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NOVEL TITANIA NANOTUBE BASED ELECTROCHEMICAL DETECTION IN MICROTOTAL ANALYSIS SYSTEM

Harikrishnan Jayamohan*, Himanshu Sant*, York R. Smith§, Swomitra K. Mohanty§, Bruce K. Gale*and Manoranjan Misra§

*State of Utah Center of Excellence for Biomedical Microfluidics, University of Utah, USA

§Metallurgical Engineering Department, University of Utah, USA

We report the modification of titania (TiO2) nanotubes for quantitative electrochemical (EC) detection of biomolecules on a microfluidic platform. Highly sensitive detection based on carbon nanotubes (CNT) is an established area of research. But growing CNT on a substrate involves techniques like chemical vapor deposition (CVD) which require use of a catalyst and a high temperature CVD furnace. In contrast, TiO2 nanotubes are a novel material that can be grown on titanium substrate by anodic oxidation with good control over voltage and length[1]. TiO2 nanotubes are found to be nontoxic, biocompatible and have a large surface area making it effective in the area of sensitive detection. This work reports the first instance of attachment of oligonucleotides to TiO2 nanotubes by surface modification. We propose to use this platform for cost-effective field based analysis and quantification.

The TiO2 nanotubes were fabricated by electrochemical anodization of titanium foil in ethylene glycol solution at 40 V for 45 minutes. The resulting TiO2 nanotubes (Fig. 1-a) were characterized using scanning electron microscopy (Hitachi S4800). The TiO2 nanotube surface was then modified by silanization in 2% aminopropyltriethoxysilane (APTES) and activated with 25% glutaraldehyde using a modified method used for Silicon nitride[2] . Cyanine-3 (cy3) fluorescent probes (Applied Biosystems) were covalently attached to the modified TiO2 nanotube substrate by treating the surface in 1nM Cy3 solution. The covalent attachment was confirmed by imaging the sample (Fig. 2-a) using a fluorescent microscope (Olympus IX81-Microfire CCD). Subsequently we attached non-labeled probes to the modified surface and complimentary target nucleotides with cy-5 labels were hybridized to these probes to validate surface chemistry protocol (Fig. 2-b).

Characterization of electrochemical (EC) performance was done by running cyclic voltammetry with TiO2 nanotube substrate as working electrode in 10 mM potassium ferricyanide in 1 M potassium chloride solution. To enhance the conductivity, the TiO2 nanotube substrate was coated with carbon and annealed in an Nitrogen atmosphere at 550 C[3]. The resultant Carbon-TiO2 composite nanotube arrays (Fig. 1-b) showed enhanced electrochemical sensitivity compared to the metallic titanium (Fig. 3). Electrochemical impedance spectroscopy (EIS) on the Carbon-TiO2 nanotube arrays proved lower charge transfer resistance compared to bare Ti and TiO2 nanotubes.

We had earlier reported a multi-wall carbon nanotube (MWCNT) electrochemical biosensing platform with an integrated sample preparation and PCR system developed using multi-scale manufacturing techniques. The microfluidic EC cartridge (Fig. 4) has a counter and reference electrodes and a microfluidic channel, and was fabricated on a glass substrate. We replace the MWCNT with C-TiO2 as working electrodes. The C-TiO2 chip and microfluidic EC cartridge is packaged into a manifold with sample inlet/outlet, electrical connectors and miniaturized potentiostats.

[1] K. Raja, T. Gandhi, and M. Misra, “Effect of water content of ethylene glycol as electrolyte for synthesis of ordered titania nanotubes,” *Electrochemistry communications,* vol. 9, no. 5, pp. 1069-1076, 2007.

[2] J. Diao, D. Ren, J. R. Engstrom *et al.*, “A surface modification strategy on silicon nitride for developing biosensors,” *Analytical biochemistry,* vol. 343, no. 2, pp. 322-328, 2005.

[3] L. Yang, S. Luo, S. Liu *et al.*, “Graphitized carbon nanotubes formed in TiO2 nanotube arrays: a novel functional material with tube-in-tube nanostructure,” *The Journal of Physical Chemistry C,* vol. 112, no. 24, pp. 8939-8943, 2008.

