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

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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

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)

**Growth Process**
- Heated to 650°C
- Plasma discharge 500 W, 530 V, 0.97 A
- 150 sccm NH₃/50 sccm C₂H₂, 5-6 Torr
- Growth rate: 1000 nm/min
- Quality is good, alignment is good

Define CNF Placement by Catalyst Placement

- Continuous Layer of Catalyst
- Photolithography Defined Catalyst Spots
- Electron Beam Lithography Defined Catalyst Spots

As Grown CNFs

SiO₂ 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

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

- 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

Stimulating Electrode: Bare CNFs with high capacitance and low impedance

Recording Electrode: CNFs embedded in SiO₂ with ultrahigh sensitivity
Nanoelectrodes for Chemical Sensing

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

Background: $i_n \propto C_d^0 A$

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

- Nanoelectrodes are at the scale close to molecules
  - with dramatically reduced background noise
  - Multiple electrodes results in magnified signal and desired redundancy for statistical reliability.
Simultaneous Detection of Neurotransmitters

Glassy Carbon Electrode

Carbon Nanofiber Electrode

Ascorbic Acid  Dopamine  Serotonin

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

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.

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

Experimental Setup

Custom-Designed Flow Cell

Cross-section:
- Solution in (2 mL/min)
- Solution out
- Electrical lead
- Polycarbonate
- Sample

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

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.
Dopamine Detection

Carbon Nanofiber Electrode

a) CNF BGS CV

b) CNF Calibration

R² = 0.9870

Carbon Fiber Microelectrode

d) CFM BGS CV

e) CFM Calibration

R² = 0.9618


Multichannel Recording

Device: 3x3 Array

Instruments: 2 WINCS

Waveforms

Multichannel Crosstalk

Overlapped Waveforms

- Channel 1: Triangle Shape
  - -0.4 V
  - 1.0 V
  - -0.4 V
  - 0.0 V

- Channel 2: N-Shape
  - -1.3 V
  - 0.0 V
  - 0.2 V
  - 0.0 V

Interleaved Waveforms

- Channel 1: Triangle Shape
  - -0.4 V
  - 1.0 V
  - -0.4 V
  - 0.0 V

- Channel 2: N-Shape
  - -1.3 V
  - 0.0 V
  - 0.2 V
  - 0.0 V

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

Channel 1: Oxygen

Channel 2 Oxygen
Multichannel Detection: Dopamine and Oxygen

Channel 1: Dopamine

Channel 2: Oxygen

Background Subtracted Voltammograms

Dopamine Calibration

Oxygen Calibration

Increasing Oxygen with Constant Dopamine
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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