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Silicon Carbide for advanced in-vivo medical devices

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ICMA 2021
1st International Conference on Micromachines and Applications
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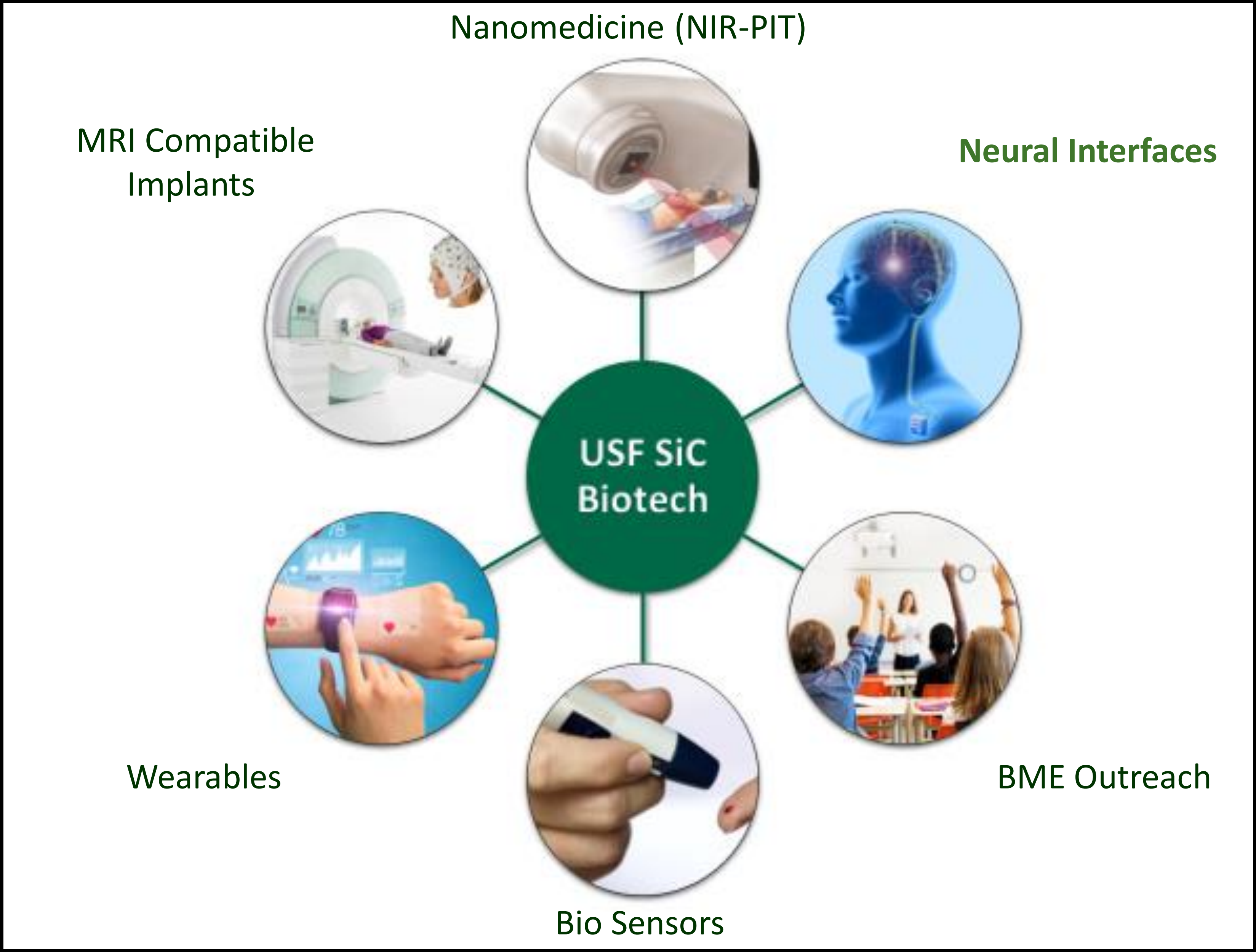

Nanomedicine (NIR-PIT)
MRI Compatible Implants
Neural Interfaces
USF SiC Biotech
Wearables
BME Outreach
Bio Sensors

Bionics –restoring human functionality

- Prosthetics
- Spinal cord repair
- Neural bridge

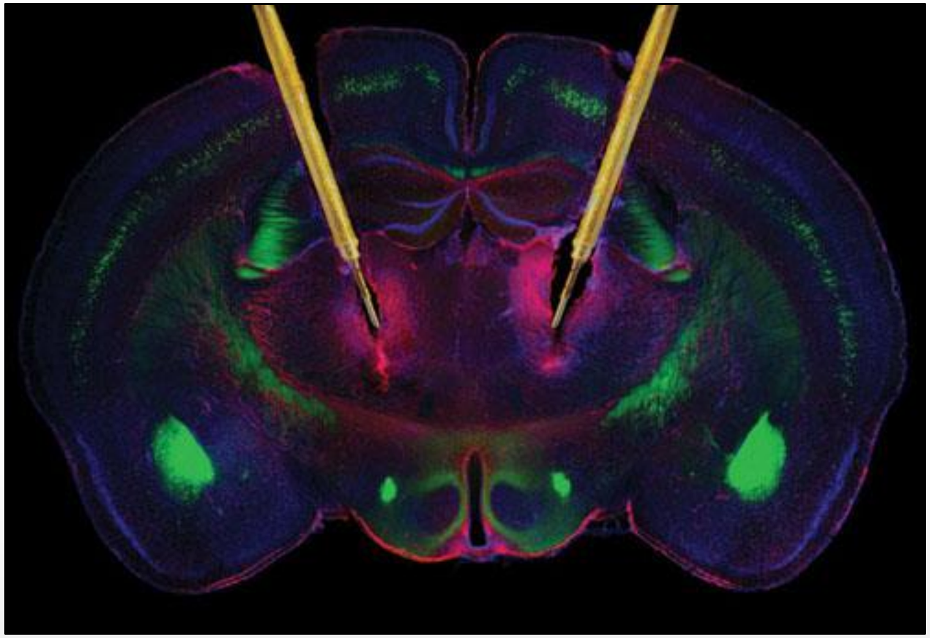
Playing piano with a mind-controlled robotic arm

Johnny will tell you the movement is slow → neural interface would allow more natural movements

Neural Interfaces face many challenges

Long-term in-vivo results in:

- Device failure (50% device failure)
- Tissue damage
- Loss of functionality/performance



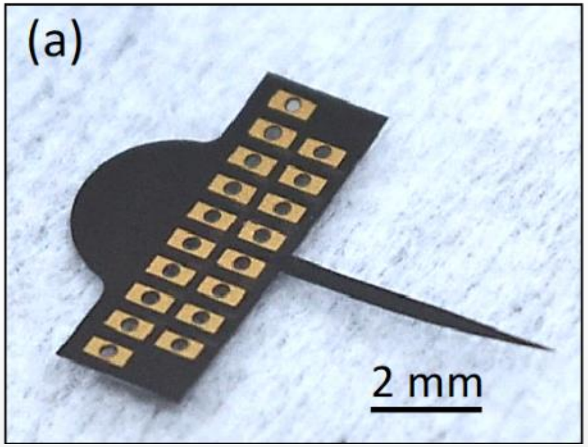
Severe tissue death with W probes

- Si arrays (Michigan and Utah) ~ 1-6 months
- Polymer arrays ~ 6-12 months
- Novel coatings ~ 4 years MAX
- A new strategy is clearly needed!
- Cubic SiC → excellent neuro and hemacompatibility
- In-vitro and In-vivo (1 month) data → solution?

