Multifunctional nanomechanical systems for multiplexed highly selective and sensitive biological detection

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Prediction of risk factors and early diagnosis of disease are the best means to preserve health and to avoid costly and inefficient medical interventions after symptoms and disease have developed. Current platforms for analysis require large amount of sample, have many sample pre-treatment steps prone to human error, are relatively slow, suffer of low sensitivity for the detection of multiple malignancies, and often provide false positives and negatives. In addition, these instruments are bulky equipment that is frequently not available to clinics or point of care diagnosis. The goal of discovering new devices and new transduction concepts for biological detection remains of paramount importance. Nanotechnology based approaches are promising candidates for providing portable and low cost nanosensor devices, capable of analyzing tiny amounts of sample, and specifically disease markers from patients. Also, the advancement of new approaches that provide the needed robustness and reproducibility of the response, as well as a high degree of multiplexing, is needed. MEMS/NEMS devices are good candidates to attain this goal, but this approach needs the further development of advanced instrumentation which demands combined expertise in fabrication, design, engineering and modelling. We have found that a private – public partnership is especially suitable to attain the cited purposes. In this work, two spin-off companies Mecwins S.L. and Nanosens Gmbh have collaborated with our group to develop an instrument with the capability for highly multiplexed detection (up to 128 sensors in parallel already demonstrated) together with an accurate control of the gas environment[1] and a biochip comprising 128 cantilevers in groups of 8 cantilevers for differential measurements.

The developed nanomechanical systems and transduction schemes and techniques have been tested and applied to solve problems in the field of biomedicine but also in other areas such as polymer science. The largest potential is in the detection of the hybridization of nucleid acids for early disease detection, including the early detection of cancer based on downregulation or overexpression of genes. Also, the detection of harmful pathogens by nanomechanical systems is in need of a cost-effective and rapid technique, as the one described here, for detecting pathogens in the early stages to avoid epidemics. The advantage of immunosensors based on nanomechanical sensors over traditional diagnosis systems such as Enzyme-Linked Immunosorbent Assay (ELISA) is that intact bacteria or viruses can be detected without need of secondary markers. More interestingly, nanomechanical sensors proposed provide unprecedented levels of sensitivity and specificity as we demonstrate in this work[1,2].

References:

[1] Mertens, J., Rogero, C., Calleja, M., Ramos, D., Martín-Gago, J.A., Briones, C. & Tamayo, J., Nature Nanotechnology **3** (2008) 301.
[2] D. Ramos, M. Arroyo-Hernandez, E. Gil Santos, H. Duy Tong, C. van Rijn, M. Calleja, J.Tamayo, Analytical Chemistry 81 (2009) 2274

Figures:

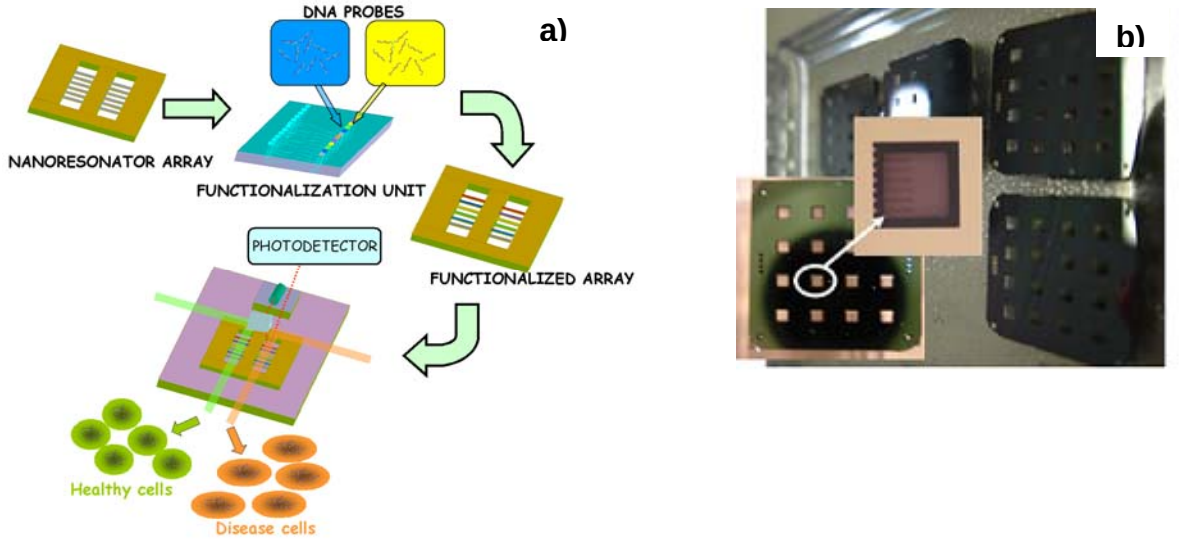

Figure 1. a) Conceptual drawing of the Mecwins chips and platform. The fabricated array consists of several separated rows of cantilevers. Each row of cantilevers is sensitized with the same combination of DNA probes by means of a microfluidics or microinjection techniques. The sensitised array is then inserted in the readout instrument composed of a scanning optical system for measuring the resonant frequency and mechanical deformations of each cantilever. 128 cantilevers have been detected simultaneously. In a possible application, the gene expressed content of disease and healthy cells is flowed over each row of cantilevers for comparison of the gene expression pattern and determination of genes responsible of disease. A picture of the actual chips manufactured by Nanosens is also shown in b).