Transport properties of water at functionalized molecular interfaces

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Understanding transport properties of solvent such as diffusion and viscosity at interfaces with biomacromolecules and hard materials is of fundamental importance to both biology and biotechnology. Our study utilizes equilibrium molecular dynamics simulations to calculate solvent transport properties at a model peptide and microarray surface. Both diffusion and selected components of viscosity are considered. Solvent diffusion is found to be affected near the peptide and surface. The stress-stress correlation function of solvent near the hard surface exhibits long time memory. Both diffusion and viscosity are shown to be closely correlated with the density distribution function of water along the microarray surface. © 2009 American Institute of Physics. [doi:10.1063/1.3224122]

I. INTRODUCTION

Biological processes such as protein adsorption, structural attachments, and some enzyme catalysis all take place in aqueous environments near hard surfaces. In micro- and nanofluidic applications, the presence of surfaces strongly affects properties of the fluid components. Both the presence of surface and water molecules in the vicinity of macromolecules can significantly affect structural and thermodynamic properties.¹ For instance, a minimum amount of water is needed for protein to maintain its biological structure and functionality.² Protein desolvation plays a driving force in ligand-receptor recognition and binding.³ The presence of surfaces affects both the thermodynamics and kinetics of proteins.

Kinetics of enzymatic reactions are known to be closely related to solvent viscosity.^{4,5} In self-assembled microdisperse systems such as micelles used as reaction media/vessels, interfacial water plays an important role in the reaction kinetics.⁶ Solvent transport properties are also modified at macromolecular or biomaterial interfaces. A hydration layer is formed at the surface of biomolecules in which the structural organization and hydrodynamic properties of water differ significantly from those in bulk. Viscosity is a central parameter in the design of microfluidic biochips and other lab-on-a-chip applications. Understanding the hydrodynamic properties of water molecules in the hydration layer surrounding biomolecules and near functionalized surfaces is of paramount importance and has been a research topic drawing enormous interest from both theoreticians and experimentalists.^{7–11}

Computer simulations provide a useful tool to study the intrinsic structural and dynamic properties of solvent at the atomic scale.^{12,13} The causes for changes in transport properties of solvent, such as diffusion and viscosity at protein/

nucleic acid surfaces, in confined nanopores or biomaterial interfaces, are approachable using molecular dynamics simulation methods. Solvent diffusion in the bulk is often evaluated using the Einstein relation that relates the self-diffusion coefficient of solvent to the slope of the mean square displacement at infinitely long time. While rigorously valid for a fluid in infinite isotropic conditions, the long time limit is not always suitable to calculate solvent diffusion defined locally in a finite inhomogeneous space.

It is well recognized that solvent mobility is limited near a surface. By considering water molecules in a finite volume element around biomolecules, numerous attempts have been made to calculate solvent diffusion in the hydration layer of proteins/DNA as a function of distance to the surface.^{10,14–16} For viscosity as opposed to diffusion, the stress-stress autocorrelation is often used to calculate the viscosity of the bulk fluid from equilibrium molecular dynamics simulations.^{17,18} To access the local viscosity of inhomogeneous fluid, such as fluid confined in nanopores or near imposing walls, nonequilibrium molecular dynamics (NEMD) has been utilized to simulate fluid under shear flow.^{19–21} The position-dependent viscosity coefficient of the fluid is related to the ratio of local shear stress to velocity gradient. Local shear viscosity of equilibrium fluid can also be estimated by extrapolation at zero shear rate in NEMD. However, Pozhar reported failure of bulk-fluid based and heuristic approximations in the calculation of local viscosity by NEMD.²² Very often, density profiles are also found to be closely correlated with diffusion²³ and viscosity.^{22,24}

In this article, we focus on the strong correlation between solvent density profile and transport properties at biofunctionalized surfaces. Diffusion and viscosity of solvent at interfaces of an experimentally used microarray surface and peptide are investigated by analysis of equilibrium molecular dynamics simulations of a molecular model. The procedure is briefly introduced in the methodology section and the method used to calculate diffusion and viscosity coefficients is described in detail. Analysis results are presented and

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FIG. 1. Snapshots from the simulations of the free peptide (a), unfunctionalized (b), and functionalized microarray surfaces (c). All three systems are solvated by explicit water (not shown).

compared with earlier work on transport properties of solvent in the results and discussion section, which is followed by the conclusion section.

