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DNA and its bending: a glimpse of mechanism and implication in bacteriology

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Abstract

The double helical DNA structure varies from one species to other. Bend DNA is also available in the cell. Bending is expressed by the supercoiling of DNA structure. The mechanism of DNA bending is based on two basic models: the A-Tract model where the phasing of 6/A residues are important and in-junction bending model, where the heteronymous poly (dA), poly (dT) and B-DNA junction are responsible for causing bend in the helix axis. DNA bending has several implications, like transcription, replication, regulation etc., that induce the protein- protein and protein-DNA interaction. This DNA bending mechanism with multidimensional attributes has important applications such as drug preparation, cancer therapy and so on.

The biochemical investigation on DNA began with Friedrich Miescher (1868). Miescher isolated a phosphorus – containing substance which he called as nuclein from the nucleus of leukocytes and he also found that, 'nuclein' consists of an acidic portion and a basic portion, i.e. protein. The acidic portion, today is known as DNA. The first direct evidence that DNA is the bearer of genetic information came in 1944 through a discovary made by Oswal T. Avery, Colin Macleod and Maclyn McCarty. These investigators found that, the DNA which is extracted from a virulent strain of *Streptococcus pneumoniae* genetically transformed a non-virulent strain of this organism to a virulent form.

Avery and his colleagues extracted the DNA from heat killed virulent pneumococci, removing the protein as completely as possible and added this DNA to non-virulent strain, which were permanently transformed to virulent strain and when injected to mouse, it died. They concluded that, the DNA which is extracted from the virulent strain carried the inheritable genetic message for virulence. But this concept was not accepted to all, as protein impurities present in the DNA could be the carrier of genetic information.

But this idea was soon eliminated after the second important experiment in 1952 by Hershey and Chase. They provided the evidence that DNA carries genetic information. They used radioactive phosphorus (32 P) and radioactive sulfer (35 S) and when infected by bacteriophage (T2 infects the host cell i.e. *Escherichia coli*) it was found that the phosphorus containing DNA of viral particle enters into the host cell instead of the sulfur containing protein particle of the viral coat. The DNA material entered into the host cell for different functions like viral replication, transcription and translation. Thus, they proved that DNA is the genetic material rather then a protein.

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DNA Structure

Rosalind Franklin and Maurice Wilkins used the powerful method of X-ray diffraction to analyze DNA fibres. The beams are diffracted or broken down by the atoms in a pattern that is characteristic of the atomic weight and the spatial arrangement of molecules. Later, Franklin concluded that, DNA is a helical structure with two distinctive regularities of 0.34 nm and 3.4 nm along the axis of the molecule.

A most important clue to the structure of DNA came from the work of Erwin Chargaff and his colleagues in late 1940s.

They found that the four nucleotide bases of DNA occur in different ratios in the DNA of any organism and the amount of certain bases are closely related. They concluded that-

The base composition of DNA in a given species does not change with organism's age, nutritional state or changing environment.

In all cellular DNA the number of adenosine resideues is equal to the number of thymidine residues i.e. A = T and the number of gunnosin residues is equal to the no of cystocin residue, i.e. G = C

Thus it can be said, that $A + G = T + C$

This quantitative relationship is sometime called as "Chargaff's rules"

It is very difficult to understand the DNA structure in two dimensional plane. The best way to conceptualise DNA is in three dimensional plane. In 1953, Watson and Crick postulated a three dimensional model of DNA structure that accounted for all the available data, i.e. x-ray diffraction data of Franklin and base equivalence

Table 1: DNA Characteristics

DNA:	Polymer of Deoxyribonucleotide
Linked by :	5' – 3' phosphodiester bonds
Nucleotide :	Sugar + base + phosphate
Sugar :	Deoxyribose sugar having 5' – OH group
Base :	Purine and Pyrimidine
Purines :	A and G
Pyrimidines :	T & C
Base Pairing :	A with T G with C
H bonding :	A = T G ° C
Rationale of base pairing :	A – G large enough to fit with in 2.0 nm dia of DNA. T – C small enough to fit with in 2.0 nm dia of DNA.

observed by Chargaff (Table 1).

For the sake of simplicity it is assumed that the base pair step is coplanar but it is not exactly so (Mohan and Yathinadra, 1992). There is an element of propeller twist as a result of which the 2H bonded bases may be twisted some what like a propeller. The H-bonding may result not only between two bases in a base pair but also between the units of the adjacent base pairs also. Propeller twist is partly responsible for this.

