These observations confirm that the γ-chain cross-link site is in the outer nodules of the trinodular fibrinogen molecule and that the mode of cross-linking is that diagrammed in Fig. 1. They also confirm that the outer nodule contains Fragment D, a large, globular proteolytic fragment of fibrinogen, since this fragment is known to include the γ-chain cross-link site (*7*). Finally, the images show that the molecules in the dimer are joined at the distal tips of the outer nodules and that there is little, if any, intrinsic bend at this junction.

In our preparation, the fibrinogen molecules are cross-linked in solution, in contrast to the cross-linking in situ of fibrin monomers in the fibrin fiber. It is therefore important to demonstrate that these fibrinogen dimers are cross-linked in the same arrangement as the molecules in the fibrin fiber. We find that after treatment with thrombin the fibrinogen dimers polymerize to form banded fibrin fibers indistinguishable from those formed from thrombin-treated fibrinogen molecules. We therefore conclude that the arrangement of the molecules in the fibrinogen dimers is the same as in the fibrin fiber.

Since the fibrin fiber is an extended three-dimensional polymer, there must be lateral contacts, probably of the staggered overlap type shown in Fig. 1, in addition to the end-to-end contact we have shown here. These lateral contacts are probably the ones activated by thrombin and may play the most important role in the initial stages of polymerization. The important conclusions of our work are that the end-to-end contact is the site of the γ-chain cross-link and that the linear arrangement of molecules connected through these contacts must be a feature of the molecular packing in fibrin fibers.

W. E. FOWLER
H. P. ERICKSON
Department of Anatomy, Duke University Medical Center, Durham, North Carolina 27710
R. R. HANTGAN
J. MCDONAGH
J. HERMANS
Departments of Biochemistry and Pathology, School of Medicine, University of North Carolina, Chapel Hill 27514

References and Notes

1. C. Hall and H. Slayter, *J. Biochem. Biophys. Cytol.* **5**, 11 (1959).
2. W. E. Fowler and H. P. Erickson, *J. Mol. Biol.* **134**, 241 (1979).
3. R. Doolittle, R. Chen, F. Lau, *Biochem. Biophys. Res. Commun.* **44**, 94 (1971).
4. B. Ly, P. Kierulf, E. Jakobsen, *Thromb. Res.* **4**, 509 (1974); H. Kanaide and J. Shainoff, *J. Lab. Clin. Med.* **85**, 574 (1975).
5. L. Lorand, D. Chenoweth, A. Gray, *Ann. N.Y. Acad. Sci.* **202**, 155 (1972).
6. Twenty-six molecules were measured. Since the standard deviation represents the real variation in molecular lengths and not the error involved in measurement, this is a sufficient number of measurements.
7. S. Pizzo, L. Taylor, M. Schwartz, R. Hill, P. McKee, *J. Biol. Chem.* **248**, 4584 (1973).
8. C. Kettner and E. Shaw, in *Chemistry and Biology of Thrombin*, R. L. Lundblad, J. W. Fenton, K. G. Mann, Eds. (Ann Arbor Science, Ann Arbor, Mich., 1977), pp. 129–143.
9. Supported by NIH grants HL 23454 (H.P.E.) and HL 20319 (J.H.) and by a grant-in-aid (R.R.H.) from the American Heart Association, with funds contributed in part by the North Carolina Heart Association.

2 April 1980; revised 30 June 1980

Deoxyribonucleic Acid Structure: A New Model

Abstract. *Models of deoxyribonucleic acid (DNA) having chain directions opposite to those of the Watson and Crick model offer strikingly different alternatives for DNA structures. Satisfactory models of the B and C forms of DNA have been built. Left-handed models readily form by twisting right-handed ones, and models can be bent into tight supercoils.*

There are two specific features of the widely accepted, generalized Watson and Crick model for DNA structures (*1*, *2*) which have not been well characterized. These are (i) the direction of each deoxyribophosphate chain and (ii) the handedness of the several double-helical forms of DNA. Consider two right-handed, intertwining helical chains asymmetrically disposed about a common helical axis as shown in Fig. 1. If each arrow represents the 5′ → 3′ direction in the deoxyribofuranose (sugar) residues in a DNA chain, two possible antiparallel chain configurations can be defined. As viewed with the helical axis held vertically, the chain on the left side of the minor groove can have the direction 5′ → 3′ either upward (configuration I, Fig. 1a) or downward (configuration II, Fig. 1b), while the chain on the right has the opposite direction. Although there is no mention of the justification, Watson and Crick used chain configuration I [see figure 7 in (*2*)]. In this initial report it is proposed that the family of model structures based on configuration II, which includes both right- and left-handed double helices, is more appropriate for representing DNA, in general.

