A comparative study of the force constants from different force fields

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Abstract: The force constants in internal coordinates can be derived from the hessian matrix in Cartesian coordinates. Selecting the bond coordinates from the hessian matrix allows the construction of the force constants of all types of internal coordinates upon eigen-decomposition of each interaction matrix. Force constants for bonds or for any pair of atoms ingeneral are defined by means of the eigenanalysis of their pair interaction matrix. Force constants for the angles are derived from their corresponding submatrices of the two bonds or distances forming the angle, the Urey-Bradley interaction can be treated the same way as bonds, and the improper force constants are similarly obtained using their corresponding three-pair interaction matrices. This method helps to find the force constants for all force fields, especially CHARMM, AMBER and MMFF. The resulting force constants were validated against other force fields.

1. Introduction

Classical molecular dynamics methods that analyze the time evolution of macroscopic systems for several thousands of time steps or conformations have become very effective tools for gaining insight into a variety of macroscopic systems and processes. Most of this work has involved the use of empirical force fields obtained from experimental measurements of geometries, heats of formation, vibrational frequencies, and barrier heights. However, with the increasing accuracy and availability of first-principles methods (standard ab initio and density functional theory), there is a growing tendency to obtain the force field data from high-level computations on the basic molecular units. This makes it possible to treat macroscopic systems that have not yet been investigated experimentally or that may not even exist at present.

Molecular mechanics (MM) and molecular dynamics (MD) simulations are very effective tools for the quantitave investigation of macroscopic systems and mechanisms. Therefore, attempts were carried out to provide the required parameters to obtain the desired information from these calculations. One of these attempts is to develop the generalized force fields such as CHARMM[1], AMBER[2], OPLS[3], and GROMOS[4]. These force fields were optimized to model the chemistry of condensed phases, with particular emphasis on the study of biological constituents and those of biological interest. Emphasis in the development of these force fields was placed on supplying highly optimized molecular fragments. Atom types and the corresponding parameters of these optimized fragments are then stored in large tables. From these tables, and by means of atom type matching, parameters of a broad spectrum of organic molecules can be determined.

Optimized force constants of harmonic internal coordinates can be obtained by fitting the MM PES to the QM PES. But, this procedure is computationally expensive and requires a set of carefully chosen constraints to keep the parameters within the physical values. An alternative strategy is to calculate the vibrational frequencies at the optimized structure and use the hessian to determine the force constants. This strategy works well to determine the harmonic internal coordinates[5].

2. Methodology

The parameterization of the harmonic internal coordinates was based on the calculation of the hessian matrix (i.e. the second derivative of the energy with respect to the coordinates), obtained as a byproduct after frequency calculations. From this matrix, force constants can be calculated using the method suggested by Jorge Seminario[6]This method was shown to improve the results of the vibrational frequencies, and consequently, the structure prediction and molecular dynamics.[7]

Hessian is an 3N*3N matrix where N is the number of atoms in the investigated molecule. In a digitized form, hessian matrix is an N*N submatrices, each submatrix $[H^{ij}]$ is a mathematical description of the interaction between atoms i and j. Then, by some mathematical methods, the submatrix $[H^{ij}]$ is analyzed to determine the eigenvalues and eigenvectors associated with the interaction between the atoms i and j. Finally, by means of projections, the force constants are calculated. Here we briefly discuss the

basic concept on which the projection method depends to calculate force constants from hessian matrix.

In terms of Cartesian coordinates, an interaction between two atoms, A and B, can be described as the reaction force on atom A, $\partial \hat{F}^A$, due to the displacement of atom B, $\partial \hat{r}^B$, in the effective direction. By the effective direction we mean the direction in which the displacement effectively increases the value of an individual internal coordinate. Determining the effective direction of each type of internal coordinates will be briefly discussed later, for more details see Bright Wilson[8] and Vebjørn and Trygve[9]. Equations and show this form of description as an 3*3 submatrix, $[H^{AB}]$, of the hessian matrix.

$$\begin{bmatrix} \partial F_{Ax} \\ \partial F_{Ay} \\ \partial F_{Az} \end{bmatrix} = \begin{bmatrix} \dfrac{\partial^2 E}{\partial B_x \partial A_x} & \dfrac{\partial^2 E}{\partial B_y \partial A_x} & \dfrac{\partial^2 E}{\partial B_z \partial A_x} \\ \dfrac{\partial^2 E}{\partial B_x \partial A_y} & \dfrac{\partial^2 E}{\partial B_y \partial A_y} & \dfrac{\partial^2 E}{\partial B_z \partial A_y} \\ \dfrac{\partial^2 E}{\partial B_x \partial A_z} & \dfrac{\partial^2 E}{\partial B_y \partial A_z} & \dfrac{\partial^2 E}{\partial B_z \partial A_z} \end{bmatrix} \cdot \begin{bmatrix} \partial B_x \\ \partial B_y \\ \partial B_z \end{bmatrix}$$

(1)

In compact notation,

$$\partial \hat{F}^A = -\left[H^{AB} \right] \partial \hat{r}^B$$

(2)

where the subscripts x, y and z are the Cartesian coordinates, E is the total energy of the molecule and the minus sign means restoring force.

