Separating and Detecting *Escherichia Coli* in a Microfluidic Channel for Urinary Tract Infection Applications

Yongmo Yang, Sangpyeong Kim, and Junseok Chae

**Abstract**—We report a lab-on-a-chip (LOC) that can separate and detect *Escherichia coli* (*E. coli*) in simulated urine samples for urinary tract infection (UTI) applications. The LOC consists of two (concentration and sensing) chambers connected in series and an integrated impedance detector. The two-chamber approach is designed to reduce the nonspecific absorption of a protein, e.g., albumin, that potentially coexists with *E. coli* in urine. We directly separate *E. coli* K-12 from cocktail urine in a concentration chamber containing microsized magnetic beads conjugated with anti-*E. coli* antibody. The immobilized *E. coli* is transferred to a sensing chamber for the impedance measurement. The measurement at the concentration chamber suffers from nonspecific absorption of albumin on the gold electrode, which may lead to false-positive response. By contrast, the measured impedance at the sensing chamber shows a $\sim$60-k$\Omega$ impedance change. This is a clear distinction between $6.4 \times 10^4$ and $6.4 \times 10^5$ CFU/mL, covering the threshold of UTI ($10^5$ CFU/mL). The sensitivity of the LOC in detecting *E. coli* is characterized to be at least $3.4 \times 10^4$ CFU/mL. We also characterized the LOC for different age groups and white blood cell spiked samples. These preliminary data show promising potential for application in portable LOC devices for UTI detection.

**Index Terms**—*Escherichia coli* (*E. coli*), lab-on-a-chip (LOC), point-of-care testing, urinary tract infection (UTI).

**I. INTRODUCTION**

Human urine is commonly used in regular medical checkups and tests to identify the cause of symptoms [1]. Urine is a rich source for evaluating overall health, especially kidney function, for instance, because urine contains hundreds of body wastes that kidneys filter from the blood. Urinary tract infections (UTIs) are common kidney-related diseases in humans, especially women. They account for 8 million hospital visits annually in the U.S. [2]. Moreover, UTI has a high recurrence rate: among individuals of a first infection, 20% has their second infection within six months, and 3% has a third infection within six months [3], [4]. *Escherichia coli* (*E. coli*) is responsible for up to 80% of such UTI [5], [6], and conventional detection methods (bacteria culture) for a urine sample require 24–48-h cultivation and labor-intensive procedures [7]. Being able to rapidly identify living cells without culturing is very important to medical diagnosis and treatment because microorganisms can cause severe diseases [8], [9], and some progress very quickly [5], [10]. Although more rapid test methods do exist, such as the dip-stick method for *E. coli* detection, such method is based on nitrite and esterase and offers fast detection, but it does not provide sufficient sensitivity [11].

Immunomagnetic separation (IMS) [12], [13] and impedance spectrometry (IS) techniques have been used to capture and detect *E. coli* [32]. Some have been implemented in a miniaturized form of detector [32]. These IMS/IS techniques presented focus on detecting *E. coli* O157, which is a cause of foodborne illness [14]. Wright et al. used IMS to collect and detect *E. coli* O157 from minced beef samples. They used magnetic beads (MBs) coated with anti-*E. coli* antibody to isolate *E. coli* O157 from the beef samples and cultured them to count colony forming unit (CFU) [12]. Perez et al. presented IMS to capture *E. coli* O157 and detected them using electrochemical method [13]. They also measured a calibration curve of CFU against electrochemical response. Besides these works, there are a number of prior work using IMS/IS techniques to collect and detect *E. coli* [15]–[17]. Varshney et al. used magnetic nanoparticle conjugated antibody for the detection of *E. coli* O157 in food samples [32]. The nanoparticles immobilized biotin-labeled polyclonal goat anti-*E. coli* antibodies to separate and concentrate *E. coli* O157:H7 from ground beef samples. Then, the impedance of the cluster of the nanoparticles and *E. coli* was measured using interdigitated microelectrodes. The lowest detection limits of their biosensor in pure culture and ground beef samples were $7.4 \times 10^3$ and $8.0 \times 10^3$ CFU/mL. By miniaturizing electrodes and by using nanoparticles, the sensitivity enhances, and the flexibility of electrode fabrication improves. Miniaturized electrodes also allow us to perform IS in low conductivity solution since they require lower concentrations of electroactive ions to form a double layer as compared to macrosized counterparts. An excellent review on miniaturized impedance biosensors for detecting bacteria is available in [31].

