Mathematical relationships between bond-bending force fields

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Molecular mechanics softwares adopt various set of force field functions. In some cases, reliable data from one set of force field parameters cannot be used in a software that adopts another set of force field. Using mathematical approach, exact relationships between parameters from three bond-bending force fields, namely the (i) harmonic cosine angle, (ii) polynomial series, and (iii) Fourier series, are herein developed. Parameters from these three potential functions are further related to the approximate form, the harmonic angle function, which is valid for small change in chemical bond angle.

KEY WORDS: bond-bending, force field, Fourier series, harmonic potential, polynomial form

AMS subject classification: 70C20, 74B15, 74E40

1. Introduction

Molecular mechanics can be broadly categorized into two groups: (a) bonded interactions, and (b) non-bonded interactions. The former includes 2-body interaction (stretching between two atoms), 3-body interaction (bending amongst three atoms) and 4-body interaction (torsion of dihedral angle). In the molecular mechanics approach, the potential energy of bending in chemical bonds has been quantified by the harmonic angle form

$$U_\theta = \frac{1}{2}k_\theta(\theta - \theta_0)^2 = \frac{1}{2}k_\theta(\delta\theta)^2 \tag{1}$$

where k_θ is the stiffness constant of the harmonic angle form, while θ and θ_0 are the bond angle and equilibrium bond angle respectively, in radians. The harmonic angle potential has been applied in the following molecular mechanics softwares: MM2 [1], CVFF [2–4], CHARMM [5], TRIPOS [6], COSMIC [7], AMBER [8], MOMEC [9] and OPLS [10] and GROMOS [11]. The harmonic angle form is a special case of polynomial form of order 2. Better fit can be attained from potential function with polynomial series

of higher orders

$$U_{\mathrm{S}} = \frac{1}{2} \sum_{n=2}^{m} k_{\theta n} (\delta\theta)^n,$$ (2)

where m refers to the polynomial order. Third-order polynomial series ($m = 3$) has been employed in the EAS [12], EFF [13,14] and MMFF [15] softwares. Fourth-order polynomial series ($m = 4$) has been incorporated in the CFF91/93/95 [16] software. Sixth-order polynomial series ($m = 6$) has been used in the MM3 [17] and MM4 [18–21] softwares. As an alternative to the polynomial forms, potential functions have been introduced in the form of Fourier series

$$U_{\mathrm{F}} = k_{\mathrm{F}} \sum_{n=0}^{m} C_n \cos(n\theta)$$ (3)

in the SHAPES [22] and UFF [23] softwares, and the harmonic cosine angle function

$$U_{\mathrm{C}} = \frac{1}{2} k_{\mathrm{C}} (\cos\theta - \cos\theta_0)^2$$ (4)

in the DREIDING [24] and ESFF [25] softwares.

Recently a set of conversion matrices have been formulated to relate parameters of three commonly adopted bond-twisting force fields [26]. In this paper a set of equations is developed to connect the parameters k_θ, $k_{\theta n}$, k_{F}, C_n and θ_0 so that the bond-bending potential functions can be mathematically related, as schematically depicted in figure 1.
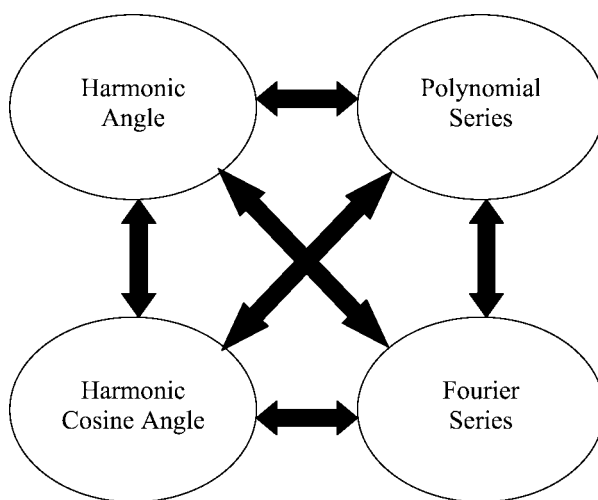

Figure 1. Schematic for relationships developed herein between bond-bending force fields.

