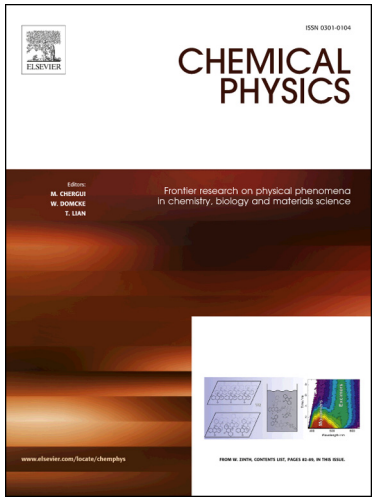

Molecular Dynamics and Monte Carlo Simulations Resolve Apparent Diffusion Rate Differences for Proteins Confined in Nanochannels

J.W. Tringe, N. Ileri, H.W. Levie, P. Stroeve, V. Ustach, R. Faller, P. Renaud

PII: S0301-0104(15)00128-7
DOI: http://dx.doi.org/10.1016/j.chemphys.2015.04.021
Reference: CHEMPH 9310

To appear in: *Chemical Physics*

Received Date: 26 December 2014
Accepted Date: 24 April 2015

Please cite this article as: J.W. Tringe, N. Ileri, H.W. Levie, P. Stroeve, V. Ustach, R. Faller, P. Renaud, Molecular Dynamics and Monte Carlo Simulations Resolve Apparent Diffusion Rate Differences for Proteins Confined in Nanochannels, *Chemical Physics* (2015), doi: http://dx.doi.org/10.1016/j.chemphys.2015.04.021

Molecular Dynamics and Monte Carlo Simulations Resolve Apparent Diffusion Rate Differences for Proteins Confined in Nanochannels

J. W. Tringe,[a]* N. Ileri,[ab] H. W. Levie,[a] P. Stroeve,[b] V. Ustach[b], R. Faller[b] and P. Renaud[c]

[a] Lawrence Livermore National Laboratory, 7000 East Avenue, Livermore, California, USA.

[b] Department of Chemical Engineering & Materials Science, University of California, Davis, California, USA.

[c] Swiss Federal Institute of Technology, Lausanne, (EPFL) Switzerland.

*Corresponding author, tringe2@llnl.gov.

We use Molecular Dynamics and Monte Carlo simulations to examine molecular transport phenomena in nanochannels, explaining four orders of magnitude difference in wheat germ agglutinin (WGA) protein diffusion rates observed by fluorescence correlation spectroscopy (FCS) and by direct imaging of fluorescently-labelled proteins. We first use the ESPResSo Molecular Dynamics code to estimate the surface transport distance for neutral and charged proteins. We then employ a Monte Carlo model to calculate the paths of protein molecules on surfaces and in the bulk liquid transport medium. Our results show that the transport characteristics depend strongly on the degree of molecular surface coverage. Atomic force microscope characterization of surfaces exposed to WGA proteins for 1000 s show large protein aggregates consistent with the predicted coverage. These calculations and experiments provide useful insight into the details of molecular motion in confined geometries.

Keywords: Molecular Dynamics; Monte Carlo; nanochannel; protein; molecular transport; nanopore; membrane

1.0 Introduction

Protein transport in nanochannels and nanopores is important in separations, microfluidics and in biology.[1-9] Many recent studies have examined the transport of proteins and other molecules near surfaces and in confined geometries.[10-21] For example, lysozyme adsorption to charged surfaces was investigated using Monte Carlo (MC) by Carlsson et al., and it was found that adsorption was favoured by high protein concentration and high protein net charge, among other conditions.[22] Ziemys et al. combined experiments and Molecular Dynamics (MD) to study glucose in silica nanochannels. It was observed that the coupling of concentration and confinement effects led to inhibited transport in the nanochannel.[23] The adsorption potential of α-lactalbumin (ALC) and the hen egg white lysozyme (HEWL) on a poly(vinylimidazole) polymer was modeled with classical molecular mechanics calculations at the atomistic level by Noinville, Vidal-Madjar and Sébille. Calculations were performed for molecule-surface separations ranging from the bulk to contact, and preferred orientations were identified for the surface-bound proteins as well as effective net charges for the proteins.[24] HEWL adsorption to charged surfaces was also studied by Ravichandran, Madura, Talbot using Brownian Dynamics, and it was determined that the net positively-charged protein can adsorb to a positively-charged surface because of the nature of the charge distribution around the protein molecule.[25] Karnik et al. found that the diffusion of molecules in a nanochannel can strongly depend on the concentration of diffusing molecules in the reservoir,[26] which has particular relevance for the present investigation. These studies all provide useful and important insight into molecular transport in confined environments, but they do not fully illuminate the complementary bulk and surface transport mechanisms for individual molecules.

In this work we resolve differences in two molecular transport studies with wheat germ agglutinin (WGA) protein molecules. In the first study, Durand et al. measured diffusion coefficients for fluorescently-labelled wheat germ agglutinin (WGA) in nanochannels, and found an effective diffusion coefficient for confined molecules which is four orders of magnitude lower than its free diffusion coefficient.[27] In the second set of experiments, WGA molecules were observed by fluorescence correlation spectroscopy (FCS) in a nanochannel formed by two parallel borosilicate glass plates separated by 50 nm.[28] The FCS observation volume is well approximated by a right circular cylinder with radius 420 nm. It was found that, depending on the concentration, net charge of the proteins, and the ionic strength of the solution, diffusion was dominated by steric exclusion, the reversible surface adsorption of the biomolecules, or the exclusion-enrichment effect. Under some conditions the effective diffusion coefficient in the nanochannel was comparable to the free diffusion coefficient. The number of charges in the nanochannel 'bulk' and on the surface was