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Fundamental approach for optoelectronic and microfluidic integration for miniaturizing spectroscopic devices

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ABSTRACT

We have described an approach for miniaturizing spectroscopic devices by using the advantages presented by elastomeric based microfluidics and semiconductor detectors/emitters. Elastomers allow for both absorption and fluorescent spectroscopy in the visible range to be conducted on small volumes of solution and allow for easy integration with existing detectors such as CMOS imagers, CCD imagers, and silicon photodiodes. Results of some basic experiments are presented to demonstrate the effectiveness of the system. In addition, several ideas for emission sources are also discussed with their relevance yet to be determined.

Keywords: microfluidic, optoelectronic, soft lithography

1. INTRODUCTION

Over the past few years, the application of micromachining techniques has grown rapidly to include many devices such as accelerometers[1,2], pressure sensors[3], ink-jet print heads[4], fiber optic communications[5,6], displays[7], and microfluidics[8-12]. Two of the most common methods for the production of microelectromechanical systems (MEMS) include bulk micromachining and surface micromachining. These methods employ silicon as their main substrate component. Bulk micromachining involves etching away single crystal silicon to form three-dimensional structures, while surface micromachining centers around the addition of different materials such as polysilicon, metals, silicon nitride, silicon dioxide, etc. to define structures. Both methods are somewhat limited by the semiconductor substrates which increase the difficulty of multilayer device production. Careful consideration must also be given to production facilities and process conditions to realize acceptable device yields.

An alternative microfabrication technique that has gained popularity in recent years is elastomer replica molding, loosely referred to as soft lithography. It has been used to make blazed grating optics[13], stamps for chemical patterning[14], and microfluidic devices[15-19]. This technique involves curing an elastomer, typically silicone, on a micromachined mold. The mold can be generated using bulk or surface micromachining, but is typically generated via photolithography. A standard mold can be generated by exposing a thick UV sensitive photoresist through a high-resolution contact mask. The pattern can then be developed and baked for a short while to finish the mold. Through the use of these techniques many microfluidic devices such as peristaltic pumps, valves, mixers, and cell sorters have been developed[20].

A major problem that exists with most semiconductor based microfluidic structures is the inability to perform optical analysis on the device's contents. Due to the absorption of silicon, these devices are limited to use in the infrared range. Visible/UV spectroscopy is virtually impossible to perform without an amazingly elaborate device. In fields such as biochemistry, this becomes a very limiting factor since many experiments are based on visible/UV absorption and fluorescence spectroscopy. Specific silicone elastomers circumvent this problem since they are optically transparent and have similar UV absorption characteristics to those of glass. This property allows for integration of elastomer microfluidic devices and optoelectronic devices to perform spectroscopy.

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Miniaturization for absorption spectroscopy has advanced dramatically over the past few years, due to development of short wavelength LED's and faster computer interconnects. A prime example of this is the Ocean Optics fiber optic spectrometer, which communicates and is powered via a personal computer USB interface. The entire unit has the footprint of a large matchbox. However, these systems still do not take advantage of microfluidics. They rely on cuvettes and test tubes to perform analysis of solutions.

Fluorescence spectroscopy using a silicone elastomer chip has been effectively demonstrated for both cell[17] and DNA sorting[21]; however, the external equipment setup includes a 488 nm Ar ion laser, focusing optics, CCD camera, upright microscope with 60x oil immersion lens, beam splitter, dichroic mirror, photomultiplier tube and a preamplifier[21-22]. This setup is quite typical for a cell sorting apparatus, and although the majority of the equipment is not needed for simple fluorescence/absorption experiments, a pump source and a microscope are almost always involved. Therefore, in order to truly miniaturize the system, the external hardware must be minimized and implemented at a much smaller scale.

2. INTEGRATION FOR SPECTROSCOPY

A simple approach to solving this problem is to eliminate the need for focusing optics by placing the microfluidic device directly on the imager. The imager can consist of silicon based avalanche photodiodes (APDs), charge coupled devices (CCDs), or CMOS imagers. All of these devices are available commercially at reasonable costs. Although the resolution of these imagers cannot match that of an optical microscope, it is suitable for most visible spectroscopy experiments. The maximum resolution of the system is dependent upon the pixel size and the active area of the pixel. Two other factors that contribute to the overall performance of the imager are its sensitivity and dynamic range. These factors become very critical when examining picoliter volumes of solutions.

