Chiral Discrimination in DNA−Peptide Interactions Involving Chiral DNA Mesophases: A Geometric Analysis

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Abstract: The notion that "L-proteins interact more avidly (than D-proteins) with D-nucleic acids" (Hegstorm, R. A.; Kondepudi, D. K. *Sci. Am.* **1990**, *253*, 98−105) represents a direct extension to the concept of stereochemical complementarity. This notion, considered as a central tenet to theories concerned with the origin of biochemical homochirality, is however completely refuted by currently available experimental data that indicate identical DNA affinities towards L- and D-peptides. Here we show that chiral discrimination in nucleic acid−peptide interactions necessitates a substantial amplification of macromolecular geometric constraints. Thus, DNA molecules are found to exhibit a higher affinity toward L-peptides—but *only* under conditions that enhance their chiral identity by promoting the formation of cholesteric DNA mesophases. The results allow for new reflections on the concept of molecular complementarity, and indicate that spontaneously obtained chiral DNA mesophases might have played a key role in determining the terrestrial L-homochirality of proteins. Moreover, the observations provide an intriguing example to the notion that new properties of DNA molecules emerge in their condensed state, in which a higher structural order is imposed.

Introduction

The requirement for homochiral biochemistry is accounted for by two fundamental extensions of the "key and lock" hypothesis, namely the enantiomeric cross-inhibition of template-directed replication processes, and the structural complementarity between D-nucleic acids and L-proteins.[1] Yet, whereas enantiomeric cross-inhibition has been demonstrated,[2,3] the theoretically predicted[4] and quite generally accepted higher affinity of nucleic acids towards L-proteins than toward the corresponding D-enantiomers is experimentally refuted. Specifically, poly-L- and poly-D-lysines were found to exhibit identical DNA-binding parameters under conditions that allow reversible complexation.[5] Similarly, D-peptides were shown to be as effective as the L-polymers in promoting a *binding-dependent* nuclease activity.[6] In both cases, heteropolymers composed of both L and D residues exhibited a lower affinity toward DNA molecules than the homopeptides, suggesting that complexation depends upon a well-defined secondary structure of the peptide—but not upon its particular chiral sense.[5−7]

DNA molecules have been shown to possess a large intrinsic tendency to self-organize into a cholesteric mesophase or into tightly-packed cholesteric microdomains.[8−14] Although the ordered chiral organizations, which have been detected *in-vitro* as well as in living systems,[13,15] are likely to substantially affect the modes of DNA interactions, their scope and significance have not yet been fully recognized. Here we report that interactions of such cholesteric DNA mesophases with peptides are characterized by a prominent chiral discrimination, revealing a significantly higher affinity toward the naturally-occurring L-peptides than toward the corresponding D-polymers. This discrimination, uniquely exhibited by chiral DNA mesophases, is directly and specifically ascribed to a substantial enhancement of the DNA asymmetric properties and chiral imprint that accompanies the spontaneous formation of the cholesteric organization.

Geometric Model

We consider two packed DNA structures, each of which has been obtained through the folding of a right-handed double-helical DNA molecule into a superhelical rod-like conformation (Figure 3A). The superhelical rods are coupled to each other by a peptide (Figure 3B) which binds at the surface of the rod along helical trajectories whose handedness is dictated solely by the peptide chirality. Thus, a right-handed peptide forms a right-handed curve along the surface of the DNA rod whereas a left-handed peptide adopts a left-handed trajectory. The attraction between the peptide and the affinity curves acts to maximize the length of the peptide segment that is bound to the DNA and to minimize the unbound part. Hence the free segment, represented by a curve γ in space, is short, and we allow ourselves to ignore the intrinsic tendency of the peptide to bend in this region.

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The energy of the system is given by:

$$E = C_1\text{length}(\gamma) + C_0\int_\gamma k(s)^2\,ds$$

where s is the arc-length parameter along γ, $k(s)$ is the curvature of γ at s, and C_1 and C_0 are constants. The first term in the expression represents the affinity energy, and the second results from the intrinsic resistance of the peptide to bending. The DNA rods and the peptide are free to move in space to achieve the lowest energy configuration. Within such a configuration the rods will assume the shortest possible distance in order to allow the shortest and smoothest trajectory of the unbound segment γ.

