MATLS 701 Seminar
Electrochemical Deposition of Organic-Inorganic Coatings with Advanced Functionality for Biomedical Applications

Imran Deen
Supervisor: Dr. Igor Zhitomirsky

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Outline

• Introduction
  ▫ What is an orthopaedic implant?
  ▫ Project Background/Motivation

• Literature Review
  ▫ Materials Used
  ▫ Current Technology/Drawbacks

• Objective

• Approach & Methodology
  ▫ Advantages
  ▫ Experimental Techniques

• Results & Discussion

• Summary
What is an Orthopaedic Implant?

• Medical devices used to replace or fix parts of the skeletal system
  ▫ Used mainly in the case of osteoarthritis (degenerative joint disease), but can also be used to mend broken bones

• Orthopaedic implants must be able to:
  ▫ Match the composition and structure of bone
  ▫ Be well-tolerated by the body
  ▫ Withstand cyclic loading in everyday use

• Biofunctionality
  ▫ Ability of the device to perform desired function
  ▫ High mechanical properties (yield strength, ductility, fatigue strength, etc.)
  ▫ Not as severe as those found in other engineering applications

• Biocompatibility
  ▫ Acceptance of materials with the body
  ▫ Promotes growth/adhesion of environment
Project Background

- Many different materials are used for orthopaedic implants
- Implant-tissue response varies depending on material:
  - Toxic material – surrounding tissue dies
  - Bioinert material – fibrous tissue forms
  - Bioactive material – promotes bone growth/tissue adhesion
    Bioreabsorbable material – the surrounding tissue replaces it
- Films deposited on materials show great promise in terms of biocompatibility and biofunctionality
  - Can meet all the criteria necessary of implantation
  - Very versatile
- New and advanced bioactive materials can be used to create the next generation of biomedical implants!
Current Technology Used

Materials used in medical implants

- Metals
  - Cobalt-chromium based alloys
  - Titanium alloys
  - Iron-chromium alloys (316L SS)

- Glass/Ceramics
  - Bioglass
  - Alumina
  - Zirconia
  - Hydroxyapatite

- Polymers
  - Chitosan
  - Hyaluronic acid
  - Alginic acid
Bio-ceramics

Hydroxyapatite (HA)

- Bioactive calcium phosphate ceramic
  - $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$
- Osteoconductive - promotes bone growth along surface
- Well-suited for bone implants
  - Similar composition
  - Biocompatibility
  - Osteoconductivity
- Used as bio-ceramic coatings and bone fillers

Hydroxyapatite-coated implants
Bio-polymers

Hyaluronic acid (HYH)

- A natural, anodic, polysaccharide found in skin, joints and cornea.
- Supports progenitor cell development
  - Cells proliferate and differentiate into appropriate phenotypes
  - Restore damaged/missing tissue
- Associated with inflammation regulation, control of tissue functions
- Assists in regenerative repair

Sources of Hyaluronic Acid in the body

Structure of Hyaluronic Acid

Vitreous humor
95% Hyaluronic acid
Bio-polymers

**Chitosan (CHIT)**

- A natural, cationic, polysaccharide
  - Derived from the deacetylation chitin
  - Similar in structure to cellulose
  - Soluble in acidic environments, maintains structure in basic/neutral environments
- Does not cause allergic reaction/rejection, breaks down to amino sugars
  - Reabsorbed by body
- Possesses antimicrobial properties
- Excellent film-forming properties, used in tissue scaffolding, biosensors implants, etc.
  - Cationic in nature

Chitosan is derived from the chitin in shrimp and other crustaceans.
New Bio-materials

**Chiral Polymers**

- Poly-L-Ornithine (PLO)
- Poly-L-Lysine (PLL)
- Used as coating agents to promote cell adhesion
  - Surface charge, ligands, microstructure, surface roughness all factors controlling cell adhesion
- PLL provides perm-selectivity in microcapsules
  - Cell microencapsulation and transplantation.
- PLO coated microcapsules are mechanically stronger, provide better perm-selectivity than PLL
New Bio-materials