In-vivo challenge – suitable materials for 25+ year operation in the human body

Monolithic 'All-SiC' INI a possible solution

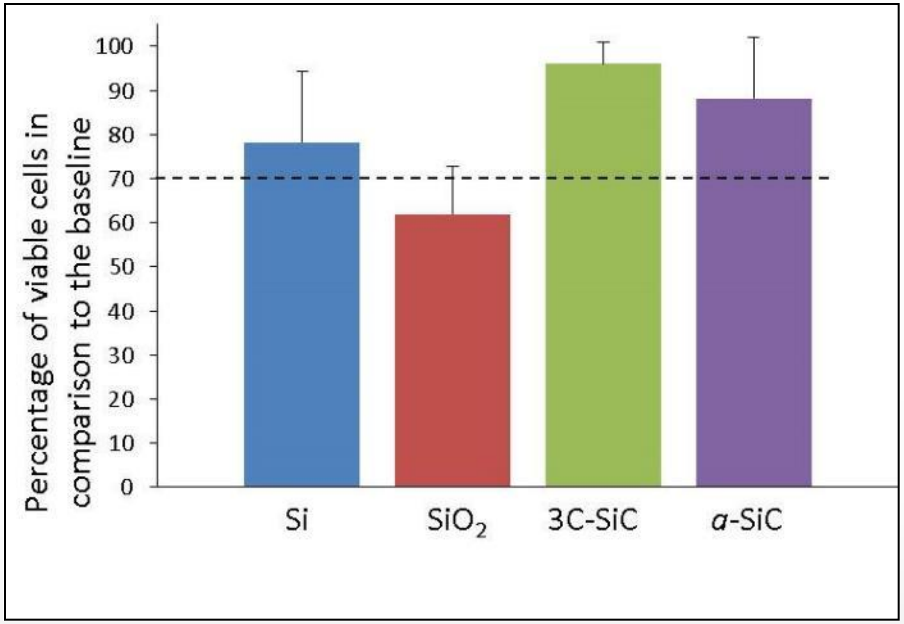
http://www.jhuapl.edu/newscenter/pressreleases/2016/160112.asp

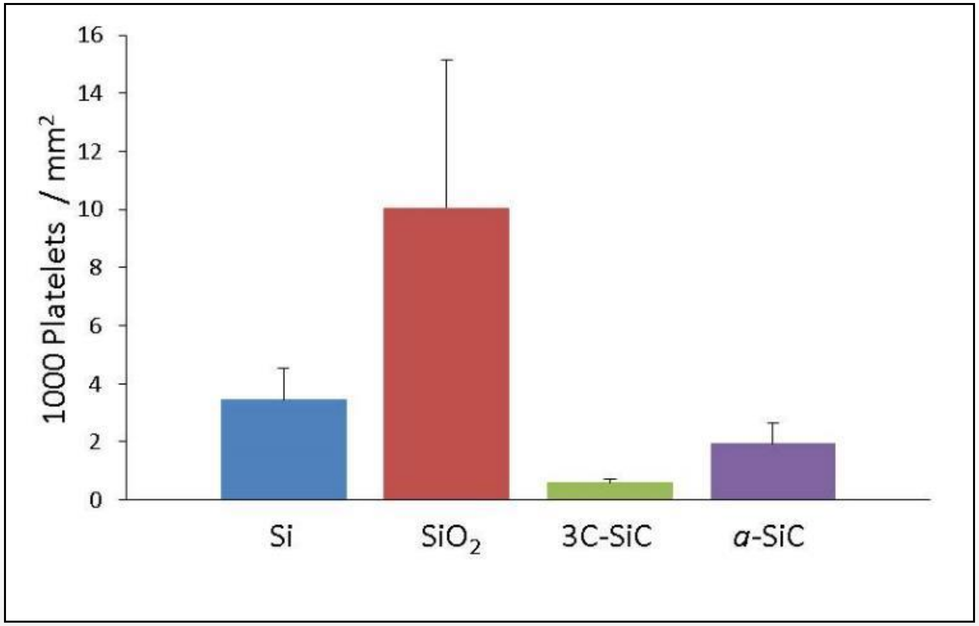


All-SiC neural probe to be packaged with an Omnetics 18 pin nanoconnector to a ZIF connector for animal testing

Osseo-integrated – lets integrate with a robust, long-term neural interface!

In-vitro performance





Biocompatibility

Hemocompatibility

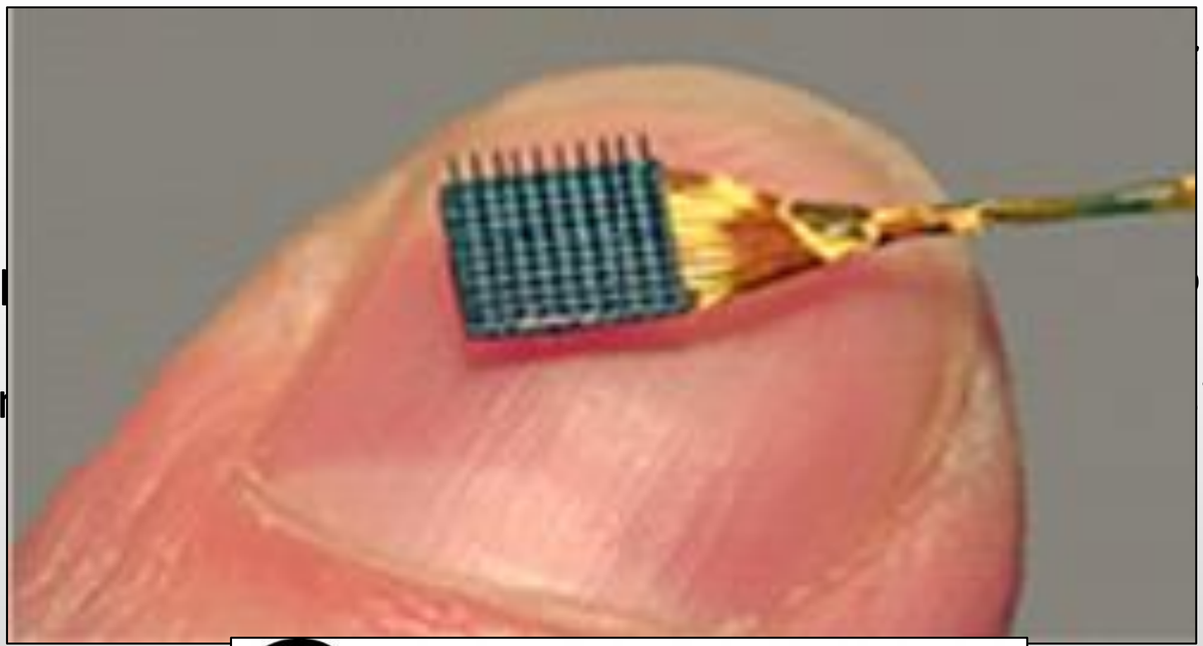
Only 3C-SiC passed all ISO 10993 tests (chem stability, bio- and hemo-compat.)