2. Analysis

Writing equation (2) as

$$U_S = \frac{1}{2}k_{\theta 2}\left[\sum_{n=2}^{m}\frac{k_{\theta n}}{k_{\theta 2}}(\delta\theta)^{n-2}\right](\delta\theta)^2 \tag{5}$$

and upon comparison with equation (1), we see that

$$k_\theta = k_{\theta 2}\left[\sum_{n=2}^{m}\frac{k_{\theta n}}{k_{\theta 2}}(\delta\theta)^{n-2}\right]. \tag{6}$$

Hence the bending stiffness parameter from the harmonic angle form is related to those of the polynomial series in terms of the change in bond angle, $\delta\theta$. To relate the polynomial series form with the harmonic cosine angle function, we expand the following term from equation (4):

$$(\cos\theta - \cos\theta_0)^2 = \cos^2\theta_0\left[\cos^2(\delta\theta) - 2\cos(\delta\theta) + 1\right]$$
$$+ 2\sin\theta_0\cos\theta_0\sin(\delta\theta)\left[1 - \cos(\delta\theta)\right] + \sin^2\theta_0\sin^2(\delta\theta), \tag{7}$$

whereby $\delta\theta = \theta - \theta_0$. Substituting the Maclaurin's series

$$\sin x = \sum_{n=0}^{+\infty}\frac{(-1)^n x^{2n+1}}{(2n+1)!} \tag{8}$$

and

$$\cos x = \sum_{n=0}^{+\infty}\frac{(-1)^n x^{2n}}{(2n)!} \tag{9}$$

into equation (7) and neglecting orders of seven and above, then equation (4) can be written as

$$U_C = \frac{1}{2}k_C\sin^2\theta_0(\delta\theta)^2 + \frac{1}{2}k_C\sin\theta_0\cos_0(\delta\theta)^3$$
$$- \frac{1}{2}k_C\left(\frac{1}{3}\sin^2\theta_0 - \frac{1}{4}\cos^2\theta_0\right)(\delta\theta)^4 - \frac{1}{2}k_C\left(\frac{1}{4}\sin\theta_0\cos\theta_0\right)(\delta\theta)^5$$
$$+ \frac{1}{2}k_C\left(\frac{2}{45}\sin^2\theta_0 - \frac{1}{24}\cos^2\theta_0\right)(\delta\theta)^6. \tag{10}$$

Neglect of higher order terms is valid when the trigonometric series expansion is convergent, i.e. $|\delta\theta| < 1$. To relate the polynomial series potential with the Fourier series form, we expand equation (3) up to $m = 2$ as considered by Rappe et al. [23]

$$U_F = k_F(C_0 + C_1\cos\theta + C_2\cos 2\theta). \tag{11}$$

Substituting $\theta = \theta_0 + \delta\theta$ as before, we have

$$
\begin{aligned}
C_0 + C_1 \cos\theta + C_2 \cos 2\theta = C_0 &+ C_1 \big[\cos\theta_0 \cos(\delta\theta) - \sin\theta_0 \sin(\delta\theta) \big] \\
&+ C_2 \big[\cos 2\theta_0 \cos(2\delta\theta) - \sin 2\theta_0 \sin(2\delta\theta) \big].
\end{aligned}
\tag{12}
$$

Applying equations (8) and (9) for equation (12) leads to

$$
\begin{aligned}
C_0 + C_1 \cos\theta + C_2 \cos 2\theta = C_0 &+ C_1 \cos\theta_0 \left[1 - \frac{1}{2}(\delta\theta)^2 + \frac{1}{24}(\delta\theta)^4 - \frac{1}{720}(\delta\theta)^6 \right] \\
&- C_1 \sin\theta_0 \left[(\delta\theta) - \frac{1}{6}(\delta\theta)^3 + \frac{1}{120}(\delta\theta)^5 \right] \\
&+ C_2 \cos 2\theta_0 \left[1 - 2(\delta\theta)^2 + \frac{2}{3}(\delta\theta)^4 - \frac{4}{45}(\delta\theta)^6 \right] \\
&- C_2 \sin 2\theta_0 \left[2(\delta\theta) - \frac{4}{3}(\delta\theta)^3 + \frac{4}{15}(\delta\theta)^5 \right].
\end{aligned}
\tag{13}
$$

Therefore, upon rearranging equation (13) in increasing indices of $\delta\theta$, equation (11) becomes

$$
\begin{aligned}
U_F = k_F (C_0 &+ C_1 \cos\theta_0 + C_2 \cos 2\theta_0) - k_F (C_1 \sin\theta_0 + 2C_2 \sin 2\theta_0)(\delta\theta) \\
&- \frac{1}{2} k_F (C_1 \cos\theta_0 + 4C_2 \cos 2\theta_0)(\delta\theta)^2 + \frac{1}{6} k_F (C_1 \sin\theta_0 + 8C_2 \sin 2\theta_0)(\delta\theta)^3 \\
&+ \frac{1}{24} k_F (C_1 \cos\theta_0 + 16C_2 \cos 2\theta_0)(\delta\theta)^4 - \frac{1}{120} k_F (C_1 \sin\theta_0 + 32C_2 \sin 2\theta_0 (\delta\theta)^5 \\
&- \frac{1}{720} k_F (C_1 \cos\theta_0 + 64C_2 \cos 2\theta_0)(\delta\theta)^6.
\end{aligned}
\tag{14}
$$

