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RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

Keynote: Molecular Sensing Based on Optical Whispering-Gallery Mode Microsensors

Zhixiong "James" Guo

3rd International Conference and Exhibition on Biosensors & Bioelectronics
August 11-13, 2014, San Antonio, Taxes, USA

Rutgers — Jersey Roots, Global Reach



- Chartered in 1766, Rutgers has a unique history as a colonial college, a land-grant institution, and a state university. In 1864, Rutgers prevailed over another major college in NJ to become the state's land-grant college.

- With more than 65,000 students on campuses in Camden, Newark, and New Brunswick, Rutgers is one of the nation's major public institutions of higher education.



The Birthplace of College Football

Major Campus – New Brunswick/Piscataway



Land: 2,688 acres
Students: > 50,000

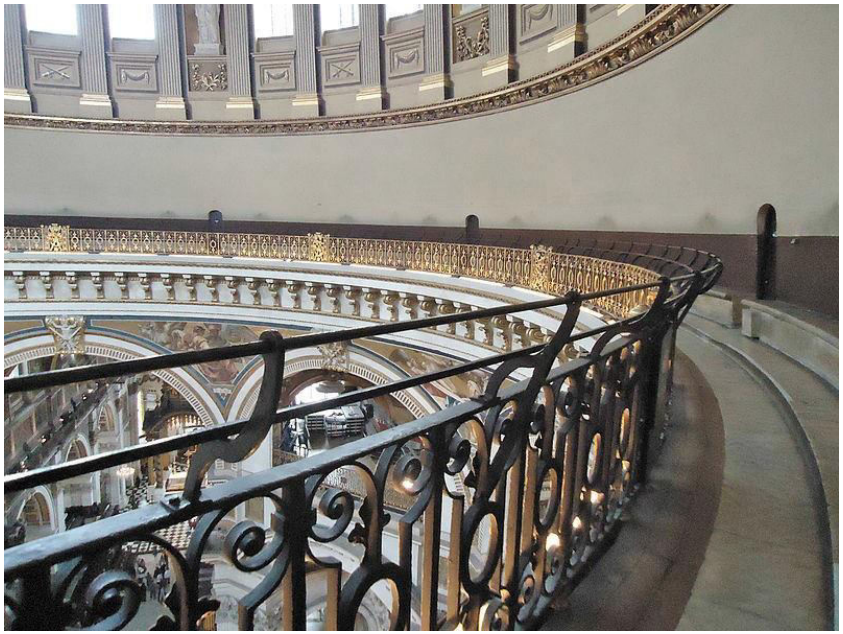
< 40 miles to Times Square, NYC



Presentation Outline

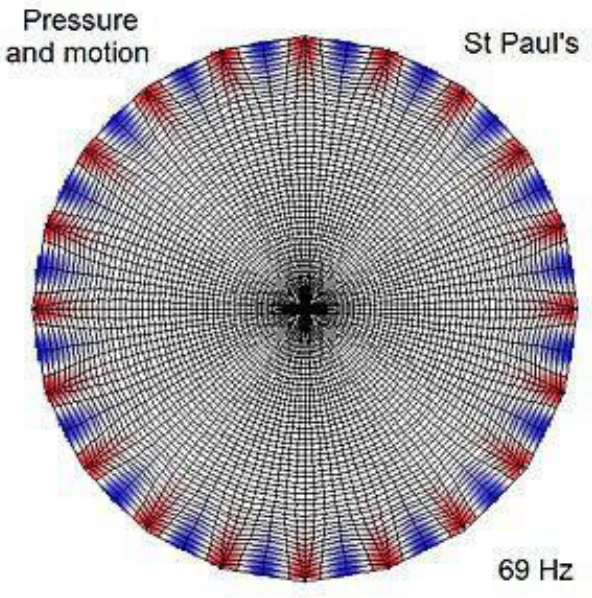
- **Introduction**
  - *What is whispering-gallery mode?*
  - *Lab fabrication of optical WGM devices*
  - *Molecular sensing based on optical WGM*
- **Physical and Mathematical Description**
  - *WGM sensor in a micro-opto-electro-fluidic system (MOEFS)*
  - *Governing equations*
    - *---- Charge and fluid transport*
    - *---- Dynamics of adsorption and desorption*
    - *---- Maxwell's equations*
- **Results and Discussion**
  - *Validation with experimental measurement*
  - *Influence of applied electrical potential*
  - *Dynamics of adsorption*
  - *Influence of resonance modes*
  - *Sensor curves*
- **Concluding remarks**

Whispering Gallery



Whispering gallery at St. Paul's Cathedral

Images from Wikipedia

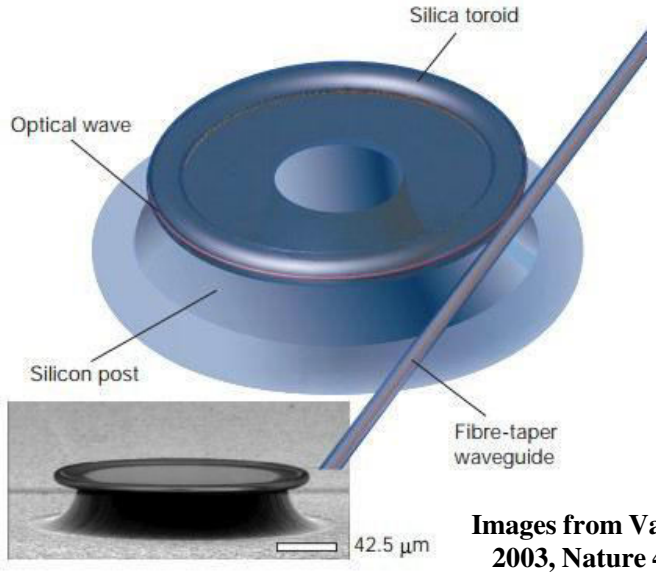


Simulation of the whispering gallery at St. Paul's Cathedral

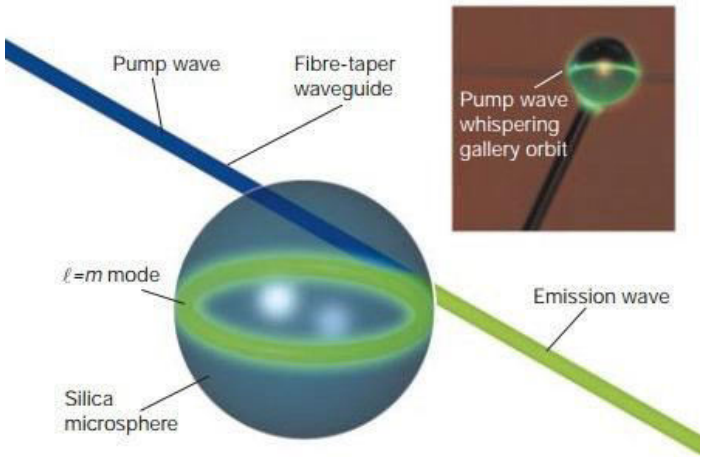
- The study of acoustic whispering gallery began in St. Paul's Cathedral, London
- Lord Rayleigh was the first to describe how sound waves were reflected around the walls of the gallery due to its circular shape in 1878
- The term 'whispering gallery' has been borrowed in the physical sciences to describe other forms of whispering-gallery waves such as light

