BMC Bioinformatics



Poster presentation

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NanoSNP: A computational platform for high throughput Quantum Dot encoded microsphere SNP genotyping

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from BioSysBio: Bioinformatics and Systems Biology Conference Edinburgh, UK, 14–15 July 2005

Published: 21 September 2005

BMC Bioinformatics 2005, 6(Suppl 3):P5

We report the development of a novel computational system, NanoSNP. The system is based around semiconductor nanocrystals or quantum dots (QDs), QDs herald the arrival of bio-nanotechnology and due to inherent advantages are currently replacing organic dyes as the probe of choice in fluorescent measurement for biology. QD encoded microspheres consist of various sizes of QD at various intensities polymerized within a latex or polystyrene bead to yield a unique spectral signature. To facilitate high-throughput SNP genotyping using QD encoded microspheres we have integrated bioinformatics and spectral analysis to create a user friendly system. Features of the system include SNP selection, QD microsphere design, oligonucleotide conjugate sequence output and QD microsphere identification.

For experimental design the system is integrated with HGVbase allowing the user to select the SNPs of interest for a population. A panel of QD encoded microspheres is designed by the system, each microsphere assigned to a SNP allele. Once the QD encoded microspheres have been prepared in the laboratory. An allele specific oligonucleotide is prepared and conjugated to its respective QD encoded microsphere.

During the experimental stage of the procedure described by Mahoney et al 2003, DNA is extracted from the sample, purified and subjected to multiplex PCR around each SNP location. The QD encoded microspheres are added to the amplified PCR products, the oligo conjugates on the surface of the QD microsphere hybridise to complementary PCR product only when there is a prefect match. Hybridisation is detected via a biotinstreptavidin system and QD encoded microsphere spectra are resolved using a flow cytometer. NanoSNP identifies hybridised spectra from a database of theoretical spectra thus identifying the allele present creating a SNP profile for each sample. We believe that this system and integration with bioinformatics recourses represents the future of real time, automated and user friendly genetic determination due to advantages such throughput, accuracy, automation and simplified instrumentation.