Microfluidic Development Platform for Nanowire-based BioSensor Applications

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Summary

The Board of Regents awarded the Advanced Materials Research Institute (AMRI) at the University of New Orleans along with its partner's funds from the Post-Katrina Support Fund Initiative (PKSFI) [1]. The project (called Post-Katrina project) addresses several aspects including development of advanced materials for sensor and energy applications. In the FRG1 sub-project partners from AMRI, LSU's Health Science Center (LSUHSC) in New Orleans, and LSU-CAMD (CAMD) in Baton Rouge are combining bio-functionalized nanomaterials with microfluidic systems to build BioMEMS based sensor devices. This report is summarizing primarily the LSU-CAMD efforts. A separate contribution showing some of AMRI's efforts is in the user section.

Introduction

The overall project goal along with the partner responsibility is illustrated in Fig. 1. The main idea is to engineer biomolecules with specific binding affinity to targeted sample molecules (task performed by LSUHSC) and covalently bind them to nanowires synthesized or nanomachined (task performed by AMRI). These 'bio-functionalized' nanowires are then integrated on silicon or glass substrates patterned with a conductive pad layout and assembled into a fluidic package for convenient testing (task performed by CAMD). Microfluidic packaging is an effort started at CAMD about 8 years ago as part of CAMD's participation in the Center for Bio-ModularMicrofludic Systems (CBM^2) and the DARPA BioMagneticIC project in which researchers from CAMD and AMRI developed a microfluidic detection system based on functionalized magnetic beads. The key ideas of the modular stack is using molded fluidic chips with passive alignment features and open areas into which customized, bio-functionalized chips can be inserted and easily interconnected. After assembly the stack forms a compact unit providing convenient ports for fluidic, optical, and electrical interconnects. Figure 2 illustrates the concept and shows a first generation result used for developing the technology. Fabrication methods include micromachining and hot embossing of microfluidic chips with packaging and interface functions, optical lithography and thin-film etching for conductive layer patterning, assembly of stack components using a passive alignment approach with features being an integral part of the chip design, and bonding and interconnecting to peripheral instruments needed for operation and testing. References [2,3,4,5,6,7] describe some of the design, process, and application details of the modular stack concept.

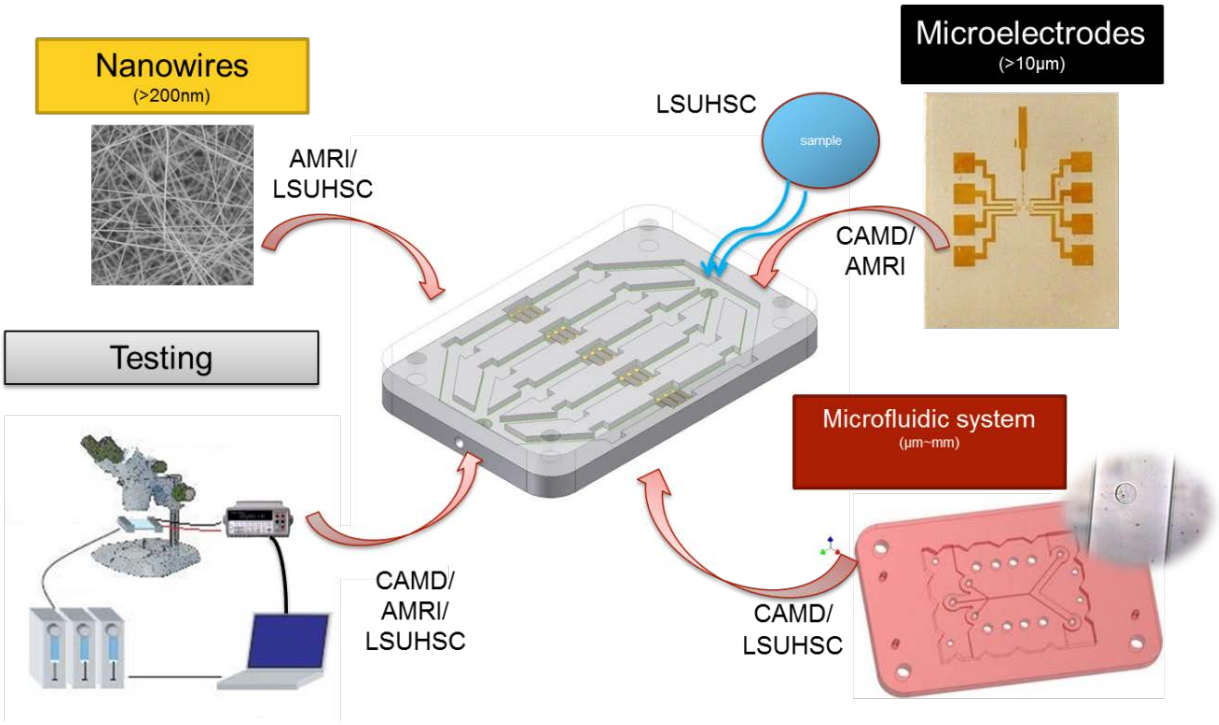


Fig. 1: Project goal and assignments of partner projects of the FRG1 team, Post-Katrina project.