Saddow *et al,* IEEE NMDC, Catania, Sicily (IT) October 2014

SiC Intracortical Neural Interfaces (INI)

3C-SiC has properties useful for many biomedical devices, such as neural interfaces:

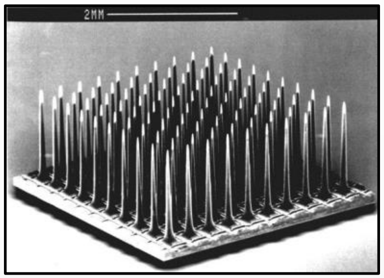
- 3X hard *surgical* ***trauma***
- Biocomp lyimide
- Can be r iC

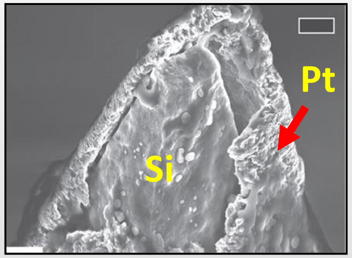


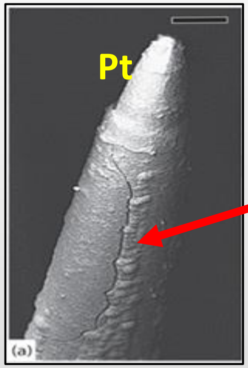
BLACKROCK® MICROSYSTEMS

Implantable Microelectrode Challenges

Utah Array







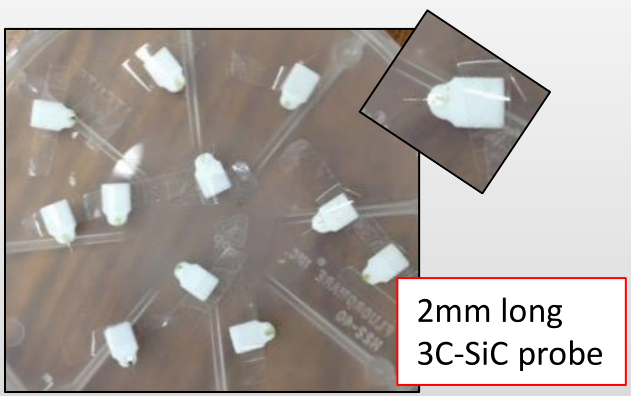
Single unit recordings not advantageous due to reliability challenges

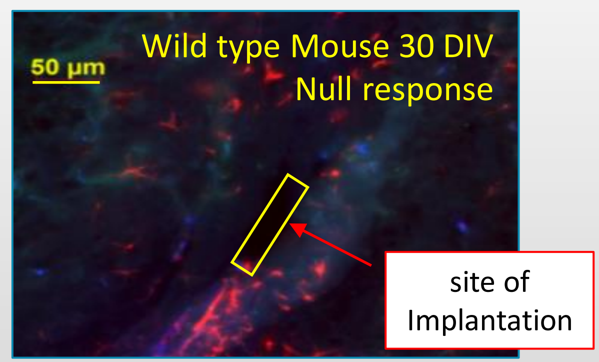
- Parylene C, Pt-Ir used for device insulation and conductors.
- Parylene C cracking/delamination Pt-Ir for micro-scaled devices has Limited current density

* [1] J. C. Barrese, J. Aceros, and J. P. Donoghue, "Scanning electron microscopy of chronically implanted intracortical microelectrode arrays in non-human primates," *J Neural Eng.,* vol. 13, p. 026003, Jan 29 2016.
.

Cubic SiC – Robust Microelectrode?

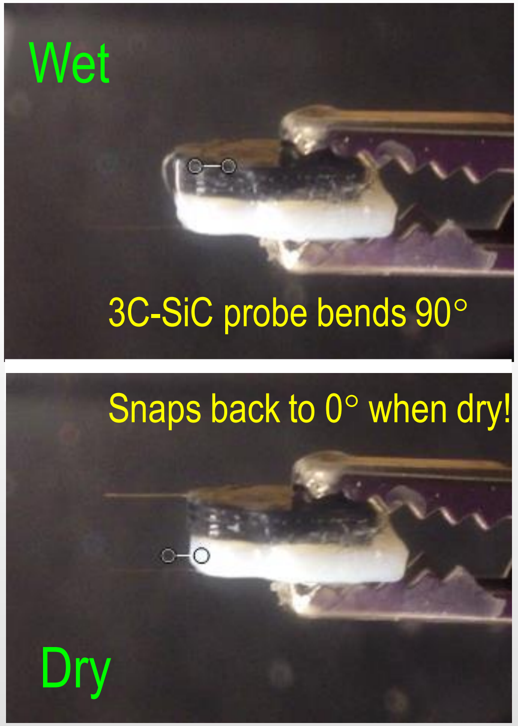
- SiC is a well-known chemically inert semiconductor:
  - Processed like Silicon (Neuronexus, etc.) → Microelectrode array (MEA) capable
  - Grown on Si wafers (low-cost) and micromachining/fab ~ identical to Si
  - Offers larger junction voltages (1.6 V vs. only 0.7V for Si) → simulation possible?
- No measured chronic inflammatory response in 2 animal models
- Multitude of solid-state forms:
  - Poly-crystalline and amorphous SiC (*a*-SiC which is an excellent insulator)
  - Single crystal polymorphs (hexagonal and cubic): 3C-SiC with 2.3 eV
  - Allows for microelectrode support, conductor and insulator in single material system





No Immune response in 3 animal models (Mouse, Rat, Pig) to date…

3C-SiC probes vs. coated Si probes



Si and 3C-SiC probes fabricated using same technology
3C-SiC 3X as hard and 3X as flexible:

Measured Mechanical Properties*

Material Type	Hardness [GPa]	Elastic Mod. [GPa]	Fracture tough. [$MPa \cdot m^{1/2}$]**
(100)Si	12.46 ± 0.78	172.13 ± 7.76	1.59 ± 0.21
(100)3C-SiC	31.19 ± 3.7	433 ± 50	4.6
Poly-3C-SiC	33.54 ± 3.3	457 ± 50	2.18

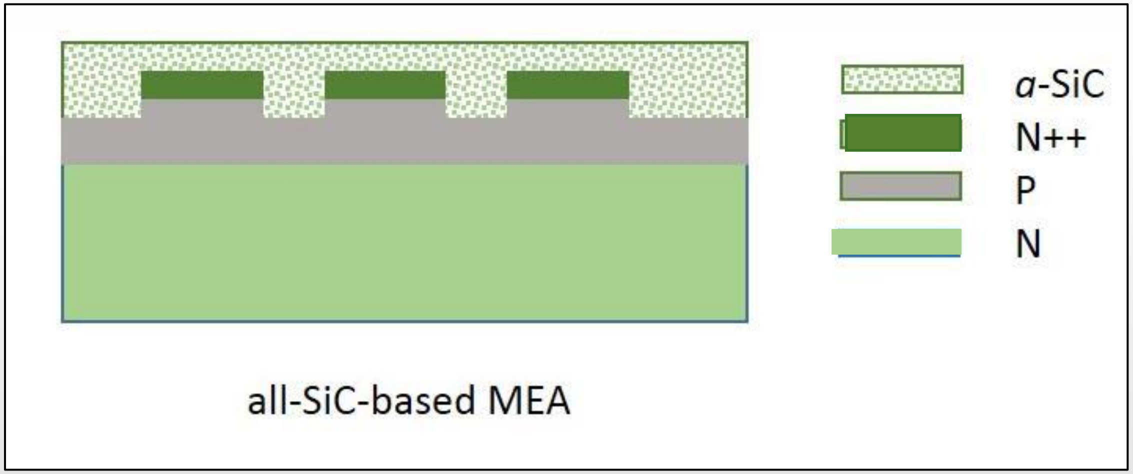
* Measured via nanoindentation.
** Crack lengths used to calculate the film fracture toughness.

