

## HYLE Article

# Towards a Process Philosophy of Chemistry

*Ross L. Stein\**

**Abstract:** Molecular change is central to chemistry and has traditionally been interpreted within a metaphysical framework that places emphasis on things and substance. This paper seeks an alternative view based on process metaphysics. The core doctrines of process thought, which give ontological priority to becoming over being, cohere well with modern chemical thinking and support a view of molecules as dynamic systems whose identities endure through time as patterns of stability. Molecular change is then seen as excursions to new stability patterns. Finally, when molecular change is viewed as foundational to emergent complexity, process metaphysics allows evolution to be seen as creative molecular advance.

**Keywords:** *process philosophy, metaphysics, ontology, enzymes, evolution.*

## 1. Introduction

Chemistry is the science of molecular change. During the past century, experimental and theoretical chemists have probed the mechanisms of chemical reactions and, through these studies, have acquired a detailed understanding of how molecular change occurs. The mechanisms we propose for the reactions we study are invariably described in terms of atomic rearrangement, in which bonds between atoms are formed and broken in accordance with well documented tenets of chemistry. Foundational to this understanding of molecular change is an ontology of material substance in which molecules are machines and change is a rearrangement of parts.

But is such an ontology really an adequate foundation for chemistry? Can an ontology that, in its limit, reduces chemistry to 'ball-and-stick' machinations provide sufficient explanatory resources to account for all aspects of molecular change, especially its foundational role in the evolution of complex molecular structures and life? I believe that the answer to these questions is No; substance ontology is incapable of providing adequate metaphysical underpinnings to allow us to build a comprehensive theory of molecular change. To understand the deep structure of molecular change [1], we must replace material substance with process.

In this paper, I will attempt to lay the groundwork for a process philosophy of chemistry with emphasis on chemical change. We will first review principles of process thought that are relevant to this project and see that process thinking stresses becoming over being and gives ontological priority to environmentally-

conditioned transformation. Next we will examine the ontological status of molecules and lay the groundwork for a conceptual framework which draws on a natural, mutually reinforcing relationship between quantum chemistry and process thought. From this discussion, an intriguing concept emerges in which molecules are likened to ecosystems. This is a powerful metaphor and shapes our thinking about chemical change, allowing us to recognize molecular change as creative advance. Of nature's many chemical systems, enzymes and their biocatalytic functions may best exemplify the concept of 'molecule-as-ecosystem'. A relational and holistic enzymology is advanced that places emphasis on the enzyme as fluctuating protein matrix and on the enzyme's simultaneous interactions, along the reaction coordinate, with its bound substrate and the energy-rich thermal bath of aqueous solvent. Catalytic transformation of substrate by enzyme is then seen to be the outworking, through time, of the chemical potential that is inherent in solvent-protein-substrate, a dynamic unity. The enzyme as ecosystem-in-process is seen to be at once the result of and a condition for evolution.

## 2. A Primer of Process Metaphysics

Metaphysics seeks to answer questions about the ultimate nature of reality. Throughout the history of Western philosophy, various answers to these questions have been offered starting as early as the 6<sup>th</sup> century B.C. in Miletus [2] with Thales and Anaximander who are thought to be the first to offer rationalistic rather than mytho-poetic accounts of reality. One strand of metaphysical thinking in which material substance is seen as the fundamental constituent of reality can be traced from the atomism of Leucippus and Democritus in 5<sup>th</sup> century B.C. through Aristotle's metaphysics of substance to concepts of substantial reality that emerged as part of the Newtonian development of a clockwork and deterministic cosmology.

A metaphysical position of radical reductionism underlies the Newtonian universe. In this ontology of material substance, every-thing can be reduced to a set of basic elements (*i.e.*, particles, atoms) that are external to one another and have no interiority themselves. The fundamental nature of each particle is independent of the nature of other particles and, because the elements or particles only interact mechanically, the forces of interaction do not affect inner natures. Substances are material things and every-thing is a 'machine', comprising independent parts, each adapted for a specific function and moving in a specific manner within the machine.

