Bacteria detection with interdigitated microelectrodes: noise consideration and design optimization

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Abstract

Impedimetric biosensors are promising for label-free, real-time, sensitive and selective detection of bacteria. However, these sensors do typically not detect below $10^3$ colony forming unit (CFU) per ml in absence of dielectrophoresis and labels. This work shows that the noise source due to random distributions of bacteria on the biosensor surface strongly restricts the limit of detection (LOD) for an interdigitated microelectrode (IDE) configuration. 3D finite-element simulations also indicate that the bacteria diameter and the surface coverage influence both the sensitivity and the signal-to-noise ratio (SNR). Optimization of the IDE design suggests that the SNR is maximized, i.e., the LOD is minimized, as the electrode gap is approximately five times the bacteria diameter and the electrode width and thickness are minimized and maximized with regards to current technological limitations, respectively. The paper finally highlights the critical design trade-off between SNR and sensitivity maximization.

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1. Introduction

Detecting ultra-low concentrations of bacteria in solution and in few minutes is an urgent matter for environmental and hospital safety. Despite improvements compared to the traditional SPR method [1], interdigitated microelectrodes (IDEs) for impedimetric measurements are still limited to the $10^3$–$10^6$ CFU/ml range [1-4]. Optimization of the sensitivity to bacteria were reported for large electrode dimensions (> 10 μm), showing that the electrode perimeter and area must be maximized and minimized, respectively [4]. Simulations of IDEs has also focused on improving the sensitivity to bacteria, but

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usually appear inaccurate, as they consider only fixed patterns of cylindrical-shape bacteria and 2D simulations [5].

In this paper, we show that the noise due to random distribution of bacteria on the IDE surface strongly restricts the limit of detection (LOD). By performing an exhaustive statistical analysis of the sensor impedance variation due to captured bacteria on the sensor surface, we show the strong influence of the bacteria diameter, electrode geometry and surface coverage on the transducer noise source. To reduce the LOD, we investigate which electrode design maximizes the signal-to-noise ratio (SNR). We show that the optimization based only on sensitivity maximization drives conflicting conclusions. With these electrode design considerations, this paper suggests that LOD below $10^3$ CFU/ml can be achieved.

2. Model

To avoid previous reported limitations, we have implemented 3D finite-element simulations of pseudo-random configurations of bacteria on a two-electrode system topology (Fig. 1). The real and imaginary parts of the admittance between electrodes are extracted at 10 MHz. The double electrical layer is not modeled since the double layer capacitance prevails only at low frequencies. The multi-shell model for bacteria must be considered as the frequency is varying [6]. In our case, we simply model bacteria as spheres with an equivalent relative permittivity and conductivity. As bacteria are captured on the surface, the dielectric properties of the medium between electrodes are altered and therefore the admittance changes. The sensitivity expresses this change $|\Delta Y|$ with regards to the initial admittance $Y_0$:

$$S = \frac{|\Delta Y|}{Y_0}, \quad (1)$$

and the SNR is defined as the ratio in decibels (dB) between the mean and standard deviation of the admittance change:

$$SNR = 20 \log_{10}(|\Delta Y| / \sigma_Y). \quad (2)$$

| Parameters                      | Values |
|---------------------------------|--------|
| Bacteria diameter               | 1 µm   |
| Bacteria relative permittivity  | 200    |
| Bacteria conductivity           | 0.1 S/m|
| Medium conductivity             | 0.01 S/m|
| Medium relative permittivity    | 80     |
| Electrode length                | 10 µm  |

Fig. 1. 3D representation of random distributions of bacteria on the IDE surface and parameters used for simulations.

3. Transducer noise source

To extract statistical information (mean and standard deviation), forty random distributions of bacteria over the sensing area were implemented at a fixed surface coverage ranging from 0 to 100%. Due to the higher relative permittivity and conductivity of bacteria, the mean sensitivity increases with the surface coverage (Fig. 2(a)). The linearity is explained by the proportional dependence of the volume occupied by bacteria between electrodes with the surface coverage. Fig. 2(a) also highlights the physical nature of the transducer noise, which is maximal as half the bio-surface is saturated with bacteria. In contrast, empty and full surface coverage show a zero standard deviation.
Fig. 2. Influence of the surface coverage on the mean and standard deviation of the sensitivity (a) and on the SNR (b). Bacteria have a 1 μm diameter and the electrode thickness, width and gap are 0.5 μm, 1 μm and 2 μm, respectively. Influence of the bacteria diameter on the sensitivity and the SNR at a fixed surface coverage (c). The electrode thickness, width and gap are 0.5 μm, 5 μm and 2.5 μm, respectively.

To highlight the relative importance of noise compared to the mean admittance, we computed the SNR based on Eq. (2). As shown in Fig. 2(b), more captured bacteria lead to higher admittance variations compared to the noise floor so that the SNR increases with the surface coverage. The limit of detection is defined as the bacteria concentration at which the SNR is equal to five or equivalently to 14 dB [7]. In this particular geometry, the LOD corresponds to approximately 20% of surface coverage by bacteria (Fig. 2(b)). This value can be troublesome to achieve detection of bacteria concentration lower than 10^3 CFU/ml.

For a given electrode geometry, the size of considered bacteria has a strong impact on figures of merits. If the bacteria diameter decreases by a scaling factor S, the number of bacteria must increase by S^2 to keep the surface coverage identical. On the other hand, the total volume per area occupied by bacteria between electrodes decreases by S. These two phenomena explain the smaller sensitivity and larger SNR in Fig. 2(c).

On the other hand, if the microelectrode geometry is scaled identically to the bacteria diameter, simulations show that both the SNR and the sensitivity are unchanged. Figures of merit (sensitivity, SNR, LOD) are therefore identical for constant geometry to bacteria diameter ratios.

4. Electrode design optimization

As suggested by Fig. 2(b), it is required to push the SNR curve up in order to reduce the LOD. The maximal averaged SNR is achieved as the electrode gap is approximately five times the bacteria diameter and the electrode thickness is maximized, with regards to micro-fabrication constraints. Smaller electrode gaps result in strong dependence to bacteria positions, increasing the standard deviation and reducing the SNR. On the other hand, larger electrode gaps reduce the mean admittance change with regards to its standard deviation, decreasing the SNR value.

However, this optimal electrode design does not maximize the sensitivity. As shown in Fig. 3(b), the mean sensitivity is indeed larger for smaller electrode gaps but the electrical response is noisier. This trade-off between SNR and sensitivity maximization is solved with regards to electrical readout circuit performances [8]. If the lower detectable admittance change by the readout circuit is smaller than the
LOD defined by the previously reported SNR, then the designer must choose the electrode gap maximizing the SNR. However, if the readout circuit is not sensitive enough, the designer must minimize the electrode gap to improve the sensitivity, even if the SNR decreases.

Fig. 3: (a) Influence of the electrode gap and thickness on the SNR. The electrode width is 1 μm. (b) Influence of the electrode gap on the sensitivity and the SNR. The electrode width and thickness are 1 μm and 3 μm, respectively.

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