Twenty-seven years ago, the structure of the high humidity B form of DNA (B-DNA) was elucidated (*1*, *2*) as a sodium salt. Some modifications to this right-handed, double-helical model have been published (*3*, *4*), but its more salient features have remained unchanged. X-ray diffraction analyses of crystalline or semicrystalline fibers of natural DNA offer evidence of other forms such as the A form (A-DNA) at lower humidity (*5*, *6*) for which a right-handed structure has been proposed (*7*), and the C form of the lithium salt (C-DNA) at still lower humidity, which is also postulated to be a right-handed double helix (*8*).

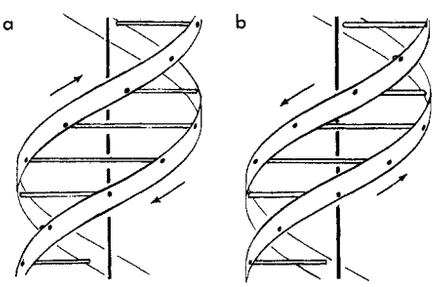

Fig. 1. (a) Configuration I and (b) configuration II of intertwining double-helical chains asymmetrically disposed about their common helical axis. The arrows represent the 5′ → 3′ deoxyribofuranose directions in DNA models.

These x-ray diffraction studies provide firm evidence for the double-stranded helical character of the original model, with the deoxyribophosphate chains on the outside of the helix. Other compelling features of the Watson-Crick model have been supported subsequently as follows. (i) The complementary purine and pyrimidine bases on the two strands being held in pairs by the specific hydrogen bonding scheme originally proposed is consistent with more recent x-ray studies (*9*) and (ii) the two chains being antiparallel has been confirmed by research on DNA replication (*10*).

Despite its major explanatory strengths, however, the original Watson-Crick B-DNA model was found to be consistent with neither density measurements nor x-ray intensity data (*5*), both of which strongly favor a more compact helical structure. In reaffirming these inconsistencies, x-ray data were interpreted using shortened bond lengths resulting from a postulated ionic compression (*3*). Other models (*4*, *7*, *8*) have required dihedral angles of 8° to 16° between the planes of the paired, hydrogen-bonded nucleotide bases. Although plausible, there has been a vague, lingering skepticism about the details of such DNA structures (*11*). Still other attempts

0036-8075/81/0116-0289$00.50/0

to account for the properties of DNA led to an unusual "side-by-side" model (*12*).

The reversed chain directions of configuration II may be the key for resolving the uncertainties in the structures of natural DNA. In fact, support for this hypothesis is provided by a report (*13*) on a left-handed structure for a small fragment of DNA which shows that it has chain configuration II (that is, the 5′ → 3′ direction is downward on the left side of the minor groove). Support is also provided by similar structures for other alternating DNA copolymers (*14*). To more fully demonstrate the feasibility and some consequences of the alternative chain directions, scaled space-filling models have been built. Two models, satisfactory from the standpoints of symmetry, stereochemistry, and consistency with experimental data, are described.

The dimensions of the models made from space-filling parts (*15*) are reported in scaled angstrom units (1.65 cm represents 1.00 Å). Each model contains 11 base pairs (bp), of which 6 bp represent A · T (A, adenine; T, thymine) and 5 bp represent G · C (G, guanine; C, cytosine). The A · T and G · C base pairs alternate along the axial direction, and all four bases occur once in each chain for every 4 bp. Two hydrogen-bonded bases remain coplanar in all models, and all glycosidic bonds have a *syn* conformation.

The model (B′ model) on the right in Fig. 2, a and b, was constructed after fixing the axial base pair interval at 3.40 ± 0.05 Å, which lies between 3.46 Å for the sodium salt (*3*) and 3.36 Å for the lithium salt (*4*) of B-DNA. The base planes of this right-handed model are approximately perpendicular to the helical axis. The chains make one complete turn for each 10 bp, giving a pitch of 34.2 ± 0.2 Å. Each phosphorus atom lies at a distance of 8.7 ± 0.3 Å from the axis of the helix, a value consistent with 8.5 Å estimated from equatorial x-ray diffraction intensities (*5*). The torsion angle about the C4′–C5′ bond in the sugar residues, which have a C3′ *endo* pucker, corresponds to a nearly *trans* conformation.

