PROTEIN ADSORPTION TO SILICA NANOPARTICLES: THE EFFECT OF NANOPARTICLE SIZE ON PROTEIN STRUCTURE, STABILITY, AND ORIENTATION

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An Abstract of a Thesis Submitted to the Graduate

Faculty of Rensselaer Polytechnic Institute

in Partial Fulfillment of the

Requirements for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject: CHEMICAL AND BIOLOGICAL ENGINEERING

The original of the complete thesis is on file
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April 2011
(For Graduation May 2011)

ABSTRACT

The work presented in this thesis was directed at investigating the effect of spherical nanoparticle size on the structure, function, stability, and orientation of adsorbed proteins. While protein structure and function has been characterized for several protein-nanomaterial systems, solvent denaturation techniques to determine protein stability present a new opportunity to further our understanding of proteins adsorbed to nanomaterials. This thesis work reports on the unfolding behavior of ribonuclease A and cytochrome c on silica nanoparticle surfaces and quantitatively demonstrates that nanoscale size and surface curvature play key roles in influencing the stability of adsorbed proteins. Urea denaturation analyses showed that the thermodynamic stability of both proteins decreased upon adsorption onto the silica nanoparticles, with greater decreases on larger silica nanoparticles. Additionally, chemical modification and quantitative proteomics have been coupled to identify lysine residues involved in cytochrome c binding to silica nanoparticles. Preferred orientations of cytochrome c to silica were near the N- and C-termini on its front face and lysine 39 on the back face. There was consistently increased acetylation and therefore lower lysine protection for cytochrome c adsorbed to 4 nm silica compared to 15 nm silica. This was direct evidence that proteins on smaller nanoscale surfaces interacted less with the surface, leading to more native-like properties. This work, therefore, provided fundamental information on the effect of nanoscale surfaces on protein structure, function, stability and orientation.