Optical Whispering Galleries

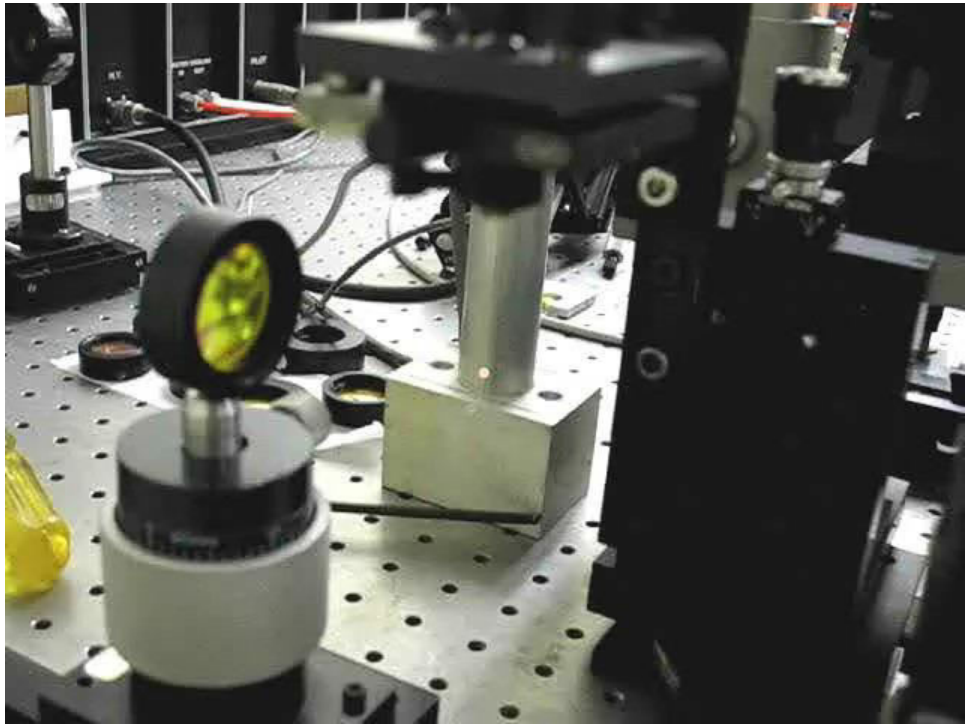
- Sound waves have a wavelength on order of meters. Light, on the other hand, has a wavelength on the order of microns or less
- Optical whispering-gallery mode (WGM) occurs in small dielectric circular shapes such as spheres, rings, or cylinders, with diameters on the micrometer scale
- Optical WGM resonators are characterized as having extremely high Quality factors (*Q*-factors) and very small mode volumes
- Such features them ideal for micro/nano photonic devices, such as lasers, filters, sensors, and quantum systems
- Distinct researchers include Stephen Arnold at NYU-Poly, Kerry Vahala at Caltech, Russian scientist V.S. Ilchenko, French scientist Serge Haroche (Nobel Laureate in Physics, 2012), etc.

