Construction of Molecular Mechanics Energy Functions by Mathematical Transformation of *Ab Initio* Force Fields and Structures

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A method is presented by which *ab initio* (or empirical) force fields and structures can be converted to molecular mechanics energy parameters. Using Cartesian coordinates, the effect of van der Waals and other nonquadratic interactions is eliminated from the original spectroscopic force field, and molecular mechanics force constants and reference geometry parameters are derived. The computed parameters yield molecular structure and vibrational frequencies that are identical to the original ones. The transformation produces a complete general valence force field, which in most cases is impractical, and a procedure to reduce the number of force constants is therefore described. Different ways of applying the transformation are outlined.

INTRODUCTION

High level *ab initio* calculations on increasingly complex organic compounds have become an important tool in the construction of empirical potential energy functions used in molecular mechanics (MM), molecular dynamics (MD), and Monte Carlo (MC) calculations. The reason is that *ab initio* calculations can produce results which in many cases would be difficult or even impossible to obtain, with comparable reliability, in any other way.[1] One drawback, though, is that *ab initio* calculations often yield different results depending on the choice of basis functions, inclusion of polarization functions, configuration interactions, etc.,[2-4] and when force fields and vibrational frequencies are computed, proper scale factors also have to be used. The choice of basis set level in each case is based largely on experience. So are scale factors, when they are not directly optimized to experimental frequencies. However, as experience with basis sets and other options increases, the quality of *ab initio* calculations on large molecules is certainly expected to improve. To be able to keep the MM, MD, and MC calculations up to date with the *ab initio* results, methods are therefore needed by which these results can be conveniently converted to MM potential energy function parameters, preferably without sacrificing too much of the original accuracy.

Quadratic force fields are among the quantities that are most suitable to study by *ab initio* methods, since, for large molecules, these are otherwise difficult to determine uniquely,[5] and the transferability of the scale factors has generally been found to be good.[6] It is a subject of debate as to what extent interaction force constants should be included in the energy function[7,8] if the main purpose is to reproduce molecular structures properly. It is clear, however, that vibrational frequencies, at least, cannot be computed very accurately without a significant number of cross terms. Also, as has recently been pointed out,[9] if the initial force field is too crude, substantial problems arise with retaining the assignments in the optimization of force constant parameters to vibrational frequencies. The question is then which cross terms to include, i.e., which cross terms cannot be neglected without severe consequences for the frequencies. Although this can easily be studied within the framework of the original (spectroscopic) *ab initio* force field, the conclusions from such a study are not necessarily transferable to the MM potential energy function. Neither are the values of the spectroscopic force constants. This is because nonquadratic interactions (van der Waals, Coulombic, etc.) are accounted for separately in the MM model, but implicitly included in a spectroscopic force field. What needs to be done before the selection of important cross terms can be made, is therefore a transformation in which the contribution of the nonquadratic interactions is eliminated from the spectroscopic force field, and true MM force constants are produced.

The aim of the present article is to describe the formalism of this transformation. In addition to the MM force constants, the transformation also gives the reference geometry parameters that pertain to the quadratic terms of the MM potential energy func-

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tion. An energy function containing the computed force constants and reference geometry, together with the original nonquadratic interactions, then yields exactly the same structure and vibrational frequencies as the *ab initio* calculation itself, and thus constitutes a good starting point for the subsequent reduction of the number of cross terms, and other modifications that may be necessary in the further refinement of the energy function.

As indicated above, we initially assume that the parameters of the nonquadratic interactions are known. This is not a serious restriction, however, since they can to a good approximation be determined independently of the parameters of the quadratic terms, for instance by fitting to crystal properties[10-13] and to *ab initio* electrostatic potentials.[14,15] Using *ab initio* (or empirical) results for several conformations of a group of related molecules, it may even be possible to refine a complete set of MM potential energy parameters for these molecules.

Thus, our conversion can be used as a fast method to fully utilize new spectroscopic force fields and structures, as well as new information concerning nonquadratic interactions. An interesting application is also the evaluation of the ability of existing functions for nonbonded interactions to yield a consistent set of energy parameters.

