Coarse-Grained Modelling of Protein-Nanoparticle Interactions

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Introduction

The increased use of nanoparticles (NP) and nanomaterials is pushing scientific research into trying to understand the mechanisms governing interactions between biomolecules and inorganic materials.
It is known that, once an NP is in contact with a biological medium, a protein corona forms on its surface [1], and that the nature of the corona is what regulates the interaction between the NP and the other biomolecules.
We aim to construct a coarse-grained model for the interaction of an arbitrary protein with common industrial nanoparticles such as gold (Au), TiO_2, CdSe and carbon nanotubes.

Methods

Coarse-Graining of the protein

We use a one-bead-per-aminoacid model with bead centres placed at the α-carbon atoms of the AA. The model preserves both the overall shape of the protein and its total charge [2]. The protein is treated as a rigid body.

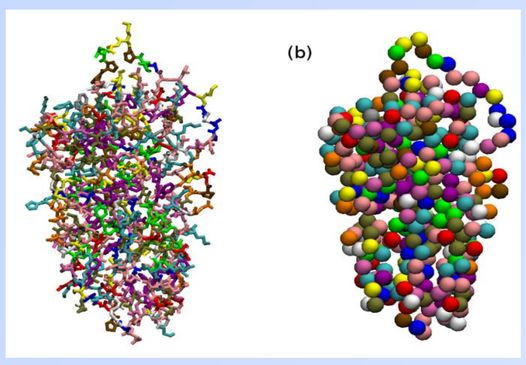


Fig. 1 α1-antitrypsin (PDB: 3NE4), in full atomistic (left) and CG model (right)

Coarse-Graining of the NP

We divide the NP into two parts. The shell is modeled as individual CG beads and accounts for solvent effects too. The core interacts with the protein via long-range forces. Pairwise interactions between beads are modeled using Lifshitz theory of macroscopic bodies.

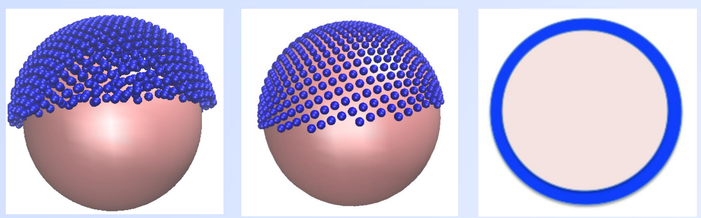


Fig. 2 Three types of surface built. 3 layer sphere (left), single layer sphere (middle), completely smooth surface (right). Shown here is a 5nm NP

The surface beads have been placed via a golden spiral algorithm.

Procedure

Generation of CG bead-AA pair potential

We use atomistic PMF as reference [3] to map the CG model to and calibrate it.

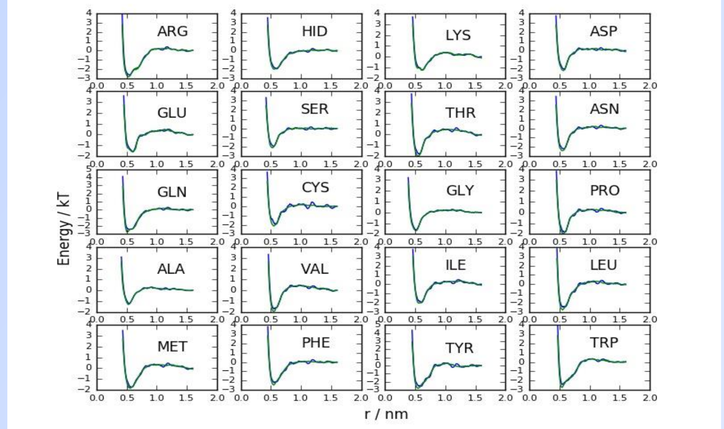


Fig. 3 CG PMFs (blue) vs atomistic reference PMFs (green).

Generation of core-AA potential

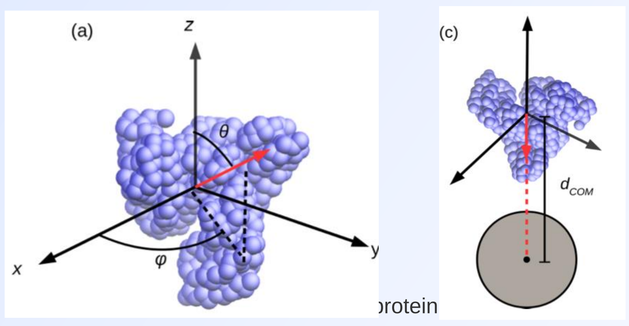
Use Lifshitz theory for macroscopic bodies. The only material-dependent property is Hamaker constant (A):

$$E_{core} = -\frac{A}{12kT}\left(\frac{4R_1R_2}{D^2-(R_1+R_2)^2}+\frac{4R_1R_2}{D^2-(R_1-R_2)^2}+2\ln\left(\frac{D^2-(R_1-R_2)^2}{D^2-(R_1+R_2)^2}\right)\right)$$

For two spheres of radii R_1 & R_2 at distance D the Hamaker constant is calculated from dielectric constants. The radius of the core was set equal to the NP radius minus the cutoff used in the atomistic calculations of PMFs (1.6 nm).

