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Sodium dodecyl sulfate decorated *Legionella pneumophila* for enhanced detection with a GaAs/AlGaAs nanoheterostructure biosensor

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ABSTRACT

The net electric charge associated with a bacterial strain is primarily defined by the number of available functional groups at its surface and we observed that it can determine the limit of detection of a charge-sensing biosensor. We have investigated the dynamic range of bacterial electric charge variations through binding negatively charged sodium dodecyl sulphate (SDS) molecules, with the objective of improving the detection limit of a charge-sensing GaAs/AlGaAs nanoheterostructure biosensor designed for detection of *Legionella pneumophila*. A two-fold increased zeta potential of *L. pneumophila* was measured at *p*H 7.4 following the exposure of these bacteria to an SDS solution at 0.02 mg/mL. Subsequently, it was possible to detect SDS decorated and heat-inactivated *L. pneumophila* at 10^3 CFU/mL. This illustrates the fundamental role of the bacterial electric charge in the operation of photocorrosion-based III-V semiconductor biochips. We discuss the mechanisms of bacterial interaction with SDS, critical aspects of decorating bacteria with this anionic surfactant and the channels responsible for charge transfer.

1. Introduction

Outbreaks of *Legionella* from contaminated water sources, resulting in mortality and morbidity, have been recorded periodically in numerous countries. Inhalation of *Legionella*-contaminated aerosols causes Legionnaires' disease and Pontiac fever. Among the about 60 known-species of *Legionella*, *L. pneumophila* ssp1 have been identified as the most common cause of severe pneumonia, or Legionnaires' disease [1–3]. Since conventional bacteria detection techniques have not been effective in preventing *Legionella* spread, numerous biosensing platforms have been investigated and proposed [4] with the aim of providing prospective identification of *L. pneumophila* with automated devices outside a laboratory setting. Sensors addressing detection of electrically charged molecules represent a significant portion of the biosensing field. For instance, electrochemical impedance spectroscopy [5] and field effect transistor [6] immunosensors have been investigated for detection of electrically charged biomolecules. In photonic materials, such as III-V semiconductors, adsorption of electrically charged biomolecules at the surface of a semiconductor in an electrolytic environment can induce perturbation of the near-surface band structure [7–9], which could be monitored with the photoluminescence (PL) effect.

The photonic characteristics of GaAs/AlGaAs nanoheterostructures has provided a compelling platform for detection of electrically charged bacteria [10–12]. This technique relies on the PL-monitored dissolution of III-V semiconductors through, so-called, digital photocorrosion (DIP) in electrolytic environments at rates that could be controlled with nanoscale precision [13,14]. The perturbation of GaAs-electrolyte and

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AlGaAs-electrolyte interfaces by negatively charged bacteria resulted in reduced photocorrosion rates, which allowed detection of *Escherichia coli* K12 at 10^3 CFU/mL [12] and heat-inactivated *L. pneumophila* at 10^4 CFU/mL [11].

The limit of detection (LOD) is one of the most important parameters for biosensing devices, thus numerous techniques, such as charged self-assembled monolayers [15], electrophoresis [16], chemotaxis [17], three-dimensional polymer brushes [18] or centrifugation [19] have been examined to enhance this aspect. Most bacteria are known to be negatively charged under physiological *p*H conditions [20] and the amplitude of bacterial zeta potential could reflect LODs achievable with a charge sensing device. Previously, we reported that heat-inactivated *L. pneumophila*, extracted from industrial water, carried a smaller negative charge than that of *E.coli* K12 [11], which was considered as the potential reason of the inferior LOD for *L. pneumophila*. In this context, conjugation of synthetic molecules that carry multiple negative charges to the surface of bacteria seems a viable approach for enhancing performance of electric charge transducers. Whereas many studies have focused on modifying bacterial membrane properties to improve bio-production or drug delivery [21,22], amplifying bacterial negative charge with the purpose of achieving enhanced LOD has not been addressed. We note that, recently, anionic surfactants have been used for amplifying the signal of electrochemical field effect transistors detecting buckwheat allergenic proteins [23].

In this study, addressing the replacement of industrial standard methods of culture (which require several days for *L. pneumophila*) and polymerase chain reaction (which requires as much time for extraction and amplification from environmental water samples as our method), we have tried to improve the sensitivity of our DIP method by decorating *L. pneumophila* with sodium dodecyl sulfate (SDS). This procedure should increase bacterial negative charge and eventually enhance the LOD of GaAs/AlGaAs biosensors. We utilized zeta potential measurements to assess the charge modification of the decorated bacteria and studied the effect of SDS on bacterial immobilization using our standard bio-architecture. Here, we report detection of SDS decorated *L. pneumophila* (heat-inactivated) with an enhanced LOD reaching 10^3 CFU/mL based on in situ-monitored DIP of GaAs/AlGaAs nanoheterostructures.

2. Materials and chemicals

Semi-insulating undoped GaAs (001) wafer (AXTG108, AXT Inc., USA) and molecular beam epitaxy fabricated GaAs/$Al_{0.35}Ga_{0.65}As$ nanoheterostructures (CPFC, National Research Council of Canada, Ottawa) were utilized. Details of III-V nanoheterostructure can be found in the Supplemental information (SI) file (Fig. S1).

The following chemical/biological compounds were used in our experiments: OptiClear (National Diagnostics, Mississauga, Canada), acetone (ACP, Montréal, Canada), isopropyl alcohol (Fisher Scientific, Ottawa, Canada), ammonium hydroxide 28% (Anachemia, Richmond, Canada), anhydrous ethanol (Commercial Alcohols Inc., Brampton, Canada), biotinylated polyethylene glycol (Prochimia Surfaces, Gdansk, Poland), hexadecanethiol (Sigma-Aldrich, ON, Canada), neutravidin (Molecular Probes, Burlington, Canada), polyclonal biotinylated antibody and Fluorescein isothiocyanate (FITC) antibody against *L. pneumophila* and *E. coli* (ViroStat, Portland, Maine), aspartic acid, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC), N-Hydroxysuccinimide (NHS), SDS, Dimethylformamide (DMF), Stains-All (all from Sigma-Aldrich, ON, Canada), FITC (Sigma-Aldrich, MO, USA), bovine serum albumin (BSA), Dimethyl sulfoxide (DMSO) and bicarbonate buffer (all from Thermo Fisher Scientific, USA). In all experiments, we used deionized (DI) water with a resistivity of 18.2 MΩ.

