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A Biological Microcavity Laser

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Abstract

We have demonstrated a new semiconductor laser device that may be useful in high speed characterization of cells for diagnosis of disease. This device has critical advantages over conventional cytometers because it integrates biological structures with semiconductor materials at the wafer level.

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We have demonstrated a new semiconductor laser device that may be useful in high speed characterization of cell morphology for diagnosis of disease. This laser device has critical advantages over conventional cell fluorescence detection methods since it provides intense, monochromatic, low divergence light signals that are emitted from lasing modes confined by a cell. Further, the device integrates biological structures with semiconductor materials at the wafer level to reduce size and simplify cell preparation.

This microcavity semiconductor laser illustrated in Fig. 1 employs intracavity biological cells to provide transverse optical confinement for spontaneous and stimulated emission. The laser comprises a vertical cavity surface-emitting semiconductor, to provide gain and feedback for light confined by cells, and a dielectric mirror to close the cavity. Transparent cells loaded into the cavity act as dielectric waveguides to define transverse electromagnetic modes. Light emitted from the microcavity can be resolved into narrow spectral modes, high-contrast/coherent light images, or time-dependent pulses that reveal cell morphology and size. We have used this laser device as a cytometer in two basic configurations. First, as a probe of individual cells by spectral analysis of cell modes. Second, as scanning cytometer for rapidly probing large numbers of cells by pulse height spectroscopy.

We have used the first configuration to study red and white blood cells and dielectric spheres by examining lasing spectra.[1] We find that these cells have unique spectral signatures that can be used to identify them and determine their size and shape. Similar results can be obtained by examining spontaneous spectra obtained below the lasing threshold condition. Fig. 3 shows 3 spectra for the bare cavity (no cell present), loaded with a red blood cell, and loaded with a lymphocyte, respectively. The spectral changes from the bare cavity to the cell-loaded cavity are evident as additional modal peaks near 850 nm. The number of modes, their spacings, intensity distribution, and red shifts from the bare cavity mode are distinctive for each cell type. The average spacings of transverse modes (open points) are plotted against cell diameters in Fig. 2. These data are well described by simple 2-dimensionaly mode theory indicated by the solid line labeled B/d^2 where B is a constant and d is the cell diameter. This dependence is contrasted with the mode spacings observed for polystyrene spheres, also plotted in Fig. 2. In those data (solid points), the modes are well described by a three-dimensional mode spacing indicated by the solid line labeled A/d.

The device can also be operated as an intracavity scanning cytometer to probe many cells placed within the laser cavity, as shown in Fig. 1. A scanning pump laser (cw or pulsed nanosecond or femtosecond) excites electron-hole pairs in the semiconductor wafer to create gain. A cell loaded in the cavity acts as dielectric waveguide to confine light and lower the laser threshold. When the scanning spot passes over the cell, an intense pulse of laser light is emitted from the cavity. Many cells can be probed in a short period of time with high signal-to-noise pulses. Using this principle, we have accumulated pulse height spectra of cell and dielectric sphere populations within a few seconds to minutes. Pulse height spectra for populations of blood cells and polystyrene spheres exhibit distinctive features that reflect the uniformity and size of the cell or sphere populations.

References

1. P. L. Gourley, K. E. Meissner, T. M. Brennan, B. E. Hammons, and M. F. Gourley, *Proceedings of the International Symposium on Biomedical Optics*, San Jose Feb. 4-10, 1995, SPIE vol. 2387, p 148.

Figure Captions

Fig. 1. Schematic of the intracavity laser device showing a pump beam scanning over the biological microcavity laser (biocavity laser) resonator that is emitting a lasing beam toward a detector/spectrometer.

Fig. 2 Spontaneous emission spectra of the bare cavity, cavity loaded with a red blood cell, and loaded with a white blood cell, respectively. The longitudinal modes of the bare cavity are labeled with arrows. The transverse modes of the cavity loaded with a cell are indicated with vertical lines.

Fig. 3. Average transverse mode spacings as a function of measured cell diameter. Red and white blood cells and yeast cells are indicated with open points. These data are well described by the solid theoretical line labeled B/d^2 where B is a constant and d is the diameter. The mode spacings for polystyrene spheres (solid points) are also shown. These data are described by the theoretical line labeled A/d.

