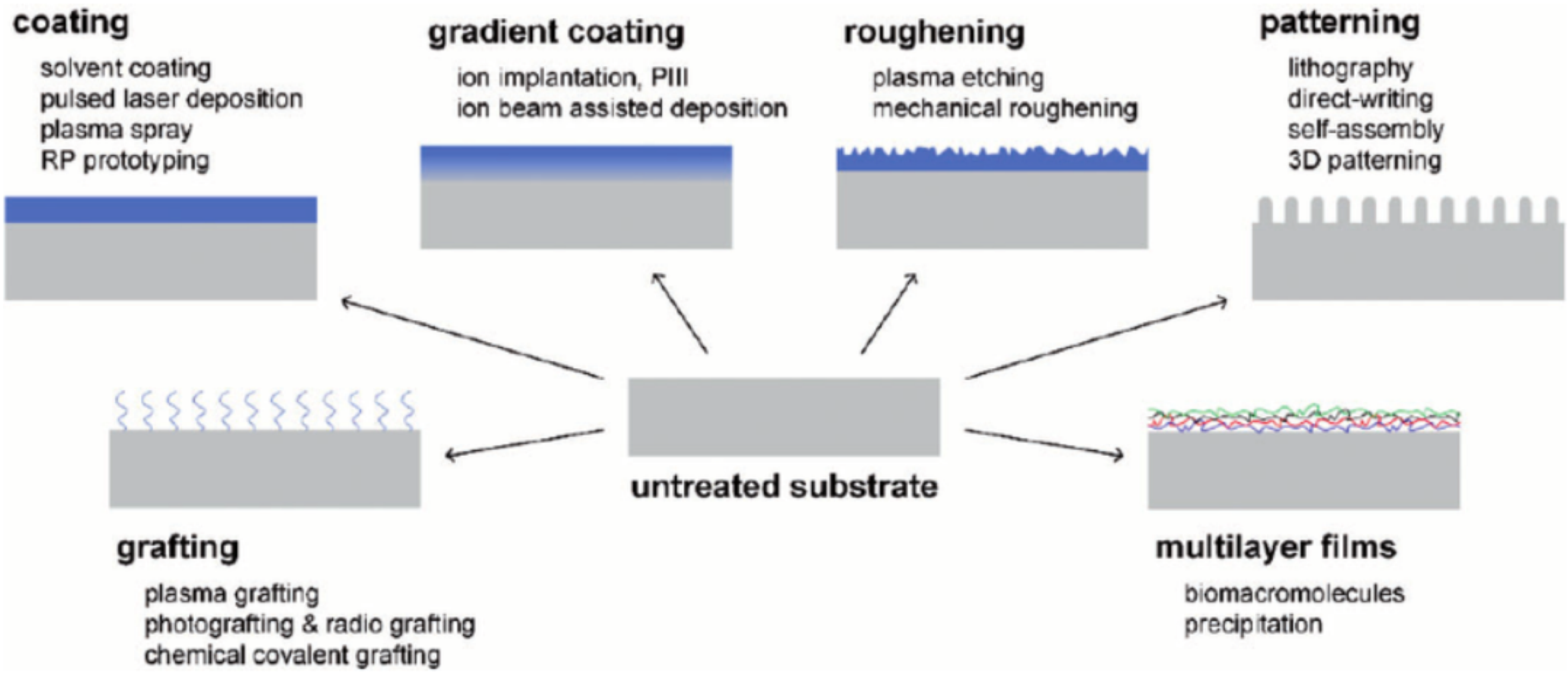
# Surface Modification of Biomaterials



# Surface Modification

**Purpose:** alter surface properties to enhance performance in biological environment while retaining bulk properties of device