E. coli ATCC 25922 (*E. coliA)* and *S. aureus* ATCC 43300 were cultured overnight in Tryptic Soy Broth medium (Thermo Fisher Scientific, USA). *E. coli* K12 *(E. coliK)* was grown overnight in Luria-Bertani nutrient broth (Thermo Fisher Scientific, USA) and colonies of *L. pneumophila* ssp1 were cultured on L-cysteine Buffered Charcoal Yeast Extract (VWR, Canada) agar medium. All bacteria were suspended in 1X phosphate-buffered saline (PBS) at a concentration of 10^9 CFU/mL. To inactivate bacteria, *E. coliK* and *L. pneumophila* were either exposed to UV light (λ = 250–260 nm, P = 100 mW/cm^2) or were heat-treated (90 °C, for 20 min). In either case, the efficiency of inactivation was verified by culture (data not shown here).

3. Experimental methods

3.1. Decorating Bacteria with SDS

Bacterial samples obtained from culture media were exposed in PBS to various concentrations of SDS (0.001 mg/mL to 0.02 mg/mL in PBS), while reference bacterial samples were kept in PBS, all for 30 min in a thermomixer (at 37 °C and 175 rpm). The washing procedure to remove excess reactants from bacterial solutions consisted of two steps. First, centrifugation at 3000 rpm for 25 min, removal of the supernatant and resuspension of the pelleted bacteria in 1 mL of PBS, followed by a second centrifugation at 3000 rpm for 15 min and resuspension in 1 mL PBS solution.

3.2. Zeta potential measurements

Zeta potential of bacteria was measured with a Zetasizer Nano system (Malvern Instruments) and analyzed using the Helmholtz-Smoluchowski equation [20]. Measurements were carried out in folded capillary cells (DTS 1064) using 1 mL of bacterial suspension at 10^6 CFU/mL, with a 180-s delay before each run.

3.3. Spectrophotometric measurements

An optimized method developed by Rupprecht et al. was adopted to measure SDS concentrations [24]. The absorbance was determined using a UV-1800 UV–vis Spectrophotometer (SHIMADZU) at λ = 453 nm. Measurements were carried out with a mixture of 25% Stains-All solution (stored at 2 mg/mL in DMF and then diluted 20 times in 1X PBS for use) and 75% SDS solution in 1X PBS (v/v). A solution of 1X PBS was used to determine the zero optical density (reference). A 10^9 CFU/mL suspension of heat-inactivated *L. pneumophila* in 1X PBS was exposed to 0.02 mg/mL of SDS for 30 min and then bacteria were removed by filtration using a PVDF membrane 0.22 μm filter (Millex-GV, Millipore, Canada).

3.4. Fourier transform infrared (FTIR) spectroscopy

E. coliA at a concentration of 10^9 CFU/mL was exposed for 30 min to 0.02 mg/mL of SDS in 1X PBS, and rinsed twice with 1X PBS. FTIR spectroscopy data of liquid samples were collected with a Perkin-Elmer Spectrum 100, using standard PTFE membrane cards. A solution of 1X PBS was used to determine the baseline. Measurements were conducted with a 1 cm^{-1} resolution.

3.5. Bio-functionalization and PL based detection

Bulk GaAs biochips were used for enumerating captured bacteria and GaAs/$Al_{0.35}Ga_{0.65}As$ nanoheterostructures were used for PL based detection tests. Biochips with surfaces of 2 mm by 2 mm were thiolated with a mixture of 0.15 mM biotinylated polyethylene glycol thiol and 1.85 mM hexadecanethiol in anhydrous ethanol, which had been deoxygenated with ultra-high purity nitrogen (5.0 UHP) prior to the thiolation process. The thiolated biochips were exposed for 2 h to 0.2 mg/mL neutravidin, and for 1 h to 0.1 mg/mL polyclonal biotinylated antibody against *L. pneumophila* or *E. coli*. The quantum semiconductor photonic biosensing (QSPB) reader employed in this work used a 660 nm light emitting diode (LED) for the intermittent excitation

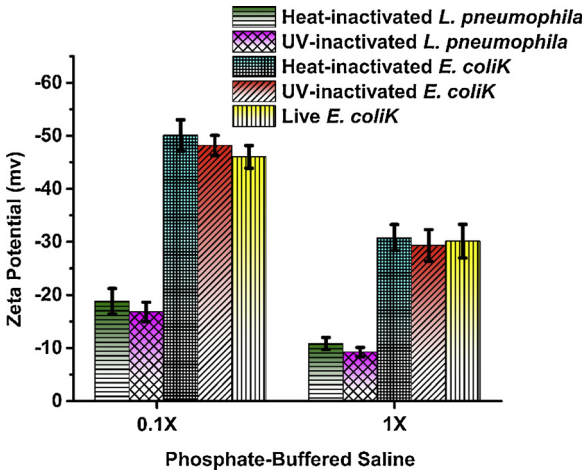

Fig. 1. Zeta potential of *L. pneumophila* and *E. coliK* in two different concentrations of PBS.

of GaAs/AlGaAs biochips (3 s in every 60 s period) at P = 25 mW/cm^2. The specificity of the employed biosensing procedure has already been established in our previous publications [10,25–27] and further illustrated in [11,28–30].

3.6. Fluorescence microscopy

An Olympus IX71 fluorescence microscope was used to collect images of bio-functionalized GaAs biochips exposed to *L. pneumophila* or *E. coli* (30-min incubation). The surface of the biochips coated with bacteria was rinsed with 1X PBS and exposed in the dark to 0.05 mg/mL of FITC-antibody against *L. pneumophila* or *E. coli* for 1 h. Next, the samples were rinsed with DI water and dried with a gentle flow of high-purity nitrogen (4.8 HP).