Let ρ be the distance between the axes of the DNA superhelical rods and p1 and p2 be points on the axes of the two rods that are a distance ρ apart. We choose a coordinate system so that the x axis coincides with the axis of the top rod, p1 is at the origin (0,0,0), and p2 lies directly below it, thus p2 = $(0,0,-\rho)$. It follows that the axis of the bottom rod is orthogonal to the z axis. The trajectory on the top rod is a helix of the form:

$$\beta(t) = (x_0 + rt\cot\psi,\ r\cos t,\ r\sin t)$$

where r is the radius of the rod, t is the angular parameter along the rod, and ψ denotes the angle between the peptide trajectory and the axis of the rod. The point $\beta(t_0)$ on the trajectory β of the top rod is the point where the curve γ leaves the rod, hence $\beta(t_0) = \gamma(0)$, and γ is tangent to β at $\beta(t_0)$. The minimality of γ and the presence of a force that resists sharp bendings of the peptide requires that the projection of γ onto the $x-y$ plane would be a straight line segment; this claim can be rigorously proven by geometrical considerations.

We now claim that $\beta(t_0)$ is on the bottom half of β, where the z coordinate of $\beta(t)$ is non-positive, that is, $\sin(t_0) \le 0$. Suppose that this is not the case and $\sin(t_0) > 0$; then, the z coordinate of $\beta(-t_0)$ is negative. Since the z coordinate of the direction of β at t_0 is equal to the z coordinate at the direction of β at $-t_0$, we may lower the bottom rod together with γ, rotate them about the z axis, and translate them parallel to the x-y plane, so that the initial point and direction of the modified γ match with the location and direction of β at $-t_0$. In the new configuration the distance between the rods has increased. It follows that the increased distance can be used to reduce the energy of the configuration. This contradicts the minimality of the energy of γ, and establishes $\sin(t_0) \le 0$.

Let us estimate the angle between the axes of the two rods. We first look at the angle between the positive direction of the x axis and $P\gamma$ (the orthogonal projection of γ onto the xy plane). At the points where $\sin(t) < 0$ the angle between the x axis and direction of $P\beta$ is positive, and its maximal value is ψ. Thus the angle θ_1 between the x axis and $P\gamma$ is in the range $0 < \theta_1 \le \psi$. Identical considerations show that θ_2 (the angle between $P\gamma$ and the axis of the bottom rod) is in the range $0 < \theta_2 \le \psi$. Thus the angle $\theta = \theta_1 + \theta_2$ between the axes of the two rods is in the range of $0 < \theta \le 2\psi$.

The part of a right-handed spiral, whose axis lies in the $z = 0$ plane, that is below the plane (that is, $\sin(t_0) < 0$), has necessarily a direction that is toward the left of the axis, whereas for a left-handed spiral, this part will have a direction toward the right of the axis. This observation and the fact that the projection of γ onto the $x-y$ plane is a straight line segment indicate a minimal energy configuration where two rods form a left-handed screw when coupled by a right-handed spiral. The above presented considerations concerning the angle θ indicate that this conclusion holds as long as $\psi \le \Pi/4$. This is assumed to be the case since minimal bending of the peptide trajectory β requires small ψ values. A left-handed spiral will, on the other hand, couple the rods into a right-handed screw.

Materials and Methods

Nucleic Acids. Highly polymerized calf thymus DNA (type I, Sigma) was dissolved in 20 mM Tris (pH 7.5) and sonicated for 2 × 30 s (Ultratip Labsonic system, model 9100) at 4 °C. DNA fragments were loaded on a Sephacryl S-400 (Pharmacia LKB Biotechnology Inc.) column and eluted with 20 mM Tris (pH 7.5), 0.25 M NaCl. Fractions of 5 mL were collected and the size distributions of the DNA fragments were determined by electrophoresis on 0.75% agarose gels. Fragments of 3000−4000 base pairs were used. Samples were extensively dialyzed against 5 mM Tris (pH 7.5), 5 mM EDTA. DNA concentrations were determined by measuring absorption at 260 nm, using an extinction coefficient of 6600 M^{-1} cm^{-1}.

