Structuralism in Chemistry

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Abstract

An analysis of the use of the notions of "structure" and "function" in chemistry is presented. It is investigated how this can contribute to illuminate the current discussion concerning self-organization and natural selection in biology. Starting from the methodology used in organic syntheses it will be illustrated that in chemistry the natural way to link structure and function is offered by a reaction mechanism i.e. a particular sequence of events. Analysis of the methodology used in the kinetic modeling of complex chemical processes reveals that this link is being exploited but becomes obliterated in the final description of the behavior of the process. The relation with semiosis, the genotype/phenotype dichotomy, development system theory (P. Griffiths), process structuralism in biology (B. Goodwin) and the local/global dichotomy will be examined. Recent models on the origin of life as presented by S. Kauffman and Fontana's Alchemy will be discussed from this point of view.

Keywords : structure, function, self-organization, structuralism, mechanistic explanation.

1. Introduction

Darwin accepted that the major phenomenon of life that required explanation was the adaptation of organisms to their environment. The explanation Darwin put forward was given in terms of random hereditary variations among the menbers of a species and natural selection of the fitter variants over long periods of time. The formalization of Darwinism and Mendelism, known as the "Modern Synthesis", describes the evolutionary process as the dynamics of alleles (genes) within populations : the frequency of the latter in the former is the relevant variable. The behavior is given by differential equations that express the frequency of a gene as jointly determined by fitness (Darwinism) and transmission (Mendel) relations. A striking paradox thus has

emerged from the way in which the "Modern Synthesis" approaches biological phenomena. Organisms - which Darwin accepted to be the primary examples of life - disappeared as fundamental and unreducible units of life. Modern biology views organisms as complex molecular machines controlled by their genes and not as distinctives intergrated entities in their own right. As a consequence of the sharp focus on the molecular level of organisms, modern biology has become dominated by historical explanations in terms of the evolutionary adventures of genes. Although Darwin's assumption that the tree of life is a consequence of the gradual accumultion of small hereditary differences can explain the small scale aspects of evolution, the "Modern Synthesis" as such must assume the prior existence of the entities it is meant to explain. This existence problem was recognised a century ago by De Vries who stated that "natural selection may explain the survival of the fittest, but it cannot explain the arrival of the fittest" (Fontana, 1994a). The theory as such cannot account for the origin of life nor for the large-scale biological order. The core of the existence problem is the determation of how biological organizations arise in ontogeny and in phylogeny. New theories, originating in mathematics and physics, are expected to offer a solution to the problems of emergent life and order in evolution. Related with this topic is the discussion concerning contingency and necessity in the evolution of life. Steven Jay Gould e.g. asked whether the biological diversity that surrounds us today would be different if "the tape were to be played twice". Would the life forms that arose from the chance variation of evolution look like anything we see in the world surronding us ? A fundamental problem associated with an analysis of the questions concerning contingency and necessity in past evolution is precisely the fact that the processess occured in the past. The systems as they might have existed billions of years ago are not at our disposal for experimental explorations. The only approach is to study a model universe that does not assume the prior existence of organisms (Fontana, 1994b).

As Stuart Kauffman showed with his catalytic sets, the spontaneous formation of order is not unlikely to occur in a "chemical soup". Above a certain threshold of complexity a self-sustaining network - a metabolism - spontaneously arises (S. Kauffman, 1993). Fontana and Buss (1994, 1996) took this idea a step further and tried to show that once a metabolism was formed, the laws of complexity made it natural for it to join into an organization with another metabolism and for the organization to combine in higher hierarchies. In several specific instances Fontana and Buss showed that a number of features that occur in the history of life were generated spontaneously and robustly. This suggests that these features arise generically and, hence, might be expected to reappear if the "tape were played twice". Moreover, the fact that the major features of evolution arise in a system that does not give a role to Darwinian selection raises the problem of determining which features of biological organization can be attributed to the emergence of the origanization and which features are attributable to natural selection. At stake is then the primacy of natural selection in shaping the major features of biological organization.

