A Framework for Environmental Thinking

A critical scientific look at the biotechnology industry

by Barry Commoner, Ph.D.

Pesticides are an enormously important signal of the way in which we have misused our knowledge of chemistry, in order to place very severe strains on living things — and doing it in a way that is dangerous, because of the ignorance that is involved. We know a lot about the chemistry, but we do not know enough about living things to really be able to predict what the chemistry is going to do. I want to run through with you the history of this predicament because it is not only important to know where we came from, but it is a very important indicator of where we are going, if we do not do something about it.

Synthetic, Organic Compounds: Their impact on Living Things

Take the example of DDT. A chemist made DDT by putting together various atoms around a network of carbon atoms. He had to be very skilled to do it because the chemistry of carbon is very complicated. It took chemists until 1823 to learn how to make a very simple carbon compound in the laboratory. It happened to be urea, which is extremely simple. Over the years, chemists have learned how make bigger and more complicated natural chemicals, things that occur in life. Well, DDT was made, but it does not occur in any living thing. By the time this work had been done, and thousands of Ph.Ds had been granted to people told, "Here's a molecule that's made in a plant, learn how to put it together in the laboratory," enough was learned by doing. People knew the rules and regulations of how to put all these complicated atoms together. Then, they began to put together atoms that did not occur in nature. If you went to any chemist's laboratory in a university, there was a room, usually dark, with bottle after bottle of the products of Ph.D theses. A whole series of unnatural chemicals, that were sort of mementos, had been created by people. A science had been built up that had taught chemists how to make these things in unnatural forms. One of the things on the shelf was DDT. Every now and then, people would take something off the shelf and expose it to living things. As you know, DDT turned out to be a way of killing insects.

Jay Feldman, executive director, Beyond Pesticides/NCAMP introduces Dr. Barry Commoner at the Eighteenth National Pesticide Forum *Beyond Pesticides: Solving a Public Health Crisis*, April 8, 2000 in New York City.

During World War II, an enormous amount of DDT was produced and used very widely. I have to make a confession. I had something to do with the dispersion of DDT during WWII when I was in the Navy. What I was told was, "Here's this stuff. It's dissolved in fuel oil and a very tiny drop of it will kill a mosquito. You have to do it quickly because we're going to invade the islands in the Pacific and there are mosquitoes that threaten the health of the marines when we land." That is all I was told. We began to work to do that. One of the experiments we had to do was to try it out in the jungle of Panama. I learned that it does more than kill mosquitoes. It makes snakes very nervous. By the time we had sprayed the jungle, they were all over the road. I also learned that DDT kills fish. We were told to help out an installation up in Delaware and the flies were bothering them, so we sprayed it. Two days later, they said, "You had better come back," because the flies were all over the place from the dead fish that the DDT had killed.

What I'm saying, very simply, is this. Here was a piece of chemistry, to make something that did not occur in nature, that kills insects. Turns out, it irritates snakes and kills fish. As you know, it took years before we learned that DDT, and other pesticides, are endocrine disruptors and can cause birth defects. So what we are dealing with here is a situation in which a science was developed that learned how to manipulate a form of chemistry that, beforehand, had been exclusive to living things. Before 1823, every organic, that is carbon containing, chemical on earth was made by a living thing. After 1823, and in the 1900s, very rapidly, synthetic, organic chemicals were made. For the first time, we had the power, and used it, to produce organic chemicals that were originally produced in living things exclusively. As you know, billions of pounds of these things have been disseminated: insecticides, herbicides, fungicides, and so on.

