Biostability and corrosion resistance of a biocompatible encapsulation and interconnect technology for implantable electronics

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Intro: advanced biomedical packaging

Traditional Ti-box

New package for implants:
- Small
- Soft, flexible
- Biomimetic

Essential requirements for package materials:
- biocompatibility
- biostability
- bi-directional diffusion barrier:
Advanced biomedical packaging: Packaging sequence

• Selection of all individual components essential to fabricate the functional implant
  → chips, sensors, passives, battery,..

• Packaging of all individual components
  → Fabrication of bi-directional diffusion barrier
  → biocompatible & biostable materials

• Assembly of all components

• Electrical interconnection
  corrosion-resistant metallization such as Pt or Au

• Embed all components and substrate
  → use biomimetic elastomer
  → if needed local adjustments for sensors, electrodes

Biocompatibility and biostability not required

Creation of bi-directional diffusion barrier

All materials should be biocompatible and biostable
Advanced biomedical packaging: process sequence

Phase 1: hermetic encapsulation of chips and components
- Insulating diffusion barrier
- Rounded chip edges
- Electrodes
- Thinned die
- 2nd diffusion barrier, e.g., parylene

Phase 2: Interposer containing encapsulated chips
- Biocompatible polymer embedding
- Inter-die connections incl. fan-out, contact pads
- Die 1 and die 2

Phase 3: system embedding in bio-mimetic material
- Sensor area (implanted deeper in the body)
- Main part of electronic implant
- Passives, crystal, ...

Sensor chip

Main part of electronic implant

Passives, crystal, ...

die 1

die 2

die 2

die 1
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Sensor chip
- die 1
- die 2

Thinned die
- Electrodes
Requirements for encapsulation materials for chips

- **electrical properties:** both insulators and conductive materials are needed

- **good step coverage of the insulating layers**

- **biocompatible materials** (no harm from material → body)

- **biostable materials** (no harm from body → material)

- **bi-directional diffusion barrier**
  - Protect the chip from corrosive body fluids
  - Protect body for harmful IC materials such as Cu

- **as much as possible wafer level processing in std. clean room**
  - controlled, repeatable processes, hence well known material properties
  - wafer based processing, hence high throughput

  → Investigation of standard CMOS materials as barrier:
    - insulators: oxide, nitride
    - conductive materials: Ta, TaN, Ti, TiN
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**Phase 1: sloped dies: fabrication concept**

Partial dicig of sloped groove in scribeline followed by deposition of top capping layer(s)

**Electrode fabrication**

- Gluing of wafer on carrier (upside down), wafer thinning
- Low temperature deposition of bottom capping layer(s)
- Release from carrier

**Start:** wafer with std. IC processing

**Top capping layer(s)**

**Bottom capping layer(s)**

**Carrier glue**

Max $200^\circ C \rightarrow \text{glue!}$

Possible issues:
- quality of layers
- step coverage

Phase 2 of packaging process

40~50um
Phase 1: biocompatible materials, diffusion barriers
Cell cultures for diffusion tests

Test of diffusion barrier properties of top layer for Cu diffusion
Layer under test: typical 100nm thick

Optional: extra leaching step @ 37°C or 70°C

5 days in vitro co-culture using primary cells.
  - Fibroblasts
  - Cardiomyocytes → most sensitive for Cu
  - Hippocampal cells

Cell staining using life-death cell assays
  → Determination of cell viability
Cytotoxicity and barrier test of insulating layers

After 5 days co-culture with cardiomyocytes

<table>
<thead>
<tr>
<th>Dep.t.</th>
<th>Oxide</th>
<th>Nitride</th>
</tr>
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<tbody>
<tr>
<td>400°C</td>
<td>OxM</td>
<td>NM</td>
</tr>
<tr>
<td>200°C</td>
<td>OxL</td>
<td>NL</td>
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</tbody>
</table>

- Med. Temp. oxide and nitride have good diffusion barrier properties.
- 100nm Low temp. Oxide and Nitride do not stop Cu diffusion sufficiently.