The possible impact of complex self-organizing system theories on biological theories of evolution forms a vast topic of discussion. Current theories on complex self-organizing systems directly challenge the idea that evolution can adequately be described in terms of random generation of heritable variants and natural selection of these variants alone. Self-organization deals with the material principles and mechanisms operative in the generation of variants and in the dynamical development of structured organisms. Attention is given to the material details of how something gets structured into a complex whole. Since the evolution of a system is considered to influence the conditions of its own adaptation, evolution becomes co-evolution and an interactionist point of view taking into account the whole network of interacting species becomes necessary. If one adopts the neo-Darwinian point of view then there is indeed no need to consider the internal structure of the organism or its developmental dynamics. Depending on the relative importance attributed to selection and/or self-organization, three major tendencies can be seen (Van de Vijver et al., 1998). Firstly, variation and natural selection is the major source of order and adaptation at all biological levels. Secondly, selection and self-organization are seen as complementary explanatory principles. There are problems, however, in seeing exactly how these two principles are to be combined (Burian & Richardson, 1996). Self-organizational principles are seen as either enhancing or weakening the power of selection and function as a null hypothesis (Depew & Weber, 1995, chpt. 16). A third tendency attributes a more prominent role to self-organizational principles to explain biological order. The problem of self-organization and complexity involves an adequate account of how to arrive at a global description of complex evolving systems that is consistent with its local dynamics. At this point, divergencies in the structuralist approach can be noticed. Although Goodwin & Websters's structuralist project deals with developmental issues in evolutionary biology, their view on structure is not in terms of the details of material interactions with an environment.

A discussion of the use of the notion of "structure" in chemistry can be usefull to illuminate the debate on self-organization and selection. From an analysis of the methodology of organic synthesis a tentative proposal for the combination of selectional and self-organizational principles can be made. The problem of consistency between local mechanics and global descriptions can be illustrated by means of an analysis of the methodology used in the kinetic modeling of complex chemical processes.

2. Methodology of Organic Chemical Synthesis

This discussion of the methodolgy used in chemical organic synthesis is strongly based on E.J. Corey's The Logic of Chemical Synthesis (E.J. Corey & X.-M. Cheng, 1989). It has to be mentioned that "organic chemical synthesis" pertains to the synthesis of

carbogens e.g. terpenes, steroids, prostaglandines, vitamins. From the point of view of organic chemical synthesis complexity arises from molecular size, elements and functional-group content, cyclic connectivity, stereocenter content, chemical reactivity and structural instability. How does a chemist find a way to synthesize a complex target molecule ? The answer to this question depends on the chemist and on the problem. The process begins with perception of structural features that are used as information which aids in the logical analysis of the problem. Iterative cycles of perception and logical analysis applied to a target structure and to the "data field" of chemistry ultimately contribute to the synthesis of the desired molecule. Since the "data field" of chemical knowledge changed over time, the answer to the question also changed over time.

In the first century of organic chemistry much attention was devoted to the analysis of the structure of organic compounds and to their transformations. During the 19th century, synthesis was based on the availability of starting materials and guided by associative thinking and thinking by analogy. The starting point for a synthesis was generally the most closely related aromatic hydrocarbon - readily available from industrial coal tar - and the synthesis was arrived at by selecting the reactions required for attachment or modification of the substiuent groups. Thus, synthesis remained restricted to simple aromatic compounds and little planning was needed for these simple syntheses. After the second World War organic synthesis was approached in a different way and depended on the knowledge of reactions suitable for the formation of polycyclic molecules. A detailed planning was needed in order to find a way to apply these reactions. This shift in approach was stimulated by the confluence of various factors. Among these, the formulation of detailed electronic mechanisms for the basic organic reactions, the conformational analysis of organic structures and transition states based on sterechemical principles and the development of spectroscopic methods for structural analysis were of prominent importance. Molecules and reactions were classified according to types of substrates that underwent a certain chemical change. The central question was : which structural subunits can be combined to reach a given structural subunit ? Chemists were thaught to see organic chemistry as a body of transformations characteristic to a structural class or to a structural subunit. In textbooks this was usually represented as an exhaustive list of all known transformations of e.g. alcohols, aldehydes, esters, α,β-keto-carbonyls, α,β-enones. Attention was directed to the structure of the reactants. The focus was put on chemical change in the direction of the products : reactants ———> products. As a result, in the period from 1945 to 1960 some complex molecules were synthesised e.g. vitamin A, cortisone, penicillin, morphine, reserpine. Consequently, until the 70's, in most schools organic synthesis was thaught by the presentation of a series of unrelated cases of actual syntheses. This "case" method had has a consequence that each synthetic problem was approached as a special case with an indivudualized analysis. By the mid 1960's a more systematic way was developped. This strategy concentrates on the perception of structural features in the reaction products as opposed to the focus being put on the starting materials. In

this approach structures are manipulated in the reverse-synthetic sense. The method is known as retrosynthesic or antithetic analysis : products ———> reactants. The focus thus shifted to the possible functions the reactants can perform. The central question now became : how can a given structural subunit be reached by a combination of structural sunbunits ? In textbooks, reactions are now presented as an exhaustive list of all possible transformations leading to the formation of a characteristic structural subunit e.g. alcohols, aldehydes, esters, amides can be synthesised by means of these known transformations of structural subunits. From then unwards the design of a synthesis for any new synthetic target molecule was simplified and accelerated.

