Whisper Sense

DETECTION. QUANTIFICATION. KINETICS.

LABEL-FREE BIOANALYSIS PLATFORM

Features

- Label-free bioanalysis in real-time (measurement frequency 10Hz), in smallest spaces (sensor size ~10µm)
- Optical sensing of any changes at and around the sensor surface, where the sensor is a free microparticle
- Measurements are based on optical Whispering Gallery Modes

Applications

- Studying biomolecular interations *e.g.* protein - protein, antibody - antigen
- Multiplex diagnostics
- Surface studies

Benefits

- Rich multiplexing options thanks to small sensor size (~10 µm) and microfluidc arrays
- Analysis in micron scale volumes e.g. cell arrays, inside large cells, organ-on-a-chip or microfluidic chips
- High spatial resoultion of ~10 µm
- Remarkably low costs per measurement

Stand-alone bench-top platform

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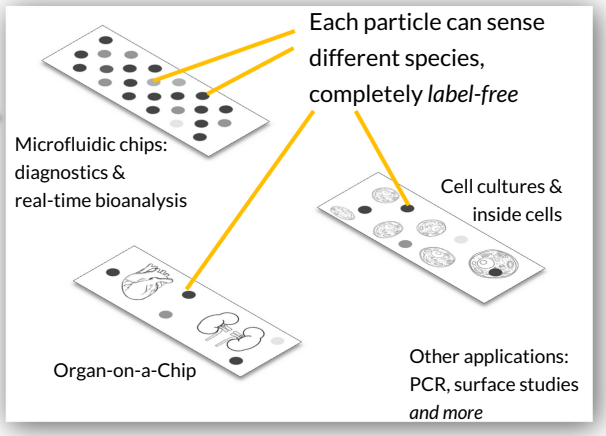
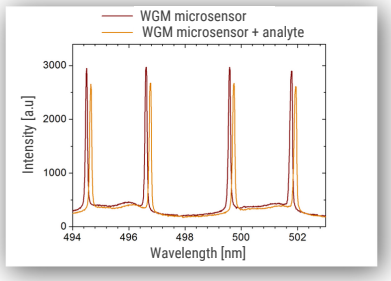
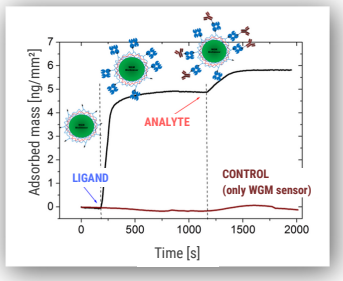


data collected online



conversion to quantity and interaction kinetics



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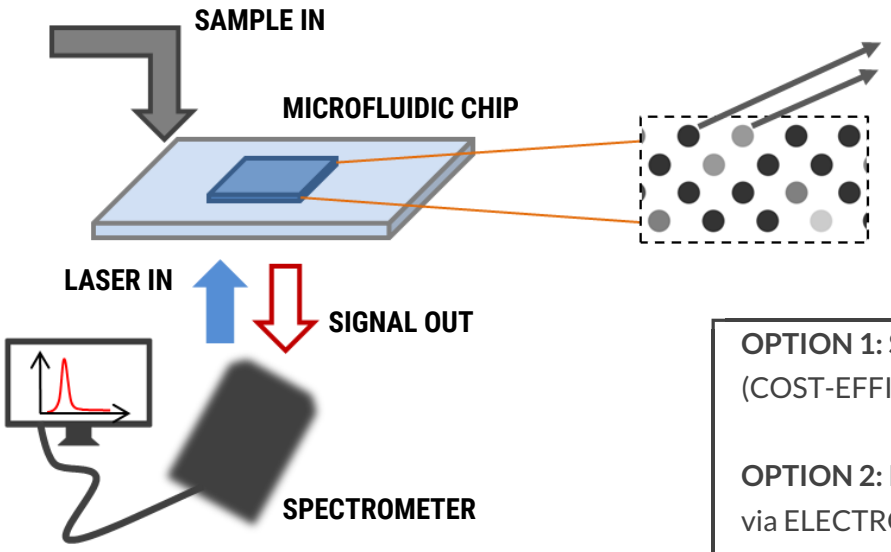
Application Example

Real-time detection and quantification of biologics in microfluidic chips



Individual microparticles as biosensors:
Each particle can sense a different analyte (*label-free*)

>1000 sensors per chip!

