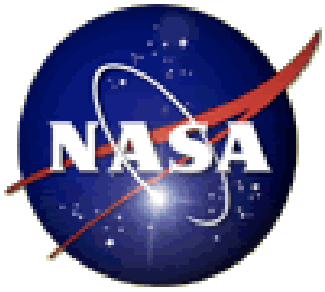


Carbon nanofiber nanoelectrodes for neural stimulation and chemical detection The era of “smart” deep brain stimulation

Jessica E. Koehne

NASA Ames Research Center

Moffett Field, CA

Biosensor Motivation

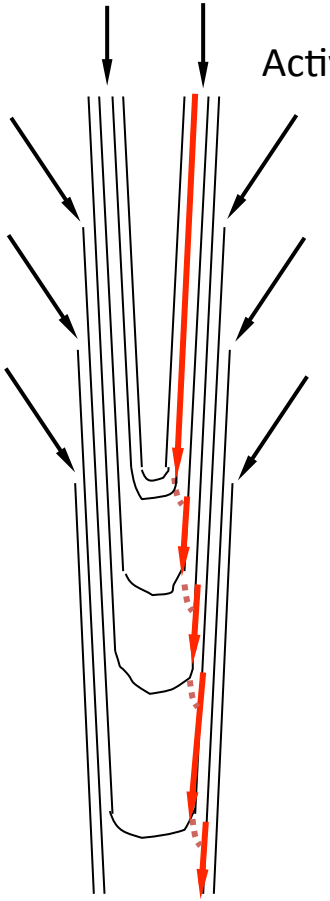
NASA Applications

- Astronaut health monitoring
  - Lab-on-a-chip
- Water Quality monitoring
  - Pathogen detection on ISS and long duration missions
- Planetary exploration
  - Life on other planets

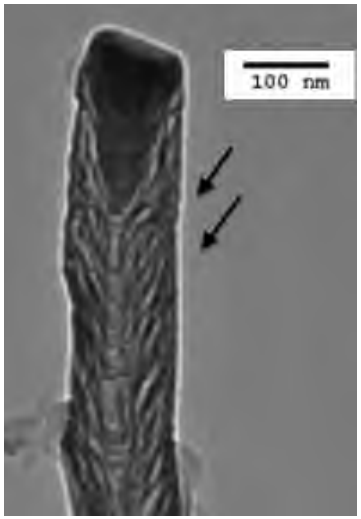
Outside Applications and Customers

- Medical Diagnostics
  - NIH, DARPA
- Environmental Monitoring
  - EPA, NIH
- Biowarfare agent detection
  - DHS, DARPA
- Food Safety
  - FDA

What are Carbon Nanofibers (CNFs)?

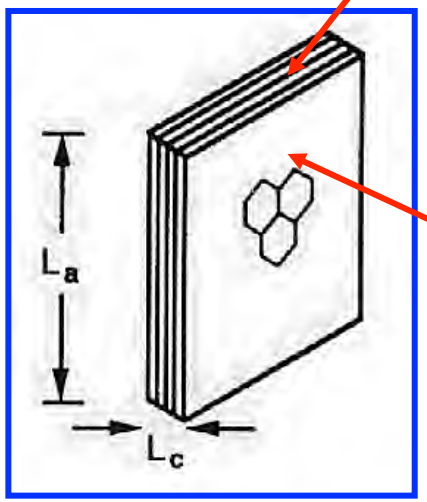


Bamboo-like CNFs



TEM of CNF

HOPG



Edge Plane:

(1) High electron transfer rate (~ 0.1 cm/s)

(2) Very high specific capacitance (>60 μF/cm^2)

Basal Plane:

(1) Low electron transfer rate (< 10^{-7} cm/s)

(2) Anomalously low capacitance (~1.9 μF/cm^2)

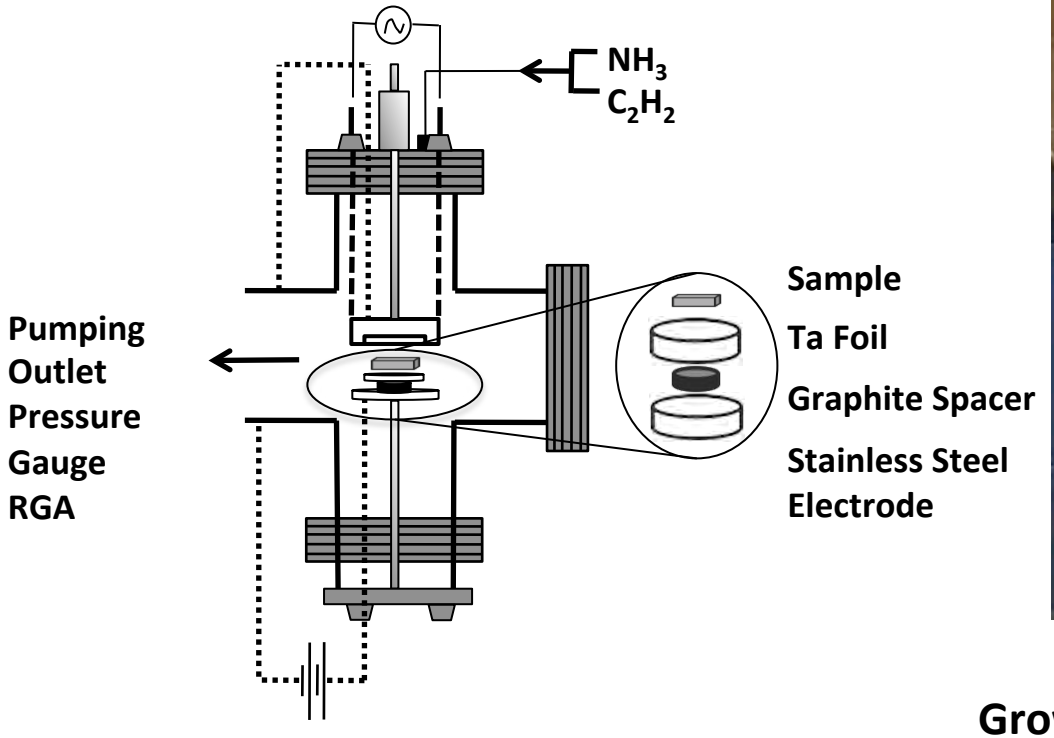
R. L. McCreery, A. J. Bard, in *Electroanalytical Chemistry*, Ed., 1991, 17, 221.

Why CNF as biosensor electrode material?

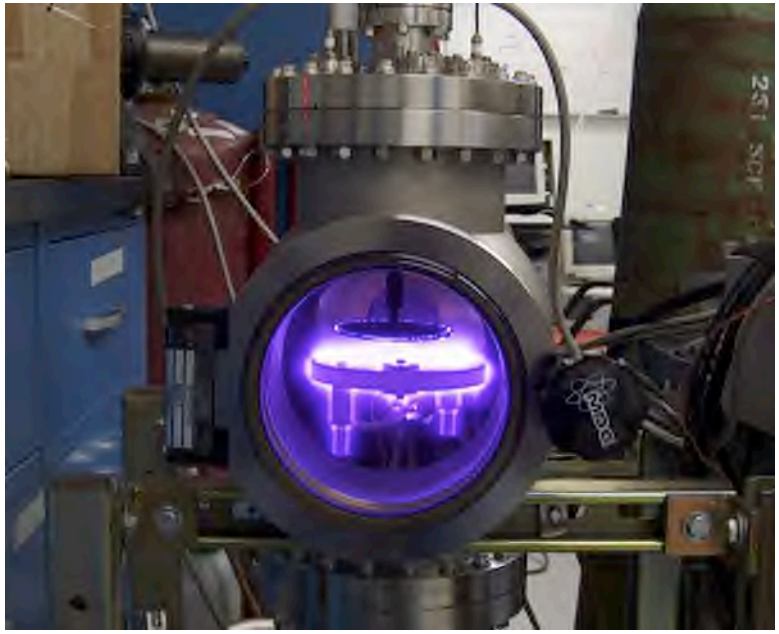
1) Good conductivity
2) Wide potential window
3) Many active sites for electron transfer
4) Easy to pattern, grow and process on silicon devices

CNF Growth by Plasma Enhanced Chemical Vapor Deposition (PECVD)

PECVD Reactor Schematic



Custom Built PECVD Reactor

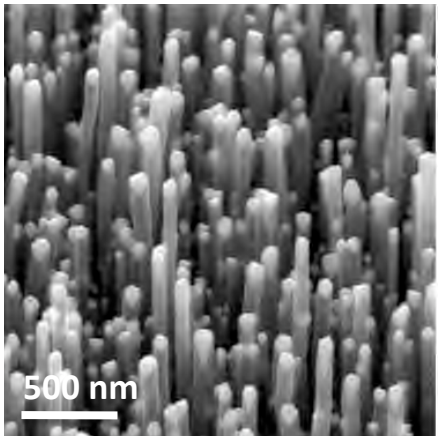
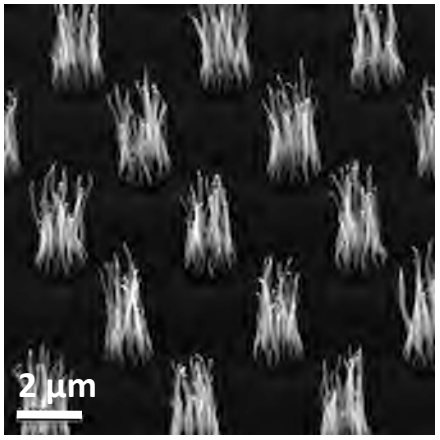
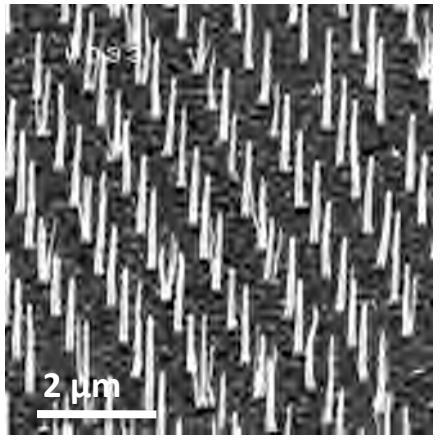
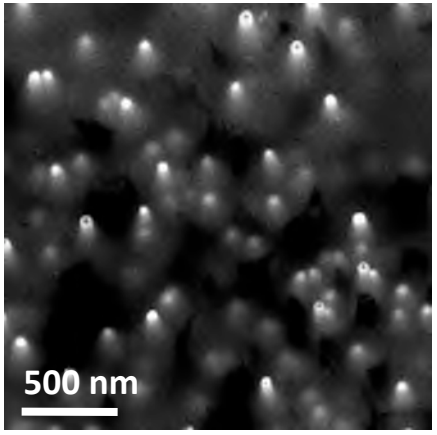
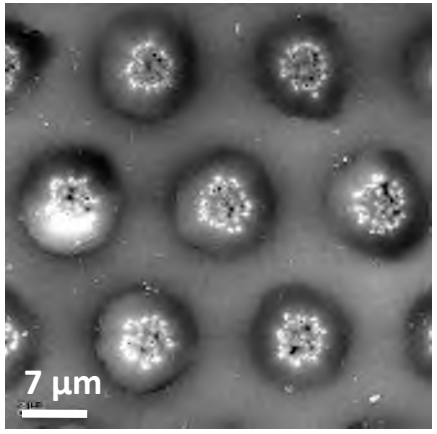
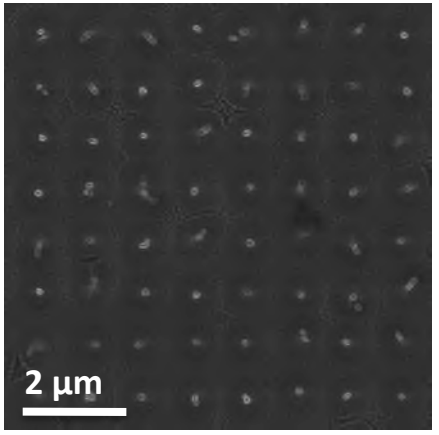