II. METHODS

A. Simulations

We wish to understand how a peptide tethered to a surface affects the local viscosity profile. To study that, we must also know the effect of a surface without a peptide and the effect of a peptide without a surface on the quantities of interest. We utilize three equilibrium molecular dynamics simulations to compare solvent diffusion and viscosity near both unfunctionalized and functionalized microarrays as well as a free peptide's surface.²⁵ Three model systems are thus needed: A free peptide in solution, a microarray surface with an organic (aminosilane) coating in solution, and the same system with the peptide tethered. Snapshots from each of these last two simulations are shown in Fig. 1.

Modeling of the microarray surface is based on a previously studied peptide chip.²⁶ Briefly, 64 acetylated aminosilane derived linkers grafted on a silica surface defining the xy -plane form a 9.2 Å thick layer. Then, 1337 TIP3P water molecules fill the remaining space above the microarray surface. The system is simulated under glide-plane boundary condition²⁷ in a $4.05 \times 3.50 \times 3.89$ nm³ box. Thus we have a controlled surface density of ~ 0.07 nm⁻². The system is studied at zero ionic strength. The functionalized microarray surface simulation is adopted from a previous study of salt effects on surface tethered peptide.²⁸ The pentapeptide RHSVV chosen for the simulation is an epitope of the anti-cancer p53 protein antibody used in previous peptide chip experiments²⁶ and simulations.²⁵ The C-terminal carboxylic

group of the peptide is neutralized and capped as *N*-methanamide. For the peptide free in solution 2164 TIP3P water molecules are added and the system is simulated under periodic boundary condition in a box of dimension $4.01 \times 4.01 \times 4.01$ nm³. Two Cl⁻ ions are added to neutralize the positively charged peptide.

All simulations are performed in the microcanonical (NVE) ensemble at 300 K using the ESP (Ref. 29) molecular dynamics simulation program. The unfunctionalized microarray surface simulation is performed for 4 ns and the coordinates and pressure are collected every 2 fs. We use a 4 ns trajectory from the simulation of functionalized microarray surface²⁸ with coordinates and pressure saved every 2 fs. A 1 ns trajectory of peptide simulation is utilized in the analysis of solvent diffusion and is taken from our former 160 ns simulation with coordinates saved every 100 fs.²⁵ More detailed description of the modeling and simulation procedures can be found in our previous study.²⁸

B. Solvent distribution function

Water density, ρ , as a function of distance, d , to the surface is defined by $\rho(d) = n(d)/V(d)$, where n is the number of water within a finite volume V . The relative water density, ρ' , is then defined by $\rho'(d) = \rho(d)/\rho^{\text{bulk}}$, where ρ^{bulk} is the bulk water density far from the surface. In the microarray simulations, the aqueous interface surface is formed by a layer of densely packed, methyl terminated aminosilane derived linkers. Thus, we regard the mean plane of the rough -CH₃ layer as the microarray surface, in both the unfunctionalized and functionalized systems. Here, d is the vertical distance (along the z -direction) from the water oxygen to the microarray surface and V is the volume of a finite slice (parallel to the xy -plane). For water density around the peptide, which has a closed surface of irregular shape, d is defined as the distance from the water to the nearest heavy peptide atom and $V(d)$ is estimated as the volume of a spherical shell of radius $d+d_0$, where $d_0=6.4$ Å is the radius of a 1097.4 Å³ sphere (concentric with the spherical shell) that geometrically approximates the peptide. In calculating water density profiles, we are mostly interested in locations of its maxima and minima and, more importantly, how they correlate with that in diffusion coefficient and viscosity. More precisely normalizing the water density is not important and has little impact on our findings.

