Fibrinogen Adsorption on Biomaterials – A Numerical Study

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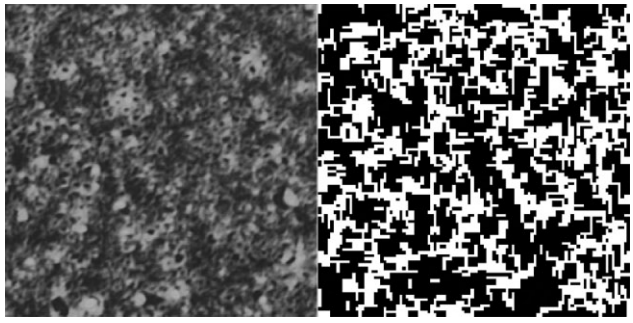
A model for the adsorption of fibrinogen or, in general, non-globular shaped proteins on solid surfaces are presented. Two-dimensional cellular automata simulations of the adsorption of fibrinogen on two different surfaces were performed. The model includes mass transfer toward the surface, adsorption of fibrinogen molecules, and surface diffusion mechanisms for both fibrinogen molecules and clusters. We show that the major physical processes are represented in the recent model. Particularly, the influence of the surface hydrophobicity on the behavior of fibrinogen. Atomic force microscopy images of fibrinogen adsorption on Si model surfaces with different hydrophobicity are compared to the results.



Introduction

The interaction of blood plasma proteins with the surface of implanted materials plays a key role in biocompatibility, as newly implanted material is coated by plasma proteins within a few milliseconds.[1] For blood coagulation and platelet adhesion, the third most abundant blood plasma protein, fibrinogen, has an eminent influence.[2,3] Furthermore, not only the amount of adsorbed fibrinogen affects biocompatibility, but also the arrangement of fibrinogen on the surface.[4] It is thus desirable to study the formation of protein films on surfaces in detail. Due to the difficulties of time-resolved in situ measurements of protein film formation, simulation of protein adsorption and coagulation is expected to be crucial for a better understanding of the underlying physical processes.

The first approaches to simulating adsorption and clustering of proteins on solid surfaces date from early 1990s.[5] A two-dimensional cellular automaton with a hexagonal lattice is first used to simulate the adsorption of a globular plasma protein, ferritin.[6] The model considers diffusion driven adsorption and coagulation. This previous study compares simulation results with experimental results. Later on a simulation study of the adsorption and clustering of a globular protein (lysozyme) on mica using a Monte-Carlo approach has been carried out.[7] For predicting the quantity of lysozyme transported toward the interface, Fick's second law was solved for lysozyme in aqueous solution. Additionally, the kinetics of the adsorption process was considered with different static adsorption probabilities at the interface and compared to experimental findings.

For protein adsorption on solid surfaces, only few atomistic simulations were documented due to the complexity of the proteins and the extensive computer resources required.[8] First contributions in this field dealt with small proteins and conformational changes in contact with different surfaces.[9,10] Recently an approach for

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simulating larger proteins has been developed.[8,11,12] One of the important results is the identification of a protein independent, surface specific interaction energy. It is introduced as the energy required to detach the protein from the surface. A study simulating parts of fibrinogen has been carried out in ref. [13] According to this study, there is no evidence of conformation changes of adsorbed fibrinogen in the simulated timescale of 5 ns for hydrophilic and hydrophobic surfaces.

Despite the progress in the field of macroscopic simulation of protein adsorption and coagulation with models for globular-shaped proteins and their surface diffusion, there are still numerous open questions, and the existing models are to be extended by a series of features. Especially the consideration of non-globular-shaped proteins involving a different type of surface- and inner-cluster diffusion is an important issue. In addition, the thermodynamics of simulated adsorption processes is often not compared to experimental findings and analytical descriptions in previous work.

Recently a review including protein adsorption on polymeric biomaterial surfaces has been published.[14] An overview over molecular dynamics and surrogate modeling approaches focusing prediction of the adsorbed protein amount is given.

The present study is the first macroscopic simulation approach dealing with rod-shaped proteins (fibrinogen), their diffusion in aqueous solution, their adsorption onto the surface, and their diffusion on the surface and within a cluster. Different kinetic and thermodynamic aspects like an environment dependent diffusion description or different driving forces are considered. Finally a qualitative and semi-quantitative comparison to experimental results obtained by AFM images is presented.

