



# **‘Slippery’ surfaces and anti-fouling coatings on catheters**

**Josh Carson**

Licensing Manager

JCarson@warf.org



# Opportunity: coated catheters meet large need in controlling infections and thrombosis

- UW-Madison researchers have developed a coating technology for catheters that can reduce the rates of infection and thrombotic complications
- Catheter-associated infections are a huge burden on patients and health systems world-wide
- Thrombosis is a frequent complication of catheter use
- Global market for catheters with antimicrobial properties worth \$3B in 2015
- One US patent granted, additional applications filed in the U.S.

# Catheter-associated infections and thrombosis are a huge burden on patients and payers

Bloodstream infections associated with the use of central venous (or central line) catheters (CLABSI) are common and costly

- **~5M** central venous catheters are inserted per year in the U.S.
- **92,000 total cases** of CLABSI in U.S. each year
- Average reported CLABSI cost per case: **\$70,696**

Thrombosis is a **frequent complication** of central venous (CVC) catheters and peripherally inserted central catheters (PICCs)

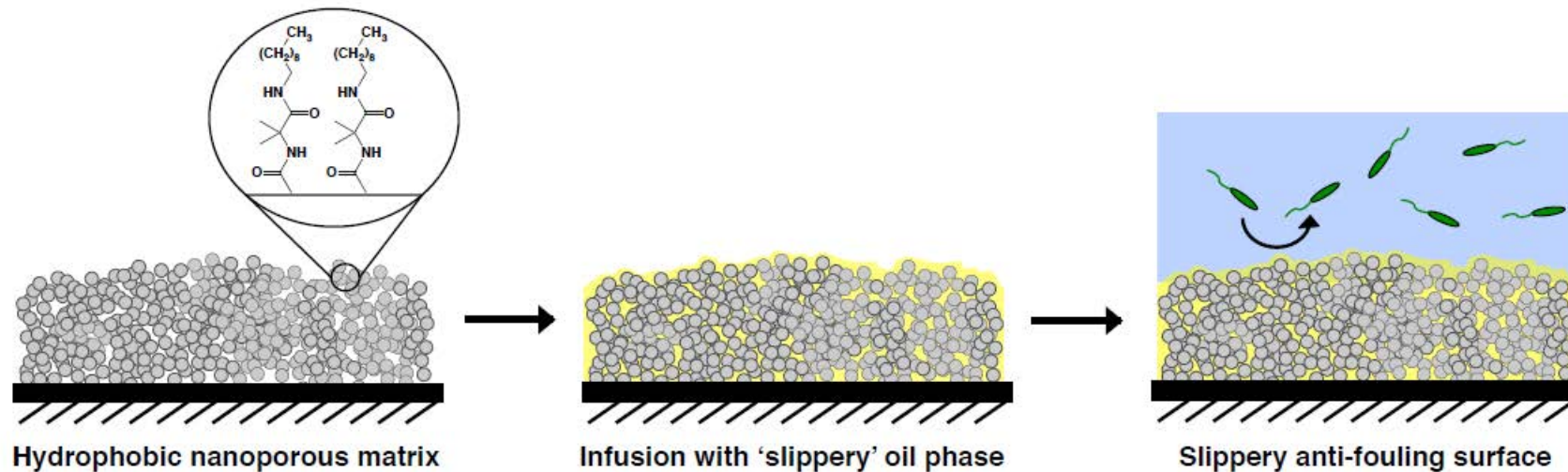
- Thrombotic complications during CVC use occur with an overall rate of **14-18%**
- The incidence of deep vein thrombosis for PICCs is between 5% and 15% for hospitalized patients (2% and 5% for ambulatory patients)
- Formation of a fibrin sheath around the catheter can promote infection, reduce flow and increase the risk of pericatheter thrombosis

# A nanoporous liquid infused surface based solution

UW-Madison researchers have developed a platform for the fabrication of catheters with anti-fouling and anti-microbial surfaces that