Results

The model is tested on 2 proteins: lysozyme (2LYZ) and human serum albumin (1N5U). The NP radii are, in nm: 5, 10, 25, 40, 100, 150, 200 and 250. Protein is kept rigid and rotated about 3 axes and allowed to adsorb 'vertically' on the NP. The distance between the NP surface and the protein COM is reported. Pairwise E-summation at fixed D:



All pair potentials have been optimized for the type of surface involved in the calculation (see Procedure sect.).

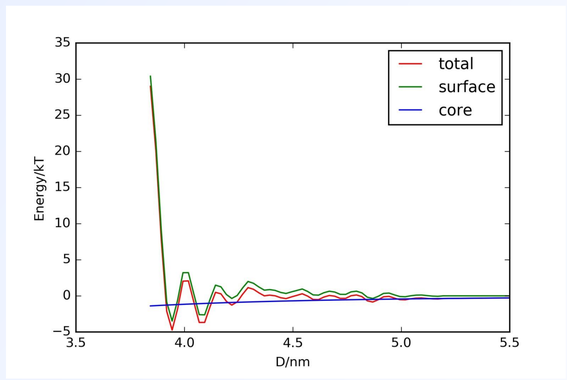


Fig. 5 separate contributions from core and surface for a single 1N5U orientation.

Results (Continued)

Boltzmann average over 11,664 orientations (ϕ_i, θ_j) [2] on a TiO_2 NPs:

$$E(f_i,q_j) =$$

$$-k_BT\ln\left[\frac{3}{\left(R+a\left(f_i,q_j\right)\right)^3-R^3}\times\int_R^{R+a\left(f_i,q_j\right)}D^2\exp\left(\frac{-U\left(D,f_i,q_j\right)}{k_BT}\right)dD\right]$$

$$E_{bind}=\frac{\sum_i\sum_j P_{ij}E(f_i,q_j)}{\sum_i\sum_j P_{ij}}$$

$$P_{ij}=\sin\left(q_j\right)\exp\left(-E(f_i,q_j)/k_BT\right)$$

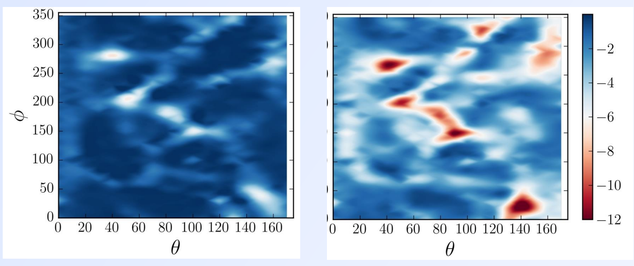
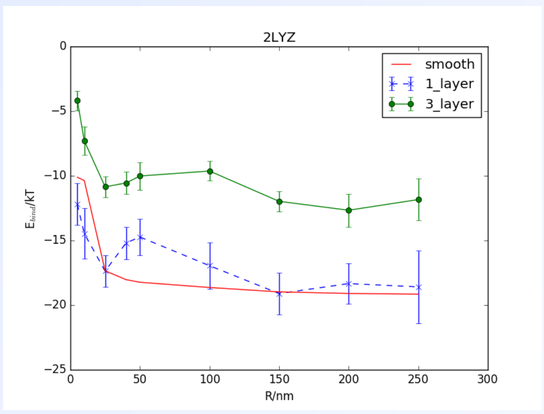


Fig.5 E_{bind} as a function of protein orientation. Left, 2LYZ on 5nm NP and right, 2LYZ on 250nm NP



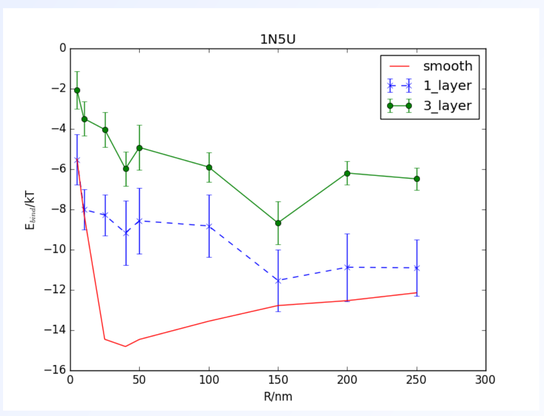


Fig.6 Average binding energies (E_{bind}) vs NP radius for 2LYZ and 1N5U.

Conclusions

- Adsorption energy profile is strongly dependent on protein shape and size. It is non-monotonous.
- The binding is reversible for small proteins/NPs and irreversible for large ones.
- Contribution from the core is minor compared to the surface.
- One can scan large number of proteins and produce a ranking based on their adsorption affinity to the material.
- The process can be completely automated using physical properties and composition of the nanomaterial.

References

[1] M. Rahman, S. Laurent, N. Tawil, L. Yahia, and M. Mahmoudi. Protein-Nanoparticle Interactions, volume 15 of Springer Series in Biophysics. Springer-Verlag, 2013
[2] H. Lopez, V. Lobaskin, J. Chem. Phys.,143:243138, 2015.
[3] E. Brandt and A. P. Lyubartsev, J. Phys. Chem. C, 119:18126, 2015

Acknowledgments

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