Peptides. Hydrobromide poly-L-lysines (degree of polymerization (DP) = 60, 115, 153), poly-D-lysines (DP = 48, 62, 72, 120), poly-DL-lysines (D/L, 1/1; DP = 65, 110), poly-L-(lys-ala) (lys/ala, 1/1; DP = 200), and poly-L-(lys-ala) (lys/ala, 3/1; DP = 195) were purchased from Sigma. Poly-DL-lysines (D/L ratio, 0.3/1, 0.5/1, 3/1; DP = 160−180), poly-L-(lys-ala) (lys/ala molar ratio, 0.3/1, 0.2/1; DP = 150), and poly-D-(lys-ala) (lys/ala ratio, 3/1, 2/1, 1/1, 0.5/1, 0.3/1; DP = 150−180) were synthesized according to the Leuchs method, using protected α-amino *N*-carboxy anhydride derivatives for solution polymerization. The desired mean length of the polypeptides was obtained through ultrafiltration and the size distribution was estimated by 12% PAGE. Dansylated derivatives of poly-L- and poly-D-lysines for fluorescence studies were prepared following the procedure givenin ref 16; dansyl to amino acid ratio (1/20) was estimated by using extinction coefficients for dansyl derivatives.

Circular Dichroism (CD) Experiments. CD spectra were recorded on a Jasco J500-C spectropolarimeter equipped with a DP-500N data processor, using 1-cm path-length quartz cells. Samples were prepared by mixing DNA (final concentration, 5×10^{-5} M in base pairs), salt, and polypeptides (final concentration, 5×10^{-5} M in amino acid residues) in water with the condensing agent (EtOH to a final concentration of 35% v/v); measurements were conducted 5 min after the addition of the EtOH to allow equilibration.

Fluorescence Studies. Fluorescence studies were conducted on a Shimadzu RF-540 spetrofluorophotometer, using 1-cm path-length quartz cuvettes. Excitation and emission slits were set at 2.0 nm. Samples were prepared under conditions identical to those used to prepare the CD samples.

Infrared Measurements. Condensed DNA and DNA−peptide pellets were prepared by centrifugation (Eppendorf, 14000 rpm, 10 min) of 1-mL solutions containing the polymers, salt, and dehydrating agent at the same ratio used to prepare samples for the CD experiments. Wet pellets thus obtained were placed between two calcium fluoride windows separated by a 5 μm Mylar spacer, and FTIR spectra were recorded on a Nicolet 510 FTIR spectrophotometer at 2 cm^{-1} resolution (200 scans). The presence of water was indicated by the broad OH-stretching band at 3500 cm^{-1}. Spectra shown are difference spectra of the DNA−peptide complexes against samples of packed DNA. Fourier self-deconvoluted spectra (up to a bandwidth of 33.4 cm^{-1} and a relative enhancement of 2.6) were further deconvoluted using the Voigt function.[17] The relative amplitudes of the amide I and II peaks obtained following this deconvolution were used for structure analysis.

Wide-Angle X-ray Scattering. Condensed DNA and DNA−peptide pellets were prepared by a gentle centrifugation (Dynac II tabletop centrifuge, 1000 rpm, 30 min) of 50-mL solutions containing the same ratio used to prepare samples for the CD experiments. Pellets immersed in supernatant were transferred into Li-glass capillaries without any attempt to pull fibers or to flow align the sample. Two dimensional diffraction patterns were collected (4 h, 19 °C) on imaging plates using a Searle camera with Ni-filtered Cu Kα radiation. The imaging plates were scanned with a He−Ne laser. Data were processed

