Combinatorial Studies of Biopolymer Deposition and Surface Functionalization for Biomolecular Reactions in BioMEMS Environments

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Chitosan (polysaccharide)

- Cationic polyelectrolyte
- pH dependant solubility (pH < 6.3)
  - Selective deposition
- Rich amine groups (DNA, protein, cell adhesion)
  - Good interface material

MEMS technology  ➔  Science and medical applications (medical, pharmaceutical)
Chitosan selective deposition

- Localized high pH region generated electrochemically due to hydrogen evolution
- Chitosan molecules deprotonate and immobilized at electrode surface

Chitosan film

2H⁺ + 2e⁻ → H₂

Cathode

pH gradient

NH₃⁺

NH₃⁺

pH > 6.3

Combinatorial material analysis
(Discrete sample library with in-situ, ex-situ measurements)

Chitosan material
(w/ process parameter)
Combinatorial material research

► Reproducible and multiple sample production
► Electronic and optical real-time measurement of deposition process (I/V measurement, laser reflectivity)
► Ex-situ materials analysis (Profilometer, AFM)
► Monitoring technique development for MEMS device
In-situ process monitoring

Electrical measurement

- As thickness increases, voltage at the cathode increases due to film resistance increasing

Optical reflectivity

- Reflectivity results show that film thickness increases with increasing deposition time
As current density increases, voltage at the cathode increases.

Reflectivity results show that reflectivity increases with increasing current density.
Deposition characteristics

Deposition time vs. thickness

- Film thickness is dependant on deposition time and current density.
- Ex-situ profilometer and reflectivity measurement results show the higher deposition rate of chitosan film after 150 sec process time elapsed.
Solution effect

- Thin high pH region in buffer and thick high pH region in HCl
- Thicker film deposition in HCl solution case.
Microfluidic systems

- Micro-scale on-chip elements to connect to fluid and electrical sources at the macro-scale for surface biofunctionalization
- Re-usable, multi-tasked, simple in design and manufacture, reliable
Chip design and material selection

- Multistep biofunctionalization in microfluidic system
- Combinatorial microfluidics: 32 max test sites in 4” wafer
- Different channel dimension: 10 to 200 μm wide
- Geometry: choking constriction

<table>
<thead>
<tr>
<th>Substrate: Kapton, Pyrex</th>
<th>Fluidic flow layer: SU-8, PDMS</th>
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<tbody>
<tr>
<td>• Temperature-resistant (to 95°C)</td>
<td>• Patternable with photolithography</td>
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<tr>
<td>• Smooth and rigid enough to withstand processing</td>
<td>• High aspect ratios</td>
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<tr>
<td>• Not damaged by chemicals</td>
<td>• High optical transparency</td>
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<tr>
<td>• Transparent</td>
<td>• Good chemical, thermal resistance</td>
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<tr>
<td>• Electrically insulating</td>
<td>• Compatible thermal expansion</td>
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<tr>
<td>• Transparent</td>
<td>with other chip materials</td>
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</tbody>
</table>
Packaging design

- Parallel connection of fluidic and electrical inputs/outputs
  - Multi-tasked and multi-functional
  - Clear access to in-situ microscopy
- Leak free packaging
  - 2 layers of SU-8 with PDMS gasket on top
  Micro-knife-edge applies extra force to gasket near channel, improving sealing

Kapton based SU-8 MEMS device

Micro-Knife-Edge Channels
Surface biofunctionalization

- Chitosan solution 1% (w/v), pH 5
  Labeled with NHS-fluorescein
  excitation = 490-495 nm, emission = 520-525 nm

- Microfluidic system
  channel width: 500μm

- Deposition conditions
  Flow rate: 0.1 mL/min
  Current density: 6A/m²
Surface biofunctionalization

- Successful chitosan deposition on working electrode in microfluidic channel

- Estimated thickness: 1 ~1.5μm

- Closest working electrode has most of deposition
Upcoming experiments

- Analysis of flow parameter (flow velocity, residence time, channel geometry) and dependency of surface biofunctionalization (built in micro-heater and thermocouple under microfluidic channel)

- Multistep surface biofunctionalization on the chitosan film deposited in microfluidic system (Enzyme, protein, DNA etc)
Conclusion

► Combinatorial analysis system for electrochemically driven chitosan deposition was developed with in-situ and ex-situ measurements techniques.

► Chitosan deposition show dependency of current density, deposition time, and pH condition of solution.

► Several microfluidic system and leak free packaging scheme were proposed.

► Fluidic and electrical in/output were integrated for rapid multistep biofunctionalization processing.

► Chitosan deposition in microfluidic system was demonstrated for the first time.