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# Detection and characterization of exosomes via a polystyrene-coated silica microresonator

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**Abstract.** Exosomes are promising biomarkers for early-stage cancer diagnostics. We present a lab-on-chip biosensor capable of detecting and characterizing single exosomes using a 30 $\mu$m silica microresonator coated with a tailored polystyrene nanoshell. The shell enhances the microresonator's sensitivity, enabling not only single-exosome detection but also characterization based on protein content relevant to cancer diagnostics. Simulation results show that the polystyrene coating increases the resonance wavelength shift by 52% in the presence of an exosome, allowing the detection of subtle variations in protein composition.

## 1 Introduction

Optical microresonators sustaining whispering gallery modes (WGMs) are highly attractive for single-bioelement sensing due to their ultra-high sensitivity to local refractive index changes, enabled by their high quality factors $Q_f$ [1]. Enhancing their functionality can significantly improve both specificity and detectivity at the single-particle level—such as for exosomes, which are nanoscale vesicles involved in intercellular communication and recognized as key biomarkers for early-stage cancer diagnostics.

To this end, we propose coating a 30 $\mu$m silica microresonator with a nanometer-thick polystyrene (PS) shell of higher refractive index than the core [1]. This dielectric shell not only reduces radiation losses and increases $Q_f$ but also shifts the optical mode profile outward, enhancing the local field intensity at the sensing interface and effectively reducing the mode volume. Together, these effects yield a significant boost in sensor sensitivity [1]. Nevertheless, the influence of such coating on coupling efficiency and mode accessibility requires further investigation [2]. In this work, we present full-field driven-mode simulations of the PS-coated microresonator, coupled to a tapered optical fiber—an approach not yet reported in literature. Beyond detection, our system enables the discrimination of single exosomes based on effective refractive index (ERI) variations linked to their protein content, thus offering a non-invasive, label-free tool for exosome characterization relevant to cancer diagnostics [3].

## 2 Biosensor functionality

To evaluate the functionality of the proposed biosensor, a polystyrene (PS)-coated 30 $\mu$m silica microdisk immersed in an aqueous medium is simulated using the finite element method

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(FEM) via the simulation platform COMSOL Multiphysics. Driven-mode simulations are performed, where the microresonator is excited through a single-mode silica optical fiber, both in the presence and absence of a 100 nm PS shell. The optical fiber and shell characteristics are adopted from our previous works [1, 2].

Key sensing parameters are extracted to assess the biosensor performance: the transmittance $T$ from the optical fiber to the microdisk, the quality factor $Q_f$ of the microdisk, the mode volume $V_{mode}$, and the normalized electric field intensity $|\boldsymbol{E}_{norm}|$ at the sensing interface. Results are summarized in Table 1, showing that the PS coating significantly enhances light confinement within the resonator, increases the $Q_f$ by 15%, reduces the mode volume by 25.8%, and amplifies the local electric field intensity by a factor of 1.75, all of which contribute to substantially improved sensing capabilities.

In the next step, a 50 nm exosome with 5% and 10% protein content—corresponding to effective refractive indices of $n_1 = 1.384$ for a healthy exosome and $n_2 = 1.394$ for cancerous, respectively—is placed near the resonator surface, and the resulting resonance wavelength shifts $\Delta\lambda$ are computed. The PS coating leads to a pronounced enhancement in $\Delta\lambda$ by up to 52.0%. In particular, increasing the exosome's protein content to 10% (a possible cancer marker) induces a wavelength shift of 0.24 pm, which is 51.8% larger than that observed for the uncoated case. These results confirm that the PS coating not only improves the fundamental optical parameters of the microresonator but also enables sensitive detection of subtle refractive index variations linked to protein content. This demonstrates the feasibility of the proposed platform for label-free, single-exosome characterization in cancer diagnostics.