Model Description

The common configuration for a protein adsorption experiment consists of the adsorbent material in contact with an aqueous protein solution. Fibrinogen molecules get adsorbed at the interface, and further fibrinogen molecules diffuse toward the surface of the adsorbent. Once the fibrinogen molecules are adsorbed, they undergo translative movement on the surface, possibly forming clusters with two or more fibrinogen molecules. Within a cluster, movements of single proteins can also occur.

The model used in this study contains the four parts mentioned above: (1) mass transfer toward the surface (diffusion); (2) adsorption; (3) surface diffusion; (4) inner-cluster diffusion.

All model parts are executed successive by the order of mentioning. One time step in the simulation is finished if all parts are performed once. The model is developed and written within the numerical computing environment MATLAB (The MathWorks, Inc., Natick, MA, USA).

All lattice sites of the simulated surfaces possess two states. The first state indicates a surface cell covered by a part of the protein, the second an uncovered cell. Every fibrinogen molecule and cluster movement or fibrinogen molecule adsorption can cause a change of the states of the involved lattice sites. Surface diffusion movement of a fibrinogen molecule for example determines a change of the previously occupied lattice sites to the uncovered state.

Diffusion

It is assumed that fibrinogen molecules are initially homogeneously distributed in an aqueous solution. At the protein-adsorbing surface there is a decrease of protein concentration directly at the interface. The consequence is a gradient generated by the local concentration decrease, resulting in diffusion in the solution.

The diffusion is described by Fick's second law:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \tag{1}$$

where c is the concentration of fibrinogen in the solution, t the time, x the position in the solution and D is the diffusion coefficient. In aqueous solution (temperature: 303 K; pH: 7.4) the diffusion coefficient of fibrinogen is $D = 3 \times 10^{-11}\,\mathrm{m^2 \cdot s^{-1}}$.[15]

For solving the diffusion equation, a Neumann boundary condition (imposed gradient) is used. This boundary condition describes a defined flux S out of the solution which is that of adsorbed proteins:

$$\frac{\partial c}{\partial x}\Big|_{x=0} = S \tag{2}$$

Proteins that are not directly adsorbed remain in the solution. This is an important feature for defining the boundary condition realistically which has, to our best knowledge, not been considered in earlier work. The boundary condition at the limit of the calculated domain in the liquid is also of Neumann type (imposed gradient of zero):

$$\frac{\partial c}{\partial x}\Big|_{x=\max} = 0 \tag{3}$$

Equation (1) is numerically solved using explicit finite differences with 60 nodes at a constant spacing of 50 μm.

Adsorption

The solution of the diffusion Equation provides the amount of fibrinogen molecules that are diffusing toward the

interface. A part of these fibrinogen molecules will be adsorbed, another part will be rejected into the solution. The retained fibrinogen molecules affect the concentration distribution in the solution and thus the ongoing diffusion process. Every single fibrinogen molecule is subject to rotational Brownian motion.[16] The orientation of a fibrinogen molecule is considered by attributing an angle with respect to the surface (0–90°). The smaller the angle, the more parallel is the molecule to the surface. The critical angle α_c defines the maximum angle that leads to adsorption of the molecule. Fibrinogen molecules with a higher angle will be rejected.

The characteristics of the surface, particularly the wettability, have a crucial influence on the adsorption of fibrinogen. It is thus necessary to introduce a parameter which reflects the surface characteristics. In the present model the parameter is expressed in analogy to the atomistic simulations[12] with an interaction energy E_i. For hydrophobic graphite, Raffaini and Ganazzoli[11] calculate an average interaction energy of $-1\,200\ \mathrm{kJ \cdot mol^{-1}}$. It is about one order of magnitude lower for a hydrophilic surface like mica.

For the calculation of the surface dependent probability for adsorption, the following Equation is used:

$$P_a = 1 - \exp\left(\frac{E_i}{Z}\right) \tag{4}$$

P_a is the probability of surface dependent adsorption and Z is the virtual lattice temperature in R units. A random number between 0 and 1 is generated. If this number is below the calculated probability, the fibrinogen molecule gets adsorbed.

The structure of fibrinogen is elongated with three globular domains (D–E–D domains) with a total length of ca. 45 nm and a height of ca. 6.5 nm.[17] Recent studies indicate two additional domains, so called αC-Domains[18] (not considered in the present work). The dimensions of an adsorbed fibrinogen molecule on different solid surfaces range between 43–55 nm in length and 7–15 nm in width.[19]

Following these studies, the present model uses an aspect ratio of 3:1 for each fibrinogen molecule. The lattice spacing is 15 nm, hence a molecule is set to $45 \times 15\ \mathrm{nm^2}$. The possible orientations in the numerical grid are horizontal (3×1 lattice points) and vertical (1×3 lattice points). Periodical boundary conditions at the edge of the simulated area are used. Fibrinogen molecules are randomly placed onto the surface with a random orientation (horizontal or vertical). Perpendicular orientation of the fibrinogen molecule with respect to the surface is not considered due to the chemical equality of the two D domains. If a randomly selected lattice point is already occupied, the arriving molecule is rejected and remains in solution.