Growth Process

- Heated to 650 C
- Plasma discharge 500 W, 530 V, 0.97 A
- 150 sccm NH_3/50 sccm C_2H_2, 5-6 torr
- Growth rate- 1000 nm/min
- Quality is good, alignment is good

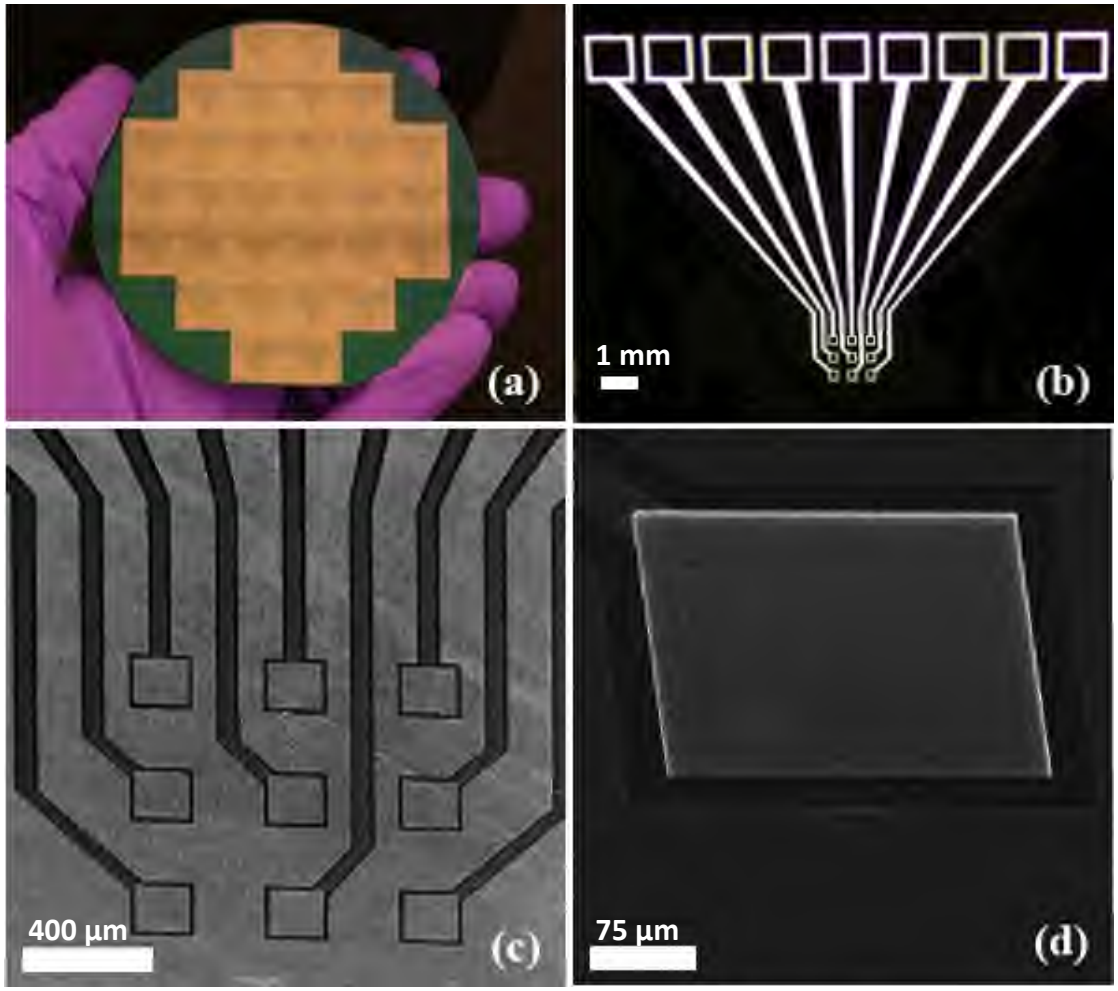
Cruden, B., et al., *Appl. Phys. Lett.* **2003**, 94, 4070-4078.

Define CNF Placement by Catalyst Placement

	Continuous Layer of Catalyst	Photolithography Defined Catalyst Spots	Electron Beam Lithography Defined Catalyst Spots
As Grown CNFs			
SiO_2 Encapsulated CNFs			

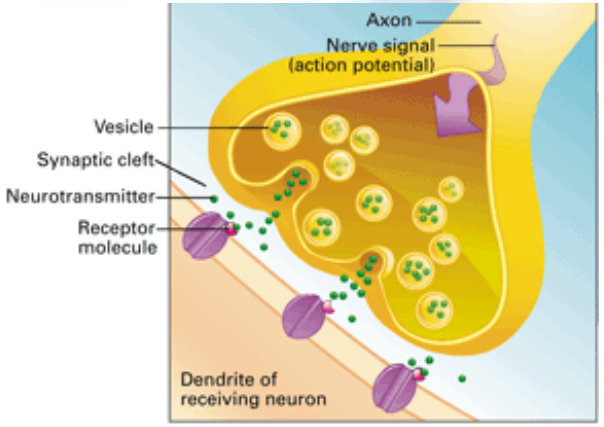
Fabrication of 3x3 Array

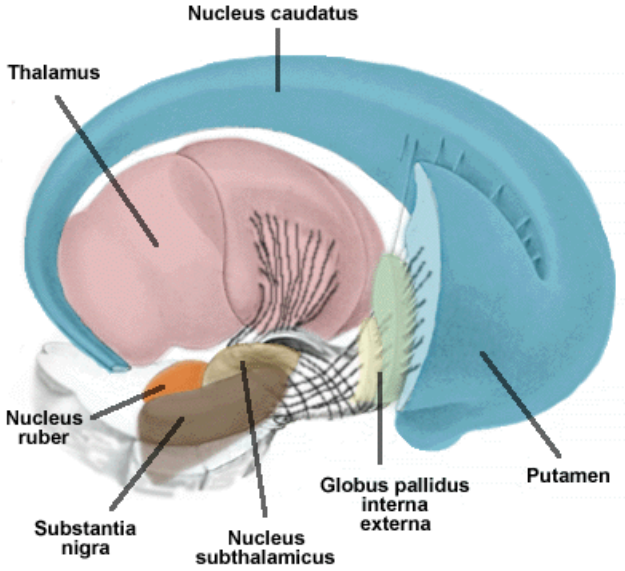
30 devices on a 4” Si wafer



- 200 µm by 200 µm electrode dimensions
- 9 individually addressed electrodes
- potentially 9 different target molecules

Motivation: Parkinson's Disease





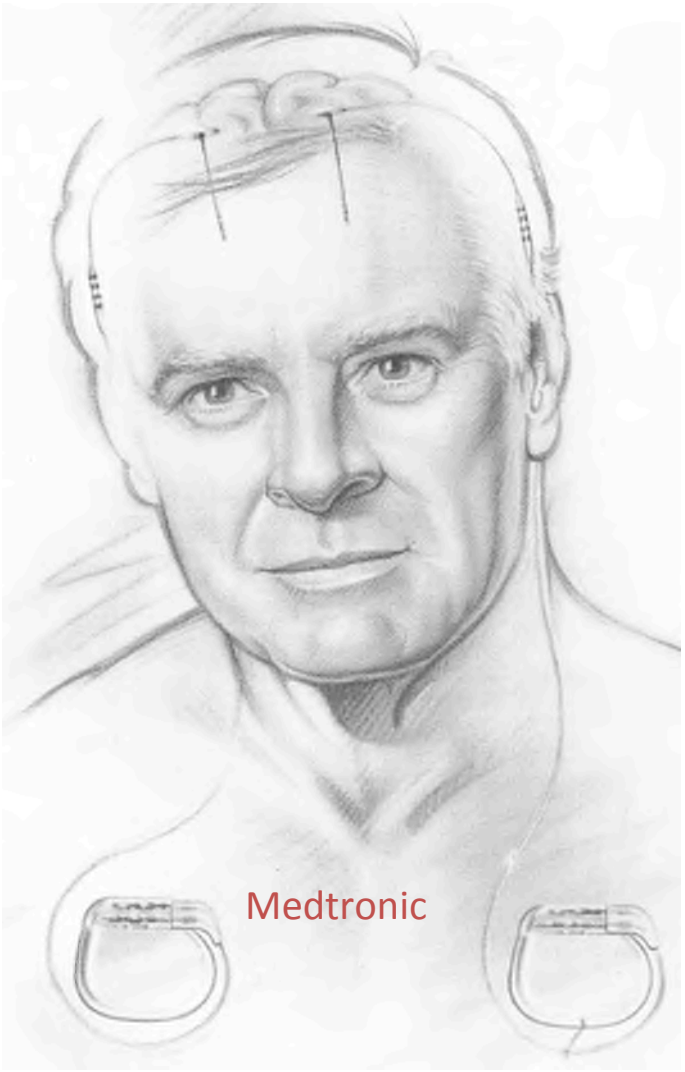
Parkinson's disease is a neurodegenerative disorder in which patients have insufficient production of dopamine from dopaminergic cells in the substantia nigra

Current treatments include L-dopa, dopamine agonists, MAO-B inhibitors, surgery (ablation and deep brain stimulation)

http://knight.noble-hs.sad60.k12.me.us/context/exploringLife/text/chapter28/concept28.2.html

http://www.profelis.org/webpages-cn/lectures/neuroanatomy_1ns.html

Deep Brain Stimulation



Deep Brain Stimulation (DBS)

-Started in the 1960's

-Over 80,000 successful surgeries

-Has been demonstrated to be an effective neurosurgical treatment for several pathologies including:

- tremor
- epilepsy
- Parkinson's disease
- depression
- Tourette syndrome
- chronic pain

How DBS Works

- Brain pacemaker, electrical impulses to different areas of the brain
- Stimulation 24/7

Potential Improvements

-Time consuming and difficult to program without feedback

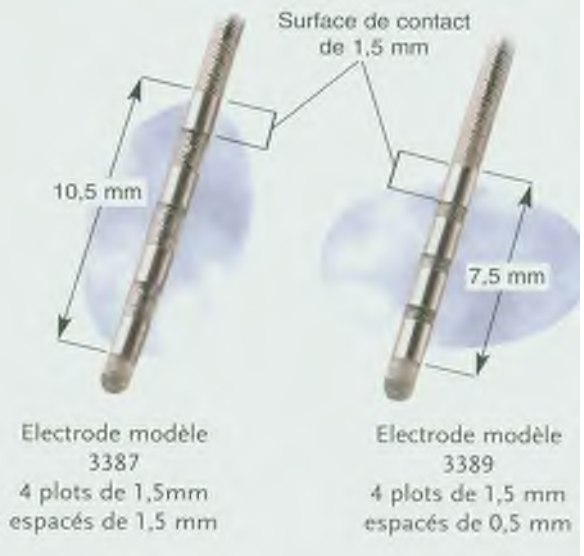
-Want real-time monitoring of the neurochemical output

-Development of chemically-guided placement of DBS electrodes *in vivo*.

