A 16 Fabry-Perot Optical-Channels Array for Biological Fluids Analysis using White Light

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Summary: *This paper describes a biosystem (biological system) used to measure the concentration of biological substances in urine, serum, plasma or cerebrospinal fluid. Rather than just one channel, it comprises 16 optical-channels that enable the measurement of the concentration of 16 different biological substances. An array of 16 optical filters based on Fabry-Perot thin-films optical resonators has been designed. Each optical-channel is sensitive in a single wavelength with a Full-Width-Half-Maximum (FWHM) of 7 nm. The filter fabrication requires only 4 masks, used with different etch time. A commercially available band-pass optical filter with a band-pass wavelength in 450-650 nm is used. The biosystem requires only a white light source for illumination due the use of selective optical filters.*

Keywords: *biosystem, optical filter array, Fabry-Perot*
Category: *7 (Fluidic Devices)*

1 Introduction

Spectrophotometric analysis (the study of the interaction of electromagnetic radiation with chemical compounds) is one of the most commonly used analytical techniques for biological fluids analysis in clinical diagnostics. This technique is used to determine the concentration and/or amount of a particular compound in biological fluids samples [1]. Usually, the samples need to be sent to a laboratory for spectrophotometric analysis, and the results become available after several hours or days. The need for rapid and on-line measurements led to the development of biosystems with the fluidic, detection and readout systems integrated in a single-chip [2]. The advantages associated with shrinking clinical analysis systems include improved efficiency with respect to sample size, integration, automation, response times, analytical performance, laboratory safety and costs. Previously developed biosystems on-a-chip with absorbance detection require a wavelength dependent light or waveguides inserted into the biosystem for illumination [3, 4]. Illumination using only a white light source requires the use of selective optical filters.

2 Design of the 16 optical-channels array

A biosystem to measure the concentration of biological substances in biological fluids, by optical absorption, was previously implemented [4]. Its operation was successfully demonstrated in uric acid concentration detection (Fig. 1 and Fig. 2). However, the measurements were carried out with a wavelength dependent light source (monochromatic light).

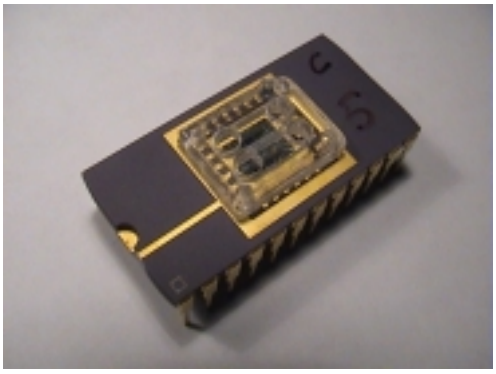

Fig. 1. Biosystem [4].

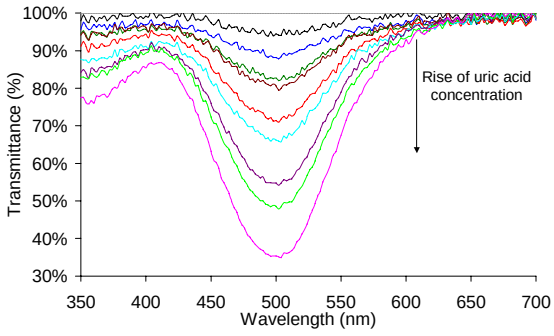

Fig. 2. Measured transmittance spectra for different uric acid concentrations [4].

An optical filter placed on the top of the biosystem allows the use of only a white light source. Rather than just one optical filter it has been developed a 16 optical filters array based on

Fabry-Perot thin-films optical resonators. The device, schematically shown in Fig. 3 and Fig. 4, allows the measurement of the concentration of 16 biological substances in human's fluids (Table 1). The biosystem is composed by a glass die that contains the fluidic channels, including the optical filters, and a silicon die that contains the photodetectors and readout electronics. A commercially available band-pass optical filter on the top of the biosystem is used to avoid the non-visible spectrum.

