The Rhetoric of Informational Molecules: Authority and Promises in the Early Study of Molecular Evolution

Edna Suárez Díaz

Science in Context / Volume 20 / Issue 04 / December 2007, pp 649 - 677
DOI: 10.1017/S0269889707001482, Published online: 09 November 2007

Link to this article: http://journals.cambridge.org/abstract_S0269889707001482

How to cite this article:
Edna Suárez Díaz (2007). The Rhetoric of Informational Molecules: Authority and Promises in the Early Study of Molecular Evolution. Science in Context, 20, pp 649-677 doi:10.1017/S0269889707001482

Science in Context **20**(4), 649–677 (2007). Copyright © Cambridge University Press
doi:10.1017/S0269889707001482 Printed in the United Kingdom

The Rhetoric of Informational Molecules: Authority and Promises in the Early Study of Molecular Evolution

Edna Suárez Díaz

Facultad de Ciencias, Universidad Nacional Autónoma de México, Max Planck Institute for the History of Science, Berlin

Argument

This paper explores the connection between the epistemic and the "political" dimensions of the metaphor of *information* during the early days of the study of Molecular Evolution. While preserving some of the meanings already documented in the history of molecular biology, the metaphor acquired a new, powerful use as a substitute for "history." A rhetorical analysis of Emilé Zuckerkandl's paper, "Molecules as Documents of Evolutionary History," highlights the ways in which epistemic claims on the validity and superiority of molecular evidence for evolution were intimately connected with authority issues in evolutionary biology. The debate is situated within the framework of the battle for resources between traditional evolutionists and molecular biologists at the beginning of the 1960s. The architects of evolutionary synthesis questioned the idea that molecular characters constitute "cleaner" and "more direct" evidence of evolution. Nevertheless, the information *discourse* constituted a productive space for the development of a new research program that, paradoxically, has made explicit the limitations of the information metaphor in reconstructing life's history.

Introduction

> Despite the acknowledged technical impotence of information theory in molecular biology, its discursive potency intensified by compromising its technical structures . . . . Information – as meaning and commodity – came to signify the privileged status of DNA as "master molecule." Emptied of its technical content, it actually became a metaphor of a metaphor, a signification without a referent. This, however, did not diminish its scientific and cultural potency. (Kay 2000, 127)

> I dislike this metaphor [the Book of Life applied to the genome] because it is superficial to the point of being false. There is no "book of life" because the text of this book really is written in ways that are in no acceptable sense analogous to "a book." (Emilé Zuckerkandl, email communication, November 5, 2005)

In 1965 Emilé L. Zuckerkandl, an Austrian biochemist, and Linus Pauling, Nobel Prize winner for chemistry, published the English version of a paper called "Molecules as Documents of Evolutionary History" (Zuckerkandl and Pauling 1965a).[1] A version in Russian had appeared some months earlier (in 1964) in a *Festschrift* volume celebrating Alexander Oparin. The paper was eloquent in its defense of one type of biological molecules, namely *semantides* (literally, molecules with meaning), as sources for reconstructing evolutionary history. Semantides, a category that includes nucleic acids and proteins, were not considered primary evolutionary data in those days. Nevertheless, the authors aimed to convince their audience not just of their potentialities as evidence for reconstructing the past, but also of their privileged status as sources of *information* for biological evolution. In defense of the value of molecular traits in evolutionary studies, their paper made a series of promises of what the field of Molecular Evolution would achieve in the future. Such promises stood in contrast with traditional evolutionary studies, and represented the culmination of five years of an intensive debate with Ernst Mayr, Theodosius Dobzhansky and, notably, paleontologist George G. Simpson (Dietrich 1998; Aronson 2002), which raised important questions of scientific authority within the realm of evolutionary biology.

In this article, I aim to explore the social and epistemic dimensions of information rhetoric, in particular the role of the *information metaphor*, in a territory previously unexplored, the early days of the field of molecular evolution. There the meaning of information was stretched to reach new limits: information was not only a set of instructions "written" in the "language" of DNA, to be "transcribed" and "translated" into RNA and proteins (Crick 1958; see Kay 2000 for an extensive historical account; see Brandt 2005 for other meanings); in the context of the disputes between traditional and molecular evolutionists, information became also a metaphor for "historical record." According to Zuckerkandl, DNA, RNA, and proteins were the privileged *documents* of the new historians of life.

The 1965 paper cannot be easily categorized as an experimental report. It contains a good deal of speculation and it is written in a deliberative style that invites the student of science to attempt a rhetorical analysis. It seems relevant to ask who the intended audience was and why the authors were so confident of the privileged status of their (still) non-existent molecular data in dealing with the reconstruction of the phyletic relations among species. An equally intriguing issue concerns the epistemic content of the information rhetoric, and the metaphor of semantides or informational molecules in particular. Given the obvious success of the molecular approach in the establishment of phylogenetic relations (extending to the contemporary comparative analyses of the genome projects), how can we account for the incorporation of rhetoric and metaphors as powerful epistemic resources?

---

[1] Although the paper was co-signed by Linus Pauling, according to Zuckerkandl, Pauling "did not participate at all" in its writing. "I remember being surprised that he co-signed it under these conditions – this was not his habit. [But] probably he co-signed it because he had committed himself to delivering a paper for the volume in honor of Oparin" (Zuckerkandl email communication, November 5, 2005; see also Morgan 1998 on this subject). Zuckerkandl must have written that text between the end of 1963 and the beginning of 1964.

First, a brief characterization of what is understood by rhetoric and metaphors will be useful. If rhetoric is the art – and the practice – of using language so as to persuade and influence others, then metaphors are one of the most common resources within a given rhetorical practice. As Lakoff and Johnson have argued (1980), metaphors allow people to understand abstract and perplexing situations in terms of everyday referents. They are able to do this by transferring words, names, or phrases to a different, but analogous, object or action. The idea that metaphors are part of scientific discourse is nowadays almost a truism (Kay 2000; Fox Keller 2002), as is the idea that rhetoric operates in different and multifarious ways in the exercise of scientific practices (Krips et al. 1995). What interests me here, however, is the fact that certain rhetorical practices, if thoroughly entrenched, may constitute a *discourse*, that is, a new space of representation and signification in which names, metaphors, and other resources acquire new and powerful meanings. Such is the case of *information discourse* or *information rhetoric* (which I will treat as synonymous) that has dominated molecular biology since the 1950s (Kay 2000).

In the context of scientific discourse metaphors deserve attention as resources in the generation and communication of knowledge. So, from a historical perspective, they deserve attention as "representations that can unfold an operational force on their own" (see Brandt 2005, 629). In particular, the metaphor of information in molecular biology has been the focus of attention in historical and philosophical studies, in view of the general implications of information discourse in contemporary society and in enterprises such as the Human Genome Project (Sarkar 1996; Kay 2000; Fox Keller 2000; Godfrey-Smith 2000; Segal 2003; Boniolo 2003; Barbieri 2003; Brandt 2005).

Thus, the goal of a rhetorical analysis of the 1965 paper published by Zuckerkandl and Pauling is not only to provide one more example of the power and pervasiveness of the information discourse in molecular biology, but also to render an analysis of the epistemic promises (either failed or fulfilled) attached to the information metaphor that gave way to the research program of Molecular Evolution. In contrast to the pitfalls generated by information discourse in molecular biology in the 1950s and even in the 1960s when it was used according to its technical meaning,[2] the field of Molecular Evolution acquired enormous momentum in the wake of information discourse, eventually leading to some of the major developments that we witness today in molecular phylogenetics and bioinformatics. Because rhetorical analysis cannot be carried out with exclusive focus on a single paper (the "nude" text), much of this essay

---

[2] Lily Kay's study on the history of the genetic code has become the *locus classicus* in which this thesis has been developed in its historical, sociological and even cognitive dimensions. In particular, chapters 3 and 4 deal with the impotence or the failures of information *theory* when it was pretended to be applied technically. As the quote at the beginning of this essay points out, this fact did not preclude the information *discourse* to transform research agendas and the ways in which biological knowledge came to be represented (Kay 2000). Segal points out, however, that Kay and others have missed the crucial point that "information theory must be understood in its historical context, as an imprecisely defined theory close to *cybernetics*" (Segal 2003, 276; my emphasis). An exception to this general failure is Creager and Gaudilliere (1996).

will present the broader historical context or *rhetorical situation* (Bitzer 1968) in which Zuckerkandl and Pauling's paper was written and published.

I have organized this essay in four sections. The first deals with relevant contemporary work on the uses of molecular data for evolutionary comparisons; in particular, it focuses on the comparisons of amino acid sequences of proteins at the beginning of the 1960s by Emilé Zuckerkandl and Linus Pauling at Caltech, and by Emanuel Margoliash and his colleagues in Chicago.[3] The second section presents the broader context in which Zuckerkandl and Pauling published their ideas on molecules as evolutionary characters. That context was marked by authority controversies between "traditional" organism-centered evolutionists, and the "new" molecular biologists interested in evolution. The issue at stake was whether molecules could count as evidence for evolutionary processes; in this sense, questions of epistemic authority became entangled with questions of social legitimacy. As I will try to show, the controversies can be better understood as part of what has been called "the molecular wars" (Wilson 1994). The third section presents the rhetorical analysis of the 1965 paper, seeking to locate the sources of epistemic and social power of the information metaphor. In the last part of the paper I will attempt a somewhat outstanding goal for a historical paper: I will consider whether the promises of the information discourse of the 1960s failed or were fulfilled, in light of the contemporary uses of bioinformatics in phylogenetic studies. This should not be interpreted as an evaluation of scientific research, but as a means to reflect on the ways in which rhetoric and metaphors may become constitutive resources of scientific knowledge.

The Nascent Field of Molecular Evolution

The idea of studying evolution through the molecules of living beings was not new in the 1960s. During the first part of the twentieth century the techniques of immunology and biochemistry were used to obtain a measure of the affinity and relatedness between species. As early as 1904, George G. Nutall used serological immune reactions for this purpose and other scientists seemed to have followed this line (Reichert and Brown 1909). Research on human blood groups in the 1950s using serological techniques also produced empirical data on the genetic variability of human populations, providing the foundation for a molecular approach to micro-evolutionary processes (see Powell 1994 for extended references).