This B′ model is proposed as an alternative to the Watson-Crick structure for B-DNA. The two right-handed models (Fig. 2a) have strikingly different appearances. The overall diameter of the B′ model is narrower than the diameter of the other model, yet its gross dimensions are compatible with values reported for B-DNA (*3–5*). While the Watson-Crick structure is much more open and has a large external surface area, the B′ model is relatively smooth and compact with a wider major groove and an almost nonexistent minor groove. Figure 2b shows more details of the backbone structure,

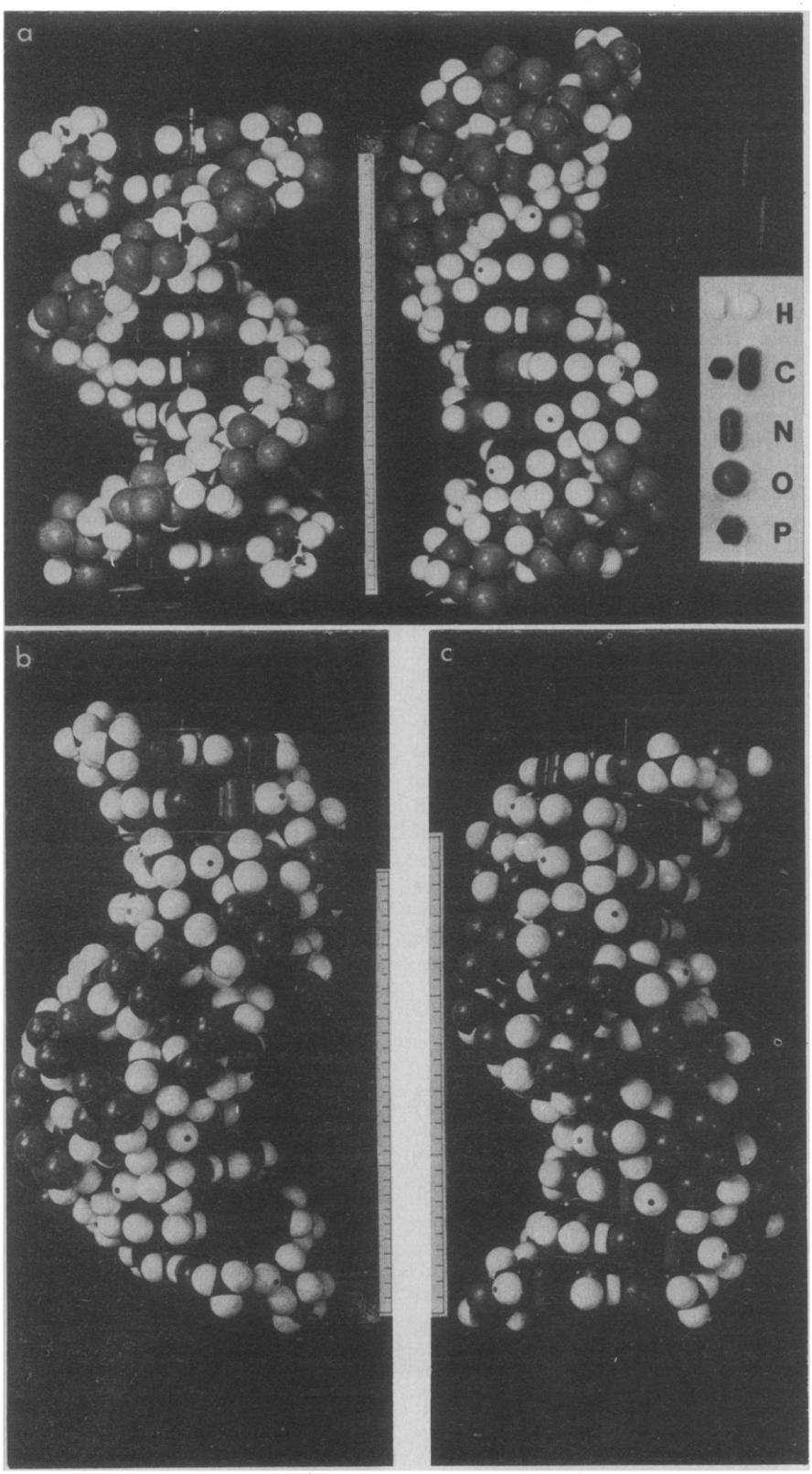

Fig. 2. (a) Two right-handed models of DNA built to the same scale. The commercial model (*15*) on the left corresponds to the original Watson and Crick structure with 10 bp and chain configuration I. The model on the right has 11 bp and chain configuration II. The C4 hydrogen on each pyrimidine base and the C8 hydrogen on each purine base is identified by a darkened dot in the model on the right in (a) and in (b) and (c). (b) An 11-bp model of right-handed DNA with chain configuration II. (c) An 11-bp model of DNA with left-handed chain configuration II. The scale in each case represents 30 Å.

including the close proximity of the two chains. The anionic phosphate groups in the adjacent chains are positioned favorably for cations to link the chains together through ionic bonds, in a way similar to the original suggestion by Franklin and Gosling (*6*). Anionic repulsion would surely cause the two chains to be further apart than shown, however.

Several interesting things occur when one physically twists an upper section of the B′ model in a left-handed or unwinding manner. The effect of a small twist is to readily open up a gap between the base pairs adjacent to the twisted and stationary sections of the model. This gap could easily accommodate intercalator molecules such as ethidium bromide or the phenoxazone chromophore of actinomycin D. Larger twists begin to result in the formation of a section of left-handed helix which is quite compatible with the adjacent section of right-handed helix. The complete transition from right- to left-handed helix or vice versa can be accomplished with only 2 bp in the transition region and in a rather confined space, such as in a hydrated crystalline structure.