In retrosynthetic analysis the structure of a target molecule is transformed to a sequence of progressively simpler structures along a pathway that ultimately leads to readily available starting materials. The transformation of a molecule to a synthetic precursor is accomplished by the application of a transform, the exact reverse of the synthetic reaction, to a target molecule. Repetition of this process leads to a tree of intermediates with chemical structures as nodes and having pathways from bottom to top corresponding to possible synthetic routes. As the iterative process of perception and logical analysis continues, questions are raised and answered, propositions are formed and evaluated. This results in ever more penetrating insights that often lead to very subtle combinations of the knowledge concerning types of possible transformations and conformations of structures and of transition states i.e. it leads to an anticipation of the occuring reaction mechanism. The aim of the strategy is to obtain a regio- and stereoselective synthesis of the target molecule with the highest possible overall-yield in the lowest possible number of steps. Retrosynthetic analysis is a problem solving technique that, with some modifications, can be implemented as an interactive program for computer-assisted synthetic analysis.

What is aimed at in this strategy is the knowledge how two interacting structures excert their function and thereby give rise to a new molecule. In chemistry this is presented as a reaction mechanism based on structural, electronic, stereochemical and conformational considerations i.e. on the material details of the interacting structures. A reaction mechanism is a formal representation of a particular sequence of individual events at the molecular level i.e. it is the reconstruction of the actual pathway by which a certain molecule originates. Examples of reaction mechanisms and of the importance of the conformational and stereochemical aspects of a reaction mechanism can be found in any textbook on organic synthesis. Moreover, if one knows how a molecule is formed, one also knows why it is being formed. In turn then, this knowledge expands the "data field" of chemistry and thereby influences the itterative procedure used in designing new syntheses.

3. Methodology of kinetic modeling of complex chemical processes.

In chemical processes new products are created from starting materials. One of the main problems chemical industry faces is the accurate simulation of processes involving complex reactions. How to predict the conversion of the feedstock ? What is the product distribution in the effluent ? Will product specifications be satisfied ? The methodology used to answer these questions will be illustrated by means of the modeling of thermal cracking. (A thorough going technical discussion of the approach can be found in Vynckier & Froment, 1991 and Froment, 1993). Thermal cracking of hydrocarbons is one of the major sources of olefins and aromatics. The modeling of this process aims at improving industrial operation and design of thermal cracking furnaces. The feedstocks processed in thermal cracking consist of a large number of components, each leading to complicated reaction paths. Over the years, the modeling of the cracking of a complex mixture, like naphtha, has gone through increasing levels of complexity. In the first models the actual reaction network was reduced to a single overall reaction ; naphtha was considered as one big lump that disappeared through a first order reaction. In a second stage, three lumps based on the PIONA-analysis of the feedstock were considered : normal and iso-paraffins and naphtenes were converted through a first order kinetics (olefines are usually not present in the feedstock and aromatics not only disappear but are also formed). The kinetic parameters determined on the basis of these models inevitably depended on the feed composition and, in most cases, even on the type of reactor in which they were determined. As a consequence, product specifications cannot be predicted by this models. Moreover, for each feedstock exhaustive experimentation is required. In recent years, a complete analysis of naphtha's using gas chromatografy has become possible. A number of components typical for normal-, iso-paraffins and naphthenes were then selected and their disappearance was described using first order kinetics. This detailed braikdown of the feedstock still gave rise to a rate coefficient for a given component that varied with the feedstock used. The reason for this variation was traced back to the interaction between reacting species. Evidently, the chemical environment in which a given component is cracked depends on the naphtha composition. This dependence cannot be accounted for on the basis of simple molecular disappearance kinetics. The accurate prediction of the effluent composition requires sets of kinetic equations describing the production of the reaction products. In the seventies, this was attempted by considering molecular equivalents of the actual occuring radical reactions. This simplification was introduced mainly to reduce the number of differential equations and to circumvent mathematical problems related to the solution of sets of stiff differential equations associated with a rigourous radical model.