It was not until the 1950s that immunological techniques were refined by Alan A. Boyden, and taken up during the 1960s by Curtis Williams, Ann Hafleigh, Morris

---

[3] The uses of molecular techniques and molecular data in studies of evolutionary biology were the hallmark of different types of scientific approaches at that time. I have dealt with some of these uses within *theoretical traditions* concerning the origins of the Neutral Theory of Molecular Evolution (Suárez and Barahona 1996), and in experimental traditions, concerning the establishment of satellite-DNA (Suárez 2001).

Goodman, and John Buettner-Janusch, among others (Suárez 1996; Dietrich 1998; Aronson 2002). Significantly, all these researchers were interested in the evolution of primates, and not surprisingly, some of the most heated debates and extreme positions in the years to come focused on the problem of human evolution and its relation to primates.

Meanwhile, in 1949, biochemist Marcel Florkin published an influential book in which he addressed biological evolution by comparing metabolic pathways and many types of molecules present in different organisms (Florkin 1949). Along similar lines, Christian Anfinsen published *The Molecular Basis of Evolution* ten years later (Anfinsen 1959). These books might have spurred other uses of molecules in evolution, namely, the studies of the origin of life and exobiology (Jukes 1966 and Woese 1967 are illustrations of these concerns in the mid-1960s).

By the end of the 1950s the use of molecules in the study of evolution received a new impulse as the most recent molecular techniques centered on the analysis of two types of macromolecules: proteins and nucleic acids (Suárez 2001). Using these molecular techniques in combination with serological techniques, one of the first and obvious goals of molecular evolutionists in the 1960s included the development of methods for establishing and *measuring* genetic affinities, or degrees of evolutionary relation, among species. The academic and social setting of biology, however, was not the same as the one that had prevailed a couple of decades earlier. The approach to evolution now climbed on the "molecular biology bandwagon."

The elaboration of phylogenies had been one of the main subjects of evolutionary biology in the century after Darwin. Paleontology, comparative anatomy and embryology, biogeography and, in general, evolutionary systematics, had dedicated some of their most important research efforts to the establishment of phyletic relations among species and to the calculation of temporal divergence among lineages using different methods. By the beginning of the 1960s these fields had not only succeeded in giving an account of the relations between important groups of organisms (basically, Eukaryota), but they had reached a high degree of consensus on the mechanisms of evolution (Smocovitis 1996). Also, as in the work of paleontologist George G. Simpson, there were attempts to measure the rates of evolution of lineages. Simpson coined the terms "tachychelic" for "fast" evolving lineages, "horotelic" for standard rate distributions, and "bradytelic" for the so-called "living fossils" (Simpson 1944). The meanings of these terms, however, were comparative and qualitative.

By contrast, the new molecular biologists focused almost exclusively on giving *quantitative* measures of the degree of relatedness among species and their evolving rates. They thought that their experimental techniques allowed them a quantitative approach not available within the more traditional toolbox of evolutionary biology. In 1959 Ellis T. Bolton and Roy J. Britten, both working at the Department of Terrestrial Magnetism of the Carnegie Institution of Washington, began to use the phenomenon of DNA renaturation (later known as DNA- hybridization) as a technique for measuring what they called the "proportion of relatedness" among species. Invariably, the measurements they obtained for "genetic homology" between a pair of biological species was a quantitative measure of the proportion of re-association between the single stranded DNA of two species (Suárez 2001).[4] Bolton and Britten restricted their experiments to the few DNA species available in those days, so they compared some bacteriophages, *Escherichia coli*, tuna, mice, yeast, and lettuce in a typical experiment.

Using different techniques, other teams focused on the evolution of proteins. In the tradition of immunological studies, Morris Goodman (1960, 1964) and Curtis A. Williams (1967), for instance, used two-dimensional electrophoresis and anti-serum reactions to study the serum proteins of primates. This paper, however, will focus on the parallel work of Emmanuel Margoliash (then at Abbot Laboratories in Chicago) and Emilé Zuckerkandl and Linus Pauling at Caltech. Because of the privileged role played by Zuckerkandl as spokesman of the new molecular evolutionists in the ensuing debates and in the construction of the new research agenda, I shall give a more detailed reconstruction of his work.[5]

Zuckerkandl's collaboration with Pauling began in 1959, when he arrived at Caltech and was asked to study hemoglobin from an evolutionary perspective (Hager 1995; Morgan 1998). Pauling arranged that he work with graduate student Richard T. Jones to analyze the hemoglobin of various primate species using the technique of "fingerprinting" (Ingram 1957). This technique – also used by immunlogists – combined electrophoresis and chromatography for a two-dimensional comparison of peptides (Zuckerkandl, Jones, and Pauling 1960). Very soon, however, Zuckerkandl and Pauling abandoned this experimental approach, mainly because the data obtained were not suitable for a quantitative analysis. Nevertheless, the fingerprinting analysis of peptides gave Zuckerkandl and Pauling their first polemic results concerning the evolutionary relation of man and primates. Their (still) qualitative conclusions established that gorilla, chimpanzee, and human hemoglobin patterns were almost identical in appearance. But it was clear that a quantitative analysis of different

---

[4] Actually, "genetic homology" cannot be measured; what can be "measured" is "similarity." Either a couple of characters (genes, functions, behaviors) share a common ancestor (that is, they are homologous) or they do not. Such incorrect uses of evolutionary terms were common among the new molecular evolutionists, coming from disciplines like biophysics (the case of Britten).

[5] Zuckerkandl's biography could certainly throw light on his prominent role. He was born in 1922 to an aristocratic, intellectual family in Vienna (his grandfather was the dean of the University of Vienna, and several family members were prominent figures in the academic and artistic world). He was trained as a piano recitalist and as a scientist. After the Second World War, he studied at the Sorbonne in Paris and at the University of Illinois. Having returned to France, he obtained a job at the Marine Laboratory at Roscoff, Brittany, but he was more attracted to molecular problems. In 1957 he arranged an appointment with Linus Pauling, who was on a trip in France, and proposed that they carry out a research project on hemocyanin and copper oxidases, to be developed at Caltech. Pauling agreed, but on September 1959, when Zuckerkandl arrived in California, Pauling was very enthusiastic about evolutionary genetics. He had become involved in the debate on the effect of radiation on mutations *and* molecular diseases, as part of his growing concern with the uses of atomic energy, and this was the beginning of his growing interest in biological evolution at the molecular level (Hager 1995). More details of Zuckerkandl's biography are given in Morgan 1998. On Zuckerkandl as a "discipline builder," see Suárez 1997.

hemoglobin molecules required a more detailed description of their amino acid sequences.

Thus, in 1961 Zuckerkandl switched to amino acid sequences as a means to compare proteins. He collaborated with Walter Schroeder, also at Caltech, to determine the amino acid composition of gorilla hemoglobin (Zuckerkandl and Schroeder 1961). Their results indicated that the α-chains of human and gorilla hemoglobin differed by two residues (today it is established that they differ by one) and the β-chains by only one. The similarities between the molecules pointed towards a common molecular ancestor (meaning they were *homologous*), but Zuckerkandl was not able to publish these conclusions at that time because of Schroeder's opposition to the theory of evolution (Morgan 1998; Zuckerkandl personal communication November 2005, see note 6).

At the same time other teams were working on the complete amino acid sequence of the α- and β-chains of human hemoglobin, the most important ones being Lyman Craig's laboratory at the Rockefeller Institute of Medical Research in New York, Gerhard Braunitzer's laboratory at the Max Planck Institute in Munich, and Schroeder's laboratory at Caltech. Zuckerkandl benefited from his access to the sequences obtained in those laboratories, and in particular from the 30 terminal residues of the human β-chain brought back to Caltech by Max Delbrück after a visit to Braunitzer's laboratory in Germany.[6] He compared this sequence with the preliminary results of Schroeder's team and concluded that the α- and β-chains of human hemoglobin were homologous, something that had been previously hypothesized by Itano in 1957 and Ingram in 1961 (Hager 1995; Morgan 1998).

With those data at hand, Zuckerkandl and Pauling attempted a new comparative analysis of adult hemoglobins. They published their results in a 37-page paper relating molecular disease and Molecular Evolution, in a volume dedicated to Albert Szent-György (Zuckerkandl and Pauling 1962). The implications of this paper were far reaching. First, they corroborated the similarities between man and gorilla. Connecting the variability of populations and the idea of molecular disease, they claimed that "since

---

[6] I quote extensively: "I had gotten no pre-publication communication of any of Braunitzer's sequences, except the sequence fragment that Delbrück had scribbled on a piece of paper. Pauling had nothing to do with that communication. I knew Delbrück privately and independently of Pauling. Pauling's presence thus played no role in the unexpected access that I had found to that one sequence fragment. Neither any collaboration nor any competition played a role in this communication – only pure scientific interest. Max Delbrück knew about my ongoing work and knew that I would be interested. Walter Schroeder, who was aware of Gerhard Braunitzer's competition, was away on a sabbatical. Did Braunitzer know about an intent on the part of Max Delbrück to pass on the sequence fragment to me? I rather doubt it. It is quite possible that Delbrück had no such intent, and that the idea of the communication occurred to him after his meeting with Braunitzer, perhaps only after his return to Caltech .... In any case, because of Schroeder's opposition to the concept of evolution, I never got to publication of the sequence homology concept, of its application to globin evolution and to proteins in general, and of this particular illustration of the importance of gene duplication in evolution. I was only able to incorporate this evolutionary insight into all subsequent thinking" (Zuckerkandl email communication, November 5, 2005).

gorillas get along well with their hemoglobin, as they prove by existing, it is not likely that the gorilla β-chain, if it were present in humans, would cause molecular disease . . . . Thus, if the gorilla β-chain occurred in a human family the physician's attention would probably not be attracted to it" (ibid., 200).

