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New technology for high throughput THz BioMEMS.

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***Abstract*— We propose a new technology for high throughput bioMEMS based on a mixed technology polymer on silicon. This technology is compatible with microelectronic processes, the electromagnetic propagation, the microfluidic circulation and the biological solutions. We use a new process and a new polymer deposited by a 'cold" plasma technique. We can use it for a surface functionalization or for the encapsulation with plasma assisted wafer bonding.**

***Index Terms*— BioMEMS, Microsystems, Microfluidic, Terahertz, Biosensor, Microtechnology, Plasma polymer**

I. INTRODUCTION

Biosensors are very useful for the investigation of complex media such as chemical or biological mixtures. Many applications are done today in medicine, biological analysis, environment, food processing or defense. But more and more novel uses are possible if we develop a large panel of new technological approaches and new transduction functions.

These sensors are benefited of the electronic integration, as the physical sensors, and have won in response time for example. Today, the emergence of the microtechnology, combined with the microelectronic process, allows designing very sophisticated miniaturized object such as MEMS (MicroElectroMechanical Systems). In these integrated circuits, we mix electronic and mechanical functions such as the fluid mechanic which becomes an electro-microfluidic circuit. This orientation is a chance for the biosensors for improving two other critical points: the sensitivity and the life time. Sensitivity is dramatically increased if we see the ration between the surface and the volume when we work in the microscopic scale. Life time also can be increased by the creation of repaired functions inside the MEMS.

The classical transduction functions (electrochemical, optical, calorimetry, acoustic surface waves…) can be integrated inside these BioMEMS [1]. But the radiofrequency electromagnetic spectrum is not really investigated for the design of biosensors. Some interesting results are presented concerning the GHz spectrum on different biological entities [2]. The results are expressed in term of the dielectric spectroscopy. The development of the THz spectrum domain could bring new interesting response. Note that THz band is not much investigated and corresponds to the "gap" between radiofrequencies and optical waves. A great activity is going to progress, in terms of advanced technology, but also for scientific interest in this transition area between the relaxation phenomena and the rotation-vibration models. The energy of the THz photon corresponds to the energies of bound inside heavy molecules, such as biomolecules [3],[4]. This spectrum could bring interesting new information in molecular biology, as for example the conformation studies of proteins [5].

The planar waveguide technology allows high measurement accuracy and high circuit versatility and leads to the possible integration of them inside new types of BioMEMS. A major problem is to find a substrate compatible with the microfluidic circulation and the high frequency electromagnetic propagation. We have decided to work with a mixed technology keeping a silicon substrate covered with a low loss polymer. Silicon substrate is important for the future development of our BioMEMS to integrate the signal treatment electronic circuit closely to the detector. We have synthesized a new polymer highly compatible with the microelectronic process, including the realization of the metallic waveguides. We explain here the different steps of the conception of our THz BioMEMS, now well optimized and we demonstrate that could be extended at all microfluidic MEMS.

II. PTMDS TECHNOLOGY.

A. Synthesis of the pTMDS (Plasma polymerized TMDS)

We have selected to work with a multilayer structure which is a polymer deposited on a silicon substrate. The silicon is suitable for the design of the embedded electronic functions. The response on the biological material is generally done with a low signal to noise ratio indeed.

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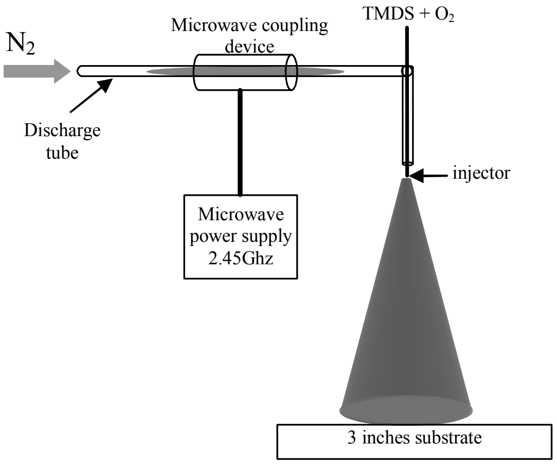

Fig. 1. Experimental after glow principle.

The design of integrated circuits becomes a good argument for treating the signal very closely to the detector. We use also the silicon substrate for the microfluidic interconnects with the external pumps. In the other hand, the polymer is dedicated to (1) the fabrication of microfluidic component (reactor, pump, tanks) in the polymer, including a very important knowledge on the surface treatment such as hydrophobic/hydrophilic property control and the surface functionalization, (2) a good electromagnetic propagation at high frequencies[6]. Figure 1 shows the scheme of the experimental deposition reactor. The nitrogen plasma is created by coaxial cavity resonating at 2450 MHz. Nitrogen is introduced with a 1.8 slpm (Standard Liter per Minute) flow-rate in the tube at 4.3 torr. The gas with excited species is extracted from the 200W microwave power discharge. The monomer used is the TMDS (TetraMethylDiSiloxane). It is introduced in the reaction chamber with 5 sccm (Standard Cubic Centimeter per Minute) and premixed with 25 sccm flow-rate oxygen. Decomposition of this molecule in the reaction cone leads to its partial polymerization. Resulting films, named pTMDS (Plasma polymerized TMDS), are bounded to silicon substrates. More detailed procedure and chemical characteristics are described in [6],[7].

