Global Langevin model of multidimensional biomolecular dynamics

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The consideration of the dynamical behaviour of proteins is of crucial importance to understand their functionality. Since it is often difficult to obtain this information in experiment, molecular dynamics simulations represent a useful tool to access molecular motions down to timescales of picoseconds. However, the data, delivered by these simulations, is so extensive that a suitable interpretation framework is needed to detect the essential characteristics of the simulated system. Frequently, the dynamics are described by a diffusive motion on a low-dimensional free energy landscape $F(\vec{x})$. The system-bath approach of Zwanzig can be used as theoretical basis of this description. Based on this ansatz, a Langevin equation can be derived. By furthermore assuming a timescale separation between the slow dynamics along the system coordinate $\vec{x}$ and the fast fluctuations of the bath, this Langevin equation can be simplified to a memory-free, i.e., Markovian, one. So, the motion of the system on the free energy landscape can be completely described by uniting all influences of the bath to a frictional force, which damps the motion, and a stochastic force. Both forces are related by the fluctuation-dissipation theorem. While the theoretical approach of Zwanzig typically assumes a extremely idealised description of the bath degrees of freedom and a specific form of the system-bath coupling, it would be desirable to extend the approach to realistic biomolecular systems, i.e., to data.

In this thesis, a practical method is proposed to construct an analytically defined global model of biomolecular dynamics. This approach uses an "empirical valence bond"-type model to describe the free energy and results of the data-driven Langevin equation to deduce frictional and random force. By considering molecular dynamics simulations of three different systems, alanine dipeptide, heptaalaine and bacteriophage T4 lysozyme, it is proven that the approach reproduces the dynamics of the references and that it is extremely suitable to describe multidimensional systems. For the considered systems, it is shown that the frictional force, as well as the random force, is sufficiently described by constants which is a nontrivial finding. It is shown that the correct interpretation of the data-driven Langevin equation includes the mass of the system and that the Langevin fields, estimated by the data-driven Langevin equation, depend on the time step of it. For the example of heptaalanine, it is presented that the model can easily be modified which is a strength of the proposed approach. This allows to study the effects of system changes on the overall dynamics without the need of calculating an expensive molecular dynamics simulation.

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