Fall 1982

Intellectual Traditions In The Life Sciences: Molecular Biology And Biochemistry

Scott F. Gilbert
Swarthmore College, sgilber1@swarthmore.edu

Follow this and additional works at: http://works.swarthmore.edu/fac-biology

Part of the Biology Commons

Recommended Citation
http://works.swarthmore.edu/fac-biology/161

This Article is brought to you for free and open access by the Biology at Works. It has been accepted for inclusion in Biology Faculty Works by an authorized administrator of Works. For more information, please contact myworks@swarthmore.edu.
Intellectual Traditions in the Life Sciences: Molecular Biology and Biochemistry

Scott F. Gilbert

Perspectives in Biology and Medicine, Volume 26, Number 1, Autumn 1982, pp. 151-162 (Article)

Published by Johns Hopkins University Press

DOI: 10.1353/pbm.1982.0009

For additional information about this article

http://muse.jhu.edu/journals/pbm/summary/v026/26.1.gilbert.html
INTELLECTUAL TRADITIONS IN THE LIFE SCIENCES: MOLECULAR BIOLOGY AND BIOCHEMISTRY

SCOTT F. GILBERT*

I

Biological science is a vibrant, collective human endeavor consisting largely of controlled experiments and their critical interpretations. This does not, however, constitute an exhaustive catalog of the component parts of the life sciences. Another element is the context in which these experiments are integrated [1]. I am not speaking here of Kuhnian paradigms or of heuristic constructs, but of intellectual traditions which are not proved or disproved by experiment and which, of themselves, rarely suggest new investigations. Nevertheless, these intellectual traditions subtly guide the direction of the entire enterprise of biology.

Most analyses of the intellectual traditions in biology have focused on the integration of biological sciences into the larger intellectual ferments of the eighteenth and nineteenth centuries. This essay, however, will attempt to look at the intellectual currents which led to the separation of molecular biology and biochemistry during the mid-twentieth century. Both of these disciplines attempt to understand the physical basis of life; yet molecular biology was founded by scientists who not only were untrained in biochemistry but were antagonistic to it. In particular, one of the most influential founders of molecular biology, Max Delbrück, “deprecated biochemistry,” claiming that the analysis of the cell by biochemists had “stalled around in a semidescriptive manner without noticeably progressing towards a radical physical explanation” [2, p. 22]. This bias was transmitted to several of his students and colleagues. Replying in unkind, the famed nucleic acid biochemist Erwin Chargaff has

This paper was submitted in the first Dwight J. Ingle Memorial Young Writers’ competition for authors under 35.

*Department of Biology, Swarthmore College, Swarthmore, Pennsylvania 19081.

Foucault has suggested the term “episteme” for such a concept; but as he claims that only one episteme defines the condition of scientific knowledge at any time, I find that “intellectual tradition” denotes what I mean more readily.

© 1982 by The University of Chicago. All rights reserved.

0031-5982/83/2601-0316$01.00
accused the molecular biologists of “practicing biochemistry without a license” [3, p. 140] and believes that molecular biology has severely impeded the flow of scientific creativity. This animosity between biochemists and molecular biologists was especially vigorous in the 1940s and 1950s. This essay will attempt to show that biochemistry and molecular biology are the current incarnations of two complementary traditions in biological science, and that they embody radically different ideas concerning the nature of life.

II

“The ultimate goal of biochemistry” according to Fruton and Simmonds, “is to describe the phenomena that distinguish the ‘living’ from the ‘nonliving’ in the language of chemistry and physics” [4, p. 1]. But neither they nor anyone else has been able to create a set of criteria for the definition of life.

To Claude Bernard, the founder of the cell physiology, which eventually gave rise to the disciplines we will be discussing, “... there is no need to define life in physiology.” Such attempts, he claimed, were “stamped with sterility.” Bernard concluded, “It is enough to agree on the word life to employ it; but above all it is necessary for us to know that it is illusory and chimerical and contrary to the very spirit of science to seek an absolute definition of it. We ought to concern ourselves only with establishing its characteristics and arranging them in their natural order of rank” [5, p. 19].