Today, a more rigourous approach retains the full detail of the reaction pathways of the individual feed components and reaction intermediates. This approach has become possible through a better understanding of the underlying chemistry, advances in

analytic techniques and expansion of computational means. To obtain the reaction network, the cracking process is decomposed into elementary steps reflecting its radical chemistry. Written in terms of the elementary steps : initiation, proton abstraction, addition, isomerization, radical decomposition etc. thermal cracking leads to enormous networks for a single hydrocarbon already. For mixtures the task of developing such networks manually is evidently not feasible; e.g. in the reaction scheme for the cracking of a naphtha containing some 200 components some 120 000 elementary steps are involved. The networks thus are computer generated starting from a binary relation matrix describing the structure of the hydrocarbons. Reactions then are simulated by mathematical operations on the relation matrix taking into account the radical chemistry of the process. In addition to a reaction network, the prediction of product distributions requires rate coefficients. In a network of reactions at the molecular level, the number of rate constants equals the number of reactions. An approach based on elementary steps can circumvent this problem since the elementary steps pertain to a restricted number of types and rate coefficients depend upon the structure of the reactant and the product only. A systematic scrutiny of these structures thus enables to determine the number of rate parameters and their definition. The number of differential equations can be reduced by expressing the concentration of some of the intermediate radicals in terms of the concentration of a limited number of other radical or molecular species by the introduction of Bodenstein's quasi-stady state approximation for the radicals. The core of the simulation model thus consists in a library containing 1680 reaction networks for some 550 hydrocarbons. The kinetics relate to the elementary steps of the networks and are invariant i.e. independent of the feedstock composition. Rate equations, describing the concentration change of each component, are generated by a search process through the library. Rate coefficients are estimated by minimalization the difference between simulated and experimental concentrations. This model accurately predicts the operation of thermal crackers under a wide variety of operating conditions.

Essential in this approach is the knowledge of the reaction mechanisms underlying the process on the basis of which the rules to generate the reaction network are derived and the library is constructed. Accurate predictions require an extensive library of reactions.

4. Relations to Biology

In chemistry a functional group is defined as a structural subunit of a molecule that can be transformed by interaction with another functional group thereby producing a new molecule. The transformation consists in a particular sequence of events that is completely determined by the structural, electronic, conformational and stereochemical properties of both interacting molecules.

As Kampis argues (1991, p. 273 - 274), a reaction mechanism is a material-implication-based theoretical explanation that introduces a history i.e. a sequence of particular events that has no other explanation than the events themselves. The retrosynthetic analysis confines itself to a reconstruction of possible events that ultimately lead to a target molecule. The analogy with the descriptive aspect of evolutionary theory, that confines itself to the reconstruction of events leading to a "target species", is striking. This will be discussed later.

The actual occuring transformation is completely determined by every indivual material detail of the interacting structures and is inherently context dependent. This introduces a relational, semantical aspect. As a consequence, it is very hard to anticipate what will actually occur during a synthesis. The difficulty arises mainly because during interaction an interplay of electronic and spatial factors often play a crucial role and these factors cannot be completely obtained from an analysis of the structure and the properties of the interacting molecules viewed separately. In the transition state, an intermediate state between reactants and products, induced polarities and "forced" conformations due to steric effects often play a crucial role. This is why the study of structure and properties of transition states can be of a tremendous help in designing a synthesis. However, in most cases a transition state is a very short living species. Usually it is studied in situ, by spectroscopic and others means (e.g. NMR, IR, TAP), but analysis and interpretation of experimental data often remains a very difficult task. Despite the enormous "data field" of chemistry surprises often occur.

