Dielectrophoresis of Biological Cells and Single-walled Carbon Nanotubes

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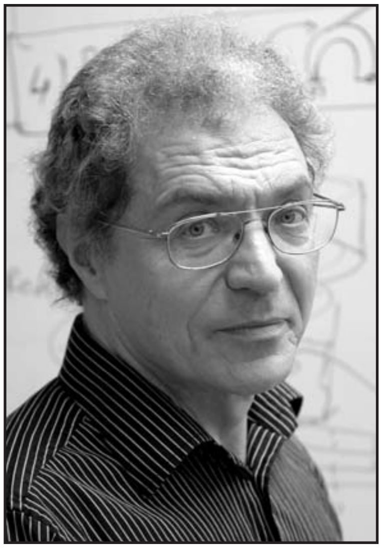
ABSTRACT—Our research is a continuation of the development and refinement of devices that can be used for the characterization of electromagnetic properties of biological and nano-size materials. In framing this approach, which is the follow-up of our earlier work on Martian Meteorite ALH84001 characterization, we have developed several capacitors with a gap between electrodes of the order of tens nm. For cell and carbon nanotubes manipulation, we have studied the technique of dielectrophoresis. Electrical phenomena play a role in living organisms. They can be used to modify and change biological samples.



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MINIATURIZED SENSORS AIMED AT cellular analysis and bio-diagnostics has become increasingly important in biomedical sciences. They are expected to play an especially prominent role in space missions. If one can monitor responses of cells to effects such as radiation or other deleterious effects related to toxicity induced by the space environment to access the mechanisms of cells modification or degradation, our space missions not only will be safer but they will contribute a better understanding of cellular mechanisms and processes to be used in medical fields on Earth.

We continue the development and refinement of devices, which can be used for characterization of electromagnetic properties of biological and solid state materials. In the scope of this approach, which is a continuation of our earlier work on Martian Meteorite ALH84001 characterization, we have developed several probes for operation in the rf and microwave frequency range. They work as broadband and single frequency probes and are used for complex permittivity measurements of liquid suspended biological cells and also for biomedical applications of oriented single-walled carbon nanotubes (SWNT).[1] Our study focused on the characterization and manipulation of biological cells and SWNT. Using silicon/silicon oxide integrated circuit technology, we fabricated structures needed for such a study.

Growing interest of dielectric properties of nano and micro scale particles is a result of great expectations in understanding mechanisms that control many basic processes and phenomena in live organisms and in the nanoworld of physics and chemistry. At the same time, miniaturization of tools available now through nanotechnology provides the venue for delivering these answers. Electrical phenomena play a considerable role in living organisms[2] and can be used to modify, change, and also to interrogate biological samples in order to provide information on their structures and various kinetic processes in the cells[3]. By interaction with electric and magnetic fields, the cells, through changes of electrical charges, conformation, polarization and conductivity, can provide structural information as well as data on functional and metabolic behavior in cell membranes, mitochondria, chloroplasts, motor proteins, and cytoskeletal proteins.

Especially important is the dependence of these properties on frequency, which, in turn, can help to identify various bio-physical and bio-chemical effects and parameters of living organisms. Widely used methods for such measurements include frequency dependent capacitance/conductance and impedance performed using electrical test structures made as part of fluidic systems with embedded electrodes.

Electrical characterization of biological samples is difficult.[4] Due to conductive losses, there is a quite pronounced polarization effect at the electrode/electrolyte interface, which results from charge accumulation and distribution at the electrode site.[5] It introduces an additional interfacial capacitance, which increases quickly at low frequencies thus obstructing the real picture of behavior of the sample. One way of alleviating this effect is to use capacitors with a very small dielectric thickness[6, 7] that would be comparable to Debye length, *i.e.*, a parameter characteristic of the electrical potential decay from the electrode.