In the absence of any consensual accord, biology has evolved two traditional approaches to characterize the physical basis of life. In each, the “natural order of rank” is the reverse of the other. The first tradition emphasizes the phenomena of growth and replication as the major vital characteristics. Organisms are seen to increase in size and numbers and are thus akin to crystals. The second perspective focuses on metabolism as life’s prime requisite, whereby an organism retains its form and individuality despite the constant changing of its component parts. In this respect, living beings resemble waves or whirlpools. These alternative crystalline and fluid models of organisms have interacted with each other for the past hundred years. It will be shown that “classical” biochemistry largely retained the metabolic model of life whereas molecular biology, a discipline with ostensibly the same goals, formulated its research program around the crystalline model.

If the basis of living organisms is to be found, not in a “life force,” but in organizations of nonliving materials, what better program is there than to look for inorganic substances which contain rudiments of living processes? To the scientists of the seventeenth and eighteenth centuries, such lifelike substances were to be found as crystals. The forces re-
sponsible for such arborescent growths of silver amalgam (*arbor Dianae*), and *arbre de Mars* (iron silicate and potassium carbonate) were often compared with those responsible for the formation of living structures [6], and such analogies can be found in the writings of Bacon, Hooke, and Coxe. Nehemiah Grew (1674) wrote that the processes of growth were the same as those responsible for the crystallization of salt and that plants were composed of crystalline formations [8, p. 14]. French scientists Beaumont (1676), Maupertuis (1744), and Buffon likewise employed crystals as useful analogues to living organisms; Guéneau de Montbéliard presented spontaneous generation as a crystalline process, and de la Métherie (1811) saw in crystallization the mechanism of organic growth and development: “The seeds of the male and of the female, being mixed, act as two salts would and the result is the crystallization of the fetus.” The culmination of this crystalline model of organic development was the cell theory of Theodor Schwann and Matthias Schleiden. In 1839, Schwann published his researches on plant and animal structure including his “theory of organisms.” Herein he established a new “mode of explanation” which sought to explain organic phenomena solely through physicochemical causes and to drive vitalism out of biology [10]. In so doing, Schwann took any discussion of life from the level of the total organism to the level of the cell and hypothesized that cell formation and growth could be explained by the same processes which govern the formation of inorganic crystals. “Organisms,” said Schwann, “are nothing but the form under which substances capable of imbibition crystallize” ([11, p. 257] quoted in Mendelsohn [10]). In this view, the nucleus (cytoblast) would condense out of solution around the nucleolus and then the cell substances are deposited on the nucleus in the manner of a growing crystal [6].

Nevertheless, Schwann accepted that crystals represent only an instructive model to study living cells.

The attractive power of the cells manifests a certain degree of election in its operation; it does not attract every substance present in the cytoblastema, but only particular ones; and here a muscle cell, there a fat cell is generated from the same fluid, the blood. Yet crystals afford us an example of a precisely similar phenomenon, and one which has already been frequently adduced as analogous to assimilation. If a crystal of nitre be placed in a solution of nitre and sulphate of soda, only the nitre crystallizes; when a crystal of sulphate of soda is put in, only the sulphate of soda crystallizes. Here, therefore, there occurs just the same selection of the substances to be attracted. [6]

---

2The analogy that the earth generates metals as a mother produces an embryo has been detailed in M. Eliade [7].

3The history of the view that a fetus “precipitates” from a fluid mixture is given in Needham [9]. Needham, as we shall see, was extremely influential in the reintroduction of the crystal analogy into embryology.
And although Schwann has reservations concerning the identity of cellular and crystalline processes, he concludes that “the process of crystallization in inorganic nature ... is, therefore, the nearest analogue to the formation of cells.” In her study of organic metaphors in twentieth-century developmental biology, Donna Haraway has seen the critical ways in which the analogy of crystallization has influenced embryology. “If one sees the world in atomistic terms (metaphysically and methodologically), the crystal is a smaller, simpler version of the organism in a nearly literal sense. If one sees the world in terms of hierarchically organized levels (the organism becomes the primary metaphor), the crystal becomes an intermediate state of organization” [12, p. 11]. Although Haraway is analyzing twentieth-century embryology, crystals were being used in the same way by the physiologists and cytologists at the turn of the century. Several cytologists analyzed protoplasm in terms of a geometrical space lattice, and entire classifications of organisms were constructed around this type of crystalline symmetry. Even Claude Bernard, who believed life is without direct analogy to any nonliving entity [5], referred to the ability of crystals to regenerate their form such that “the physical force that arranges the particles of a crystal according to the laws of a wise geometry has results analogous to those which arrange the organized substance in the form of an animal or a plant.” However, Bernard was cautiously aware that “these comparisons between mineral forms and living forms certainly constitute only very different analogies and it would be imprudent to exaggerate them. It suffices to mention them.”

