

Applied biochemistry meets microfabrication and nanotechnology: Micro- and nano-labels for biomedical diagnostics

Richard Willson

University of Houston

Many bioanalytical technologies use a biological molecular recognition tool such as a DNA probe or antibody to bind specifically to a target such as a biomarker, pathogen, or nucleic acid. Equally important, these technologies also usually employ a label to signal that binding of the target has occurred, and 3-beam technologies can be used to allow the use of better labels.

After a brief review of biological recognition and its applications, this talk will discuss several micro- and nano-scale labels which we are developing along with collaborators expert in micro- and nanofabrication. In decreasing order of size, these are micron-scale retroreflectors, nanoscale GMR sensors, and immunomagnetic nanoparticles tagged with amplifiable DNA sequences.

Along with Paul Ruchhoeft (UH), we are using magnetic sample-prep particles as light-blocking labels in optical assays based on micron-scale microfabricated retroreflectors. Retroreflectors return light directly to its source and are readily detectable with inexpensive low-NA optics. When the target is present, magnetic sample-prep particles decorated with anti-target antibodies (as routinely used in cleaning up complex clinical samples) can assemble on the Retroreflector surface and substantially reduce reflectivity. The assay can easily detect the presence of a single magnetic sample-prep particle bound to the surface. The magnetic properties of the particles are useful in sample preparation and concentration, and particle capture. Magnetic forces, as well as microfluidic fluid flow shear, are used to increase specificity by discriminating against non-specific interactions. Shear force discrimination, reproducibility, and convenience are enhanced by the implementation of the technology in a microfluidic cartridge format.

Along with Dmitri Litvinov (UH), we are developing biomarker diagnostics based on nanofabricated GMR sensors. These assays use nanoscale magnetic particles as labels which are bridged by antibodies onto the sensor in the presence of the analyte. The detection sensitivity of GMR sensors is good enough to raise the possibility of labels small enough to be captured through a single molecule of analyte, with enhancement of specificity by magnetic force stringency.

Finally, we have used magnetic nanoparticles as the basis of an immunoPCR-style assay in which particles are captured via antibodies, and sensitively detected by quantitative PCR. Detection limits are very low, as low as 10-40 particles. This assay may be particularly applicable to detection of viral and bacterial pathogens, as a single cell can capture 5-20 reporter particles, each displaying up to thousands of DNA labels in an accessible format, ready for PCR detection without laborious cell lysis and DNA purification.