Progress Towards An Aberration-Corrected Low Energy Electron Microscope for DNA Sequencing and Surface Analysis

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The emerging opportunities in the biosciences have a growing need for imaging at the sub-nm scale. In genome research in particular, there is great demand for imaging techniques that enable high quality DNA sequencing at high speed and low cost. Recently, we proposed[1] to develop a novel monochromatic, aberration-corrected dual-beam low energy electron microscope (MAD-LEEM) capable of imaging a DNA sequence of unlimited length at a cost of $1,000/genome with the accuracy needed for full-scale sequencing. The key advantages of this approach compared to current sequencing techniques are long read length, the absence of heavy-atom DNA labeling needed e.g. for transmission electron microscopy approaches, and use of low energy imaging. Longer reads reduce computational complexity needed to assemble the sequence, and the exclusion of labels reduces sample preparation and improves accuracy. The use of low energy electrons for imaging ensures that radiation damage is minimized, i.e. high electron doses critical to achieving high throughput and low cost can be used.

In this paper, we focus on the critical objectives needed to establish the feasibility of this novel imaging technique. In particular, we analyze the performance of the key electron-optical components of a MAD-LEEM, i.e. the aberration corrector combined with a symmetry mirror and magnetic prism array (Fig. 1). Initial results indicate that an electrostatic electron mirror has negative spherical and chromatic aberration coefficients that can be tuned over a large range. The negative aberrations generated by the electron mirror can be used to compensate the aberrations of the LEEM objective lens for a range of electron energies and provide a path to achieving sub-nanometer spatial resolution. We also present first experimental results of characterizing DNA molecules on Au substrates. Images (Fig. 2) obtained in a spin-polarized (SP)LEEM show that small changes in landing energy have a strong impact on the achievable contrast. A qualitative comparison of the LEEM results to that of an AFM reveal the topography of the islands formed by attachment of single-DNA base oligomers on Au substrates (Fig. 3). Electron reflectivity measurements (Fig. 4) performed in a SPLEEM over a range of landing energies from 0 to 10eV demonstrate the high contrast achievable at low electron energies.

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[1]Mankos, M.: A Novel Low Energy Electron Imaging Technique for DNA Sequencing and Surface Analysis, EIPBN Abstracts, 2011.

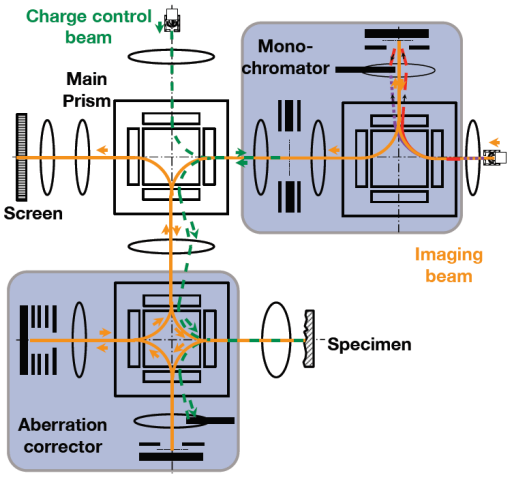

Figure 1: Electron-optical layout of a novel low energy electron microscope for DNA sequencing.

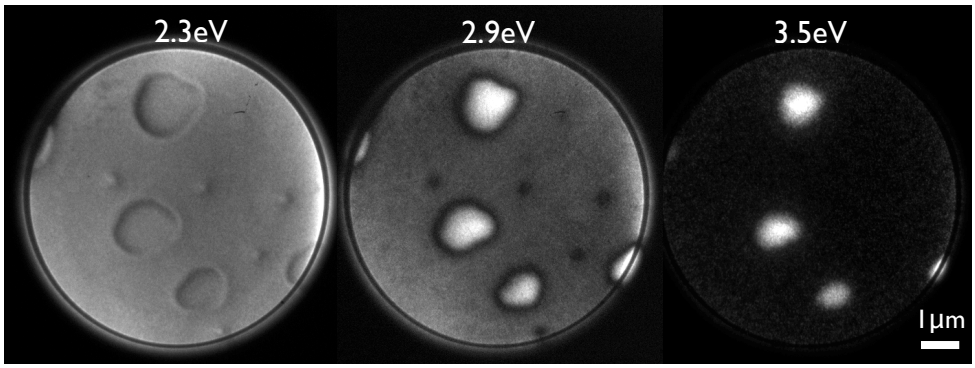

Figure 2 : SPLEEM images of DNA islands formed by attaching 5'dithiol-Cytosine 20mers on Au substrate for 3 landing energies (field of view 8 µm).

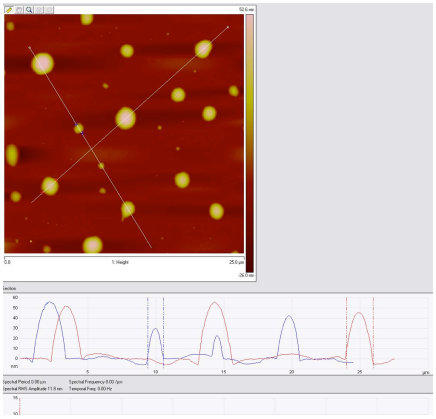

Figure 3: AFM image of 5'dithiol-cytosine-20mer islands attached on Au substrate (field of view 25 µm).

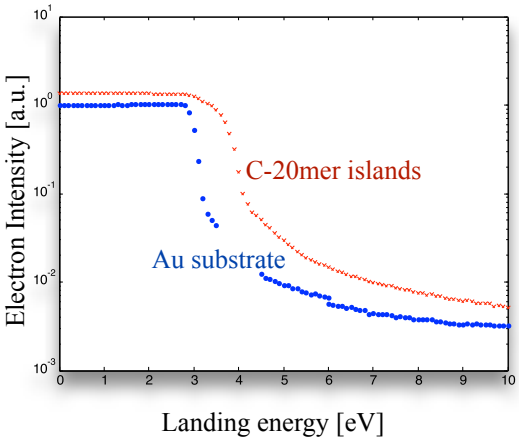

Figure 4 : Electron reflectivity vs. landing energy for Au substrate (blue) and attached 5'dithiol-Cytosine 20mer islands.

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