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Semiconductor Microlasers with Intracavity Microfluidics for Biomedical Analyses

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Abstract

Recently demonstrated microfluidic "chips" have the potential to be useful bioanalytical tools for DNA, protein, and cellular studies.[1] To realize this potential, means for introducing fluids, separating their components, and detection must be integrated onto the chip. We have investigated semiconductor laser microcavity spectroscopy as a means for ultrasensitive detection of various fluids, cells, and particulates.[2]

Two methods for implementing this laser device are illustrated in Fig. 1. Fig. 1a shows a scanning method for reading the light signals from a static fluid in the microcavity. The device illustrated in Fig. 1b shows a microfabricated flow structure formed between two surfaces, a vertical cavity surface-emitting laser and a glass dielectric mirror. The resonance frequencies of this Fabry-Perot microcavity are very sensitive to the dielectric properties of the fluids confined inside the cavity. Further, the resonance linewidth or cavity Q is sensitive to the optical length of the cavity, light absorption, and light scattering from the fluid and the surfaces forming the cavity. If cells or particulates are present in the fluid, they confine light transverse to the cavity length and develop additional sub-frequencies between the Fabry-Perot frequencies as shown in Fig. 2. Thus, the spectrum of light emitted from or transmitted through the cavity comprises a wealth of information about the cavity contents.

DISCLAIMER

Fig. 2 shows spectra for 4 different types of cells, including red and white blood cells, platelets, and placental tumor cells. The transverse modes are evident as the smaller peaks to the right of the large peak (Fabry-Perot mode) in each spectrum. The mode spacing, mode shift, and intensity relative to the longitudinal mode are plotted in the 3-dimensional cluster plot. This plot shows that the cell types can be identified solely on the basis of the spectral emission from the microcavity.

Fig. 3 shows how the transverse mode spacings can be used to caliper the cell dimensions. The average mode spacings (open points) are plotted against cell diameter d for red and white blood cells and yeast cells. These data are well described by a simple 2-dimensional mode theory (solid line labeled B/d^2) because the cells lie flat in the cavity. On the other hand, polystyrene sphere mode spacings (solid points) are better described by a three dimensional theory (solid line labeled A/d), because they are rigid spheres. Thus, the emission spectra can reveal reveal cell size and 3-dimensional shape.

Finally, we will report current investigations of different methods for pumping fluids through the microcavity space using mechanical or electromotive forces.[3] These forces can be used to drive molecules, cells, or particulates through an analysis region in the cavity.

References

1. Conference on Microfabrication Technology for Biomedical Applications, San Jose, CA October 24-25, 1996, Cambridge Healthtech Institute, Newton Upper Falls, MA (1996).
2. P. L. Gourley, *Nature Medicine* 2, 942-944 (1996).
3. D. J. Harrison, K. Fluri, K. Seiler, Z. Fan, C. S. Effenhauser, A. Manz, *Science* **261,** 895 (1993).

Figure Captions

Fig. 1a. Laser scanning method for detecting light signals from the microcavity laser (BL). GM-galvo-mirrors, LD-laser diode, PD- photodiode, BS- beam splitter.