Moreover, they developed the idea that the time of divergence between two species could be calculated from their evolutionary rate, assuming that the rate of mutation was relatively constant (that is, it conformed to a mean). They estimated the number of differences between the α-chains of horse and human to be eighteen amino acid substitutions (based on previous work by Braunitzer). This number was correlated with the time of divergence between human and horse, as calculated by paleontologists (between 100 and 160 million years), and they obtained an average of about one amino acid substitution every 14.5 million years. Taking this as the rate of evolution of hemoglobin, they calculated the time of divergence of gorilla and man from their common ancestor to be approximately 11 million years. Such a figure fell within the lower limit of the range that most paleoanthropologists considered acceptable at that time (between 11 and 35 million years). Moreover, they had developed (and applied) an idea with multiple implications for evolutionary studies: the so-called *molecular evolutionary clock*.[7] As Morgan has stated, "the idea of using the number of amino acid substitutions to make temporal divergence estimates evolved as Zuckerkandl wrote the paper" (Morgan 1998, 164). And, as Alex Rich put it, "at one stroke [Zuckerkandl and Pauling] united the fields of paleontology, evolutionary biology and molecular biology" (quoted in Hager 1995, 541).

Despite their brave conclusions, the paper included a long section on the possible sources of "error" for these calculations: the lack of preservation of deleterious mutants, mutations that completely transform the hemoglobin molecules, back mutations, change in ecological conditions, and population size. Most of these reservations would disappear in the following years, but they point to the fact that neither Pauling nor Zuckerkandl were unaware of the many drawbacks of the molecular clock hypothesis; this attitude was not always shared by other molecular evolutionists, notably by Margoliash, whose work I now focus on.

Margoliash's work revolved around cytochrome *c*, a small heme-protein conserved across the whole evolutionary tree. In 1961, together with Emil Smith, Gunther Kreil, and Hans Tuppy, Margoliash published the complete amino acid sequence of horse cytochrome *c*. First doing research for a private laboratory, Margoliash had explicitly manifested his interest in evolutionary studies and focused on sequencing a set of homologous proteins. In 1963 he published a comparative study of the seven

---

[7] The "molecular evolutionary clock" or molecular clock, for short, was not given this name in the 1962 paper, but in another joint paper published three years later (Zuckerkandl and Pauling 1965b). The molecular clock is the hypothesis that the rate of evolution of a given protein (or DNA) molecule is approximately constant over time and among evolutionary lineages. For a detailed historical reconstruction of the hypothesis of the molecular clock, see Morgan 1998.

known cytochrome *c* sequences, including horse, human, pig, rabbit, chicken, tuna, and yeast. Margoliash concluded that the "most plausible interpretation of the abundant structural similarities" of these proteins was that they derived "phylogenetically from a common primordial cytochrome *c*," that is, they were "truly *homologous* structures in the evolutionary sense." Making use of Zuckerkandl and Pauling's molecular clock, Margoliash adhered to the idea that it would be possible to estimate the period of time at which two biological lineages diverged based on the differences in amino acid substitutions (Margoliash 1963). But in contrast with the cautionary attitude of Zuckerkandl and Pauling, Margoliash's commitment to the molecular clock went further, assuming that "the number of residue differences between the cytochromes *c* of any two species is mostly conditioned by the time elapsed since the two lines of evolution leading to these two species originally diverged" (ibid., 677).

Margoliash's work, like that of Bolton and Britten, corroborated the phylogenetic trees established by more traditional approaches, but it was clearly more ambitious. He aimed at reconstructing the complete ancestry of living beings using only *one* molecule as a phylogenetic trait, a promise that – as we will see – was part of the early research project of molecular evolutionists and one that he enthusiastically defended. Moreover, he used his comparative approach to draw inferences as to the existence of genetic "hot spots" and "cold spots" in cytochrome *c*. Hot spots were sites in which a variety of amino acid sequences could be found, suggesting that function in that area could be compatible with a variety of primary structures; invariant residues or cold spots, instead, could be an expression of properties of the corresponding DNA "which make them impervious to mutagenic influences, just as well as of selection for functionally necessary structures" (ibid., 675).

Margoliash argued that a correct interpretation of the similarities and differences between proteins could only be achieved by means of a quantitative analysis, and thus that "many more homologous cytochromes *c* from suitable chosen species will be required to establish the statistical validity" of such relations (ibid., 677). In pursuing this program, Margoliash's team had already sequenced 20 different cytochrome *c* molecules by 1966, more than for any other protein. These data were crucial to his future collaboration with Walter Fitch on the development and application of the first computer programs for the construction of phylogenies (Fitch and Margoliash 1967; see also Fitch 1988, for his recollections of these events).

Organismic *versus* Molecular Approaches to Evolution

The incursion of molecular biologists in evolutionary biology was not welcomed everywhere. The 1960s were a difficult time for evolutionary biologists, who were feeling, and actually suffering, the impact of the molecular biology bandwagon. As previous authors have noticed, Ernst Mayr, Theodosius Dobzhansky, and George G. Simpson emerged as spokesmen for the more "classical" branches of biology, not least because in those years they occupied prestigious academic positions and participated in important scientific and institutional committees (Beatty 1990 and 1994; Wilson 1994; Smocovitis 1996; Dietrich 1998). Beatty (1990, 1994) has made a powerful case to prove that there was a legitimate battle for resources behind the scientific and conceptual issues rising during the so-called "molecular wars" (naturalist Edward O. Wilson's label). This should be understood not only as a battle for financial support (which it was), but for the best human resources and a fair distribution of prestige between the "new" and the "classical" fields of biology (Mayr 1963).[8]

The degree to which the concern for resources was blended with broad conceptual considerations regarding the place of organism-oriented studies in biology is amazing. Mayr seems to have developed his famous distinction between "ultimate and proximate causes" of biology as a defense of the complementary nature of evolutionary and molecular approaches (Mayr 1961). As Director of the Museum of Comparative Zoology since 1961 and, in particular, as a member of important committees in which the institutional structure of the new biology and its future funding were being debated (at the National Academy of Sciences-National Research Council and at Harvard University), Mayr forcefully and constantly used this distinction to promote the view that there is more to biology than the study of proximate causes (Beatty 1994). Complaining of the (American) inclination to equate "classical" with "old-fashioned" and "passé" he said:

> Even scientists have succumbed to this psychology. Whenever there is a new breakthrough we tend to abandon the previously active areas. A massive follow-up of new discoveries is normally highly productive, and no damage would be done if it were not for the fact that the abandoned fields are rarely exhausted. When science is diverted from them, science suffers an irreparable loss of know-how in the form of specialized information and methodology.... This development is followed by other trends.... Bright young students quite naturally look for the greenest pastures. Recruitment thus becomes a serious problem. This is aggravated by the attitude of the Young Turks in the new areas. They tend to regard the more classical branches of their science with unconcealed contempt. At worst, this intolerance leads them to attempt to cut off funds from the more classical fields. The situation is further aggravated by the attitude of some foundations and science administrators.... The follow-up of breakthroughs rarely requires large foundation support. The bandwagon tendency takes care of this automatically. (Mayr 1963, 765)

In the same vein, Dobzhansky published in 1966 an article entitled "Are naturalists Old-Fashioned?" where he warned that "the reductionist notion that knowledge about

---

[8] E. O. Wilson recalls this time at Harvard University as one of "conflict with the molecular faction centered with increasing heat on new faculty appointments" (Wilson 1994, 227), as the molecular biologists led by James D. Watson tried to get rid of what they called "stamp collectors." Mayr, Dobzhansky and Simpson had already been denied financial support from the Rockefeller Foundation during the 1950s, for the development of systematics and evolutionary biology (Beatty 1994; Smocovitis 1996).

lower levels provides deeper insight unfortunately reinforces the equally ridiculous notion that, corresponding to the hierarchy of organic nature, but running in reverse, there is a hierarchy of the biological sciences, with molecular biology on top" (Beatty 1990, 210).

Mayr, Dobzhansky, and Simpson were united in "their desire to ensure that organismic biology continued to receive support in the age of molecular biology" (Aronson 2002, 444). Their attitude was not confrontational, and in general they argued for the need to integrate the study of molecules and organisms as complementary approaches, without reducing biology to physics and chemistry. However, as molecular biologists entered the field of evolutionary biology, the *architects* expressed their doubts on particular conceptual issues. Mayr and Dobzhansky were uncertain of the value of molecules as evidence of evolutionary processes, and Simpson's response to the value of the molecular approach was even more skeptical. Historians of science who have studied the conflict between traditional and molecular evolutionists have detected this uneasiness (Beatty 1990; Dietrich 1998; Aronson 2002).

There were several reasons for Simpson's position, all of them deeply rooted in his earlier work and previous conceptions. According to Simpson's philosophy of science, biology occupied "the center of all science" (Simpson 1964a, 88). Simpson argued that biology, contrary to physics and chemistry, could deliver not only reductionist, but also teleological explanations. Biology, in Simpson's view, "should be a *historical science* that seeks ultimate causes and highlights contingency (i.e., the unique interactions of an organism with its constantly changing environments)" (Aronson 2003, 445, emphasis added; Simpson 1964c). Paleontology was in Simpson's view the most important biological science insofar as it provided the framework upon which all other contributions needed to be organized (Aronson 2003, 444), and the fossil record was seen as the ultimate source of evidence for evolutionary (historically contingent) events and processes.

More particularly, Simpson's position rested on the fact that the results of Molecular Evolution concerning the evolution of primates contradicted some of the most important findings of paleoanthropology. Simpson himself had made previous exhaustive evaluations of the state of taxonomy in this field (Simpson 1964a; also see Aronson 2002). As molecular evolutionists approached this area of research (Zuckerkandl, Jones, and Pauling 1960; Zuckerkandl and Pauling 1962; Goodman 1960), Simpson began to deal with the evidence they presented and with their conclusions regarding the evolution of primates.

