Biological science at the crossroads

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AIDS (Acquired Immunodeficiency Syndrome) has produced a crisis in biological science every bit the equal of its impact as the major lethal epidemic of the last half of the 20th century, and possibly of all time. This crisis is hinted at in the introductory paragraphs of the sixth chapter of the National Academy of Sciences report *Confronting AIDS*. This chapter, entitled "Future Research Needs," begins with the following statements:

"In the brief period since the first descriptions of HIV and its unambiguous identification as the cause of AIDS, a tremendous amount has been learned about the genetic structure and transmission of the virus. Much less is known, however, about how it initiates infection, how it maintains infection, and what determines the progression and diversity of the resulting illness.

"Research has been very effective in discovering the routes of viral transmission, enabling public health and education programs to be designed that incorporate increasingly accurate and specific information. Research has also been particularly effective in elucidating the complete genomic structure of the virus, allowing definition of many, if not all, of the virus's genes.

"Such insights, however impressive, are only the beginning of what promises to be a long and difficult path toward effective therapeutic interventions to minimize or eliminate the debilitating effects of HIV infection and toward eliminating the spread of the virus by safe and effective vaccines."

Leaving aside the issue of the systematic cover-up of the role of environmental factors in the transmission of HIV infection, and the fact that "public health and education programs—-that incorporate increasingly accurate and specific information" have been singularly ineffective in stopping the spread of this pandemic, which according to the director-general of the World Health Organization will infect over 100 million people in the next five years, there is another issue that transcends mere bureaucratic venality. This relates to the first paragraph quoted above and is emphasized by the subsequent statements that, in spite of knowing the entire genomic structure of the virus, we know very little about how it causes disease in living human beings.

Problem of modern molecular biology

The crux of this problem lies in the essential nature of modern molecular biology as a scientific discipline. The ability to know every nucleotide in the genetic material of the AIDS virus, or more correctly AIDS viruses, and yet not know how it actually functions in a living system is exemplary of the more general issue involved. That issue is the current concept of DNA as simply a computer tape carrying linear data bits which are capable of being read and analyzed according to the precepts of information theory.

The basic tenet of this theory is that information is transmitted in a one-way path from DNA to RNA to protein. Once information is translated into protein it cannot return and the only way the DNA code can be changed is by random point mutations in the DNA base sequence. The process of producing new DNA from pre-existing DNA is known as replication and is done by enzymes known as DNA polymerases. The sequence of nucleotide bases in the DNA molecule serves as a template for the synthesis of a complementary RNA by a process called transcription. The DNA-dependent RNA polymerases which catalyze this reaction are called transcriptases. The messenger RNA thus formed is then used as a template for the synthesis of proteins by a process known as translation. Thus, DNA is transcribed into RNA which is in turn translated into protein.

The model is that of a computer tape from which code sequences are read and then translated into proteins, more specifically into enzymes, which then automatically catalyze all the reactions necessary to create living organisms. The gene is thus defined as a sequence of DNA bases which coded for a single enzyme. This is also known as the "one gene, one enzyme" theory. A number of early experiments appeared to confirm this idea, and it became "the central dogma of molecular biology" that information is irreversibly transmitted from DNA to RNA to protein.

Not surprisingly, the AIDS virus belongs to a group of viruses whose mechanism of reproduction first shook the foundations of the central dogma. These viruses, the retroviruses, were demonstrated to have RNA as their genetic material; however, unlike other RNA viruses which simply reproduced by replicating RNA copies, the retroviruses synthesized a DNA copy of their RNA genomes, known as a provirus, which then in turn served as a template to synthesize new virus RNA. This provirus DNA could then integrate into the nuclear DNA of the host cell and become an inherited cellular gene!

The scientists who discovered this phenomenon, such as

Howard Temin (who shared the Nobel prize with Renato Dulbecco and David Baltimore), claimed to have overthrown the central dogma since they had demonstrated that information could flow from RNA to DNA. However, they were, and are, still enmeshed in the information theory paradigm as exemplified
polymerase by which the retroviruses synthesized the proviral DNA as a "reverse transcriptase."

