**Why Ultrasensitivity Matters for Clinical Diagnosis**

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A major challenge for many clinical diagnostic applications is the quantification of low-abundance proteins and other biomolecules in biological fluids. For example, traditional techniques, such as enzyme-linked immunosorbent assay (ELISA), can only measure several hundred proteins in human blood, which is limiting because there are thousands of proteins present at low concentrations that are of potential diagnostic utility. Single-molecule technologies allow for digital counting of individual protein molecules and have enabled 1000-fold increases in sensitivity over conventional protein detection methods. We have pioneered the development of these technologies that provide for multiplexed measurements with femtomolar sensitivities or below. I will discuss the technologies and describe their application to neurodegenerative disease, cancer, and infectious diseases.