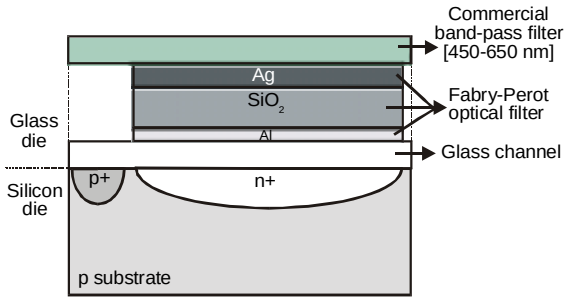

Fig. 3. Schematic structure of the biosystem for an individual optical-channel in cross-section.

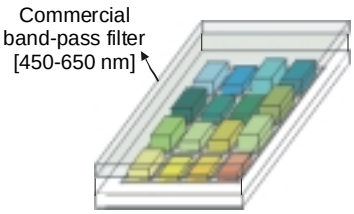

Fig. 4. An artist impression of the 16 optical filters (4x4 array) and the commercial band-pass filter. Each of the Fabry-Perot cavities is tuned to transmit in different spectral band.

Table 1. The 16 biological substances that can be analyzed in the biosystem. U (Urine), S (Serum), P (Plasma) and CSF (cerebrospinal fluid) [1].

Biological Substance	Biological Fluid	Absorption spectra maximum peak (nm)
Uric Acid	U, CSF	495
Cholesterol	S	500
Glucose	S	505
Glutamic oxalacetic / pyruvic transaminase	S, P, CSF	510
Creatinine	U, S, P	515
Magnesium	S	520
Aldolase	S	525
Bile acids	S	530
Blood urea nitrogen	S, P	535
Salicylate	S	540
Hemoglobin	P	545
β Glucuronidase	S, U	550
Urea nitrogen	U, S, P	555
Bilirubin	S	560
Leucine aminopeptidase	U	565
Calcium	S	570

The device operation is based on optical absorption in a well-defined wavelength of the visible spectrum. The impinging spectrum is filtered by the optical filters to a single wavelength, and the intensity of the selected spectral component transmitted through the fluid is measured using an underlying photodetectors array. Thus, each optical-channel is composed by a Al/SiO_2/Ag layer stack functioning as the Fabry-Perot optical filter with an optical detector underneath (a CMOS standard photodiode). The 16 optical filters are tuned for a specific wavelength (third column of Table 1). The thickness of the SiO_2 layer determines the tuned wavelength.

The optical filters use metallic mirrors instead of high-performance dielectric mirrors due to the simplicity of their fabrication: only 3 layers are deposited and the wavelength selection is performed by changing only the thickness of the SiO_2 layer.

A thin-film optics software package (TFCalc 3.4) was used for the structural optimization of the optical filters. Simulation results show that a 20 nm Al / SiO_2 / 40 nm Ag layer stack is the best option for the optical filters in terms of optical characteristics and feasibility. The SiO_2 layer thickness changes between 637 nm and 742 nm with 7 nm steps. The simulated transmittances for all the 16 optical filters show that each of the channels is sensitive to a single spectral band, with a FWHM = 7 nm (see Fig. 5).

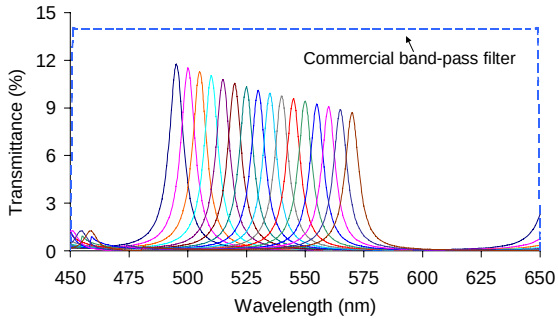

Fig. 5. Simulated transmittance vs. wavelength for the 16 optical filters array.