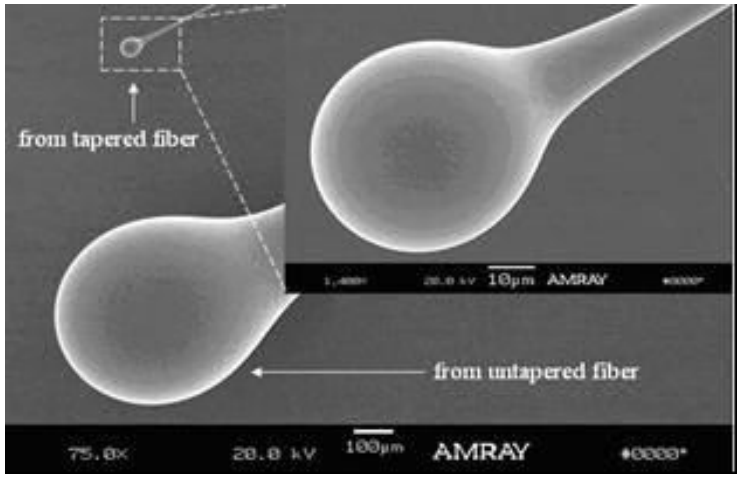


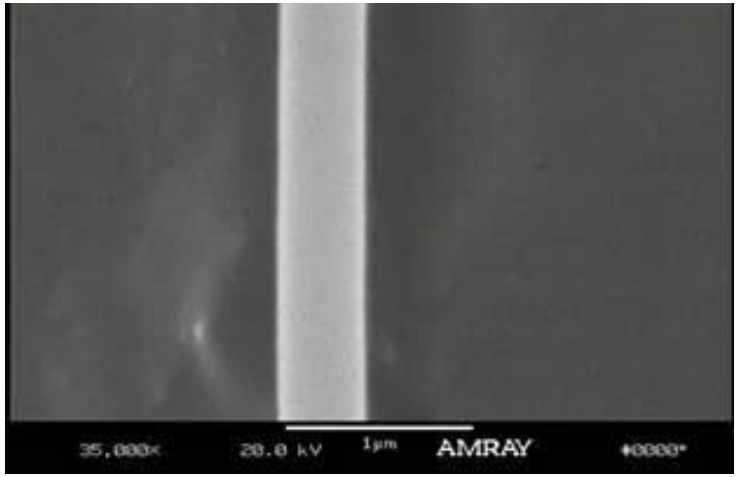
Images from Vahala 2003, Nature 424



Fabrication of Microbeads & Tapers

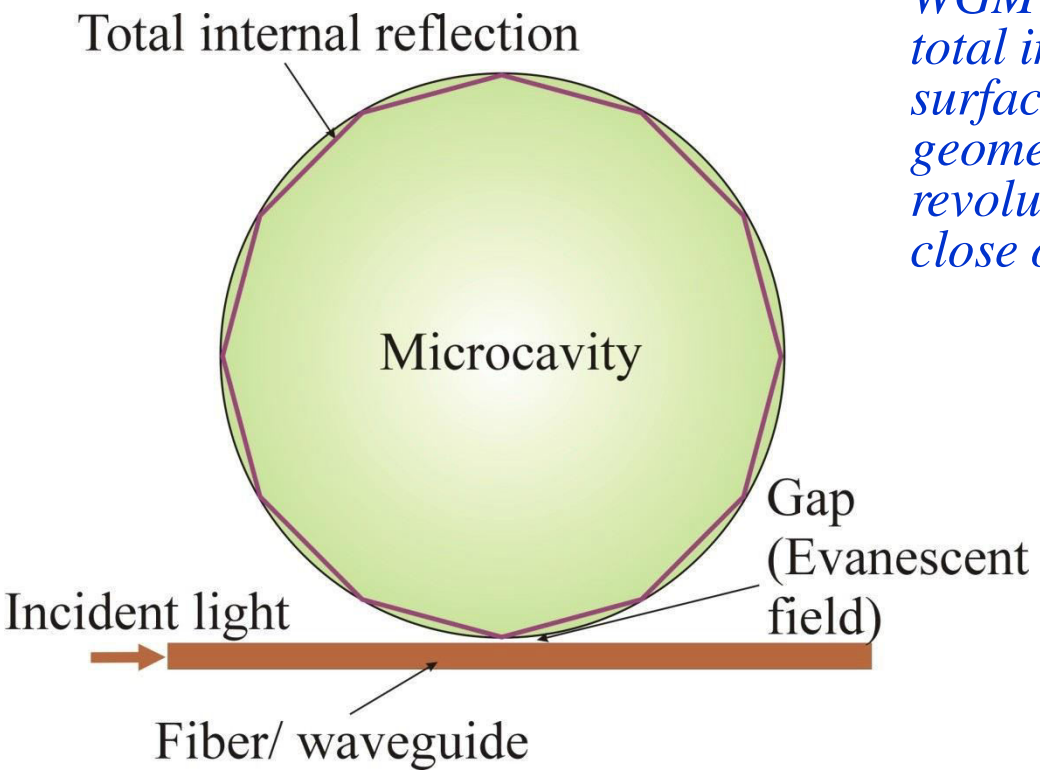




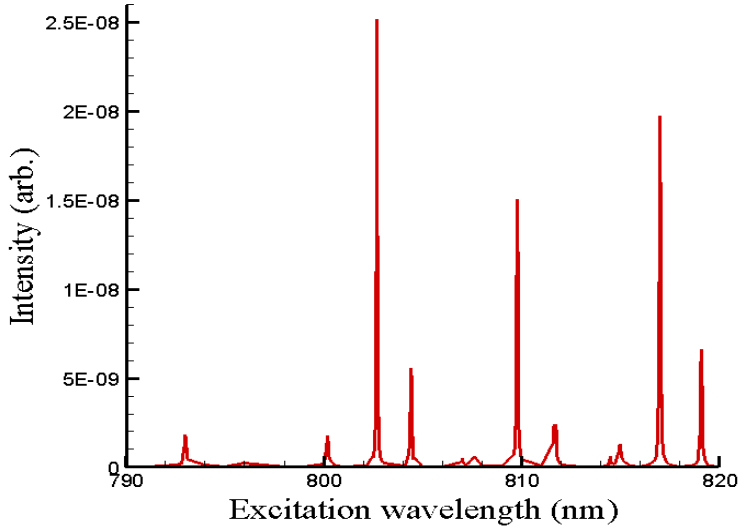


Images from Ma, Rossmann & Guo, 2008, J. Phys. D

Generation of Optical WGM



WGM occurs when light, confined by total internal reflections, orbits near the surface of a dielectric medium of circular geometry and returns in phase after each revolution. The electromagnetic field can close on itself, giving rise to resonance.

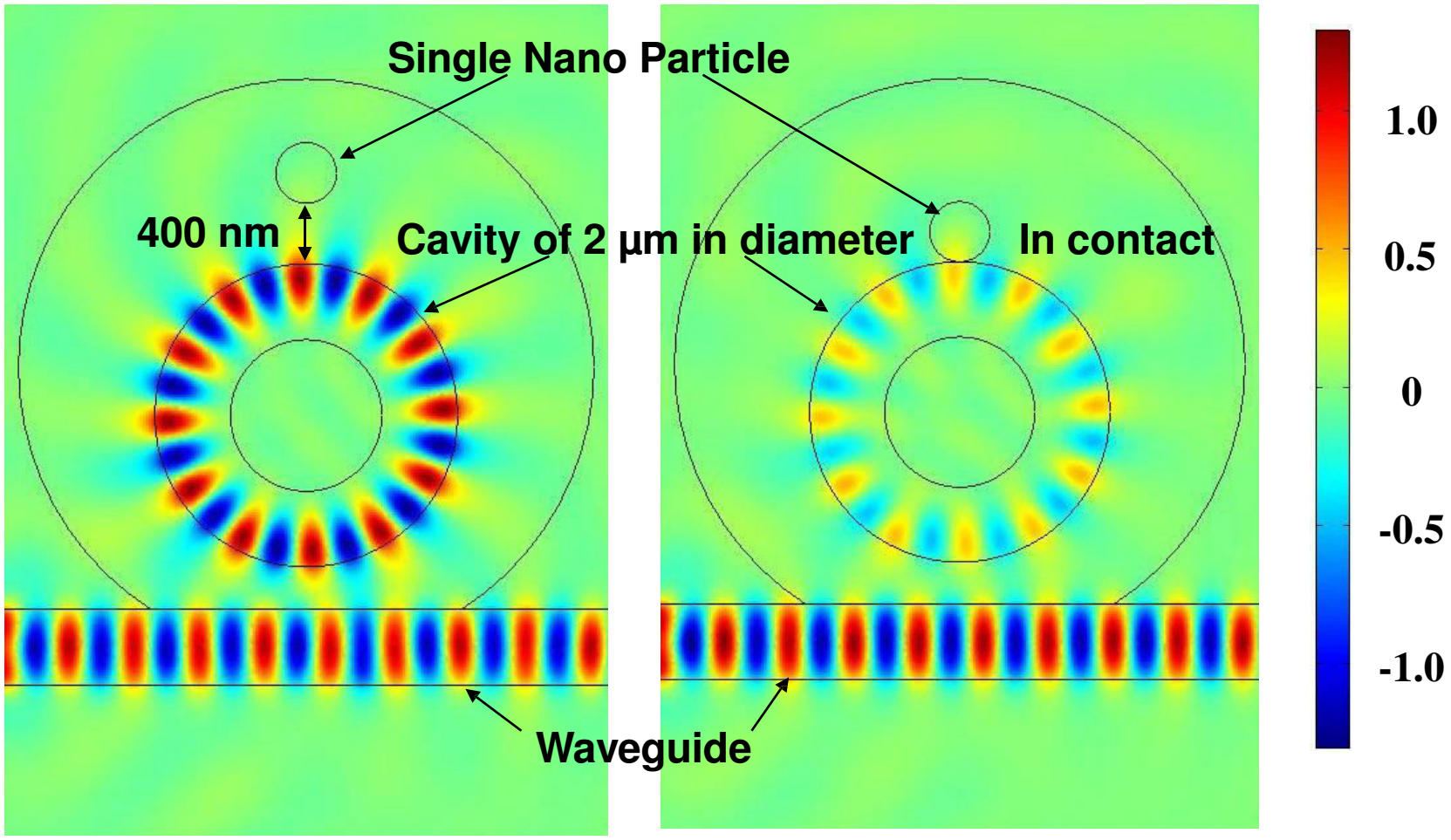


Typical resonance spectrum

Sensing Principle:

$$\Delta f / f = -\left(\Delta r / r + \Delta n / n\right)$$

Example: Sensing of A Single Nano-Entity



H. Quan & Z. Guo, Nanotechnology, 2007; or Haiyong Quang, Ph.D. Dissertation, Rutgers University, 2006.

Earlier Literature on Single Molecule Detection

- Science 10 August 2007: Vol. 317 no. 5839 pp. 783-787
  Received for publication 11 May 2007

  Label-Free, Single-Molecule Detection with Optical Microcavities

  (Dr. Zhixiong Guo proposed such a similar ideal back in early 2005, See below)
- NSF Proposal Number: CTS-0541585**. Starting Date: August 15, 2005**
  Principal Investigator: Guo, Zhixiong
  Proposal Title: **SGER: Single Molecule-Radiation Interaction in Whispering Gallery Mode Evanescent Field**

- Nanotechnology 18 (2007) 375702 (5pp)

  Received 9 May 2007. Published 22 August 2007

  Simulation of single transparent molecule interaction with an optical microcavity.
  Haiyong Quan and Zhixiong Guo

  Results from

  Haiyong Quan, Ph.D. Dissertation, Rutgers University, May 2006

  Characterization of Optical Whispering Gallery Mode Resonance and Applications

- *Nature Methods* - **5**, 591 - 596 (2008)
  Whispering-gallery-mode biosensing: label-free detection down to single molecules. Frank Vollmer & Stephen Arnold

Earlier Literature on Layered Detection

- Appl. Phys. Lett. **80**, 4057 (2002)
  Protein detection by optical shift of a resonant microcavity.
  F. Vollmer, D. Braun, A. Libchaber, M. Khoshsima, I. Teraoka, S. Arnold.

