



## Photonic studies on polymer-coated sapphire-spheres: A model system for biological ligands



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### ABSTRACT

In this study we show an optical biosensor concept, based on elastic light scattering from sapphire microspheres. Transmitted and elastic scattering intensity of the microspheres (radius 500  $\mu\text{m}$ , refractive index 1.77) on an optical fiber half coupler is analyzed at 1510 nm. The 0.43 nm angular mode spacing of the resonances is comparable to the angular mode spacing value estimated using the optical size of the microsphere. The spectral linewidths of the resonances are in the order of 0.01 nm, which corresponds to quality factors of approximately  $10^5$ . A polydopamine layer is used as a functionalizing agent on sapphire microspherical resonators in view of biosensor implementation. The varying layer thickness on the microsphere is determined as a function of the resonance wavelength shift. It is shown that polymer functionalization has a minor effect on the quality factor. This is a promising step toward the development of an optical biosensor.

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### 1. Introduction

Development of biological, chemical and biochemical sensors is one of the current needs of the society. Label-free detection of DNA was studied by elastic measurements at the level of a single DNA molecule [1] via force-induced denaturation [2], electrochemistry [3,4], field-effect sensors [5,6], and by monitoring the denaturation dynamics in real-time using impedance spectroscopy [7] and the heat transfer method [8]. Label-free detection of protein–protein interaction was shown recently using nanowires [9], nanoparticle probes [10], biochips [11], and mechanical cantilevers [12]. Optical measurement techniques can provide high sensitivity, compactness, fast response and real-time measurements [13]. They

are non-destructive to the sample, and the transduction processes generally take place on a surface and can be tailored to sense almost any kind of (bio)chemical molecules [14].

Optical sensing can be performed using plasmonic biosensors [15], ring resonators [16], confocal microscopy [7], prism couplers [17], and spherical cavities [18,19]. Optical microcavities such as spherical resonators, where optical rays are confined by total internal reflection, are promising optical label-free detection setups and play a prominent role in modern optics [20].

Recently, a silicon-on-insulator (SOI) microring resonator for sensitive label-free biosensing was fabricated [21]. Hereby, microring surface functionalization with biotin and a detection limit of 0.37 fg avidin mass (3260 molecules) was achieved [22,23]. In an optical microcavity, the target molecules can be sampled hundreds of times due to the recirculation of light within the microcavity by total internal reflection (TIR) [20]. The target molecule induces a change in the optical microcavity properties such as its size. As a result, a change in the whispering gallery mode (WGM) resonant wavelength is encountered [24]. In order to preserve the high quality of the transducer and the interaction with the sensing layer and

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the WGMs [14,24–26] a good control of surface functionalization of the transducer surface is a crucial step for producing reliable biosensors for the binding of the biological recognition element to it. The circumnavigating light within the microcavity will evanesce to the external medium and extends about 200 nm [24]. Hence, the functional layer has to be very thin, i.e.  $\approx 10$  to  $\leq 200$  nm, and homogeneous.

So far, silicon-on-insulator ring resonators [23] and glass microspheres [18] have been used as microcavity-based biosensors. However, silicon and glass are known to degrade easily in aqueous media, especially at longer time scale and in non-neutral pH circumstances [27,28]. Hence, the usability of these two materials as biosensors is somehow limited. To overcome the drawback of limited chemical stability, recently, diamond ring resonators [29] and nearly spherical diamond resonators were developed [30]. However, their fabrication is expensive and diamond surface

modification with proteins or DNA still requires a good control of the functionalization steps [27,31].

