Polymer 129 (2017) 44–56

Contents lists available at ScienceDirect

Polymer

journal homepage: www.elsevier.com/locate/polymer

Nanorheology of poly - and monodispersed polymer brushes under oscillatory flow as models of epithelial cancerous and healthy cell brushes

J.D. Hernández Velázquez [a], S. Mejía-Rosales [a], A. Gama Goicochea [b, *]

[a] Centro de Investigación en Ciencias Físico – Matemáticas, Facultad de Ciencias Físico - Matemáticas, Universidad Autónoma de Nuevo León, San Nicolás de los Garza 66450, Nuevo León, Mexico
[b] División de Ingeniería Química y Bioquímica, Tecnológico de Estudios Superiores de Ecatepec, Av. Tecnológico s/n, Ecatepec 55210, Estado de México, Mexico

ARTICLE INFO

Article history:
Received 18 July 2017
Received in revised form
15 September 2017
Accepted 21 September 2017
Available online 22 September 2017

Keywords:
Polydispersed polymer brushes
Tribology
Dissipative particle dynamics

ABSTRACT

In this work we study the rheology of polymeric brushes at the nanoscale interacting with an explicitly included atomic force microscopy (AFM) tip, using dissipative particle dynamics simulations, as models for pericellular brushes on epithelial cells. Two types of cells brushes are modeled: normal cells, whose surface is covered by brushes of uniform length, and cancer cells, which are covered by brushes of non-uniform length. To study their rheology, an external oscillatory shear acting on the surface of the model cells is applied, at two values of stiffness of the chains that conform the brushes. Properties such as viscosity, the coefficient of friction and interfacial tension are reported as profiles along the direction normal to the surface of the cell and are found to depend on the amplitude of the external oscillatory shear. Additionally, it was found that the mean thickness of the brush decreases with increasing amplitude of the external motion. Moreover, it is noteworthy that the properties of the uniform brush are qualitatively different from those of the polydispersed one when the oscillatory shear acts on the sample. It is argued that these differences arise from the collective effect of the chains that conform the brushes. These results illustrate the usefulness of applying physical methods such as AFM in studies of diagnosis and characterization of cancer cells.

1. Introduction

Carcinomas are one of the most common types of cancer in humans. They arise in cells of the epithelial tissue and have attracted special interest because they cause more than 80% deaths due to cancer in the Western Hemisphere alone [1]. In 2012, GLOBOCAN estimated that 14.1 million new cancer cases and 8.2 million deaths occur each year, and these numbers are expected to increase because of lifestyle factors and the aging of the population [2]. To further the understanding of the nature of this disease, much of the research has focused on finding differences on the morphology and the biophysical properties between normal and cancerous epithelial cells (NECs and CECs, respectively) [3]. Physical methods like scanning electron microscopy have been able to image the pericellular coat of epithelial cells [4]. Also, atomic force microscopy (AFM) has proven to be an effective technique to analyze the physico-mechanical behavior of epithelial cells [3,5–7] through studies of properties such as viscoelasticity [8], rheology [9] and mechanical properties [10,11]. In recent decades AFM has been used for understanding the mechanism of metastasis [12–14], and even to discriminate between normal and cancer cells [15]. The morphological differences in the extracellular matrix of healthy and cancer cells are well known. Their molecular brush-like coating is composed of a glycocalyx layer, proteins, polysaccharides etc. The study of the brush covering cancer or healthy cells becomes very important due its correlation with the degree of invasiveness and progression of this disease [16,17]. AFM measurements [6] show that NEC brushes are made up of arrays of uniform length, while the brushes on CECs are made up of arrays of non-uniform length (see Fig. 1). Furthermore, it has been established that the grafting density in NEC brushes is substantially lower than that found in CEC brushes [6].

* Corresponding author.
E-mail address: agama@alumni.stanford.edu (A. Gama Goicochea).