Other philosophers claim that this cannot be the whole story and believe that although the notion of material substance "expresses a useful abstract for many purposes of life" and has a "sound pragmatic defense" (Whitehead [1929] 1978, p. 79), reliance on such an ontology gives a deficient and impoverished view of reality. To accept such an ontology is to be drawn into self-deceit, to allow abstractions from reality to pass as reality itself:

The error does not consist in the employment of the word 'substance', but in the employment of the notion of an actual entity which is characterized by essential qualities and remains numerically one amidst the changes of accidental relations and of accidental qualities. [Whitehead (1929) 1978, p. 79]

In opposition to substance ontology, a metaphysical position developed that sees process and change as a fundamental descriptor of reality. In the West,[3] this strand of thinking can be traced to Heraclitus who reminds us that "one cannot step twice into the same river". Since Heraclitus, process thinkers have included Gottfried Wilhelm Leibniz, Henri Bergson, Charles Peirce, William James, and, its leading 20<sup>th</sup> century exponent, Alfred North Whitehead.

Process thought, as a metaphysical system, focuses principally on change and the temporal. Becoming, not being, is ontologically central. Contingency, emergence, and creativity are essential elements and take precedence over determinism and the static.

Process thought is pragmatic in its approach and insists that we take very seriously that which is actual. And the actual is change. The process philosopher tells us to simply look around and see that nothing is constant; every-thing is in flux.

[...] reality appears as a ceaseless upspringing of something new, which has no sooner arisen to make the present than it has already fallen back into the past" [Bergson (1907) 1998, p. 47].

The process philosopher tells us to look within; see the experiences of our life and understand that they are not *things* that happen to us, but rather are the fundamental elements of the real that comprise us. We are our experiences and "we change without ceasing" (*ibid.*, p. 2).

Keep in mind how fast things pass by and are gone – those that are now, and those to come. Existence flows past us like a river: the ‘what’ is in constant flux, the ‘why’ has a thousand variations. Nothing is stable. [Marcus Aurelius (*ca* 170) 2002, p. 61]

This view, which maintains merely that process is an important conceptual descriptor of substantial objects, can rightfully be called Weak Process Ontology when contrasted with a more ardent appraisal of reality, Strong Process Ontology, which asserts boldly that processes are existentially fundamental; substance is mere appearance (Rescher 1996, p. 57). In Strong Process Ontology, *the* fundamental ontological category is process.

The champion of Strong Process Ontology is Alfred North Whitehead (1861-1947), for whom "the reality is the process" (Whitehead [1925] 1967, p. 72). Through his speculative metaphysics, Whitehead gives us a remarkably innovative picture of reality in which the basic unit of nature is not static material substance, but rather is creative, experiential events, ‘actual occasions of experience’. Significantly, these basic unit-events of the world are not vacuous, but rather possess a subjective nature that allows them attributes that might be called ‘feeling’, ‘memory’, and ‘creativity’. Every event, while influenced by the past through a process Whitehead calls ‘prehension’, exercises some amount of self-determination or self-creation. Every event has some power to exert creative influence on the future. Whitehead’s cosmos is characterized by the ‘creative advance into novelty’.

Note that Strong Process Ontology is not merely echoing Heraclitus and asserting that things are constantly in flux, but rather is making the extraordinary claim "to be *actual* is to be a process" (Cobb & Griffin 1976, p. 14). But, how can this be? How can process, and not material substance, constitute reality? To answer this question, we need to understand better the difference between the fundamental claims of substance ontology and process ontology.

According to substance ontology, reality comprises material substance, static and non-experiencing. Material substance has an objective nature only, lacking both subjective and temporal natures. That is, material substance is not only incapable of enjoying experience, it also does not change through time. In substance ontology, processes rearrange matter and, since matter lacks a subjective nature, processes happen *to* matter. In contrast to this is process ontology, according to which reality comprises process, dynamic and capable of experience. Processes have an objective nature (*i.e.*, processes can be experienced by subjects), a subjective nature (*i.e.*, processes can experience, are partly self-determining, and can enter into relation with other processes), and a temporal nature (*i.e.*, processes happen through time or, perhaps, define time). The distinctive features that characterize substance and process ontologies raise a key question: How is it that the objects that populate our world can endure through time?