Halloysite Nanotubes (HNT)

- $\text{Al}_2\text{Si}_2\text{O}_5(\text{OH})_4 \cdot \text{nH}_2\text{O}$,
- Charge difference between $\text{SiO}_2$ and $\text{Al}_2\text{O}_3$
  - facilitates loading with anionic drugs (e.g. salicylate)

Zeta potential vs. pH

Comparison of HNT and CNT

<table>
<thead>
<tr>
<th></th>
<th>HNTs</th>
<th>CNTs</th>
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<tbody>
<tr>
<td>ID/length</td>
<td>15 nm/1000 nm</td>
<td>2 nm/1000 nm</td>
</tr>
<tr>
<td>Compatibility</td>
<td>biocompatible</td>
<td>toxic</td>
</tr>
<tr>
<td>Price</td>
<td>$4$ per kg</td>
<td>$500$ per kg</td>
</tr>
<tr>
<td>Availability</td>
<td>thousand tons</td>
<td>grams</td>
</tr>
</tbody>
</table>

Loading with anionic drugs
Bone Structure

- Porous organic-inorganic composite
  - 56–68% apatites
  - 32–44% organics
- Recent discovery (2007) showed that bone is composed of organic and mineral components with a polysaccharide layer as an interface between the two
- Polysaccharides are most closely bound to minerals
  - Central role in biomineralization
  - Modulate mineral growth and crystallinity

<table>
<thead>
<tr>
<th>Organic phase (collagen)</th>
<th>Interface (polysaccharide)</th>
<th>Inorganic phase (mineral)</th>
</tr>
</thead>
</table>

Collagen fibril composed of collagen molecules and bone crystals (Kobayashi, 2010)
Drug Delivery

- Microencapsulated chitosan microspheres have previously been used for drug delivery
  - Developed using layer-by-layer (LbL) technique
  - Physical, chemical properties can be controlled

- Formation of polyelectrolyte hollow capsules via the LbL assembly (Johnston et al, 2006)

- Formed by consecutive deposition of polymers onto colloidal particles, which is then removed.
- Release rate was adjustable depending on amount of polymer used

SEM pictures of a loaded chitosan microparticle (Ko et al. 2002)
FGM & Multilayer Coatings

- Coating can be modified to suit multiple needs using layers
  - Creation of a gradient in the composition profile
- Multiple layers, each made up of different materials
  - Advanced functions
  - Drug delivery
  - Anti-microbial agents

Schematic illustration of FGM (Wang et al., 1998)

- High degree of biocompatibility/bioactivity or bioreabsorbability
- Transition layer loaded with drugs & antimicrobial agents
- High adhesive property + biocompatibility
How can all these goals be achieved?

First look at current fabrication processes
Current Methods of Fabrication

- Problems related to sintering of ceramic coatings
  - Sintering shrinkage, cracking, diffusion of components, chemical reactions with substrate, substrate degradation at elevated temperatures
  - Microstructure of sintered HA differs from natural HA
- Would result in decomposition of HNT
- Formation of chiral surfaces problematic
- Unable to replicate FGM/multilayer

Problems to be addressed:

- Possibility of incorporation of functional biomaterials
  - Proteins, drugs, antimicrobial agents
- Possibility of fabrication of composites, multilayer and FGM coatings
- Control of microstructure → coating similar to natural material
Electrophoretic Deposition (EPD)

- Charged particles or polymer macromolecules in solvent
- Electrophoresis → charged particles move towards electrode
- Particles coagulate on electrode → form coherent deposit

Electrophoretic Deposition (EPD)

- Low cost
- Room temp
- Simple
- Scaleable
- Complex surfaces
- Fast
- Control properties

