Nanotechnology in the life sciences

A FRONTIS LECTURE SERIES

organized by

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# Nanotechnology in the life sciences

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Self-assembly of molecular structures

OUTLINE

• General comments
• Self-assembled monolayers (SAMs)
• Self-assembly of macromolecular structures on surfaces
• Layer-by-layer deposition of polyions
• Stamping
• Self-assembly of diblock polymers
• Self-assembly of macromolecules
Applications

• Catalysts
• Integrated circuits
• Data Storage
• Drug Delivery
• Sensors
• Medical Devices
• Biomaterials
• Nanoparticles
• Microfluidics
• Separation and purification
Self-assembly can be influenced by

- Interface
- Reaction
- Electric field
- Flow
- Temperature
- Solvent
- Ionic strength
- pH
Self-assembly of molecular structures

- Self-assembled monolayers (SAMs)
- Self-assembly of macromolecular structures on surfaces
- Layer-by-layer deposition of polyions
- Stamping
- Self-assembly of diblock polymers
- Self-assembly of macromolecules
Self-assembled monolayers

- Thiols on metals (Whitesides)
- Silanes on oxides (Sagiv)
- Alkenes and alkynes on silicon hydride (Sudholter)
Self-assembly of thiols on gold films

\[ X = \text{-CH}_3, \text{-OH, -COOH, -SO}_3^-, \text{-PO}_4\text{H}_2, \text{N}^+\text{(CH}_3)_3, \text{-OCH}_2\text{CH}_2\text{OH}, \ldots \]

Gold is usually deposited by vacuum evaporation techniques. Electroless gold is also of interest for complex geometries.
XRD data on gold: information on crystallographic planes

X-ray diffraction patterns of films of electroless gold and evaporated gold supported on a variety of substrates.

Hou, Stroeve et al., Langmuir 1998
IR data on alkane thiols on gold: orientation of molecules

Grazing-angle infrared spectra of SAMs formed from CH$_3$(CH$_2$)$_{15}$SH on
(a) evaporated gold,
(b) electroless gold on glass microscope slides, and
(c) electroless gold on high-index glass.

Hou, Stroeve et al., Langmuir 1998
Thiol oriented with tilt angle alpha

Aliphatic chain within a SAM formed from an alkanethiol on a surface of gold. Directions of transition dipole moments corresponding to C–H stretching modes are shown. The projections of the transition dipole moments along the surface normal (z) are determined by the tilt angle (\(\alpha\)) and twist angle (\(\beta\)) of the chain. In this diagram, \(\alpha = 30^\circ\) and \(\beta = 0^\circ\).
Cyclic voltammetry on gold and SAMs on gold in 0.1 M H$_2$SO$_4$:  
(a) evaporated gold;  
(b) electroless gold on glass microscope slides;  
(c) electroless gold on high index glass slides;  
SAMs on gold

Alkanethiols on single crystals of gold. Open circles represent gold atoms, and shaded circles represent alkyl chains.

(a) Au(111). The smaller rhombus shows the Au(111) lattice. The larger rhombus shows a unit mesh with \( a = b = 4.97 \text{ Å} \) and \( \alpha = 120 \) (angle between \( a \) and \( b \)).

(b) Au(110). Also shown is a unit mesh with \( a = b = 4.99 \text{ Å} \) and \( \alpha = 109.5 \).

(c) Au(100). Also shown is an oblique mesh with \( a = b = 5.97 \text{ Å} \) and \( \alpha = 95 \).

Self-assembled monolayers (SAMs) on gold

- Molecules are close-packed (if $C_{10}$ or greater)
- Crystallographic surface of gold determines packing
- Large choice of functional groups
- Template for assembly of macromolecules
Self-assembly of molecular structures

- Self-assembled monolayers (SAMs)
- Self-assembly of macromolecular structures on surfaces
- Layer-by-layer deposition of polyions
- Stamping
- Self-assembly of diblock polymers
- Self-assembly of macromolecules
Example: the cell membrane - a macromolecular assembly
Supported lipid bilayers by vesicle fusion

H.M. McConnell, S. Boxer, E. Sackman
Lipid bilayer/peptide on SAM substrate ➔ biosensor

Requirements (to mimic the real cell membrane):
• Stable planar bilayer
• Fluid bilayer (lateral mobility)
• Aqueous environments on both sides of bilayers
• Preserve biological activity for molecules inserted
• Sensing or screening proteins/peptides/ligands

Zwitterionic Lipid POPC

Negatively Charged Lipid SOPS

Red blood cell membrane

Au

SiO₂

Peptide

PDDA

Mercaptoalkanoic acid

Zwitterionic Lipid POPC

Negatively Charged Lipid SOPS

Red blood cell membrane
Experimental set-up: SPR with CV

Detector

Laser

θ

WE (Au)

PC 1

PC 2

Potentiostat

RE

CE (Pt)

Lock-in Amplifier

Current density, i/mAcm$^{-2}$

Potential, E/V(Ag/AgCl)

Reflectivity R

Reflected light intensity, I

$\theta_{obs}$

$\Delta R$

$\theta$

$\Delta R$

$R_1$

$R_2$

$R_3$

Time t
SPR: layer by layer deposition

SPR Curves of Layer by Layer Deposition

Reflectivity vs. Angle (degree)

- MUA on Gold
- PDDA
- SOPS Bilayer

Layer Deposition Schematic:
- Au
- SiO2
- ~4 nm
- 1 nm
- 1-2 nm
Lateral mobility of lipid bilayers