Reality, as we see it around us, has complexity that endures through time. According to process thought, the enduring objects of our experience are nothing more than stable patterns of sequential actual occasions. In the language of Whitehead, complex objects are ‘societies’ or ‘nexus’ of actual occasions that endure cooperatively. Complex objects are no mere aggregates, but possess a defining unity. Ivor Leclerc explains that this emergent unity arises from the reciprocal ‘acting’ of the constituents of a compound object:

The entities in relation act on each other reciprocally, and are thus each modified, in some respect, by the relationship, that is, by their acting. This reciprocal acting constitutes a tie or bond between them, this bond being the relation which exists only in the acting. [...] With this, it is clear, there is unity between the entities so related, a unity which is more than that of an aggregate. [...] As so combined into one, this one must transcend the many constituents – for we have a ‘one’ here which is not that of an aggregate. Further, this one is an actual one, that is, an actualized unity. In the same way there could be compounds with the previous compounds as their constituents, and so on in increasing orders of complexity. [Leclerc 1972, pp. 309-312]

We see then that enduring material substance is mere appearance and exists as the stable patterns established by sequential processes. To quote Rescher: "...process philosophers tend to be realist about processes but idealist about substances" (Rescher 1996, p. 58).

Process philosophers justify all of these claims on the existential grounds that we can only truly understand the units comprising the physical world by analogy with our own experience that we know from within. Experience shapes the very process of becoming that is enjoyed by all actual entities. Process thought admits a new sort of relationship between experience and consciousness. All actual entities, and not just conscious beings, enjoy experience. In Whitehead's words: "Consciousness presupposes experience, and not experience consciousness" (Whitehead 1929, p. 53).

### 3. The Ontological Status of Molecules

What can such metaphysical claims mean to the chemist? How can physical reality *not* have its foundation solidly set in substance? What would it even mean to speak of a molecule as a ‘process’ rather than an elemental bit of matter?

Chemistry is deeply rooted in substance ontology. Chemical compounds, when considered at the molecular level, are defined by their structure, that is, the arrangement of their constituent atoms in 3-dimensional space. The attribute of possessing, and of being ultimately defined by, a fixed arrangement of parts allows us to view molecules as deterministic machines. It is axiomatic in chemistry that molecular structure gives rise to molecular properties.

However, a moment's reflection will reveal that this presents something of a dilemma for the substance ontologist. Process philosopher John Cobb makes the insightful comment that "the fact [that structure engenders molecular properties] would not be so if the world were *really* composed of material substances" (Cobb 1988, p. 107). Cobb is pressing all who embrace an ontology of substance to ask themselves: How is it that molecular properties emerge from atomic arrangement?

Process thought tells us that to answer this question, notions of static material and substance must be rejected and be replaced with a philosophy of dynamism and relatedness.

[...] the properties of an atom are always the properties of that atom as its existence is determined by its relations to its environment. Atoms acquire different properties when they are arranged in different molecular structures because these different structures constitute different environments. *Instead of viewing molecules as machines, we should view them as ecosystems.* Science may continue to ask what properties a certain type of atom continues to have in great varieties of contexts, but it should add the question as to the diverse properties the atom acquires in different relationships. This ecological approach to the study of atoms can subsume the materialistic one, whereas the materialistic approach cannot subsume the ecological." [Cobb 1988, p. 108, italics mine]

While this concept of ‘molecules as ecosystems’ may initially strike us as strange, it is, in fact, a central

part of contemporary chemistry. That the properties of atoms and molecules are contextual is precisely what quantum chemical theories are telling us. I believe it is worth a short digression to see that this is so.