THEORY

In the molecular mechanics method,[16a,16b] the potential energy function may be considered to consist of a quadratic part V_q and a nonquadratic part V_{nq},

$$V = V_q + V_{nq} \tag{1}$$

V_{nq} accounts for van der Waals interaction, Coulombic interaction, periodic torsions, etc., while V_q is the potential energy arising from deformation of valence bonds and angles. Explicitly, V_q can be written

$$V_q = \frac{1}{2} \sum_{i,j} F_{ij}(R_i - R_{i0})(R_j - R_{j0}) \tag{2}$$

where the F_{ij}'s are called MM force constants, the R_i's are valence coordinates and the parameters R_{i0} define the reference (or intrinsic equilibrium) geometry. The reference geometry corresponds to the minimum of the quadratic part of the potential but does not in general represent the equilibrium geometry of any real molecule. The real equilibrium geometry is obtained by minimizing the total potential energy, usually in Cartesian coordinates. In the conversion from *ab initio* we assume, at first, as explained in the introduction, that V_{nq} is known and we only determine the MM force constants and the reference geometry.

If the Cartesian coordinates of the molecule are denoted by $x_{k\alpha}$, where k runs over the atoms and $\alpha = 1, 2, 3$, we have for the first derivatives of the potential energy

$$\frac{\partial V}{\partial x_{k\alpha}} = \frac{\partial V_q}{\partial x_{k\alpha}} + \frac{\partial V_{nq}}{\partial x_{k\alpha}} \tag{3}$$

and for the second derivatives

$$\frac{\partial^2 V}{\partial x_{k\alpha} \partial x_{l\beta}} = \frac{\partial^2 V_q}{\partial x_{k\alpha} \partial x_{l\beta}} + \frac{\partial^2 V_{nq}}{\partial x_{k\alpha} \partial x_{l\beta}} \tag{4}$$

or

$$\frac{\partial^2 V_q}{\partial x_{k\alpha} \partial x_{l\beta}} = \frac{\partial^2 V}{\partial x_{k\alpha} \partial x_{l\beta}} - \frac{\partial^2 V_{nq}}{\partial x_{k\alpha} \partial x_{l\beta}} \tag{5}$$

where $l\beta$ is defined in the same way as $k\alpha$. The second derivatives of V with respect to the Cartesian coordinates represent the *ab initio* force field, and since we assume that V_{nq} is known its first and second derivatives can be computed. Thus, in Cartesian coordinates, the contribution of the nonquadratic interactions can be subtracted from the spectroscopic force constant matrix to yield a new matrix that is purely associated with V_q. To obtain the second derivatives of V_q with respect to the internal coordinates, i.e., the MM force constants, we use the chain rule

$$\frac{\partial V_q}{\partial R_i} = \sum_{k\alpha} \left(\frac{\partial V_q}{\partial x_{k\alpha}} \cdot \frac{\partial x_{k\alpha}}{\partial R_i} \right) \tag{6}$$

which applied twice yields

$$\begin{aligned}
\frac{\partial^2 V_q}{\partial R_i \partial R_j} &= \frac{\partial}{\partial R_j} \left(\sum_{k\alpha} \frac{\partial V_q}{\partial x_{k\alpha}} \cdot \frac{\partial x_{k\alpha}}{\partial R_i} \right) \\
&= \sum_{k\alpha} \left[\left(\frac{\partial x_{k\alpha}}{\partial R_i} \right)_{\bar{R}_{min}} \frac{\partial}{\partial R_j} \left(\frac{\partial V_q}{\partial x_{k\alpha}} \right) \right. \\
&\quad \left. + \left(\frac{\partial V_q}{\partial x_{k\alpha}} \right)_{\bar{x}_{min}} \frac{\partial}{\partial R_j} \left(\frac{\partial x_{k\alpha}}{\partial R_i} \right) \right] \\
&= \sum_{k\alpha} \left[\left(\frac{\partial V_q}{\partial x_{k\alpha}} \right)_{\bar{x}_{min}} \left(\frac{\partial^2 x_{k\alpha}}{\partial R_i \partial R_j} \right)_{\bar{R}_{min}} \right. \\
&\quad \left. + \sum_{l\beta} \left(\frac{\partial x_{k\alpha}}{\partial R_i} \right)_{\bar{R}_{min}} \left(\frac{\partial x_{l\beta}}{\partial R_j} \right)_{\bar{R}_{min}} \cdot \left(\frac{\partial^2 V_q}{\partial x_{k\alpha} \partial x_{l\beta}} \right)_{\bar{x}_{min}} \right]
\end{aligned} \tag{7}$$

where $\bar{x}_{min}$ and $\bar{R}_{min}$ denote the minimum of the total potential V in Cartesian and internal coordinates, respectively. In the expression above we have three unknown quantities, the gradient of V_q with respect to the Cartesians and the first and second derivatives of the Cartesians with respect to the internal coordinates, all these taken at the minimum of the total potential V. The Cartesian gradient of V_q is readily obtained from (3) since, at the minimum, the total gradient is zero. Hence,

$$\left(\frac{\partial V_q}{\partial x_{k\alpha}} \right)_{\bar{x}_{min}} = -\left(\frac{\partial V_{nq}}{\partial x_{k\alpha}} \right)_{\bar{x}_{min}} \tag{8}$$