B. Surface characteristics of pTMDS.

We have optimized our process and we obtain today a roughness of 0.1µm peak to peak for a thickness deposition of 40 µm. Note that we have done layers up to 140 µm thickness without any cracks. This high thickness is necessary for digging the microchannels where the biological fluid will circulate. The deposition is processed on 3” silicon wafers. Some theoretical and experimental studies are led for improving the flatness. We have studied the hydrophobicity of our polymer by the measurement of the droplet angle. We have recently demonstrated recently that this character can be modulated with a surface treatment based on 0_2 plasma. It is important for the functionalization of the pTMDS or for the sealing of the microsystems.

C. Electromagnetic characteristics of pTMDS.

No dielectric information exists on this polymer, especially in the THz spectrum. We have realized coplanar waveguides on it, with a layer height of 40µm to avoid interactions between the electric field and the silicon substrate. We have developed the data inversion to retrieve the complex permittivity of pTMDS. Note that we obtain a very flat dispersion of its real part in [8]. It is an excellent point for the well matched design of the waveguides on a broadband from some ten GHz up to some THz.

III. THZ BIOMEMS DESIGN

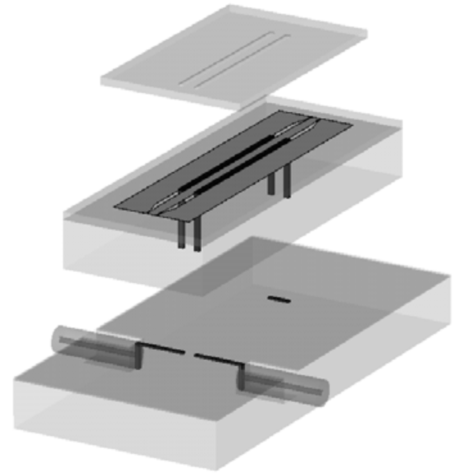

Fig. 2. Split of level representation of BioMEMS.

The microfabrication using this mixed technology is high throughput and low cost, as the integrated circuits. We think it is important for having disposable BioMEMS and for avoiding contaminations. Each bioMEMS consists of tree parts. Figure 2 describes such microsystem. The top level contains the up half microchannels. The middle level deals with the coplanar lines and the bottom half part of microchannels. Note that we only dig them inside the coplanar slots. Under this condition, we have a hard coupling of the electric field inside the biological fluid, with a good increase of the sensitivity measurement. The bottom level is connected with the microfluidic supplies channels where capillaries will be sealed. Three inches double-side polished <100> silicon wafer are used for each level. The top and the middle one are built with thinner silicon wafers. So Bosch process plasma is used to thinning down the silicon wafer at a thickness of about 200 micrometers. The resulting roughness is better than the one obtained through a simple plasma etching method.

A. Bottom level.

Silicon wafer is used to build the lower level where the capillary tubing is connected to the BioMEMS. This one are dug into the silicon layer thanks to the Bosch process. Their depth size is not critical if they are superior.

All bottom level technological process is represented in figure 3. The first fabrication step consists to pattern AZ9260 thick photoresist in a 3" silicon wafer as the mask for the etching step. We apply after a deep Reactive Ion Etching (dRIE) provided by Surface Technology Systems company with the reference Multiplex ICP-ASE. It permits to realize a Bosch process which is etching/passivation succession. We obtain a high aspect ratio and high selectivity with the photoresist. The anisotropic etching constitutes the capillary tubing access of about 130 µm diameter size. The photoresist is removed with acetone. The microfluidic supply channels and their connections to the capillary tubing access are made in the same manner, but with about 20 µm etching depth. Finally, we deposit a thin pTMDS layer using to the bonding with the middle level.

