Carbon nanofiber electrode array for neurochemical monitoring

Jessica E. Koehne
NASA Ames Research Center
Moffett Field, CA

14th Annual Society for Brain Mapping & Therapeutics Congress, Los Angeles, CA. April 2017.
Background: 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
- 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
- Has been shown to induce dopamine release

Potential Improvements
- Time consuming and difficult to program without feedback
- Want real-time monitoring of the neurochemical output

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.
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.
What are Carbon Nanofibers (CNFs)?

Bamboo-like CNFs

Active sites

TEM of CNF

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

Edge Plane:
1) High electron transfer rate (~ 0.1 cm/s)
2) Very high specific capacitance (>60 µF/cm²)

Basal Plane:
1) Low electron transfer rate (< 10⁻⁷ cm/s)
2) Anomalously low capacitance (~1.9 µF/cm²)

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 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

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
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

**Recording Electrode:**
CNFs embedded in SiO₂ with ultrahigh sensitivity
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

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
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

$R^2 = 0.98$

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

Triangle (Dopamine)
N-shaped (Oxygen)

Dopamine

Oxygen

Multichannel Crosstalk

Overlapped Waveforms

Interleaved Waveforms

Implantable Style CNF Electrode Needle

Penetrating multiplexed array
- Ability to spatially resolve
Needle Assembly
Simultaneous Multichannel Oxygen Detection

Device: Needle

Instrument: WINCS Harmoni

Channel 1: Oxygen

Channel 2 Oxygen

Background Subtracted Voltammograms

Potential (V)

time

0 10 20 30 40 50

-0.2

-1.1

-0.2

-1.1

-0.2

-23

-0.2

-23 nA

-1.1 V

0.2 V

5 nA

Channel 1

Channel 2
Multichannel Detection: Dopamine and Oxygen

**Channel 1: Dopamine**

**Channel 2: Oxygen**

**Background Subtracted Voltammograms**

- **23 nA**
- **-1.1 V**
- **0.9 V**
- **-30 nA**

Dopamine Calibration:

- \( R^2 \) channel 1 = 0.9981
- \( R^2 \) channel 2 = 0.9969

Oxygen Calibration:

- \( R^2 \) channel 1 = 0.9847
- \( R^2 \) channel 2 = 0.9625

Increasing Oxygen with Constant Dopamine:

- Current (nA)

Injection #:

- 1
- 2
- 3
- 4
- 5

- Dopamine
- Oxygen
Next Steps

Device

Rat implant
Neurochemical sensing

Porcine DBS surgery
Stimulation and Sensing

Human Clinical Trial

Wikimedia Commons: Vdegroot

Medtronic
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 ready for animal testing
Acknowledgements

• NASA Ames Research Center
  • Emily Rand
  • Adwoa Boakye
  • Brandon Douglas
  • Jason Driver
  • Russell J. Andrews
  • M. Meyyappan

• Mayo Clinic
  • Department of Physiology and Bioengineering
    • Michael Marsh
    • Su-youne Chang
    • Inyong Kim
    • Kendall H. Lee
  • Department of Engineering
    • Christopher J. Kimble
    • Kevin E. Bennet

Funding
NASA Ames Research Center
NIH (R01 Ns75013)
Presidential Early Career Award for Scientists and Engineers (NASA)