4. Results and discussion

Fig. 1 shows the zeta potential measurement of *L. pneumophila* and *E. coliK* in 1X and 0.1X PBS (*p*H 7.4). In 1X PBS, *E. coliK* had a zeta potential of approximately −30 mV, which increased to approximately −50 mV in 0.1X PBS. The zeta potential values for *L. pneumophila* were close to −10 and −20 mV in 1X and 0.1X PBS, respectively. It can be seen that zeta potentials of UV- and heat-inactivated *E. coliK* were in the same range as that of live bacteria. Due to safety precautions, we were unable to measure zeta potential of live *L. pneumophila*, however considering the *E. coliK* results, it seems reasonable to assume that the zeta potential of live *L. pneumophila* would be very close to that of UV- or heat-inactivated bacteria. Halder et al. observed a reduction of zeta potential in 0.5 mM potassium phosphate buffered solution (*p*H 7.4) for heat treated (100 °C for 10 min) *E.coli* (MTCC 2939) versus live bacteria, whereas a 10-min heat exposure at 100 °C had no significant impact on the zeta potential of *S. aureus* (MTCC 96), which was attributed to the thicker peptidoglycan layer of Gram-positive bacteria [31]. Since in the present study bacteria were heat-inactivated at only 90 °C, this might explain why a zeta potential difference between live and dead *E. coli* was not observed. As it can be seen in Fig. 1, both bacteria exhibited higher negative zeta potentials in 0.1X PBS. This feature, potentially important for the performance of an electric charge biosensor, could be explained by the dependence of bacterial cell surface electric charge on the ionic strength of the surrounding solution

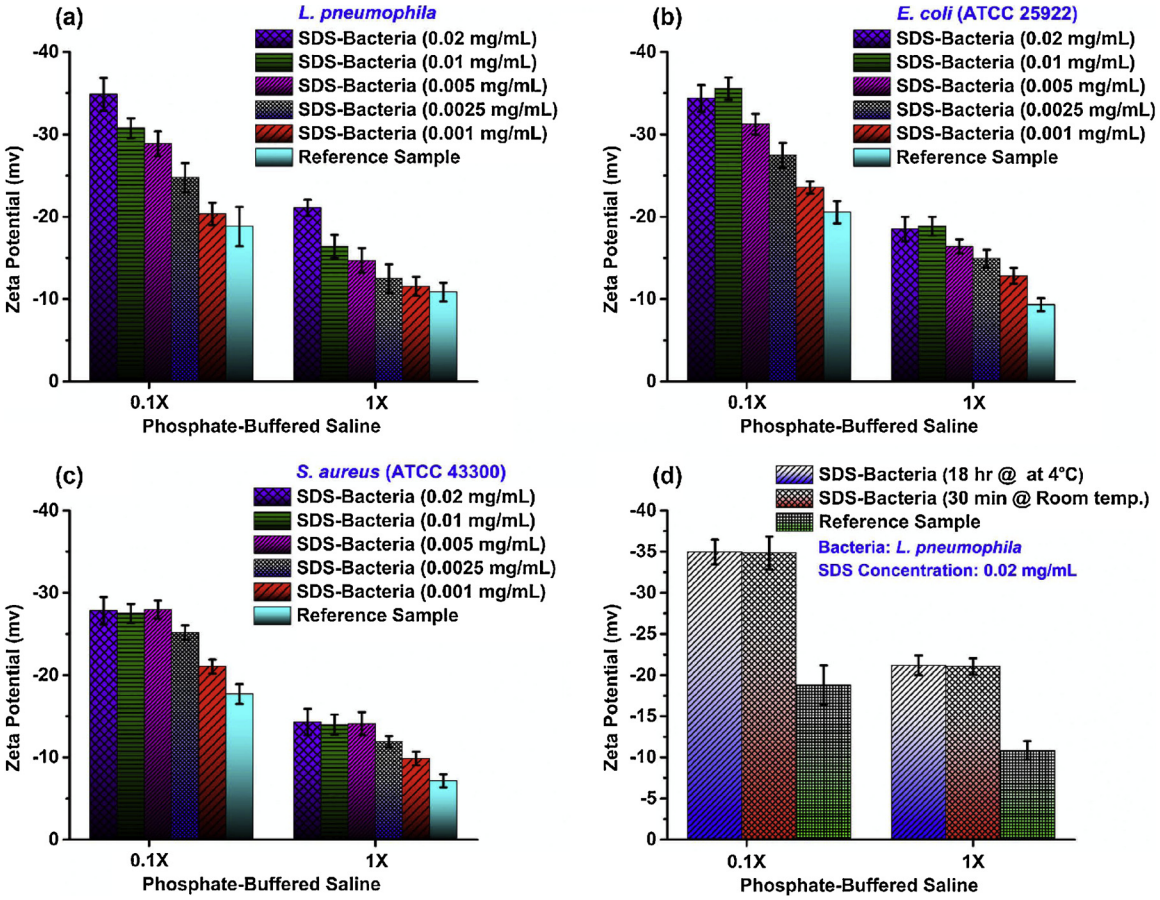

Fig. 2. Effect of various concentrations of SDS on zeta potential of heat-inactivated *L. pneumophila* (a), live *E. coliA* (b), live *S. aureus* (c), and effect of incubation time on zeta potential of heat-inactivated *L. pneumophila* (d).