3 Fabrication of the 16 optical-channels array

The filter fabrication starts with the deposition of a 20 nm Al layer by evaporation. Then a 742 nm thick SiO_2 layer is deposited by chemical vapor deposition. In subsequent plasma etching steps, for which a mask is used and each of them with different etch time (see Fig. 6), the total thickness of the SiO_2 layer is decreased from 742 nm to 637 nm, in 7 nm steps. The different thicknesses of the SiO_2 layer and the correspondent filters are described in Table 2. The fabrication ends with the deposition of a 40 nm Ag layer. The 16-filter fabrication requires only 4 masks and 4 etching steps. The filters can be easily tuned to different spectral bands by adjusting only

the thickness of the SiO_2 layer without affecting the biosystem layout.

Table 2. Thicknesses of the SiO2 layer.

Filter Number	SiO_2 layer thickness (nm)	Absorption spectra maximum peak (nm)
1	637	495
2	644	500
3	651	505
4	658	510
5	665	515
6	672	520
7	679	525
8	686	530
9	693	535
10	700	540
11	707	545
12	714	550
13	721	555
14	728	560
15	735	565
16	742	570

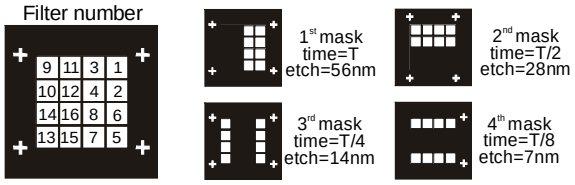

Fig. 6. The 4 masks used in the SiO_2 etching process. The filter number 1 (λ = 495 nm) is for uric acid; the filter number 2 (λ = 500 nm) is for cholesterol, and so one according to Table 1. The crosses are alignment marks.

4 Experimental Results

The 16 optical filters are now being fabricated. Meanwhile a single channel was previously fabricated and its operation demonstrated in the measurement of uric acid concentration (λ = 495 nm). A 200 W quartz tungsten halogen lamp was used as the white light source for biosystem illumination. The photodiode current was measured using a Keithley 487 picoammeter. A monochromator is also used in order to obtain the photodiode current versus the wavelength. The optical filter is composed of the 20 nm Al / 637 nm SiO_2 / 40 nm Ag layer stack. Optical spectra measurements on the biosystem show that the single channel is sensitive to its specific wavelength (λ = 495 nm), with a FWHM of 7 nm (Fig. 7). These measurements, when compared with the measurements without the optical filter (Fig. 2), allow concluding that it can be used only a white light source for the biosystem illumination. However, Fabry-Perot filters using metallic mirrors cannot provide both high-transmittance and low FWHM due to the optical absorption in the metal layers. From Fig. 7 it can be seen that with a FWHM = 7 nm the transmittance of the highest concentration fall off from 35% (see Fig. 2) to 4.5%. This can be avoided using high-performance dielectric mirrors. However the filters fabrication will be significantly more complex.

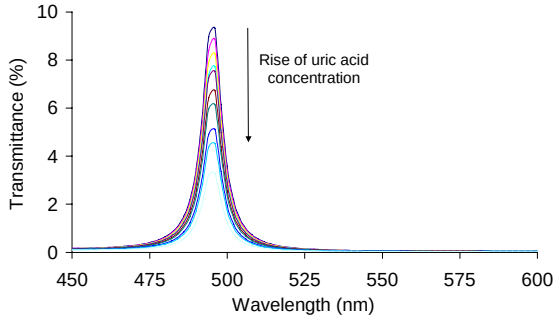

Fig. 7. Measured transmittance for a single channel for the same uric acid concentrations measured in Fig. 2 (λ = 495 nm).

5 Conclusions

The reported biosystem offers a new approach for clinical analysis due to the measurements of the concentration of 16 different biological substances in human's fluids, with the same device. This performance is obtained with an array of 16 optical filters based on Fabry-Perot thin-films optical resonators. Moreover, the 16 optical-channels array allows the use of only a white light source for illumination. Therefore, the measurements can be performed in any place and the results of those measurements become available immediately.

Acknowledgments

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