In the summer of 1962 the Wenner-Gren Foundation organized a conference on "Classification and Human Evolution" at Burg Wartenstein, Austria. The *architects* were present, as were the main researchers in primate Molecular Evolution. As Dietrich (1998) has claimed, this was a key event for the unraveling of future arguments and attitudes of molecular and organism-oriented evolutionists. Zuckerkandl presented his and Pauling's results on the evolution of hemoglobins in man and primates (Zuckerkandl 1964). Morris Goodman presented his conception of the phylogeny of man based on his work with serum proteins (Goodman 1964). Simpson's talk focused on "The meaning of Taxonomic Statements," while Mayr dealt with the taxonomic evidence of fossil hominids, and Dobzhansky with the genetics of hominid evolution.

One of the most important outcomes of the Burg Wartenstein conference was the direct discussion, among a "restricted committee" including Zuckerkandl, Goodman, Dobzhansky, Mayr, and Simpson (among others) of the "potentialities of the molecular approach to anthropology and the study of evolution" (Zuckerkandl 1964, 254). Dietrich has given a detailed account of the exchanges between the architects of the evolutionary synthesis and Zuckerkandl and Goodman as representatives of the molecular evolutionists. He has hypothesized that the exchange at the Burg Warterstein conference was pivotal to the launching of Mayr, Simpson, and Dobzhansky's "most pointed attacks on molecular biology" (Dietrich 1998, 95). The same can be said about Zuckerkandl. After 1962 he felt compelled to express his views in a more open, direct manner (see below). The main arguments developed by the architects against the use of molecular evidence set the tone of the rhetorical situation in which the informational discourse was developed and the metaphor of information acquired a wide range of implications for evolutionary studies.

Drawing on the discussions that took place during the meetings of the "restricted committee," Zuckerkandl presented – in the written version of his talk – a list of the advantages and the disadvantages of studying human evolution at the molecular level. Among the latter, he explicitly recognized that molecular studies did "not lead to the elucidation of the causality of evolutionary trends," and he acknowledged the importance of other biological levels: "Molecules make proposals, and these proposals are taken up or dropped at other levels." He further specified that the "molecular, supra-molecular, cellular, tissue, organic, systemic, individual, and further the ecological, sociological and psychological levels" had to be considered key elements in the "determinism of the evolutionary trends" (Zuckerkandl 1964, 258). Addressing Mayr's concerns, he also conceded that the analysis of protein sequences had nothing to say about the openness or the closeness of a genetic pool, a very important issue for the notion of biological species.

Despite his cautionary approach, Zuckerkandl emphasized that one of the advantages of using proteins for phyletic considerations was that molecular characters were "cleaner" material than morphological characters (ibid., 260). This was a direct response to the doubts expressed by Mayr and Dobzhansky, who had claimed that the majority of functional traits in organisms were polygenic. Zuckerkandl's assertion had several implications. Some of them can be grouped broadly as methodological. As Zuckerkandl said: "morphological characters of living matter undoubtedly are among the most complex effects in existence in the universe and as such should be among the poorest analytical tools" (ibid., 243). In this sense, he seemed to equate the analytical approach of physics (directed towards "simple" or basic phenomena) with the molecular approach to evolution, adding the explicit clarification that an analysis of complex traits was clearly inferior. A second sort of implication was more epistemological in tone, and pointed to the *fundamental* character of molecular – genetic – explanations: "While morphological characters can be ascribed to an almost hopelessly complex interweaving of causes and effects, different characters being partly affected by the same causes and one given character by different causes, this network is relatively disentangled at the molecular level" (ibid., 260–261).

On the architects' view it was feasible to concede the convenience of studying evolutionary processes at the molecular level *in addition to* the organismic level. Though it was difficult to accept Zuckerkandl's claim that molecules represented "cleaner" and more direct evidence for evolutionary processes, they remained open to what Molecular Evolution could offer. Zuckerkandl remembers that Dobzhansky told him at the Burg Wartenstein conference: "Perhaps in twenty years you will be able to say 'I was right!'" (Zuckerkandl personal communication, November 2005).[9] However, Simpson's attitude was more critical and might have been important in explaining the future interventions of Zuckerkandl: "Only in the case of Simpson did I have the impression that his mind was pretty well closed in regard to conceding to the field of Molecular Evolution the place that I thought was its rightful one within the field of evolution in general" (ibid.).

As already mentioned, Simpson's view of evolutionary biology was very different. So was his understanding of evolutionary processes, which he linked to his most general and important contributions to paleontology and evolutionary synthesis, namely, his ideas on the *tempo* and the *mode* of evolution. Based on paleontological evidence, he had concluded that evolution did not occur at a stable rate (as the molecular clock hypothesis maintained), but rather proceeded at varying rates; actually, this was the finding that supported his corresponding terminology of bradytelic, horotelic, and tachytelic species. According to Simpson, evolution was intimately historical, that is, contingent on environmental conditions that would never be repeated.

In his intervention at the conference Simpson maintained that the wealth of taxonomic data and their difficult interpretation supported the conclusion that the rates and modes of morphology changed greatly from earlier to later parts of the primate phylogeny (Simpson 1964a, 15). He also claimed that the postulate that Hominidae and Pongidae belonged to different families should be accepted (ibid., 16), even though he recognized that there was no universal agreement (and even that an agreement may not be desirable) among taxonomists on the affinities between primate species and their translation into formal classification (ibid., 18). Nevertheless, Simpson clarified that man, gorilla, and chimpanzees were "not almost identical," and

---

[9] Zuckerkandl enjoyed a friendly relationship with Dobzhansky, one with many contacts. Zuckerkandl's wife, Jane, was the daughter of cytogeneticist C. W. Metz, and through him he had known Dobzhansky for many years. But the relationship between Zuckerkandl and Ernst Mayr "was very special." They had met before, in the 1950s, when Mayr spent time at the Station Biologique of Roscoff, in Brittany, where Emilé and his wife worked and lived. "Though over the years (our) contacts suffered interruptions, they were always reestablished, and we became friends in the strong sense of the word" (Zuckerkandl email communication, November 5, 2005).

responding to Zuckerkandl's (and Goodman's) claims, he further stated: "Seemingly contradictory evidence, e.g., that of the hemoglobins as reported by Zuckerkandl (in this book), indicates merely that in *certain* characters *Homo* and its allies retain ancestral resemblances and that *these* are not the characters involved in their otherwise radical divergence" (ibid., 25).

Simpson reacted with a still more comprehensive response to molecular evolutionists in an article entitled "Organisms and Molecules in Evolution," published in *Science* almost at the same time as the Burg Wartenstein conference memories were published (Simpson 1964b). There, he questioned the hypothesis of the molecular clock, that is, the view that proteins "have evolved by some sort of internal constant-rate mutational process and not in an irregular or a specifically adaptive way" (ibid., 146). Simpson focused his attention on the molecular biologists' work on the evolution of primates. He pointed to the contradictory evidence brought forth by Goodman (1960), Zuckerkandl and Pauling (1962 and 1965b), and Hafleigh and Collins (1966). Although the work of the immunologists Buettner-Janusches (1963) deserved his praise, in general he was exasperated by the molecular evolutionists' arrogance in their entrance to the field of paleoanthropology. Simpson again attacked Goodman's controversial claim that chimpanzees, gorillas, and humans were so similar from an immunological point of view that they deserved to be grouped in the same family, despite their numerous physical differences and all the previous and contemporary work on the subject. (See Washburn 1964 and Buettner-Janusch 1963 for examples of the research done at that time.)

Simpson also reacted forcefully to Zuckerkandl's assertion (published in the Burg Wartenstein memories edited by Washburn 1964) that "from the point of view of hemoglobin structure, it appears that gorilla is just an abnormal human, or man an abnormal gorilla, and the two species form actually one continuous population." To this, he responded: "From any point of view other than that properly specified, that is of course nonsense. What the comparison really seems to indicate is that in this case, at least, hemoglobin is a bad choice and has nothing to tell us about affinities, or indeed tells us a lie" (Simpson 1964b, 1536). Simpson practically questioned the validity of molecules as evidence of evolutionary processes, and claimed that "if one (protein molecule) can be misleading, so can many" (ibid.).

Triggered by the opposition of some "reputable scientists," the scenario was set for a major defense of what Zuckerkandl considered the "rightful place" of Molecular Evolution. It is in this context that Zuckerkandl recounts:

> It prompted me to spell the "tenants and aboutissants" of the field more broadly than I would probably have done, had the opposition not been present. The task was to establish what the semantide level – and the interactions-among-semantides level! – contributed to the knowledge of biological systems, especially in relation to the organismic level that many thought to be the only one from which we could "really" understand evolution, all other levels being useful accessories at best. (Emilé Zuckerkandl, email communication November 5, 2005)

Molecules as Documents of History

The paper published in 1962 marked the beginning of a fruitful collaboration between Zuckerkandl and Pauling. Since that year, and up to 1965, they published a series of essays in which they exposed some of the most far-reaching conclusions in the study of evolution at the molecular level, and they retooled important evolutionary concepts to fit the molecular perspective. Beginning with the proposal of the molecular clock in 1962, and culminating with the reformulation of concepts such as the convergence and divergence of proteins, the importance of functional constraints, and the role of gene duplication in Molecular Evolution (Zuckerkandl and Pauling 1965b), these papers developed the basic themes of the research program in Molecular Evolution for the next decades. And, as Morgan has already noted, their 1962 collaboration set a "tone": "Pauling would be invited to submit to a *Festschrift* volume without peer review, and together they would publish pioneering papers on Molecular Evolution" (Morgan 1998, 164). This fact should be kept in mind when analyzing their 1965 article. All these papers fail to conform to the standard experimental report: they are too long and contain more speculation than a typical peer-reviewed publication would allow. They are, nevertheless, scientific texts in so far as they portray the authors' wide knowledge of the field and they present arguments supported by a wealth of empirical evidence.