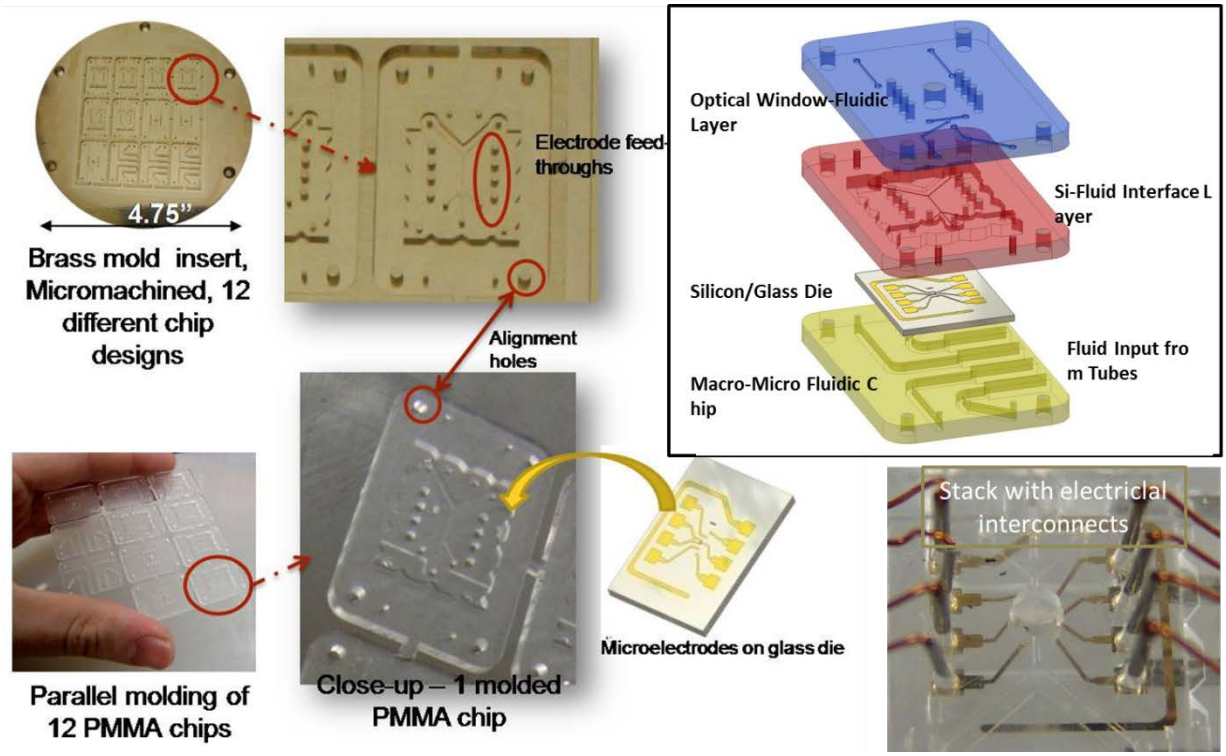


Fig. 2: Concept and example of a modular fluidic sensor package with passively aligned Si or glass based sensor chip.

Fabrication and Integration

In 2011 research from previous years was focused on building a fluidic package compatible with nanowire-assembled Si chip integration. Several approaches have been discussed and are outlined in Figure 3.