In this article, an experimental study of an optical biosensor concept based on elastic light scattering from sapphire microspheres and the corresponding shift of WGMs, after an add-on polydopamine (PDA) layer to the sphere, is performed. Mussel-inspired polydopamine coating have been intensely studied in recent years [32–34]. Surface functionalization using this biopolymer is especially robust. By simply dipping any substrate into an aqueous solution of dopamine, a surface-adherent polydopamine thin film is first formed within hours through oxidative self-polymerization and subsequently bounded to the sapphire surface via hydrogen bonds [32,35]. The thickness of the formed polymer can be tuned by varying the concentration of the dopamine used or by adapting the immersion time of the substrates. Using atomic force microscopy (AFM), Lee et al. found that the thickness of the polymers formed

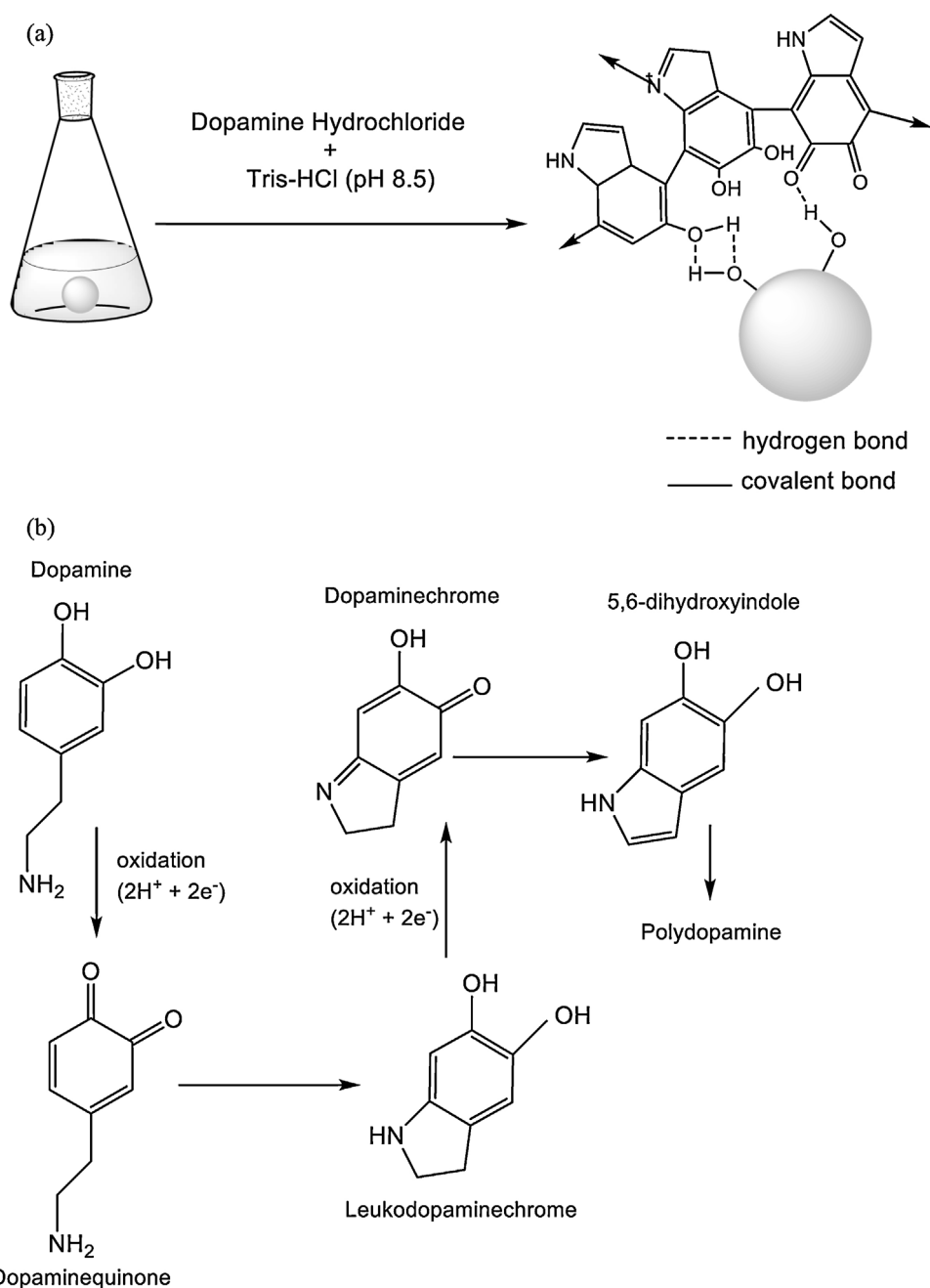


Fig. 1. (a) Sapphir surface functionalization with PDA. (b) Polymerization mechanisms of dopamine adapted from Lee et al.