Main advantage of 3C-SiC instead of polymer-coated Si is thinner probe thickness (**6 um vs. 15 um for Si**)

*C. Locke, G. Kravchenko, P. Waters, J. Deva Reddy, A. A. Volinsky, C. L. Frewin, S. E. Saddow, ECSCRM ‘08

Monolithic All-SiC MEA: a robust solution

- In all-SiC technology, a pn diode blocks current flow and an amorphous SiC (*a*-SiC) insulator caps the metallic-like electrodes:

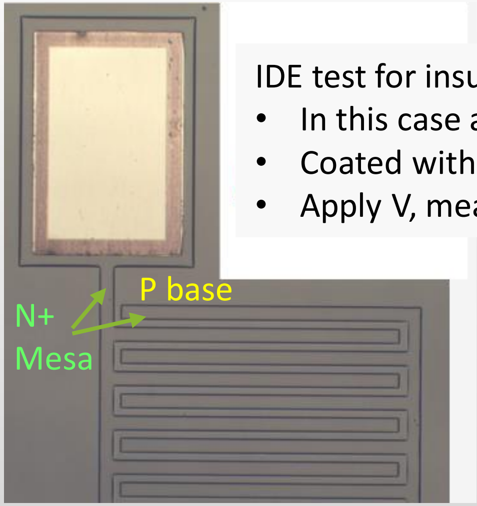


No metals or plastics → robust SiC only

How does this work?

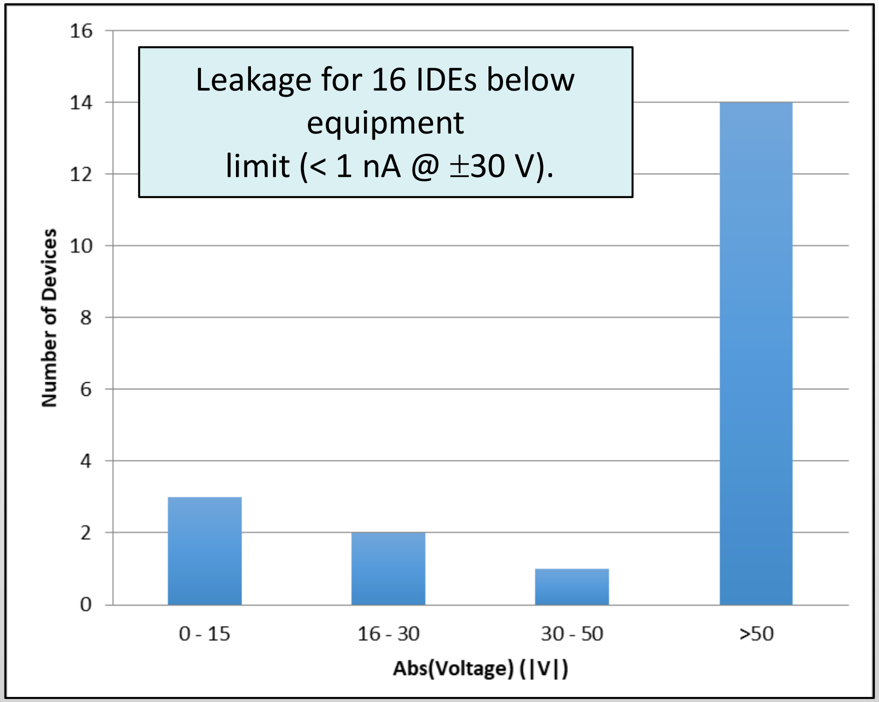
- Degenerately doped semiconductors → semi-metallic conduction
  - no need for metal electrodes to carry bi-directional signals
- Metal electrodes, such as PtIr, typically processed to form ceramic-like properties
  - 3C-SiC is already a ceramic
- *a*-SiC is highly insulating
  - All-SiC materials integrated to create a monolithic device

All-SiC IDE

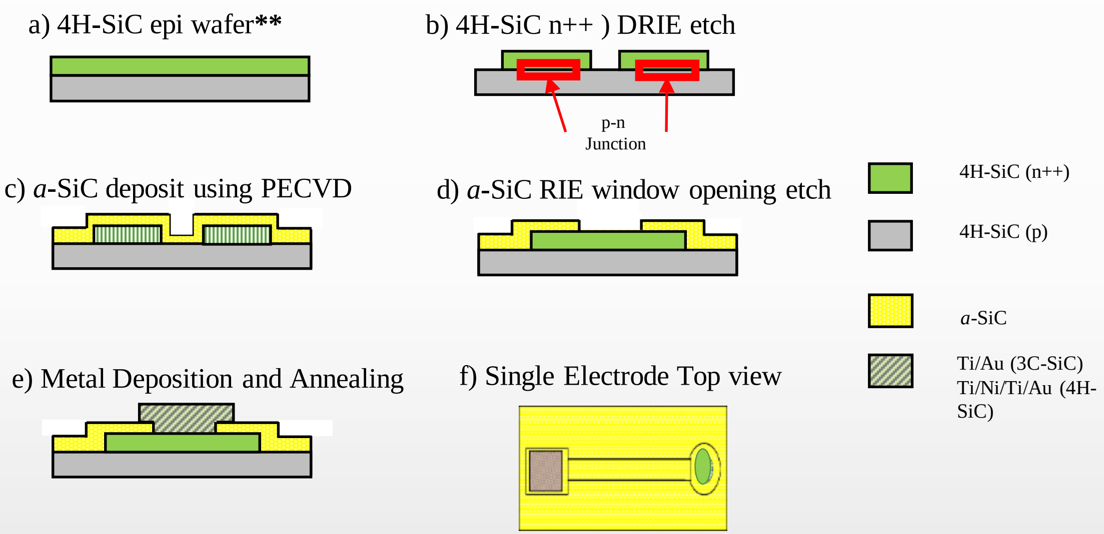


IDE test for insulation

- In this case also isolation
- Coated with *a*-SiC
- Apply V, measure I

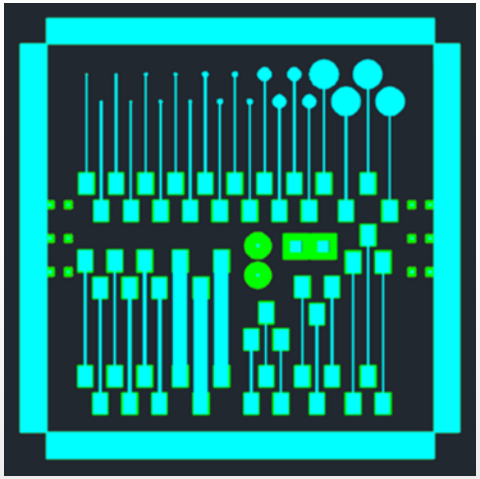


All-SiC INI Fabrication flow



Fabrication flow (a through f) for 4H- all-SiC planar neural microelectrode.

Fab for 3C-SiC devices identical with underlying Si substrate.



