Lecture 9:

Surface Modification of Biomaterials

Supporting notes

Purpose:

Alter surface properties to enhance performance in biological environment while retaining bulk properties of device

The modified zone at the surface of the device should be as thin as possible. Ideally < 1 nm
Specific objectives:

1. Clean a surface
2. Reduce/eliminate protein adsorption
3. Reduce/eliminate cell adhesion
4. Reduce bacterial adhesion
5. Reduce thrombogenicity
6. Promote cell attachment/adhesion
7. Alter transport properties
8. Increase lubricity
9. Increase hardness
10. Enhance corrosion/degradation resistance
Preparation of non-fouling surfaces
to prevent non-specific protein/cell or bacterial adhesion
to reduce thrombogenicity

Surfaces should be hydrophilic or very hydrophobic.
Example of “gold standard”

Surface modification with PEO derivative.

PEO-PPO-PEO, Pluronic

Physical adsorption

Short-time use
Ex. Drug delivery

Chemical immobilization

Long-time use
Other strategies for hydrophilic surfaces 1

**Albumin coating surface**

Serum albumin:
High water solubility and stability
No affinity to proteins and platelets

**Phospholipid-mimicking surface**

Hydrophilic phosphocholine head
Hydrophobic acyl chain
Other strategies for hydrophilic surfaces 2

**Heparinized surface**

Heparin:
Immobilized covalently and ionically
Inhibitor for thrombin or platelet adhesion

**Endothelial cell attachment**

Natural blood vessel lining:
Fibrinolytic activity (hydrolysis of fibrin)

**Plasma treatment**

Water soluble polymer

Will be discussed soon
NR6 WT fibroblast adhesion triggered by RGD recognition

Photos removed for copyright reasons.

NR6 WT:
mice fibroblast bearing human integrin

Taniguchi, *Polym Int.* submitted
Biomolecule immobilization method for specific surfaces

<table>
<thead>
<tr>
<th>Physical adsorption</th>
<th>van der Waals</th>
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<tbody>
<tr>
<td></td>
<td>Electrostatic</td>
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<tr>
<td></td>
<td>Affinity</td>
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<td></td>
<td>Adsorbed and cross-linked</td>
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<td></td>
<td>Barrier system</td>
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<td>Physical “entrapment”</td>
<td>Hydrogel</td>
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<td>Dispersed system</td>
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<tr>
<td>Covalent attachment</td>
<td>Soluble polymer conjugate</td>
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<tr>
<td></td>
<td>Solid surface</td>
</tr>
<tr>
<td></td>
<td>Hydrogel</td>
</tr>
</tbody>
</table>

Biomolecules: proteins/peptides, saccharides, lipids, drugs, ligands, nucleic acids/nucleotides, (cells,) etc.
Chemical modification of materials

ref. Ratner, *Biomaterials Science*, p. 229

For covalent binding to an inert solid polymer surface, the surface **must first be chemically modified** to provide reactive groups for the subsequent immobilization step.

- $\text{-OH}$
- $\text{-SH}$
- $\text{-NH}_2$
- $\text{-CH}=\text{CH}_2$
- $\text{-COOH}$

etc.
Protein/peptide immobilization strategies 1

Major reacting groups: -NH₂

Activation of -OH

All the procedures must be carried out under anhydrous condition.
Protein/peptide immobilization strategies 2

Major reacting groups: -NH$_2$

**Activation of -NH$_2$**

[Diagram showing the activation of an amino group (NH$_2$) through chemical reactions.]

**Activation of -COOH**

[Diagram showing the activation of a carboxylic acid (COOH) through chemical reactions.]

Be careful!
Protein/peptide immobilization strategies 3

Major reacting groups: -COOH

**Activation of -NH$_2$**

\[
\text{R—COOH} \xrightarrow{\text{carbodiimide}} \text{R$_1$—N=\text{C}—\text{N}—R$_2$} \xrightarrow{\text{H—N$\text{C}$—R} + O=C} \text{R—C—O—C} \xrightarrow{\text{HN—R$_1$} + O=C} \text{HN—R$_2$}
\]
Protein/peptide immobilization strategies 4

Chemoselective ligation

Reactions take place between selected pairs of functional groups.
Other chemical surface modifications

Preparation of hydrophobic and inert surfaces

**Fluorination**

[Diagram showing the reaction of OH groups with a fluorinated compound (Cl(CF₂)₃) to produce a fluorinated surface with CF₂ and CF₃ groups.]

**Silanization**

[Diagram showing the reaction of OH groups with a silane (OSi(O)OSi) to produce a silanized surface with OH and Si groups.]

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Summary:

- Clean a surface
- Reduce/eliminate protein/cell/bacteria adsorption, reduce thrombogenicity

Non-fouling and bioinert surfaces

- Promote biological response

Immobilization of biomolecules

Short time - Physical adsorption
Long time - Covalent bonding