Closely related is the genotype/phenotype distinction. This is refelected in the practice of the design of new biological active drugs or peptides. The aim here is thus to construct a molecule with a target function. Early attempts started from the presupposition that a small change in structure will be accompanied by a small change in function. In practice, however, this presupposition very often turned out to be wrong. Usual practice is guided by trial-and-error and by intuition i.e. one synthesizes a number of products that for one reason or another are expected to be active and then screens the activity of the lot. The difficulty will be illustrated in relation to peptides. One of the most striking things about peptides is the tremendous range of biological functions which they perform. This diversity in functions is paralleled by an equal diversity in properties. It is however not possible to account for the properties of a peptide solely in terms of its primary structure i.e. the sequence of amino acids. Due to folding of the peptide chain, amino acids that seem to be widely separated in the primary structure can be close toghether in the three dimensional arrangement of the amino acid residues. There are various levels of structural complexity. Apart from the peptide bonds which can occur in two conformations (cis and trans), parts of the peptide chain can be coiled (secundary structure) and these coiled chains are folded in a tertiary structure. Two or more peptide molecules can also be arranged in a quaternary structure. The myoglobin molecule, the oxygen transporting proteïn in whales, e.g. is

a globular proteïn that occurs in a unique and extremely compact conformation. Approximately 75% of the amino acid residues reside in a α-helical region. These regions are folded upon each other in such a way that nearly all of the polar groups are directed towards the surface of the molecule. All hydrophobic groups are directed towards its inside. All of the polar groups at the surface form bonds with water molecules. Despite its size (M = 17 000), there are no interior spaces or channels apart from the pocket containing the haem group, the active site of the molecule. This heam moiety, the iron bearing porphyrine structure, is coordinated between non-polar side chains of two histidine residues. The side chains are in close contact and most of the stabilization energy derives from van der Waal's forces, rather than from polar interactions or intrachain hydrogen bonds. From this example it is clear that the active site of a peptide consists in residues of the side chains that are held in spatial proximity by a supporting structure. Solely this active site of the molecule will interact with oxygen. Changes in the primary structure may or may not result in a change of the conformation of the molecule and thereby alter or even completely destroy the activity of its active site. This completely depends on the ability of the resulting supporting structure to maintain the required spatial arrangement of the active site. Each and every sequence of amino acids that is capable to support the spatial requirements of the active site is able to perform the same function. Moreover, in the case of myoglobin e.g., the conformation of the active site and its biological functioning is also influenced by the iron atom enclosed in the heam pocket. A further difficulty arises from the fact that a peptide can occur in different conformations. The relative concentrations of the different conformations are proportianal to their relative stabilities. This means that the same sequence of amino acids can occur in different three dimensional shapes. Moreover, peptide conformations are solvent dependent. Peptide folding is thus a context dependent phenomenon. From the point of view of functional properties then, the sequence of amino acids is not very informative. The mechanism by which a sequence of amino acids folds into its three dimensional shape is very hard, if not impossible (R. Rosen, 1991, par. 11F), to anticipate from its primary structure. The design of new biological active peptides is greatly hampered by the chemists inability to more or less predict the three dimensional shape of a peptide from the sequence of its constituting amino acids. A more systematic approach, as in the case of carbogen synthesis, remains impossible and every case thus needs and individual analysis. The case is even worse for other biological active molecules. For peptides, one can start from the idea that the conformation of the active site is the factor that determines its biological functioning and this facilitates the determination of which parts of the molecule relate to its functioning. For other molecules a carefull comparison of conformational and structural aspects of active and inactive molecules is usually needed in order to establish what features of a molecule are decisive for its biological functioning. A more systematic approach would require knowledge of the mechanism by which a molecule excerts its function. As was shown in the previous discussion this can only be obtained by an in depth analysis that proceeds in the reverse sense and that often requires knowledge of

structure and properties of intermediates.

The inherent context dependence of transformations can also be formulated as follows: the information content stored in a molecule is expressed in different ways in different environments. The philosophical analogue of this situation is called the "frame problem". A biological analogue of this situation can be found in the discussion concerning the role of the genome in development. In genetics the sequence of the base pairs in DNA is usely referred to as "genetic information". A gene is taken to be a "code" for a phenotypic trait. From the previous discussion it is clear that the information content of a molecule is inherently context dependent. What is expressed from the information contained in a molecule depends completely on what other molecule it interacts with. The outcome is determined by every material detail of both molecules that plays a role in the interaction itself. As a consequence, the descission which molecule is regarded as substrate and which as reagent is completely arbitrary and it thus becomes impossible to decide which molecule is being interpreted and which molecule interpretes. This chemical point of view on "genetic information" coincides with the criticism of a DNA-centered view on develeopment advanced by the adherents of "development systems theory" (Griffiths P., 1994, p. 283).