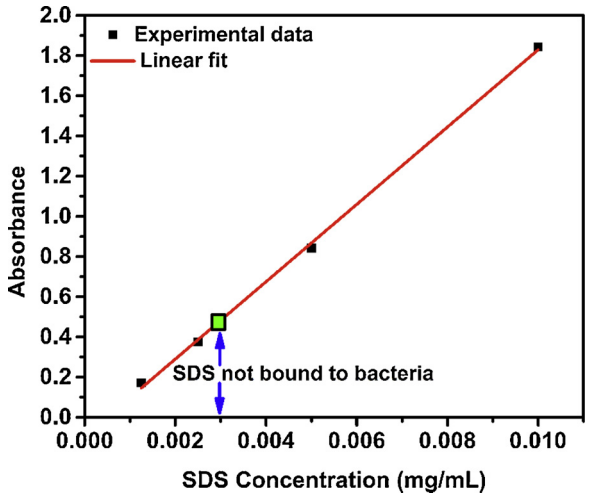

Fig. 3. Quantification of SDS molecules using spectrophotometry in 1X PBS. The free SDS after removal of bacteria from a bacteria-SDS (0.02 mg/mL) suspension is presented as a green (bold) square (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

[20]. The zeta potential of bacteria increases in solutions of reduced ionic strength, however further reduction of the ionic strength strongly diminishes the buffering capacity of PBS [32] and undermines its *p*H stabilizing performance. It was reported that the *p*H condition can directly affect photocorrosion of GaAs/AlGaAs nanoheterostructures [33]. Thus, it was more desirable to increase the negative charge of bacteria, without further reducing the ionic strength of PBS (less than 0.1X), by decorating them with materials and molecules providing an additional negative charge.

Fig. 2 displays zeta potential measurements for *L. pneumophila* (heat-inactivated), *E. coliA*, and *S. aureus*, all decorated with SDS molecules after premixing the bacteria with SDS solutions at concentrations ranging from 0.001 mg/mL to 0.02 mg/mL. It has been reported that SDS at a concentration of 0.05% resulted in destruction of the bacterial membrane accompanied by a displacement of the nuclear material [34]. To avoid this problem and maintain the integrity of a bacterial cell membrane, a maximum concentration of 0.02 mg/mL was utilized in these experiments. For *L. pneumophila,* as shown in Fig. 2a, SDS amplified the negative zeta potential of bacteria a maximum of 1.9 times, from - 10.8 mV in 1X PBS, and 1.8 times, from - 18.8 mV in 0.1X PBS. The zeta potential of *E. coliA* (See Fig. 2b) was improved 2 times, from -9.3 mV in 1X PBS, and by 1.7 times, from -20.5 mV in 0.1X PBS. However, increases of zeta potential for *E. coliA* continued only up to 0.01 mg/mL of SDS, and no further increase of zeta potential was observed for *E. coliA* exposed 0.02 mg/mL of SDS. Zeta potential values of *S. aureus*, as shown in Fig. 2c, increased 2 times, from ~ -7.1 mV in 1X PBS, and by 1.6 times, from ~ -17.7 mV 0.1X PBS, though zeta potential increment continued merely up to 0.005 mg/mL of SDS and further increments of SDS exhibited no major effect on zeta potential values of this Gram-positive bacteria.

The electric charge of each bacterial strain is determined by the available groups at its surface and its hydrophobicity [20]. Consistent with the literature, our results revealed that the zeta potential of Gram-positive bacteria was weaker than that of Gram-negative bacteria, probably related to the presence of an additional negatively charged lipopolysaccharide (LPS) layer in Gram-negative bacteria [31,35]. Furthermore, we observed that under the same conditions, the increment of zeta potential for *S. aureus* was saturated at a much lower concentration of SDS (0.005 mg/mL), compared to that of *E. coliA* (0.01 mg/mL). Such a trend of zeta potential variations in Gram-negative bacteria could be due to the higher density of anionic groups and O-antigen in their LPS membrane, as well as their thin peptidoglycan layer [36]. The interaction between SDS and membrane proteins is not well understood, however SDS has been modeled as a 'lipid-like' amphiphile affecting helical rearrangement of proteins, resulting in protein denaturation [37]. It is relevant to mention that the concentrations of SDS utilized in our experiments was not enough to induce protein denaturation [34] nor to kill bacteria (See Supplementary Material). Binding of SDS to bacteria is mainly governed by hydrophobic interactions between long hydrophobic chains of SDS and the proteins at the surface of the bacteria [38]. Since LPS of *L. pneumophila* is hydrophobic, due to the presence of the deoxy groups and N- and O-acyl substituents in polylegionaminic acid [39], it may promote adherence of SDS molecules to the bacterial surface. It was reported that the highly hydrophobic surface of *L. pneumophila* promoted their adherence to alveolar macrophages [40] that contain negatively charged sialic acid on their membranes [41].

Fig. 2d compares zeta potential measurements for two different incubation times, for *L. pneumophila* exposed to 0.02 mg/mL of SDS. Comparable zeta potential values obtained for different exposure times suggested the rapid formation of a stable *L. pneumophila*-SDS complex. Decreased and stable zeta potentials of *E. coli* and *S. aureus* have been reported for low concentrations of cetyl trimethyl ammonium bromide (CTAB), however at higher concentrations of CTAB, the zeta potential changed over time [31].

We have investigated other negatively charged molecules for modulation of bacterial electric charge. We observed that electrostatic interactions of aspartic acid with *L. pneumophila* were much less stable and efficient compared to hydrophobic interactions with SDS (Fig. S2 in SI file). Specific binding of BSA showed low efficiency and involved extra chemical steps (Fig. S3 in SI file). Consequently, it was deduced that SDS provided the best solution for providing extra negative charge to bacteria. This approach was also much simpler and faster to apply, therefore it was further investigated for enhanced detection of *L. pneumophila*.