Surface Diffusion

Lateral movements of fibrinogen molecules on mica have been observed in ref. [20] In the present model, surface diffusion of fibrinogen molecules and of clusters is also considered. Obviously clusters have a lower diffusion rate than fibrinogen molecules, since a cluster is attached by a higher number of bonding sites to the surface. The model provides this dependency using a power law:[7]

$$P_o = P_{max} \cdot s^{-\mu} \tag{5}$$

where P_o is the probability of migration for a fibrinogen cluster or molecule, P_{max} the maximum probability of migration for a fibrinogen cluster or molecule, s the number of fibrinogen molecules in a cluster and μ the cluster mobility coefficient ($\mu > 0$). The mobility coefficient μ is a scaling exponent.

A small value of μ yields a high mobility of the clusters.

In analogy to Adsorption Section we also introduce an influence of the adherent surface that effects the migration of clusters and fibrinogen molecules according to:

$$P_s = \exp\left(\frac{E_i}{Z}\right) \tag{6}$$

where P_s is the surface dependent migration probability of clusters and fibrinogen molecules. The product of the two probabilities P_o and P_s [Equation (5) and (6)] gives the overall migration probability of a cluster or fibrinogen molecule for the diffusion on the surface. In analogy to Adsorption Section a random number is generated. A resulting value below P_s causes the fibrinogen clusters or molecules to move.

The geometry of the lattice limits the moving directions to up, down, left, and right. Movement perpendicular away from the surface is not considered in the present work due to the large interaction energy between the molecule and the surface. For a free fibrinogen molecule without any cluster or molecule in the neighborhood cells, the probability of moving in all possible directions is equal. Depending on the neighborhood, the two clusters or fibrinogen molecules can be "attracted". The physical reason is the hydrophobic nature of the D and E domains[21] which causes an affinity to each other. Thus the migration probability for the directions combining fibrinogen molecules or clusters is higher than that for isolated fibrinogen molecules.

Inner-Cluster Diffusion

Merely the surface diffusion of fibrinogen molecules and clusters is not sufficient to explain the experimental findings[22,23] of fibrinogen layer formation on different surfaces. Many fibrinogen molecules which are part of a

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cluster undergo certain energetic and conformational changes.[24] One possibility to model this is to introduce the diffusion of fibrinogen molecules within the clusters. Basically there are two types of movements for non-globular shaped proteins like fibrinogen: translative and rotative. The 3 to 1 shape of the fibrinogen molecule in the present model is introduced by considering rotations around all three molecule parts. Theoretically there are ten possible movements: four translative and six rotative.

The probabilities of rotation and translation are determined by considering the overall distance covered by the different parts of the fibrinogen molecules. For all translative movements, the fibrinogen molecule has to move by 1 lattice space. In terms of all fibrinogen molecule parts this yields a total distance of 3 lattice units. For the rotation around the middle part of a molecule the total distance is $2\sqrt{2}$ units, and for the rotation around the outer parts $3\sqrt{2}$ units. This is illustrated in Figure 1.

The moving probability is set inversely proportional to the overall moving distance.

Not all theoretically possible movements are feasible in a simulation because of spatial restrictions due to the neighborhood of other fibrinogen molecules within a cluster. Figure 2 shows three of nine possible movements in a cluster consisting of two fibrinogen molecules.

In the present model, it is assumed that interfaces between fibrinogen molecules within a cluster are energetically more favorable than surfaces of a cluster to the aqueous solution. The value of the free surface of a cluster correlates with the number of free edges of a cluster, implying that a lower number of free edges is more favorable. The three movements shown in Figure 2 demonstrate different changes of the number of the free edges after the inner cluster movement of a fibrinogen molecule. In Figure 2(a) the number of the free edges is constant, Figure 2(b) shows a decrease, and Figure 2(c) an increase of the number of the free edges.

The movements which increase the number of the free edges are attributed a lower movement probability P_b.