Planar MEA

Single ended electrodes

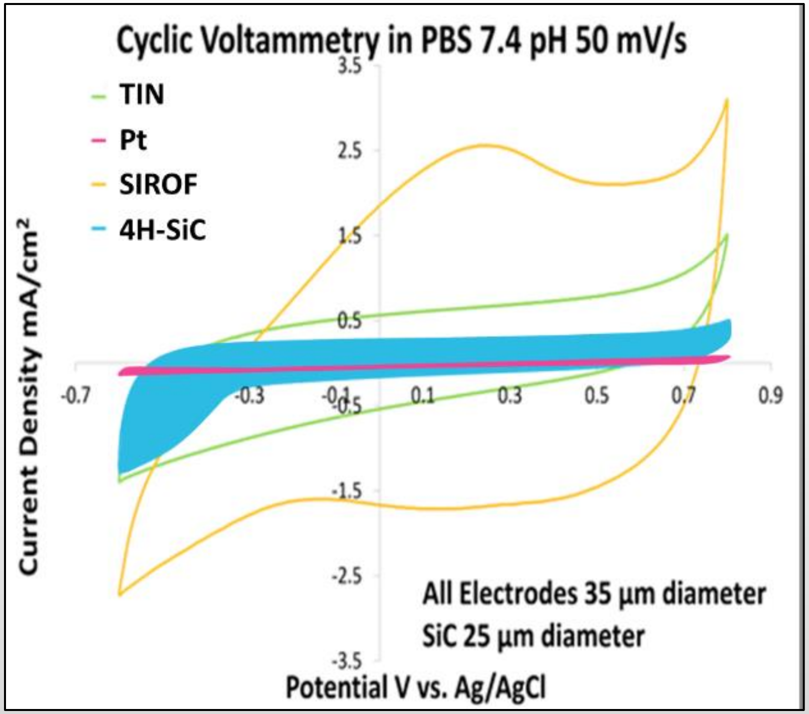
Double ended resistors

PN Diodes

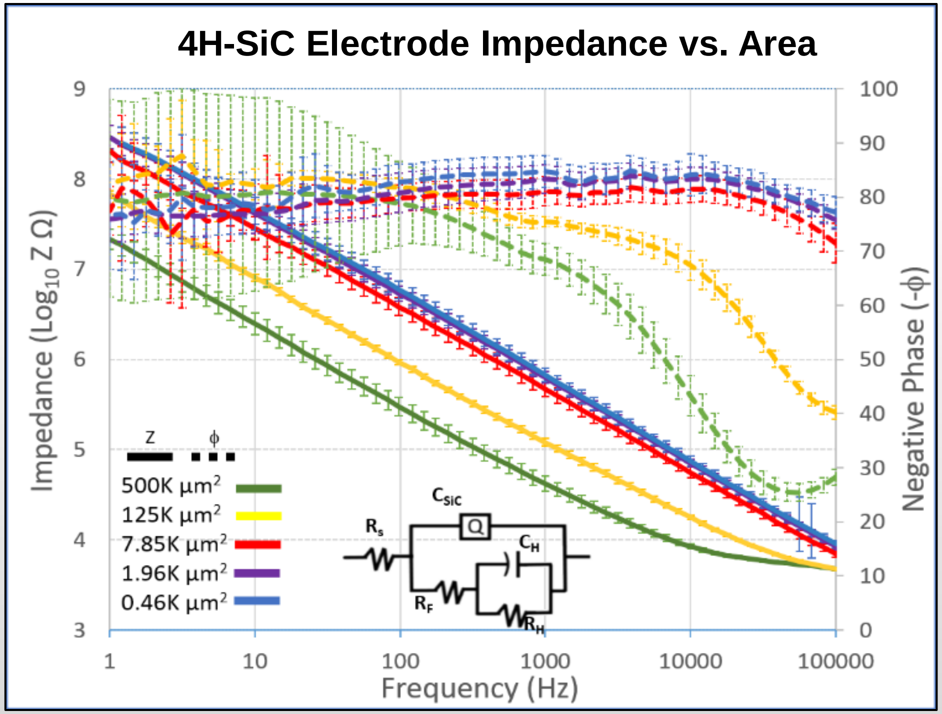
Bernardin, E.K.; Frewin, C.L.; Everly, R.; Ul Hassan, J.; Saddow, S.E. Demonstration of a Robust All-Silicon-Carbide Intracortical Neural Interface. *Micromachines* **2018**, *9*, 412. https://doi.org/10.3390/mi9080412

Electrochemical Performance

- Impedance and cyclical voltommetry performed
- Planar all-SiC MEA consistently displayed electrode-like performance
- Dependence on electrode tip area studied
- Capacitive characteristic, as expected, observed



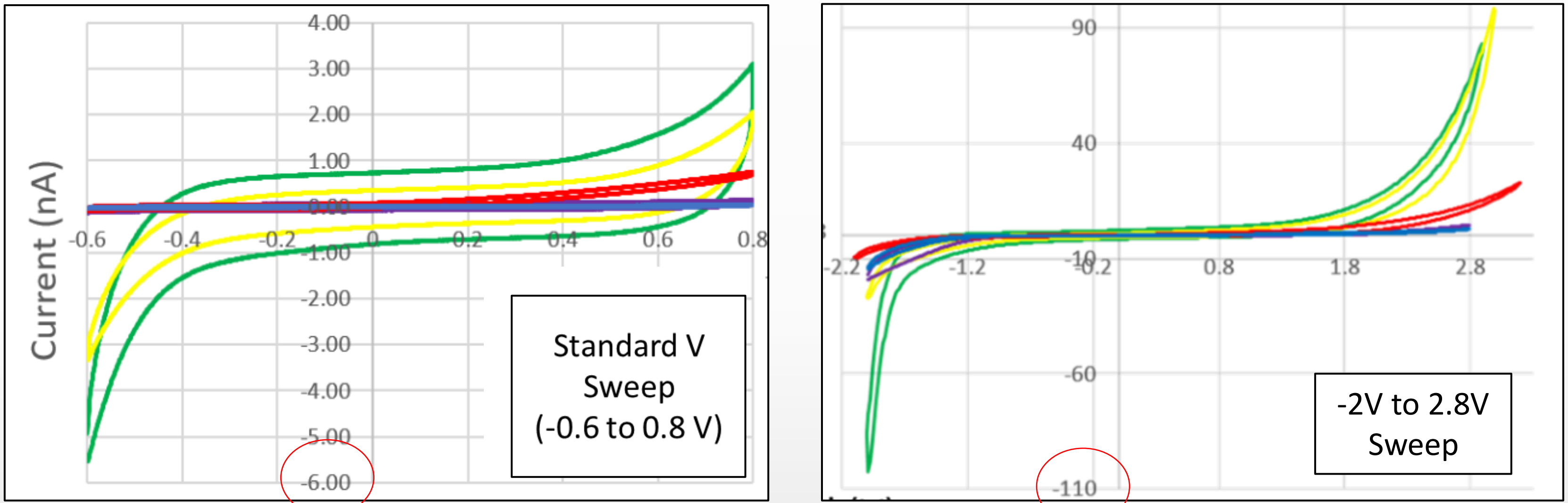
4H-SiC performed better than Pt electrode



|Z| ~675kΩ (496 μm²) and ~46kΩ (500K μm²)

Electrochemical Performance

4H-SiC Electrode CV vs. Area



Note scale difference

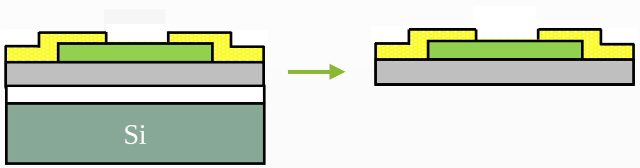
500K μm^2
125K μm^2
7.85K μm^2
1.96K μm^2
0.46K μm^2

Increasing recording/stim tip area decreases Z and increases Charge capacity, as expected.

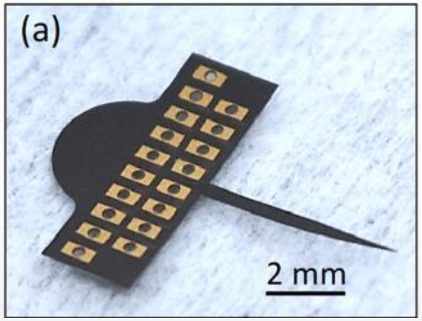
Advantages of Cubic SiC over 4H-SiC

- Biggest challenge is removal of the substrate for implantable MEA's
- One solution is to grow 3C-SiC on SOI → oxide release layer
- Films grown at IMM-CNR (Catania)
- Allows for integration with electronics (Si) on tab.