Steric hindrance between two adjacent purines is again partly influenced by propeller twist. The DNA stability is due to the double helical structure. This stability is not only maintained by H-bond of complementary base pairs but also by electronic interactions between the stacked bases as well as hydrophobic interactions. The two anti-parallel strands are not identical- rather they are complementary to each other.

WHY HELIX

If the DNA is considered as an untwisted ladder, then a considerable space would be present in between which would be accessible to water. But the bases are oily or hydrophobic in nature, they would try to expel those water molecules from this space. This phenomena will occur only when the bases slide over each other or by twisting. Sometime sliding of bases occur through twisting. Thus twisting conformation is more stable.

The bases are not exactly coplanar somewhat like propeller twist occurs. Thus, the H-bonding is not only present in between two bases in a base pair but between the units of adjacent base pair also. This propeller twist also cause the steric hindrance between the adjacent purines by which the helical conformation of DNA is maintained (Mohan and Yathinadra, 1992). If the base pairs are forced to open by EtBr and chloroquine like elements, then it is shown that DNA can get back to its untwisted conformation. Thus, it can be said that the way of base stacking plays an important role in the structure of the DNA which favours the twisted form for stability. The bases are stacked in such a manner that the bases are particularly accessible from the major groove side than the minor groove side. If the base stacking manner are tried to unstack it will require energy and a tension will build up in DNA structure unable to rotate freely.

STRUCTURE VARIATION

The basic of DNA structure is the dinucleotides. The dinucleotides also undergo deformation in various ways. The deformation occurs due to the movement of bases along three different axes (Tolstorukov et al., 2007) like, Twist axis, Roll slide axis, Front back axis. So, they are deformed in major 3 ways: Roll, Twist, Slide. Along the twist axis the dinucleotide twists, along the roll or slide axis, dinucleotides roll or slide.

There may be positive roll and negative roll, also positive slide and negative slide. When two adjacent dinucleotides move away from each other then it is known as +ve slide, where as when they move closer to each other then it is –ve slide. 'Steric hindrance' is caused when two adjacent bases come closer, there is a repulsive interaction i.e. steric hindrance, where the bases twist to each other. In another case, when two purines are located on the opposite strand like, G-G, A-T that repulsion occurs due to the propeller twist. This phenomenon is known as purine clash. To avoid the purine clash, the purines must slide away from each other (+ve slide) or slide over one another (-ve slide) and pyrimidines will have to rotate away from one another.

Deformation of dinucleotide also occur in case of charge -charge repulsion. G-C base pair possess dipole as G contain '- ve' charge and C contain '+ve' charge. Thus when one G-C base pair stacked over another there is repulsion due to same charge and thus it causes sliding and/or rolling deformation of dinucleotide. But in case of A-T it has no dipole, thus it need not to deform due to the charge difference it only deform by the steric hindrance phenomena and propeller twist phenomena.

Aternative double helical structure

Variations in the conformation of the dinucleotide of DNA associated with conformation of its varieties. The double helical structure of DNA are present in 6 different forms i.e. A, B, C, D, E & Z. Among these the A, B and Z forms are important (Table 2).

Certain DNA sequences adopt unusul structures. When in DNA identical DNA sequences are present in the reverse orientation they are called inverted repeat. The sequences of inverted repeats together is called palindrome. The inverted repeat may cause the formation of secondary structure in SSDA or in dsDNA. In a longer palindromic sequence the complementary sequences pair to form a hairpin. In dsDNA the formation of two opposite hair pin is produced forming cruciform structure, which is so called because it represents the junction of four duplex regions.

Other types of DNA structure

Besides double stranded helical structure, DNA also exists in certain unusual structure and believes as important for molecular recognition of DNA by protein

Table 2: Comparison of structural features of different conformations of double helical DNA.

Types of DNA	B[1]	A[2]	Z[3]
Helix type	Right handed	Right handed	Left handed
Helical diameter (nm)	2.3	2.5	1.8
Distance per each complete turn (nm)	3.4	3.2	4.5
Rise per base pair (nm)	0.34	0.29	0.37
No. of bp per complete turn (nm)	10.5	11	12
Base till normal to the helical axis	6°	20°	7°

[1]B-form: Most predominant form
[2]A form: Occurs in DNA-RNA hybrid, conformation similar with the dsRNA
[3]Z-form; Available *in vitro* under high salt condition

and enzymes.