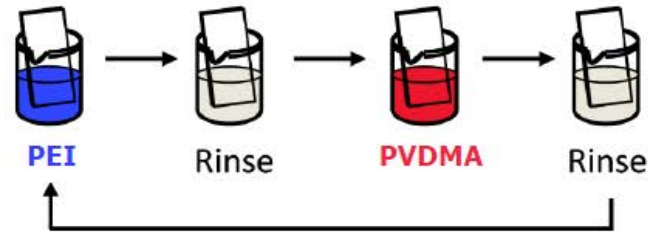
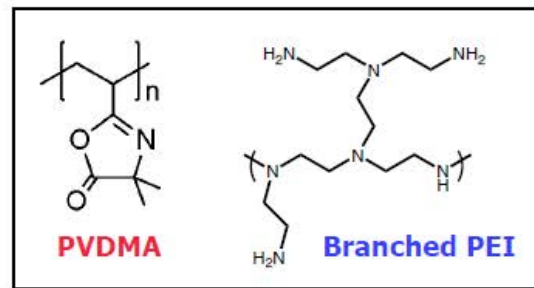
- can prevent bacterial colonization and the formation of biofilms
- can reduce systemic infections by controlled release of antimicrobials

The approach is based on nanoporous surfaces fabricated by the infusion of a hydrophobic liquid oil into polymer multilayers

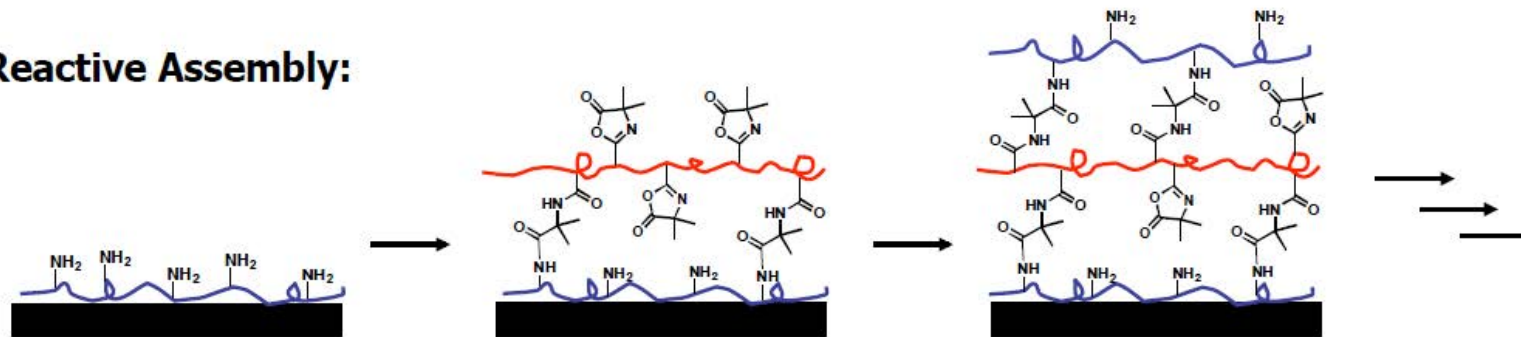


# Reactive assembly

Coatings are applied using a stepwise process with PVDMA and PEI resulting in a thin nanoporous layer that can be infused with silicon oil

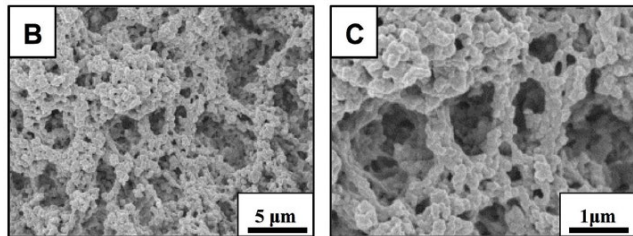


Reactive Assembly:



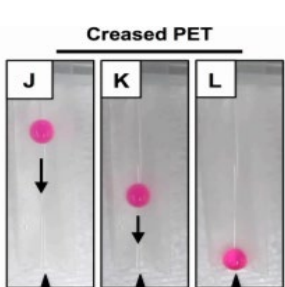
# Flexible and robust surfaces

- Surfaces can be fabricated with micro- and nanoporous morphologies containing voids and other features

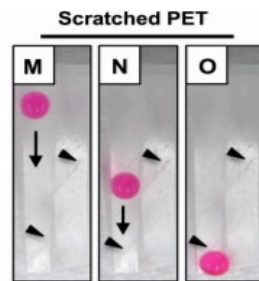


Low- and high-magnification Scanning Electron Microscope images of multilayers showing micro- and nanoscale porosity