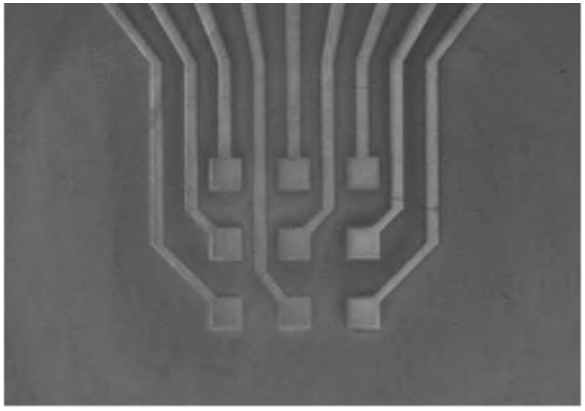
Clinical efficacy is not questioned, but mechanisms are very poorly understood

Deep Brain Stimulation Electrodes

DBS Electrodes from Medtronic

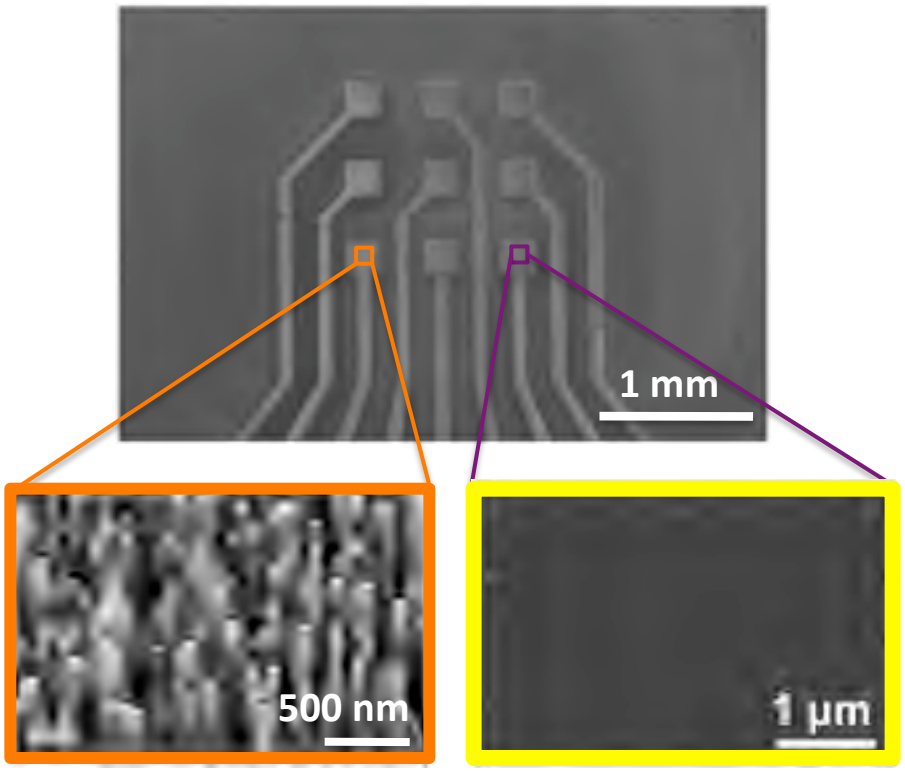


CNF Electrodes



Current 3x3 CNF device does not have an optimal geometry for implantation but can be used for preliminary in vitro investigations.

Electrochemical Detection of Neurotransmitters



Stimulating Electrode: Bare CNFs with high capacitance and low impedance

Recording Electrode: CNFs embedded in SiO_2 with ultrahigh sensitivity

- Molecules of Interest
  - Dopamine
    - Movement disorders, addiction
  - Serotonin
    - Depression, hunger
  - Adenosine
  - Oxygen
  - pH

- Techniques
  - Differential Pulse Voltammetry
    - More sensitive
  - Fast Scan Cyclic Voltammetry
    - Better temporal resolution

Nanoelectrodes for Chemical Sensing

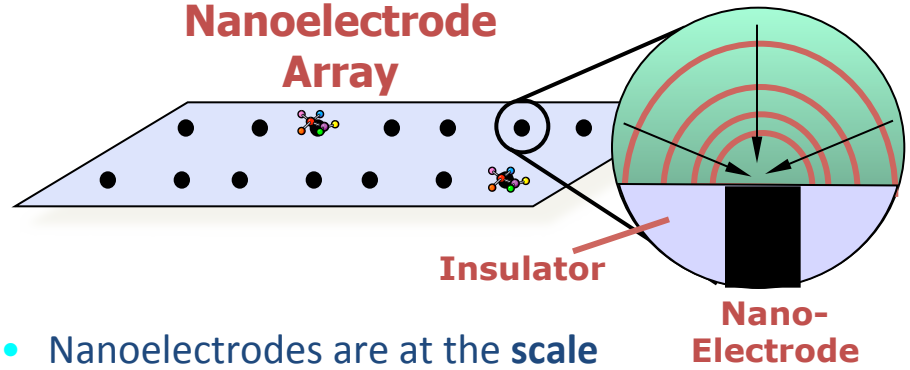
Nanoscale electrodes create a dramatic improvement in signal detection over traditional electrodes for small analyte concentrations

Background: $i_n \propto C_d^0 A$

Traditional Macroelectrode

- **Scale difference** between macroelectrode and molecules is tremendous
- **Background noise** on electrode surface is therefore significant
- **Significant amount** of target molecules required

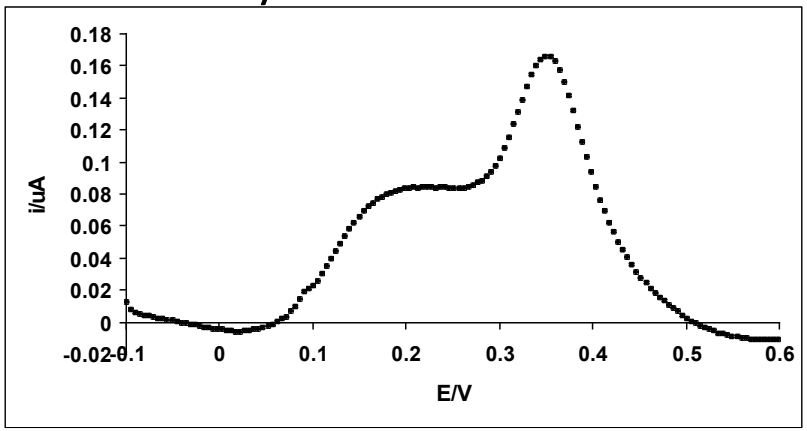
Nanoelectrode Array



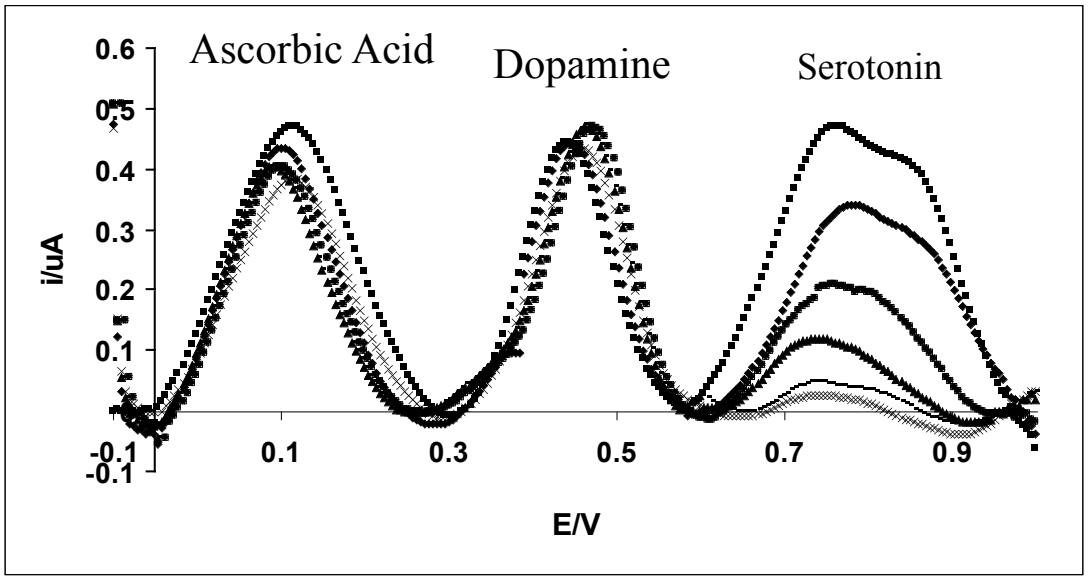
- Nanoelectrodes are at the **scale close to** molecules
- with dramatically **reduced background noise**
- Multiple electrodes results in **magnified signal** and **desired redundance** for statistical reliability.