- Optics Letters, Vol. 28, Issue 4, pp. 272-274 (2003)
  Shift of whispering-gallery modes in microspheres by protein adsorption.
  S. Arnold, M. Khoshsima, I. Teraoka, S. Holler, and F. Vollmer

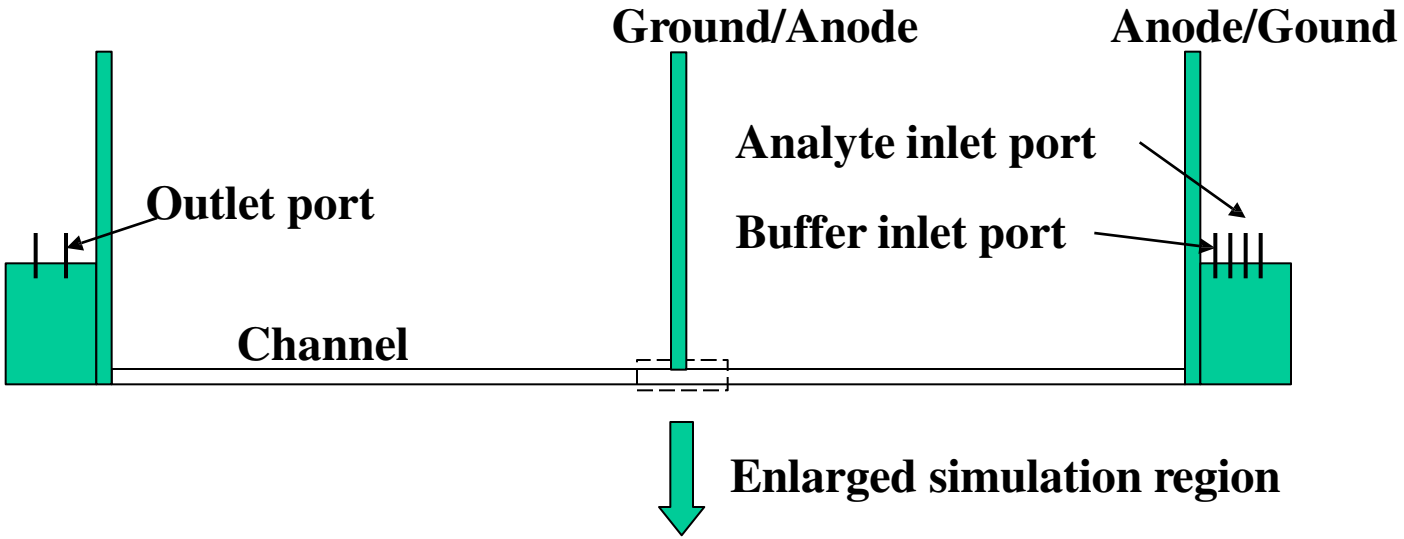
- Selected Topics in Quantum Electronics, IEEE J, vol.12 (1) , 2006
  Polymer microring resonators for biochemical sensing applications
  C.Y. Chao, W. Fung, L. J. Guo

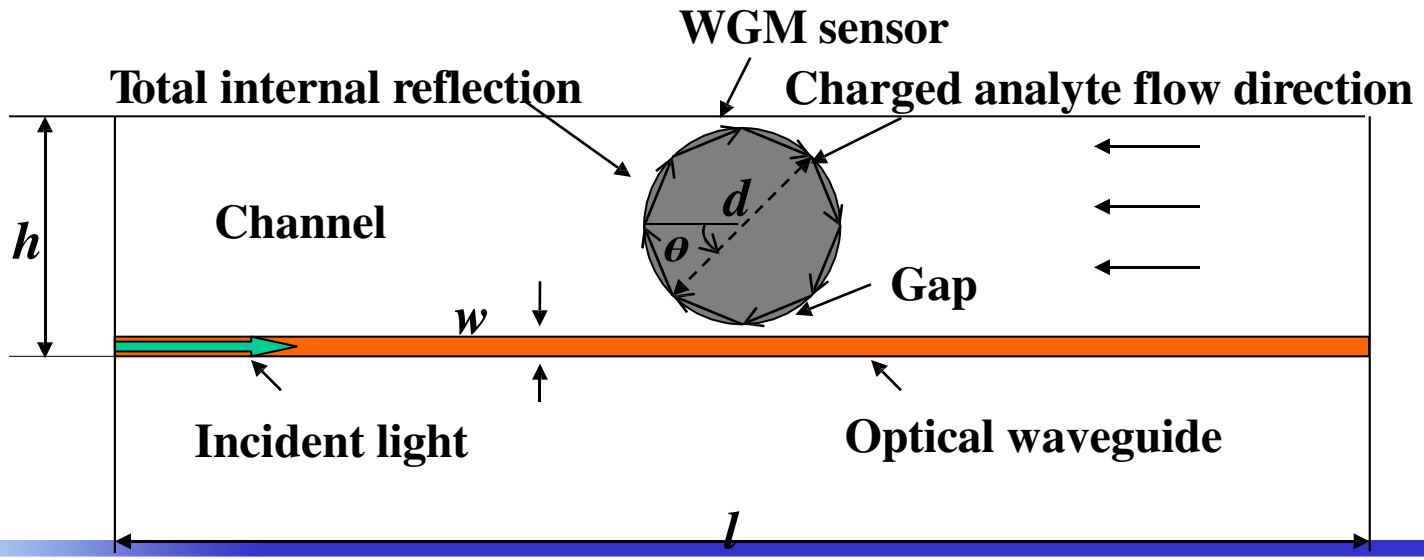
- Advanced Functional Materials, vol. 15 (11), pp. 1851-1859, 2005
  Macroporous Silicon Microcavities for Macromolecule Detection
  H. Ouyang, M. Christophersen, R. Viard, B. L. Miller and P. M. Fauchet

- JQSRT, vol. 93 (1-3), pp. 231–243, 2005
  Simulation of whispering-gallery-mode resonance shifts for optical miniature biosensors
  H. Quan and Z. Guo