- Creasing and severe scratching of treated surfaces has little effect on coating

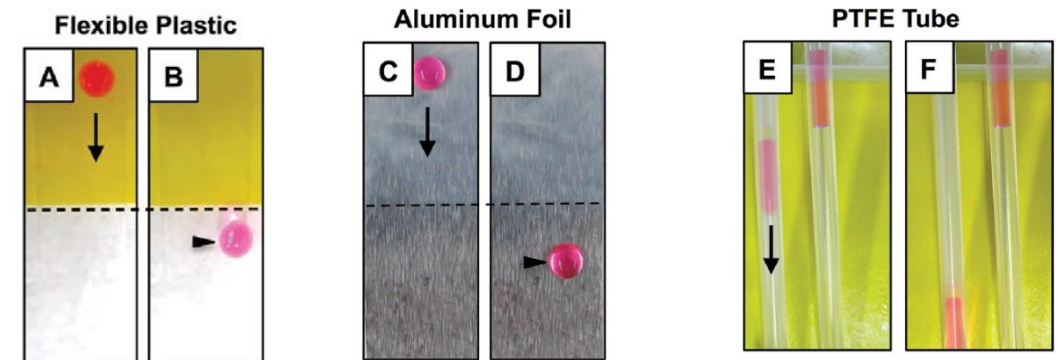


Droplets are observed to contact and wet the crease (marked by black arrowheads)



Droplets slide unperturbed over severe scratches (marked by black arrowheads)

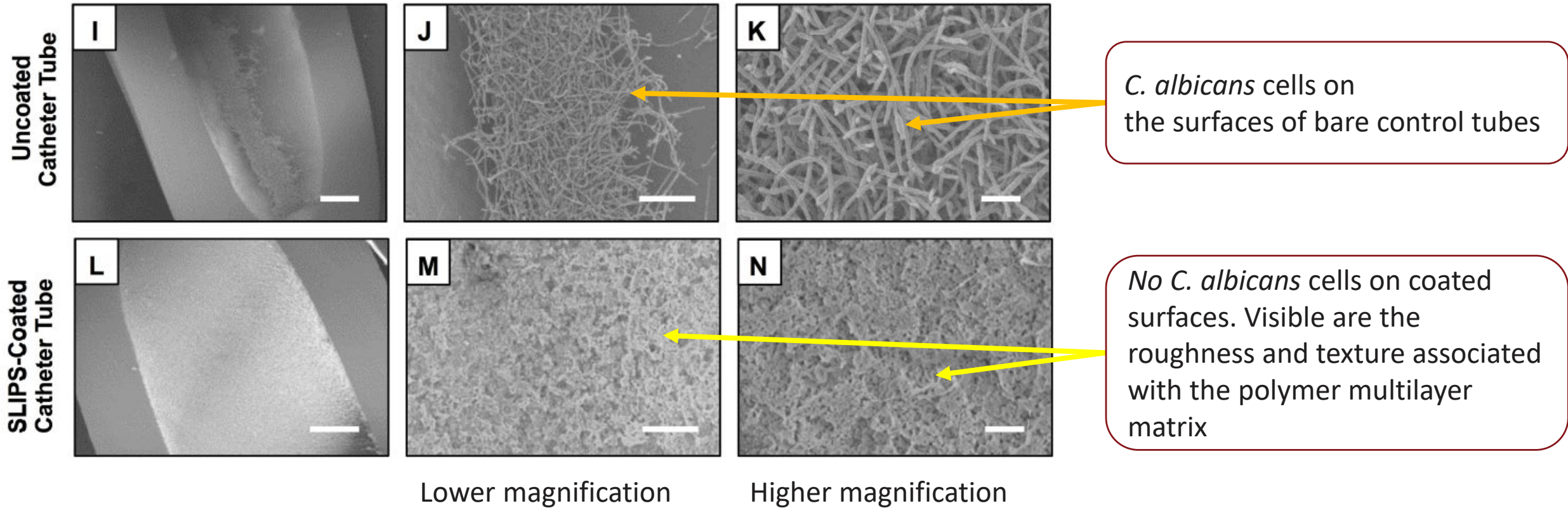
- Layer-by-layer approach is well suited for fabrication on surfaces of arbitrary composition (paper, PET, aluminum foil) and shape (flat surfaces, tubes)