In "Molecules as Documents of Evolutionary History" (1965), Zuckerkandl seems to be responding to the need for a more objective, direct, and quantitative way to study biological evolution, by focusing on the differences between types of molecules and between morphological and molecular characters and, even more importantly, by the various uses he gave to the metaphor of information. His defense of studies at the molecular level towards the accomplishment of a more direct and quantitative analysis, however, did not commit him to the physicalism and reductionism that might be observed in later molecular evolutionists.[10] In fact, a large part of the paper is geared towards explaining the possibility that "isomorphisms" in amino acid sequences – resulting from the so-called degeneracy of the genetic code – might be subjected to natural selection because of the interactions among molecules and other levels of biological organization.

---

[10] For instance, Motoo Kimura, Jack King, and Thomas Jukes, authors of the Neutral Theory of Molecular Evolution, defended, from different positions and in different contexts, the idea that biological evolution could be understood as a mere physical statistical phenomenon at the molecular level. Kimura (1983) wanted his Neutral Theory to be the equivalent of the thermodynamic theory of gases where genetic drift was a stochastic phenomenon analogous to the behavior of gases. King and Jukes (1969) defended the idea that DNA substitution rate might have a behavior analogous to "radioactive decay" based on the idea of the molecular clock. Although he was one of the authors of the idea of the molecular clock, Zuckerkandl cannot be considered a defendant of neutralism. Moreover, he has never been the reductionist that Simpson claimed him to be, even if we take literally some of his expressions. For Zuckerkandl's "sophisticated" conception of evolution, in particular his conviction that it takes place at different levels, see below.

Zuckerkandl's paper meets what Swales (1990) has identified as the rhetorical "move sequence" in contemporary research articles: a centrality statement (the importance and localization of the problem to be addressed) is followed by a gap statement (the absence of a satisfactory or adequate solution), and finally by a gap filling statement (an argument presenting a solution). However, it meets this rhetorical move in unorthodox ways. The problem is presented within an exceptionally general assertion together with a philosophical reference and a rhetorical question, stating the centrality of the subject and the need for a different approach:

> Of all natural systems, living matter is the one which, in the face of great transformations, preserves inscribed in its organization the largest amount of its own past history. Using Hegel's expression, we may say that there is no other system that is better *aufgehoben* (constantly abolished and simultaneously preserved). We may ask the questions where in the now living system the greatest amount of their past history has survived and how it can be extracted. (Zuckerkandl and Pauling 1965a, 357).

If one is acquainted with Zuckerkandl's background, his familiarity with the language of philosophy is understandable (see note 6). His reference to Hegel, however, is unexpected in a scientific paper. As we shall see, it seems to point towards a "sophisticated" biological perspective that has deep roots in Zuckerkandl's formative years; at the same time, the reference unveils his particular use of the information metaphor, namely, as an *historical* resource. A closer analysis of the rhetorical question, and his answer to it, will bring us back to Hegel. The gap-filling answer is given next: "At any level of integration, the amount of history preserved will be the greater, the greater the complexity of the elements that have to be affected at that level and the smaller the parts of the elements that have to be affected to bring about a significant change" (ibid.).

What followed, however, was not an analysis of what terms like "complexity" meant. Because of its later connection with "information" it might be hypothesized that complexity is loosely related with one of the many meanings of information in *physics*, the idea that "ordered" systems contain more information: "Gain in entropy always means loss of information" (Segal 2003, 278). Even more abruptly, the paper jumps to a proposal for classifying different types of biological molecules according to how much *information* is contained in each type. Thus, the text exhibits a "terminological displacement" analogous to displacements in other historical cases. In this case "history" is replaced by "information."[11] Zuckerkandl offered the following classification of molecules:

---

[11] Lily Kay (2000), and previously Michael Morange (1998) have identified the terminological displacement of biochemical or biological "specificity" in the molecular biology of the 1930s and 1940s, and its substitution with "information" in the 1950s. According Christina Brandt's study, the term "function" was displaced by "information" in the work of German biochemist Gerhard Schramm on the TMV (Brandt 2005).

i) *Semantophoretic* molecules or *semantides* carry the largest amount of information; they carry the information of genes or a transcript thereof. Genes are the primary semantides, messenger-RNA molecules are secondary semantides, and polypeptides (at least most of them) are classified as tertiary semantides.
ii) *Episemantic* molecules are synthesized under the control of tertiary semantides; and
iii) *Asemantic* molecules are not produced by the organism, and therefore do not express – either directly or indirectly – any of the information that this organism contains.

The rhetorical question of *where is the greatest amount of history preserved in the living systems* meant a reformulation of the classical question of taxonomists and paleontologists: *which are the best characters to study in order to reconstruct biological evolution?* The text gives two answers: at the molecular level, semantides or semantophoretic molecules are privileged characters in the construction of phylogenies. Along these lines, Zuckerkandl says, for example, that "there may be a region of overlap of semantides with the lowest degree of complexity and of episemantic molecules with the highest degree of complexity. The former, however, will still contain more information than the latter about the present and the past of the organism." Moreover, he states, "the most rational, universal and informative molecular phylogeny will be built on semantophoretic molecules alone" (Zuckerkandl 1965a, 359). This answer, though definitive about the privileged character of semantides, still leaves room for phylogenies made from more conventional, morphological characters, a point reinforced by Zuckerkandl's broader anti-reductionist approach to evolution.

In a passage where he deals with other levels of evolution, Zuckerkandl gives a second, stronger answer to his rhetorical question:

> Even these small changes (in which an amino acid is altered in a polypeptide) can have profound consequences at higher levels of organic integration, through an alteration of the established pattern of molecular interaction. Therefore, in macromolecules of these types there is more history in the making and more history preserved than at any other single level of biological integration. (Ibid., 360)

It is reasonable to think that Simpson interpreted Zuckerkandl's views in accordance with this answer; moreover, this was the view that the majority of molecular evolutionists held at that time. In any case, in both answers the metaphor of molecules as historical documents was closely related to a second metaphor of common use among molecular biologists. The idea that information "flows" from nucleic acids to proteins and phenotypic characters, and that the fundamental "code" or "archive" resides in nucleic acids was first formulated by Francis Crick in 1958 (see below). Zuckerkandl's classification of biological molecules stated that information – which is relevant for historical reconstructions – was *lost* as one passes from semantides to episemantophoretic and asemantic molecules:

> The relevance of molecules to evolutionary history decreases as one passes from semantides to asemantic molecules, although the latter may represent quantitative or qualitative characteristics of groups. As such they are, however, unreliable and uninformative. It is plain that asemantic molecules are not worthy of consideration in inquiries about phylogenetic relationships. (Ibid., 358).

This statement had epistemic consequences directly connected to the position that Zuckerkandl wanted to defend for molecular characters. Episemantic molecules could be used to reconstruct parts of the phylogenetic tree, for instance, but it was "characteristic of those studies that they need independent confirmation. Such independent confirmation may be obtained by direct or indirect studies of semantides" (ibid.). Thus, semantides *alone* could be the basis for the determination of phylogenetic relationships, something that episemantic molecules could not be. However, given Zuckerkandl's second answer (regarding the amount of information preserved in semantides compared to molecules in other biological levels) and his previous statement that molecular characters were "cleaner" than morphological ones, he gave the impression of asserting that molecular phylogenies could stand alone.

The idea that the *most* informative characters are at the semantide level were clearly not in accord with the ideas and practices of field biologists. Simpson, for one, argued that morphological characters were essential to the action of natural selection on individuals and populations (Simpson 1964b). Moreover, the long tradition of research on the history of biological species depended *not* on the amount of information (or history) contained in *a single* character (or *type* of character), but on the idea and the practice that it was desirable to gather all sorts of independent evidence in order to make "robust" inferences of phylogenetic relations.

Among other advantages of using semantides, Zuckerkandl repeatedly pointed out that the discrete (quantized) nature of the substitutions would allow an easy *quantitative* comparison between homologous peptide chains and, eventually, the comparison between DNA segments (something that looked well into the future). In this case, again, the metaphor of information is connected to "history": "Our purpose," wrote Zuckerkandl, "was to spell out principles of *how to extract evolutionary history from molecules*, rather than to write any part thereof in its final form" (Zuckerkandl 1965a, 360).

Zuckerkandl's argument is enlightening regarding the way in which the political and epistemic dimensions of his rhetoric are entangled. As I have described above, traditional and molecular evolutionists had already mixed such dimensions in their battle for resources and academic authority. Within this context, Zuckerkandl seems to be responding to Simpson's contention that molecules did not constitute proper evidence for studying evolution, and that the fossil record was the only reliable evidence in the reconstruction of the biological past. The political dimension of Zuckerkandl's statement is as clear as its epistemic implications: by saying that semantides do not need independent confirmation, he privileges molecular evolutionary studies on the ground that they are based on direct, clean evidence (documents) of the past.

Many tensions underlie the different uses of the information metaphor in Zuckerkandl's paper. As already mentioned, the idea that "information" is lost in the passage from semantides to episemantides is reminiscent of the original account of the central dogma of molecular biology. Francis Crick had described the *flow of information* from nucleic acids to proteins, and stated, "once information has passed into protein it cannot get out again. Transfer of information from protein to nucleic acid or from protein to protein is impossible" (Crick 1958).