Characteristics of EPD

Schematic of EPD cell showing cathodic deposition

Electrogenerated base

\[2\text{H}_2\text{O} + 2\text{e}^- \rightarrow \text{H}_2 + 2\text{OH}^-\]

Electrogenerated acid

\[2\text{H}_2\text{O} \rightarrow \text{O}_2 + 4\text{H}^+ + 4\text{e}^-\]
Goals

- Develop **films with advanced functionality** for biomedical applications
  - EPD of bioactive polymers and halloysite nanotubes for controlled release of drugs and antimicrobial agents
- EPD of **composite, multilayer and FGM coatings**
  - CHIT-HNT/CHIT-HA
  - HYH-HNT/HYH-HA
- EPD of **chiral biopolymers** and composites
- Investigate different factors controlling the coating microstructure, kinetics of deposition and deposition mechanism.
We know what we want, how do we go about getting it?
Approach and Methodology

Materials used in medical implants

- **Metals**
  - 316L SS
- **Ceramics**
  - HNT
  - HA
- **Polymers**
  - CHIT
  - HYH
  - PLL
  - PLO

- Used alone, materials have significant drawbacks
  - Metals susceptible to degradation and rejection
  - Polymers, ceramics lack strength/ductility
- Combine metal base with ceramics and polymers
- Create implant with necessary properties
  - Biocompatibility and biofunctionality
Approach and Methodology

• Develop process for EPD of HNT-polymer composites and chiral polymers
  ▫ No need to sinter end product

• Investigate the effects of concentration, additives and dispersants
  ▫ Influence stability of suspension (no agglomeration)
  ▫ Determine different morphologies

• Investigate the deposition of new bio-polymers/ceramics
  ▫ Mechanics/kinetics of deposition
  ▫ Properties of film (e.g. corrosion in SBF, adhesive tests)

• Drug delivery capabilities
  ▫ Use of HNT for drug delivery using inner tube for loading drug
  ▫ Modify release rate base on concentration of polymer, viscosity of fluid

• Use EPD for multilayer/FGM coatings
Experimental Techniques

- Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM)
  - Analyse morphology, structure, thickness
- Thermogravimetric and Differential Thermal Analysis (TGA/DTA)
  - Analyse composition
- X-Ray Diffraction (XRD)
  - Analyse composition
- Quartz Crystal Microbalance (QCM)
  - Measure deposition yield
- Electrochemical testing in simulated body fluids
  - Measure corrosion protection
### EPD of Polymers

<table>
<thead>
<tr>
<th>Reaction in solution</th>
<th>Reaction at electrode</th>
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<tbody>
<tr>
<td>CHIT–NH₂ + H₃O⁺ → <strong>CHIT–NH₃⁺</strong> + H₂O</td>
<td>CHIT–NH₃⁺ + OH⁻ → <strong>CHIT–NH₂</strong> + H₂O</td>
</tr>
<tr>
<td>HYH-OH + OH⁻ → <strong>HYH-O⁻</strong> + H₂O</td>
<td>HYH-O⁻ + H₃O⁺ → <strong>HYH-OH</strong> + H₂O</td>
</tr>
<tr>
<td>PLO–NH₂ + H₃O⁺ → <strong>PLO–NH₃⁺</strong> + H₂O</td>
<td>PLO–NH₃⁺ + OH⁻ → <strong>PLO-NH₂</strong> + H₂O</td>
</tr>
<tr>
<td>PLL–NH₂ + H₃O⁺ → <strong>PLL–NH₃⁺</strong> + H₂O</td>
<td>PLL–NH₃⁺ + OH⁻ → <strong>PLL-NH₂</strong> + H₂O</td>
</tr>
<tr>
<td>PAA–COOH + OH⁻ → <strong>PAA–COO⁻</strong> + H₂O</td>
<td>PAA–COO⁻+H₃O⁺ → <strong>PAA-COOH</strong> + H₂O</td>
</tr>
</tbody>
</table>

