Conductometric analysis in bio-applications: A universal impedance spectroscopy-based approach using modified electrodes

Chiara Canali\textsuperscript{a}, Layla Bashir Larsen\textsuperscript{b}, Ørjan Grøttem Martinsen\textsuperscript{b,c}, Arto Heiskanen\textsuperscript{a,∗}

\textsuperscript{a} Department of Micro- and Nanotechnology, Technical University of Denmark, Produktionsstørket 423, 2800 Kgs Lystby, Denmark
\textsuperscript{b} Department of Physics, University of Oslo, Sem Sælands vei 24, Fysikkbygningen, 0371 Oslo, Norway
\textsuperscript{c} Department of Biomedical and Clinical Engineering, Oslo University Hospital, 0372 Oslo, Norway

\textbf{A R T I C L E   I N F O}

Article history:
Received 15 December 2014
Received in revised form 5 February 2015
Accepted 7 February 2015
Available online 16 February 2015

Keywords:
Electrochemical impedance spectroscopy
Universal protocol for impedance-based conductivity determination
Customised Matlab-based algorithm for automated spectral analysis
Protein-repellent electrode modification
Conductivity measurements in cell culture medium

\textbf{A B S T R A C T}

We present a universal protocol for quick and reproducible conductivity determinations in bio-applications using electrochemical impedance spectroscopy (EIS), electrode modification and automated spectral analysis. Two-terminal EIS measurements may be acquired using any standard impedance analyzer adjusting the applied sinusoidal potential and frequency range for spectral analysis. An implemented Matlab algorithm displays the acquired spectra, automatically identifies the frequency at which the phase angle (\(\psi\)) is closest to 0° and determines the impedance magnitude, i.e. the solution resistance (\(R_0\)). The corresponding conductivity value is immediately calculated as the ratio of the conductivity cell constant (\(\kappa\)), determined based on calibration, and \(R_0\). This protocol eliminates the need for evaluating a specific equivalent circuit followed by non-linear regression based curve fitting that is generally required in EIS-based conductivity determinations. The protocol is applicable to conductivity determinations using different conductivity cell configurations in any electrolyte solution regardless of its composition, i.e. in solutions with or without electroactive species that give rise to faradaic interface impedance. Conducted measurements showed high reproducibility in good agreement with a commercial conductometer in a wide range of ionic strengths up to five times that of physiological PBS. Since measurements in cell culture medium with bare gold electrodes indicated the need for recalibration to counteract the effect of biomolecule physisorption, the validity of the protocol was further extended using a protein-repellent coating of poly(ethylene glycol) methyl ether thiol self-assembled monolayer. This effectively eliminated electrode fouling, facilitating high reproducibility in repeated conductivity determinations in the presence of proteins.

© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Measurement of solution conductivity is a classical analytical technique that finds application in a wide variety of chemical and biochemical studies, e.g., evaluation of solvent purity, determination of relative ionic strength in solutions, assessment of critical micelle concentration, monitoring of enzymatic reactions and calculation of basic thermodynamic quantities [1], as well as biosensing [2,3]. Although bio-applications most frequently involve measurements in the physiological conductivity range [4,5], low conductivity solutions have been used for, e.g., impedance-based affinity biosensing [6,7], while high conductivity solutions are used as supporting electrolytes in voltammetric analysis, where concentrations may range up to 3 M [8,9].

Solution conductivity can be explained in terms of ionic mobility, which is directly proportional to temperature with an immediate effect of typically 1–3% per °C with respect to tabulated values at 25 °C. It is also influenced by shifts in pH; acidic or basic solutions increase conductivity since hydrated protons and hydroxyl ions are the most mobile cations and anions, respectively. Variation of conductivity over time may also convey a high degree of information about the chemical dynamics of biological processes. A culture medium containing proliferating or dying cells is an extremely heterogeneous chemical environment, the composition of which is continuously changing depending on cellular metabolism [10]. Conductivity of culture media was correlated to microbial concentration and fermentation activity already in 1898 [11], paving the way to impedance microbiology [12], which gained increased significance in the 1970s
with the emergence of frequency response analysers. However, although electrical impedance spectroscopy (EIS) potentially provides extensive information about electron transfer mechanisms, mass transfer phenomena and biochemical activity, the design of an optimised analytical strategy may be highly demanding [13]. Simplified approaches have been devised based on conductivity measurements. Parsons and Sturgis developed and tested a simple and relatively quick approach to correlate culture medium conductivity to the total amount of ammonia and amino nitrogen produced by putrefactive anaerobic bacteria [14,15]. Allison et al. extended this technique to metabolic studies on aerobes producing ammonia and lactic acid [10]. Similarly, cell culture medium conductivity may be a key parameter for analysing the complex dynamics that modulate mammalian cell cultures over time [16]. This is particularly relevant for biomedical research which is currently undergoing a shift of paradigm toward 3D cell cultures, needing new non-invasive on-line monitoring technologies [17,18]. Furthermore, EIS has already been shown to be a valuable tool for defining the porosity of 3D cell culture scaffolds by yielding the conductivity of the bulk electrolyte filling the pores [19,20].

