Orchestrated Attachment of Antibiotic Monolayers to Polymeric Surfaces

Isolated Nano-Objects and Organized Nano-Networks

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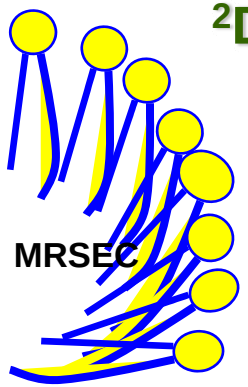

How All Started: N. Aumsuwan, S. Heinhorst, M.W. Urban,
"Antibacterial Surfaces on Expanded Polytetrafluoroethylene; Penicillin Attachment,"
Biomacromolecules, 2007, *8*(2), 713-718.

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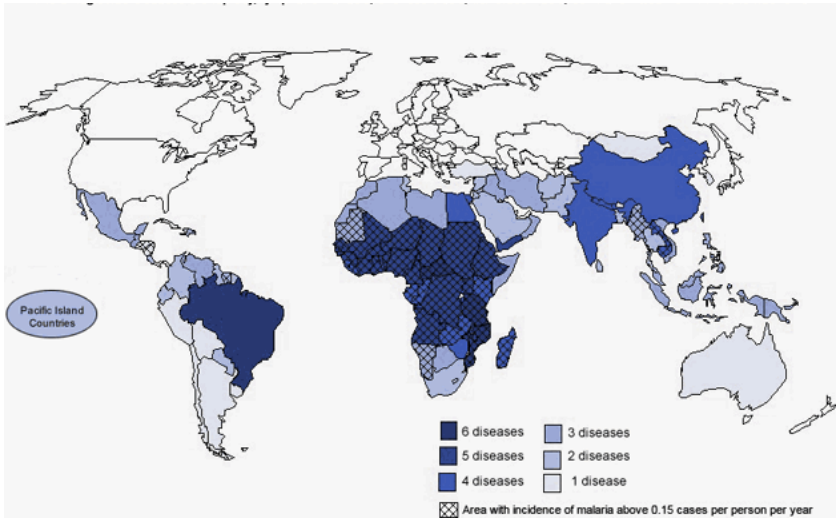


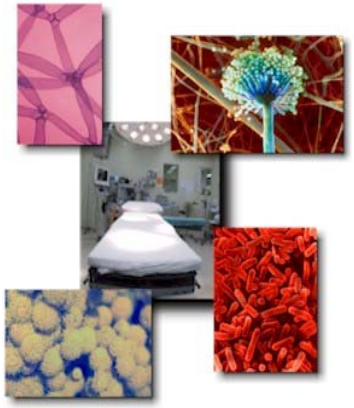
- Each Year, 2 Million Infections Are Acquired in Hospitals, 88,000 of Which Are Fatal (CDC).
- These Infections Add $5 Billion to the Cost of Health Care in the U.S.

- Approach: Control the Infection Before it Starts

Urban Research Group

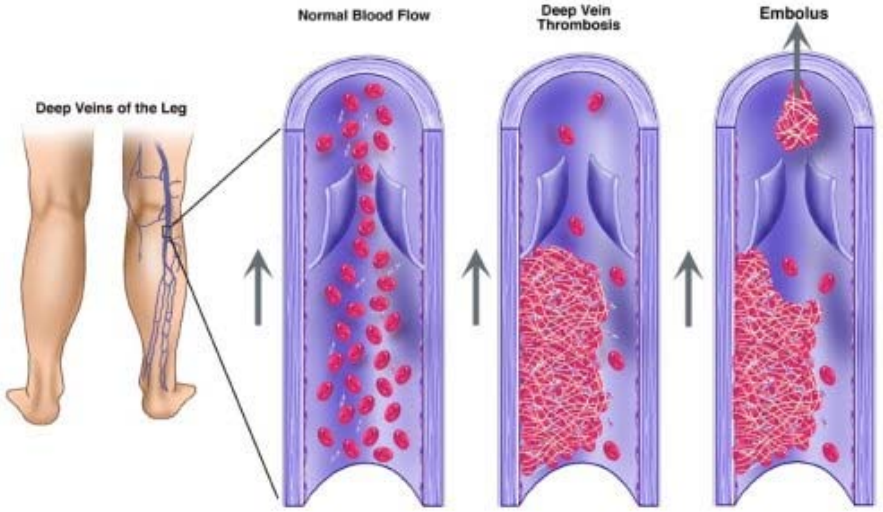
CDC. Press Release, March 6, 2000, *http://www.cdc.gov/ncidod/eid/vol7no2/wenzel.htm*

While many organizations are working hard to prevent infections and fight antimicrobial resistance in U.S. healthcare settings, this issue continues to be a challenge. These problems are larger than any one institution or agency can solve alone. Individuals at the federal, state, and local levels, in the public and private sector, need to work together to improve strategies to meet this healthcare challenge.



March 2006, House of Representatives
Denise Cardo, M.D.
Director, Division of Healthcare Quality Promotion
National Center for Infectious Diseases
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services

- When a Foreign Object Enters the Body and Vascular Damage Results, Proteins are Adsorbed to the Surface of the Object which Causes Clotting
- Triggering of a Fibrin Network Formation called a Thrombus
- One Approach to Simultaneously Address These Problems is to Utilize Bio-Functional Surfaces
- Selected Useful Bio-Functional Molecules
  - Antibiotics
    - *Beta*-lactam Antibiotics
    - Aminoglycosides
  - Anti-Thrombogenics
    - Glycosaminoglycans



Key Issues:

Orchestrated NANO
Isolated NANO

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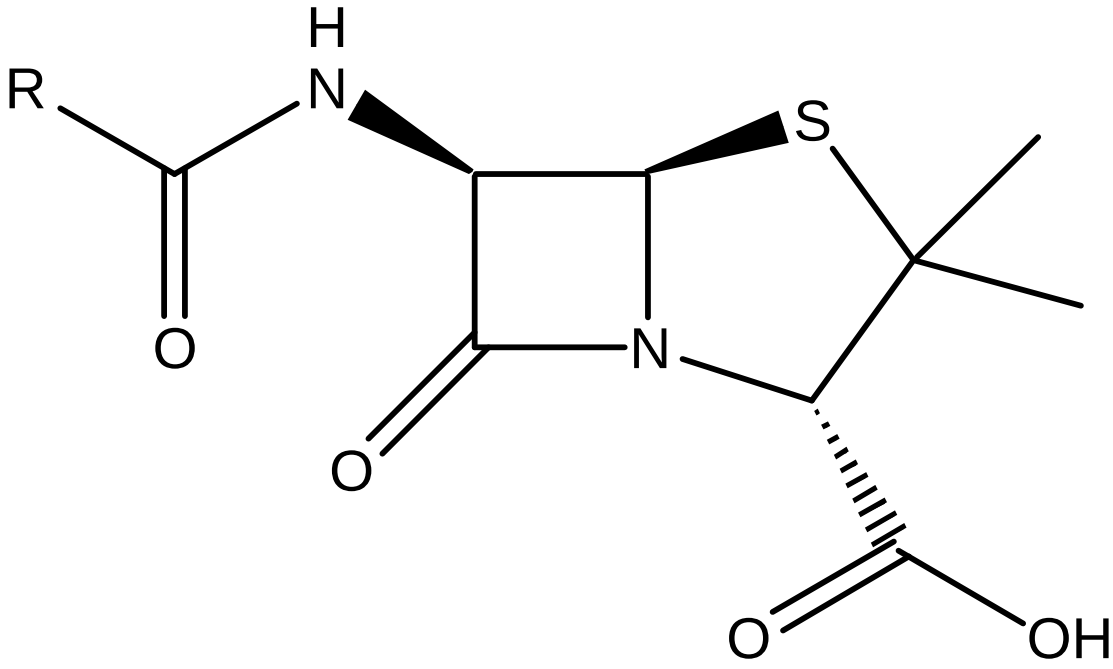
Antibiotics

Beta-lactam Antibiotics

Orchestrated NANO



Penicillin Nucleus

- The Active *Beta*-lactam Group Binds to a Bacterial Enzyme Known as Transpeptidase