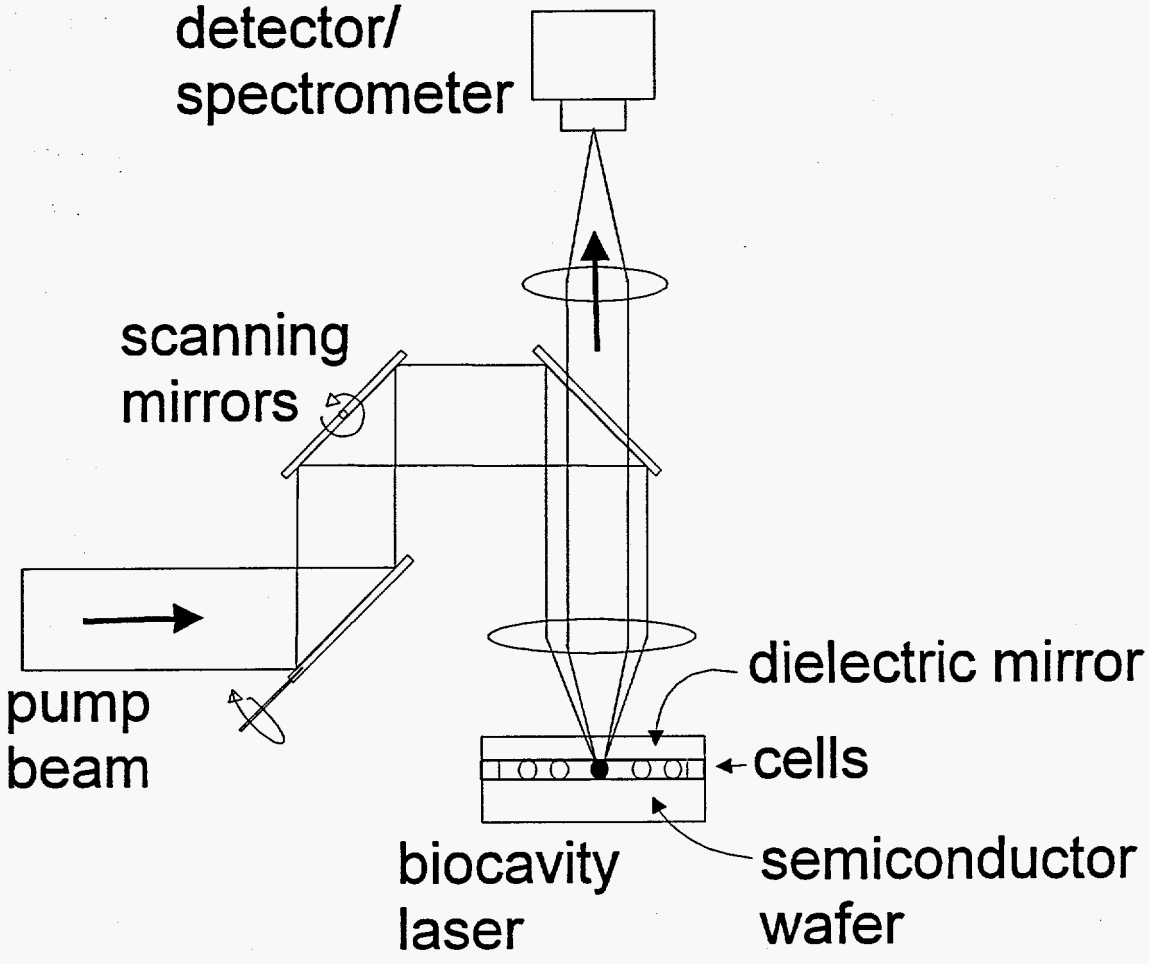
detector/
spectrometer
scanning
mirrors
pump
beam
dielectric mirror
cells
biocavity
laser
semiconductor
wafer