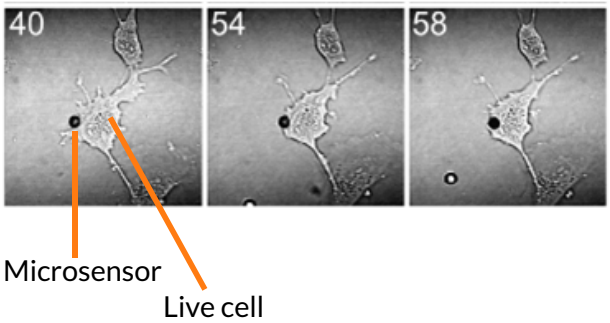
OPTION 1: SIMPLE MICROFLUIDIC ARRAYS
(COST-EFFICIENT)

OPTION 2: PARTICLE POSITION CONTROL
via ELECTROPHORESIS
(SUPERIOR MULTIPLEX) *under development*

Application Example

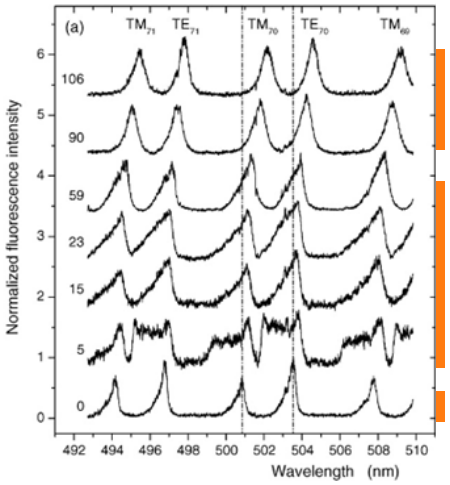
Real-time bioanalysis inside a cell

- Large cells can internalize 6-7 µm sensor particles
- Online analysis during particle uptake & inside cells is possible



M. Himmelhaus, A. Francois
Biosensors and Bioelectronics, 25 (2009) 418–427

SENSORS POSITION



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WHISPERING GALLERY MODES (WGM) BASED SENSORS

Setup

The setup consists of a laser to activate the sensor, a spectrograph to detect the signal from the sensor, and the sensor (microparticle) itself, immobilized in a microfluidic chip. The sample is introduced easily into this microfluidic chip, optionally via an auto-sampler. The main advantages of using a microfluidic chip in this case are the small sample amounts, compact instrument architecture and freedom of creating multiplex assays. As each microparticle is a sensor in WhisperSense and hundreds of microparticles can be placed in a microfluidic chip, multiplex assays can be performed with an unmatched flexibility without need of manual work or robotics. The only pre-requisite is to functionalize different particles with specific ligands such as oligonucleotides or antigenes. Surflay Nanotec's wide experience, IP and network ensured the construction of an analysis device with a high spectral resolution (10 pm) as well as the preparation and functionalization of the specific sensor particles. Finally as a crucial part of the setup, the computer hardware and software are embedded in WhisperSense in order to ensure a compact device and ease-of-use.

Sensing mechanism

The following figure visualizes the main steps in a WGM sensing process. WhisperSense uses polymeric microparticles as WGM sensors. The principle of detection is temporarily trapping light within a particle and measuring the wavelengths of the escaping light before, during and after sample introduction. The escaping light creates peaks at certain wavelengths due to constructive waves, which are an outcome of the whispering gallery modes. How WGM are created is as follows: some photons are trapped within the sensor particle due to a total reflection at the particle/medium interface and start travelling along the inner particle walls. If a photon, after one circulation, comes back to the point it was first reflected, it interferes constructively with photons of the same wavelength; before eventually escaping the particle (all photons escape the particle at some point). This set of constructive interferences (resonances) at discrete wavelengths is called whispering gallery modes, in analogy to a gallery in St. Paul's cathedral in London, where sound waves resonate within the circular walls so that even whispers can be heard from the other side of the gallery.

The wavelength of the WGM depends on the particle (i.e. sensor, resonator) size as well as the refractive index of the particle and the medium. Therefore WGM sensors are sensitive to the smallest changes at their surfaces and in the medium surrounding them: Any change results in a shift in the wavelength. Once the particle surface is functionalized by a chosen ligand, it will be sensitive specifically to a certain analyte.