One may observe that if U_C is zero as well as a minimum then both the zeroth and first orders, i.e. coefficients of $(\delta\theta)^0$ and $(\delta\theta)^1$, should be set as zero. Therefore

$$
C_0 + C_1 \cos\theta_0 + C_2 \cos 2\theta_0 = 0,
\tag{15}
$$

$$
C_1 \sin\theta_0 + 2C_2 \sin 2\theta_0 = 0
\tag{16}
$$

and

$$
\begin{aligned}
U_F = &-\frac{1}{2} k_F (C_1 \cos\theta_0 + 4C_2 \cos 2\theta_0)(\delta\theta)^2 + \frac{1}{6} k_F (C_1 \sin\theta_0 + 8C_2 \sin 2\theta_0)(\delta\theta)^3 \\
&+ \frac{1}{24} k_F (C_1 \cos\theta_0 + 16C_2 \cos 2\theta_0)(\delta\theta)^4 - \frac{1}{120} k_F (C_1 \sin\theta_0 + 32C_2 \sin 2\theta_0)(\delta\theta)^5 \\
&- \frac{1}{720} k_F (C_1 \cos\theta_0 + 64C_2 \cos 2\theta_0)(\delta\theta)^6.
\end{aligned}
\tag{17}
$$

Comparing equations (2), (10) and (17), the parameters from the (i) polynomial series, k_θ, (ii) harmonic cosine angle, $k_{\theta n}$, and (iii) Fourier series, (k_F, C_n) can be simultaneously related as

$$
\begin{Bmatrix} k_{\theta 2} \\ k_{\theta 3} \\ k_{\theta 4} \\ k_{\theta 5} \\ k_{\theta 6} \end{Bmatrix} = k_C \begin{Bmatrix} \sin^2 \theta_0 \\ \sin \theta_0 \cos \theta_0 \\ -\dfrac{1}{3}\sin^2 \theta_0 + \dfrac{1}{4}\cos^2 \theta_0 \\ -\dfrac{1}{4}\sin \theta_0 \cos \theta_0 \\ \dfrac{2}{45}\sin^2 \theta_0 - \dfrac{1}{24}\cos^2 \theta_0 \end{Bmatrix} = k_F \begin{Bmatrix} -(C_1 \cos \theta_0 + 4C_2 \cos 2\theta_0) \\ \dfrac{1}{3}(C_1 \sin \theta_0 + 8C_2 \sin 2\theta_0) \\ \dfrac{1}{12}(C_1 \cos \theta_0 + 16C_2 \cos 2\theta_0) \\ -\dfrac{1}{60}(C_1 \sin \theta_0 + 32C_2 \sin 2\theta_0) \\ -\dfrac{1}{360}(C_1 \cos \theta_0 + 64C_2 \cos 2\theta_0) \end{Bmatrix}.
$$

(18)

For infinitesimal bond-bending the harmonic angle form is valid and, upon comparing equations (1), (2), (10) and (17), parameters from the (i) harmonic angle potential, (ii) polynomial series, (iii) harmonic cosine angle, and (iv) Fourier series can be simultaneously related as

$$
k_\theta = k_{\theta 2} = k_C \sin^2 \theta_0 = -k_F(C_1 \cos \theta_0 + 4C_2 \cos 2\theta_0)
$$

(19)

with $k_{\theta n} = 0$ for $n \geqslant 3$.

3.   Results and discussion

For verification of the mathematical relationships, we consider the C–C–C bending stiffness according to the harmonic angle potential $k_\theta = 605$ kJ rad^{-2} mol^{-1}, and its equilibrium angle $\theta_0 = 111°$, as furnished by Noid et al. [27] in the case of a general polymeric chain. The parameter k_C can be obtained from the first row of equation (18) whereby $k_{\theta 2} = k_\theta$, and, whereupon k_C is known, subsequent parameters ($k_{\theta n}$, $n \geqslant 3$) are obtainable from other rows in the same equation. The parameter k_F can be obtained by considering the following relationships from Rappe et al. [23]:

$$
C_0 = C_2\left(2\cos^2 \theta_0 + 1\right),
$$

(20)

$$
C_1 = -4C_2 \cos \theta_0 \quad \text{and}
$$

(21)

$$
C_2 = \frac{1}{4\sin^2 \theta_0}.
$$

(22)

Substituting equations (21) and (22) into any row shown in equation (18) leads to the same relation

$$
k_F = k_C \sin^2 \theta_0 \equiv k_\theta.
$$

(23)

In addition to this consistency, the conditions laid out in equations (15) and (16) are fulfilled when the coefficients are substituted from equations (20)–(22).

