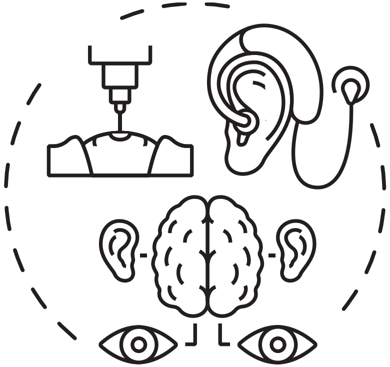
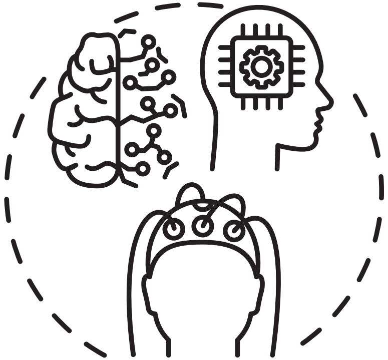
EPFL





Neural Interfaces

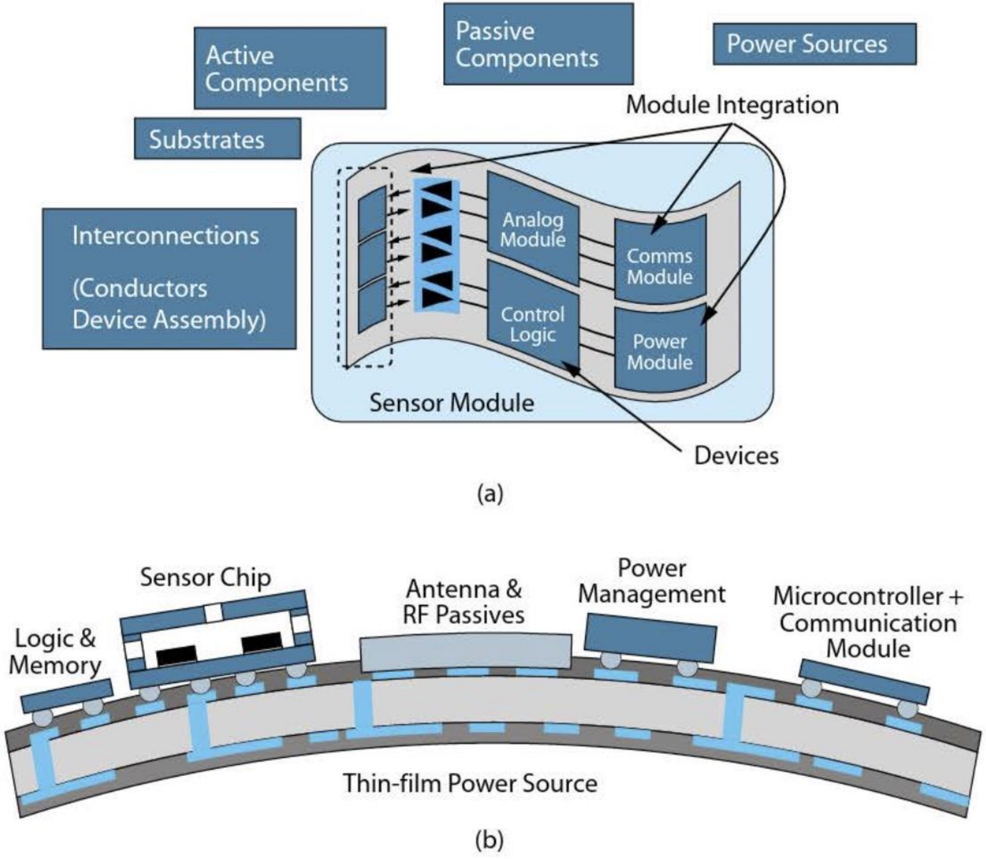
NX-422

Packaging

Giuseppe Schiavone

Neuro-X Institute

Packaging: one term, many meanings



Packaging in flex electronics =
How to assemble, interconnect and protect:

- A thin flexible substrate (up to ~ 50 μm)
- Active devices such as sensors and transistors
- A processor and memory ICs
- Passive components such as capacitors, resistors, and inductors
- (electrodes)
- Power sources, such as a flexible battery and interconnections.
- Etc.

Packaging: one term, many meanings

Packaging of medical devices (pacemaker example)