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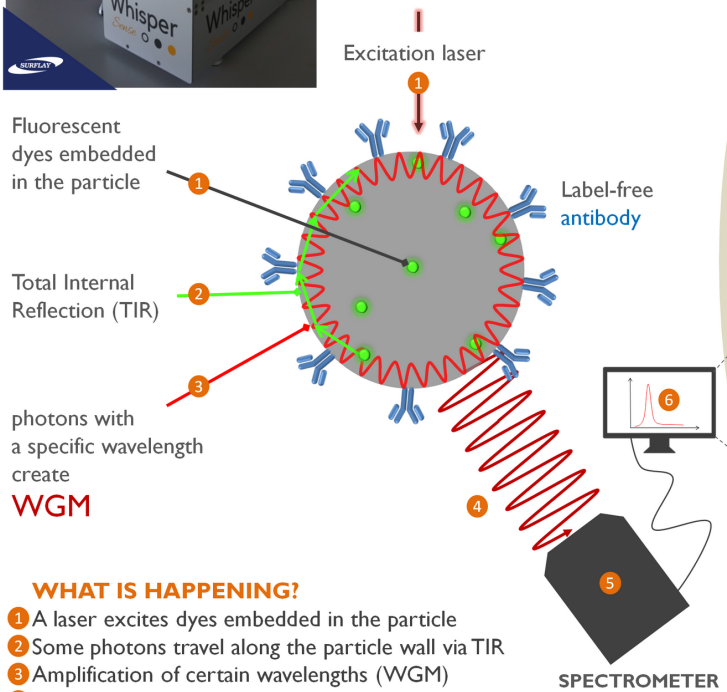
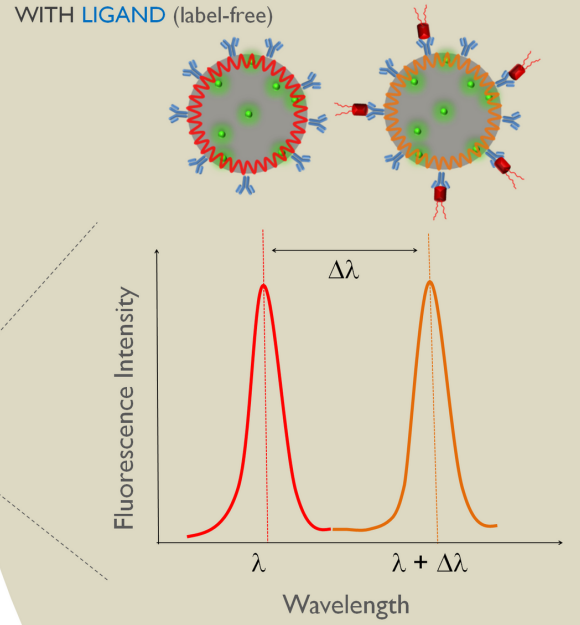
How does WhisperSense work?

WhisperSense sensor
Surface functionalized microparticle
(R = 6 - 15 µm)

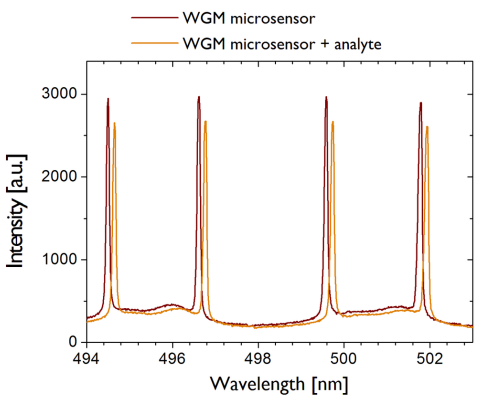


WHAT IS HAPPENING?

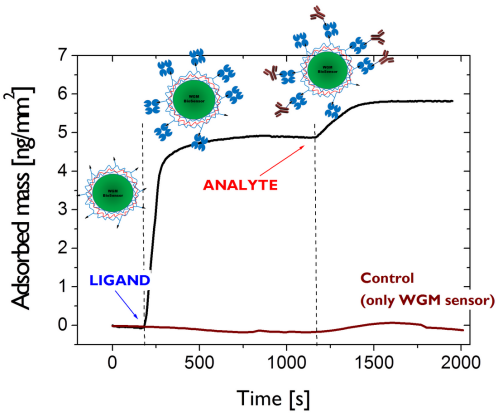
1. A laser excites dyes embedded in the particle
2. Some photons travel along the particle wall via TIR
3. Amplification of certain wavelengths (WGM)
4. Photons escape after >1000 roundtrips
5. A detector monitors all wavelengths: WGM = peaks
6. WGM wavelength shifts during analyte binding



Online and quantitative determination of interactions based on the peak shift



Conversion of raw data to interaction kinetics monitor in real-time



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