One could formulate the inherent context dependence also as : the total information content of a molecule, as contained in its chemical structure and in its conformational, stereochemical and electronic properties, is only partly interpreted by the interaction partner. The relation with the notions of "syntactical" and "functional" information, as introduced by Kampis (1991, p. 423) is obvious : "Structural information characterizes structure in terms of the arrangements and properties of its parts. Functional information can be conceptualized as the informational effect of the structure on systemic functions, or, in more general terms, on causal behavior." Moreover, from a chemical point of view, it becomes clear that the idea of information content of a molecule is inherently associated with interaction. Every combination of molecules can behave differently. What properties of a molecule are important completely depend on which other molecules it interacts with. The properties of a single molecule on its own are undefined. The total range of its properties can only be known if it is paired with all other molecules. The interactionist aspect thus implies that the properties of a molecule can only be known in retrospect. As a consequence a molecule on its own cannot be considered as a unit i.e. a "thing" with certain fixed properties. A molecule starts to behave as a "thing" when it is put in a context. The true unit is the network of interactions the molecule enters into in a context (Kampis G., 1991, p. 266-268). The structure of a chemical system thus consists in the integrative network of all molecules and their formation processes. A biological analogue can be found in the fact that animals and plants that belong to an ecosystem behave totally inpredictable when they enter another ecosystem. The true unit that has to be considered is the whole network of interactions the plant or the animal enters into in a given ecosystem.

The requirement of an extensive library for accurate kinetic modeling is a consequence of the relational, semantical, interactionist aspect of chemical processes. In a dynamical description the chemical compounds are represented as quantifiable variables i.e. as their concentrations and interaction is seen as occuring between these quantifiable variables. Molecules are not considered as entities with a distinct structure that determines the behavior of the system. Instead they are represented as structureless variables that quantify properties of a class of molecules. As a consequence, the behavior of the system is captured as a temporal change in the concentration of the molecules. The relevant molecules and the network of their kinetic (functional) couplings (the systemic structure) are fixed and are to be known a priori. Within this description it is impossible to understand how the molecules themselves are generated. In a dynamical description a molecule is "reduced" to its concentration. In nature interaction does not occur between the numerical values that represent molecules in a dynamical description. As stated previously, in nature interaction involves material details of molecules. A causal description of the process is a description of the temporal sequence of how the molecules are formed from one another that makes use of the properties of the interacting molecules. The information needed for a causal description is contained in the types of molecules involved and, as discussed previously, is context dependent and can only be known a posteriori. Moreover, this information is qualitative. In fact, the construction of the library is a fixation of the interpretation frame. This enables the "transformation" of a causal description based on qualitive information carried by the type of molecules involved into a dynamical description based on quantative information carried by the amount of molecules present and thereby makes an accurate mathematical description of the process possible.

We will now turn to the previously mentioned analogy with the descriptive aspect of evolutionary biology. The Darwinian approach to a taxonomy of organisms is to classify morphological traits on the basis of descent from ancestral forms. The organizing principle is common descent and the associated explanatory scheme, convincingly advocated by Griffiths (1996b), is called the "adaptive-historical" approach (not to be confused with "adaptationsism" as defended by Dennett (1995)). In contrast, the process structuralists' ideal is some kind of periodic table of form whose "equivalent in physics is the periodic table of the elements, constructed on the basis of a theory that tells us the dynamically stable patterns of electrons, protons and neutrons." (Goodwin B., 1995 p. 103). Technically, a form is a stable solution to the dynamic morphogenetic field equations. A morphogenetic field refers "to spatial organization activities that involve clearly defined physical and chemical processes combined in a way that is characteristic to the living state." (Goodwin B., 1995, p. 88). Form is seen as the result of the unfolding of the dynamics of self-organizing, self-generating processes. A generic form is defined as a structure or form that is common to all members of a group (Goodwin B., 1995, p. 95) and devides the space of biological possible forms into regions accesible to a particalur type of organism. The tetrapod limb e.g. is defined as "the set

of all possible forms that can be generated by the rules of focal condensation, bifurcation and segment condensation in the morphogenetic field of the limb bud" (Goodwin B., 1995, p. 141). The reconstruction of the historical pathway followed to reach a viable region in the space of possible forms is not credited with any real explanatory status. They argue that genuine explanations should be cast in terms of the dynamics that govern the self-organizing processes (Goodwin B., 1990). The paradigm of rationality is taken to be Newtonian dynamics and the comparison is often presented to justify the approach : from the inverse square law it can be deduced that the elliptical orbit of the planets is one of the possible forms of planetary motions (the other possiblities being a circle, a parabola and a hyperbola). Both programmes thus are opposed to each other. According to Griffiths (1996a, 1996b), a possible way out of this situation is to historicize the idea of generic form.

