

Sensitivity Limit of Nanoparticle Biosensors in the Discrimination of Single Nucleotide Polymorphism

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Single-nucleotide polymorphism (SNP) is a random replacement of a nucleotide in a given genetic location that occurs in human genome at every few hundred of bases across the genome¹. These replacements alter functioning of proteins, leading to cancer, cardiovascular or neurodegenerative diseases². Therefore, the ability of sensitive detection of specific SNPs has considerable value in diagnosis, prediction of patient's responses to treatments, and risk of relapse of diseases. LSPR-based detection methods offer some significant advantages: applicability to a wide range of analytes, ease of use, elimination of the use of toxic organic solvents, point-of-care applications, as well as high sensitivity in the detection of some biological species³.

The main factor limiting colloidal sensor sensitivity is the number of available target DNA molecules able to aggregate nanoparticles and therefore produce an optical output. A systematic study for SNP detection using AuNPs of 13, 46 and 63 nm using conventional sandwich assay is proposed⁴. It has been found that by increasing particles diameter at constant gold concentration, one can improve limit of detection by two orders of magnitudes (Figure 1). At constant gold concentration and varying particles size, the best sensitivity was reached with the large particles, 63 nm. This tendency was explained by a higher ratio of target-to-particles as compared to the smaller AuNPs. Using 63 nm particles we could differentiate match from mismatch sequences down to 10 pM. The results show that colloidal biosensors based on the aggregation possess an intrinsic limitation which is the number of target molecules per particles.

References

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Figures

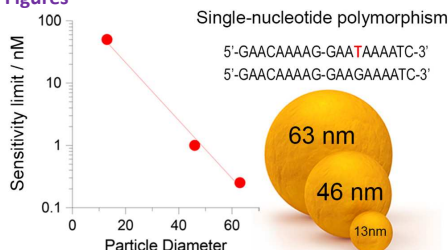


Figure 1: Sensitivity limit versus particle size, showing a linear dependence in a logarithmic scale.