Table 1: Figures of merit for sensing performance of uncoated and 100 nm PS-coated microresonators.

| | $d_x$ (nm) | $\lambda_{res}$ (nm) | $T$ (%) | $Q_f$ | $V_{mode}$ ($\mu m^2$) | $\lvert\boldsymbol{E}_{norm}\rvert$ (V/m) | $\Delta\lambda_{5\%}$ (pm) | $\Delta\lambda_{10\%}$ (pm) |
|---|---|---|---|---|---|---|---|---|
| **Uncoated** | 350 | 786.92 | 85.56 | $1.81\times10^4$ | 73.88 | $0.87\times10^5$ | 0.98 | 1.14 |
| **PS-coated** | 400 | 789.38 | 92.39 | $2.09\times10^4$ | 54.79 | $1.52\times10^5$ | 1.49 | 1.73 |

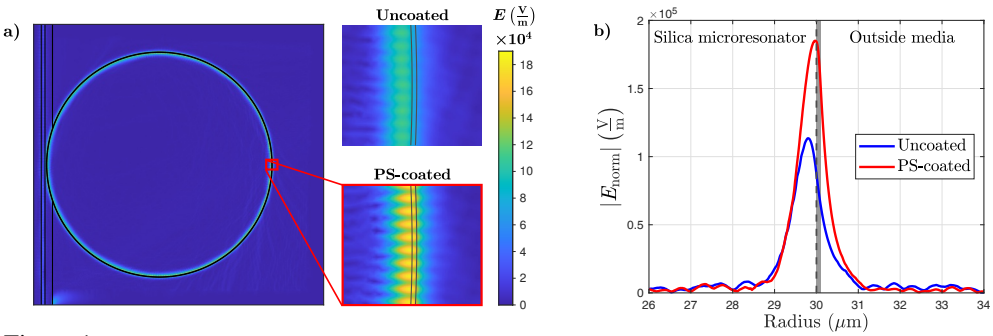


Figure 1: a) Electric field intensity of the PS-coated microdisk coupled to the single-mode optical fiber at a resonance wavelength of 789.38 nm. Zoomed mode profiles of the two microdisks, uncoated (top) and PS-coated (bottom), at their respective resonance wavelengths of 786.92 nm and 789.38 nm are shown. b) Electric field intensity distribution at the resonant wavelength along the microdisk radius for both configurations. The gray-shaded region indicates the coating layer.

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# Detection and characterization of exosomes via a polystyrene-coated silica microresonator

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*Offen im Denken*

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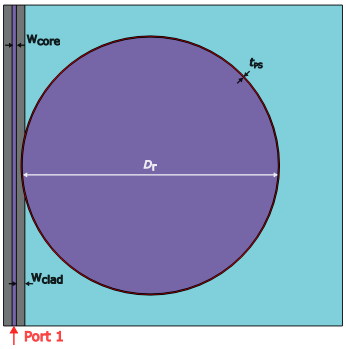
## Introduction

Optical microresonators capable of sustaining whispering gallery modes (WGMs) are highly attractive candidates for single-bioelement sensing due to their ultra-high sensitivity to local refractive index changes, enabled by their high quality factors $Q_f$ [1]. Enhancing the sensing functionality of such optical sensors can add specificity to detection at the single-particle level. Such specificity can be leveraged to determine the health status of exosomes — nanoscale extracellular vesicles recognized as key biomarkers for early-stage cancer diagnosis.

To achieve this, we improve optical microresonator performance by functionalizing silica resonators with a tailored polystyrene (PS) nanoshell, thereby increasing sensitivity. This dielectric shell not only reduces radiation losses and increases $Q_f$ but also shifts the optical mode profile towards the shell, enhancing the local electric field intensity at the sensing interface and reducing the mode volume [1,2].

In the present work, we present full-field driven-mode simulations of the proposed PS-coated microresonator coupled to a tapered optical fiber. The enhanced sensitivity of the proposed microresonator enables single-exosome detection and the discrimination of single exosomes based on effective refractive index (ERI) variations linked to their protein content, thus offering a non-invasive and label-free tool for exosome characterization suitable for early-stage, non-invasive cancer diagnostics [3].

## Biosensor modelling




- Biosensor geometry:
  - A silica microdisk (diameter $D_r$= 60μm) is immersed in an aqueous medium and coupled to a single-mode optical fiber with a silica core with 1μm width ($w_{core}$) and a cladding of teflon ($w_{clad}$=2μm, $n_t$=1.343).
  - The microdisk is modeled both with and without a polystyrene (PS) shell with 100nm thickness ($t_{PS}$).
- Driven-mode simulations using the finite element method based simulation platform *COMSOL Multiphysics* are performed.
- The light is coupled within the microresonator through the tapered optical fiber.