The Chemistry of Life

The question is, how did this happen? How did it happen that we were unaware of the consequences of what we had

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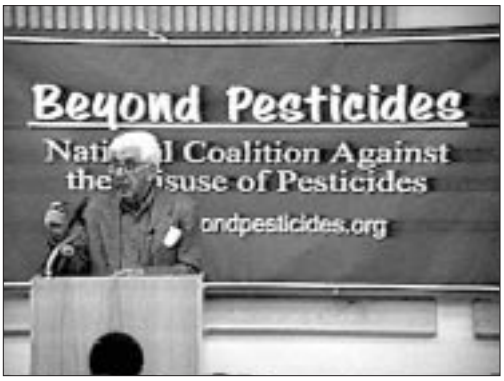
done? This came about because the chemistry of the living thing itself was largely ignored. Sure, they needed to know why the insect died, but no one bothered to ask what would happen when this stuff got into mother's milk. The lesson to learn from that is that an organic chemical that does not occur in living things is inherently dangerous to life. Why? Because the chemistry of life is something that began four billion years ago. It is extraordinarily complicated. Over those four billion years, many different types of chemical reactions could take place and what we now have in living things is an enormously selective group of molecules that are compatible with each other.



Dr. Commoner explains how scientists, by the mid 1800s, learned to manipulate atoms and create chemicals that were not produced by living things. Scientists originally rejected the possibility that these new chemicals, like DDT, could affect birds, when they were designed specifically to kill insects.

To think about this simplistically, understand that a protein is a string of amino acids. Well, you see, it is a string. (*At this point, Dr. Commoner shows a length of colored cord, which is rolled into a ball.*) It is hard to unravel. These colored sections indicate the position of an amino acid. There are 20 different amino acids in a normal protein, 20 different kinds. Theoretically, they can be put together in any sequence that you want. Some time ago, a very smart physicist named L. Sasser did the following calculations. He said, suppose that we synthesize one molecule of each of the proteins that can take 20 of these different amino acids, say 100 units long, until we make one molecule of each of the possible ones. Then, weigh all of those possible molecules. How much would it weigh? It turns out, it weighed more than the weight of the known universe. What does that mean? It means that the proteins that are made in living things are a very narrowly selected group of molecules from among the various kinds of proteins that could be made. Now, so much has been learned about proteins that there are chemists busily, right now, synthesizing not-normal proteins. That is, proteins with an amino acid sequence that no one has ever seen in a living cell. I have not seen any results yet, as to what happens when anybody eats it, but I mention this simply to get across to you the idea that in living chemistry there is a fantastic, specific, limitation to the kinds of molecules that can be compatible living in a single cell. What that says is that you have to automatically regard any synthetic, organic chemical (like DDT, Dioxin, PCBs, all of the herbicides, etc.) as likely to be dangerous because, in a sense, they are evolutionary rejects. Think of it this way. At some point 20 million years ago, or more, some living cell took it into its head to synthesize DDT, and it has not been heard from since. In other words, what this tells you is that there is a conflict between the business of making these unnatural things and widely disseminating them into the environment without taking precautions to see what the consequences are going to be.

Regulating Pharmaceuticals

It so happens that we have created an industry of making synthetic, organic compounds, which has very carefully taken this lesson and practiced it. What is the industry? Pharmaceutical drugs. What are pharmaceutical drugs? They are synthetic, organic compounds that are made in the laboratory. They do not occur in living things, but after a lot of work it has been found that they can be usefully taken into the body to correct or change some internal condition. We always knew that they do a lot more. Look at all the adds for drugs now in the paper. There is a full page of tiny type describing the side effects. In other words, if you are taking something for an acid stomach, it turns out that you have to worry about dizziness, under certain circumstances. They are completely aware of the side effects. Look at the precautions. You cannot take most of these things unless you first go to a doctor who looks at you, does a diagnosis, and figures out what might work and what might not work. You cannot get the stuff until the doctor writes it down on a piece of paper, with your name on it, that allows you, personally, to get that particular chemical from a druggist, who goes to jail if he fools around with it. There is a whole structure in the U.S. Food and Drug Administration (FDA) that sets up rules and regulations about it. We have learned that the business of putting synthetic, organic compounds into living things is inherently dangerous. If there are certain things that will help people who have asthma or cancer or diabetes and it is worth doing, with all the precautions being carefully looked at, then we do it.

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So what we have been doing in disseminating insecticides, fungicides and herbicides in millions of pounds per year, has been spreading pharmaceutical drugs into the environment, which everybody is exposed to, whether they are sick or not, young, old, without a prescription. We are doing exactly what the FDA was set up to prevent. That is the situation that we have gotten into. We have gotten into it by not paying attention to the evolutionary significance of synthetic, organic compounds as rejects.

