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Historical perspective

The polymer physics of single DNA confined in nanochannels

Liang Dai [a], C. Benjamin Renner [b], Patrick S. Doyle [a,b,*]

[a] BioSystems and Micromechanics (BioSyM) IRG, Singapore-MIT Alliance for Research and Technology (SMART) Centre, 138602, Singapore
[b] Department of Chemical Engineering, Massachusetts Institute of Technology (MIT), Cambridge, MA 02139, United States

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ABSTRACT

In recent years, applications and experimental studies of DNA in nanochannels have stimulated the investigation of the polymer physics of DNA in confinement. Recent advances in the physics of confined polymers, using DNA as a model polymer, have moved beyond the classic Odijk theory for the strong confinement, and the classic blob theory for the weak confinement. In this review, we present the current understanding of the behaviors of confined polymers while briefly reviewing classic theories. Three aspects of confined DNA are presented: static, dynamic, and topological properties. The relevant simulation methods are also summarized. In addition, comparisons of confined DNA with DNA under tension and DNA in semidilute solution are made to emphasize universal behaviors. Finally, an outlook of the possible future research for confined DNA is given.

Contents

* Corresponding author.
E-mail address: pdoyle@mit.edu (P.S. Doyle).

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1. Introduction

In recent years, experiments on DNA in nanochannels [1–7] and their relevant applications [8–14] have stimulated the systematic study of the physics of confined DNA molecules. These experiments have been made possible due to concurrent advances in nanofabrication techniques [15–27]. Beyond practical applications, DNA has often been used as a model semiflexible polymer for single-molecule experiments for the purpose of exploring general polymer physics under confinement [28]. Single DNA molecules with well-defined length can be prepared by the molecular biology techniques, and visualization of single DNA molecules is convenient with the aid of various fluorescence dyes. Two examples [2,29] of the visualization of single DNA molecules in two types of confinement: tube-like channels [2], and the slit-like channels [29] are shown in Fig. 1.

One promising application of confining DNA in nanochannels is genome mapping [9,30]. The basic premise, shown in Fig 2, involves labeling specific sequence motifs in DNA molecules by fluorescence dyes, confining and stretching these molecules in nanochannels, and then inferring the number of base pairs between sequence motifs by measuring the distances or the fluorescence intensities between motifs. The sequence motif map can be used directly or facilitate the assembly of short DNA sequences [30]. Many experiments [14,24,31] and simulations [32] have been performed towards the development of this technological platform. Confining DNA in nanochannels has been also applied for other applications, such as DNA sorting [26,33,34], DNA denaturation mapping [11,35], recognizing barcoded DNA [12], and studying DNA-protein interactions [36].

From the viewpoint of polymer physics, confinement is a type of perturbation to polymer systems, providing many fundamental questions to be answered. Intuitively, confining a DNA molecule within a nanochannel will elongate the DNA and slow down its dynamics. Theoretical studies are motivated to obtain more quantitative relationships between the size of channels and resultant DNA physical properties, often expressed as scaling relationships. The dependence of DNA

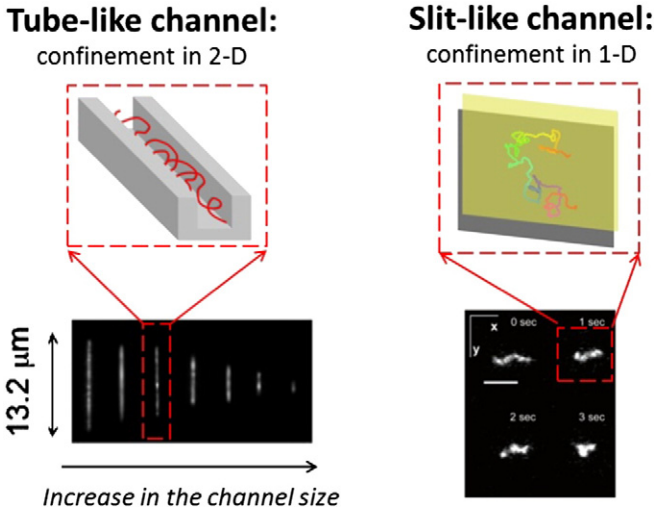

Fig. 1. Schematic illustration of single DNA molecules in square/rectangular channels and slit-like channels. The left-bottom image shows experimental results [2] of the averaged intensity of λ-DNA in the 30 nm × 40 nm, 60 nm × 80 nm, 80 nm × 80 nm, 140 nm × 130 nm, 230 nm × 150 nm, 300 nm × 440 nm, 440 nm × 440 nm channels (left to right). The right-bottom image shows experimental results of 2λ-DNA in a 545 nm tall slit-like channel [29].

