Systematic Coarse-graining: Fundamentals and Applications

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Coarse-grained (CG) models provide a computationally efficient means to study biomolecular and other soft matter processes involving large numbers of atoms correlated over distance scales of many covalent bond lengths and long time scales. Variational methods based on information from simulations of finer-grained (e.g., all-atom) models – for example the multiscale coarse-graining (MS-CG) and relative entropy minimization methods – provide attractive tools for the systematic "bottom up" development of CG models. These methods can also be extended to the "ultra coarse-grained" (UCG) regime, e.g., at a resolution level coarser or much coarser than one amino acid residue per effective CG particle in proteins. This extension leads to the possible existence of multiple metastable states "within" the CG sites for a given UCG model configuration, which can also be treated by systematic variational methods. Additionally, certain aspects of this theory connect back to single-state force matching and open up new avenues for method development in that arena. These results taken as a whole provide a formal statistical mechanical basis for CG methods related to force matching and relative entropy minimization and suggest practical algorithms for constructing optimal CG models from fine-grained simulation data, or for utilizing CG models to bias new fine-grained simulations and to enhance their sampling. Representative applications to challenging liquid and biomolecular systems will be described.