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Multiplexed electrical sensor arrays in microfluidic networks

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ABSTRACT

A major limitation of many microfluidic platforms is their inability to perform large scale, real time, sensing, routing, or scheduling of the materials moving through them. This paper seeks to address the first of these deficiencies by introducing a multiplexed sensing architecture capable of monitoring the movement of liquid droplets in large microfluidic networks. We describe the design and fabrication of the sensor array, as well as its integration and testing in microfluidic networks. Individual sensors consisting of small electrical components (resistors, capacitors, or conduction gaps) are addressed using a multiplexing approach that allows an array of $m \times n$ sensors to be supported by only $m+n+1$ electrical contacts, as compared to the $2 \times m \times n$ contacts traditionally necessary. For example, a multiplexed 10×10 array of sensors can be operated with 21 contacts, as opposed to the 200 contacts needed in a traditional configuration. The multiplexing relies on the fact that each sensing element is connected to two electrical leads, and each electrical lead is connected to multiple sensing elements. Here we show the principle using a 4×4 multiplexed arrays of resistive and capacitive sensors to monitor the passage of discrete liquid plugs through a microfluidic network.

1. Introduction

As microfluidic devices continue to decrease in size and increase in complexity, the ability to monitor the passage of material through them becomes ever more important. In recent years, microfluidic systems have been used in many chemical and biological applications, including: DNA analysis [1], capillary electrophoresis [2], cell cytometry [3], high throughput screening for combinatorial chemistry [4], fuel cells [5], combining multiple biological assays onto a single chip [6], and the generation of multistream segmented flow regimes [7]. However, as impressive as these microchemical systems are, during operation one typically has little to no exact information about the position and speed of material moving through them. This inability to monitor and control the position of discrete liquid elements becomes a significant issue when scaling up from microfluidic configurations with only a few channels to configurations comprised of extensive channel networks designed for the high throughput processing of multiple droplets flowing within a carrier stream. For microfluidic devices to continue to evolve, better real time routing and scheduling methods are needed. Such a control system will depend on the ability to detect the position of material throughout a microfluidic network using an array of appropriate sensors [8]. Ideally, the sensors used should be easy to fabricate and integrate with current microfluidic devices, require a small footprint of space within the device, and consume only a small amount of power.

Numerous reports and reviews have appeared in the literature on various types of sensing in microfluidic devices. Optical detection techniques based on fluorescence [9,10], absorbance [9,10], luminescence [11], and waveguides [12,13] are the most prevalent. Others have used some form of electrochemical detection during electrophoretic separations, including amperometry [14–18], conductimetry [19–22], and potentiometry [22–24]. Still others have used electrical sensors such as resistors [25–28], capacitors [29–33], and conduction gaps [34–39] for the detection of specific chemical species or biological cells, or the measurement of certain fluid properties (e.g. concentration, temperature, or flow rate). These electrical sensing principles can also easily be applied to the detection of a discrete liquid element (e.g. in plug [40–42] or slug [43] flow regimes) at a specified position within a microfluidic network, which is the goal of this study [44].

In this work, we integrate arrays of multiplexed electrical sensors into microfluidic networks. Whereas most optical sensing methods rely on an external light source and detector, electrical sensors can be incorporated directly within a microfluidic device because of their inherent minimal thickness. Additionally, they are easy to fabricate by standard photolithographic techniques, and require only a small amount of power for operation. For the purposes of liquid droplet detection, a small constant current or potential is applied across a sensing element (either a resistor, capacitor, or conduction gap) patterned in a microchannel, and the corresponding output signal is continually monitored. A change in

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the output signal indicates a change in a physical property (thermal conductivity, dielectric constant, or electrical conductivity, depending on the sensor type) of the liquid surrounding the sensor, thereby detecting when a liquid element arrives at or passes a certain point.

Scaling these individual sensors up into large arrays spanning an entire microfluidic network is logistically complex. As the number of sensors increases, the number of electrical leads necessary to connect the sensors with external monitoring equipment will also increase. This rapid growth renders the design, fabrication and, implementation of the sensor array exceedingly difficult. The creation of a large array of sensors that also minimizes the number of electrical leads necessary is therefore desirable. Previous work on creating arrays of similar sensors has resulted in either small arrays that are difficult to scale up [45–47], or complicated fabrication procedures [8]. Others have extensively characterized individual electrical sensors for microfluidic droplet position detection, yet have not reported on the possibility of scaling those sensors up into arrays [44]. Here we describe a fully scalable and planar sensor configuration that employs a multiplexing approach allowing an array of $m \times n$ sensors to be controlled by only $m+n+1$ electrical leads, as opposed to the usual $2 \times m \times n$, corresponding to 2 leads per sensor. We will discuss the design, fabrication and testing of resistive, capacitive, and conductive sensors in single channels, as well as 4×4 multiplexed arrays of resistive and capacitive sensors within microfluidic networks.

