A Model for Recognition Scheme between Double Stranded DNA and Proteins

S. H. Kim, J. L. Sussman,
and G. M. Church

ABSTRACT

It is likely that there are many modes by which DNA can be recognized by proteins. A model for the complex between a double stranded DNA and an antiparallel β-ribbon is proposed as a possible mode of recognition between double stranded DNA and proteins. In this model, the symmetry elements, as well as the repeat distances of two components, coincide, thus providing a nice complementary contact. The contact is occurring on the narrow groove of DNA, and the polarity of each DNA strand is antiparallel to the backbone of the peptide with which the complementary hydrogen bonds are formed.

INTRODUCTION

The recognition between DNA and protein is one of the fundamental molecular processes going on in all the living cells. Examples of such DNA-protein complexes are numerous: histone-DNA complex, repressor-DNA complex, restriction enzyme-DNA complex, etc.

The specific recognition between a double stranded DNA (ds DNA) and a protein can occur in two ways: one case, in which ds DNA opens up and the base sequence of the single stranded region is recognized by the protein, and the other case, in which the base-paired double strand itself is recognized. The model proposed is a general scheme for the latter type of recognition.

Carter and Kraut (1) proposed a model for a double stranded RNA (ds RNA) and a two-stranded antiparallel β structure where the $2'$ hydroxyl of ribose in

571

RNA forms a hydrogen bond to the free carbonyl oxygen of the backbone and the free NH group forms two hydrogen bonds with the ring oxygen and the 2' hydroxyl oxygen of the next molecule through a water molecule on the narrow groove of the ds RNA. They also pointed out that because the narrow groove of the ds RNA is so shallow, there is no room for α-carbons in the antiparallel β structure to have any residues other than very small sidechain groups. Even though ds DNA can assume a ds RNA type of conformation, this scheme is inapplicable to ds DNA which do not have the 2' hydroxyl group.

The proposed model in this paper contains the feature which allows the narrow groove of ds DNA to be recognized by various amino acid sidechains on the inside of antiparallel "β-ribbon."

MODEL BUILDING

Space filling (CPK) models and skeletal (Kendrew-Watson) models were built for ds DNA according to the coordinates of Arnott et al. (2) and for an antiparallel two-stranded β structure. Since ds DNA has two kinds of pseudo 2-fold axes perpendicular to the helix axis, one on the plane of each base pair, the other between two adjacent base pairs, we considered only the antiparallel β structure, which also contains the two kinds of pseudo 2-fold axes. As was observed in many protein structures and pointed out by Chothia (3), β structures usually have right handed helical twist. The antiparallel β-ribbon was slightly twisted, then fitted to the ds DNA while optimizing van der Waals contacts and possible hydrogen bondings between the DNA and the β-ribbon, at the same time keeping the DNA structure as close to the DNA B conformation as possible. The coordinates for the final complex were measured from the skeletal model so built and the coordinates were "idealized" by a computer program, written by Hermans and McQueen and modified by Sussman, which idealizes the bond distances, bond angles, certain dihedral angles, and van der Waals contacts, by allowing only those conformational angles to vary which are known to be variable from the results of x-ray studies; for example, two phosphoester bonds (ω,ω' angles) in DNA and two bonds of α-carbons in the polypeptide chains (ϕ,ψ angles) as major variables.

STRUCTURAL FEATURES OF THE MODEL

When two antiparallel peptides form a β-ribbon, all alternating peptide nitrogens are hydrogen bonded to the opposite strand, leaving one free peptide nitrogen per dipeptide. These free nitrogens are utilized to form hydrogen bonds to the 3' oxygens of the polynucleotide backbone, thus utilizing all the peptide nitrogens. All alternating carbonyl oxygens are involved in the hydrogen-bonded anti-

parallel β-ribbon. The free carbonyl oxygens are in position to form a hydrogen bond with the polynucleotide backbone phosphate oxygens through a water molecule. But this is neither an important nor a necessary feature of this model. Within the antiparallel β-ribbon, the alternating α-carbons of each peptide chain are facing the narrow groove of the ds DNA, and the remaining α-carbons are pointing outward.

Any basic residues attached to the α-carbons on the outside of the β-ribbon will be able to neutralize the negative charges of the phosphates. So can other positive ions in the solution. This feature of neutralization by the basic group is shown in Figure 1. However, it is not shown in Figure 2, which shows the interaction of the DNA backbone and the peptide backbone more clearly.
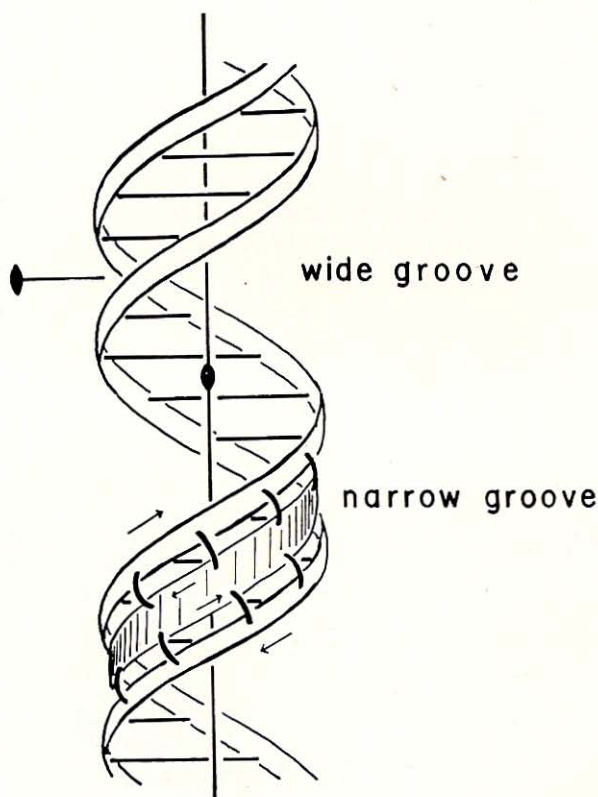

wide groove

narrow groove

Figure 1. A possible model for the Histone F2a2-DNA Complex. Arrows indicate the polarity of the chain; 5′→3′ direction for DNA; N terminus → C terminus for peptide. Thick dark arcs connecting DNA and β-ribbon represent the basic residue on the β-ribbon neutralizing the phosphate charges of DNA. The β-ribbon is assumed to be only a small portion of F2a2 protein; the remaining portion of this molecule is assumed to be in hydrophobic contact with other histone molecules.

