

MODELING DNA SEPARATIONS IN SELF-ASSEMBLED MAGNETIC ARRAYS: COMPARISON OF THEORY AND EXPERIMENT

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Summary We present a theoretical model of macroscopic DNA transport in a self-assembled array of magnetic posts. The model parameters are determined either experimentally or from a microscale model. Experiments confirm our scaling results, and we achieve reasonable quantitative agreement with an experimental measurement of the average trapping time.

INTRODUCTION

Microfluidic arrays of posts proffer great potential for rapid, reproducible electrophoretic separations of long DNA. Moreover, such arrays provide an ideal platform for testing fundamental theories of polymer dynamics in confined media, since the arrays are strongly organized, tunable, and highly reproducible between experiments. We focus here upon predicting the macroscale motion and separation properties for arrays formed by the self-assembly of nanosize magnetic beads [1] under the influence of an external magnetic field.

EXPERIMENTAL METHOD

Microchannels with widths of 150 μm and depths of either 10 or 12 μm were fabricated in PDMS using rapid prototyping technology. The magnetic matrix is formed reversibly by injecting an emulsion of monodisperse superparamagnetic beads (size 570 nm, dispersion 5%, kind gift of Ademtech SA, Pessac, France) into the channel and applying a magnetic field of approximately 10mT, as in Fig. 1a. The size-dependent interaction of the DNA with the post (Fig. 1b) gives rise to the separation. We compute the average column diameter d and center-to-center spacing a from the autocorrelation function of an image of the array. Mixtures containing λ (48.5 kbp), 2λ (97 kbp) and/or T4 DNA (168.9 kbp), stained with Yoyo-1, were injected using a double-T and detected by epifluorescence at the entrance (to measure the initial plug half-width l_0) and at a distance $L = 7.5\text{mm}$ downstream, the latter depicted in Fig. 1c. Further details of the experimental setup are available in Ref. [2].

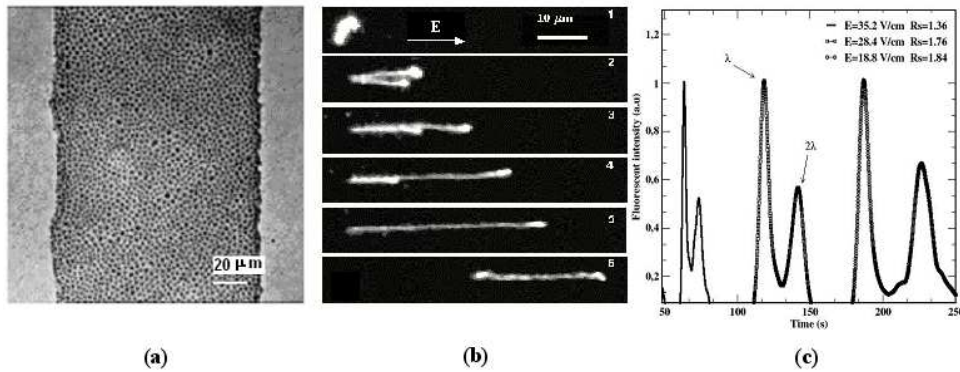


Figure 1: (a) Image of a typical matrix. (b) Mechanism of separation. Long DNA become hooked on the posts and extend in the field direction. The retention time on the post depends upon the the size of the DNA. (c) An electrophoregram of a separation between λ and 2λ DNA.