The overall movement probability (decision if the molecule moves at all) is influenced by the fibrinogen molecules in the neighborhood and, in analogy to Adsorption and Surface Diffusion Sections , by a surface dependent term. The more neighboring lattice points of a fibrinogen molecule are occupied, the lower is the movement probability. The present model considers this with a linear dependence because it is assumed that the binding sites of a molecule are equal. The surface dependent moving probability of fibrinogen molecules within clusters P_c is defined by:

$$P_c = \exp\left(\frac{E_i}{Z}\right) \tag{7}$$

Similarly as in the adsorption and surface diffusion parts of the present paper, a random number between 0 and 1 is generated. A value below P_c causes movement of the fibrinogen molecule within the cluster.

The key parameters of the model are: the simulation time $t_s(s)$, the interaction energy E_i ($kJ \cdot mol^{-1}$), the movement probability for increasing free edges P_b, the critical adsorption angle $\alpha_c(^\circ)$ and the initial concentration of fibrinogen in solution c_s ($\mu g \cdot mL^{-1}$).

Experimental

Adsorption Experiments

For comparing the simulated results with experiments under comparable conditions, two different surfaces of Si with adsorbed fibrinogen were characterized by AFM.

The substrates (Si wafer, diameter: 11 mm) were activated with oxygen plasma. The hydrophilic samples were used right after the plasma treatment. The hydrophobic substrates were coated with chlorodimethylsilane (Sigma–Aldrich, Schnelldorf, Germany).

Human plasma fibrinogen (Calbiochem, Merck KGaA, Darmstadt, Germany) emerged in phosphate buffer saline was deposited onto the silicon wafer segments under stagnant and quasi-physiological (pH 7.4, $T = 37\,^\circ C$) conditions. With an initial fibrinogen concentration in solution of $10\ \mu g \cdot mL^{-1}$ the samples surfaces were incubated for 180 min. After adsorption the samples were rinsed twice with deionized water and dried under compressed air.

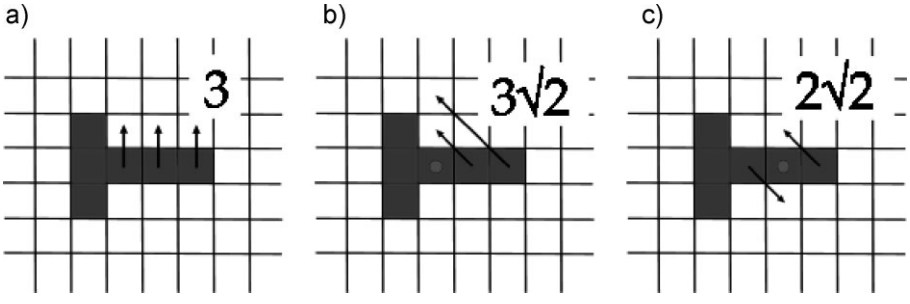

Figure 1. Three examples for covered distances upon movement of a fibrinogen molecule. (a) Translative movements, (b) rotation around the outer parts, and (c) rotation around the middle part.

AFM-Imaging

The AFM measurements were performed with a Nanoscope IV (Digital Instruments, Santa Barbara, CA, USA) operating in tapping mode (scan rate: 2 Hz) under ambient temperature in air. Standard tapping mode silicon cantilevers (Olympus OMCL-

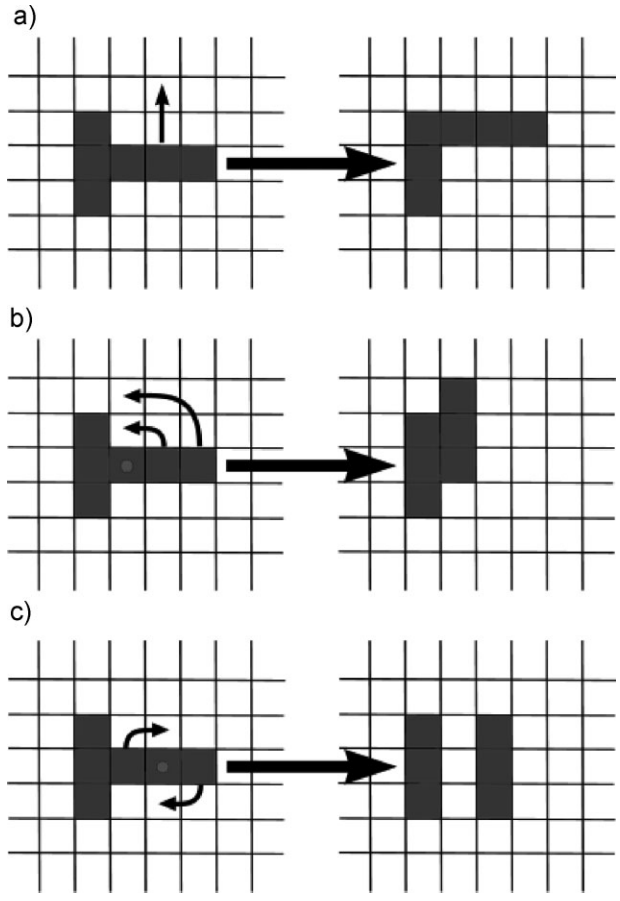

Figure 2. Three examples for possible movements in a two fibrinogen molecule cluster. (a) Translative movement, (b) rotation around left molecule part, and (c) rotation around the middle molecule part.