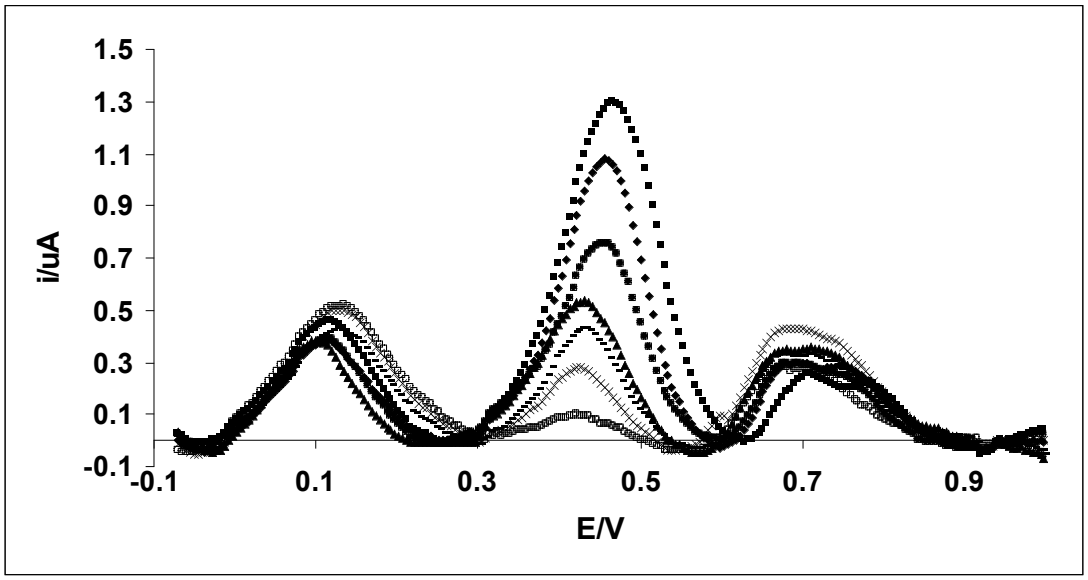
Simultaneous Detection of Neurotransmitters

Glassy Carbon Electrode



Carbon Nanofiber Electrode





-CNF electrode has ability to distinguish multiple electroactive brain chemicals in a mixture!
-Detection limits 50nM for DA and 100nM for 5-HT

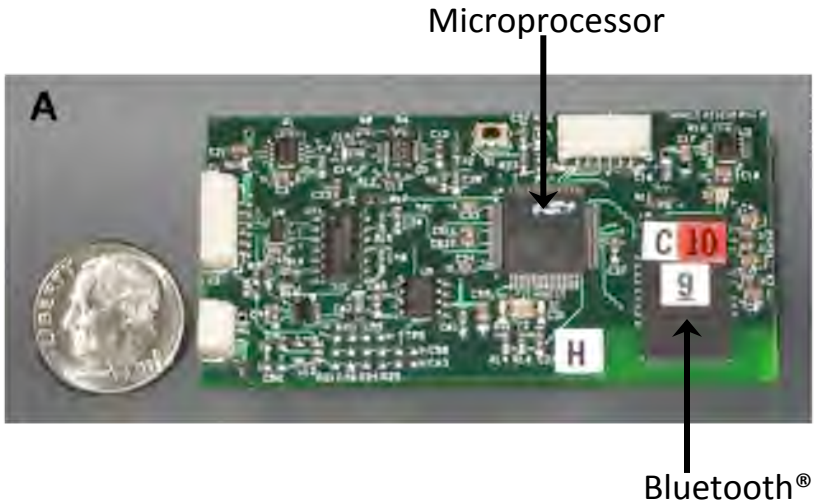
E. Rand, A. Periyakaruupan, Z. Tanaka, D. A. Zhang, M. P. Marsh, R. J. Andrews, B. Chen, M. Meyyappan, K. H. Lee, J. E. Koehne *Biosens Bioelect* **2013**, 42, 434-438.

Wireless Instantaneous Neurotransmitter Concentration Sensor (WINCS)

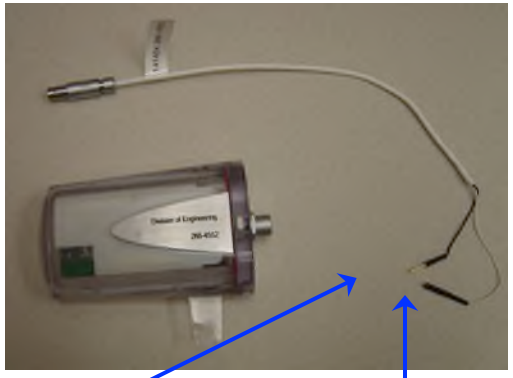
The Mayo Clinic-developed WINCS is a microprocessor-controlled, MRI-compatible, battery-powered instrument that combines Bluetooth® digital telemetry with fast scan cyclic voltammetry and constant potential amperometry.

Standard Potentiostat

Printed Circuit Board



Sterilizable WINCS Unit



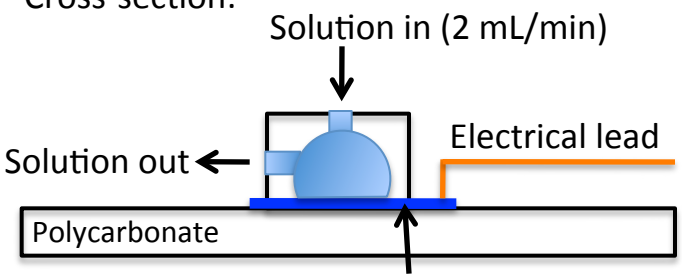
WINCS was designed in compliance with FDA-recognized standards for medical electrical device safety.

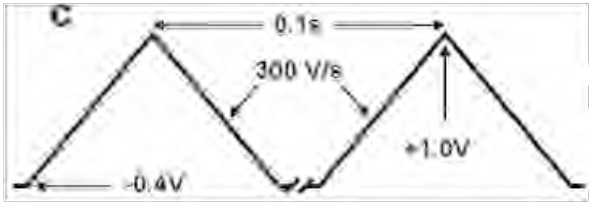
Bledsoe, J. M. et al., *J. Neurosurg*, **2010**, 11, 712-723.

Experimental Setup

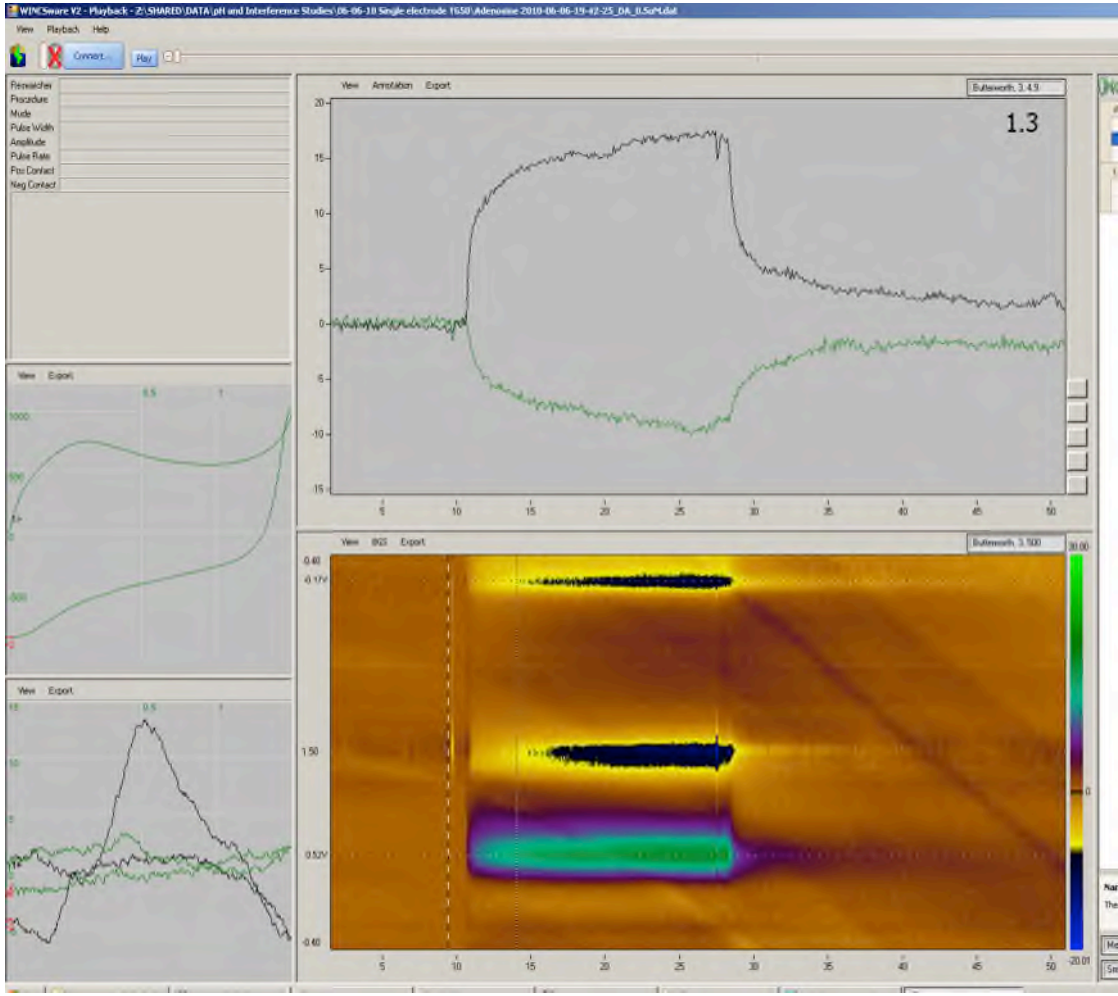
Custom-Designed Flow Cell

Cross-section:



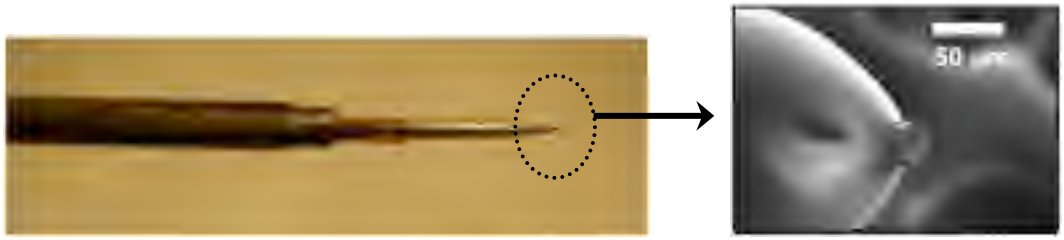


WINCSware User Interface



WINCSware allows viewing of the data in nearly real-time

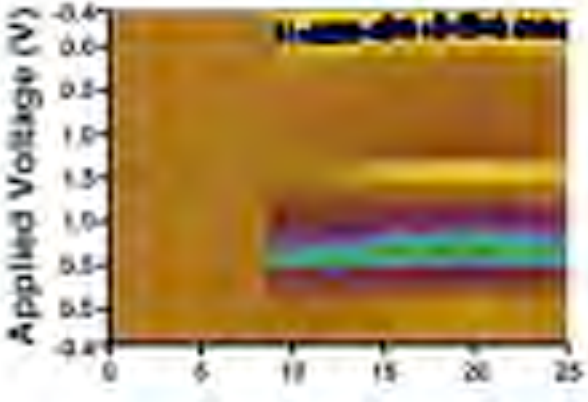
WINCStrode for the Detection of Dopamine



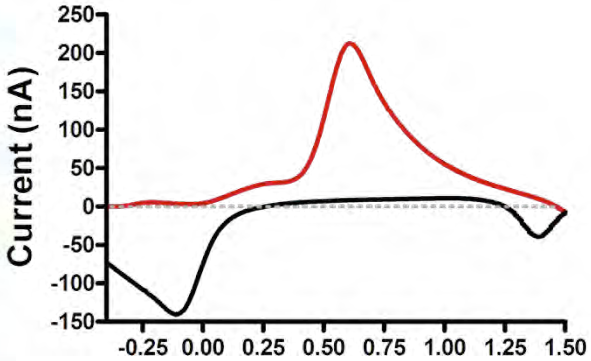
The WINCS carbon fiber electrode (WINCStrode) is based on an approved human extracellular tungsten electrophysiology electrode that was modified by the addition of a short section of carbon-fiber to enable FSCV recordings.

