Optofluidic Intracavity Spectroscopy for Single Cell Detection

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Summary

Biological cells inside an optofluidic cavity modify the optical cavity modes, providing a probe for optical properties of the cells that can be used to detect and differentiate single cells. The fabrication and characterization of an optofluidic Fabry-Perot (FP) cavity in glass substrates[1] for this purpose and initial results on obtaining single biological cell spectra[2] were previously reported. Spectra of single biological cells including yeast cells and human blood cells using the optofluidic resonant cavity will be reported in this work. A method for spectral correlation is also presented to verify the preliminary results of the single cell spectra. The correlation calculation demonstrates that the method is able to differentiate some types of single cells.

Motivation

Low cost and label-free detection of single biological cells is of broad interest in a variety of fields, including clinical diagnostics, drug discovery, food safety, environmental monitoring, biology, and homeland security. Cell detection, identification, and monitoring are important capabilities for these applications. The potential capabilities of optofluidics in terms of fluidic control, miniaturization and optical property tuning afforded by microfluidics provide an ideal platform upon which to build such devices. This work combines microfluidic and optical sensing techniques to realize real-time, label free detection of single biological cells. Detection and differentiation of cells are based on the transmission mode spectra of cells in 10 to 30 μm deep fluid filled FP cavities fabricated on glass substrates and illuminated by an LED as schematically illustrated in Figure 1. The transverse mode structure of the cell-loaded cavity is determined by the refractive index structure of the cell including its type, size, and shape. Single cell spectra obtained using this method qualitatively appear to have characteristics such as the number of modes and mode spacing that can be used to differentiate cells.

Optofluidic resonant cavity fabrication

A sealed dielectric coated FP cavity with a finesse higher than 30 was successfully fabricated using thermocompressive gold bonding of glass and was used in the spectroscopic experiments. The cavity was formed by etching 10~30 μm deep channels in Pyrex glass and coating the surfaces with broadband thin dielectric mirror coatings. The reflectors are then joined using a thermo compressive gold-to-gold diffusion bonding technique inside a $350^{o}C$ oven in a 10^{-3} torr vacuum in order to form a FP interferometer. The low bonding temperature is compatible with the dielectric mirror materials. Figure 2 shows the optical transmission spectrum of a ~15μm deep cavity with a finesse higher than 30.

Experimental cell spectra

Light from a broadband LED with a FWHM of 50nm was focused onto the cell, and the transmitted light was directed to a 0.3nm resolution spectrometer through a customized microscope system. Figure 3 shows the multiple transmission spectra for single (a) yeast (b) red blood and (c) white blood cells. Narrow, higher order transverse mode peaks induced by the cells are clearly seen in the spectra in addition to a broad, low wavelength fundamental mode. The transverse mode structure groups are repeated three to four times in the 865 to 935 nm range due to the presence of multiple longitudinal modes associated with the cavity's free spectral range (FSR) of 15 to 20 nm. The spectral data were prepared for correlation computations. The correlation coefficients between four red blood cells, two other blood cells, and three yeast cells were then computed and recorded in Table I. The correlation data shows that the two types of blood cells can be differentiated, but that this initial method is not sufficient to differentiate red

[1] H. Shao, D. Kumar, S. A. Feld, and K. L. Lear, " Fabrication of a Fabry-Perot cavity in a microfluidic channel using thermocompressive bonding of glass substrates", *IEEE J. of MEMS,* vol. 15, pp. 756-762, 2005.
[2] H. Shao, D. Kumar, and K. L. Lear, "Single cell detection using optofluidic intracavity spectroscopy", *IEEE Sensors J.*, 2006 (in press).

blood cells from yeast cells. Additional measurements and analysis on malignant and normal cells are in progress and will be presented at the conference.

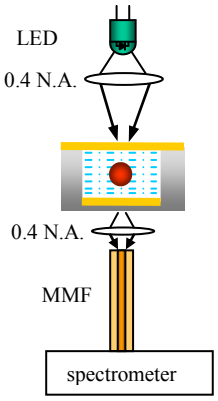

Figure 1. Experiment setup for single cell spectroscopy.

