An electrostimulation cell device with patterned $Nb:TiO_2$ thin films as bio-electrodes

Marc Jobin, Cédric Pellodi, Cosmin Sandu, Giacomo Benvenuti, Antonin Sandoz and Luc Stoppini

***Abstract*—**We present a cellular test device based on $Nb:TiO_2$ (niobium dooped titania) transparent conductive oxide (TCO) as bio-electrodes. The device is intended to easily provide electrical stimuli to a given cell tissue and to monitor its response. The $Nb:TiO_2$ thin film deposition were performed with combinatorial chemical beam epitaxy (C-CBE) which allows for linear and well controlled gradients of both Nb concentration (ranging from 3% to10%) and oxide thickness in predefined directions (usually orthogonal). We have systematically characterized the $Nb:TiO_2$ films with Atomic Force Microscopy, Scanning White-light Reflectometry, and sheet resistance Finally, we show the device, i.e the electrodes design and patterning in order to perform to electrical stimuli to the various ways to measure the cell's response.

***Keywords*—** Transparent conductive oxide (TCO), doped titania, cell culture, bio-electrode, white-light reflectometry.

I. Introduction

We are looking for a biocompatible and versatile (in terms of electrical sheet resistivity) transparent conductive oxide which can be used as thin electrodes in biomedical devices. Indeed, the most common TCO, namely ITO (indium tin oxide) is not convenient because of its poor biocompatibility and its predictable lack of availability at a reasonable price in the near feature (indium). Titania (TiO_2) based materials, on the other hand, appear as a prime choice as TiO_2 is the flagship material in term of biocompatibility. Its large bang gap (3eV) makes it optically transparent in the visible range: as a consequence, the device can be used under an epi-fluorescence microscope during the test, which is very valuable in most experiments. Titania is a highly resistive material which can be made electrically conductive with a small concentration of Nb (1) ranging from2% to 10%, i.e. up to the limit of solubility. Nb doping atoms are substitutional to Ti atoms in anatase phase. Conductivity of typically 0.4 $\mu\Omega$cm has been reported (2) which makes $Nb:TiO_2$ competitive to ITO

In this research, we aim to design a versatile device which can be used to study the electro-stimulation of various cell cultures, typically neurons or cardiocytes. Titanium dioxide has already been reported to be a convenient material to promote neural cell growth (3).

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II. Fabrication of the device

A. Deposition of $Nb:TiO_2$ by CBE

Chemical Beam Epitaxy (CBE) is a UHV thin film deposition technique which enables various types of gradients such as chemical and thickness gradients. Its working principle (shown in Fig. 1) is to flow one or several gas of molecular precursors in the chamber, with molecules distributions that are inhomogeneous in a very well controlled way. When the precursor molecules reacts with the heated substrate (again with a controlled temperature distribution) at a specific substrate location, the film will grow at a rate depending on the substrate temperature and with a chemical composition depending of the precursor concentration at this location. As a result, a very large number of films parameters can be synthetized in a single wafer (4'' in our case). This so-called combinatorial approach is very efficient to find the optimal film properties for a given application.

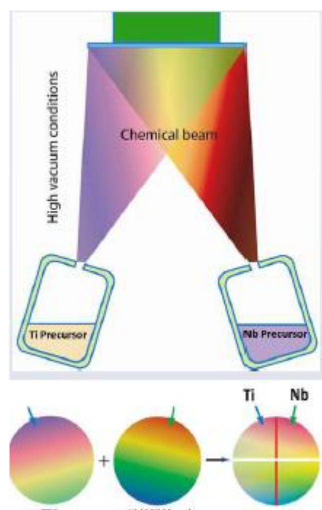

Fig. 1 Schema of CBE with explanation of the gradient

B. Electrode design and etching

The bio-electrodes pattern is shown in Fig. 2a). It consists of three spatially separated patterns, each containing three set of electrodes. The two outer sets of electrodes (i.e those not connected each other) are intended to measure the effects of a *dc* or *ac* electric field on the cell, while the inner set of electrodes (connected by a channel in the middle) can be used the measure the effect of a *dc* or *ac* electric current. We first produced standard metallic electrodes (such as aluminum or Au/Cr) in order to have a control, as Au is the material standard for this application. For the final device, we have used Nb:TiO_2 electrodes deposited by CBE with the optimal Nb concentration. An example of such deposited electrodes on 4'' glass wafer is shown in Fig 2b).