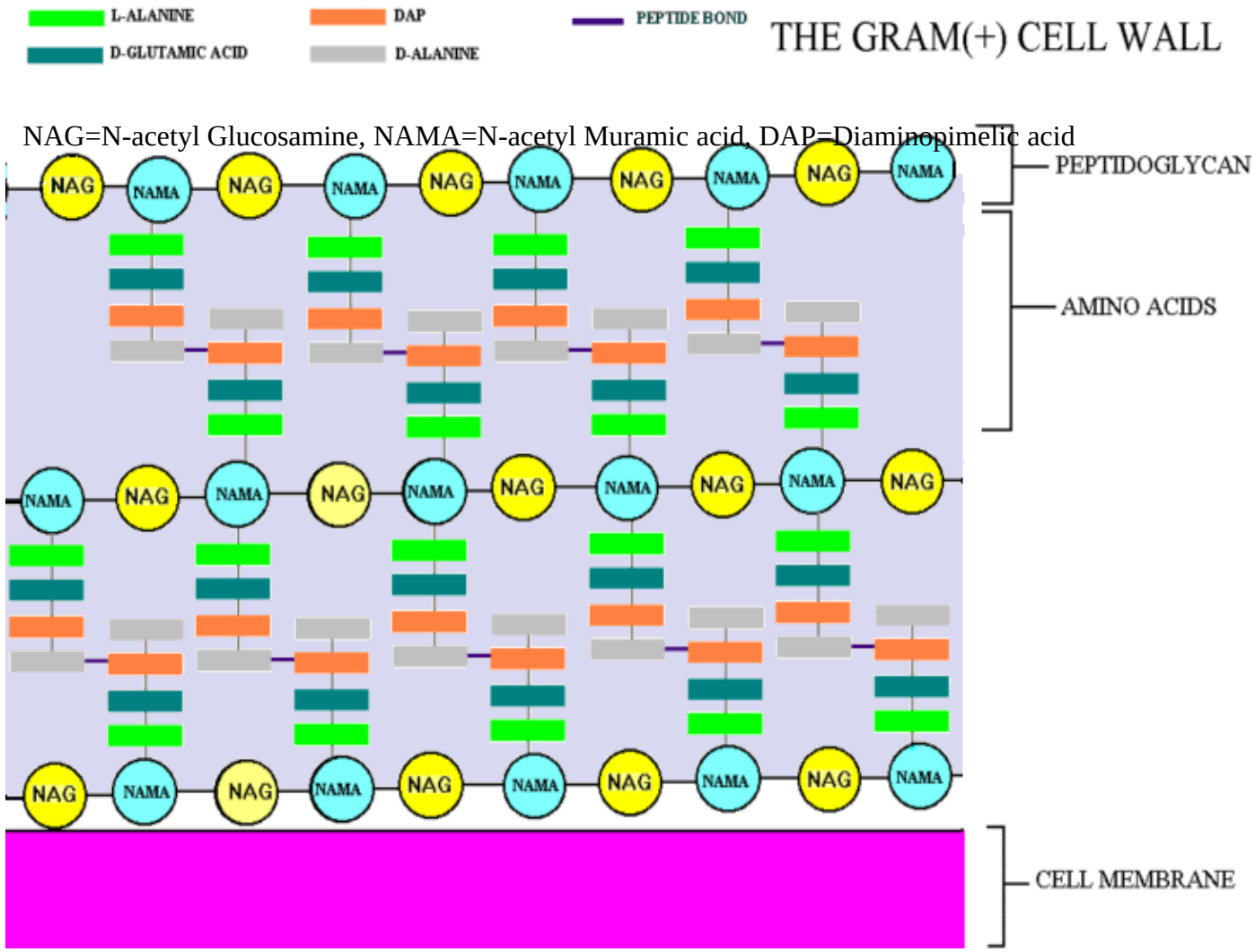
- Without this Enzyme, the Cell Wall Cannot Form a Crosslinked Network, and the Bacteria Succumbs to Osmotic Forces

Strominger, J.L.; Park, J.T.; Thompson, R.E. *The Journal of Biological Chemistry* **1959**, 234(12), 3263-8.

Antibiotics

Beta-lactam Antibiotics

Orchestrated NANO



Copolysaccharide Backbone

Oligopeptide Side Chains

Formation of a Precisely Orchestrated Crosslinked Network

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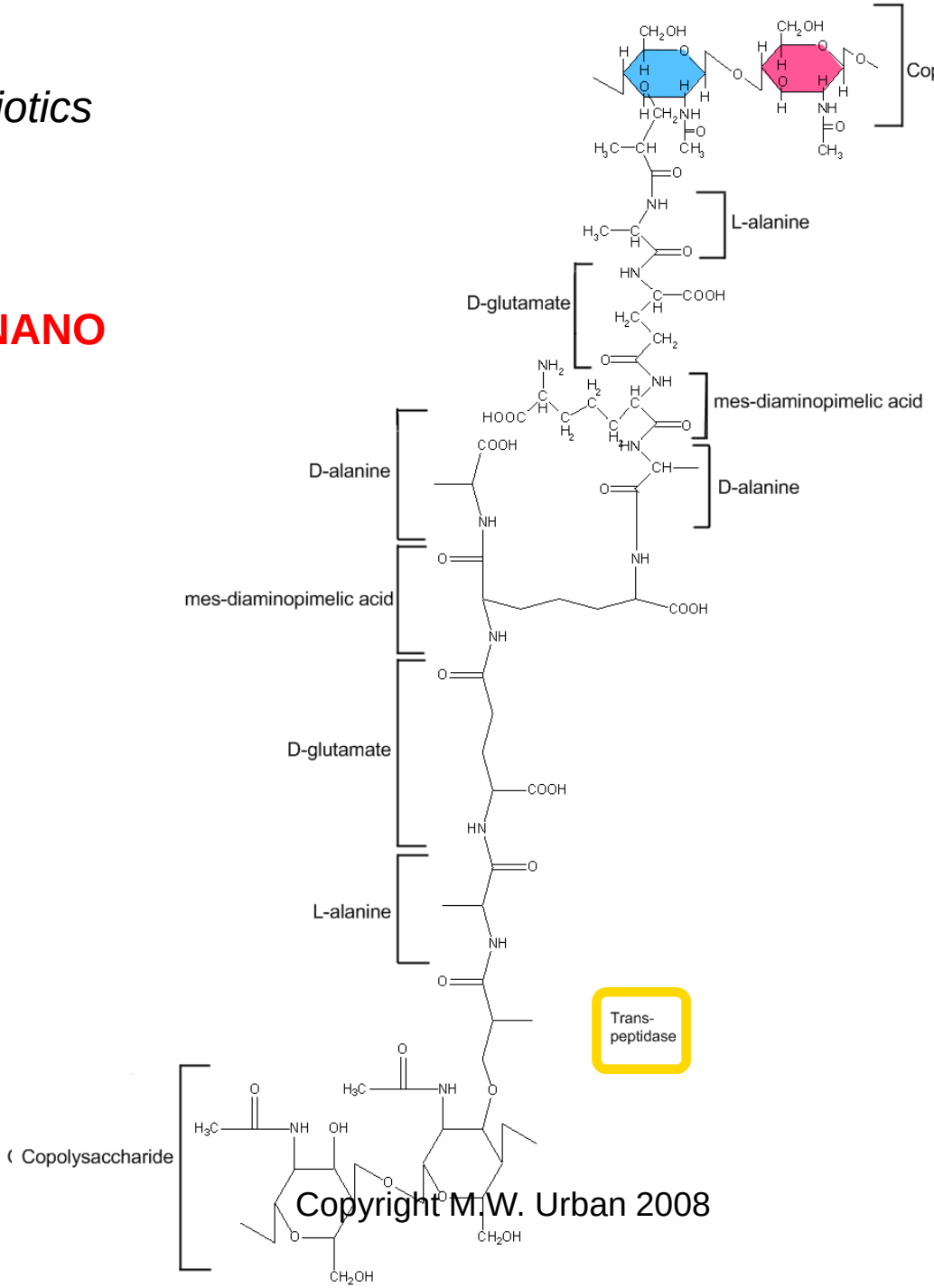
Paustian, T. and Roberts, G. *Through the microscope: A look at all things small* 2nd ed. Madison, Wisconsin, **2002**.