on gold surfaces increases linearly with time at the beginning of the reaction and saturates after 20 h [32]. Polymers with similar thickness were also obtained by Pop-Georgievski et al. on hydrogen and oxygenated diamond surfaces measured by spectroscopic ellipsometry [35]. Various post-modification reactions are possible to create a variety of ad-layers on this polymer coating to fulfill various purposes [34,36–39]. WGMs have been used in polymeric microresonators [40]. Surface functionalization of this biopolymer on sapphire microspheres is an alternative to polymeric resonators and can be used as a platform for future bio-optical biosensing applications. In this article we therefore address sapphire, not only the second hardest material next to diamond but it also shows outstanding chemical inertness, wear resistance, and biocompatibility [41]. Hence, it is widely used for implants such as hip [41], dental [42], and endosseous implants [43]. Moreover, its wide optical transmission band from the ultraviolet (UV) to the near-infrared (near-IR) [44] suggests application potential in optical biosensors.

## 2. Experimental method

### 2.1. Surface functionalization

2-Amino-2-(hydroxymethyl)-1,3-propanediol hydrochloride (TRIS-HCl) (reagent grade, minimum 99%) and dopamine hydrochloride (98.5%) were purchased from Sigma and used as received. The formation of a polydopamine film was carried out by immersing the sapphire microsphere (Edmund Optics) into a solution of dopamine hydrochloride (2 mg/mL) in 10 mM Tris-HCl buffer that was adjusted to pH 8.5 by adding 0.5 M NaOH. Immersion times were varied (2 h, 5 h, 10 h and 20 h) to create polydopamine films with different thicknesses [32]. To prevent the formation of microparticles in the dopamine solution, the solution together with the sapphire microsphere was stirred with a shaker during the reaction. After the reaction, the coated sapphire microsphere was thoroughly rinsed with deionized water and dried under a stream of nitrogen (Fig. 1 a).

Fig. 1 b presents a brief illustration of the polymerization mechanisms of dopamine adapted from Lee et al. [32]. Briefly, under an oxidative condition, e.g., alkaline buffer, dihydroxyl group protons in dopamine are deprotonated, becoming dopamine-quinone. Dopamine-quinone is then rearranged via intramolecular cyclization to leukodopaminechrome. Further oxidation and rearrangement leads to 5,6-dihydroxyindole, which oxidation causes intermolecular cross-linking to yield a polymer that is structurally similar to the biopigment melanin [32].

### 2.2. X-ray photoelectron spectroscopy (XPS)

For reference purposes, X-ray photoelectron spectroscopy (XPS) measurements were performed on a single crystalline sapphire chip instead of sapphire sphere in order to confirm the presence of the PDA layer after polymerization. Given the respective dimensions of the molecules used in the PDA layer synthesis and the sapphire microsphere, the microsphere surface will appear “flat” to the molecules binding to the surface. The surface roughness of the sapphire microsphere and the sapphire chip are on the same order of magnitude, therefore the sapphire-chip XPS data can be applied to the sapphire microsphere. Moreover, sapphire chips have a well defined take-off angle. A sapphire chip (1 cm × 1 cm) with crystalline orientation [0,1,-1,2] as measured using X-ray diffraction (XRD) was used for the XPS measurements. It was functionalized with PDA (5 h immersion) just as described in Section 3. Section 2.1. Photoemission experiments were carried out using a Scienta ESCA 200 spectrometer in ultrahigh vacuum with a base pressure of  $1 \times 10^{-10}$  mbar (Linköping University, Sweden). The