Evidently, in biology the situation is far more complex than in chemistry and a systemic view on structure is certainly needed. However, equating a target molecule with a target species, a tentative comparison can be made. In chemistry, the reconstruction of the pathway followed to reach a particular molecule causally explains the presence of that particular molecule, provided that it is given in the form of a mechanism that is related to the material details of interacting structures that gave rise to the new molecule. The foregoing discussion also reveals that, in chemistry, it is taken into account that besides a structure, a molecule necessarily has a certain three dimensional shape but that the relation between structure-shape need not be a one-to-one mapping. In the debate concerning the Darwinian and the process structuralist approach to taxonomy, no clear distintinction between form and structure is apparent. In chemistry, a form is necessarily related to a structure but the interaction and transformation of structures is seen as central. As shown, this transformation is not independent of three dimensional shape as it is completely determined by all material details of the molecules involved. In the Darwinian approach, the notion of structure is completely lacking and the transformation of one form into another is seen as the result of chance. Since variant forms are seen as produced by chance, evolution is regarded as contingent and Darwinians thus insist on historical explanations. In chemistry, complete determinsm related to the creative capacities of interacting structures does not exclude the requirement for a historical explanation. Process structuralists, on the other hand, do see the transformation of one form into another as a completely determined process. The morphogenetic field could be seen as a systemic structure. However, process structuralist insist on an explanation in dynamical and a-historical terms. The morphogenetic field equations can be compared with the dynamic equations that govern pattern formation in the Beloussov-Zhabotinsky reaction. These equations accurately describe the macroscopic behavior of the system. In chemistry, however, dynamical descriptions of the macroscopic behavior are not considered as explanatory sufficient. As shown previously, a description of the actually occuring events at the molecular level is required. At the molecular level the events that occur are collisions, structural

transformations and interactions regulated by physical forces. Goodwin & Websters's view on structure is not in terms of the material details of interactions occuring in the morphogenetic field. The sructural transformations occuring in the chemical processes in the morphogenetic field require the introduction of a mechanistic (historical) explanation related to the material details of the interacting chemical structures involved. This tentative comparison thus suggests that, from a chemical point of view, both approaches could be reconciled if the idea of generic form is related to the explanatory scheme required by the creative capacities of the chemical structures involved in tissue formation i.e. if the idea of generic form is related to a mechanistic, historical explanation.

The fact that molecules possess an internal structure that gives rise to the occurence of specific interactions that modify or create other molecules has consequences for the dynamical models describing the origin and evolution of life. Firstly, the set of molecules present and the kinetic (functional) couplings between them must be open and constanly evolving. Conventionally, the set of variables in a dynamical system and the dynamical couplings between them are fixed at the outset. Thereby a fixed state space of the system, i.e. a fixed interpretation frame, is specified. The state of the system at every moment in time can then be represented by a point in the phase phase and the system's dynamical trajectory can be represented as a trajectory through the phase state. Secondly, if the origin of the network of interactions is to be captured, it is necessar to consider that the change in the numerical values of the variables in the classical dynamical description is caused by an interaction that changes the molecules themselves. The causal linkage between the internal structure of a molecule and the type of interactions through which it participates in the construction of other molecules requires that a molecule is to be seen as a syntactical (structural) component that causes interaction with other molecules whereby the molecules are integrated in network relations. The functional relationships in this network then determine the meaning (semantics) of the molecules.

The models presented by Kauffman (1993) and Fontana (1994, 1996) take into account that the formation of a new molecule in the system requires an expansion of the network of interactions and both make use of a "metadynamic" approach (Bagley & Farmer, 1992). However, in Kauffman's model amino acids and peptides are considered as structurless entities. Consequently, although the set of components in the system is not explicitly fixed in advance, the rules according to which new molecules are generated and on the basis of which the interaction network is generated are fixed a priori i.e. only coupling and hydrolysis reactions of peptides are taken to be possible. Thereby the creative capacities of the chemical structures present in the system are completely tied up and the various reaction mechanisms underlying the process are implicitly specified.