All-SiC (3C-SiC) Device on SOI



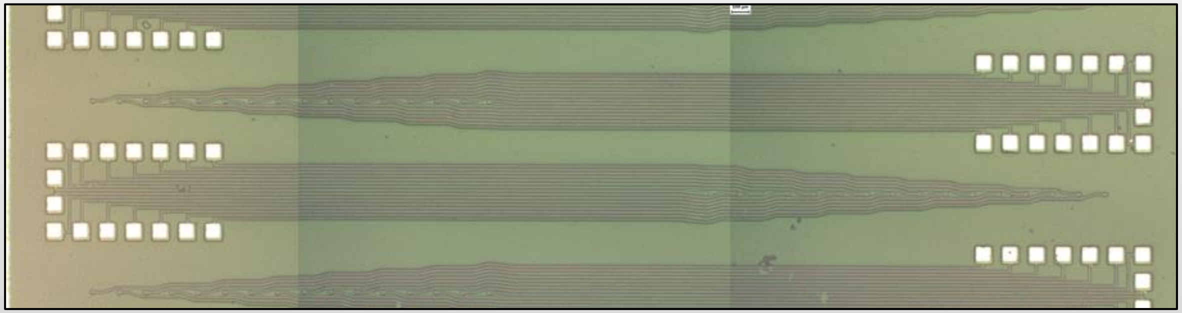
Probe release (HF)



Shank → 5.1 mm long

Tab → 6.64 x 2.3 mm

Newest 16 electrode Monolithic 3C-SiC Implants

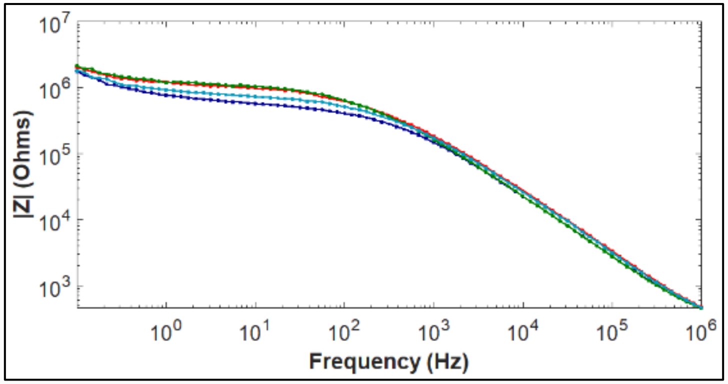


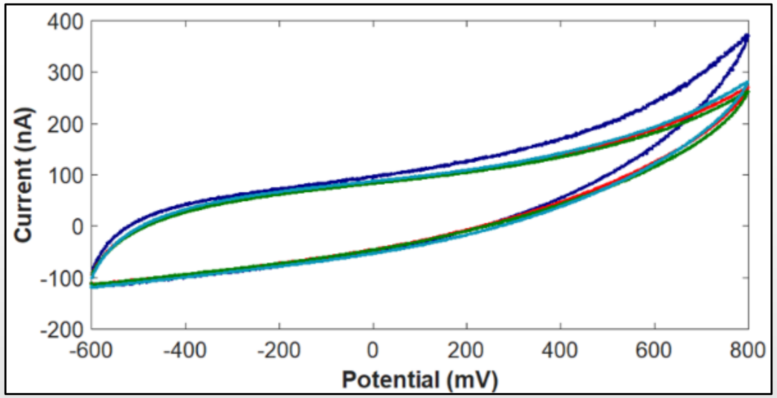
Beygi, M., et al, "Fabrication of a Monolithic Implantable Neural Interface from Cubic Silicon Carbide."
Micromachines, **10** (7), p.430 2019

Fabrication of a Monolithic 3C-SiC/SOI Implantable Neural Interface

EIS & CV measurements

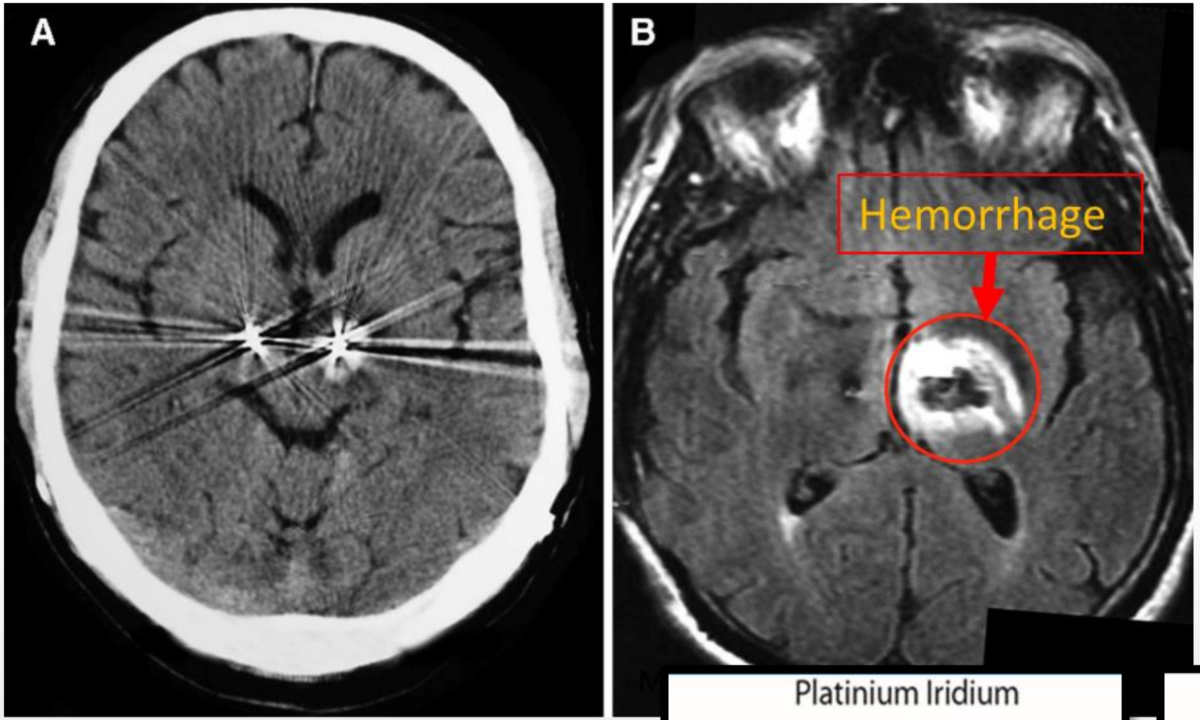
- Results of 4 microelectrodes
- Average of 3 replicates
- |Z| @ 1kHz → ~165 kΩ
- Electrode-electrolyte shows a predominantly capacitive behavior
- Rate of 50 mV/s