FIG. 1

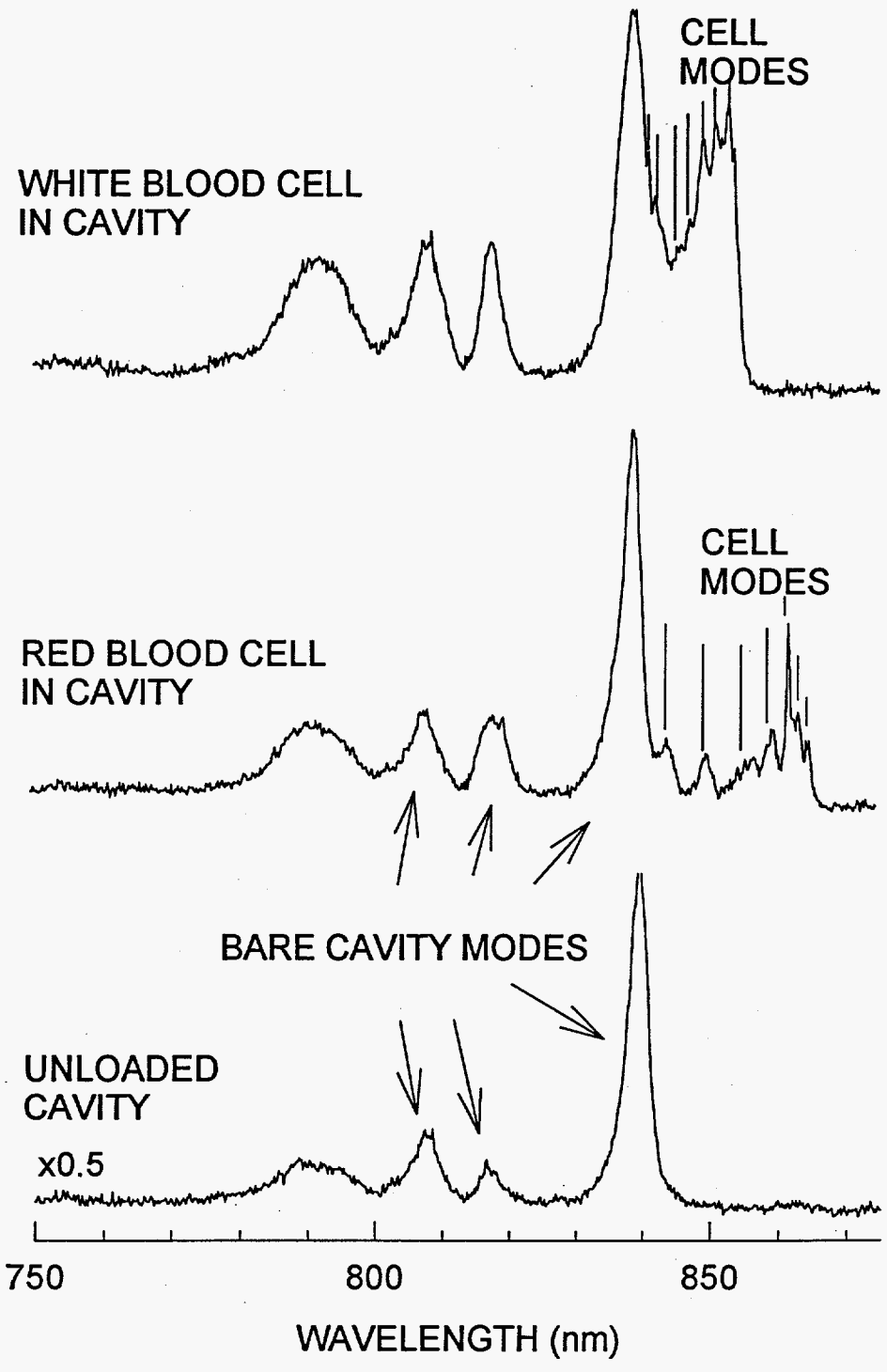
CELL
MODES
WHITE BLOOD CELL
IN CAVITY
CELL
MODES
RED BLOOD CELL
IN CAVITY
BARE CAVITY MODES
UNLOADED
CAVITY
x0.5
750
800
850
WAVELENGTH (nm)