A. Triple stranded DNA

Triple stranded DNA formation may occur due to additional H-bonds between the bases. T can selectively form 2 Hoogsteen

hydrogen bond to A, of A-T pair forming T-A-T where as a protonated C can also form two Hoogsteen H-bond with G of G-C pair forming C^+ - G-C. The N-7, O^6 of guanine and N^6 of Adenine atoms are involved in Hoogsteen H-bonding; thus these are referred to as Hoogsteen positions in non Watson-Crick base pairing, first described by Karst Hoogsteen (1963).

By this Hoogsteen pairing the triplex DNA is formed (Aishima *et al*, 2002). The triplex DNA strands are less stable than double helix, because of the 3 negatively charged back bone. Strands in triple helix produce increased electrostatic repulsion. The triple DNA is most stable in low pH because. C ≡ G C+ require a protonated C. Some triplex DNA contain two pyrimidine strand and one purine strand or vice versa, called H-DNA having alternating pyrimidine and purine tract.

B. Four stranded DNA

Polynuceotide with very high content of guanine can form a novel tetrameric structure called G-quartates. These structure are planar and are connected by Hoogsteen H-bonds. (Aishima *et al*, 2002) Antiparallel four stranded DNA structures are referred to as G-tetraplex.

The end of the eukaryotic chromosomes- namely telomeres are rich in guanine and therefore form G-tetraplexes. Telomeres have become the targets of anticancer chemotherapy. G-tetraplexes have been implicated in the recombination of immunoglobulin genes and in dimerization the dsRNA of HIV. The G-tetraplex is quite stable over a wide range of conditions.

C. Bent DNA

In general a base containing DNA tract is rigid and straight but bent conformation also occurs. Bending in DNA structure happens due to photochemical damage or mispairing of bases. Certain antitumor drugs e.g. cisplatin induce bent structure in DNA such changed structure can take up protein that damage DNA.

DNA supercoiling

The DNA double helix represents DNA as a linear molecule. But DNA *in vitro* generally shows a closed structure. It lacks free end. Cellular DNA is extremely compacted, implying a high degree of structural organization. The folding mechanism must not only pack the DNA but also permit access to the information in the DNA.

Before considering its accomplishment in processes like replication, transcription, it is important to understand the property of DNA supercoiling.

Supercoils, the coiling of a coil, occur in DNA when a duplex is twisted in space around its own axis. The twisting introduced by supercoiling places a DNA molecule under torsion. Supercoil occurs only in closed structure because an open molecule can release the torsion simply by untwisting. A closed molecule must not have any breakage on either strand of DNA; any break even in one strand of a circular molecule allows untwisting.

A molecule that lacks supercoiling whether is open or closed is said to be relaxed. Supercoiling is of two types: Negative supercoiling and Positive supercoiling.

Negative supercoils twist the DNA around its axis in the opposite direction from the clockwise turn of the right handed double helix. This allows in principle to relieve the torsional pressure of DNA by adjusting the structure of the double helix. The relief takes the form of loosening the winding of the two strands about each other- DNA with negative supercoiling is said to be underwound.

The opposite type of effect is caused if DNA is supercoiled in the same direction as the intrinsic winding of the double helix. The positive supercoils tighten the structure applying torsional pressure to wind the double helix even more tightly. DNA with positive supercoil is known as overwound. It has been shown that many circular DNA molecules remain highly supercoiled even after they are extracted and purified, freed from protein and other cellular components. This indicates that, supercoiling is an intrinsic property of DNA tertiary structure. It occurs in all cellular DNA and are highly regulated.

Supercoiling is the combination of Twisting number (Tw) and Writhing number (Wr)

Twisting number (Tw):

It is property of the double helical structure itself, representing the rotation of one strand about the other. It represents the total number of turns of a duplex and determined by number of bp per turn. The twist angle 34^0 in B-DNA results in a helical repeat of about 10.5 bp/turn.

Writhing number (Wr):

It is the turning of the axis of the duplex in space. The global wrapping of the axis of the double helix around itself.

Linking number (Lk)

It is the number of times one DNA strand wraps the other when the molecule lie in a plane. Thus, Lk is the number of revolution that one strand make around the other when the DNA is considered to lie flat on a plane surface. Lk is equal to the sum of Wr and Tw, be written as: L=Tw+Wr

The DNA supercoil can be of two types: Toroidal and Plectonemic. In a protein free state, the DNA will remain plectonemicly supercoiled but in the presence of DNA binding protein it may be present as toroidal supercoil.