To compute the first and second derivatives of the Cartesians with respect to the (nonredundant) internal coordinates we make use of Taylor expansions of both types of coordinates, in terms of one another, around the minimum of V. Thus, if ΔR_n and $\Delta x_{i\alpha}$ denote displacements, from the minimum, of the internal coordinate R_n and the Cartesian coordinate $x_{i\alpha}$, respectively, we can write

$$\Delta R_n = \sum_{i\alpha} \left(\frac{\partial R_n}{\partial x_{i\alpha}}\right)_{x_{\min}} \Delta x_{i\alpha}$$
$$+ \frac{1}{2} \sum_{i\alpha} \sum_{j\beta} \left(\frac{\partial^2 R_n}{\partial x_{i\alpha}\partial x_{j\beta}}\right)_{x_{\min}} \Delta x_{i\alpha}\Delta x_{j\beta} + \dots \quad (9)$$

and

$$\Delta x_{i\alpha} = \sum_{k} \left(\frac{\partial x_{i\alpha}}{\partial R_k}\right)_{R_{\min}} \Delta R_k$$
$$+ \frac{1}{2} \sum_{k} \sum_{m} \left(\frac{\partial^2 x_{i\alpha}}{\partial R_k\partial R_m}\right)_{R_{\min}} \Delta R_k\Delta R_m + \dots \quad (10)$$

The derivatives that occur in (9) can be evaluated analytically so we denote

$$B^n_{i\alpha} = \left(\frac{\partial R_n}{\partial x_{i\alpha}}\right)_{x_{\min}} \quad \text{and} \quad b^n_{i\alpha,j\beta} = \left(\frac{\partial^2 R_n}{\partial x_{i\alpha}\partial x_{j\beta}}\right)_{x_{\min}}$$

Substitution of (10) into (9) then yields (to the second order)

$$\Delta R_n = \sum_{i\alpha} B^n_{i\alpha}\left[\sum_{k}\left(\frac{\partial x_{i\alpha}}{\partial R_k}\right)_{R_{\min}}\Delta R_k\right.$$
$$+ \frac{1}{2}\sum_{k}\sum_{m}\left(\frac{\partial^2 x_{i\alpha}}{\partial R_k\partial R_m}\right)_{R_{\min}}\Delta R_k\Delta R_m\bigg]$$
$$+ \frac{1}{2}\sum_{i\alpha}\sum_{j\beta}b^n_{i\alpha,j\beta}\left[\sum_{k}\left(\frac{\partial x_{i\alpha}}{\partial R_k}\right)_{R_{\min}}\Delta R_k\right.$$
$$+ \frac{1}{2}\sum_{k}\sum_{m}\left(\frac{\partial^2 x_{i\alpha}}{\partial R_k\partial R_m}\right)_{R_{\min}}\Delta R_k\Delta R_m\bigg]$$
$$\times\left[\sum_{k}\left(\frac{\partial x_{j\beta}}{\partial R_k}\right)_{R_{\min}}\Delta R_k\right.$$
$$+ \frac{1}{2}\sum_{k}\sum_{m}\left(\frac{\partial^2 x_{j\beta}}{\partial R_k\partial R_m}\right)_{R_{\min}}\Delta R_k\Delta R_m\bigg] \quad (11)$$

and equating left-hand side and right-hand side linear and quadratic terms we have

$$\sum_{i\alpha} B^n_{i\alpha}\left(\frac{\partial x_{i\alpha}}{\partial R_k}\right)_{R_{\min}} = \delta_{kn} \quad (12)$$

and

$$\sum_{i\alpha} B^n_{i\alpha}\left(\frac{\partial^2 x_{i\alpha}}{\partial R_k\partial R_m}\right)_{R_{\min}}$$
$$= -\sum_{i\alpha}\sum_{j\beta}b^n_{i\alpha,j\beta}\left(\frac{\partial x_{i\alpha}}{\partial R_k}\right)_{R_{\min}}\left(\frac{\partial x_{j\beta}}{\partial R_m}\right)_{R_{\min}} \quad (13)$$