Antibiotics

Beta-lactam Antibiotics

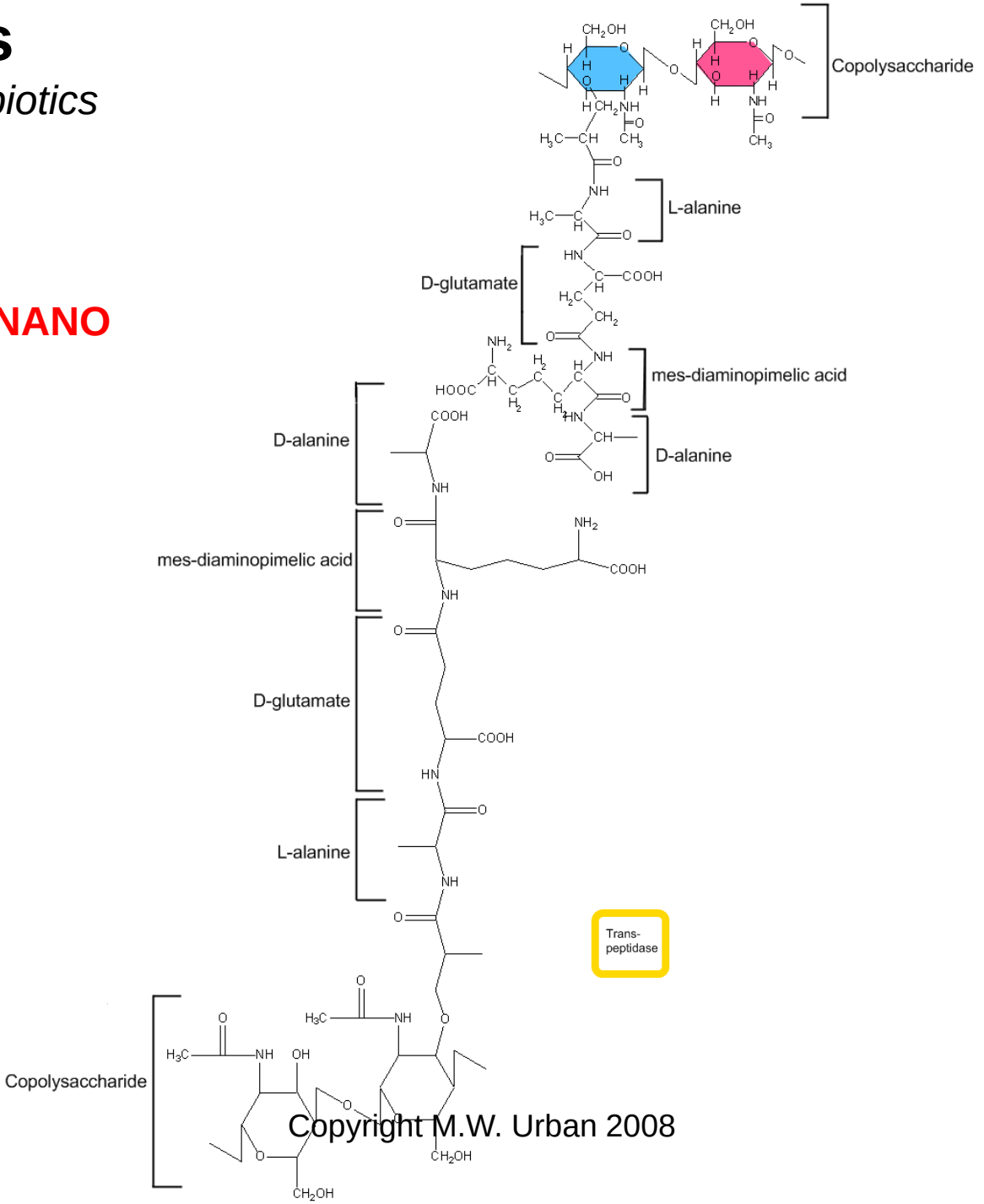
Orchestrated NANO



Antibiotics

Beta-lactam Antibiotics

Orchestrated NANO



Surface Approaches

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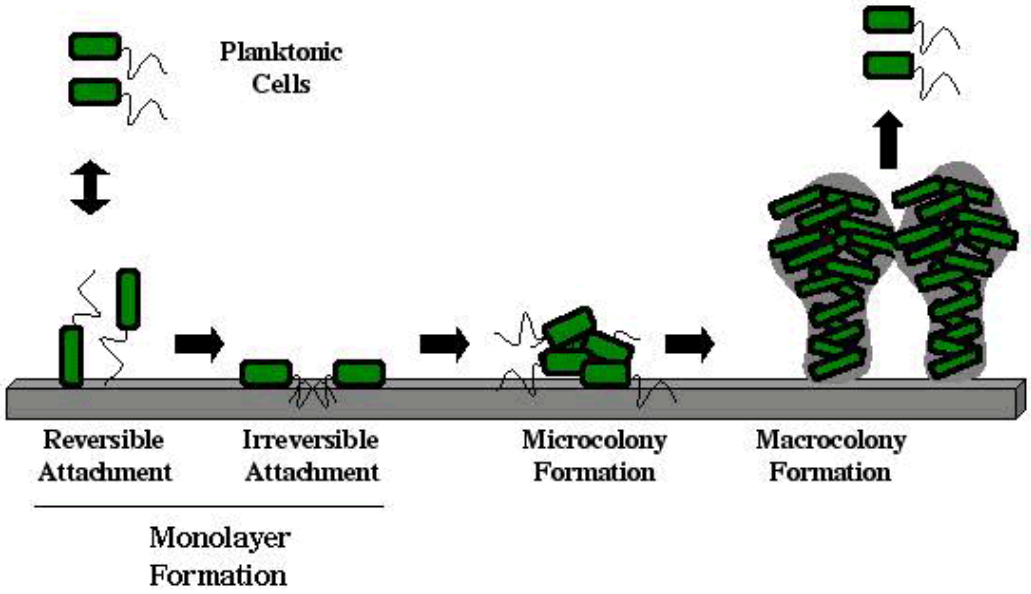
- How Can Implants or Objects in Contact with Blood be Simultaneously Resistant to Bacterial Attachment or Thrombosis?

- Surface Modifications
  - Many Surface Modification Methods Do Not Have the Intimate Combination of Chemical and Morphological Adjustments



Approach: **Orchestrated NANO**

Enhanced Specific Binding

Reduced Non-Specific Binding

Senaratne, W.; Andruzzi, L.; Ober, C.K. *Biomacromolecules* **2005**, 6(5), 2427-2448.

Zegans, M.E.; Becker, H.I.; Budzik J.; O'Toole, G. *DNA and Cell Biology* **2002**, 21(5), 415-420.