2.1 Absorption Spectroscopy

Since the typical size of an elastomer microfluidic channel is on the order of 50 to 250 microns wide by 10 to 20 microns deep, the absorption path length is quite small. According to the Beer-Lambert law the absorbance A is proportional to c and l so that

$$A = \epsilon(\nu)cl$$

Where ϵ is a function of ν the wave number and is the molar absorption constant or molar absorptivity, c is the concentration of absorbing material in solution and l is the absorption path length. Thus the difference in detected intensity inside the channel versus outside the channel is very small for dilute solutions. Therefore the better the sensitivity of the detector, the greater the range of experiments that can be conducted.

A basic absorption experiment was performed using a ten-bit resolution black and white CMOS imager provided by NASA's Jet Propulsion Laboratory. The imager has a typical pixel size of 12 μm, a dynamic range > 65 dB, and a responsivity > 1.3 μV/photon (specifications given at room temperature.) The active pixel area consisted of 512 x 512 pixels. The experiment conducted tested the absorptivity of various concentrations of bromophenol blue(Aldrich Chemical Company, Inc. #62625-28-9.) Control data was measured on

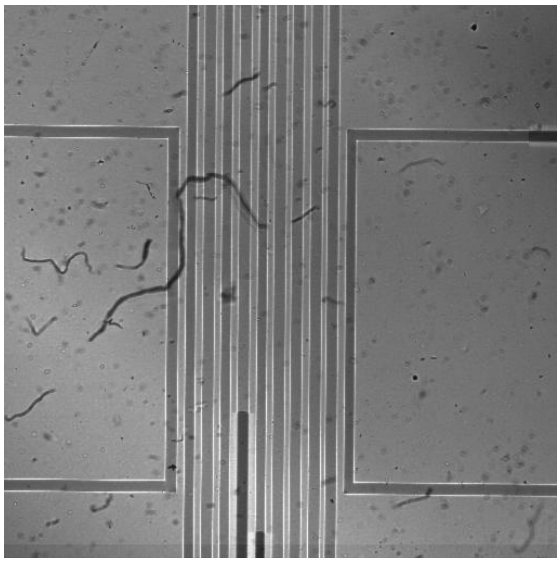

Figure 1. A PDMS microfluidic chip imaged by the JPL APS CMOS imager. The light source is a 588 nm λ_{max} AlInGaP LED and the channels contain bromophenol blue solutions. The dark channel areas are where air entered the channel. This sample also illustrates the fact that PDMS chips can still function correctly even with minor contamination such as the fibrous particulate present.

a calibrated Shimadzu BioSpec 1601 in 1 cm cuvettes. The molar absorption constant was then calculated and a curve fit was applied to generate the control data for a 14 μm channel. A polydimethylsiloxane (PDMS) microfluidic chip consisting of eleven 100 μm wide by 14 μm deep channels spaced 100 μm apart was placed directly on the imager. Two channels were filled with each concentration of interest and one channel was filled with water for background measurements. Figure 1 shows a typical image of the channel structure captured by the CMOS imager. The illumination source consisted of a Yellow AlInGaP LED (LITEON #LTL-2R3VSKNT) with λ_{max} = 588 nm and I_o = 1500 mcd. The results of the experiment are shown in Figure 2.

