consequences. For example, the curvature might distort the DNA so that some of the factors that regulate gene transcription are encouraged to bind, while others are not.

The distribution of the contacts between DNA and protein also allows researchers to envisage how a large enzyme complex like the one that replicates DNA can travel along the DNA strand without completely displacing the nucleosome. "The DNA is like a piece of Velcro on the outside of the histone octamer," explains Richmond. An enzyme could displace 30 or 40 base pairs of DNA from the protein at a time, but when it has passed, that DNA can stick back to the very same nucleosome, so the histone octamer may never be totally removed from the DNA.

Previous biochemical studies had indicated that the histone tails extend beyond the DNA. The new structure provides a more direct view of the position of the tails, which may play an important role in making contact with adjacent nucleosomes as the chromatin folds back on itself to form the higher order structure needed to pack all the chromatin into the nucleus.

That folding would make large stretches of the DNA inaccessible when the genes encoded in them need to be kept inactive. The structure suggests how active genes become accessible. The projecting histone tails contain some of the sites that are modified by histone acetyl transferases—the enzymes that have been hot news in the past couple of years because of their role in regulating transcription. By adding acetyl groups to the tails that poke out, these enzymes would almost certainly disrupt a higher order structure and open up the chromatin to infiltration by the transcriptional machinery.

An atomic-level description of the nucleosome core particle is a tremendous technical achievement in itself but is only the first step toward understanding chromatin structure. To see the structure of two particles connected by the linker DNA would be nice, Richmond says. The structure of three particles, the central one wrapped by uncut DNA, might be even better. But the real goal is "to see what two or three turns of a higher order structure looks like." With luck, this next quest will not take another 2 decades.

–Carol Featherstone

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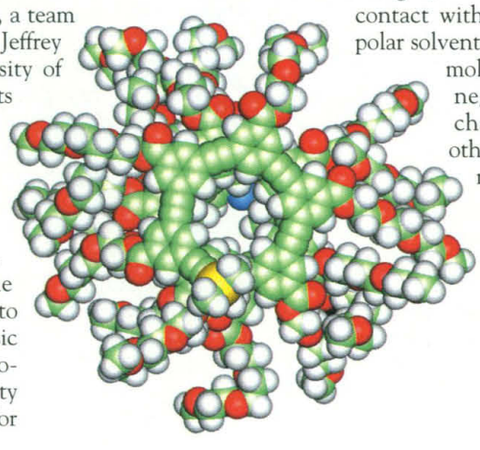
ORGANIC CHEMISTRY

Polymer Folds Just Like a Protein

The exact linear arrangement of amino acids in a protein is not the only thing that determines how it behaves: Also key is the protein's precise three-dimensional shape. For decades, chemists have sought to understand what forces make a string of amino acids bend and curl into a particular configuration, with the hope of one day making their own synthetic polymers that can duplicate the functions of natural proteins. But they have had a hard time getting anything other than a protein to fold in solution.

Now on page 1793, a team led by organic chemist Jeffrey Moore of the University of Illinois, Urbana, reports achieving this goal with a polymer they made from repeating units of a hydrocarbon molecule called phenylacetylene. They found that the polymer readily coils into a helix, one of the basic folding motifs of proteins, and forms a cavity that can be modified for different purposes.



NELSON *ET AL.*

21st century chemistry. This spontaneously folding polymer may be the wave of the future.

Other organic chemists are enthusiastic, because it is a new addition to the small number of synthetic polymers, sometimes called "foldamers," that they have coaxed into folding. The achievement shows "Mother Nature doesn't have a monopoly on folded structures," says Brent Iverson, a chemist at the University of Texas, Austin. "This is a very important new direction for chemistry."

Researchers hope that the work will point the way to new types of tailor-made complex molecules that have the specificity and self-organizing capabilities of proteins. If they can be made to catalyze chemical reactions as the body's own enzymes do, these tailor-made molecules could be useful as industrial catalysts or as biomedically active substances that would not degrade as easily as proteins themselves.

The new results may also shed light on a long-standing disagreement among protein chemists. Some chemists think that proteins in solution fold to protect those amino acids that are uncharged, or "hydrophobic," from contact with water, a so-called polar solvent because each water molecule carries partial negative and positive charges. In contrast, others have argued that relatively weak links between a hydrogen atom and two adjacent atoms are responsible for a protein's kinks and curls. But the phenylacetylene polymer folded even though it has no such hydrogen bonds, showing that at least in this case "you can drive the ordering and folding just using a hydrophobic effect," says Moore's collaborator Jeffery Saven, now at the University of Pennsylvania, Philadelphia.

To test his ideas about protein folding, Illinois physical chemist Peter Wolynes teamed up with Moore 2 years ago to make a nonprotein polymer that could fold like a protein. For their polymer building block, they chose a molecule, phenylacetylene, that has no nitrogen or oxygen atoms in its backbone and thus lacks the key hydrogen-bond ingredients. Computer modeling by Saven and Wolynes indicated that if a chain had at least eight of these uncharged, ring-shaped phenyl groups, it would be able to twist into a helix and thereby avoid contact with a polar solvent.

The team then synthesized a selection of polymers, ranging in length from two to 18 links, and dissolved them in different polar organic solvents. Using several different spectroscopic techniques, the team found that chains 10 links or longer did form helices as predicted. The Illinois team also showed that the new foldamer, like proteins, can be made to fold, unfold, and then refold.

Changing the solvents also confirmed that hydrophobic-like forces were responsible for the folding. The more polar the solvent, the "stronger the induced organization," Moore says, adding: "This is a step along the way of understanding the rest of protein behavior."

Not everyone is convinced, however, that this polymer reflects what is going on in proteins. "The network of forces [in the polymer] is very clearly different from [the forces] in a protein," comments organic chemist Sam Gellman of the University of Wisconsin, Madison. He points out that proteins are a mosaic of uncharged and charged amino acids, and that the latter could also help drive folding.

But even if foldamers aren't complete protein mimics, researchers hope they will be able to duplicate the sophisticated chemistry that goes on in cells. "This is a field in which almost anything you can imagine, you can try to do," Gellman predicts. "For chemists, it will be the challenge of the 21st century."

–Elizabeth Pennisi