**soluble** | **insoluble**
TEM of Halloysite Nanotubes
Comparison of CHIT-HNT film at (a) 5000X (b) 30000X (c) 5000X (d) 30000X

0.5 g/L CHIT
0.3 g/L HNT

0.5 g/L CHIT
0.6 g/L HNT
0.5 g/L HYH
0.3 g/L HNT

Comparison of HYH-HNT film at (a) 5000X (b) 30000X (c) 5000X (d) 30000X
Comparison of CHIT-HNT-HA film at (a) 5000X (b) 3000X (c) 5000X (d) 30000X
Deposition/Analysis of CHIT-HNT Films

Deposition of 
(a) 0.1 g/L CHIT  
(b) 0.1 g/L CHIT + 0.05 g/L HNT  
(c) 0.1 g/L CHIT + 0.10 g/L HNT solution measured using QCM

XRD analysis of 
(a) as-received HNT  
(b) as-received HA  
(c) pure CHIT film  
(d) CHIT-HNT film  
(e) CHIT-HNT-HA film

DTA/TGA of 
(a) as-received HNT  
(b) film prepared from 0.5 g/L CHIT + 0.3 g/L HNT solution
Deposition/Analysis of HYH-HNT Films

XRD analysis of (a) as-received HNT (b) as-received HA (c) pure HYH film (d) HYH-HNT film (e) HYH-HNT-HA film

DTA/TGA of (a) as-received HNT (b) film prepared from 0.5 g/L HYH + 0.3 g/L HNT solution
PAA films with (a) 0.1 g/L HNT (b) 0.3 g/L HNT (c) 0.6 g/L HNT. (d) DTA/TGA of 1 g/L PAA + 0.6 g/L HNT
Comparison of (a) 2 g/L PLO, 2 g/L HA, (b) 2 g/L PLO (c) 2 g/L PLL, 2 g/L HA films
CHIT-HNT-HA (a) single layer (b) multilayer (c-d) alternating layer films
Summary

- Demonstrated the feasibility of using EPD to deposit organic-inorganic coatings containing HNT
- Multilayer coatings of CHIT-HA-HNT are possible
- Testing shows coatings contain properties similar to bone
- EPD was used to successfully deposit PLL & PLO

Future Work

- Continue investigating FGM coatings
  - Incorporate chiral polymers into FGM coatings
- Attempt to incorporate drugs into coatings, investigate release
- Continue testing under physiological conditions
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- My colleagues in the lab

Thank You!
References


References


References


<table>
<thead>
<tr>
<th>Technique</th>
<th>Thickness</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dip Coating</td>
<td>0.05-0.5mm</td>
<td>• Inexpensive • Coatings applied quickly • Coat complex substrates</td>
<td>• Requires high sintering temperatures • Thermal expansion mismatch</td>
</tr>
<tr>
<td>Sputter Coating</td>
<td>0.02-1mm</td>
<td>• Uniform coating thickness on flat substrates</td>
<td>• Line of sight technique • Expensive • Time consuming • Cannot coat complex substrates</td>
</tr>
<tr>
<td>PLD</td>
<td>0.05-5mm</td>
<td>• Same as for sputter coating</td>
<td>• Same as for sputter coating</td>
</tr>
<tr>
<td>Hot Pressing and Hot Isostatic Pressing</td>
<td>0.2-2.0mm</td>
<td>• Produces dense coatings</td>
<td>• HP cannot coat complex substrates • High temperature required • Thermal expansion mismatch • Expensive • Removal of encapsulation material</td>
</tr>
<tr>
<td>EPD</td>
<td>0.1-2.0mm</td>
<td>• Uniform coating thickness • Rapid deposition rates • Can coat complex substrates</td>
<td>• Difficult to produce crack-free coatings • Requires high sintering temperatures</td>
</tr>
<tr>
<td>Thermal Spraying</td>
<td>30-200mm</td>
<td>• High deposition rates</td>
<td>• Line of sight technique • High temperatures induce decomposition • Rapid cooling (\rightarrow) amorphous coatings</td>
</tr>
<tr>
<td>Sol-Gel</td>
<td>&lt;1mm</td>
<td>• Can coat complex shapes • Low processing temp. • Relatively cheap</td>
<td>• May require controlled atmosphere processing • Expensive raw materials</td>
</tr>
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</table>
Top-down Approach

