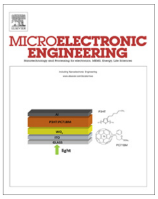
Microelectronic Engineering 132 (2015) 156–175

Contents lists available at ScienceDirect

Microelectronic Engineering

journal homepage: www.elsevier.com/locate/mee



Review Article

Lab-on-a-chip devices: How to close and plug the lab?

Yuksel Temiz *, Robert D. Lovchik, Govind V. Kaigala, Emmanuel Delamarche *

IBM Research GmbH, Säumerstrasse 4, 8803 Rüschlikon, Switzerland

ARTICLE INFO

Article history:
Received 16 May 2014
Received in revised form 14 October 2014
Accepted 16 October 2014
Available online 28 October 2014

Keywords:
Microfluidics
Lab on a chip
Microfabrication
Sealing
Fluidic interconnect
Electrical interconnect

ABSTRACT

Lab-on-a-chip (LOC) devices are broadly used for research in the life sciences and diagnostics and represent a very fast moving field. LOC devices are designed, prototyped and assembled using numerous strategies and materials but some fundamental trends are that these devices typically need to be (1) sealed, (2) supplied with liquids, reagents and samples, and (3) often interconnected with electrical or microelectronic components. In general, closing and connecting to the outside world these miniature labs remain a challenge irrespectively of the type of application pursued. Here, we review methods for sealing and connecting LOC devices using standard approaches as well as recent state-of-the-art methods. This review provides easy-to-understand examples and targets the microtechnology/engineering community as well as researchers in the life sciences.

1. Introduction

Miniaturization techniques have been continuously shaping the microelectronics technology and its ability to produce devices for a broad range of applications. In the late 1950s, "planar" processes were introduced for the manufacturing of integrated circuits. Since then, downscaling the dimensions of transistors has been rigorously pursued in the industry to fulfill the ever-increasing demand for smaller, faster, and more energy-efficient electronic systems [1]. In addition to conventional processes used in the microelectronics, new techniques were developed for the fabrication of high-aspect ratio structures and suspended layers, which opened up new possibilities particularly for sensing applications. In the early 1970s, it was possible to fabricate microsensors using bulk and surface micromachining of silicon. With progress in the processing technologies and the integration of nonconventional (i.e. not silicon-based) materials, a new field named microelectromechanical systems (MEMS) emerged [2]. Following the early examples of silicon-based pressure sensors and accelerometers in the mid-1970s, inkjet printing nozzle arrays were developed using anisotropic etching of silicon [3]. First implementations of inkjet printer heads demonstrated that minute amounts of liquids can be manipulated in micromachined channels. A few years later, Terry et al. presented a micromachined gas chromatograph in silicon [4]. The following studies also demonstrated handling of small volumes of liquids, and it was the pioneering paper of Manz et al. in 1990 that introduced and established the concept of miniaturized total chemical analysis systems (μTAS) [5]. Soon after, early companies were founded to utilize these systems for life science applications. Rapid prototyping and replication of polymers as an alternative to silicon processing boosted the academic research and new terminologies such as "microfluidics" and "lab-on-a-chip" (LOC) emerged (we here use both terms interchangeably).

Over the last 10–20 years, LOC devices have demonstrated their potential and benefits for many applications, including point-of-care diagnostics, genomic and proteomic research, analytical chemistry, environmental monitoring, and the detection of biohazards. These miniaturized systems offer many advantages compared to bulkier and "historical" analytical instruments: they support precise control of liquids flowing usually under laminar regime, minimize consumption of reagents and samples, favor short reaction times, enable highly parallel and multiplexed analysis, require little or less power to operate, are portable, and potentially have low cost of production. Today, structures can be fabricated with sub-micrometer precision, flows of liquids can be sustained and precisely controlled using integrated or external pumps and valves, and quantitative detection of different analytes can be done in high sensitivity using optical-, electrical- or magnetic-based techniques.

This review is not about the applications and markets of LOC devices, the detection mechanisms and sensing principles of these devices, microfluidic pumps and valves, the integration of reagents, or the theory of LOC devices. Insightful reviews on different aspects of LOC devices and applications can be found elsewhere [6–14].

---

* Corresponding authors.

E-mail addresses: yte@zurich.ibm.com (Y. Temiz), emd@zurich.ibm.com (E. Delamarche).

http://dx.doi.org/10.1016/j.mee.2014.10.013
0167-9317/

Instead, we focus on two important practical challenges: sealing and interfacing LOC devices. These challenges are common to nearly all LOC devices and affect how these devices are conceived and perform.

