Long-term Pulmonary Retention for Sustained PTX Release

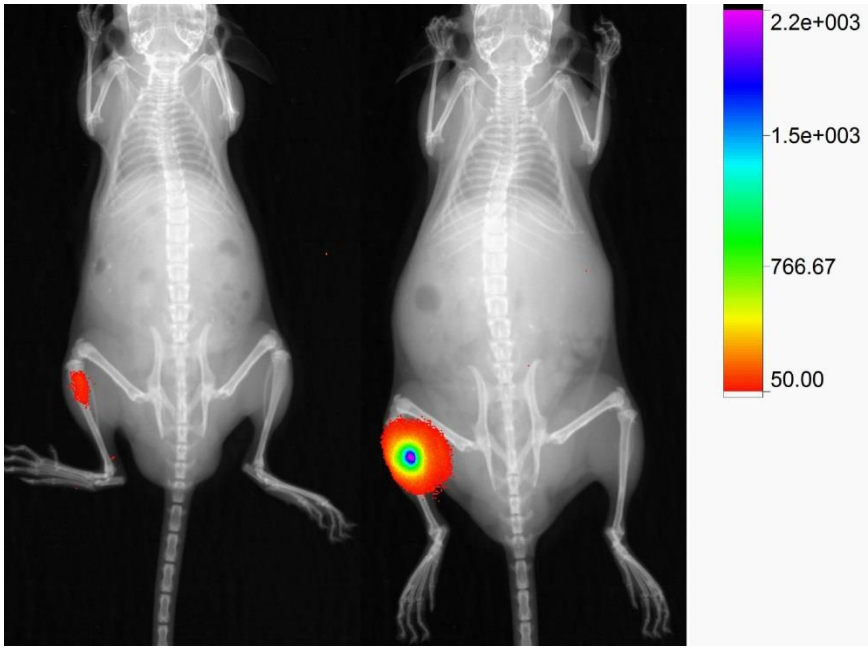


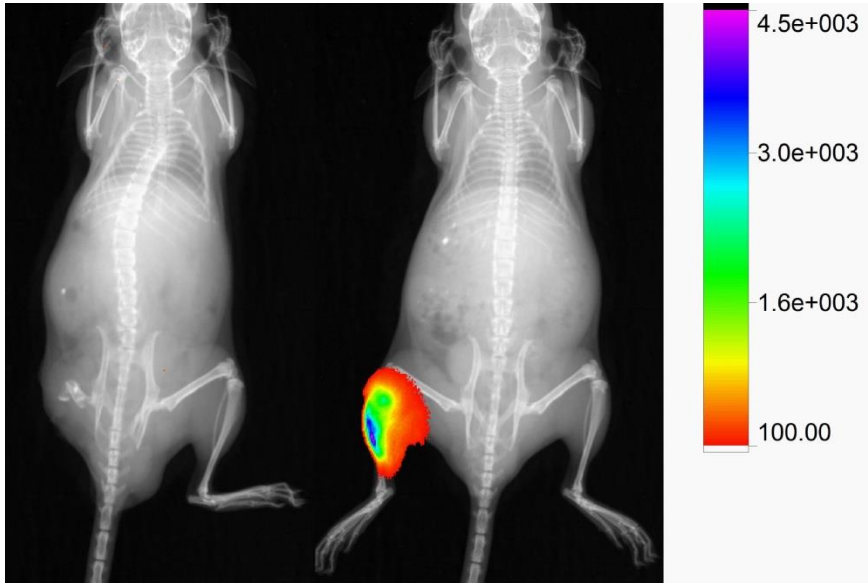




Bioluminescence is Visualized from OS-O Cells *In Vivo*

140404_TG-AS1-024E OS-O
at 1 week and 9 weeks



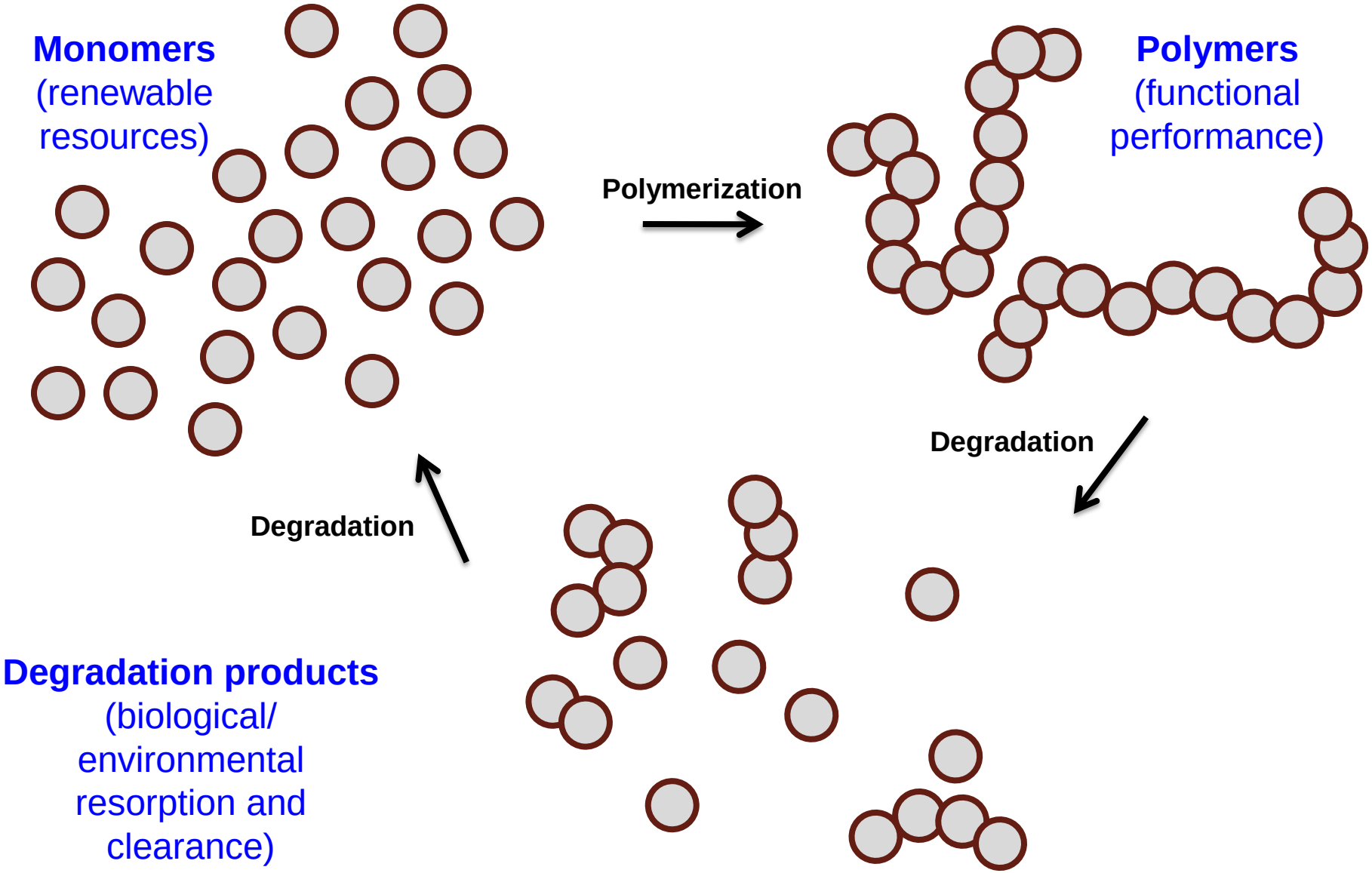


140404_TG-AS1-024C OS-O
with and without amputation
at 9 weeks

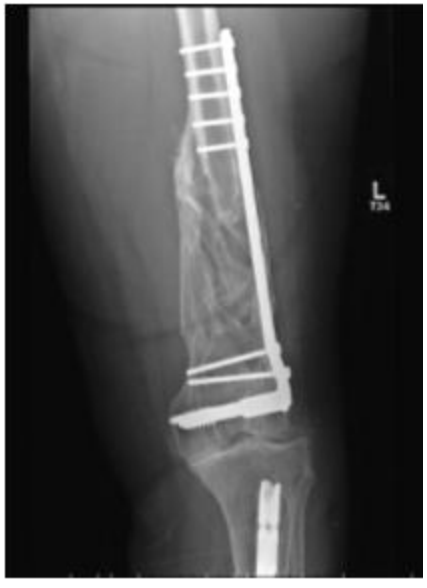
A few functional polymer chemistry goals:

- Antimicrobial nanoparticles for infectious disease treatment
- Chemotherapeutic nanoparticles for treatment of osteosarcoma lung metastases
- Engineering polymers derived from natural products
- Anti-biofouling and anti-icing coatings
- Advanced photoresist technologies

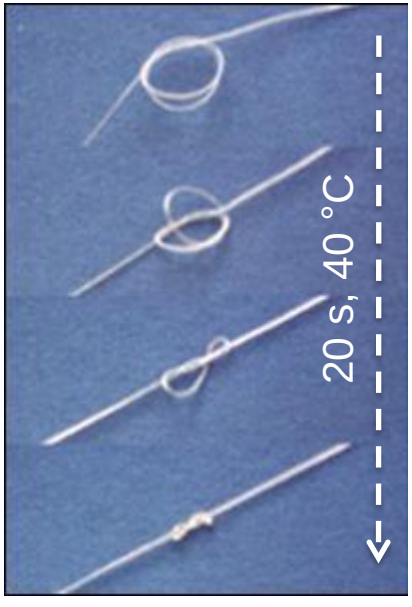
Idealized Polymer Life Cycle



Challenges for Materials for Orthopedic Applications



www.ceessentials.net

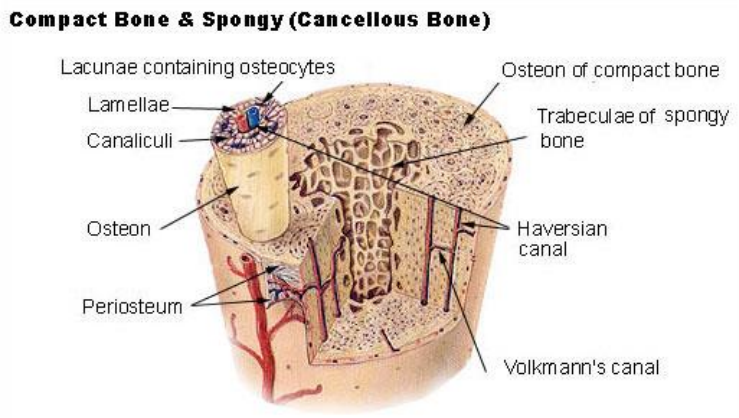


www.plastemart.com

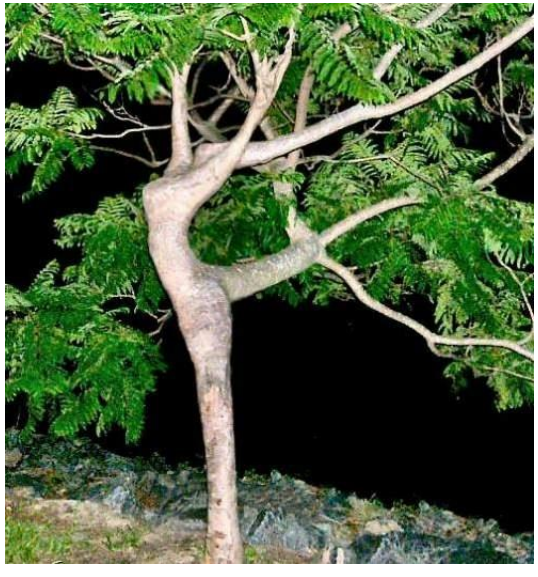
http://ajs.sagepub.com

- Metal materials:
  - Mismatch with mechanical properties of bone (Young's moduli, *E*, are ~100 GPa *vs*. ~20 GPa)—stress-shielding, osteopenia
  - Permanent implantation, unless secondary surgical removal is performed
- Degradable polymers:
  - Insufficient mechanical properties (*E ca*. 0.1-5 GPa)
  - Corrosive/inflammatory degradation products

