

Double Helix Reveals New Twist

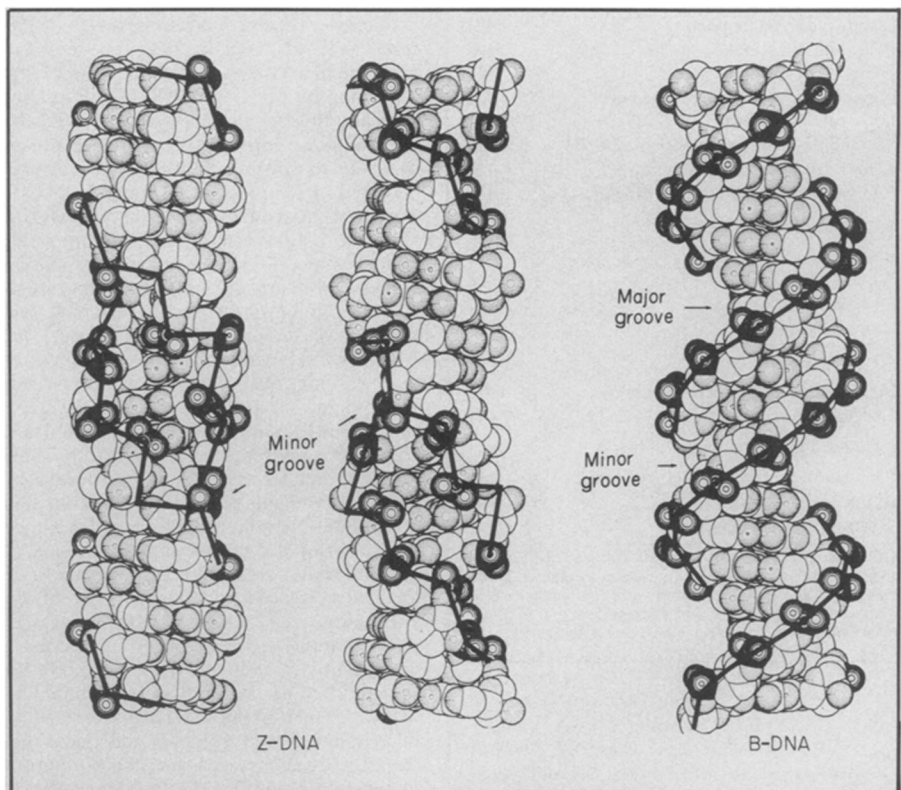
Stretches of double helix jaggedly twisting to the left may be scattered throughout a cell's more traditionally structured DNA, which curves smoothly, corkscrew-style to the right. This new picture arises from the first data that directly reveal DNA's structure at an atomic level.

The right-spiraling model of the genetic material was proposed 26 years ago by James D. Watson and Francis Crick when they first described DNA as a twisted ladder with pairs of chemical groups called bases linking chains of sugar and phosphate groups. Studies of long synthetic DNA molecules, resembling those in cells, have confirmed this structure using low resolution data interpreted with known lengths and angles of bonds between atoms. Research has turned up more than 20 variations on the right-twisting helix, such as molecules in which the bases are tilted at different angles or stacked more closely or in which the helix is wound more tightly than in the standard double helix, known as B-form.