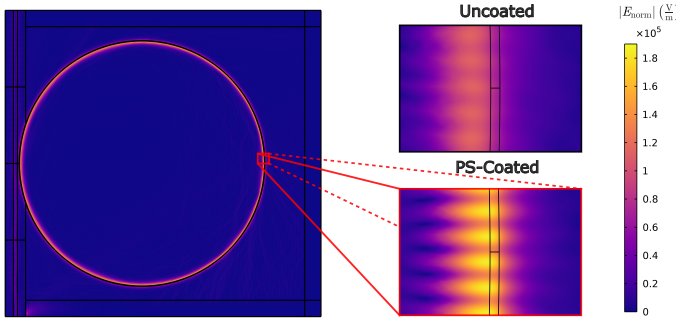
## Biosensor performance evaluation

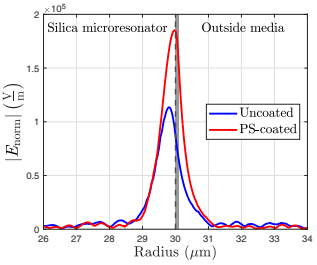
- To maximize light coupling into the microresonator, we optimized the fiber-resonator separation $d_x$ (measured from the optical fiber core to the resonator). The optimal gaps are 400nm for the coated case and 350nm for the uncoated one.
- The best resonance mode is searched for both microresonators by analyzing the key sensing performance parameters: Transmittance $T$ from the optical fiber to the microdisk, the quality factor $Q_f$ of the microdisk, the normalized electric field intensity $|E_{norm}|$ at the sensing interface, and the mode volume $V_{mode}$ [4].
- Single-exosome detection and characterization is evaluated by placing a 50nm exosome at the immediate vicinity of the microresonator.

## Biosensor functionality

- The sensing performance parameters for the best configurations for the uncoated (azimuthal mode number $m$ = 335) and PS-coated ($m$ = 339) microresonators were evaluated and presented in the following table:

| | $\lambda_{res}$ (nm) | $T$ (%) | $Q_f$ | $V_{mode}$ (μm²) | $\|E_{norm}\|$ (V/m) |
|---|---|---|---|---|---|
| Uncoated | 786.92 | 85.56 | $1.81\times10^4$ | 73.88 | $0.87\times10^5$ |
| PS-coated | 789.38 | 92.39 | $2.09\times10^4$ | 54.79 | $1.52\times10^5$ |



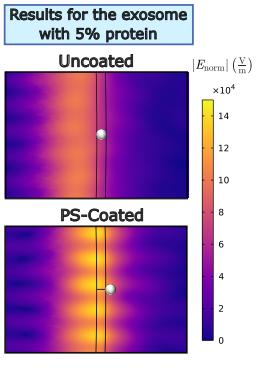




- The PS coating leads to an overall enhancement in the sensitivity: It increases the $Q_f$ by 15%, reduces the $V_{mode}$ by 25.8%, enhances the transmittance to the microresonator, amplifies the light confinement and the electric field at the sensing location by a factor of 1.75.

## Detection and characterization of exosomes

- Simulations varying the protein content for both a healthy exosome (5% protein, $n_1$= 1.384) and a cancerous exosome (10% protein, $n_2$= 1.394) are done [1].
- Resulting resonance wavelength shifts show that the PS coating increases $\Delta\lambda$ by 52% in the presence of an exosome.

| | $\Delta\lambda_{5\%}$ (pm) | $\Delta\lambda_{10\%}$ (pm) |
|---|---|---|
| Uncoated | 0.98 | 1.14 |
| PS-coated | 1.49 | 1.73 |




- PS coating exhibits enhanced detection capability of subtle refractive index variations linked to protein content: a 5% increase in the protein content produces 0.24pm wavelength shift.
- This demonstrates that introducing the tailored PS shell to the microresonator substantially improves its sensing performance.

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[1] M. Jalali, and D. Erni, Early stage, label-free detection of breast cancer based on exosome's protein content alteration, Proc. SPIE 12139, Opt. Sens. and Detect. VII, 121390G (2022).
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