The regular left-handed helix (Fig. 2c) which forms by twisting the B′ model was adjusted to have axial base pair intervals of 3.32 ± 0.05 Å, the value determined (*8*) for C-DNA. The planes of the base pairs are approximately perpendicular to the helical axis. The helix makes one complete turn for each $9^1/_3$ bp, resulting in a pitch of 31.4 ± 0.2 Å. The radial distance to each phosphorus atom from the helical axis is 9.4 ± 0.3 Å, a value not wholly inconsistent with 9.05 Å proposed from x-ray-diffraction studies (*8*). The sugar residues attached to pyrimidine bases have a C1′ *endo* pucker while sugar residues attached to purine bases have a C3′ *endo* pucker, and both have a nearly *trans* conformation about the C4′–C5′ bond. This model (C′ model) is suggested as an alternative structure for C-DNA. Nonetheless, a right-handed model with $9^1/_3$ bp per turn and acceptable dimensions for C-DNA can also be built. Like the B′ model, the C′ model is relatively smooth and compact, but has an even less distinct minor groove.

Significantly, the right- to left-handed B′ → C′ (also C′ → B′) transition is hindered in those chain segments attached to pyrimidine bases. The O2 atom on a pyrimidine base restricts the sugar rotation during the transition by interfering with hydrogens on C5′ and C3′ (or on C3′ and C5′ for C′ → B′) in the absence of "thermal" chain motions. Thus, each pyrimidine sugar is initially rotated counterclockwise about its glycosidic bond by about 70° less than a purine sugar during the transition. The resulting irregular *syn* chain pattern might lead directly to a form like alternating B- (*16*) or Z-DNA (*13*) in alternating copolymers, or perhaps to an irregular form associated with A-DNA. No regular configuration II models were found which have 11 or more base pairs per turn as in A-DNA (*6*, *7*); however, the study was in no way exhaustive nor were irregular chain models considered.

The configuration II family of models provides a topologically direct path for transitions between right- and left-handed DNA forms. This scheme is consistent with model 2 of Pohl and Jovin (*17*) on the cooperative, reversible, salt-induced transition in the synthetic DNA copolymer having alternating G · C and C · G base pairs. This transition is suggestively referred to as being between R and L forms, since the circular dichroism spectrum inverts in going from one form to the other. In the transition from right-handed B′-DNA to a left-handed form, the activation energy would be associated primarily with the disruption of the stacking interaction between one or more adjacent, intact base pairs.