III

By this time, however, an alternative view of life had reached maturity. This tradition held that living beings were in a constant flux and therefore analogous to waves of water—that is, just as a wave maintains its individuality while constantly changing its component parts, so do living organisms. This tradition concentrated on existing organisms rather than emerging ones, and its principle supporters were French biologists. Flux was the central focus of de Blainville’s view of life, and Cuvier claimed that “the living being is a whirlpool constantly turning in the same direction, in which matter is less essential than form.” Flourens paraphrased the vital whirlpool concept, stating that “life is a form served by matter” [5].

The idea that crystals provided a framework to order life continued to have adherents throughout the nineteenth century. Foremost among them was Ernst Haeckel, who utilized crystalline symmetries for his studies of development and who declared that “the secure promorphological foundation makes possible a mathematical understanding for organic individuals just as crystals” [13, p. 543].

154 | Scott F. Gilbert · Intellectual Traditions in Life Sciences
The contrast between the two models was demonstrated by Thomas Huxley, who clearly stated his preference. A unicellular organism, he stated, "is a perfect laboratory in itself, and it will act and react upon the water and the matters contained therein, converting them into new compounds resembling its own substance, and at the same time giving up portions of its own substance which have become effete. Furthermore, the Euglena will increase in size; but this increase is by no means unlimited, as the increase in crystal might be" [14].

Furthermore, following the French biologists, Huxley postulated that each individual organism was formed by the temporary combination of molecules which

stand to it in the relation of particles of water to a cascade or a whirlpool; or to a mould into which the water is poured. The form of the organism is thus determined by the inherent activities of the organic molecules of which it is composed; and as the stoppage of a whirlpool destroys nothing but a form, and leaves the molecules of water, with all their inherent properties intact, so what we call death and putrefaction of an animal or of a plant, is merely the breaking up of the forms, or manner of association, of its constituent organic molecules. [15, p. 355]

Not having a theory of intermediary metabolism to underwrite his views, he speculated on the special nature of these biologically active molecules and the remarkable interconvertibility of such molecules from species to species.

Nutrition was the paramount criterion for this view of life. Indeed, this was the vital characteristic that Bernard had ranked most highly. Huxley's view of the chemical nature of nutritive metabolism "flowed" directly from this tradition: "The particles of matter that enter the vital whirlpool are more complicated than those that emerge from it .... The energy set free in this fragmentation is the source of the active forces of the organism" [5].

This view is common among the founders of biochemistry, and in 1907 Emil Fischer defined the "ultimate aim of biochemistry" as the gaining of "complete insight into the unending series of changes which attend plant and animal metabolism" [6, p. 136]. As biochemistry improved, so did this model. Whereas Huxley could only intuit that life had a "tendency to disturb existing equilibrium," L. J. Henderson could relate the vital whirlpool of life to the laws of thermodynamics. His work, The Fitness of the Environment, popularized the view among scientists that "living things preserve, or try to preserve, an ideal form, while through them flows a steady stream of energy and matter which is ever changing ..." [16]. Here was a context in which intermediary metabolism could be studied, and the triumphs of intermediary metabolism caused the eclipse of the crystal model for decades. The biologist-philosopher
Edmund Sinnott of Yale gave the following explanation: “There is good reason to believe that the sort of formative found in living things is really different from that in such lifeless ones or crystals. First, the crystal system is stable. Its molecules are at rest. Whatever change there is results from the addition of new molecules along the crystal surface. A living organism, on the contrary, is in a continual state of change . . . . An organism has a sort of fluid form like a waterfall, through which water ceaselessly is pouring, but which keeps in its descent a definite pattern” [17, pp. 116–117].