Challenges for Degradable Polymers for Orthopedic Applications



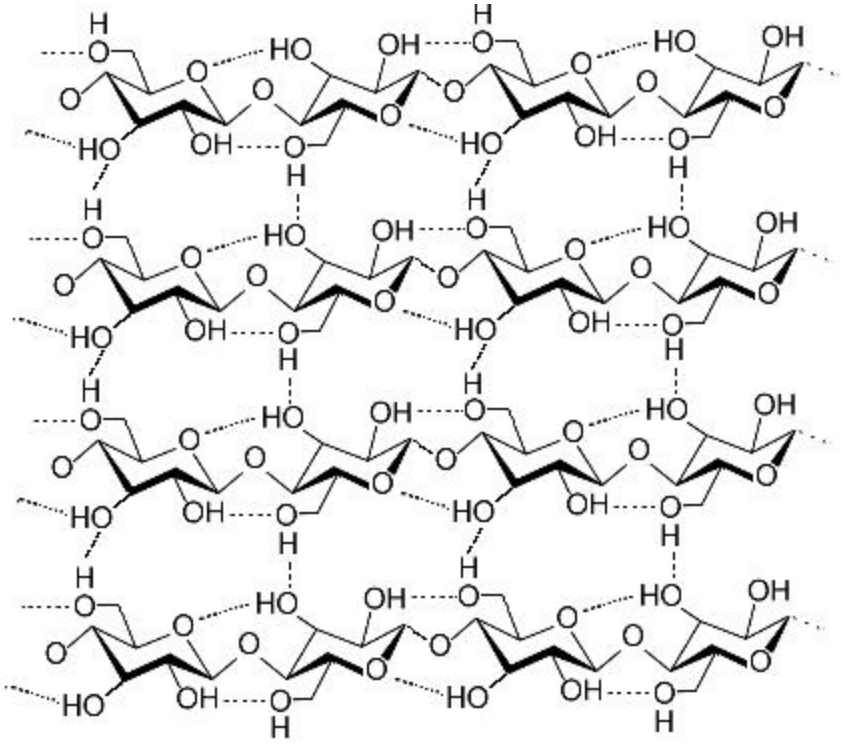
http://en.wikipedia.org/wiki/Osseous_tissue



http://yovia.com/blogs/1milliontrees/files/2009/06/dancin-tree.jpg

- Among Nature's supportive/engineering construction materials:
  - Bone—complex composite of osseous tissue as the supportive matrix—hydroxyapatite (mixture of collagen (proteins) and minerals) (*E ca*. 20 GPa)
  - Plants, cellulose (*E ca*. 10 GPa)
  - Also crustacean exoskeletons, *etc*. (*e.g.*, polysaccharides, silicas)

Orthopedic Degradable Polymer Materials Design

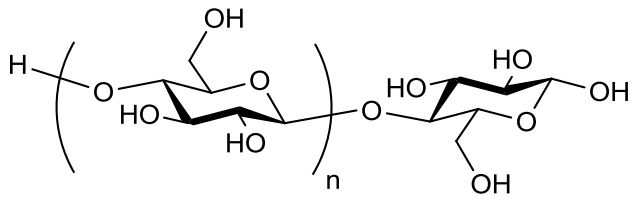


- Cellulose as a model material
- Good mechanical properties
  - 1,4-β-D-glucose linkages allow interchain packing and crystallization
  - Intermolecular H-bonding adds to the mechanical integrity
  - *E ca*. 10 GPa
- Design: Replace the glycosidic linkages with bonds that can be hydrolyzed more readily, in the absence of cellulases

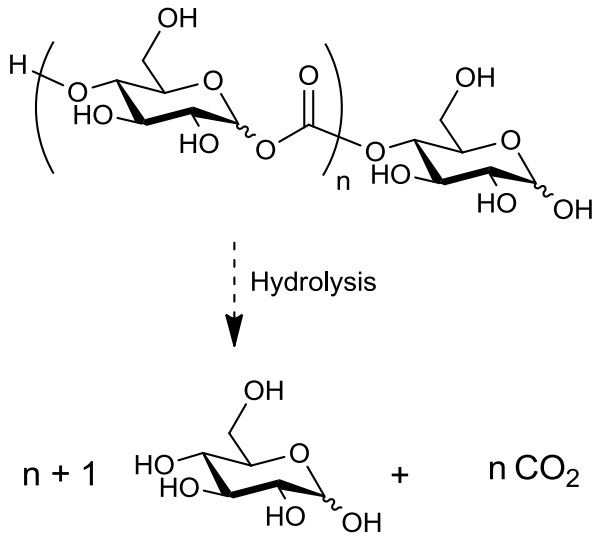
http://upload.wikimedia.org/wikipedia/commons/c/c3/Cellulose_strand.jpg

Orthopedic Degradable Polymer Materials Design

Cellulose: A polyacetal of glucose



Synthetic Target:
A polycarbonate of glucose

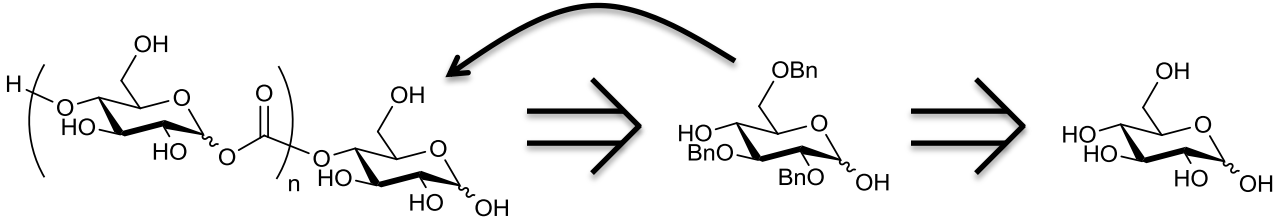


- Cellulose as a model material
- Design: Replace the glycosidic linkages with bonds that can be hydrolyzed more readily—acetal-type carbonates
- Good mechanical properties are expected
- Hydrolytic degradation will produce glucose plus CO_2

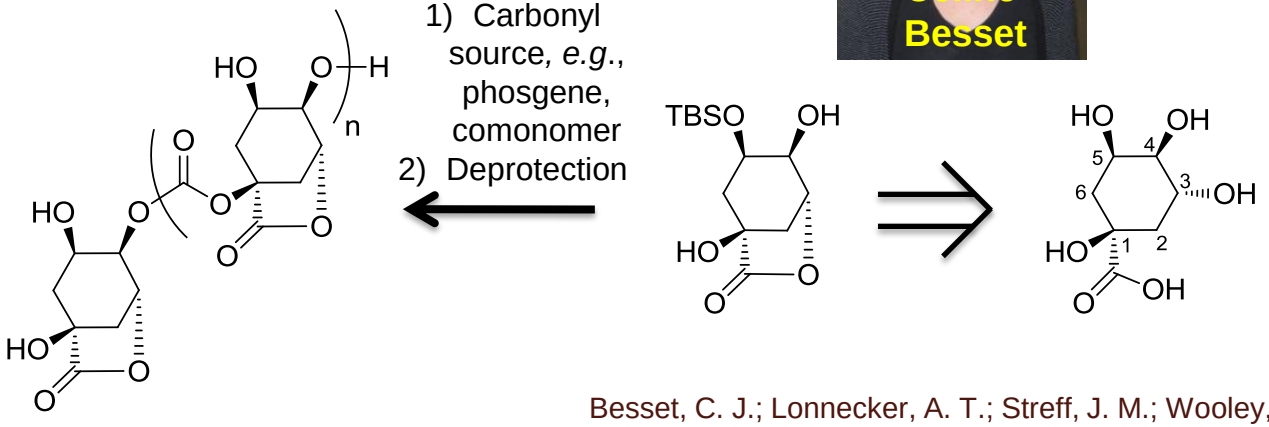
Orthopedic Degradable Polymer Materials Design

Synthetic Target:
A polycarbonate of glucose

1) Carbonyl source, *e.g.*, phosgene, comonomer
2) Deprotection



Synthetic Target:
A polycarbonate of quinic acid



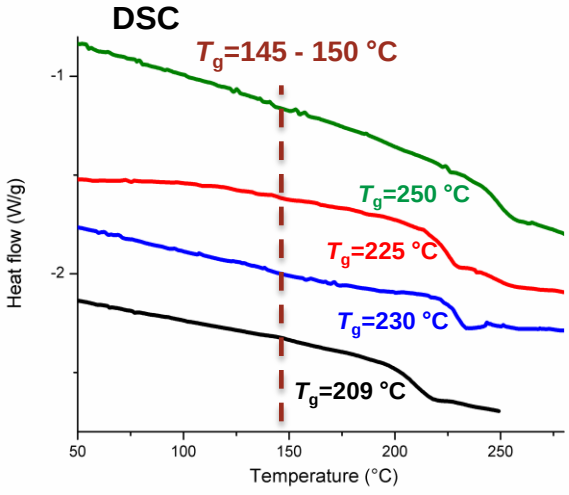
- Polyhydroxyl natural products as starting materials (monomers)
- Polyhydroxyl natural products as hydrolytic degradation products
- Glucose is an energy source
- Quinic acid has growth-promoting properties and is a chiral starting material for pharmaceuticals
- Rigid cyclic or bicyclic backbones
- Interchain H-bonding

Besset, C. J.; Lonnecker, A. T.; Streff, J. M.; Wooley, K. L. *Biomacromolecules*, **2011**, *12*(7), 2512

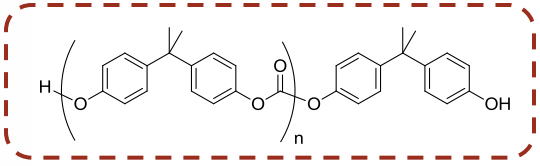
K. L. Wooley, C. Besset, A. Lonnecker, "Degradable Polycarbonates from Polyhydroxy Natural Products", *Patent App. No. PCT/US2011/56204*, October 13, 2011