Dopamine Detection:

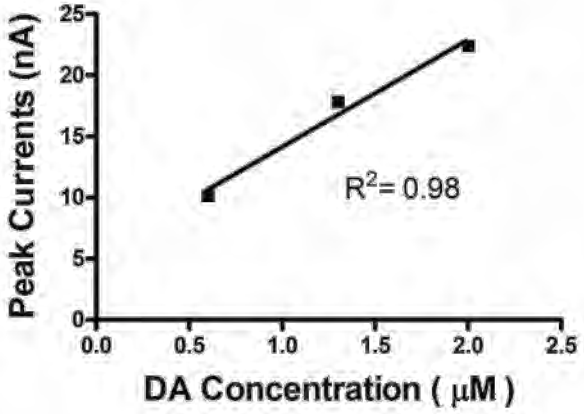
3D Color Plots



Background Subtracted Cyclic Voltammogram



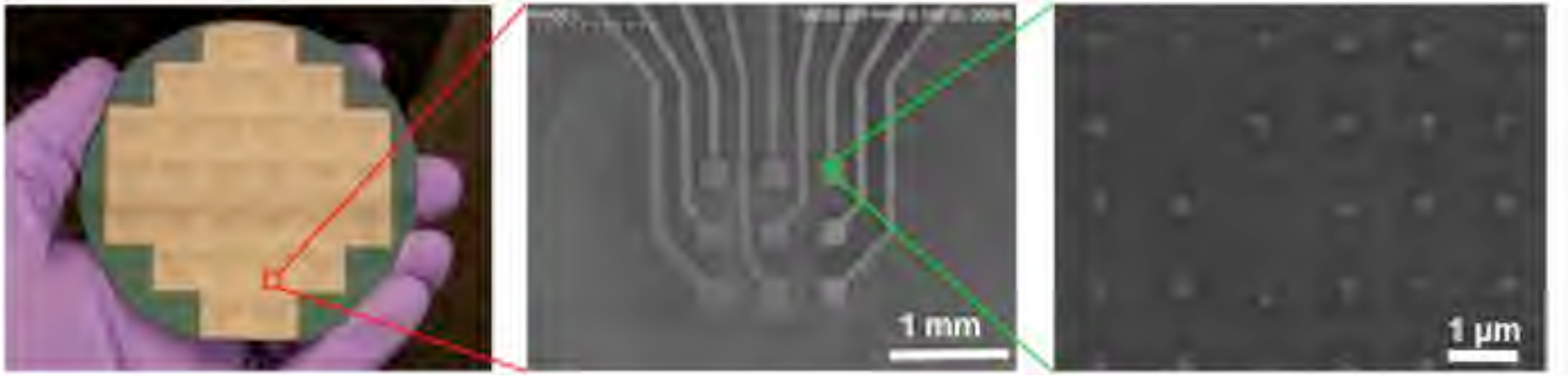
Calibration Curve



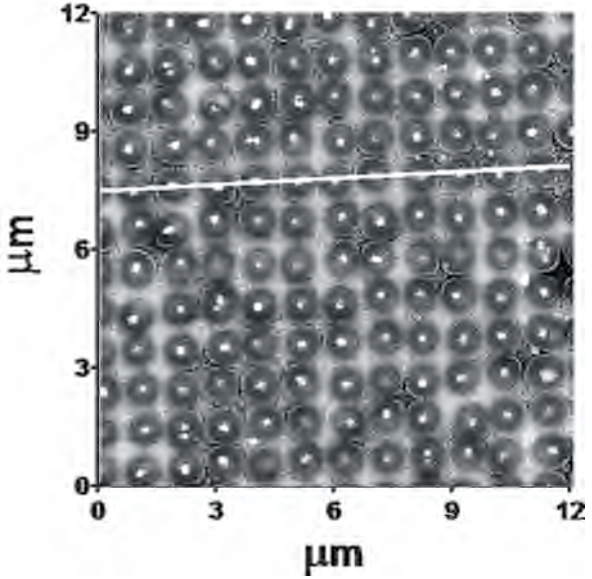
Agnesi, F. et al., *J. Neurosurg*, **2010**, 11, 701-711.

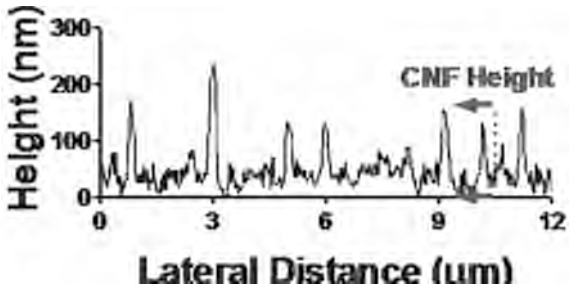
WINCS Carbon Nanofiber Electrode (WINCSnanotrode)

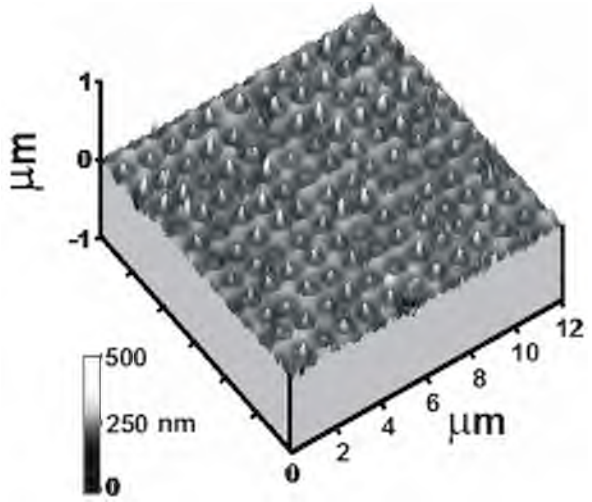
Scanning Electron Microscopy (SEM) Data:



Atomic Force Microscopy (AFM) Data:





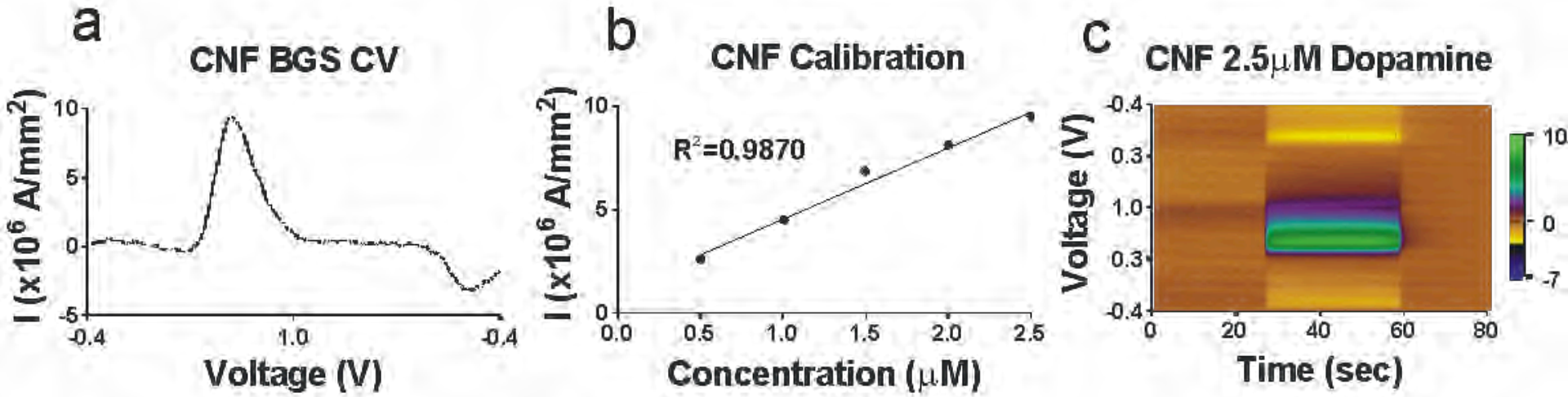


Use a combination of SEM and AFM analysis to determine total electrode surface area

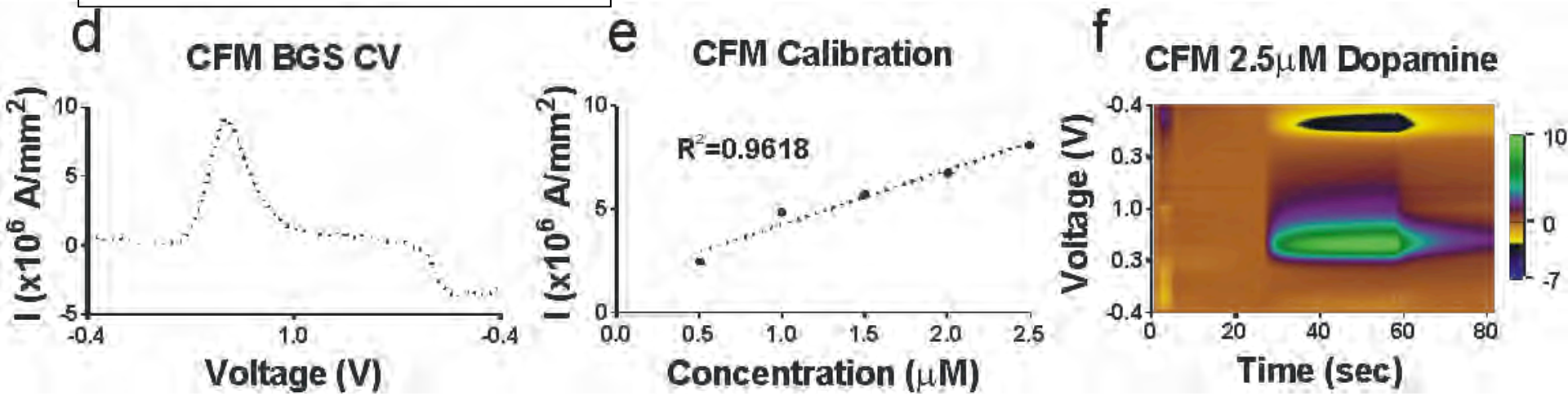
Koehne, J. E., et al. *Analyst* **2011**, 136, 1802-1805.

Dopamine Detection

Carbon Nanofiber Electrode



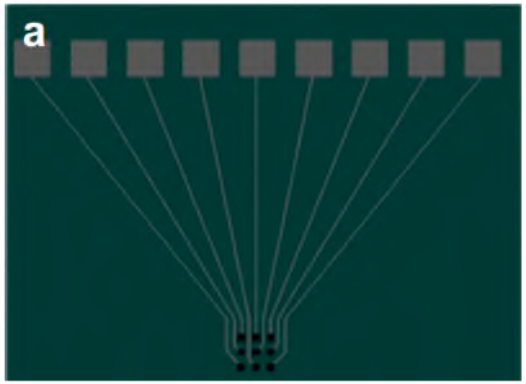
Carbon Fiber Microelectrode



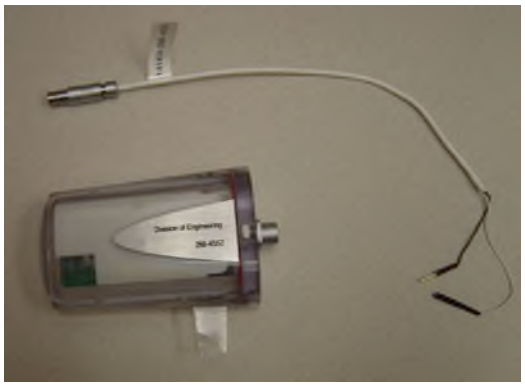
J. E. Koehne, M. Marsh, A. Boakye, B. Douglas, I. Y. Kim, S. Y. Chang, D. P. Jang, K. E. Bennet, C. Kimble, R. Andrews, M. Meyyappan, K. H. Lee *Analyst* **2011**, 136, 1802-1805.