Surface Modification Methods

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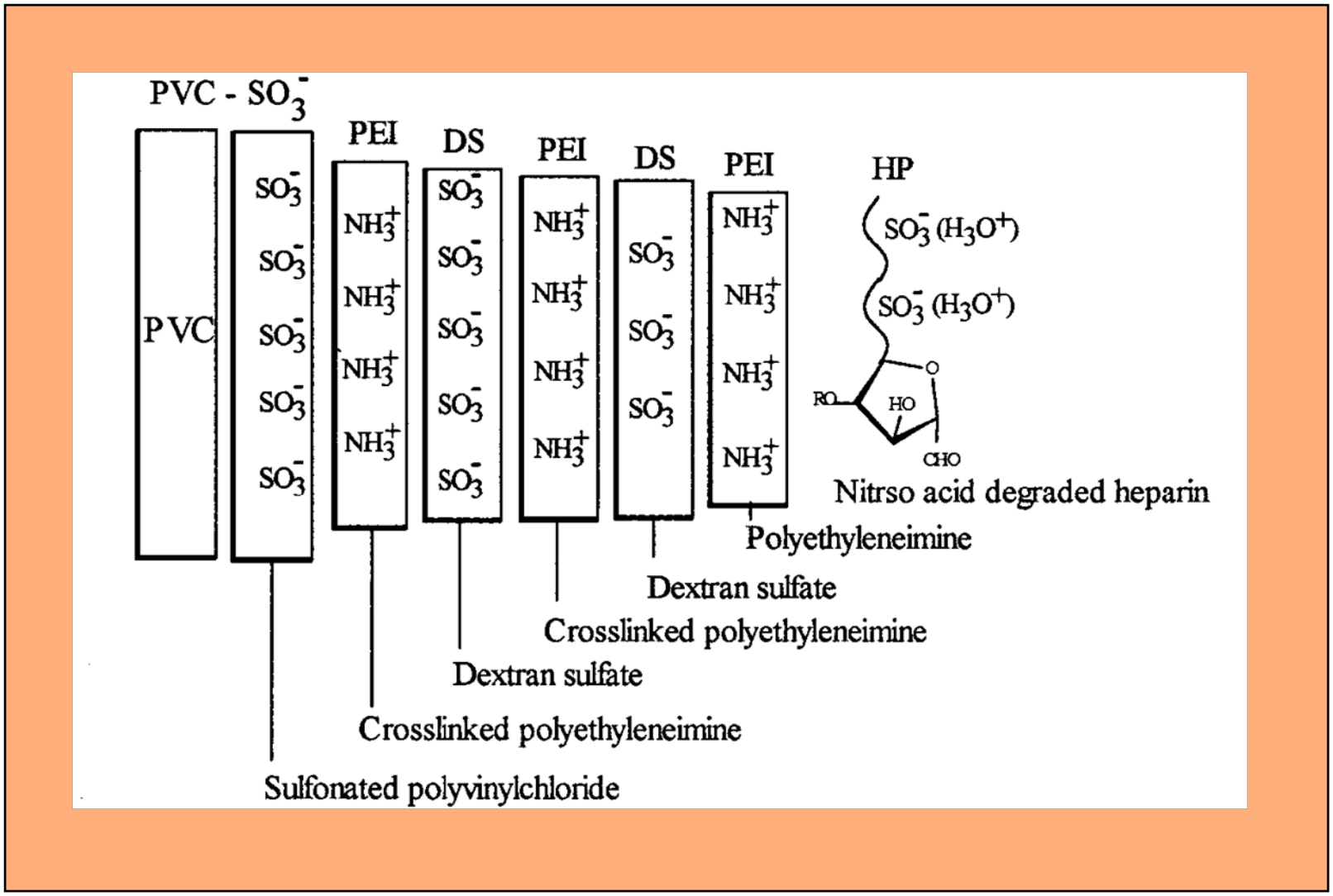
Layer-by-Layer Thromboresistant Surfaces



Orchestrated NANO

Kim, H.; Urban, M.W. *Langmuir* **1998**, 14(25), 7235-7244.

General Approach

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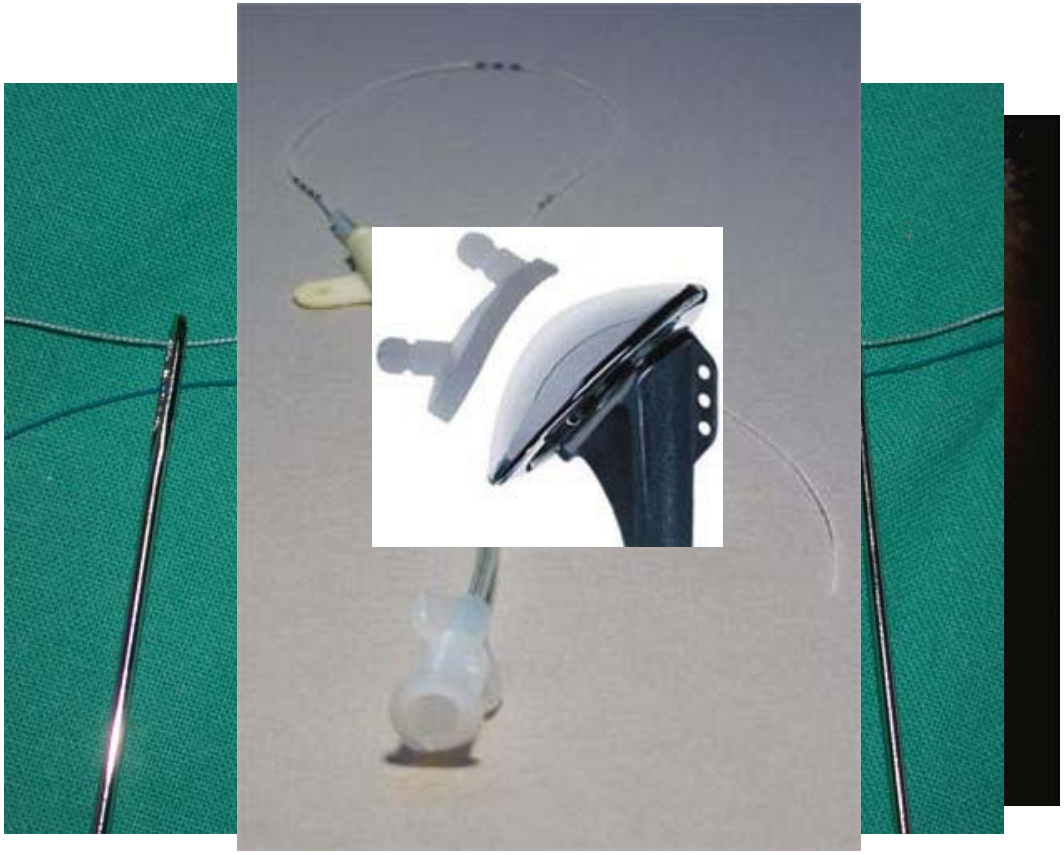
- Substrates:
  - Polytetrafluoroethylene
  - Polyurethane
  - Polyethylene (UHMW)
  - Polypropylene
  - Polymethyl methacrylate
- The Objective is to Create Controllable Surface Reactive Groups

Orchestrated NANO



Microwave Plasma Reactions

Orchestrated NANO

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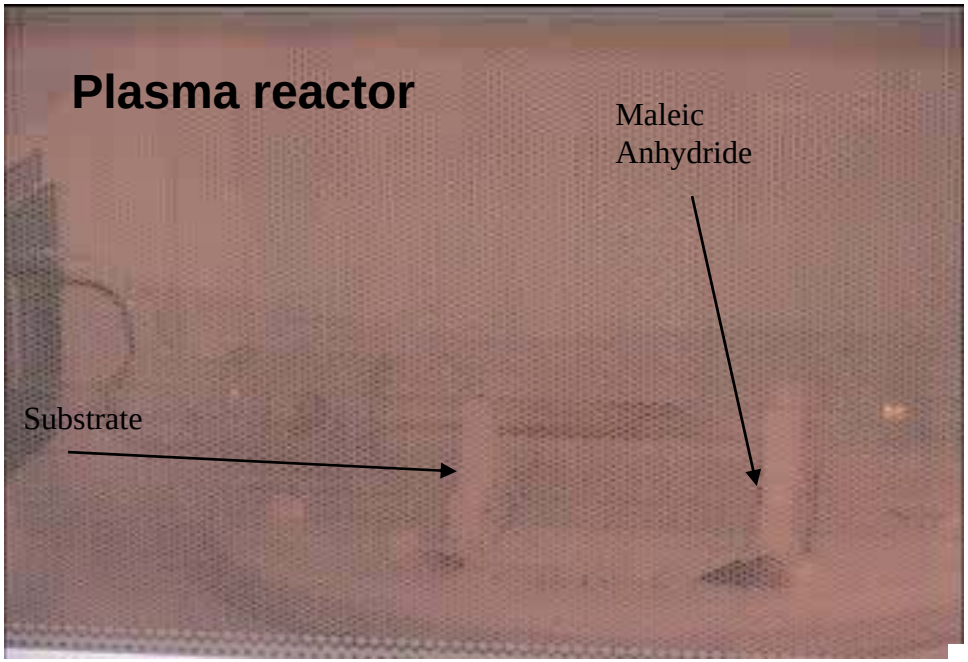
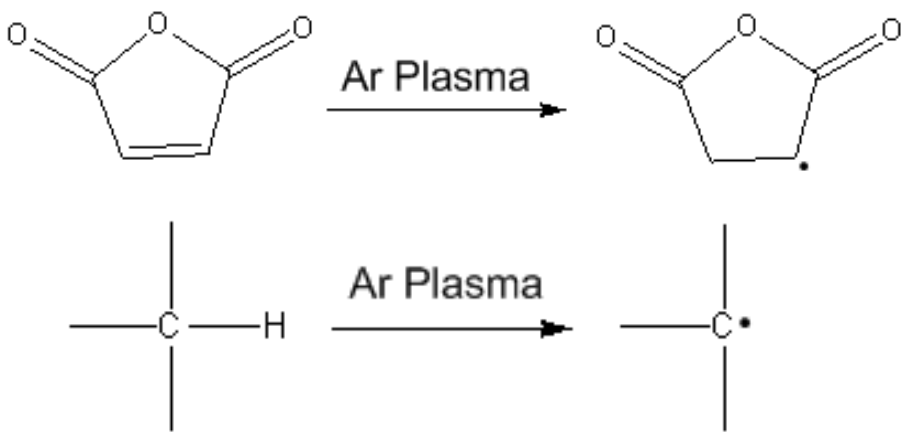
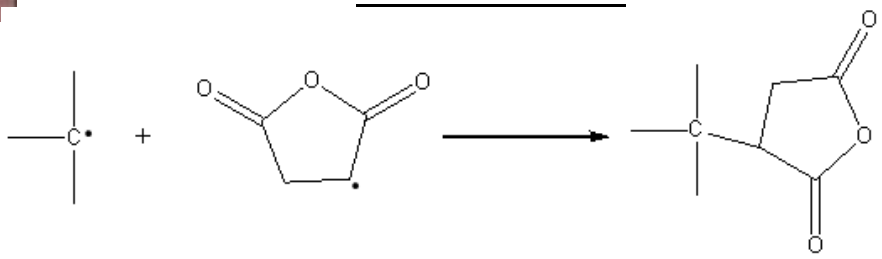
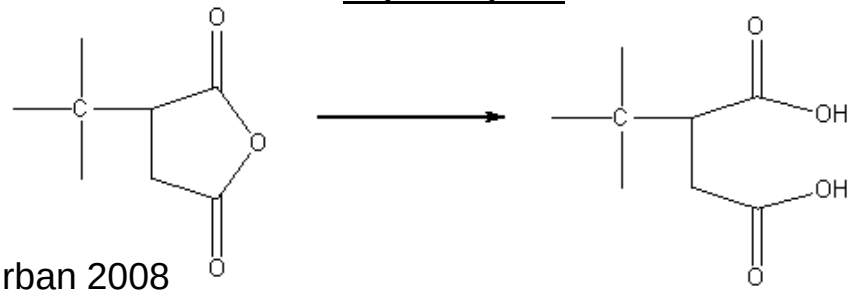


