Development of flexible process to manufacture lab on Chip systems on polymer substrates to predict the first earlier detection of the transplanted organs rejection

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Abstract:

Heart failure (HF) is the most increasing cause of death in Western Countries. For that reason, together with the difficulty of having a sufficient number of donor organs, it is recognized that the device-based therapeutic approaches will assume an increasingly important role in treating the growing number of patients with advanced heart failure, not only as bridge to transplant, but also as destination therapy, by considering also the ageing population. In fact, HF is primarily a disease of the elderly. Approximately 6% to 10% of people older than 65 years have HF, and approximately 80% of patients hospitalized with HF are more than 65 years old. During the last 10 years, the annual number of hospitalizations has increased from approximately 550,000 to nearly 900,000 for HF as a primary diagnosis and from 1.7 to 2.6 million for HF as a primary or secondary diagnosis. Nearly 300,000 patients die of HF as a primary or contributory cause each year, and the number of deaths has increased steadily despite advances in treatment.

Clinical inflammation is both a cellular and biochemical event (1-3). Both pro-inflammatory cytokines such as Tumour necrosis factor-alpha, Interleukin-1, and Interleukin-6 and anti-inflammatory cytokines such as interleukin 10, and interleukin 1 receptor antagonist are participants in the basic inflammatory process and mediators of cellular infiltration (4-5). These biomarkers are at high level in the serum of patients experiencing a cytokine storm.

Increasing need for a fast, real-time and reliable medical diagnosis has led to growing interest in new point-of-care biological sensors capable of the sensitive and specific detection of biomolecules [6]. Lab on Chip field constitutes a peculiar research area of SensorART project. From the evaluation of early detection of inflammation and/or sepsis markers as well as water retention sensor for heart failure monitoring in patients with VADs.
This work surveys a few of the emerging Lab on a chip technologies based on the combination of the “Soft” fabrication techniques and Self-assembled monolayers (SAMs) at Laboratoire de Sciences Analytiques (LSA) for improved, inexpensive health care. The developed lab-on-a-chip system is devoted to the detection of Tumour Necrosis Factor-alpha (TNF alpha) as a biomarkers in the serum of patients experiencing an inflammation due to the rejection of the transplanted organ. The Lab on a Chip is based on a flexible polymer substrate (Polyimide or PI) (Figure1) and it consists on the integration of a platinum counter electrode, a silver pseudo reference microelectrode and an array of gold microelectrode. A specific

monoclonal antibodies are immobilized on a gold substrate by several methods [7] in order to detect the corresponding cytokines involving in the inflammation process (TNF alpha) by Electrochemical impedance spectroscopy (EIS). The limit detection of cytokine in vitro is 0,1 Pg/ml (See Fig.2). Finally, the developed Lab on chip will be used to detect a specific cytokine (IL-1, TNF alpha and IL-10) and predict the first earlier detection of the transplanted organs rejection.

Figures :

