Integrated System for Cancer Biomarker Detection

PCA: Nanoscale devices and systems

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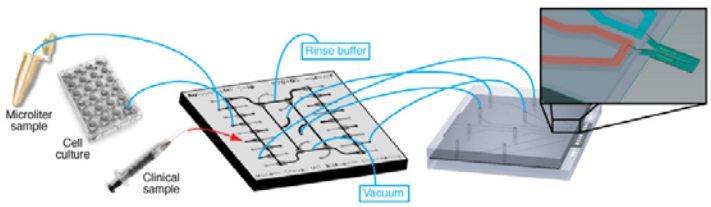
Early detection of cancer is a vital key in the fight against cancer. By the time patients are diagnosed with breast, lung, colon or ovarian cancer, more than 60% already have hidden or known metastases. For example, more than two thirds of ovarian cancer cases are detected at an advanced stage, and the 5-year survival rate is 40%. However, if this disease is detected and treated at Stage I (when it is still confined to the ovary) the survival rate increases to 90%. Additionally, early diagnosis of breast cancer could bring survival rates up to 98%.

While immunoassays such as ELISA are well established for antigen-based biomarker detection, the fidelity of the assay is governed by the dissociation constant, Kd, of the antibody-antigen complex. If the antigen concentration is significantly below Kd, then the binding kinetics are slow and readout precision of the antibody-antigen complex can be degraded by noise.

For decades, resonant mass sensors have been excluded from applications requiring fluid because mechanical vibrations are hindered by viscous drag. The Manalis laboratory solved this problem by placing the fluid inside the resonator instead of immersing the resonator in the fluid. Using these Suspended Microchannel Resonators (SMRs), they showed that viscous loss from the fluid is negligible compared to the intrinsic damping of the silicon crystal resonator, which, when combined with the low intrinsic weight of the resonator, led to the million-fold improvement in sensitivity.

By integrating the SMRs with a nanofluidic device that controllably concentrates dilute samples, the Manalis laboratory has been able to detect specific proteins in serum and to analyze the mass and density of single cells with high precision.



Ultra-sensitive detection of circulating tumor cells using suspended microchannel resonant mass sensor (SMR)

Since the amplification (or gain) of the concentrator is adjustable, the dynamic range and detection limit of the immunoassay can be governed by the properties of the concentrator and not Kd. By increasing the dynamic range of the immunoassay, more stringent filtering can be used to remove abundant background proteins, and low-affinity capture agents such as peptides or protein fragments can be used if high-affinity antibodies do not exist.