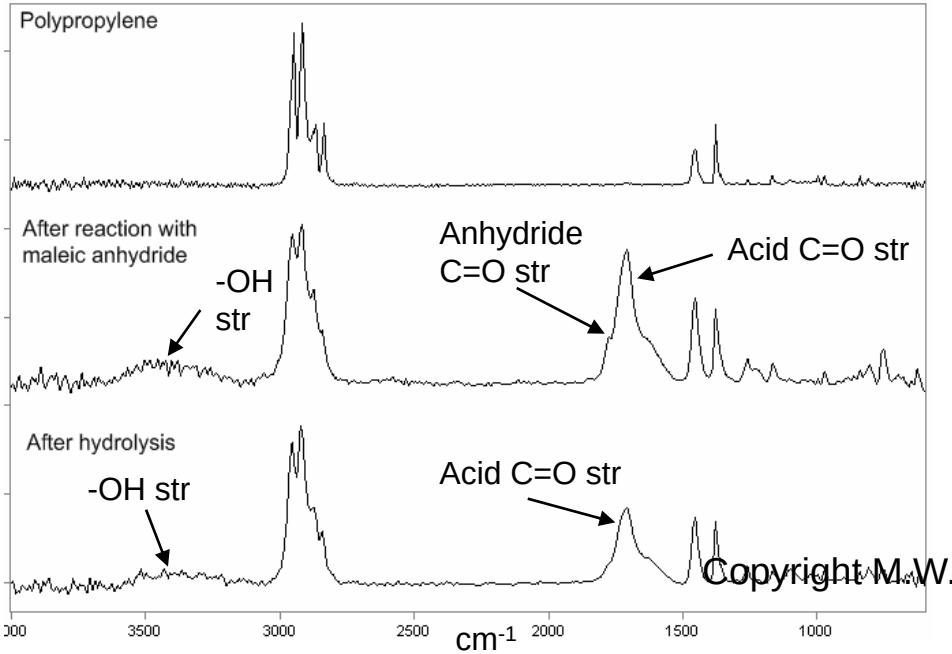


Combination



Hydrolysis





Gaboury, S.R.; Urban, M.W.*Langmuir* **1993**, 9(11), 3225-3233.

Formation of Orchestrated Polymer "Cushions"

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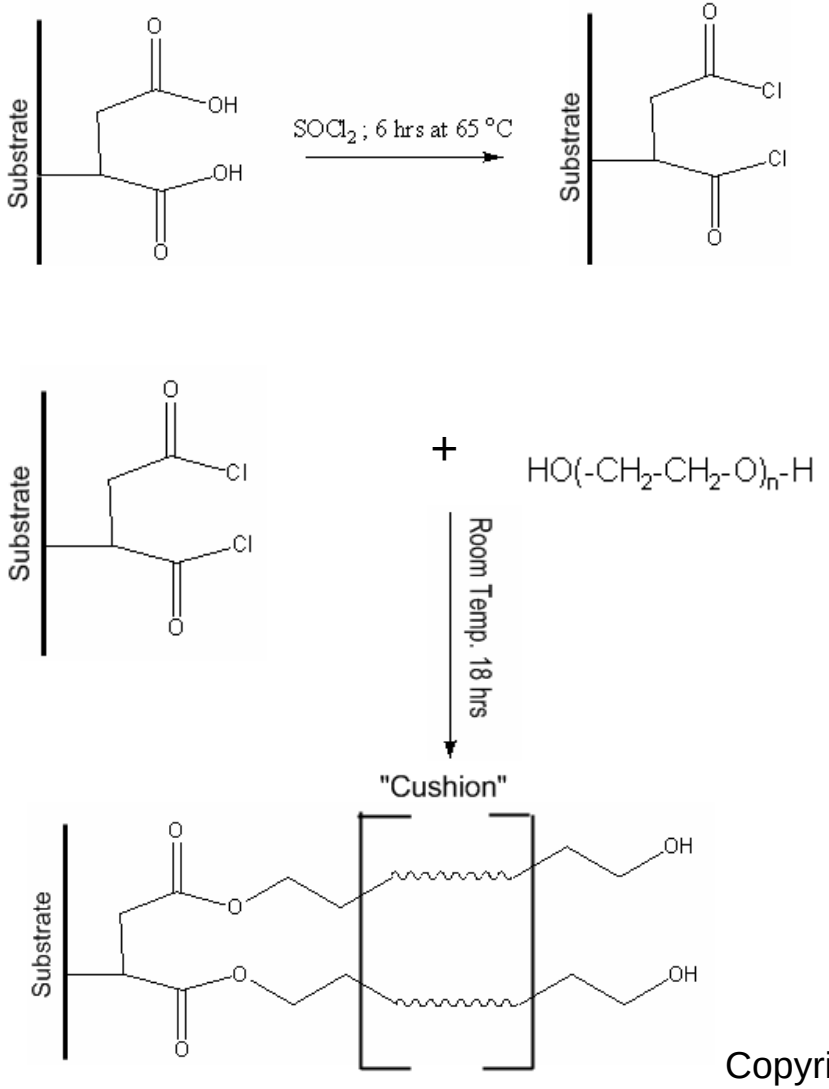
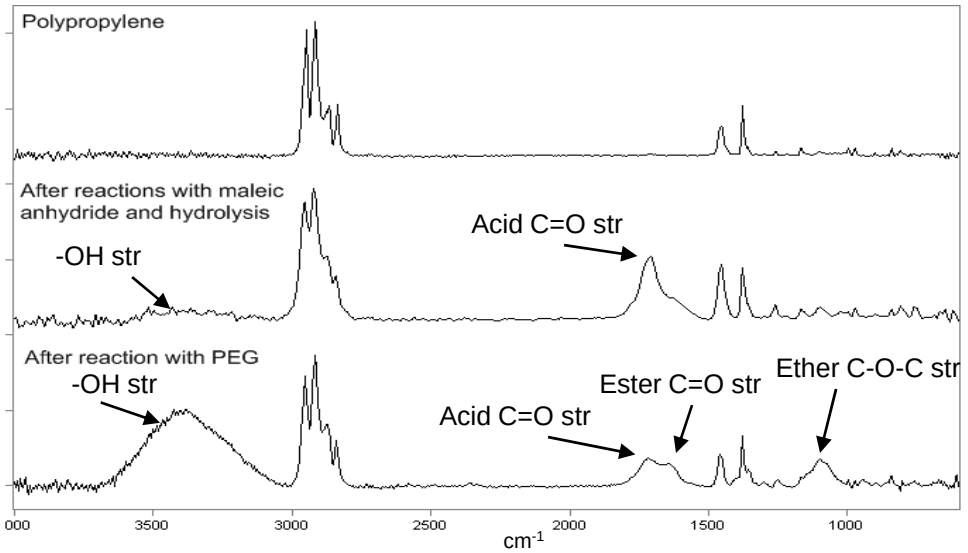
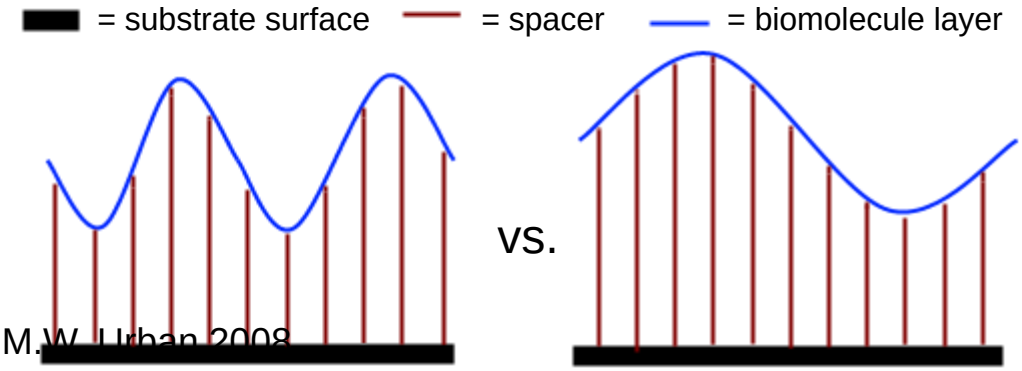