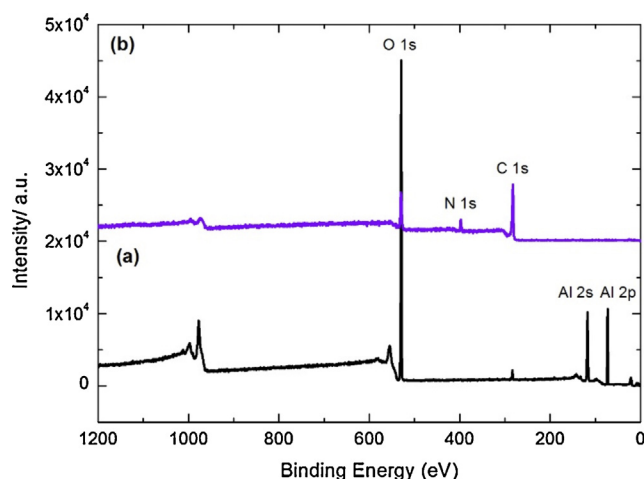


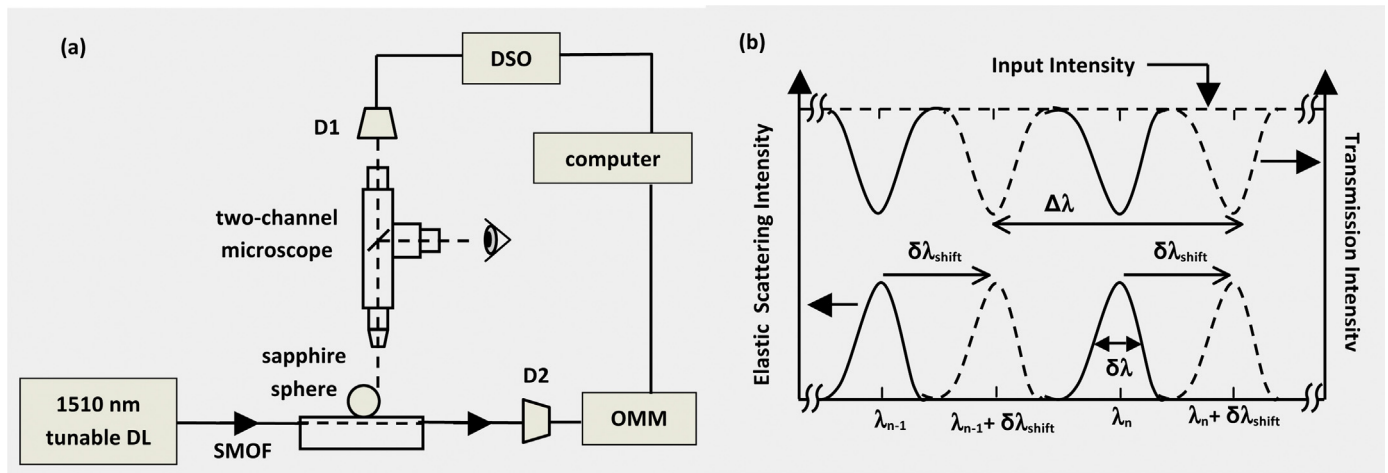
Fig. 2. XPS spectra of a sapphire chip before (a) and after (b) 5 h functionalization with PDA layer. The curves are displaced vertically for better clarity.

measurement chamber was equipped with a monochromatic Al  $K_{\alpha}$  X-ray source (1486.6 eV). The XPS experimental conditions were set so that the full-width-at-half-maximum of the clean Au 4f<sub>7/2</sub> line was 0.65 eV. All spectra were recorded under a photoelectron take-off angle of 0°, i.e. normal emission.

Spectrum a in Fig. 2 shows the XPS spectrum of a blank sapphire chip. The blank sapphire shows three major peaks at 118 eV, 73 eV, and 532 eV, which corresponds to Al 2s, Al 2p, and O 1s peaks, respectively. A negligible C 1s peak appears at 284 eV, which might be attributed to contamination. Simple immersion of substrates in a dilute aqueous solution of dopamine, buffered to a slightly basic pH (2 mg of dopamine per milliliter of 10 mM Tris-HCl buffer, pH 8.5), resulted in spontaneous deposition of a thin adherent polymer film. X-ray photoelectron spectroscopy (XPS) analysis of the sapphire chip coated during 5 h (Fig. 2 spectrum b) shows two additional peaks at 400 eV and 284 eV which are related to N 1s and C 1s, respectively. The presence of these peaks can be attributed to the nitrogen (N) and carbon (C) atoms in the PDA layer. Moreover, XPS analysis also revealed the absence of signals specific to the sapphire chip (Al 2p and Al 2s peaks), indicating the formation of a polymer coating is greater than 10 nm in thickness [32]. We will show in Section 4 on paragraph 4 that 5 h of polymerization corresponds to a PDA layer of 25 nm thickness.