Droplets of aqueous TMR sliding on flexible plastic film (A,B) and aluminum foil (C,D). Dotted lines show borders between coated (top) and uncoated (bottom) regions; droplets slid freely at angles of  $\approx 10^\circ$  on coated regions and came to rest upon contact with uncoated regions

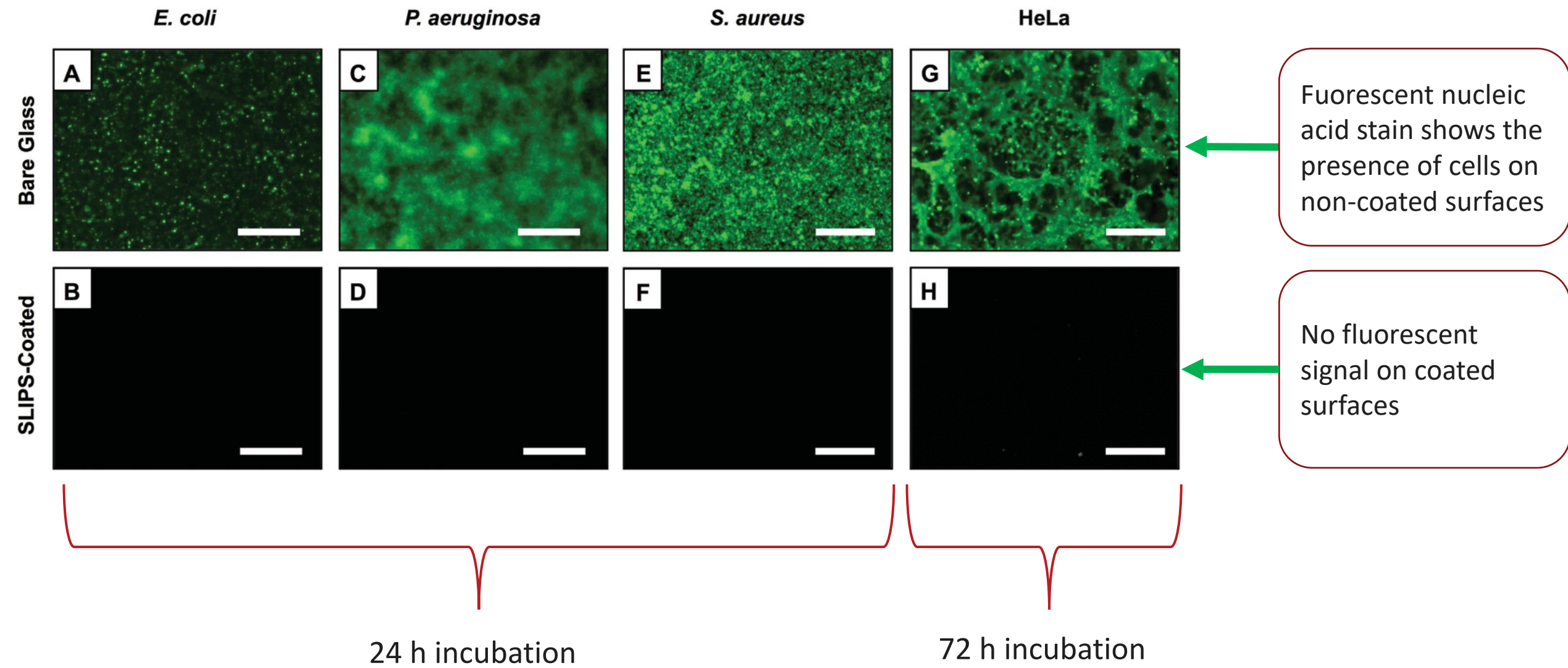
Left in each panel: droplets slide inside coated flexible PTFE tubing. Right: plugs form in uncoated tubes

# Coated catheters resist the formation of *C. albicans* biofilm



Scanning electron microscope images of bare (top) and SLIPS-coated (bottom) catheter tubes after inoculation with suspensions of *C. albicans* for 4 hours.