https://doi.org/10.1016/j.polymer.2017.09.046
0032-3861/

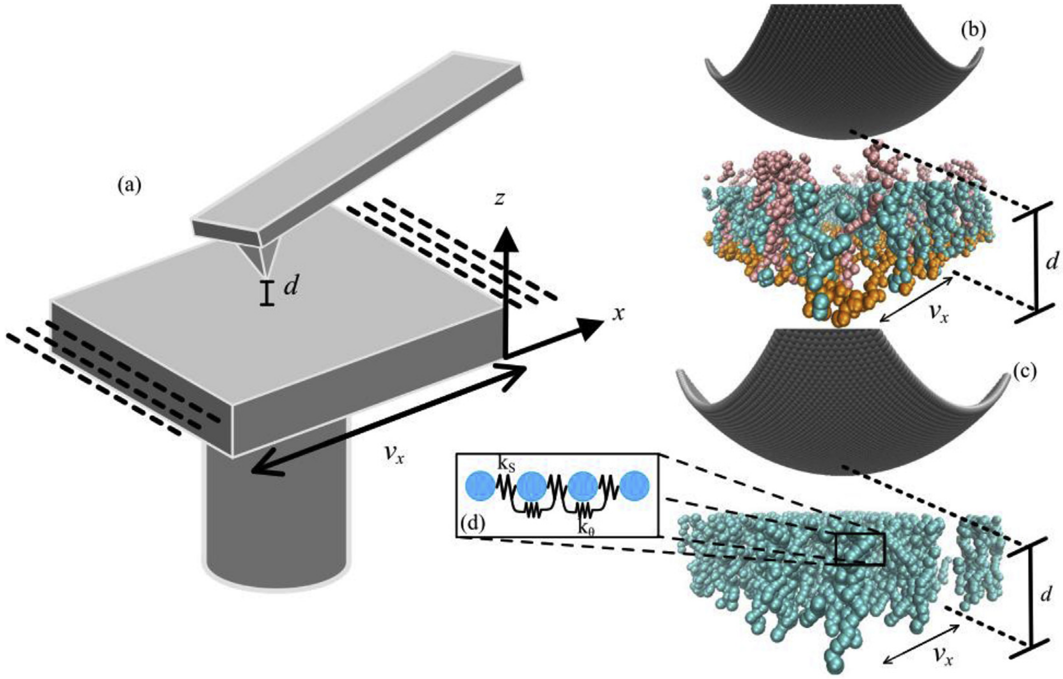

Fig. 1. Schematic representation of the system set up; (a) *d* is the distance between the cell's surface that is placed on the *xy*-plane and the AFM tip; $\boldsymbol{v_x}$ is the oscillatory velocity along *x*-direction applied on the chains' heads fixed on the flat surface. (b) and (c) show the DPD models of CEC and NEC pericellular brushes (orange, cyan and pink beads in (b) and cyan beads in (c), gray beads represent the surface of AFM tip), respectively. The brushes on the CECs have three different chain lengths, where orange beads are the shortest, cyan beads are the medium sized, and pink beads are the largest chains. NEC brush models are conformed by chains with a uniform length (cyan beads). To hold together two consecutive beads of the chains we use Hookean springs and to model the rigidity of the chains we use angular harmonic springs between two adjacent bonds (see inset (d)). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

In this work we present novel results on the characterization of monodispersed and polydispersed brushes compressed by the tip of an AFM, for the study of their rheological properties, by means of dissipative particle dynamics (DPD) simulations. DPD is a coarse − grained technique that has been used to simulate the rheology of suspensions [18] as well as properties of polymer brushes [19], among many other applications. Among the novelties of this work is the inclusion of an explicit surface made up of DPD beads with a radius of curvature *R* representing a nanometric AFM tip. The reason behind this representation is that experiments show how mechanical properties correlate with the morphology of the probe [20], while simulations show that the mechanical properties of fluids confined by explicit surfaces depend on the geometry of such surfaces [21]. Another novel aspect is the introduction of an oscillatory shear acting on the beads grafted on the surface of the cells. This feature is inspired by experimental studies of polymer brushes wherein an oscillatory force is implemented [22,23], which showed how frictional forces depend on the amplitude of the oscillatory movement [22]. With this setup, we predict rheological properties at the nano-scale of CEC and NEC brush models, by reporting profiles along the direction normal to the applied shear. We also study the effects of the oscillatory shear on the CEC brushes varying the amplitude and frequency of the oscillatory motion, while keeping the tip of the AFM fixed at a certain distance from the surface of the cell. Our primary aim is to contribute to the understanding of the physical responses of polymer brushes to the AFM probe through the insights provided by DPD simulations under the influence of oscillatory motion. Furthermore, we show that important knowledge on the nanomechanics and nanorheology of poly − and monodispersed brushes can be gained using this methodology. It is to be emphasized that our results are applicable in general to monodispersed and tri − modal brushes under oscillatory flow, which have various important applications of practical interest such as in lubrication, membrane modification and adhesion [24–26].

2. Models and methods

We performed a set of simulations using DPD [27,28], a technique that has been widely used to study mechanical properties of polymeric [29–33] and biological [34,35] brush models under shear. The DPD interactions can be found in the "Model Details" section of the supplementary information (SI). For the modeling of the brushes we use the bead − spring model [36], with the spring stiffness and equilibrium position chosen appropriately to avoid bond crossing [37]. Here we have included explicitly the surface of an AFM tip located at a distance *d* from the cell's surface, maintaining *d* fixed throughout the simulations; it is designed as a curved surface, made up of frozen beads. The flat surface on which polymer chains are grafted is defined by an effective force, see eq. (S7) in the SI. We have introduced an oscillatory velocity $\boldsymbol{v_x}$ on the chains' heads along the *x*-direction during the entire simulation time (see Fig. 1), to generate oscillatory shear, as is customarily done [31,35]. The velocity is given by eq. (1),

$$\boldsymbol{v_x}(\Delta t) = A cos(\omega \Delta t)\widehat{\boldsymbol{x}}, \tag{1}$$

where *A* and ω are the amplitude and the frequency of the applied velocity, respectively, Δt is the time step, and $\widehat{\boldsymbol{x}}$ is the directional unit vector of the velocity. The oscillatory shear gives rise to highly non-stationary flow near the implicit flat wall that represents the cell's surface.

To model the brushes on CECs and NECs, we have designed an array of linear chains made up of beads joined by harmonic springs, which are anchored from one end to the implicit flat surface, with the length of the chains depending on whether the cell is normal or