DNA Detection by Differential Perturbation of two Microsphere Cavities

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Abstract.
We report the detection of unlabeled DNA oligonucleotides on microsphere probes from a response of their photonic resonance modes. Narrow linewidth resonant modes (called whispering-gallery-modes, WGMs) occur from a light ray orbitting inside the microsphere due to total internal reflection. The resonance thus improves the detection limit by orders of magnitude as compared to existing single pass techniques. The ultimate detection limit of an optical cavity has been estimated to be on the order of a single, unlabeled macromolecule.

1 Whispering Gallery Modes,
A light ray can be confined inside a dielectric sphere due to total internal reflection at the sphere surface. The long confinement time (high Q) allows the light to circumnavigate the sphere for many orbits. If used for biosensing, such an optical resonance (WGM) enables the light to interact with the same analyte molecule for several thousand times. The resonance thus improves the detection limit by orders of magnitude as compared to existing single pass techniques. The ultimate detection limit of an optical cavity has been estimated to be on the order of a single, unlabeled macromolecule.

2 Detection Principle,
Resonances in glass microspheres can be excited by the light transmitted through an optical fiber. Coupling of light between fiber and sphere occurs only for specific resonance wavelengths. Experimentally, a resonance is detected as a dip in the spectrum of the light intensity transmitted through the fiber-sphere system. Detection of biomolecules is possible due to the evanescent field which extends from the evanescent field that extends from the sphere surface. Dielectric material such as DNA and protein molecules polarize when entering the evanescent field of the microsphere. This perturbation of the optical cavity leads to a red shift of a given resonance wavelength.

3 Theory,
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References:
2 “Shift of Whispering Gallery Modes in Microspheres by Protein adsorption”, Optics Letters 28 (4), 2003, 272-274

6 Results,
Shift of Resonances. (A) Shows the time trace of the two resonance positions from S1 and S2. The arrows indicate when the two complementary DNA oligonucleotides were injected into the sample solution. Hybridization saturates within minutes and the resonance wavelength of the corresponding sphere increased about 0.038 nm each.

Single nucleotide mismatch discrimination. (A) Time traces of resonance wavelengths in two spheres S1 and S2. S1 was modified with a 11-mer oligonucleotide (CTATCTCAGTC). The oligonucleotide immobilized on sphere S1 was identified as Lorentzian dips in the transmission spectrum. A hybridization event of a label-free oligonucleotide on sphere S2 is detected by an increase of the S1-specific resonance wavelength.

4 Setup,
(A) Light from a tunable laserdiode L (1.3 µm) is transmitted through a single mode optical fiber F. Two silica microspheres S1 and S2 are evanescently coupled to the fiber. A photodetector P records the intensity at the other fiber end. Optical resonances from each sphere are identified as Lorentzian dips in the transmission spectrum. A hybridization event of a label-free oligonucleotide on sphere S1 is detected by an increase of the S1-specific resonance wavelength.

(B) Micrograph of two spheres coupled to the same optical fiber running horizontally through the center of the image. The image shows resonances of light orbitting inside each sphere.

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