Numerical simulation of the effect of liposomes on a quartz crystal microbalance

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With the advance of nanotecnology in life-science, the measurement of small quantities of mass has become an important issue on some applications. Quartz crystal microbalance (QCM) is a very popular device to do such a task, due to its high sensibility (10^{-16} kg) and to the simple physical concepts involved in those systems [1]. The base of the QCM is a small disk-shaped piezoelectric quartz crystal resonator which oscillation at high frequencies (of the order of Mhz) can be controlled by the application of an electrical voltage. When the QCM is in contact with bio-fluids, changes in the attached mass to the resonator can be determined through changes on the dissipation and frequency of the crystal.

In this work, we will focus in the case of liposomes attached with DNA molecules to the resonator. Such kind of systems are currently being tested to diagnose cancer in blood. This is done through binding events with tumoral cells: a target protein is attached on the DNA chain anchor to the resonator in order to bind mutant cells; the increase of mass is then detected by the QCM and can be used as a biomaker for cancer allowing its early detection and/or its monitorization [2]. Although the binding mechanism is quite simple, its effect in experiments is understood only qualitatively through very simple mathematical models which can only be applied to very simple situations. For a more quantitative knowledge is necessary to study the system from a more fundamental point of view.

To understand better this problem we have performed mesoscopic simulations with different numerical methods, such as Finite Volume with Immersed Boundary method [3], Langevin dynamics or Dissipative Particle Dynamics (DPD). The scheme of the simplified model used to address this problem is depicted at Fig. 1. The liposomes (represented by a sphere in the figure) are modeled as small spheres linked by Hookean springs. The DNA anchor of the liposome on the QCM is given by another Hookean spring, or by a semiflexible chain. The crystal is modeled as an oscillating wall and its hydrodynamic dissipation is calculated from the velocity gradient on the wall position.

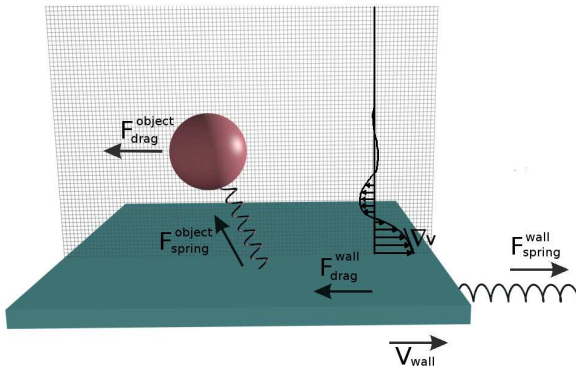

Fig. 1. Scheme of the model.

Resolution studies and comparison with analytical solutions will be shown to check the accuracy of the code. Results about the influence of different features, such as hydrodynamic effects, mass, concentration, radius, length of anchor or rigidity of the liposomes will be also presented.

This work is part of an ongoing FET-OPEN project *Capturing non-Amplified Tumor Circulating DNAwith Ultrasound Hydrodynamics (CATCH-U-DNA)*, whose objective is to increase the mass sensitivity of the QCM setup using dissipative structures, so as to be able to detect minute bulk concentrations (femto to attomolar) of mutant DNA in the sample.

[1] C. Steinem and A. Janshoff (Eds.), *Piezoelectric Sensors, Vol. 5* (Springer Science & Business Media, 2007).

[2] Y. Uludag and I. E. Tothill, Cancer biomarker detection in serum samples using surface plasmon resonance and quartz crystal microbalance sensors with nanoparticle signal amplification, Anal. Chem. **84** 5898-5904 (2012).

[3] A. Vázquez-Quesada, F. Balboa-Usabiaga, and R. Delgado-Buscalioni, A multiblob approach to colloidal hydrodynamics with inherent lubrication, J. Chem. Phys. **141**, 204102 (2014).