It is clear that the projection method operates on the Cartesian coordinates, therefore, this procedure has the advantage of being automatic and fully invariant with respect to the choice of internal coordinates. This invariance is a fundamental requirement for any physical quantity.

Briefly, after sufficient iterations of Eigen decomposition of a submatrix matrix $[H^{AB}]$, an 3*3 upper triangular matrix $[T]$ results such that $T_{1,1}$, $T_{2,2}$, $T_{3,3}$ are the eigen values of $[H^{AB}]$.

Let
$$\lambda = \left[T_{1,1}, T_{2,2}, T_{3,3} \right]$$

(3)

As a physical problem of displacement, these eigenvalues are the magnitudes of the atomic displacements. If atoms A and B are in a stable interaction, a bond at the equilibrium length for example, the three eigenvalues will be all real and positive. For each eigenvalue, there is the unit eigenvector which defines the direction associated with the displacement. Finally, using standard methods of linear algebra and geometry, the projection

method derives force constants from the eigenvalues depending on the projection of the eigenvectors onto the effective direction of the displaced atom (declared below).

Basically, the interaction $[H^{AB}]$ contributes to all internal coordinates which include A-B as one of the constituting bonds. In other words, an internal coordinate can be described utilizing all the submatrices of its constituting bonds.

Here we will explain briefly how to determine force constants of the harmonic internal coordinates by projection method. Without loss of the generality, we will assume the displacements which increase the values of the individual internal coordinates. See figure (1) to realize the general notation of the effective directions.

For projection method, we will introduce a general notation. Atoms will be labeled with capital letters from A to D. Cartesian coordinates for each atom well be denoted by the subscripts x, y and z for its atom label.

The bond

$$k_b = \sum_{i=1}^{3} \lambda^i \left| U \cdot P^i \right|$$

(4)

Where λ^i is the ith element of the eigen values determined for the submatrix $[H^{AB}]$ and P^i is the corresponding eigenvector.

The Angle

$$\frac{1}{k_\theta} = \frac{1}{r_{AC}^2 \sum_{i=1}^{3} \lambda_{AC}^i \left| U_A \cdot P_{AC}^i \right|} + \frac{1}{r_{BC}^2 \sum_{i=1}^{3} \lambda_{BC}^i \left| U_B \cdot P_{BC}^i \right|}$$

(5)

Where r_{AC} and r_{BC} are lengths of the bonds A-C and B-C, respectively, λ_{AC}^i and λ_{BC}^i are the ith eigen values of the submatrices $[H^{AC}]$ and $[H^{BC}]$, respectively, and P_{AC}^i and P_{BC}^i are the corresponding eigenvectors.

The improper angle

$$k_\omega = s^2 \sum_{j} \sum_{i=1}^{3} \lambda_j^i \left| U \cdot P_j^i \right|$$

(6)

where j denotes one of the bonds B-A, C-A and D-A, one after another, λ_j^i is the ith eigen value of the corresponding submatrix, and P_j^i is the corresponding eigenvector.

3. Results and Discussion
Water Molecule

Water molecule was used to test how the parameters of different force fields are consistent.

The force constants of water from three force fields are shown in table 1. Good consistency was observed between different force fields.

Table 1: The stretching (kcal mol-1 Å-2) and bending (kcal mol-1 rad-2) force constants of water in comparison between CGenFF, AMBER and MMFF.

The internal coordinate	CGenFF	AMBER	MMFF
Bond	450	553	567.1
Angle	55	100	47.4

Glycine amino acid

Force constants of glycine amino acid from different force fields are shown in table 2. Good consistency was observed between different force fields.

Table 2: The force constants of glycine in comparison between AMBER and CGenFF.

