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Normal-mode analysis without the Hessian: A driven molecular-dynamics approach

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We point out that normal modes and frequencies of molecules and molecular complexes can be obtained directly from a harmonically driven molecular dynamics calculation. We illustrate this approach for HOD and H_5O_2^+ and then discuss its potential advantages over the standard Hessian-based approach for large molecules. © 2003 American Institute of Physics.

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Normal-mode analysis is a time-honored technique in chemistry¹ to obtain vibrational frequencies and the corresponding motions of molecules, molecular complexes, adsorbates, etc., in the harmonic approximation. It is finding renewed use in the area of biomolecular simulations, where, however, it can be very computationally demanding due to the large number of atoms.² The standard normal-mode analysis is based on a calculation and subsequent diagonalization of the mass-weighted force constant matrix, also known as the Hessian. The normal-mode frequencies are directly related to the eigenvalues and the normal modes to the eigenvectors of this matrix.

The order of the Hessian matrix is typically $3N$, where N is the number of atoms in the system of interest. The computational procedure to obtain the eigenvalues and eigenvectors of the Hessian matrix is an $O(N^3)$ process, i.e., the computational effort scales like N^3 . For small and moderately-sized molecules, N is of the order of 100 or less and the Hessian-based approach is easily carried out. However, as recently stressed by Li and Cui,² this approach becomes very difficult to implement for biomolecules where the number of atoms can approach and even exceed 10 000.

A full normal-mode analysis, as described above, yields both frequencies and normal modes. Another, quite different approach is based on the calculation of certain time correlation functions.³ This approach, however, only yields the frequencies and requires the Fourier transform of an appropriate autocorrelation function, e.g., the velocity or dipole correlation function. The quantum version of the method,³ when applied to vibrational motion, yields, in principle, the exact excitation frequencies (in contrast to a normal-mode analysis, which is based on the harmonic approximation). The classical version of this theory is widely used in both isolated molecule and condensed matter applications;^{4–6} however, most often not within the small amplitude, harmonic limit. It is well known that in this limit the method does yield the correct normal-mode frequencies. To obtain sharp spectral

features, a molecular dynamics calculation must be done for sufficiently long time to permit a well-resolved Fourier transformation of the time correlation function.^{4,5} In recent, very promising work,⁷ “Filter Diagonalization” has been shown to yield a sharper spectrum compared to a standard Fourier transform method.

An important limitation of current time-correlation methods is the absence of information about the corresponding molecular motions, i.e., the normal modes, in the limit of small amplitude motion. In the context of condensed matter calculations, this limitation motivated, in part, the development of “instantaneous normal-mode analysis.”^{5,6} This approach requires the calculation and diagonalization of the Hessian (actually many such diagonalizations) and so is subject to the limitations of the Hessian-based method mentioned above.

In this paper, we propose and demonstrate a method to perform a full normal-mode analysis that does not require a calculation of the Hessian. We show how normal modes can be obtained using a straightforward molecular dynamics (MD) approach. The method employs an external, harmonic driving term that can be used to scan the spectrum in a continuous wave fashion to determine resonant absorptions, which for weak signals are the normal-mode frequencies. The molecular motions, induced by driving at resonant frequencies, are (by definition) the normal modes. This approach follows from a basic characteristic of normal modes, i.e., that a classical system executing small amplitude motion about a minimum can be driven resonantly at the normal-mode frequency of the unperturbed system. It is also clear that the system will respond to a given resonant driving frequency by executing the corresponding normal-mode vibration. To our knowledge, this approach has not been used in MD simulations to obtain normal modes. (We note that harmonically-driven, MD calculations have been reported previously to simulate multiphoton absorption of light.^{8,9} In these studies, a single bond was coupled classically to an external driving term with the object of creating a highly excited molecule. The external driving was not aimed at de-

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termining normal modes, nor was that possibility mentioned.)

We give the details of one implementation of this approach and validate the method by applying it to two molecules. We note some advantages this method may have over the conventional Hessian-based approach for very large systems and conclude with some comments about extensions to anharmonic motion.

