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# Acoustic Trapping of Proteins under Physiological Conditions

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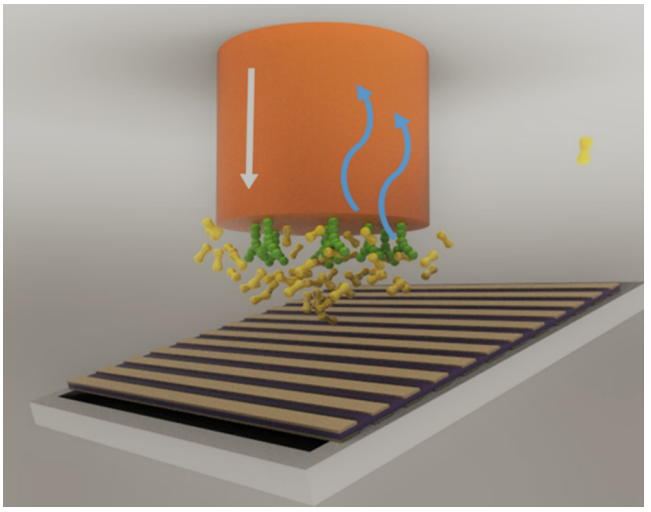
**An acoustic resonator can act as concentrator, boosting performance of bioassays via enhanced binding of low-abundance biomolecules.**

Essential proteins, hormones, and drugs circulate in human blood at concentrations that often do not exceed picomolar levels, which presents a challenge to existing sensors. Detection of biomolecules at such ultralow concentrations can be achieved by miniaturizing bioanalytical and biodiagnostic sensors by involving nanotechnology and by developing devices with novel transduction concepts.[1] Miniaturized biosensors are expected to increase their signal-to-noise ratio due to the high surface-to-volume ratio, yet mass transfer limitations and insufficient binding affinities prove severe challenges to achieving and improving ultrasensitive detection. Most surface-based biosensors require liquid media for analyte molecules to bind to their complementary receptors immobilized on the device's surface. In order to overcome diffusion and affinity limitations in these biosensors, the binding can be electrically, magnetically, or optically enhanced.[2] However, the persistent issue of excessive sample preparation steps or complicated device structures of existing approaches might have motivated Duan and co-workers from Tianjin University to search for biocompatible tools that ensure simple and direct trapping of biomolecules under physiological conditions.[3]

The authors demonstrate a novel approach to trap and concentrate proteins by controlling molecular motion via induced flow patterns using an acoustic nanoelectromechanical system (NEMS) resonator in both buffer and serum. It is well-known from the hydrodynamic trapping research in the field of microfluidics that biomolecules in a vortex flow preferentially migrate from regions of high fluid velocity to regions where the fluid velocity becomes negligible.[4] Therefore, biomolecules depart from the vortex



Schematic representation of an acoustic NEMS resonator as biomolecule concentrator.

and accumulate at the bottom of virtual micropockets, which was conclusively shown by digital image-plane holographic microscopy.[3] The research team has achieved the concentration factor of $10^5$ by breaking the mass transfer limitation and enhancing the kinetics of molecular surface binding, which increased the *in vitro* limit of detection of low-abundance target (bio)molecules by a factor of up to 1000. A quick and efficient process of protein concentration could be used in virtually any concept of rapid biomarker detection and diagnosis. The trapping of biomolecules occurs in open spaces, and the position of the virtual

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micropocket, where the biomolecules are massively trapped and concentrated, is easily predictable by numerical simulations. These advantages facilitate integration of such devices into optoelectronic bioassay platforms, as the transducer can easily be located at, or close to, the virtual micropocket to create a universal biomolecular concentrator and to enhance real-time label-free biosensing. The authors have demonstrated the feasibility of this approach by detecting immunoglobulins and antigens through specific antibody−antigen interactions using a resonator-enhanced immunoassay integrated into a biolayer interferometry sensor.[3] In this device, the acoustic NEMS resonator accumulates the analyte at the interface of the probe (an optical fiber) to enhance the surface absorption kinetics of analyte molecules.

In general, this type of device is biocompatible and can be applied universally to concentrate molecules or proteins irrespective of their physical and chemical properties. Further studies should now focus on the selective trapping of specific proteins that are present in complex media, such as whole blood. Label-free sensors have the potential to detect disease markers rapidly, specifically, and sensitively, providing point-of-care diagnosis at low cost. However, detecting these biomarkers in physiological fluids will likely be impeded by common problems such as biofouling and nonspecific binding, and as a result, the need to use ultrapure reagents and prepurification or the need to develop multistep sample preparation procedures will challenge the clinical relevance of any such type of sensor.

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