Special Session 5: Hybrid Monte Carlo

Elena Akhmatskaya, Basque Center for Applied Mathematics, Spain
J. M. Sanz-Serna, Universidad de Valladolid, Spain

The hybrid Monte Carlo (HMC) method was first introduced by Duane and his coworkers in 1987 in order to combine the best features of two well established simulation techniques, molecular dynamics and Monte Carlo. The HMC method proved itself to be both an efficient sampling device and an effective realization of a stochastic thermostat. Some of its weakness are its inability to reproduced dynamical properties and its lack of efficiency in the simulation of large systems.

An important development came in 1996, when Neal successfully applied HMC to neural network models, thus demonstrating its suitability for statistical computations. Recent developments have aimed at increasing the capability of simulating large molecules, retaining dynamical information and solving large dimensional statistical problems.

The purpose of this session is to bring together researchers with interests in different application fields in physics, chemistry and statistics, as well as in numerical and optimization techniques, to promote further development and dissemination of the method.

Generalized shadow hybrid Monte Carlo: from theory to useful tools

Elena Akhmatskaya
Basque Centre for Applied Mathematics (BCAM), Spain
akhmatskaya@bcamath.org
S. Reich, B. Escribano, J.M. Asua, J.I. Mujika

Recently introduced Generalized Shadow Hybrid Monte Carlo (GSHMC) method has found applications in areas such as atomistic simulation, particle simulation and Bayesian computation. This required the development of four variants of the original GSHMC technique: (1) the standard GSHMC (a thermodynamically consistent implementation of constant-temperature molecular dynamics); (2) MTS-GSHMC (a multi-time stepping GSHMC); (3) meso-GSHMC (a Metropolis corrected dissipative particle dynamics method) and (4) the GSHmMC) (a Generalised Shadow Hamiltonian Monte Carlo approach employing modified Hamiltonians in the Metropolis test). We highlight the ideas behind the GSHMC methods, while focusing on their implementation and on the range of applications expected to benefit most from their introduction. We describe implementation of GSHMC and MTS-GSHMC in two popular molecular simulation software packages, GROMACS and PROTOMOL, aimed at high performance computers. Performance of GSHMC methods is analysed in some detail and illustrated by the examples of two on-going studies: dynamic modeling of multiphase polymer morphology development and large-scale simulations of Serum Transferrin- Aluminium complexes.

⟶ ∞ ◇ ∞ ⟵

Constant-pH molecular dynamics using stochastic titration: theory and applications

Antonio Baptista
Universidade Nova de Lisboa, Portugal
baptista@itqb.unl.pt
Miguel Machuqueiro, Sara R. R. Campos, Pedro R. Magalhaes

Although the behavior of many biomolecules of interest depends markedly on the acid/base equilibrium of their protonatable groups, molecular dynamics (MD) simulations are traditionally performed using a fixed and somewhat arbitrary protonic state based on the pK_a values of those groups in solution. This talk discusses the stochastic titration method for constant-pH MD, where protonatable groups vary their state along the simulation according to the pH value of the solution, addressing its theoretical basis and some illustrative applications.

⟶ ∞ ◇ ∞ ⟵

Hamiltonian Monte Carlo with endogenous splitting

Martin Burda
University of Toronto, Canada
martin.burda@utoronto.ca
John Maheu

Splitting methods for Hamiltonian Monte Carlo have been shown to exhibit improvements in sampling efficiency over standard Hamiltonian Monte Carlo approaches. Splitting methods separate the Hamiltonian function and apply varying effective stepsizes for the split terms. In this paper we explore Hamiltonian splitting determined endogenously based on the underlying structure of the economic model. Preliminary output suggests efficiency gains of the endogenous split method relative to the regular HMC.

⟶ ∞ ◇ ∞ ⟵

Hybrid Monte Carlo for long timestep Langevin dynamics

Jesus Izaguirre
University of Notre Dame, USA
izaguirr@gmail.com
Haoyun Feng, Chris R. Sweet

Langevin dynamics is an efficient thermostatted form of molecular dynamics. We have introduced the Normal Mode Langevin (NML) dynamics that accurately integrates low frequency motions and approximates fast frequency motions near equilibrium using Brownian dynamics. This allows for long timesteps (100 fs and above) and large speedups (10x to 50x) compared to plain Langevin dynamics. It is attractive to combine Langevin dynamics with Hybrid Monte Carlo to make sampling more rigorous. I will present Hybrid Monte Carlo extensions of NML that can be used for rigorous sampling of either the low or fast frequency motions or both. These HMC extensions will be derived using the Nonequilibrium Driven Dynamics approach recently introduced by Crooks and Chodera.

