Studies of cellular informative transfer by THz BioMEMS

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Abstract **— We have designed a nanometer THz probe based on a Planar Goubau Line (PGL). This probe is integrated in a Biological MicroElectroMechanical System (BioMEMS) for characterizing the molecular information transfer between the microfluidic environment and the membrane of a single cell.**

Index Terms**—Biological Micro-Electro-Mechanical Systems, Planar Goubau Line, Submillimeter wave devices, Biological cells.**

I. Introduction

The use of micro/nanotechnologies for life science investigations is a new key for a better understanding of biological activities, especially in the field of intra and extra-cellular communication. This work is focused on the area of ligand-receptor interaction analysis. We have recently demonstrated that the nucleoline, a nuclear protein, has been recognized as a binding site of lactoferrin on the cell membranes [1]. The purpose is to follow this specific interaction in a real time, without using molecular labels. The new instrument used to reach this goal is the THz BioMEMS. The principal interest in THz electromagnetic spectrum is the probing of low binding energies inside heavy molecules like proteins [2]. But this trend is difficult due to the very high absorption of THz in aqueous solutions, except if we work on very small volumes. The development of BioMEMS brings us interesting solutions by combining microfluidic circuits and THz planar waveguides. We have recently shown that the submillimeter wave propagation is possible with a wire with a high efficiency.

II. THz Probe

The very innovative investigation of biological entities with THz waves is confronted today with the technological approach we want used. We have demonstrated that THz propagation is possible on a planar metal wire put down a dielectric substrate. The propagation is the same as Goubau propagation [3], but the main difficulty lies in the excitation of this mode. We have designed a coplanar–PGL transition for transferring THz signals issued from the measurement systems to the BioMEMS (Fig. 1). The structure is composed of two transitions and a wire of 5µm of width. The reflection and transmission parameters are measured on the wafer by Vectorial Network Analysers (frequency domain). They are connected to wafer probes designed for Coplanar Waveguides (CPW) up to 0.22 THz. The measurements of this structure in G-band present a transmission coefficient at a relatively high level S_{21}=-2.5dB at 180GHz [4].

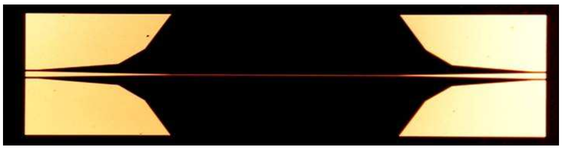

Figure1: Photographs of two CPW to PGL transitions with a Goubau line of 5µm of width and 2mm of length

The challenge is to probe a part of the cell membrane. Molecular assemblies occur during a biochemical event with a size around 1 µm. We have solved this problem by using nanometre wire. We have quantified the spatial resolution. For example, a wire of 100nm width gives us a spot of 2.2µm [5]. The same results could be obtained when we put a cell on the PGL. CHO cell has typically a size of 20µm long when it adheres on the surface (Fig. 2).

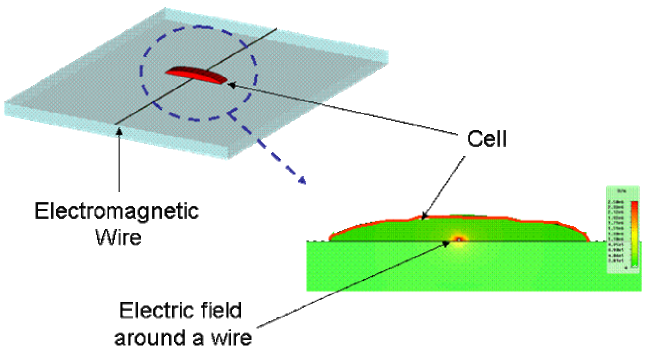

Figure2: Interaction of electric field with a cell along a wire

III. BioMEMS Design

A new mixed technology is required for the BioMEMS fabrication (Fig. 3a). The BioMEMS is composed of 2 parts. A first one is the microfluidic circuit constituted by microchannels and sucking up sub-circuit (Fig. 3b). The measurement channel size is defined by the CHO cell dimensions. We dig microchannels of 50µm width by 150µm depth for guaranteeing a good circulation of the nutritional fluid. The connection of the BioMEMS is carried out by using capillaries of 150µm diameter with 50µm internal diameter. The biological fluid as well as the cells will be injected by using microsyringes connected to the capillaries, and fitted with precise flow control. This flow can be decreased down to 1,6nl/mn and computations are in progress to confirm that very small flow intensity does not create stress on cells.