- Experiment with the deposition of known materials
  - Chitosan, hyaluronic acid, hydroxyapatite, SS
- Attempt to co-deposit new materials
  - PLO, PLL, halloysite
  - Use materials whose properties will complement each other
- Examine coatings using different experimental techniques
  - Determine which parameters are best suited for deposition
  - Determine feasibility
- Investigate if coatings with different functions can be created
  - Drug delivery, FG coatings
- Test coatings in SBF, physiological conditions
  - Investigate whether or not they fulfill biofunctions (drug delivery, corrosion protection)
Deposition

- Chitosan is protonated and dissolved in acidic solutions, become a cationic polymer:
  \[ \text{CHIT–NH}_2 + \text{H}_3\text{O}^+ \rightarrow \text{CHIT–NH}_3^+ + \text{H}_2\text{O} \]

- Hyaluronic acid forms an anionic species:
  \[ \text{HYNa} \rightarrow \text{HY}^- + \text{Na}^+ \]

- Electric field provides electrophoretic motion of charged macromolecules to the anode or cathode, insoluble deposit forms:
  - **Cathodic reaction:**
    \[ 2\text{H}_2\text{O} + 2e^- \rightarrow \text{H}_2 + 2\text{OH}^- \]
    \[ \text{CHIT–NH}_3^+ + \text{OH}^- \rightarrow \text{CHIT–NH}_2 + \text{H}_2\text{O} \]
  - **Anodic reaction:**
    \[ 2\text{H}_2\text{O} \rightarrow \text{O}_2 + 4\text{H}^+ + 4e^- \]
    \[ \text{HY}^- + \text{H}^+ \rightarrow \text{HYH} \]
  - Charged polymers carry larger, neutral, molecules to be deposited

Charged polymers and neutral ceramics deposited cathodically
Potential change in EPD cell (Van der Biest and Vandeperre, 1999)

\[ V_a = \Delta \phi_1 + IR_{dep}d_1 + IR_s(d - d_1) + \Delta \phi_2 \]

Film thickness, \( d_1 \)

Electrode spacing, \( d \)

Resistances in EPD cell (Van der Biest and Vandeperre, 1999)

- \( V_a \) = the applied potential
- \( I \) = current
- \( R_d \) and \( R_s \) = resistance per unit length
- \( d \) = electrode separation
- \( d_1 \) = thickness of the deposit
- \( \Delta \phi_i \) = potential drop at one electrode
DLVO Theory

- Developed by Derjaguin, Landau, Verwey and Overbeek
- Describes relationship between stability of suspension using repulsive/attractive energies
- Dominant, attractive energy (LvdW)
  \[ V_A = -\frac{Aa}{12D} \]
  - \( A = \text{Hamaker's constant} \)
  - \( D = \text{separation of particles} \)
  - \( a = \text{particle radius} \)
- Repulsive energy (coulombic double-layer repulsion)
  \[ V_R = 2\pi\varepsilon\varepsilon_0 a\psi^2 \ln[1 + e^{-\kappa H}] \]
- The energy of interaction \( V_T \) of two particles
  \[ V_T = V_A + V_R \]

Energy of interaction between two particles (Sarkar and Nicholson, 1996)
Double-layer (DL) distortion as particle moves

- DL is thinner ahead of the particle
- Counter ions move along with particle, could recombine

Incoming particles also have thinned DL

- Repulsion is decrease
- Particles overcome repulsive barrier

Schematic of the deposition mechanism by lyosphere distortion and thinning (Sarkar and Nicholson, 1996)
Deposition Kinetics of Composite Films