AC160TS, Atomic Force F&E GmbH, Mannheim, Germany) with a nominal constant force of 0.42 $N \cdot m^{-1}$ and a typical resonance frequency of 300 kHz were used.

Contact Angle Measurements

The contact angles were obtained from the shape of axisymmetric menisci of sessile distilled water drops wits a DSA10 drop shape analysis system (Kruss GmbH, Hamburg, Germany).

Results

For verification purposes, the model has been tested in two different ways. To determine the correctness of the underlying physical assumptions, we compare results with experimentally confirmed analytical descriptions of the adsorption process.

The simulation in this section are carried out with $\alpha_c = 90°$, i.e., there is no protein rejection due to unfavorable orientation with respect to the surface. The mobility coefficient μ has been set to one in all simulations for which results are shown.

The calculation times are between ca. 2 h for the hydrophilic and ca. 8 h for the hydrophobic surfaces. These values are typical for the uncompiled program in the MatLab environment. A reduction in calculation time could be easily achieved by employing a compiled version of the program.

Fibrinogen Diffusion Kinetics

Figure 3 shows the fibrinogen concentration distribution in the solution at different simulation times t_s. The present model produces a stable and consistent concentration distribution. The high flux of fibrinogen out of the solution at the beginning of the adsorption process and the decrease at later times reflect the interaction of diffusion and adsorption. Note that the fibrinogen concentration gradient directly at the surface flattens for longer diffusion times. This is a consequence of the fibrinogen molecules that are rejected at the surface and remain in the solution.

Adsorption Thermodynamics with Analytical Equations

The fibrinogen adsorption process has been shown to follow a Langmuir type adsorption up to an initial fibrinogen concentration in solution of 1 $mg \cdot mL^{-1}$.[24,25] Thus, the thermodynamics of this adsorption process is described by the Adsorption isotherm as characterized mathematically by:[26]

$$\theta = \theta_{max}\left(\frac{L \cdot c_e}{1 + L \cdot c_e}\right) \quad (8)$$

where θ is the degree of surface coverage, θ_{max} the maximum surface coverage, L the Langmuir sorption

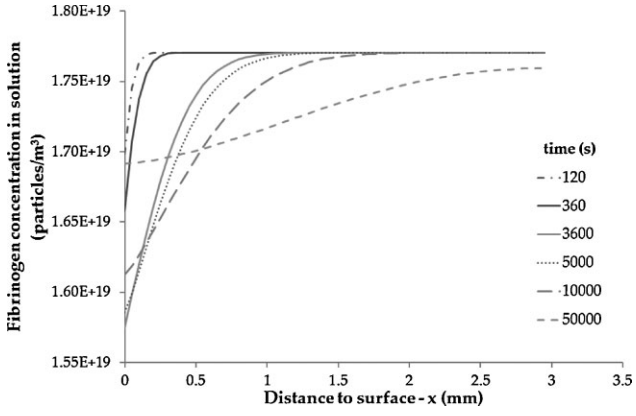

Figure 3. Diffusion profiles: $E_i = -1140$ kJ $\cdot$ mol^{-1}; $c_s = 10$ µg $\cdot$ mL^{-1}; $P_b = 0.02$.

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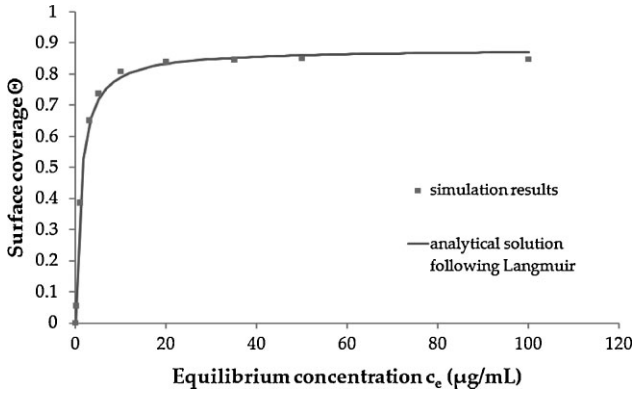