Table 1
Equivalent bond-bending parameters for $\theta_0 = 1.9373$ radian [27].

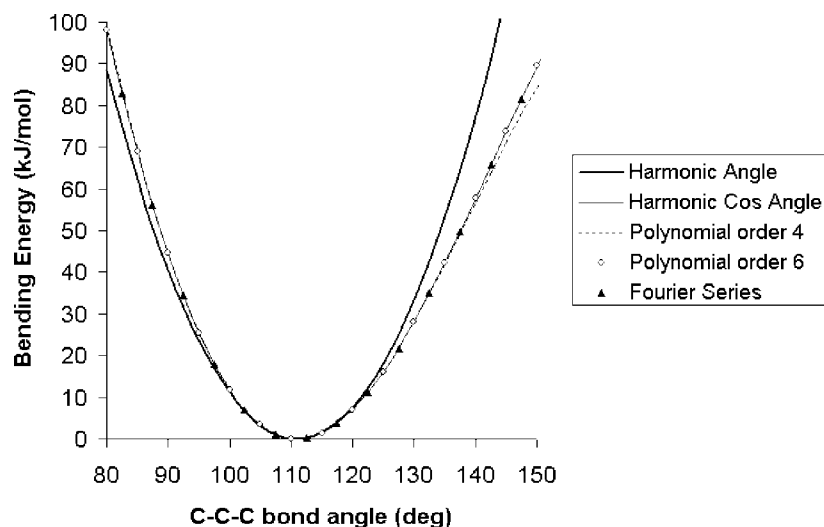|	Harmonic angle	Harmonic cosine angle	Polynomial series	Fourier series
k_θ (kJ rad^{-2} mol^{-1})	605	n.a.	n.a.	n.a.
k_C (kJ mol^{-1})	n.a.	694.12	n.a.	n.a.
$k_{\theta 2}$ (kJ rad^{-2} mol^{-1})	n.a.	n.a.	605	n.a.
$k_{\theta 3}$ (kJ rad^{-3} mol^{-1})	n.a.	n.a.	−232.25	n.a.
$k_{\theta 4}$ (kJ rad^{-4} mol^{-1})	n.a.	n.a.	−179.38	n.a.
$k_{\theta 5}$ (kJ rad^{-5} mol^{-1})	n.a.	n.a.	58.063	n.a.
$k_{\theta 6}$ (kJ rad^{-6} mol^{-1})	n.a.	n.a.	23.174	n.a.
k_F (kJ mol^{-1})	n.a.	n.a.	n.a.	605
C_0	n.a.	n.a.	n.a.	0.36051
C_1	n.a.	n.a.	n.a.	0.41119
C_2	n.a.	n.a.	n.a.	0.28683

Figure 2. Results of generated harmonic cosine angle, polynomial series and Fourier series functions based on data from harmonic angle function.

Summary of the bond-bending force field parameters, based on $k_\theta = 605$ kJ rad^{-2} mol^{-1} [27] and the mathematical relationships described by equation (18) is listed in table 1. Using these parameters, bending potential energy of C–C–C according to the harmonic angle function, harmonic cosine angle function, polynomial series function (of orders 4 and 6) and Fourier series function are plotted in figure 2 for comparison. That both the harmonic cosine angle and Fourier series functions agree well with one another is not surprising since the relationship shown in equation (18) is exact. The polynomial series of order 6 gives excellent agreement to the harmonic cosine angle and Fourier series forms within the considered range of bond angle. Polynomial series of order 4

is obtained by neglecting the fifth order and above, i.e. equation (2) is expanded up to $m = 4$. When expanded up to $m = 2$, we have the commonly used harmonic angle form, as described in equation (1). This approximate form can obtained from any of the other three force field function – i.e. equations (2), (3) or (4) – by using equation (19).

4. Conclusions and suggestion

Four of the most commonly adopted force fields for quantifying the potential energy due to bending of chemical bonds have been mathematically related to one another. These connections have been made possible by using the Maclaurin series for expansion of trigonometric terms. Simultaneous relationships among the bond-bending parameters is useful for molecular drug designers and computational chemists when reliable force field parameters are available in a certain form, but the force field in purchased software uses another force field function.

Development of a subroutine – consisting of the bond-bending connections formulated herein and the bond-torsion connections formulated earlier [26] – for incorporation into available established molecular mechanics software is therefore suggested for future work. Should there be any mismatch between the input parameters and the adopted force field functions, this subroutine converts input parameters into those corresponding to the force field employed in the software.

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