The stance taken by Fontana is to view chemical molecules as compositional objects capable of constructive interactions. Fontana takes Lambda-calculus as a proxy for chemistry and places it in a constrained dynamical setting and claims that "organizations emerge from the collective behavior of primitive objects without any prior assumption regarding the nature of the objects and their kinetic couplings beyond that required by logical consistency with established physics and chemistry" (Fontana, 1996). The core idea of Fontana's approach is to consider a molecule to be a mathematical function and its interaction upon collision with another molecule to be a functional application. It is crucial to Fontana's approach to substantiate this view. Here originates Fontana's stress on the syntactical and functional aspect of molecules i.e. the usual way in which chemical formulas are manipulated in ordinary chemical practice. According to Fonatana, a chemist uses the well-known chemical symbols to represent molecules and uses the chemical formulas in much the same way as a mathematician uses strings of symbols e.g. "1 + x" or "$\sqrt{}$xdx". These strings have a structure that stands for an action that depends on the value of x. In the same vein a chemist sees a chemical formula as a statement about an action that depends on its structure and on the structure of the objects it interacts with. However, the elaborated system of rules to link the action of molecules to their formulas is an informal one. It is not grounded in a mathematical framework in which one could discover emperically verifiable truths by "calculation". Having demonstrated that a molecule can be taken as a function and interaction between molecules can be considered as a functional application, Fontana then makes the link to computation. The foundations of computation provides a theory of the kind of objects that molecules can be seen to be : i.e. syntactical and functional entities. Fontana explains that the key aspect of computation is to distinguish between "behavior" and "that which behaves". One view considers "behavior" as a function in the sense of a hugh look-up table, which assigns inputs to outputs without considering how an output is obtained from an input. The classical dynamical discription, based on an interaction matrix between numerical values representing the objects, corresponds with such a look-up table. Another view sees a function as a rule of computation i.e. as a process of symbolic manipulation that produces a value when applied to an argument. Thereby, the infinite look-up table (the infinity of possible behaviors) is compressed into a finite rule or procedure specifying how an input is transformed to an output. According to Fontana, this corresponds to take seriously that in the physical world the objects "behave" and interaction involves the objects directly and never the numerical values describing them. To express a rule some formal language is needed. The required representation of chemistry thus must be a "specification language" designed to abstract the features characteristic of molecular actions. Fontana considers this features to be : 1. the *constructive capability* of chemistry which is reflected in the compositional syntax of molecules. The combination of molecules causes specific structural rearrangements given by the laws of chemistry. Such rearrangements start with a collision between molecules followed by the formation of a transition complex that rearranges to stable products. The sequence is driven by thermodynamics. 2.

equivalence relations i.e. the same product can be synthesized by a variety of chemical reactions. Constructive capability permits diversity and equation relations enable network formation. From this it follows that a theory of biological organization must be an axiomatic theory that contains at least 1. a grammar to express the syntactical structure of the molecules (objects) and 2. a formal way to connect these structures with actions on syntactical structures, such that 3. structures bear equivalence relations.

This leads Fontana to an abstract chemistry based on an analysis of the fundamental concept "function". However, what actually happens in the model is that starting from a series of Lambda-expressions, another series of Lambda-expressions is obtained but the basic rule according to which interaction between Lambda-expressions occurs is fixed a priori, i.e. only substitution reactions are possible. The type of interaction that occurs is thus ultimitately independent of the structure of the molecules. This a priori specification of the type of interaction together with the equivalence relation is what ultimately makes Fontana's model work. The equivalence relation required by Fontana's approach is a consequence of an externalist, global view. At a molecular level, presence versus absence of a molecule in the system is important. From the point of view of the other molecules present in the system the fact that a particular molecule is being formed by a single pathway or by various pathways is totally unimportant, instead the molecule's accessibility for the other molecules present in the system is decisive.

5. Conclusion

The creative capacities related to the internal structure of molecules introduces a relational, semantical aspects of chemical interactions. In different contexts different material properties of molecules are assessed. The interactions in a given chemical system, its organization, are determined by the properties of the molecules present in the system. The appearance of a new molecule in the system changes the context and thereby new and unexpected behavior can emerge. This leads to a mutuality between the identity of the parts and the whole : the properties of the molecules can only be conceived in the existing organization of the system and the organization of the system is defined by the properties of its constituting molecules. Associated with the creative capacities of molecules is a mechanistic, historical explanation. From a chemical point of view it seems that self-organizational and Darwinian theories of evolution could be reconcilied if the idea of "generic form" to which Goodwin & Webster appeal is associated with the explanatory scheme required by the chemical structures involved. Perhaps this simply reflects the fact that, after all, life and evolution on earth started from a chemical soup.

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