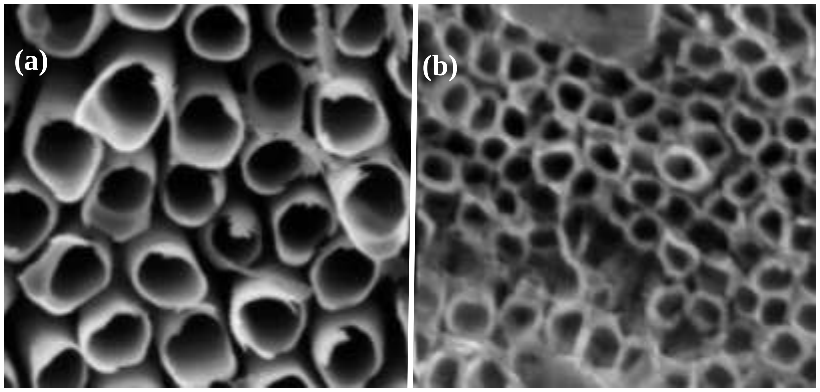

Figure 1: SEM image of TiO2 nanotubes anodized in ethylene glycol (a) and deposited with carbon (b)

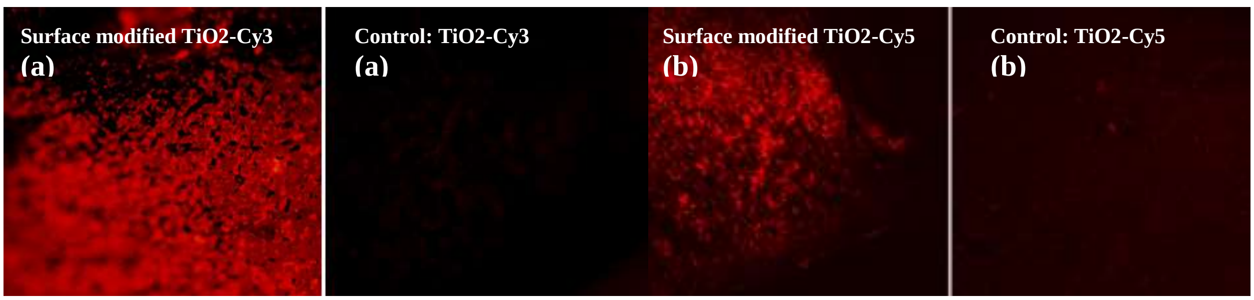

Figure 2: Surface modified Titania nanotubes and normal TiO2 nanotube substrate (control) treated with Cy3 probes (a) and Cy5 probes (b)

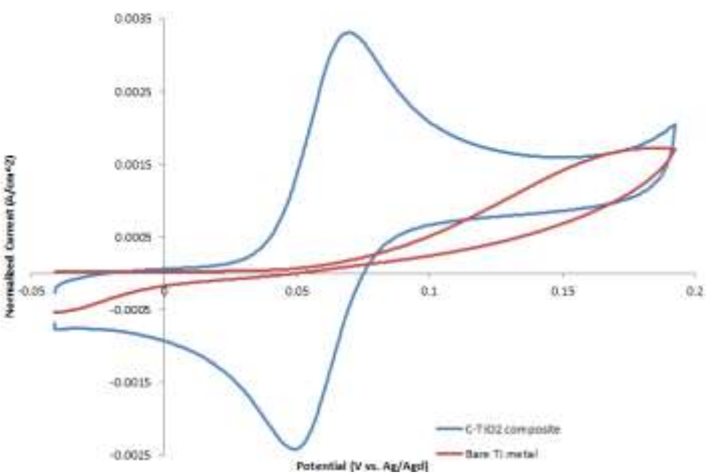

Figure 3: CV of 10 mM $[Fe(CN)_6]^{3-}$ in 1.0 M KCl using Ti metal (red) and C-TiO2 composite nanotubes (blue)

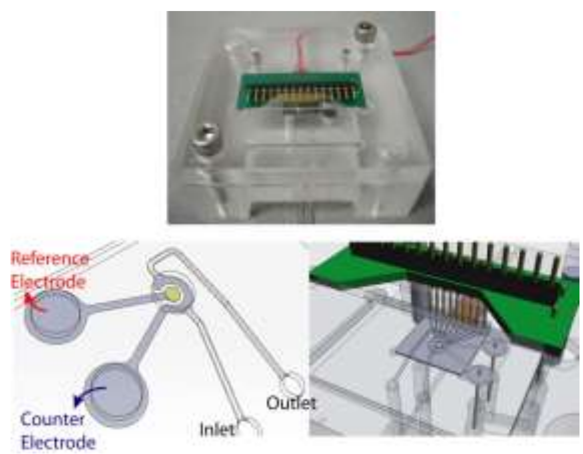

Figure 4: Microfluidic EC (electrochemical) detection system including microfluidic EC cartridge, electrical connectors and miniaturized potentiostats