- Deposition described by the Haymaker equation:
  \[ M = \mu E t S C_s \]
  - \( C_s \) = concentration of colloidal particles
  - \( E \) = electric field
  - \( t \) = Deposition time
  - \( \mu \) = particle mobility
- However, does not take moving boundary into account
  \[ M = \mu E t S C_s \frac{C_c}{C_c - C_s} \]
  - \( C_c \) is the particle concentration in the deposit
- For two-component system with chitosan:
  \[ M = \mu E t S C_s \left(1 - \frac{C_s}{C_c}\right)^{-1} + \mu' E t S \psi_s \left(1 - \frac{\psi_s}{\psi_c}\right)^{-1} \]
  - \( \mu' \) = CHIT mobility
  - \( \psi_s \) is the concentration of CHIT in suspension
  - \( \psi_c \) is the concentration of CHIT in the deposit
Deposition Kinetics

• 1940, deposition described by the Haymaker equation

\[ M = \mu E t S C_s \]

- \( C_s \) = concentration of colloidal particles
- \( E \) = electric field
- \( t \) = Deposition time
- \( \mu \) = particle mobility
- \( S \) = surface of electrode

• Given many variables held constant, we have

\[ M = \mu E S C_s \quad t = kt \]

- \( k = \mu E S C_s \)

• Mass deposited is linearly dependant on time
• Model ignore the change of concentration during deposition
• 1994, Zhang et al. derived kinetic equation incorporating change
\[ \int dw = \int \int fudSC(t) = fu \int dSC(t) dt \]
  □ \( u \) = average velocity of particles
  □ \( C(t) \) = concentration of particles in suspension
  □ \( f \) = efficiency factor (i.e. if all particles is suspension deposit, then \( f = 1 \); otherwise \( f < 1 \))
• If suspension is homogeneous, no change in particles concentration due to sedimentation, only due to EPD, then mass balance condition can be imposed
\[ C(0) = w_0 \]
\[ C(t) = \frac{[w_0 - w(t)]}{V} \]
  □ \( w_0 \) = initial weight of the powder in the suspension
  □ \( V \) = volume of suspension
• The following solution is obtained
\[ w(t) = w_0(1 - e^{-kt}) \]
\[ \frac{dw}{dt} = w_0ke^{-kt} \]
• \( k \) = kinetic parameter \( (k = Sfu/V) \)

Deposited weight (fraction of initial weight of solid in the suspension) as a function of time under constant current conditions (Sarkar and Nicholson, 1996)
• There was still disagreement between calculated and experimental results
  ▫ At higher times, calculated weight as significantly higher than actual
  ▫ Constant value of $k$ cannot be used
  ▫ In a constant-voltage process, current decreases during deposition

Deposited weight (fraction of initial weight of solid in the suspension) as a function of time under constant voltage (Sarkar and Nicholson, 1996)

Normalized current $I_N$ and $kI_N$ as a function of time during constant voltage deposition (Sarkar and Nicholson, 1996)
\[
\int dw = f \int dSu(t)C(t) \, dt = f \int dS \mu E(t)C(t) \, dt
\]

\[
\int dw = k' \int E(t)[w_0 - w(t)] \, dt, \quad k' = \frac{\frac{Sf \mu E}{V}}{(\text{kinetic parameter})}
\]

- \( E(t) = \) voltage drop/unit length of suspension normal to depositing electrode
- As deposit forms, it replaces an equal thickness of suspension
- Total resistance of system changes

\[
L_{\text{equiv}} = L + L_{\text{dep}}(R_r - 1), \quad L_{\text{dep}} = \frac{\text{deposit volume}}{\text{area}} = \frac{w(t)/\rho}{S}
\]