The interesting thing about this is that every time an is-

sue would come up with Rachel Carson and DDT, now with hormonally active compounds and the endocrine disruptors, the first reaction of the industry is to say, "You don't know what you're talking about." You have to remember, Rachel Carson was viciously attacked by Monsanto. They said that it was absolutely, scientifically incorrect to say that birds are susceptible to something that we have synthesized to kill insects. So the result is that we now have a globe, a planet, saturated with these compounds, over which we have almost no control. There are epidemiological studies and so on, but everyone knows that it is not healthy.

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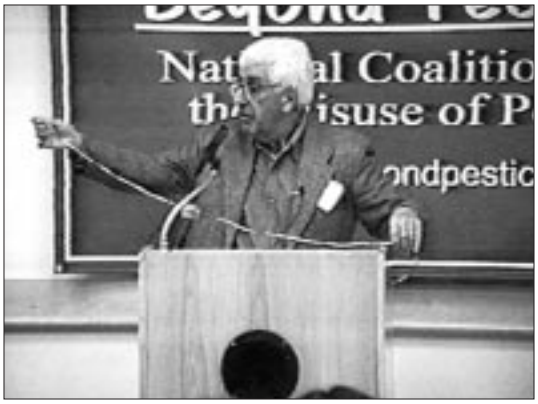
Biotechnology

There is an interesting argument that has come up in the biotechnology industry. You know the Bt gene, which makes a toxic insecticide in bacteria, has been transferred to corn plants and cotton plants. Monsanto makes the following argument. This is a good thing to do because it will cut back on the use of synthetic pesticides. They are now acknowledging that synthetic pesticides ought to be controlled. Why are they doing that? Because they have gotten out of that business. As you know, Monsanto split off its chemical business into a separate company, got heavily into biotechnology, got into real financial trouble and they have now been taken over by a pharmaceutical company and are a subsidiary company within this pharmaceutical company. That is indicative of what? Of the transformation of the whole petrochemical industry into biotechnology. The big biotechnology companies were set up by Monsanto, Ciba, and Hoffman-Laroche. They have transformed themselves into biotechnology companies.



Dr. Commoner uses a colored string as a visual aide to explain that different proteins are particular sequences of amino acids. A small segment of a species' DNA dictates each sequence of amino acids. Genetic engineers can introduce these small segments of DNA from one species into the genetic makeup of a different species, creating novel forms of life with unpredictable results.

What I want to talk about now is whether they have learned their lesson this time and what the dangers are. You notice that in order to deal with this, you have to get the science of it. I had to talk about carbon atoms and so on. Well, when we get to biotechnology we are going to have to do the same thing. Why? Because if you criticize biotechnology, you have to know what it does. The biotechnology industry, through genetic engineering, takes a molecule of DNA, which carries genetic information, from one organism, for example the bacterium that produces the Bt insecticide, and puts it into a corn plant, with the expectation that it will do in the corn plant exactly what it does in the bacterium. That is, there will be an insecticide produced and no other effect on the corn plant. The whole safety issue in biotechnology hinges on that single theoretical point —that the DNA gene has exclusive control over a particular event in the living cell and that no other part of the cell can affect what the DNA does. It is a strict code that says, "Do this."

Now, many people have used the evolutionary argument against biotechnology and that is absolutely true. Evolution tells us that the transfer of a gene from one organism to a wholly unrelated organism flies in the face of four billion years of evolution because one of the characteristic consequences of evolution is species. We are humans. There are humans, mosquitoes, snakes, monkeys, elephants, etc. Living things come in discrete packages, which do not breed with each other. There is no way, in nature, to pick up a gene from another species. The argument has been made. This is an unnatural thing to do and, therefore, dangerous. The argument you get from the other side is, "Well, you don't understand. That's evolution. We're doing molecular genetics." You've heard this, "We do this with surgical precision; we're not just breeding. We're taking one molecule at a time and putting it into another organism."