Poly(quinic acid carbonate)s - Overview

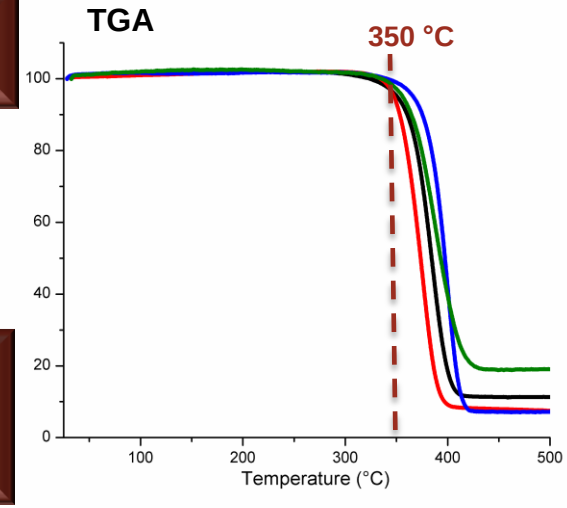
Thermal properties

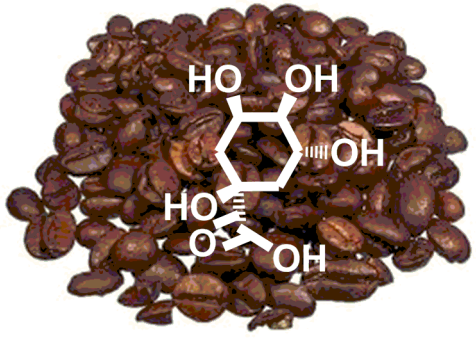


Carbonate's linkage flexibility: O-1,O-4 > O-1,O-5

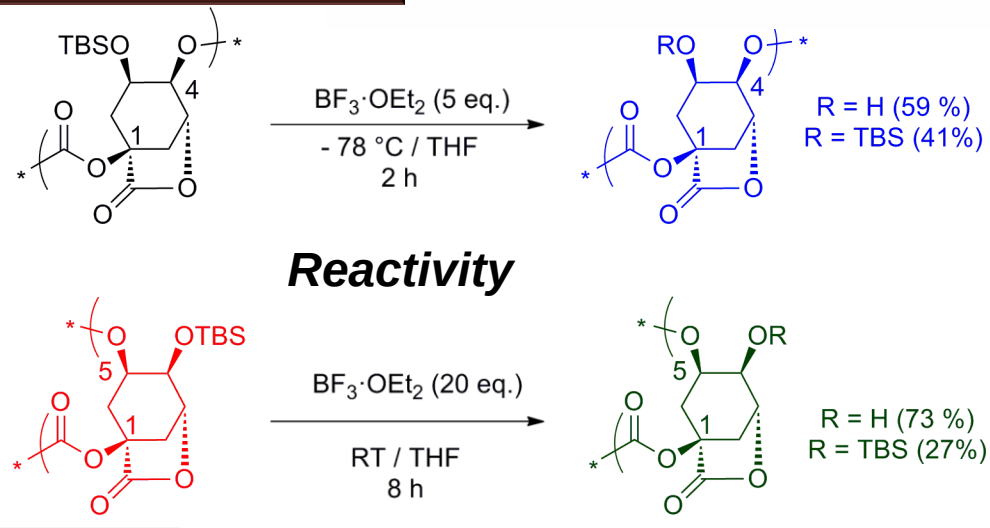


T_g poly(quinic acid carbonate) >> T_g poly(bisphenol A carbonate)





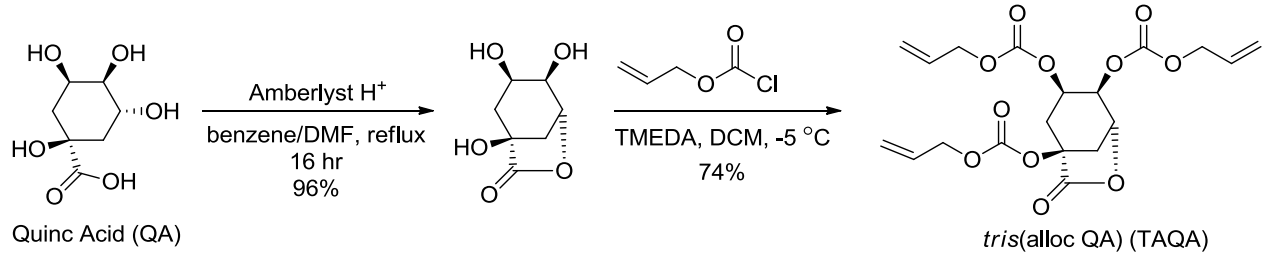
Lactonization → Silylation → Co-polymerization

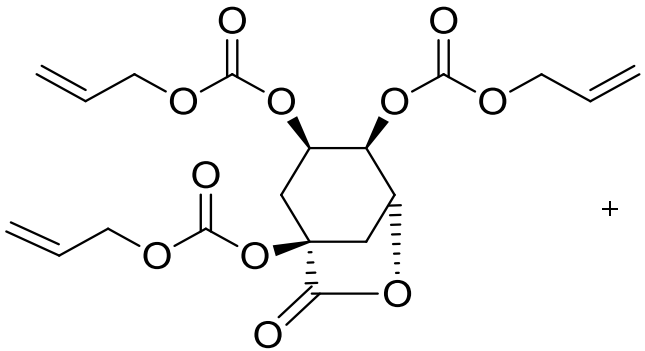


Reactivity

Carbonate's linkage stability: O-1,O-4 << O-1,O-5

Poly(quinic acid thioether-*co*-carbonate) Networks





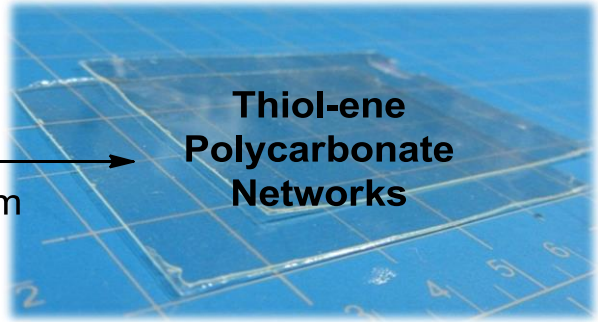
TAQA

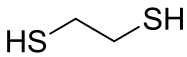
+

Multifunctional Thiols

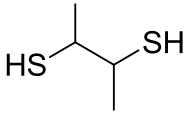
DMPA

λ=365 nm
15 min

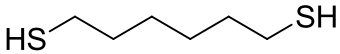




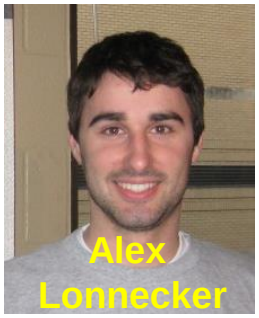
1,2-EDT

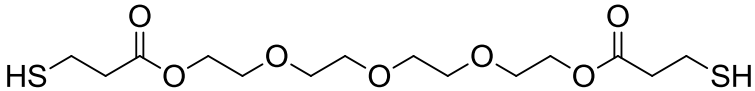


2,3-BDT

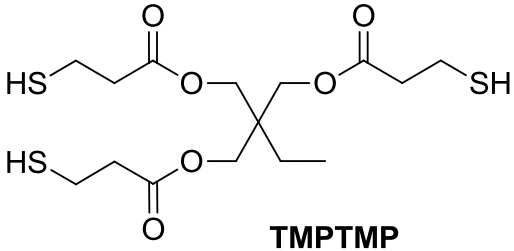


1,6-HDT



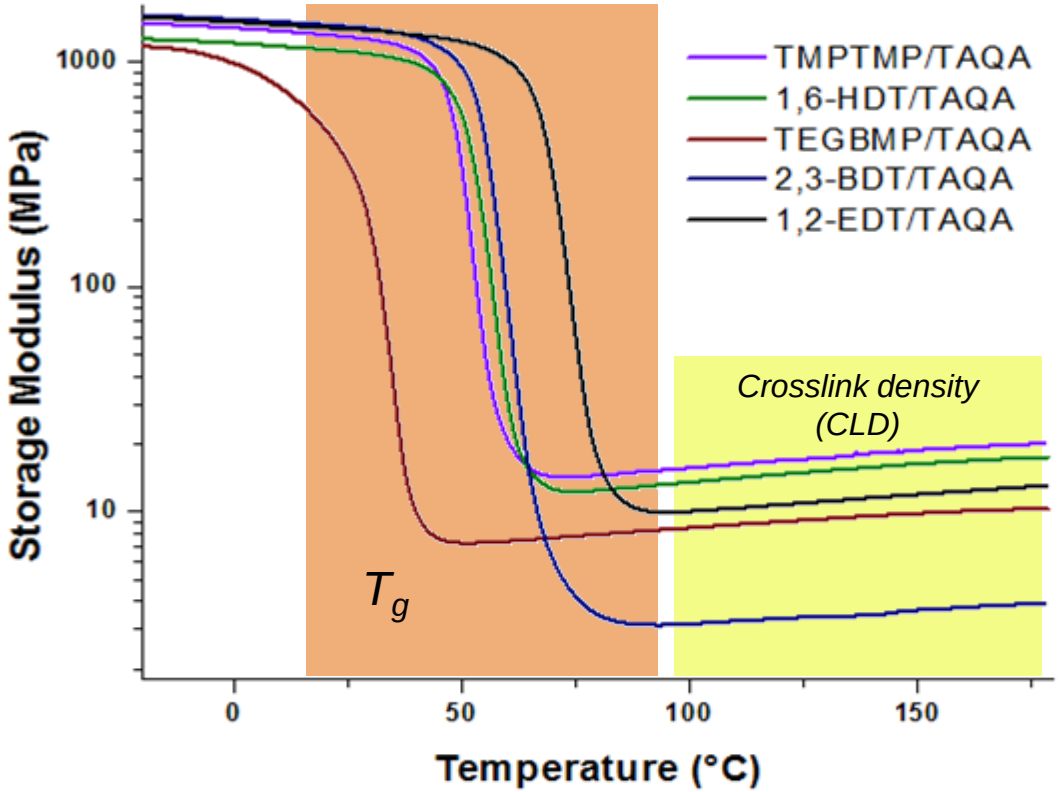


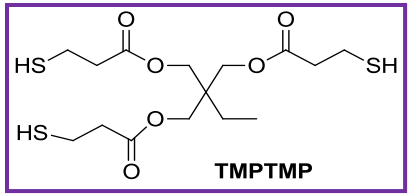
TEGBMP

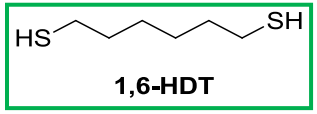


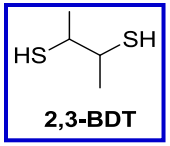
TMPTMP

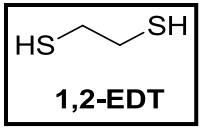
Thiol Composition and Structure Tune Network Properties

