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# Multi-Scale Modelling Of the Formation of the Nanoparticle-Protein Corona

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## Extended Abstract

A nanoparticle (NP) immersed in a biological medium does not remain in its native state for long, but instead rapidly acquires a corona of adsorbed proteins. This protein corona masks the original physical and chemical properties of the NP and is known to determine its biological fate, uptake by cells, and potential adverse outcomes [1]. Thus, the prediction of the corona content is crucial for the evaluation of the safety of novel biomaterials to avoid the requirement of experimentally investigating each of the large number of these biomaterials being introduced to the market.

A given medium may consist of hundreds of proteins with the corona evolving over the course of several hours. With current computational tools, the simulation of the interaction between a single protein with an NP at an atomistic scale of accuracy is limited to at most a few nanoseconds of time and so clearly an alternate approach is necessary. The vast majority of proteins consist of only the twenty standard amino acids (AAs), suggesting that it should be possible to pre-compute these NP-AA interactions and use these to construct a model for the interaction of the entire protein with the NP, significantly simplifying the task of predicting the affinity of a given protein to the NP in question. Further coarse-graining of the system can then allow for modelling of the long-term adsorption and desorption of proteins, enabling the prediction of the content of the corona.

Here, we present an overview of our multi-scale methodology for the prediction of the content of the protein corona. Our methodology employs atomistic simulations to parameterise the interaction between individual amino acids and a nanomaterial, with the output used as part of the UnitedAtom [2] method to predict the orientation-specific adsorption energies of proteins to the specific nanoparticle. These adsorption energies are used together with our recently-developed hard-sphere model of particles adsorbing to curved surfaces [3] to predict the time-dependent corona composition. We compare the results of our methodology for corona prediction to the results of a recent experimental study, finding good agreement [4]. Our workflow can easily be adapted to cover novel nanomaterials and is applicable to spherical, cylindrical, and planar NPs, allowing for the investigation of a wide range of combinations of nanoparticles and biological media. We thank EU H2020 grant no. 814572 and SFI grant no. 16/IA/4506 for funding.

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