the size of the sample to about 1 or 2 milligrams. But placing the magnetic field around the sample means that conventional, well-developed light sources can be used. One of the most difficult problems with the type 2 instrument has been the development of a light source that can operate reliably within a high magnetic field (on the order of 15 kilogauss).

Hadeishi and his colleague Ralph McLaughlin have recently developed a new light source, called the magnetically confined lamp, that seems to have solved this problem. And because the magnetic field is around the light source, the type 2 instrument can accommodate much larger samples, even larger than those that can be accommodated in conventional atomic absorption spectrometers. Because detection is proportional to the absolute amount of an element in the sample, the type 2 instrument can often detect smaller concentrations than either the type 1 or the conventional instrument.

The chief advantage of ZAA spectrometry—a direct result of the ability to monitor an element in the presence of high background absorptions—is that sample preparation is greatly simplified. In conventional atomic absorption spectrometry, the sample frequently must be put into solution or otherwise manipulated to increase the concentration of the element being monitored or to decrease the concentration of extraneous smoke-producing materials. With ZAA spectrometry, according to McLaughlin, this is generally not necessary. Most of the time, he says, an untreated sample can simply be put into the graphite cuvette and vaporized. This simple procedure greatly reduces the possibility that the sample might be contaminated during preparation, that the element to be analyzed might not be completely dissolved, or that it might be absorbed onto the walls of the glassware.

ZAA spectrometry thus has a large number of potential applications where the ability to detect an element in the presence of a high background absorption makes it clearly superior to conventional atomic absorption spectrometry. One good example is the analysis of trace elements in seawater. Extensive treatment of seawater samples prior to analysis is generally required for atomic absorption spectrometry because the sodium chloride in a sample generates too much smoke for accurate analysis. ZAA spectrometry, however, is able to compensate for the background interference produced by the sodium chloride, so that almost all analyses can be performed directly.

In a similar fashion, analyses can be performed directly on blood and urine samples. The technique can also be used, for example, to analyze trace elements in steel. This generally cannot be accomplished with conventional atomic absorption spectrometers because the numerous spectral lines of iron generally produce too high a background absorbance. Among the other substances that Hadeishi's group and NSI have been able to analyze without prior treatment are cow's liver and other tissue samples, coal, ash, ceramic pots, geological samples, sediments, and oil shale.

Hadeishi and McLaughlin and the investigators at Hitachi have done most of the initial work demonstrating the utility of both types of ZAA spectrometry. One other investigator in this country who is familiar with the instrument's potential is James Westhoff of the Corps of Engineers' Waterways Experiment Station in Vicksburg, Mississippi. Westhoff has a prototype type 2 ZAA spectrophotometer built by NSI specifically for the measurement of mercury, selenium, arsenic, and cadmium. The instrument is used at the station to detect these metals in industrial wastes, urban waste treatment products, and solid wastes. It is also used to measure trace concentrations of these elements in river waters and sediments and to determine the uptake of metals by plant tissue.

Westhoff says that many of the samples studied at the station require much more extensive prior treatment when analyzed by conventional atomic absorption spectrometry than when analyzed by ZAA spectrometry. All of his experiences, Westhoff says, point to the great utility of ZAA spectrometry and to the advantages of its superior background correction capabilities relative to conventional instruments.

ZAA spectrometry does not solve one of the major problems that is inherent in atomic absorption spectrometry, the extraneous formation in the cuvette of molecular products that interfere with measurement of the desired element. It does, however, partially solve a second problem, the inability of atomic absorption techniques to assay more than one element at a time. The great speed of measurement achievable with ZAA makes it possible to assay a large number of elements sequentially in about the same time that would be required for other techniques that assay them simultaneously, such as nuclear activation analysis or x-ray fluorescence. In any case, the greater sensitivity of ZAA spectrometry compared to these other techniques may still make it desirable in many cases even if sequential analysis should take longer. It thus seems safe to say that ZAA spectrometry will find its own niche in the instrument world and will prove to be a valuable analytical tool.—THOMAS H. MAUGH II

Bacterial Genetics: Action at a Distance on DNA

Conventional views of the structure and function of DNA molecules are being extended by some recent studies of bacterial DNA. Researchers have now found evidence of "action at a distance" on these molecules. That is, a protein will bind to the DNA at one spot and will affect gene expression at a position some distance away. How this can occur is a matter of some speculation, but the existence of the phenomenon indicates that DNA is far from the "inert" molecule assumed by many models in molecular biology.