Multichannel Recording

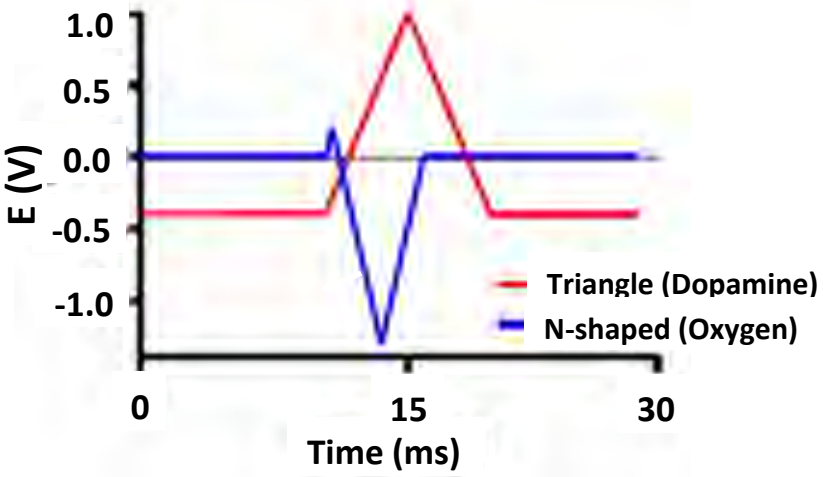
Device: 3x3 Array

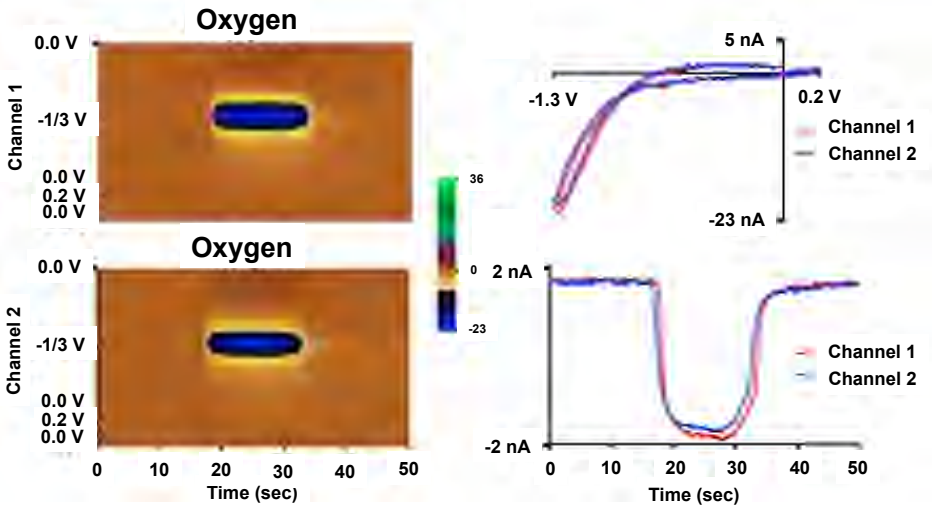


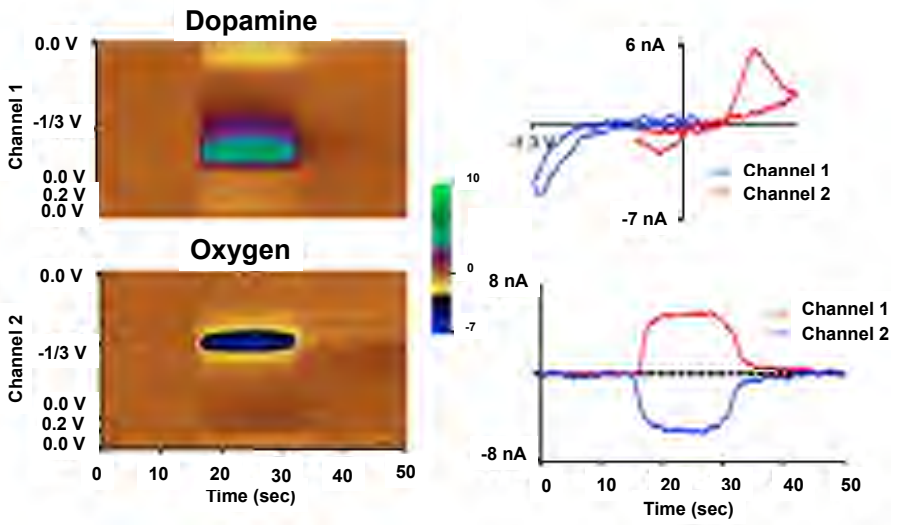
Instruments: 2 WINCS



Waveforms



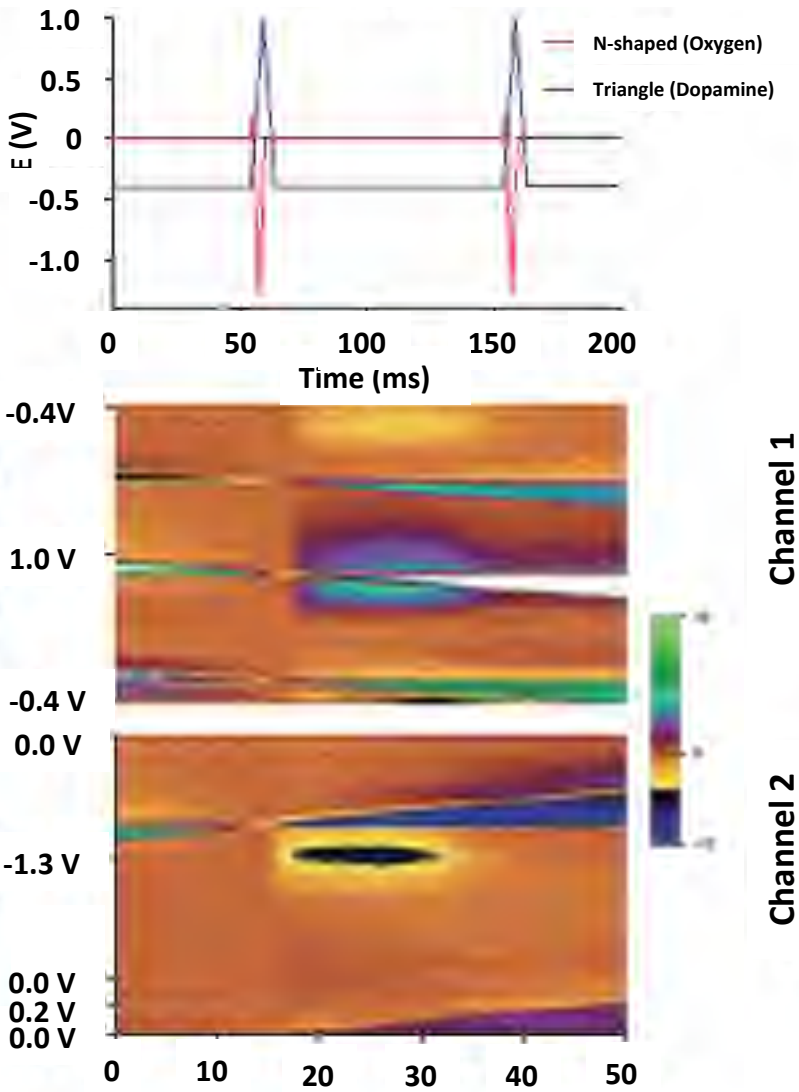




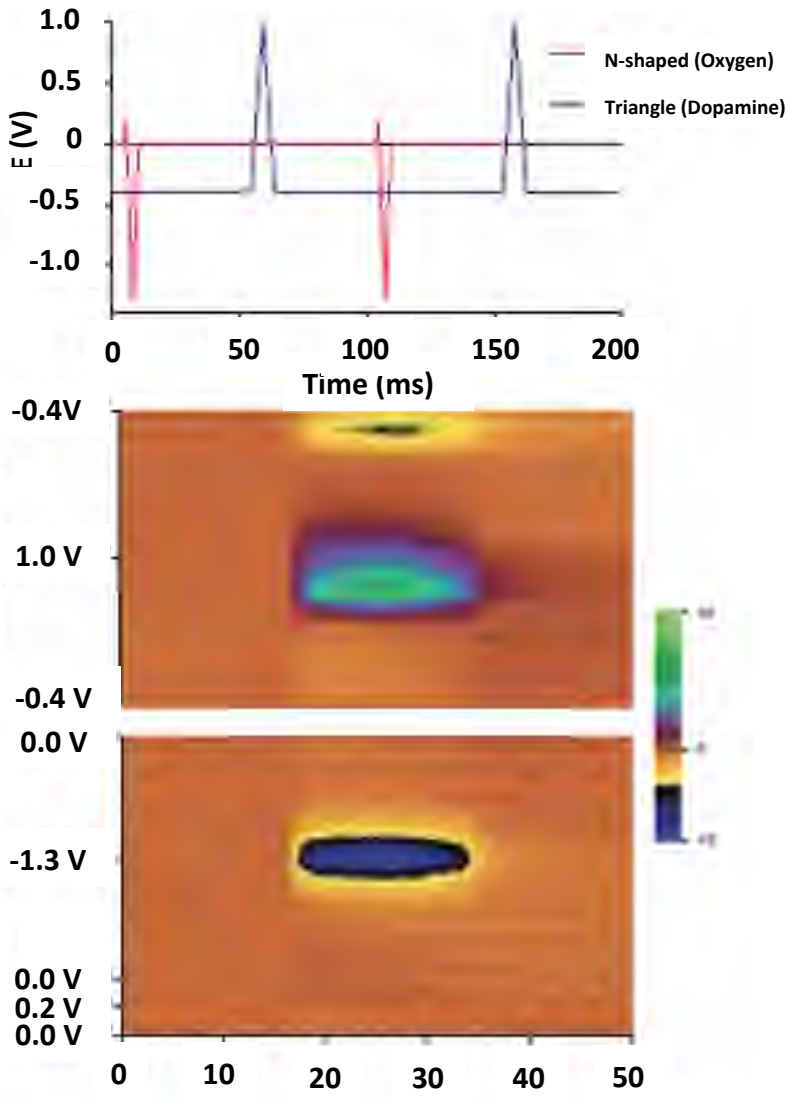
M. P. Marsh, J. E. Koehne, R. J. Andrews, M. Meyyappan, K. E. Bennet, K. H. Lee *Biomed Eng Lett,* **2012**, 2,271-277.