Fabrication of such small nm range structures is also very difficult, especially if vertical structures are to be made. However, they can be precisely controlled if horizontal structures are used such as those in Integrated Circuits (ICs). Planar capacitors with a very small (*n*m) oxide thickness can be fabricated; after etching a cavity around the electrode perimeter, it can be used to entrap minute particles or fragments of bio samples. For other biological samples, such as cells that are of the order of μm, these capacitors can be used for sensing the properties of cells via their fringing electric fields. Also they can be used for characterization of smaller objects such as carbon nanotubes.

To deliver cells to the site of this electric field, we used cell manipulation by a phenomenon called dielectrophoresis (DEP).[8] It is a process that relies on electrical polarization of neutral particles present in a solution.[9, 10] DEP occurs in a nonuniform electric field created by specially configured and patterned electrodes operating under an ac signal condition. The process depends on dielectric and conductive properties of both the cells and solution and is controlled by the signal amplitude and frequency.[9, 10] Particles can migrate to the maximum of electric field in positive dielectrophoresis (*p*-DEP) or to the minimum of electric field in negative dielectrophoresis (*n*-DEP). Additional effects affecting the motion of particles and their attachment to the electrode

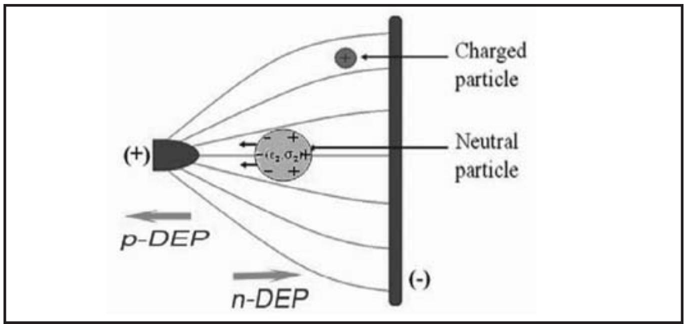

Figure 1. Dielecrophoresis results in the polarization of a neutral particle (formation of a dipole). As a result, such a particle will move in an electric field either toward a positive or a negative electrode, depending on permittivity and conductivity parameters of the whole system.

include rotation, levitation, chain formation, and bubbles that are all affected by temperature, flow and concentration of solution. In Fig. 1, a sketch explaining DEP is shown. The goal of this part of the work is to use a controlled and effective entrapment of particles or cells for their further electrical interrogation.

We designed test structures to attract, agglomerate, and attach particles to the electrodes and to perform electrical measurements of capacitance and conductance with high sensitivity. Capacitors were fabricated using *Si* technology where oxide layers of 17 nm and 150 nm were produced as dielectrics and electrodes were formed by doping and polysilicon deposition processes to ensure high conductivity (Fig. 2). Such structures have so small a gap between capacitor electrodes that even carbon nanotubes can be characterized this way. Structures of various geometries and dimensions, including interdigitated capacitors, were patterned by a photolithography process. We characterized these devices to verify proper electrical parameters prior testing of the samples.

Using minute drops of sample electrolytes, we conducted tests of particulate entrapment and then measurements of capacitance and conductance as a function of DC electric field, frequency of probing ac signal, and as a function of time. By changing conductivity of the suspension of yeast cells (*S. cerevisiae* and *S. pombe*) and parameters of the ac power supply (amplitude and frequency), we obtained positive or negative DEP *i.e.*, accumulation of cells at the highest or lowest E-field sites, respectively. Figure 3 shows an agglomeration of *S. pombe* aligned 3a) and misaligned 3b) in *p*-DEP around an electrode. Orientation of cells is affected by DEP conditions (voltage and frequency).

Similarly, we used single wall carbon nanotubes (SWNT) suspended in water with two surfactants (Pluronic™ F108 or SDBS) and samples with varying conductivity for measurements. SWCNT, first placed homogeneously over test structures with electrodes, were subjected to ac signals of frequencies up to 15 MHz and voltage amplitudes up to 10 Vpp until they dried up.