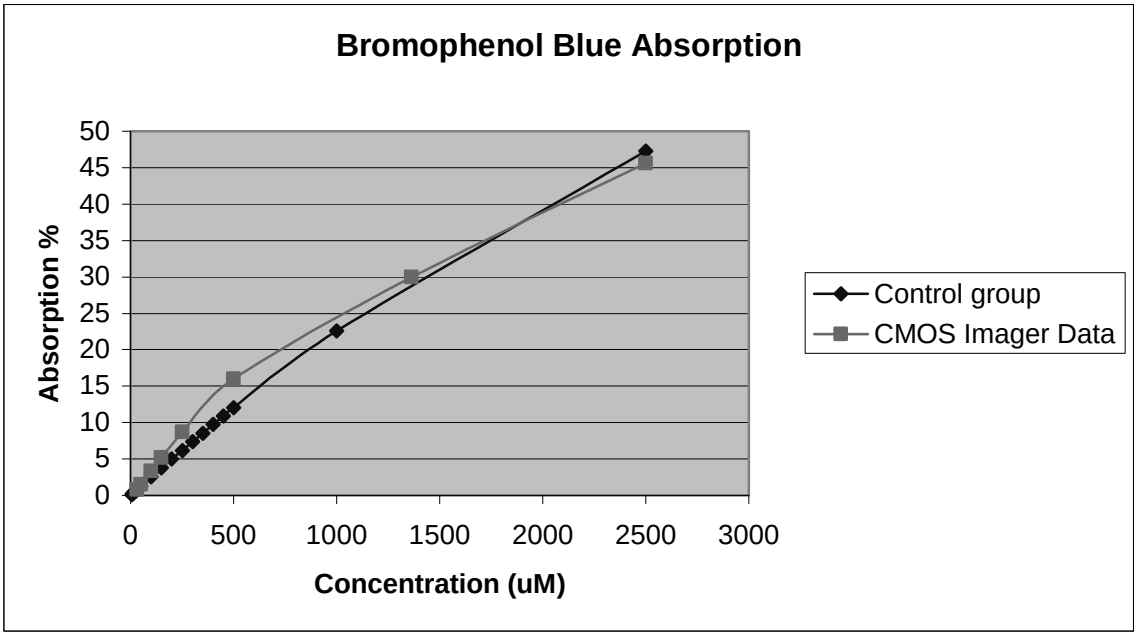

Figure 2. Absorption spectra of various bromophenol blue concentrations taken with a Shimadzu spectrophotometer and the JPL APS CMOS imager.

2.2 Fluorescence Spectroscopy

An issue that arises during fluorescence spectroscopy involves the need to excite the sample under test with a light source whose wavelength is close, usually 40-80 nm away, to the emitted fluorescent light. Typically the pump source is much brighter than the fluorescence especially for those experiments involving single units of fluorescence, such as single cell detection. The pump tends to saturate the imager thus blocking any chance of identifying the fluorescent unit. In order to compensate for this fact, a blocking filter that is tuned to the pump wavelength must be placed between the microfluidic device and the imager. This filter can easily be fabricated as a λ/4 dielectric thin-film stack (Fig. 3). The filter is transparent at the fluorescent wavelength, but blocks over 99% of the pump wavelength (Fig. 4). An example of this technique is shown using 5 μm latex beads in Fig 5.

