WHY DO DNA HELICAL MODELS EXHIBIT WEDGE ROLLS? A MATHEMATICAL RATIONALE*

DHANANJAY BHATTACHARYYA and MANJU BANSAL

Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560 012, India.

ABSTRACT

The base-pair parameters wedge-tilt and wedge-roll are extremely useful for describing curved DNA structures. The wedge effect has generally been assumed to be due to the differences between the base-pair tilts and rolls of two successive base-pairs in a DNA molecule. A mathematical formalism has been established here, which shows that, wedge-roll is a function of base-pair tilt and helical twist, similarly the wedge-tilt is a function of base-pair roll and helical twist. This provides a straightforward explanation for the reported wedge-roll in A-DNA helical model of 12° and gives a value of $-3.8°$ for B-DNA fiber model. The wedge-rolls and wedge-tilts calculated for the oligonucleotide crystal structures, using these relations, are in excellent agreement with the values reported earlier, which were calculated directly from the coordinates, using a global helix axis.

INTRODUCTION

THE uniform helical models proposed on the basis of X-ray fiber data assume that all the nucleotide units have an identical structure. Since there is no variation between the units, the base-pairs in them are simply characterized in terms of their orientation with respect to the helix axis (Z-axis). The base-pair orientation is described in terms of two angles: tilt(Θ_x) and roll(Θ_y) and the displacement (D Å) of the base-pair centre from the helix axis[1-3]. However the recently studied oligonucleotide crystal structures[2,4] and the models for curved DNA[5-9] indicate that the relative orientations of neighbouring base-pairs may also be described in terms of two wedge parameters, wedge-roll(Θ_R) and wedge-tilt(Θ_T). The wedge-roll in a straight B-DNA model has been assumed to be zero while the large wedge-roll value for fiber A-DNA has been explained descriptively and pictorially[4,6] as being due to the large displacement of the tilted base-pairs from the helix axis. However no rigorous mathematical or geometrical explanation is available. We show here, from simple mathematical relations between the orientation vectors of two neighbouring base-pairs in a regular helix that the wedge-roll can be simply expressed in terms of the base-pair tilts and helical twist, a relationship shown graphically in our earlier paper[3]. Similarly the wedge-tilt is related to the intrinsic rolls of the base-pairs.

METHOD

The orientation vectors for each base-pair have been termed as the local base-pair axes. The average of the two base normals defines the base-pair normal (local Z-axis) while the line joining C8 (purine)-C6(pyrimidine) defines the Y-axis. The X-axis is now defined by the direction normal to both this axis and the base-pair normal, such that a right-handed frame of reference is obtained (figure 1). These axes can be defined in an external cartesian frame of reference by their direction cosines (l_x, m_x, n_x) and (l_y, m_y, n_y), and the unit vectors along the X and Y-axes of the first base-pair are given by

$$X_1 = l_x i + m_x j + n_x k \tag{1}$$

$$Y_1 = l_y i + m_y j + n_y k. \tag{2}$$

Since the Z-axis of the external frame can be chosen to coincide with the helix axis, the second base-pair is related to the first by a rotation (corresponding to helical twist Θ) and a translation (helical rise) about this axis. The unit vectors X_2 and Y_2 are therefore given by the following relations

$$X_2 = (l_x \cos\Theta - m_x \sin\Theta)i$$
$$+ (l_x \sin\Theta + m_x \cos\Theta)j + n_x k \tag{3}$$

$$Y_2 = (l_y \cos\Theta - m_y \sin\Theta)i$$
$$+ (l_y \sin\Theta + m_y \cos\Theta)j + n_y k, \tag{4}$$

where Θ = helical twist angle; $n_x = \sin(\Theta_y)$ and $n_y = \sin(\Theta_x)$.

The wedge-roll and wedge-tilt are defined[1,8] by the inclination of the base-pair X- and Y-axes to the mean plane defined by the two neighbouring base-pairs (figure 1). The X- and Y-axes of this mean plane are defined as

$$X_m = \frac{X_1 + X_2}{|X_1 + X_2|} \quad \text{and} \quad Y_m = \frac{Y_1 + Y_2}{|Y_1 + Y_2|}. \tag{5}$$

The normal Z_m to the mean plane is then given by

$$Z_m = X_m \times Y_m. \tag{6}$$

Hence the value of wedge-roll (Θ_R) as defined above is given by

$$\text{Sin}(\Theta_R/2) = -X_1 \cdot Z_m = X_2 \cdot Z_m =$$

$$\left[\frac{-n_y \sin \Theta}{[(1 + \cos\Theta)^2 + (n_x^2 + n_y^2)\sin^2\Theta + n_x^2 n_y^2(1 - \cos\Theta)^2]^{1/2}} \right]. \tag{7}$$