Figure 4. Adsorption isotherm: $E_i = -1140$ kJ · mol^{-1}; $t_s = 5 \times 10^4$s; $P_b = 0.02$.

coefficient and c_e is the equilibrium fibrinogen concentration. Equation (8) is generally used to fit experimental data.[25,27]

Figure 4 shows an example of simulated data fitted with Equation (8) of the resulting equilibrium concentration of fibrinogen in solution c_e when the initial concentration of fibrinogen in the solution c_s is varied. The data illustrate the good agreement with the theoretical Langmuir adsorption, confirming that the major physical processes are represented in the model.

Simulation Examples for Surfaces with Different Hydrophobicity Compared to Experimental Findings

By varying the model parameters, adsorption processes on different surfaces were simulated. A main issue is the different hydrophobicity of surfaces.

In Figures 5 and 6, simulation results are shown in combination with the in-house experimental results on fibrinogen adsorption on surfaces with different hydrophobicity.

In Figures 5 and 6, white color indicates adsorbed proteins and black indicates uncovered surface.

For the hydrophilic surface there are 59 clusters with an average cluster size of 5.05 fibrinogen molecules for the hydrophilic surface after the simulated process. The number of adsorbed single fibrinogen molecules is 299. The hydrophobic surface consists of only one adsorbed cluster with a cluster size of 1 371 fibrinogen molecules. The number of adsorbed single fibrinogen molecules is 12.

A variation of the cluster mobility coefficient μ between 0.5 and 1.5 has some effect on the number of adsorbed fibrinogen molecules and the average cluster size. Values for μ smaller than unity have relatively little effect, whereas larger values lead to an increase of cluster size and a decrease of the number of the clusters. As now specific information is available about cluster mobility, a value of $\mu = 1$ has been used for the results presented here.

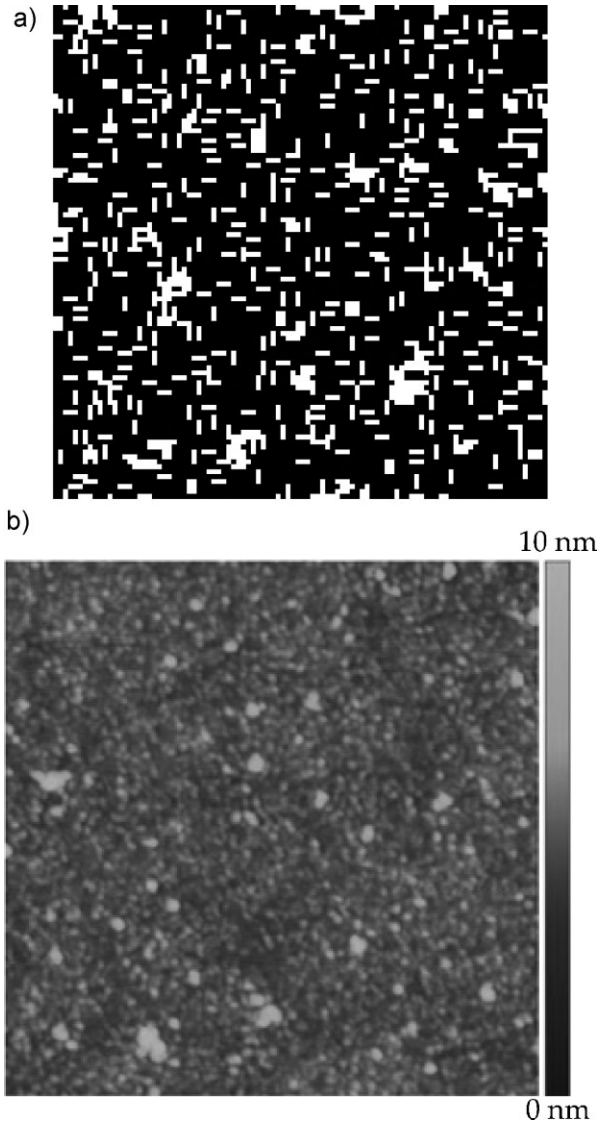

Figure 5. Simulation and experimental results for the hydrophilic surface. (a) Simulation result for a hydrophilic surface: $E_i = -300$ kJ · mol^{-1}; $c_s = 10$ μg · mol^{-1}; $P_b = 0.2$; $t_s = 2\,700$ s; simulated area: 1.5×1.5 μm^2. (b) AFM picture of hydrophilic surface (Si wafer oxygen plasma treated); contact angle with water $37.3 \pm 1.5^\circ$; scan size: 1.5×1.5 μm^2.