Other biochemists followed this tradition, reflecting on the flow inherent in biological systems [18]. Thus, by 1940, biochemistry had allied itself to the tradition of flux.

IV

While biochemists could use the waterfall to analogize the metastable state of the adult organism or cell, it never became fully acceptable to those scientists concerned with the genesis of living beings—that is, geneticists and embryologists. In 1924, geneticist J. Arthur Thomson noted Thomas Huxley’s comparison of the living body to the great whirlpool beneath Niagara Falls. However, while agreeing that “the whirlpool of the body is a useful metaphor,” Thomson criticized it for lack of completeness, especially since the body “has the power of giving rise to other whirlpools like itself” [19, p. 123].

At the same time, geneticists were having a difficult time trying to integrate the gene into the context of biochemistry. To do this, the gene was often viewed as an enzyme catalyst, yet one that could catalyze its own replication (autocatalysis). This linked genes not only to crystals but also to viruses.

One of the first attempts to equate autocatalytic genes with heterocatalytic enzymes was Leonard Troland’s “enzyme theory of life,” first presented in 1914 and expanded in the 1917 volume of American Naturalist. Linking the new biochemistry of Fischer to the new genetics of Morgan, Troland proposed that the genes of the nucleus were composed of catalytic enzymes. “Although the fundamental life property of the chromatin is that of autocatalysis, it is necessary and legitimate to suppose that the majority of them sustain specific heterocatalytic relationships to reactions occurring in living matter” [20].

This idea was seconded in a review by J. B. S. Haldane, who attempted to squeeze genes into the tradition of flux. “The ultimate goals of biochemistry may be stated as a complete account of intermediary metabolism, that is to say, of the transformations undergone by matter passing through organisms” [21]. Moreover, to Haldane, as to Troland, “The gene has two properties. It intervenes in metabolism . . . and it re-
produces itself.... The most economical hypothesis is that these two processes are closely related, and that the primary products of genes during the 'resting' stage differ from the genes themselves in not being attached to the chromosomes, but perhaps in no other respect" [21]. To account for gene replication, Haldane uses a variety of crystallizations.

The growth and reproduction of large molecules are not, it may be remarked, hypothetical processes. They occur, it would seem, in certain polymerizations which are familiar to organic chemists. In my opinion, the genes in the nuclei of cells still double themselves in this way. The most familiar analogy to the process is crystallization. A crystal grows if placed in a supersaturated solution, but the precise arrangement of the molecules out of several possible arrangements depends on the arrangement found in the original crystal with which the solution is "seeded." The metaphor of seeding, used by chemists, points to an analogy with reproduction. [22, p. 156]

Haldane claimed that "the problem of gene reproduction is very similar to that of virus reproduction" [21] and eventually linked the process to crystallization [23]. "[The] gene is within the range of size of protein molecules, and may be like a virus. If so, the chemist will say, we must conceive of reproduction as follows. The gene is spread out in a flat layer, and acts as a model, another gene forming on top of it from pre-existing materials such as amino acids. This is a process similar to crystallization in the growth of a cellulose wall" [23]. In this we can see one tradition trying to break away from the other, and in 1937 Haldane predicted that “classical” biochemistry, focusing on degradative phenomenon, would be superseded by a “new branch of biochemistry which will, I believe, arise from genetics . . . and its final goal will be the explanation and control of the synthesis of genes” [21]. As we will see, this is the field in which the tradition of crystalline models is strongest. Thus, while the classical biochemistry of intermediary metabolism is retained the model of flux, a “new” biochemistry was emerging which would reject that tradition.