Significant research efforts have focused on shortening analysis time and on detecting *E. coli* with increasing sensitivity and high accuracy. One example is Klodzinska et al., who separated *E. coli* using capillary zone electrophoresis and the presence of negatively charged ions of carboxyl and phosphate groups on the bacterial cell wall [18]. The capillary surface was...
modified to separate E. coli, and spectrophotometry measured the concentration of bacterial cells. High voltage (20 kV), however, could cause electromagnetic interference, posing a bottleneck in the development of a portable handheld unit for use at a patient’s bedside [19], [20]. In another example, Ruan et al. immobilized anti-E. coli antibodies on a planar electrode to detect E. coli O157:H7 [21]. The surface of glass electrodes coated by indium tin oxide was modified, and it detected E. coli, but a low capturing rate was shown. This may lead to false-negative results under normal use. These difficulties add urgency to our work as it is our belief that microfluidics in IMS may overcome such limitations. Despite of such success of many microscaled platforms, a few studies have focused on detecting bacteria in urine for UTI applications. This motivates our research, developing a microchip to integrated IMS/IS to detect E. coli for UTI applications.

In this paper, we present a lab-on-a-chip (LOC) to separate E. coli and to measure its concentration using MBs directly from a cocktail urine sample. The E. coli captured by MBs was evaluated by miniaturized IS, and those IS measurements were further evaluated using the current standard practice of counting cultured CFUs. An E. coli concentration of $10^5$ CFU/mL or higher in urine is typically considered a UTI, and several different E. coli serotypes can cause UTI [22]–[24]: O1 : K1 : H7, O6 : K15 : H31; SmR, O6 : K2 : H1, O18 : K1 : H7; SmR, and O4 : K6; NaI. Since UTI-related E. coli demands high safety requirements, we used E. coli K-12 instead of serotypes such as O1 : K1 : H7 and O6 : K15 : H31; SmR. Normal urine does not contain any protein, or it contains only trace amounts of it [25], [26]. For UTI patients, however, albumin may be excreted and contained in the urine. We attempted to make the closest possible simulation of UTI-infected urine sample by spiking albumin and E. coli K-12 in cocktail urine. We also characterized the LOC using the simulated urine having different concentrations of E. coli, coexisting with white blood cells (WBCs).

II. DEVICE DESIGN AND FABRICATION

The design of the E. coli separator is shown in Fig. 1. Two chambers (one for concentration and the other for sensing) are connected in series with two mechanical valves [27] to control the fluidic stream. The dimension of the chambers and inlets is $1.8 \times 3 \times 0.05$ mm$^3$ ($W \times L \times H$), and that of the microfluidic channels is $0.5 \times 5 \times 0.05$ mm$^3$ ($W \times L \times H$). The two gold electrodes for IS measurement are $1 \times 1.5$ mm$^2$ ($W \times L$), and these are placed in the concentration and sensing chambers. MBs are retained and transported inside and between the chambers using two permanent magnets (K&J Magnetic, Inc.) placed above and beneath the chamber.

We used the replica-molding technique, which transfers surface patterns on a mold to an elastomeric material. Silicon substrate and PDMS were used for the mold and elastomeric material, respectively. The fabrication of the Si mold shown in Fig. 2 required a one-mask process using AZ 4330 photoresist and one deep-RIE (50 μm deep) step.

Once the Si mold was fabricated, PDMS was prepared by mixing silicone elastomer and curing agent in a 10:1 ratio and by pouring it on the Si mold. After curing, the PDMS replicate was peeled off and assembled. Two screws were mounted and used for mechanical valves. The gold electrodes [chrome/gold (10/200 nm)] were lithographically patterned on the glass slide. The glass slide and PDMS replicate were treated with oxygen plasma (Harrick Plasma) for 1 min at 100 W and were bonded and then cured for 20 min at 80 °C in the oven. The fabricated LOC is shown in Fig. 3(a).