All materials are non-cytotoxic

±10% viability of control

Cell viability after 5 days co-culture (%)

Cytotoxicity Test

Diffusion Barrier Test using 100nm thick layers
bio-stability of SiN: Long time immersion at 37°C

200nm SiN on Cu, 4 weeks immersion @ 37°C using various fluids:
- **DI**: de-ionized water
- **PBS**: simulating blood serum (phosphate buffered saline)
- **Cardio cell culture medium**: simulating tissue fluid

Front side: 400°C SiN (MT)  
Back side: 200°C SiN (LT)

→ **Color change caused by all fluids.**  
  For LT SiN: color change obvious already after a few days immersion  
→ **Potential mechanism:** etching? Absorption? Chemical reaction?
Bio-stability of SiN

Dedicated tests are performed to understand non-stability of SiN in water-based fluids

FTIR analysis
XPS analysis
Etch tests

→ No material change due to immersion
→ SiN dissolves in water

Immersion tests proved that H concentration in SiN is origin!
- 200ºC PECVD SiN → H conc. of ~ 20-25%
- 400ºC PECVD SiN → H conc. of ~15%
- 400ºC LPCVD SiN → H conc. of ~3%

Options for final use:
- material improvement
  - cover SiN with biostable insulating material (SiC? Parylene-c?)
Soaking of SiC in biological fluids

SiC: from literature: very stable in solutions
→ Put SiC on top of SiN as protection
  test: 45nm SiC on top of SiN
  2 weeks immersion in PBS and DI @ 70ºC

→ No clear color change observed when immersing SiN protected by a SiC layer
  (only some deposition of products from PBS)
→ SiC layer can protect SiN layer.
→ more tests needed for full characterization of SiC layer
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Conductive barriers
2 types of electrodes:

- Good biocompatible is reported in literature, but this is depending on the deposition process / chemical composition of the material
- Has interesting diffusion barrier properties for std. CMOS applications

Interesting CR materials: Ti, TiN, Ta, TaN,...
Cytotoxicity and barrier test of conductive layers

- Ti and TaN have good diffusion barrier properties.
- TiN and Ta are not performing well

Typically, Ti/TiN or Ta/TaN are used
→ always one good barrier metal
→ Long term diffusion tests are essential

All materials are non-cytotoxic
Bio-stability of conductive barrier materials

Cu + 15/40 nm Ta/TaN
→ Immersion for 10 days at 37°C in various biofluids
→ surface damage in PBS*

* Phosphorate buffered saline: similar ionic concentration as blood serum
Bio-stability of conductive barrier materials

Cu + 15/40 nm Ta/TaN

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→ surface damage in PBS

Ta / TaN / Ti / TiN are all exposed to biofluids to mimic later exposure in body:
  - Cardio cell culture medium: good
  - DMEM (for fibroblast* cell culture): good
  - PBS**: surface damage

→ Biostability problems in certain biofluids.
→ solution: cover material with noble metal such as Pt or Au

* Phosphorate buffered saline: similar ionic concentration as blood serum
Protection of conductive barriers

Cu-pads:
→ cover with Ta/TaN as diffusion barrier
→ cover with Ti/Pt to protect barrier for etching by biofluids (50nm Pt)

Highest risk for moisture diffusion at contact pad edge
→ Test device for biostability/corrosion has extra contact pads to create worst case scenario test

Materials related to std. CMOS

- Si
- Standard CMOS passivation
- TaN/Ta
- Metal (e.g. Cu)

Biocomp. capping layers, being also a diffusion barrier
Passive/Active corrosion test method

Passive test: corrosion study without current; only immersion

Active test: Predict corrosion behavior in operational environment
  Current running through devices
  Bio-fluid contacting the top surface of devices
Passive corrosion tests

Corrosion tests in PBS (most aggressive biofluid for Ta/TaN):
- real time testing: 1 week immersion at 37°C
- accelerated testing: 2 months immersion at 70°C *

→ No corrosion

4-point resistance measurements of Cu interconnects with 1 - 5 - 10 - 40 µm width.
No change in resistance!

*corresponding to corrosion resistance of at least 2 years at 37°C (assuming acceleration factor Q_{10}=2)
Active corrosion test

Active test: current is running through the device to mimic operation

**Test procedure:**
- Fill PDMS chamber with PBS, room temperature
- Contact bond pads through needles.
- Apply current (AC, DC)
- Monitor resistance during the tests.