In 1929, Paul Dirac claimed that "the underlying [quantum mechanical] laws necessary for the mathematical theory of [...] all of chemistry are completely known" (Dirac 1929). Such optimism was based on the work of a generation of theoretical physicists that culminated with Erwin Schrödinger whose theoretical treatment allows a mathematical representation of quantum systems and the calculation of the total energy of those systems. It was soon realized that analytical solutions to the Schrödinger equation for systems larger than hydrogen would be impossible due to incursion of the 'many-body problem', so approximate methods were developed for the quantum mechanical analysis of more complex molecular systems that are of interest to chemists.

Something astonishing emerges from these quantum mechanical treatments. Classical chemical depictions of molecules as rigid assemblies of balls-and-sticks give way to radically dynamic pictures in which the system's electrons are delocalized across the whole of the system's nuclei. Discrete bonding between pairs of atoms, a central dogma of traditional chemistry, emerges only under the constraint of the restricted Hartree-Fock model with its concept of a set of molecular orbitals each occupied by an electron pair. In fact, it can be argued that chemical structure cannot be derived from pure quantum mechanical formalism since it is only imposed under the Born-Oppenheimer approximation. English theoretical chemist R.G. Woolley warns that "it is wrong to regard molecular structure as an intrinsic property of a molecule" (Woolley 1978). Structure cannot be considered a property of the individual molecules, but only as it arises in an environmental context. Molecular structure emerges under the influence of environmental influences that provide constraints which lead to distinguishable spatial atomic distribution. (Bogaard 1993, p. 266; Zeidler 2000 and references therein).

We see then that quantum chemical treatments of molecules provide an emphasis upon relatedness in which molecules are a part of a continuum of relational interactions. At a primary level of this 'holoarchy' [4] are internal atomic interactions that are defined by the relation between nucleus and electrons and that give the atom its chemical identity. At a secondary level, atomic interactions manifest as quantum chemically allowed bonding interactions – the molecular 'glue' that prevents the molecule from falling into bits and, thus, gives the molecule endurance through time. Finally, a molecule interacts with the environment. In this relation, the former gains structural definition while the latter gains depth of compositional complexity.

Quantum chemical understanding coupled with elements of process thought provide the basis for the development of a contemporary molecular ontology in which molecular entities are not mere objects, 'vacuous entities', but rather can be said to possess a subjective nature [5] that is able to 'prehend' and respond to its environment. Such an ontology can provide John Cobb a physico-chemical basis for his assertion that molecules should be viewed as ecosystems. We will see that it is a molecule's interiority and ability to respond to its environment that can account for seemingly diverse chemical phenomena including molecular change, molecular complexification, and, ultimately, the evolution of life.

## **4. Molecular Change as Creative Advance**

We have just seen that molecules can rightly be characterized as environmentally conditioned ensembles of atomic processes. Moreover, they are dynamic. Constantly in flux, molecules possess multiple reactivities that differentially manifest themselves depending on environmental conditions. If chemical stability is an illusion,[6] as it appears that it must be, what then is chemical change?

Metaphysics based on Weak Chemical Processism supports the notion that change is fundamental to chemical thinking and goes on to explain that molecular change is a simple rearrangement of parts. For example, Henri Bergson explains that the

[...] *idea of change is that of a displacement of parts which themselves do not change.* If these parts took to changing, we should split them up in their turn. We should thus descend to the molecules of which the fragments are made, to the atoms that make up the molecules, to the corpuscles that generate the atoms, to the 'imponderable' within which the corpuscle is perhaps a mere vortex. In short, we should push the division or analysis as far as necessary. *But we should stop only before the unchangeable.*" [Bergson (1907) 1998, p. 8, my italics]

By this reckoning, chemical change occurs in 'ball-and-stick' fashion as a repositioning in 3-dimensional space of a molecule's constituent atoms, the 'unchangables'. Of course, this view can be informed by concepts of contemporary chemistry in which we might speak of the adjustment and/or creation of orbitals to house the electrons that are shared in bonds between adjoining atoms. Nonetheless, this represents, through and through, an ontology of substance.