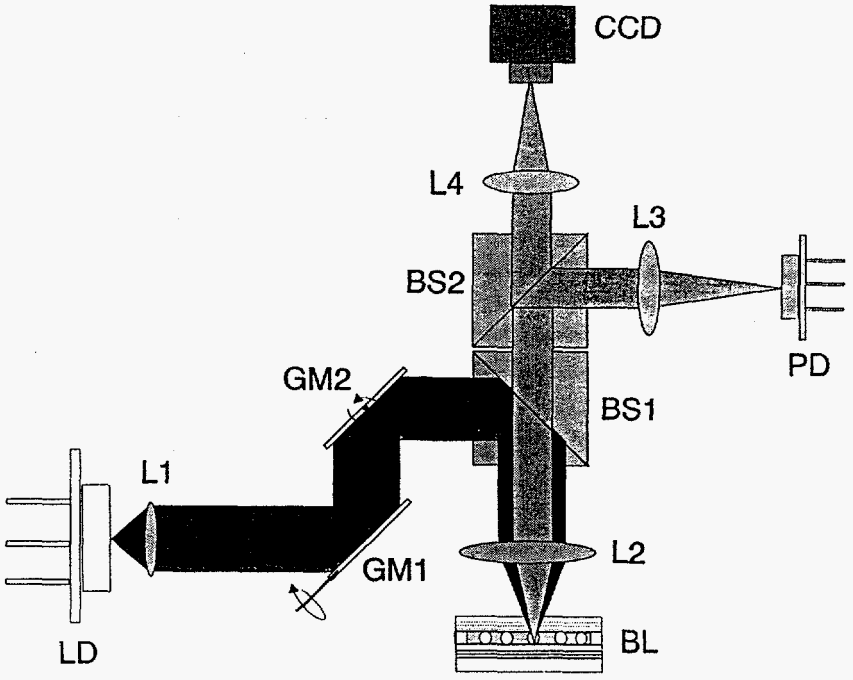
1b. Method for detecting flow of cells through a microcavity laser formed between a vertical cavity surface-emitting laser wafer and a glass dielectric mirror.

Fig. 2. Cluster plot of normal blood cells (red, white, and platelets) and cancer cells (spindle cells from a placental cancer) showing spectral method for differentiating cell types. Representative spectra for each cell type are displayed in the corners.

Fig. 3. Average transverse mode spacings as a function of cell measured cell diameter for cells and polystyrene spheres. The lines labelled B/d^2 and A/d are theoretical computations for 2- and 3-dimensional analyses, respectively.

LASER SCANNING CYTOMETER
FOR CELL, DNA, OR SINGLE MOLECULE DETECTION

(a)



FLOW CYTOMETRY ON A CHIP

(b)