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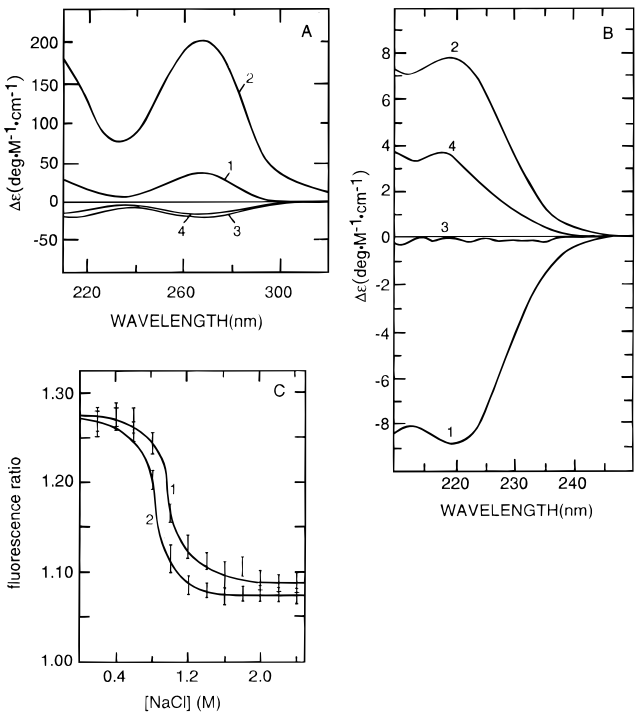

Figure 1. (A) Circular dichroism (CD) spectra of DNA−peptide complexes obtained under conditions that promote the formation of DNA mesophases (see under Experimental Procedures): 1, DNA; 2, DNA + poly-D-lysine; 3, DNA + poly-L-lysine; 4, DNA + a racemic mixture composed of poly-D- and poly-L-lysine. NaCl concentration in all samples was 0.8 M. Note the virtually identical spectra exhibited by the complexes obtained in the presence of poly-L-lysine and of the racemic peptide mixture (curves 3 and 4, respectively). (B) Detection of unbound poly-D-lysine following complexation of packed DNA with a racemic peptide mixture. 1−3, CD spectra of poly-L-lysine, poly-D-lysine, and a racemic mixture of both peptides, respectively; 4, CD spectrum exhibited by the supernatant obtained by precipitation of the DNA−peptide complexes formed in the presence of a racemic peptide mixture. DNA−peptide complexes were prepared as in part A; precipitation was induced by centrifugation on an Eppendorf centrifuge at 4000 g for 30 s. The enrichment of the supernatant by the D-peptide should be noted. Similar results were obtained when mixed peptides were used (see text). (C) Effects of the ionic strength on the fluorescence ratio of (1) DNA−poly-L-lysine, and (2) DNA−poly-D-lysine complexes prepared as indicated in part A but with dansylated peptides. The fluorescence values represent the ratio between the fluorescence of the peptides in the presence and absence of DNA.

using a home-made circular-averaging analysis program (E. J. Wachtel and R. deRoos, Chemical Services Unit, The Weizmann Institute of Science).

Results

Under conditions which induce the formation of chiral DNA mesophases, DNA molecules interact with positively charged peptides to form highly chiral supramolecular assemblies whose long-range asymmetry is dictated by the handedness of the peptides. Specifically, a left-handed supramolecular structure is obtained in the presence of the L-peptides, whereas D-peptides induce a right-handed long-range organization (Figure 1A, curves 2 and 3, respectively). The sense of the long-range handedness is indicated by the sign of the circular dichroism signals exhibited by the chiral complexes; negative non-conservative CD maxima have been shown to indicate a left-handed cholesteric organization whereas positive signals correspond to a long-range right-handed twist.[9,13,18] The most remarkable feature of the cholesteric DNA phase is its prominent chiral discrimination, that is, a substantially higher affinity toward the L-peptides. The discrimination is clearly indicated by three independent observations: first, the virtually identical optical properties exhibited by the DNA−peptide assemblies prepared in the presence of the L-peptides alone, and those characterizing complexes obtained in the presence of a racemic mixture, composed of L- and D-peptides in a 1/1 molar ratio (Figure 1A, curves 3 and 4, respectively); second, the large enrichment of unbound D-peptides in the supernatant that is obtained following the interaction of a racemic mixture of the peptides with the DNA (Figure 1B), and third, a fluorescence analysis of the DNA-bound peptide which reveals a significant difference in the salt-concentration dependence of the binding affinities of the L- and D-peptides (Figure 1C). Notably, the different binding affinities are specifically detected at the range of ionic strength in which chiral DNA mesophases are induced, being the largest at 0.8 M NaCl.