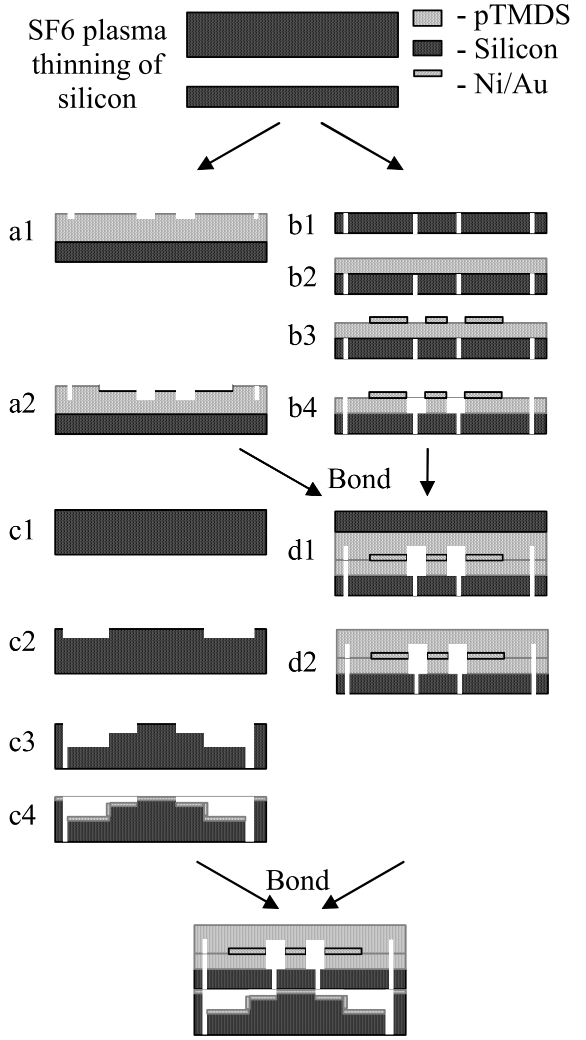

Fig. 3. All BioMEMS technological steps. Step a1 to a2: fabrication of the top level: half upper microchannel and the anchor sytem. Step b1 to b4: fabrication of the middle level: the columns, the coplanar lines and lower microchannels. Step c1 to c4: fabrication of the bottom level: connects to the capillary tubing. Step d1 tod4: the middle and the top level bonded. Etching of the top level silicon wafer.

B. Top level.

The fabrication of the top level is like the bottom level. The main difference is about the pTMDS layer which thickness is now 30 µm. The polymer etching is realized with an Oracle system provided by the Trion company. The gas is a fluorine and oxygen mixture. The mask is also AZ9260 photoresist. The top level technological process is a succession of photolithography and etching to realize the half upper microchannel and the lineprint.

C. The middle level.

This level hold the coplanar lines, the lower half microchannels and the supply columns for bringing the biological solution between the bottom level to the microchannels. The first step is to dig these columns from the upper face of thinner silicon wafer to the lower face. The etching is realized with optimized Bosch process to obtain the ratio aspect 20 µm length on 200 µm depth. We take into account the different etching rates due to the small size. Then, we deposit a ten micrometers thickness of pTMDS. We sputtered 40 nm of nickel as binding layer, followed by 1 µm of gold. For the design of planar waveguides, we realize a photoresist mask and we etch with an argon ion physical attack in Plassys MU350 system. The photoresist is stripped with acetone and with RIE attack in oxygen gaz. Then a photolithography permits to etch the microchannels in the polymer material. The chemical structure is mainly based on inorganic Si-O-Si chains and organic methyl terminal groups and consequently near of composed siloxan material as polydimethilsiloxane (PDMS), methylsesquioxane (MSQ). A mixture gaze with a Tetrafluoromethane (CF_4) with addition oxygen is used to etch the pTMDS layer in ICP with RIE Oracle system. We obtain 0.4 µm per minute etch rate with about 3:1 selectivity to photoresist on nickel film.

D. Assembly

Two pTMDS layer are necessary to bond two levels with few micrometers precision. It consists in a reactivation of the surface with oxygen plasma realized in a parallel plate polarized reactor. The levels are put in a double side mask aligner (Karl Suss MA6) and the bonding is realized with a Karl Suss SB6 bonder. In first, the top level and the middle level are bonded. The thinner silicon of the top level is etching up to the pTMDS layer. Secondly, the top and middle levels are bonded to form the full structure. Each BioMEMS are released with cleave anchor system designed into each wafer.

IV. BIOLOGICAL INTEREST AND MEASUREMENTS.

A. Procedure of measurement (figure 4)

The measurement of complex dielectric procedure requires microfluidic pump. For instance, we use ten microliters syringes placed in a constant rate pump. The capillary tubings are a standard polyimide coating Flexible Fused Silica produced by Polymicro Technologies. They are connected to the syringe with sleeve and fitting system. It is possible to connect several inner diameters from 2 to 75 µm at the BioMEMS, with the same technology process.