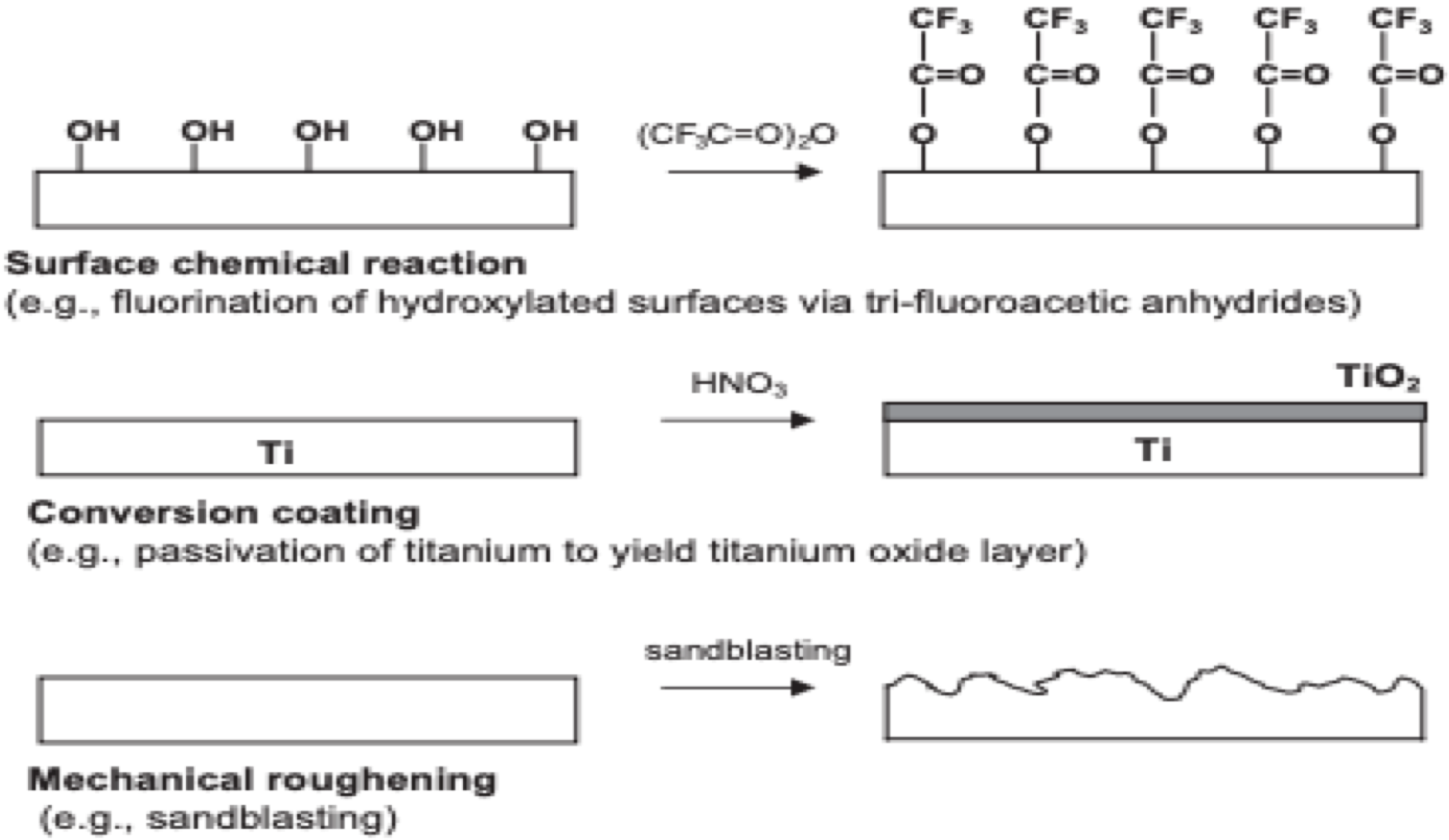
**Modifying the surface doesn’t make a change in bulk properties**

The modified zone at the surface of the device should be **as thin as possible**.

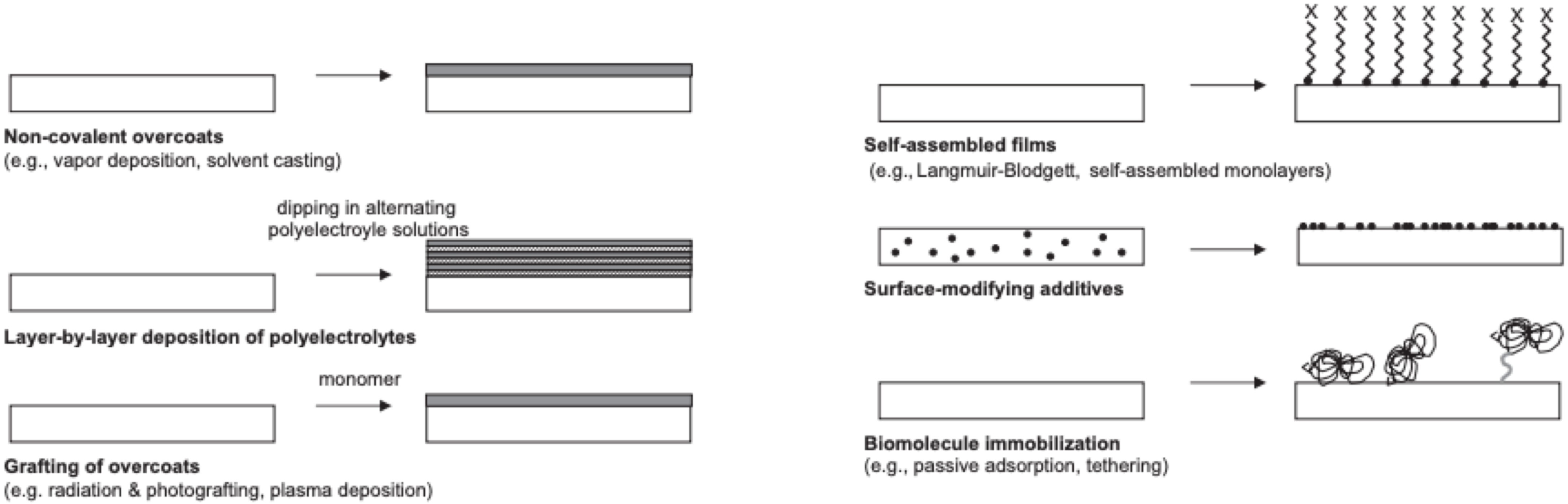
# How can we modify the surfaces for a better cell response?

