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# Ordering in fibrinogen layers: A numerical study

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ABSTRACT

Ordered protein layers are the subject of active biomedical research for their usually interesting physicochemical properties, e.g. permeability, stiffness and pours structure. In the present work, we focused on layers build of fibrinogen molecules characterized by strong shape anisotropy. Using Random Sequential Adsorption (RSA) method, we simulated adsorption process in which the orientation of adsorbate was described by a non-uniform probability distribution. Covering layers obtained this way had different level of global orientational ordering. This allowed us to find relationship between main properties of layers, such as maximal random coverage ratio, and order parameter. For better description and deeper understanding of the obtained structures, the autocorrelation function as well as the distribution of uncovered space were determined. Additionally, we calculated the Available Surface Function (ASF), which is essential for determining adsorption kinetics.



## 1. Introduction

Structure of monolayers formed during an adsorption process is strongly related to the properties of underlying substrate, environmental conditions and adsorbate molecules themselves [1–3]. Earlier works on structured protein coverages indicate a high potential of such layers for material, medical and food sciences as well as pharmaceuticals and cosmetics industries e.g. [4,5]. In this study we focused on ordered fibrinogen layers. We assumed that strongly anisotropic fibrinogen molecules tend to align along a specific axis. Latest experiments show that ordering can have considerable impact on covering layers, e.g. [3,6–8]. The primary mechanism of formation of such layers is adsorption on a patterned surface. However, orientationally ordered phases can be observed in microfluidic cells, in which elongated particles flowing through them may accumulate on their walls [9]. Similar phenomenon causes atherosclerosis [10].

Earlier theoretical works investigating adsorption of anisotropic molecules assumed uniform distribution of molecules directions in a bulk phase [11,12]. Nevertheless, local orientational ordering has to appear as a result of adsorption simply because the probability of parallel alignment is higher, especially when molecules are close to each other. This phenomenon, however, has been noticed and investigated only recently [13].

Orientationally ordered adsorption layers may find application also in other areas of the fundamental science. For example, much interest has been recently shown in diffusion processes in a crowded, yet orientationally oriented environment [14–17]. A natural system for experimental verification of formulated theoretical approaches is liquid crystal [16–18]. It is hard, thought, to control the level of its ordering as it is a result of phase transition. Therefore in practice, liquid crystal is either almost fully ordered or disordered. Adsorption processes can provide an alternative way for obtaining a well controlled, oriented environment.

Aim of this paper is to give quantitative insight into the effect of orientational ordering of elongated particles in a bulk phase on the main properties of adsorption layers. The study focuses mostly on fundamental features which are usually measured by experimentalists such as maximal random coverage ratio, density autocorrelations, and adsorption kinetics. To achieve our goal, we performed extensive numerical simulations of ordered fibrinogen adsorption using RSA algorithm.

## 2. Model

A fibrinogen molecule is modeled as a component of three spheres of 6.7, 5.3 and 6.7 nm in diameter, connected by two chains of ten small 1.5 nm spheres; see Fig. 1.

Such a model was used earlier in [19,20] and it turned out to be the most effective in reproducing maximal coverages and adsorption kinetics obtained in experiments.

Fibrinogen molecules are placed on a flat homogeneous collector surface according to the Random Sequential Adsorption (RSA) algorithm [21], which iteratively repeats the following steps:

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**Fig. 1.** Approximation of fibrinogen molecule shape used in simulations. The side balls have diameter of 6.7 nm whereas the middle one is a little smaller with 5.3 nm. Each of the small spheres between them is of 1.5 nm diameter.

1. a virtual fibrinogen molecule is created with its position on a collector chosen randomly according to the uniform probability distribution, however, centers of all the components (see Fig. 1) are required to be on a collector;
2. the molecule orientation is chosen randomly according to the normal probability distribution having specific expected value $\overline{\varphi}$ and variance $\sigma^2$;
3. an overlapping test is performed for previously adsorbed nearest neighbors of the virtual molecule. The test checks if a surface-to-surface distance between each of the spheres is greater than zero;
4. if there is no overlap, the virtual molecule is irreversibly adsorbed and added to an existing covering layer. Its position does not change during further calculations;
5. if there is an overlap, the virtual fibrinogen molecule is removed and abandoned.

The number of RSA iterations $N$ is typically expressed in dimensionless time units:

$$t = N\frac{S_F}{S_C}, \tag{1}$$

where $S_F = 127.918\,\text{nm}^2$ is an area covered by a single fibrinogen molecule and $S_C$ is a collector's size. In case of our simulations, algorithm was stopped after $t = 10^4$. Example coverages obtained this way are presented in Fig. 2.

