Linear Thermodynamics of Rodlike DNA Filtration

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***Abstract*—Linear thermodynamics transportation theory is employed to study filtration of rodlike DNA molecules. Using the repeated nanoarray consisting of alternate deep and shallow regions, it is demonstrated that the complex partitioning of rodlike DNA molecules of different lengths can be described by traditional transport theory with the configurational entropy properly quantified. Unlike most studies at mesoscopic level, this theory focuses on the macroscopic group behavior of DNA transportation. It is therefore easier to conduct validation analysis through comparison with experimental results. It is also promising in design and optimization of DNA filtration devices through computer simulation.**

***Index Terms* —DNA, Electrophoresis, Filtration. Entropy barrier, Transportation, Linear thermodynamics**

I. Introduction

THE electrophoretic migration of polyelectrolyte in polymeric gels forms the foundation of gel separation of biomolecules such as DNA and proteins. The result of fractionalization is determined by characteristic size of the random porous network and that of molecules in solution. Because of the irregularity in random pores of the polymeric gel, theoretical study of fractionation results is difficult. Recently, microfabricated structures with controlled geometry are developed as a substitute for gel in electrophoresis. Patterned periodic regular sieving structures are ideal for study of molecular dynamics of electromigration of polyelectrolytes because the dimension of obstacles and channels can be easily controlled.

Han and his group used an array of channel with regions of two different depths to study the motion of long DNA[1,2], rodlike short DNA[3] and proteins[4] . The thick regions of the channels are of the order of 1 μ m while the depth of the shallow regions is less than 100 nm. As the radius of gyration of the molecule is of the same order larger than the depth of shallow region, entropic barrier plays a dominant role in the electrophoretic migration of these molecules. The configurational entropy barrier is associated with the steric constraints that prevent the molecules from penetrating the wall. For rigid molecules, this configurational entropy barrier can be quantified using statistical theory of equilibrium distribution in simple-shape channels.

In this paper we will develop the theoretical model of filtration of short rodlike DNA molecules using linear thermodynamics theory. A unified electrochemical potential will be defined, from which flux rate of DNA molecules at any point in the field can be derived. We will employ smoothed particle hydrodynamics methods to discretize the fluid domain and integrate the control equations of DNA transportation. From the traveling time and peak broadening over one repeat of nanofilter, the result of DNA partitioning passing though multiple repeats is predicted. By adopting the experimentally obtained parameters of diffusion coefficients and electrophoretic mobilities, it will be shown that separation of rodlike DNA molecules using periodic

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nanofluidic filter arrays is dominated by the configurational entropy effects.

II. Linear thermodynamics theory of DNA transportation

A unified electrochemical potential for the transportation of multi-component charged solute particles in fluidic solvent can be expressed as [5]:

$$\mu_i = \mu_i^0 + RT\ln C_i + z_i F\phi - TS_i \quad (1)$$

where R is the gas constant, T is the temperature, F is faraday number, and ϕ is the external electric potential . C_i, z_i, S_i are concentration, charge, and configurational entropy of component i respectively. μ_i^0 is the standard-state chemical potential, which is a hypothetical reference potential of component i at unit concentration, temperature of 25℃and pressure of 1 atm.

When the volume flow velocity is zero, the flux density $\mathbf{J}$ (the number of moles carried through a unit area in unit time) of a component at steady state is proportional to the driving forces acting on the particle,

$$\mathbf{J} = -U\cdot C\nabla\boldsymbol{\mu} = -\{D_d\nabla C + U_e C\nabla\boldsymbol{\varphi} - UTC\nabla\mathbf{S}\} \quad (2)$$