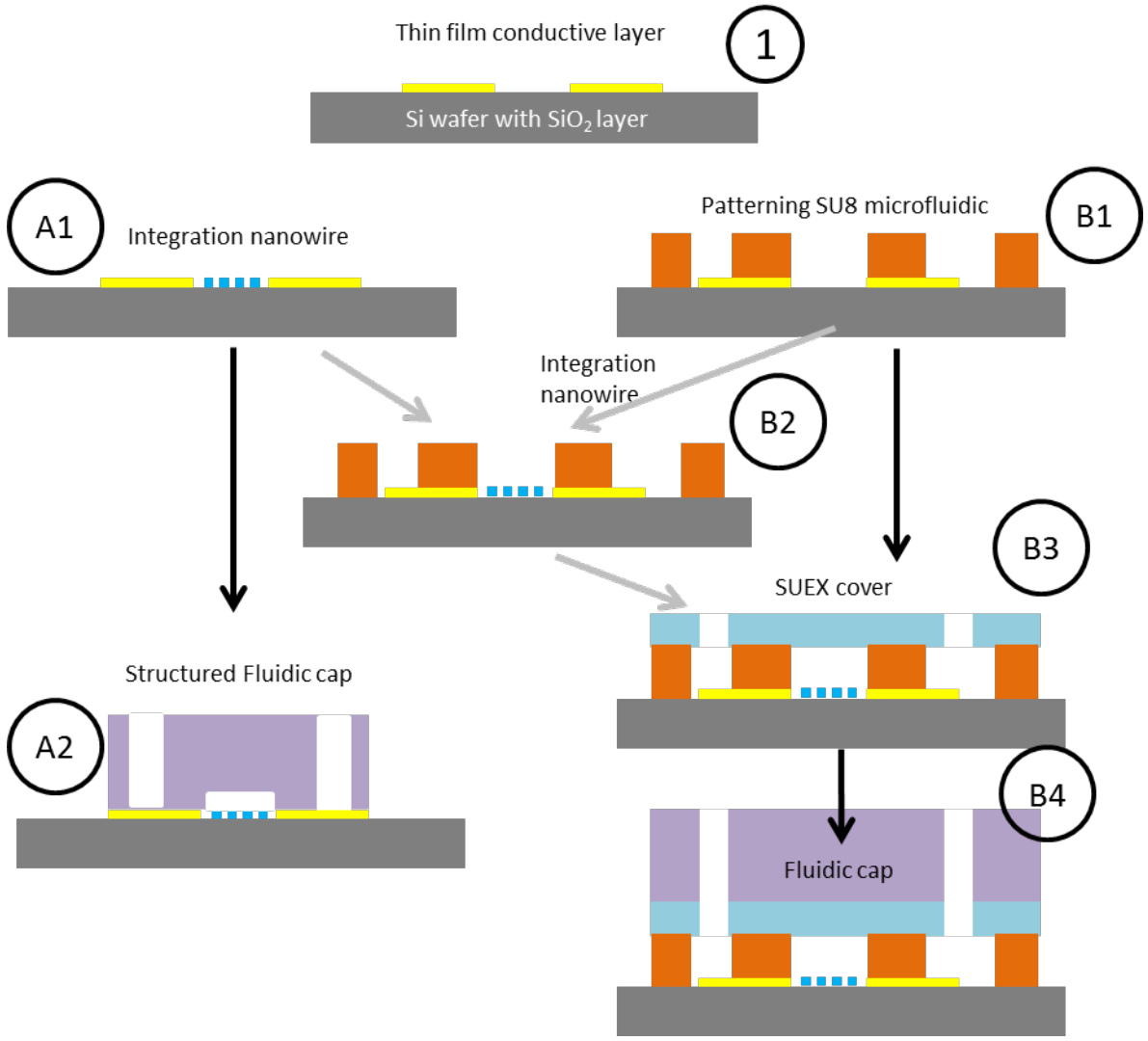


Fig. 3: Schematic of different fabrication approaches applied and tested in this project.

Starting with a silicon wafer covered with a 1-2µm thick SiO_2 insulation layer a thin metal layer (Cr/Au) is deposited by e-beam evaporation, coated with a thin photoresist and subsequently patterned with the micro/macroelectrode design (Fig. 4a) using optical lithography and wet-etching. In process sequence A1-A2 the nanowires are assembled into the fingers of the microelectrode pattern (Fig. 4b, c) thereby connecting them to the micro/macroelectrodes [8]. Process is completed by aligned attaching/gluing a PDMS casted fluidic cap that also contains a microfluidic channel to the Si substrate (Fig. 4d-f). While this simple approach is suitable for prototyping a number of issues compromise the results. For example proper PDMS bonding of the microfluidic channel requires

oxygen plasma treatment which compromises the adhesion to the Au electrodes (leakage). Manual alignment to precisely place the channel above the electrode field requires a liquid film of PDMS to allow sliding until properly positioned. This often results in covering the electrodes and also clogging the microfluidic channel. Lastly, additional liquid PDMS is pasted around the cap occasionally blocking electrode pads and resulting in poor electrical connections making the entire approach very unreliable with poor fabrication yield.

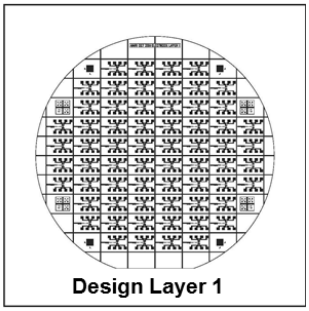


Fig. 4a: Layout of 64 chips with micro/macroelectrode designs.

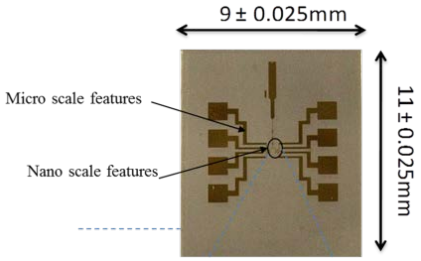


Fig. 4b: Diced Si chip with integrated nanowires.

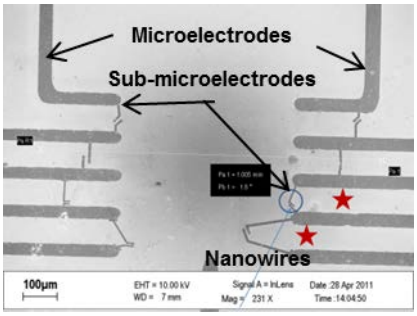


Fig. 4c: SEM picture of electrode and nanowire assembly.

