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Final Project Report

Mimicking Human Vision by Photo-stimulation of Blind Retinas based on NR-CNT sensor

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ABSTRACT

The goal of this project is to present an idea to mimic the human vision i.e. the development of electronic eyes or Bionic Eyes with the aid of a nanosensor. In this project the progress made in the field of visual prosthesis, particularly in the photo-stimulation of a blind retina with the help of nanotechnology is discussed. A wire-free photo-reception approach has been adopted. A novel structure for the retinal photo-stimulation, based on a combination of two nanomaterial systems ideally suited for neurostimulation: semiconductor nanorods (NRs) and carbon nanotubes (CNTs) has been presented. The complete design paradigm along with the fabrication techniques adopted and the complete characterization of such complex optoelectronic systems has been given. It is our belief that successful stimulation of such a light-sensitive system suggests the potential use of these novel platform in future artificial retina applications.

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1. INTRODUCTION

Vision is one of the most important senses in a person's life. There are several diseases that can lead to partial or total loss of vision. According to the World Health Organization, there are 314 million visually impaired individuals worldwide [1]. Some of the most important are:

- Glaucoma refers to four different eye conditions that damage the optic nerve that carries visual information to your brain
- Cataracts cause cloudy vision and are more common in older people
- Optic neuritis is inflammation that can cause temporary or permanent vision loss
- Retinitis pigmentosa refers to retina damage, but leads to blindness only in rare cases
- Tumors that affect the retina or optic nerve can also cause blindness
- Macular degeneration destroys the part of your eye that enables you to see details

Age-related macular degeneration (AMD) is the leading cause of central vision around the globe. The common condition affects the macula, a small region near the center of the retina. This area is responsible for gathering light from objects straight ahead of the viewer. Although the condition does not cause total blindness, the symptoms often get worse over time [2].

Therefore, much progress has been made with the help of medicine and technology to compensate for the loss of vision and invent new methods for making the life of patients with such impairment easier. Visual prosthetics are being developed as a potentially valuable aid for individuals with visual degradation. A visual prosthesis, often referred to as a bionic eye, is an experimental visual device intended to restore functional vision in those suffering from partial or total blindness.

The idea of using electrical current (i.e. electrically stimulating the retina or the visual cortex) to provide sight dates back to the 18th century discussed by Franklin, Tiberius Cavallo and Charles LeRoy. In 1983, Joao Lobo Antunes, a Portuguese doctor, implanted a bionic eye in a person born blind [3].

2. LITERATURE REVIEW

There is a great need to help the ever growing number of patients suffering from age-related macular degeneration in which the photoreceptors in the retina degenerate. In essence, a retinal based visual prosthesis would replace the function of the degenerated photoreceptor cells by stimulating the surviving retinal neuronal machinery. A particular challenge is the need for high-resolution stimulation, along with effective interfacing with the remaining neurons in the retina [4].

An approach of photovoltaic retinal prosthesis to restore sight in blind patients due to degenerative retinal diseases is suggested by Wang L. et al. where a silicon photodiode array for sub-retinal stimulation has been fabricated by a silicon-integrated-circuit/MEMS process. Each pixel in the two-dimensional array contains three series-connected photodiodes, which photovoltaically convert pulsed near-infrared light into bi-phasic current to stimulate nearby retinal neurons without wired power connections. The fabricated device delivers efficient retinal stimulation at safe near-infrared light irradiances without any wired power connections, which greatly simplifies the implantation procedure [5].

Different approaches have been proposed including conducting polymers; such as by Ghezzi D. et al. where soft organic materials are used to couple artificial sensors with neuronal tissues. In their paper, they interface a network of primary neurons that can be grown onto a polymer layer without affecting the optoelectronic properties of the active material or the biological functionality of neuronal network [6]. As suggested by Hintz et al., the major disadvantages of CPs are their low stability under continuous stimulation, exposure to ultraviolet (UV) light or heat which may gradually degrade their properties, as well as the risk of toxic residues [7].

Methods of using quantum dots films are proposed by Lugo K. et al where remote switching of cellular activity by optical QD excitation by integrating QDs with cells. This method make cells photosensitive without using genetic or chemical manipulation, which alters natural cells, in conjunction with Quantum Dots (QDs) [8].

An additional emerging approach to vision restoration is optogenetics, most commonly including the introduction of bacterial opsins into neurons through viral transfection. Particularly, to restore photosensitivity, they genetically targeted a light-activated cation channel, channelrhodopsin-2, to second-order neurons, ON bipolar cells, of degenerated retinas in vivo in the Pde6b (also known as rd1) mouse model. Recent studies have demonstrated the use of optogenetics for restoring light-sensitivity to residual cells in a degenerate retina. The optogenetics approach offers high temporal resolution and cell specificity, and it is minimally invasive [9]. Nevertheless, there are still many challenges that have to be overcome to make this technology suitable for application in vision restoration.

In this project we present a new idea suggested by Lilach Bareket et al. making use of semiconductor nanocrystal (SCNC) systems which are particularly attractive for neuronal stimulation applications due to their tunable optical and electronic properties, photostability, and chemical interfacing diversity.