Connections between leads and feedthroughs

Hermetic housing for electronic circuit and battery

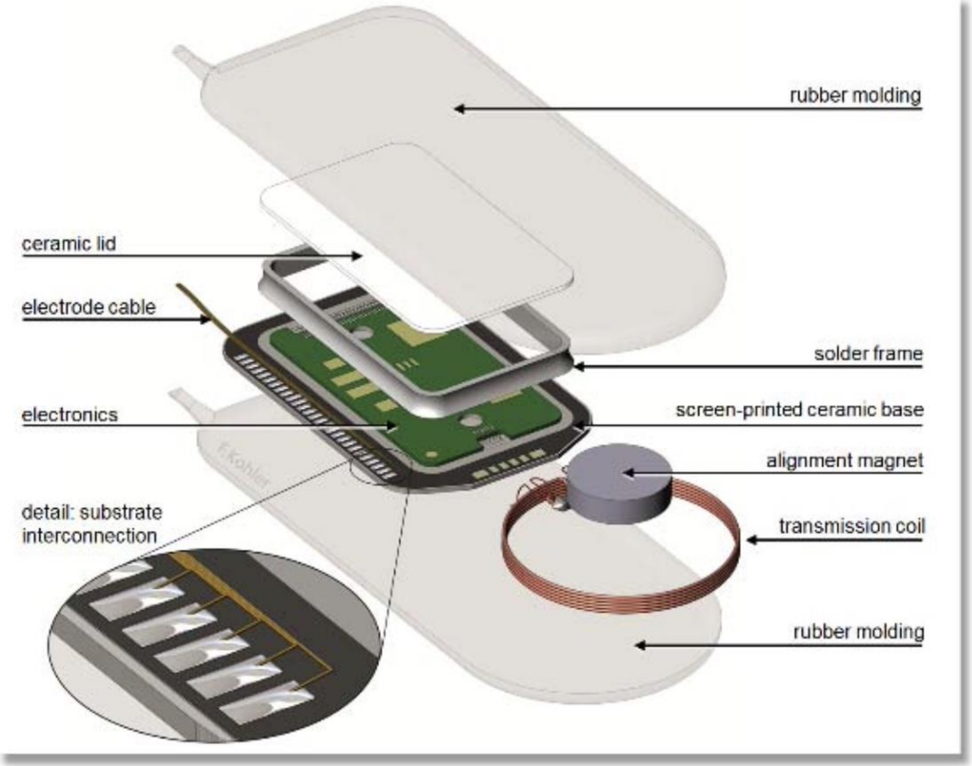
Leads for connections of electrodes to electronic circuit

Electrodes for sensing and stimulation

Example

Cortec BrainCon

by CorTec GmbH & University of Freiburg



Kohler et al. IEEE/EMBS-NER, 2013

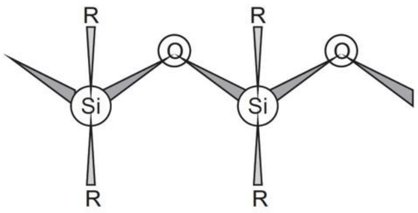
Encapsulation – the outer « shell »

- Many insulating materials but few are suitable for direct immersion into biological systems
  - Evaluation under saline conditions is required
  - In vitro vs in vivo

- Accelerated testing
  - insulator monitor, 4-point resistance,
  - Young’s modulus monitor, surface bonding monitors

- Accelerating degradation
  - Elevated temperature (10-deg rule, but can alter chemical reactions)

Silicones encapsulation / packaging



- Long-lasting material
- **Polymer** with simultaneous presence of organic groups attached to inorganic atoms

- Silicone elastomers (rubbers)
  - Molding, injection, spin-coating, printing
  - Cross-linked polymer

- Soft polymer : elastic modulus range: 10 kPa – 10 MPa

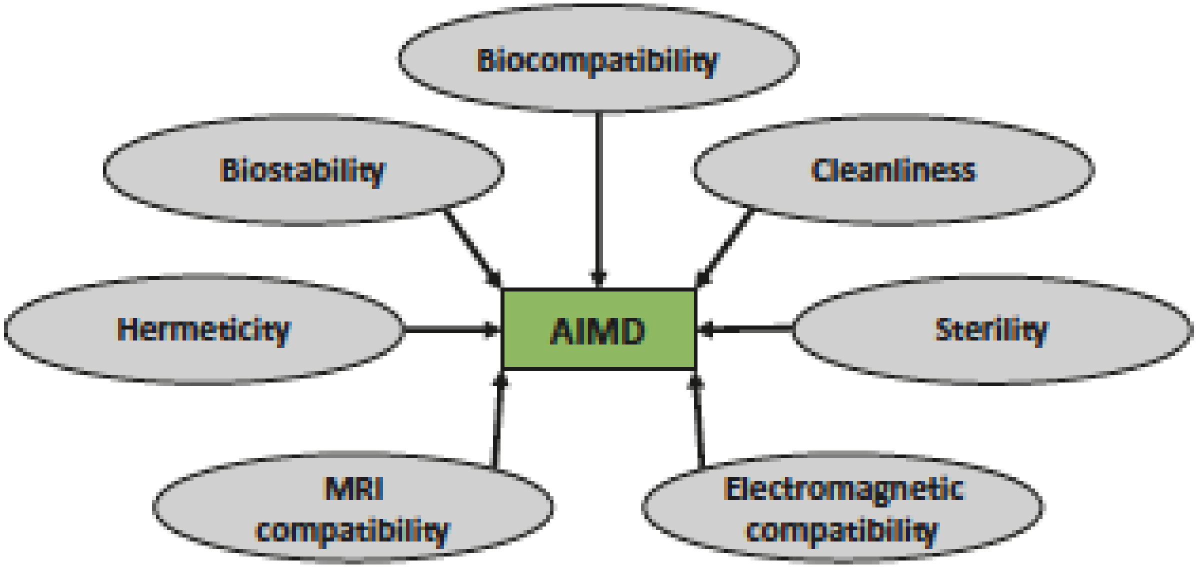
- Very good protection over corrosion of silicon and oxidizable materials
- Very good electrical insulators (esp. Fluoropolymers)