What early molecular biologists meant by "information," however, has been the subject of debate. Lily Kay has claimed that the attempts of molecular biologists to link their uses of "information" to Wiener and Shannon's classical theory were full of drawbacks because Shannon's analysis was restricted to the syntactic level of communication. Coming from a different perspective Peter Godfrey-Smith has reached similar conclusions. He reminds us that there is a weak sense of information "in which anything is a source of information if it can occupy a variety of states" (Godfrey-Smith 1999, 311). This is the sense of information present in Shannon's mathematical theory, sometimes called "natural meaning." But in this case, anything is a source of information: proteins are a source of information about nucleic acids, or the environment is a source of information about phenotypic traits, or phenotypic traits a source about the environment. The semantic properties ascribed to genes, within this view, are understood simply as meaning that one type of molecule (nucleic acids) serves as template of a second different type of molecule (proteins), in a combinatorial (in triplets) and arbitrary way (Godfrey-Smith 1999, 2000).[12]

Nevertheless, in Crick's characterization genes are described as containing instructions, that is, carrying "imperative semantic content" (Godfrey-Smith 1999, 311). Moreover, in Zuckerkandl's text "semantics" *did* matter and the technicalities of the mathematical theory of communication were not even considered. The term he invented, *semantides*, refers explicitly to semantics: "I took the Greek word for meaning (semanté) and added 'ide' by analogy with peptide," he recalls (Zuckerkandl email communication November 5, 2005). In this sense an informational molecule was also the equivalent of a "message": "The most direct effect of a message is its meaning. Thus, I no doubt felt that one could use the notion of meaning to stand

---

[12] This is not the place to include a broad philosophical discussion on the validity and/or the conceptual role played by the attribution of semantic properties to informational molecules (DNA and proteins), the genetic code or the processes involved in replication, transcription, translation, and transmittance of traits. Some authors are deeply suspicious of any attribution of semantic properties to such structures and processes (for instance, Sarkar 1996; Oyama 1985; Griffiths and Gray 1994), while others have attempted an analysis of such semantic properties, although arriving at the conclusion that those are very limited (Sterelny and Griffiths 1999; Godfrey-Smith 1999, 2000).

in for *specificity of effect*" (Zuckerkandl, email communication November 5, 2005, my emphasis). Crick and Zuckerkandl's position, thus, goes beyond the idea of "natural meaning" and takes us back to one of the most common meanings that information has taken up, that of *function* (see note 11). Zuckerkandl's recollection coincides with the position he expresses in other papers written in the early 1960s (Zuckerkandl 1964, for instance), as well as in his later work (Zuckerkandl 2002). Moreover, Zuckerkandl's choice of the word *semantide* had to do with a broader (and more problematic) research project for molecular evolutionary studies, as he recalls:

> I was very conscious at that time – trained in this respect already as an adolescent by absorbing my father's philosophical and biological concepts – of the hierarchical structure of the living world. "Information," in my mind, no doubt then stood for specific effects of a sequence at all hierarchical levels of a living system and the participation of these effects in functions. (Zuckerkandl email communication, November 5, 2005)

Further elaboration of the metaphor allowed him to speak of the ways in which "information" was deployed at different levels of organization, with a *dialectical* movement in which previous stages are incorporated in the ensuing processes. This, of course, takes us back to Hegel's reference:

> As I used the notion of information in "genetic information" it merely referred to the encoding of amino acid sequences in the protein-coding polynucleotide sequence, and, beyond, to the further effects that the amino acid sequence specifies – to the expression of this information in ensuing higher-order actions of the transcript of a coding sequence of DNA, in particular the specific folding of the polypetide chain, the specific interaction of the folded chain with other molecules, and the specific build-up of more complex cellular structures and their specific functions. (Ibid.)

A different idea is present when information is used as a metaphor for history, as explicitly stated in the title of the text: "molecules as documents of evolutionary history," that is, as *records* of life's past. Semantides are said to carry information of evolutionary relationships, something that molecular evolutionists considered particularly useful for their phyletic reconstructions. In this sense, information is something "that *we* use, not information that is part of any explanation of the causal role that genes play in development or evolution" (Godfrey-Smith 1999, 312), and has nothing to do with the semantic properties of the genes. Nevertheless, when Zuckerkandl says that information is "lost" in the passage from semantides to episemantides, he seems to point not to the rather standard view that records from the past often get lost. On the contrary, in Zuckerkandl's argument there are (causal) *processes* which are "information destroying" (like the passage from semantides to asemantides) and the past can be better retrieved from a special type of trace: molecules which preserve history. Thus, the metaphor of history is reinforced by its connection with Crick's basic idea that genes have semantic properties.

These alternative uses of the metaphor of information point to different aspects in Zuckerkandl's research program, and their interchangeability seems to have been very productive.[13] The metaphor of information, however, could not be stretched without limits on Zuckerkandl's view of biological evolution. The reference to Hegel is all the more illuminating because it underlines the importance he ascribed to interactions between semantides and between semantides and other levels. This conviction accounts for Zuckerkandl's critical position towards what he (and many others) consider illegitimate – ultimately determinist – uses of the linguistic metaphor in biology. The quotation at the beginning of this paper refers to his reaction against the metaphor of "the script of life," an expression that he heard in the voice of James Watson during a televised interview (email communication November 5, 2005). His criticism of the metaphor of the "Book of Life" extends to his present research (Zuckerkandl 2002, 122–123). He has said, for instance:

> The genome can be likened to a long text or a book, but the genome is only one of the essential ingredients of life, it does not make life by itself. By itself it is dead and would never have generated itself. The genome is the master stabilizer of the living system, but it is not its master determinant. The reason why it is not is that there is no single master determinant. (Zuckerkandl email communication, November 5, 2005)

In conclusion, like many of his contemporaries, Zuckerkandl was *not* familiar with the mathematical theory of information developed by Shannon and Wiener: "The notion of information as linked to molecular biology must have been in the air," he says, giving a familiar interpretation of what Kay has characterized as the *epistemic rupture* in the representations of heredity that led to the pervasiveness of "information discourse." According to Kay, even though "these informational representations of genetic phenomena were imprecise, sometimes self negating, and often metaphorical, they proved remarkably seductive and productive both operationally and culturally. They aided the scientific imagination in the process of meaning making, in and beyond the laboratory" (Kay 2000, 327–328).

A promising research project was announced in the 1965 paper. In particular, Zuckerkandl's defense of research at the molecular level gave a new and powerful meaning to the need for "genotypic" studies of evolution. A consensus on what was the causal level of evolution, namely, the "gene" and the genotype, had been reached with the Synthetic Theory of Evolution. The absence of "genetic data," however, had caused that consensus to be developed only in an abstract and general way, in the models of theoretical population genetics.[14] By highlighting that evolution, and even

---

[13] I am defending the productiveness of the flexibility of metaphors, in contrast to Barbieri who expresses a somewhat negative view by asserting that information is a metaphor "but no more than that" (Barbieri 2003, 244). However, this flexibility is not infinite; see below on the limits of Zuckerkandl's metaphor.

[14] A notable description of the situation was expressed by Richard C. Lewontin: "For many years population genetics was an immensely rich and powerful theory with virtually no suitable facts on which to operate. It was

natural selection, acted at the genotypic level, molecular evolutionists were directing their arguments against the architects of the Synthesis, even to the point of ridiculing Simpson (King and Jukes 1969).[15] In a broader context, the techniques and concepts of the new field of Molecular Evolution made the study of microbial phylogenies and of the origins and early evolution of life possible, thus entertaining the Darwinian dream of reconstructing life's complete lineage (but this subject deserves a different paper).

Failed and Fulfilled Promises

The epistemic content of a discourse cannot be detached from its rhetorical aspects. It is through a given text that ideas and concepts are proposed, contrasted, and *differentiated* from other ideas and concepts (in a Derridean sense). From a historical perspective we can evaluate which elements in a given discourse came to infuse the activities and forms of representation of a scientific field, creating new coordinates for the construction of knowledge. But even if we recognize the epistemic value of rhetoric, science cannot be reduced to a discursive practice. The history of Molecular Evolution shows us the complexities of constructing new scientific territories (Suárez 1996; Suárez and Barahona 1996). It would be misleading to suggest that a single paper, or even a sustained discourse or rhetorical situation, was responsible for the development and expansion of the molecular approach to evolution. Nevertheless, the discourse of informational molecules, as presented in the 1965 paper by Zuckerkandl and Pauling, was "an act of creativity, an interpretative act" (Vatz 1973), aimed to generate a socio-professional space, a place that had not been granted before for studies of Molecular Evolution. It cannot be seen as a mere response to a given rhetorical requirement (or *exigence*) of presenting molecular characters as evidence of evolution; what emphasized the differences between the traditional (morphological) approach and the molecular approach to evolution was a *choice* of elements and an organization of arguments. More particularly, a new hierarchy was given to evolutionary characters by contrasting semantides and episemantic molecules. The more informative ones

---

like a complex and exquisite machine, designed to process a raw material that no one has succeeded in mining. Occasionally some unusually clever or lucky prospector would come upon a natural outcrop of high-grade ore, and part of the machinery would be started up to prove to its backers that it really would work. But for most part the machine was left to the engineers, forever tinkering, forever making improvements, an anticipation of the day when it would be called upon to carry out full production" (Lewontin 1974, 189).

[15] In their provocative paper "Non-Darwinian Evolution" King and Jukes direct their satirical tone against G. G. Simpson, who had said that natural selection was "the composer of the genetic message and DNA, RNA, enzymes, and other molecules . . . its messengers." King and Jukes answered: "We cannot agree with Simpson that DNA is a passive carrier of the evolutionary message. Evolutionary change is not imposed upon DNA from without; it arises from within. Natural selection is the editor, rather than the composer, of the genetic message. One thing the editor does *not* do is to remove changes which it is unable to perceive" (King and Jukes 1969, 788).

were not the complex, polygenic, morphological traits of the paleontologists, but the discrete, quantitative data of molecular sequences. As a corollary, the *fossil record* was implicitly and rhetorically (though not practically) substituted with the *molecular record*.

Nowadays, the fruitfulness of the "informational molecules" discourse in evolutionary biology is clear to everyone that looks into the field of molecular phylogenetics. In many cases, phylogenetic relations are difficult to assess in any other way (Li and Grauer 1991, 99). The accumulation of DNA data sequences allows biologists to infer phylogenetic relationships among closely related species such as human and apes, to study very ancient evolutionary events such as the origin of mitochondria and chloroplasts, and to assess the divergence of phyla and kingdoms (Woese 1987). The results of such research have led, in some cases, to what might be called "phenomenological surprises," like the establishment of Archaea as a third domain of life, and the discovery of the pervasiveness of horizontal – or lateral – genetic transfer.