				CGenFF	AMBER
Bond type					
CG2O2	CG321			200	317
CG2O2	OG2D1			750	570
CG2O2	OG311			230	450
CG321	NG321			263	367
CG321	HGA2			309	340
NG321	HGPAM2			453.1	434
OG311	HGP1			545	553
Angle type					
CG321	CG2O2	OG2D1		70	80
CG321	CG2O2	OG311		55	70
OG2D1	CG2O2	OG311		50	80
CG2O2	CG321	NG321		43.7	80
CG2O2	CG321	HGA2		33	50
NG321	CG321	HGA2		32.4	35
HGA2	CG321	HGA2		35.5	35
CG321	NG321	HGPAM2		41	50
HGPAM2	NG321	HGPAM2		42	35
CG2O2	OG311	HGP1		55	35
Urey-Bradley distance					
CG321	CG2O2	OG2D1		20	
OG2D1	CG2O2	OG311		210	
CG2O2	CG321	HGA2		30	
NG321	CG321	HGA2		2.14	
HGA2	CG321	HGA2		1.802	
Improper angle					
CG2O2	CG321	OG2D1	OG311	65	

N-methyl acetamide (NMA)

Force constants of NMA from different force fields are shown in table 3. Good consistency was observed between different force fields.

We have presented a simple method to parameterize the different force fields that is largely independent of the choice of coordinates. The hessian matrix is the only requirement for this method. From this method bond, angle and improper force constants can be determined. Each internal coordinate in was treated as a group of bonds. Small molecules were used to compare different force fields.

Table 3: The force constants of NMA in comparison between AMBER, MMFF and CGenFF.

				CGenFF	AMBER	MMFF
Bond						
CG2O1	CG331			250	317	301.54
CG2O1	NG2S1			370	490	419.5
CG2O1	OG2D1			620	570	931.96
CG331	NG2S1			320	337	335.65
CG331	HGA3			322	340	342.99
NG2S1	HGP1			440	434	479.51
Angle						
CG331	CG2O1	NG2S1		80	70	70.814
CG331	CG2O1	OG2D1		80	80	67.50
NG2S1	CG2O1	OG2D1		80	80	65.27
CG2O1	CG331	HGA3		33	50	46.78
NG2S1	CG331	HGA3		51.5	50	53.26
HGA3	CG331	HGA3		35.5	35	37.13
CG2O1	NG2S1	CG331		50	50	59.08
CG2O1	NG2S1	HGP1		34	30	41.38
CG331	NG2S1	HGP1		35	30	39.72
Urey-Bradley distance						
CG2O1	CG331	HGA3		30		
HGA3	CG331	HGA3		5.4		
Improper angle						
CG2O1	CG331	NG2S1	OG2D1	120		

Pyrrolidine

Force constants of pyrrolidine from different force fields are shown in table 4. Good consistency was observed between different force fields.

Table 4: the force constants of pyrrolidine in comparison between AMBER, and CGenFF.

			CGenFF	AMBER
Bond Type				
CG3C52	CG3C52		195	310
CG3C52	NG3C51		400	367
CG3C52	HGA2		307	340
NG3C51	HGP1		450	434
Angle Type				
CG3C52	CG3C52	CG3C52	58	40
CG3C52	CG3C52	NG3C51	84	80
CG3C52	CG3C52	HGA2	35	50
NG3C51	CG3C52	HGA2	54	35
HGA2	CG3C52	HGA2	38.5	35
CG3C52	NG3C51	CG3C52	140	50
CG3C52	NG3C51	HGP1	43	50
Urey-Bradley distances				
CG3C52	CG3C52	CG3C52	11.16	
CG3C52	CG3C52	HGA2	22.53	
HGA2	CG3C52	HGA2	5.4	

General consistency was observed between the different force fields despite of the different potential energy functions. All values were seen to be within the physical values. In addition, all force constants are internally consistent that is their values relative to each other are conserved among different chemical environments. As examples for this finding, the C-N force constants and the associated bending force constants. Seminario and Bautista reported that C-N bonds had showed the most variability with respect to their environment. In addition, electron delocalization and the presence of exchangeable protons are often associated with these findings. An important conclusion of this article is that the force constants have a strong influence on the final geometry and for the mechanistic implications of the structure. Large changes in the force field change a dynamics of the molecule.

Conclusion

In this paper we showed a comparative study of the force constants from different force fields. This study can help in selecting and developing a new force field. Different empirical force fields with supply consistent force constants in spite of the different potential energy functions. Differences may be larger for large molecules. However, qualitatively acceptable results still achieved. All values were seen to be within the physical values. The used force fields were designed to yield condensed phase properties. These force fields can be used for docking studies, free energy determinations and detailed structure function studies. Different types of macromolecules like proteins, nucleic acids, lipids and carbohydrates can be studied using theses force fields. When selecting a force field for calculations care must be taken that the different portions of the force field (e.g., lipid and protein) have been adequately tested.

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