C. Diffusion coefficient calculation

According to the Einstein relation, the self-diffusion coefficient of water, D , can be estimated numerically with the finite difference expression^{14,30} $(\langle |r(t_2) - r(t_0)|^2 \rangle - \langle |r(t_1) - r(t_0)|^2 \rangle) / (t_2 - t_1) = 2nD$, where $r(t_0)$, $r(t_1)$, and $r(t_2)$ are the positions of water oxygen at time "zero," 1, and 2 ps, respectively; $\langle \dots \rangle$ denotes the average over time origins and water molecules and n refers to the spatial dimension. The microarray surface is placed on the xy -plane, perpendicular to the z -direction. Thus, the mean square displacement can be decomposed into x -, y -, and z -directions in order to compare the parallel (x - and y -direction) and perpendicular (z -direction) solvent mobility. Therefore, the perpendicular

FIG. 2. Geometry illustration of diffusion calculation.

diffusion coefficient of water, D_z , which also depends on the distance d from the microarray surface, is calculated by $D_z(d) = (\langle |z(t_2) - z(t_0)|^2 \rangle - \langle |z(t_1) - z(t_0)|^2 \rangle) / (2(t_2 - t_1))$, where d is the mean distance of water oxygen from the surface between time t_0 and t_2 , defined as $d = (d(t_0) + d(t_1) + d(t_2)) / 3$. We use $t_2 - t_1 = 1$ ps to estimate the diffusion coefficient where t_1 is 1 ps from the time origin, which is long enough for water molecules to reach the diffusional regime but also short enough to resolve its spatial dependence.^{14,27,30} The parallel diffusion coefficient D_x and D_y are calculated in a similar way.

In addition to the microarray surface, the influence on the solvent mobility of biomolecules functionalizing the surface, such as proteins, is evident on the diffusive properties of hydration water. In a similar manner, the diffusion coefficient as a function of distance to the peptide is calculated by $D(d) = (\langle \Delta r^2 \rangle) / (6(t_2 - t_1)) = (\langle |r(t_2) - r(t_0)|^2 \rangle - \langle |r(t_1) - r(t_0)|^2 \rangle) / (6(t_2 - t_1))$. We can decompose the overall diffusion coefficient into components parallel and perpendicular to the peptide surface: $D_{\parallel}(d) = (\langle \Delta r_{\parallel}^2 \rangle) / (4(t_2 - t_1)) = (\langle |r_{\parallel}(t_2) - r_{\parallel}(t_0)|^2 - |r_{\parallel}(t_1) - r_{\parallel}(t_0)|^2 \rangle) / (4(t_2 - t_1))$ and $D_{\perp}(d) = (\langle \Delta r_{\perp}^2 \rangle) / (2(t_2 - t_1)) = (\langle |r_{\perp}(t_2) - r_{\perp}(t_0)|^2 - |r_{\perp}(t_1) - r_{\perp}(t_0)|^2 \rangle) / (2(t_2 - t_1))$, where $\langle \Delta r_{\parallel}^2 \rangle$ and $\langle \Delta r_{\perp}^2 \rangle$ are, respectively, the mean square displacements locally parallel and perpendicular to the proximal region of a peptide or protein surface.^{10,14} The decomposition is illustrated in Fig. 2. For any water molecule, at any time instant, we can always find a heavy atom of the protein closest to the water oxygen. For instance, at fixed time $t_0 = 0$ ps, $t_1 = 1$ ps, and $t_2 = 2$ ps, the oxygen atom of water molecule located at $r(t_0)$, $r(t_1)$, and $r(t_2)$ is $d(t_0)$, $d(t_1)$, and $d(t_2)$ away from the nearest protein atom, which is located at $p(t_0)$, $p(t_1)$, and $p(t_2)$, respectively. Three points $p(t_0)$, $p(t_1)$, and $p(t_2)$ form a plane and two points $r(t_0)$ and $r(t_2)$ define a line segment. We define the projection of the line segment on the plane as the parallel displacement $|r_{\parallel}(t_2) - r_{\parallel}(t_0)|$ and the projection of the line segment on the normal of the plane as the perpendicular displacement $|r_{\perp}(t_2) - r_{\perp}(t_0)|$, between t_0 and t_2 with respect to the peptide. The parallel displacement $|r_{\parallel}(t_1) - r_{\parallel}(t_0)|$ and perpendicular displacement $|r_{\perp}(t_1) - r_{\perp}(t_0)|$ from time “zero” to time t_1 are defined similarly. For any time interval t , we have

$\Delta r^2(t) = \Delta r_{\parallel}^2(t) + \Delta r_{\perp}^2(t)$. The average distance of water from the peptide surface in the 2 ps interval is estimated by $d = (d(t_0) + d(t_1) + d(t_2)) / 3$.

