dent adenosine triphosphatases (*24*), none of the gene products has known homologies. Biochemical evidence indicates that polar granules, isolated from pole cells, have a major component of approximately 95 kilodaltons (*7*), but none of the cloned posterior group genes codes for a protein of this size.

In spite of the association of the posterior polar plasm with germ cell determination, none of the posterior group genes appears to be specifically responsible for pole cell formation. The presence of polar granules remains the common component essential for a functional germ plasm and for the posterior localization of *nos* RNA. Thus, there are probably additional gene products that are key to germ cell formation but may have little effect on posterior development. Saturation screens for true grandchildless mutations remain to be conducted. Organelles comparable to polar granules are also found in the amphibian germ plasm (*25*) and may be present in other organisms (*26*). These organelles may have multiple functions wherever they are found.


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# β Ribbon: A New DNA Recognition Motif


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THE TWO MOST STRIKING FEATURES OF DNA ARE ITS BEAUTY and symmetry. The beauty is displayed by the curvature of the right-handed double helix and the symmetry arises from the two twofold rotation axes per base pair, one in the plane of each base pair and the other between every two adjacent base pairs. Both twofold axes are perpendicular to the helix (Fig. 1A). Since these two features are so striking, it was widely recognized that they would be used by proteins that recognize DNA.

What types of symmetries do protein structural elements such as α helices and β sheets have? An α helix has neither a twofold axis nor a helical curvature comparable to double-helical DNA. However, an antiparallel β ribbon (two-stranded β sheet) contains two types of twofold axes (Fig. 1B) that have separations comparable to those of the twofold axes of double-helical DNA. The twist curvature is also comparable to that of DNA. This striking similarity prompted molecular modeling of the recognition between a β ribbon and double-helical RNA (*1*) and DNA (*2*), in which the curvature and symmetry axes of the β ribbon and double-helical DNA were matched (Fig. 1C).

When crystallographic evidence for such a model was sought by soaking short peptides such as protamines into transfer RNA crystals, it came as a surprise that the α helix rather than the β ribbon was bound in the minor groove of a double-helical region of transfer RNA (*3*). The real surprise came when higher resolution crystal structures of DNA complexes of several DNA-recognizing proteins were determined [reviewed in (*4*)]. In all of these structures, DNA was recognized by a helix-turn-helix motif in which neither the symmetry nor the helical curve of DNA was used by the recognizing protein. More recently, the structure of another DNA recognition motif, the zinc finger, revealed that the α helix again was the recognition element (*5*). It almost appears as if nature has taken the second best option. What advantage do these motifs have as a structural element for recognizing double-helical DNA? These motifs have neither helical twist nor symmetry elements similar to those of DNA. The examination of the helix-turn-helix motif in various different DNA complexes reveals that the first helix serves as a stage on which to present the second helix, which protrudes out of the protein to interact with the DNA grooves. In the zinc finger motif, a zinc ion holds the β ribbon and the α helix together to form the entire peptide into a compact package. In both cases, the recognition helix orients in such a way that the positively charged amino-terminal end of the helical dipole points toward the groove, which is surrounded by the negatively charged phosphates of DNA.

A recent crystallographic study of MetJ repressor complexed with DNA by Somers and Phillips (*6*) finally revealed the antiparallel β ribbon as a DNA recognition motif, as was predicted from nuclear magnetic resonance studies of Arc repressor by Breg, Kaptein, and their colleagues (*7*). The crystal structure shows that the motif recognizes the major groove of double-helical DNA, bringing the twofold symmetry axes of the ribbon coincident with those of double-helical DNA (the upper option in Fig. 1C is assumed by the repressor dimer, as shown in Fig. 1D).

The MetJ repressor is a dimer of identical 104-residue subunits, binds two corepressors, *S*-adenosyl-L-methionine, noncooperatively, and recognizes each eight–base pair "met box" in six known operators (each operator contains two to five "met boxes") that negatively regulate the expression of the enzymes of the methionine biosynthetic pathway in *Escherichia coli*. In the crystal structure, an amino-terminal β strand of ten residues (residues 20 to 29) of one monomer and its twofold symmetry-related counterpart of the other monomer form a β ribbon. This ribbon binds to the compressed major groove of an operator DNA so that the two types (types a and b in Fig. 1B) of twofold axes of the ribbon coincide with both types of twofold axes of the DNA (Fig. 1A). The amino acid side chains on the DNA-facing side of the ribbon recognize the edges of the base pairs on the major groove or phosphate. Specifically, a set of hydrogen bonds are formed between $Thr^{25}$ and N7 of an adenine, $Lys^{23}$ and N7 of a guanine, and $Lys^{22}$ and a phosphate oxygen and another set of hydrogen bonds related by a twofold axis (Fig. 1E). If a β ribbon is bound to the minor groove, similar base recognition might be difficult because of the