| Surface Modification | | | | | |
|---|---|---|---|---|---|
| **Physicochemical Modification** | | | **Surface Coatings** | | |
| Chemical Reaction | Etching | Mechanical roughening/ polising and patterning | Grafting | Covalent and non-covalent bondings | Thin film deposition |

# Common **physicochemical** surface modifications of biomaterials



# Common overcoating technologies for surface modification



# Expected Characteristics of Surface Modifications

While the specific requirements of the surface modification approach vary with application, several characteristics are generally desirable.

- **Thin surface modification layer** (too thick can change the mechanical and functional properties of the material. Thick coatings are also more subject to delamination and cracking. Ideally: 10-15 A˚ , Practically: 10-100 nm)
- **Stability of the modified surface**

# Common Surface Analysis Techniques...

| | Principle | Operation | Spatial resolution | Info. depth | Sensitivity | Texture | Chemical composition info. | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Elements | Compounds | Isotopes | Additional |
| Contact angle | Liquid wetting of surfaces | Air Liquid | NA | 3–20 Å | NA | Indirect | | | | Surface energy |
| AFM | Records interatomic forces between tip and sample | Air Aqueous | Atomic | NA | Single atom | Yes | No | No | No | |
| SEM | Secondary electron emission caused by electron bombardment is imaged | Vacuum | 40 Å | 5–10 Å | High | Yes | No | No | No | Crystallinity |
| EDXA | X-ray emission caused by electron bombardment | Vacuum | 40 Å | 1 μm | $10^{-7}$ g/cm$^2$ | No | $Z > 5$ | No | No | |
| AES | Auger electron emission caused by electron bombardment | Vacuum | 100 Å | 15–50 Å | $10^{-10}$ g/cm$^2$ 0.1 atom % | No | $Z > 3$ | Chemical shift | No | |
| XPS | X-rays cause emission of photoelectrons with characteristic energies | Vacuum | 10 μm | 10–150 Å | $10^{-10}$ g/cm$^2$ 0.1 atom % | No | $Z > 3$ | Chemical shift (excellent) | No | |
| SIMS | Ion bombardment causes secondary ion emission | Vacuum | 3–10 μm | 10 Å | $10^{-13}$ g/cm$^2$ | No | All | Yes | Yes | |
| FTIR | Molecular vibrations resulting from adsorption of IR radiation | Air Aqueous (ATR) | 10 μm | $<1$ μm | 1 mole % | No | Indirect | Vibration frequency | No | Monolayer orientation |

# PHYSICOCHEMICAL SURFACE MODIFICATIONS

Involve alterations to the atoms, compounds, or molecules on the material surface

# Topographical Modifications

The size and shape of topographical features on a surface influence cellular and host responses to the material. For example, surface macro-,micro- and nano-texture alters cell adhesion, spreading, and alignment

Increasing surface roughness/porosity

promotes cell attachment (↑ surface area for binding)

**But is it always good???**

# Roughness or topography?

Methods for generating surface texture can be grouped into approaches for engineering either roughness or topography


Surface roughness : a random or complex pattern of features of varying amplitude and spacing, typically on a scale smaller than a cell (10-20 mm)

Surface topography: patterns of well-defined, controlled features on the surface

(traditional modifications: via sandblasting, plasma spraying, and mechanical polishing as well as ion beam, electric arc, photolithography combined with reactive plasma and ion etching)

# Chemical Modifications

- Chemical reactions, including UV/laser irradiation and etching reactions to clean, alter, or crosslink surface groups, have been developed to modify biomaterial surfaces.
- *Non-specific reactions* yield a distribution of chemically distinct groups at the surface, and the resulting surface is complex and difficult to characterize due to the presence of different chemical species. Nevertheless, non-specific chemical reactions are widely used in biomaterials processing.
- In contrast, *specific chemical reactions* target particular chemical moieties on the surface to convert them into another functional group with few side (unwanted) reactions. Acetylation, fluorination of hydroxylated surfaces via tri-fluoroacetic anhydrides, silanization of hydroxylated surfaces, and incorporation of glycidyl groups into polysiloxanes are examples of specific chemical reactions.