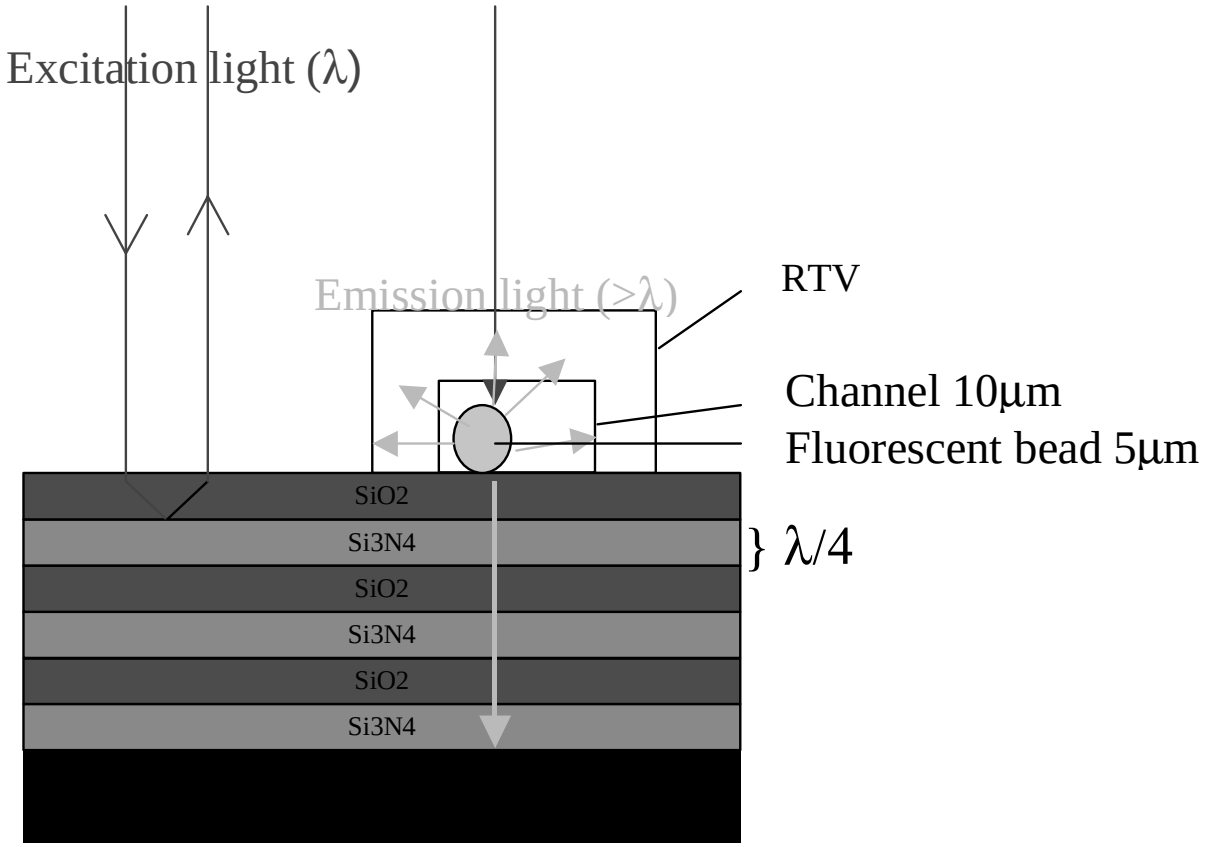

Figure 3. A schematic diagram illustrating the principles of a dielectric thin-film blocking filter placed directly on top of the imager. The filter allows emission light to pass while quenching the excitation light.

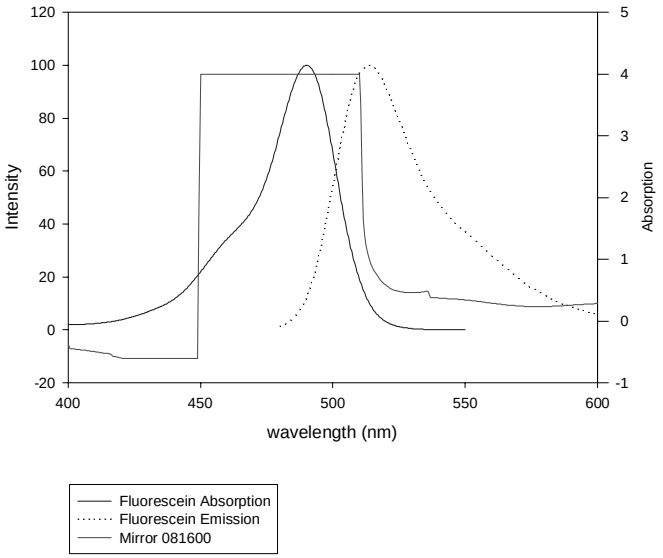

Figure 4. Fluorescent absorption and emission spectra for Fluorescein. Blocking filter absorption spectrum shown in relation to second y axis. The emission peak corresponds to a region just outside the block band where the transmission is roughly 50%. This can easily be improved by constructing a narrower band-blocking filter.

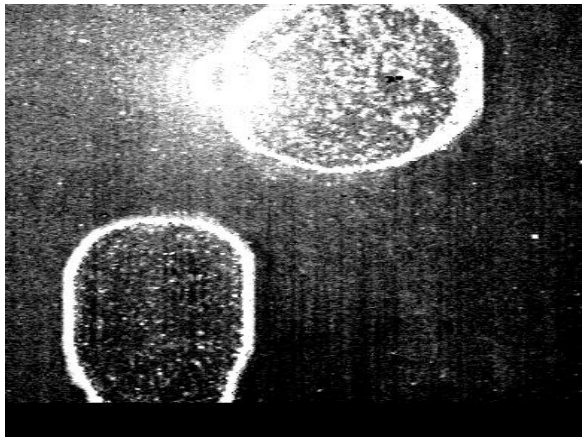

Figure 5. CMOS image of both 5 μm fluorescent and non-fluorescent latex beads under the excitation of 488 nm Ar ion laser. Blocking filter used on the imager.

2.3 Emission sources

With the microfluidic device directly on the imager, the next component of the system becomes a light source. In a typical visible spectrophotometer the light source is generally a tungsten or tungsten-iodine filament lamp with some models also including light emitting diodes. The appropriate light source depends heavily upon the application, but several alternatives include light emitting diodes, laser diodes, white light sources, and perhaps even the sun. The source might be a tungsten filament lamp in a laboratory with a specific color filter placed directly over the microfluidic device. For other applications an array of vertical cavity surface emitting lasers (VCSELs) could be placed directly on top of the microfluidic device to create a fully functional on-chip visible spectrometer.

3. CONCLUSION

Since the microfluidic device is inexpensive and disposable, the rest of the system remains reusable for many more experiments. With the appropriate information processing, the integrated system could yield rapid, accurate results in a very short time. This coupled with the flexibility of soft lithography shows much promise toward completion of a lab on a chip.

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