RICHARD LEWONTIN

THE TRIPLE HELIX

gene

organism

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Gene, Organism, and Environment

RICHARD LEWONTIN

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CONTENTS

I GENE AND ORGANISM

➾ It is not possible to do the work of science without using a language that is filled with metaphors. Virtually the entire body of modern science is an attempt to explain phenomena that cannot be experienced directly by human beings, by reference to forces and processes that we cannot perceive directly because they are too small, like molecules, or too vast, like the entire known universe, or the result of forces that our senses cannot detect, like electromagnetism, or the outcome of extremely complex interactions, like the coming into being of an individual organism from its conception as a fertilized egg. Such explanations, if they are to be not merely formal propositions, framed in an invented technical language, but are to appeal to the understanding of the world that we have gained through ordinary experience, must necessarily involve the use of metaphorical language. Physicists speak of "waves" and "particles" even though there is no medium in which those "waves" move and no solidity to those "particles." Biologists speak of genes as "blueprints" and DNA as "information." Indeed, the entire body of modern science rests on Descartes's metaphor of the world as a machine, which he introduced in Part V of the *Discourse on Method* as a way of understanding organisms but then generalized as a way of thinking about the entire universe. "I have hitherto described this earth and generally the whole visible world, as if it were merely a machine in which there was

nothing at all to consider except the shapes and motions of its parts" (*Principles of Philosophy,* IV).

While we cannot dispense with metaphors in thinking about nature, there is a great risk of confusing the metaphor with the thing of real interest. We cease to see the world *as if* it were *like* a machine and take it to *be* a machine. The result is that the properties we ascribe to our object of interest and the questions we ask about it reinforce the original metaphorical image and we miss the aspects of the system that do not fit the metaphorical approximation. As Alexander Rosenblueth and Norbert Weiner have written, "The price of metaphor is eternal vigilance."[1]

A central problem of biology, not only for biological scientists but for the general public, is the question of the origin of similarities and differences between individual organisms. Why are some short and others tall, some fat and others thin, some prolific setters of seed and some nearly sterile, some clever and others dull, some successful and others failures? Every individual organism begins life as a single cell, a seed or fertilized egg, that is neither tall nor short, neither clever nor dull. Through a series of cell divisions, differentiations, and movements of tissues, an entire organism is formed that has a front and a back, an inside and an outside, and a collection of organs that interact with each other in a complex way. Changes in size, shape, and function occur continually throughout life until the moment of death. As we grow older we grow taller at first and then shorter, our muscles become stronger and then weaker, our brains acquire more information and then seem to lose it. The technical term for this life history change is *development,* and the study of the process is called *developmental biology* (or, in cognitive and behavioral studies, *developmental psychology*).

But the term *development* is a metaphor that carries with it a prior commitment to the nature of the process. Development (*svillupo* in Italian, *desarrollo* in Spanish, *Entwicklung* in German) is literally an unfolding or unrolling of something that is already present and in some way preformed. It is the same word that we use for the process of realizing a photographic image. The image is already immanent in the exposed film, and the process of development simply makes this latent image apparent. This is precisely the view that developmental biology has of the development of an organism. Modern developmental biology is framed entirely in terms of genes and cell organelles, while environment plays only the role of a background factor. The genes in the fertilized egg are said to determine the final state of the organism, while the environment in which development takes place is simply a set of enabling conditions that allow the genes to express themselves, just as an exposed film will produce the image that is immanent in it when it is placed in a chemical developer at the appropriate temperature.

One of the most important issues in the premodern biology of the eighteenth century was the struggle between the preformationist and epigenetic theories of development. The preformationist view was that the adult organism was contained, already formed in miniature, in the sperm and that development was the growth and solidification of this miniature being. Textbooks of modern biology often show, as an example of the quaint notions of past eras, a seventeenth-century drawing of a tiny homunculus packed into a sperm cell (see Figure 1.1). The theory of epigenesis was that the organism was not yet formed in the fertilized egg, but that it arose as a consequence of profound changes in shape and form during the course of em-

bryogenesis. It is usually said that the epigenetic view decisively defeated preformationism. After all, nothing could seem to us more foolish than a picture of the tiny man inside the sperm cell. Yet it is really preformationism that has triumphed, for there is no essential difference, but only one of mechanical details, between the view that the organism is already formed in the fertilized egg and the view that the complete blueprint of the organism and all the information necessary to specify it is contained there, a view that dominates modern studies of development.