The particular chirality of the supramolecular DNA−peptide assembly, the manifestation of a chiral discrimination depend upon the properties of the peptides: the phenomena are detected in the presence of polylysines as well as of poly (Lys-Ala), provided that the Lys/Ala ratio is larger than 3, and only when the positively-charged peptides are longer than 60 residues; shorter peptides do not affect the optical properties exhibited by the DNA. Significantly, optically-pure peptides are not required in order to affect chiral discrimination: interactions between DNA and polylysines composed of both L and D residues in a random order exhibit the same unique patterns as those characterizing chirally-homogeneous polymers, provided that the peptides are enatiomerically enriched in a chiral ratio that is equal to or larger than 3. Thus, poly (L-lys-D-Lys) in which the L/D ratio is larger than 3 interact more avidly with a cholesteric DNA mesophase than a mixed peptide characterized by a L/D ratio that is equal to or smaller than 0.3. Mixed peptides composed of both L and D residues in a 1/1 ratio do not modulate the optical properties of the chiral DNA mesophase,[19] further supporting the previously mentioned notion that DNA−peptide complexation depends upon a well-defined secondary structure of the peptide.[5−7]

In order to unravel the factors responsible for the chiral discrimination, the various complexes were studied as a function of the ionic strength. Infrared analysis of the DNA−peptide complexes[20] reveals a conspicuous salt-dependent structural change of the DNA-bound peptides, undergoing a transition from a predominant (88−90%) α-helical conformation at 0.4 M NaCl into an extended flexible structure (66−70%) as the ionic strength is increased to 0.8 M (Figure 2). In addition, the bound peptide-to-DNA molar ratio significantly decreases upon the increase of salt concentration. X-ray scattering experiments indicate that throughout the studied range of ionic strength (0.4 to 1.0 M NaCl), the DNA molecules are tightly packed but reveal a salt-dependent transition from an hexagonal to a tetragonal arrangement (results not shown). Identical scattering patterns are exhibited by the different complexes at a given ionic strength, thus indicating that the basic structural features sampled by the X-rays are not affected by the chirality of the peptide. Fluorescence experiments conducted on the DNA−peptide complexes (Figure 1C) point toward a narrow range of ionic strength, centered at 0.8 M NaCl, at which a large difference in the binding affinity of DNA to the L- and D-peptides is detected. Notably, a higher ionic strength results

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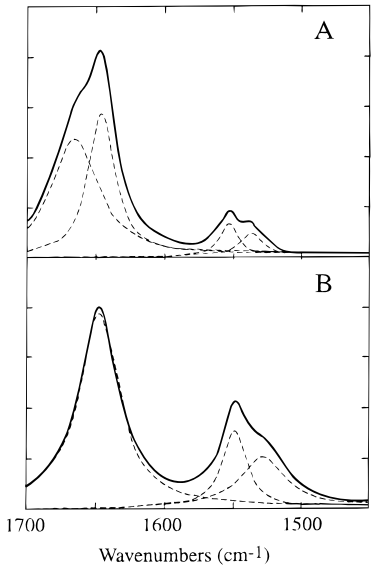

Figure 2. Difference FTIR spectra and their deconvolution (solid and broken curves, respectively) of DNA−poly-L-lysine complexes at (A) 0.4 M NaCl and (B) 0.8 M NaCl. Full lines are the experimental spectra; broken curves represent deconvoluted spectra. Details concerning the preparation of samples and the deconvolution procedure are provided under Experimental Procedures.

in the dissociation of the complexes, as indicated by the infrared analysis as well.

Discussion

At a relatively low ionic strength, discrete DNA double helices are presumably interspersed by α-helical peptide chains to form a non-chiral hexagonal arrangement. Such a symmetrical organization has been previously suggested for complexes in which the peptide-to-DNA molar ratio is relatively large.[21] As the ionic strength is increased, three processes occur: DNA spontaneously collapses into a cholesteric-like organization[8−15,18] within which the molecules have been shown to assume a tightly-packed rodlike structure.[8] At ionic strength values where chiral discrimination is detected, these rods are characterized by a superhelical right-handed conformation (Figure 3A), as indicated by the positive non-conservative circular dichroism signals (Figure 1A, curve 1). In addition, the increase of the ionic strength results in a conformational change of the DNA-bound peptides from an α-helical to an extended form, as well as in a decrease of the relative amount of peptide molecules that are bound to the DNA.

