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Path-space variational inference for non-equilibrium coarse-grained systems

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ABSTRACT

In this paper we discuss information-theoretic tools for obtaining optimized coarse-grained molecular models for both equilibrium and non-equilibrium molecular simulations. The latter are ubiquitous in physicochemical and biological applications, where they are typically associated with coupling mechanisms, multi-physics and/or boundary conditions. In general the non-equilibrium steady states are not known explicitly as they do not necessarily have a Gibbs structure.

The presented approach can compare microscopic behavior of molecular systems to parametric and non-parametric coarse-grained models using the relative entropy between distributions on the path space and setting up a corresponding path-space variational inference problem. The methods can become entirely data-driven when the microscopic dynamics are replaced with corresponding correlated data in the form of time series. Furthermore, we present connections and generalizations of force matching methods in coarse-graining with path-space information methods. We demonstrate the enhanced transferability of information-based parameterizations to different observables, at a specific thermodynamic point, due to information inequalities.

We discuss methodological connections between information-based coarse-graining of molecular systems and variational inference methods primarily developed in the machine learning community. However, we note that the work presented here addresses variational inference for correlated time series due to the focus on dynamics. The applicability of the proposed methods is demonstrated on high-dimensional stochastic processes given by overdamped and driven Langevin dynamics of interacting particles.

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1. Introduction

Molecular dynamics simulations at microscopic (e.g. atomistic) level have capability of providing quantitative information about rheological, mechanical, chemical and electrical properties of molecular systems, [48,21]. However, the enormous range of length and time scales involved in such complex materials presents a challenging computational task, in particular, due to a wide disparity of relaxation times.

A standard methodology in order to overcome problems of long relaxation times of complex systems is to abandon the chemical detail and describe the molecular system by fewer (the most relevant) degrees of freedom. The choice of the latter depends entirely on the physical problem under question. Such particle-based, systematic *coarse-grained* (CG) models of molecular systems are developed by averaging out the details at the molecular level, and by representing groups of atoms by a single CG particle. Then the effective coarse-grained interaction potentials (more precisely free energies) are derived from the microscopic details of the atomistic model. The coarse-grained potentials and force fields can be derived through different methods, such as the inverse Boltzmann method, force matching and relative entropy, [53,52, 70,27,33,34,69,12]. Applying these methods in the context of best-fit procedures in parametrized families of CG models the structural properties of systems at *equilibrium* can be described with accuracy which is related to a metric used for the parameter fitting procedure. However, the above mentioned coarse-graining parametrization techniques do not address dynamical properties of the model and are restricted to systems already at a (equilibrium) Gibbs state.

Furthermore, there are several important issues related to systematic CG models using microscopic information for molecular systems under non-equilibrium conditions: (a) the whole approach is based on the fact that there is a direct connection between structural properties (like pair distribution functions) and CG interaction potentials; i.e., the renormalization group map or Boltzmann relation, see for instance [53,72,27]. This is certainly true at equilibrium and near to equilibrium but may not be the case for systems far from equilibrium; (b) since the CG interaction potential intrinsically involves entropy, it is not clear what is the dependence of the effective CG force field with respect to the external forces (if they are present); (c) predicting the dynamics (or incorporating the proper friction in the equations of motion) in the CG non-equilibrium model is not clear, [25,3]. All these aspects are, in principle, relevant in any application of a systematic CG model for a molecular system under non-equilibrium conditions.

Recently, several methods for coarse-graining of stochastic models based on information theory have appeared in the literature, [14,5,6]. These methods employ entropy-based techniques that estimate discrepancy between (probability) measures. Using entropy-based analytical tools has proved essential for deriving rigorous results for passage from interacting particle models to mean-field description, e.g., [47]. Applications of these methods to the error analysis of coarse-graining of stochastic particle systems have been introduced in [46,39,44,45,40,41]. Independently of such rigorous mathematical work, the engineering community developed entropy-based computational techniques that are used for constructing approximations of coarse-grained potentials for models of large biomolecules and polymeric systems (fluids, melts), where the optimal parametrization of effective potentials is based on minimizing the relative entropy between *equilibrium* Gibbs states, e.g., [14,10,13,5,6]. Note, that other works in the literature are primarily based on observable-matching using either structural distribution functions, such as the inverse Boltzmann method, inverse Monte Carlo methods, [70,53,52], or averaged forces on CG particles [34,33]. These methods were used with a great success in coarse-graining of macromolecules, see, e.g., [72,58,27–29,25,3]. Recent review articles [25,67,68] give a detailed overview of coarse-graining techniques applied to systems at equilibrium. Finally, effective coarse equilibrium dynamics for systems with temporal scale separation modeled by overdamped Langevin dynamics were studied in [49].

Evolution of coarse-grained variables corresponding to Hamiltonian microscopic dynamics can be described exactly with the Mori–Zwanzig formalism leading to a stochastic integro-differential system with strong memory terms, known as the generalized Langevin equation (GLE) [75,57], that is in principle computationally intractable. Therefore either a scaling of CG dynamics or approximations of the GLE are used [62,29,30,25,63,15,31,54,18,51]. Approximate dynamical models in a parametrized formulation have also been considered in recent studies, most of them based on the well established equilibrium parametrization methods described above. For example, authors in [35,19] propose optimal CG parametrized Langevin dynamics based on the force matching method.

In order to extend the information-theoretic approach developed in [69] for coarse-graining of Gibbs states to dynamics, a parameter fitting procedure for dynamic coarse-grained models was developed in [23]. The method proposed there is based on minimization of the relative entropy between discrete two-time transition probabilities associated with the diffusion process, in this case Langevin dynamics. Moreover, authors demonstrate that the relative entropy minimization can be interpreted as a force-matching problem. The use of the two-time step probability limits the applicability of the approach to short time dynamics while the discretization time step appears explicitly in the minimization problem leading to time step depended optimal parameters. In a recent article, [20], authors attempt to overcome the short time limit using Bayesian inference to identify most probable parameters for a given time series of microscopic states, i.e. in a path space perspective. The authors provide also the connection with force-matching where though again the optimal parameter set depends on the time step of the numerical discretization scheme. The *relative entropy rate* (RER) functional for Markov Chains proposed in [64] and [42] is similar to the functional that defines the best-fit optimization in [23], being the relative entropy per unit time for stationary processes. The formulation of path-space relative entropy for continuous time process in the present work illustrates that both path-space relative entropy and RER are independent of the time step for any numerical dis-