- Important Considerations
  - Effect of Polymer "Cushion" Thickness
  - Effect of Polymer "Cushion" Thickness Dispersity



MORPHOLOGY OF THE CUSHION

Formation of Bio-Functional Surfaces

Antimicrobial Surfaces

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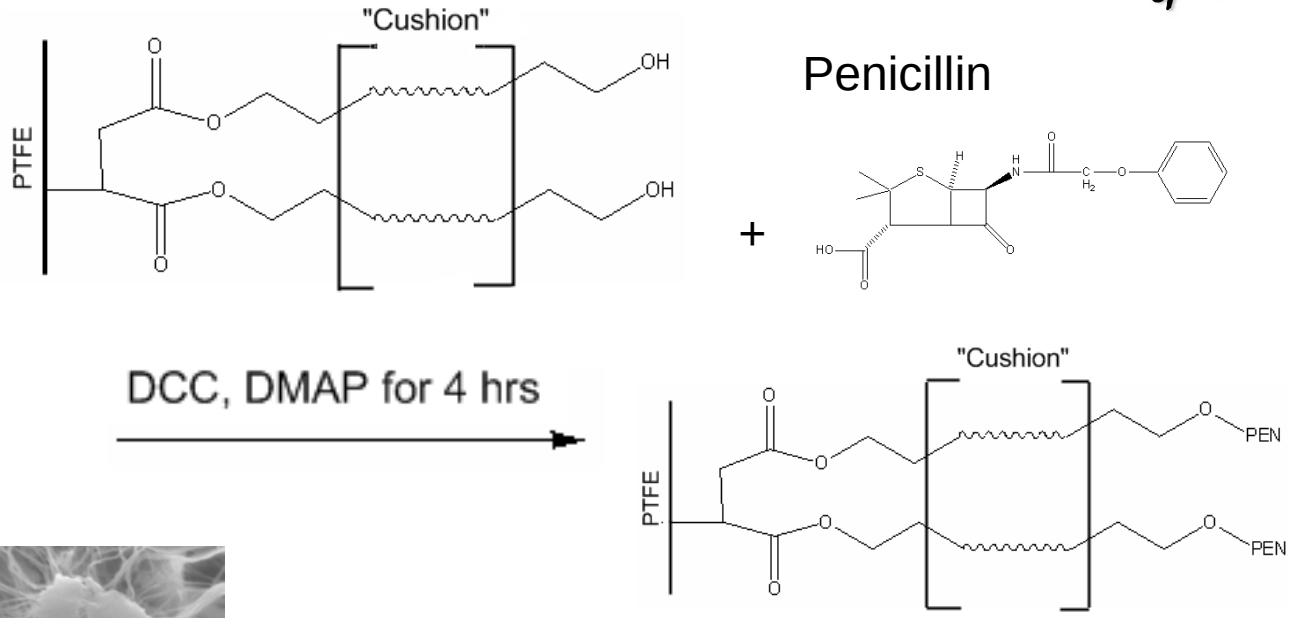
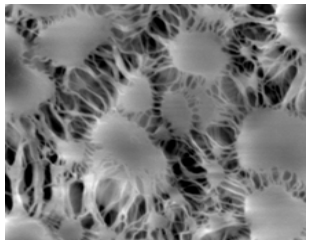
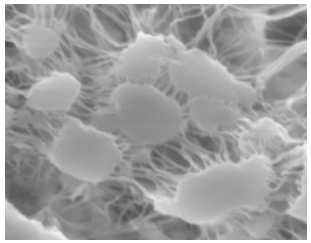
Orchestrated NANO





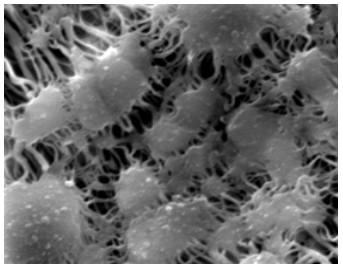
Unmodified ePTFE

(A)



Plasma reacted ePTFE surface

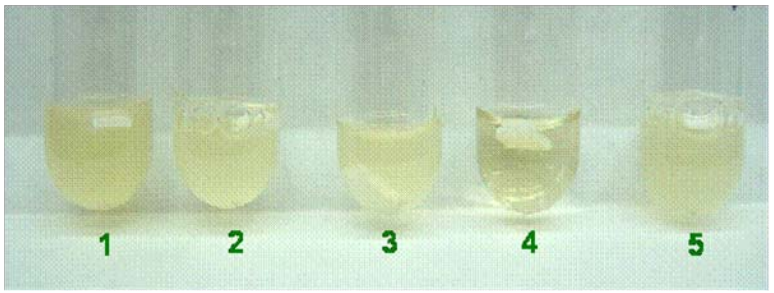
(B)



5 μm

Plasma reacted
maleic anhydride ePTFE

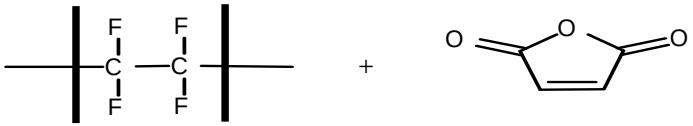
(C)



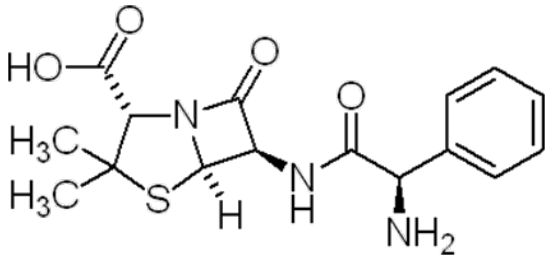
Staphylococcus aureus

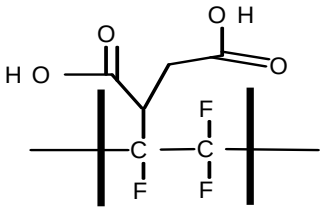
Aumsuwan, N.; Heinhorst, S.; Urban, M.W. *Biomacromolecules* **2007**, 8(2), 713-718.