Discussion

The model for the adsorption process of the non-globular shaped protein fibrinogen shows a good performance compared to experimental findings, analytical descriptions, and recent simulation studies. One of the most important and novel features is the possibility to simulate the adsorption process on surfaces with different hydrophobicity.

It has been shown experimentally[25] that fibrinogen adsorbs up to an initial concentration in the solution of 1 mg · mL^{-1} following the Langmuir adsorption theorem. One precondition of the Langmuir adsorption process is that

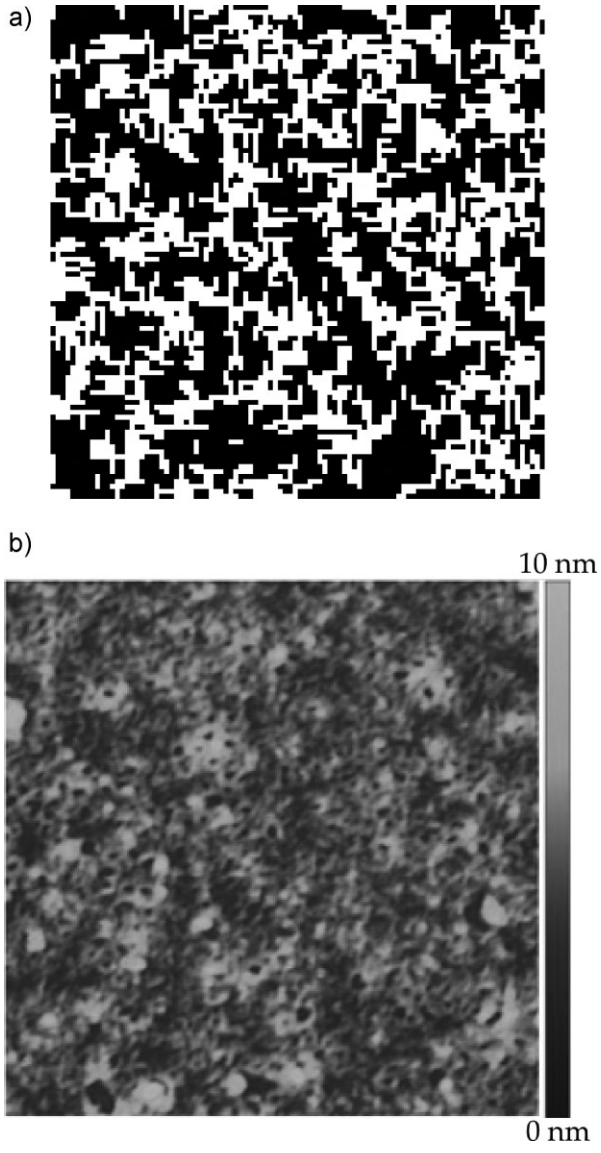

Figure 6. Simulation and experimental results for the hydrophobic surface. (a) Simulation result for a hydrophobic surface: $E_i = -1630\,kJ \cdot mol^{-1}$; $c_s = 10\,\mu g \cdot mol^{-1}$; $P_b = 0.02$; $t_s = 3\,500\,s$; simulated area: $1.5 \times 1.5\,\mu m^2$. (b) AFM picture of hydrophobic surface (Si wafer with self-assembled monolayer of chlorodimethylsilane); contact angle with water $97.6 \pm 2^\circ$; scan size: $1.5 \times 1.5\,\mu m^2$.

no multilayer adsorption occurs.[28] Due to the low initial fibrinogen concentration in solution that was used here in the simulation and the experiment ($10\,\mu g \cdot mL^{-1}$) the assumption of monolayer adsorption is justified. This is confirmed by the excellent agreement that of the adsorption isotherm of the simulated adsorption process (Figure 4) and the Langmuir adsorption isotherm.

The limitation to two possible fibrinogen molecule orientations limits the model only in few aspects: for inner-cluster diffusion there are consequences for the achievable cluster packing density, which is lower for less orientations. However, the overall quality of the simulation results is not affected (Figures 5 and 6).