Let ω_n be a given normal-mode frequency, obtained either from a standard time-correlation calculation, or by a method we illustrate below. The suggestion is to perform a MD calculation, with the system initially at rest at a stationary point, with a weak, harmonic, driving force at the frequency ω_n . We investigated several forms for a driving force, including one that is linearly coupled to the Cartesian coordinates of each atom. This form does work, but it does require additional constraints in order to avoid mixing translational and rotational modes into the conventional normal modes of vibration.¹⁰ Here we present results using a driving force that depends only on internuclear distances. This driving is obviously rotationally and translationally invariant, and thus the center of mass translation and overall rotation will not be excited by it. (Of course, other forms of the driving that are translationally and rotationally invariant are possible; however, we chose to use this particularly simple form here.)

The Hamiltonian for driven molecular dynamics (DMD) of a molecular system consisting of N atoms is given by

$$H(\mathbf{p}, \mathbf{q}, t) = H_0(\mathbf{p}, \mathbf{q}) + U(t), \quad (1)$$

where \mathbf{q} and \mathbf{p} represent the $3N$ atomic Cartesian coordinates and conjugate momenta, respectively. In this equation, the molecular Hamiltonian, H_0 , is given by

$$H_0(\mathbf{p}, \mathbf{q}) = \sum_i \frac{p_i^2}{2m_i} + V(\mathbf{q}), \quad (2a)$$

where V is the molecular potential, and $U(t)$, the driving term, is given by

$$U(t) = \sum_{i,j} \lambda_{ij} r_{ij} \sin \omega_n t, \quad (2b)$$

where r_{ij} are internuclear distances, and λ_{ij} are the (small) coupling constants. Hamilton's equations of motion are

$$\begin{aligned} \dot{q}_{\alpha,i}(t) &= \frac{p_{\alpha,i}(t)}{m_i}, \\ \dot{p}_{\alpha,i}(t) &= -\frac{\partial H_0}{\partial q_{\alpha,i}} - \sum_{i,j} \lambda_{ij} \frac{\partial r_{ij}}{\partial \alpha_i} \sin \omega_n t \\ &= -\frac{\partial V}{\partial q_{\alpha,i}} - \sum_{i,j} \lambda_{ij} \frac{\alpha_i - \alpha_j}{r_{ij}} \sin \omega_n t; \\ i &= 1, \dots, N, \quad \alpha = x, y, z. \end{aligned} \quad (3)$$

Thus, the only modification to standard MD codes is the addition of the harmonic driving term, which, as seen, is quite simple to evaluate. More details about the coupling constants are given below.

If, as assumed, ω_n is a normal-mode frequency, then the system should respond to the driving force by executing motion that is a normal mode, provided the driving is not too hard, i.e., the motion remains in the small amplitude limit. This is easily achieved by choosing suitably small values of the coupling constants. In addition, it should be clear that the normal-mode frequency spectrum can also be determined by doing the analog of a continuous wave absorption experiment. That is, the driving frequency can be varied through a frequency range and energy absorption should maximize locally at the normal-mode frequencies. An examination of the molecular motion at a given "resonance" will provide the corresponding normal mode. We now illustrate this approach for HOD and the molecular complex H_5O_2^+ .

Consider HOD first. This triatomic represents this simplest nontrivial example of a molecule with normal modes. We chose to present results for HOD (instead of H_2O) because of its low (C_s) symmetry, and thus there are no symmetry conditions on the coupling matrix λ_{ij} . A realistic potential was used,¹¹ the equations of motion were integrated using a standard integrator, and the coupling constants λ_{ij} all equal 0.0001 Hartree (22 cm^{-1}). Note the choice of equal coupling constants is not necessary and was made for convenience.

The absorption measure we adopt is the average total internal energy of the molecule, which is given by

$$\langle E \rangle = \frac{1}{T} \sum_i H_0(t_i), \quad (4)$$

where T is the total driving time. The resulting spectrum for T equal to 20 000 atomic time units, which corresponds to 1000 time integration steps, is shown in Fig. 1(a). As seen, there are three absorption peaks. The maxima of these peaks are at frequencies that are in excellent agreement (less than 1 cm^{-1} difference) with those from a Hessian-based, normal-mode analysis. It should be noted that these "absorption" features are fairly broad and better resolution can be obtained using the more conventional correlation function method. Also, note that the energy absorbed is of the order of 1.0 cm^{-1} , which indicates very mild driving.