### 2.3. Detection setup

Fig. 3(a) shows the detection setup used in this experiment. The diode laser was tuned from 1510 nm to 1512 nm with a step size of 5 pm. The laser light was coupled to the sapphire sphere through a side polished single mode optical fiber (SMOF). When the resonances wavelength of the laser matches the resonances wavelength of the sapphire sphere, the laser light couples to the sapphire sphere and circumnavigates the sphere by total internal reflection [24]. The elastically scattered light from the sapphire microsphere at 90° is collected by a two-channel optical microscope and detected by a germanium (Ge) photodiode (D1). The elastically scattered light is separated by a beam splitter placed at an angle of 45° with respect to the collected beam. The Ge photodiode signal is sent to a digital storage oscilloscope (DSO) for signal monitoring and data acquisition (DAQ). The transmitted power through the optical fiber is detected by a second Ge photodiode D2 and recorded by an optical multimeter (OMM). All the optoelectronic equipment is controlled using the general purpose interface bus (GPIB) standard.



**Fig. 3.** (a) Schematic geometry of the microsphere coupled to a single mode side polished optical fiber. (b) Schematic of WGMs ( $\lambda_{n-1}$  and  $\lambda_n$ ) of same mode order and consecutive mode number, and their shift due to the sphere's surface modification.

#### 2.4. Detection mechanism

The system was modeled using the Generalized Lorenz-Mie Theory (GLMT), which describes the electromagnetic scattering of an arbitrary light beam by a spherical microparticle [45]. The elastic scattering intensity from the sphere and transmittance intensity at the output of the optical fiber for transverse electric (TE) and transverse magnetic (TM) polarization were calculated for sapphire spheres before and after surface modification with biomolecules [46]. Fig. 3(b) shows the excited resonances manifested due to the circumnavigating light in the sphere. The mode spacing  $\Delta\lambda$  of consecutive resonances having the same mode order (number of nodes or maxima of the intensity distribution in the radial direction) and consecutive mode number (the number of maxima between  $0^\circ$  and  $180^\circ$ ) in the angular intensity distribution of the mode can be calculated using the following equation: [46]

$$\Delta\lambda = \frac{\lambda^2 \arctan \sqrt{m^2 - 1}}{2\pi a \sqrt{m^2 - 1}} \quad (1)$$

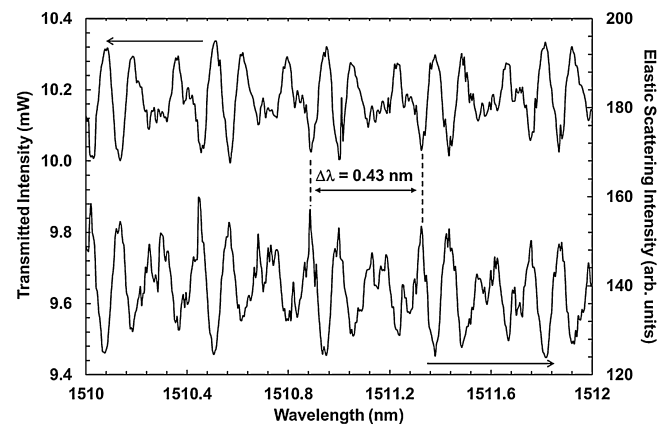
where  $m$  is the relative refractive index of the sphere (refractive index of the sphere/refractive index of the surrounding medium),  $\lambda$  the wavelength of the laser source in vacuum, and  $a$  is the sphere's radius. If molecules are tethered onto the sphere's surface, these molecules will induce a change of the optical properties of the sphere, especially its effective size and refractive index. As a result, the resonance wavelength will change further and result in the phenomenon of resonant shift [24]. The wavelength shift  $\delta\lambda_{shift}$  can be calculated by the equation:

$$\frac{\delta\lambda_{shift}}{\lambda} = \frac{\delta a}{a} \quad (2)$$

Here,  $\delta a$  is the change in sphere radius due to the interaction between the adsorbed molecules [24].

