

Bibliographical Entry: "Single-Nucleotide Polymorphism Genotyping by Nanoparticle-Enhanced Surface Plasmon Resonance Imaging Measurements of Surface Ligation Reactions." Yuan Li, Alastair W. Wark, Hye Jin Lee, and Robert M. Corn, *Anal Chem*, 2006, 78(9), 3158-3164.

Bioanalysis and Sample: The authors use an array-based technology with surface plasmon resonance imaging (SPRI) to qualitatively detect the presence of a single-nucleotide polymorphism (SNP) in unamplified genomic DNA. As a proof of concept, the authors first performed their method using short synthetic DNA sequences. They then applied their method to the BRCA1 gene, a gene commonly associated with hereditary breast and cervical cancer. Again, they were able to demonstrate an ability to identify an error in a single base.

Importance: Clinical analysis of genomic DNA to identify the presence and identity of SNPs could prove highly beneficial in the early diagnosis of genetically transmitted diseases. Included in this goal is the need for a method that is rapid and simple. This requires elimination of PCR amplification of the DNA before array analysis. The authors demonstrate detection limits to 1 pM, which is sufficient for detection of specific SNPs in unamplified DNA.

Technique: The probe DNA used in this study is complementary to the target DNA and terminates after incorporation of the SNP of interest. Probe strands are linked via a thiol group to the gold surface of the array.

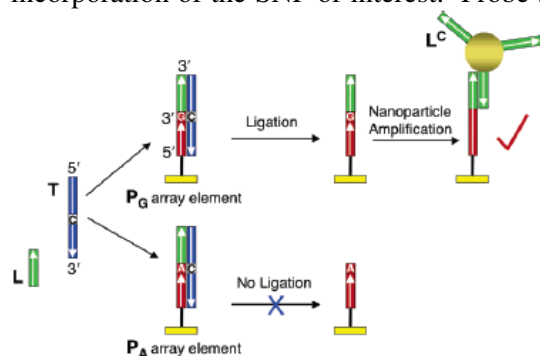


Figure 1: Ligation scheme for detection of an SNP
Li, et. al. *Anal Chem*, 2006, 78(9), 3158-3164

A $(\text{CH}_2)_6$ followed by T_{20} spacer is used to separate the probe DNA from the array surface. Following hybridization of the target to probe DNA, a ligase probe is hybridized to the target DNA and *Taq* ligase enzyme is introduced. Because the *Taq* enzyme is specific to correct base pairing, only DNA that has the correct pairing will undergo the ligation reaction. After denaturing to remove the target DNA, a nanoparticle probe containing a DNA strand complementary to the ligation probe is introduced and hybridized. See Figure 1 for a pictorial representation of the ligation process. SPRI is then performed to determine the presence of nanoparticle labels using a commercially available instrument.

Results: An example of the results obtained using the BRCA1 gene is shown in Figure 2. The figure on the left is a sample taken from a normal cell. Because a normal gene is a C-C homozygote, hybridization to the G-terminated probe is expected and observed. On the right is an abnormal C-T heterozygous cell. As expected, hybridization is observed for both the A-terminated and G-terminated probe sequences.

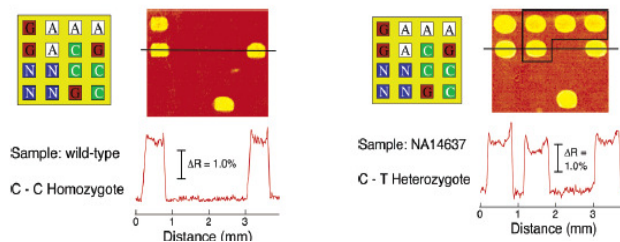


Figure 2: Example of array results for BRCA1 genomic DNA
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Comments: This paper successfully demonstrates the ability to detect a single SNP in 1 pM samples of DNA. This is promising for creating probes that are capable of determining the presence of a specific SNP a clinical setting. By creating several sample cells on the same chip with varied lengths of probe DNA, simultaneous detection of several SNPs could be possible. I have concerns about the cost and time per analysis of this method. With the goal of clinical implementation, one must take these factors into account and authors do not mention either factor.