The obtained patterns, recorded by scanning electron microscopy (SEM), show the agglomeration of SWCNT around the perimeters of electrodes in the regions of high electric fields (positive DEP) with SWCNT clearly aligned with the electric field (Fig. 4c). The electrodes in our structures acting for SWCNT manipulation were also used as capacitors for complex permittivity measurements as a function of frequency. We found that increasing frequency in DEP manipulation of SWCNT resulted in the increased capacitance and in larger conductance of the capacitors. We have correlated SEM recorded patterns with simulated applied electric field and resulting DEP force distribution over the electrodes of nanogap capacitors.

The correlation and the obtained pattern of the DEP aligned SWCNT were found to be a function of applied frequency and the semiconducting/conducting nature of measured samples.

Capacitance and conductance measurements of capacitors with entrapped cells and with SWNT done as a function of frequency when compared with non-trapped capacitors show differences indicating that there is an effect of the fringing electric field in probing the agglomerated particles.

The efficiency of DEP in creating force-inducing motion of particles was verified using numerical simulations. The electrophoresis force that exerts on a nano-particle of radius *R* with dielectric constant $\varepsilon 2$ and conductivity $\sigma 2$ suspended in a liquid with dielectric constant $\varepsilon 1$ and conductivity $\sigma 1$, due to non uniform the electric field can be calculated as:

$$F_{DEP} = 2\pi\varepsilon_1 R^3 K(\varepsilon_1, \varepsilon_2, \sigma_1, \sigma_2, \omega)\nabla|E|^2 . \tag{1}$$

The factor *K* is a Clausius-Mossetti coefficient, which is a function of frequency. It is determined by the electrical properties of the medium and particles. Its sign determines whether the force is attractive or repulsive.

The last factor is the geometric gradient of the square of the field intensity, which means that the direction of the dielectrophoretic force is independent of the sign of the applied field. In this work we only analyze this field factor

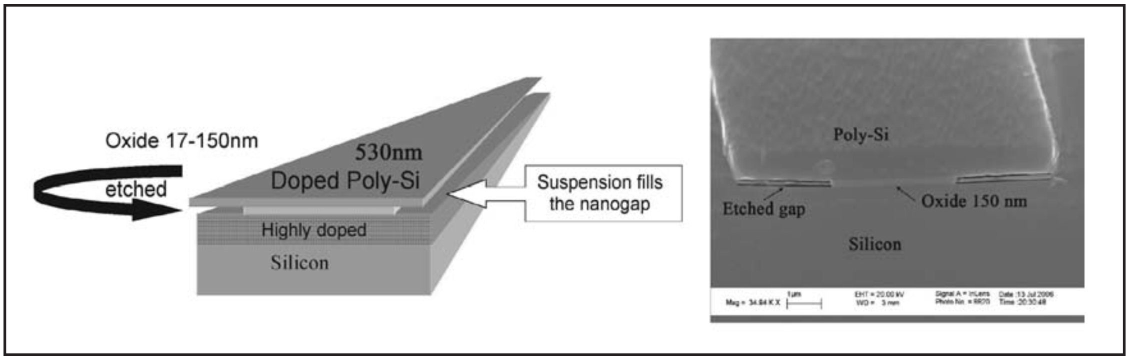

Figure. 2. Nanogap capacitor represented as a cartoon (a) and as a fabricated structure with 150 nm oxide (b).