- \( L_{\text{equiv}} = \) suspension with equal resistance
- \( L = \) distance between electrodes
- \( L_{\text{dep}} = \) thickness of deposit
- \( R_r = \) ratio of deposit resistivity to that of suspension
- \( \rho = \) deposit density

\[
L_{\text{equiv}} = L + \frac{w(t)/\rho}{S} (R_r - 1) = L + w(t)R', \quad R' = \frac{(R_r - 1)}{\rho S}, \quad \therefore E(t) = \frac{V_a}{L_{\text{equiv}}} = \frac{V_a}{L + w(t)R'}
\]

\[
\int dw = k' \int \frac{V_a}{L + w(t)R'} [w_0 - w(t)] \, dt
\]

\[
R'w(t) + (R'w_0 + L) \ln \left( \frac{w_0 - w(t)}{w_0} \right) + k'V_a t = 0
\]
Different Deposition Kinetics

- Curve I – Constant current/constant concentration
  \[ w(t) = kw_0t \]

- Curve II – Constant current/variable concentration
  \[ w(t) = w_0(1 - e^{-kt}) \]

- Curve III – Constant voltage/constant concentration
  \[ R'w^2 + Lw(t) + k'w_0V_at = 0 \]

- Curve IV – Constant voltage/variable concentration
  \[ R'w(t) + (R'w_0 + L) \ln \left( \frac{w_0 - w(t)}{w_0} \right) + k'V_at = 0 \]

Deposited weight (fraction of initial weight of solid in the suspension) for different conditions (Sarkar and Nicholson, 1996)
New Bio-materials

Halloysite Nanotubes (HNT)

- $\text{Al}_2\text{Si}_2\text{O}_5(\text{OH})_4 \cdot n\text{H}_2\text{O}$,
  - $n=0 \text{ or } 2$
- Dual-layer aluminosilicate
  - Octahedral alumina
  - Tetrahedral silica
  - Layer of water
  - Siloxane $\text{SiO}_4$ surface
- Lattice mismatch in the alumina/silica layers creates strain
  - Curving occurs, creates hollow tube structure.
- 30-50 nm OD and 1-3 $\mu$m in length

Schematic diagrams of (a) the crystalline structure of halloysite-(10 Å) and (b) the structure of a halloysite nanotube (Yuan et al., 2008)
New Bio-materials

• Can trap different reagents within either the inner tube or void spaces
• Outermost surface composed of silica, and inner of alumina
  ▫ At pH < 8.5, ζ-potential of silica is negative, and alumina is positive
  ▫ Positive inner surface → enables loading of negative macromolecules
• Controlled drug release, significantly better than microcrystals
  ▫ Initial burst within 10 min, then prolonged 8-10 h release
  ▫ A linear release rate can be achieved by increasing the viscosity of the loading solvent

Release curves of drugs from halloysite and crystals in water, pH 7 (Lvov et al., 2008)
Electrophoretic Deposition (EPD)

- EPD of cathodic polymer
  - Protonation
  - Electrophoresis
  - Charge compensated
  - Neutralized
  - Coherent deposit

Base generation:
Electrogenerated base
\[ 2\text{H}_2\text{O} + 2\text{e}^- \rightarrow \text{H}_2 + 2\text{OH}^- \]

Base generation:
Electrogenerated acid
\[ 2\text{H}_2\text{O} \rightarrow \text{O}_2 + 4\text{H}^+ + 4\text{e}^- \]

Anode
Cathode

Low pH

High pH

Acidic solution, pH < pI
Electrophoretic Deposition (EPD)

- EPD of cathodic polymer
  - Protonation
  - Electrophoresis
  - Charge compensated
  - Neutralized
  - Coherent deposit
- EPD of anodic polymer
  - Deprotonation
  - Electrophoresis
  - Charge compensated
  - Neutralized
  - Coherent deposit

Base generation:
- Electrognerated base
  \[2\text{H}_2\text{O} + 2\text{e}^- \rightarrow \text{H}_2 + 2\text{OH}^-\]
- Electrognerated acid
  \[2\text{H}_2\text{O} \rightarrow \text{O}_2 + 4\text{H}^+ + 4\text{e}^-\]