Where U is the mobility of the solute particle (with the unit of $(cm/s)\cdot(mol/N)$) corresponding to the velocity of the solute obtained if $1N$ of force is applied to $1\,Mole$ of solute molecules. For small solute particles, mobilities corresponding to diffusion term and electrostatic term are identical. In this case, $D_d = RTU$, $U_e = zFU$ and Nernst-Einstein relation $D_d/U_e = RT/zF$ holds. However for the DNA molecules, mobilities corresponding to different driving forces are found not the same and Nernst-Einstein relation is not valid anymore [6]. Specifically, it is established that the diffusivity D_d of DNA molecules of M base pairs changes as $D_d = RTU_d \sim M^{-\nu}$, where $\upsilon = 0.5 - 0.67$ depending on different theoretical models and experimental observations. In this case, it is clear that $U_d \sim M^{-\nu}$. On the other hand, it is well established that the electrophoretic mobility of DNA molecules longer than a few hundred base pairs is independent of the DNA size, i. e. $U_{DNA}^{ep} \sim M^0$. This means that the apparent mobility $\tilde{U} = U_{DNA}^{ep}/zF$ is inverse to the molecular charge $z \sim M$. Therefore in our work, experimentally obtained diffusivity D_{DNA} and free-flow electrophoretic mobility U_{DNA}^{ep} of DNA molecules are used to describe transport parameters corresponding to diffusion and electro-driven motion of DNA molecules. Assuming that the mobility of DNA driven by configurational entropic gradient is the same as that driven by diffusion, the expression for the flux of DNA molecules is modified as

$$\mathbf{J}_{DNA} = -\left(D_{DNA}\nabla C + U_{DNA}^{ep} C\nabla\boldsymbol{\varphi} - \frac{1}{R}D_{DNA}C\nabla\mathbf{S}\right) \quad (3)$$

The conservation of the solute mass implies the evolution of concentration

$$\frac{\partial C_{DNA}}{\partial t} = -\nabla\cdot\mathbf{J}_{DNA}. \quad (4)$$

Equations 3 and 4 are the basic differential equations for the DNA transportation systems. They describe how concentration varies with time and location. As the analytical solution to Equation 4 is not available, it is solved numerically to describe the macroscopic transportation of the charged solute molecules driven by electric field. The configurational entropy of DNA molecules are difficult to calculate, thus we will focus on the short rod-like rigid molecules.

III. Configurational entropy of rod-like solid molecule near solid boundaries

According to statistical arguments made in [7], configurational entropy of short rod-like solid molecules can be defined as $S(\mathbf{r}) = -R\ln\Omega(\mathbf{r})$, where $\Omega(\mathbf{r})$ represents the accessible microscopic configuration state integrals at location $\mathbf{r}$. Specific to the rodlike rigid DNA molecules, the entropy of interest in nanofilter can be calculated from partition function $K(\mathbf{r})$ by $\tilde{S}(\mathbf{r}) = R\ln K(\mathbf{r})$. In Ref [7], the partition function of rigid molecules in various nanopore of infinite length was defined by the ratio of the permissible configurations to the total number of possible configurations, i.e. $K(\mathbf{r}) = P_{permissible}(\mathbf{r})$. This definition of partition function gives a negative entropy $\tilde{S}(\mathbf{r})$ at boundary regions, it poses no problem because only gradient of entropy is relevant. The gradient of entropy is then,

$$\nabla\tilde{\mathbf{S}}(\mathbf{r}) = R\frac{1}{P(\mathbf{r})}\nabla P(\mathbf{r}). \quad (5)$$

Replacing the entropy gradient to the flux expression,

$$\mathbf{J}_{DNA}(\mathbf{r}) = -[D_{DNA}\nabla C(\mathbf{r}) + U_{DNA}^{ep}C(\mathbf{r})\nabla\boldsymbol{\varphi}(\mathbf{r}) - D_{DNA}\frac{C(\mathbf{r})}{P(\mathbf{r})}\nabla P(\mathbf{r})]. \quad (6)$$

As the geometry of the nanofilter is too complex to obtain analytical results of partition function, we calculate the partition function numerically. Fig. 1 shows an example of a rod-like molecule of length L centered at point $C(\mathbf{r})$ near a solid boundary for 2D cases. The permissible configurations are those that lie in the shadowed region. The partition function $K(\mathbf{r})$ is equal to the ratio area of shadowed region to that of the circle.