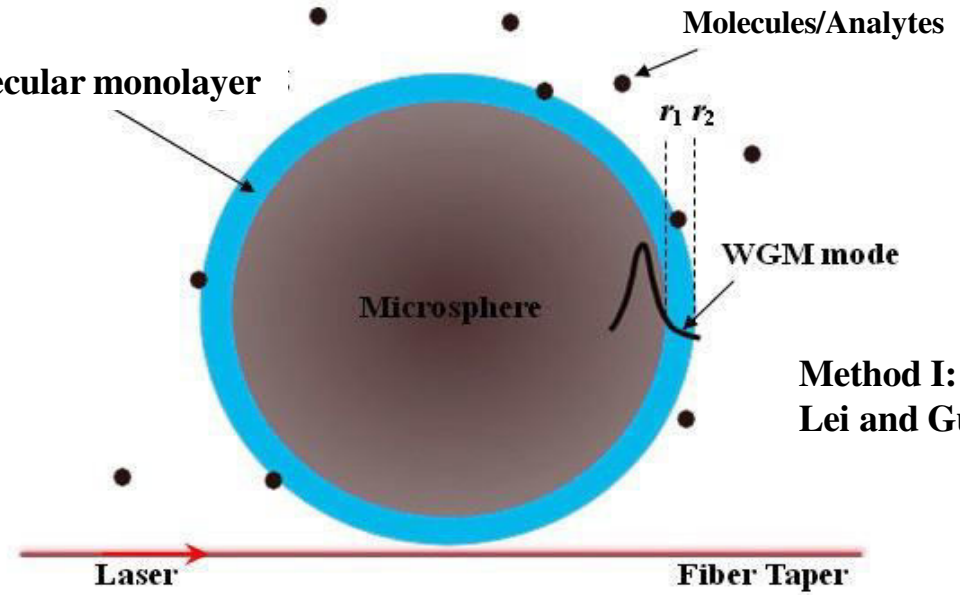
and many others

Proposed MOEFS with a WGM Sensor



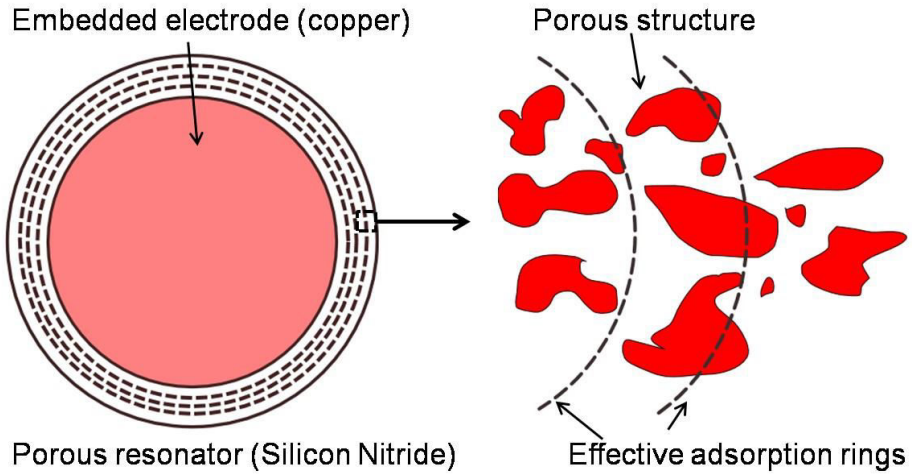


Adsorption and Sensing of Small Molecules



Method I: Surface attachment of analytes
Lei and Guo 2011, Biomicrofluidics

Method II: Filtration and trapping of analytes in porous layer
Lei and Guo 2012, Nanotech.



Governing Equations

- Charge transportation equations

$$\frac{\partial C_i}{\partial t} + K_{i,c}\vec{V}\cdot\nabla C_i = \nabla\cdot(z_i w_i F C_i \nabla\Phi) + K_{i,d} D_i \nabla^2 C_i, \quad i = 1,2,3$$

for the charged analyte, hydroxide ion and hydrogen ion.

- Poisson equation for electrical potential

$$\varepsilon_f \nabla^2 \Phi = -\tau\rho_E \qquad \rho_E = F\left(\sum_i c_i z_i\right)$$

- Navier-Stokes equation with porous medium model

$$\frac{\partial \vec{V}}{\partial t} + \vec{V}\cdot\nabla\vec{V} = -\frac{}{\tau\rho} + \frac{}{\tau}\nabla^{-}\vec{V} - \frac{'\ E}{\tau\rho}\nabla\Phi + \frac{\acute{\jmath}\Gamma}{\tau}$$

- Langmuir model for adsorption

$$\frac{\partial C_{s}}{\partial t} = K_{ads}\left(\frac{C_{1}}{\xi}\right)(\Theta - C_s) - K_{des}C_s$$

Governing Equations (cont.)

- Time-dependent Maxwell's equations

$$\begin{cases} \nabla \cdot \vec{E} = \dfrac{\rho}{\varepsilon}; \quad \nabla \times \vec{E} = -\mu \dfrac{\partial \vec{H}}{\partial t} \\ \nabla \cdot \vec{H} = 0; \quad \nabla \times \vec{H} = \vec{J} + \varepsilon \dfrac{\partial \vec{E}}{\partial t} \end{cases} \qquad \begin{cases} \dfrac{1}{\mu} \nabla^2 \bar{E} + \omega^2 \varepsilon_c \bar{E} = 0 \\ \dfrac{1}{\mu} \nabla^2 \bar{H} + \omega^2 \varepsilon_c \bar{H} = 0 \end{cases}$$

where

$$\varepsilon_c = \varepsilon - i\frac{j}{\omega} = \varepsilon_{cr}\varepsilon_0 \qquad \omega = \frac{2\pi c}{\lambda}$$

j=1,2 indicate the electrical conductivity of bulk solution and micro resonator, respectively .

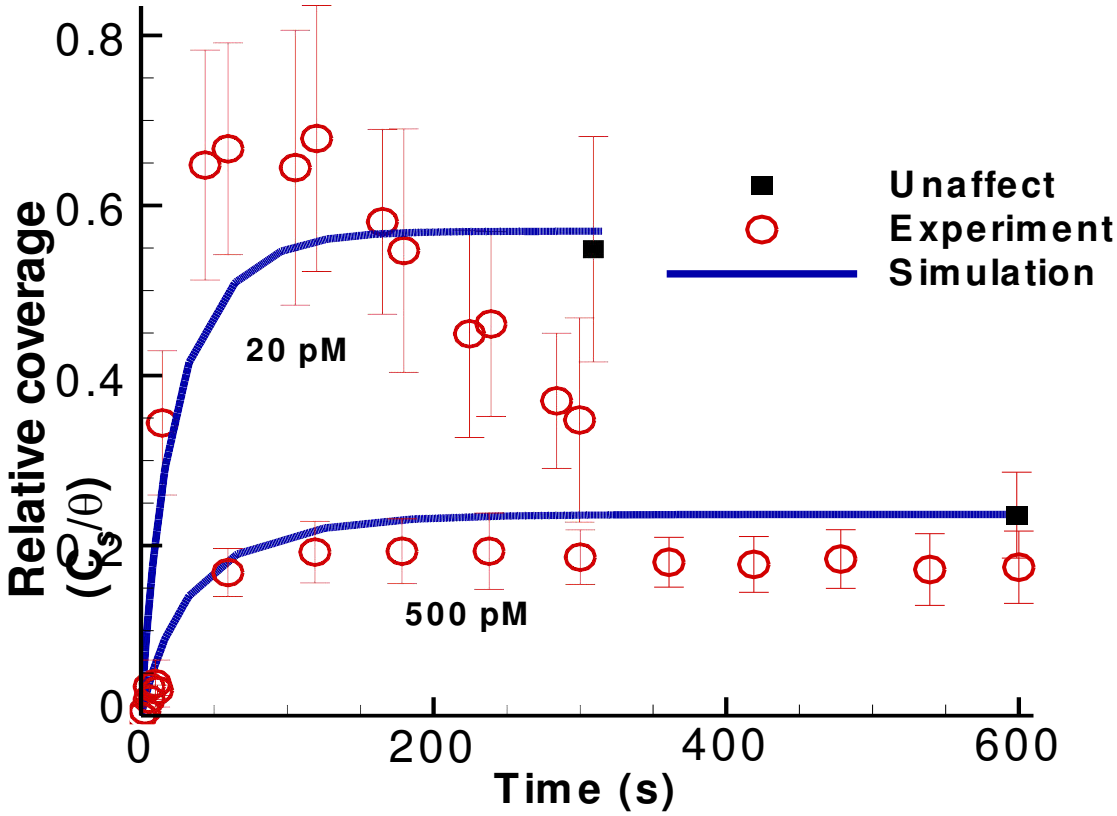
- In-plane TE waves

$$\bar{E}(x, y, t) = E_z(x, y)\bar{e}_z e^{i\omega t}$$

$$\bar{H}(x, y, t) = [H_x(x, y)\bar{e}_x + H_y(x, y)\bar{e}_y]e^{i\omega t}$$

Validation with Experiment

Sample analyte: Bovine Serum Albumin (BSA) proteins that carry negative charges at neutral pH