➢ The use of the concept of development for the changes through which an organism goes during its lifetime is not simply a case of available language influencing the content of ideas. When it was decided to make an ancient language, Hebrew, into a modern one with a technical vocabulary, the word chosen for the development of an organism, *Lehitpateach,* was the same as the word chosen for the development of a film, but in the reflexive form, so an organism literally "develops itself." Moreover, the word *evolution* has the same meaning of an unfolding, and for this reason Darwin did not use the word in the first edition of the *Origin.* Before Darwin the entire history of life on earth was seen as an orderly progression of immanent stages. While Darwin freed the theory of this element of predetermination, its intellectual history has left its trace in the word.

What is reflected in the use of these terms is the deep commitment to the view that organisms, both in their individual life histories and in their collective evolutionary history, are determined by internal forces, by an inner program of which the actual living beings are only outward manifestations. This com-

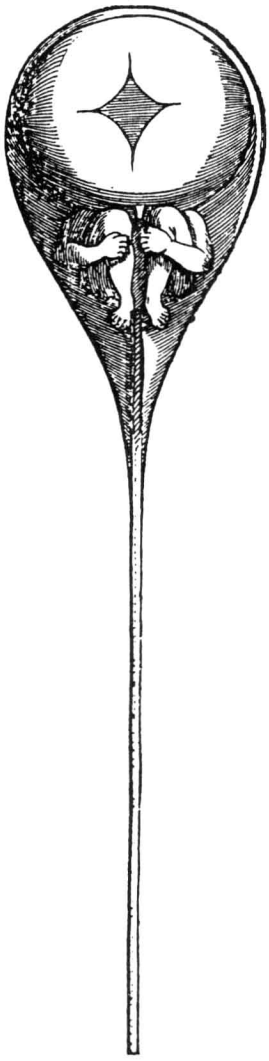

Figure 1.1. A picture by the seventeenth-century microscopist Nicolaas Hartsoeker of the human sperm, showing it as containing a microscopic infant folded in a fetal position. This already-formed infant supposedly grew larger during fetal development, with the mother's egg providing only the nutrition for its growth.

mitment is an inheritance from the Platonic typological understanding of nature according to which actual material events, which may differ in varying degrees from each other, are the imperfect and accidental realizations of idealized types. The actual is the ideal seen "as through a glass, darkly." This was the view of species that was dominant until the twentieth century. Each species was represented by a "type" description, and an actual specimen was deposited in some collection as representative of the type, while all other individuals of the species, varying from the "type," were regarded as imperfect realizations of the underlying ideal. The problem of biology, then, was to give a correct anatomical and functional description of the "types" and to explain their origin. Modern evolutionary biology rejects these Platonic ideals and holds that the actual variation among organisms is the reality that needs to be explained. This change in orientation is a consequence of the rise of the Darwinian view that the actual variation among organisms is the material basis on which evolutionary change depends.

The contrast between the modern Platonic theory of development and Darwinian evolutionary theory is the contrast between two modes of explanation of the change of systems through time. Development is a *transformational* theory of change. In transformational theories the entire ensemble of objects changes because each individual object undergoes during its lifetime the same law-like history. The cosmos is evolving because all stars of the same initial mass go through the same sequence of thermonuclear and gravitational changes on their way to a predictable position in the main sequence. As a group, seventy-year-olds are grayer and more forgetful than thirty-five-year-olds because all the individuals have been aging in body and mind. In contrast, the Darwinian theory of organic

evolution is based on a *variational* model of change. The ensemble of individuals changes, not because each individual is undergoing a parallel development during its life, but because there is variation among individuals and some variants leave more offspring than others. Thus the ensemble changes as a whole, by a change in the proportional representation of the different variants, which are themselves unchanging in their properties. If insects are becoming more resistant to insecticides, it is not because each individual is acquiring greater and greater resistance during its lifetime, but because the resistant variants live and reproduce while the susceptible organisms are killed.

A consequence of the difference between these two models of change is a difference in the problematic of biological disciplines that incorporate them. For evolutionists the differences between individual organisms and the differences between closely related species are at the center of attention. The variation is the primary object of enquiry. Its causes need to be explained and it needs to be incorporated into the explanatory narratives of the origin and evolution of species. Similarities between organisms are taken to be largely historical consequences of common ancestry, of the expected similarity between close relatives, rather than as consequences of functional laws. Indeed the entire science of systematics, whose purpose is to reconstruct the relationships and ancestry patterns of species, uses as its only data the observed patterns of similarity.