However, I believe that the lessons of quantum chemistry demand an explanation of chemical change that can only be fashioned from the doctrines of Strong Chemical Processism. We turn first to Whitehead for whom the molecule is a structured society, or nexus, of actual occasions of experience (Whitehead [1928] 1978, p. 99) that possesses endurance through time by virtue of the serial order of its constituent actual occasions. Thus, he explains that "a molecule is an historic route of actual occasions" and that "changes in the molecule are the consequential differences in the actual occasions" that comprise the nexus (Whitehead [1928] 1978, p. 80).

Alternatively, we can build on John Cobb's metaphor of 'molecule-as-ecosystem'. Similar to a macro-ecosystem, the molecule endures through time and maintains identity, not because it is static and unchanging, but rather because it is a dynamic system exhibiting a stability pattern through time. Seen in this way, molecular change represents an excursion to a new pattern of enduring stability. Transformations of the molecule-as-ecosystem should not be viewed as rearrangements of parts, but rather as ensemble progression from one dynamic state to another.

## 5. Enzymes as Molecular Ecosystems

The metaphor of molecule-as-ecosystem is particularly applicable to enzyme molecules. Enzymes are protein catalysts that accelerate the critical reactions of an organism's metabolic and catabolic processes. Enzymes effect catalysis by providing their reactant substrates a low energy pathway to product and are able to achieve remarkable rate accelerations.<sup>[7]</sup> As an example, we will consider the hydrolytic cleavage of *p*-nitroacetanilide (PNAA) to *p*-nitroaniline and acetic acid. Both the enzymatic (Stein 2002) and non-enzymatic reactions (Stein 1981, Stein *et al.* 1984) have been studied in some detail and allow comparison from both a mechanistic and thermodynamic point of view. The second-order rate constant for reaction of aryl acylamidase from *Pseudomonas fluorescens* with PNAA is about  $10^9$ -times larger than the second-order rate constant for non-enzymatic reaction of PNAA with hydroxide anion (Stein 2002). How does one account for this extraordinary rate enhancement?

The reaction catalyzed by aryl acylamidase, like all enzymatic reactions, proceeds by a mechanism in which the substrate is initially extracted from aqueous solvent and bound by the enzyme within a micro-environment that is known as the 'active site'. Within the enzyme's active site, chemical transformation of substrate to product occurs. After completion of the reaction, the product dissociates from the active site and, in so doing, liberates the enzyme for another round of catalysis.

For aryl acylamidase, active site chemistry involves two distinct steps: enzyme acylation followed by hydrolytic deacylation. In the first step, the carbonyl carbon of the bound -substrate undergoes nucleophilic attack by the hydroxyl moiety of the active site serine residue. This reaction is subject to general-base catalysis by the imidazole of a nearby histidine. This first reaction produces *p*-nitroaniline, which dissociates into bulk solvent, and an acyl-enzyme intermediate. In the second step of this reaction,

the acyl-enzyme reacts with water to produce the second product, acetic acid, and to liberate the enzyme. Again, the active site histidine residue acts as general catalyst.

From the foregoing discussion, it is evident that the chemical transformations occurring at the active site of aryl acylamidase are nothing special; they are identical to the transformations that one would observe in aqueous solution if studying general acid-base catalysis by imidazole of any acyl-transfer reaction (Jencks 1969). Thus, the key to understanding enzyme catalysis must be sought elsewhere; it must be sought in the protein matrix in which the active site is embedded.