The molecular motions corresponding to each resonant-driving frequency are given in Figs. 1(b)–1(d). As seen, the lowest-frequency mode corresponds to a bend, followed by the local OD-stretch, and finally the local OH-stretch, in agreement with the normal modes from the conventional analysis. Indeed, the normalized, mass-scaled Cartesian displacement vectors are in perfect agreement with the ones from the standard normal-mode analysis. We prefer to show the time dependence of the molecular modes because they clearly indicate that the system is monotonically absorbing energy with increasing time. Obviously, as the molecule continues to absorb energy, deviations from small amplitude harmonic motion will occur and anharmonic motion will develop. Such motion would be expected to detune the resonant frequency from the harmonic one⁹ and could be exploited to study anharmonic deviations from harmonic motion.

The second example is the complex H_5O_2^+ (the protonated water dimer). This is an interesting and challenging

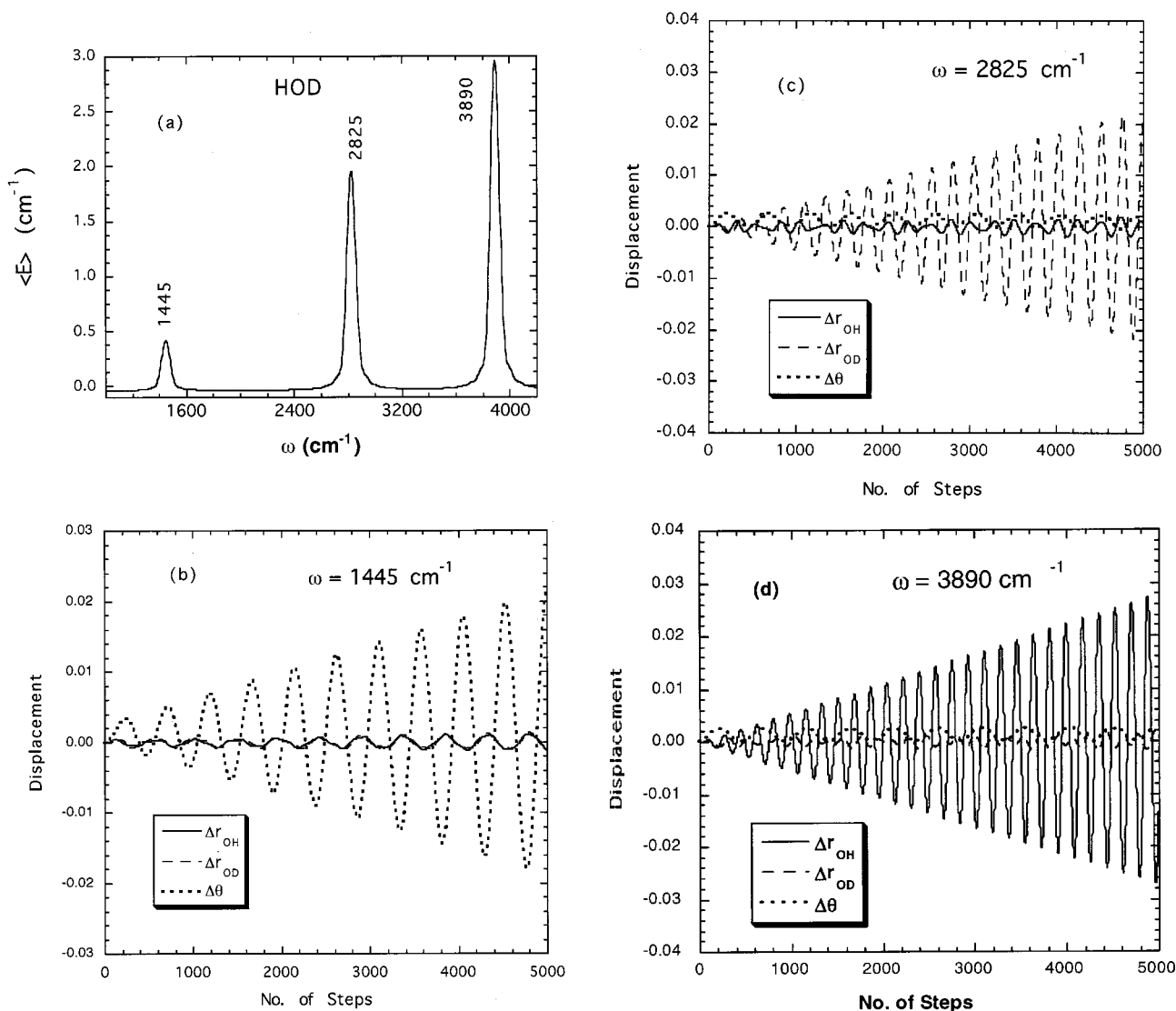


FIG. 1. Absorption spectrum from driven molecular dynamics calculation for HOD (a), and time dependence of the two bond stretches and the bond angle relative to the equilibrium values, measured in bohrs and radians, respectively, for the three normal modes with indicated frequencies (b)–(d).

system in several respects. First, there are a number of low-frequency, torsion-type normal modes that require no overall rotational mixing to describe properly. (This condition is met by the form of the driving used.) Second, the system is quite floppy, with two equivalent minima (of C_2 symmetry) which are separated by a second-order saddle point 97 cm^{-1} above the minima. The minima are for a slightly nonlinear O–H⁺–O configuration, and the saddle point is at a linear configuration. Thus, these stationary points are separated from each other by a small variation in the O–H⁺–O bending angle.

