Protein Detection by Optical Shift of a Resonant Microsphere

Frank Vollmer[1], Maziar Khoshsima[2], Dieter Braun[1], Iwao Teraoka[2], Albert Libchaber[1], Stephen Arnold[2]

[1]*Center for Studies in Physics and Biology, The Rockefeller University, New York, NY 10021*
email: vollmef@rockvax.rockefeller.edu

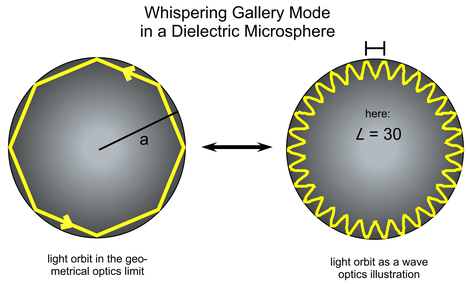
[2]*Microparticle Photophysics Lab, Polytechnic University, Brooklyn, NY 11201*
www.poly.edu/microparticle

Abstract

We present a novel **optical biosensor** with unprecedented sensitivity for detection of unlabeled molecules. Our device uses optical resonances in a dielectric microparticle (**Whispering Gallery Modes**) as the physical transducing mechanism. The resonances are excited by evanescent coupling to an eroded optical fiber and detected as dips in the light intensity transmitted through the fiber at different wavelengths. Binding of proteins on the microparticle surface is measured from a shift in resonance wavelength. We demonstrate the sensitivity of our device by measuring adsorption of bovine serum albumin and we show its use as a biosensor by detecting streptavidin binding to biotin.

Whispering Gallery Modes

An **optical resonance** (or **Whispering Gallery Mode**, WGM) occurs when circumnavigating light, trapped by total internal reflection, constructively interfers with itself. Each resonance can be characterized by the number of wavelength L within an orbit.



Experimental Setup

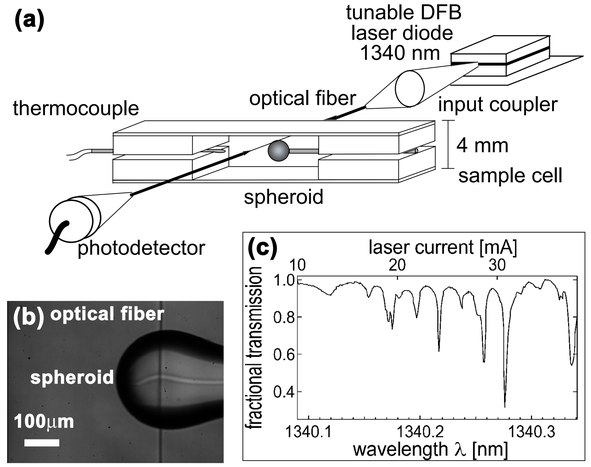
(a) A spheroidal microparticle fabricated by melting the tip of a fiber is placed in contact with the eroded part of a single mode optical fiber.

The output wavelength of a distributed feedback laser diode is tuned by its laser current. Resonances are detected as dips in the transmitted intensity at different wavelength.

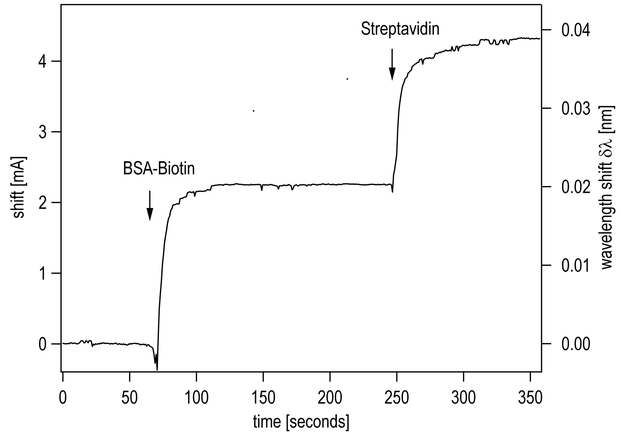
Buffer solution is retained in the sample cell due to surface tension, a thermocouple measures the solution temperature.