On the basis of these observations we suggest that whereas at low ionic strength DNA molecules are coupled through positively-charged α-helical peptide chains to form a non-chiral hexagonal organization,[21] highly asymmetric supramolecular assemblies are formed as the salt concentration is increased. Within these complexes the cholesteric-like DNA rods are coupled to each other by the conformationally-extended peptide. If sufficiently long, the peptide chains bridge the right-handed superhelical DNA rods such that their DNA-bound portion resides along "affinity trajectories" on the DNA. The sense of these trajectories is defined solely by the chirality of the peptide, being right-handed for L-peptides and left-handed for D-peptides. Notably, since the cholesteric-like DNA rods assume a *right-handed superhelicity* at the range of ionic strength in which chiral discrimination is observed, these rods are capable of specifically accommodating an extended—but still right-handed—L-peptide along their right-handed superhelical grooves. Within such an assembly, stabilizing DNA−peptide interactions are maximized. A trajectory defined by a left-handed D-peptide cannot fit into the right-handed DNA rod, resulting in substantially fewer binding interactions and hence in a relatively reduced affinity of the DNA molecules in a cholesteric organization toward D-peptides.

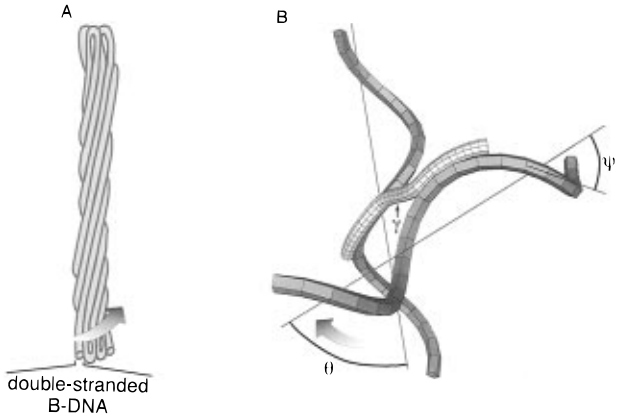

Figure 3. (A) Schematic representation of the proposed mode for DNA cholesteric-like intramolecular packaging.[8] A single right-handed double-stranded B-DNA molecule is depicted by a continuous tube-like segment that folds on itself into a tightly packed right-handed superhelical rod. The darker lines denote superhelical grooves within the tertiary conformation. The long-range right-handed twist is indicated by the non-conservative CD signal exhibited in Figure 1A, curve 1. (B) Optimized conformation of the chiral DNA−peptide complex. The darker curves represent *peptide trajectories* on two DNA rods; for a right-handed L-peptide, these trajectories are right-handed and hence may coincide with the rod's right-handed superhelical groove. The coupling peptide is modeled by the lighter curve. ψ is the angle between the peptide trajectory and the rod axis; γ represents the unbound segment of the peptide. θ denotes the angle between the axes of two DNA rods which are coupled into a left-handed supramolecular organization by a right-handed peptide. Note that the left-handed relationship between the two superhelical DNA rods represents a direct outcome of the right-handed trajectory of the peptide.

By using Onsager's approach it has been shown that helical rod-like species take up less space when packed in a twisted, cholesteric arrangement compared to a parallel, nematic organization, due to the larger excluded volume of the parallel arrangement.[22] Fitting of right-handed screws under tight packaging conditions will form, in general, a left-handed long-range helical configuration[23] (see Figure 6 in ref 22). A geometric analysis in which two rods are tightly coupled to each other by means of a right- or a left-handed spiral results in an identical conclusion. Thus, in a tightly-packed DNA−peptide assembly, a *left-handed supramolecular* organization of right-handed DNA rods is stabilized as a result of both the superhelical twist of the rods and trajectory assumed by the right-handed L-peptide (Figure 3B). Conversely, a left-handed D-peptide stabilizes a supramolecular assembly in which the supercoiled DNA rods are related to each other in a right-handed configuration, as indeed indicated by the circular dichroism results. This situation results not only in a poorer packaging of the right-handed DNA rods but also in fewer DNA−peptide binding interactions, as discussed above. Thus, both the optical properties exhibited by the DNA−peptide assemblies and the chiral discrimination can be directly and specifically ascribed to geometric constraints. This observation underlines the notion that the amplification of these constraints, associated with the

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DNA cholesteric organization and its intrinsically emphasized asymmetry, represents a crucial factor in the determination of the specific mode of the chirally-discriminating interaction between DNA and peptides.