### 3. Experimental results

Fig. 4 shows the measured spectrum of the elastically scattered light from the sapphire microsphere. The  $\Delta\lambda$  of the WGMs is observed to be 0.43 nm, which is comparable with the  $\Delta\lambda$  estimated using Eq. (1) for a 1 mm diameter sapphire microsphere with refractive index of 1.77. For each maximum in the elastic scattering spectrum, there is a corresponding minimum in the transmittance spectrum. The minima in the transmittance spectrum correspond to a fraction of the light coupled from the fiber into the sphere.



**Fig. 4.** Measured elastic scattering intensity (lower curve) and the corresponding transmitted intensity (upper curve) spectra from sapphire sphere of radius 500  $\mu\text{m}$  and refractive index 1.77.

The linewidth ( $\delta\lambda$ ) of the resonances is about 0.01 nm, which corresponds to a quality factor  $Q$  of the order  $10^5$  (using  $Q = \lambda/\delta\lambda$ ).

When adding layers of PDA to the surface of the sphere, we obtain the results in Fig. 5 (a and b). Fig. 5a represents the transmitted spectra and Fig. 5b represents the elastic scattering intensity spectra for the non-modified and the modified sapphire sphere in the wavelength range from 1510 to 1512 nm. Spectrum A represents the resonances from the non-modified sapphire sphere. Then, the sapphire sphere was polymer-coated for 2 h and afterwards spectrum B was collected. As a result, the resonances were red-shifted by 0.05 nm. The spectra were collected again for 5 h, 10 h, and 20 h polymerization time, which corresponded to a shift of 0.075 nm (spectrum C), 0.11 nm (spectrum D), and 0.155 nm (spectrum E), respectively with a resolution of 0.005 nm (cfr. Table 1).

**Table 1**

Resonance wavelength shift and the corresponding resulting polymer film thickness as a function to polymerization time.

Polymerization time (h)	Resonance wavelength shift (nm)	Polymer film thickness (nm)	Quality factor ( $Q$ )
0	NA	NA	$7.5 \times 10^4$
2	$0.05 \pm 0.005$	$16.6 \pm 1.7$	$6.04 \times 10^4$
5	$0.075 \pm 0.005$	$24.8 \pm 1.7$	$5.03 \times 10^4$
10	$0.11 \pm 0.005$	$36.4 \pm 1.7$	$3.35 \times 10^4$
20	$0.155 \pm 0.005$	$51.2 \pm 1.7$	$4.3 \times 10^4$

