

# Sensitivity Analysis for Stochastic Molecular Modeling of Complex Chemical Systems

Anastasios Tsourtis,<sup>1, a)</sup> Yannis Pantazis,<sup>2, b)</sup> Markos A. Katsoulakis,<sup>2, c)</sup> and Vagelis Harmandaris<sup>3, d)</sup>

<sup>1)</sup>*Department of Mathematics and Applied Mathematics, University of Crete, Greece*

<sup>2)</sup>*Department of Mathematics and Statistics, University of Massachusetts, Amherst, USA*

<sup>3)</sup>*Department of Mathematics and Applied Mathematics, University of Crete, Institute of Applied and Computational Mathematics (IACM), Foundation for Research and Technology Hellas (FORTH), GR-70013, Heraklion, Crete, Greece*

Molecular simulations of complex chemical systems at multiple length and time scales are very powerful tools, which, nowadays, are used extensively to predict structure-properties relations of complex chemical systems. The properties of the model chemical systems depend on a large number of parameters, which are usually obtained utilizing optimization techniques matching specific data taken obtained either from more detailed (e.g. quantum) calculations simulations, or from experiments.<sup>1,2</sup>

Here, we propose a sensitivity analysis (SA) method for molecular modeling of complex chemical systems based on information-theoretic (and thermodynamic) quantity of relative entropy (RE) in order to estimate information change or loss upon perturbations of the parameters of the modeled systems.<sup>3,4</sup> We further use the associated components of relative entropy rate (RER) and Fisher Information matrix (FIM) and we validate the proposed SA method to a diverse range of observable functions. We show that the proposed methodology accurately predicts the parameter sensitivities of stochastic systems of different complexity. In more detail, we performed large molecular dynamics (MD) computer simulations and calculations of the RE and the associated RER along with computation of observable quantities and we carried out the sensitivity analysis (SA) on the system parameters.

The RER method for sensitivity analysis carries sufficient level of generality and can be used to carry out feasible large scale computations of complex molecular systems. The adopted approach on RE quantification is between time-series distributions that originated from the same initial phase-space state, therefore we refer to it as "pathwise". The method used requires analytic form of the transition probabilities based on the integration scheme at hand and computations from the continuous-time RER regime validate our results as the discretization time-step becomes sufficiently small.

We apply the above methodology to various systems, such as the prototypical LJ fluid and a more complex one (methane, CH<sub>4</sub>)<sup>4</sup>. SA was based on the potential parameters for all systems. Static and dynamic observable quantities such as the radial distribution function, the mean square displacement and the pressure are used to validate the proposed SA approach. We also investigated the effect of the potential cutoff radius by numerically computing the RER.<sup>4</sup>

Our results lie on the stationary regime of stochastic dynamics but recent ongoing research proves that the methodology we utilized can be extended to the transient regime, i.e study of non-equilibrium chemical systems, such as non-equilibrium MD simulations of polymer nanocomposites, lattice kinetic Monte Carlo models of catalysis, modeling of reaction networks etc.

Furthermore, we apply the current SA methodology for high-dimensional systems using RE as a measure of loss of information in coarse-graining. Coarse-graining (CG) methods of stochastic systems allow for constructing optimal parametrized Markovian coarse-grained dynamics within a parametric family, by minimizing the information loss (i.e., the relative entropy) on the path space. Recent ongoing work on is application of the RE framework for CG in the non-equilibrium regime where there's no Gibbs structure<sup>5</sup>.

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<sup>a)</sup>E-mail: tsourtis@uoc.gr

<sup>b)</sup>E-mail: yannis.pantazis@gmail.com

<sup>c)</sup>E-mail: markos@math.umass.edu

<sup>d)</sup>E-mail: harman@uoc.gr

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