Pure SOPS and SOPS/POPC Mixtures on PDDA

Diffusion Coefficient: $D (\text{cm}^2/\text{s}) = 0.224 \omega^2 / t_{1/2}$

$\omega$ (cm): radius of bleached spot; $t_{1/2}$ (s): half time of recovery

- 100% SOPS: $D \sim 1 \times 10^{-9} \text{ cm}^2/\text{s}$
- 75% SOPS + 25% POPC: $D \sim 2 \times 10^{-9} \text{ cm}^2/\text{s}$
- Natural membranes: $D \sim 10^{-8} \text{ cm}^2/\text{s}$; Immobile membranes: $D \sim 10^{-11} \text{ cm}^2/\text{s}$

Fluorescence Recovery After Photobleaching (FRAP)
Cyclic voltammetry on lipid bilayers

Lipid bilayer/Protegrin on SAM substrate → biosensor

Requirements (to mimic the real cell membrane):
• Stable planar bilayer
• Fluid bilayer (lateral mobility)
• Aqueous environments on both sides of bilayers
• Preserve biological activity for molecules inserted
• Detecting or screening proteins/peptides/ligands

Zwitterionic Lipid POPC

Negatively Charged Lipid SOPS

Mercaptopropionic acid (MPA)

Red blood cell membrane

Au
Uptake of protegrin-1 by lipid bilayer

Use of SPR to monitor peptide uptake

Reflectivity

Time (Minutes)

Inject Protegrin-1

Rinse
Cyclic voltammetry on lipid bilayers: Protegrin

- Protegrin/
- (SOPS+Cholesterol)/PDDA/MPA/Au
- (SOPS+Cholesterol)/PDDA/MPA/Au

Potential (V)

Current density (μA/cm²)

MPA/Au
AFM studies on layer by layer deposition

- Surface roughness decreases with each layer deposited on gold surface.
- Surface roughness increases with addition of peptide.
AFM of supported lipid bilayers

Lipid bilayer **before** uptake of protegrin-1
AFM of supported lipid bilayers

AFM of supported lipid bilayer after uptake of protegrin-1
Supported lipid bilayers as micro-array biosensors

- Micron sized electrodes connected to each gold pad
- Glass substrate
- PDMS polymer
Supported lipid bilayer as biosensor for avidin

Detector for protein avidin. Also shown is use of PEG-lipid at about 10 mole %, to prevent disrupting species from reaching the bilayer.
Self-assembly of molecular structures

- Self-assembled monolayers (SAMs)
- Self-assembly of macromolecular structures on surfaces
- Layer-by-layer deposition of polyions
- Stamping
- Self-assembly of diblock polymers
- Self-assembly of macromolecules
Layer-by-layer deposition of polyions

\[\begin{align*}
- & = \text{Polystyrene sulfonate, (PSS)} \\
\{\text{benzene ring}\}_n & \quad \text{Polydiallyldimethylammonium chloride, (PDDA)}
\end{align*}\]
Layer-by-layer deposition of polyions

Applications

- Lifting supported bilayers
- Biosensors
- Permselective membranes
- Catalytic films
- Coatings
Lifting the bilayer

Anionic Lipid
Zwitterionic Lipid
Lipid Bilayer
PDDA Layer
PSS Layer
PDDA Layer
Alkylthiol
Self-Assembled
Monolayer
Au
S\textsubscript{i}O\textsubscript{2}

Protegrin-1

C. Ma, Stroeve et al., Coll. & Surf. B, 2003
Layer-by-layer deposition on SWCNT

Arthyukhin et al., Langmuir, 2004

Polystyrenesulfonate

PDDA
Carbon nanotube sensor
Arthuykhin, Stroeve et al., 2004

pore forming protein
(α-hemolysin)
lipid bilayer
polymer
carbon nanotube
gold electrode
α-Hemolysin

Side view

Top view

N
Cap
C

Stem

Rim

T129

52 Å
70 Å
100 Å

26 Å
100 Å
Self-assembly of molecular structures

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- Stamping
- Self-assembly of diblock polymers
- Self-assembly of macromolecules
Stamping (microcontact printing)

Patterning of supported lipid bilayers

**Use of stamping or microcontact printing.** Srinivasan, Stroeve et al., Langmuir 2001
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Self-assembly of diblock polymers

TEM micrographs of polystyrene-polybutadiene diblock copolymer film masks (a,c) and lithographically patterned silicon nitride (b,d).

(C. Harrison, Science)
Nanowire-array formation. a) An asymmetric diblock copolymer is annealed above the glass transition temperature of the copolymer between two electrodes under an applied electric field. b) After removal of the minor component, a nanoporous film is formed. c) Nanowires formed by electrodeposition in 20 nm pores.

(from M.T. Tuominen, Science)
Self-assembly lithography (IBM)

Self-assembly patterning occurs when a diblock copolymer is heated, thereby separating the two polymers in the material into defined areas before the PMMA is etched away. The template of cylindrical holes is transferred into the silicon dioxide before the holes are filled with nanocrystalline silicon used to store data (20 nm size).
FLASH MEMORY: A layer of self-assembled silicon nanocrystals is inserted into an otherwise standard device as part of a novel IBM manufacturing process.

Image: SAMUEL VELASCO
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Self-assembly of a double rosette superstructure 19 through the interaction, mediated by hydrogen bonds, of barbiturate 17 with melamine derivative 18.

R.N. Reinhoudt, U of Twente, Angew. Chemie, 1996
Self-assembly of molecular structures

CLOSING COMMENTS:

• Molecular assemblies can be built on a variety of substrates.
• Combination of bottom up and top down techniques can lead to patterned features.
• Research on self-assembling structures on surfaces has stimulated the development of new products.