Fig. 4d: Micromachined brass mold.

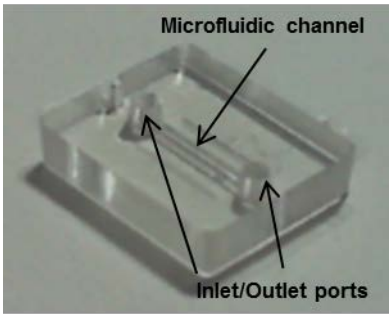


Fig. 4e: Casted PDMS fluidic cap with microchannel and ports.

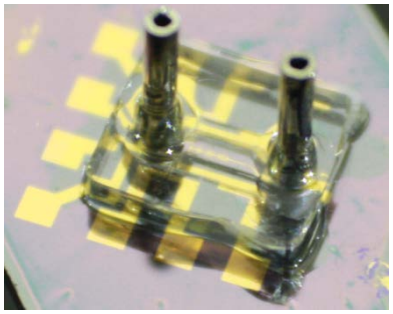


Fig. 4f: Assembled fluidic cap on Si dice with fluidic ports.

In order to overcome the alignment and handling issues an additional microfluidic pattern was designed and patterned in thick SU8 directly on top of the micro/macroelectrode design using aligned UV lithography. The current efforts include process steps B1, B3, B4 shown in Figure 3 and the assembled device is illustrated in Fig. 5a. After standard fabrication of the thin film micro/macroelectrode layer (1) a microfluidic layer is precisely patterned relative the electrodes using aligned optical lithography and thick SU8 resist (B1). The fluidic layout also includes mechanical structures defining a glue reservoir that is preventing any glue needed for cap assembly from reaching either electrode or contact pads thus ensuring good electrical interconnects. The fluidic cap can either be molded in PDMS or also hard plastic (e.g. PMMA) using a brass mold. The cap also provides ports for tubing that are connected to pumps via rubber tubes (Fig. 5c). When using hard plastic cover an additional seal layer is needed covering the microfluidic channel and providing openings for the cap. Step B3 in Fig. 3 shows an example for cover application using SUEX dry resist sheets (for details see contribution in this annual report from D. Johnson et. al. on SIEX resist for microfluidic applications) laminated onto the open channels and patterned using UV lithography. With the microfluidic channels properly protected the cap can now glued to the chip completing the fabrication process (step B4 in Fig. 3).

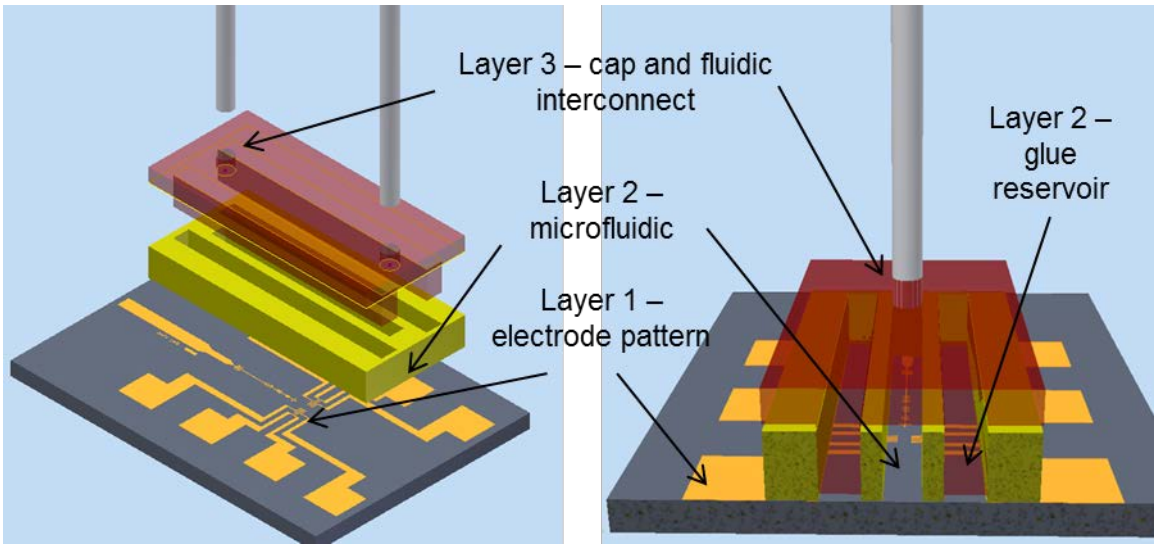


Fig. 5a: Schematic of the different layers/fabrication steps of the fully packaged sensor device.

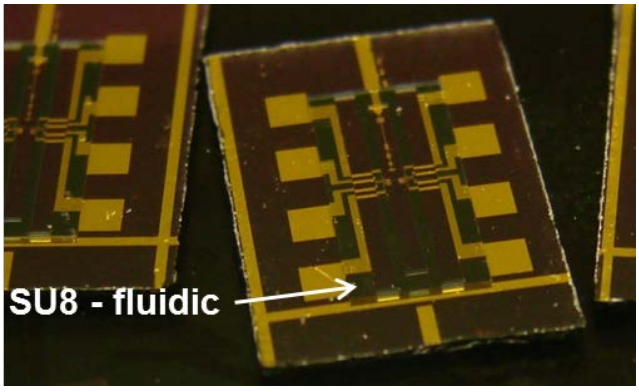


Fig. 5b: Si dice with layers 1 and 2 after dicing.