Still, we may ask what has been the role of information discourse as an epistemic resource for evolutionary biology, and which "promises" originally stated in a rhetorical manner have not been met. There is the apparent paradox that empirical research resulting from the molecular approach has shown the practical and methodological limitations of the ideals foreseen by Zuckerkandl and others. Let us focus, very briefly, on the fate of two of the most publicized "advantages" or promises of the molecular approach: the access to quantitative – objective – data (due to the discrete nature of molecular evidence), and the primacy of molecular characters.[16]

According to molecular evolutionists, given the primary structure of homologous proteins or genes, the number of differences among these could be codified as a single number, independently of the place and the person who did the comparison. In contrast, paleontological work seems to be attached to *interpretation* and *judgment*: what one paleontologist (or embryologist or comparative anatomist) could *interpret* as a generic difference in a given structure, another could interpret as a specific one.[17] Organismic/morphological traits need to be interpreted. Numbers seem not to require such interpretation.

---

[16] Very old and general presuppositions are of course involved in the claim that quantitative evidence is somehow superior to qualitative evidence. Without digging into the more philosophical reasons for this preference, I would like to draw attention to some pragmatic aspects. As Theodore Porter (1995) has pointed out "in modern times quantification has been as closely tied to administration as to science. Indeed, its use in science derives not only from a faith that the laws of nature are written in mathematical language but also from the rigors of scientific communication, the administration of knowledge, and the need for trust." A shift towards the objectivity of numbers "implies a move towards a more public form of knowledge."

[17] This picture describes what critics have said of "Evolutionary Systematics." Cladistics (either supported by morphological or by molecular characters) is said to avoid many of these problems, by a commitment to identifying monophyletic groups.

This picture, however, does not describe the realities of the quantitative approach in molecular phylogenetics. In the 1960s amino acid sequences were said to allow an easy, computable way of establishing affinities and differences between species. Very soon, and in concert with theoretical developments in the general field of taxonomy, computer programs were developed for measuring the "overall similarity" between two sequences (*phenetics*). The first computer program of this kind was developed by Walter Fitch in 1966 and put to use for a comparison of cytochrome *c* sequences by Fitch and Margoliash (1967). However, many difficulties emerged soon, and some of them had been already detected by Zuckerkandl and Pauling (1962 and 1965a).

Among the difficulties mentioned were the degeneracy of the genetic code and also the fact that intermediate mutations (*multiple hits*) might have occurred in the past that are not "visible" in the extant molecules. This fact required the development of models to calculate the *minimal number of mutational events* that hypothetically separate two chains on the evolutionary scale. Different proposals, based on different methodological commitments, were made. Also, there are deep methodological issues involved in the alignment of sequences, the different ways to measure resemblance, the alternative methods for inferring ancestor-descendant relations, and the selection of the best tree (Li and Grauer 1991).

But a deeper methodological and even philosophical debate surfaced: the methods used in the calculation of mutational events rely not only on experimental work (the detection that some nucleotide pairs mutate more often than others, for instance), but also on the assumption of the principle of *parsimony*. The same situation occurs when comparing molecules of different lengths (which is a common case). Dependence on molecular data has not made computerized sequence alignment easier or more "reliable." Moreover, the computer programs for choosing among the many possible trees resulting from a given number of sequences and alignments incorporate problematic methodological presuppositions, and again rely on the controversial principle of parsimony (Schejter and Agassi 1981; Sober [1988] 1991).[18] The coming of DNA sequences has not solved, but only re-localized the problems associated with "hidden mutations." The molecular phylogenetics literature is full of recommendations of *when* (in which cases) and *how* to use a combination of analytical tools in order to have reliable analyses and "interpretations" of the raw data. It seems that the generation of quantitative data faces the same old problems, plus some new ones, related to data interpretation and the inevitability of judgment in scientific practice.

This fact is related to the second promise, according to which the level of semantides possesses the largest amount of information regarding biological evolution.

---

[18] It should be noticed that the number of possible trees increases exponentially as a result of the number of *operational taxonomic units* (OTUs), which are the extant units (that is, the external branches of a tree) under comparison. For 3 OTUs the number of possible rooted trees is 3 and the number of unrooted trees is 1; for 5 OTUs the number of possible rooted trees rises to 105 and for unrooted trees to 15.

Today, things are more complicated. The concept of information has acquired even more multiple meanings in contemporary biological research; it is common to read that *morphogenesis* multiplies structural information many times and that information should also include *epigenetics*. Moreover, the assumption that the developmental causal arrow goes in the direction from informational molecules to phenotypic characters has been at the center of a serious debate that originated in independent research and literature in the 1980s within the Developmental Systems approach (Oyama 1985).

Certainly, the most challenging argument to the idea that genes and proteins are "the most informative characters" in the traditional sense, and do not require "independent confirmation," has come from molecular phylogenetics itself. In the last few years, the accumulation of molecular data on the evolution and classification of organisms has brought forth the conclusion that different trees of life result from choosing different types of homologous molecules. In order to choose a *tree* among the many (statistically equivalent) possibilities delivered by computer programs, molecular evolutionists rely heavily *on several other pieces of evidence*, in particular, from paleontology, but also from ecology and biogeography. As a molecular evolutionist has said: "a molecular tree needs to have biological meaning" (Antonio Lazcano, personal communication, Mexico City, June 22, 2005).

But conceptual and empirical uncertainty is heightened in the field of evolutionary microbiology. The unexpected discovery of large amounts of horizontal genetic transfer among bacteria, and the impossibility of reconciling trees built from different genes, have turned out to be challenges with profound implications not only for the overall goal of phylogenetic studies, but for the basic principles of evolutionary biology. In light of these challenges, vertical inheritance, and the clear genealogies that result from it, are contested. Instead of trees, "the relationships between major lineages of many bacterial species take the form of webs or networks" (O'Malley and Boucher 2005, 190). As horizontal genetic transfer becomes a privileged source for evolution among bacteria, the concept of species acquires its most extreme nominalism, and the relations among groups of microorganisms are taken to be not the result of ancestry but of "the intimacy of environmental relationships between organisms and populations" (ibid., 191).

As we can gather from the rhetorical situation in which Zuckerkandl and Pauling's paper was published, their intentions were directed towards convincing others that molecular studies of evolution deserved "their rightful place." That they succeeded in modifying biology's socio-professional field by appropriating "history" (a notion traditionally in the hands of morphologists) and, eventually, by creating a new epistemic space, is nowadays quite clear. Even if the molecular approach has been shown to have its own limitations, it would be deeply misleading to conclude that this is so *because* of the rhetorical nature of the promises and the strategies announced forty years ago. By creating new spaces for representing evolutionary (historical) relations, the information metaphor allowed new quantitative, statistical, and computer-based analyses of data.

Such analyses were not constrained by "information theory." Rather, they were inspired by metaphors, and maybe that is why so many "surprises" in our understanding of the history of life have resulted from them.

Acknowledgments

I thank the Universidad Nacional Autónoma de México for granting a sabbatical fellowship (PASPA 2005–2006) and the Max Planck Institute for the History of Science in Berlin for its generous support. I also thank Ana Barahona, Hans-Jörg Rheinberger, Angela Creager, Marie-Claude Lorne, the members of Department III at the MPIWG, and anonymous referees for their useful comments and suggestions.

References

Anfinsen, Christian. 1959. *The Molecular Basis of Evolution*. New York: Wiley.

Aronson, Jay D. 2002. "'Molecules and Monkeys': George Gaylord Simpson and the Challenge of Molecular Evolution." *History and Philosophy of the Life Sciences* 24:441–465.

Atkinson, Dwight 1999. *Scientific Discourse in Sociohistorical Context. The Philosophical Transactions of the Royal Society of London, 1675–1975*. New Jersey: Lawrence Erlbaum.

Barbieri, Marcello. 2003. "Biology with Information and Meaning." *History and Philosophy of the Life Sciences* 25:243–254.

Beatty, John. 1990. "Evolutionary Anti-reductionism: Historical Reflections." *Biology and Philosophy* 5:199–210.

Beatty, John. 1994. "The Proximate/Ultimate Distinction in the Multiple Careers of Ernst Mayr." *Biology and Philosophy* 9:333–356.

Bitzer, Lloyd. 1968. "The Rhetorical Situation." *Philosophy and Rhetoric* 1:1–14.

Boniolo, Giovanni. 2003. "Biology without Information." *History and Philosophy of the Life Sciences* 25:255–273.

Brandt, Christina. 2005. "Genetic Code, Text and Scripture: Metaphors and Narration in German Molecular Biology."*Science in Context* 18(4):629–648.

Britten, Roy J. 1963. "Complementary Strand Association between Nucleic Acids and Nucleic Acids Gels." *Science* 142:963–965.

Buettner-Janush, John, ed. 1963. *Evolutionary and Genetic Biology of Primates*. Vols. 1 and 2. New York: Academic Press.

Creager, Angela and Jean-Paul Gaudilliere. 1996. "Meaning in Search of Experiments and Vice-Versa: The Investigation of Allosteric Regulation in Paris and Berlin, 1959–1968." *Historical Studies in the Physical and Biological Sciences* 27:1–89.

Crick, Francis J. 1958. "On Protein Synthesis." *Symposium of the Society for Experimental Biology* 12:138–163. New York: Academic Press.

Dear, Peter, ed. 1991. *The Literary Structure of Scientific Argument*. Philadelphia: University of Pennsylvania Press.

Dietrich, Michael R. 1998. "Paradox and Persuasion: Negotiating the Place of Molecular Evolution within Evolutionary Biology." *Journal of the History of Biology* 31:85–111.

Dietrich, Michael. 2007. "Representando el objeto de la controversia. El caso del reloj molecular." In *Variedad Infinita. Ciencia y Representación, un enfoque histórico y filosófico*, edited by Edna Suárez, 351–366. México: Universidad Nacional Autónoma de México/Limusa, Noriega Editores.

Fitch, Walter. 1988. "This Weeks Citation Classic." *Current Contents* (27):16.

Fitch, Walter and Emanuel Margoliash. 1967. "The Construction of Phylogenetic Trees. A Generally Applicable Method Utilizing Estimates of the Mutation Distances Obtained from Cytochrome C." *Science* 155:279–284.

Florkin, Marcel. 1949. *Biochemical Evolution*. New York: Academic Press.