For a nonlinear molecule composed of N atoms eq. (12) gives a set of $3N - 6$ linear equations for the $3N$ unknown derivatives of the Cartesians with re-

spect to an internal coordinate R_k. The unknowns can be solved for if we require that the solution does not represent any translation or rotation of the molecule as a whole.[17] This criterion gives the six additional equations needed to make the set complete. Similarly, eq. (13) forms a set of $3N - 6$ equations for the $3N$ second-order derivatives of the Cartesians with respect to a pair of internal coordinates, R_k and R_m. These second-order derivatives can be solved for if we first compute the first order derivatives that occur on the right-hand side, and then again add the six equations for elimination of translation and rotation of the whole molecule.

Thus, all the unknowns of the right-hand side of eq. (7) can be determined, and we are able to calculate the MM force constants. In fact, what we obtain are the second order derivatives of V_q, with respect to the internal coordinates, at the minimum of the total potential V. But if V_q is quadratic (as we assume here) the second derivatives are independent of the actual values of the internal coordinates and therefore directly identical to the MM force constants. If V_q is not quadratic, but contains e.g., Morse potentials, an additional transformation must be performed to produce the MM parameters.

It is interesting to note that the problem of finding the MM force constants, as described here, is similar to the problem of finding the spectroscopic force constants for a nonequilibrium ab $initio$ geometry, as described by Pulay.[18]

In addition to the MM force constants, we also want to compute the reference geometry, i.e., the values that the internal coordinates would have without V_{nq}. This can be done as follows. The derivative of V_q with respect to an internal coordinate R_n is

$$\frac{\partial V_q}{\partial R_n} = \sum_{j} F_{nj}(R_j - R_{j0}) \quad (14)$$

which, when equated to what is obtained using the chain rule (6), gives

$$\sum_{j} F_{nj}(R_j - R_{j0}) = \sum_{k\alpha}\left(\frac{\partial V_q}{\partial x_{k\alpha}}\right)_{x_{\min}}\left(\frac{\partial x_{k\alpha}}{\partial R_n}\right)_{R_{\min}} \quad (15)$$

where, for a nonlinear molecule composed of N atoms, the only unknowns are the $3N - 6$ R_{j0}'s. For $n = 1, \dots, 3N - 6$, eq. (15) forms a set of $3N - 6$ linear equations which can be solved to yield the reference geometry $R_{j0}, j = 1, \dots, 3N - 6$. If V_q contains nonquadratic terms, the set of equations becomes nonlinear.

The force constants and the reference geometry obtained in the transformation refer to a set of nonredundant internal coordinates, whereas a MM energy function is usually defined in terms of redundant coordinates. However, this is not a problem since it is easy to transform the force constants into any redundant set of coordinates.[16b] The refer-

ence geometry pertaining to a redundant coordinate basis can also be derived, simply by solving the linear system of equations that is formed by the redundancy relations, the definitions, and the calculated reference values of the nonredundant coordinates.

REDUCTION OF THE FORCE FIELD

The transformation described in the previous section is mathematically exact, and comprises the complete general valence force field. For example, for a molecule containing 20 atoms this means altogether 1485 force constants, which clearly is an impractical number in a MM force field. The number is, however, greatly reduced if the interaction force constants that do not significantly affect the vibrational frequencies are omitted.

In order to extract the important force constants to be included in the final MM energy function, we need to compute the derivatives of the frequencies with respect to the force constants. In Cartesian coordinates, the frequencies are obtained from the eigenvalues of the mass-weighted Hessian. The elements of the Hessian are the second derivatives of the total potential V, as given by eq. (4). If Λ is a diagonal matrix containing the eigenvalues, U is a matrix whose columns are the eigenvectors, $M^{-1/2}$ is a diagonal matrix containing the square-roots of the reciprocal atomic masses, and H is the Hessian, the following relation holds

$$\Lambda = U^t M^{-1/2} H M^{-1/2} U \qquad (16)$$

and the frequencies are

$$\nu_k = s\sqrt{\lambda_k} \qquad (17)$$

where s is a constant and $\lambda_k, k = 1, \ldots, 3N$, are the eigenvalues. The derivative of a frequency ν_k with respect to a force constant F_{ij} is then