One final promising result shows that the B′ and C′ models are consistent with the supercoiling of DNA which occurs in chromatin. An outward bend of about 60° toward the almost nonexistent minor groove is readily allowed in the chains lying between each adjacent base pair. The hinge axis is approximately horizontal and passes across the minor groove. As a result, a 180° supercoil bend of these double-helical models can be accommodated over the distance of a small number of nucleotides.

ROBERT C. HOPKINS
University of Houston at Clear Lake City, Houston, Texas 77058

References and Notes

1. J. D. Watson and F. H. C. Crick, *Nature (London)* **171**, 737 (1953).
2. F. H. C. Crick and J. D. Watson, *Proc. R. Soc. London Ser. A* **223**, 80 (1954).
3. M. Feughelman *et al.*, *Nature (London)* **175**, 834 (1955).
4. R. Langridge *et al.*, *J. Mol. Biol.* **2**, 38 (1960); S. Arnott and D. W. L. Hukins, *ibid.* **81**, 93 (1973).
5. R. E. Franklin and R. G. Gosling, *Nature (London* **172**, 156 (1953).
6. ———, *Acta Crystallogr.* **6**, 673 (1953); *ibid.*, p. 678; *ibid.* **8**, 151 (1955).
7. W. Fuller, M. H. F. Wilkins, H. R. Wilson, L. D. Hamilton, *J. Mol. Biol.* **12**, 60 (1965).
8. D. A. Marvin *et al.*, *ibid.* **3**, 547 (1961).
9. S. Arnott, M. H. F. Wilkins, L. D. Hamilton, R. Langridge, *J. Mol. Biol.* **11**, 391 (1965); M. A. Viswamitra *et al.*, *Nature (London)* **273**, 687 (1978).
10. J. Josse, A. D. Kaiser, A. Kornberg, *J. Biol. Chem.* **236**, 864 (1961).
11. J. Donohue, *Science* **165**, 1091 (1969).
12. G. A. Rodley, R. S. Scobie, R. H. T. Bates, R. M. Lewitt, *Proc. Natl. Acad. Sci. U.S.A.* **73**, 2959 (1976).
13. A. H. J. Wang *et al.*, *Nature (London)* **282**, 680 (1979).
14. S. Arnott *et al.*, *Nature (London)* **283**, 743 (1980).
15. Science Related Materials, Inc., Janesville, Wis. 53545.
16. A. Klug, A. Jack, M. A. Viswamitra, O. Kennard, Z. Shakked, T. A. Steitz, *J. Mol. Biol.* **131**, 669 (1979).
17. F. M. Pohl and T. M. Jovin, *J. Mol. Biol.* **67**, 375 (1972).
18. I thank Drs. W. Ronald Mills and Carroll Lassiter for advice and Mrs. Star Hopkins for help and encouragement.

25 June 1980; revised 9 September 1980

Hydra Mesoglea: A Model for Investigating Epithelial Cell–Basement Membrane Interactions

Abstract. *Isolated hydra mesoglea served as a suitable substrate for the attachment and spreading of hydra cells in vitro, irrespective of the species tested. Hydra cells did not attach and spread on substrates typically used for culturing mammalian cells. Mammalian and* Drosophila *cells attached and spread on plastic culture dishes but not on isolated mesoglea.* Xenopus *epithelial cells spread on both plastic and mesoglea. Because of the similarities of hydra mesoglea to vertebrate basement membranes, suggestions are offered for using mesoglea to study the interactions of epithelial cells with their basement membranes.*

The extracellular matrix influences a number of normal cellular and developmental activities, such as cell migration, differentiation, and proliferation (*1*, *2*). It has also been implicated in abnormal cellular behaviors, including neoplasia (*2*). The matrix exists as a primitive basement membrane in the freshwater hydra, where it is sandwiched between the two epithelial layers that make up the animal. Known as the mesoglea, it has physical and biochemical similarities to the basement membrane of vertebrates (*3*). We used isolated mesoglea to study the interactions of epithelial cells with an extracellular matrix in vitro.

Intact mesogleas totally free of adhering cells were isolated from cultures of *Hydra attenuata* (*4*) by a modification of the technique of Barzansky *et al.* (*5*): a 0.1 percent solution of the detergent Nonidet P-40 was substituted for Sarkosyl NL-97. The isolated mesoglea retained the hydroid shape of the polyp (Fig. 1a) and often exhibited a rectilinear fiber system (*6*) under phase-contrast mi-

0036-8075/81/0116-0291$00.50/0