Fox Keller, Evelyn. 2000. *The Century of the Gene*. Cambridge Mass: Harvard University Press.

Fox Keller, Evelyn. 2002. *Making Sense of Life. Explaining Biological Development with Models, Metaphors, and Machines.* Cambridge Mass: Harvard University Press.

Godfrey-Smith, Peter. 1999. "Genes and Codes. Lessons from the Philosophy of Mind." In *Biology Meets Psychology*, edited by V. Hardcastle, 305–331. Cambridge, MA: MIT Press.

Godfrey-Smith, Peter. 2000. "On the Theoretical Role of 'Genetic Coding'." *Philosophy of Science* 67 (March):26–44.

Goodman, Morris. 1960. "On the Emergence of Intraspecific Differences in the Protein Antigens of Human Beings." *American Naturalist* 94:153–166.

Goodman, Morris. 1964. "Man's Place in the Phylogeny of the Primates as Reflected in Serum Protein." In *Classification and Human Evolution*, edited by Sherwood L. Washburn, 204–234. London: Methuen.

Griffiths, Paul E. and Russell Gray. 1994. "Developmental Systems and Evolutionary Explanation." *Journal of Philosophy* 91:277–304.

Hafleigh, Anne S. and Curtis A. Williams Jr. 1966. "Antigenic Correspondence of Serum Albumins among the Primates." *Science* 151:1530–1535.

Hager, Thomas. 1995. *Force of Nature: The Life of Linus Pauling*. New York: Simon and Schuster.

Ingram, Vernon M. 1957. "Gene Mutation in Human Haemoglobins: The Chemical Difference between Normal and Sickle Cell Haemoglobin." *Nature* (180):326–338.

Jukes, Thomas. 1966. *Molecules and Evolution*. New York: Columbia University Press.

Kay, Lily, E. 2000. *Who Wrote the Book of Life? A History of the Genetic Code*. Stanford: Stanford University Press.

Kimura, Motoo. 1968. "Evolutionary Rate at the Molecular Level." *Nature* 217:624–626.

Kimura, Motoo. 1985. "Genes, Populations and Molecules: A memoir." In *Population Genetics and Molecular Evolution*, edited by Tomoko Ohta and K. Aoki, 459–481. Tokyo-Berlin: Jap. Sci. Soc. Press-Spring Verlag.

King, Jack and Thomas Jukes. 1969. "Non-Darwinian Evolution." *Science* 164:788–798.

Krips, Henry J. E. McGuire, and Trevor Melia, eds. 1995. *Science, Reason and Rhetoric.* Pittsburgh: University of Pittsburgh Press.

Lakoff, George and Mark Johnson, 1980. *Metaphors We Live By*. Chicago: University of Chicago Press.

Lewontin, Richard C. 1974. *The Genetic Basis of Evolutionary Change*. New York: Columbia University Press.

Li, Wen-Hsiung and Dan Grauer. 1991. *Fundamentals of Molecular Evolution*. Sunderland Mass: Sinauer.

Margoliash, Emanuel. 1963. "Primary Structure and Evolution of Cytochrome C." *Proceedings of the National Academy of Sciences* 50(4):672–679.

Marmur, J. and D. Lane, "Strand Separation and Specific Recombination in Deoxyrribonucleic Acids: Biological Studies." *Proceedings of the National Academy of Sciences* 46(1960):453–461.

Mayr, Ernst. 1961. "Cause and Effect in Biology." *Science* 134(3489):1501–1506.

Mayr, Ernst. 1963. "The New versus the Classical in Science." *Science* 141(3583):765.

Morgan, Gregory J. 1998. "Emilé Zuckerkandl, Linus Pauling, and the Molecular Evolutionary Clock." *Journal of the History of Biology* 31:155–178.

Myers, Greg. 1990. *Writing Biology. Texts in the Social Coonstruction of Scientific Knowledge.* Madison: University of Wisconsin Press.

O'Malley, Maureen A. and Yan Boucher. 2005. "Paradigm Change in Evolutionary Microbiology." *Studies in History and Philosophy of Biological and Biomedical Sciences* 36:183–208.

Oyama, Susan. 1985. *The Ontogeny of Information.* Cambridge Mass: Cambridge University Press.

Powell, J. R. 1994. "Molecular Techniques in Population Genetics: A Brief History." In *Molecular Ecology and Evolution: Approaches and Applications*, edited by B. Schierwater, B. Streit, G. P. Wagner and R. De Salle, 131–183. Switzerland: Birhäuser Verlag Basel.

Porter, Theodore M. 1995. *Trust in Numbers. The Pursuit of Objectivity in Science and Public Life*. Princeton: Princeton University Press.

Reichert, Edward T. and Amos P. Brown. 1909. *The differentiation and specificity of corresponding proteins and other vital substances in relation to biological classification and organic evolution: the crystallography of hemoglobin*. Washington: Carnegie Institution of Washington.

Sarkar, Sahotra. 1996. "Biological information: A Skeptical Look at Some Central Dogmas of Molecular Biology." In *The Philosophy an History of Molecular Biology: New Perspectives*, edited by S. Sarkar, 187–231. Dordrecht: Kluwer Academic Press.

Schejter, Abel and Joseph Agassi. 1981. "Molecular Phylogenetics: Biological Parsimony and Methodological Extravagance." In *Scientific Philosophy Today*, edited by J. Agassi and R. S. Cohen, 333–356. Dordrecht: D. Reidel

Segal, Jerome. 2003. "The Use of Information Theory in Biology: A Historical Perspective." *History and Philosophy of the Life Sciences* 25:275–281.

Shapin, Steven and Simon Schaffer. 1985. *Leviathan and the Air Pump.* Princeton: Princeton University Press.

Simpson, George G. 1944. *Tempo and Mode in Evolution.* New York: Columbia University Press.

Simpson, George G. 1964a."The Meaning of Taxonomic Statements." In *Classification and Human Evolution*, edited by Sherwood L. Washburn, 1–31. London: Methuen.

Simpson, George, G. 1964b. "Organisms and Molecules in Evolution." *Science* 146(3651):1535–1538. Reprinted in *Biology and Man*, 1968, edited by George G. Simpson, 32–41. New York: Harcourt, Brace and World.

Simpson, George G. 1964c. "The Historical Factor in Science." In *This View of Life: The World of an Evolutionist*, edited by George G. Simpson, 253–271. New York: Harcourt, Brace and World.

Smocovitis, Vasiliki B. 1996. *Unifying Biology: The Evolutionary Synthesis and Evolutionary Biology*. Princeton: Princeton University Press.

Sober, Elliot. [1988] 1991. *Reconstructing the Past. Parsimony, Evolution and Inference*. Cambridge, Mass: MIT Press.

Suárez, Edna. 1996. "El origen de disciplinas como integración de tradiciones científicas: el caso de la Evolución Molecular." Ph.D thesis. México: Universidad Nacional Autónoma de México.

Suárez, Edna. 1997. "Emilé Zuckerkandl, Arquitecto de la Evolución Molecular." *Arbor* 158(623–624):305–332.

Suárez, Edna. 2001. "Satellite DNA: A Case Study for the Evolution of Experimental Techniques." *Studies in the History and Philosophy of Biological and Biomedical Sciences* 32(1):31–57.

Suárez, Edna and Ana Barahona. 1996. "The Experimental Roots of the Neutral Theory of Molecular Evolution" *History and Philosophy of the Life Sciences* 17:3–30.

Swales, J. 1990. *Genre analysis: English in Academic and Research Settings.* Cambridge: Cambridge University Press.

Vatz, Richard. 1973. "The Myth of the Rhetorical Situation." *Philosophy and Rhetoric* 6:154–161.

Washburn, Sherwood L., ed. 1964. *Classification and Human Evolution.* London: Methuen.

Williams, Curtis A. 1967. *Methods in Immunology and Immunochemistry.* New York: Academic Press.

Wilson, Edward O. 1994. *Naturalist.* Washington, D. C.: Island Press/Shearwater Books

Woese, Carl. R. 1967. *The Genetic Code. The Molecular Basis for Genetic Expression.* New York: Harper and Row Publishers.

Woese, Carl R. 1987. "Bacterial Evolution." *Microbiol. Review* 51–221-271.

Woolgar, Steve. 1981. "Discovery: Logic and Sequence in a Scientific Text." In *The Social process of Scientific Investigaction*, edited by Karin Knorr Cetina, Roger Krohn and Richard Whitley, 239–268. Dordrecht: D. Reidl.

Zuckerkandl, Emilé. 1964. "Perspectives in Molecular Anthropology." In *Classification and Human Evolution*, edited by Sherwood L. Washburn, 243–272. London: Methuen.

Zuckerkandl, Emilé. 2002. "Why so Many Non-Coding Nucleotides? The Eukaryotic Genome as an Epigenetic Machine." *Genetica* 115:105–129.

Zuckerkandl, Emilé. 2005. Personal communication via email, November 5, 2005.

Zuckerkandl Emilé and Linus Pauling. 1962. "Molecular Disease, Evolution and Genic Heterogeinity." In *Horizons in Biochemistry: Albert Szent-György Dedicatory Volume*, edited by Michael Kasha and Bernard Pullman, 189–225. New York, Academic Press.

Zuckerkandl, Emilé and Linus Pauling. 1965a. "Molecules as Documents of Evolutionary History." *Journal of Theoretical Biology* 8:357–366.

Zuckerkandl, Emilé and Linus Pauling. 1965b. "Evolutionary Divergence and Convergence in Proteins." In *Evolving Genes and Proteins*, edited by Vernon Bryson and Henry Vogel, 97–166. New York: Academic Press.

Zuckerkandl, Emilé, Richard. T. Jones, and Linus Pauling. 1960. "A Comparison of Animal Hemoglobins by Triptic Peptide Pattern Analysis." *PNAS* 46:1349–1360.

Zuckerkandl, Emilé and Walter Schroeder. 1961. "Amino-Acid Composition of the Polypeptide Chains of Gorilla Haemoglobin. *Nature* 192:984–985.