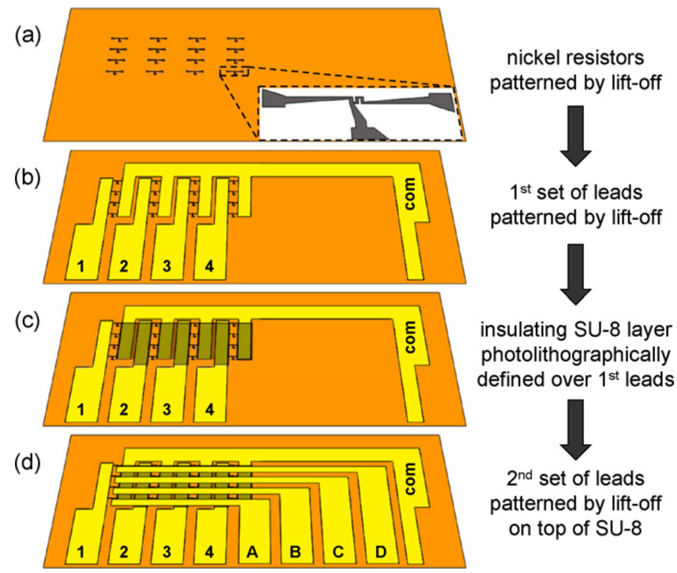

Fig. 2. Step-by-step fabrication procedure of a typical substrate with a 4×4 array of multiplexed resistive sensors. (a) Array of 80 nm thick nickel resistive sensors patterned by lift-off; (b) the first set of leads (vertical; no. 1–4) as well as the common lead (com), all 100-nm Au, patterned by lift-off; (c) insulating layer of 4-μm SU-8 photoresist, selectively patterned on top of the underlying first set of leads; (d) second set of leads (horizontal; no. A–D), 300-nm Au, patterned by lift-off.

2. Electrical sensing principles for microfluidics

2.1. Resistive sensing

The resistive sensors discussed here are thin-film serpentine resistors, similar to traditional resistive heaters used as flow and temperature sensors [25,48–51]. When a small constant potential is applied, the resistor quickly heats up to some constant temperature in proportion to its temperature coefficient of resistance (TCR) and the thermal conductivity of the surrounding liquid. When liquids of varying thermal conductivity flow over the resistor, the temperature of the resistor fluctuates correspondingly, resulting in changes to the overall resistance of the resistor, and thus to the output current. Therefore, a change in the liquid contacting the resistor is detected when the current through the resistor changes.

2.2. Capacitive sensing

The capacitive sensors used in this study consisted of two coplanar gold electrodes separated by a small gap [32], instead of the more common parallel plate capacitor geometry [33]. A coplanar geometry was used because it allows for a simpler microfabrication procedure than a parallel plate structure. Previous experimental and theoretical work has shown that the maximum capacitive signal in the coplanar configuration is obtained when the electrode gap spacing is minimized, and the exposed electrode width is comparable to the height of the channel surrounding them [32,52].

Most of these capacitive sensing elements are operated in an AC mode. A difference in capacitance is measured upon a change in liquid composition between the electrodes. *In contrast, we will operate our coplanar capacitive sensors in a constant potential mode, measuring a short induced current upon a change in liquid composition.* A small constant potential is applied across the gap between the electrodes and the current is monitored as a function of time. Equal and opposite charges build up on the ends of the electrodes and no change in current is detected until a liquid with a different dielectric constant passes over the sensor. The change in dielectric constant manifests itself a change in the charge distribution on

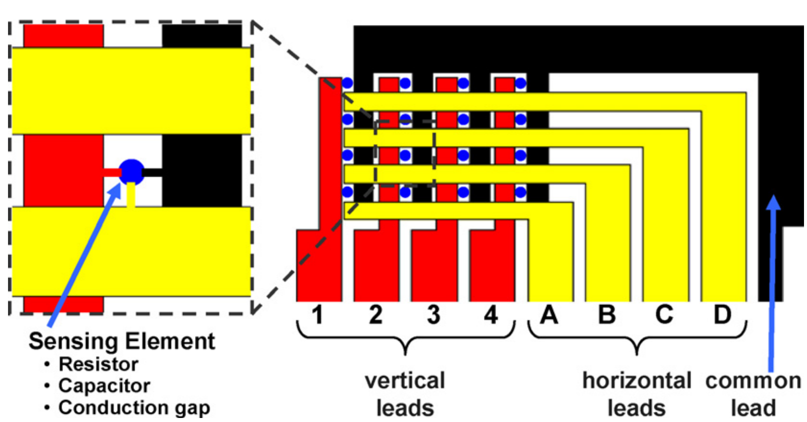

Fig. 1. Schematic illustrating the multiplexing detection principle, here in a 4×4 array of sensing elements (blue dots). Each sensing element (a resistor, a capacitor, or a conduction gap) is connected to two separate input leads (red and yellow) and one common output lead (black). Each lead is connected to multiple sensing elements. A unique combination of the responses from leads 1–4 and leads A–D pinpoints the location at which a sensing event, e.g. a change in liquid composition, takes place. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)