# Coated glass resists adhesion & colonization by bacteria & mammalian cells



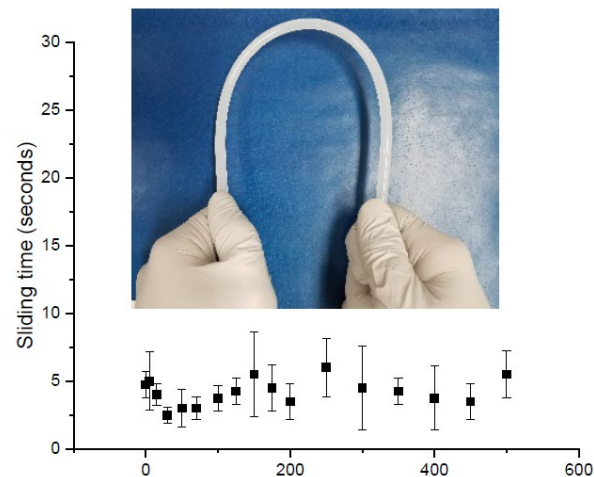


# Coated tubes retain their slippery properties under various conditions

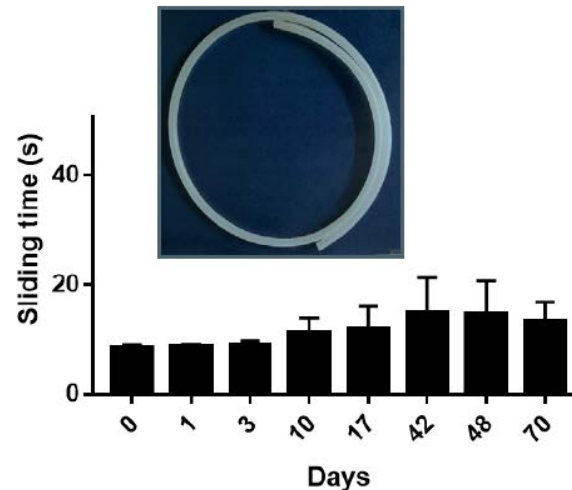
Physically robust nature of PEI/PVDMA multilayers allows coatings to maintain slippery properties under various conditions

- Repeated bending and flexing, permanent creasing and deep scratching
- Cooling/dry storage and storage in buffer
- Flow and simulated urine
- Ethylene oxide sterilization

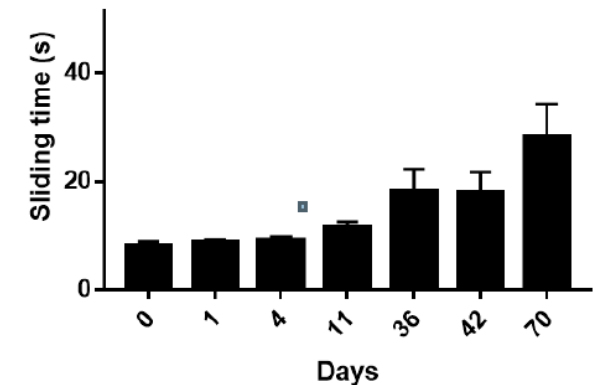
**Repeated bending & flexing (500X)**



**Coiling/dry storage (>70 days)**



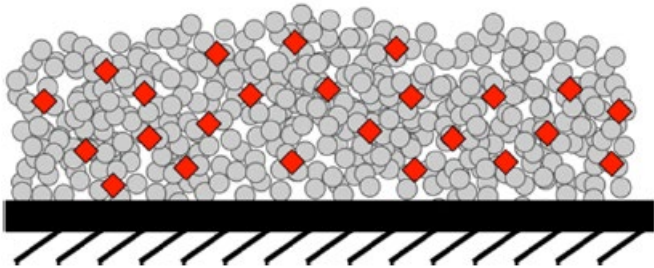
**Storage in buffer (>70 days)**



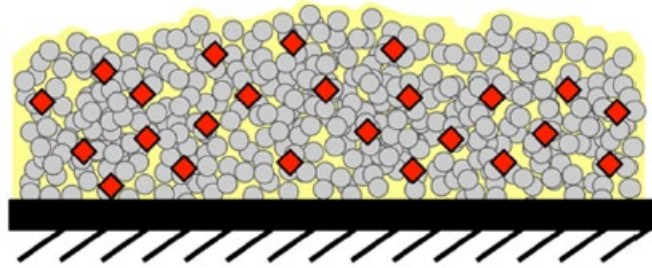
# PEI/PVDMA-based coatings enable drug delivery