In toroidal supercoil DNA is stable. But isolated in laboratory condition, it may be in plectonemic form, as all proteins have been removed from it. Supercoiling is intricately linked to biological activity of the DNA. DNA supercoiling has an important role to bring the distal segment of DNA in close proximity as it is required for recombination event. Thus, DNA compaction requires for the DNA supercoiling.

DNA Bending

DNA does not exist as linear form in a cell rather, in twist, turn and supercoil. The supercoiling is required for compaction and also for several biological functions. For the twist, turn or supercoiling DNA requires to be flexible enough, initiating the bending process.

Nucleosomal bending

Nucleosome model is very useful model for DNA bending. In nucleosome model 2 nm DNA is wrapped around the central core i.e. the histone octamer. DNA (160 bp) wrapped into core molecule via roll and slide with the bp twisting. The tight bending of DNA in the nucleosome suggests its ability to bend in a particular direction, that's a crucial factor. Experiments performed to understand if there was any intrinsic sequence dependence and revealed a periodic modulation of dinucleotide AA/TT and a dinucleotide GC but this happens in opposite direction. (Goodsell *et al*, 1993) The phasing of AA/TT and GC/CG in the nucleosomal model consider that AA step is rigid and they present at the low roll position, where as GC is localized in the high roll position (Tolstorukov *et al*, 2007).

The sequence of the bound DNA affects the binding of DNA to histones in nucleosome cores. The histone core does not bind randomly to the DNA, rather they tend to place themselves at certain locations. This positioning is not fully understood. In some cases, it appears to depend on abundance of AT base pairs in the DNA helix where it is in contact with histones. The tight wrapping of the DNA around the nucleosome- histone core require compression of the minor groove of the helix and a cluster of 2 or 3 A=T bp makes this compression more likely. (Goodsell *et al*, 1993)

Mechanisms for DNA bending

The relationship between DNA sequence, structure and function has been studied and discussed extensively in last few decades. To reveal the structural basis of DNA bending/curvature effort has been directed towards the structure of a short run of 4-6 A-T residues known as A-tract. The DNA curvature is induced when the 'A-tract' that is inserted in phase, with the helical periodicity.

The structural basis of 'A-tract' that induce 'DNA bending' has remained enigmatic. Because no single structure could explain the whole phenomenon, it is necessary to rely on several models which have been confirmed by 'gel migration data' (Kerppola, 1997) This data suggests that the center of curvature is towards the minor groove of the 'A-tract' and towards the major groove of intervening general sequence.

DNA bending at A-T tracts

It is quite common to use the variation in gel mobility for mapping a bending locus contained in a sau 3 - a restriction fragment isolated from *Leishmania tarentolae* kinetoplast DNA and the sequence identified as–

GAATTCCCAAAAAGTCAAAAAATAGGCAAAAA ATGCSAAAAATCCCAAAC– (Wu and Crothers, 1986). This is a striking feature that a regular repeat of the sequence element $CA_{5-6}T$ with 10bp periodicity is present around the center of the bend.

Presumably, each A-tract produces a small bend in the DNA helix axis repetition of these elements in phase with the helix screw results in their coherent addition to form a large overall bend. Thus, for DNA bending, it requires a continuous run of 'A-tract' residues and the potential role of the junctions with other bases flanking the A-tract. For DNA bending phasing is also very essential (Kerppola, 1997). It is shown that bending elements must be repeated in phase with the helix screw in order. The importance of continuous run of A-residues for the bending phenomenon was investigated by interrupting the A-tract with another nucleotide at the central base it is shown that the single bp change causes the gel mobility to revert nearly to normal.