To check the importance of boundaries shape, simulations were performed using both round and square collectors. Obtained results do not show any significant dependence on the collector shape. Coverages generated using a round collector of 500 nm diameter were chosen for further analysis.

As mentioned above, the orientational order inside a layer is controlled by a parameter $\sigma^2$ bound up with the width of Gaussian probability density function used during simulations. However in possible experiments, ordering can be evoked by many different factors, e.g. collector structure, electrostatic interactions or flows. Each of them will generally produce different orientation probability distributions with variance being typically a non-linear function of experimentally controlled parameters. On the other hand, this study focuses on the properties of ordered layers regardless of how they were created. Therefore, it is worth to introduce a separate parameter describing orientational order, irrespectively of underlying phenomenons promoting parallel alignment of molecules. The order parameter can be expressed as follows [13]:

$$q = 2\left[\frac{1}{N}\sum_{i=1}^{n}(x_i\cos\phi + y_i\sin\phi)^2 - \frac{1}{2}\right], \tag{2}$$

where $n$ is a number of molecules in a layer, $[x_i, y_i]$ describes a unit vector parallel to orientation of the $i$th fibrinogen, and $\phi$ denotes a mean direction. Parameter $q$ defined as above is 0 for a totally disordered layer and rises up to 1 with the growth of orientational order. The maximum value is reached when all molecules inside a coverage are parallely aligned.

## 3. Results and discussion

### 3.1. Orientations distribution inside a layer

At the beginning of an adsorption process, when the collector is almost empty, orientations of adsorbed molecules reflect the probability according to which they were drawn in the RSA procedure.

$$p(\alpha \in (-\pi, \pi)) = \sum_{k\in Z}\frac{1}{\sqrt{2\pi}\sigma}\exp\left[\frac{(\alpha + 2k\pi)^2}{2\sigma^2}\right] \tag{3}$$

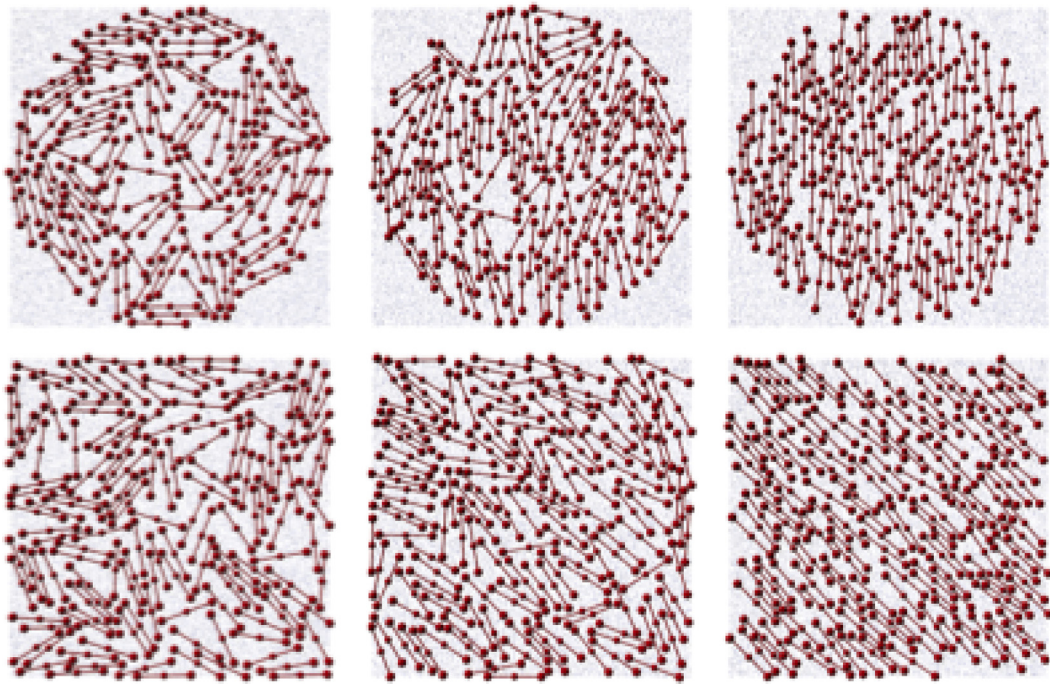

**Fig. 2.** Example coverages for two different collector shapes and three different $\sigma^2$. From left to right, $\sigma^2 = 1.0$, 0.5 and 0.1 which, according to (2), corresponds to the order parameter $q = 0.188$, 0.668 and 0.982, respectively. The expected direction was $\overline{\varphi} = \pi/2$ for round collectors and $\pi/4$ for square ones.