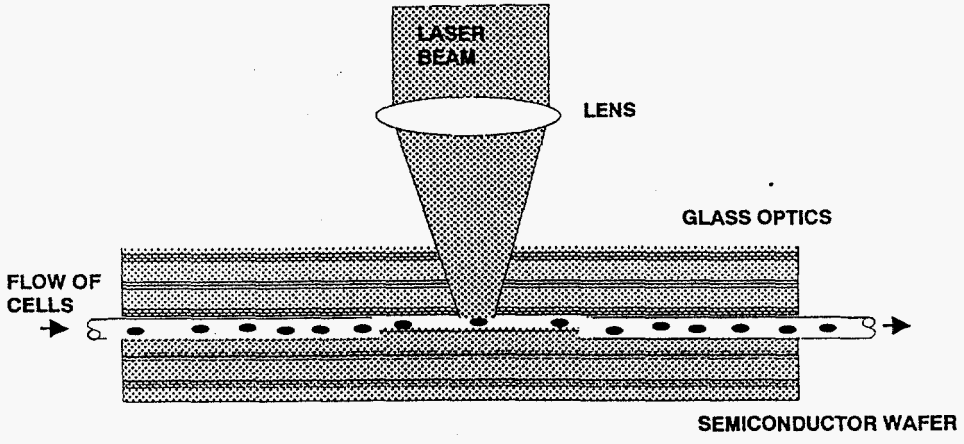


FIG. 1

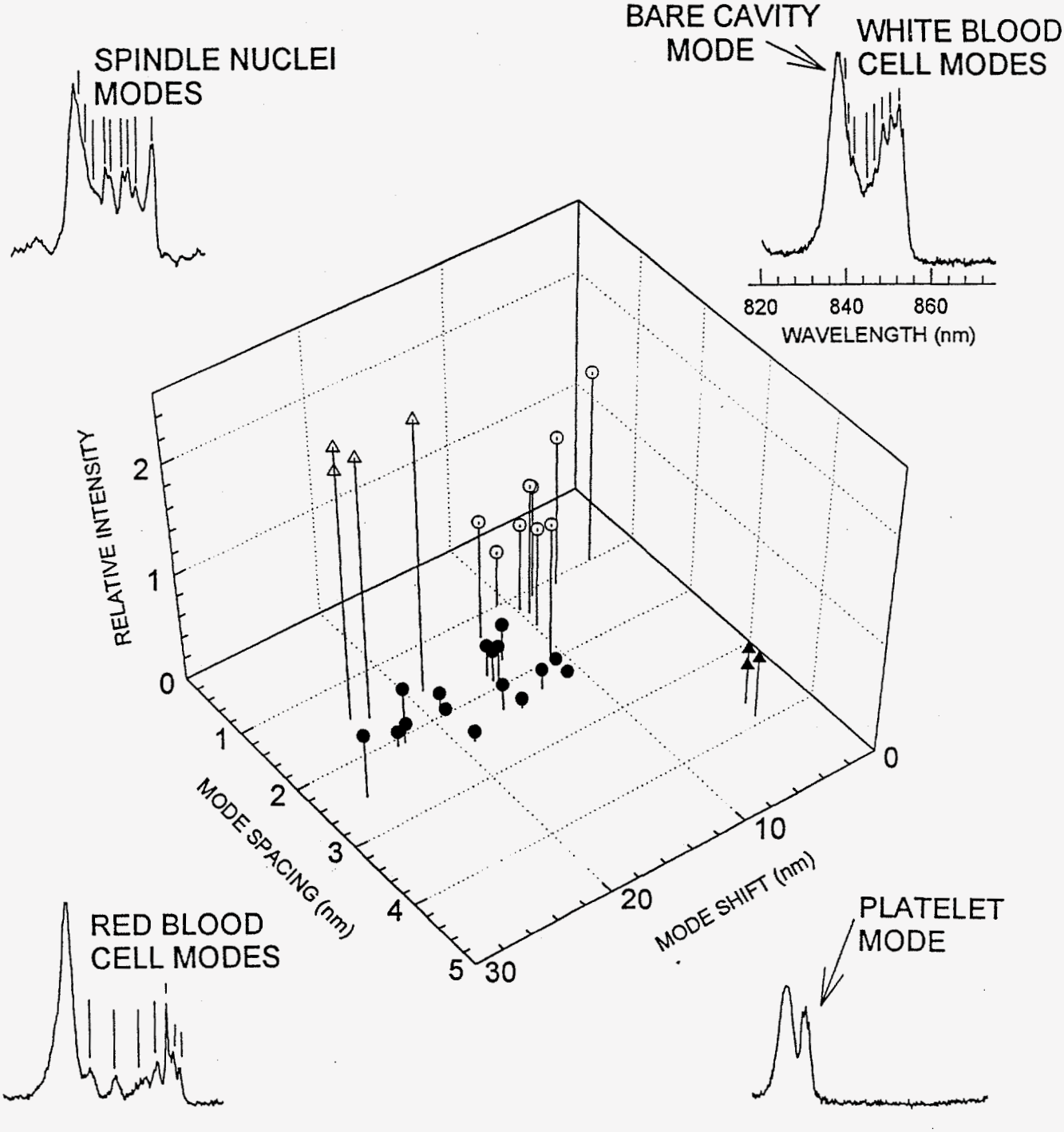

SPINDLE NUCLEI MODES
BARE CAVITY MODE
WHITE BLOOD CELL MODES
820
840
860
WAVELENGTH (nm)
RELATIVE INTENSITY
0
1
2
MODE SPACING (nm)
1
2
3
4
5
MODE SHIFT (nm)
0
10
20
30
RED BLOOD CELL MODES
PLATELET MODE