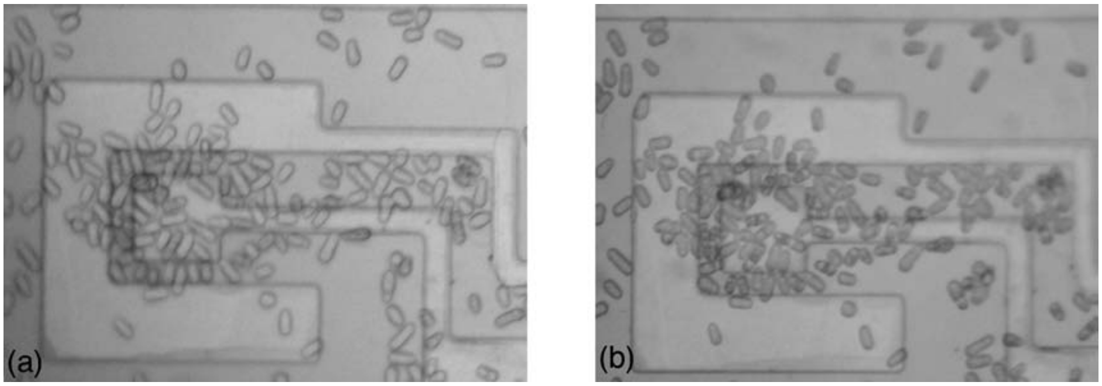

Figure 3. Dielectrophoresis for *S. pombe* shows positive DEP behavior. Researchers obtain better alignment (circled) along the electric field lines (a) compared with less oriented entrapped cells (b).

with a special configuration of device.

In our numerical calculation we used the normalized equation (1) and its corresponding boundary conditions. The results are shown in Fig. 5 (a, b), where an excellent agreement is shown between a pictured SWNT entrapment between two electrodes and the calculated electric field lines distribution and the force factor. Calculated electric field values showed very high electric fields on the edges of the electrodes, such as 5x10^{8} V/m. The actual values of the field factor (which for given frequency and ε and σ parameters) proportional to the force acting on nanotubes are 1.3x10^{22} V^{2}/m^{3}, and 4x10^{19} V^{2}/m^{3}, at inner and outer electrodes edges. In Fig. 4 we show the field factor values.

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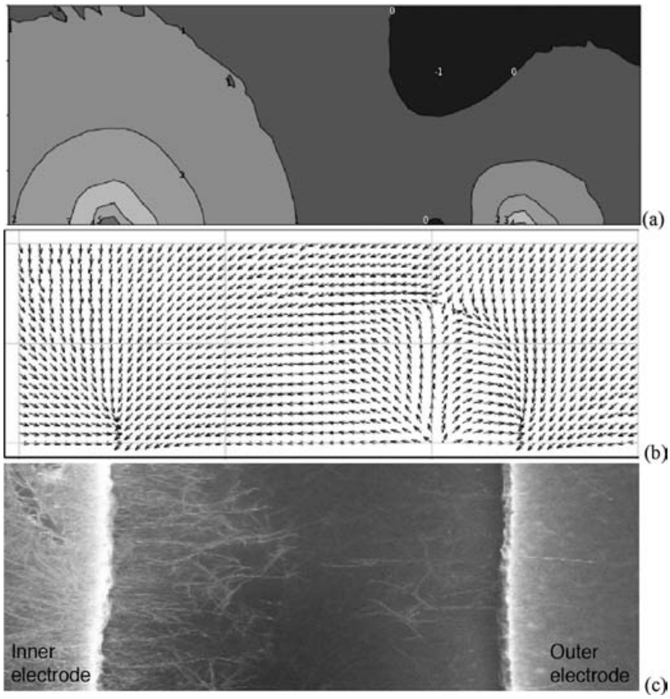

Figure 4. (a) The contour plot (in log scale) of the magnitude of electric field factor is shown. At center is the highest amplitude. (b) The plot of the vector of electric field factor distribution is shown according to equation (1). One can see clearly that the DEP forces are concentric toward the edge of the electrodes and that the force is the strongest toward the inner edge, weaker at the outer electrode edge. Because of the structure of the device in the gap region, particles experience a repelling force. (c) Entrapment of SWNT is seen in this SEM picture on a patterned electrode due to a positive DEP force at 10MHz at 10V peak-to-peak applied to the electrode.

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