(b) Picture of the spheroid coupled to the optical fiber.

(c) Resonances (WGMs) versus wavelength.

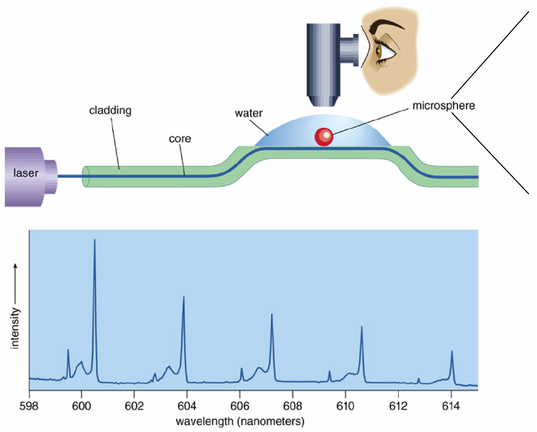


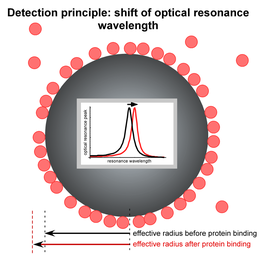
Biosensor



Streptavidin binding to previously surface immobilized BSA-biotin. The initial shift is due to adsorption of BSA-biotin. After injecting Streptavidin, a second shift is observed.

Detection Principle





Proteins binding to the microsphere surface increase its effective radius.

A given optical resonance will shift its resonance wavelength to accomodate the larger circumverence.

WGMs of a microsphere can be excited by **evanescent coupling** to the core of an optical fiber. Resonances are detected in the scattered light from the microsphere or by dips in the transmitted intensity through the fiber end.

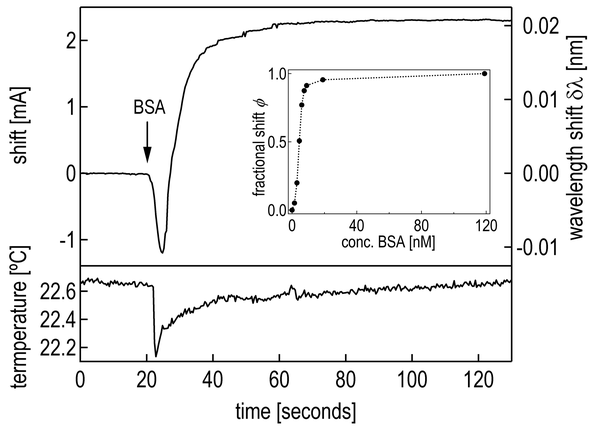
BSA Adsorption

BSA solution is injected into the sample cell to a final concentration of 1.5 μM (PBS, pH 7.4).

A Labview program traces the wavelength shift of one given optical resonance.

The initial negative shift is due to thermal contraction of the spheroid. The overall positive shift is entirely due to BSA adsorption onto the aminosilanized microparticle.

The inset shows the binding isotherm.



Theory

In the asymptotic limit for the number of wavelength within an orbit $L >> 1$, the resonance wavelength shift δλ is caused by the energy needed to polarize a protein molecule. The protein needs only be characterized by its excess polarizability. The resulting shift is

$$\frac{\delta\lambda}{\lambda} \approx \frac{\alpha_{ex}\sigma_s}{\varepsilon_0(n_1^2 - n_2^2)R}$$

λ ... wavelength
$\delta\lambda$ ... wavelength shift
α_{ex} ... excess polarizability of the bound protein
σ_s ... surface density of the bound protein
n_1, n_2 ... refractive indices of the sphere and the buffer solution, respectively
R ... orbital radius
ε_0 ... vacuum permittivity

FV is supported by a fellowship of the Boehringer Ingelheim Fonds, DB by a Fellowship of the Deutsche Forschungsgemeinschaft, research at the Polytechnic is supported by a National Science Foundation grant BES-0119273.