Spectrophotometry experiments were carried out to determine the incorporation of SDS molecules in bacteria. Absorbance increased in a linear fashion for SDS concentrations between 0.0025 mg/mL and 0.01 mg/mL, in 1X PBS solution, with a background absorbance of 0.042 for the reference sample, as shown in Fig. 3. After exposing 10^9 CFU/mL of heat-inactivated *L. pneumophila* to SDS at concentration of 0.02 mg/mL in 1X PBS, the SDS that had not reacted with the bacteria was determined after removing the bacteria by filtration. The absorbance data of this solution is presented with a green (bold) square. This indicated that the concentration of SDS in the supernatant was $\sim$ 0.003 mg/mL, while the rest of the SDS molecules (0.017 mg/mL) must have been bound to bacteria, assuming negligible loss of molecules during this experimental procedure. Quantification of SDS molecules using conductivity measurements in DI H_2O resulted in comparable numbers (Fig. S4 in SI file). Given that the number of SDS molecules bound to the bacteria (0.017 mg/mL) was $\sim 35.5 \times 10^{15}$, it was calculated that an average $\sim 35.5 \times 10^6$ SDS molecules were attached per bacterium (at a concentration of 10^9 CFU/mL). As expected, such a number of SDS molecules had no effect on bacterial viability, which was confirmed by live/dead assay (Fig. S5 in SI file). Theoretical calculations based on the Gouy-Chapman model [42,43] showed that the surface charge density of *L. pneumophila*, exposed to 0.02 mg/mL of SDS, was almost doubled from $\sim$ - 0.01 C/m^2 ($\sim 1.3 \times 10^5$ *e*) for bacteria without SDS to $\sim$ - 0.02 C/m^2 ($\sim 2.6 \times 10^5$ *e*) for bacteria with 0.017 mg/mL of bound SDS (Fig. S6 in SI file). Even though the absolute values could be underestimated, the ratio of the final charge density per initial number seems reasonable, considering that the employed model predicted the proper trend of charge variation as reported in [42,43]. This information is of importance for molecular simulations as well as fundamental studies of the interaction of SDS with proteins and other biochemical compounds [44].

Fig. 4 shows FTIR spectra of *E. coliA* and SDS conjugated *E. coliA*. The FTIR transmittance spectra of bacteria contain overlapping signals

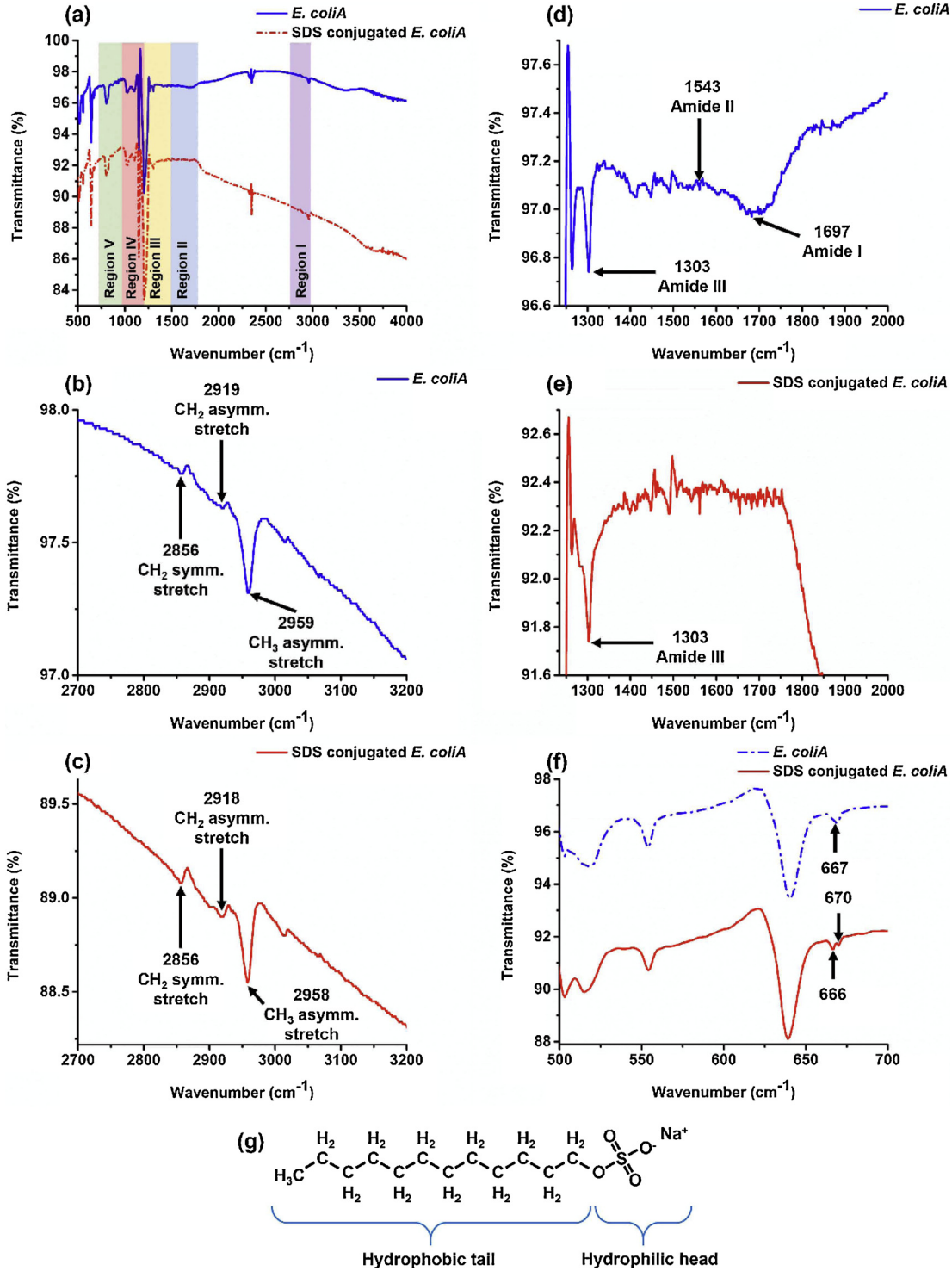

Fig. 4. FTIR transmittance of SDS conjugated *E. coliA* versus unconjugated bacteria (a), magnified spectra at 2700–3200 cm^{-1} (b) and (c), magnified spectra at 1250-2000 cm^{-1} (d) and (e), magnified spectra of 500–700 cm^{-1} (f), and chemical structure of SDS (g).