We did a standard, Hessian-based, normal-mode analysis at one minimum using the full-dimensional potential of Ojamäe *et al.*¹² There are seven normal modes of B symmetry and eight of A symmetry. These sets of modes can be driven separately with a coupling-matrix that transforms according to the appropriate irreducible representation of the C_2 point group. The driving was done for 20 000 atomic time units with all λ_{ij} equal in magnitude to 0.000 01 Hartree but with signs chosen to conform to B symmetry. The resulting

energy absorption spectrum for the B -modes is shown in Fig. 2. As seen, there are seven peaks, and the corresponding frequencies agree very well with the normal-mode frequencies. Note, these driving conditions are much milder than in the HOD example. This was necessary owing to the very shallow minima in this example, compared to HOD.

As an illustration of the normal modes obtained from the DMD calculation, we show the lowest frequency (178 cm^{-1}), counter-rotating torsional normal mode (which is of A symmetry) in Fig. 2.¹³ The mode obtained using the Hessian approach is also shown, and, as seen, there is excellent agreement with the DMD mode. We note that this type of torsional mode is of interest in conformational studies of biomolecules,² and we are gratified that DMD can yield a correct description of it.

These two examples clearly demonstrate that a normal-mode analysis can be done using DMD, without recourse to the Hessian. Thus, the method provides a viable alternative to the standard Hessian-based method. In comparing the computational effort of the two methods, it must be stressed