OK, let's talk molecules. What I want to do now is to tell you what can be learned from the enormous amount of data that has developed over the last 40 years, when the DNA double helix theory was first announced by Francis Crick, the more thoughtful member of the Watson and Crick team who developed the double helix. What biotechnology does is to take a molecule of DNA, which they say is a molecule that dictates a series of very precise chemical events in the cell that leads to an inherited characteristic. So if you have blue eyes, there is some little bit of DNA that broke off from one of your parents that produces chemical changes to make you end

up with blue eyes. The claim here is that DNA has two prime characteristics. One is that it will dictate what happens in a living cell that is inherited, and two, the reason it is inherited is that it also makes itself. A gene makes another gene and that gets transmitted down generations. So, what comes out of it is that the gene, the DNA, is the only source of self-replication and the exclusive source of the individual characteristics that are inherited.

Biotechnology: A Corporate Takeover

Now, what is this sequence? What are these chemical reactions? I thought I would share with you a statement at a U.S. Senate hearing in October of 1999, on biotechnology, in which Senator Richard Lugar (R-IN) brought in all the people from the industry to defend against, what he called, the recent hysteria from Europe. The first witness was Ralph W.F. Hardy, who is president of the National Agricultural Biotechnology Council, an industry group, and formally director of life sciences at Dupont. Here is the way he describes what is called, officially, in the academic world, the central dogma. That is the theory that Dr. Crick, Ph.D developed. And I quote, "DNA (top management molecules) directs RNA formation (middle management molecules), which directs protein formation (worker molecules)." Now it so happens that this is an absolutely accurate description of the Crick theory. You can think of what biotechnology does as, basically, a corporate takeover. It takes the top management of an organism and injects it into another species with the idea that that top management will now dictate what happens in that new organism.

Dr. Commoner compares biotechnology to a corporate takeover. Newly introduced segments of DNA dictate the production of proteins that were never before made by the original host cell.

So, it is a corporate takeover. It says that the rules that are set up by the management are in the DNA that transfers over. The middle management does exactly what the DNA tells it, and then the middle management tells the workers exactly what to do and disregard what they did before. There is a funny piece of irony here because the man who has been the ideological leader in this whole biotechnology reincarnation, Robert Shapiro, is a victim of a corporate takeover. When Monsanto was taken over, not merged, it was announced that Shapiro would retire within the following year. There was an article in *The New Yorker* with a very wistful ending with Shapiro going back to gardening.

An Industry to Prove Safety

At any rate, what I want to make clear here is that the biotechnology industry is absolutely bound to the situation of putting a management, a governing DNA, into a living cell without any other side issues happening. As it turns out in the petrochemical industry, the safety problem deals exactly with that. Are there side effects? There are going to be side effects if you can show that this idea that the DNA is exclusively in control, that there is nothing else in the cell that can do these things other than DNA, is false. If you can show that DNA is in total control, then maybe you are safe. If not, then you are in trouble.

As I said, there has been a lot of research over the last 40 years. In January 2000, a paper came out in *Science* with an exquisitely done molecular study, which proved that this theory was wrong. It proved that at least one aspect of the theory was wrong —that only DNA can replicate itself and that no other molecule can. What was done? Well, it so happens that there are certain types of viruses, called prions. These types of viruses were originally discovered in goats, a disease called Scrapie. Scrapie is closely related to the mad cow disease and a whole series of virus diseases that are known as "slow viruses" because the disease developed very slowly. As early as the 1950s, researchers tried to purify the Scrapie virus and discovered that they could not detect any nucleic acid in it. All other known viruses have nucleic acid as DNA or RNA, but Scrapie has no nucleic acid in it. Ever since then, people have been battling over how this could be. This virus is infectious and it can replicate itself. So, what they did was to show that they could make a normal protein, a pure normal protein, into an infectious prion by attaching to it a piece of protein from the original virus. In the same issue of *Science* it was admitted, in a

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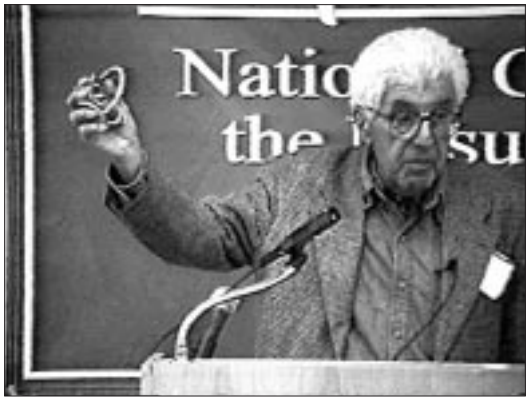
commentary on the front cover of the magazine, that this contradicted the central dogma on which the biotechnology industry is founded. Have you read about that in the newspaper? No. What you have here is the development of very important facts that are not being acknowledged by the people who discovered them.