D. Viscosity coefficient calculation

We wish to consider viscosity as a local property. Usually one refers to viscosity as the familiar bulk transport property. Here the interest is in how this property is modified in the boundary layer near a surface. While various methods using semimacroscopic concepts such as slip length have been used to describe this phenomenon, we take a different approach.

Solvent viscosity is a tensor quantity and its components may be calculated by integration of the time autocorrelation function of shear stress tensor components. For example, following the Green–Kubo formula, the xy -component is $\eta_{xy} = (1/kTV) \int_0^\infty \langle J_{xy}(t) J_{xy}(0) \rangle dt$, where k is the Boltzmann constant, T is the absolute temperature, V is the volume, and J_{xy} is the xy -component of the stress tensor.³¹ We will concentrate on the xy -component of the viscosity (η_{xy}) of solvent as a function of the distance from the surface. This is a quantity that can be diagnostic of the dynamics of surface proximal or associated solutes hopping from one functional site to another on the surface.

In a system with defined volume V and constant number of particles N , the xy -component of the shear stress tensor J is calculated as $J_{xy} = \sum_{i=1}^N m_i v_{i,x} v_{i,y} + (1/2) \sum_{i=1}^N \sum_{j=1}^N r_{ij,x} F_{ij,y}$, where m_i is the mass of the i th particle, v is the velocity, $r_{ij,x}$ is the distance between particle i and j on the x -direction, and $F_{ij,y}$ is the force between i and j in the y -direction. The first term of the stress tensor expression comes from the kinetic contribution, which sums over all particles within the volume. The second part is due to the potential contribution, which runs over all pairwise particle interactions. To calculate the shear viscosity of water near the microarray surface, we divide the simulation box into slices of finite volume along the z -direction, with thickness δz equal to 0.5 Å. For any atom i within a particular slice, its contribution to the stress tensor is then $J_{i,xy} = m_i v_{i,x} v_{i,y} + (1/2) \sum_{j=1}^N r_{ij,x} F_{ij,y}$. The summation in the potential part runs over all atoms (both inside and outside the slice) interacting with atom i . The total stress tensor within a finite volume is, therefore, summed over the contribution from all atoms within the volume slice $J_{xy} = \sum_{i=1}^n J_{i,xy}$. We consider water hydrogen atoms within the volume slice if the oxygen atom of the molecule is inside the volume.

Solvent viscosity near the microarray surface is calculated, following the Green–Kubo formula, by integrating the time autocorrelation of the shear stress tensor within a finite volume slice as a function of distance to the surface. It should be noted that a bin size of 0.5 Å is chosen as a compromise between the spatial resolution and statistical error. In both the unfunctionalized and functionalized microarray surface simulations, the shear stress tensor is saved every 2 fs and time autocorrelation function is evaluated over a 4 ns trajectory. An error bar is estimated by the standard deviation of four 1 ns segments of the trajectory. It should be noted that in the simulations, the electrostatic interactions are

FIG. 3. Comparison of calculations on bulk water viscosity with or without k -space Ewald contribution. Both stress-stress correlation calculations utilize 200 ps of trajectory written out every 2 fs step in the simulation of 512 TIP3P water molecules at 300 K in the NVE ensemble.

calculated with an Ewald sum including both the real space and k -space part. However, only the real space contribution of the electrostatic interactions is included in the final stress tensor analysis of the anisotropic systems. We do not include the less local k -space contribution to the stress tensor which, given our use of Ewald sums, would be problematic in the anisotropic case. As a check of this, in Fig. 3, we compare the solvent viscosity of bulk water with and without k -space contribution. The results differ by 3%–5%. The slight difference is less than statistical errors in some cases and therefore apparently negligible for our conclusions for the anisotropic cases.