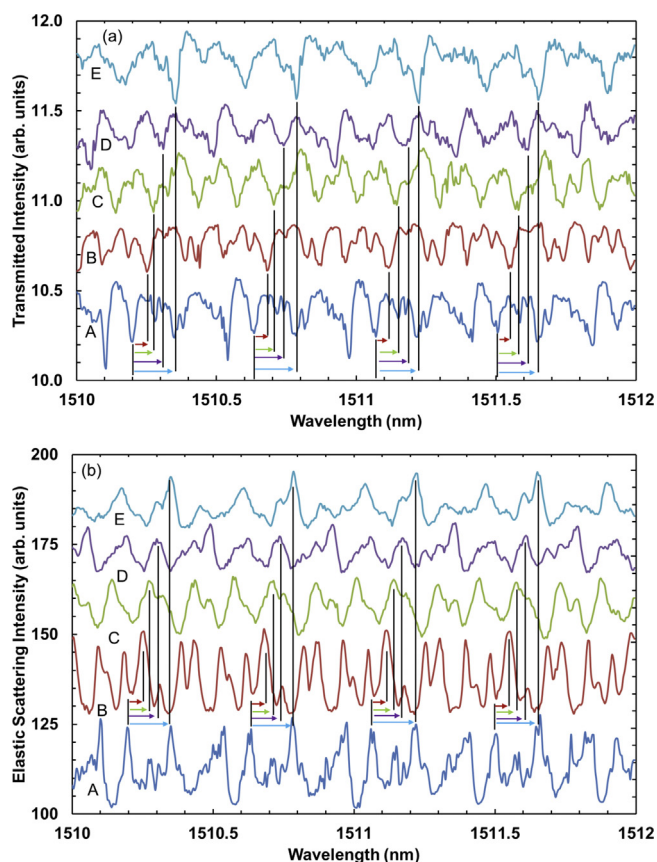


Fig. 5. Transmitted intensity (a) and elastic scattering intensity spectra (b) from a sapphire sphere with different polymerization time and the corresponding shift. A: Non-modified sphere; B: 2 h; C: 5 h; D: 10 h; and E: 20 h of polymerization.

By treating the refractive indices of PDA (1.6) and sapphire (1.77) as being almost identical and using Eq. (2), these wavelength shifts, given with a resolution of 0.005 nm, correspond to a thickness of 16.6 nm, 24.8 nm, 36.4 nm, and 51 nm (see Table 1). This correlates rather well with the thickness data determined by Lee and coworkers which are  $\approx 8$  nm, 25 nm, 40 nm, and 51 nm for 2 h, 5 h, 10 h and 20 h polymerization time, respectively [32]. In the case of 2 h polymerization time, our shift (16.6 nm) is more pronounced than reported by Lee et al. (8 nm) in ref. [32]. The higher growth rate in the initial polymerization phase might be attributed to a faster nucleation due to the spherical geometry.

The spectrum of the non-modified sphere showed resonances with a quality factor of  $1.5 \times 10^5$  while the spectra of the modified sphere showed resonances with a maximum quality factor of  $6.04 \times 10^4$ . This is possibly due to the fact that higher polymer concentrations lead to the formation of an inhomogeneous coating, with the presence of clusters [13]. This scatters the photons out of the WGM and decreases the Q as shown in Table 1 [47].

Fig. 5(a) and (b) were zoomed into one resonance to study the relationship between the PDA layer thickness and the resonance quality factor. It can be seen from Fig. 6(a) and (b) that as the PDA layer thickness increases, the resonance linewidth increases.

As shown in Table 1 the quality factors of the analyzed resonances were on the same order ( $Q \approx 10^4$ ) and this verifies that the PDA layers are widely homogeneous. As the polymer thickness is increasing, the quality factor of the resonances is decreasing; this might be due to the fact that the PDA surface is becoming more heterogeneous with increasing polymer thickness. Fig. 7 represents the resulting shift in resonance wavelengths as a function of the polymer film growth time. The polymer thicknesses corresponding to

