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Technologies for autonomous integrated lab-on-chip systems for space missions

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ABSTRACT

Lab-on-chip devices are ideal candidates for use in space missions where experiment automation, system compactness, limited weight and low sample and reagent consumption are required. Currently, however, most microfluidic systems require external desktop instrumentation to operate and interrogate the chip, thus strongly limiting their use as stand-alone systems. In order to overcome the above-mentioned limitations our research group is currently working on the design and fabrication of "true" lab-on-chip systems that integrate in a single device all the analytical steps from the sample preparation to the detection without the need for bulky external components such as pumps, syringes, radiation sources or optical detection systems. Three critical points can be identified to achieve 'true' lab-on-chip devices: sample handling, analytical detection and signal transduction. For each critical point, feasible solutions are presented and evaluated. Proposed microfluidic actuation and control is based on electrowetting on dielectrics, autonomous capillary networks and active valves. Analytical detection based on highly specific chemiluminescent reactions is used to avoid external radiation sources. Finally, the integration on the same chip of thin film sensors based on hydrogenated amorphous silicon is discussed showing practical results achieved in different sensing tasks.

1. Introduction

Chemical and biochemical analysis is a very important task for space missions, both manned and unmanned, with tasks ranging over a very broad spectrum of applications. In case of manned missions, analytical tasks include astronaut's health monitoring [1], on-board food and environment safety assurance [2], monitoring of microorganisms on spacecraft surfaces, like certain fungi species [3], that may damage structural materials with a big impact in long lasting missions or permanent installations like the International Space Station (ISS). Another important class of tasks includes the planetary exploration ranging from the sampling of the ground [4] and of the atmosphere to the search for complex organic molecules up to, eventually, biotic precursors or traces of ancient life [5]. The importance of chemical and biochemical analysis extends also to satellite experiments that may take advantage of the peculiar properties of the Low Earth Orbit (LEO) space environment. In particular, satellite missions may include experiments to explore the properties of materials grown or assembled in microgravity conditions. However, currently there is a growing interest in using the space environment as a biology laboratory [6] to study the combined effect of microgravity and radiations on living cells [7]: experiments may include metabolic studies, drugs development and testing, study of the space environment effects on individual cell components from DNA to mitochondria or other cell structures.

One of the key requirements for an analytical device to be considered for a space mission is surely its size and, in part connected with it, its weight. For this reason, integrated solutions as the ones that fall under the generic definition of "lab-on-chip" are extremely interesting, in particular for satellite missions and especially for nanosatellite (cubesat) missions. In addition to the advantages in terms of weight and size of the analytical device itself, lab-on-chip systems achieve their analytical performances working with very limited volumes of both samples and reagents, typically in the microliter or even nanoliter scale.

However, a more detailed analysis of practical lab-on-chip systems, including both commercial or research devices, indicates that most of the proposed systems are just microfluidic chips that allow to perform their analytical tasks on tiny volumes of fluids but, nevertheless, need complex external bench-top instrumentation to be operated. They can be referred to "chip-in-a-lab" [8]. Typically, fragile interconnections between the microfluidic chip and external fluid supplying systems like syringes or

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pumps are needed to actuate the fluidics. These actuation systems are themselves bulky and may have a non-negligible power consumption. Furthermore, often the analysis relies on optical detection methods (e.g. fluorescence or absorption) that proved to be among the most efficient and sensitive techniques for the analytical purposes. However, such techniques need complex optical systems including radiation sources, lenses and optical filters, e.g., for the rejection of the excitation wavelength and selection of the proper analytical signal. Finally, additional weight, size and complexity are needed for implementing the optical detection system that might include simple optics and a CCD or more complex microscopy systems.

Recently, different groups began to address the main issues related to fluidics actuation and signal detection, moving toward systems that do not require additional external instrumentation to perform the analysis. Tools for following the route toward the 'true' lab-on-chip involve physics, chemistry, materials engineering, electronics but also biomedicine. In this framework, our research group is working on the development of systems that can perform on-chip biological assays, in a stand-alone fashion by integrating all the analytical steps into a single device, from sample preparation to detection and quantification of multiple biomarkers simultaneously, without the need of preliminary off-chip sample pre-treatment procedures and bulky external systems for managing the fluidic flow and for signal generation and detection. The path toward 'true' lab-on-chip devices begins with the addressing of each individual limitation of present systems and it ends with the proposal of technically feasible solutions, which are described in detail in the next sections. In particular, the next section focuses on the microfluidic actuation and control: in order to avoid complex microfluidic joints and bulky external fluid actuation systems like pumps and syringes, we propose the combined use of Electro-Wetting on Dielectric (EWOD) and autonomous capillary flow for the handling of samples and reagents. The following section addresses the elimination of external radiation sources by means of the use of chemiluminescent reactions that ensure high chemical specificity and sensitivity. Finally, we propose the use of thin-film hydrogenated amorphous silicon (a-Si:H) photosensors integrated in the system for the detection of the radiation emitted by the chemiluminescent reactions. The main advantage of the use of amorphous silicon is the possibility to deposit high-performances photosensors on a wide range of substrates including quartz, glass and plastics that are used in most of the lab-on-chip systems. The resulting device will only need an electrical interface toward the control and readout electronics that also includes the signal processing unit, the data storage and the external communication interface. Preliminary results of all the proposed technologies are also presented.