Polymers for medical devices

	Copper Film	PI Film	LCP Film	TPU Film	Silicone Rubber
Melting Temperature [°C]	1’085	None	285-330	220	none
Density [g/cm3]	8.9	1.4	1.4	1.2	1.0
Ultimate Tensile Strength [MPa] @ max. Elongation	280 @ 8%	231 @ 72%	282 @ 4%	40 @ 400%	3 @ 600%
Young’s Modulus [MPa] at 23°C	75’000	2’500	4’000	150	0.5-2
Coefficient of Thermal Expansion (CTE) [ppm]	17	20	18	150	900
Thermal Conductivity [W/m*K]	390	0.12	0.2	0.19	0.15
Electric Volume Resistance [Ω*cm] at 23°C	1.7 E-6	1 E17	1 E18	1 E11-E13	1 E15

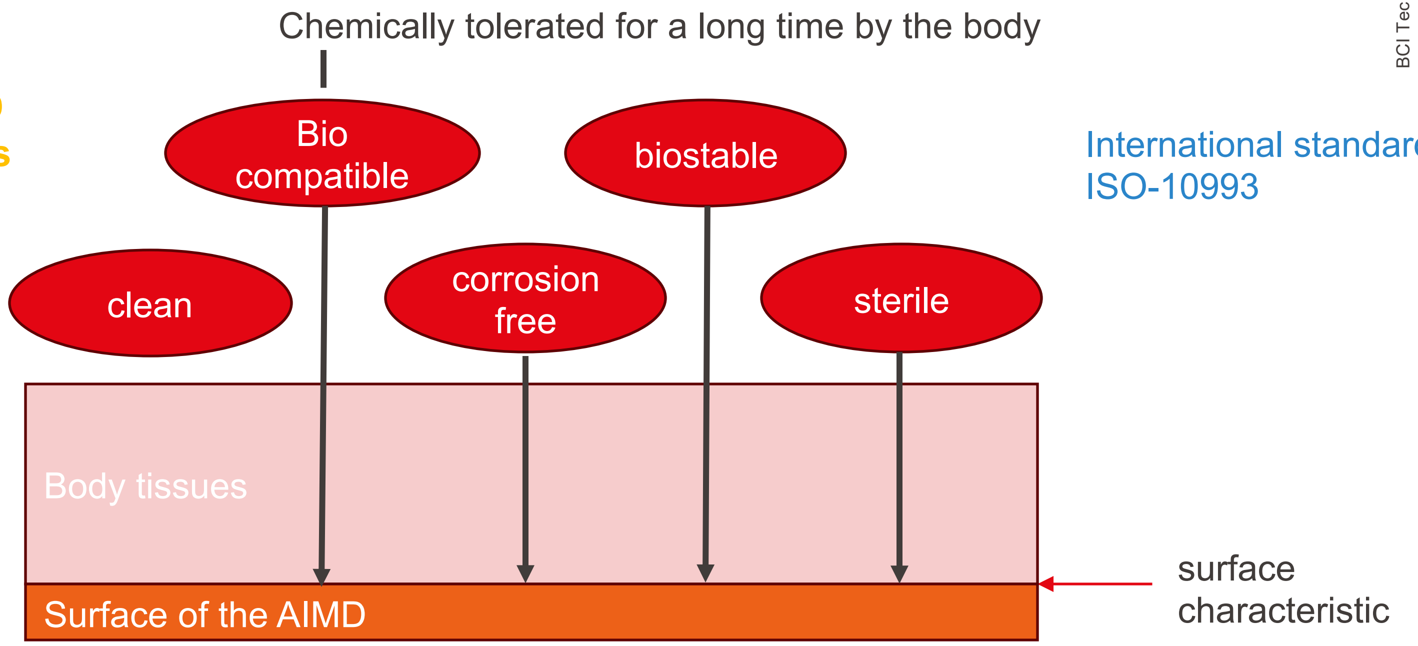
Peripheral nerves: ≈ 0.5 MPa
Brain cells: ≈ 0.01 MPa

Active Implantable Medical Devices AIMDs



Biocompatibility

On an assembled AIMD
Not individual materials



International standard ISO-10993

inert – resorbable - bioactive

Biocompatibility

- i.e. Compatibility with biology

- Not a simple concept. Biocompatibility is a property of a system when used in a specific way.

  → Are the materials toxic?
  → Is the geometry of the system affecting the physiological operation of the tissue?
  → Is the system assembly robust enough to avoid complications?
  → Is the use of the system safe?
  → etc.

- Just for easier understanding: many clinically approved implantable electrodes are made of Pt-Ir alloy.
  → BUT you cannot say “Pt-Ir” is biocompatible. How was your Pt-Ir formed? Where is it integrated? How is it going to be used?