MBs were conjugated with anti-E. coli antibody. First, 400 mM of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) and 100 mM of N-hydroxysulfosuccinimide (NHS) were freshly prepared in DI water and were mixed with MBs to activate COOH-terminated self-assembled monolayers (SAMs). After 15 min of incubation, the mixture of MBs with NHS and EDC was washed with PBS solution. The anti-E. coli antibody was prepared with 10-mM NaAc (sodium acetate; pH 5.3 solution), and the anti-E. coli antibody and NaAc mixture was mixed with MBs to conjugate with activated COOH-terminated SAM on the surface of the MBs. After completing the antibody bonding to the COOH-terminated SAM, the unbound activated COOH-terminated SAM was blocked by ethanolamine [28], [29].
There are several prior arts that modeled the equivalent circuit of \textit{E. coli} on thin-film electrodes [30] and \textit{E. coli} conjugated with magnetic particles [32]. Radke et al. modeled \textit{E. coli} O157:H7 on interdigitated electrodes [30]. The equivalent model of \textit{E. coli} consists of the resistance of the cytoplasm, the resistance of the cell membrane, and the capacitance of the cell membrane. Additionally, the parasitic capacitance represents the double-layer capacitance at the electrode surface and the capacitance created from the oxide separation of the gold electrodes and the silicon. Varshney et al. presented an equivalent circuit model of magnetic nanoparticles attached to \textit{E. coli} on a thin-film electrode [32]. The model consists of double-layer capacitance, stray capacitance (associated with electrodes, shielding, wires, cables, and adhesives), and resistance of medium or bulk that represents the cluster of magnetic nanoparticles and \textit{E. coli}. The equivalent model was characterized by a series of measurements, and the measurements fit very well to the model. It is very difficult to model the undefined number of magnetic particles and \textit{E. coli} clusters between sensing electrodes. One cannot assume a distributed model of a cluster of a magnetic particle and \textit{E. coli} since the electric field density is not uniform inside the chamber.

We used a non-Faradaic equivalent circuit to model IS measurements of the LOC, as shown in Fig. 3(b). The equivalent circuit consists of two double-layer capacitances ($C_{dl}$), connected in series with a bulk medium resistor ($R_s$), and a stray capacitor ($C_s$) connected in parallel with $C_{dl}$ and $R_s$ [31], [32]. $C_{dl}$ comes from the effect of ionic species near the electrode surface. $R_s$ reflects the conductivity change in bulk medium and charge transport across the bulk solution. $C_s$ represents the stray capacitance associated with shielding, electrodes, and adhesion layer between the gold electrode and the glass. Contributions to the total impedance value can be expressed by the following:

$$
|Z_1| = \sqrt{R_s^2 + \frac{1}{(\pi f C_{dl})^2}}\quad |Z_2| = \sqrt{\frac{1}{(2\pi f C_s)^2}}
$$

where $f$ is the frequency, $Z_1$ is the impedance of $R_s$ and $C_{dl}$, $Z_2$ is the impedance of $C_s$, and $Z_{total}$ is the total impedance of $Z_1$ and $Z_2$. The current cannot pass through $C_s$ at low frequency. This results in an open circuit, and only the $C_{dl}$ and $R_s$ path is active and contributes to the total impedance. At high frequency, however, current passes through $C_s$, and $R_s$ and $C_{dl}$ can be ignored.

### III. Experiments and Results

#### A. Reagent and Analyte

Affinity-purified rabbit anti-\textit{E. coli} antibody (1.0 mL; 4.6 mg/mL) was purchased from ViroStat (Portland, ME) and was diluted with PBS (0.01 M, pH 7.4) from Fisher Scientific. MBs from Spherotech, Inc., were 4.5 µm in diameter and were coated by COOH-terminated SAMs on the surface. The activating reagents that couple anti-\textit{E. coli} antibody to the COOH-terminated SAMs on the MB are EDC and NHS, as purchased from Pierce. NaAc was obtained from Mediatech, Inc. Ethanolamine from Sigma was used as a blocking buffer. One-tenth molar solution of mannitol (Sigma-Aldrich) in DI water from Millipore (Milli-Q; 18.2 MΩcm) was used for washing and IS measurement. Simulated urine cocktail was prepared by mixing ingredients A and B in 1 L of sterilized DI water, and all chemicals are from Sigma-Aldrich, shown in Table I. \textit{E. coli K-12} (ATCC 10798) was obtained from American Type Culture Collection (Rockville, MD). The pure culture of \textit{E. coli K-12} was prepared in tryptic soy broth (BD, Franklin Lakes, NJ) at 37 °C for 24 h. For enumeration, pure cultures were serially diluted in PBS and were surface plated on nutrient agar plate (PML Microbiologicals), incubated at 37 °C for 20–24 h.

#### B. Test Procedure and Test Setup

Fig. 4 shows the test setup of the fabricated LOC \textit{E. coli} separator/sensor. Three different syringe pumps contain MBs with anti-\textit{E. coli} antibody, mannitol solution, and \textit{E. coli} K-12 in cocktail urine and deliver them to a six-way valve.
Fig. 4. Schematic of characterizing the fabricated LOC E. coli separator integrated with on-chip IS.