Fig. 5c: Molded fluidic caps (PMMA) with lateral ports to accommodate tubing.

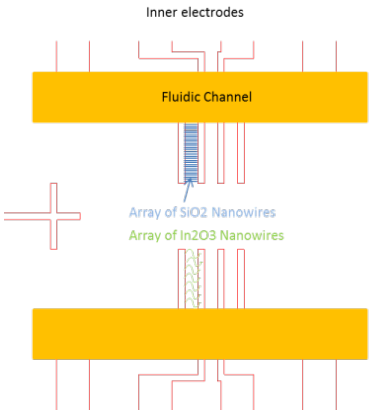


Fig. 5d: Different assembly options to integrate nanowires into the electrode layout.

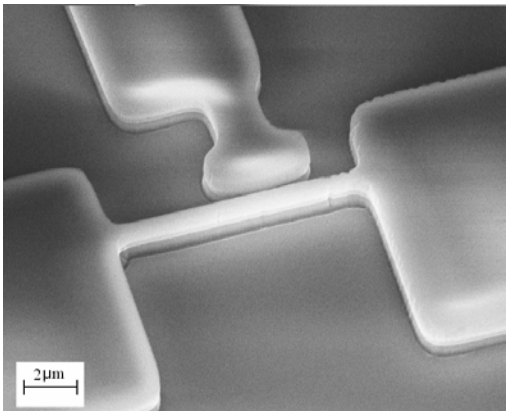


Fig. 5e: Nanowire patterned into SOI wafer using E-beam writing and DRIE-etching.

It should be noted that our current efforts where only using Si dice without integrated nanowires. These have to be added in the device as shown in Step B2, Fig. 3. Partners at AMRI are

investigating two different approaches as illustrated in Fig. 5d. Using orientation of nanowire bundles (either by flow or combing, [9]) nanowires will be randomly positioned in the electrode area and connecting with the Au electrodes. This process allows for separate fabrication of the wires and takes advantage of well-defined flow conditions via the surrounding fluidic channel. The other approach is a conventional top-down approach in which Si nanowires are patterned by E-beam lithography and DRIE-etched into a Silicon-on-insulator (SOI) wafer as illustrated in Fig. 5e and connected to the micro/macroelectrodes via thin-film deposition and lift-off processing.

Device Testing

Sensor chip testing has another focus at CAMD strongly supported by Y. Jin. The main idea outlined in Figure 6 is combining commercial solutions in conjunction with customized sensor chips. This approach is very flexible and offers highest performance for initial laboratory testing and can be transferred into a smaller footprint using advanced fluidic chip designs and integration with Printed Circuit Board technology for real sensor application at a later time.