- Biocompatibility is a system-level “property” and can only be verified by means of specific testing

Biocompatibility

ISO 10993 Standard

- The International Organisation for Standardisation (ISO)
  - Federation of national standards bodies
- The ISO 10993 International Standard pertains to:
  - Surface devices on the skin, mucosal membranes, breached or compromised surfaces.
  - External communicating devices with blood, tissue, bone, dentin.
  - Implantable devices.
- Its purpose is to protect humans and to serve as a framework for selecting tests to evaluate biological responses.
- In so doing consideration has been given to minimize the number and exposure of test animals.

Tissue Response to Materials (ISO 10,993)

- Cytotoxicity
- Sensitization
- Irritation
- Intracutaneous reactivity
- Systemic toxicity
- Subchronic toxicity
- Chronic toxicity
- Genotoxicity
- Implantation
- Hemocompatibility
- Carcinogenicity
- Reproductive and Developmental toxicity
- Biodegradation
- Immune system

Cell damage from materials, leachable agents – in vitro cell culture

Allergic reactions – test leachable agents in suspension Guinea pigs (skin, eye, mucosa)

Harmful and adverse effects from single or multiple Exposures – time period from 24h – 90 days/lifetime Mice, rats & rabbits.

DNA effects, gene mutation, chromosomal aberrations Rodents.

Local pathological effects – histological examinations Mice, rats, guinea pigs, rabbits – 12 weeks Dogs, sheep, pigs, calves – long term

Effects on blood and blood constituents (thrombosis, coagulation, platelets, hemtaology, immunology).

Tumor induction – major part of lifespan (polyethylene control)

Reproductive function, embryonic, pre/post natal development

Biodegradable material, biodegradation products

Immunotoxicity – function/structure/dysfunction Damage on implant

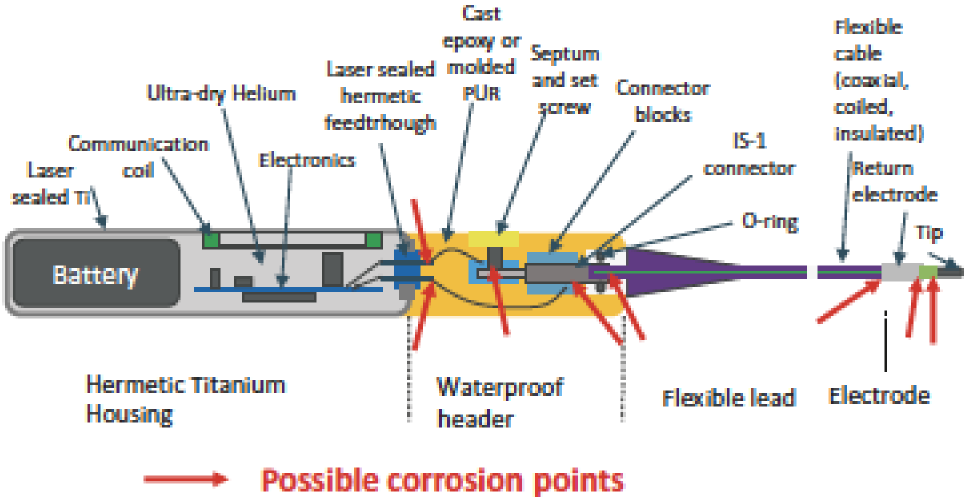
Biostability

- The body does not damage the implant
  - Linked to time scale
  - Dissolution in biological fluids
  - Residues and geometrical scale
  - Corrosion induced by the ionic composition of biological fluids
    - ✓ Noble metals
    - Avoid intermetallics and moisture
    - Never apply DC bias
    - Avoid gaps and cavities (fluid pockets)
    - avoid particle based polymers e.g. epoxies

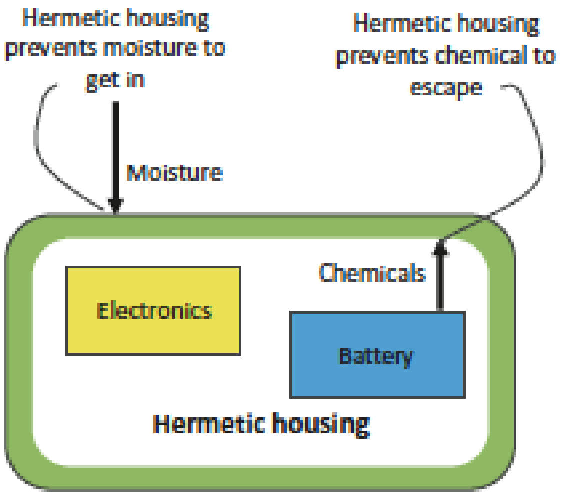
Corrosion

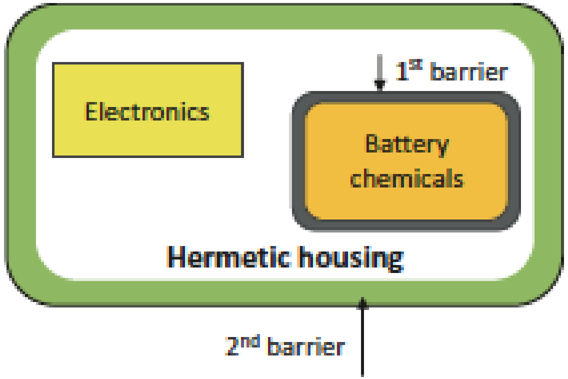
Human body: 37 ℃, 100% humidity and salty