that originate from different biomolecules and appear distinctively in five main regions (Fig. 4a) as defined in [45]. Full FTIR spectra of *E. coliA* and that of SDS conjugated bacteria, shown in Fig. 4a, looked very similar, because SDS molecules have CH_2, CH_3, S—O and S═O groups that are also common in bacterial cells. However, Fig. 4b and c show that in region I the CH_3 asymmetric stretch, the CH_2 asymmetric stretch and the CH_2 symmetric stretch bands were more intense, well-defined and clearer in SDS conjugated compared to unconjugated *E. coliA*. These are the characteristic peaks related to the fatty acid region of bacterial FTIR spectra [46] and, in the case of SDS coated bacteria, the long CH_2 chain of SDS could lead to an increased signal-to-noise ratio in this region. Moreover, the FTIR spectra of bacteria include amide I, II and III peaks, but the signal from these peaks was masked due to the presence of SDS on the surface of bacteria, as shown in Fig. 4d and e. In Fig. 4a, the intensity ratio between peaks in regions III and IV has also been changed upon binding of SDS to *E. coliA*. The peaks associated with the SO_3^- group of SDS could be indicative of an interaction between SDS and bacteria. The asymmetric or antisymmetric stretching

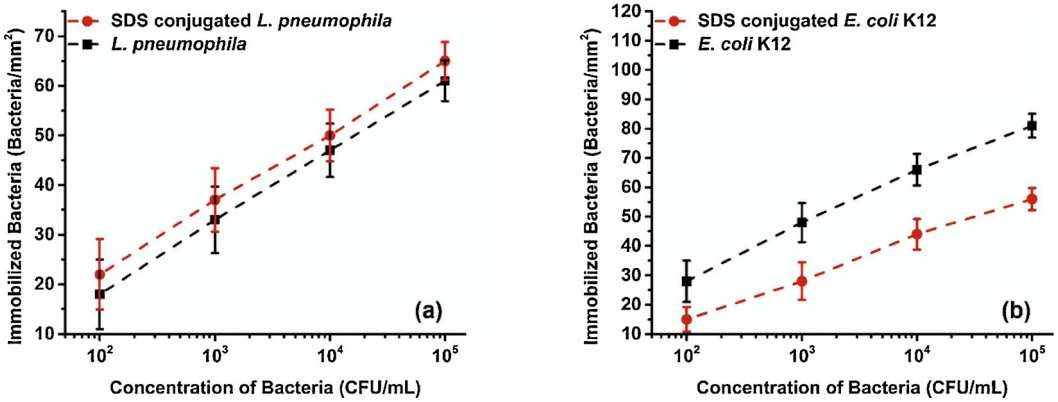

Fig. 5. Surface coverage of bio-functionalized GaAs biochips exposed to heat-inactivated *L. pneumophila* (a) and *E. coli K12* (b), determined by fluorescence microscopy.

and symmetric stretching vibration of SO_3^- groups (at 1274 cm^{-1} and 1117 cm^{-1} respectively) overlapped with those peaks of bacteria, as shown in Fig. 4a. However, a new distinguishable peak was observed in the case of SDS conjugated bacteria at 670 cm^{-1}, which was related to the vibration of the SO_3^- group [47], as it can be seen from a magnified portion of the spectra, presented in Fig. 4f. The preceding dataset confirmed the presence of SDS on the bacterial surface, while it pointed to the fact that there was no chemical binding/shifting for the two involved components. This is consistent with the literature reporting that the interaction between negatively charged SDS and proteins only involves electrostatic and mainly hydrophobic interactions [38,48].

Fig. 5 compares the number of heat-inactivated *L. pneumophila* and *E. coliK* bacteria immobilized at the surface of GaAs biochips for both bare and SDS conjugated bacteria. In the case of *L. pneumophila*, Fig. 5a, no statistically significant differences were found between the two experiments, indicating that SDS did not impact bacterial capture. However, in the case of *E. coliK*, a substantial decrease in bacterial capture was observed. Hassen et al. reported that *E. coliK* has strong affinity toward the neutravidin coated surface of GaAs biochips [17]. This was verified for our employed bio-architecture by exposing GaAs biochips, coated only with SAM and neutravidin but without grafting antibody to *E. coliK* or *L. pneumophila* (Fig. S7 of SI file). Thus, the difference observed in the capture of *E. coliK*, shown in Fig. 5b, could be the result of reduced non-specific binding. Alternatively, reduced affinity between SDS decorated *E. coliK* and antibodies, in Fig. 5b, might also have an impact. As established by the live/dead assay (Fig. S5 in SI file), at an SDS concentration of 0.02 mg/mL, the loss of bacteria through lysis by SDS could not be considered as a major parameter in capture efficiency of bacteria. Moreover, disaggregation of the bacterial cell walls requires a much higher concentration of SDS, typically 0.2% (w/v) [49]. These results showed that SDS did not interfere with the immobilization of *L. pneumophila* and they suggested that it can improve the selectivity of the employed bioreceptor architecture in the case of a solution containing a mixture of *E. coli* and *L. pneumophila*. However, for other types of bacteria commonly found in industrial water samples more investigation is required.

