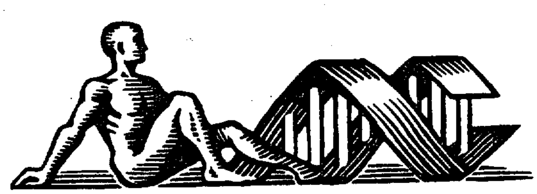
Illustrations by Bill Sanderson

Genes and history

DNA is a historical record that molecular biologists are now beginning to read. At last, we may be able to understand the story of life on Earth. But we should give up the illusion that we will ever discover "laws" that will predict its future

Robert Pollack

HISTORIANS and scientists differ profoundly in their beliefs. Scientists believe that patterns found in the past or uncovered by experimentation can be predictive, that "laws of nature" will follow as generalisations from experimental results. Historians, not held to an obligation to find laws, draw their mission from the simpler hope that a historical record can be recreated, and that we can learn from it.



Molecular biologists are now coming to realise that human DNA is a historical record, as well as a biological molecule subject to experimental modification. Species have been born and died since life began. Their history is written in their DNA. In the DNA of each of us there are passages that can be found in every plant and animal alive today. These are ancient passages, successful parts of the failed survival strategies of the long-gone ancestors of us all.

Comparing the texts of DNA from different species alive today has already begun to provide new details of the idiosyncratic history of the coming and going of species on this planet. No previous species has had the skill to understand its origins, and none the ability to search its origins for clues to its future fate. As the human genome is decoded and deciphered, we can hope to do both.

Can the unique history of life really be studied as a problem in molecular biology? Molecular biology has been built upon the assumptions of physics, chemistry and the other so-called "hard" sciences: laws of great generality and perfect stability do exist in nature; living things are governed by these laws. Yet the study of natural selection stands outside this framework, even though many students of the process begin as scientists and use the tools of various scientific disciplines. Students of natural selection can have no hope and no wish for eternal laws. Physicists can predict the next solar eclipse, but no one can predict the next species. Trained as scientists but thinking like historians, students of natural selection are pleased to accept the contingent aspects of current and past life, the certainty that we will not come this way again.

The study of the sequences of genomes has now drawn molecular biology into thinking of life in this historical way. It is arguably a "paradigm shift", in the terms of the philosopher of science Thomas Kuhn. Our ability to decipher and understand the genomes of many species, including our own, has made molecular biologists into historians despite ourselves. As we read out the details of our origins in the evolved differences between our DNA and the DNAs of neighbouring species, we will begin to think more and more like historians. We have begun to see the texts encoding individuals and species as historical records. We should begin to approach them not as molecules alone, but as one would a library of ancient books documenting the history of life on this planet. The DNA texts of species alive today are full of references to this common past, references which we first recognised by the visible characters they encoded, and that we now can read in their original DNA language. We have also found examples of the richness of a true historical record: meaning in DNA is encoded in many layers, some fully predictable, others not.

The myth of objectivity

As we shift to history, we need not surrender any of the tools of science, nor even the methodologies of experimentation. But we will have to accept the innate incompleteness of the historical record, in place of the ideal of perfectly objective description that lies at the heart of science. We will also have to accept the fact that the same species do not evolve twice. When we choose which part of the historical record, or the human genome, to reconstruct or analyse, we will be able to admit that our priorities are subjective, as they really always have been. The shift will happen as we think about DNA differently, as we come to accept the limits of history. Natural selection, the author of our DNA texts, is a network of causal relationships so complex that we will never break the final code linking DNA sequences to the survival of species. We simply have to admit that, no matter how many sequences we unravel, we will not be able to reduce natural selection to a set of predictable laws.

This change in paradigms will also help those biologists who struggle to understand natural selection without a full grasp of the powerful generalities and tools molecular biology has brought to the subject. For example, historically-based scientists assess the degree of difference between species by counting the number of different "characters" between them. Molecular biology is needed to bring sense to the notion of characters. A "character" may have any molecular complexity. A single base-pair difference may count as a character in one study, while another study will take as one character the difference between chimpanzees, who lack spoken language, and humans, who possess it. Because about four-tenths of all the messenger RNAs made from the human genome are made specifically and only in the human brain, it is likely that such a "character" as the ability to form languages has the molecular complexity of tens of thousands of genes.

To give another example of the value of a historical perspective, a common path to the origin of new species is the appearance of incompatibility in mating. We would like to know which DNA sequences, if any, block the appearance of fertile offspring in the mating of sister species such as donkey and horse or lion and tiger. Learning this, we would then begin to learn the extent to which the evolution of species involves chromosomal incompatibilities, and the extent to which it involves complex genetic changes that somehow subtly alter the behaviour of animals, making them unable to reproduce.

Perhaps the most useful place for the historical paradigm to take hold would be within America's federal research establishment, especially in the multi-billion-dollar apparatus of the National Institutes of Health. Infectious diseases are, after all, monuments to our intertwined genetic past and present coexistence with a zoo of invisible organisms, while our inherited diseases are entirely a matter of our own particular history as a species.

Up till now, the clash of paradigms has not been easy. It has brought discord and confusion to the conversations among evolutionists and molecular biologists, and it has pushed many molecular biologists into fanciful and unconvincing arguments for seeing the sequence of human DNA not as an historical document, but only as a "database" to guide further molecular biology. Mapping molecular biology to natural selection does not work very well, because it is so hard to figure out how to use the tools of the trade if there will not be any new laws to discover. Seeing DNA as a text is the way to relieve these tensions. No one wants to be told that a book, or a doctrine, or an historical train of events, will predetermine their fate. Similarly, even molecular biologists should be pleased, when they think about it, to realise that they will not find rules and laws and codes in the functions of the genome which might restrict the free will of their own brains.

Why is this paradigm shift important, beyond its discomforting effects on a few of my colleagues? Because the vision of DNA as a text is closer to reality than the vision of it as a molecule from which laws may be found. Molecular biology, and biology generally, carry a considerable burden of unexamined determinism. No serious historian expects the historical record to yield rules that predict the course of history, or which order historical and political events by their closeness to an historical "ideal". Every claim to have found such laws of history has turned out to be premature, and many have also been excuses for terrible, murderous behaviour. Yet, many molecular biologists continue to expect to find such laws in their work, because unlike historians they have sometimes succeeded: the self-copying double helix and the genetic code are examples of such powerful and fertile generalisations.

To use human DNA wisely, we cannot approach it looking for ways to outwit natural selection, or for rules and codes with which to describe an "ideal" or "best" human genome. The best insurance against these mistakes is to see the genome as an historically grounded text. Then the notion of an ideal human DNA would be seen for what historians know it to be—a mistaken dream. As historians using the tools of molecular biology, we will be able to appreciate the human genome, without allowing ourselves to be drawn into empty dreams of perfection. Let us look at DNA as an interesting text, and take both pleasures and lessons from the past by learning to read it as clearly as we can. Each of us owns a copy that has its own particular typographical errors and novel phrases, and in it we can find the reasons we must die. □

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