The simplest approach for conductivity determination is to apply an alternating electric field between two electrodes and measure the impedance magnitude as an estimation of the solution resistance ($R_S$), which can be used to calculate conductivity. Alternating current at frequencies above 1 kHz should be used instead of direct current that may lead to electrolysis and electrode polarization [21]. Commercial conductometers are standalone devices which typically operate maximally at few predetermined frequencies. During calibration using a conductivity standard solution, an internal algorithm selects the frequency value depending on the conductivity range to give an accurate estimation of $R_S$. However, the algorithm may vary between manufacturers and depending on the instrument quality, increasing the possibility of systematic errors in the analysis. Moreover, although commercially available conductivity sensors are manufactured from robust metals, e.g., platinum, stainless steel and titanium, that provide high mechanical stability, they are not designed for measurements in biological solutions. Biomolecule adsorption on the electrode surface increases the measured impedance, hence, yielding a lower apparent conductivity value.

EIS-based conductivity measurements, relying on analysis of complete spectra using equivalent circuits, have been proposed in order to eliminate the need of choosing a specific frequency that may result in measurement inaccuracy [22]. To our best knowledge, such approach has been used especially for lab-on-a-chip devices in impedance microbiological applications [23–25]. Generally, such analysis depends on the electrolyte composition and hence, whether the measured impedance is contributed to by faradaic and/or non-faradaic processes. Additionally, the structure/geometry of a conductivity cell imposes requirements on the used equivalent circuit [22], especially when microfabricated devices having interdigitated electrodes (IDEs) are used [26]. Hence, this approach complicates conductivity determinations, requiring a different equivalent circuit depending on the composition of the used electrolyte solution [13,27] or structure of the conductivity cell [22,26].

To avoid the limitations described above, we hereby present a universal protocol that relies on acquisition and automated analysis of complete impedance spectra as the basis for quick conductivity determinations, as well as electrode modification applicable for measurements in biomolecule containing electrolytes. Conventional two-terminal EIS measurements can be used with the flexibility of choosing both the sinusoidal potential of excitation and frequency range for analysis. A Matlab-based algorithm displays Bode plots for impedance magnitude ($|Z|$) and phase angle ($\varphi$) while it automatically identifies the most suitable frequency for determining $R_S$, i.e., $|Z|$ at the frequency where $\varphi$ is closest to 0°. This approach provides two major advantages: the calculated solution conductivity value is (1) based on an accurately determined $R_S$ unlike in the case of an algorithm relying on a few predetermined frequencies, and (2) independent of validation and analysis of a specific equivalent circuit. A commercial conductometer was used for validation and a good agreement between the two methods was found for ionic strength (1) values up to five times that of physiological PBS. Our universal protocol facilitated stable, precise and accurate measurements using inexpensive electrodes and a standard impedance analyser. Moreover, the validity was further extended to conductivity measurements in biomolecule containing electrolytes (i.e., cell culture medium). The influence of protein physiosorption on conductivity determination was eliminated using a protein-repellent self-assembled monolayer (SAM) modification of poly(ethylene glycol)-terminated alkanethiol. High precision and reproducibility was achieved in repeated measurements in cell culture medium without the requirement for recalibration during measurements or labour-intensive electrode cleaning after measurements.

2. Materials and methods

2.1. Chemicals and solutions

Potassium hydroxide (semiconductor grade), hydrogen peroxide (30% solution in water), cell culture tested PBS (physiological and 10× concentrate), Roswell Park Memorial Institute medium 1640 (RPMI), fetal bovine serum (FBS), penicillin/streptomycin (P/S), and poly(ethylene glycol) methyl ether thiol (mPEG, average Mₐ 800) were purchased from Sigma–Aldrich Corporation (St. Louis, MO, USA). Electrochemical measurements were performed on serial dilutions of PBS in the range of 0–1.5 M NaCl (chemical composition of the 10× concentrate given by the supplier: 0.03 M Na(P0₄)₂ . 1.5 M NaCl, 0.0105 M KH₂PO₄). Ultrapure deionized water (18.2 MΩ cm) from Milli-Q system (Millipore Corporation, Billerica, MA, USA) was used for diluting PBS samples and rinsing electrodes. Standard solutions of known conductivity ($8.4 \times 10^{-2}, 1.4 \times 10^{-2}, 1.3, 11.2 \text{S/m}$) were purchased from Hanna Instruments (Kungsbacka, Sweden).

