**Prediction of peptide-driven exfoliation and assembly on 2D nanosheet materials**

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**Introduction.** Peptides provide a versatile platform for the generation, organisation and activation of nanomaterials in aqueous media. However, their application and use on two dimensional (2D) nanosheet structures such as graphene and *h*-BN is hampered, due to a lack of fundamental data regarding the structure/function relationships of these bio-nano interfaces. Together with experimental characterisation, molecular simulations can provide complementary insights into the structure/functional relationships of these challenging interfaces. Here, our strategy of using bioconjugate hybrids of peptides and fatty acids to exfoliate materials into 2D nanosheets is introduces, and the role of molecular simulations in revealing the molecular scale characteristics of the exfoliation process are discussed for graphene. The extension of our simulation approach to peptide/*h*-BN will also be presented.

**Methods.** We used replica-exchange with solute tempering (REST) molecular dynamics (MD) simulations to predict the most likely structures of a graphene-binding peptide, P1, with a fatty acid chain attached at either the N- or C-terminus, adsorbed at the aqueous graphene interface (denoted F10-C-P1 and P1-C-F10, respectively). Interfacial interactions were described using the polarisable GRAPPA force-field. Additionally, we used standard MD simulations to explore potential peptide-driven exfoliation mechanisms of graphene. To accomplish this, we modelled a stack of graphene sheets in the presence of multiple bioconjugate peptide/fatty-acid molecules, in liquid water. Finally, we have created a force-field for describing bio-interactions at h-BN nanosheet interfaces in aqueous media, based on first-principles calculations, and have used this to predict binding free energies for a range of amino acids using well-tempered metadynamics simulations.

**Results and Discussions.** Our simulations predict that the most likely structures of graphene-adsorbed P1-C-F10 and F10-C-P1 differ remarkably from those predicted for P1 alone adsorbed on graphene. In other words, the conjugation of the fatty acid influenced the binding conformation of the P1 peptide. The degree of residue/surface contact was similar for the two molecules, consistent with QCM experimental data. We also identified differences in predicted adsorption geometry between P1-C-F10 and F10-C-P1 which are consistent with AFM observations. These data indicate that both biomolecules broadly support similar trends in overlayer morphology as a function of solution concentration. In terms of graphene exfoliation, our multi-molecule graphene stack simulations suggest a unique ‘side-swipe’ ingress mechanism. The fatty-acid chain is typically found to wrap around the edge of the graphene sheet, offering potential protection from damage, which is consistent with our experimental exfoliation data. Extending our work to bio-interfaces of *h-*BN, we fitted first-principles binding data to introduce a new bio/BN interfacial force-field. Tests of force-field performance include recovery of the experimental water droplet contact angle on *h-*BN. Our predictions of the adsorption free energy for nine amino acids suggest that Arg is one of the strongest binders in our set, with Asp amongst the weakest.

**Conclusion.** In summary, we have used molecular simulation to complement experimental efforts, including AFM and QCM observations, to explore the functional potential of peptide bioconjugates as exfoliation and organisation agents of 2D nanomaterials. The outcomes of our simulations provide a strong foundation for future work to design and deploy these molecular bioconjugates in the self-assembly of 2D heterostructures.