

POSSIBLE SEPARATION OF INTERTWINED NUCLEIC ACID CHAINS BY TRANSFER-TWIST

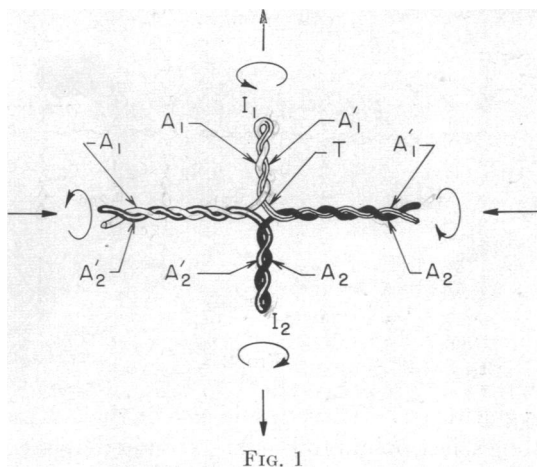
BY JOHN R. PLATT

PHYSICS DEPARTMENT, UNIVERSITY OF CHICAGO

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To separate the strands of a twisted rope it is not necessary to unravel them from the end. It is mechanically simpler and energetically easier to make a "transfer-twist," pulling the strands apart in the middle and letting each strand twist about itself. This suggests a method of separating two twisted intertwined helical molecules without expending excessive energy. It might be an alternative to the method suggested by Delbrück.¹

In particular, Figure 1 shows how transfer-twist might apply to intertwined duplicate nucleic acid chains like those in the Watson and Crick model of DNA.² The A_1 and A_2 halves of the two DNA chains are identical and are the complements to the other halves, A_1' and A_2' . Thus A_1 will intertwine perfectly with either A_1' or A_2' in a "lock-and-key" relationship but not with A_2 , and so on. If we now start with A_1 linked with A_2' and A_1' linked with A_2 and make a transfer-twist which pulls the chains apart at their centers of inversion, I_1 and I_2 , then an extensive motion in the direction of the arrows will cost almost nothing in energy or entropy. The energy of twist is transferred to the self-twisted strands, A_1-A_1' and A_2-A_2' . The bonds formed at the transfer point, T , are identical with those broken, the two processes perhaps even facilitating each other to give a very low activation energy.



The motive force to drive the twisting forward along the arrows in Figure 1 might come from a change of environment. Perhaps hydration or dehydration of the chains might start to be favored, leading to more hydrogen bonding, or less, per nucleotide. With hydration favored, water molecules might be added to each nucleotide as it separates from its usual bonds in passing the transfer point T in the forward direction. Once started, there would be a continual energy gain in going forward in the same direction and none in going backward. Other environmental alterations might favor similar changes in the chain structure and energy per unit length.

After separation of A_1-A_1' , the regeneration of another duplicate from it can proceed in from the ends in reverse fashion, with the self-twisted center untwisting as fast as suitable new fragments, a_3 and a_3' , grow and retwist around the ends.

The general features of transfer-twisting may be followed by manipulating a

two-strand piece of rope. A more elaborate model, constructed as follows, will show the lock-and-key relationship in duplicate chains. Take two equal lengths of round soft rubber rod (gaskets). Twist each tightly the same number of turns and fasten them flat side by side on a table. With a wet knife, slice both together from one end almost to the other, keeping the knife parallel to the table and roughly near the center line of the rods, but making arbitrary hills and valleys. The top halves of the two rods (A_1 and A_2) are then alike and are complementary to the bottom halves (A_1' and A_2'). The uncut ends are the centers of inversion (I_1 and I_2). When the rods are released, each will have its complementary halves tightly twisted together; but, when the cut ends are separated, each can be made to twist in a unique way with its complementary duplicate in the other rod, as in Figure 1.