Since that time it has been discovered that this phenomenon of RNA-dependent DNA synthesis is not unique to the so-called retro (from reverse) viruses but is quite common throughout the biosphere. Viruses such as Hepatitis-B, which is a DNA virus, can synthesize RNA which is then "reverse transcribed" into DNA which can be inserted into the genetic material of a host cell. These viruses are called pararetroviruses. In addition, there are segments of DNA which show a similar organization to retrovirus DNA (retrotransposons) and other DNA sequences which indicate that they have been transcribed from an RNA template (retrotranscripts). These sequences of integrated DNA copies of RNA make up over 10% of the genetic material of mice and men.

The real significance of these findings is that the linear information-theory computer code model of DNA function is totally inadequate to deal with these phenomena. Putting all the terminology of translation and transcription aside, we now have evidence that DNA is not a static molecule which only changes by random point mutations over the lifetime of a single organism, but that changes in cell DNA occur in the normal course of tissue function. In this regard, it is noteworthy that most of the retroviruses which have been studied, in animal and man, arise from and infect cells of the immune system, especially lymphocytes and macrophages. Self-induced genetic change appears to play a role in such processes as synthesis of new immunoglobulins (antibodies) by lymphocytes. This is directly relevant to the question of the human AIDS retroviruses, which characteristically attack the immune system and the nervous system.

A different way to look at DNA

If instead of looking at DNA as a computer tape, we study it as a harmonic oscillator which absorbs low energy photons and re-emits them coherently at a shorter wavelength, i.e., as a biological laser, then we can begin to approach a number of problems which are inexplicable by the computer tape model, or even its later, more sophisticated variants. The work of Dr. Fritz Popp of Kaiserslautern University in Germany, indicates that the effect of various carcinogenic chemicals is a function of their optical activity and that carcinogenesis is a result of efforts by the cell to eliminate or counteract these optical properties. In other words, in order to function as a biological laser, DNA, and probably RNA as well, needs to maintain long-range coherence of optical activity. This long-range coherence is based on resonant harmonic structures, and if these are disturbed, then the DNA seeks to regain its harmonic coherence by elimination or addition of what are essentially discords.

There is evidence for this thesis in the large number of repetitive sequences in human DNA, up to a thousand or more copies in some cases, which code for no protein but function as so-called regulatory sequences. In both mice and humans, some of these repetitive sequences show evidence of having been transcribed from RNA, i.e., they are retrotranscripts.

The regulatory function is most probably that of maintaining long-range coherence in the DNA molecule by stabilizing standing waves in the molecule. The amplification of these genetic sequences, up to 1,000 or more copies per genome, is much more consistent with such a harmonic resonance function, than with the idea that they function as on-off switches for gene expression. As a result, changes in these sequences would have a much more global effect on cell function by altering the harmonic characteristics of the DNA molecule. Some of these repeated sequences apparently can recombine with exogenous retroviruses and thus provide another mechanism for alteration of both cellular and viral DNA.

What is evident is that retroviruses represent singularities in the life process, which is itself a singular phenomenon. The real Achilles heel of current biological science is that the statistical information theory model, based on the second law of thermodynamics, is by its nature incapable of dealing with singular events which it by necessity regards as highly improbable. To quote Jacques Monod in *Chance and Necessity:* "Life appeared on earth; what *before the event,* were the chances that this would occur? The present structure of the biosphere far from excludes the possibility that the decisive event occurred *only once*. Which would mean that its *a priori* probability was virtually zero.—The universe was not pregnant with life nor the biosphere with man. Our number came up in the Monte Carlo game. Is it any wonder if, like the person who has just made a million at the casino, we feel strange and a little unreal?"

This radical rejection of causality permeates molecular biology and is the basis of the paradox of knowing the entire genetic structure of the AIDS virus but not understanding how it causes disease in the living host. On the more banal level it assists such people as CDC bureaucrats and the leadership of the California Medical Association in denying the existence of non-sexual, non-needle transmitted AIDS, in spite of the existence of documented cases, and in denying the relevance of cofactors in the development of the disease. On a larger scale, it enables organizations, such as the World Bank and International Monetary Fund, to pursue economic policies which create the conditions for the outbreak of pandemic diseases. Finally, it has created an epistemological *cul-de-sac,* from which biological science must emerge if it is going to deal with the crisis of AIDS and the longer term issues of cancer and aging.