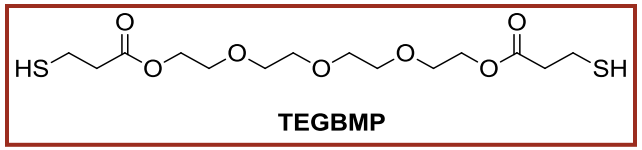










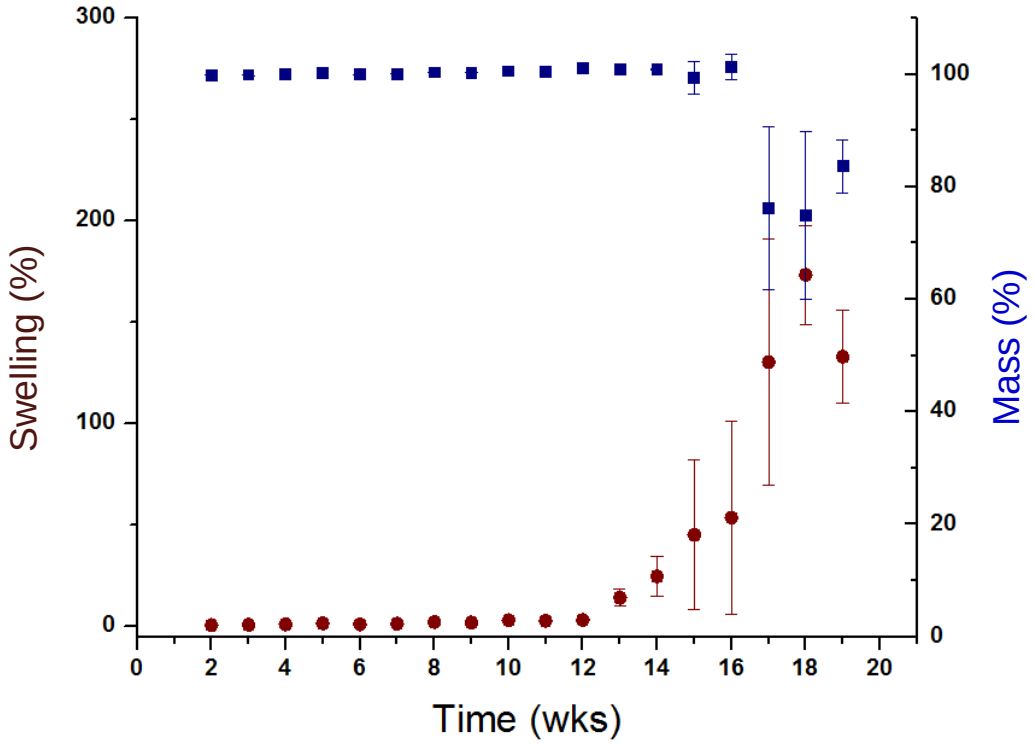


- DMA behavior characteristic of crosslinked thermosetting polymers
- Increased functionality of thiol increases CLD (decreases toughness)
- Increased length and flexibility of thiol decreases T_g

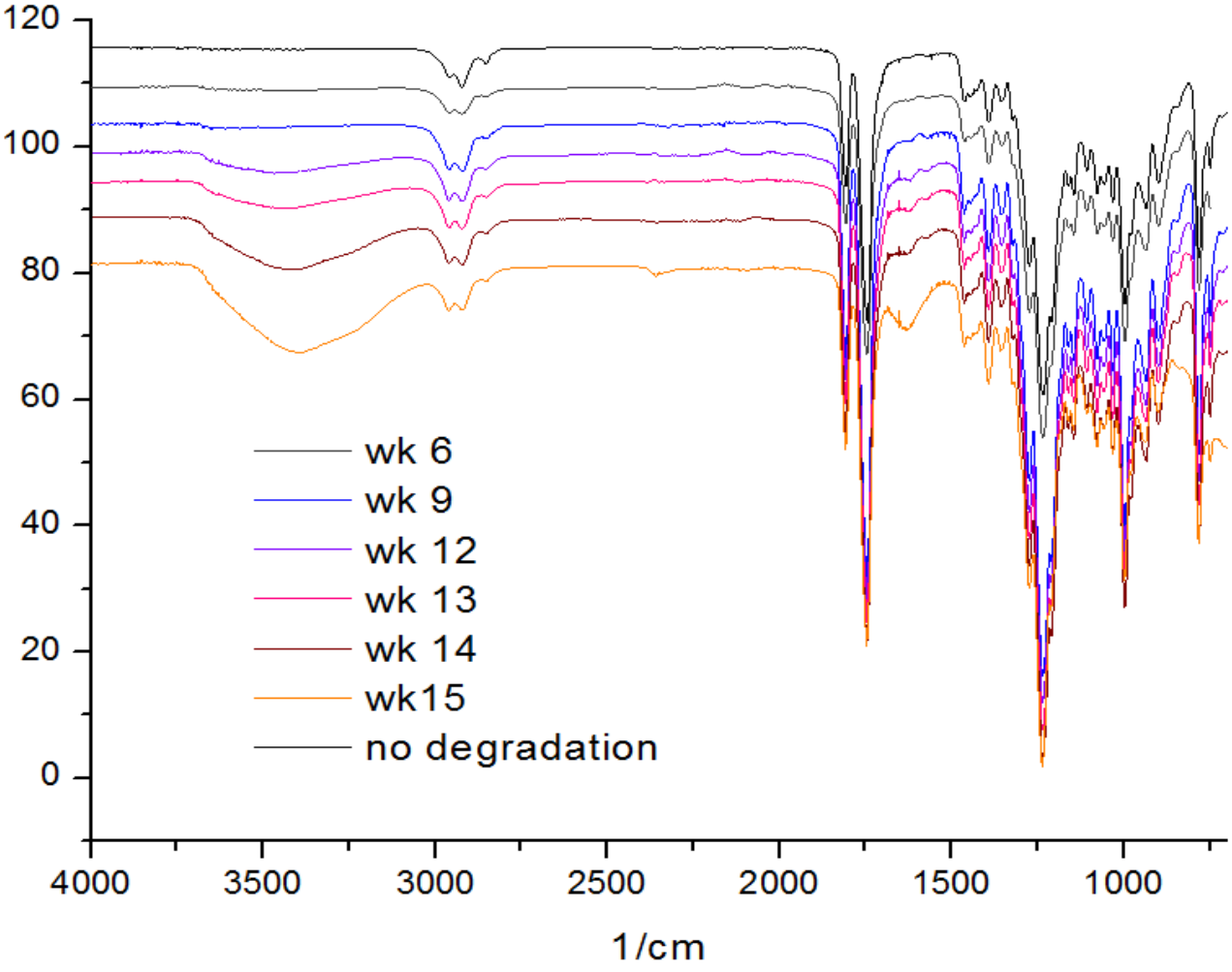
Hydrolytic Degradation of 1,2-EDT-*co*-TAQA

Hydrolytic degradation studies of 1,2-EDT/TAQA were performed in phosphate-buffered saline solution (pH 7.4, 37 °C, 60 rpm)

- Swelling increased suddenly at 13 wks
- Mass loss was observed at 15 wks and reached *ca.* 25%
- No changes in surface contact angle
- Degradation by bulk erosion



Hydrolytic Degradation of 1,2-EDT-*co*-TAQA



WEEK 15
Bulk Erosion

- *No changes in contact angle*
- *IR spectra of dry films underwent change after 9 weeks*

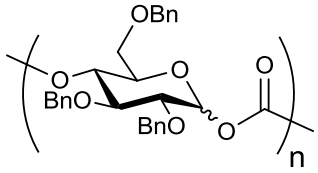
Link, L. A.; Lonnecker, A. T.; Hearon, K.; Raymond, J. E.; Maitland, D. J.; Wooley, K. L. "Photo-crosslinked Poly(thioether-*co*-carbonate) Networks Derived from the Natural Product Quinic Acid", *Chem. Mater.*, under revision.

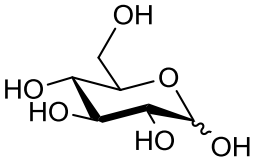
Current Status for Wooley Group Natural Product-based Polymers

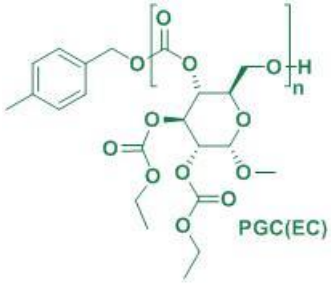
Linear Polycarbonates w/control Over Regiochemistry

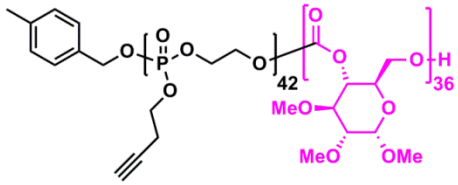
Linear Polycarbonates and Block Copolymers by ROPs

Glucose

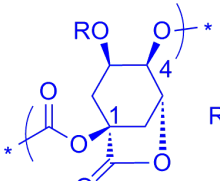




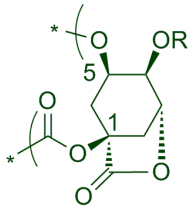




Quinic Acid

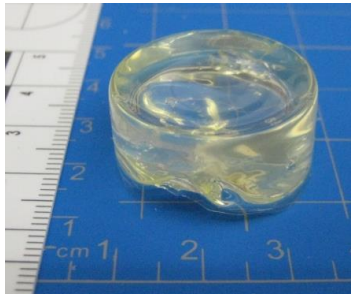


R = H (59 %)
R = TBS (41%)

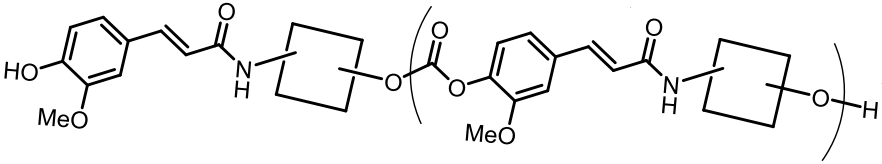


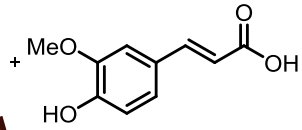
R = H (73 %)
R = TBS (27%)