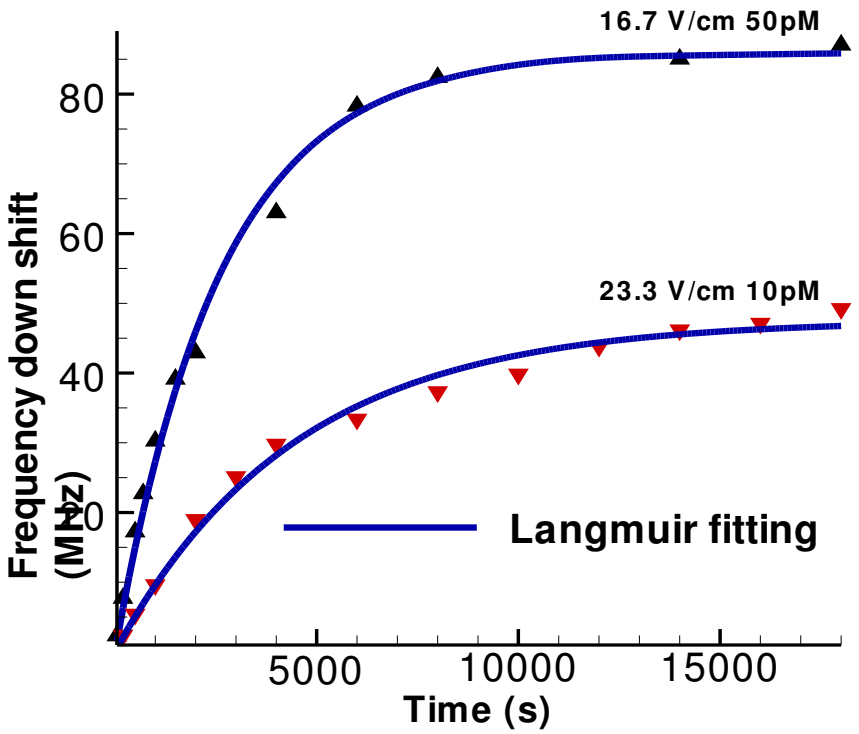


Adsorption of BSA at two different concentrations onto a silica micro resonator at pH 6.6 in the absence of external electrical field (experimental results by Yeung *et al*. 2009, Colloids and surfaces B: Biointerfaces)

•On a hydrophilic surface, the electrostatic attraction between oppositely charged material is often the major driving force for adsorption of bio molecules. In a Si_3N_4/H_2O solution, the $SiNH_3^+$ species remains the charged one.

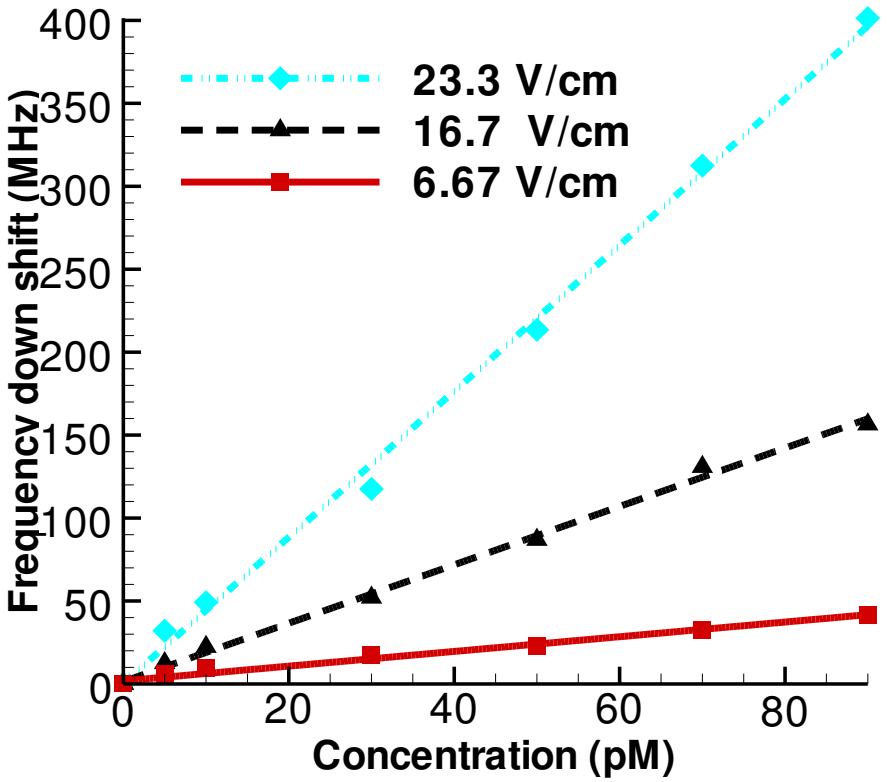
•Langmuir approach is adopted to describe the protein adsorption process. The key assumptions are: (a) only a monolayer forms by adsorption; (b) the adsorbing surface is composed of discrete, identical, and non-interacting sites; (c) the adsorption process for each molecule is independent; and (d) there is no molecule-molecule interactions since the concentration is very low.

Results: Detection of BSA Proteins



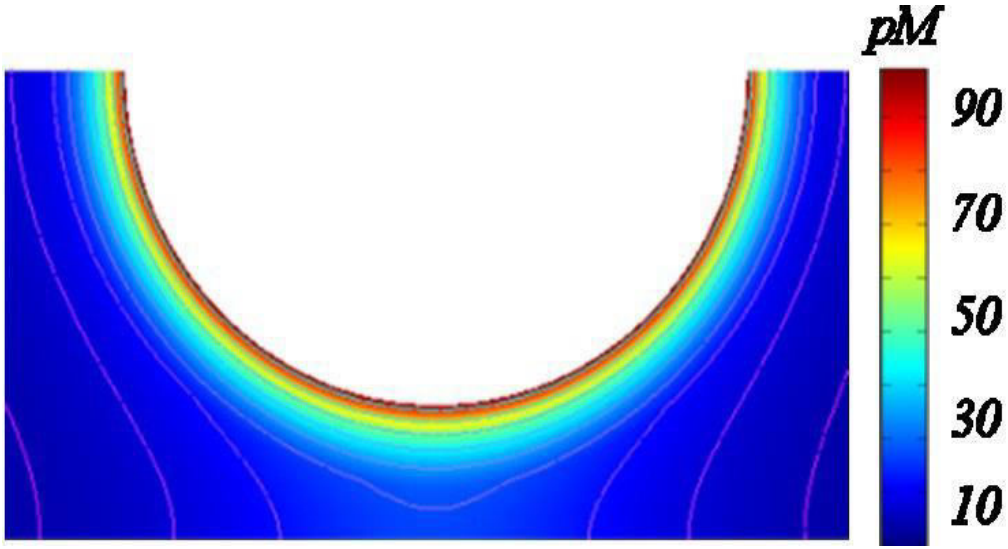
Time trace of optical resonance frequency down shifts induced by BSA adsorption, showing the Langmuir adsorption pattern

The resonance frequency shifts versus the bulk BSA concentration for different applied voltage gradients at steady state



Results: Aminoglycoside Adsorption in Porous Layer

Sample molecules: Neomycin, an aminoglycoside antibiotic, that carries positive charges at neutral pH