V

The term “molecular biology” was coined in the same year that Haldane’s article showed the strains within biochemistry. There was obviously a need to describe the new discipline that was ready to formulate its own research program for the physicochemical basis of life and which was receiving its input from some nontraditional sources—genetics, virology, and two new branches of physics, X-ray crystallography and quantum mechanics. The term was first used (and in large type) by Warren Weaver, the director of the Rockefeller Foundation's funding for natural science and the man responsible for the recruitment of sev-
eral physicists and chemists into this new science [24]. It was used in the
decision to fund a new research institute which Joseph Needham pro-
posed, in 1935, to investigate the biological importance of crystal physics.
Needham, as well as other embryologists, were aware of the recent ad-
vances in crystallography and were impressed by Bernal's beliefs that
crystallography could help elucidate biological problems. In his pro-
posal, Needham stated that crystals were not only models or analogues
for the living process, but are the physical components of cells. “Next,
there is the profound importance of the paracrystalline state of biology.
The 'liquid crystal' is not merely a model for what goes on in the living
cell; it is in point of fact a state of organization actually found in the
living cell” [24].

This raises the stakes considerably. We are no longer talking about
speculative hypotheses that the processes of life and crystallization are
governed by the same laws, or facile similies that life is somehow like a
crystal. What is now being proposed is that the crystalline state is, in fact,
found in the living cell. A “proof” for this was soon forthcoming, since
the same year that Needham proposed this institute, Wendell M. Stanley
crystallized tobacco mosaic virus.

This was a philosophical as well as biological breakthrough, similar in
its significance and interpretation to Wohler's synthesis of urea, and it
was recognized as such by biochemists. Stating that this feat demon-
strated “that there is no definite boundary between the living and the
nonliving,” the authors of one textbook relate that “certain viruses have
been isolated in highly purified crystalline form and studied extensively
in the laboratory. Yet these substances, isolated in the laboratory and
having no apparent or obvious features characteristic of living mat-
ter . . . an inanimate crystalline compound, when introduced into the
proper environment, appears to behave as though it were a living viral
agent” [25, p. 1].

Within a year, geneticist Hermann Muller was willing to claim that this
crystallized virus was apparently a pure protein capable of “auto-
synthesis” and that “it represents a certain type of gene” [24]. At the
Genetical Congress in Edinburgh in 1939, no less than three crystallog-
raphers, Astbury, McKinney, and Gowen, put forth analogies between
viruses and genes. Astbury said that viruses and chromosomes were the
two simplest reproductive systems known. Thus, autocatalysis, which was
thought to occur by crystalline duplication, was now seen to occur in
viruses which could themselves be crystallized. Furthermore, since this
process is also common to chromosomes, the chromosomes, too, must be
crystalline in nature.

Dr. Hans Oberdiek has pointed out to me that each of the three “prophets” of molec-
ular biology (Bernal, Needham, and Haldane) was a committed Marxist. There may be,
then, a further ideological reason for their demanding a chemistry of biological “produc-
tion.”
Thus, by 1940 the lines were being drawn. Biochemistry, concerned with intermediary metabolism and the energy that drives it, worked well within the tradition of flux and thermodynamics. However, the portion of the life sciences concerned with the transmission and expression of inherited characteristics rejected this view for the tradition of crystalline morphogenesis. Not only did the gene just not fit into the whirlpool model, but it looked as if functional genes (i.e., viruses) could even be crystallized. Whereas the principal characteristic of life for the biochemist was metabolism, life's principal characteristic for the molecular biologist was replication. Furthermore, the primary unit of life for the biochemist was the resting cell (metabolically active but not replicating), whereas the unit of life for the molecular biologist was the virus—crystalline, nonmetabolizing, and capable of enormous feats of replication (see, e.g. [26, pp. 12-13, 18]).

One approach to the study of life was proposed in 1944 when Schroedinger published his essay, “What Is Life?” The importance of this essay has been attested to by such researchers as Crick, Watson, Wilkins, Luria, Benzer, and even Chargaff. The only major dissenter appears to be Seymour Cohen, who called the book marginal. Yoxen has studied the influence of this volume and claims that it “exerted on some scientists a powerful and transient influence in suggesting and validating a particular line of research” [27]. This line of research was predicated on the idea that crystallinity is a state unifying all of matter and that “the most essential part of a living cell—the chromosome fiber—may suitably be called an aperiodic crystal.”