Crosslinked Networks

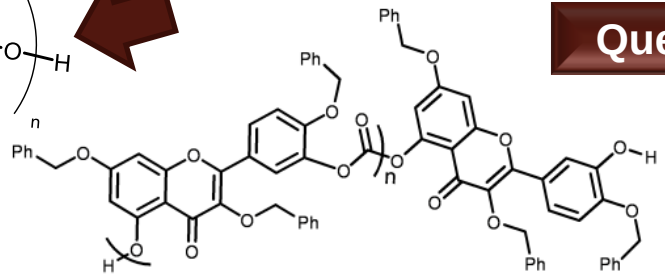


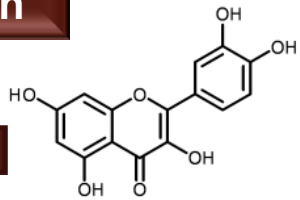
Ferulic Acid





Quercetin





A few functional polymer chemistry goals:

- Antimicrobial nanoparticles for infectious disease treatment
- Chemotherapeutic nanoparticles for treatment of osteosarcoma lung metastases
- Engineering polymers derived from natural products
- Anti-biofouling and anti-icing coatings
- Advanced photoresist technologies

Treacherous Terrain-based Anti-fouling Surfaces:

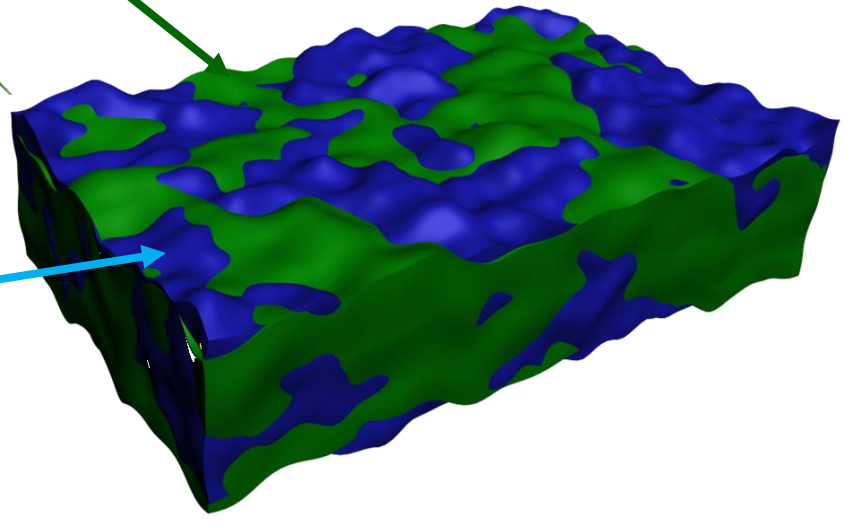
Hybridization of molecular architectures, compositions, and dimensions

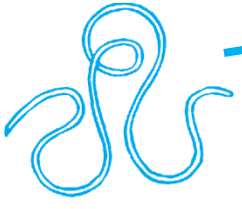
Hydrophobic, low surface energy, crosslinkable polymer

Complex Morphology Leads to:

- Topography/Texture (nm + μm)
- Patchy Composition
- Hydrophobic + Hydrophilic
- Flexible/Dynamic + Rigid
- Differential Surface Energies

Secreted protein "glue" must adhere to the surface for the organism to thrive





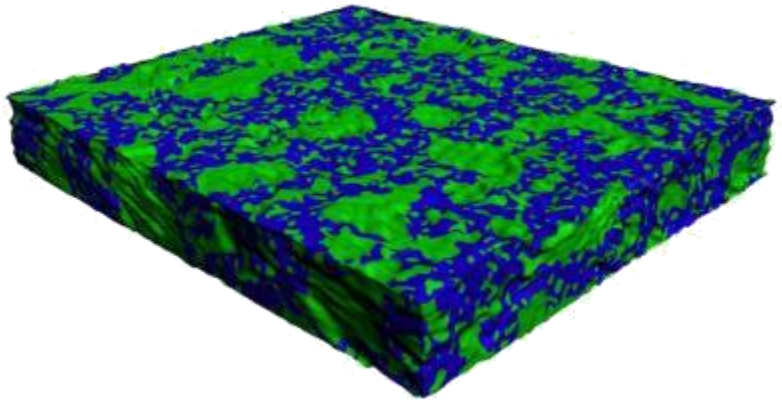
Hydrophilic, water soluble polymer

Nanoscopically-resolved morphological and topographical surface domains composed of crosslinked networks

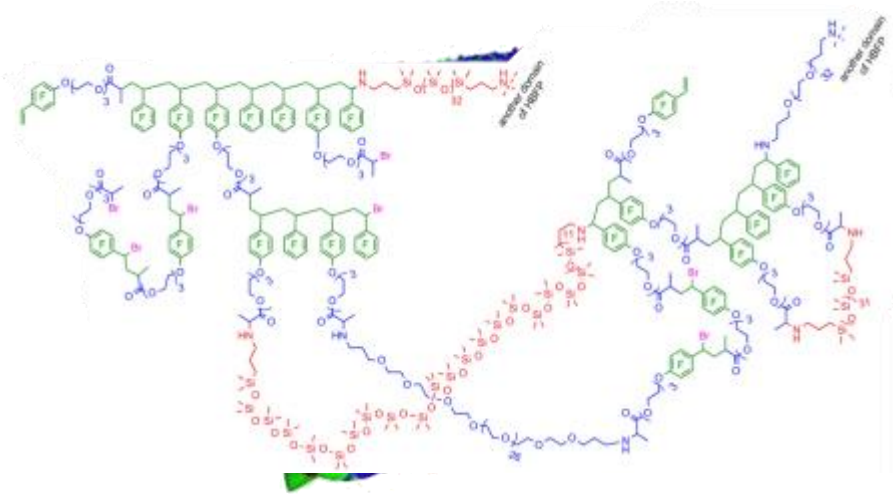
The proteins are nanoscale, therefore the coating surface features should also be nanoscale in dimension to intercept/inhibit adhesion

(Algae spore image courtesy of AMBIO)

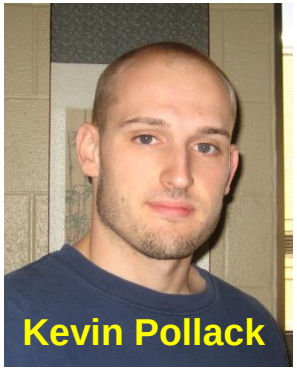
HBFP-PEG-PDMS Ternary Coatings: Synthesis



vs.

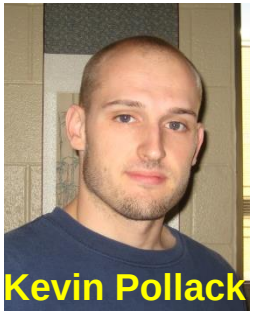


- Synthesized by crosslinking **HBFP** with diamine-**PEG** and diamine-**PDMS**
- By incorporation of three classes of anti-fouling polymers, the ternary system is expected to take advantage of each of their unique properties
- The key challenge is to determine the optimal proportions of each component

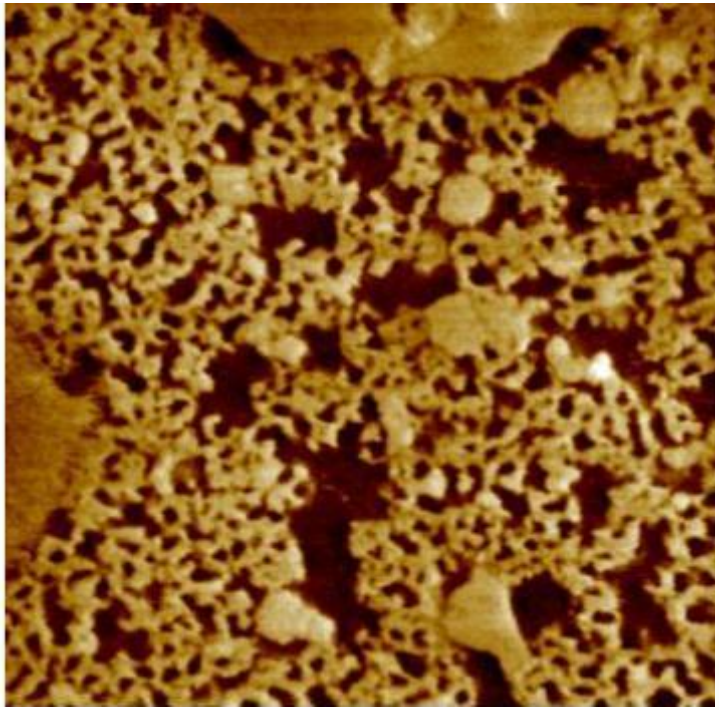


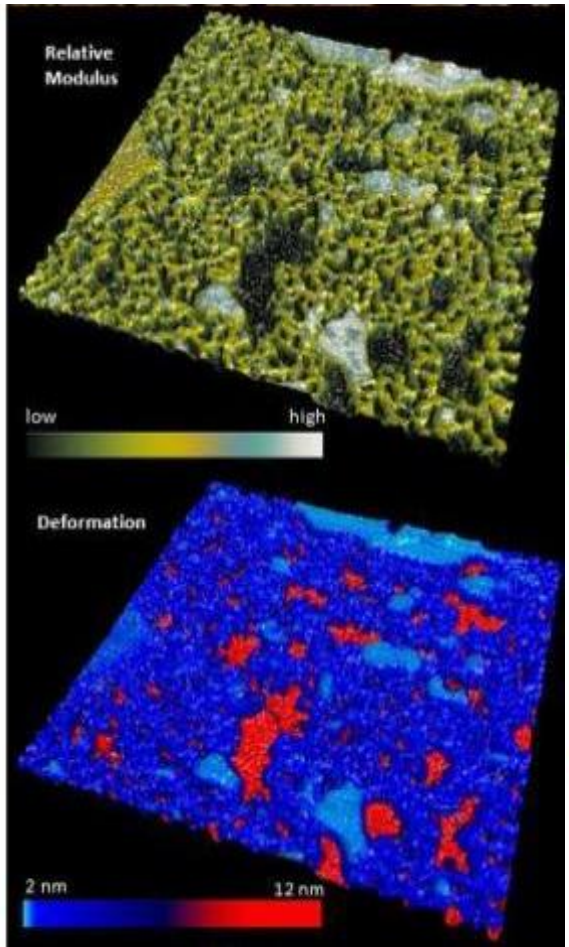
HBFP-PEG-PDMS Ternary Coatings: Physicochemical Surface Analysis