It appears that the continuous run in 'A' residues is the basis for bending phenomenon. In this case the purine 'A', and 'G' are not equivalent. In addition, it is also found that the sequence of 'G' has normal gel electrophoretic mobility which conform the special role of A-tracts. It is found that 'A' tract of length 3 produces only a minor electrophoretic anomali, the effect is substantial with 4 in a row and increases to maximum for a tract of length 6, that becomes another important factor for DNA bending (Crothers *et al*, 1990). It is the junctions of A-tracts on which the extent of bending would depend on the flanking bases. It is probable that the greatest degree of bending is seen when the 5'-flanking base is C and the 3'-base is T as it is found at natural bending locus in *L. tarentolae*. When C is present in both 3' and 5' end, it is less bent and when G is present in both 3' and 5 end the bending property reduces further (Crothers *et al*, 1990)

There are two general classes of models for the origin of sequence – directed DNA bending (Goodsell and Dickerson, 1994). Class I includes the sequence –

periodicities. Sequeunces should favour bending by compressing the minor groove, where as pyrimidine – purine sequence should bent into the major groove. All these observations support the 'A-tract' DNA bending.

Class-2 model shows that poly (dA) poly (dT) has an anomalous structure as revealed by fibre diffraction, its 10.1 bp helical screw, its Raman spectrum and its inability to be reconstituted into nucleosomes. It is possible that oligo dA-dT tracts in DNA can adopt one or more alternative structures in addition to the B-configuration. This model appeals to a longer range structural polymorphism at the A-tract to focus the properties of junctions between it and adjacent B-DNA. According to this, the heteronymous poly (dA) poly (dT), then a bend in the helix axis is expected at the junction with B-DNA. The junction bending model serves as an effective working hypothesis (Nadeau and Crothers, 1989). This model holds that the 'A-tract' adopts a conformation similar to the poly (dA) poly (dT) structure deduced from fibre diffraction studies the key feature of which is the substantial tilt of the bp relative to the helix axis. When a segment of B-DNA is adjoined to the filled bases of the A-tract the helix axis is deflected at the junction between the two dissimilar structure for maintaining favourable base stacking. Concerted phasing of these local junction bends then yields to a global curvature of the DNA.

The distinguishing assumption of the original junction model is that 'A-tract' residue will remain in a B-conformation unless they are long enough to overcome the free energy barriers to nucleation of altered structure responsible for bending (Nadeau and Crothers, 1989). The structures of several similar 'A-tract' containing duplexes have been determined by x-ray crystallography, each of which is bent and displays a minor groove narrowed by strong propeller twisting of the A-T pairs without significant bp tilt. The bends are at the roll of the junction and the responsible factors are groove compression, whether results from propeller twisting bp tilt, some other structural features or combination of several.

In order to inhibit gene expression proteins need to bind to specific DNA target site such that recognition is often accompanied by 'DNA bending'. Scanning force microscopy (SFM) studies revealed crucial differences in DNA bending induced by protein of non specific and specific sequence. However, the significance of DNA bending is not clearly understood.

From the studies on 'Cro' protein i.e. the protein that regulates the genes in bacteriophage, it has been shown that 'Cro' first binds loosely to DNA at non specific sites and produces 'binding wave' and travel along the chain until it recognize a specific target site where it binds very tightly. The SFM studies revealed an increase in DNA bending angle where the protein is bound to a specific site. This molecular recognition is not only important in gene regulation but in many other biological processes. Thus it can be said that DNA bends to bind (Kanhere and Bansali, 2004)

DNA Bending and transcription

The $\alpha_2B\beta'\sigma$ *E. coli* RNA polymerase holoenzyme is capable of promoter binding, accurate initiation and response to diverse transcriptional regulators some of which alter the conformation of DNA in the upstream promoter region. Architectural changes in DNA may be important to initiate the formation of a DNA loop around RNA polymerase. Wrapping of DNA around *E. coli* RNA polymerase in the preinitiation complex has been observed.

The largest dimension of *E.coli* RNA polymerase holoenzyme is 160 A^0, but footprints of holoenzyme on promoter DNA in both closed and open complexes extend to 310 A^0 or more (Coulombe and Burton, 1999). This footprinting is explained by wrapping the DNA round RNA polymerase. The prominent common features of the RNA polymerase is the presence of finger like projections in RNA polymerase that is close to form a channel large enough to accommodate DNA. For *E. coli* RNA polymerase the channel is open in the initiating holoenzyme and remains closed to the elongating core enzyme. This suggests that DNA penetrates the channel which closes around template during elongation to prevent transcription.

In both the closed and open complex the topology of promoter is altered to introduce negative supercoiling. Upstream promoter DNA may be partially wrapped around RNA polymerase in closed complex, with a significant DNA bend near the – '35' region of the promoter (Perez – Martin and Lorenzo, 1997). During transcription there is a conformational change in the holoenzyme that closes the 'hand' of RNA polymerase around the DNA and introduces another major DNA bend near the transcriptional start site. This conformational change has the effect of developing significant strain on the DNA helix around + 1.