Fig. 6 presents PL data for the detection of SDS conjugated *L. pneumophila* (heat-inactivated) in 0.1X PBS, and the calibration curve for this biosensor. This technique relies on *in situ* monitoring of the photocorrosion rate of GaAs/AlGaAs nanoheterostructures. The time of appearance of the PL maximum-intensity has been used as an indicator of the photon-induced etching rate. The presence of negatively charged bacteria delayed the appearance of the PL maximum-intensity as a result of the reduced photocorrosion rate [11,12]. In Fig. 6a, the blue curve (solid line) corresponds to a biochip exposed to a solution of 0.1X PBS, as the reference test, and the resultant PL maximum-intensity occurred at around $t = 43$ min. The green (full triangles), purple (full circles) and red (full rectangles) show data corresponding to individual biochips exposed to, respectively, 10^2, 10^3 and 10^4 CFU/mL of SDS decorated *L. pneumophila*. These biochips had PL maxima positioned at 55, 70 and 120 min, respectively. It can be seen in Fig. 6b that the temporal delay of the PL maximum-intensity position increased linearly with the concentration of *L. pneumophila*. This enabled us to correlate the appearance of PL maximum-intensity with the concentration of *L. pneumophila* in a given solution. Fig. 6c compares the delay of PL maximum-intensities obtained for unconjugated and SDS decorated *L. pneumophila* using GaAs/AlGaAs nanoheterostructure biosensors. It shows that exposing biochips to SDS-*L. pneumophila* resulted in a noticeable shift of the detection signal, compared to unconjugated *L. pneumophila* at the same concentration. For biochips exposed to 10^4 CFU/mL of SDS-*L. pneumophila*, an average delay of ~ 70-min versus the reference biochip was observed. For the same concentration of bacteria, only a ~ 10-min delay was observed for the unconjugated *L. pneumophila*. Most importantly, we were unable to resolve the difference between the PL maximum-intensity of reference biochips and that of biochips exposed to the unconjugated *L. pneumophila* at 10^3 CFU/mL, however for the biochips exposed to 10^3 CFU/mL of SDS decorated bacteria we observed a ~ 30 min delay in the PL maximum-intensity. The surface coverage data, presented in Fig. 5, indicated that decorating *L. pneumophila* with SDS had no effect on the bacterial surface coverage, compared to unconjugated bacteria, whereas the PL data shown in Fig. 6, revealed a substantial difference in the appearance of PL maximum-intensity for these two cases. This pointed out the role of bacterial electric charge in decreasing the photoetching rate of GaAs/AlGaAs nanoheterostructures.

Chemical dissolution of III-V materials is, for the most part, governed by the number of hole carriers drifted into the solid/electrolyte interface [50]. The excess hole carriers generated by photoexcitation of the semiconductor can contribute either to surface state mediated recombination [51], or by participating in the charge transfer reaction with the surrounding electrolyte via surface states [52]. While recombination by means of surface states is non-radiative and independent of the surface band bending [53], the hole-driven photoetching reactions can be changed according to band bending conditions. It was observed that photocorrosion of n-GaAs was slower under flat band conditions, compared to n-GaAs with upward band bending [54]. Chemical- and physical-induced band bending variation of semiconductors has been studied extensively [9]. Hilal et al. studied Mott-Schottky behavior of n-GaAs and reported that attachment of positively charged metalloporphyrin shifted the flat band voltage of the semiconductor toward positive values by 200–300 mV [55]. Moreover, it has been reported that adsorption of electron acceptor molecules, such as Cl_2 and O_2, and electron donor molecules, such as CH_3OH, affected band bending of titanium oxide (TiO_2) and regulated the rate of hole transfer at the surface of TiO_2 [56]. Furthermore, in several studies, charge transfer between bacteria and a conducting or

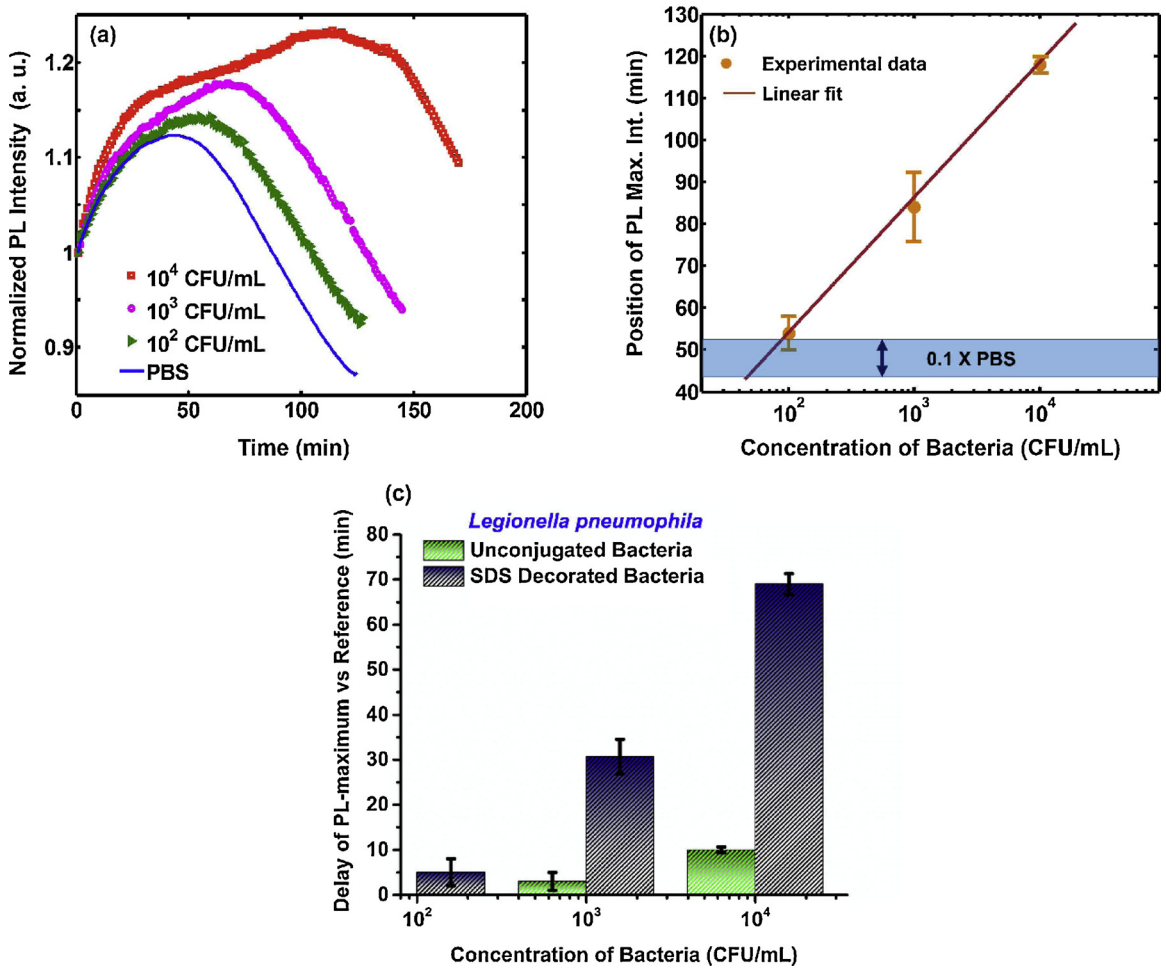

Fig. 6. Representative PL data from bio-functionalized samples exposed to different concentration of SDS decorated *L. pneumophila* (a), statistical analysis of PL maximum-intensity vs time for numerous repeated detection tests (b), and comparison of PL maximum-intensity delay versus reference (unconjugated) and SDS conjugated *L. pneumophila* (c).

semiconducting substrate was observed [57,58]. It has been experimentally demonstrated that, on average, around 10^{-14} C of charge per single bacterium has been exchanged upon bacterial adhesion to the semiconducting indium tin oxide surface. This amount corresponds to only a fraction of the total charge at the surface of the bacteria [58].