The tube-like space formed in the narrow groove of the ds DNA B form by the β-ribbon is of such a size that almost all amino acid sidechains attached to the α-carbons on the inside of the β-ribbon can be accomodated, thus allowing the narrow groove side of base pairs to be recognized by various sidechains of the β-ribbon.

The ds DNA contains two pseudo 2-fold axes per base-paired two nucleotides, one on the plane of each base pair and the other between two adjacent base pairs, and both are perpendicular to the helix axis. The antiparallel β-ribbon also has two kinds of pseudo 2-fold axes.

In the model of the complex, these two pseudo 2-fold axes from ds DNA are coinciding with those from the β-ribbon. In addition, the repeating unit of the β-ribbon has a length of about 7 Å, which again coincides with the repeating distance of the phosphate groups along the ds DNA helix.

The unique portion of the complex is composed of one nucleotide and two peptides. Given the coordinates of this unique portion, the rest of the complex can be generated by a simple set of helical parameters. The polarity of the chains are as follows: one strand of DNA going from 5' end to 3' end forms hydrogen bonds with one strand of β-ribbon going from the C terminus to the N terminus, as does the relation between the remaining strands of DNA and β-ribbon. In other words, the polarity between the DNA strand and the polypeptide strand is "antiparallel."

DISCUSSION

The model proposed here is a plausible way in which a secondary structure of a protein can interact with ds DNA in a non-specific way by utilizing the
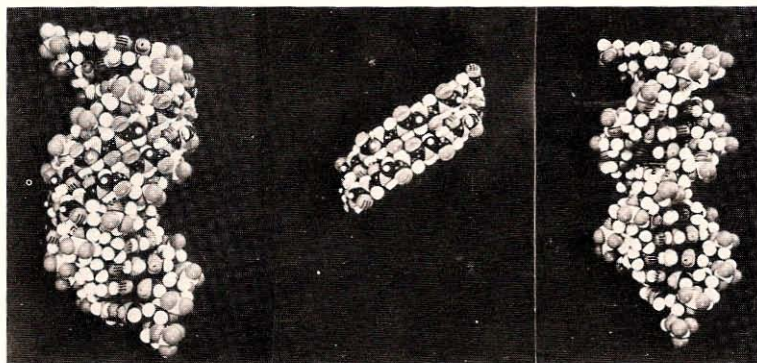

Figure 2. CPK model of the double stranded DNA B form (*right*), antiparallel β-ribbon (*middle*) and the DNA-β-ribbon complex (*left*), where the β-ribbon occupies the narrow groove of DNA. Side residues of the β-ribbon are not shown for clarity.
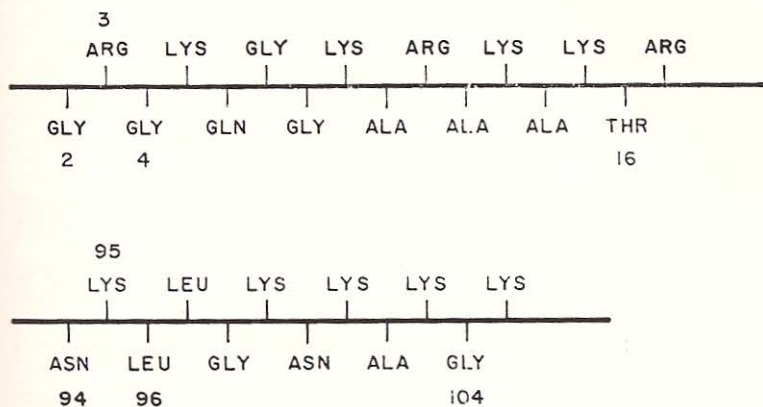
Figure 3. Two regions of Histone F2a2 where basic residues appear alternatingly along the sequence, which is indicated by the numbers.

symmetry elements of ds DNA and also provide sufficient room for various sidechains from the inside of the β-ribbon to interact specifically with base pairs on the narrow groove.

One requirement of this model is that most of the basic residues be outside of the β-ribbon. There are a few histones whose sequence shows just such regions, e.g., F2a2, where many alternating residues are basic. This is shown schematically in Figure 3. It is likely that certain histones interact with ds DNA using the α-helix; some interact with β-ribbons. The details of this model with some possible examples as well as "idealized" coordinates will be published elsewhere.

ACKNOWLEDGMENT

REFERENCES

1. Carter, Jr., C. W. and J. Kraut. 1974. A proposed model for interaction of polypeptides with RNA. Proc. Natl. Acad. Sci. USA 71: 283.
2. Arnott, S. and D. W. L. Hukins. 1972. Optimized parameters for A-DNA and B-DNA. Biochem. Biophys. Res. Commun. 47: 1504.
3. Chothia, C. 1973. Conformation of twisted β-pleated sheets in proteins. J. Mol. Biol. 75: 295.