Similarly wedge-tilt Θ_T is given by the relation

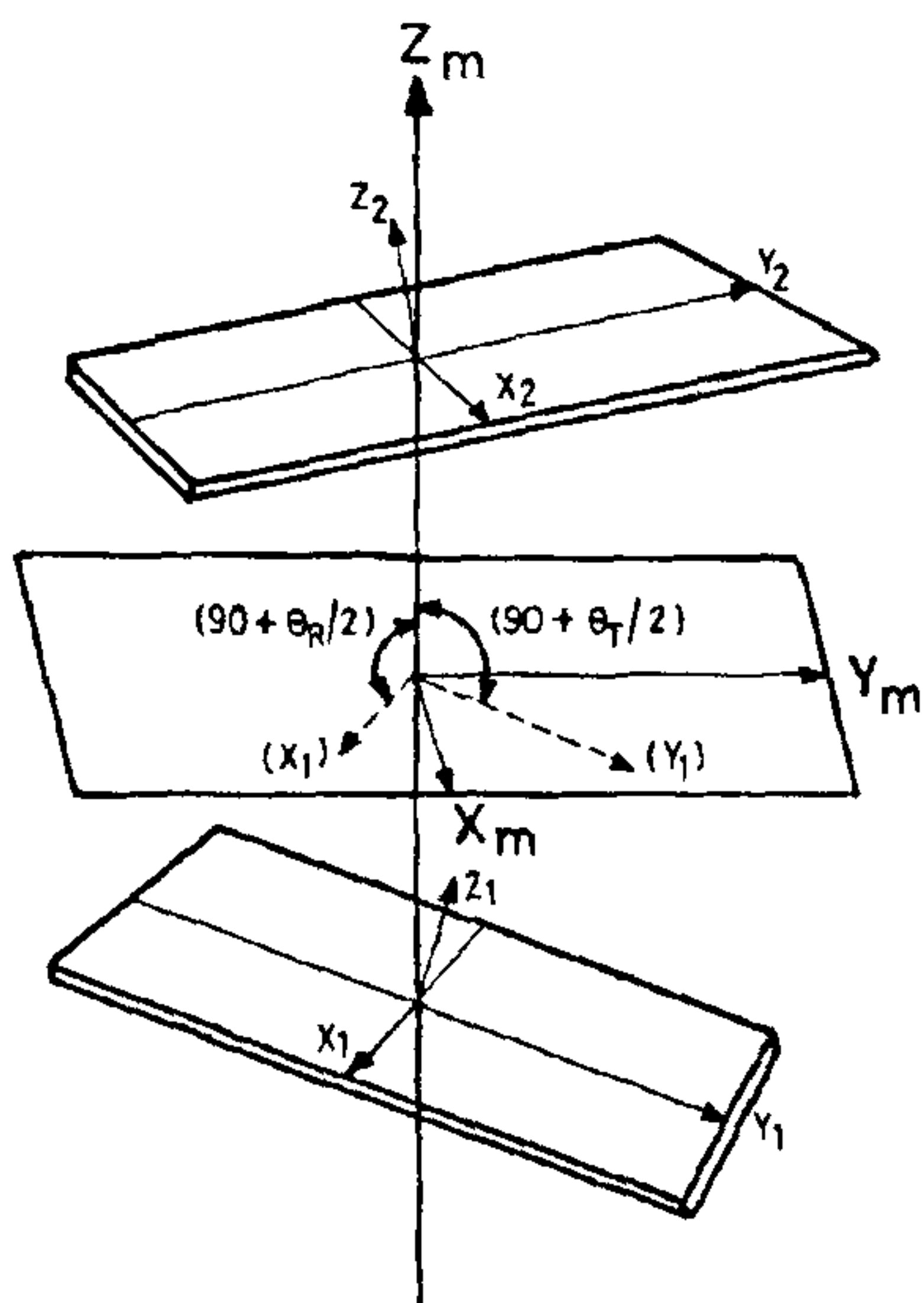**Figure 1.** Schematic drawing showing two local base-pair axes and the imaginary mean plane axes (X_m, Y_m, Z_m). The wedge parameters Θ_R and Θ_T which are related to the angles between X_1 (or X_2) and Z_m, Y_1 (or Y_2) and Z_m respectively are also shown.

