Microfabricated Nanoporous Gold Electrodes for Triggered Drug Release

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Statement of Purpose: There is a continuous demand for biomedical devices that can monitor and modulate physiological activity for effective treatment of disorders. Nanomaterials with unique features have shown high potential in engineering multifunctional devices, including advanced biosensor and drug delivery platforms. Nanoporous gold (np-Au), produced by a selective dissolution process, is a promising material that has found use in catalytic applications, but its biomedical potential remains underexplored. Np-Au films, displayed in Figure 1, offer high-effective surface area, opportunity for surface functionalization via thiol-based chemistry, high electrical conductivity, tunable porosity, and biocompatibility. We have previously demonstrated np-Au's application in monitoring neural electrical activity[1] and modulating cellular proliferation via passive drug release[2]. Here, we assess the performance of microfabricated np-Au thin film electrodes in electrically-actuated release of small molecules.

Methods: The prototype devices consist of np-Au and gold electrode traces patterned on glass coverslips, as shown in Figure 2 inset. In order to produce a 1 mm by 10 mm np-Au electrode, 300 nm-thick $Au_{0.25}Ag_{0.75}$ film was sputter-deposited onto an acid-cleaned glass cover slip through a laser-cut silicone elastomer stencil mask. The deposition involved the sequential sputtering of an adhesive chrome layer and an intermediate gold layer, followed by co-sputtering of gold and silver to produce the precursor alloy to the np-Au film. A gold counter-electrode with the identical planar geometry was similarly patterned. The np-Au morphology was obtained by dealloying the samples in nitric acid (65%) at 55°C for 15 minutes and rinsing them extensively with deionized (DI) water. The resulting pore morphology was quantified by processing the scanning electron micrographs of the electrodes with ImageJ. The electrodes were then loaded with fluorescein as a surrogate for small-molecule drugs. The samples were immersed in a 10 mM aqueous solution of fluorescein sodium for 5 hours and were subsequently rinsed with DI water. A ~3 mm-thick 0.6% agarose-PBS gel was placed over the electrodes and the electrodes were biased at several voltages to release of fluorescein molecules into the gel. The gel composition has been shown to mimic diffusive properties of brain tissue[3]. The fluorescence intensities in the gel above the np-Au and gold regions were captured at 10 second intervals with a monochrome camera connected to a fluorescence microscope. The image sequences were analyzed by ImageJ to plot fluorescence intensity with respect to time (Figure 2) to quantify fluorescein release.

Results: The dealloying process created a continuous open-pore structure (Figure 1) with an average pore size of 50 nm and average porosity of 65%.

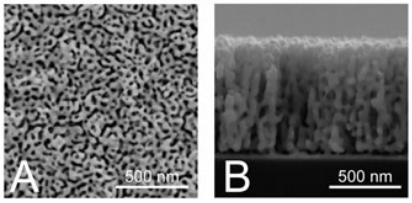

Figure 1. Scanning electron micrographs of typical np-Au morphology: (a) top view, (b) cross-sectional view.

Figure 2 illustrates that there was no molecular release from the Au electrode (also soaked in fluorescein solution), slight passive diffusion from the untriggered np-Au electrode, and significant release from np-Au electrode at a negative voltage compared to the counter gold electrode.

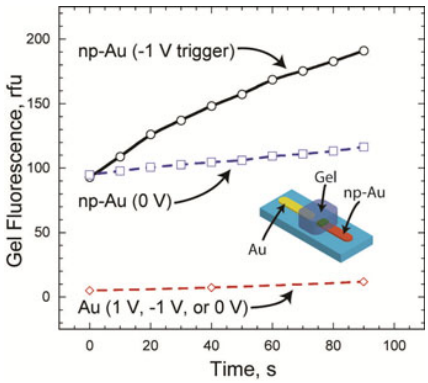

Figure 2. Fluorescence intensity in agarose gel for different experimental conditions.

Conclusions: We demonstrated that np-Au thin films can retain small molecules, such as fluorescein (~330 Da), within their nanoporous network and release them on demand with the application of a small electrical potential. In the example here, the negative potential repels the negatively-charged fluorescein ions. We are currently exploring the effect of pore morphology and molecular properties on the release profile. As the production of np-Au electrodes is compatible with conventional microfabrication techniques, we expect this technique to benefit drug delivery application using miniature biomedical devices.

References:

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