In Simulaton Examples for Surfaces with Different Hydrophobicity Compared to Experimental Findings Section two simulation runs for surfaces with different hydrophobicity (Figures 5(a) and 6(a)) are shown. A comparison between our own measurements (Figures 5(b) and 6(b)), different experimental studies and the simulation results shows qualitative agreement in several respects. The experimental studies[20,22] show that the clustering behavior and the adsorbed amount of fibrinogen change on surfaces with different hydrophobicity. For hydrophobic surfaces, the adsorbed amount of fibrinogen with a constant initial fibrinogen concentration in solution is higher compared to hydrophilic surfaces. This is due the surface dehydration phenomena on hydrophobic surfaces that facilitate protein adsorption as opposed to hydrophilic surfaces where the displacement of surface bound water by proteins is energetically prohibited.[29]

The simulation results for the hydrophilic surface (Figure 5) show a large fraction of fibrinogen molecules and small clusters (average cluster size ca. 5 fibrinogen molecules). Unlike this, on a hydrophobic surface (Figure 6) there is a close network of proteins (only one cluster) and few fibrinogen molecules. The amount of adsorbed fibrinogen is much higher on the hydrophobic surface.

A further quantitative comparison between simulation results and AFM images is problematic due to the difficult interpretation of the AFM images and has not been carried out in the present study.

The different simulation parameters for surfaces with different hydrophobicity are mainly the movement probability for increasing free edges P_b and the interaction energy E_i.

The interaction energy E_i is used on the basis of the molecular dynamics studies of Ganazzoli and Raffaini,[8] even though they simulate the adsorption of different blood plasma proteins on surfaces with different hydrophobicity. Albumin has a dimension of ca. $14 \times 4 \times 4\,nm^3$,[30] fibronectin of ca. $70 \times 25 \times 4\,nm^3$.[31] Ganazzoli and Raffaini introduce an interaction energy E_{int} as the energy needed to detach the adsorbed protein from the surface and converting it to the native state. E_{int} depends on the number of the protein residues in contact with the surface. For all considered proteins the average number of residues in contact with the surface is about 20. Thus the interaction energy E_{int} for the average number of residues of different proteins is for hydrophobic graphite ca. $-1\,200\,kJ \cdot mol^{-1}$ and for the hydrophilic polymer PVA ca. $-260\,kJ \cdot mol^{-1}$, respectively. Fibrinogen has a dimension of ca. $47 \times 5 \times 5\,nm^3$,[32] between the sizes of the two other blood plasma proteins studied by Ganazzoli and Raffaini.

The value of the interaction energy changes drastically depending on the hydrophobicity. The values for hydrophilic surfaces are lower, implying that less energy is needed to detach the proteins.[8] Ganazzoli and Raffaini

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observe a higher probability for water molecules to stay much closer to the hydrophilic surface as compared to the hydrophobic one. Thus the reversible process of protein detachment and re-hydration of the surface is more favorable for hydrophilic than for hydrophobic surfaces.[33] Additionally the conformation changes are more likely for adsorbed fibrinogen on hydrophobic surfaces[34] which leads to a stronger binding.

In analogy to Ganazzoli and Raffaini, the present model shows for the hydrophobic surface a larger value of the interaction energy E_i than for the hydrophilic surface. The variation of the exact value is due to the different surfaces (graphite and PVA *vs.* treated Si wafer).

The movement probability for increasing the number of free edges P_b describes the clustering behavior of fibrinogen especially for the inner-cluster diffusion. It is thus a parameter specifying the interaction of adsorbed fibrinogen molecules among each other. It has been shown that conformation changes and denaturation processes of proteins depend on the amount of adsorbed protein and the hydrophobicity of the surface.[34] Particularly the secondary structure of fibrinogen changes dramatically after adsorption on surfaces with different hydrophobicity.[35] For the initial concentration of fibrinogen in solution as considered here, the α-helix on hydrophilic surfaces and the β-sheet structure on hydrophobic surfaces prevails.[35] The β-sheet secondary structure is responsible for the interaction between fibrinogen molecules.[33] Thus, changes of the secondary structure of adsorbed fibrinogen molecules have an eminent influence on their interaction among them and leads to a modification of the clustering behavior. This process is represented by a variation of P_b.

Conclusion

We propose a model for simulating the adsorption and coagulation process of non-globular proteins on different surfaces. Adsorption principles found in molecular dynamic studies were included in our mesoscopic simulation approach. Considering main physical effects, the simulated adsorption process follows recent experimental findings and theoretical mathematical descriptions of the fibrinogen adsorption process. By modifying the two key parameters, the movement probability for increasing free edges P_b and the interaction energy E_i, it is possible to adapt the model to surfaces with different hydrophobicity. The in-house adsorption experiments and experimental studies on surfaces with different hydrophobicity show a good agreement with the simulation results.

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