It is proved that two DNA bends are spaced in such a manner that as the DNA wrap is tightened, the short stretch of helix between the 2 bends are forced to unwind.

DNA upstream and downstream of the two DNA bends to act as two levers and to force the helix into the unwound conformation that preceeds open complex formation. Transcriptional regulators can affect this mechanism by pulling the upstream DNA lever the downstream lever or both.

DNA Bending and transcriptional control

The α-subunit of RNA polymerase are important for interaction with upstream promoter DNA and regulators. The α-structure comprises an amino-terminal domain (α -NTD) and a CTD (α-CTD) domain separated by a flexible central region.

A DNA wrapping model describes catabolite gene activator protein (CAP) cyclic AMP (CAMP) medicated activation of 'lac' promoter. CAP binding sites can be located at variable positions relative to the transcriptional start site but the face of the helix on which CAP lies relative to RNA polymerase for

activation (Perez – Martin and Lorenzo, 1997) Maintaining the orientation of CAP relative to RNA polymerase is to serve two purposes- (i) to allow specific CAP-RNA polymerase interactions, and (ii) to maintain the directionality of the CAP-induced bend in DNA towards RNA polymerase.

CAP-CAMP bends DNA by 90°, bending promoter DNA back to RNA polymerase. CAP-CAMP on the lac promoter make specific contact with activation region on the α-CTD. DNA bending and α-binding by CAP-CAMP might contribute to promoter strength in two ways: i) by enhancing RNA polymerase binding to promoter and ii) by promoting isomerisation (Coulombe and Burton, 1999). Initial binding of holoenzyme induce DNA bending in the upstream promoter region, DNA bending by CAP-CAMP could stimulate binding. RNA polymerase binding is also expected to be stimulated by interaction bent CAP-CAMP and α-subunit of RNA polymerase.

According to DNA wrapping model, however appropriately phased bends in upstream DNA initiate DNA wrapping round RNA polymerase so that DNA bending in the upstream promoter region can also contribute to isomerisation (Spronk *et al*, 1999). Formation of appropriate DNA loop around holoenzyme requires bending and wrapping of the DNA, facilitated by a multitude of protein-protein and protein-DNA contacts.

Thus DNA bending by CAP-CAMP in upstream promoter region, appear to cause DNA to wrap around RNA polymerase.

DNA bending and regulation of gene expression

The most common example regarding gene expression is the 'lac operon'. The lac repressor protein is one of the key enzyme in the lactose digestion chain of *E.coli* bacteria. This protein turns off the genes that are responsible for lactose digestion when lactose is absent from the bacterial environment.

The lac repressor functions through clamping two out of the three DNA sites i.e. O_1, O_2, O_3 called operator site. The DNA bend - site is forced to form a loop which interferes with the reading the genes by another protein i.e. RNA polymerase (Mahadevan and Schulten, 1999). A single repressor molecule binds to two operators that are between 93 and 401 bp apart. One suggested mechanism is that the repressor tetramer binds to separate operator sequences forcing the DNA to conform to a loop structure.

For DNA interaction to occur there must be a sufficient length between the operator sequence in addition to certain other properties of DNA. The formation of the loop structure makes RNA polymerase binding even more unfavourably than only one repressor tetramer bound to the DNA. DNA loop induced by the lac repressor between the operator sites O_1 and O_3.

Conclusion

It is experimentally proved that DNA bending depends on the binding competition between monovalent and multivalent components. DNA bound p53 core domain causes local DNA conformational change, that results in DNA bending. Local distortion mechanism, induced by polyamine treatment, could be related to DNA condensation. Further implication for transcription activation lies with p53 induced DNA binding. Since p53 is an important factor for cancer suppression thus DNA bending can be used in cancer therapy. Based on a few examples it is speculated that updating of knowledge suggests that there may be a relation between drug molecule and DNA bending where structural and conformational change in the DNA and drug molecule occurs. Thus to understand the mechanism of drug action, DNA-drug interaction during DNA bending is very essential.

Thus DNA curving is also very important in biotechnological field which helps to regulate the synthetic plasmid replication and transcription. When polyamine ion is immobilized in the middle of major groove, the DNA chain could bent upto the largest angle which is sterically allowed.

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