**Test of 1µm wide interconnects:**
- Apply for 3 days
  1 mA, 1Hz AC current
  → no corrosion
- Apply for 14 days
  1 mA, DC current
  → no corrosion

➢ For multiple test devices, no corrosion was observed under the test conditions mentioned above
More efficient accelerated active corrosion tests

- Al bonding wires are protected prior to immersion:
  - By globtop
  - By a dedicated epoxy
  - By epoxy + Parylene-c

- Test: immersion in PBS @ 70°C
  0.1 mA DC current (active test)

- Failure: zero current
  - By globtop → after 7 days
  - By epoxy → after 9 days
  - By epoxy + Parylene-c → after 10 days

- We checked the immersed bond path chains: no corrosion!
- Remove protection to investigate failure
  → connections on Si chip and on PCB are good.
  → Al wire bonding failed in the test, in spite of protection
  → Moisture/liquid at high temperature caused failure in the wire bonding.
  → Need for better protection which can withstand elevated temperatures (ie. Parylene-HT)

Remark: Globtop: Stycast 50500, moisture absorption at RT: 7 days 0.2%. 24 hr boil test: 0.5%.
Biostability in case of tissue inflammation

Inflammation process after implant surgery results in more aggressive bio-environment for the implanted materials:

- macrophages secret reactive oxygen, which converts to H$_2$O$_2$ (strong oxidant).
- Concentration of H$_2$O$_2$ rises sharply within ~1 week after implant, then decreases markedly, continuing at a very slow decreasing for several years.
- Local pH decreases from ~7.4 down to ~5.2 due to inflammation

→ 2 test conditions to simulate inflammation:

**Incubation of material / device at 37° C for 1 week**

- 50 mM H$_2$O$_2$, PBS, pH 5.2 adjusted by HCl
- 150 mM H$_2$O$_2$, PBS, pH 5.2 adjusted by HCl

Reference:
2. C. Fonseca, M.A. Barbosa, Corrosion behaviour of titanium in biofluids containing H2O2 studied by electrochemical impedance spectroscopy, 2000
Passive corrosion tests simulating inflammation: results after 1 week

After 1 week immersion of corrosion device:

• No visible corrosion on device surface for both solutions
• pH of both immersion solutions are still 5.2
• Resistance measurement before and after immersion

⇒ No significant change in resistivity
⇒ device is stable under the testing conditions.

⇒ test is prolonged with one more week immersion for safety.
Passive corrosion tests simulating inflammation: results after 2 weeks

For further verification, 1 more week immersion in solutions

→ Resistance measurements: no changes

➢ Our test device with electrodes protected by Platinum is resistant under inflammatory reaction conditions.
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Implantable packaging concept: phase 2

(sub-)system package or interposer:
- polymer encapsulation
- bio-metallization

Start: Imec’s ultra-thin chip package (UTCP) for wearable devices

Currently under investigation / investigation planned:
- encapsulation of various thin dies (alignment essential)
- encapsulant: biocompatible polyimide or alternative polymer → HD PI2611, LCP
- current chip adhesive is not biocompatible → epoxy-based alternative
- Pt or Au based metallization process instead of Cu
- Parylene as extra moisture barrier
Platinum & gold for interconnects

- Both are very interesting material for medical applications:

- Very expensive materials, especially Pt.

- Deposition and patterning:
  - subtractive technique: sputtering and lift-off
    - easier to deposit alloys
    - More than 50% of the deposited metal is not used
      → COST !! Recycling is important but process remains expensive.

  - additive technique: selective electroplating
    - conductive seed layer needed
    - less expensive
Optimization of plane Pt-plating on small area

→ Investigate uniformity, adhesion, max. thickness, stress, roughness, purity of Pt layer, ... as function of basic plating parameters such as:
  • seed layer (material, thickness)
  • various electrolyte solutions
  • current or voltage settings for galvanostatic / potentiostatic control

→ Optimized plating process:
  • Pt thickness up to ~800 nm
  • Good adhesion, smooth film, reproducible process

- plating solution: Dihydrogen dinitrosulfatoplatinate (DNS); room temperature
- -3mA/cm² current density, galvanostatic process control, 32% current efficiency
Fabricated Pt interconnects on PI Substrate