III. RESULTS AND DISCUSSION

A. Solvent diffusion near peptide surface

Many studies have shown that water mobility in the proximity of a protein surface is restricted.^{7,10,14,16,32,33} The self-diffusion coefficient of solvent is expected to decrease when approaching the protein surface. We evaluate the diffusion coefficient of water, along with its parallel and perpendicular components, as a function of distance to the peptide surface (Fig. 4). As expected, diffusion in radial shells around the peptide reveals reduced solvent mobility near the peptide surface. Water diffusion also correlates with the solvation structure around the peptide surface. From 1.5 to 4.5 Å, diffusion decreases rapidly within the region of the first hydration shell. From 4.5 up to 10 Å in the second hydration shell and beyond, the water diffusion is still slightly slower than the bulk value of 0.58 Å²/ps. At around 2.5 and 5.5 Å, which correspond to the first and second hydration peaks, the solvent diffusion rate is low, also corresponding to local viscosity maxima. The reduced mobility of hydration water has been shown to be closely correlated with the distance dependence of hydrogen bond relaxation time and water residence time near the protein surface.⁷ In addition, water molecules also diffuse anisotropically near the peptide surface. The diffusion rate perpendicular to the peptide surface is slower than the overall diffusion while the parallel diffusion is found to be faster. As observed in other simulations^{14,32} and experi-

FIG. 4. Density distribution (upper), total, parallel, and perpendicular diffusion (lower) of water as a function of distance to the peptide surface.

mental results,³³ the anisotropy in the parallel and perpendicular water mobility seems to be connected to the dipole and H-bonding of structured water, especially in the first hydration layer of the protein surface.^{10,34} Interactions of protein residues with neighboring water molecules can orient water dipoles normal to the protein surface. The hydrogen bond networking organization at the protein-solvent interface also drives the surrounding water to move preferentially along the macromolecule surface rather than away from it. The relative increase in the parallel diffusion rate can be viewed as being related to the equipartition of energy principle.¹⁴ It is noteworthy that spatial confinement and geometrical complexity of the biomolecular surface and the heterogeneity of protein-solvent interactions always result in a non-Brownian dynamics behavior of hydration water, which usually leads to anomalous diffusion of water at protein surface. We choose a time window of 1 ps, a relatively short time scale, to calculate the diffusion rate, and our investigation clearly shows the position-dependence of water diffusion.

B. Solvent diffusion near a microarray surface

Solvent density and diffusion coefficients for the x -, y -, and z -directions as a function of distance to the unfunctionalized and functionalized microarray surfaces are plotted in Figs. 5 and 6, respectively. As expected, solvent density as well as diffusion is similar in both simulations. Nevertheless, due to the nature of the tethered peptide in the vicinity (mostly within 12 Å) of the functionalized microarray surface,²⁵ water diffusion is slower than that near the unfunctionalized surface. It also takes a somewhat longer distance from the hard surface as opposed to a protein surface for water to reach its bulk mobility. Water forms two distinctive hydration layers along the hydrophobic microarray surface, with a third layer less prominent. Diffusion of hydration water in the perpendicular direction near the hydrophobic surface is not necessarily (universally) slower than the bulk water and is sometimes even faster in the low density regions (Fig. 5).

FIG. 5. Density distribution (upper) and diffusion (lower) of water as a function of distance to the unfunctionalized microarray surface.

We observe an inverse correlation between water diffusion and density along the microarray surface. Increased solvent mobility is observed in the dominant low density region while restricted solvent mobility is shown in the high density region. The first peak of the diffusion coefficient in the perpendicular direction (z) appears at about 4.5 Å, corresponding to the low density region between the first and second water coordination layer. Correspondingly, the second peak of diffusion coefficient at around 7.5 Å correlates with the low density region between the second and third water coordination layer. The inverse correlation of diffusion and density can be explained from an energetic point of view. High water density corresponds to a low free energy region where the effect of the hydrogen bonding network and packing are maximized.

In contrast, water diffusion on the parallel direction to the microarray surface shows a pattern similar to water diffusion around the protein surface. Parallel diffusion is restricted near the hydrophobic microarray surface. As expected, water mobility in the x - and y -directions, parallel to

the microarray surface, is uniform in nature. The water diffusion coefficient gradually reaches the bulk value at 15 and 20 Å, respectively, as the distance increases from the unfunctionalized and functionalized microarray surfaces. Although the linkers of microarray surface are highly packed, the small shoulders within 3 Å from the surface shown in the water density distribution and diffusion coefficient may be induced by surface roughness. It should also be noted that value of bulk water diffusion constant in the unfunctionalized microarray surface simulation is slightly larger than that in the functionalized peptide microarray surface simulation.