$\longrightarrow \infty \diamond \infty \longleftarrow$

Monte Carlo sampling of RNA 3D graphs

Namhee Kim
New York University, USA
kimnamhee@gmail.com
Christian Laing, Shereef Elmetway, Segun Jung, Jeremy Curuksu, Tamar Schlick

RNA structure prediction is a mathematical and computational challenge with important biological applications in RNA structure and function. In this talk, I present a hierarchical Monte Carlo approach to predict RNA helical arrangements by a coarse-grained sampling of 3D graphs guided by knowledge-based potentials derived from geometrical measures based on solved structures. The coarse-grained model using newly developed 3D RNA graphs accelerate global sampling of candidate RNA topologies. Monte Carlo results are compared to reference graphs from both solved structures and predicted structures using current available programs. The comparison indicates promise for our graph-based sampling approach for characterizing 3D global helical arrangements in large RNA from a given secondary structure and offer reasonable candidate for further refinement.

$\longrightarrow \infty \diamond \infty \longleftarrow$

Langevin dynamics with constraints

Tony Lelievre
Ecole des Ponts ParisTech, France
lelievre@cermics.enpc.fr

We consider Langevin processes with mechanical constraints. The latter are a fundamental tool in molecular dynamics simulation for sampling purposes and for the computation of free energy differences. We will present three main results:(i) We propose a simple discretization of the constrained Langevin process based on a splitting strategy. We show how to correct the scheme so that it samples exactly the canonical measure restricted on a submanifold, using a Metropolis-Hastings correction in the spirit of the Generalized Hybrid Monte Carlo (GHMC) algorithm. Moreover, we obtain, in some limiting regime, a consistent discretization of the overdamped Langevin dynamics on a submanifold, also sampling exactly the correct canonical measure with constraints. (ii) For free energy computation using thermodynamic integration, we rigorously prove that the long time average of the Lagrange multipliers of the constrained Langevin dynamics yields the gradient of a rigid version of the free energy associated with the constraints. A second order time discretization using the Lagrange multipliers is proposed.(iii) The Jarzynski-Crooks fluctuation relation is proved for Langevin processes with mechanical constraints evolving in time. An original numerical discretization without time discretization error is proposed, and its overdamped limit is studied. This talk is based on the following reference: T. Lelivre, M. Rousset and G. Stoltz, Langevin dynamics with constraints and computation of free energy differences, to appear in Mathematics of Computation.

$\longrightarrow \infty \diamond \infty \longleftarrow$

A superconvergent method for configurational sampling using Langevin dynamics

Charles Matthews
University of Edinburgh, Scotland
charles.matthews@ed.ac.uk
B. Leimkuhler

In Molecular Dynamics, trajectories are often treated from a statistical perspective: we use them to sample the overall phase space with respect to a desired statistical ensemble. In sampling the Canonical (NVT) ensemble, typically a stochastic perturbation to Newton's equations is used to generate such trajectories. However, once such a thermostatted system has been defined, the challenge remains to integrate the equations in an efficient and robust manner, particularly in a Molecular Dynamics context where rugged potentials and the high cost of force evaluations can stymie such efforts. In this talk, we will present some mathematical results on invariant measures for methods based on splittings of Langevin Dynamics,

and give some innovative numerical methods where the goal is exclusively configurational sampling.This talk describes joint work with Ben Leimkuhler.