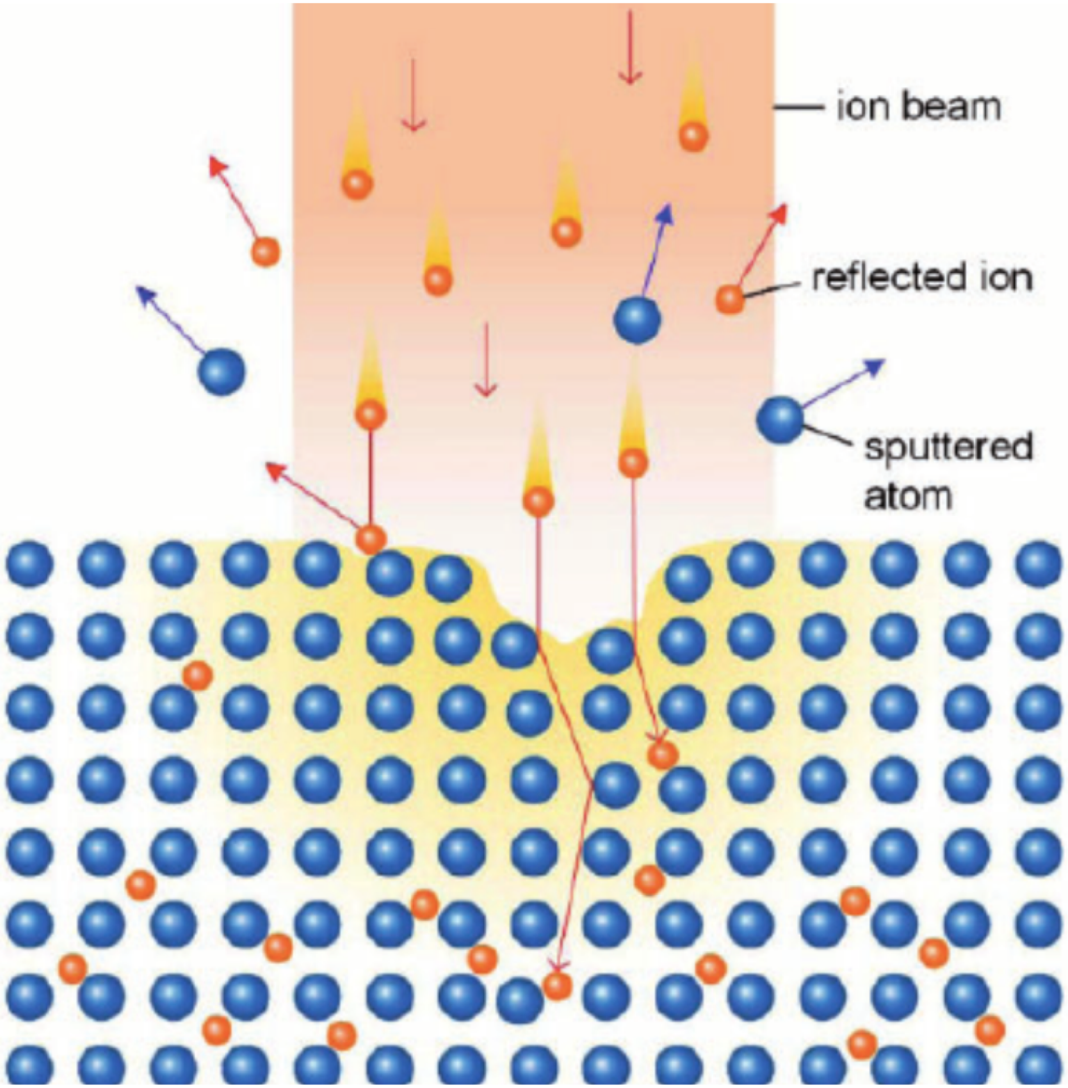
# Chemical Modifications

- Reaction of metal surfaces to produce an oxide-rich layer that conveys corrosion resistance, passivation, and improved wear and adhesive properties are common surface modifications in metallic biomaterials. For example, nitric acid treatment of titanium and titanium alloys to generate titanium oxide layers is regularly performed on titanium-based medical devices.
- Implantation of ions into surfaces via a beam of accelerated ions has been applied to modify the surface properties of mostly metals and ceramics.
- For example, ion beam implantation of
    - **nitrogen** into *titanium* and *boron* improves <u>wear resistance</u>
    - **carbon** into *stainless steel* Improves <u>fatigue life</u>
- Ion beam implantation of *silicone* and *silver* can also enhance the **blood compatibility** and **infection resistance** of silicone rubber catheters.

