

Electrical Impedance Spectroscopy as a Powerful Analytical Tool for Monitoring Microbiological Growth on Medical Implants

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INTRODUCTION

Hospital-acquired infections (HAI) are defined as infections that are neither present nor incubating when a patient enters the hospital (Bourn, 2000). Their effects vary from discomfort to prolonged or permanent disability and they may contribute directly or substantially to a patient's death. HAI's are estimated to cost the National Health Service (NHS) in England £1 billion annually (Bourn, 2000) with as many as 5,000 patients dying as a result of acquiring such an infection (Anon, 2001). Not all hospital-acquired infections are preventable but Infection Control Teams believe that they could be reduced by at least 15%, with yearly savings of £150 million (Anon, 2001). Central intravascular catheters have been found to be a common source of infection. Catheters can become infected via a number of different routes with the infection proliferating in multiple areas along the catheter surface. It has been reported that over 40% of the identified micro-organisms causing hospital-acquired infection were *Staphylococci*, an organism that is typically found on the natural skin flora (Bourn, 2000).

If an infection associated with the device is suspected, clinicians can either treat the infection with antibiotics or replace the catheter. Both of these methods increase patient discomfort, place an additional workload upon hospital staff, drain hospital resources, and increase the patient's length of stay within the hospital. It would be hugely beneficial to patients and clinicians if the onset of subclinical biofilm formation on medical implants could be detected, and thus treated, at an early stage.

The idea of using impedance to monitor bacterial growth is not a new one; indeed impedance microbiology was first introduced over 100 years ago (Stewart, 1878). Traditional impedance microbiology involves the application of a sinusoidal voltage or current typically across two-electrodes and the resulting impedance (or conductance) response is monitored at only one-frequency during the growth of the micro-organism under investigation. Although the area has shown promise, advances have been limited. The majority of published works have focused on changes in the bulk electrolyte with few studies examining the electrode-electrolyte interface and only a few recent studies have

examined the development of sensors for monitoring bacterial growth (Gomez, Bashir, & Bhunia, 2002; Gomez et al., 2001; Oliver et al., 2006; Yang, Li, Griffis, & Johnson, 2004).

An alternative to monofrequency measurements is Frequency Response Analysis using Electrical Impedance Spectroscopy (EIS) and equivalent circuit modelling. When used to study electrochemical systems, EIS can give accurate, kinetic, and mechanistic information using a variety of techniques and output formats. For example, consider a small alternating voltage of known angular velocity, (ω) and small amplitude (v) applied to the system under investigation. The current response (i) and phase difference (ϕ) of the resultant waveform is measured for a range of applied frequencies (ω). The relationship between the applied voltage and resultant current waveform is the impedance (Z) of the system. During measurements, the amplitude of the applied perturbation waveform is carefully controlled to ensure minimal disturbance to the test system. EIS is therefore considered to be a nondestructive and safe method for studying biological systems. Established AC and electrochemical theory can be used to characterise the impedance of the electrochemical cell and to represent it in terms of an equivalent circuit model.

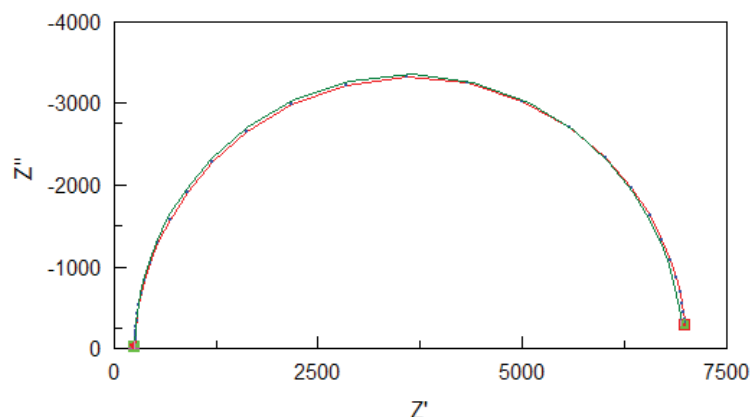
BACKGROUND: IMPEDANCE MICROBIOLOGY

The need to monitor bacterial growth effectively is apparent in the areas of food science, water quality, and

medicine. However, there have been relatively limited advances in improving the means of detecting microbial growth. Conventional detection methods require long sample turnaround times, have low reproducibility, produce high error rates, and are costly in terms of labour (Noble, 1994). Automating microbiological detection would be advantageous as it would increase productivity and relieve human beings from having to perform mundane, menial, and repetitive tasks (Trotman, 1978). Impedance microbiology has been presented as a mechanistic alternative to monitoring the growth of bacteria and has become an accepted method of monitoring growth of micro-organisms in the brewing industry. Although this acceptance has been a promising advance, the monofrequency method used to date limits the potential of the technique. In the microbiology field, there have been relatively few studies which have explored the multifrequency impedance analysis method. It is proposed that a multifrequency approach will not only facilitate the monitoring of microbial growth rates but will also provide a means of monitoring microbial-environment interactions.

Electrical impedance spectroscopy differs from traditional impedance microbiology measurements in that it measures the impedance response over a wide range of frequencies and the data can be modelled using an equivalent circuit which can be interpreted in terms of the electrochemical reactions occurring within the system. The combination of a multifrequency approach, improved electrode design, and the use of meaningful equivalent circuit modelling enables the simultaneous examination of the electrode-electrolyte interface and

Figure 1. A typical complex impedance plot showing one partial semi-circular arc



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