To go on. We now know a lot about how the prion does this trick of being free of nucleic acid, but replicating itself and being infectious. The work was done out in San Francisco in the early 1980s by a man named Stanley Prusiner. He got the Nobel prize two years ago for this work on prions.

He has now worked out how the prion works. The prion is a protein, a pure protein that when biochemically active is folded up and has a particular shape of twists and turns. What Prusiner showed is that this virus, the prion, when it gets into the brain (because that is where the attack takes place), encounters a normal brain protein. That brain protein assumes the folded up shape of the prion and becomes infectious. It then bumps into another normal protein and transforms that, explaining why they are "slow viruses." This is a very slow process. As this goes on over tens of years in humans, finally the brain goes dead. These diseases are universally fatal.



Dr. Commoner illustrates how a sequence of amino acids fold into a specific, functional protein, with the use of a colored string. He explains how the molecular genetic system is under the control of both the DNA and protein folding systems which co-exist and have evolved together.

Here is the key thing about the folding. Remember I said that the whole purpose of this stream of genetic information was to get to the activity of the protein. If it is an enzyme, it is completely dead. In order for it to be active, it needs to be put together into a particular configuration, which brings together two particular amino acids, sometimes three, sometimes another chemical. That is called the active site. The chemical reactivity takes place on the surface of that particular point. You can see how important the folding is because if it were not folded, these two amino acids would be far apart. Folding is an absolutely essential step to making a protein biochemically active and, therefore, capable of bringing about the inherited effect.

Here is the problem that Dr. Crick has. Crick has described, and all the evidence supports it, how the DNA transmits its code to RNA and how the RNA transmits its code to this sequence of the protein. Full Stop! That is the end of the theory. The theory ends by saying we know how the DNA makes a dead protein. Incidentally, Crick said that the information in the protein cannot get out and he said that if you could ever show that genetic information is transferred directly from one protein to another, and I quote, "It would shake the intellectual foundation of molecular biology." Well, that happens.

You will hear this argument. Oh that is a disease. That is not a normal thing. What does this have to do with normal inheritance? Another thing that has happened in the last 20 years in this area of research is the discovery that the folding up of proteins requires a protein. In Crick's theory, he knew that the protein needed to be folded to be active. He said, "We will assume that when you have specified the sequence of the amino acids in the strung out form, then the protein will automatically fold itself up to a highly specific three dimensional form." How specific is that? IBM has announced a new high-speed computer. They also announced that this computer would have a test. This test would be to figure out how many different twists and turns can be made in order to specify the particular arrangement of a folded up protein. And the answer is one, with one hundred zeros after it. In other words, there are zillions of ways of doing this. Then they said that the computer would have to run continuously for a year to work that all out. In the cell, proteins are made linearly and fold up in exactly the right way in two seconds. How do they do it? There are proteins called chaperones. These chaperones are cup shaped and when the linear protein gets into it, it comes out properly folded. In other words, it does exactly what the prion does, a protein combining with another protein and bringing about its proper fold.

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So, Crick was right up to the point of the stretched out protein. But that does not answer the question of how you get the inherited characteristic. A different genetic process, which involves only protein, is essential to carry out the final step. Incidentally, the two are absolutely essential. The scheme to make the stretched out protein is necessary, but not sufficient. The folding up is necessary, but not sufficient without something to fold. Now these two systems, the Crick system and the folding up protein system, coexist in current living things. They must have evolved together and they must be compatible with each other. Otherwise, you have got the same problem that you have got with DDT, when you put an evolutionary reject chemical into a living thing.