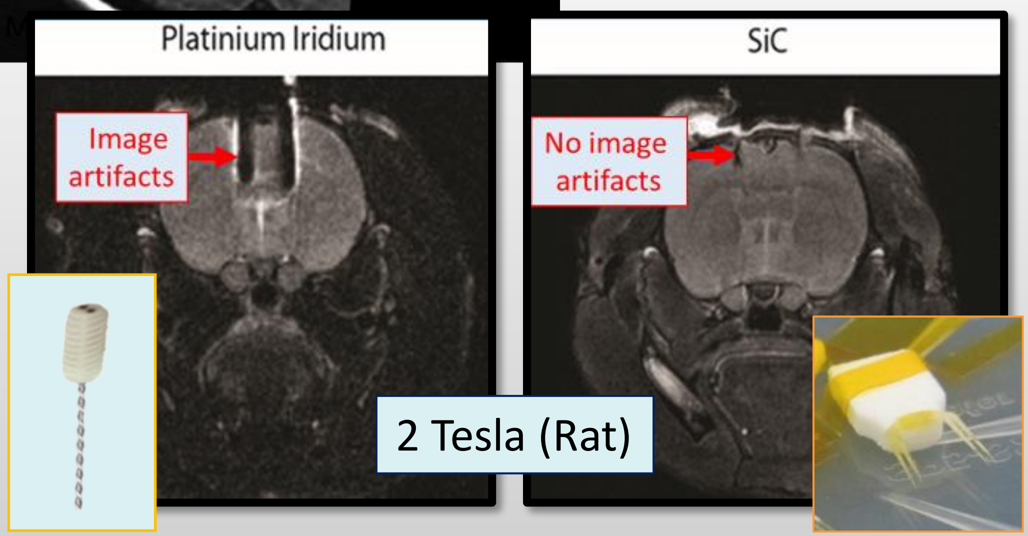


	Anodic	Cathodic
Average Charge Storage Capacity (mC/cm^2)	15.4 ± 1.46	15.2 ± 1.03
Average Charge Per Phase (nC)	75.4 ± 5.06	74.8 ± 5.06

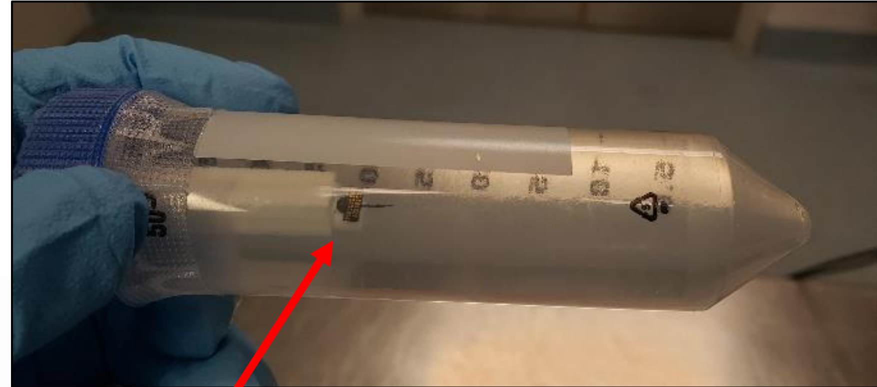
MRI compatible neural interfaces



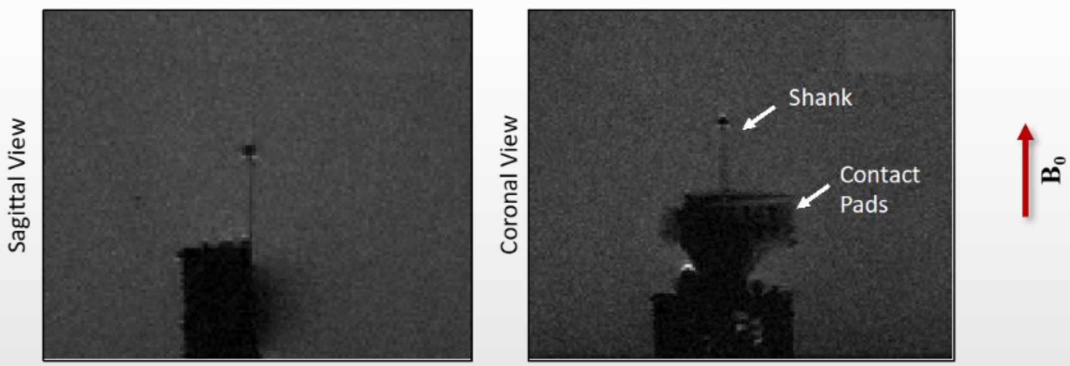
Left: Dual-shank MRI compatible PtIr electrodes (12.1 mm L, 160 μm diameter)
Right: 3C-SiC dual passive probe (7mm L, 15 μm thick, ~ 1015 n-doped)



MRI Images @7T

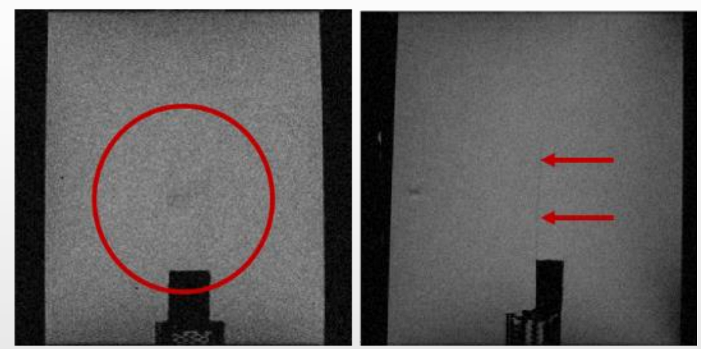


- Even a thin (~27 um) Si layer results in noticeable image artifacts
- All-SiC free-standing probe displays no artifact @7T and is barely visible!



All-SiC INI

(Si device layer)



Free-standing *All*-SiC INI

No Si device layer

Beygi, M.; Dominguez-Viqueira, W.; Feng, C.; Mumcu, G.; Frewin, C.L.; La Via, F.; Saddow, S.E. Silicon Carbide and MRI: Towards Developing a MRI Safe Neural Interface. *Micromachines* 2021, **12**, 126. https://doi.org/10.3390/mi12020126

Summary

- Silicon Carbide is highly neuro-compatible
  - In-vitro and in-vivo (3 animal models) → no immune system trigger
- It is possible to create a monolithic INI with only SiC
  - No plastics (polymers) or metals to degrade in-vivo
  - Use of PN junction substrate isolation
  - Use of amorphous SiC capping layer
    - IDE data shows greater than ± 50V breakdown (I < 1 nA) in 4H-SiC devices
- 3C-SiC on Si and SOI promising to allow for low-cost manufacturing
  - SOI → HF dip probe harvest
  - Higher CSC than 4H-SiC but with higher leakage current (Gen 1)
  - Gen 2 fabricated – packaging and testing pending
- Preliminary MRI compatibility testing in tissue phantom @7T
  - No visible image artifacts (SiC only)
  - Numerical modeling → below SAR limit (not presented)
  - In-vivo confirmation planned (summer 2021)

Acknowledgments

SiC Bio/Materials Studies
C. Coletti (Tissue)
N. Schettini (Blood)
C. Frewin (Brain)

Glucose Sensing
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Biosensors
S. Iannota, IMEM-CNR
R. Bange, E. Bano, V. Stambouli (DNA)

Simulations
M. Beygi

Deep-Tissue Cancer (NIH R21)
P. Choyke, NCI (Bethesda)
A. Gali, Wigner (Budapest)
G. Salviati, IMEM-CNR (Parma)