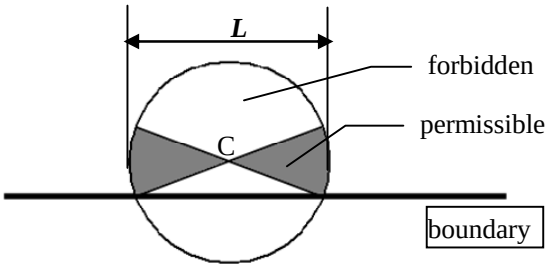

Fig. 1 Definition of partition functions

IV. Diffusivity and Diffusive Mobility of Rod-Like DNA Molecules

The diffusion mobility for short rod-like molecule (12-180bp) is found to be [8]

$$D = \frac{k_B T}{3\pi\eta_0 L}\left(\ln(\frac{L}{d}) + \nu\right), \quad (7)$$

where L and d are the length and diameter of the rod, respectively. The parameter $\nu = 0.312 + 0.565\frac{d}{L} - 0.100\left(\frac{d}{L}\right)^2$ represents the correction term in the end effect. η_0 is the viscosity of the solvent. This formula corresponds to an apparent hydrodynamic radius $R_h = \frac{L}{2\pi\left(\ln(\frac{L}{d}) + \nu\right)}$. The DNA mobility corresponding to this from is $U = \frac{1}{3\pi\eta_0 L}\left(\ln(\frac{L}{d}) + \nu\right)$.

V. Discretization and Integration Using Smoothed Particle Thermodynamics Method

Smoothed particle hydrodynamics (SPH) discretizes the hydrodynamic equations using a set of particles that follows the flow field. It has been successfully applied in simulation of various fluid dynamics problems. In SPH, a field function and its derivatives are approximated as the weighted summation over the neighboring particles through a smoothing function $W(r)$. As one example of implementation, a field function $A(r)$ and its derivatives $\partial A(r)/\partial r$ can be approximated by weighted summation of kernel functions $W(r)$ and their derivatives $\nabla W(r)$ of at neighboring points,

$$A_i = \sum_j m_j \frac{A_j}{\rho_j} W_{ij} \quad (8)$$

$$\frac{\partial A_i}{\partial x_i} = \sum_j \frac{m_j}{\rho_j}(A_j - A_i)\nabla_i W_{ij} \quad (9)$$

$$\left(\nabla^2 A\right)_i = -2\sum_j \frac{m_j}{\rho_j}\left(A_i - A_j\right)F_{ij}, \quad (10)$$

Substituting Equations (9-11) to Equation (4) and (6), the evolution of concentration at any location and any time instance can be obtained.

VI. Numerical Results

As the rodlike DNA molecules pass through the each repeat of the nanoarray channel as shown in Fig. 2, DNA concentration distribution is changed as the result of translation and diffusion process and presence of entropy barrier. The concentration profiles are commonly described by Gaussian functions. Differences in peak location(mean) and peak width (variance) can be obtained for a single repeat from the simulation results. The outcome of multiple repeats can be predicted accordingly.

In this paper, the specification of the nanofilter array is $d_S = 55nm$, $d_d = 300nm$, and $p = 1.0\mu m$, as has been used in experiments described in Ref [3]. The lengths of simulated rod-like DNA molecules are 10nm, 30nm, 50 nm and 70nm respectively.

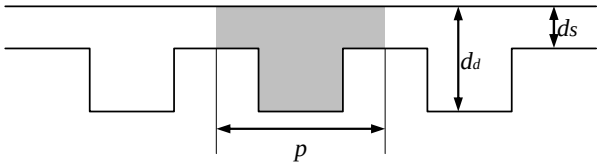

Fig. 2 The nanofilter that consists of a deep region and a shallow region

The computational structure and initial configuration are shown in Fig. 3. In the region represented by particles shown in red near the injection point, the initial concentration of the DNA molecule is 0.1M. The concentration in other regions is 0. DNA concentrations are monitored at two inspection points L and R, which corresponds to the left and right boundary of the shaded repeat in Fig. 2. As the boundary conditions, the concentrations beyond the left and right ends of the channel are set to zero. The applied electric field is 63.42V/cm which was the highest value used in Ref. 3.