An extended—yet still well-defined in terms of the handedness sense[4,24]—conformation of the peptides is deemed to be essential for their accommodation into the cholesteric superhelical DNA grooves. Indeed, such a conformation is shown to predominate at the ionic strength range in which chiral discrimination is manifested. Moreover, peptides which cannot assume an extended conformation, such as poly (Lys-Ala) with an Lys/Ala ratio lower than 3 (in which an α-helical structure is strongly stabilized), or chirally-heterogeneous peptides composed of L and D residues in equal or near to equal ratios, do not affect the DNA optical properties. The requirements imposed upon the coupling peptides (i.e. their ability to bind avidly and non-specifically to DNA and a significant conformational flexibility) limit the range of peptides that could be tested. The finding that a geometrical model which is based solely upon the chiral sense of the bridging peptides predicts the experimentally observed chiral selectivity points, however, to the generality of the phenomenon.

Chiral discrimination in interactions involving double-stranded DNA has been hitherto observed only in reactions with small, optically active intercalators.[25−27] Chiral selectivity is however reduced—or altogether eliminated—in DNA−polymer interactions, presumably due to the non-specific nature of the overlapping binding terms between polymeric species. In order to allow chiral selectivity in polymer−polymer interactions, a suppression of these non-specific terms,[5] and an enhanced asymmetry of one of the interacting polymers are required. Both requirements are met under the high salt conditions that promote the formation of cholesteric DNA mesophases and attenuate electrostatic interactions which dominate the binding of macroions. Thus, whereas a "two-dimensional" helical configuration is sufficient to affect chiral recognition between DNA and small ligands,[25−27] a higher order of a chiral identity, attained in this case by both the suppression of non-specific electrostatic terms and an enhanced cholesteric-related asymmetry, is required to counteract cooperative effects and hence to allow chiral selectivity in DNA−peptide interactions. As such, the observations presented in this study provide an intriguing example to the notion that new properties of the DNA molecule emerge in its condensed state, in which a higher structural level is imposed.[28,29]

It is generally held that the basic question that must be answered when terrestrial biochemical chirality is dealt with revolves around the predominance of D-sugars and L-amino acids over its classically equal alternative, namely L-sugars and D-amino acids.[30] By challenging the unanimously accepted notion of structural complementarity between polymers composed of D-sugars and L-amino acids, the considerations presented above raise an additional question hitherto unconsidered: why a biochemical homochirality based on D-sugars and L-amino acids rather than on D-sugars and D-amino acids? Notably, whereas the predominance of D-sugars might be accounted for by parity-violating weak nuclear interactions,[30−34] any initial excess of L-amino acids is likely to be negated by racemization processes that are particularly effective for amino acids incorporated in proteins.[35] We submit that if, as currently believed, the early biosphere consisted of D-nucleic acids, the L-based homochirality of proteins might represent a direct outcome of conditions that induced the formation of chiral DNA mesophases. This assumption is buttressed by the well-documented large intrinsic tendency of DNA molecules to form cholesteric mesophases, as well as by the observation that chiral discrimination in interactions involving such mesophases does not require optically-pure peptides. Moreover, due to its significantly enhanced asymmetry, the cholesteric DNA organization might act as an efficient chiral template in chemical polymerization processes of peptides, thus enabling a chiral selective elongation and hence a chiral enrichment, following the demonstrated initial selective binding. Indeed, enantiomeric enrichment has been shown to be particularly effective in polymerization processes of peptides that assume an extended conformation,[36] shown here to be essential for a chiral discrimination upon interaction with DNA.

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