Implantable Neural Interfaces
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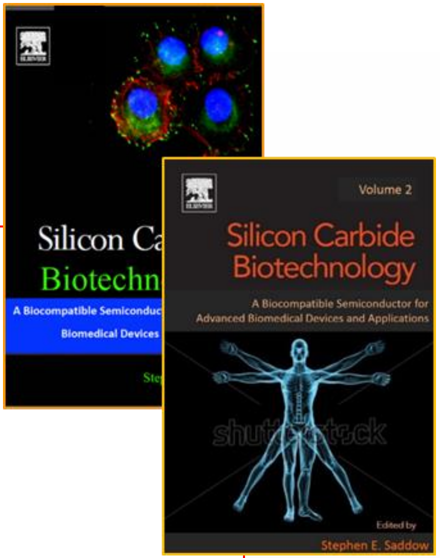
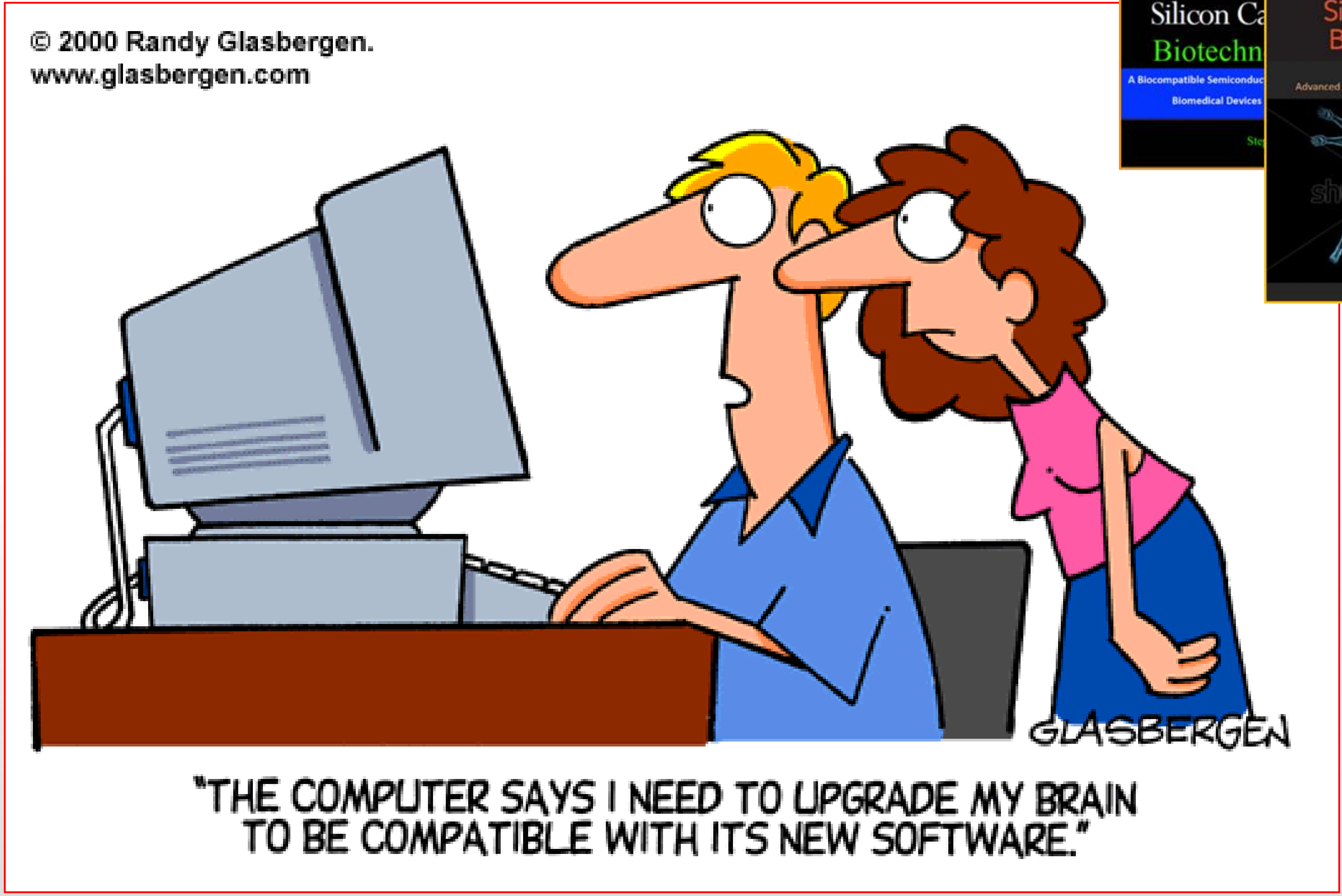
Our team at USF

Spring 2020

USF Silicon Carbide Biotechnology Group

Thank you for your kind attention!





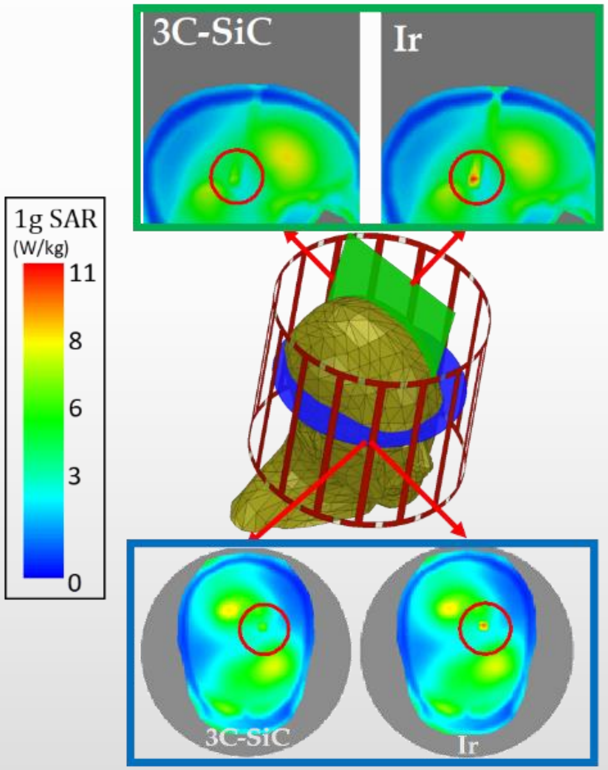
Prof. Dr. Saddow Overview

- PhD in Electrical Engineering (electrophysics) 1993 (Uni of Maryland)
- Professor of Electrical and Medical Engineering, Uni of South Florida, Tampa, FL
- Develop silicon carbide (SiC) materials and devices for biomedical applications
  - Neural interfaces: Bionics, BMI, etc.
  - In-vivo sensors: blood, etc.
  - Bioelectronics: wearable sensors (wireless sleep, personal locator beacon, etc.)
  - Nanotechnology to treat deep-tissue cancer

- Innovation comes when you work at the nexus of different technologies/fields of endeavor
- In my case EE, physics, chemistry, medicine, material science, mechanics…

Simulation of INI Materials – Brain Phantom

Induced heating caused by interaction with MRI fields → tissue damage



Simulated SAR* vs. implant probe material

Material	SAR (W/kg)			
	Whole Head	Inside the box		
		Max 10 g	Max 1 g	Max 0.1 g
Ref.	2.55	5.83	6.68	7.28
All-3C-SiC	2.54	5.91	7.16	21.15
3C-SiC Tip	2.55	5.87	6.75	7.32
iridium	2.55	6.01	10.82	39.24
titanium	2.54	5.98	9.51	32.73
platinum	2.54	5.97	10.36	37.05
IrO_2	2.55	6.00	9.39	32.19
TiN	2.55	5.98	8.87	30.04

*SAR Specific Absorption Rate (W/kg)

Simulation of INI Materials – Brain Phantom

Image Artifacts caused by interaction with MRI fields → difficult to 'see' detail near INI

- Estimated ΔB_0 caused by $\Delta\chi$
- Assumed B0=7 T
- FOV=256×256 pixels
- Voxel size 1mm×1mm×1mm
- Max ΔB_0=100μT & Min ΔB_0=-0.3μT
- Averaged χ from literature

1) 3C-SiC
2) Si
3) Pt