PEI/PVDMA-based coatings sustain the long-term release of small-molecule antimicrobial agents

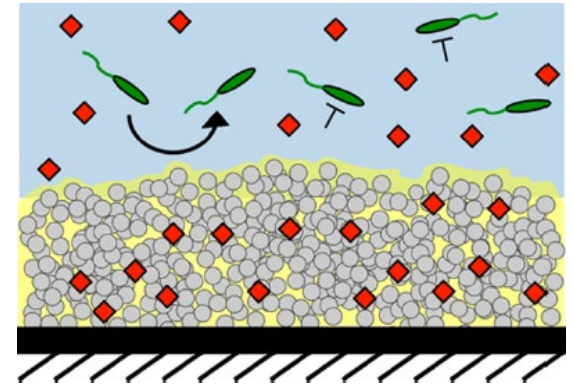
Solvent-assisted loading of agent into the nanoporous multilayers



Infusion with slippery oil phase

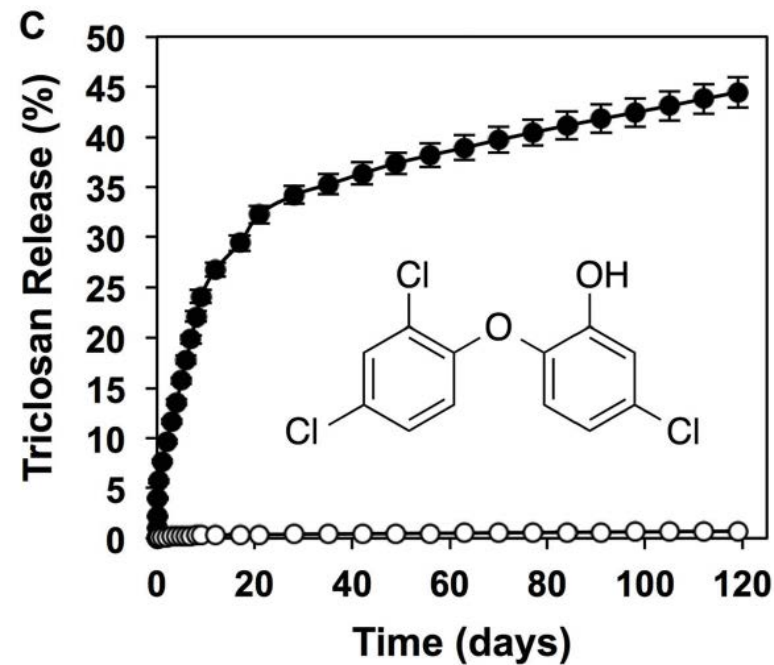


Controlled release



# Delivery proof of concept: PEI/PVDMA-based coating delivers triclosan

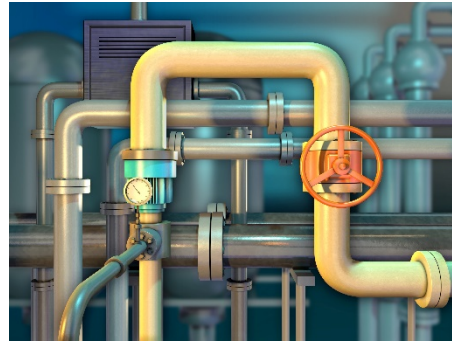
Triclosan infused surfaces remain slippery and slowly release compound



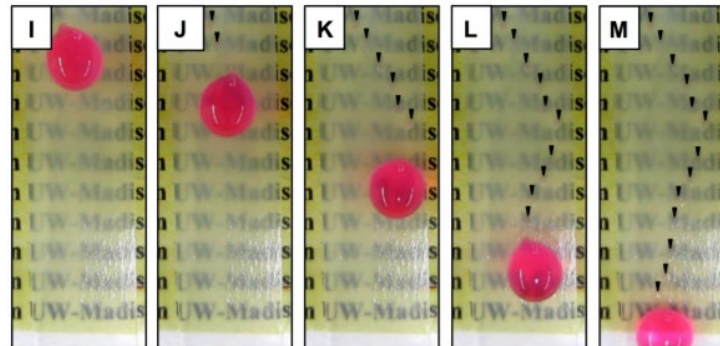
Release of triclosan from triclosan-loaded surfaces (closed circles) upon incubation in PBS buffer at 37 °C