Fig. 5. Test procedure. (a) MB retention, direct E. coli separation from cocktail urine, and IS measurement in the concentration chamber. (b) MBs’ transfer and retention and IS measurement in the sensing chamber.

An LCR meter (Agilent E4908A) measured from 10 Hz to 1 MHz at the concentration and sensing chambers. Fig. 5 shows the test procedure. First, when valve 2 closed, mannitol solution flew into the separator at 1 µL/min, and MBs with anti-E. coli antibody were inserted, as shown in Fig. 5(a). The mannitol solution was used to allow E. coli to live and to enable impedance measurement as it has high impedance. Two permanent magnets were placed at the top and bottom of the concentration chamber, and they retained the MBs, which were then washed by mannitol solution for 15 min at 1 µL/min. Injected through the chip was 5 µL of cocktail urine containing different concentrations of E. coli K-12 and albumin. Once MBs captured E. coli K-12 in the cocktail urine, mannitol solution again flew to wash the concentration chamber for 15 min at 1 µL/min, and then, IS was performed using an LCR meter (E4980A Precision LCR Meter from Agilent Inc.). When valve 1 closed and valve 2 opened, the two permanent magnets above and beneath the concentration chamber were relocated at the sensing chamber, as shown in Fig. 5(b). Mannitol solution then transported MBs with E. coli K-12 from the concentration chamber to the sensing chamber at 1 µL/min. Then, the impedance was measured. Both electrode pairs in the concentration and sensing chambers were used as they were without any surface modification. At the end of each measurement, the E. coli separator was washed with 0.1-M sodium hydroxide for 30 min, DI water for 30 min, 0.1-M hydrochloric acid for 30 min, and DI water for 30 min.

Table II shows the step-by-step procedure of the microchip operation and associated time to complete each step. The total analysis time is roughly 100 min. Please note that this does not include fabricating microchips and immobilizing MBs with anti-E. coli antibodies. We assume that these steps are performed before the analysis. We used mannitol solution to rinse microfluidic channels and chambers. The rinsing step is used to ensure that we remove all unnecessary entities to enhance sensitivity of the microchip.

C. CE

One of the biggest advantages of using IMS is in capture efficiency (CE). Prior art using IMS reported up to 100% CE [32], [33]. We characterized CE in a single chamber configuration using a standard fluorescent intensity measurement. MBs having anti-E. coli antibodies were placed inside the chamber and were held by permanent magnets at the top and bottom of the chamber. After packing the chamber, we flew 3 µL of 10^7 E. coli/mL that were conjugated with red fluorescent dye and chemically dialyzed (E-2863; Invitrogen Inc.). Then, the permanent magnets were removed, and we collected the MBs with E. coli at the outlet. The fluorescent intensity was measured using an inverted microscope. We compared the measured fluorescent intensities to that of E. coli before being captured by MBs. We repeated the experiments for a different length of the column from 1 to 6 mm, as shown in Fig. 6. As the column length increased, CE improved; however, the applied fluidic pressure also increased. At the length of 3.2 mm, the fluidic pressure reaches 100 psi (structural failure point) based upon the geometry. This determined the channel length as 3 mm.

D. Results

Fig. 7 shows the bode plot and phase angle of the IS measurement and fitted impedance spectra for 6.4 × 10^8 CFU/mL of E. coli K-12 attached to the antibody of the MBs retained in the sensing chamber. The fitting was generated by ZSimp software [34], [35]. Mean errors of impedance and phase angle shown in Table III were 6% and 0.8°, respectively. Based on the phase angle, there are two distinct regions in the impedance spectra, which correspond to two elements in the equivalent circuit. The double-layer capacitance can be measured below 10 Hz; however, we were not able to measure it because the LCR meter cannot measure below 10 Hz. When the frequency is between 10 Hz and 10 kHz, current cannot pass through C_s, resulting in an open circuit in the equivalent circuit. Only the C_dl and R_s become active, but R_s is more dominant because the captured E. coli membrane becomes an insulator that increases
### Table II

