

**Kalim Mir (Oxford University) - Spatially addressable self-assembly, combing and nanoparticle binding of single DNA polymers**

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Background - coming from the human genetics/genomics point of view. 4 billions bases, 30,000 genes, and several million sites of common variation. Need to link sequence/genes with traits/disease. Ordered array, spatially addressed (shows schematic of single chromosome). Diagnostic device "gene-chip" to sort complex mixtures of molecules. Extracted genome is disorganized, reorganized by hybridization on the chip. Microarray - synthesize probes and spot onto slide is one way, other approach is in-situ synthesis on a chip (photolithography). Digital microlithography aims: to develop massively parallel methods for genomic analysis in which single molecules can be viewed individually. Look at long range feature such as the genome and analyze short range feature of the genome. We want to sequence the human genome for \$1000. A platform for single molecule analysis - sort, resolve, display, examine. Wants to be able to look into microarray spot and look at individual dye molecule markers. Can tell if single molecule by photobleaching characteristics. Use digital data extraction to count individual molecules and amplification of signal from single molecules using nanoparticle labeling. Self-assembly and combing of genomic DNA on microarrays, fragments sizes of up to 200kb, capture on microarray, comb, spot gives whole genome coverage that can be labeled with sequence specific probes. Haplotype: diploid genome, one copy from each parent, haplotype is the linear association of alleles on single parental chromosome. SNP typing does not resolve which set of alleles from which parent. Enables better correlation of genomic regions with disease. Haplotyping by spatial addressing: oligonucleotide nano-array, novel spatial arrangement of array elements identifies each allele the gene is from. Another way is to measure electrical continuity from each pad. Bridging DNA between probe coated electrodes: sequencing-by-synthesis on arrays, monitoring template-directed sequencing.