2.2. Measurement protocol

Prior to the first EIS measurement, gold plate electrodes, fabricated by e-beam evaporation on oxidized silicon wafers as previously described [18,20], were cleaned by a 10-min treatment with a mixture of 25% (v/v) H₂O₂ and 50 mM KOH followed by a potential sweep from −200 mV to −1200 mV in 50 mM KOH [27]. Electrodes were mounted on a 3D printed conductivity cell as described in Supplementary Information S1 and shown in Fig. S-1. Impedance spectra were acquired using a Reference 600 potentiostat (Gamry Instruments, Warminster, PA, USA). An alternating potential (rms) of 10 mV was applied in the frequency range between 10 Hz and 1 MHz. The geometrically determined cell constant ($k$) was verified by acquiring and analysing three EIS spectra in triplicate samples of each conductivity standard solution. This allowed calculation of the experimental value for $k$, which is defined as the product of the solution conductivity and solution resistance ($R_S$). The results are presented as average ± standard error of mean (s.e.m.), $n = 9$. EIS data processing for automated generation of Bode plots and conductivity determination were implemented as a Matlab (version R2012b) script (detailed description in Supplementary Information S2). For-loops allowed presentation of spectra acquired in different solutions in the same Bode plot ($|Z|$ or $\varphi$). To calculate the
conductivity, $R_5$ was determined based on the $|z|$ value in a frequency range where $\phi$ is closest to $0^\circ$. This was computed using the $\min(X,Y)$ function. Three EIS spectra were acquired in triplicate samples of different PBS dilutions. The relationship between calculated conductivity and $I$ (approximated by NaCl concentration) was determined and validated against the performance of a commercial conductometer (CDM S2, Radiometer Analytical, Copenhagen). The results are presented as average ± s.e.m., $n = 9$. All the measurements were conducted at room temperature in solutions exposed to atmospheric CO$_2$.

2.3. Electrode modification for bio-applications

Three EIS spectra were acquired in triplicate samples of cell culture medium. Before and after measurements in cell culture medium, three samples of physiological PBS was analysed to evaluate the influence of medium serum proteins on the electrode performance. The results are presented as average ± s.e.m., $n = 9$. Then, three sets of electrodes were used for measurements after modification with 10 mM mPEG in water for 16 h. The results are presented as average ± s.e.m., $n = 27$. Impedance measurements were performed as described in Section 2.2. CO$_2$ level in cell culture medium samples was equilibrated in an incubator (5% CO$_2$/95% air) for 30 min prior to measurements. Between measurements in different samples, electrodes were rinsed using Milli-Q water.

3. Results and discussion

3.1. Analysis of PBS dilutions

As first validation of our universal protocol, EIS spectra were acquired in samples of different PBS dilutions (range of 0–1.5 M NaCl) and analysed using the custom-made Matlab algorithm (Supplementary Information S2) that presents data as Bode plots (Fig. 1a, b) and determines $R_5$ in a frequency range where $\phi$ is approximately $0^\circ$ (Fig. 1b). The corresponding conductivity was calculated as the ratio between the conductivity cell constant ($\kappa$) and $R_5$. The calculations were based on the experimentally determined $\kappa$, 1.77 ± 0.02 cm$^{-1}$ (average ± s.e.m., $n = 9$), obtained by calibration in standard solutions with known conductivity. The geometric definition of $\kappa$ is the ratio between the distance of the electrodes and the area exposed to the solution. Based on these factors, $\kappa$ was calculated to be 1.85 cm$^{-1}$ (Fig. S1b), indicating a good agreement between the experimental and geometric value.