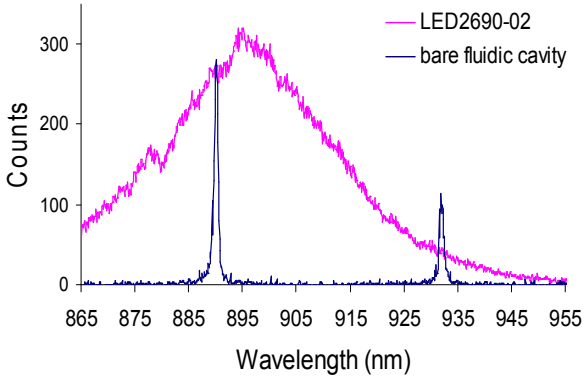

Figure 2. Water filled optofluidic dielectric coated FP cavity transmission spectrum illuminated with a well-collimated Hamamatsu LED.

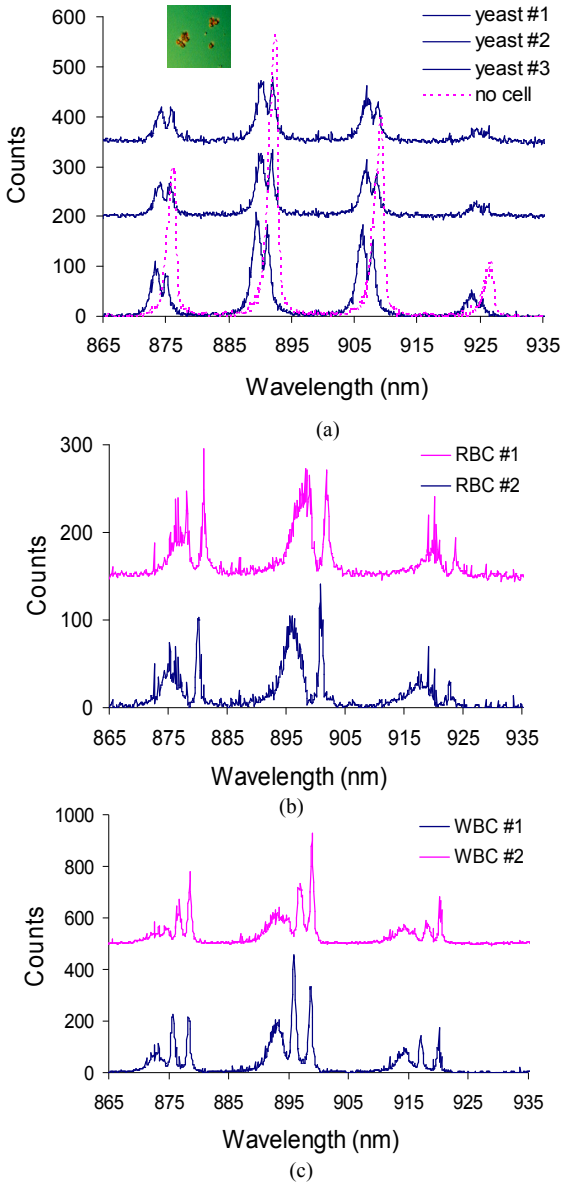

Figure 3. Transmission spectra of single (a) yeast cell, (b) red blood cell, and (c) white blood cell.

Table I. Correlation coefficient of spectra for red blood (RBC), white blood (WBC), and yeast (Y) cells.

	RBC1	RBC2	RBC3	RBC4	WBC1	WBC2	Y1	Y2	Y3
RBC1	1	0.84	0.84	0.8721	0.7016	0.6716	0.8430	0.862	0.7993
RBC2	0.84	1	0.9011	0.847	0.757	0.7442	0.820	0.8115	0.8666
RBC3	0.8721	0.9011	1	0.8784	0.7026	0.7241	0.6810	0.7660	0.7314
RBC4	0.9252	0.847	0.8784	1	0.7591	0.7223	0.9068	0.9230	0.8907
WBC1	0.7016	0.757	0.7026	0.7591	1	0.6507	0.6910	0.7690	0.7533
WBC2	0.6716	0.7442	0.7241	0.7223	0.6507	1	0.571	0.6385	0.7465
Y1	0.843	0.820	0.6810	0.9068	0.6910	0.571	1	0.9699	0.8707
Y2	0.862	0.8115	0.7660	0.9230	0.7690	0.6385	0.9699	1	0.9247
Y3	0.7993	0.8666	0.7314	0.8907	0.7533	0.7465	0.8707	0.9247	1