# Ion beam implantation...example

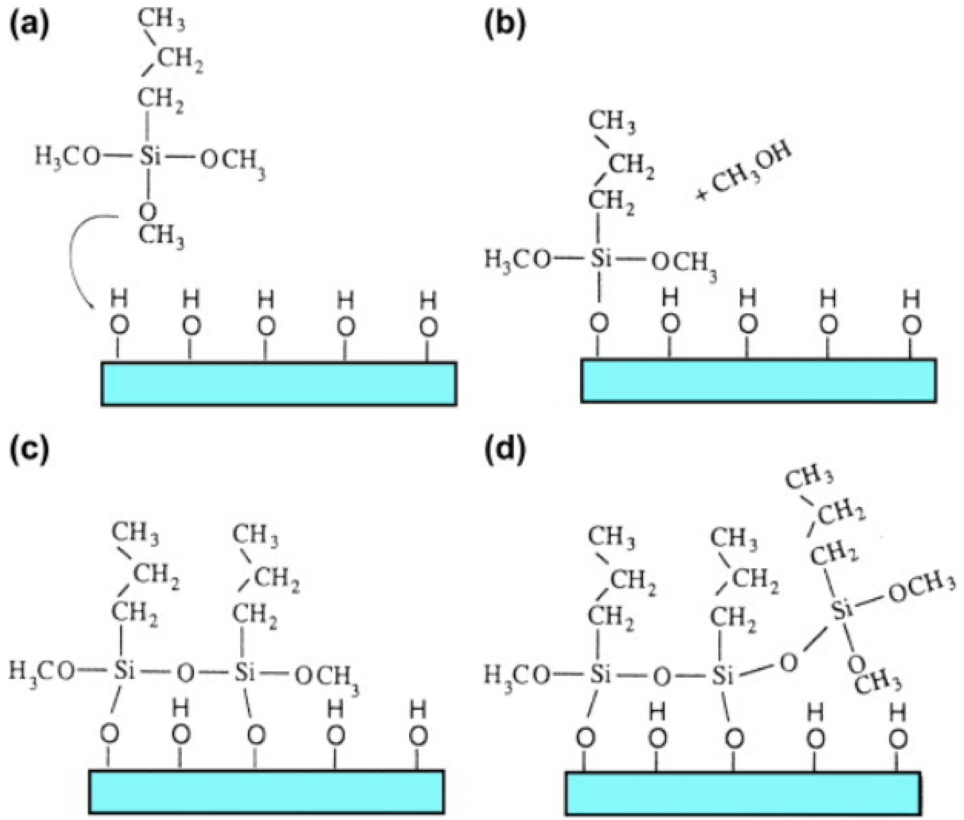
- High energy ion beam injects ions into the surface zone of a material.

- Sometimes called "electropolishing"
  - Ions prevent crack propagation
  - Alloying increases resistance to corrosion



# Silanization...example

- Silanization is a low-cost and effective covalent coating method to modify material surface that is rich in hydroxyl groups, such as titanium, hydroxyapatite, and many other metal oxide surfaces.




The chemistry of a typical silane surface modification reaction: (a) a hydroxylated surface is immersed in a solution containing n-propyl trimethoxysilane (nPTMS); (b) one of the methoxy groups of the nPTMS couples with a hydroxyl group releasing methanol; (c) two of the methoxy groups on another molecule of the nPTMS have reacted, one with a hydroxyl group and the other with a methoxy group from the first nPTMS molecule; (d) a third nPTMS molecule has reacted only with a methoxy group. This molecule is tied into the silane film network, but is not directly bound to the surface.

# OVERCOATING TECHNOLOGIES

Coating strategies rely on the deposition of a surface layer consisting of a different composition from the underlying base material. These surface modification approaches include non-covalent and covalent coatings

# Non-covalent coatings

**Major advantages of non-covalent coatings**

- simple application and
- ability to coat a variety of different base materials.

