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


1CIC biomaGUNE, Paseo de Miramón 182, 20009 Donostia-San Sebastian, Spain
2Molecular Oncology Group, Biodonostia Research Institute, 20014 Donostia-San Sebastian, Spain
3POLYMAT, University of the Basque Country, 20018 Donostia-San Sebastian, Spain
4Ikerbasque, Basque Foundation for Science, 48013 Bilbao, Spain
5CIBER-BBN, 20009 Donostia-San Sebastian, Spain
msanroman.biodonostia@cicbiomagune.es

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 genome. These replacements alter functioning of proteins, leading to cancer, cardiovascular or neurodegenerative diseases. 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 species.

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 proposed. 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


Figures

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