The transport properties such as self-diffusion coefficient and viscosity coefficient have been shown to be water model, simulation method, and even simulation box size dependent.^{35–37} Experimental values of diffusion and viscosity coefficient at room temperature are about 0.3 Å²/ps and 1.0 cP, respectively. However, simulations using TIP3P water model fail to reproduce experimental data and the reported diffusion and viscosity coefficients are around 0.53 Å²/ps and 0.35 cP, respectively. In addition to water models, translational diffusion also linearly depends on the inverse of the simulation box size, which is a known finite size effect and results in the underestimation of diffusion. We choose TIP3P because it is used in the CHARMM parametrization for our peptide. Nevertheless, the bulk diffusion coefficient and viscosity coefficient calculated in our study agree with the other reported simulations using TIP3P water model at the temperature of 300 K.^{35,38}

Our results using a model of water near functionalized surfaces should be contrasted with the results on hard spheres near surfaces.²³ In the case of hard spheres near hard surfaces, the regions of density wave maxima also have high diffusion coefficients. The hard sphere fluid confined to spaces near the wall maximizes its entropy through layering. The difference between that system and ours may be related to entropy-enthalpy compensation for an associated liquid near a wall with finite attractions. We note that the small shoulders in our diffusion data quite close to the surface are positively correlated with density and so more work is needed to understand the finer details and the thermodynamic driving forces.

C. Solvent viscosity near microarray surface

We plot the convergence of the shear stress tensor integration at different distances from the unfunctionalized microarray surface in Fig. 7. They are grouped into panels according to their rates of convergence, which correlates with the distance from the surface. While bulk water viscosity converges within 1 ps (shown in Fig. 3), the autocorrelation function of solvent near the microarray surface has a longer relaxation time. For the region within 1.5 Å from the average surface groups ($-\text{CH}_3$), due to large fluctuations resulting from the small number of water molecules and difficulties in volume estimation near the rough microarray surface, the calculation of viscosity is not shown. Longer memory time is obvious in the first hydration layer and the stress-stress correlation function takes up to 20 ps to decay to zero. As the water moves away from the surface, relaxation time quickly

FIG. 6. Density distribution (upper) and diffusion (lower) of water as a function of distance to the functionalized microarray surface.

FIG. 7. Convergence of integration of time correlation functions of the shear stress tensor in volume slices at different distances (in angstroms) from the unfunctionalized microarray surface.

decreases. At 7.5 Å away from the surface, solvent viscosity is indiscernible from the bulk, though density and diffusion still show some differences.

We also plot the xy -component of solvent viscosity as a function of distance to the unfunctionalized and functionalized microarray surfaces along with density distribution in Figs. 8 and 9, respectively. Keeping with the inverse correlation to the diffusion, the viscosity near the functionalized surface is slightly higher than that near the unfunctionalized one. The raise is due to the increased solvent viscosity in the vicinity of the immobilized peptide on the functionalized microarray surface. At a distance of 1.75 Å from the surfaces, water viscosity is estimated to be 1.2 and 1.4 cP, respectively, very high compared to the model bulk value of about 0.37 cP. Large statistic fluctuations are also associated with large

FIG. 8. Density distribution (upper) and viscosity (lower) of water as a function of distance to the unfunctionalized microarray surface. An error bar is displayed if the standard deviation is greater than 0.015 cP.

FIG. 9. Density distribution (upper) and viscosity (lower) of water as a function of distance to the functionalized microarray surface. An error bar is displayed if the standard deviation is greater than 0.015 cP.

viscosity values. Viscosity drops sharply at 2.25 Å, followed by a rise at 2.75 Å, which corresponds to the first solvation peak.

The first major peak in viscosity positively correlates with the first major density peak. We note however, a negative correlation in the first shoulder in density, nearest the wall, with the first dip in viscosity, which is reminiscent of what was found in hard sphere simulations.²³ Viscosity declines slightly below bulk value between the first and second hydration layer and then increases slightly at the second hydration peak. Local viscosity oscillations are more pronounced in the first hydration layer and become less significant in the following one. This component of viscosity smoothly drops to the bulk value after the second hydration layer. Beyond the contact region with the wall, when water density is high, the solvent viscosity is also high and with limited diffusion.