Attachment of Ampicillin
Gram “+” and “-” Bacteria



Microwave Ar Plasma
Hydrolysis

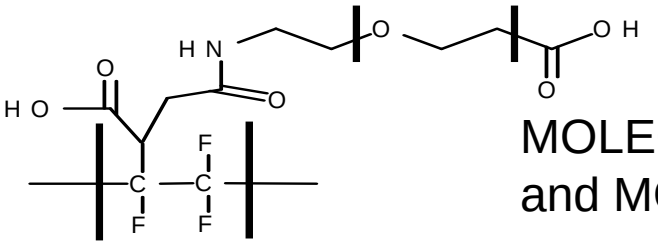




ACID GROUPS

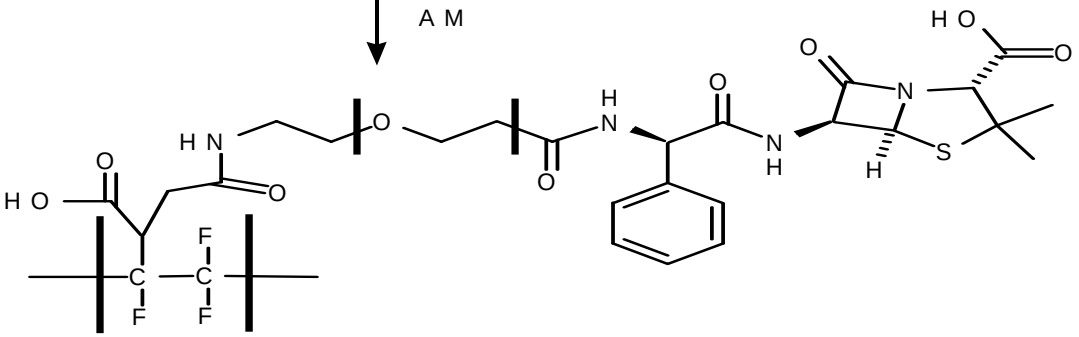
PEG

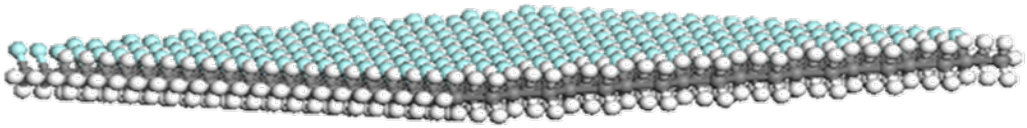
Orchestrated NANO



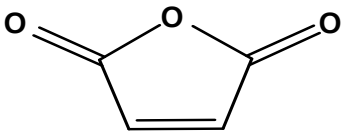
MOLECULAR CUSHION
and MORPHOLOGY

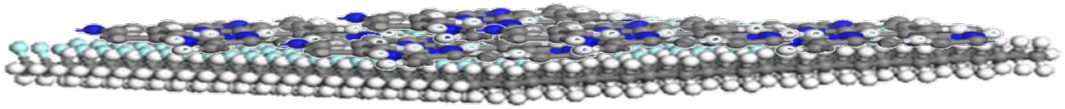
AM





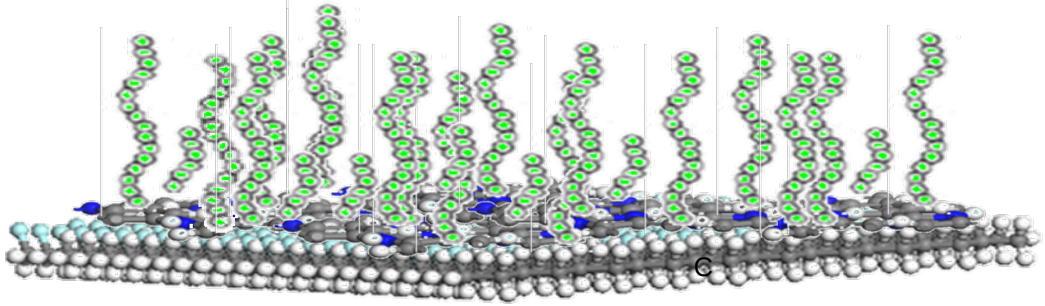
A



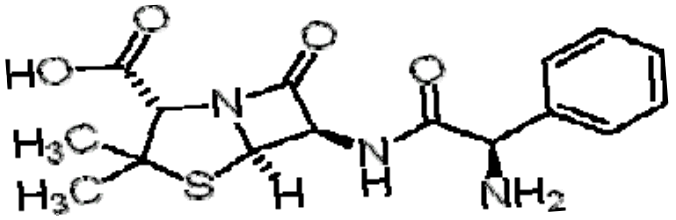


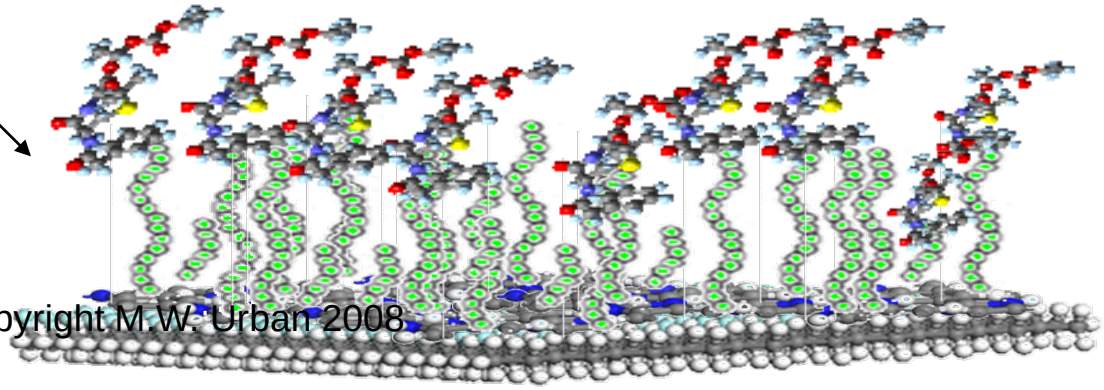
$HOOC\text{-}(CH_2\text{-}CH_2\text{-}O)_n\text{-}NH_2$