The relationship between the determined conductivity and the ionic strength ($I$) of the PBS dilutions showed very high reproducibility, the overall relative standard error (RSE%) for all the dilutions being only 0.5%. The value also comprises measurements in solutions with very low conductivity, which are more prone to be affected by artifacts due to parasitic conduction paths [28,29]. This means that in solutions with higher conductivity, such as those around physiological $I$, the obtained variation in measurements was even lower than the above mentioned overall RSE%. Corresponding measurements using the commercial conductometer resulted in an overall RSE% of 3.0%, which is clearly higher than the value obtained with our universal protocol. Further comparison between the methods is shown in Fig. 2. The linear correlation between the determined conductivity and calculated $I$ of the PBS dilutions shown in Fig. 2a indicates that the coefficient of determination ($R^2$) for our universal protocol was slightly higher (0.998) than the one obtained for the commercial instrument ($R^2 = 0.991$). The general observation based on Fig. 2a is that both approaches show good agreement in conductivity determination for solutions reaching five times the $I$ value of physiological PBS ($I = 8.12 \times 10^{-3}$ M).

However, for highly concentrated electrolytes (10 times the $I$ of physiological PBS), the commercial conductometer deviated significantly from the value obtained using our universal protocol, which retained linearity throughout the used $I$ range. Performed regression analysis (Fig. 2b) indicated a very good agreement ($R^2 = 0.999$) until $I$ five times that of physiological PBS. These results showed that the established universal protocol provides stable, accurate and reproducible measurements in a wide conductivity range.

The impedance spectra acquired in the PBS dilutions were also used to define four frequency ranges applicable for quicker determination of conductivity with single frequency analysis: (1) 1–4 kHz for very low conductivity solutions ($I < 1.62 \times 10^{-3}$ M); (2) 20–50 kHz for low conductivity solutions $(1.62 \times 10^{-3} < I < 8.12 \times 10^{-2}$ M); (3) 200–250 kHz for solutions close to the physiological $I$ $(8.12 \times 10^{-2} < I < 1.62 \times 10^{-1}$ M); (4) 300–400 kHz for solutions above the physiological $I$ ($I > 1.62 \times 10^{-1}$ M).

In the above described conductivity determinations based on EIS measurements, the applied sinusoidal potential was 10 mV$_{\text{rms}}$ and the used electrodes had large area with a deposited thin gold film. When using an impedance analyser, the amplitude of the sinusoidal potential may be freely chosen as long as it ensures linearity of the current–voltage response. However, despite the chosen potential amplitude, the measured impedance, and hence
3.2. Electrode modification for bio-applications

To further evaluate the validity of the presented universal protocol for conductivity measurements in biomolecule-containing electrolytes, we determined the conductivity of cell culture medium containing serum proteins. Physisorption of biomolecules on bare gold surfaces is well-known. To easily see the effect of electrode fouling, we determined the conductivity of physiological PBS before and after measurements in cell culture medium. The performed conductivity measurements clearly indicated that the used electrode surfaces were foulsed by physisorbed biomolecules, requiring intensive electrode cleaning and recalibration after each measurement. Therefore, we optimised a protein-repellent electrode modification using self-assembled monolayer (SAM) of a poly(ethylene glycol)-terminated alkanethiol. This approach eliminated the need for labour-intensive electrode cleaning and recalibration that are crucial when using a commercial instrument.

### 3.2.1. Effect of biological solutions on bare gold electrodes

The impedance spectra presented in Fig. 3a indicate that the spectral behaviour is in accordance with the one previously shown...
Table 1. Influence of biomolecule-containing electrolytes on conductivity measurements: conductivity [S/m] values for physiological PBS and cell culture medium determined using bare and mPEG-modified gold electrodes.

<table>
<thead>
<tr>
<th>Type of electrolyte</th>
<th>Conductivity [S/m]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bare gold electrodes</td>
<td></td>
</tr>
<tr>
<td>PBS before measurements in cell culture medium</td>
<td>1.66 ± 0.01</td>
</tr>
<tr>
<td>PBS after measurements in cell culture medium</td>
<td>1.12 ± 0.01</td>
</tr>
<tr>
<td>PBS after measurements in cell culture medium and recalibration</td>
<td>1.49 ± 0.01</td>
</tr>
<tr>
<td>Cell culture medium (RPMI)</td>
<td>1.55 ± 0.01</td>
</tr>
<tr>
<td>mPEG-modified gold electrodes</td>
<td></td>
</tr>
<tr>
<td>PBS before measurements in cell culture medium</td>
<td>1.595 ± 0.007</td>
</tr>
<tr>
<td>PBS after measurements in cell culture medium</td>
<td>1.603 ± 0.007</td>
</tr>
<tr>
<td>Cell culture medium (RPMI)</td>
<td>1.44 ± 0.01</td>
</tr>
</tbody>
</table>