$$\frac{\partial \nu_k}{\partial F_{ij}} = \frac{1}{2} \frac{s^2}{\nu_k} J_{k,ij} \qquad (18)$$

where

$$J_{k,ij} = \frac{\partial \lambda_k}{\partial F_{ij}} \qquad (19)$$

defines the Jacobian. Using eq. (16), an analytical approximation for the Jacobian may be derived if the eigenvectors are assumed to remain unchanged for small changes of the force constants, i.e.,

$$\left(\frac{\partial}{\partial F_{ij}} \Lambda\right) = U^t M^{-1/2} \left(\frac{\partial}{\partial F_{ij}} H\right) M^{-1/2} U \qquad (20)$$

Obviously, the part of the Hessian that depends on the MM force constants is obtained by taking the

second derivatives of eq. (2), which gives

$$\frac{\partial^2 V_q}{\partial x_{k\alpha} \partial x_{l\beta}} = \frac{\partial}{\partial x_{l\beta}} \left[\sum_{ij} F_{ij} \frac{\partial R_i}{\partial x_{k\alpha}} (R_j - R_{j0}) \right]$$

$$= \sum_{ij} F_{ij} \left[\frac{\partial R_i}{\partial x_{k\alpha}} \cdot \frac{\partial R_j}{\partial x_{l\beta}} \right.$$

$$\left. + \frac{\partial^2 R_i}{\partial x_{k\alpha} \partial x_{l\beta}} (R_j - R_{j0}) \right]$$

$$= \sum_{ij} F_{ij} C^{ij}_{k\alpha,l\beta} \qquad (21)$$

where, in the last row, we have defined a set of matrices, C^{ij}, with the elements

$$C^{ij}_{k\alpha,l\beta} = \frac{\partial R_i}{\partial x_{k\alpha}} \cdot \frac{\partial R_j}{\partial x_{l\beta}} + \frac{\partial^2 R_i}{\partial x_{k\alpha} \partial x_{l\beta}} (R_j - R_{j0}) \qquad (22)$$

Taking into account that $F_{ji} = F_{ij}$, eq. (20) may then be written in the following form

$$\left(\frac{\partial}{\partial F_{ij}} \Lambda\right) = U^t M^{-1/2} [C^{ij} + (1 - \delta_{ij}) C^{ji}] M^{-1/2} U \qquad (23)$$

from which the Jacobian can be calculated. Note that in eq. (23) it is not assumed that the whole energy function is quadratic, but the effect of the nonquadratic interactions is taken fully into account by using the eigenvectors obtained in the diagonalization of the complete (mass-weighted) Hessian. Thus, the quantity

$$\Delta \nu_k = \frac{1}{2} \frac{s^2}{\nu_k} F_{ij} J_{k,ij} \qquad (24)$$

which is obtained by multiplying eq. (18) by F_{ij}, is an easily computable measure of the effect that omission of the force constant F_{ij} has on the frequency ν_k. The measure is not exact, of course, since the frequencies are not linear functions of the force constants. However, for small interaction force constants it provides a good estimate. The force field may now be reduced e.g., by leaving out such interaction force constants for which all (absolute) values of $\Delta \nu_k$ are smaller than a certain limit. As an example the conversion and reduction scheme has been applied to an *ab initio* force field for trans-N-methylacetamide,[19] using different significance limits $\Delta \nu$. The number of remaining force constants in each case, along with the maximum and root-mean-square frequency deviations, as compared to the original *ab initio* results, are given in Table I. As is seen from the table, reasonable agreement with the *ab initio* frequencies is still retained even with substantial reduction in the original number of force constants. This is understandable, since it merely reflects the fact that few interaction force constants, other than the nearest neighbor ones, significantly affect the

Table I. Remaining force constants (N) and frequency deviations (in cm^{-1}) for different significance limits (in cm^{-1}) in the reduction of the MM force field for N-methylacetamide.

