DNA Electrophoresis through Microlithographic Arrays

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Electrophoresis is one of the most widely used techniques in biochemistry and genetics for size-separating charged molecular chains such as DNA or synthetic polyelectrolytes. The separation is achieved by driving the chains through a gel with an external electric field. As a result of the field and the obstacles that the medium provides, the chains have different mobilities and are physically separated after a given process time. The macroscopically observed mobility scales inversely with chain size: small molecules move through the medium quickly while larger molecules move more slowly. However, electrophoresis remains a tool that has yet to be optimised for most efficient size separation of polyelectrolytes, particularly large polyelectrolytes, e.g. DNA in excess of 30-50 kbp. Some advances have occurred through trial and error exploration; however these improvements are not sufficient and changing the media morphology may provide the greatest effects upon separation. Unfortunately, gels provide only a small window of random morphologies and are difficult to control, let alone optimize for the electrophoretic process.

Microlithographic arrays etched with an ordered pattern of obstacles would provide an attractive alternative to gel media and provide wider avenues for size separation of polyelectrolytes and promote a better understanding of the separation process. Its advantages over gels are (1) the ordered array is durable and can be re-used, (2) the array morphology is ordered and can be standardized for specific separation, and (3) calibration with a marker polyelectrolyte is not required as the array is reproduced to high precision. Most importantly, the array geometry can be graduated along the chip so as to expand the size-dependent regime over larger chain lengths and postpone saturation. The high precision available in today's silicon chip industry promises accurate and controllable electrophoretic arrays with minimum length scale of 1 micron. Recent advances in nanolithography promise even smaller dimensions.

What is the optimal array geometry for separation of DNA? In order to predict the effect of obstacles upon the chain-length dependence in mobility and hence, size separation, we study the dynamics of single chains using theory and simulation. We present recent work describing:

- The release kinetics of a single DNA molecule hooked around a point, frictionless obstacle and in both weak and strong field limits.
- The mobility of a chain impinging upon point obstacles in an ordered array of obstacles, demonstrating the wide range of interactions possible between the chain and the point obstacle. Despite the range of glancing and head on impact that a chain may suffer with the obstacle, our simulations demonstrate a surprisingly simply universal description of the interaction kinetics. This universal description allows prediction of chain length dependence of mobility as a function of row spacing of obstacles.
- The escape kinetics of a single DNA molecule impinging upon a barrier wall perforated with holes in both weak and strong field limits.