THEORETICAL MODEL

We used a coarse-grained, exactly solvable lattice Monte Carlo model [3] to compute the mean velocity and dispersivity of the DNA as it moves through a quasi-regular staggered array of columns. Interactions with the posts, quantified by the average trapping time τ and collision probability Π_c , are determined by a microscale model. The exact solution of our lattice model furnishes the mean velocity $\bar{U}^*$ and dispersivity $\bar{D}^*$

$$\bar{U}^* = \frac{U}{1 + \Pi_c(\alpha - 1)}, \quad \bar{D}^* = Ua \frac{\Pi_c(\alpha - 1)[1 + (2 - \Pi_c)(\alpha - 1)]}{2[1 + \Pi_c(\alpha - 1)]^3}, \quad (1)$$

where U is the free solution velocity obtained in a matrix-free channel. The dimensionless trapping time $\alpha = \tau U/a > 1$ measures the retardation caused by the posts. For experimentally relevant values of τ and Π_c , $\bar{D}^*$ increases with increasing Π_c for $\tau < 4/3$ and decreases otherwise. The dispersion caused by the posts is 60-300 times greater than molecular diffusion.

COMPARISON BETWEEN THEORY AND EXPERIMENT

To make a comparison between theory and experiment [2], we assumed that the trapping time is inversely proportional to the field, which is valid for strong fields, and that the collision probability only depends upon the density of posts, $\Pi_c = d/a$. Using these assumptions in eq. (1) and its associated Gaussian macrotransport equation [2], we arrive at the scalings

$$\bar{U}^* \sim E, \quad \bar{D}^* \sim E, \quad t_{1/2} \sim E^{-1}, \quad R_s \sim E^0. \quad (2)$$

where $t_{1/2}$ is the time for the half peak to pass the detector and R_s is the separation resolution. The scaling for $t_{1/2}$ and R_s follows from that for $\bar{U}^*$ and $\bar{D}^*$; thus, we can confirm our scaling results with only two experimental measurements, $\bar{U}^*$ and $t_{1/2}$.

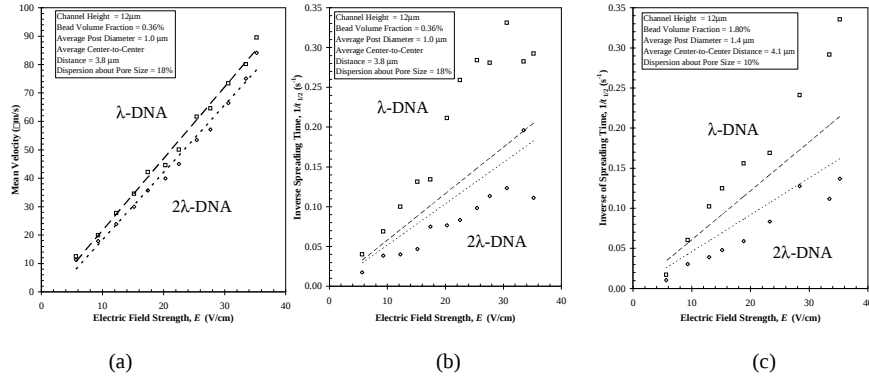


Figure 2: Comparison of theory and experiment for the mean velocity (a) and band broadening (b,c) for the matrix geometries indicated in the insets. Short dashed lines (theory) and $\square$ (experiment) refer to λ DNA; long dashed lines (theory) and $\diamond$ (experiment) refer to 2λ DNA.

As evidenced by Fig. 2, both $\bar{U}^*$ and $t_{1/2}^{-1}$ scale linearly with the field. Although not shown here, the resolution also passes through a plateau over 15-30 V/cm [2], further confirming our scaling results. We made the numerical estimates in Figs. 2b,c by computing the proportionality coefficient for τ from the slope of $\bar{U}^*$ and then computing the difference between the roots $C(t) - 1/2 = 0$ of the concentration profile at the detector,

$$C(t) = \sqrt{\frac{L/\bar{U}^* + T}{t + T}} \exp \left[-\frac{(L - \bar{U}^*t)^2}{4\bar{D}^*(t + T)} \right], \quad T = \frac{l_0^2}{16 \ln(2)\bar{D}^*}. \quad (3)$$

We achieved reasonable quantitative agreement between theory and experiment using this simple model, with much of the error attributable to the initial condition estimate. Similar values of $t_{1/2}$ in Figs. 2b,c confirm the theoretical prediction of a decrease in $\bar{D}^*$ with Π_c .

Acknowledgments

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