In many cases, expression of bacterial genes is controlled by regulatory proteins that bind to the DNA molecule near the gene. (A gene is expressed when the protein it codes for is actually produced by the processes of transcription and translation.) According to Robert Wells of the University of Wisconsin at Madison, the notion of action at a distance comes down to the question of the role of DNA in the control of gene expression. Wells asks, "Is DNA an inert molecule on which interesting [regulatory] proteins act, or does the DNA itself play an active role?" Wells's long-held belief that DNA plays an active role was not only considered a maverick idea but was also found to be very difficult to demonstrate.

The problem is that naturally occurring DNA is such a large molecule that it is hard to search for long-range effects. For several years, Wells, John Burd of Miles Laboratories, Inc., in Elkhart, Indiana, and their associates have used short strands of synthetic DNA molecules to demonstrate, as Wells puts it, that "one end of the molecule knows

what is happening at the other end." But these results left open the question of whether such effects occur in DNA in living organisms. Now Jay Hirsh of the California Institute of Technology and Robert Schleif of Brandeis University report that action at a distance occurs on bacterial DNA. Although the distance over which the action occurs is not enormous—it encompasses about one-tenth the size of a typical gene—it is far greater than any previously observed in naturally occurring DNA.

Schleif explains that their findings were made possible by recent technical improvements that allowed them to take high-resolution electron micrographs of proteins bound to specific sites on DNA. These advances include both techniques in microscopy and molecular biologists' new-found ability to obtain, by cloning, pure DNA segments encompassing one or a few known genes. If these short strands are not isolated, the DNA looks like a mass of spaghetti, and investigators have no hope of identifying particular genes and the binding, or lack of binding, of particular proteins near them.

Hirsh and Schleif studied four genes on *Escherichia coli* DNA concerned with the metabolism of the sugar arabinose. These genes, together known as the arabinose operon, consist of a regulatory gene (araC) and three genes coding for arabinose-metabolizing enzymes (araB, -A, and -D). In addition, a regulatory protein can cause or prevent gene expression, depending on biochemical conditions. In the presence of arabinose, the araC regulatory protein, which is coded by the araC gene, binds near araB and induces the transcription of the genes coding for the three arabinose-metabolizing enzymes. In the absence of arabinose, the araC protein binds near the araC gene and represses the synthesis of these enzymes.

The araC gene is physically separated by a distance of 150 base pairs of DNA from the three other genes of the arabinose operon (which are mutually adjacent). Expression of araC is controlled separately from that of araB, -A, and -D, and the araC gene is oriented in the direction opposite from that of the other arabinose genes. That is, transcription of araC begins at the far right-hand end of the gene and proceeds leftward, whereas transcription of araB, -A, and -D is from left to right (Fig. 1). Because of the distance between araC and araB—the closest of the other three genes to araC—the regulatory proteins binding at the beginning of araC would not be expected to directly affect the expression of araB, -A, and -D, nor would proteins binding at the beginning of araB be expected to affect the expression of araC. Yet this is exactly what Hirsh and Schleif found. According to Schleif, there is a distance of 100 base pairs from the edge of regulatory proteins binding near araC and the place where transcription of araB is initiated. Similarly, the distance between proteins binding near araB and the start of araC is about 100 base pairs. Thus, there are two examples of action at a distance in the arabinose operon.

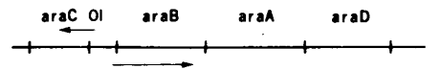

Fig. 1. The arabinose operon. Transcription of the gene araC begins in the region OI. Transcription of araB, -A, and -D begins in the I region.

