

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

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### 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  $12^\circ$  and gives a value of  $-3.8^\circ$  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 ( $\Theta_x$ ) and roll ( $\Theta_y$ ) and the displacement ( $D \text{ \AA}$ ) of the base-pair centre from the helix axis<sup>1-3</sup>. However the recently studied oligonucleotide crystal structures<sup>2,4</sup> and the models for curved DNA<sup>5-9</sup> indicate that the relative orientations of neighbouring base-pairs may also be described in terms of two wedge parameters, wedge-roll ( $\Theta_R$ ) and wedge-tilt ( $\Theta_T$ ). 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<sup>4,6</sup> 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<sup>3</sup>. 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

$$X_1 = l_x i + m_x j + n_x k \quad (1)$$

$$Y_1 = l_y i + m_y j + n_y k. \quad (2)$$

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  $\Theta$ ) and a translation (helical rise) about this axis. The unit vectors  $X_2$  and  $Y_2$  are therefore given by the following relations

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

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

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

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The wedge-roll and wedge-tilt are defined<sup>3,8</sup> 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

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

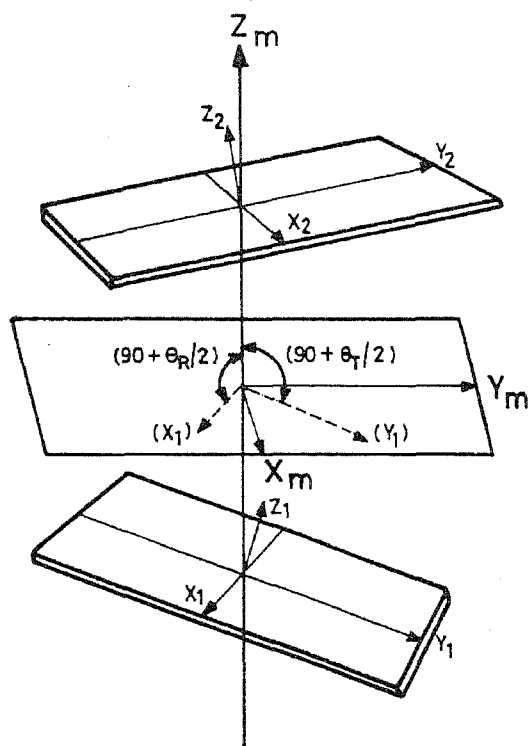
The normal  $Z_m$  to the mean plane is then given by

$$Z_m = X_m \times Y_m. \quad (6)$$

Hence the value of wedge-roll ( $\Theta_R$ ) as defined above is given by

$$\sin(\Theta_R/2) = -X_1 \cdot Z_m = X_2 \cdot Z_m = \left[ \frac{-n_y \sin \Theta}{[(1 + \cos \Theta)^2 + (n_x^2 + n_y^2) \sin^2 \Theta + n_x^2 n_y^2 (1 - \cos \Theta)^2]^{1/2}} \right]. \quad (7)$$

Similarly wedge-tilt  $\Theta_T$  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  $\Theta_R$  and  $\Theta_T$  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.

$$\sin(\Theta_T/2) = -Y_1 \cdot Z_m = Y_2 \cdot Z_m =$$

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

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

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

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

## RESULTS AND DISCUSSION

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

The values of wedge-roll ( $\Theta_R$ ) calculated for different values of base-pair tilts ( $\Theta_x$ ) 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  $\Theta_x$  and  $\Theta_y$  for any given value of the wedge parameters ( $\Theta_R, \Theta_T$ ) and helical twist ( $\Theta$ ) using the inverse relations