# Other applications

- Technology is a platform for the design of multifunctional interfaces that could prevent fouling by a variety of organic fluids and other substances, organisms, or environmental contaminants



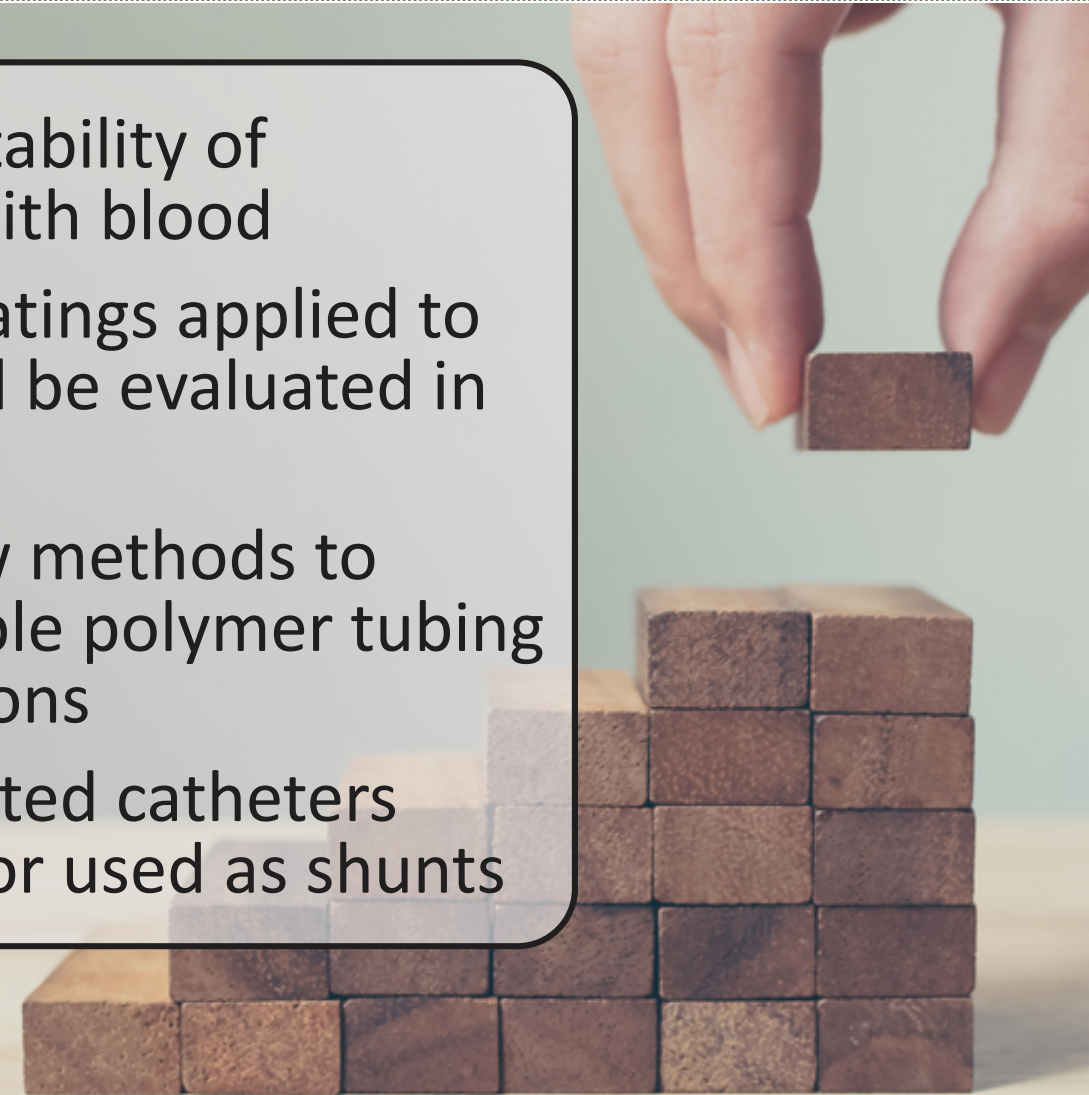
- Approach enables the creation of macroscale or microscale patterns of adhesive and non-adhesive surface features that enable passive or active control over the wetting behaviors of oils