These investigators first discovered action at a distance in the arabinose operon when they studied how the expression of araB, -A, and -D is turned off in the absence of arabinose. They found with electron microscopy that, in order for this repression to occur, proteins, including araC, must bind at or near the initiation site for transcription of the araC gene (Fig. 2).

Next, Hirsh and Schleif found that proteins binding near araB affect the expression of araC. They discovered that when RNA polymerase, the protein that copies DNA into RNA during gene expression, binds at the initiation site for transcription of araB, -A, and -D, the expression of araC is repressed. They showed that this action at a distance is mediated by the DNA between araB and araC since, when they cleaved the DNA between the sites, the effect disappeared and araC was expressed at the same time araB, -A, and -D were expressed.

These findings of long-range interactions along DNA molecules are unprecedented, and investigators are only beginning to consider how they may occur. Hirsh and Schleif propose three possible explanations. First, binding of proteins at one position may affect the tilt of the nucleotide bases that make up DNA and thereby prevent other proteins, such as those necessary for transcription, from binding within a length of several hundred nucleotides. Second, the DNA may form a hairpin loop when a protein binds, thereby bringing two distant points into contact and permitting binding at one point to affect gene activity many nucleotides away. Finally, action at a distance could be only an illusion. The protein could bind initially at one position and slide down the DNA to another position at which it would affect gene expression.

The apparent demonstration of action at a distance on bacterial DNA has profound implications for theories in molecular biology. It indicates, for example, that regulatory proteins may have multiple effects—many different proteins may all be involved in regulating a set of genes, or many sets of genes may be regulated by a single protein. It indicates that mechanisms of control of gene expression may be more subtle than previously imagined. And it indicates that molecular biologists are still far from understanding how genes are regulated, even in bacteria—the simplest organisms to study.—GINA BARI KOLATA

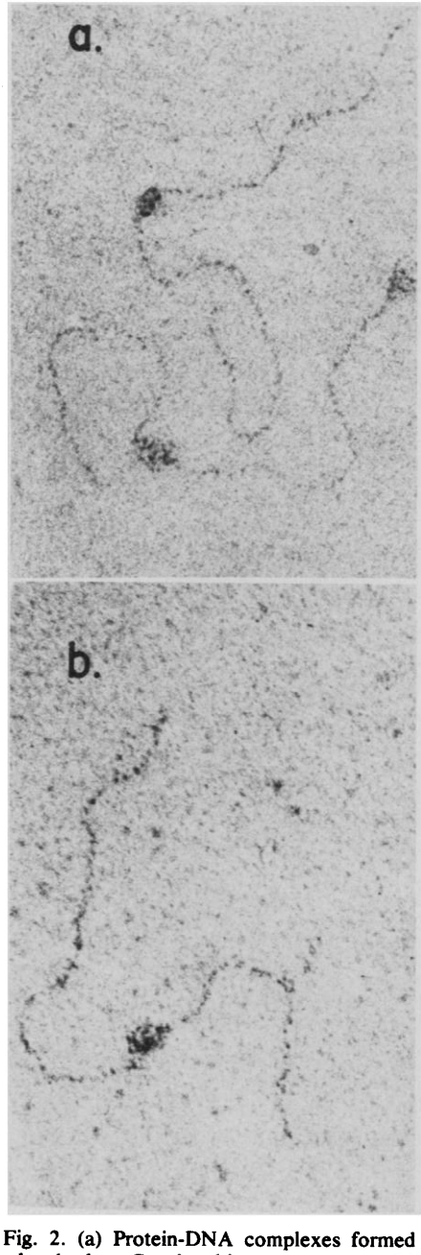

Fig. 2. (a) Protein-DNA complexes formed when both araC and arabinose are present. (b) Protein-DNA complexes formed when araC is present and arabinose is absent. (Source: Robert Schleif, Brandeis University)