* Conductivity values are reported as average ± s.e.m., n = 9.
* Conductivity values are reported as average ± s.e.m., n = 27. Three sets of electrodes were evaluated.

for PBS dilutions (Fig. 1). The decrease in conductivity corresponds to a slight upward shift in the Bode plots for |Z| at frequencies above 200 Hz and a clear separation above 5 kHz. Values of conductivity were calculated in the frequency range proposed for performing measurements on solutions with I close to the physiological range, further confirming that the protocol is fully suitable for single frequency analysis. Table 1 summarises the determined conductivity values for PBS and cell culture medium. The obtained results clearly show that measurements in cell culture medium influenced the behaviour of bare gold electrodes. The conductivity value determined for PBS before measurements in medium agreed well with previously shown results [30], whereas after electrode exposure to biomolecules the determined conductivity was clearly lower. Moreover, despite the small distribution of the determined conductivity values (s.e.m.) for cell culture medium, the individual measurements showed a clear trend in terms of decreasing conductivity, which indicates that even during a series of measurements in a biological solution the individual measurement results may be influenced by electrode fouling. When performing conductivity measurements using a commercial conductometer, which has fixed electrodes, calibration using conductivity standard solutions may alleviate the effect of exposure to biomolecule-containing electrolytes. To evaluate this possibility, we recalibrated our conductivity cell after measurements in cell culture medium and repeated conductivity determination of physiological PBS. The obtained result (Table 1) indicates that, despite recalibration, the determined conductivity was still lower than obtained in the original measurements prior to any exposure to cell culture medium. Extensive cleaning might improve electrode behaviour in subsequent measurements; however, it would easily deteriorate the performance of microfabricated thin-film electrodes, shortening their lifetime. This encourages the use of modified electrodes with a stable protein-repellent SAM so that they can be applied to a series of measurements without the influence of electrode fouling.

3.2.2. Effect of biological solutions on mPEG-modified gold electrodes

Analogously to chemical electrode modifications, which behave as capacitors in series with the double layer capacitance [27], adsorbed biomolecules also change the capacitive behaviour of the electrode–electrolyte interface. Results described in Section 3.2.1 clearly indicate that |Z| increases as a consequence of measurements in biomolecule-containing electrolytes when using bare gold electrodes. To eliminate this effect and be able to conduct EIS measurements without the need for extensive electrode cleaning and/or recalibration after each measurement, we evaluated the possibility of using electrodes modified with a protein-repellent coating. Polyethylene glycol (PEG) is a nontoxic and non-immunogenic polymer which is able to decrease attractive forces between solid surfaces and proteins. Harder et al. showed how this ability is related to PEG molecular conformation and becomes most effective when PEG chain length allows the formation of dense and predominantly helical films of PEG [31]. They speculated that the helical conformation may correlate with the degree of solvation and, consequently, with the stability of the interfacial layer of water, which may repel proteins reaching the electrode surface by diffusion. Hence, PEG-terminated alkanethiol SAMs on gold surfaces have been successfully used to facilitate selective cell patterning and reduce surface fouling [32].

To readily modify gold surfaces and increase the biocompatibility, we used water soluble mPEG-terminated alkanethiol. Initial tests followed by EIS characterisation indicated that a modification time of at least 16 h yielded a robust well-behaved functionalization (data not shown). Three sets of electrodes were calibrated after mPEG modification and k was calculated to be 1.52 ± 0.01 cm⁻¹ (average ± s.e.m., n = 9). Based on the geometric factors, k resulted 1.85 cm⁻¹. The larger difference between the calculated and the geometrically determined k is due to the fact that although k is generally referred to as the ratio between electrode distance and area, calibration takes into account the condition of the electrode–electrolyte interface, which is different for chemically modified electrodes in comparison with non-modified ones. Fig. 3b shows a set of averaged impedance spectra for PBS and cell culture medium acquired using three sets of modified electrodes (three repetitive spectra acquired for each electrode set in three electrolyte samples). Each spectrum is reported as average ± s.e.m. (n = 27). In the frequency range 200–250 kHz, where ω is approximately 0°, the spectra acquired in PBS before and after measurements in cell culture medium completely overlap, which means that the mPEG modification was able to protect the electrode surface from the influence of physiosorbed biomolecules. The spectra acquired in PBS indicate that the measurements in cell culture medium only had a slight influence on the capacitive behaviour of the electrodes as seen in the shift of ω at frequencies below 100 Hz. The conductivity values for PBS are shown in Table 1 and agree well with values reported in literature [30]. Moreover, the values shown in Table 1 also indicate that, on virtue of the electrode modification, the conducted measurements are highly reproducible between sets of electrodes.