2. Microfluidics actuation and control

2.1. Electrowetting on dielectric

As mentioned before, the handling of the fluids that are moving between the units of the lab-on-chip can be based on the combination of active techniques like the electrowetting on dielectric and passive ones like capillarity. The electrowetting on dielectric (EWOD) is a technique that allows to change the wetting behavior of a liquid droplet when it is in contact with a hydrophobic surface by applying a voltage potential between the droplet and an insulated control electrode. In particular, according to the Young–Lippmann equation [9] it is possible to modify the contact angle between the droplet and the surface from hydrophobic behavior (contact angle greater than 90°, spherical shape of the droplet) to hydrophilic (contact angle less than 90°, oblong shape of the droplet).

This structure can be organized in an array of adjacent electrodes that can be properly biased to move liquid droplets along a path by using specific voltage waveforms leading to a fully digital microfluidic system [10]. Several technological options are available to implement an EWOD system on a glass substrate, including different types of dielectric layers (as parylene or SU-8) and hydrophobic coatings (as Teflon or Cytop). As an alternative, Poly-DiMethilSiloxane (PDMS) can also be used. PDMS is an elastomeric polymer widely used for lab-on-chip fabrication and, thanks to its high dielectric strength (21 MV/m) and its high contact angle of 104°, it can be used both as insulation and as hydrophobic layer [11]. This is the case for the device the operation of which is shown in Fig. 1.

The device consists of a glass substrate on which three-layer Cr–Al–Cr metal electrodes have been deposited by thermal evaporation. The electrodes have been patterned to form a sample reservoir (round part on the right) and a droplet path (rectangular electrodes on the left). A 1 μm-thick PDMS layer is spun over the substrate and a cover glass with a PTFE-coated transparent electrode is placed on the substrate using a 100 μm spacer to achieve a closed EWOD device. Fig. 1 shows six frames of a sequence showing the dispensing of a droplet of fluid from the reservoir toward the microfluidic path achieved by properly timing the voltage on the metal control electrodes. Such structure can be used for both sample and reagent dispensing in an analytical system allowing a precise control of the timing in an automated way by simply programming the correct sequence on a microcontroller. For more reliability, a feedback signal of the droplet actuation can also be easily integrated, e.g., through the measurement of electrode capacitance that is a function of the volume of the droplet lying on the electrode.

2.2. Capillarity

Capillarity is a phenomenon that occurs when a liquid is injected in a narrow and hydrophilic micro-channel. When a liquid is inside the channel it is driven by a capillary pressure, which linearly depends on the cosine of the contact angle between the wall of the channel and the liquid and on the surface tension of the liquid and is inversely proportional to the channel width. By using particular structures as capillary pumps, directional valves and trigger junctions it is possible to control the flow rate and timing. Hydrophilic channels can be easily fabricated on glass substrates by using SU-8 photodefineable polymer by means of conventional UV-lithography processes. The SU-8 is an epoxy photoresist from Microchem with very good adhesion on glass and slight hydrophilic behavior. Moreover, the epoxy nature of SU-8 ensures good mechanical properties even in the smallest details and good chemical inertia to reagents used in biological applications. By using different formulations of SU-8 and by changing processing parameters as rotation speed of the spin coater it is possible to obtain any desired channel depth. An example of a microfluidic network consisting in a series of mixers is shown in Fig. 2. The width of the micro-channels is 600 μm and their height is 50 μm as defined by the thickness of the SU-8 layer. A cover glass is then bonded on top of the structure in order to seal the channel. Details of the fabrication process are reported in [12].

Also PDMS can be used for the fabrication of the microfluidic network. However, in order to achieve a high capillary pressure and high fluid velocity, it is important to have a hydrophilic channel. For this reason, the PDMS channel must be treated to turn its behavior from hydrophobic to hydrophilic. To increase the hydrophilicity of the PDMS a partial curing process [13] or a special treatment to incorporate PEG molecules (MW 1500) in the inner wall of the channel can be used [14].