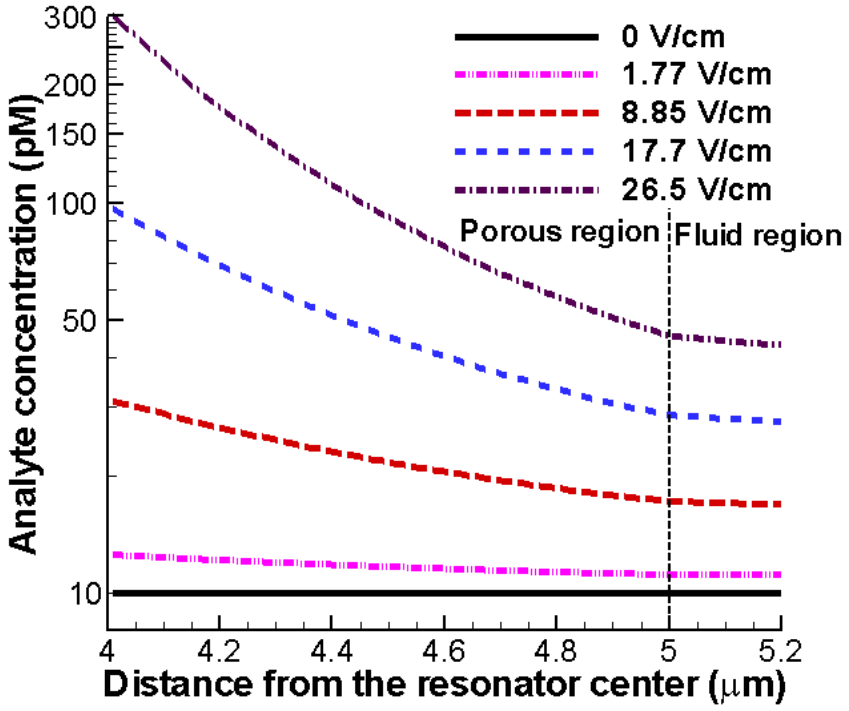


Contour of analyte concentration in the porous resonator and the equipotential lines of the electrical potential field for the case with 10 pM feed and 17.7 V/cm

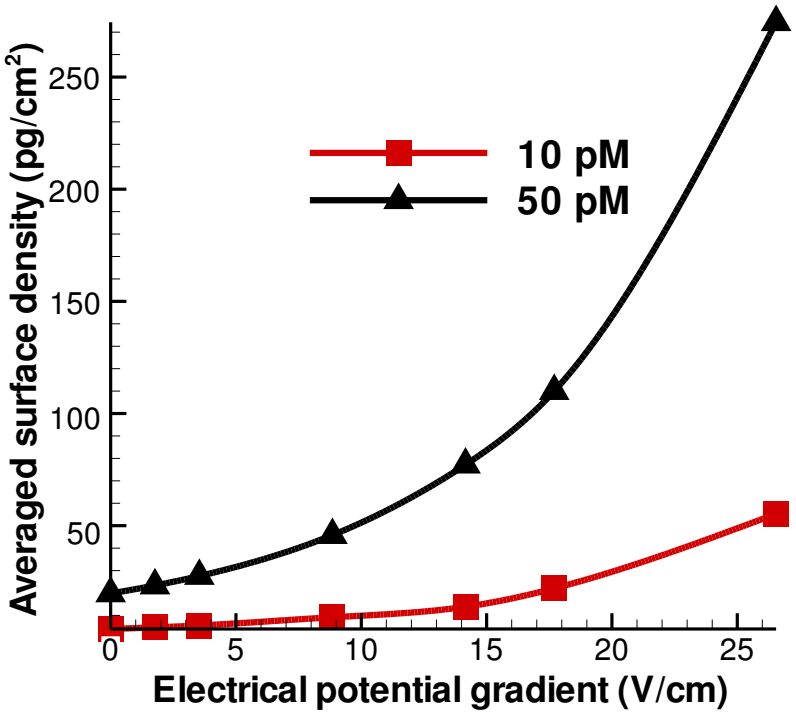
•A grounding electrode is placed inside the resonator to attract the positively-charged neomycin molecules. The porous vicinity surrounding the electrode is the most concentrated region, which justifies the fact that, the applied electrical potential is a predominant driven mechanism over the convection and diffusion for the charged analyte transport.

•Molecular concentration near the resonator can be enhanced by a magnitude of order, that is very useful for extremely low-concentration molecule detection.

Influence of Electrical Potential on Adsorption

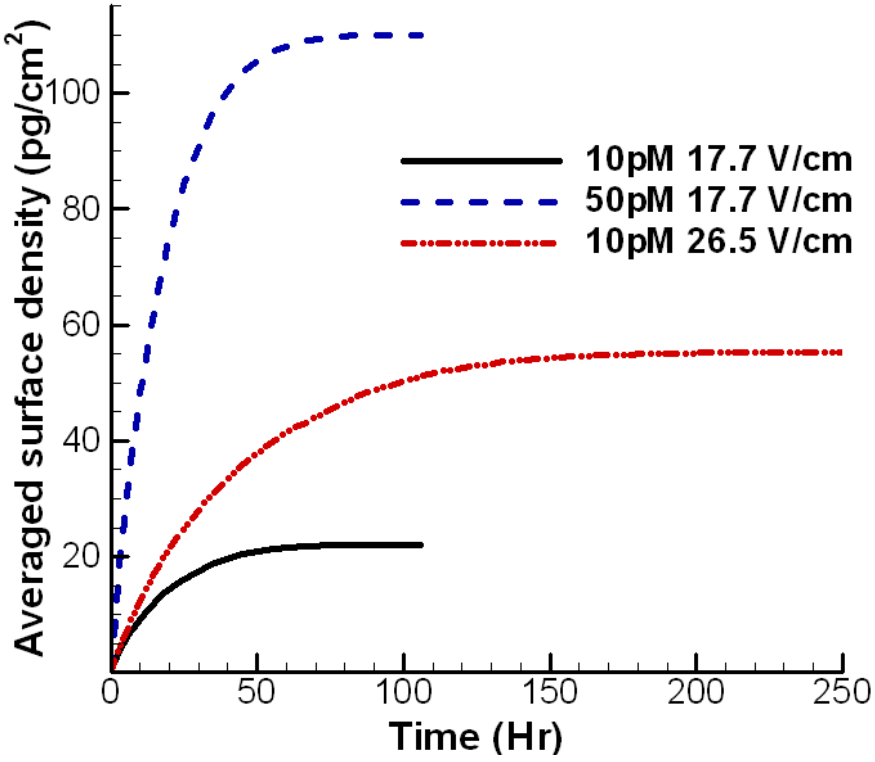


The aminoglycoside concentration profiles along the resonator radial direction with a feed concentration of 10 pM for various applied voltage gradients.