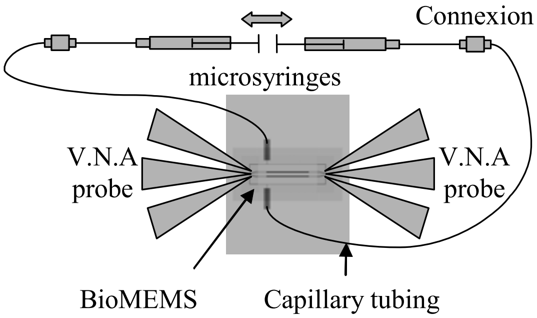

Fig. 4. Schematic measurement bench.

For the electromagnetic measurement, the first method operate on coplanar waveguide with Vectorial Network Analyzers (VNA) Agilent 8510XF in the bandwidth 0.45-110 GHz and Anritsu 37147C working in the bandwidth 140-220 GHz. It is associated with mixers of reference V05VNA2-T/R from OML (Oleson Microwave Laboratories). We use standard LRM calibration with a calibration kit of Cascade Microtech. The second method is a temporal measurement using a Ti:Al_2O_3 femtosecond laser. It is based on electroabsorption sampling [9]. LT-GaAs and LT-AlGaAs layers are bonded on the coplanar striplines. These materials are respectively used to generate a sub-picosecond electrical pulse and to sample the electric field after propagation. The maximal frequency is about 1 terahertz. The lines are designed to have about 20 to 30dB maximum transmission loss. They contain tapers to attack the microchannel and each part of the waveguide has a characteristic impedance of about 50 ohms calculated with a full 3D software named Microwave Studio® from Computer Simulation Technology (CST). The microchannels are filled with water during the simulation. Their lengths are 1000 micrometers for the VNA measurement and 500 micrometers for the electro-optical method. Water is considered as a reference for the simulation because it is generally a solvent for a great majority of proteins solutions. We use a second order Debye model for its modeling. From the scattering parameter measurements, we can calculate the complex dielectric permittivity of the solution running out the microchannel. We extract the permittivity by using Microwave Studio®.

V. CONCLUSION

We have presented a novel fabrication of a BioMEMS, especially dedicated to the THz BioMEMS design. We have shown that a mixed technology using a high thickness polymer layer on silicon is a proper way for this fabrication. Moreover, our technological approach is highly compatible with the microelectronic process leading to high throughput BioMEMS. Of course, this technology could be extended to the design of other microfluidic microsystems. We can now plan to design disposable Microsystems which is more preferable for guaranteeing the biological security and capable of a large screening analysis on a population.

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REFERENCES

[1] R. Bashir, “BioMEMS: State-of-the-art in detection, opportunities and prospects”, *Advanced Drug Delivery Reviews*, Vol.56, pp.1565-1586, 2004.

[2] G.R. Facer, D.A. Notterman, L.L. Sohn, “Dielectric spectroscopy for bioanalysis: From 40 Hz to 26.5 GHz in a microfabricated waveguide”, *APL*, Vol.78, n°7, pp 996-998, 2001.

[3] J. Hefti, A. Pan, A. Kumar, “Sensitive detection method of dielectric dispersions in aqueous-based, surface bound macromolecular structures using microwave spectroscopy”, *APL*, Vol.75, n°12, pp 1802-1804, 1999

[4] S.W. Smye, J.M. Chamberlain, A.J. Fitzerald, E. Berry, “The interaction between Terahertz radiation and biological tissue”*, Phys. Med. Biol.*, Vol.46, pp R101-R112, 2001.

[5] P.H. Siegel, “Terahertz technology in biology and medicine”, *IEEE-MTT*, Vol.52, n°10, pp2438-2447, 2004.

[6] B. Bocquet, N. Bourzgui, Y. Guhel, V. Mille, P. Supiot, C. Vivien, “Design Of Silicon-PPTMDS Bio-Mems By Cold RPECVD”, SPIE International Symposium, San Jose, California (USA), 26-27 January 2004, *Proc. of SPIE Microfluidics*, BioMEMS and Medical Microsystems II, Vol. 5345, pp. 118-129.

[7] Philippe Supiot, Céline Vivien, Agnés Granier, Angélique Bousquet, Anna Mackova, David Escaich, Richard Clergereaux, Patrice Raynaud, Zdenek Stryhal, Jaroslay Paylik, “Growth and Modification of Organosilicon Films in PECVD and remote Afterglow Reactors”, *Plasma Process. Polym. 2006*, 3, pp. 100-109.

[8] V. Mille, N.E. Bourzgui, F. Mejdjoub, L. Desplanque, J.F. Lampin, P. Supiot, B. Bocquet, “Technological development of THz microfluidic Microsystems for biological spectroscopy”, *12th IEEE International Conference on Terahertz Electronics*, Sept. 27- Oct. 1, Karlsruhe, Germany, 2004, pp. 549-550.

[9] L. Desplanque, J.F. Lampin, F. Mollot, Appl. Phys. Lett., Vol. 84, p.2049, 2004