Abstract Submitted
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Monte Carlo Simulations of Absolute Binding Free Energy of Targeted Nanocarriers to Cell Surfaces[1] JIN LIU, B. ZERN, P.S. AYYASWAMY, D.M. ECKMANN, V.R. MUZYKANTOV, R. RADHAKRISHNAN, University of Pennsylvania — We have developed a computational methodology based on Metropolis Monte Carlo and the weighted histogram analysis method (WHAM) to calculate the absolute binding free energy between functionalized nanocarriers (NC) and endothelial cell (EC) surfaces. The calculated binding affinities agree quantitatively with the measurements of specific antibody coated NCs (100 nm in diameter) to intracellular adhesion molecule-1 (ICAM-1) expressing EC surface in *in vitro* experiments. We then systematically explore the effects of experimentally tunable parameters including the antibody surface coverage σ_s of NC, glycocalyx, shear flow and NC size. Of particular biological significance, our model predicts a threshold σ_s value below which the NC binding affinities reduce drastically and drop below that of single anti-ICAM-1 molecule to ICAM-1; our results reveal that this is due to a change in the multivalency (or number of bonds formed per NC). This trend and threshold value are recovered exactly in the *in vivo* measurements of the endothelium targeting of NCs in the pulmonary vascular in mice.

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