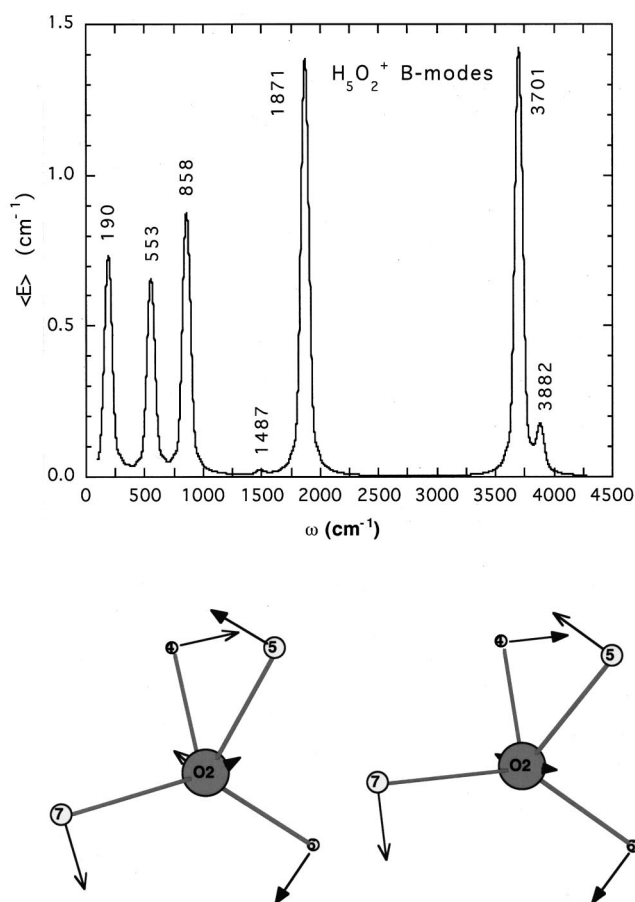


FIG. 2. Absorption spectrum from driven molecular dynamics calculation for modes of H_5O_2^+ of B -symmetry (upper plot) and comparison of normal mode for the lowest frequency mode (A -symmetry) from conventional analysis (left) and present driven calculations (right).

that because the two methods are quite different, they have different computational demands. As already noted, the conventional Hessian-based analysis requires the calculation of the $3N \times 3N$ matrix (of second derivatives of the potential at a stationary point), followed by diagonalization to obtain eigenvalues and eigenvectors. Thus, the effort to calculate the Hessian is $O(N^2)$, and the effort to obtain eigenvalues and eigenvectors is $O(N^3)$. So clearly this is not favorable scaling for large N .

The DMD approach requires $O(N)$ gradients of the potential per time step. A trajectory of N_{steps} thus is $O(N \times N_{\text{steps}})$, and to scan N_{scan} frequencies is $O(N \times N_{\text{steps}} \times N_{\text{scan}})$. If the frequencies are already known, say from a time-correlation function calculation, then per frequency the effort to obtain the corresponding normal mode is just $O(N \times N_{\text{steps}})$. A typical value for N_{steps} is 1000, so the effort in a DMD calculation does not become competitive with the Hessian-based one until N approaches 1000. (The number of time steps must be at least enough for several cycles of the driving term. However, we have found that the integration time step can be larger for driving a low-frequency mode compared to the time step to drive a high-frequency mode.)

Thus, roughly stated, the two methods become comparable for 1000 atoms if all normal-mode frequencies and modes are calculated. However, if a much smaller number of

normal modes is of interest, then the DMD could be significantly faster than the conventional approach. It should also be noted that the memory requirement of DMD is much less than the conventional approach for N greater than 1000. Further, it should be obvious that a DMD calculation for many frequencies is “embarrassingly” parallel.

Several issues clearly need further investigation for applications to biomolecules. One is the choice of internal coordinates to drive. It seems intuitive that different choices could result in more or less efficient driving of certain modes. For example, if the interest is in low-frequency torsional modes is it sufficient and perhaps even most efficient to drive nonbonded internuclear distances? Another issue is the “resolving power” of the method, i.e., the ability to distinguish modes that are very close in frequency. In principle driving can be done with arbitrary precision; however, it may be necessary to drive for longer times to separate modes with nearly the same frequency. Driving for longer times must be done with care of course (i.e., by choosing smaller coupling constants), because as the energy absorbed increases so may the deviation from harmonic motion.

In a different context driving the system beyond the harmonic limit may be of great interest since this opens a window on the study of coupled, anharmonic motion. To the extent that classical dynamics accurately describes this motion, it would be interesting to apply DMD to a system that is executing motion exceeding the harmonic limit. In the H_5O_2^+ example, we explored this in a preliminary way. We noticed that driving the two B -normal modes of frequencies 553 and 580 cm^{-1} with slightly larger values of the coupling constants led to sidebands in the absorption line shapes. Further investigation revealed that driving these two modes “pushes” the system in the direction of the second order saddle point. Indeed a normal-mode analysis at the saddle point reveals two imaginary modes with motions quite similar to these B -modes of the minima. Clearly this kind of motion is well beyond the normal-mode picture and in fact points to a breakdown of it. DMD does potentially offer a way to understand this motion as well driving it. This is clearly a topic for future investigations as are the points made in the preceding paragraph.

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normal modes due to small mixing of translational and rotational degrees of freedom.

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