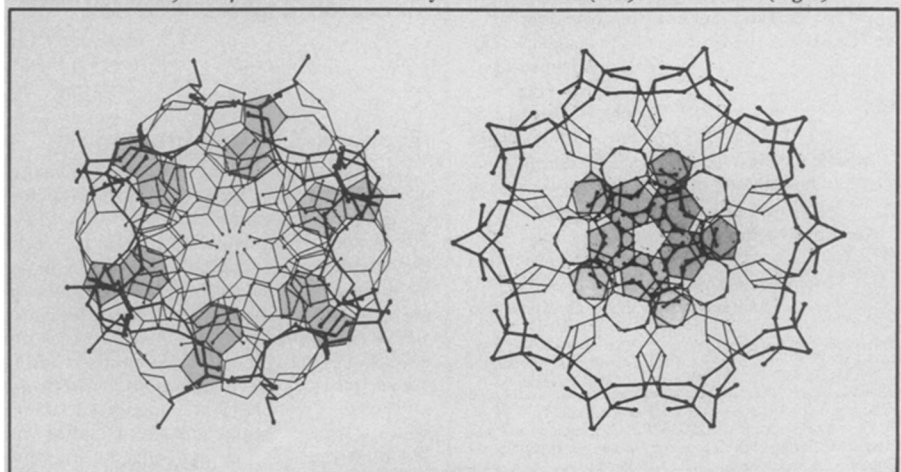
But now a dramatically different conformation for DNA is reported in the Dec. 13 NATURE. Andrew H.-J. Wang, Alexander Rich and colleagues present evidence for a DNA fragment, among the first to be studied at atomic resolution, being a left-handed double helical molecule. The Massachusetts Institute of Technology scientists worked with a stretch of DNA made up of six base-pairs in an alternating sequence of guanine (G) and cytosine (C). The segment of double helix was synthesized by scientists in the Netherlands. It was made into crystals by a new technique, and then the crystals were subjected to X-ray analysis. Because the crystals are less flexible than fibers of long DNA chains they gave higher resolution X-ray scattering (accurate to less than 1 Angstrom). The structure the scientists identified was clearly different from the standard right-handed spiral.

Another research team working at the California Institute of Technology has synthesized, crystalized and analyzed DNA fragments of four base-pairs, also alternating C and G. Richard E. Dickerson says that he and Horace Drew also see a left-handed structure, but one that is slightly different than that reported by the MIT group. Dickerson says different salt conditions are probably responsible for the variation and that he expects there to be several members of the left-handed spiral family.

The newly discovered conformation is not just a property of short DNA pieces. Within the crystals the DNA fragments stack to resemble longer molecules. In addition, Struther Arnott of Purdue University, who has done extensive analyses of the right-handed spiral conformations,



A zig-zag, left-spiraling shape for DNA, shown in two views above (Z-DNA), is determined by the bases in the molecule. End views (below) illustrate that bases (guanine of one strand is shaded) are positioned differently in the Z-form (left) and B-form (right).



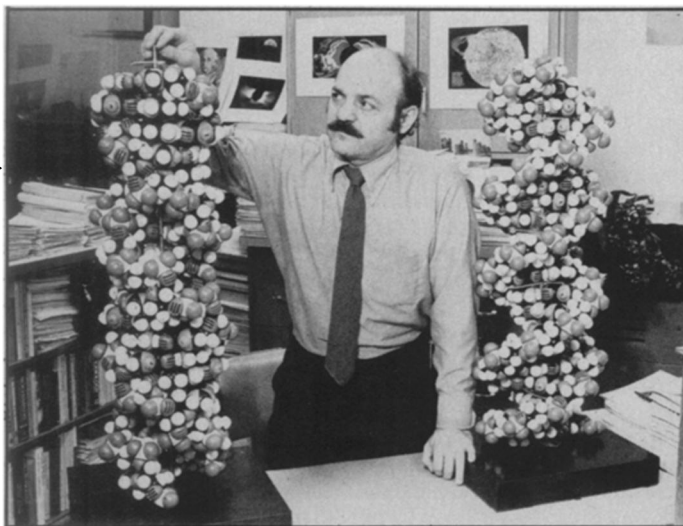
finds a left-handed structure in synthetic polymers almost a thousand base-pairs long that alternate G and C bases. Arnott has also examined other DNA sequences and finds that the left-handed spiral is not restricted to alternating G and C. The conformation doesn't seem to require any particular base, but rather an alternation of bases from the purine family (G and adenine) with bases from the pyrimidine family (C and thymine).

The significance of the left-handed spiral is still an open and fascinating question. Dickerson says that his group views

the GCGC fragment primarily as a practice run for the analysis of DNA with more biological significance. They are currently working on crystals of another tetramer, CCCG, and a 12- base-pair segment that includes the site at which an enzyme specifically cuts DNA.

Rich is more excited by the implications of the left-handed spiral. In this form, which he calls Z-DNA after the zig-zag course of the phosphate groups, the sugar-phosphate chains are closer together than in the B-form and the base pairs are on the outside of the helix in-

Rich suggests that most DNA in cells has the form of the right-handed double helix, on the right, but that sections of the molecule may be folded in the left-handed form he points to on the left.