Sensitivity of the viscosity coefficient to structure at an interface has been successfully predicted by Pozhar and Gubbins,²⁴ transport theory of dense, inhomogeneous fluids.²² Using simplified fluid models such as Weeks–Chandler–Andersen and Lennard-Jones atomic fluids, calculation of the theoretical viscosity of fluids confined in a nanoslit pore has shown a strong correlation of the local viscosity with the layered structure of the fluids. Incorporating structure details of the inhomogeneous fluids via number density profiles and/or pair correlation function contact values is central to theories of transport properties of fluids in nanoconfinement or at interfaces. Our study of water diffusion and viscosity at microarray surface using equilibrium molecular simulation data shows the importance of the contribution of fluid structure to transport properties.

Usually in isotropic viscosity calculations by the Green–Kubo formula, better statistics can be obtained by averaging shear viscosity for all three off-diagonal components: $\eta = (1/3)(\eta_{xy} + \eta_{xz} + \eta_{yz})$. However, due to the anisotropic nature of our system only the xy -component of the stress tensor as a function of z is utilized to calculate the solvent viscosity

here. We cannot use tensor components associated with the z -direction when attempting a decomposition as a function of that direction. When attempting to calculate viscosity as a function of distance to the microarray surface along the z -direction, we find that time autocorrelation function of sheer stress tensor of the xz - and yz -components show long time memory as well as size effects and do not decay to zero within tens of picoseconds. Even in the calculation for bulk water, if one divides the water box into slices in an arbitrary direction of the Cartesian coordinate α , in general, the autocorrelation function of the $\alpha\beta$ - or $\alpha\gamma$ -component of the stress tensor will have a long time tail. However, stress fluctuations in the $\beta\gamma$ -component converges. This has a geometric origin and has aspects related to the issue of our choice of ensemble.^{39–42} Unlike the whole simulation box, the thin slice of water in our calculation is not a microcanonical ensemble (NVE). With fluctuating number of particles, we should consider it as a grand canonical ensemble. A general expression for a stress fluctuation function was suggested by McLennan⁴¹ as $L = \int_0^{+\infty} dt \langle (J(0) - \hat{J})(J(t) - \hat{J}) \rangle$, where the time average of stress tensor as a function of pressure P , energy E , and particle number N was evaluated by $\hat{J}_{\alpha\beta} = \delta_{\alpha\beta} [p(\bar{E})V + (N - \bar{N}) \partial p / \partial \bar{N} + (E - \bar{E}) \partial p / \partial \bar{E}] + \dots$. In the microcanonical ensemble, we have $N = \bar{N}$ and $E = \bar{E}$, so the last two terms drop out while, with the grand canonical ensemble, both terms are present. We do not calculate the local components of viscosity around the peptide in isotropic solution.

IV. CONCLUSIONS

We show solvent diffusion coefficients as well as components of the local viscosity in the vicinity of a functionalized microarray surface and compare with an unfunctionalized microarray surface and a peptide free in solution. Both transport properties are shown to be nonmonotonic in the direction away from the surface and closely correlated with the solvent density profile.

Translational diffusion coefficients for solvent molecules in directions parallel and perpendicular to a peptide surface are both restricted, while water molecules moving in a parallel direction are slightly more mobile than in the perpendicular direction. While restricted solvent diffusion is observed in the direction parallel to the microarray surfaces, diffusion in the perpendicular direction is not necessarily slower than the bulk and shows strong correlation with local water density. In the presence of a tethered peptide near the functionalized microarray surface, the water diffusion decreases and the viscosity increases, compared to the unfunctionalized microarray surface. We note that we only consider a single surface density of peptides ($\sim 0.07 \text{ nm}^{-2}$) and that such an effect would be expected to have a surface density dependence.

While NEMD simulations of fluids under sheer flow are usually utilized to calculate local pressure tensor magnitudes and predict position-dependent viscosity, we use equilibrium molecular dynamics simulations to calculate local solvent viscosity components as a function of distance from the surface. Viscosity calculation results agree well with theoretical predictions of strong correlation with solvent density profile.

At the microarray surface, solvent in the high density regions shows limited diffusion and high viscosity while low solvent density regions always correspond to low viscosity and high diffusion rate. This is in contrast with hard sphere results²³ that may be due to a fundamental difference in mechanism between systems with and without sufficient attractions.

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