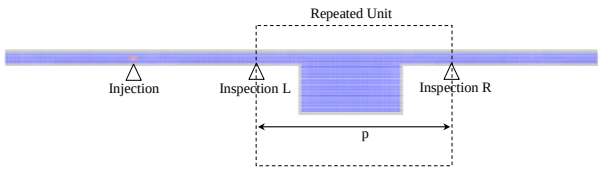

Fig. 3 Initial configuration of the single repeat nanofilter

The diameter of rodlike DNA is taken as 3 nm in calculation of the diffusion coefficients using Eq 7. After integration of the control equation, the profiles of DNA concentration at the left and right inspection points versus time are obtained as shown in Fig 4.

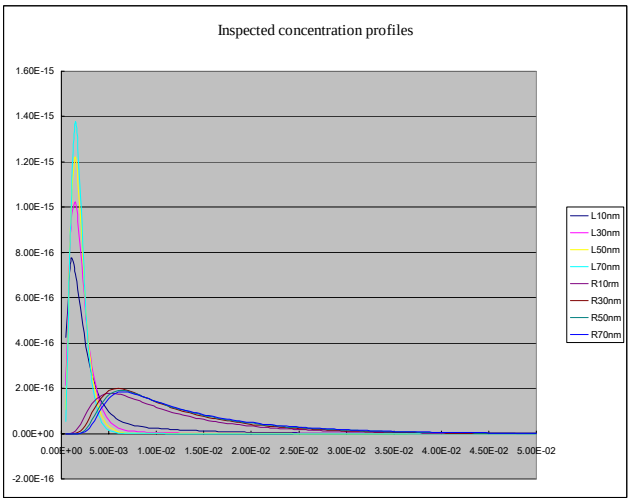

Fig. 4 Concentration profiles at the left and right inspection points

From the concentration profiles shown in Fig. 4, the traveling time passing through one period (τ_1) is calculated from the difference location of peaks of concentration curves for left (τ_p^L) and right (τ_p^R) inspection points $\tau_1 = \tau_p^R - \tau_p^L$. We can also calculate the changes in the variance ($\Delta\sigma_1^2$) by subtracting the variance of right curve ($\Delta\sigma_R^2$) by the width of left one ($\Delta\sigma_L^2$). After *n* repeats, the traveling time and the variance are simply obtained as $\tau_n = n\tau_1$ and $\Delta\sigma_n^2 = n\Delta\sigma_1^2$. As an example, concentration evolution of DNA molecules after 5000 repeats is shown in Fig. 5. It can be clearly seen that partitioning of DNA molecules of different lengths are achieved successfully. Since the current results are obtained from 2D simulation, direct comparison with experimental results is not applicable. As an extension of the current work, three dimensional version of the software is under implementation.

VII. Conclusions

In this paper, we developed a model based on linear thermodynamics for simulating transportation of rod-like DNA molecules. As the configurational entropy is properly defined based on equilibrium partition theory, linear thermodynamics transportation theory is capable of describing partitioning of rodlike DNA molecules under electrophoresis. Discretization of fluid field using SPH method enables analysis of transportation across complex geometrical channels. As this method focus on the behavior of group solute rather than one single molecule, it is capable of investigating large time scale macroscopic phenomena. Quantitative comparison of simulation results with experimental ones can be performed after the 3D version of this theory is implemented.

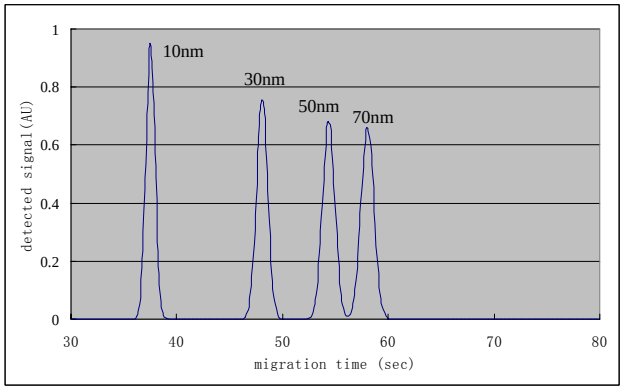

Fig. 5 Simulated DNA concentrations after 5000 repeats.

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