+ Low pH

Anode

Cathode

Acidic solution, pH > pI
Quartz Crystal Microbalance

\[ \Delta f = -\frac{2f_0^2 \Delta m}{A \sqrt{\mu_q \rho_q}} \rightarrow \Delta \text{mass} = -\Delta f \times \frac{A \sqrt{\mu_q \rho_q}}{2F_q^2} \]

- \( \Delta \text{mass} = \) Mass change
- \( \Delta f = \) frequency change
- \( \mu_q \) = AT-cut quartz crystal constant (2.947 \times 10^{11} \text{ g/cm} \cdot \text{sec}^2)
- \( \rho_q \) = Quartz crystal density (2.648 g/cm\(^3\))
- \( F_q \) = Reference frequency (9.00 MHz)
- \( A \) = Quartz crystal surface area (0.196 cm\(^2\))

\[ \Delta \text{mass} = -\Delta f \times \frac{0.196 \sqrt{2.947 \times 10^{11} \times 2.648}}{2 \times (9 \times 10^6)^2} \]
\[
= -\Delta f \times 1.06878 \times 10^{-9} \\
\Delta \text{mass} = -1.06878 \times 10^{-9} \Delta f \]
Ag-Chit/HA-Chit laminates using EPD (Pang and Zhitomisrky, 2008)
Comparison of PAA films with (a) 0.1 g/L HNT (b) 0.3 g/L HNT (c-d) 0.6 g/L HNT
0.5 g/L CHIT, 1.0 g/L HA

0.5 g/L CHIT, 0.3 g/L HNT

0.5 g/L CHIT

CHIT / CHIT - HNT / CHIT - HA Film
HA layers

HNT layers

0.5 g/L CHIT - 0.3 g/L HNT + 0.5 g/L CHIT - 1/0 g/L HA Film

1 μm
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HA layers

HNT layers

0.5 g/L CHIT - 0.3 g/L HNT + 0.5 g/L CHIT - 1/0 g/L HA Film

1 μm
2 g/L PLL - 2 g/L HA Film
(a) as-received HNT
(b) film prepared from 0.5 g/L CHIT + 0.3 g/L HNT solution
(c) film prepared from 0.5 g/L HYH + 0.3 g/L HNT solution
(d) film prepared from 1.0 g/L PAA + 0.6 g/L HNT solution
DTA & TGA Data

(a) as-received HNT
(b) film prepared from 0.5 g/L CHIT + 0.3 g/L HNT solution
DTA & TGA Data

(a) as-received HNT
(b) film prepared from 0.5 g/L HYH + 0.3 g/L HNT solution
Secondary amine group

Acetyl group

Chitin-Deacetylase

Primary amine group

Becomes protonated
Siloxane

- A chemical compound composed of $R_2SiO$
  - $R$ is a hydrogen atom or hydrocarbon group
  - $-Si-O-Si-O-$ form branched/unbranched backbone
  - Belongs to organosilicon class or compounds
- Silica particles and Siloxane networks investigated for bio-nanohybrid networks

*Stephanopyxis turris* diatom (SAHFOS, 2010)

Siloxane structure in *S. turris* (Ruiz-Hitzky et al., 2008)
Materials selection chart of tensile strength vs. Young’s modulus (Hench and Jones 2005)
Body Environment

- Body fluids have an effect similar to warm aerated seawater
  - Can contain up to 100 mL Cl\textsuperscript{-} per liter or water
- Body pH is usually 7.2-7.4,
  - Can vary between pH=4-9, especially after surgery if in the case of an infection
- Temperature is 37°C
Ionic compositions of blood plasma, interstitial fluid, and intracellular fluid. (Davis and ASM International 2003)
Hierarchical structure of bone (Kobayashi, 2010)