<table>
<thead>
<tr>
<th>Step #</th>
<th>Description</th>
<th>Time [min]</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Preparation of <em>E. coli</em> sample</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Capture the MBs using two permanent magnets in the concentration chamber</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>Flow mannitol solution to rinse the microfluidic channels/chambers</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>Flow <em>E. coli</em> sample</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>Flow mannitol solution to rinse the microfluidic channels/chambers</td>
<td>30</td>
</tr>
<tr>
<td>6</td>
<td>Perform impedance spectroscopy measurements at the concentration chamber</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>Move and immobilize <em>E. coli</em>-conjugated MBs inside the sensing chamber</td>
<td>10</td>
</tr>
<tr>
<td>8</td>
<td>Perform impedance spectroscopy measurements at the sensing chamber</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td><strong>Total time required to complete the procedure</strong></td>
<td><strong>100 mins</strong></td>
</tr>
</tbody>
</table>

### Table III

<table>
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<tr>
<th>Component in IS equivalent circuit</th>
<th>Measured</th>
<th>Fitted</th>
<th>Error</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>R</em>&lt;sub&gt;s&lt;/sub&gt;</td>
<td>1.68 MΩ</td>
<td>1.68 MΩ</td>
<td>0.3%</td>
</tr>
<tr>
<td><em>C</em>&lt;sub&gt;s&lt;/sub&gt;</td>
<td>3.8 pF</td>
<td>3.9 pF</td>
<td>0.1%</td>
</tr>
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Fig. 6. CE of the *E. coli* separator as a function of the concentrator length. At 3.2 mm, the pressure inside the concentrator reaches 100 psi, which induces a structural failure. This sets our concentrator to be at 3 mm.

Fig. 7. IS measurement of 6.4 × 10⁸ CFU/mL *E. coli*.

the impedance [31], [36]. By contrast, *C*<sub>dl</sub> and *R*<sub>s</sub> become inactive at higher frequencies (above 10 kHz). The *E. coli* membrane becomes electrically invisible, and the value of *C*<sub>dl</sub> is larger than *C*<sub>s</sub>, contributing to all of the impedance changes at a frequency above 10 kHz.

We spiked *E. coli* K-12 and albumin in urine cocktail and repeated the separation/detection procedure in the concentration chamber [Fig. 8(a)]. A large impedance change was observed between high *E. coli* concentrations (6.4 × 10⁸ and 6.4 × 10⁷ CFU/mL) and the control (MBs with anti-*E. coli* antibody). On the other hand, low *E. coli* concentrations (6.4 × 10⁵ and 6.4 × 10⁴ CFU/mL) showed almost no impedance change. We believe that this is due to the masking effect of albumin (albumin absorbed on the electrodes). Thus, low concentration *E. coli* cannot be well discriminated. Moreover, impedance changes between the low concentration samples and the control are very large. The changes may cause a false-positive response. The albumin in the urine cocktail was absorbed on the gold electrode by hydrophobic interaction in the concentration chamber [37], [38]. In the higher *E. coli* concentration, *E. coli* was the dominant factor in increasing *R*<sub>s</sub> (medium resistance), but in the lower concentration, the albumin absorbed on the gold surface resulted in a constant impedance change.

Fig. 8(b) shows the IS measurement in the sensing chamber where MBs conjugated with *E. coli* were transported from the concentration chamber. Compared to the IS measurement in the concentration chamber, lower *E. coli* concentrations became clearly distinguishable in the sensing chamber. The impedance difference between 6.4 × 10⁸ and 6.4 × 10⁴ CFU/mL was approximately 60 kΩ at 1 kHz. Fig. 9 shows the impedance change at 1 kHz in the sensing chamber. A resistance change of 60 kΩ was observed between the 6.4 × 10⁸ and 6.4 × 10⁵ CFU/mL. The threshold of UTI is 10⁵ CFU/mL [22], [23]. Therefore, the IS measurement suggests that the LOC separator/detector is capable of evaluating urine samples for UTI.

Fig. 10 shows the sensitivity characterization of the LOC. We used the same simulated urine samples and spiked *E. coli* from 3.4 × 10⁷ down to 3.4 × 10³ CFU/mL. Impedance spectrums at 1 kHz in both concentration and sensing chambers were
Fig. 8. IS measurement for different *E. coli* K-12 concentrations ranging from $6.4 \times 10^4$ to $6.4 \times 10^8$ CFU/mL in the (a) concentration and (b) sensing chambers.

Fig. 9. Impedance spectrum of different *E. coli* concentrations at 1 kHz in the sensing chamber. The sensitivity in the concentration chamber (slope of the bars) is lower than that in the sensing chamber. Also, the minimum detectable concentration of *E. coli* in the sensing chamber is lower than that in the concentration chamber.

