A Biosensor Based on Magnetic Resonance Relaxation

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Conventional culture and susceptibility tests continue to remain the “gold standard” for identifying pathogens in clinical and other settings. Many new pathogen detection approaches have aimed at replacing this standard by providing more rapid, more accurate and less expensive detection. Very promising techniques such as PCR, surface enhanced Raman, and others have proven adept at pathogen detection, but end users have not warmed up to their expense, extensive sample preparation and skill set necessary to perform them. The field continues to search for a rapid, sensitive, and specific detection technology that is cost-effective and easy to use. This work describes a biosensor based on magnetic resonance relaxation switching. The method leverages a large body of work involving nanoscale contrast agents employed in nuclear magnetic resonance (NMR) imaging. The aim was to develop a detection approach that mimics the human immune response to an invading pathogen, the release of 10^9 to 10^{12} specific antigens to guarantee quick contact with the pathogen. The technique employs magnetic nanoparticle contrast agents conjugated with specific capture agents to achieve a similar contact goal. Detection of the species involves monitoring the average relaxation time (T2) of water protons in the solution, which is highly sensitive to the concentration and distribution of the magnetic nanoparticles present. With multiple nanoparticles attaching to each individual target species their distribution will be altered, and correspondingly, the average proton relaxation time will change. Although, this method leverages well established principles of NMR imaging, this measurement can be accomplished with a simple hand-held relaxometer.

This detection technique appears to have the potential to mitigate 4 of the primary factors limiting the effectiveness of current detection strategies: **(1)** poor contact statistics between the sensor platform and target – which impacts detection time, **(2)** sample preparation – which is required to concentrate or remove pathogens from the sample and/or remove or reduce interferents, **(3)** non-specific binding – which significantly reduces sensitivity and selectivity of the detection method, and **(4)** ease and cost of use – most end users will not have PhDs or a high level of training. Our results have identified an ideal concentration of magnetic nanoparticles that imparts the highest sensitivity to changes in particle distribution. We have also discovered that increasing the concentration of particles actually reduces the sensitivity of the technique by as much as a two orders of magnitude.