MIT

stead of on the inside. Rich speculates that those base pairs are less protected in the Z-form, so they may be sites for attack by bulky carcinogens or for modification by cellular enzymes. In addition, the interaction of the Z-DNA with proteins may be altered because it has only a single groove, while B-DNA has two grooves. If different conformations of DNA dictate how the molecules interact with protein, they may control whether a gene is active or inactive at a given time in a cell.

Among biologically active sequences of

natural DNA, occasionally nature has preserved alternating sequences of G and C, the MIT scientists point out. One stretch of 20 such alternating residues is at the site where DNA replication begins in a rodent virus. Another sequence of eight alternating G and C residues is found at a mutational "hot spot" in the bacterium *Salmonella*. The overall shape of a stretch of DNA helix, dictated by the base-pairs it contains, may be a guide for protein-DNA interactions and thus control expression of genes. □

Cosmological anomaly: A trip you can't miss

Proponents of big-bang theories of the origin of the universe have usually worked from the assumption that the universe at the moment of origin was isotropic and homogeneous — that is, the same in all directions and with a smooth distribution of matter and energy throughout. There is a relic of that time present now, the famous three-degree blackbody microwave background radiation that pervades the cosmos, that could give us information on whether those assumptions are correct. If it is isotropic, so was the primeval universe.

The latest results of one of several groups of observers working on the question lead them to suggest a negative answer. Furthermore, they propose that there is a supercluster of galaxies in the constellation Virgo containing 30 to 40 percent more galaxies than might be expected to be in the volume of space they occupy, which stretches across 2 billion light years of the observable universe's total diameter of about 10 billion light-years or one percent of the visible volume.

The group of researchers is from the University of California and is led by George Smoot of the Lawrence Berkeley Laboratory. In 1978 they used a specially designed radiometer mounted on a U-2 airplane belonging to NASA and flown from Moffett Field, Calif., to measure the temperature of the cosmic background

radiation as the plane flew various paths over California. The idea was to see whether the temperature was exactly the same in all directions. It wasn't. Along a line oriented toward the constellation Virgo the radiation was a few millidegrees warmer in one direction than in the other.



John Douglas

George Smoot and his CBR radiometer.

This could be interpreted to say that the earth, the solar system, our galaxy, etc., were moving toward Virgo at a speed of about 600 kilometers a second, moving, that is, through the blackbody radiation and in addition to the expansion of the universe. Having seen this, the group decided to do a similar series of observations in the Southern Hemisphere to be sure the effect was general and not some strange Northern Hemisphere oddity. Now those results are in, and they tend to agree.

The most easily imaginable cause for this kind of motion would be the gravitational attraction of a large, dense concentration of matter. Hence the hypothesis of hypersupercluster. There are other possible explanations for a temperature anomaly in the blackbody radiation, but they tend to be more exotic. This one is supported by some other observations: Large scale structure in the direction of Virgo is indicated by X-ray astronomy studies done by A.C. Fabian of Cambridge University and R.S. Warwick of the University of Leicester. Counts of faint galaxies by J.A. Tyson and J.F. Jarvis of Bell Telephone Labs have yielded evidence of a northern supercluster of galaxies—that is, in the general neighborhood of Virgo.

The existence of such a supercluster is mind-boggling, according to Smoot. He points out that there has not been enough time since the beginning for such an agglomeration to gather together out of an originally homogeneous universe. Therefore the clump must have been present at the beginning, a lump in the leaven, so to speak. But that's not the end of it. Supposing that one such supercluster can exist, why not more? Astronomers always like to generalize: A new kind of object is suspected to be a member of a whole new class. This Virgo supercluster may be the only one we can easily detect from where we are, but, says Smoot, "if we have one such concentration of matter, there are probably others."

So the universe may have been generally lumpy at the start. Other measurements have suggested this. If the evidence gets too strong that the beginning of the universe was more like chicken soup with dumplings than a smooth gruel, it could be disturbing to most cosmologists. They prefer a smooth beginning, because their equations develop more easily from there. Given pervasive lumps, they may have to go back to their computer terminals. When they do, they will find themselves rearranging more than cosmology. An unhomogeneous universe could make serious problems for current efforts to derive a unified field theory in particle physics.

And a final note for science fiction freaks. The speed of approach toward Virgo though zippy presages a very long trip. Even if, in some later aeon, we should crash into the supercluster, all we would be likely to notice would be a rearrangement of galaxies in our sky. □