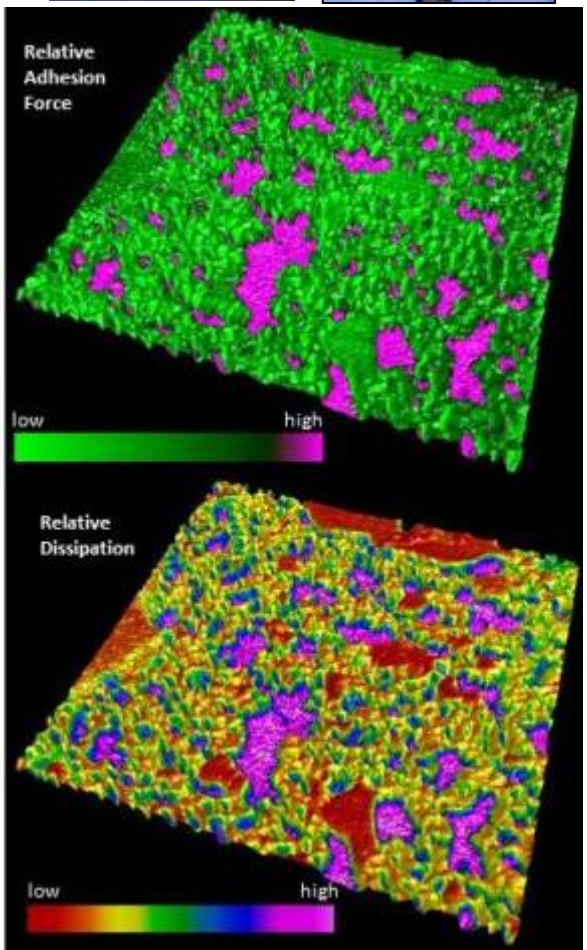
- Surface force spectroscopy demonstrates unique surface properties present on the surface of the ternary coatings with raised lattices of **HBFP** & **PDMS** and lowered regions of **PEG**


Kevin Pollack


Jeff Raymond

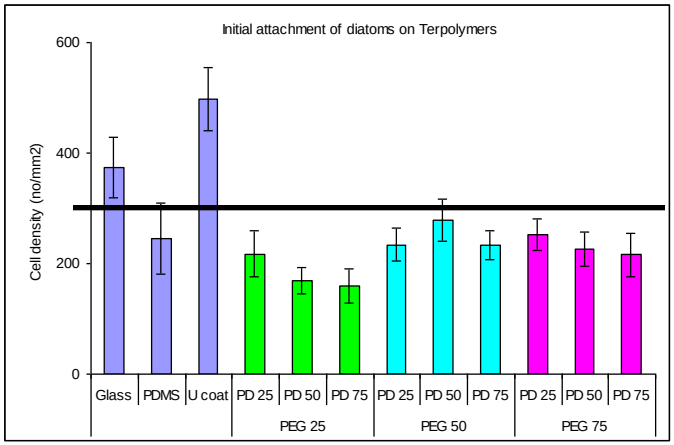


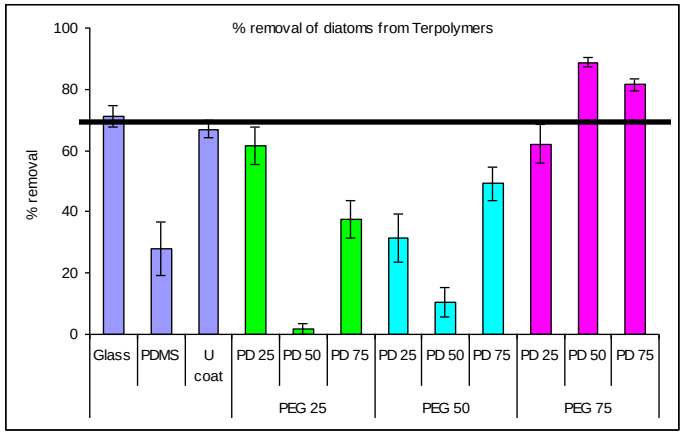




HBFP-PEG-PDMS Ternary Coatings: *Navicula incerta* Fouling Study

HBFP-PEG-PDMS Ternary System

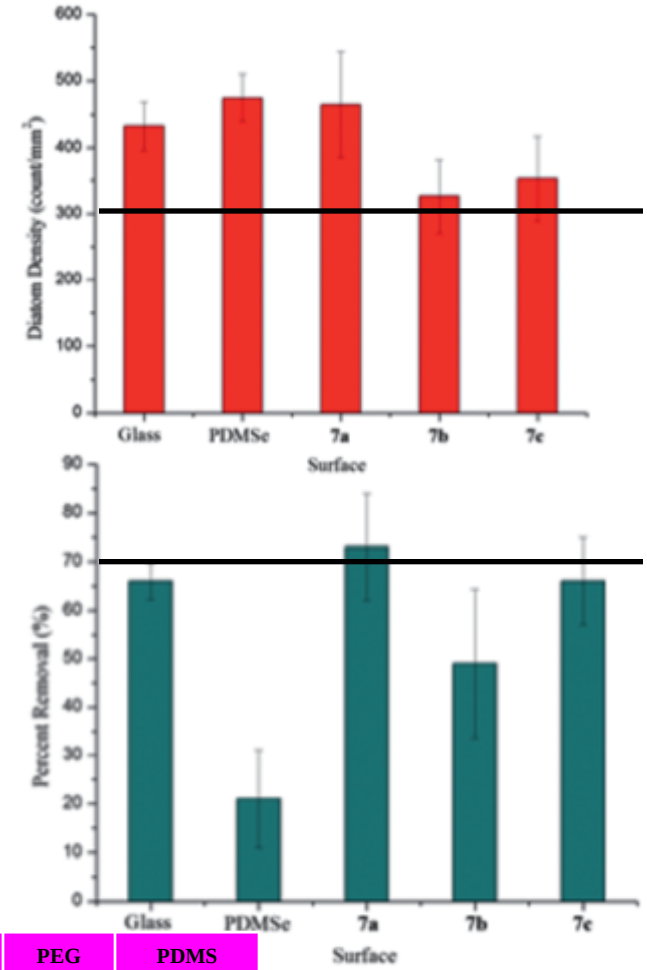




- Lower initial density of settlement than **HBFP-PEG** binary system
- Percent removal of diatoms on the **PEG** 75 series are comparable or better than for the binary systems

w/Gemma Cone, John Finlay, Sophie Hill, Maureen Callow, James Callow

HBFP-PEG Binary System



PEG 25	HBFP wt%	PEG wt%	PDMS wt%
PD 25	67	16.5	16.5
PD 50	57	14.3	28.7
PD 75	50	12.5	37.5

PEG 50	HBFP wt%	PEG wt%	PDMS wt%
PD 25	57	28.7	14.3
PD 50	50	25	25
PD 75	44	22.4	33.6

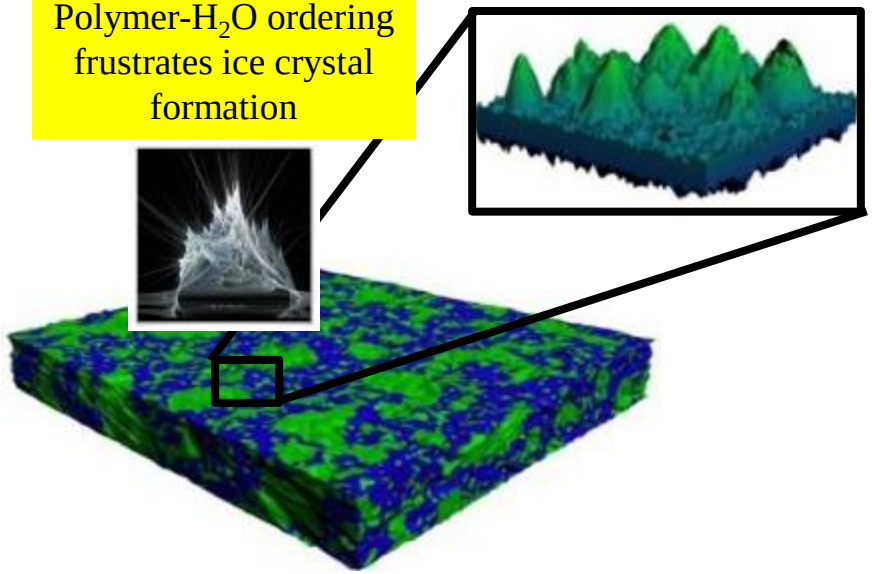
PEG 75	HBFP wt%	PEG wt%	PDMS wt%
PD 25	50	37.5	12.5
PD 50	44	33.6	22.4
PD 75	40	30	30

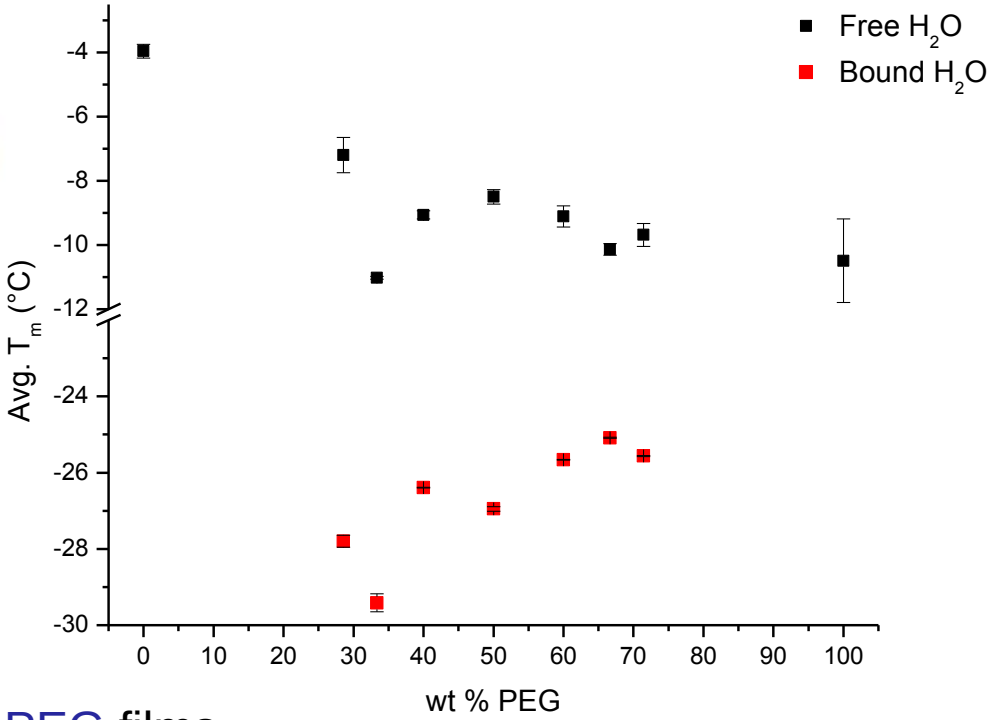
	HBFP wt%	PEG wt%
7a	67	33
7b	50	50
7c	40	60

Imbesi, P. M.; *et al. Polym. Chem.*, **2012,** *3*, 3121-3131.