$\longrightarrow \infty \diamond \infty \longleftarrow$

Calculations of binding free energies with molecular simulations: progress and challenges

David Mobley
University of New Orleans, USA
dmobley@gmail.com
Gabriel Rocklin, Pavel Klimovich

Calculation of binding strength, or affinity, between proteins, life's molecular machines, and small molecules is of substantial interest in pharmaceutical drug discovery. Accurate techniques for such calculations could yield substantial benefits in drug discovery pipelines. Here, we discuss progress calculating binding strengths, or free energies, from molecular simulations. We present the highlights of our calculations in several different binding sites, focusing on what we learned as well as on sampling challenges that can benefit from enhanced sampling techniques such as hybrid Monte Carlo. Overall, these calculations based on physical force fields are reaching the accuracy where they can, in favorable situations, yield sufficient accuracy to benefit pharmaceutical drug discovery, yet many challenges remain.

$\longrightarrow \infty \diamond \infty \longleftarrow$

An application of a hybrid Monte Carlo method in path space

Frank Pinski
University of Cincinnati, USA
frank.pinski@uc.edu
P.J. Malsom

We are investigating collections of atoms as their positions evolve under Brownian (over-damped Langevin) dynamics. In the cases where the collection changes conformation, an energy barrier often exists. Such transitions are rare events when the thermal energy is small compared to the energy barrier. The understanding of such rare events is the goal of our studies. We sample the transition paths in a thermodynamically significant manner using a Hybrid Monte Carlo (HMC) Method in Path Space. The relative probability of paths is computed using expressions generated from Ito's equation and the Girsanov formula. In implementing the HMC, auxiliary variables (velocities) are introduced with the masses chosen to help equalize the time scales. Moreover the method preserves the quadratic variation along the paths.The immediate focus of this work is to study transitions in small Lennard-Jones clusters. We consider a low energy transformation in 13-atom and 14-atom clusters. The 14-atom cluster consists of one atom sitting on the surface of a close-packed structure of the others. In this cluster, the single "surface" atom drives into the cluster and pushes an atom, initially on the opposite side of the cluster, onto the surface. In the 13-atom cluster, we investigated a similar mode.

$\longrightarrow \infty \diamond \infty \longleftarrow$

Hybrid Monte Carlo on Hilbert spaces

J Sanz-Serna
University of Valladolid, Spain
sanzsern@mac.uva.es
A. Beskos, F.J. Pinski, A.M. Stuart

We define a generalized Hybrid Monte Carlo algorithm which overcomes this problem for target measures arising as finite-dimensional approximations of measures π which have density with respect to a Gaussian measure on an infinite-dimensional Hilbert space. The performance of the algorithm does not deteriorate as the dimensionality of the problem increases.

$\longrightarrow \infty \diamond \infty \longleftarrow$

Mass tensor molecular dynamics and hybrid Monte Carlo

Robert D. Skeel
Purdue University, USA
skeel@cs.purdue.edu

In hybrid Monte Carlo and for most application of molecular dynamics, the masses are relevant only to the extent that they enhance sampling. Back in 1975, it was proposed by C.H. Bennett that, in such cases, the physical masses be replaced by an arbitary positive definite symmetric mass tensor. Much more recently, such an approach was developed independently for statistical applications by Girolami and Calderhead and applied with considerable success. Building on these insights, preliminary results will be presented concerning the possibility of applying this methodology in a rigorous fashion to molecular dynamics and hybrid Monte Carlo. This is joint work with Y. Fang, M. Calvo, and J.M. Sanz-Serna.

$\longrightarrow \infty \diamond \infty \longleftarrow$

Riemann manifold hybrid Monte Carlo and alternative metrics

Vassilios Stathopoulos
University College London, England
v.stathopoulos@ucl.ac.uk
Mark Girolami

For the purposes of statistical inference taking a geometric perspective and defining Hybrid Monte Carlo on a differentiable manifold defined by a model

based Metric tensor and associated connection provides a powerful Markov chain Monte Carlo (MCMC) method. Although the Fisher Information (FI) is the natural metric for probability density functions there are cases where the metric can be degenerate or not analytically defined. In this talk an overview of the Riemann Manifold Hybrid Monte Carlo algorithm of Girolami and Calderhead (2010) will be given and example applications where the exact (FI) is degenerate or not analytic will be discussed. For such degenerate cases we can augment the FI with the Hessian of the prior while when the FI is not analytic we can consider local or finite estimate approximations of the FI. Examples will consist of a probit and logistic regression and finite Gaussian mixture models.

$\longrightarrow \infty \diamond \infty \longleftarrow$