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

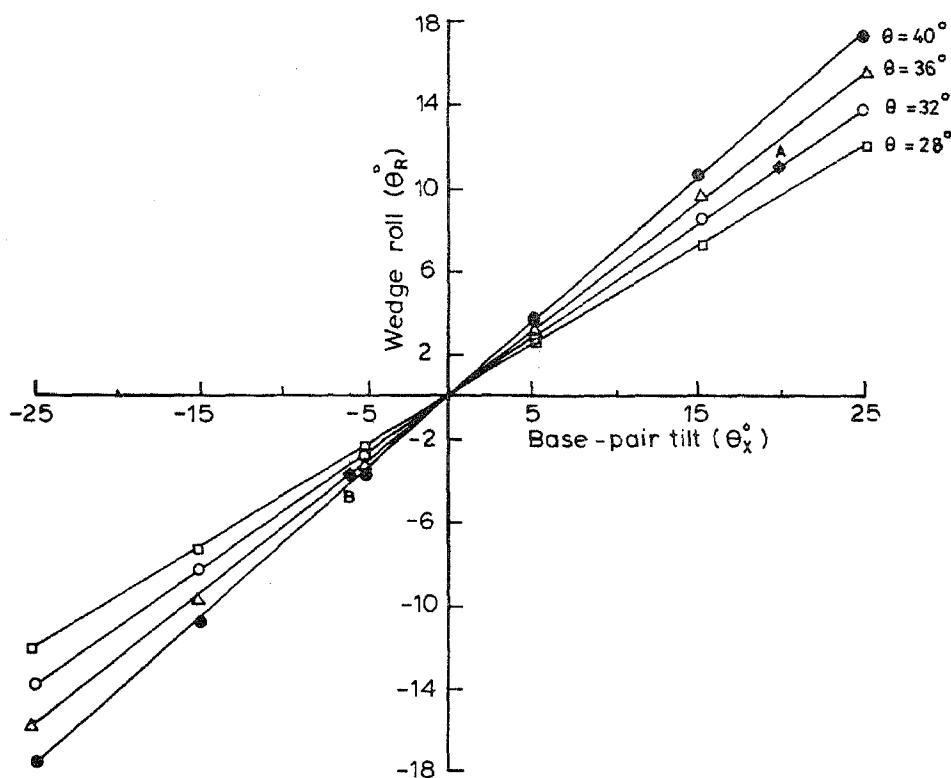
and

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

where,

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

The  $\Theta_{x1}$  and  $\Theta_{x2}$  thus obtained, for any two base-pairs, are always equal (as also the  $\Theta_{y1}$  and  $\Theta_{y2}$ ). 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<sup>11</sup> and is similar to the cylinder axis defined in reference 8. Using these values of  $\Theta_x$  and  $\Theta_y$  a non-uniform structure can be easily generated for DNA<sup>3</sup>, corresponding to



**Figure 2.** The calculated value of wedge-roll( $\Theta_R$ ) is plotted against base-pair tilt( $\Theta_x$ ) for four different values of helical twist( $\Theta$ ). The signs of  $\Theta_x$  and  $\Theta_R$  have been shown here so as to conform to the usual convention<sup>3,11</sup>, wherein  $\Theta_x$  is positive for A-DNA and  $\Theta_R$  is positive for base-pair opening towards minor groove. The points corresponding to the fiber models<sup>10</sup> for A- and B-form DNA are also shown ( $\blacklozenge$ ).

any prescribed values of the wedge parameters  $\Theta_R$  and  $\Theta_T$ .

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

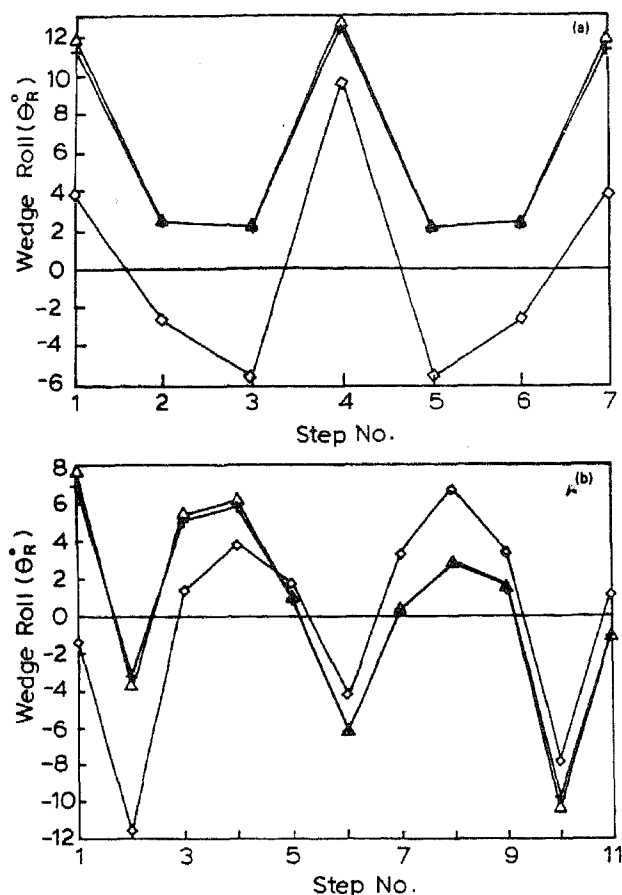
$$\Theta_R = \Theta_R(\Theta_x, \Theta_y, \Theta) + \Theta_{y2} - \Theta_{y1} \quad (13)$$

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

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  $\Theta_R$ , calculated using (13) are shown in figure 3 for the various base-pair steps in the crystal structures of the oligonucleotides d(GGCCGCC)

and d(CGCGAATTCGCG). The values reported earlier<sup>2</sup>, 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<sup>7</sup>, 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<sup>5,9</sup>, 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<sup>12</sup>, 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<sup>2</sup>. '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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#### ANNOUNCEMENT

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