3. PROJECT DESCRIPTION

We breakup the project description into sub-sections and individually continue with the design, fabrication, characterization and the application of our proposed novel structure.

3.1 DESIGN

Due to many advantages like tunable optical and electronic properties, semiconductor nanocrystal (SCNC) systems are particularly attractive for neuronal stimulation applications. In lieu of such exhaustive efforts, efficient SCNC mediated neuronal stimulation with ambient light intensities is yet to be demonstrated. In this project, we present a novel approach for wire-free retinal photo-stimulation, which is ideally based on a combination of two nanomaterial systems that are suited for neurostimulation: semiconductor nanorods (NRs) and carbon nanotubes (CNTs) (as shown in fig.1). Efficiency in light absorbance is derived from the nanorod geometry, which is followed by the effective charge separation at the NR−CNT interface [10]. CNTs are particularly suitable for this application as they are known to posses superior neuronal recording and stimulation properties [11,12] owing to their natural characteristic of high surface roughness [13,14] and also their biomimetic nature [15,16]. The use of highly porous three-dimensional CNTs as SCNC carrying microelectrodes therefore supports high SCNC loading along with the formation of an electrochemically safe interface, with excellent coupling with the neuronal tissue [17]. Most notably, not only our nano interfaces provide highly efficient photosensitivity, but on a more serious note, they form a truly three-dimensional interface with optimized binding between the optoelectronic device and the biological tissue [15,17].

3.2 FABRICATION

The figure (fig.1) depicts the fabrication process carried out on the NR–CNT films and electrode array: Part (a) provides a schematic representation of the photoactive electrode preparation. NR conjugation onto a CNT film is based on covalent binding enabled by a

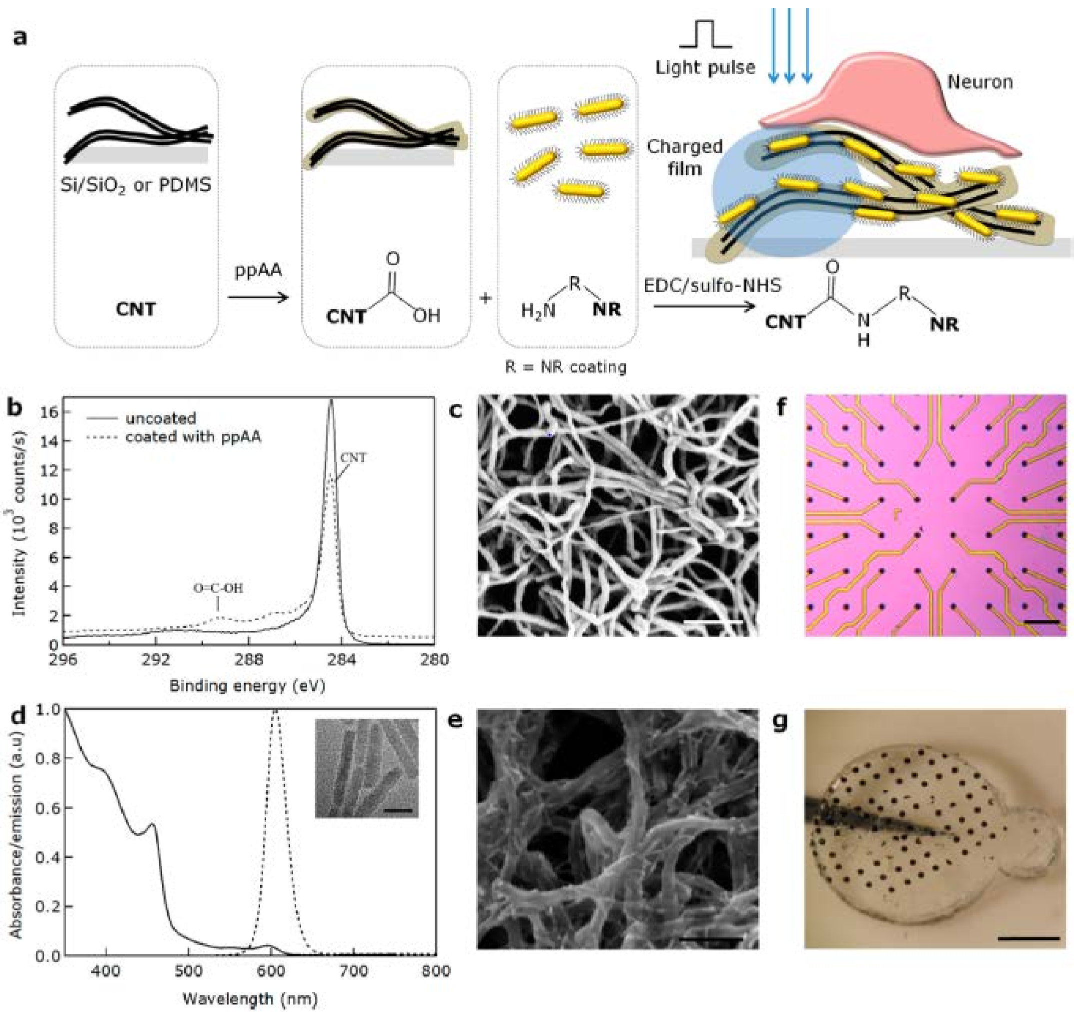

Figure 1: NR−CNT films and electrode arrays [3].