$$\text{Sin}(\Theta_T/2) = -Y_1 \cdot Z_m = Y_2 \cdot Z_m =$$

$$\left[\frac{n_x \sin \Theta}{[(1 + \cos\Theta)^2 + (n_x^2 + n_y^2)\sin^2\Theta + n_x^2 n_y^2(1 - \cos\Theta)^2]^{1/2}} \right]. \tag{8}$$

Neglecting the terms containing n_x^2 and n_y^2 in (7) and (8), the following approximate relations are obtained

$$\Theta_R = 2 \sin^{-1}[-\sin \Theta_x \cdot \tan(\Theta/2)] \tag{9}$$

$$\Theta_T = 2 \sin^{-1}[\sin \Theta_y \cdot \tan(\Theta/2)]. \tag{10}$$

RESULTS AND DISCUSSION

The expression (7) when used to calculate wedge-roll for the uniform fiber models[10] gives values of $\Theta_R = -3.8°$ and $11.6°$ for B- and A-DNA respectively while the approximate relation (9) gives values of $-3.8°$ and $11.5°$.

The values of wedge-roll(Θ_R) calculated for different values of base-pair tilts(Θ_x) are shown in figure 2. It may be mentioned that this value does not show any explicit dependence on the displacement (D) of the base-pairs from the helix-axis.

Equations (7) and (8) are a pair of quadratic simultaneous equations and can be solved to obtain the values of Θ_x and Θ_y for any given value of the wedge parameters (Θ_R, Θ_T) and helical twist (Θ) using the inverse relations

$$\text{Sin } \Theta_x = n_y = [(1/2T) \cot(\Theta/2) [(1 - R - T)$$
$$- \sqrt{\{(1 - R - T)^2 - 4RT\}}]]^{1/2} \tag{11}$$

and

$$\text{Sin } \Theta_y = n_x = [(1/2R) \cot(\Theta/2) [(1 - R - T)$$
$$- \sqrt{\{(1 - R - T)^2 - 4RT\}}]]^{1/2} \tag{12}$$