Schroedinger’s notions were derived largely from the work of another physicist who had emigrated into biology, Max Delbrück. Delbrück had worked on Drosophila, Neurospora, and bacteriophage viruses in order to study how genes replicate exactly and transmit themselves flawlessly in each generation. One of Delbrück’s most important contributions in this regard was a paper co-authored with N. W. Timoféef-Ressovsky and K. G. Zimmer [28]. This was an analysis of gene size and the mechanism of mutation by ionizing radiation, and it gave rise to what has been termed the quantum mechanical model of the gene. The stability of the gene was seen to be due to forces linking the atoms of the gene and could be overcome by causing a quantum jump from one stable configuration to another. This paper was “rediscovered” for Schroedinger by the crystallographer P. P. Ewald, and it became the basis of Schroedinger’s analysis of the gene as crystal.

The study of Delbrück’s entry into bacteriophage research and the subsequent recruitment of the “phage” group has been told several times and will not be repeated here [24, 29]. Suffice it to say that Delbrück felt that in focusing on the metabolic concerns of life, biochemists had misrepresented the cell as “a sack full of enzymes acting on substrates,
Converting them through various intermediate stages either into cell substance or waste products" [6]. He also believed that "the field of bacterial viruses is a fine playground for serious children who ask ambitious questions." These questions arise from the replication of viral genes. "He will say: 'How come one particle becomes 100 particles of the same kind in 20 minutes? This is very interesting. Let us find out how it happens! How does the particle get into the bacterium? How does it multiply? Does it multiply like a bacterium? ... Does it have to go inside the bacterium to do this multiplying, or can we squash the bacterium and have the multiplication go on as before?’" [24]. Delbrück was convinced that the problem of autocatalytic synthesis would "turn out to be simple, and essentially the same for all viruses as well as genes. The bacterial viruses should serve well to find the solution, because their growth can be studied with ease quantitatively and under controlled conditions. The study of bacterial viruses may thus prove the key to basic problems in biology" [24].

Thus, by 1945 one finds two rival claimants to the study of the physical basis of life: the older biochemical school conducting its research with cells in the tradition of flux, and the aggressive molecular biologists working with viruses in the newly resurrected tradition of the crystal nature of life. The 1950s became a golden age of research for both groups. Molecular biologists Hershey and Chase used phage to demonstrate that DNA was the basis of gene structure, and Watson, Crick, Wilkins, and Franklin used X-ray crystallography to determine the structure and chemical nature of DNA. Soon to follow were the in vitro synthesis of nucleic acids (Kornberg, Ochoa), the research into the nature of genetic mutation (Ingram), the redefining of the gene concept (Benzer), and the decipherment of the genetic code (Nirenberg and colleagues). Meanwhile, in biochemistry, the concept of allosteric interactions, the use of radioisotopes to elucidate metabolic pathways, and new techniques of isolation and separation leading to the characterization of hundreds of enzymes were highlighted in the 1950s. Thus, just as biochemistry reached its long-awaited golden age, it found its pedestal shared with molecular biology.

By the end of the 1950s, however, a new synthesis was emerging between these two disciplines. Both were needed to account for the phenomena of life. In 1953, for instance, Watson and Crick [30] hypothesized that the nitrogenous base precursors of DNA would line up ("crystallize") on their template and be zippered together. No enzyme was needed for DNA replication. The biochemists, however, had all sorts of models for the enzymatic construction of nucleic acid, most of them based on the synthesis of NAD (a dinucleotide coenzyme) or on the notion that whatever enzyme degrades a substance can also synthesize it (see [31, pp. 87–90]). When, in 1958, DNA polymerase was discovered, it
was not what biochemists had expected. "Directing enzyme function with a template was unique and unanticipated by any advance in enzymology, and was for some biochemists, even after a number of years, very hard to believe" [31].

Similarly, Jacob and Monod [32] integrated biochemistry and molecular biology into a scheme whereby DNA not only coded for proteins but the proteins could bind back to specific regions of DNA. In so doing, proteins were modulating DNA for the synthesis of other proteins. Thus, the two traditions blended into each other, neither one predominating.

In this essay I have attempted to show that two rival intellectual traditions concerning the physical basis of life were manifest in the two similar disciplines, molecular biology and biochemistry, during the earlier half of this century. Today, these traditions have merged into an integrated study which characterizes far better the complex chemistry of life.

REFERENCES