Multichannel Crosstalk

Overlapped Waveforms



Interleaved Waveforms

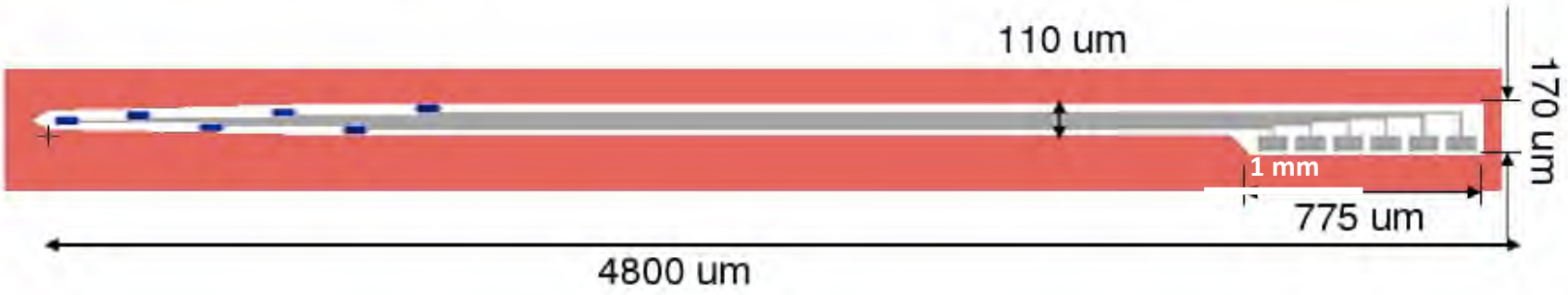


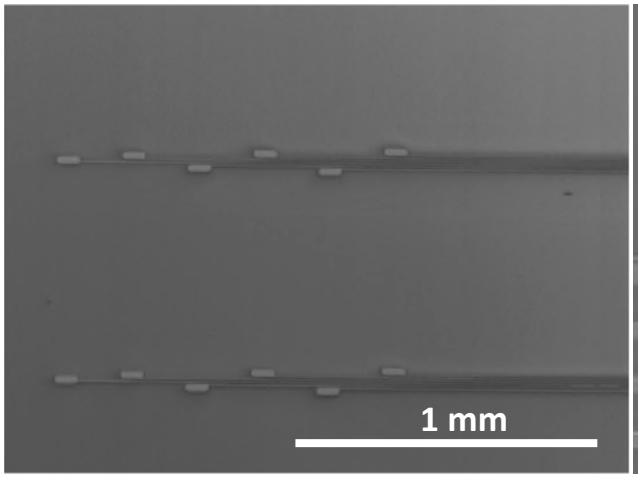
M. P. Marsh, J. E. Koehne, R. J. Andrews, M. Meyyappan, K. E. Bennet, K. H. Lee *Biomed Eng Lett,* **2012**, 2,271-277.