Generally, the band bending of a semiconductor could be affected electrostatically by the surface adsorbed bacteria and/or by possible charge transfer between adsorbed bacteria and the semiconductor [57,58]. The degree of band bending would, thus, depend on the distance between the bacteria and the surface of a biochip, the Debye length of an employed electrolytic environment [59], the charge of bacteria and the conductivity of an interfacial layer. Here, the surface of biochips was covered with thiols, neutravidin and antibodies prior to the detection experiments. The evidence of charge transport by thiol has already been reported [60,61]. Moreover, it has been shown that passivation of GaAs with thiols will not exceed 50% of the whole surface atoms [62], therefore the uncovered area could also influence the charge transfer between bacteria and the semiconductor.

The foregoing discussion underlines that the increased negative zeta potential of SDS-*L. pneumophila* has improved the interaction of bacteria with biochips by influencing the semiconductor band bending. The PL results confirmed that decorating *L. pneumophila* with SDS (at 0.02 mg/mL) enhanced the LOD of the photocorrosion based biosensor by one order of magnitude in comparison with parallel experiments, as well as with the previously reported data [11].

To implement the SDS decoration step in a detection scheme of *L. pneumophila*, a small volume of industrial, recreational or surface water, typically less than 1 L, would be filtered and, if required, concentrated [63]. After exposure to a highly acidic environment (pH ~ 2.2) to eliminate most of the non-*L. pneumophila* bacteria [64] and suspension in PBS solution, the filtrate would be mixed with an SDS solution to produce SDS-decorated bacteria. After removal of unbound SDS by washing, detection would be carried out in a PBS solution. Detailed research has yet to be carried out to verify the selectivity of the biosensor, as well as its sensitivity, reproducibility and reusability [65,66]. All of these parameters are the subject of intensive research carried out in our laboratory and they will be covered in future reports, but this exceeds the scope of the present manuscript.

5. Conclusions

We have investigated bacterial surface charge amplification by decorating *L. pneumophila*, *E. coliA* and *S. aureus* with negatively charged biomolecules. Hydrophobic interactions of SDS molecules with bacteria resulted in a nearly twofold increase in the negative zeta potential of both Gram-negative (*L. pneumophila, E. coliA*) and Gram-positive (*S. aureus*) bacteria, with an attractive stability of molecular binding. We were able to increase the zeta potential of *L. pneumophila* from - 10.8 mV to -21.05 mV in 1X PBS, and from - 18.8 mV to -34.85 mV in 0.1X PBS, by exposing these bacteria to 0.02 mg/mL of SDS. Spectrophotometry data suggested that the improved zeta potential originated from attachment of ~ 35.5×10^6 SDS molecules per

bacterium. By employing the Gouy-Chapman equation, it was estimated that at a concentration of 0.017 mg/mL of bound SDS, the surface charge density of *L. pneumophila* in 1X PBS increased from ~ - 0.01 C/m^2 to ~ - 0.02 C/m^2. This suggested that ~ 35.5 × 10^6 SDS molecules added 1.2 × 10^5 *e* per bacterium, with each SDS molecule providing the equivalent of 0.0035 *e*. Furthermore, using a maximum concentration 0.02 mg/mL of SDS caused no major damage to the cell membrane of *E. coliA* or *S. aureus*. Hydrophobic interaction of SDS with the surface of *E. coliA* was confirmed by FTIR-revealed traces of SDS molecules. Some reduction of the nonspecific interaction of SDS-decorated *E. coliA* was observed with the employed bio-architecture. In correlation with the zeta potential results, PL measurements confirmed that the LOD of the GaAs/$Al_{0.35}Ga_{0.65}As$ nanoheterostructure biosensor for *L. pneumophila* was enhanced to 10^3 CFU/mL, which is one order of magnitude better than our previously reported results. This result belongs, arguably, to the best results ever reported for detection of *L. pneumophila* with a biosensing device. For instance, Li at al. [67] and Lei et al. [68] reported detection of *L. pneumophila* with electrochemical impedance spectroscopy at 10^2 and 10^5 CFU/mL, respectively, while Enrico et al. [69] and Foudeh et al. [70] reported detection of *L. pneumophila* at ~10^4 CFU/mL with SPR technology. Recently, Martin at al. [71] reported detection of *L. pneumophila* at 10^4 CFU/mL using an amperometric magnetoimmunoassay method. Some of these biosensors have also shown slightly more rapid detection than the 3 h reported in this manuscript, but they may not become commercially successful, if they cannot be efficiently automated and employed outside of a laboratory setting as our DIP biosensor. Our approach is focused on the development of a workstation for quasi-continuous monitoring of water reservoirs for the presence of *L. pneumophila* using a biosensor with stacks of GaAs/AlGaAs nanoheterostructures for delivering a single biosensing result per day over a 30-day period without the involvement of an operator. Thus, we find that the 2–3 h detection time, in addition to the time required for biofunctionalization, has to be considered attractive for the operation of a proposed workstation. We argue that the relatively simple approach of decorating bacteria with SDS, as discussed in this report, significantly enhances the limit of detection of charge-sensing semiconductor biosensors, and it paves the way towards attractive deployment of DIP biosensors comprising stacks of GaAs/AlGaAs nanoheterostructures for semi-automated analysis of water reservoirs for the presence of pathogenic bacteria in remote locations.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.snb.2019.127007.

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