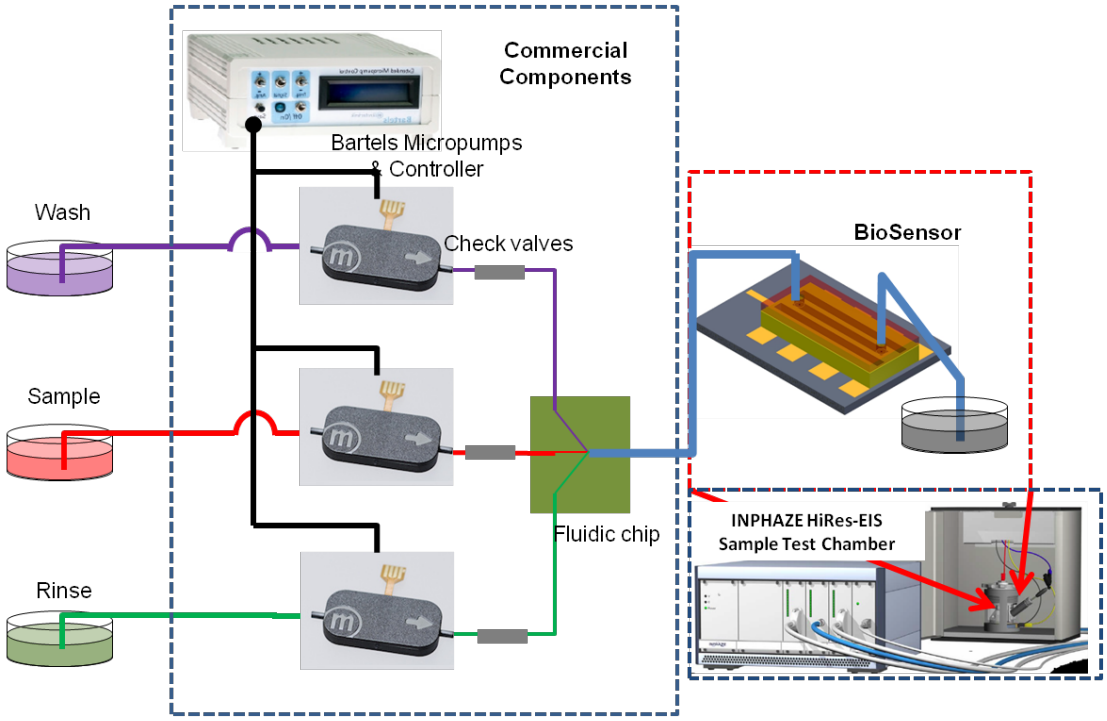


Figure 6: Principle layout of sensor test stand using commercial components (Bartels micropumps and controller) for fluidic delivery and a highly sensitive impedance measurement instrument (INPHAZE) with customized detection chamber for electrical testing. A Thinxxs chip combines three liquids into one outlet connected to the BioSensor chip.

Figure 7 shows part of the fluidic setup namely Bartels pumps (mp6) with controller, a Thinxxs mixer chip, and a BioSensor chip with no nanowires. The successful flow of liquid through the assembly demonstrates that the latest generation of Bartels micropumps is suitable for driving liquids through the fluidic system including the narrow, shallow sensor channels.

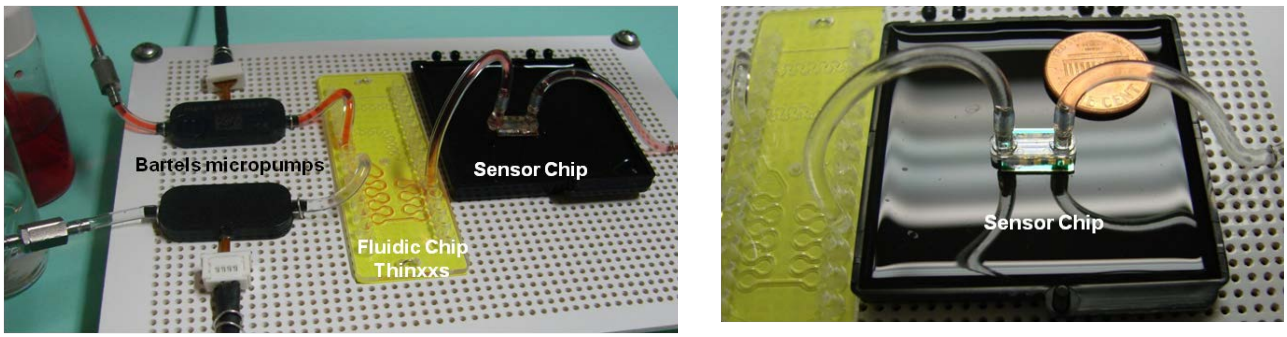


Figure 7: Fluidic setup for sensor chip testing utilizing commercial components from Bartels Mikrotechnik and Thinxxs. Colored DI water is pushed through the setup demonstrating that the micropump is capable of pumping liquid through the setup.

Electrical measurements are done in a special chamber attached to the INPHAZE impedance device (Triode chamber) illustrated in Figure 8. The sensor chip is placed inside the Triode chamber which accommodates tubes for fluidic interconnect and poco-pins providing temporary electrical connections to the electrodes on the sensor chip. A Faraday cage (not shown) is placed around the chamber for additional shielding during the actual measurements. Data are collected through INPAHAZE data acquisition unit which is connected to a laptop and controlled by LABVIEW software.