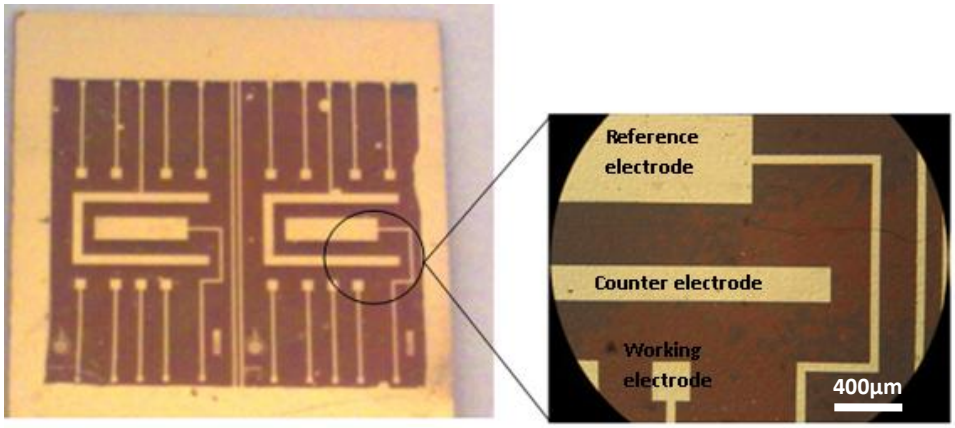

Fig. 1: Gold microelectrodes on polyimide substrate

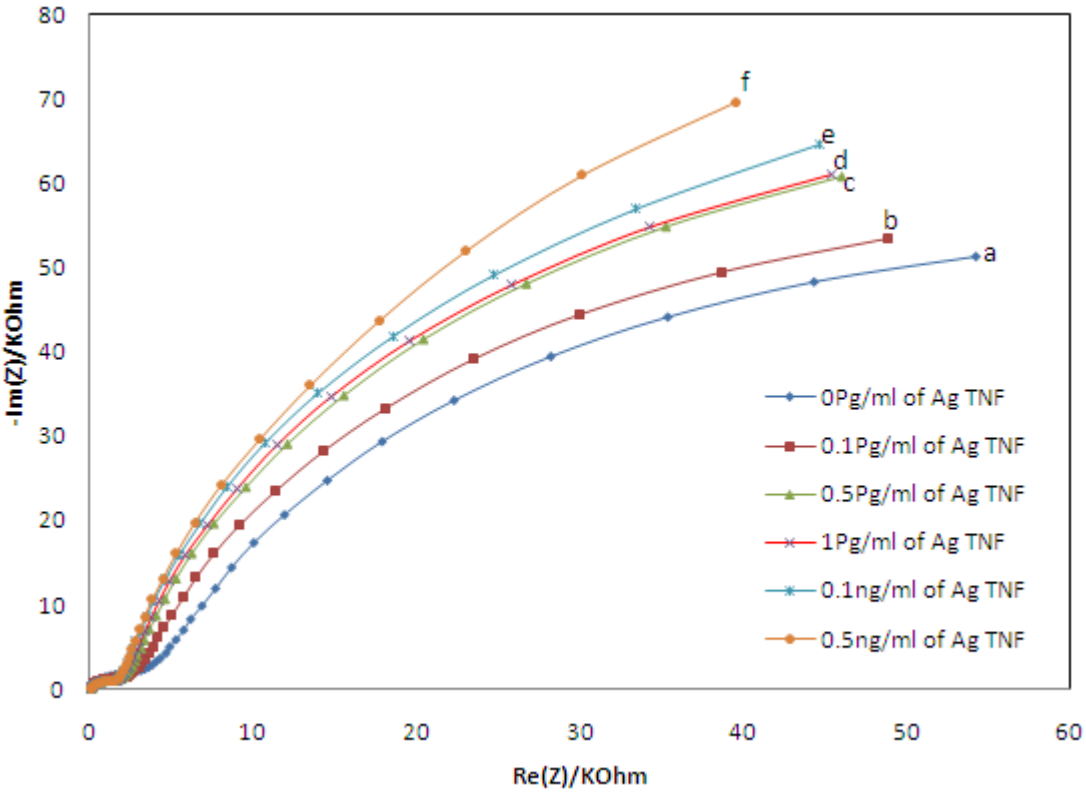

Fig. 2: Nyquist plot impedance (Z_r vs Z_i: at 5mM of $K_3[Fe(CN)_6]$/ $K_4[Fe(CN)_6]$ in PBS pH7,4 solution) at various TNF aplha antigen concentrations on its specific antybody : (a) 0Pg-ml; (b) 0.1Pg/ml;(c) 0.5Pg/ml; (d) 1Pg/ml; (e) 0.1ng/ml et (f) 0.5ng/ml

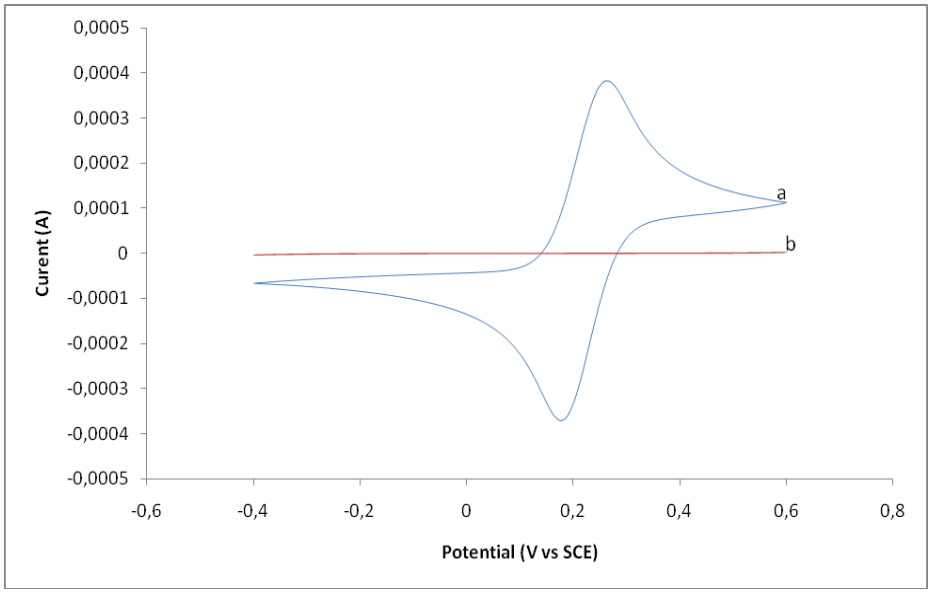

Fig. 3 : Cyclic voltammetry for :(a)bare gold electrodes and(b) mixed SAM electrodes in 5mM $K_3[Fe(CN)_6]$/ $K_4[Fe(CN)_6]$ in PBS pH 7.4 Electrodes were scanned at a rate of 100 mV/s

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