Thin-Film Sol-Gel As Controlled Delivery Platform For Neural Microelectrodes

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ABSTRACT

Long-term efficacy of neural implantation devices is a persisting challenge in neural engineering and rehabilitation. Upon implantation of a neural device, the foreign body response (FBR) is triggered and glial cells form a sheath around the electrode array. This sheath isolates the array from the rest of the brain both mechanically and electrically. Tetramethyl orthosilicate (TMOS), a thin-film polymer, has been shown to not negatively impact the impedance and charge-carrying capacity, as well as offer a controlled delivery method to deliver pharmaceuticals to mitigate inflammation without significant effect to device design. Using an *in vitro* protein delivery model to analyze the ability of multiple layers of TMOS to be used for protein delivery from both silicon wafers and microelectrodes, we evaluated the release kinetics and surface properties of the coatings. Through the wafer analysis, results reflect that adding a layer of TMOS significantly lowered 'burst release' of the protein, bovine serum albumin (BSA). Coating with freshly-made TMOS prolonged the protein release period. Total protein released per number of coats had no linear correlation, possibly due to nonuniform thickness of layers or protein trapped between multiple layers. From these findings, we speculate the possibility of a gradual release model for the utility of TMOS-coated microelectrodes in neural devices.

INTRODUCTION

- FBR initiated upon breaching the blood-brain barrier, leading to local neural cell death and electrical isolation of the microelectrode via glial sheath
- Controlled release of anti-inflammatory or neurotropic agent has shown potential to mitigate FBR
- Thin-film polymers, specifically thin-film orthosilicates, previously shown as effective drug delivery platforms for other medical implants
- **Objective: Determine effectiveness of TMOS as controlled delivery platform for neural microelectrodes**

METHODS

Preparation of Sol-Gel, TMOS:

- 1:4 ratio of TMOS to H_2O solution at room temperature and stored at -20°C

Protein Encapsulation:

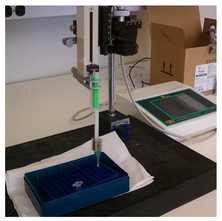
- Bovine Serum Albumin (BSA) dissolved in phosphate buffer solution to desired concentration (4.6% or 10%) before addition to prepared sol-gel

Wafer Preparation:

- Wafers cleaned with piranha solution, prepared by mixing equal parts 13M Sulfuric Acid 30% w/v Hydrogen Peroxide. Rinsed with Double Deionized (DDi) water and ethanol, to rinse any contaminants upon the surface of the substrate, and allowed to dry overnight

Wafer Coating:

- Wafers dip coated using actuator traveling at 70cm/min into protein encapsulated sol-gel at -20° C, to slow poly-condensation and allowed to dry before further coatings added according to desired design paradigm.
  - Note: One wafer was coated with freshly-made TMOS, denoted by an asterisk (*).



In Vitro Release:

- Wafers placed into 1.5mL micro-centrifuge tubes with 1.0 mL phosphate-buffer-saline (PBS) solution at 37°C
- PBS solution removed (hours 2,4,8, and every 24 hours thereafter) and replaced with fresh PBS
- Samples collected were stored at 1.4°C

BSA Release Analysis:

- Protein release quantified by Coomassie (Bradford) Protein Assay Kit and spectrophotometer at (595 nm)

RESULTS

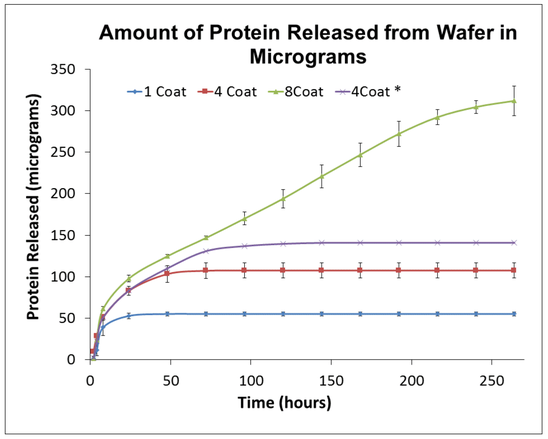
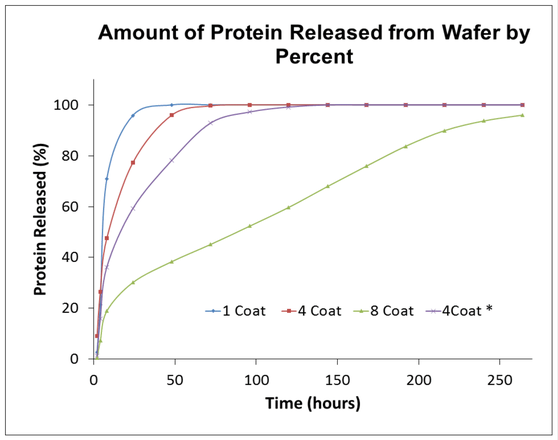


Fig 1. Amount of Protein Released from Wafer in Micrograms.
Burst release occurred within 24 hours and all protein was released by end of 48 hours for wafers with 1 coat and 4 coats of protein-encapsulated TMOS. Wafers with 8 coats, which one layer was solely TMOS, had a significantly lowered burst release and continued release after the analysis period.

Fig 2. Amount of Protein Released from Wafer in Percentage.
Different representation of data. Wafer coated with freshly-made TMOS released approximately 72 hours longer than its counterpart.



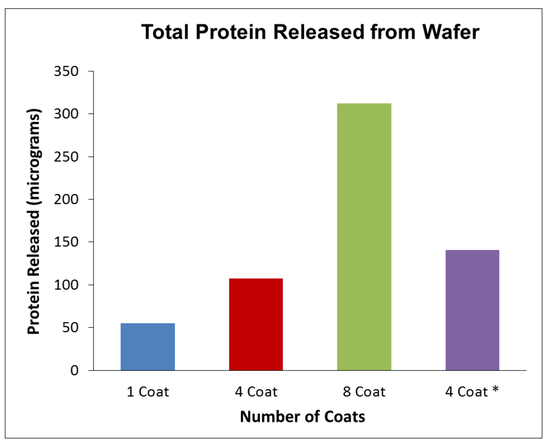


Fig 3. Total Protein Released from Wafer.
There is no linear correlation to the protein released per coat.

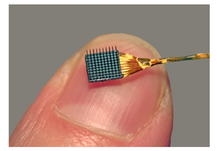
CONCLUSIONS

- A TMOS-only layer prevented 'burst release' of BSA from wafer.
- Coating with freshly-made TMOS prolonged protein release period
- Protein released per layer has no linear correlation, possibly due to nonuniform thickness layers or protein trapped between multiple layers

⇒ *Speculation of a gradual release model for the utility of TMOS-coated microelectrodes in neural devices*

FUTURE WORKS

- Quantification and analysis of BSA/TMOS-coated microelectrodes
- Quantification and analysis of Liposome/TMOS-coated microelectrodes
- Comparative analysis of TMOS performance based upon time of synthesis and time of coating



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