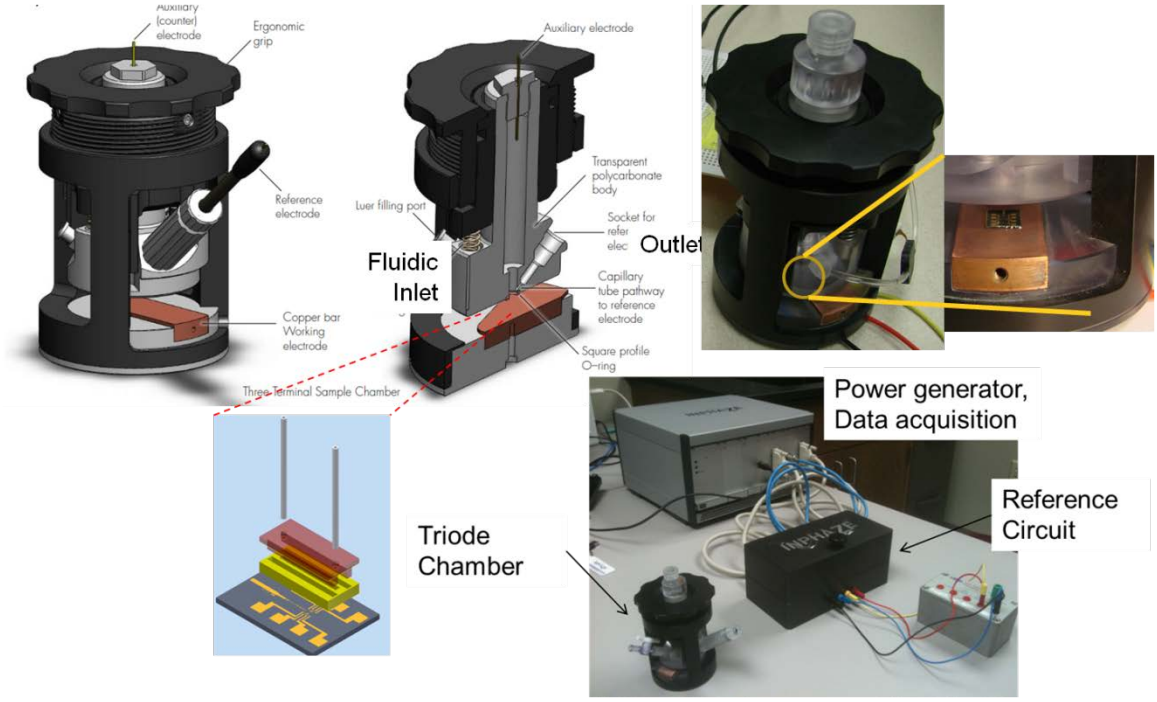
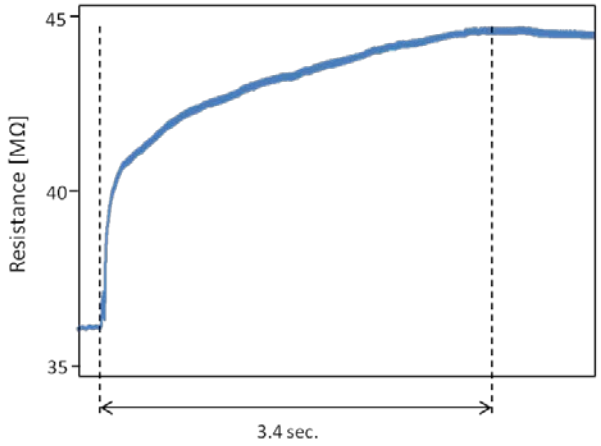


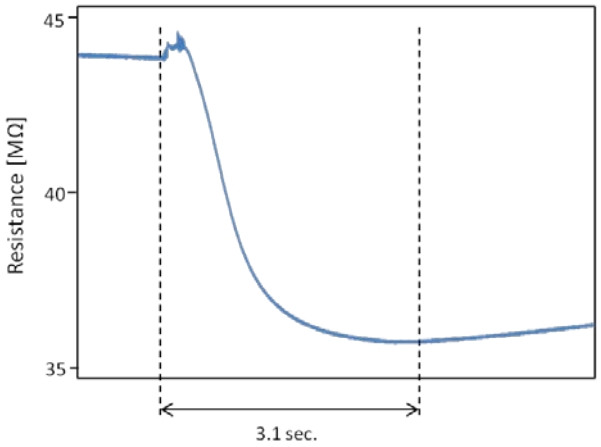
Figure 8: INPHAZE triode chamber with fluidic and electrical interconnect.

Figures 9 show the principle operation using two liquids (DI water, iso-propyl-alcohol/IPA) and an open circuit (electrode pattern without nanowire) configuration. Depending upon which liquid fills the microfluidic channel/sensor volume conductivity between the open electrodes is changed resulting in different resistance measured in the Triode chamber. Operation for different flow pattern

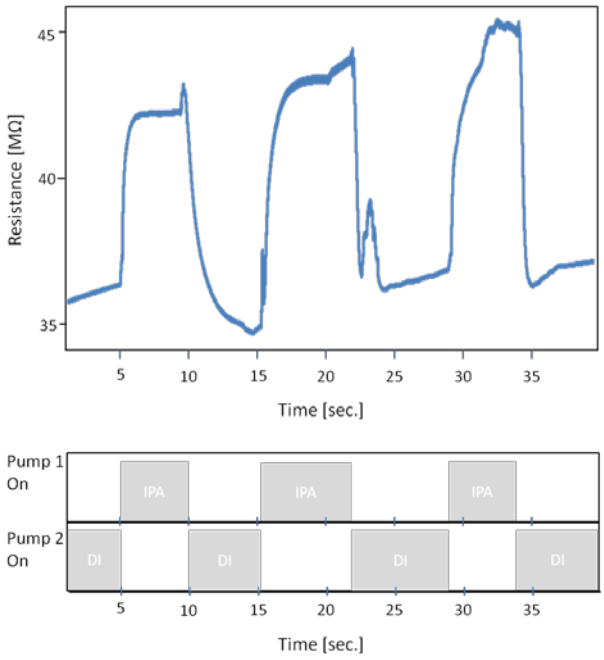
illustrate that absolute resistance measurements is a suitable means of detection but can easily be influenced by external, hard to control parameters such as temperature, bubbles, and similar.



