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TRACOM TTP n°38: Lab-on-Skin™ with Zero-Power Interface

Zero Power Microfluidics for on-Chip Integration - Enabling System on Chip wearable sensing

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Wearable technologies have become commoditized, and offer only a glimpse of the physical state of a person with limited information collected on the body: essentially activity and sleep tracking and heart rate monitoring. Access to the biochemical information of an individual is needed to get a more accurate picture of the health and wellness of an individual, today, this typically means a blood test in laboratory: a process that is precise, but invasive, and offering only a snapshot at a given point in time. Conversely, pressure to reduce medical expenditure have incited the healthcare ecosystem to look into to preventive health and look for alternatives to blood testing, notably wearable, non-invasive and continuous sweat monitoring. Indeed, it has been shown that many of the biomarkers available in blood are also available in sweat, and particular conditions (cystic fibrosis, dehydration…) have been associated with changes in biomarkers available in sweat. Until now, the biggest impediment to on-body sweat monitoring was the lack of technology to analyze sweat composition in real-time and mainly to continuously collect it, but the recent advances in nanosensors and the development of microfluidic biochips pave the way towards full biochemical microsystems.

Xsensio develops next-generation wearable devices that track biochemical information at the surface of the skin, providing unprecedented real-time information about our health and wellness, in a simple and non-invasive way. Xsensio considerably expands the potential of existing wearable products with the development of a unique tiny wearable intelligent stamp that will analyze biomarkers at the surface of the skin – e.g. electrolytes, proteins, molecules, bacteria – to provide real-time health information. Xsensio targets a highly attractive segment which is emerging at the intersection of two massive and fast growing markets, the biosensors market and the wearable market, with the development of the first "Lab-on-skin™" sensing platform, which heterogeneously integrates state-of-the-art FinFET sensor technology, computing, and wireless communication components and microfluidic interface, a natural extension of the "lab-on-chip" trend.

In this TTP, Xsensio and EPFL have achieved the integration of a novel zero-power, capillary microfluidic channels interface into the wearable sensing platform to create the first "Lab-on-Skin™" product. The zero-power, capillary microfluidic channels interface, which allows infinitesimally small sweat droplets to be collected at the surface of the skin without the need for a pump, has been chosen as the perfect interface for on-body, sweat surface-collection and delivery.

The purpose of this TTP was to investigate and develop microfluidic interface that focuses on the following challenges:

- An optimized design of capillary microfluidics for a fully passive delivery of sweat collected on the skin providing zero power consumption, a significant benefit for powered constrained wearable technologies.
- Materials and fabrication processes for the microfluidic interface fully compatible with post-processing on silicon wafer for direct on-chip integration for the wearable sensing technology, enabling large scale and reproducible industrial production and cost efficiency.
- Selection of organic materials for the microfluidics (in accordance with the targeted passive delivery system) and review for the verification of the biocompatibility as the chip is aimed to be in prolonged contact with human skin.

The proposed capillary microfluidic interface exploits material hydrophilicity and surface tension forces for passive collection and delivery of sweat; it consists of microchannels and capillary pumps

that regulate the unidirectional flow of the biofluid. Within the framework of biomarker sensing in sweat, the design provides a constant volumetric flow rate and a steady velocity profile: capillary pumps are used to achieve these features. The microfluidic interface is modeled through the Navier-Stokes equation, which expresses the velocity field of a laminar flow in a capillary system. The design variables in such equations are adjusted to obtain the desired flow rate typically ≈ 500 pL/min. The capillary pressure in the pump is increased by splitting the capillary pump into parallel microchannels. A higher flow resistance would be expected with such a configuration, however, by placing microstructures in the capillary pump, parallel flow paths are provided overcoming thus this impediment and actually lowering the flow resistance. The geometry of the capillary pumps provides then a high capillary force due to the small dimensions and the small flow resistance, this provides the capability to use capillary pressure to continuously collect sweat (at the inlets) directly on the skin after excretion from the sweat ducts and displace the biofluid, without external forces acting, in the sensing system to finally expel it at the outlets.

Fabrication of the microfluidic interface is based on bonding of patterned SU-8 layers. SU-8 is an epoxy-based negative photoresist with well-established microfabrication processes. It was initially developed as a fabrication mask in the semiconductor device industry and is now widely used in microfluidics manufacturing: a mechanically and chemically resistant polymer that can be exploited for high aspect ratio structures with hydrophilic behavior. This photoresist enables upscalable wafer level processing by leveraging standard lithography techniques. The microfluidics manufacture is then developed as a compatible post-process to the FinFET sensors fabrication on wafers providing direct integration of the capillary interface on the sensing platform in a monolithic unit.

Besides its microfabrication qualities, SU-8 has been selected as the microfluidics material due to its documented biocompatibility: a requirement for the capillary interface which, in a wearable sweat monitoring scenario, is intended to be continuously and worn for extended duration on an individual's skin. Indeed SU-8 composition comprises notably a monomer with 8 epoxy moieties that is dissolved in an organic solvent, typically gamma-butyrolactone GBL or cyclopentanone, and a photoacid generator in the form of triarylsulfonium hexafluoroantimonate salt. This latter component is key to its photolithographic properties but represents a potential source of toxicity which has motivated an in-depth study of SU-8 biocompatibility in the literature. Following ISO 10993 recommendations, absence of cytotoxicity and tissue interaction has been reported in a study for SU-8 subcutaneously implanted in mice and its hemolytic activity is comparable to FDA approved implant materials. Biocompatibility of SU-8 has also been favorably evaluated for several types of cells, notably human skin fibroblast cells but also Schwann cells, astrocytes and explanted neurons by multiple groups. When compared to the invasive neural probe application in the above-mentioned studies, the use of highly crosslinked SU-8 microfluidic interface in the non-invasive "Lab-on-Skin™" application portends no issue of biocompatibility.

In this TTP, **EPFL has successfully delivered and transferred to Xsensio a biocompatible, zero-power microfluidic interface (as well as the related technology know-how) for on-chip Integration** enabling system on chip wearable sensing within the framework of the "Lab-on-Skin™" platform. The corresponding IP created during this TTP is under filing by Xsensio.