Multi-site Analysis of Dopamine Uptake in the Somatosensory Cortex

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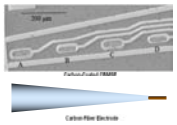
Abstract

➢Recording sites of ceramic-based multi-site electrode (CBMSE) arrays were coated with a thin film of carbon

➢In vitro and in vivo studies were performed to compare the sensitivities of the CC-CBMSE to standard carbon fiber electrodes

➢In vivo data from CC-CBMSE was compared to a mathematical model that used the standard diffusion equation with uptake



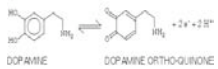
Schematic of Electrode Surface Area. The small sites (B and D) and the platinum sites have a surface area of 1216 •m². The large sites (A and C) have a surface area of 4116 •m². The small and large carbon fiber electrodes have surface areas of 5417 •m² and 7929 •m² respectively.

CBMSE Advantages

-Designed with precise intersite spacing
  -Measure the effects of the local microenvironment on neurochemical activity
  -Ability to record from several different neurons or brain-sites simultaneously
-Produce multiple, identical recording sites
-Ceramic substrates are rigid
-Ceramic substrate is a good insulator

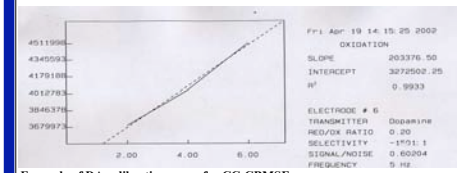
Voltammetry

➢Electrons are added to or removed from compounds by electric fields
➢Field is generated by the application of a voltage across an electrode/solution interface.
➢The chemical present at the electrode surface surrenders its electrons resulting in a small flow of current.



Example of the Electro-Oxidation of Dopamine

Sample Calibration

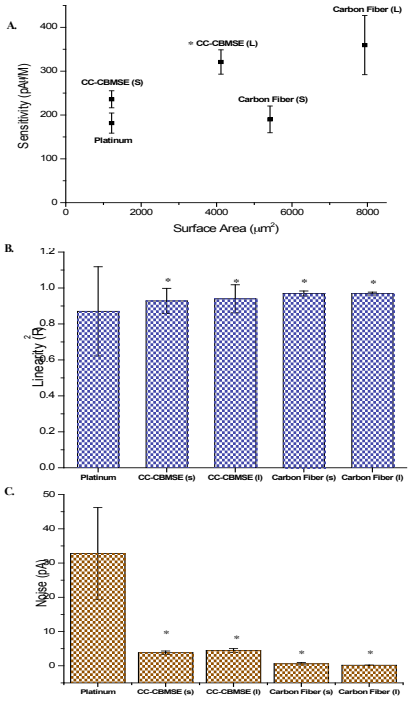


Example of DA calibration curve for CC-CBMSE array.
Sensitivity is the slope of the line in pA/•M (current vs concentration).
Linearity is Pearson Correlation Coefficient (R^2) and it should approach 1.
Noise is the amount of interfering signal detected in pA and it should be minimized.

In Vitro Comparison of Electrodes

Compared: CC-CBMSE, small and large
Platinum CBMSE Arrays
Small Carbon Fiber Electrodes
Large Carbon Fiber Electrodes

As measured by: Sensitivity, Linearity and Noise

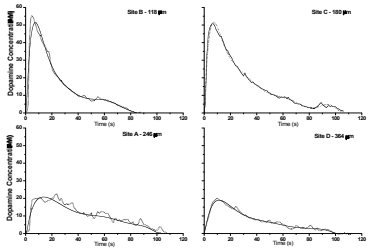


In Vitro Comparison: A: Large CC-CBMSE array had a significantly improved sensitivity over the platinum CBMSE and performed comparable to carbon fiber electrodes. Small CC-CBMSE array had improved sensitivity over the platinum CBMSE. **B:** Increased surface area improved the linear response to increases in concentration **C:** Small and Large CC-CBMSE arrays were significantly different from platinum CBMSE ***Significantly different from platinum CBMSE p<0.05**

Significance:
By applying a rough carbon surface using different surface areas, the ability of the CC-CBMSE arrays to perform voltammetry was improved and made comparable to today's standard carbon fiber electrodes.

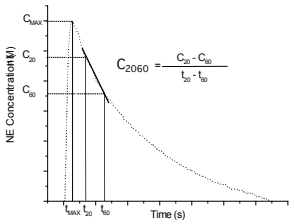
In Vivo Detection of Dopamine

Experimental Summary: Micropipettes that were filled with a known concentration of DA were attached to CC-CBMSEs. The electrode/micropipette bundle was then implanted in the rat SI and known quantities of DA were injected. The response of the electrodes was then recorded.



Dopamine concentration vs. time: Known volumes of dopamine was pressure injected into the somatosensory cortex from a micropipette. The micropipette was attached to a CC-CBMSE and the resulting dopamine concentration was recorded at each recording site as a function of time. The recorded concentration is seen above as the dotted line. The solid line depicts a best fit polynomial function that was used to overlay the concentration for clarity.

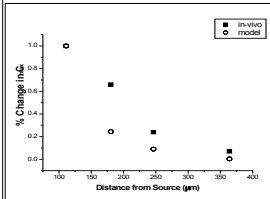
Significance: Every recording site was able to measure the concentration of dopamine after pressure injection regardless of distance from the micropipette. As expected, the sites closest to the source of injection recorded the highest concentration of dopamine while the sites further away recorded a lower concentration.



Measured Parameters: The parameters that were being measure were the maximum concentration of dopamine, C_{max}, seen at a recording site for each pressure injected volume. The slope between 20 to 60 percent of the maximum concentration seen at each recording site, C_{2060}, was used to measure The clearance of dopamine from the extracellular space.

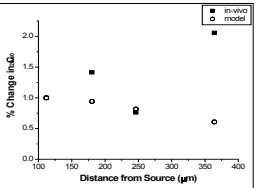
In Vivo Comparison to Model

Since dopamine is not endogenous to the somatosensory cortex, the amount of dopamine concentration that was seen was due only the amount that was pressure injected. The in vivo data was compared to a model that used the standard diffusion equation with uptake parameters. Uptake parameters were derived using Michalis-Menten kinetics, where V_{max} and K_m were taken from the literature. The measured in vivo C_{max} and C_{2060} were then compared to the C_{max} and C_{2060} from the model.



Comparison of C_{max} : The measured values for C_{max} for the in vivo data and the model were normalized to the recording site closest to the source. Although the in vivo data and the model followed the same trend, the percent change of C_{max} for the model was much greater than the percent change in the in vivo data.

Comparison of C_{2060} : The measured values for C_{2060} for the in vivo data and the model were normalized to the recording site closest to the source. While the percent change in C_{2060} remained constant for the model, the percent change in C_{2060} fluctuated in the in vivo data.



Significance : The in vivo model did not follow the prediction of the model. The model had a V_{max} that was constant for every site. The fact that the in vivo parameters did not follow the prediction of the model suggests that V_{max} is different across the different recording sites.

Conclusions

- Thin film technology can be used to create electrodes with multiple independent, identical recording sites.
- Carbon deposition onto multiple site thin film recording electrodes show predicted increases in electrode sensitivity for increases in surface area and roughness of the recording sites.
- CC-CBMSE arrays can be used to measure monoamine concentrations in vivo.
- Since the in vivo data did not follow the prediction of the model, the V_{max} across the somatosenory cortex may be different.