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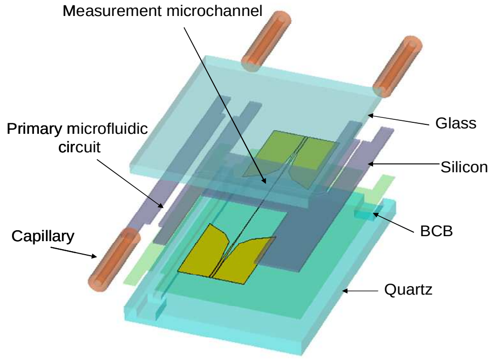
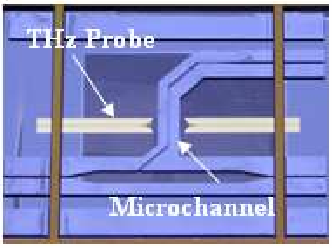


(a)



(b)

Figure 3: (a) Scheme of the BioMEMS, (b) Photography of the final BioMEMS fabricated in a mixed technology.

IV. Result

We have obtained the first measurements on biological solutions involved in the molecular informative transfer. Note that no information about these proteins in the THz spectrum exist today. Experimental results show that we can distinguish a very low concentration of lactoferrin in Phosphate Buffer Saline (PBS) (fig. 4). We can notice an interesting phenomenon: higher are the concentrations, lower are the losses. This can be explained by the replacement of water molecules by lactoferrin molecules. The next step is a best understanding of the hydration phenomena around proteins. This one demonstrates the huge potential of THz BioMEMS for free-label biological characterization.

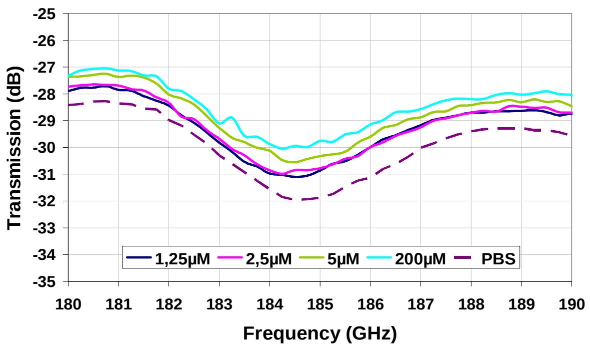


Figure 4: First experimental results obtained on different lactoferrin solution in PBS

We have demonstrated recently that CHO cells growth inside the measurement channel (Fig. 5). We have a cell culture within the microsystem close to the culture classically carried out by biologists.

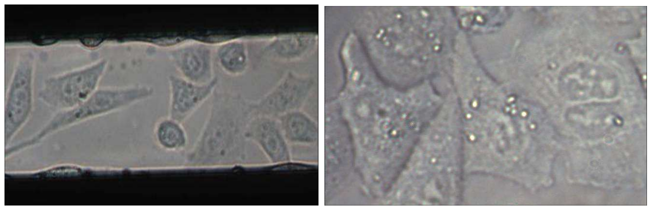


Figure 5: Survival and growth of Chinese Hamster Ovary cells in perfused microchannel

V. Conclusion

THz propagation on wires is the key for integrated probes for biological investigation. We have designed an excitation with a good efficiency and we have demonstrated that the propagation around a nanometer wire size is valid. These conditions make THz measurements on living cells possible with a high spatial resolution.

Acknowledgment

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