**Examples of common non-covalent coating methods**:

- solvent-casting,
- vapor deposition of metals, parylene, and carbons
- Langmuir-Blodgett deposition method: one or more highly ordered layers of surfactant molecules (e.g. phospholipids, amphiphiles) are placed at the surface of the base material via assembly at the air-water interface and compression of the surfactant molecules. Langmuir-Blodgett films exhibit high order and uniformity and provide flexibility in incorporating a wide range of chemistries.
- deposition of multilayer polyelectrolytes (e.g. poly(styrenesulfonate)/poly(allylamine), hyaluronic acid/ chitosan).

https://www.youtube.com/watch?v=j8yqyRr2VQg

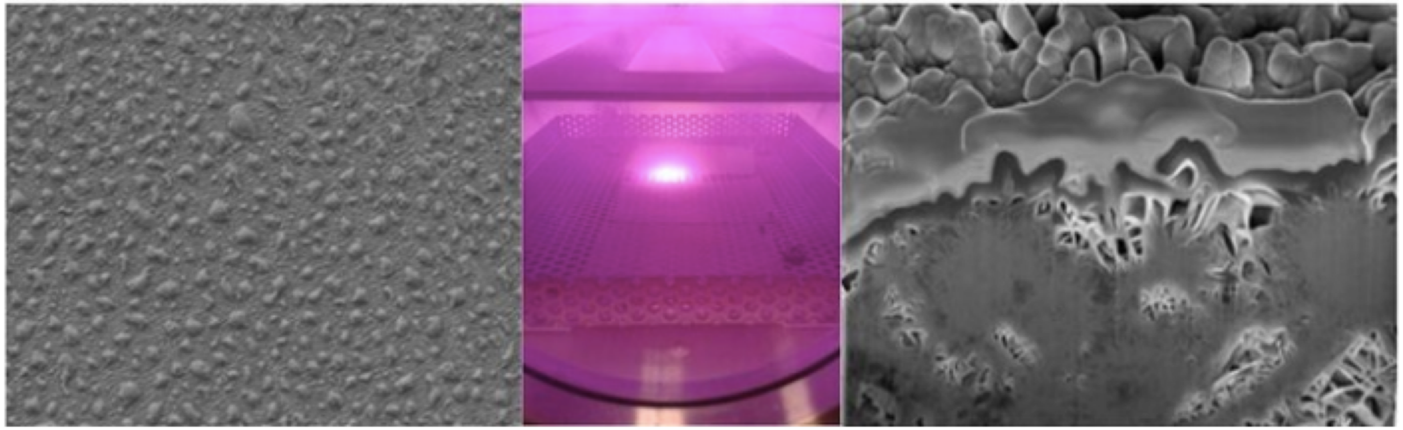
https://www.youtube.com/watch?v=NQ6H3ys6-_o&t=38s

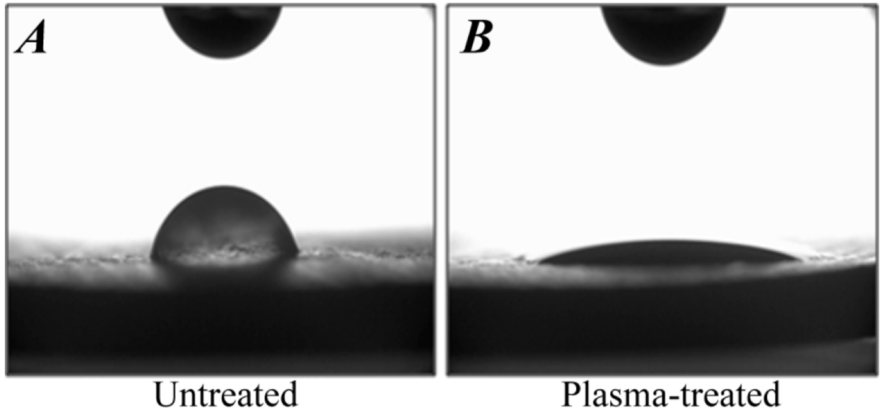
# Covalent coatings

- Covalent coating methodologies rely on direct tethering of over coats onto the base material to improve film stability and adherence.
- Radiation grafting, both with ionizing radiation and high-energy electron beams, and photografting have been extensively pursued to modify polymer substrates in order to introduce chemically reactable groups into inert hydrophobic polymers and polymerize overcoats onto the base support.
- Plasma deposition (also referred to as glow discharge deposition) via radio frequency or microwave has also been extensively applied to biomaterial surface modification.