Limit (Δv)	N	Max. dev.[a]	R.M.S. dev.[a]
0.0	465		
1.0	175	2.9 (2.9)	1.1 (1.0)
2.0	142	7.8 (7.6)	3.4 (3.1)
3.0	115	14.8 (14.8)	5.2 (4.4)
4.0	103	17.7 (17.7)	6.3 (4.7)
5.0	92	20.2 (20.2)	8.1 (5.6)
6.0	87	21.1 (19.6)	9.0 (5.8)
7.0	80	24.7 (24.7)	10.1 (7.7)
8.0	76	25.7 (22.7)	10.8 (8.5)
9.0	73	31.4 (22.9)	11.9 (9.2)
10.0	69	39.2 (23.5)	12.9 (8.5)
11.0	67	39.2 (21.8)	12.9 (8.5)
12.0	63	39.2 (23.9)	14.2 (10.9)

[a]Values in parentheses refer to the exclusion of C-H stretching frequencies.

frequencies. Further, the results listed in Table I were obtained simply by dropping the force constants not yielding a value of Δv greater than the specified limit. By reoptimizing part of the remaining force constants, much better frequency agreement would be achieved. The effect on the geometry of the neglected small interaction force constants is altogether negligible.

As a second means of reduction and simplification of the force field, force constants of the same type can, in a reoptimization, be given the same value in similar groups. This has been utilized extensively in spectroscopic force field calculations, and in MM calculations it ought to work even better because the differences in the nonbonded interactions in different parts of the molecule, or in different molecules, are no longer represented in the force constant values. To be successful, such combining and reoptimization of force constants and other parameters should preferably be done using frequency and geometrical data from several different conformations and isotopomers of a set of molecules.

DISCUSSION

The conversion procedure from *ab initio* to molecular mechanics is easy to apply and nicely yields MM force field and reference geometry parameters which, depending on the degree of reduction, produce more or less perfect agreement with the original *ab initio* results. However, the converted parameters need not always have physically reasonable values. If it is evident that something is wrong with the parameters, this indicates that either the *ab initio* results or the nonquadratic interactions (or both) are too crude. The calculated reference geometry, for instance, should not deviate very much

from a corresponding empirically obtained one. Periodic torsions may be used as a check when the intrinsic equilibrium angles are known. If a torsion coordinate is only moderately deformed, say less than 20 degrees for a three-fold torsion, the potential is, in first approximation, quadratic and a force constant and reference angle may be computed in the conversion. This reference angle should then, of course, be close to a real one. For a torsion angle which is so much deformed that the potential cannot be considered quadratic, such a check can still be made, but in this case the set of equations that gives the reference geometry is nonlinear.

A situation may also arise, where the *ab initio* force field and geometry are considered very reliable, but the conversion still yields MM force constants and reference geometry parameters that in some respects are unsatisfactory. If this happens, one may consider adjusting some part of the nonquadratic interactions. Using the conversion, such adjustment can, in fact, be done e.g., if *ab initio* results exist for several conformations of the same molecule(s), so that consistency may be required. This means that corresponding MM force constants and reference bonds and angles, respectively, should have values very close to one another. The refinement can then be carried out in the following way

Step 1. Adjust the computed force constants and the reference geometry parameters in the direction of consistency.

Step 2. For each molecule, use eq. (21) to compute the second derivatives of V_q, and solve the second derivatives of V_{nq} from eq. (5).

Step 3. Refine the selected parameters of V_{nq} in a least squares fit to the second derivatives obtained in Step 2. (If the parameters do not change, the process has converged.)

Step 4. Compute new MM force constants and reference geometry parameters, and go back to Step 1.

Note that care should be taken when applying this kind of refinement, since the adjusted parameters of the nonquadratic interactions must not become incompatible with the independent crystal or other data from which they originate.

Although the conversion is primarily designed for the utilization of *ab initio* (or empirical) spectroscopic force fields in the construction of potential energy functions, it may also be used to facilitate the implementation of new nonquadratic potentials in an existing energy function. One may want to do the latter for example in order to utilize new improved van der Waals or charge parameters, or to explicitly include totally new energy terms for some type of interaction (e.g., hydrogen bonding). If the old energy function works well for a certain group of molecules, these molecules may be used, one at

a time, to derive a set of Hessians, corresponding to chosen minima. If the conversion is then applied to these Hessians, using the new nonquadratic interactions, new force constants and reference geometry parameters are obtained, which should provide good initial values for a reoptimization to the original molecular data. The aim of an operation like this would of course be to achieve better transferability of the whole set of parameters.

Thus, the conversion offers great flexibility with regard to the choice of the most trusted data on which to base the construction or improvement of MM potential energy functions. Detailed applications to N-methylacetamides[19] and alanine dipeptides[20,21] will be the subject of subsequent papers.

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