where,

$$R = \sin^2(\Theta_R/2) \quad \text{and} \quad T = \sin^2(\Theta_T/2).$$

The Θ_{x1} and Θ_{x2} thus obtained, for any two base-pairs, are always equal (as also the Θ_{y1} and Θ_{y2}). For a uniform helix this condition is always true. However, in the case of a non-uniform structure this implies the definition of a local helix axis, different from the average or global helix axis[11] and is similar to the cylinder axis defined in reference 8. Using these values of Θ_x and Θ_y a non-uniform structure can be easily generated for DNA[3], corresponding to
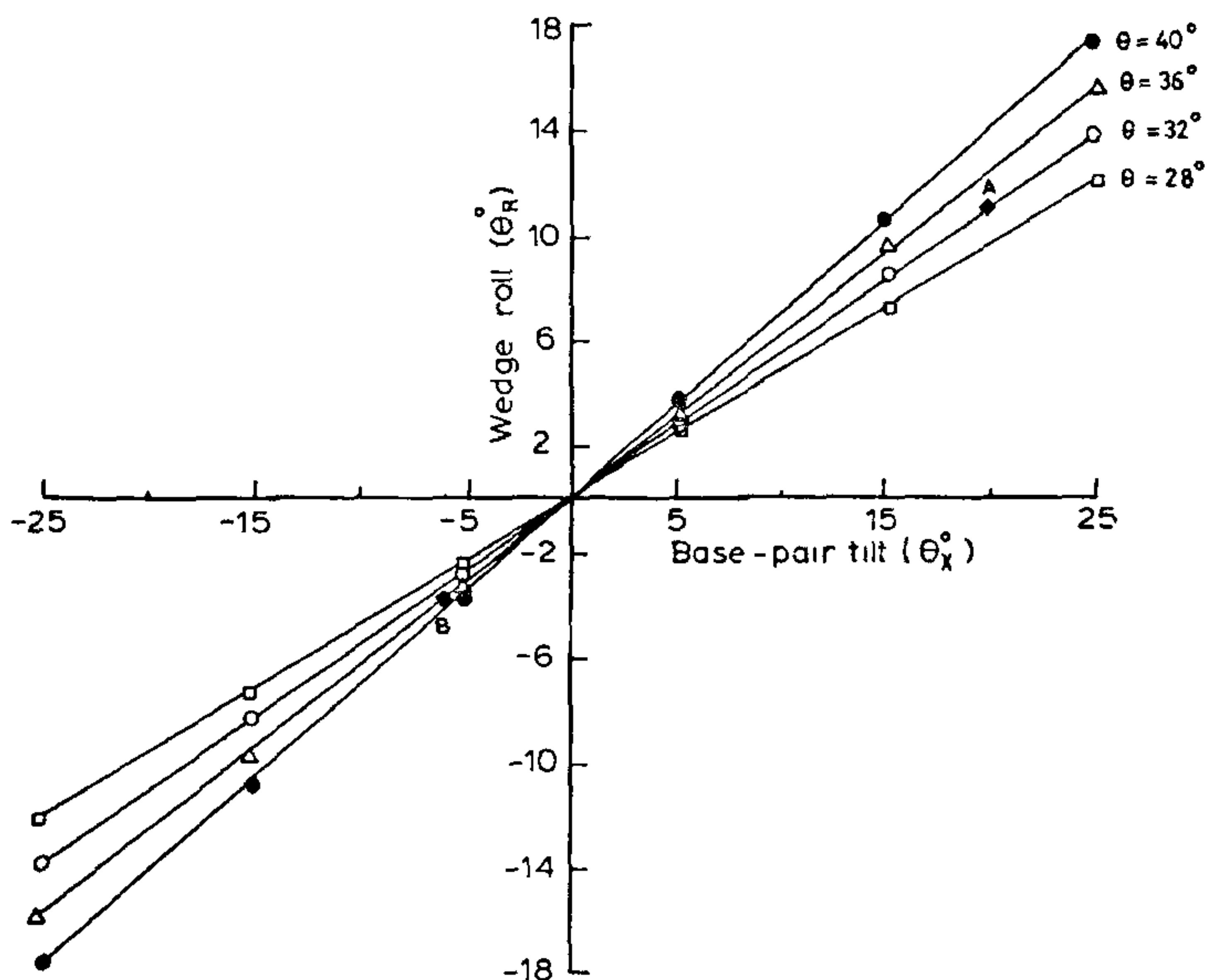
Figure 2. The calculated value of wedge-roll (Θ_R) is plotted against base-pair tilt(Θ_x) for four different values of helical twist(Θ). The signs of Θ_x and Θ_R have been shown here so as to conform to the usual convention[3,11], wherein Θ_x is positive for A-DNA and Θ_R is positive for base-pair opening towards minor groove. The points corresponding to the fiber models[10] for A- and B-form DNA are also shown (◆).

any prescribed values of the wedge parameters Θ_R and Θ_T.

The base-pair orientations in the oligonucleotide crystal structures have been earlier described in terms of an average helix axis. Because of the non-uniformity in the structure, the base-pair parameters for any two successive base-pairs have different values with respect to this axis. The wedge parameters are now related to the individual base-pair tilts and rolls by

$$\Theta_R = \Theta_R(\Theta_x, \Theta_y, \Theta) + \Theta_{y2} - \Theta_{y1} \qquad (13)$$

$$\Theta_T = \Theta_T(\Theta_y, \Theta_x, \Theta) + \Theta_{x2} - \Theta_{x1}. \qquad (14)$$

The values of $\Theta_R(\Theta_x, \Theta_y, \Theta)$ and $\Theta_T(\Theta_y, \Theta_x, \Theta)$ in the above equations are calculated using the relations (7) and (8) and making the approximation $\Theta_x = (\Theta_{x1} + \Theta_{x2})/2$ and $\Theta_y = (\Theta_{y1} + \Theta_{y2})/2$. The values of Θ_R, calculated using (13) are shown in figure 3 for the various base-pair steps in the crystal structures of the oligonucleotides d(GGCCGGCC)

and d(CGCGAATTCGCG). The values reported earlier[2], which were calculated using a global helix-axis, are also plotted and the good agreement between the two is clearly seen, thus proving the validity of this approximation.