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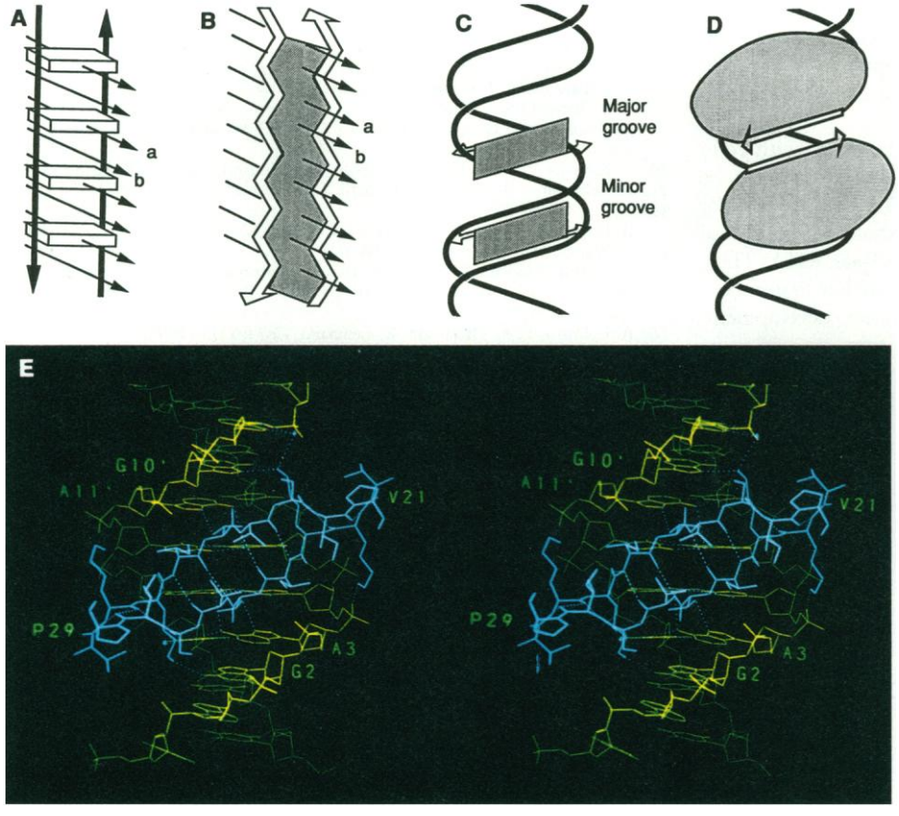


**Fig. 1.** (**A** to **D**) Schematic drawings of DNA, β ribbon, and their interactions. (A) An antiparallel double-stranded DNA. The double helix is unwound for simplicity to show two kinds of twofold symmetry axis, one (a) on each base pair and the other (b) between two adjacent base pairs. (B) An antiparallel β ribbon. The helical curvature has been removed to show two kinds of twofold symmetry axes, one (a) at each crest and the other (b) at each valley of a corrugated ribbon. (C) Two ways in which a β ribbon may bind to DNA, one in major groove (upper shaded parallelogram) and the other in minor groove (lower shaded parallelogram). There are two modes by which each interaction can occur, one in which the polarity of a DNA strand is parallel to that of the adjacent peptide, and the other antiparallel. Only one mode each is shown. (D) The crystal structure of MetJ operator-repressor dimer complex. The β ribbon is represented by a pair of antiparallel arrows, one each from two monomers (shaded). (**E**) A stereo pair showing the details of the interaction between DNA and a β ribbon in the crystal structure of MetJ repressor–DNA complex (*11*). The β-strands are in blue, DNA strands are in yellow, and hydrogen bonds are shown as dotted lines. [Courtesy of S. Phillips, University of Leeds, Leeds, U.K.]

shallow space of the minor groove. Thus, the major-groove binding mode is used for sequence-specific DNA recognition and the minor-groove binding mode may be used for nonspecific binding.

There are indications that the β-ribbon recognition may occur in other interactions, such as between DNA and the HU protein (*8*), IHF proteins (*9*), and Arc repressor (7) and between double-helical RNA and U1 proteins (*10*). These indications suggest that the β ribbon may be just as "popular" a motif as the helix-turn-helix and zinc finger motifs. Does each motif recognize a particular class of DNA sequences? More examples are needed to answer this question.

Looking into the details of interaction between the side chains of all three types of recognition motifs and the base pairs of the major groove, there appear to be no simple unified rules, such as every AT or GC base pair being recognized by a particular amino acid or structural motif. In fact, some base pairs within the binding regions are not recognized at all or recognized with ambiguity. Thus, the old question still remains: Is there yet another structural motif that is used in recognizing any DNA sequence without ambiguity by a set of simple rules? It is possible that such a motif or motifs exist but are not yet discovered, or existed in an early evolutionary period but have disappeared. If the latter is the case it should be possible to reconstruct these motifs. Such motifs may have tremendous value as tools in designing DNA sequence–specific probes for basic research as well as for medical and industrial applications. Are there yet other DNA recognition motifs still to be discovered? The answer probably is yes. After all, nature is a pluralist.

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11. Abbreviations: A, adenosine; G, guanosine; P, proline; V, valine.