In contrast, for developmental biologists the variation between individual organisms, and even between species, is not of interest. On the contrary, such variation is an annoyance and is ignored wherever possible. What is at the center of interest is the set of mechanisms that are common to all individuals and

preferably to all species. Developmental biology is not concerned with explaining the extraordinary variation in anatomy and behavior even between offspring of the same mother and father, which enables us to recognize individuals as different. Even the large differences between species are not within the concerns of the science. No developmental biologist asks why human beings and chimpanzees look so different, except to say the obvious: that they have different genes. The present agenda of developmental biology concerns how a fertilized egg becomes differentiated into an embryo with a head at one end and an anus at the other, why it has exactly two arms at the front and two legs at the back rather than six or eight appendages projecting from the middle of the body, and why the stomach is on the inside and the eyes on the outside.

The concentration on developmental processes that appear to be common to all organisms results in a concentration on those causal elements which are also common. But such common elements must be internal to the organism, part of its fixed essence, rather than coming from the accidental and variable forces of the external milieu. That fixed essence is seen as residing in the genes.

➲ One of the most eminent molecular biologists, Sydney Brenner, speaking before a group of colleagues, claimed that if he had the complete sequence of DNA of an organism and a large enough computer then he could compute the organism. The symbolic irony of this remark is that it was made in his opening address of a meeting commemorating the one hundredth anniversary of Darwin's death.[2] A similar spirit motivates the claim by yet another major figure in molecular biol-

ogy, Walter Gilbert, that when we have the complete sequence of the human genome "we will know what it is to be human."[3] Just as the metaphor of development implies a rigid internal predetermination of the organism by its genes, so the language used to describe the biochemistry of the genes themselves implies an internal self-sufficiency of DNA. First, DNA is described in textbooks and popularizations of science as "self-replicating," producing copies of itself for every cell and every offspring. Second, DNA is said to "make" all the proteins that constitute the enzymes and structural elements of the organism. The project to characterize the entire DNA sequence of humans has been called by molecular biologists "the search for the Grail," and the metaphor of the Holy Grail seems entirely apt since it too was said to be self-renewing (although only on Good Friday) and all-sustaining, providing nourishment for those who partook of it "sans serjant et sans seneschal," without servant or steward.

The metaphor of unfolding is then complete from the level of molecules to the level of the whole organism. Molecules that reproduce themselves and that have the power to make the substances of which the organism is composed contain all the information necessary to specify the complete organism. The development of an individual is explained in standard biology as an unfolding of a sequence of events already set by a genetic program. The general schema of developmental explanation is then to find all the genes that provide instructions for this program and to draw the network of signaling connections between them. The ultimate explanatory narrative of developmental biology will then be something like the following: "The division of the cell turns on gene A, which specifies a protein that binds to the DNA of the controlling regions of gene B and

gene C, which results in an activation of these genes, whose protein products combine with each other to form a complex that turns off gene A in the cell near the surface but not in the cell that is more interior, which, etc., etc."

When this complete narrative finally becomes available, as it certainly will in the not too distant future for large parts of early embryonic development of worms and fruit flies, then the fundamental problem of development, as currently understood by the communal agreement of developmental biologists, will have been solved. Moreover, some of the elements of this narrative must be common not only to individuals who are examples of the same species ideal but to a vast array of species that are organized in similar ways. The greatest excitement in the study of development has been generated by the discovery that there are genes concerned in the ordering of the parts of an organism from one end to the other, the *homeobox* genes, that can be found in humans, insects, worms, and even plants. That such genes exist is undoubtedly of very great interest, especially to the evolutionist concerned with the underlying continuities in the history of life. For the program of developmental biology, however, the excitement arises from that discovery's embodiment of the ultimate program of the science.

A last feature of the unfolding model is that the life history pattern is seen as a regular sequence of stages through which the developing system passes, the successful completion of one stage being the signal and condition for passing on to the next stage. Differences in pattern between species and individuals are then thought of as the result of adding new stages or of "arrested development" in an earlier stage. The role of the external environment in this theory is twofold. First, some environmental trigger may be necessary to start the process. Desert plants