➢ Complex electrochemistry

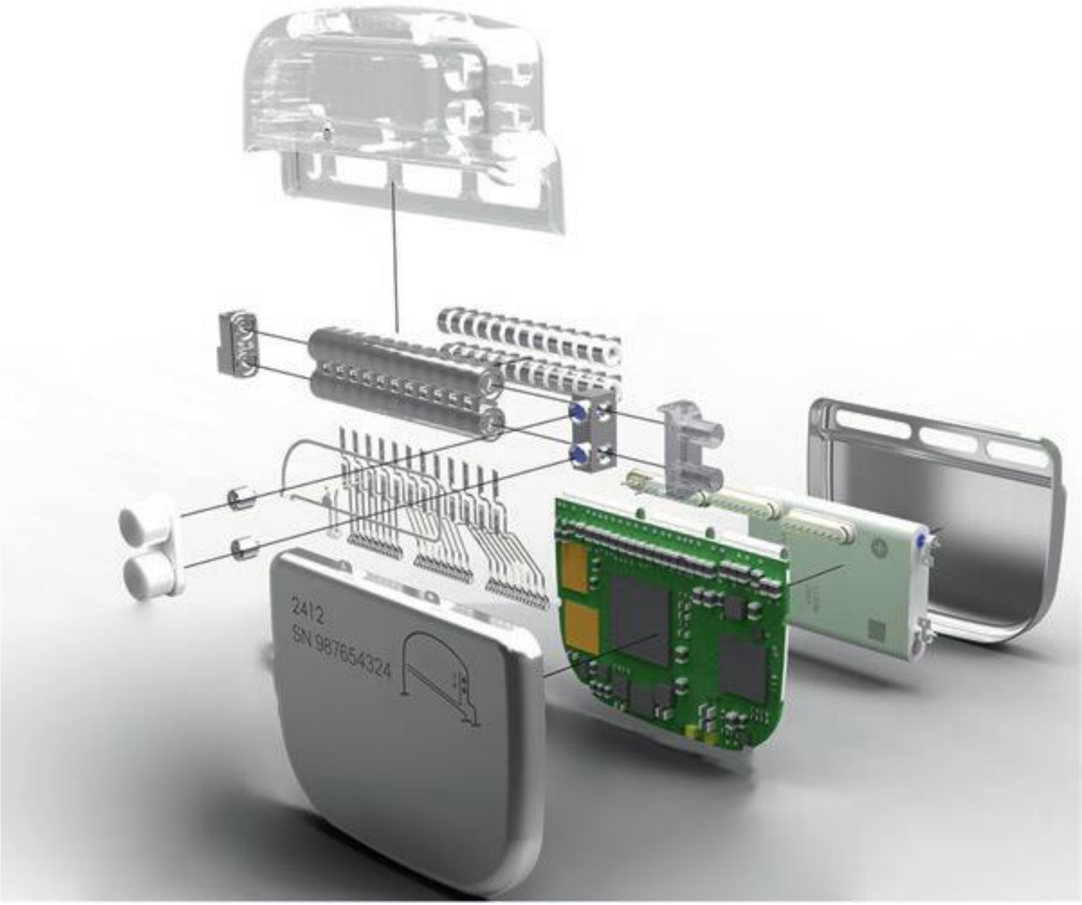


Hermetic housing





Hermetic packaging / clinical use



Ti casing

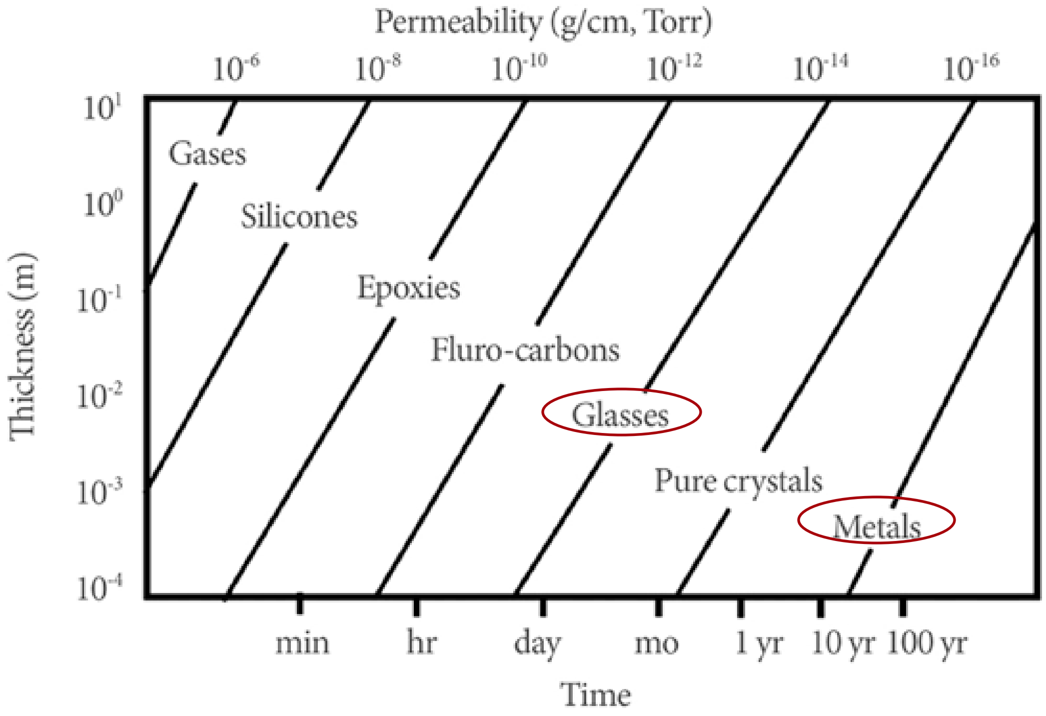
electronic components

4 single wire
FTs in a row

Hermeticity

- Standard for Class III medical devices: MIL-STD-883 Test Method 1014
  - the internal moisture content inside a cavity package must not exceed **5000 parts per million (PPM)** over the lifetime of the device.
