Zero-Mode Waveguides Fabrication for DNA Nucleosome Sequencing Application

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Primary CNF Tools Used: JEOL 6300 electron-beam lithography system

Abstract:

Cost-effective deoxyribonucleic acid (DNA) sequencing has been one of the most important goal in this era of biological and health science study. Zero-mode waveguide (ZMW) has been proven to be a promising technology for single DNA sequencing [1]. This research aims to apply this technology on directly reading DNA nucleosome sequence while detecting nucleosome modification in parallel. This could be a new innovative means of probing for epigenetics [2].

Summary of Research:

ZMW is essentially a ~ 100 nm size well that allows a confined region of laser illumination at its bottom. Once a DNA/polymerase complex is immobilized in the ZMW, the sequence can be read by imaging the incorporation of fluorescence-labeled nucleotides [1]. In our research, we plan to use it on DNA nucleosome complex instead of a simple single strand DNA. Thus the information of histone modification can be probed at the same time as we sequence the DNA, and the modification site can be located in the genome.

The proposed structure for ZMW chips is an array of ~ 100 nm holes on a thin film of aluminum on top of a glass wafer, similar to other designs under the same CNF project. We have finished a few trainings for some necessary fabrication tools, but haven't yet started the fabrication. Meanwhile colleagues Mohammad Alibakhshi and Fatemeh Farhangdoust are working on optimizing the protocol for glass wafer based ZMW fabrication.

References:

[1] Levene, M. J.; Korlach, J.; Turner, S. W.; Foquet, M.; Craighead, H. G.; Webb, W. W. Science 2003, 299, 682-686.

[2] Shema, Efrat, et al. "Single-molecule decoding of combinatorially modified nucleosomes." Science 352.6286 (2016): 717-721.