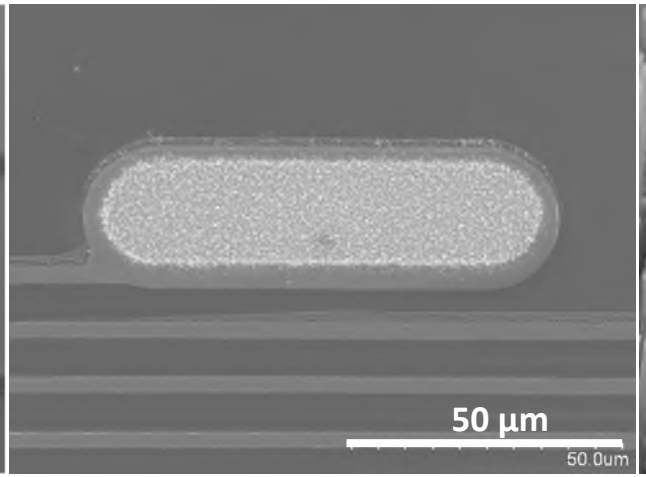
Implantable Style CNF Electrode Needle

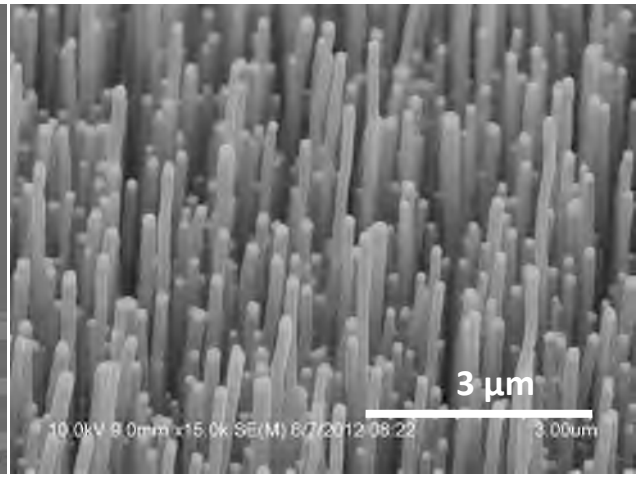
Penetrating multiplexed array

- Ability to spatially resolve

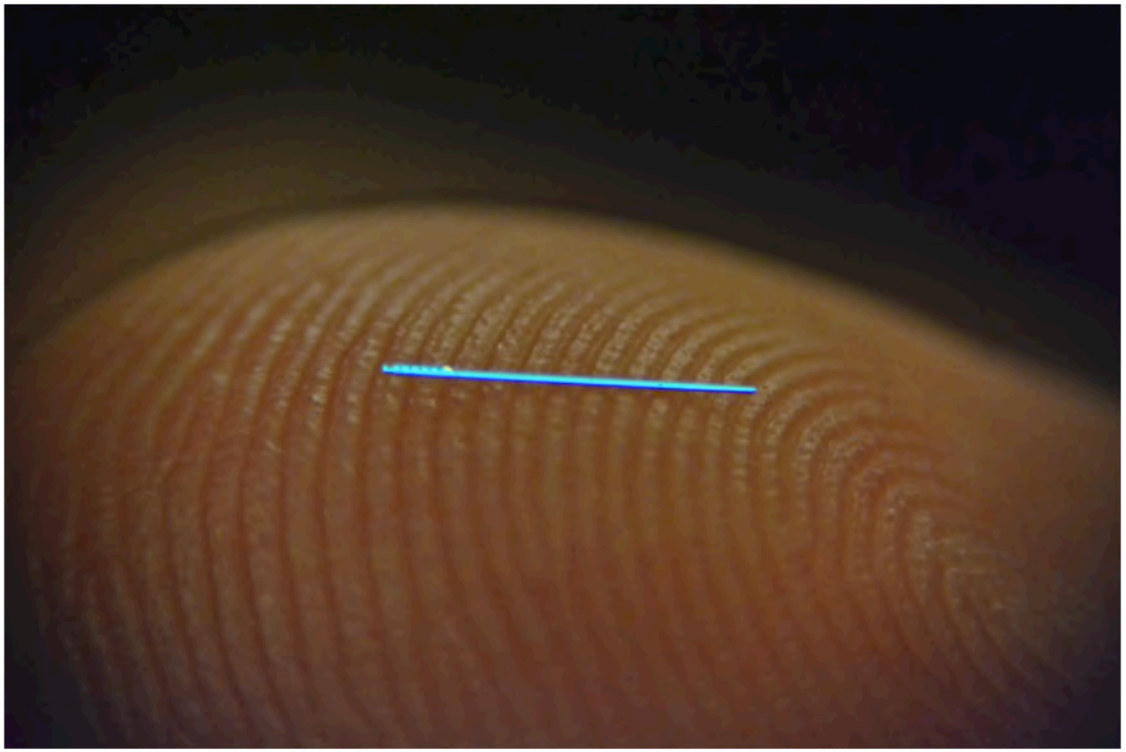


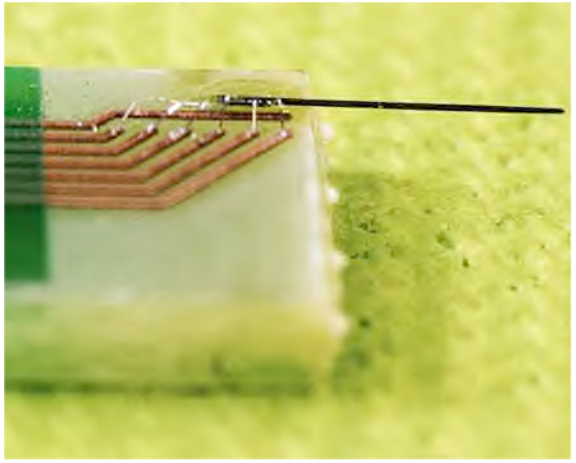


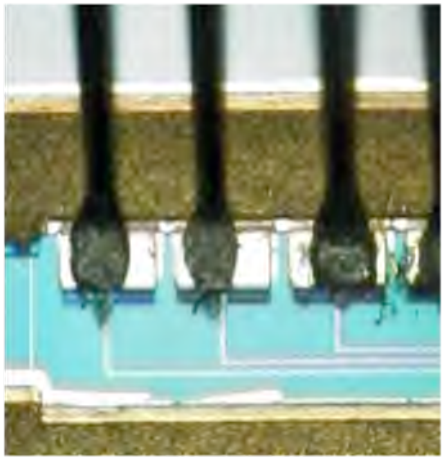




Needle Assembly

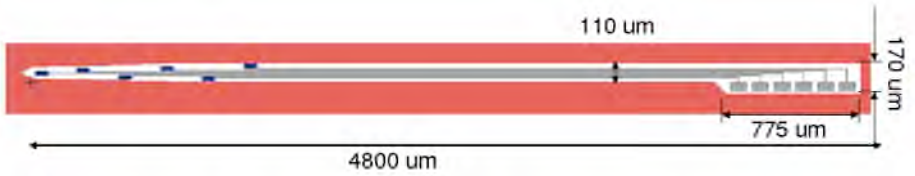




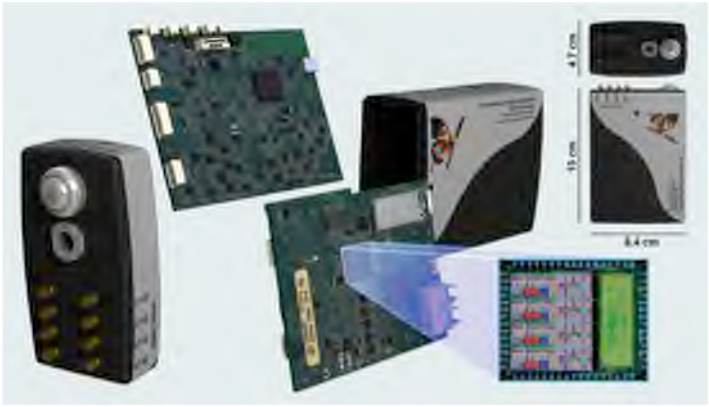


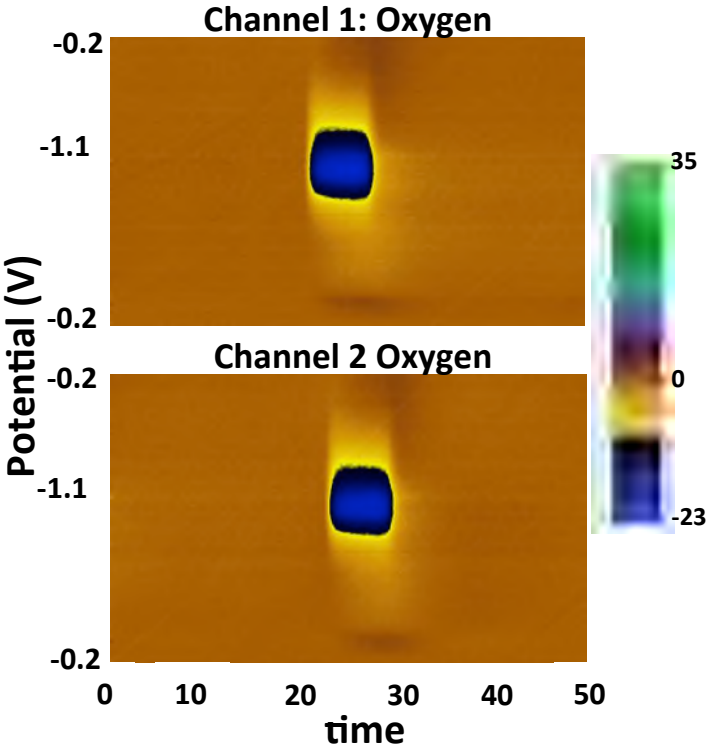
Simultaneous Multichannel Oxygen Detection

Device: Needle

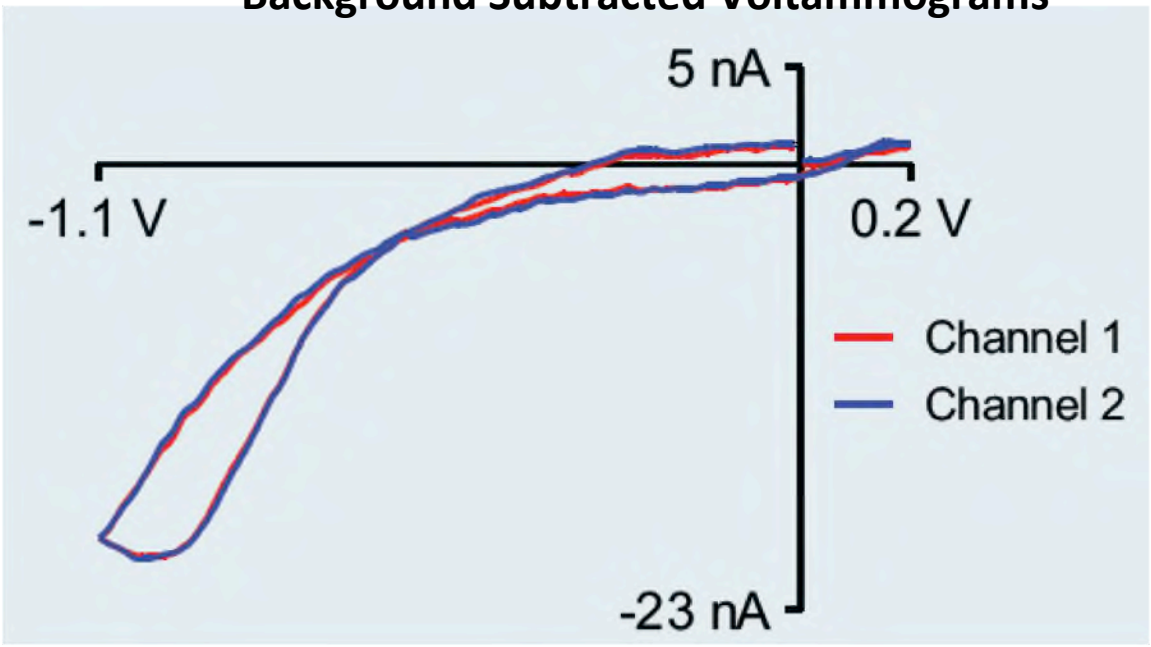


Instrument: WINCS Harmoni

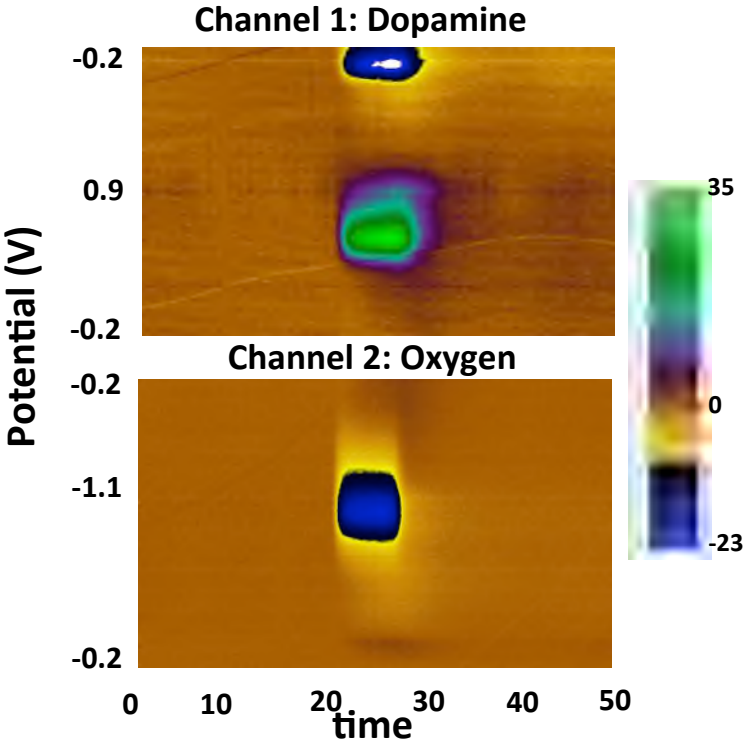


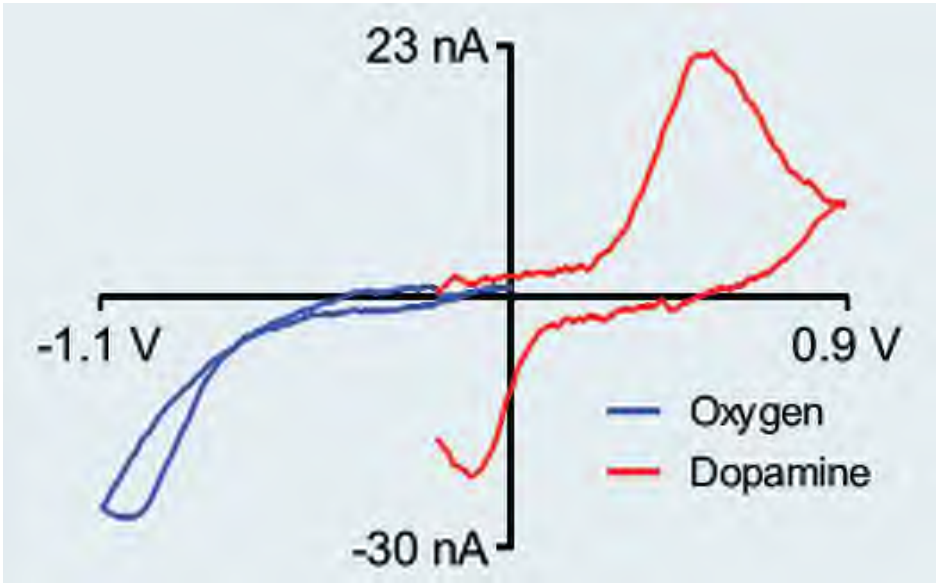


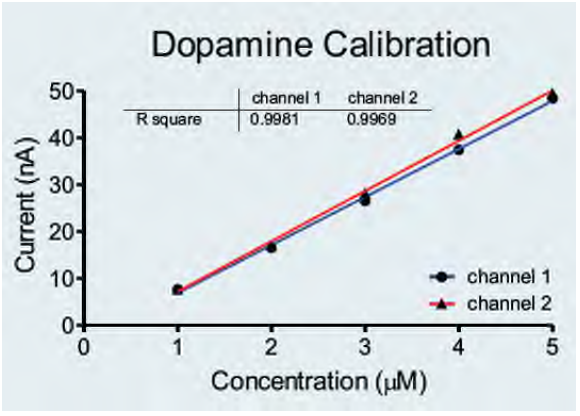
Background Subtracted Voltammograms

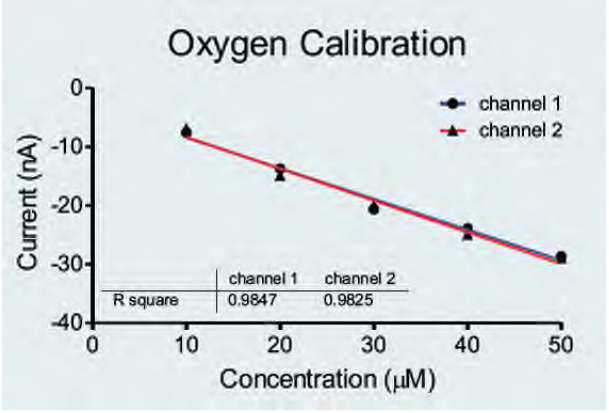


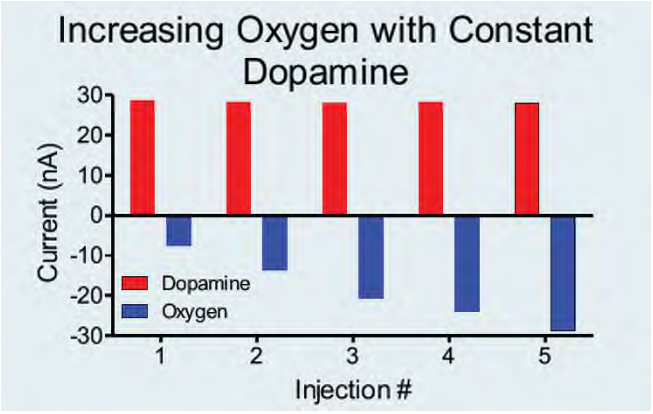
Multichannel Detection: Dopamine and Oxygen











Next Steps

Device

Rat implant
Neurochemical sensing

Wikimedia Commons: Vdegroot

Porcine DBS surgery
Stimulation and Sensing

Human Clinical Trial

Summary

- Carbon nanofiber electrode device is well suited for the next generation DBS
  - High sensitivity to act as neurochemical sensing electrodes
- Carbon nanofiber electrode sensors can distinguish between multiple analytes
  - From one electrode using differential pulse voltammetry
  - From adjacent electrodes using fast scan cyclic voltammetry
- Needle style electrode is read for animal testing

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