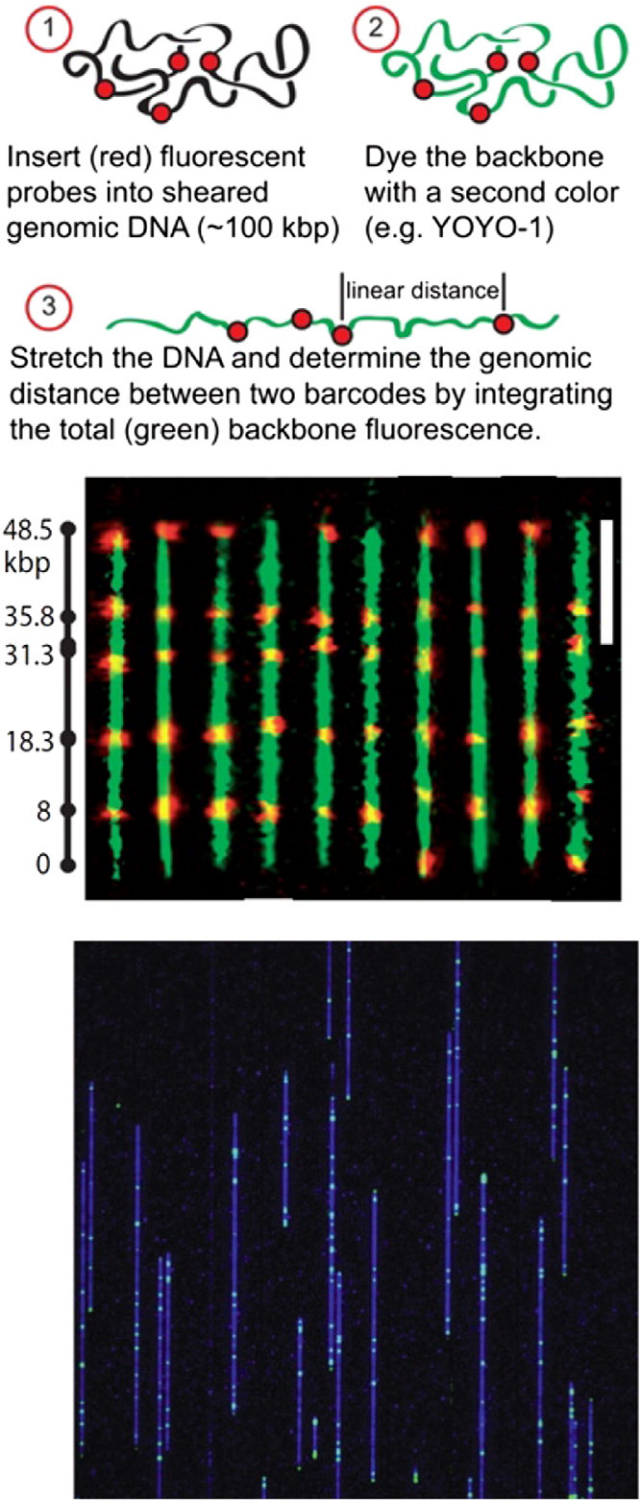

Fig. 2. (Top) Illustration of the steps in genome mapping. Adapted from Wang et al. [32] with permission. (Middle) examples of confined λ-DNA with sites labelled. The DNA molecules are coated with cationic-neutral diblock polypeptides to increase stretching and are confined in 150 × 250 nm^2 channels. The scale bar is 5 μm. Adapted from Zhang et al. [91] with permission. (Bottom) more examples of confined DNA with sites labelled. Image of a single field of view 73 × 73 μm [2]. Adapted from Lam et al. [9] with permission.