plasma-polymerized acrylic acid (ppAA) coating of the CNTs. Part (b) provides an X-ray photoelectron spectroscopy (XPS) chemical analysis of pristine (continuous line) and ppAA coated CNT film (dashed line) demonstrating the formation of carboxylic groups. We see that in Part (c) a SEM image of a ppAA coated CNT film demonstrating preservation of porous structure; the scale bar is 200 nm. Part (d) depicts the absorption (continuous line) and emission (dashed line) spectrum of the CdSe/CdS NRs; where the scale bar is 20 nm. Part (e) provides us a SEM image of a NR−CNT film; the scale bar being 100 nm. NRs appear as bright elongated elements on the CNTs.

Part (f) on the other hand, is an optical microscope image of a CNT multi electrode array (MEA); the scale bar is kept at 200µm. Lastly, Part (g) portrays a CNT electrode array on a PDMS flexible support; the scale bar is 1 mm.

To achieve clean and effective NR–CNT conjugation, a special covalent bonding scheme is developed based on plasma-polymerized acrylic acid (ppAA) coated CNT films, amine modified NRs, and carbodiimide chemistry. NRs were synthesized in a seeded growth approach [18] and High-density CNT films were first grown on titanium nitride (TiN) coated silicon/silicon dioxide (Si/SiO2) substrates using chemical vapor deposition (CVD) which supports CNT patterning, film porosity, and cleanliness. CNT films were then coated with a ppAA coating featuring carboxylic functional groups (needed for the conjugation step) using a plasma polymerization process. The plasma polymerization offers high conformity, strong adhesion, and surfaces containing no contaminates [19,20]. X-ray photoelectron spectroscopy (XPS) data of the ppAA coated CNT films show a clear carboxylic group (O=C−OH) peak component, which is absent in pristine CNT films, validating the buildup of a ppAA.

3.3 CHARACTERIZATION

The main aim is to characterize a visual scene such as color, motion, and form. In human eye the light-capturing component at the outer segment of the retina, that is, the photoreceptor cells absorbs light, which further simulates the neuronal interface within retina. Similarly, light is absorbed by the NR-CNT film, followed by charge separation at the NR−CNT interface which elicits a neuronal response. To validate the effectiveness of the NR−CNT film for optical stimulation of a light-insensitive neuronal tissue, photo-voltage and photocurrent measurements were conducted using a modulated light source.

Various conjugation procedures and SCNC configurations were systematically explored to better understand the underlying principles until highly efficient surfaces were realized. It is also important to note that, to accommodate good solubility, the maximum concentrations achievable without discernible SCNC aggregation were used (300−900nM, 100nM, and 20−40nM for CdSe−GSH QDs, CdSe/CdS−GSH QDs, and CdSe/CdS−GSH NRs, respectively). To investigate whether the films yielded good electrical properties, photocurrent measurements of coated CNT films were also carried out. Furthermore, the coating material plays a vital role in stabilizing and protecting SCNC from degradation and is therefore an important parameter in determining the safety and stability of the CdSe/CdS NR−CNT system. GSH, a well-known natural antioxidant molecule can contribute to an improved biocompatibility [21].

3.4 APPLICATION

A broad spectrum of critical medical conditions is associated with dysfunctional neuronal connectivity and sensory information transfer to the brain. The most difficult challenge is to develop a high-resolution stimulation technique, along with effective interfacing with the remaining neurons in the retina. The approaches in the recent past, to address these challenges are based on metallic electrodes and are typified by relatively low spatial resolution, rigidity, and cumbersome wiring. The novel approach as proposed in this project deals with neuronal activation along with optical stimulation of photo-responsive surfaces which offers an alternative, wire-free route to address the need for artificial vision, to aid in visual prosthetics.

4. CONCLUSION AND RECOMMENDATIONS

Further optimization of the stability of the system toward implementation in long term in-vivo applications will be needed and is beyond the scope of this investigation. According to our study, by effectively incorporating SCNCs onto CNT surfaces, highly efficient photo-responsive porous films has been realized, demonstrating that a nanomaterial based approach for retinal photo-stimulation will yield better performance and pave way a path for further optimization. Fully understanding the underlying mechanisms of light harvesting, charge separation, and photocurrent generation in our novel nano-structured device remains a challenge, under our ongoing study. The use of a bottom up approach used in this project implies that the technology can be further improved, owing to massive activity in this field. The CdSe/CdS−GSH NR−CNT photo-responsive electrodes presented here represent a major step toward achieving a wire free retinal prosthesis and a paradigm shift from two dimensional to significantly superior three-dimensional biomimetic opto-electrical interfacing.

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