It is possible that two intertwined complementary molecular chains may each be made of many segments like those in Figure 1. Opposite segments are duplicates but are oriented oppositely with their neighbors. Each segment may undergo transfer-twist about its own center, as suggested in Figure 2, provided viscous

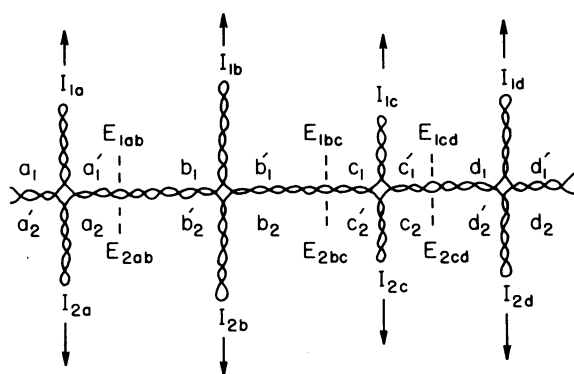


FIG. 2

resistance of the medium does not prevent the necessary twist of the transverse axes around the longitudinal axis. There would be no such twist of the axes if the segments were equal and were alternately right-handed and left-handed helices.

It is tempting to speculate on whether such a polysegment DNA chain might be a principal fragment of a chromosome. It has the property that regeneration could begin simultaneously at the numerous ends of

segments, E . These would also be the last points to separate from a duplicate and the easiest points to break. Hundred-segment chains, when almost ready to separate, would appear of the order of a hundred times shorter and a hundred times wider than the extended chains and might be microscopically visible.

A rope of three or more strands may be converted by transfer-twist into two or more self-twisted strands or groups of strands, but these are not in general identical in pitch or energy with the original rope. Likewise, a one-strand helix may be pulled out at one or more points into self-twisted side arms, but these will all be double helices. While transfer-twist could be important in the transformations of one-strand molecular helices, the special facility of two-strand transformations suggests that, for all suspected helices, special attention should be paid to possible two-strand interpretations of the evidence.

Besides its possible role in self-duplication and separation, transfer-twist might serve generally to shrink long chains and to pull distant units together and also to bring together two reactants if they were associated, say, with opposite ends of the same segment in Figures 1 or 2. It might facilitate creation of duplicates or complements even of nonhelical chain molecules if they could be associated with a trans-

fer-twist helix in a noninterfering way. And it might be a reversible method, largely freed from the randomness of thermal meanderings, by which one molecule, reversing the arrows in Figures 1 and 2, may "examine" its alien neighbors for identity or complementarity so that specificity is insured in any reaction with them.

I am indebted to Dr. Aaron Novick for much helpful criticism and discussion of these questions.

¹ M. Delbrück, these PROCEEDINGS, 40, 783, 1954.

² J. D. Watson and F. H. C. Crick, *Nature*, 171, 737, 964, 1953; F. H. C. Crick, *Sci. American*, 191, No. 4, 54, 1954. That each chain is self-complementary like our A_1-A_1' was suggested by Crick's remark that "the figure looks exactly the same whichever end is turned up." With or without this feature, a Watson-Crick "zipper" replication is copied by the present model, if one of their chains is identified with a fragment such as A_1 of Figure 1, points I_1 and I_2 being broken. But the separation process in Figure 1 and the polysegment replication and separation processes indicated in Figure 2 have no counterpart in their model.

ERRATA: HAMARTIEXÉRESIS AS APPLIED TO TABLES INVOLVING LOGARITHMS

In the article of the foregoing title appearing in these PROCEEDINGS, 40, 728-731, 1954, the following corrections should be made:

P. 729, line 24: Insert subscript 1 below symbol π at right.

P. 729, line 25: *For* 117724.51130 *read* 11 77245.51130.

P. 730, top line: A closing bracket,], should precede the = sign.

P. 730, second line below table: *For* = *read* = or \doteq .

P. 731, line 14 from bottom: *For* Duarte *read* Alliaume.

P. 731, line 12 from bottom: *For* 26823155 *read* 26823 155.

P. 731, bottom line: *For* 26090359 *read* 26090 359.

HORACE S. UHLER