  - Condensation will form inside a package held a 5℃ if there is a “dry moisture” level of 8000ppm

Hermetic packaging

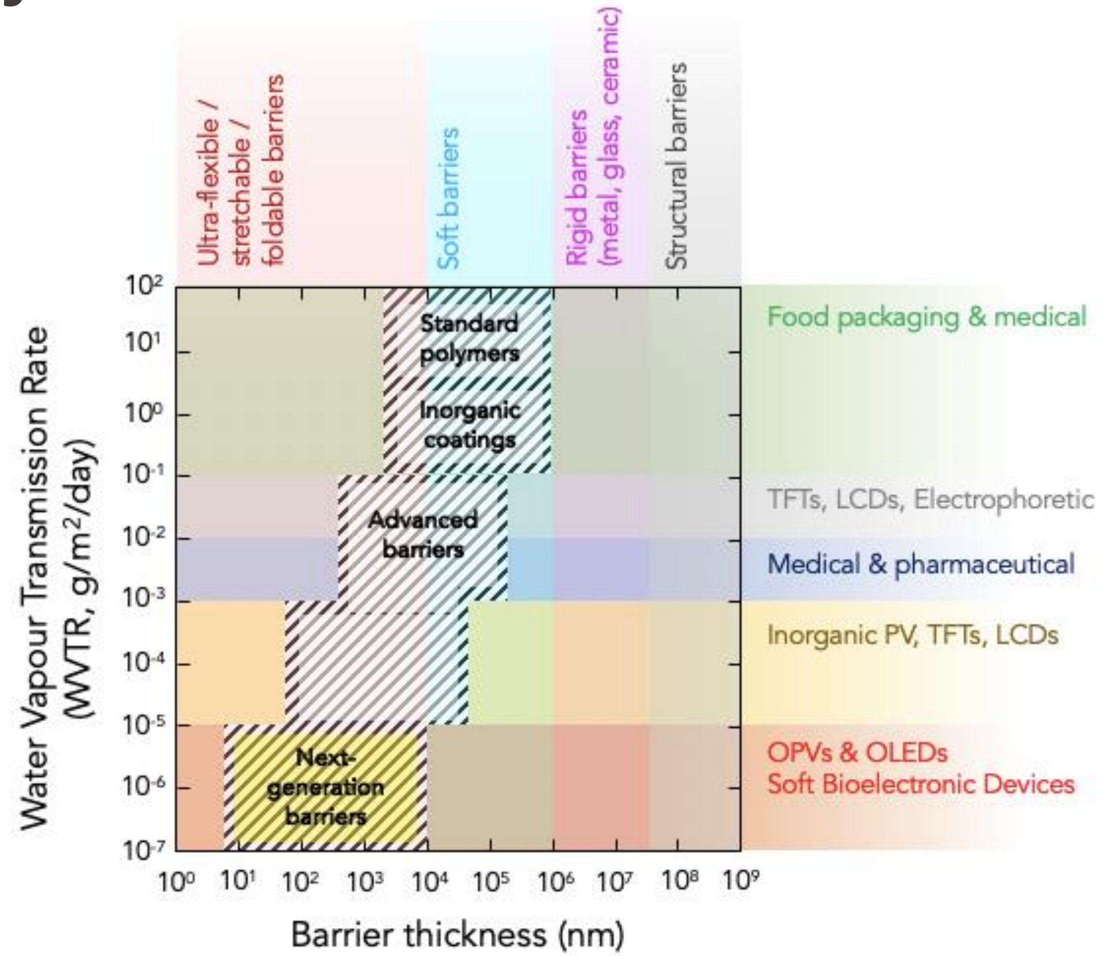


- **Permeability** is atypical metric for polymers
- Dense **titanium/alumina/glass** walls are effectively **impermeable** in normal use conditions
- Ingress happens through **defects/joints** (welds, brazes, feedthrough seals), not through the bulk.