- 165nm Pt is deposited
- released flexible substrate showed good adhesion and flexibility of interconnects
- dedicated reliability tests are planned

SEM top-down images showed no cracks or deformations in the plated interconnects
Use of Parylene for implantable packaging

Requirements for Parylene:

- Biocompatible → parylene-C, parylene-HT
- Availability of suitable patterning method → litho + etch, laser
- Good adhesion to all relevant materials
- Excellent barrier properties
- Integration compatibility:
  - Polyimide cures at 370°C
  - Polyurethane embedding is performed above 60°C
  - Pt annealing at min. 300°C
  - Sterilization
  → selection between parylene-C, parylene-HT
Adhesion: test protocol based on ASTM standard D-3359

Tape Test: ASTM standard D-3359.

Protocol:
- cut 10 x 10 grid with blade on sample,
- place tape on grid
- wait for 90s
- pull tape off.

→ Compare results with ASTM classification table

In literature, parylene adhesion to polymers and (noble) metals is poor.

Methods used to improve adhesion:
- Adhesion promoter A174
- Oxygen plasma
- Dehydration

<table>
<thead>
<tr>
<th>Level</th>
<th>Adhesion</th>
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<tbody>
<tr>
<td>0%</td>
<td>Excellent adhesion</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>Level 4</td>
</tr>
<tr>
<td>5%-15%</td>
<td>Level 3</td>
</tr>
<tr>
<td>15%-35%</td>
<td>Level 2</td>
</tr>
<tr>
<td>35%-65%</td>
<td>Level 1</td>
</tr>
<tr>
<td>&gt;65%</td>
<td>Level 0</td>
</tr>
<tr>
<td></td>
<td>Bad adhesion</td>
</tr>
</tbody>
</table>
Basic adhesion tests: Parylene-C on various materials

- **Parylene-C on Silicon:**
  - Without promoter: Level 0
  - With adhesion promoter: A-174, Level 5
  - With A-174 adhesion promoter, level 5 adhesion is achieved on Si, SiO$_2$, SiNx, Cu, Pt, polyimide PI2611, PDMS

- **Parylene-C on polymer PI 2611:**
  - Without promoter: Level 2
  - With adhesion promoter: A-174, Level 5
Severe moisture barrier test of 25 µm Parylene-C immersion of coated Cu in PBS @ 37ºC

Cu coated with 25 µm Parylene-C (multilayer):

- Locally corrosion is clearly visible.
  Limited barrier properties?
  Corrosion due to Parylene damage by handling or particles??

- Barrier test is not satisfying, more investigation needed
  Long term immersion in other biofluids or DI water is not tested yet.
Flex & stretch: Parylene-C on top of PDMS

3 µm parylene C on PDMS

- Adhesion OK
- Parylene on flexible substrate (PDMS) shows micro stretch marks due to handling/ stretching.
- Strong plastic deformation with large scale elongation.
Flex & stretch: Parylene-C on top of PDMS

- 3 µm parylene-C on PDMS, 5-10% stretching while measuring force
- 1st stretch cycle is different. Some jumps suggest small cracks in parylene film.
- During further stretch cycles, sample has elastic behavior.
- Similar behavior was observed with 16µm and 25µm Parylene-C on PDMS

→ Barrier properties?? Samples with Cu meander embedded in PDMS will be tested.
Conclusions

A flexible compact packaging concept for active medical implants is under development.

Recent process developments:

- **Phase 1: insulating barrier materials:**
  - various types of oxide and nitride are tested
  - low temperature materials: poor diffusion barrier properties.
  - SiN dissolves in water, SiN should be covered (SiC) for long term stability.

- **Phase 1: conductive barrier metals:** Ti, TiN Ta, TaN
  - Ti and TaN perform well as diffusion barrier (100nm).
  - biostability of all tested materials is not good in all biofluids.
  - barrier layers will be covered with Platinum before exposure to body fluids.
  - active and passive corrosion tests showed good stability due to Pt capping.

- **Phase 2-3:**
  - process development in ongoing, alternative encapsulating polymers are studied
  - for cost reduction: a selective Pt plating process is developed, with good results
  - Parylene-c tests: adhesion issues could be solved barrier properties?
Questions?