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Prediction of purification of biopharmeceuticals with molecular dynamics[1] VINCENT USTACH, ROLAND FALLER, University of California, Davis — Purification of biopharmeceuticals remains the most expensive part of protein-based drug production. In ion exchange chromatography (IEX), prediction of the elution ionic strength of host cell and target proteins has the potential to reduce the parameter space for scale-up of protein production. The complex shape and charge distribution of proteins and pores complicates predictions of the interactions in these systems. All-atom molecular dynamics methods are beyond the scope of computational limits for mass transport regimes. We present a coarse-grained model for proteins for prediction of elution pH and ionic strength. By extending the raspberry model for colloid particles to surface shapes and charge distributions of proteins, we can reproduce the behavior of proteins in IEX. The average charge states of titratatable amino acid residues at relevant pH values are determined by extrapolation from all-atom molecular dynamics at pH 7. The pH specific all-atom electrostatic field is then mapped onto the coarse-grained surface beads of the raspberry particle. The hydrodynamics are reproduced with the lattice-Boltzmann scheme. This combination of methods allows very long simulation times. The model is being validated for known elution procedures by comparing the data with experiments.

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