HBFP-PEG Coatings Towards Anti-Icing Applications

Hypothesis:
Polymer-H_2O ordering frustrates ice crystal formation





- With 200 *wt*% H_2O added, HBFP-PEG films (cast and cured in DSC pans) depress the freezing point of bound water by 25-30 ° C and free water by 7-11 ° C
- As the *wt*% PEG increases, the T_m of bound water increases, and the T_m of free water decreases

http://rlv.zcache.co.uk/ice_castle_fractal_by_kitty_ann_poster-rced69fd98bca49229cc82682b2c1bdad_wi4_8byvr_512.jpg

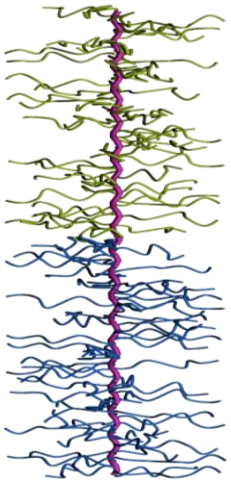
A few functional polymer chemistry goals:

- Antimicrobial nanoparticles for infectious disease treatment
- Chemotherapeutic nanoparticles for treatment of osteosarcoma lung metastases
- Engineering polymers derived from natural products
- Anti-biofouling and anti-icing coatings
- Advanced photoresist technologies

Negative-tone Resist with Vertical Alignment of Molecular Brushes as Ultra-high Resolution Macromolecular Pixels

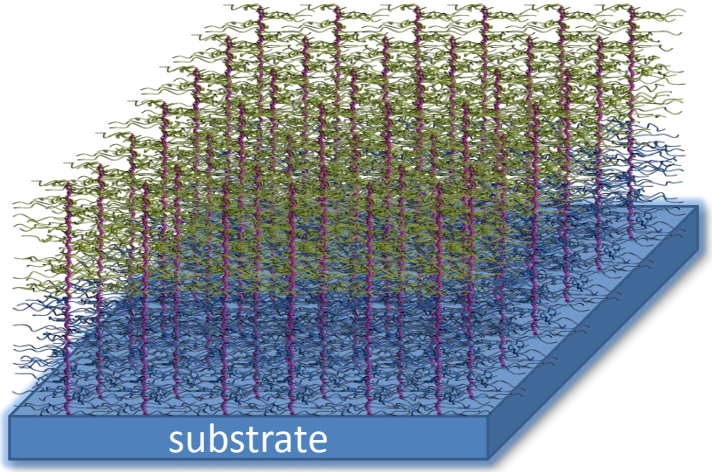
Vertical alignment

[w/Jim Thackeray and Pete Trefonas, Dow Electronic Materials]

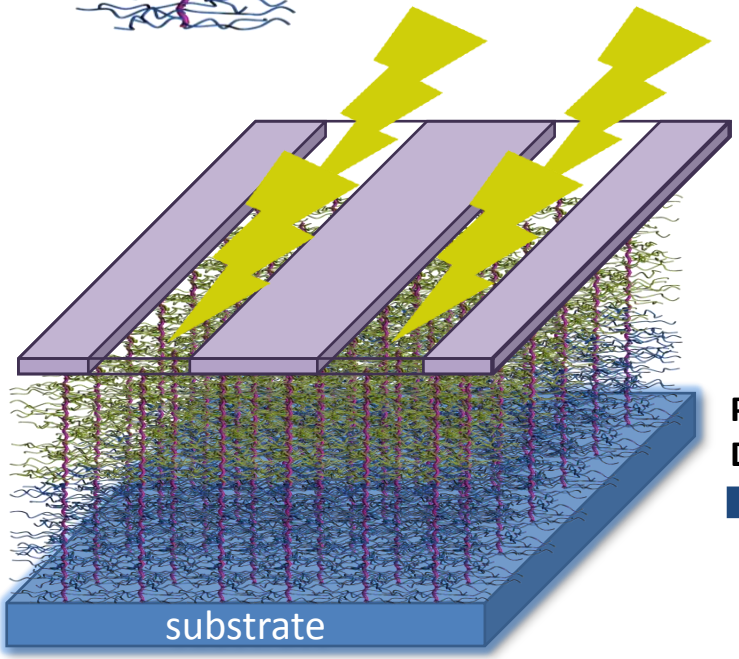


Hydrophobic segment & low surface energy

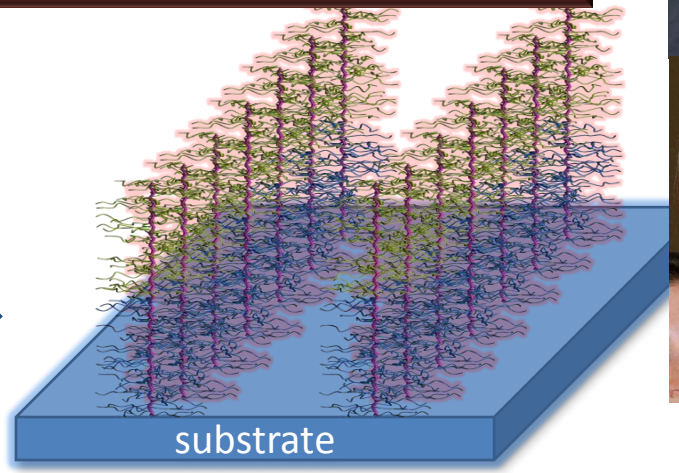
Hydrophilic segment & high surface energy & crosslinkable

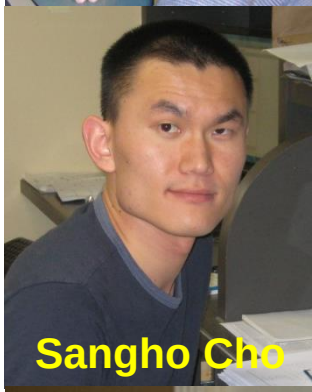


Hypothesis: Pattern dimensions can be defined by molecular dimensions and ordering

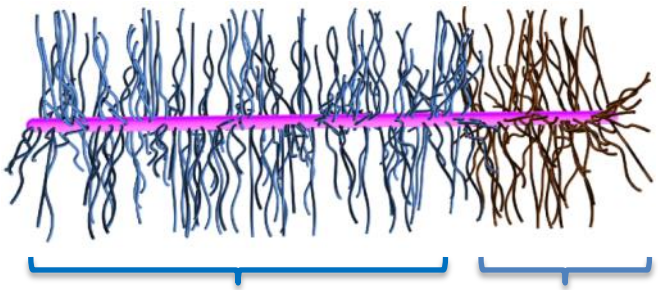


Post baking
Development



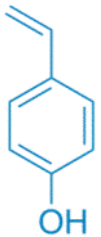


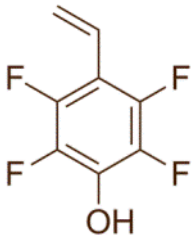
RAFT and ROMP Approach to Block Brush Photoresist Polymers