The formulation reported here and in reference 3 clearly indicates that a well-defined relationship exists between the wedge parameters and the individual base-pair orientation parameters. Thus the large wedge-roll in the oligo d(A) stretch, which forms the basis of the uniform bending model[7], could actually arise due to the larger base-pair tilts in this fragment and smaller tilt or roll for the other sequences. This would lead to a change in the helix-axis direction at the interface of the oligo d(A) stretches similar to that proposed in the junction model[5,9], thus suggesting that the two models may be geometrically equivalent. Alternatively if the bases in the oligo d(A) stretch are almost normal to the helix axis[12], then a large wedge-roll at the junction could arise due to the neighbouring base-pairs being more tilted.
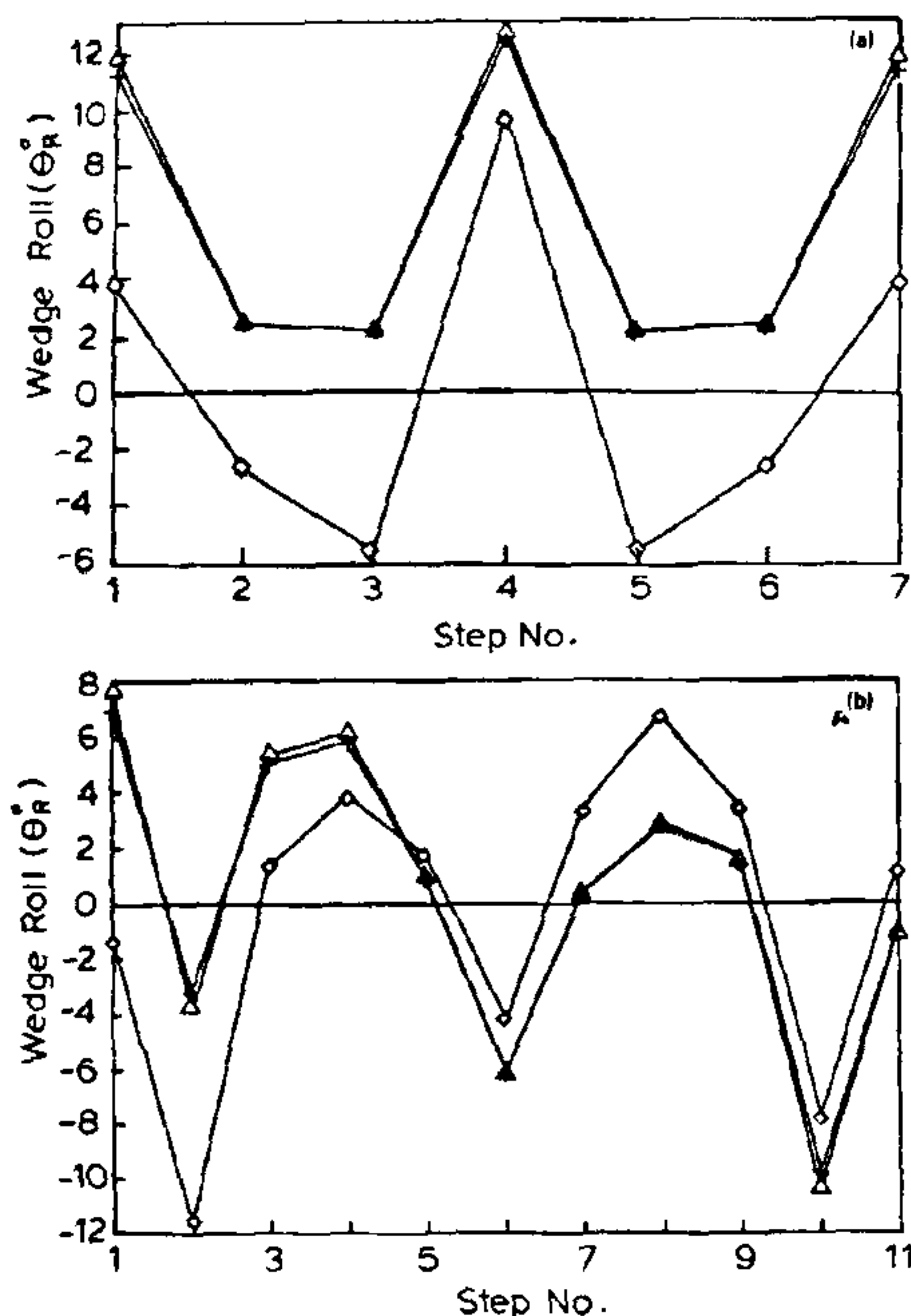
Figure 3a, b. Wedge-roll values for the various base-pair steps in crystal structures of (a) octamer d(GGCCGGCC) in *A*-form and (b) dodecamer d(CGCGAATTCGCG) in *B*-form (native). '+' The reported values[2]. 'Δ' The values calculated using equation (13). The root-mean-square deviations between the calculated and the reported values are 0.28° and 0.36° for the *A*-DNA and *B*-DNA structures respectively. '◇' The values calculated using the approximation $\Theta_R = \Theta_{y2} - \Theta_{y1}$, large deviations from the reported values are seen in this case.

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