# Plasma treatment…example

- Introduce reactive groups to a surface
- Oxygen plasma increases hydrophilicity of the surface
- Plasma spray deposition uses plasma to heat up molecules and deposit onto a surface





# Covalent coatings

- In contrast to these relatively low-energy/low-temperature plasmas, high-energy/high-temperature plasmas have also been used to apply inorganic surface modifications onto inorganic substrates. For examples; flame spraying hydroxyapatite onto titanium and cobalt chrome orthopedic improve osseointegration.

- Coatings consisting of self-assembled monolayers (SAMs) have gained significant attention as robust surface modification. These films spontaneously assemble; form highly ordered, well-defined surfaces with excellent chemical stability; and provide a wide range of available surface functionalities. The basic structure of molecules that form SAMs is an anchoring “head” group, organic chain backbone, and functional “tail” group.

# BIOLOGICAL MODIFICATION OF SURFACES

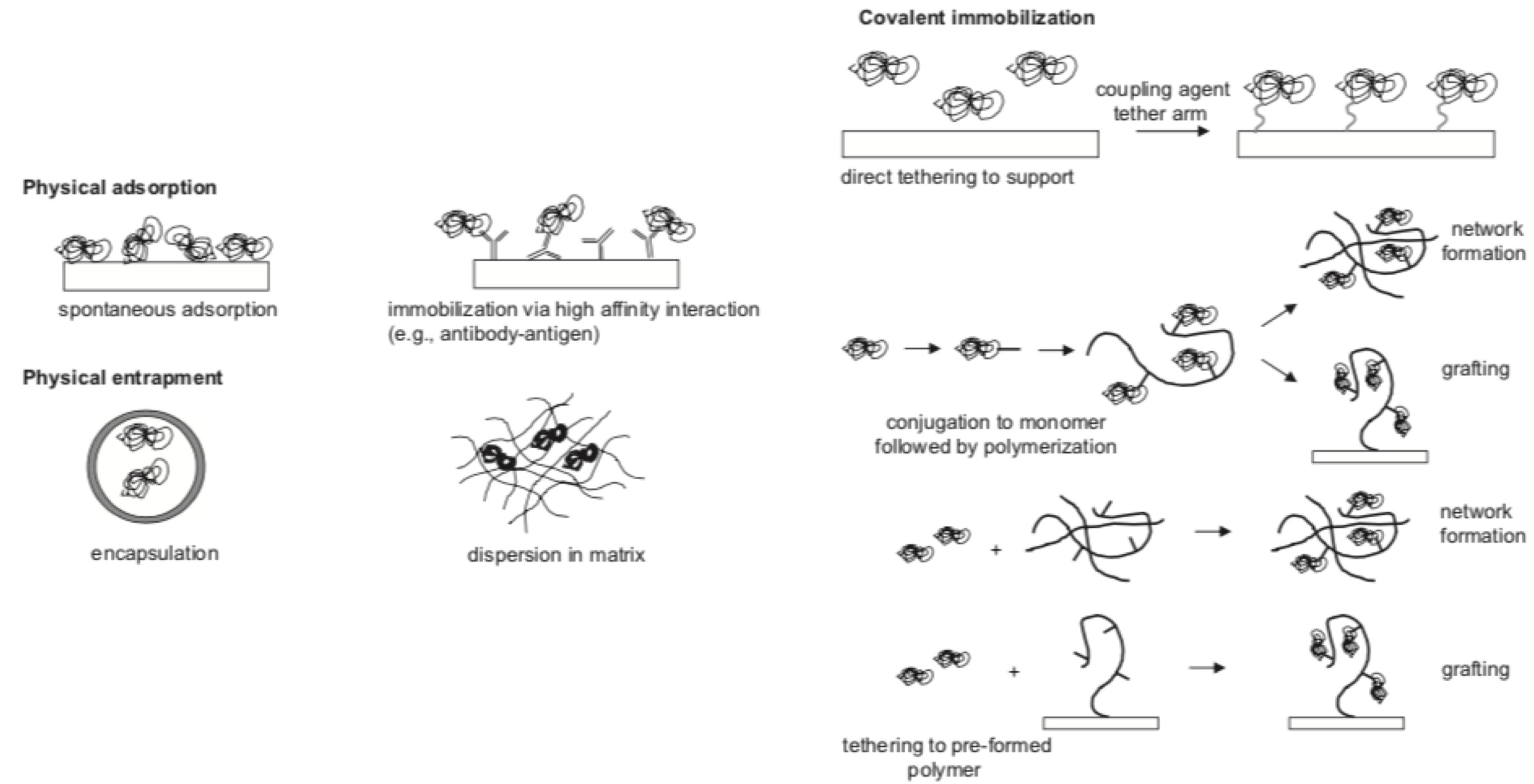
Biomolecules (e.g. cell receptor ligands, enzymes, antibodies, pharmacological agents, lipids, nucleic acids) have been immobilized onto and within biomaterial supports for numerous therapeutic, diagnostic, and bioprocess applications.

