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Journal of Computational Physics 211 (2006) 262–288
JOURNAL OF COMPUTATIONAL PHYSICS
www.elsevier.com/locate/jcp

Modal reduction of mathematical models of biological molecules

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Received 14 January 2005; received in revised form 8 April 2005; accepted 24 May 2005
Available online 14 July 2005

Abstract

This paper reports a detailed study of modal reduction based on either linear normal mode (LNM) analysis or proper orthogonal decomposition (POD) for modeling a single α-D-glucopyranose monomer as well as a chain of monomers attached to a moving atomic force microscope (AFM) under harmonic excitations. Also a modal reduction method combining POD and component modal synthesis is developed. The accuracy and efficiency of these methods are reported. The focus of this study is to determine to what extent these methods can reduce the time and cost of molecular modeling and simultaneously provide the required accuracy. It has been demonstrated that a linear reduced order model is valid for small amplitude excitation and low frequency excitation. It is found that a nonlinear reduced order model based on POD modes provides a good approximation even for large excitation while the nonlinear reduced order model using linear eigenmodes as the basis vectors is less effective for modeling molecules with a strong nonlinearity. The reduced order model based on component modal synthesis using POD modes for each component also gives a good approximation. With the reduction in the dimension of the system using these methods the computational time and cost can be reduced significantly.

Keywords: Modal reduction; Biological molecules; Linear normal mode; Proper orthogonal decomposition; Component modal analysis

1. Introduction

Biomolecular motions involve a large number of atoms and take place over a great range of time and length scales. Moreover, because of the existence of high frequency motions, the usual time step in a

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doi:10.1016/j.jcp.2005.05.021

molecular dynamics simulation is around 10^{-15} s. These characteristics make a numerical molecular dynamic simulation a computationally intensive task. There is a clear need to reduce the cost of the computation. So far several schemes have been developed to accomplish this goal. One way is to reduce the time and cost for the evaluation of non-bonded forces, electrostatics forces and van der Waals forces. Since van der Waals interactions are short ranged, their calculation can be restricted to neighboring pairs. For electrostatic forces several algorithms have been proposed such as Ewald summation [1], particle–particle/particle mesh (PPPM) method [2] and fast multipole algorithms (FMAs) [3]. Also in the widely used computer code, CHARMM [4], a cut-off is used to exclude from the force calculation those atom pairs with a distance greater than the cut-off distance. Another approach being used is to make full use of high performance software techniques. Several computer programs such as NAMD [5] and EGO [6] are designed to run simulations on parallel computers.

An alternative approach is modal reduction as presented in this paper. The premise that motivates modal reduction is that complex systems can have a relatively simple dynamic behavior which only depends on a relatively small number of essential variables. The challenge for constructing low-dimensional models for complex physical systems is the choice of basis vectors. Various basis vectors for the subspace have been proposed.

As far as linear systems are concerned, the most common method is linear normal mode (LNM) or eigenmode analysis. Modal reduction is well established for linear dynamic systems since the linear systems have the property of superposition.

By contrast, modal reduction for nonlinear systems is much more complicated. Generally linear normal modes are no longer invariant manifolds in nonlinear vibration systems. However, it is valid to simulate small fluctuations by assuming the potential energy is harmonic in the neighborhood of equilibrium states (conformations) based on linear normal modes. The interested reader is referred to [7] for a discussion of existing methods. For the basic methodology used in biological systems, see Ref. [8]. It is known that the reduced order models for nonlinear systems that are based on the linear eigenmode space can give qualitatively wrong results due to the contamination from the non-modeled modes. More specifically, it has been observed that projecting nonlinear equations onto linear eigenmodes predicts incorrect hardening and softening regions of the potential energy. See [9] and the references therein for examples. To overcome this problem, several invariant manifolds such as center manifolds [10], inertial manifolds and nonlinear normal modes (NNMs)[11] have been proposed. But these approaches are still under development and have been primarily used for low-dimensional or relatively simple systems [12–15]. For complex and high-dimensional systems these methods are often computationally intractable. Another method that has received attention recently is the proper orthogonal decomposition method (POD) also known as the Karhunen–Loeve (K–L) method or principal modal analysis (PCA).

The POD method is a procedure for extracting the essential information from a set of data obtained in experiments or numerical simulations, thus providing a optimal basis for modal reduction. For a physical interpretation of POD modes (POM), see [16–18] for detailed discussions. It has been proven that POM are actually the linear modes of vibration for linear symmetric undamped free-vibration systems with an identity mass matrix [16]. In addition to being optimal in a least square sense, the POD method has the advantage that POM are completely data dependent and do not need any prior knowledge of the system. Hence, this procedure is powerful in generating low-dimensional models for complex systems described by a high-dimensional discrete system or a continuous system. Compared with other nonlinear invariant manifold reduction methods, POD modes are much easier to compute. Because of these properties the POD method is widely used in various fields such as data analysis, image processing, and modal reduction. One of the earliest applications of POD may be traced back to turbulence modeling by Lumey in 1967 [19]. Now POD is emerging as a useful tool in structural dynamics and time-dependent fluid dynamics. It has been used to build reduced order models in a variety of contexts [20–23].

The application of modal analysis to molecular dynamics first appeared in the early 1980s. In [24], the author shows that multiple minima exist in proteins and the harmonic approximation of the potential