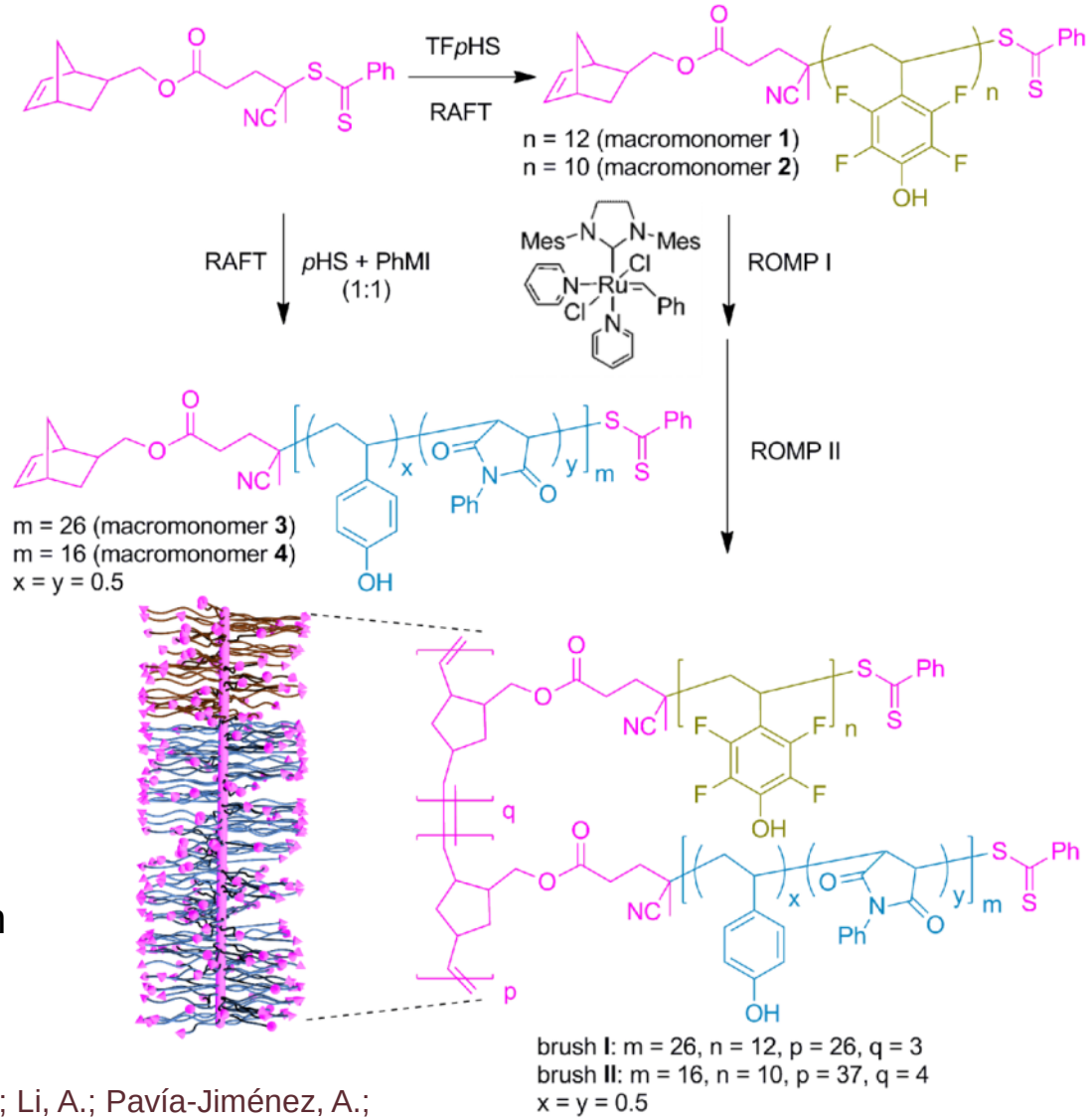


reactive moiety

surface energy reducing moiety



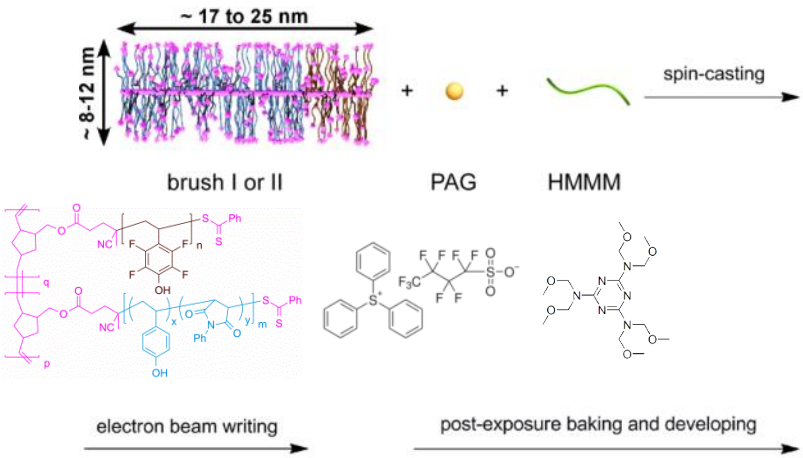


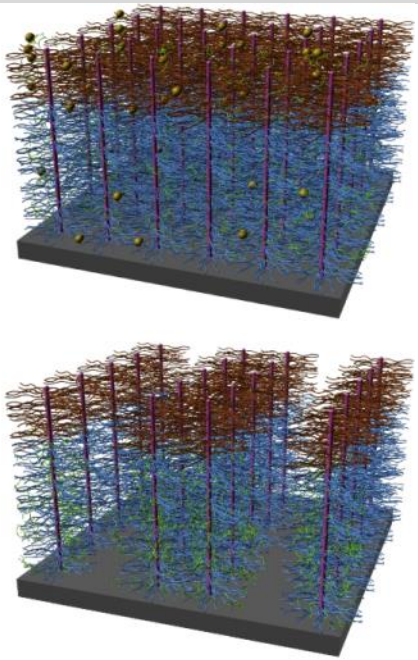


❖ Combinations of RAFT (co)polymerizations and sequential ROMPs are applied for preparing designed block brush terpolymers with dual concentric and lengthwise tunabilities.

Sun, G.; Cho, S.; Clark, C.; Verkhoturov, S.; Eller, M. J.; Li, A.; Pavía-Jiménez, A.; Schweikert, E. A.; Thackeray, J. W.; Trefonas, P.; Wooley, K. L. *J. Am. Chem. Soc.*, **2013**, *135*(11), 4203-4206.

Electron-beam Lithography (EBL) of Block Brush Terpolymer Chemically-amplified Resists (CARs)





- ***CAR solutions with polymer:HMMM:PAG = 0.75:0.15:0.10 wt% in cyclohexanone***
- ***Spin-casting onto silicon wafer; directly applying (no acetone annealing) for EBL (30 kV accelerating voltage, 10 pA beam current)***
- ***PEB at 90 °C for 1 min; 0.27 M TMAH aqueous solution developing***

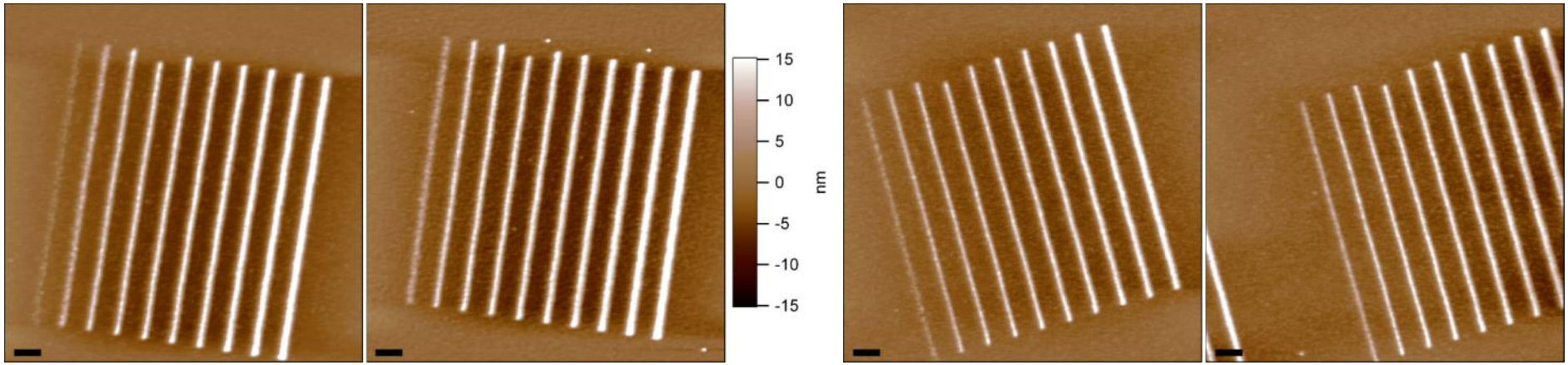
Exposure dosages:

Brush **I**

250 μC/cm^2 400 μC/cm^2

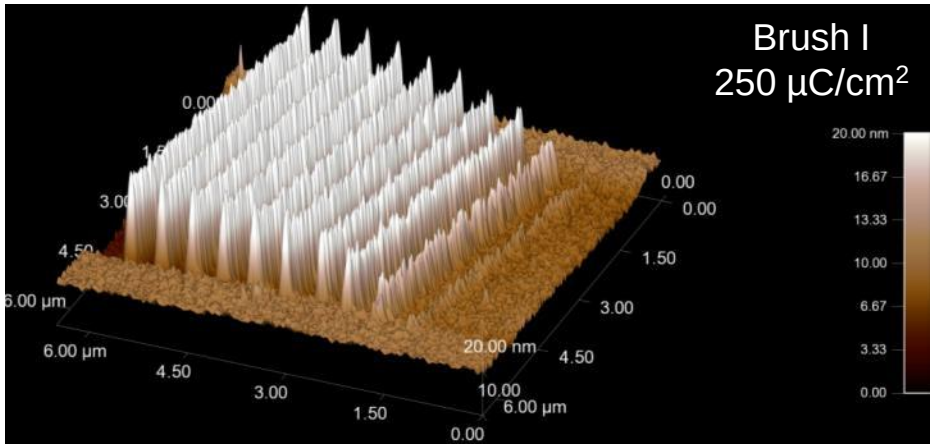
Brush **II**

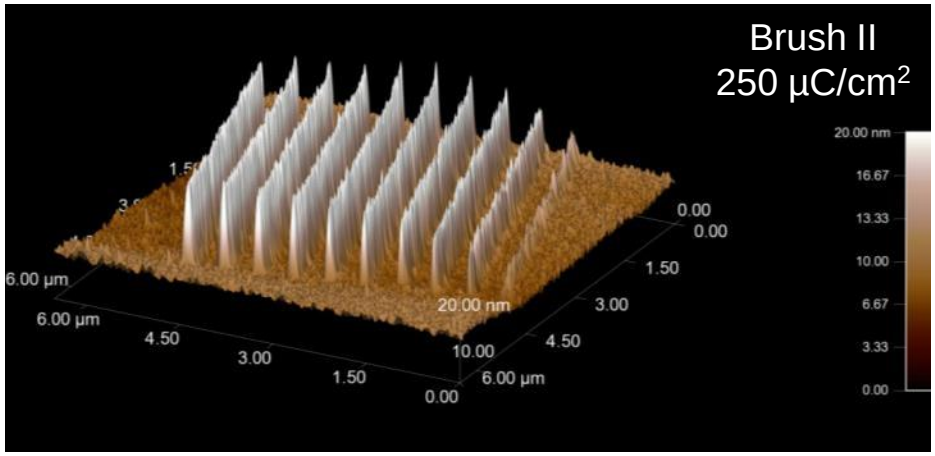
250 μC/cm^2 400 μC/cm^2

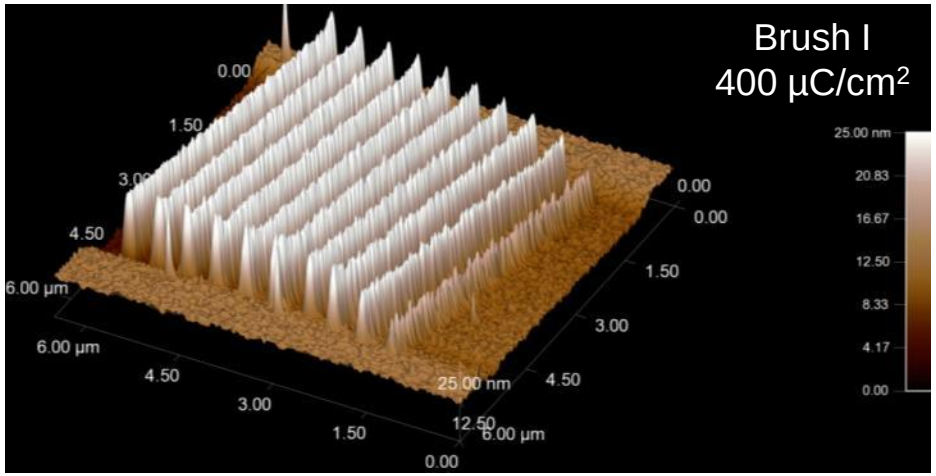


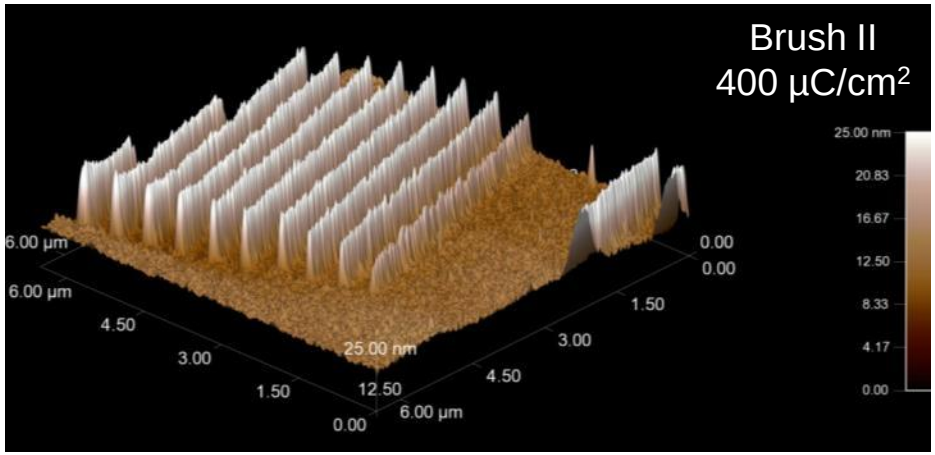
Pattern: 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 nm line/500 nm space; scale bar: 500 nm

EBL Results for Block Brush Terpolymer CARs









Negative-tone bottle-brush photoresist IP filed November 2012;
Extension to positive-tone photoresist systems, IP filed September 2013

Acknowledgements

Parth Shah
Justin Smolin
Carolyn Cannon
Matthew Panzer
Patrick Wagers
Wiley Youngs

Kristin Tiemann
David Hunstad
Tolulope Aweda
Suzanne Lapi

Laura Nelson
Dennis Hughes

Mark Lenox

Gemma Cone
John Finlay
Jim & Maureen Callow

Jim Thackeray
Pete Trefonas