Guided control over the in-plane path of a water droplet as it slides down the surface of a coated glass slide patterned with 13 strategically placed sticky spots; black arrowheads mark the locations of the sticky spots

# Next steps

1. Characterize the physical and functional stability of nanoporous coated catheters in contact with blood
2. Evaluate controlled-release antifouling coatings applied to the outside of flexible tubing; coatings will be evaluated in flow and using biological assay
3. Demonstrate feasibility of continuous flow methods to fabricate coatings in/on segments of flexible polymer tubing with lengths relevant in catheter applications
4. Evaluate the anti-fouling properties of coated catheters when inserted directly into blood vessels or used as shunts



# Limited evidence of effectiveness for clinically tested competing solutions [*alternative*]

Antibiotic-impregnated catheters	Silver alloy-coated catheters	Bactiguard urinary catheters	Heparin-coated catheters to prevent thrombogenesis
<ul style="list-style-type: none"><li>• Urinary catheters: limited evidence of clinical effectiveness from studies adopting symptomatic CAUTI as primary endpoint</li><li>• Central line catheters: significant benefits shown only in studies conducted in ICUs (most CLABSI occur outside of ICUs)</li></ul>	<ul style="list-style-type: none"><li>• High cost, unlikely to be cost-effective</li><li>• Cytotoxicity problems</li><li>• No effective reduction of incidence of symptomatic CAUTI (primary outcome) or blood stream infections</li></ul>	<ul style="list-style-type: none"><li>• (Gold, palladium and silver coating creates a galvanic effect when in contact with fluids, making it more difficult for bacteria to attach and form biofilm on the surface)</li><li>• Mixed evidence of effectiveness</li></ul>	<ul style="list-style-type: none"><li>• Heparin-coated central hemodialysis catheters not successful in preventing hemodialysis catheter thrombosis, according to retrospective studies</li><li>• Up to 5% of patients exposed to heparin develop heparin-induced thrombocytopenia</li></ul>

The CDC recommends the use of antiseptic- or antimicrobial-impregnated catheters only conditionally, after the implementation of other measures

# Patent filings

- 1) U.S. Patent No. US 8,071,210 – Covalent Assembly of Reactive Ultrathin Films
- 2) Application US-2017-0022371– Slippery Anti-Fouling Surfaces Fabricated from Reactive Polymer Multilayers
- 3) Application US-2018-0230318 – Slippery Liquid-Infused Porous Surfaces that Prevent Microbial Surface Fouling
- 4) Application filed – *Influence of Partial Side Chain Hydrolysis on the Growth and Morphology of Reactive Polymer Multilayers Fabricated Using Azlactone-Functionalized Polymers*

# Research Team



David Lynn-left, Harshit Agarwal-right

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## David Lynn

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*Chemical and Biological Engineering Dept., UW-Madison*

- Additional Affiliations: Materials Science and Engineering, Chemistry
  - Harshit Agarwal – graduate student
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## Collaborators

- **Helen Blackwell**

*Chemistry Dept., UW-Madison*

- **Sean Palecek**

*Chemical and Biological Engineering Dept., UW-Madison*



# Publications

- Michael J. Kratochvil et al. [Slippery Liquid-Infused Porous Surfaces that Prevent Bacterial Surface Fouling and Inhibit Virulence Phenotypes in Surrounding Planktonic Cells](#). ACS Infect. Dis. 2016, 2, 7, 509-517
- Uttam Manna et al. [Slippery Liquid-Infused Porous Surfaces that Prevent Microbial Surface Fouling and Kill Non-Adherent Pathogens in Surrounding Media: A Controlled Release Approach](#). Adv. Funct. Mater. 2016, 26, 3599–3611
- Uttam Manna, David M. Lynn. [Fabrication of Liquid-Infused Surfaces Using Reactive Polymer Multilayers: Principles for Manipulating the Behaviors and Mobilities of Aqueous Fluids on Slippery Liquid Interfaces](#). Adv. Mater. 2015, 27, 3007–3012
- Uttam Manna, David M. Lynn. [Synthetic Surfaces with Robust and Tunable Underwater Superoleophobicity](#). Adv. Funct. Mater. 2015, 25, 1672–1681
- **News article:** [Double dipping: Dual-action ‘slippery’ catheter fights bacteria](#), May 10, 2019