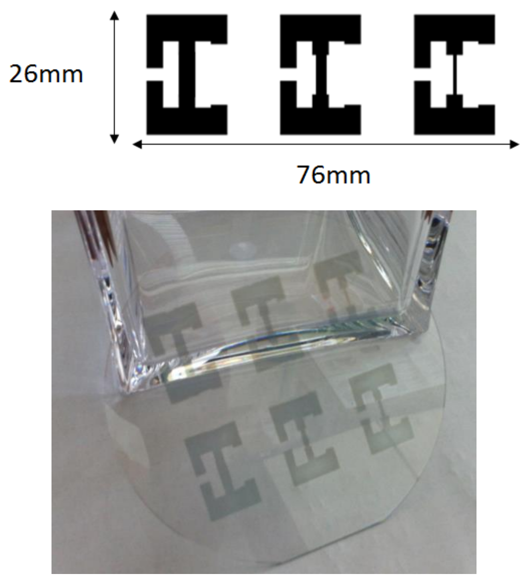

Fig. 2 *a)* Pattern of the electrodes, b) Picture of the Nb: TiO_2 electrodes on a 4 inch glass wafer

C. Encapsulation and electrical contacts

The encapsulation of the bio-electrodes on the final device is shown in Fig. 3. Apart from the integrated circuit (shown in green in Fig 3)), the other layers are made from 1mm thck PMMA layers. The fluidic channels and the openings in the PMMA layers have been made by laser machining with a CO_2 laser. The assembled device is placed in an incubator and electrically connected sine wave generator. Typical signals were 50mVpp at 1 Hz.

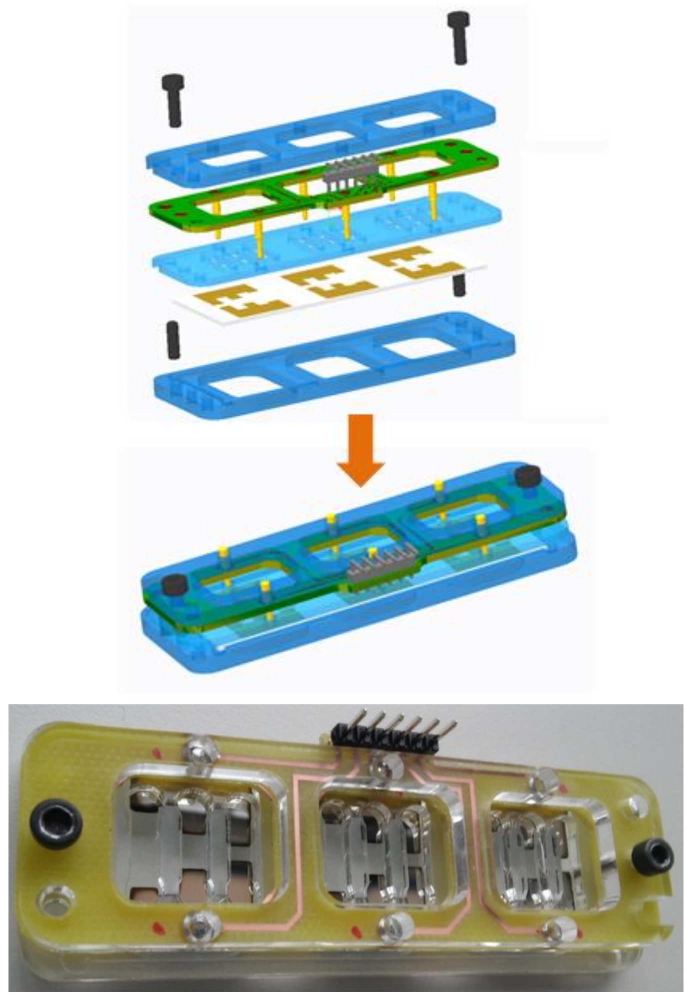

Fig. 3 a) CAD view and b) picture of the device

On the final version, the device is placed in an incubator and the electrical impedance is measured continuously during the incubation time.

III. ELECTRODE CHARACTERIZATION

As explained above, we have used a combinatorial approach for the Nb:TiO2 thin film deposition. The full 4'' wafer then has to be investigated, requiring a full-wafer metrology instrument. We have developed such an instrument (see Ref (4)) which allows for various characterizations on the full wafer, including the optical thickness and the sheet resistivity.

A. Scanning White light reflectometry

The optical thickness *nd* (*n* is the refractive index and *d* is the thickness) can be obtained with the white light reflectivity spectrum. Representative results on Nb:TiO_2 films is shown in Fig 4 and Fig 5), for homogeneous thicknesses and graded thicknesses respectively. We can see the ability of the C-CBE system to produced very well controlled thickness, from 30nm to 3um, over the 4 inch of the wafer.