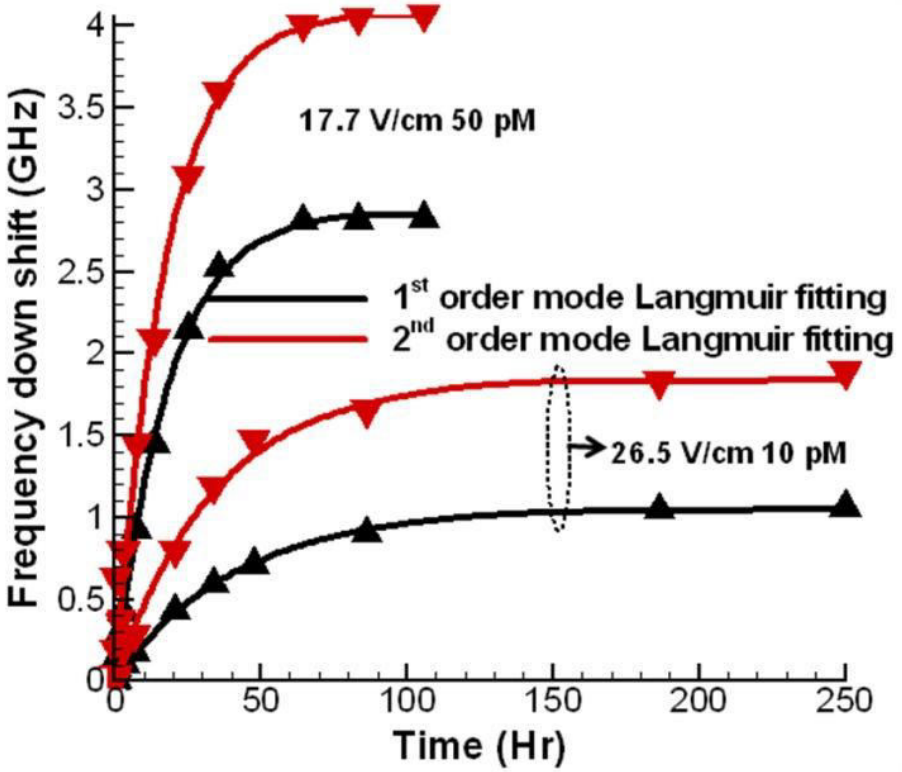


Influence of electrical potential on the surface density inside the porous resonator

Time Trace of Adsorption and Induced WGM Shifts

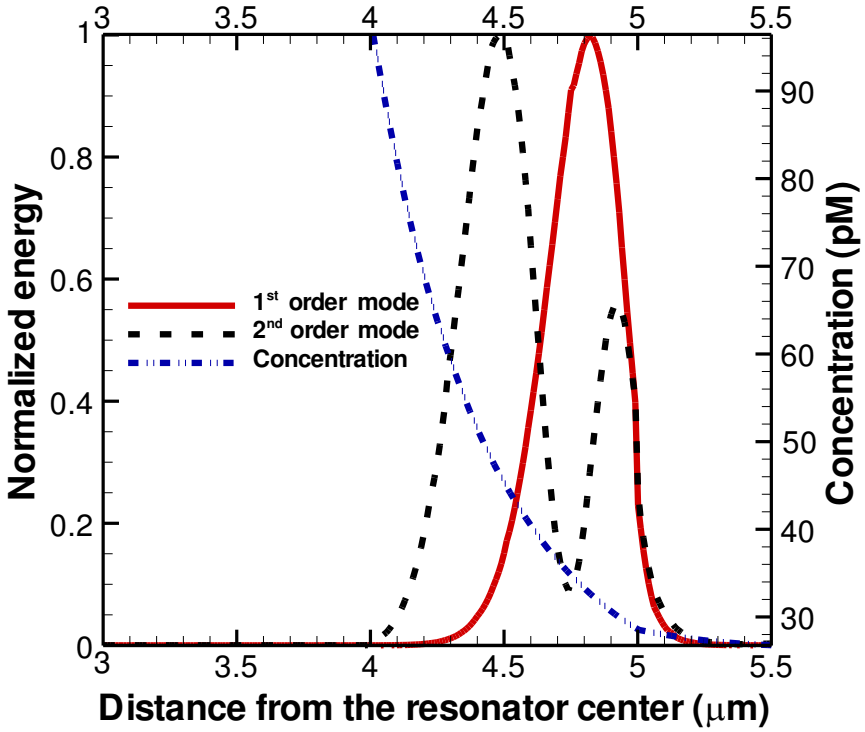


The time trace of the adsorbed aminoglycosides on the resonator surface for three different operation cases.

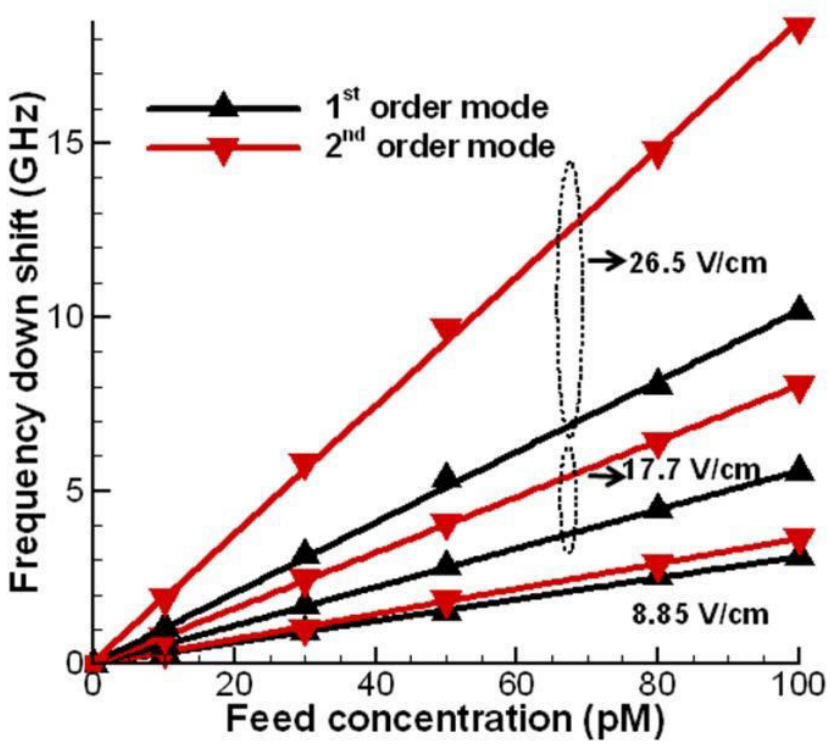


The resonance frequency down shifts with Langmuir fitting for two different feeding and applied voltage conditions under the first-order and second-order modes, respectively.

Mode Profile and Sensor Curves



Energy distributions in the resonator radial direction for the first- and second-order modes and the amino concentration profile in and outside the resonator for the case of 17.7 V/cm applied voltage gradient and 10 pM feed concentration.



The optical sensor curves at steady-state aminoglycoside deposition.

Conclusions

- A porous ring microresonator integrated in a microelectrofluidic system can function as both a filter and an optical whispering-gallery mode sensor.
- The microelectrofluidic forces augment substantially the filtration capability of the system, which separates the target molecules from its solution and enriches the analyte deposition inside the porous resonator.
- This alters the optical properties of the resonator and shifts the optical WGM resonance frequency, leading to label-free ultrasensitive detection of small molecules at picomolar concentration levels and below.
- The second-order whispering-gallery mode signal is found to give greater resonance frequency shift than the commonly adopted first-order mode of other types of WGM sensors.
- For large molecules such as proteins, they are detectable via direct surface attachment due to surface modification or electrostatic force.

Acknowledgment

Thank You!

- This material is based upon work supported by NSF grants CBET-1067141 and CTS-0541585, and by the US Department of Agriculture under grant number 2008-01336.
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  Dr. Haiyong Quan

  Dr. Lei Huang

  Dr. Qiulin Ma
- Useful discussion with Dr. Guoying Chen, Research Chemist, at Eastern Regional Research Center, USDA Agricultural Research Service, is appreciated.

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