NUCLEIC ACIDS: THE LONG STRINGY INFORMATION BEARING MOLECULES OF LIFE

Dr. Kary B. Mullis
Founder and Vice President, Research of Atomic Tags, Inc.

Life on the Earth, as we know it in this century is always associated with these very long stringy molecules which we call by the rather unfortunate name nucleic acid. The term was coined in 1899 long before the structure or the function of the nucleic acids was understood, and it sounds like something you wouldn't want to spill on your hand, much less have in all of your cells. It turned out of be a bad name. Inside of every living cell on the planet as far as we know there are nucleic acids, and remarkably every structural detail of every living creature arises from easy to read instructions on these long stringy molecules. And as if that weren't enough, there is a lot of information on these molecules which isn't currently being used by the creature bearing it. It belongs in a way to the creature's past, like old trunks in the attic. A more fitting name for nucleic acid might have been magnesium archivate or informationate or something like that, but the concept of informational molecules was not appreciated until late in the 1950s.

The threads of our modern understanding of life and it's informational molecules began to be woven somewhere around 1930. Irwin Schroedinger, one of the brilliant physicists who created quantum mechanics, wrote a little book called "What is Life?" and he puzzled in that book over the notion, "how like begat like?" The subject had been broached in the Old Testament of the Bible but no mechanistic details were offered. There had been a few thinkers, people like Charles Babbage, John von Neumann, and Alan Turing who had already imagined computing machines with evolutionary capabilities which could operate from ordered lists of coded instructions. For these few the notion of long stringy molecules bearing symbolic information from generation to generation would not have been too bizarre to take seriously but these men were not biologists. Most biologists were of the opinion that "how like begat like" was an impossible question, not likely to be answered in their lifetime. The details appeared in the 1950s starting with Oswald Avery who demonstrated that at least in one case the hereditary material was nucleic acids.

Not a lot of people were ready to accept that because no one knew then that nucleic acids were not just what the name implied, acids from the nucleus. No one knew they were the most beautiful, complex, long stringy molecules to be found on earth. The very satisfying answer arrived when Francis Crick and James Watson postulated a structure for deoxyribonucleic and which had two very remarkable qualities. The molecule seemed capable of encoding a great deal of information and it could serve as a template for its own replication. It could bear children. In its structure was the answer to the old question of begetting and indeed, the very essence of life. Watson and Crick noted this in their 1953 paper in Nature in a statement that must rank as the most cautious understatement of an earthshaking discovery in the scientific literature. They wrote, "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

Today we are completely surrounded even in the privacy of our own homes, with mechanical devices that regularly and dependably record and dispense long strings of information converying everything from mathematical descriptions of theoretical objects to high fidelity recordings of Eric Clapton playing his guitar and singing about some woman. We are accustomed to this now. Most of us know that floppy disks and CD's and tape recordings and old 78 records even are mechanical devices that allow us to assemble a long string of information into a convenient coil, where it can be stored and retrieved.

Long stringy information bearing molecules make perfect sense to us now, but our curiosity about them goes further than just knowing that they exist. We want to know what they say and some of us want to be able to manipulate them, repair broken ones, make new ones, fool around with them.

But very long stringy molecules are not so easy to work with. They break up into little irregular pieces, and if you want to examine a particular region of human DNA, for example, the gene which encodes insulin, you are looking for something in the presence of about a million other things which look very much like it. For a long time after the discovery of the structure of DNA, detailed information about it came out only very slowly. Then came molecular cloning. With this technique molecular biologists could isolate particular DNA sequences and produce them and their encoded proteins in large amounts. Biology became very exciting and biotechnology emerged as a new industry. Still it was a long, tedious process to isolate a particular DNA sequence, and the manipulations one could perform were limited.

In 1983 I was driving my Honda Civic from San Francisco to Mendocino County, which is to the north in the mountains by the coast. It was spring and the California buckeyes were in full bloom. The moist still air was saturated with their perfume. I was imagining experiments which I thought I might do in the coming weeks. It was late at night and my thoughts were very loose, almost like dreams, as the road curved right and left through the mountains. Suddenly almost by accident I had assembled in my mind the elements of what I later named the polymerase chain reaction. I was in the mood to think new thoughts, to discover new possibilities in the combination of familiar elements. I had not been looking for PCR, but I was ready to find it. I stopped the Honda. Within a minute or two I realized that I had discovered something fantastic. I tried to wake up my girlfriend, but she had heard wild new ideas from me before and most of them evaporated in the scrutiny of daylight. It could wait for morning. But I was up all night, and in the morning PCR had not evaporated.

After a few months in the laboratory it was working.

Now almost ten years have passed. PCR is a standard tool without which most biochemists would cry in their sake. It has done for DNA chemistry what the word processor did for writing. Out of long stringy molecules, complex and annoying to work with, PCR can make little, orderly, well-behaved pieces of DNA in whatever size and amount is convenient. It can splice them together, cut them apart, add something here, delete something there.

DNA has been tamed, and all the information it contains is in our hands. Our human DNA, our genome, has as many letters as a thousand long books, a fair sized library. It is our story. Each of us carries it around in our cells. Some of it is personal, some of it is public, the same in everyone. It will tell us about our health and our diseases. In it we can find traces of our past, and if we can use it wisely it will help us direct our future toward peace and prosperity for all mankind.