Fig. 10. Sensitivity of the microfluidic device in detecting *E. coli* (at 1 kHz). The sensitivity in the concentration chamber (slope of the bars) is lower than that in the sensing chamber. Also, the minimum detectable concentration of *E. coli* in the sensing chamber is lower than that in the concentration chamber.

concentration of $3.4 \times 10^4$ CFU/mL has 113 kΩ. The $3.4 \times 10^4$ CFU/mL minimum detectable concentration is lower than the threshold of UTI ($10^5$ CFU/mL).

WBC may be present in urine. Having more than 10 WBCs/µL in urine is considered to be a high chance of UTI [39]. We spiked 35 cells/µL WBC (from Innovative Research, Inc.) in the simulated urine cocktail having $3.4 \times 10^3$, $3.4 \times 10^5$, and $3.4 \times 10^6$ CFU/mL *E. coli* to see how WBC impacts the impedance measurements at the concentration and sensing chambers, respectively, as shown in Fig. 11. One can see a substantial gap of impedance measured between the control and the rest in the concentration chamber [Fig. 11(a)]. Also, the impedance measurements of three concentrations ($3.4 \times 10^4$, $3.4 \times 10^5$, and $3.4 \times 10^6$ CFU/mL) overlap each other, which we believe that it is due to the protein screening effect. On the other hand, the data in the sensing chamber [Fig. 11(b)] show a different pattern. There is no abrupt change of the measured impedance as the concentration increases. The impedance is roughly proportional to the *E. coli* concentration, as shown in Fig. 11(c). It is clear to observe that the measurements in the sensing chamber offered more consistent results than the ones in the concentration chamber when the samples were spiked by WBC.

Human urine can be very diverse, such as volume per day and pH of different age/sex groups [40]. We attempted to compare impedance responses of three different urine cocktails, as shown in Fig. 12: 20-, 40-, and 60-year-old females, respectively. We chose urine cocktails [40] for female only since up to 40% of women will develop UTI at least once during their lives [41]. The impedance measurements of the controls for three samples were largely different: 232 kΩ for 20-year-old control, 135 kΩ for 40-year-old control, and 799 kΩ for 60-year-old control. This is partially because we used three different microchips. However, it is notable that the impedance changes as a function of *E. coli* concentration showed different patterns from one to the other urine cocktails. The impedance of the 40-year-old samples showed a larger increase over that of the 20- and 60-year-old samples. It is hard to draw a conclusive evidence of any fundamental mechanism that describes the discrepancy of the three groups of samples, yet the measurements strongly suggest that the presented microchip must be calibrated for diverse nature of urine samples.
Fig. 11. Impedance spectrum of simulated urine samples having 35 WBCs/µL in three different E. coli concentrations in the (a) concentration and (b) sensing chambers. (c) Impedance comparison of concentration/sensing chambers at 1 kHz.

IV. CONCLUSION

In this paper, we have presented a microchip that is used to study UTI using simulated urine samples. The target microorganism to detect is E. coli, which is responsible for 80% of UTI. We designed a LOC which is equipped with dual chamber configuration that separates and measures the concentration of E. coli for UTI applications. MBs were conjugated with anti-E. coli antibody to capture E. coli and were transported from the concentration chamber to the sensing chamber. The integrated electrodes allowed IS to measure the concentration of the captured E. coli. The IS measurements between the concentration and sensing chambers showed that nonspecific binding from albumin could cause a false-positive response. We believe that this result comes from a hydrophobic interaction between the gold electrodes in the concentration chamber and albumin in UTI-infected urine. The IS measurement in the sensing chamber showed a significant impedance change to evaluate UTI: \( \sim 60 \) kΩ between \( 6.4 \times 10^4 \) and \( 6.4 \times 10^5 \) CFU/mL. The sensitivity of the LOC was characterized to be at least \( 3.4 \times 10^4 \) CFU/mL, which is less than the threshold of UTI (\( 10^5 \) CFU/mL). We have also characterized the LOC for the interference of WBCs to impedance measurements and for different urine cocktails, and no significant interference and discrepancy were observed. Our preliminary results using E. coli K-12 may suggest that the LOC E. coli separator/sensor can be used to detect UTI E. coli in human urine. Before testing a target bacteria (UTI E. coli), however, we will need to optimize the capture rate of the E. coli separator and to increase the sensitivity of IS measurements. The sensitivity of the device obviously needs to be improved. The threshold of UTI for asymptomatic individuals is generally given as \( 10^5 \) CFU/mL. However, the threshold can be as low as \( 10^2 \) CFU/mL for symptomatic patients or for those susceptible for recurrent infection [42], [43], and our current device is not sensitive in detecting such low concentration.

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