4. Conclusions

We established and verified a universal protocol for quick conductivity determinations using electrochemical impedance spectroscopy (EIS) and electrode modification for bio-applications with high reproducibility. The approach relies on simple spectral analysis to determine the frequency at which the phase angle (ω) is closest to 0°. The impedance magnitude (|Z|) at that frequency corresponds to the solution resistance (Rₛ), which can be used to calculate the conductivity. Unlike commercial instruments, typically operating at a few predetermined frequencies, which, depending on the solution composition, may not yield an accurate estimation of Rₛ, our universal protocol, based on analysis of complete spectra, has the advantage that Rₛ and consequently the corresponding conductivity, can be determined with certainty independent of the solution composition. A Matlab-based algorithm was implemented to display impedance spectra as Bode plots and automatically identify the suitable frequency for determining Rₛ and calculating solution conductivity. The universal protocol gave results in good agreement with a commercial conductometer in a wide range of electrolyte solutions for ionic strength up to five times that of physiological PBS. The validity of the protocol was extended to bio-applications by applying an optimised electrode modification method using a protein-repellent coating.
of poly(ethylene glycol) methyl ether thiol. This allowed precise and reproducible conductivity determinations without influence of electrode fouling, which clearly affected measurements with non-modified electrodes. Our universal protocol combined with protein-repellent electrode modification provides a fast and simple way of performing programmed conductivity monitoring using any impedance analyser, opening possibilities for diverse applications, ranging from biosensing to cell-based assays and microbiological studies. Moreover, the entire protocol for data treatment and electrode modification may be particularly beneficial for the development of stable, precise and accurate miniaturised devices.

Acknowledgements

This work and the Ph.D. fellowship of C.C. were supported by the EU-funded project NanoBio4Trans (“A new nanotechnology-based paradigm for engineering vascularised live tissue for transplantation”, grant no: 304842). Additionally, A.H. acknowledges Lundbeck Foundation (grant no. R69-A6408) for financial support.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.snb.2015.02.029.

References


Biographies

Chiara Canali received the M.Sc. degree in pharmaceutical biotechnology (summa cum laude) from University of Bologna in Italy in 2011. From 2009 to 2012 her research projects were focusing on bioanalytical chemistry and bioluminescence imaging working at University of Bologna, Leiden University Medical Center and Institut Polytechnique de Grenoble. She is currently a Ph.D. student at the Technical University of Denmark (Department of Micro- and Nanotechnology). Her project is focused on the design of bioimpedance-based sensing for applications in tissue engineering.

Layla Bashir Larsen is postdoc at the Technical University of Denmark (Department of Micro- and Nanotechnology). She is a biomedical engineer with a Ph.D. degree in Micro and Nano-engineering (University of Birmingham, UK) and prior clinical experience (within the National Health Service, UK) in the field of rehabilitation engineering. Her research focuses on the applications of engineering in medicine and includes development of sensors, microfluidic devices and tissue engineering support systems.

Ørjan Gottum Martinsen is professor at the University of Oslo (Department of Physics) since 2002 and head of the Bioprocess group. He also has a part time position as researcher at the Department of Clinical and Biomedical Engineering at Oslo University Hospital. He became elected member of the Royal Norwegian Society of Sciences and Letters in 1995 defending a thesis on the electrical properties of human skin. His research mainly focuses on the passive electrical properties of biological materials and applications of bioprocess impedometry in medicine, biology and physiology. His particular expertise is within bioimpedance basic theory, instrumentation, electrode systems and modeling. He is co-editor in chief of Journal of Electrical Bioprocess (JEB) and President of the International Society for Electrical Bioprocess (ISEBI).
Arto Heiskanen is associate professor at the Technical University of Denmark (Department of Micro- and Nanotechnology) focusing on the development of microfluidic systems with electrochemical detection for cell-based applications. He received the B.Sc. degree in biochemistry from Åbo Akademi University, Turku, Finland, in 1987, the B.Sc. degree in chemistry from the University of the Philippines, Diliman, Quezon City, in 2001, and both the M.Sc. degree in 2004 and the Ph.D. degree in 2009 from Lund University, Lund, Sweden. He has coauthored over 50 peer-reviewed publications on electrode fabrication and modification as well as development of microfluidic platforms for applications in electrochemical monitoring of cellular functions.