Permeability

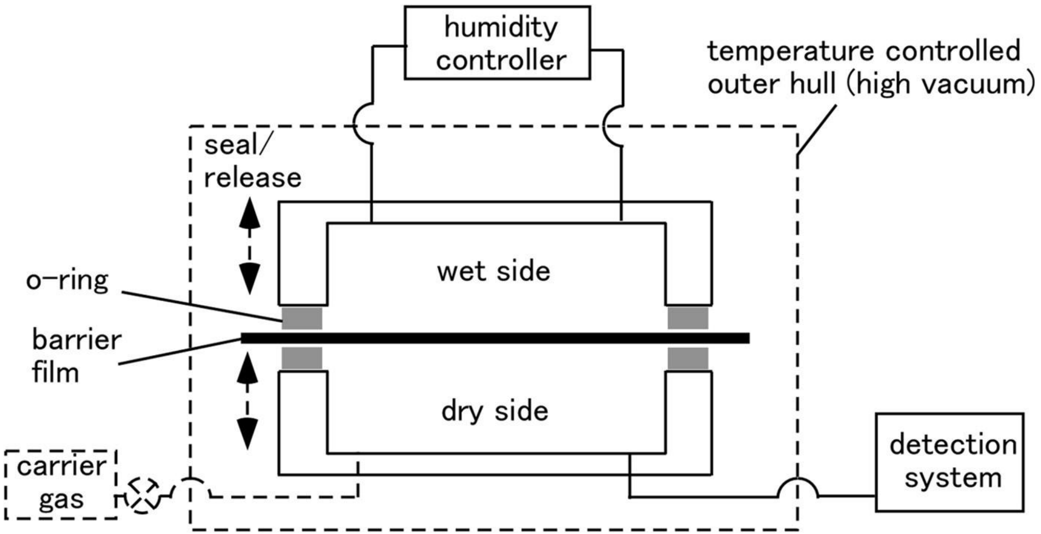
Permeability for vapor barriers

WVTR
Water vapor transmission rate
g/m²/day



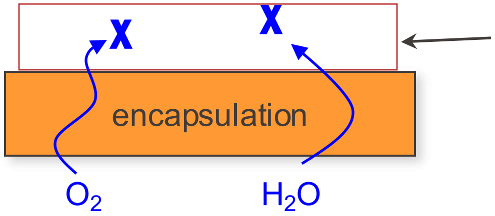
Measuring permeability

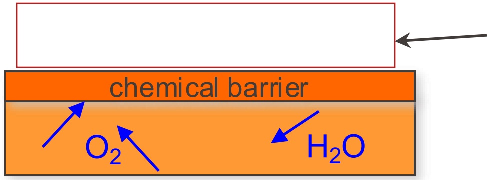
- Measure of temperature and humidity gradients across a given thickness of the encapsulation material(s)



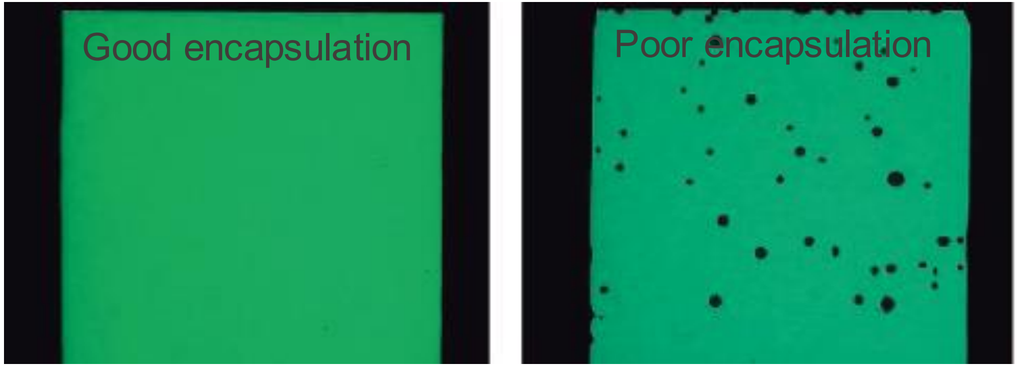
Scientific Reports **volume 6**, Article number: 35408 (2016)