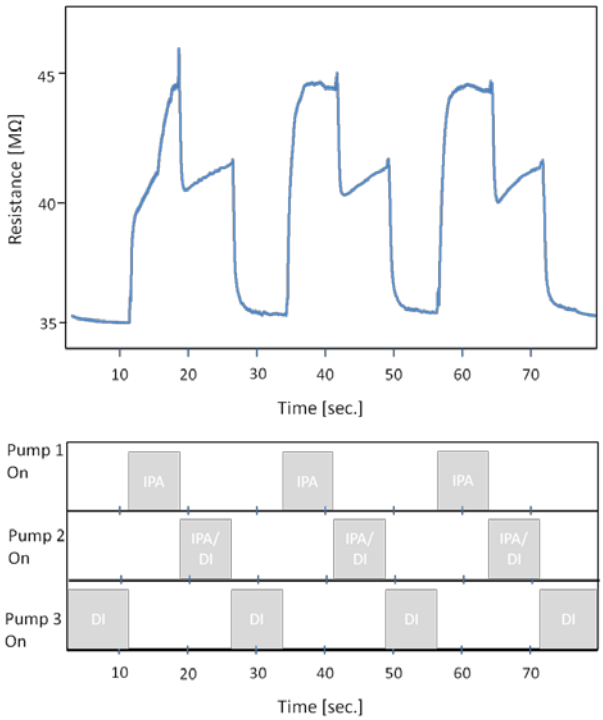
Test 1: Fluidic channel is filled with DI water and IPA is injected. A rapid signal change occurs transiting into a state-of-equilibrium after about 3.5 sec.



Test 2: Fluidic channel is filled with IPA and DI water is injected. A similar transition is measured changing the resistance back to the initial value and indicating that operation is reversed.



Test 3: Alternating flow from both reservoirs with the pumping pattern illustrated below the graph. Flow pattern is fairly repeatable but shows a slight signal drift suggesting that environmental factors (for example temperature) influence the absolute measurement.



Test 4: Alternating flow from three reservoirs, DI water, IPA, and a DI water/IPA mix using three pumps. The pumping scheme is illustrated below the graph. Similar comments as for previous measurements just with an additional intermediate signal produced by the 3rd liquid.

Fig. 6: Measurements of sensor performance using different liquids pumped across an open circuit (see text for details).

Conclusion

Our joint efforts produced a viable concept of fabricating and operating BioSensor chips with a microfluidic package. Work done at AMRI and LSUHSC will provide functionalized nanowires that can be integrated into the fluidic package at moderate process conditions (max. temperature ~60˚C) or possibly at room temperature if gluing the fluidic cap without the protecting SUEX cover is feasible. Off-the-shelf fluidic modules such as pumps and flow controller will allow flexible operation on a small footprint and ultimately enable fabrication of a portable, handheld sensor system.

Acknowledgements

The authors like to thank the Louisiana Board of Regents for continuous funding of this project since 2007, our coworkers at AMRI/UNO, LSU Health Science Center in New Orleans, and the LSU-CAMD staff for their support and contributions. Finally we would like to acknowledge the hard work and outstanding results achieved by a number of students at all institutions who have participated in this project since 2007 and have laid a solid foundation for today's results.

References

[1] Information about the P-KFSI program at http://laregents.org/P-KSFI.ppt or elsewhere at the Board of Regents homepage at http://regents.state.la.us/.

[2] P. Datta; *Modular, Polymeric Development Platform for Microfluidic Applications - Design, Fabrication, Testing and Examples*; Dissertation University Karlsruhe (2007).

[3] S. Gurung; *Passive alignment of micro-fluidic chips using the principle of elastic averging*; Master Thesis Louisiana State University, Mech. Eng. (2007).

[4] N. Frische; *Microfluidic Impedance Spectroscopy Module for label-free Particle sensing and counting*; Bachelor Thesis University of Applied Science Gelsenkirchen (2009).

[5] P. Datta, J. Goettert; *Multi-level Modular Polymer Microfluidics with Optimized Form Factor*, Proc. HARMST 2009, Saskatoon, Canada (2009), 147-148.

[6] P. Datta, G. George, S. Tiwari, J. Goettert; *Monolithic fabrication of electro-fluidic polymer microchips*, Microsyst Technol (2009) 15:463–469.

[7] N. Frische, P. Datta, J. Goettert; *Development of a biological detection platform utilizing a modular microfluidic stack*; Microsyst Technol (2010) 16:1553-1561.

[8] R. Long et. al.; *Precise Voltage-contrast Image Assisted Positioning for In-situ E-beam Nanolithography for Nanodevice Fabrication with Suspended Nanowire Structures*; Nanotechnology **20**, 285306 (2009) technique also highlighted in http://nanotechweb.org/cws/article/lab/40074.

[9] K. Wang, J. Chen, W. Zhou, Y. Zhang, H. Pern, Y. Yan, A. Mascarenhas; *Well aligned ZnO/ZnSe Coaxial Nanocables Array on Transparnet Conducting Oxide Substarte for Solar Cells;* Microscopy & Microanalysis **14** (Suppl 2), 202 (2008).