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Probing DNA on Surfaces Using Optical Interference Techniques

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Probing DNA on Surfaces **Using Optical Interference Techniques**

Mehmet Dogan, Julia R. Dupuis, Lev Moiseev, Anna K. Swan, Bennett B. Goldberg, M. Selim Ünlü, Charles R. Cantor **Boston University**





Abstract

We have developed and patented (1) a technique, Spectral Selfinterference Fluorescence Microscopy (SSFM), to determine the location of fluorescent molecules above a reflecting surface with nanometer precision. The method utilizes the spectral fringes produced by interference of direct and reflected emission from fluorescent molecules. The modified spectrum provides a unique signature of the axial position of the fluorophores. We have used the SSFM technique to determine the position of fluorescent markers attached to sub-cellular structures such as lipid bilayer membranes and DNA strands revealing conformational information. Using this technique we have estimated the height of single strand DNA, tilt angle of double strand DNA and amount of hybridization. With the patented SSFM technology, DNA hybridization and DNA-protein interactions can be studied in more detail in many areas such as molecular biological research as well as medical diagnostics, particularly cancer, genetic and infectious diseases. It is promising to be a valuable tool and have an impact in the growing DNA chip industry that utilize microarrays of DNA immobilized on surfaces.

Current State of the Art

Interference Techniques to Determine Position:



•Ellipsometer: non fluorescent technique



DNA Microarray technology (3): Parallel gene expression and processing

- •Gene analysis and discovery
- Disease diagnostics
- Drug discovery



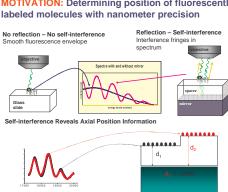
Challenges and Significance

•Current DNA microarray technologies lack determining DNA conformation *SSFM is capable of determining position of emitters that label DNA, thus reveals valuable information regarding conformation

•A Hyperspectral Fourier Transform Spectrometer (HS-FTS) is being designed and built for parallel acqusition of spectra to perform SSFM on

Technical Approach: Spectral Self-interference Fluorescence Microscopy (SSFM)

MOTIVATION: Determining position of fluorescently



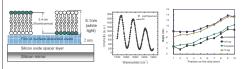
Best fit to MODEL

fitting parameter: d, axial position

Spectral Fringes

Probing Lipid Bilayers with SSFM

(Artificial cell membranes)



Probing fluorophore position in top or bottom leaflet of an artificial cell membrane

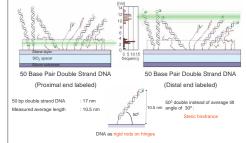
Accomplishments up through Current Year: **Probing DNA on Surfaces**

Estimating Amount of DNA Hybridization using White Light Spectral Interference





DNA Conformation Studies



In Progress: Probing DNA-Protein Interactions

Opportunities for Technology Transfer

Microarry Industry Overview (4)

- •\$ 450M, growing 10% each year
- •\$ 1 Billion revenue projected for 2010

Some of DNA microarray companies :

Affymetrix Inc., Molecular Dynamics Inc., Nanogen, Protogene Labs,

Industry members using

- microarryas: •Molecular Biological Research Healthcare
- •Pharmacology for Drug Discovery

Our proposed contribution to microarray technology:

Microarray detection with determining hybridization efficiency and position information of the fluorescent markers that leads to understanding of the DNA conformation

Opportunities for Technology Transfer

Hyperspectral Fourier Transform Spectroscopy: SSFM on Microarrays

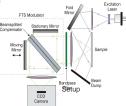
•We have demonstrated the proof of concept for SSFM

•We are now developing a hyperspectral Fourier transform spectrometer (HS-FTS) to demonstrate the SSFM principle with imaging on microarray chips

The instrument includes a small FTS modulator and a CCD camera to record the spatially resolved interferograms.

Benefits of the system:

- Good radiometric efficiency because
- of spectral multiplexing. · Background rejection due to
- synchronous detection.
- · Flexibility in spectral range by changing the spectral prefilter and sampling parameters,
- · Flexibility in spectral resolution by changing the mirror stroke length.
- . The HS-FTS is also being used for white light interferometry measurements of biological material bound to surfaces.



Contribution to CenSSIS Research Thrusts



This work falls under CenSSIS Research Thrust R1(multispectral imaging). The development of the HS-FTS nanoscope relates the project to the CenSSIS BioBED platform.

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