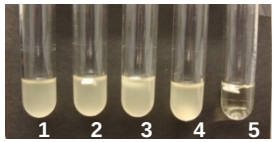
B

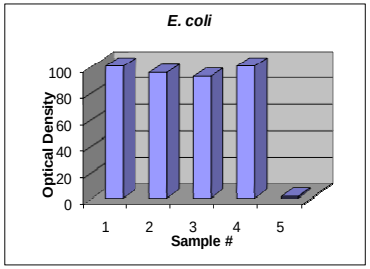


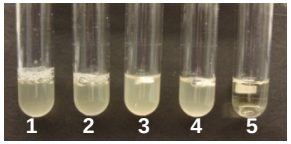
C

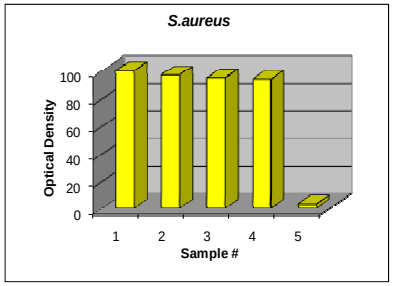


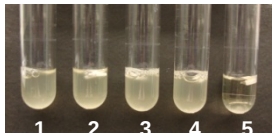


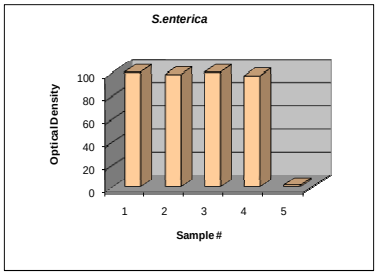


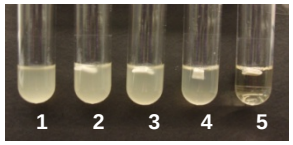


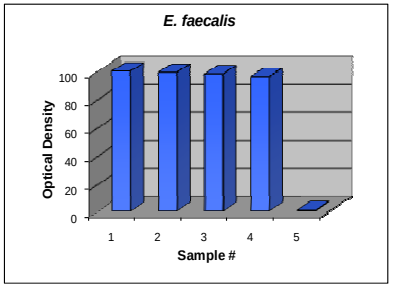


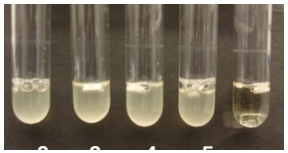


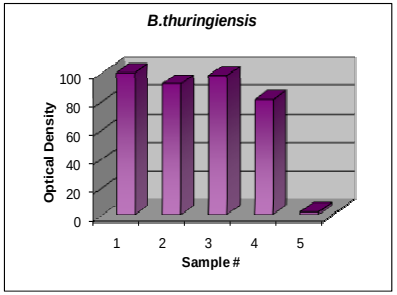






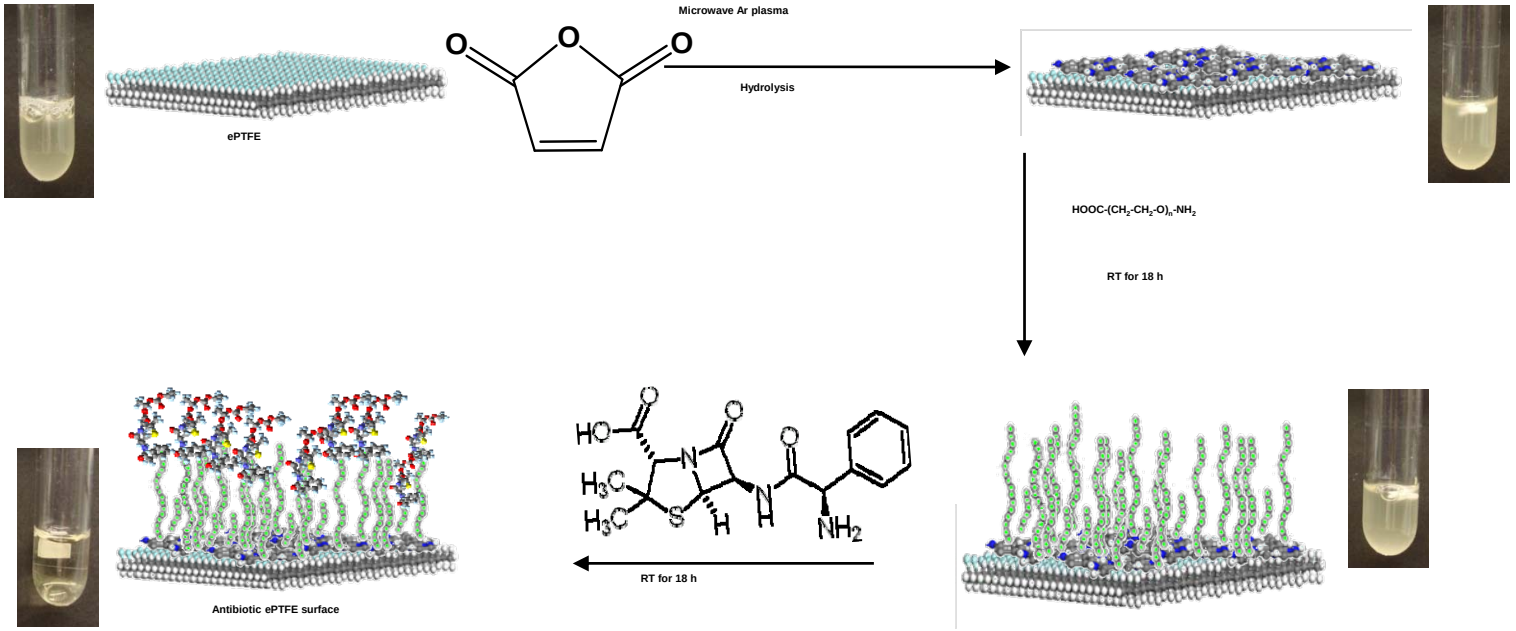






Antimicrobial Assessments

MODIFICATION OF ePTFE SURFACES EFFECTIVE AGAINST GRAM “+” AND GRAM “–“ BACTERIA

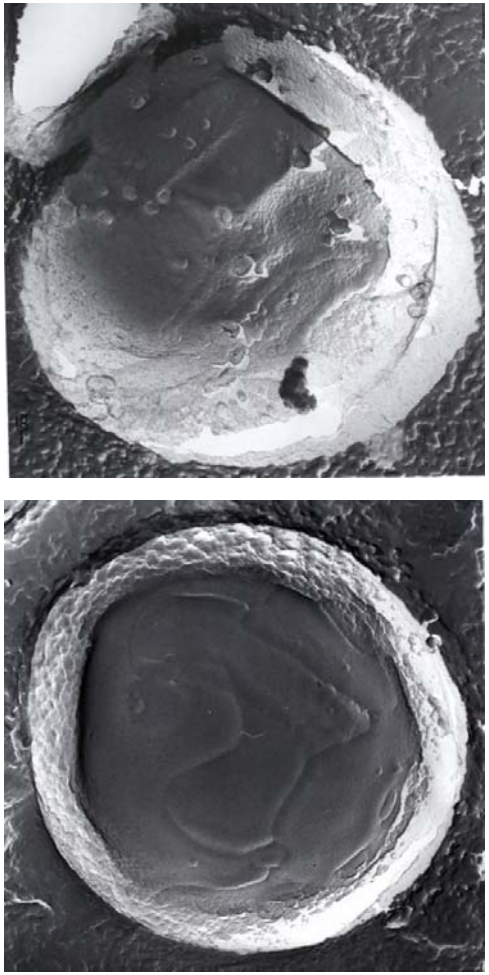


Orchestrated NANO

N. Aumsuwan, S. Heinhorst, M.W. Urban, Biomacromolecules, 2008, in press.

Isolated NANO-Objects

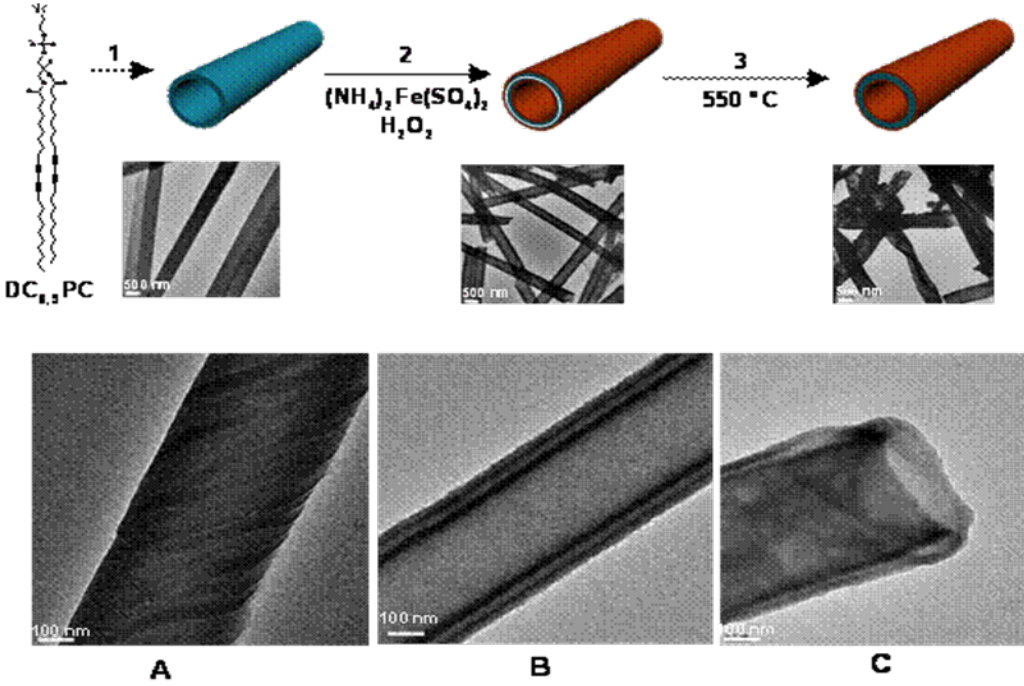
FF-TEM



200 nm

Hollow Particles

Formation of Magnetic Nanotubules from PLs



Redox Nanotubes

Blue Dye

Redox Nanotubes with Dye

M. Yu, M.W. Urban, J. Mat. Chem., 2007.

Summary

- Platform of Surface Modifications on Inert Materials
- Nano-Orchestrated Surfaces with Anti-Microbial Properties
- Biomimetic Assembly of Nano-Objects into Nano-Networks

- National Science Foundation
  - Materials Research Science and Engineering Center (DMR 0213883)
  - IU CRC in Coatings and Industrial Sponsors
- Industrial Sponsors
- Urban Research Group
  - Min Yu (PhD Student)
  - Anuradha Misro (PhD Student)
  - Laura Kolibel (PhD Student)
  - Biswajit Ghosh (PhD Student)
  - Fang Liu (PhD Student)
  - Megan Aumsuwan (PhD Student)
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