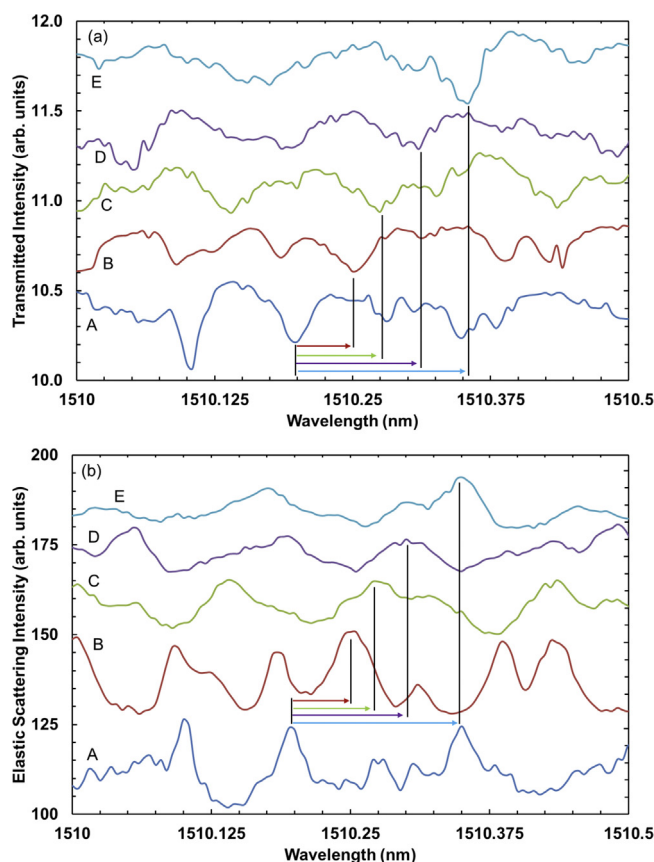


Fig. 6. Zoom of Fig. 5. Single resonance of the transmitted intensity (a) and elastic scattering intensity spectra (b) from a sapphire sphere with different polymerization times and the corresponding wavelength shift. A: Non-modified sphere; B: 2 h; C: 5 h; D: 10 h; and E: 20 h of polymerization.

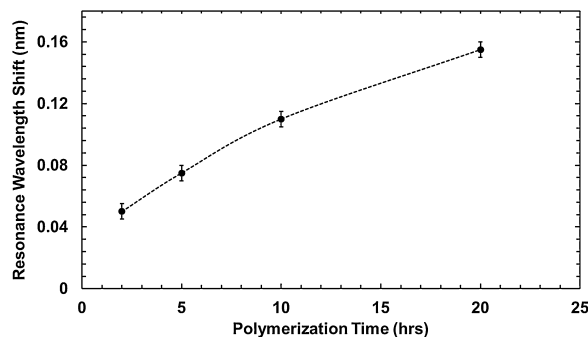


Fig. 7. Resonance wavelength shift corresponding to the sapphire surface polymerization time with PDA. Line is a guide for the eye.

the resonance wavelength shifts were calculated using Eq. (2) as shown in Table 1. As the polymerization time increases, the resonance wavelength shifts to a value, which corresponds to a thicker PDA layer on the sapphire surface.

#### 4. Conclusion

We have studied the transmitted intensity and the elastic scattering intensity of a sapphire sphere (radius  $500 \mu\text{m}$  and 1.77 refractive index) in the wavelength range of 1510–1512 nm. We have demonstrated the highest quality factor, in the order of  $10^5$ , up to date in a spherical resonator fabricated from single crystalline sapphire. The shift in resonance wavelength arising from coating the sphere with different thicknesses of PDA layers was studied.

The quality factor of the resonances was studied as a function of the change in the PDA polymer thickness, and we found that it is almost preserved despite a small decrease in the coefficients. We also verified that PDA layers are homogeneous which resulted in high  $Q$  factors, comparable with the values achieved with silica spheres coated with polylactic-acid (PLLA, a crystalline biodegradable polymer) [13], showing that PDA coating is a valid alternative method to silanization for coupling bioreceptors such as DNA, proteins and even cells to the sphere. The experimental feasibility of the photonic biosensing concept with sapphire microspheres was recently proven within DNA-characterization studies using a silane crosslinker between DNA and the sapphire spheres [48]. The PDA coatings described in this article are expected to offer even more experimental flexibility due to the numerous available coupling protocols between organic- and biological compounds.

### Authors contributions

The experimental setup was built by M.S.M. in cooperation with D.M. All experimental measurements were performed by M.S.M. in cooperation with D.M. W.-S.Y. modified the sapphire sphere with the PDA. Biological assistance and guidance was provided by L.M. XPS measurements were performed by X.L. in cooperation with M.F. M.S.M. interpreted the optical data in close cooperation with P.W., A.S., and P.B. Insights in technical improvements of the setup were provided by P.W., A.S., and K.H. All authors have given approval to the final version of the manuscript.

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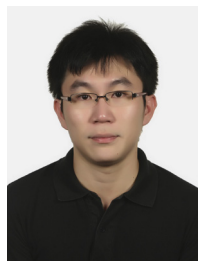
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## Biographies



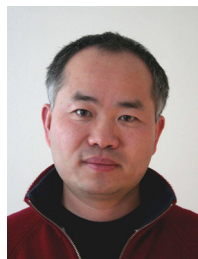
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