Nowadays, microfluidic and microelectronic devices do not follow the same scaling and manufacturing rules: microfluidics incorporate a very diverse set of materials and fabrication techniques, and they can also comprise many different functional elements. However, both types of devices still share a common challenge attendant to miniaturization. They both require reliable, low-cost and convenient interfaces to the outside world and a suitable package supporting efficient device operation. The microelectronic industry is already facing the "interconnect bottleneck" problem because the effective operation speed of the system has started to be limited by on-chip and off-chip interconnecting wires, which was previously limited by the transistor or the device itself. The amount of heat that can be removed from the package has also started to limit the performance of the circuits, which makes the bonding techniques and materials used in the package more important than ever before. Researchers have been looking for a shift in paradigm on how functional blocks are placed and connected. For example, hybrid optical/electrical interconnects and through-silicon-vias are emerging as promising solutions for replacing conventional copper connections and wirebonds. Similarly, the I/O (input/output) complexity of microfluidics systems has increased over the years because many applications now require high-density fluidic and/or electrical interconnections. There are also other packaging-related challenges that are unique to LOC systems. Microfluidic chips often need manual handling and plugging by the operator, which induces additional constraints on the final package due to practical reasons. Moreover, unlike for the majority of electronic systems, reusability or disposability is crucial for some LOC applications. This requires interconnects that are reliable, cost-effective to fabricate, and also that can be connected to LOC devices in a reversible manner. The community working on these devices demonstrated significant improvements in terms of device performance and generation of novel detection mechanisms but we think that packaging and interfacing microfluidics remain a significant technical challenge and obstacle for the commercialization and wide-spread use of microfluidics.

Fig. 1 illustrates a sealed microfluidic device having fluidic and electrical connections. Typically, after the fabrication of microfluidic structures and electrodes, various back-end processes are needed to realize a fully-functional device [15,16]. Taking the example in Fig. 1, microfluidic structures can (1) be sealed with a cover layer, which is drilled or patterned so as to create openings for fluidic/electrical interfaces, (2) chemically-treated for tuning the wetting properties of surfaces and modulating protein-surface interactions, (3) indented or fully diced to produce individual chips, and (4) connected to peripheral devices such as pumps and valves using inlet/outlet ports. Although these back-end processes are sometimes neglected in the microfluidics community, they have great impact on the manufacturing cost and performances of the final devices.

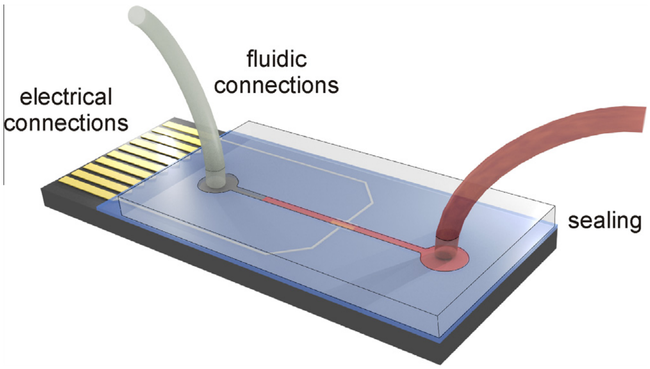


Fig. 1. LOC devices cover a broad range of applications and research areas but typically these microfluidic devices need to be sealed, connected to pumping peripherals, and often bear electrical connections. In other words, "plugging" and "closing" these small labs is a general challenge.

This review is divided into three main sections that focus on sealing (1), fluidic connection (2), and electrical connection (3) techniques developed for LOC devices. The first section on sealing surveys various bonding methods based on conformal materials (PDMS), non-conformal polymers (plastics), hard materials such as glass and silicon, intermediate adhesive layers, and recently emerged prototyping technologies, and discusses reversible bonding techniques and open-channel microfluidic devices. The next section on fluidic connections provides an in-depth overview and recent examples of reversible (inserted or contact-based), permanent (adhesive based), and monolithically integrated fluidic interfaces. The final section on electrical connections discusses commonly used connectors (sockets and spring-loaded contacts), some of the advanced packaging techniques developed for hybrid CMOS/microfluidics integration, and emerging interconnection techniques.

2. Sealing

LOC devices are typically sealed to (1) confine solvents, samples and reagents in defined volumes, (2) prevent uncontrolled spreading of liquids along wettable areas, (3) reduce contamination and biohazards, (4) minimize adversary evaporation of samples and reagents from chips, and (5) protect sensitive and fragile structures or molecules from dust or physical impacts. Depending on the materials and the constraints imposed by the application, many bonding techniques are available. An early review from Verpoorte et al. covers a wide range of fabrication and sealing techniques for microfluidic chips [17], and more recent examples are outlined in reviews by Abgrall et al. [18] and Nge et al. [19]. Here, we survey some of the most common and emerging materials and their bonding techniques.

2.1. Sealing using conformal materials

PDMS (Polydimethylsiloxane) has become by far the most popular material in the academic microfluidics community because it is inexpensive, easy to fabricate by replication of molds made using rapid prototyping or other techniques, flexible, optically transparent, biocompatible and its fabrication does not require high capital investment and cleanroom conditions. Various techniques have been adapted to fabricate microfluidic structures in PDMS, including wet and dry etching [20–22], photolithographic patterning of a photosensitive PDMS [23], and laser ablation [24]. But, it was the "soft-lithography" techniques [25] introduced by Whitesides et al. that enabled the widespread use of PDMS and opened up the era of PDMS-based microfluidics in the late 1990s. Replica molding, which is the casting of prepolymer against a master and generating a replica of the master in PDMS, has become a standard fabrication technique available in almost every research laboratory. Detailed overviews of soft-lithography techniques and their applications can be found from the reviews by McDonald et al. [26] and Sia et al. [27]. Nowadays, many tools dedicated for this purpose are available and can be purchased as a complete set (e.g. SoftLithoBox® provided by Elveflow (USA) [28]). Moreover, companies, such as FlowJEM (Canada) [29], Microfluidic Innova-