FIG. 2

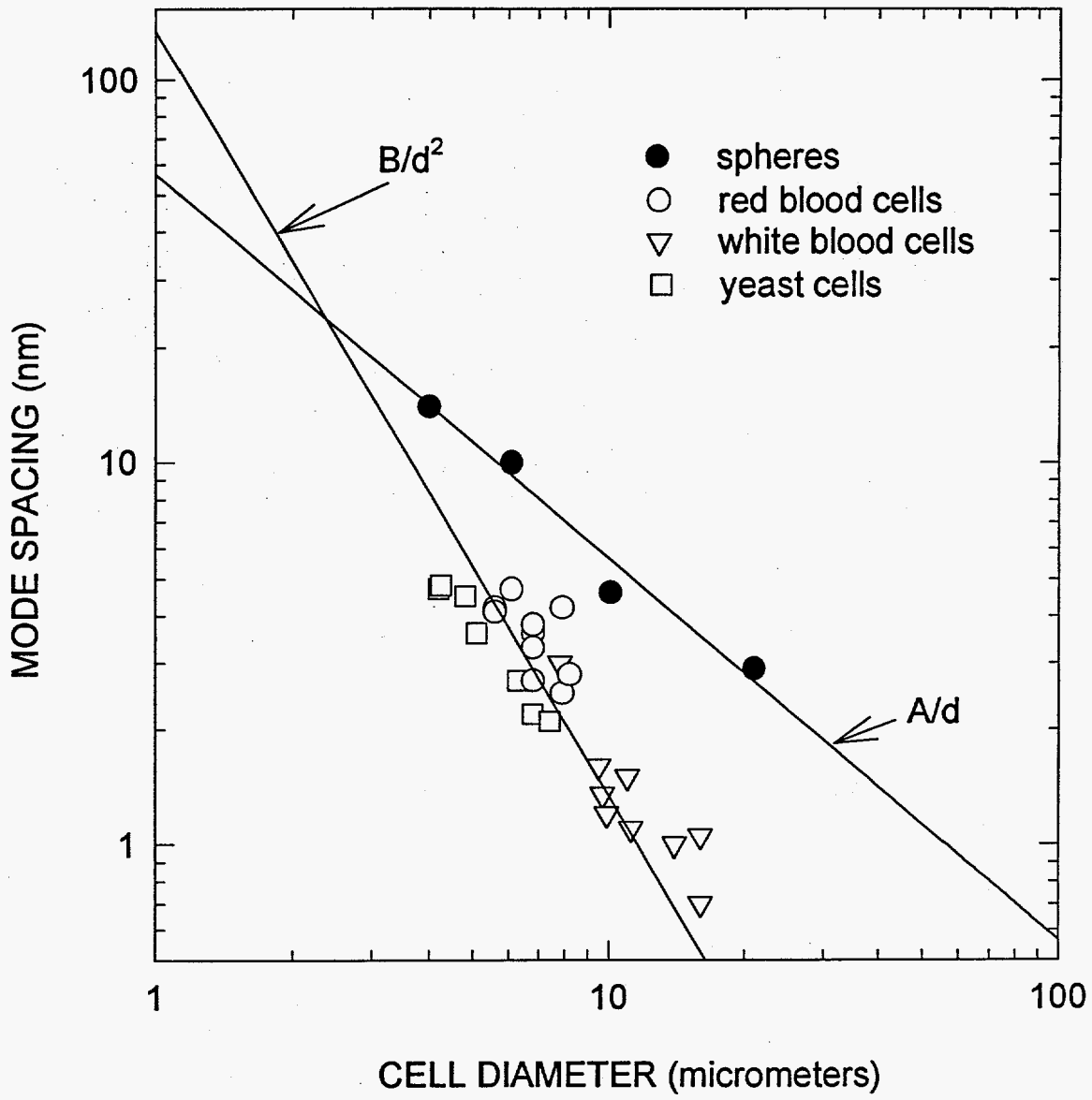
100
10
1
MODE SPACING (nm)
B/d²
A/d
spheres
red blood cells
white blood cells
yeast cells
1
10
100
CELL DIAMETER (micrometers)

FIG. 3