# Biomolecule immobilization method for specific surfaces

| | |
|---|---|
| Physical adsorption | van der Waals<br>Electrostatic<br>Affinity<br>Adsorbed and cross-linked |
| Physical “entrapment” | Barrier system<br>Hydrogel<br>Dispersed system |
| Covalent attachment | Soluble polymer conjugate<br>Solid surface<br>Hydrogel |

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

# Methods for immobilizing biomolecules onto and within biomaterials...



# Biomedical and Biotechnological Applications of Immobilized Biomolecules

| Biomolecule | Applications |
|---|---|
| Heparin | Blood-compatible surfaces; growth factor immobilization |
| Fibronectin, collagen, RGD peptides | Cell adhesion and function in biosensors; arrays, devices, and tissue-engineered constructs |
| Antibodies | Biosensors; bioseparations; anti-cancer treatments |
| DNA plasmids, antisense oligonucleotides, siRNA | Gene therapy for a multitude of diseases; DNA probes |
| Growth factor proteins and peptides | Anti-cancer treatments; treatments for auto-immune and inflammatory conditions; enhanced wound repair |
| Enzymes | Biosensors; bioreactors; anti-cancer treatments; antithrombotic surfaces |
| Drugs and antibiotics | Antithrombotic agents; anti-cancer treatments; anti-hyperplasia treatments; anti-infection/ inflammation treatments |
| Polysaccharides | Non-fouling supports for biosensors and bioseparations |

# Methods for immobilizing biomolecule..

- 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.

| | |
|---|---|
| -OH | -SH |
| $-NH_2$ | $-CH=CH_2$ |
| -COOH | etc. |

# Physical and Chemical Surface Modification Methods

| | Polymer | Metal | Ceramic | Glass |
|---|---|---|---|---|
| **Noncovalent Coatings** | | | | |
| Solvent coating | ✓ | ✓ | ✓ | ✓ |
| Langmuir–Blodgett film deposition | ✓ | ✓ | ✓ | ✓ |
| Surface active additives | ✓ | ✓ | ✓ | ✓ |
| Vapor deposition of carbons and metals* | ✓ | ✓ | ✓ | ✓ |
| Vapor deposition of Parylene (p-xylylene) | ✓ | ✓ | ✓ | ✓ |
| **Covalently Attached Coatings** | | | | |
| Radiation grafting (electron accelerator and gamma) | ✓ | – | – | – |
| Photografting (UV and visible sources) | ✓ | – | – | ✓ |
| Plasma (gas discharge) (RF, microwave, acoustic) | ✓ | ✓ | ✓ | ✓ |
| Gas phase deposition: | | | | |
| • Ion beam sputtering | ✓ | ✓ | ✓ | ✓ |
| • Chemical vapor deposition (CVD) | – | ✓ | ✓ | ✓ |
| • Flame spray deposition | – | ✓ | ✓ | ✓ |
| Chemical grafting (e.g., ozonation + grafting) | ✓ | ✓ | ✓ | ✓ |
| Silanization | ✓ | ✓ | ✓ | ✓ |
| Biological modification (biomolecule immobilization) | ✓ | ✓ | ✓ | ✓ |
| **Modifications of the Original Surface** | | | | |
| Ion beam etching (e.g., argon, xenon) | ✓ | ✓ | ✓ | ✓ |
| Ion beam implantation (e.g., nitrogen) | – | ✓ | ✓ | ✓ |
| Plasma etching (e.g., nitrogen, argon, oxygen, water vapor) | ✓ | ✓ | ✓ | ✓ |
| Corona discharge (in air) | ✓ | ✓ | ✓ | ✓ |
| Ion exchange | ✓** | ✓ | ✓ | ✓ |
| UV irradiation | ✓ | ✓ | ✓ | ✓ |
| **Chemical Reaction** | | | | |
| • Nonspecific oxidation (e.g., ozone) | ✓ | ✓ | ✓ | ✓ |
| • Functional group modifications (oxidation, reduction) | ✓ | – | – | – |
| • Addition reactions (e.g., acetylation, chlorination) | ✓ | – | – | – |
| Conversion coatings (phosphating, anodization) | – | ✓ | – | – |
| Mechanical roughening and polishing | ✓ | ✓ | ✓ | ✓ |