It is simply not true that moving DNA from one species to another is a perfectly natural thing to do. What you are doing is putting top management into a potentially hostile situation because you have got workers who do not know from Crick. In effect, the evolutionary argument tells us an essential part of the molecular genetic system is not under the control of DNA and the compatibility of the systems is related to their evolutionary development. You are exactly where you are with DDT. If you only put in one part, you have no way of knowing what will happen when it confronts another part that was built up from the course of evolution. There is enormous research on protein folding and an enormous amount of research on prions. There is tremendous activity in biotechnology. What is it? A third of the corn crops have been taken over? What you have, from the research on folding and the research on prions properly understood, is a denial of the theoretical basis that is essential to biotechnology. Without that basis, it is a completely unpredictable thing to transfer DNA from one organism to another species.

Dr. Commoner receives Beyond Pesticides/NCAMP's Environmental Protector Leadership Award at the 18th National Pesticide Forum for leading the environmental movement with thought and action.

You might say that nothing dangerous has happened. Well, proteins act slowly. DNA, when it comes into a cell, is competing with another molecule. There are thousands of protein molecules within a cell and you will not change that very fast. Very slow processes may be taking place now and at least we know that this is inherently a very unpredictable, dangerous process. The data exists, but the people who are doing the work will not talk about it. There are many reasons for this. One obvious one is that they are in the biotechnology business. Even if they are not in the business, such a huge ideology has developed in research practice that to step out of it means that you will not get many grants.

We are in a difficult situation, but we have been in difficult situations before. We know how to get out of it. The important thing to do is for those of us in the environmental movement to take on the task of educating the public about the molecular facts that show that biotechnology is an unpredictable industrial practice. It is not going to be easy, but I think it is time to do it. Thank you.

Questions & Answers

What is your response to Dr. Anfensen's work on how temperature creates protein folding?

The only knowledge that we have on the living cell is that chaperones are involved and that they are universal. There is a key thing that I should have mentioned here. If Anfensen and Crick are correct, then it is not possible for two proteins with the same amino acid sequence to fold differently. Prusiner showed that the normal protein in the brain has exactly the same amino acid sequence as the prion, yet it has a different folding from the prion. When they interact, the normal protein's shape is changed into the shape of the prion's folding. That makes it infectious. The ironic thing is that the chaperones were first discovered by the biotechnology industry. When they started to make transgenic bacteria with human genes, looking for human growth hormones, they found a lot of protein, but it was inactive. This created a problem in the industry at the beginning. They finally discovered that they could recover more active protein by putting more protein into the test tube to chaperone. So, chaperones were really discovered by the biotechnology industry.

How do we manage to propose education to a public that does not seem to want to know about organic chemistry, wants to put their herbicides on their lawns and does not care if their children and pets play there?

Well, you are describing a certain fraction of the public. I think that the way to do it is by educating people not to have that attitude. Look, we had this problem way back in the Atomic Energy Commission and with the fallout from nuclear bomb tests. How did we do it then? We got smarter than they were. We knew more about the ecology of Strontium 90 than the Atomic Energy commission did and we challenged them! I think that we should be challenging the biotechnology industry by using the paper that came out in *Science* in January — by using Prusiner's work. Prusiner will not do it. I guarantee you.

It is hard for people to go out and talk with your level of skill. How do we convince more scientists who are working on this issue to talk about the consequences of what they do?

In St Louis around the fallout date, that is exactly what we did. It is going to be harder this time. I guarantee you. It is going to take a gutsy scientist to be willing to organize around this issue. There are groups out there like the Committee for Responsible Genetics. I think that what we have to do is organize. What I have described to you is the result of maybe six months of very part-time work digging up stuff on prions and chaperones. Do you know, for example, that the gene for a given protein does not exist in a one piece? This gene exists in scattered pieces, which have to be put together in exactly the right way. In some cells they are put together one way, and in other cells a different way. Where does information come from to know exactly how to do that? Where is the blueprint? We have got to organize the scientists and start a campaign! The way to do that is to put public pressure on the scientists and say, "Come on, do your job!"