FIG. 2

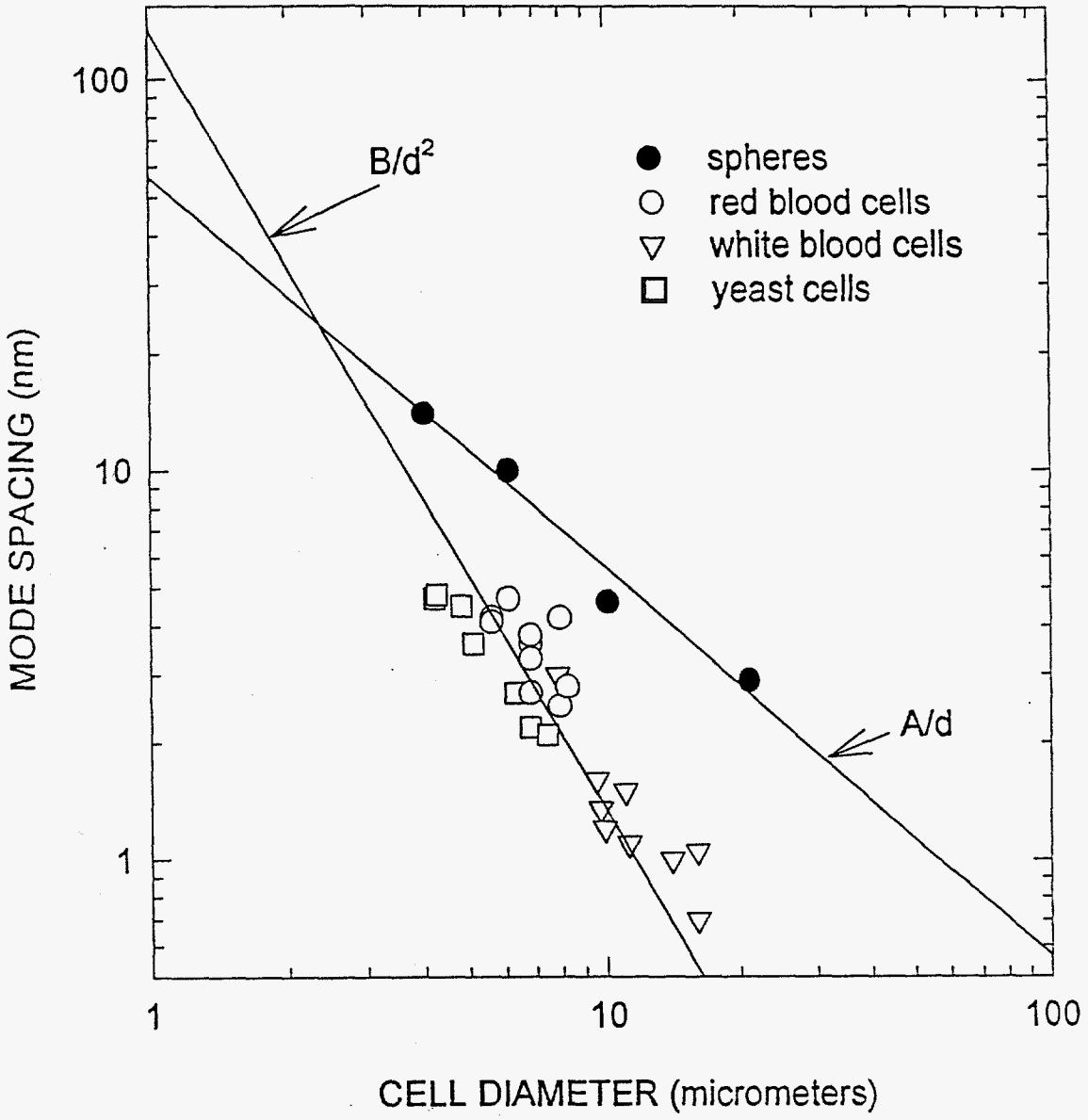

100
10
1
MODE SPACING (nm)
B/d²
A/d
spheres
red blood cells
white blood cells
yeast cells
1
10
100
CELL DIAMETER (micrometers)

FIG. 3