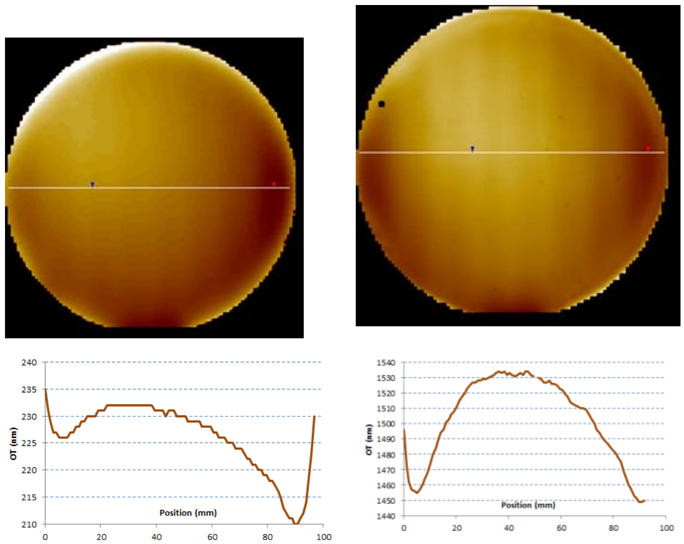

Fig. 4 Optical thickness for homogeneously thick samples. A) thin sample B)thick sample

Fig 6. Optical thickness of the final Nb:TiO2 electrodes

Fig. 6 shows the optical thickness of a bio-electrodes actually used for the biological test. The black to white scale ranges form 214nm to 275nm.

B. Sheet resistance

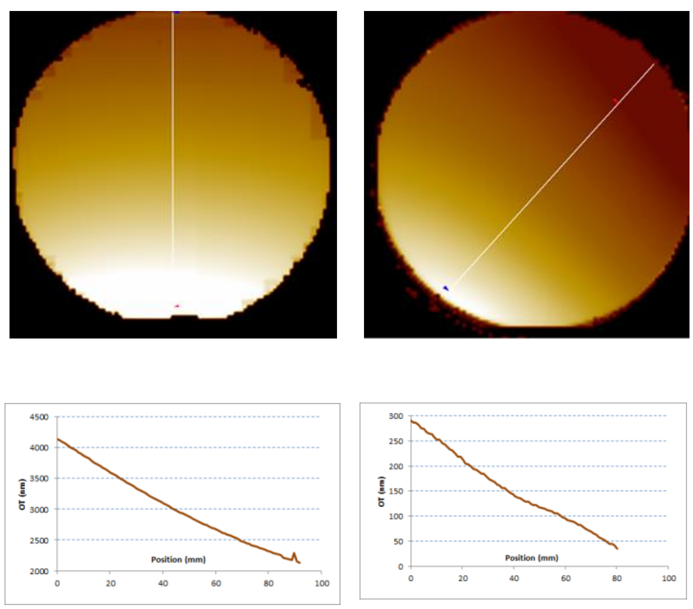

Fig. 5. Optical thickness for graded thicknesses A) thick sample B) thin sample

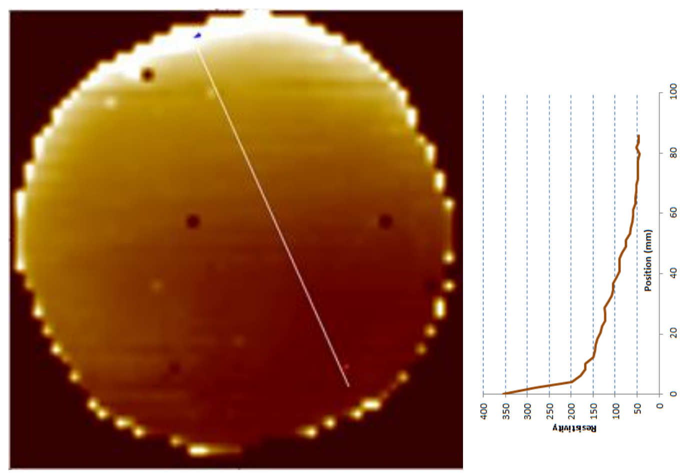

Fig. 7. Sheet resistance

Fig 7. Shows the sheet resistance over the full wafer for an homogeneous thickness Nb:TiO_2 film.

IV. Cells in Electrostimulation

Fig. 8 shows a first biological test performed on the bioelectrodes and devices reported here. We have used neural ReNcells, either with (left part of the Fig) our without (right part) electrical stimulation. These are florescence confocal microscopy images taken after 5 days on incubation. We can see that the influence of the electrostimulation on the growth of neural cells. The experiments have shown that the Nb:TiO_2 deposition is not toxic but do not allow ReNcells to attach very well so far.

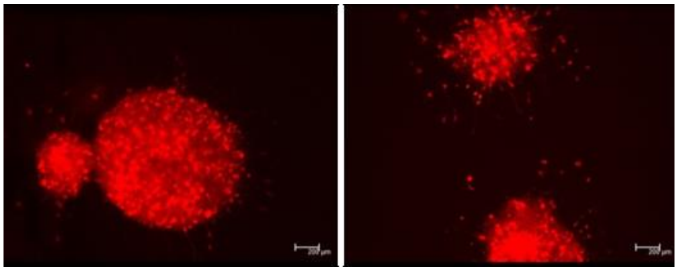

Fig. 8 Pictures of RFP-ReNcells 5 days after seeding with electrical stimulation (left part) or without electrical stimulation (right part)

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