An example of a poor hermetic encapsulation





- Illustration

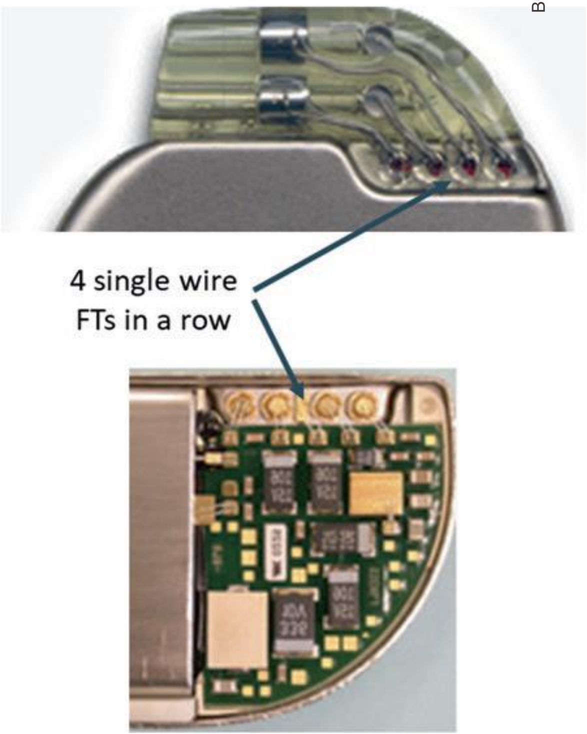


after 2,000h at 60°C and 90% humidity

From Komatsu Seiren

The challenge: Feedthroughs

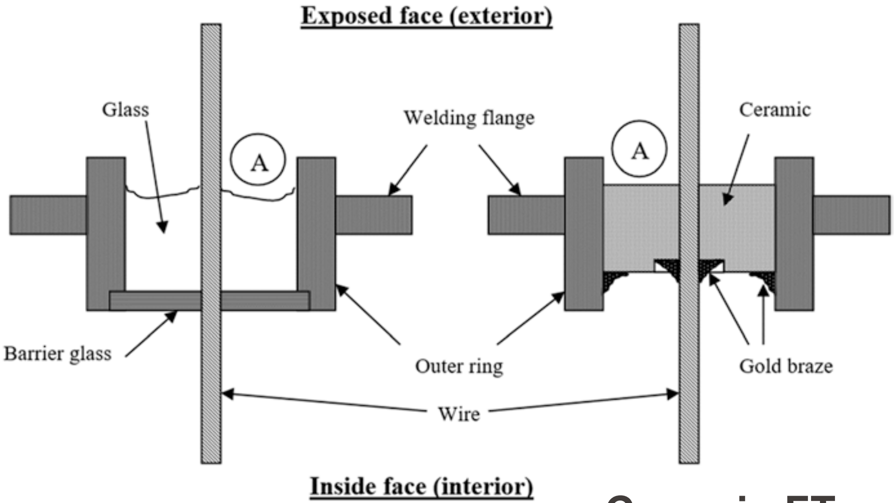
- Provide high electrical insulation (wires to casing)
  - $R >> M\Omega$, $I_{leak} << pA$
- Support high electrical conduction of signals
- Preserve hermetic seal
- Biostable
- Compatible with cleaning and sterilisation
- Integration with the casing
- Stable properties for > 1 decade of implantation



Two main technologies for feedthroughs

•**What they do:** Provide sealed electrical pathways from internal electronics to body-facing electrodes while preserving the device's hermetic barrier.

•**Core construction:** Ceramic-to-metal or glass-to-metal seals (e.g., alumina insulators brazed into titanium housings) with noble-metal pins (Pt/Ir, PtAu).



Glass FT

Ceramic FT

Cleaning!

•**Why cleaning matters:** Cleanliness during AIMD manufacturing prevents failures from organic/ionic residues and significantly boosts adhesion strength of metallizations (PtAu increased from **12.50 ± 3.83 MPa** to **21.71 ± 1.85 MPa**).

• **Notable option - "Leslie's soup" from UCL: Teepol-L 0.5 wt% + $Na_3PO_4 \cdot 12H_2O$ 2.5 wt% + DI water 97 wt%**. Or variations thereto.

•**Effect on surfaces:** "Leslie's soup" alone made contaminated ceramics highly hydrophilic (contact angle **< 10°**), whereas rinsing with only IPA + DI water left surfaces far less clean (**~76°** for flux, **~104°** for grease).

•**Residue management:** Follow-up IPA and DI-water steps (plus a DI ultrasonic bath) remove remaining organic and ionic residues (Na, P) introduced/left after the soup step; the full sequence avoids mechanical scrubbing while removing solder/flux.

Micromachines **2021**, *12*(2), 209; https://doi.org/10.3390/mi12020209

Sterility

- Remove most of biological contaminants
- Main remain even after various cleaning steps

- Step conducted on complete, assembled device

- Methods
  - Autoclave (121℃, saturated pressurized steam, 15-20min)
  - Gamma radiations (not for electronics)
  - Ethylene Oxide (gas)
  - Hydrogen peroxide (H_2O_2) (gas)

Summary

Neural tissues

- Anatomy
- Function

Cable/lead

- Insulation
- Multiple wires
- Flexibility and hermeticity

Electrodes

- Interface with tissue
- Impedance Z(f)
- Electrochemistry
- CIC and CSC

Feedthroughs

- Insulation & conductivity
- Unique link

Hermetic casing

- Permeability
- >10 years reliability