Now, it would be a mistake to think of the active site as a mere scaffold on which reactive chemical moieties are positioned for optimum reaction with the substrate. While the disposition of active site amino acid residues about the substrate in 3-dimensional space is clearly of critical importance in building a molecular edifice that can support enzyme chemistry, it is the protein matrix in dynamic communication with these residues that imparts to them the status of an enzyme catalyst. The protein matrix must not only organize these residues around the substrate in the active site, but also correlate their motions during catalysis. Furthermore, these active site dynamics, which are controlled by overall protein dynamics, are ultimately coupled to the energy bath of bulk solvent.[8] This brings us to an understanding of the origins of the catalytic power of the enzyme: to pay the energetic cost of catalysis, the enzyme protein transduces energy that is available from its stochastic interactions with the medium to the active site. The mechanism for this transduction involves solvent-driven conformational fluctuations of the enzyme combined with the substrate-dependent stabilization of specific enzyme conformers that possess active site geometries in optimal catalytic configuration.

We see then that enzymes, like all proteins, exist in solution as ensembles of conformational isomers (Lumry 1986). The ability of the enzyme to sample from among these protein conformers is not only essential to catalysis, as we just saw, but also to selectivity. Enzymes express selectivity both towards the chemical reactions they mediate and the substrates they transform. Aryl acylamidase catalyzes *only* the hydrolytic degradation of amides and *only* amides of very specific structure. This enzyme will not hydrolyze N-alkyl acetamides or anilides of benzoic acid; nor will it perform chemical reactions other than hydrolysis on preferred acetanilide substrates. These two forms of selectivity, while expressed at the active site, rely on the structural plasticity of the protein matrix and the ability of this matrix to communicate with the surrounding aqueous environment.

A picture now begins to emerge in which we see the enzyme as manifesting a molecular teleology, where I speak of teleology not as the end determining the present, but rather as the potential that exists in the present actualized as the future unfolds. The enzyme as molecular teleological expression was recognized by biophysicist G. Ricki Welch who asks us to understand that

[...] the enzyme molecule is a beautifully intricate and dynamically ‘purposive’ entity; a ‘deterministic’ mediator between the molecular chaos of the environment and the localized chemical-reaction coordinate. [Welch et al. 1982]

Latent within the polymeric sequence of amino acids that constitutes the enzyme’s primary structure is directionality and potential for its correct folding into a catalyst of remarkable power and selectivity.

Let me try to pull these thoughts together and summarize. We have seen that enzymatic reactions are initiated by a combining of enzyme and substrate to form a complex from within which chemical transformation occurs. While starting as two entities, the resultant complex, stabilized through formation of complementary hydrogen-bonding, electrostatic, and hydrophobic interactions, becomes a unity. The unity that emerges from this productive interplay between enzyme and substrate feels influence from its environment and, with its environment, defines a reacting system; a single quantum system that is appropriately described by a single wave function (Cunningham & Bash 1997, Monard & Merz 1999). This unity is not a static complex but rather exists as an ensemble of species interconverting across a rugged free energy landscape that runs perpendicular to the advancing reaction coordinate (Hirsch 1974, pp. 176-282; Ma 2000; Matthews 1995). Catalytic transformation that defines this reaction coordinate is

driven by the dynamic response of the ensemble to its aqueous environment. Free energy that is available from the thermal bath of bulk solvent is transduced through the protein matrix to the active site for productive chemical work. In the end, we will not be able to locate the origins of the catalytic power of an enzyme in a certain 3-dimensional arrangement of active site residues nor in a certain fold of the protein; rather, enzymatic catalysis will have to be analyzed as structurally specific substrates bound to an active site of definite chemical potential embedded in a dynamic protein matrix that is in thermal exchange with the aqueous environment of bulk solvent.

This holistic description of enzymatic catalysis can be solidly grounded in the metaphysical foundation of Strong Chemical Processism. Enzyme and substrate, existing as separate actualities, combine. In the combining, plurality is dissolved into unity. An intimate relation of reciprocal acting and interaction gives rise to a new actuality that endures through time as a pattern of stability or a 'nexus of actual occasions'. Significantly, existing within this new actuality is creative potentiality for a transformative chemical process. This potentiality manifests as a disruption of the stable pattern that, until that moment, has defined the unitary complex of enzyme and substrate. Driven by the energy of its environment, this potentiality provides directionality and, in a very real sense, 'navigates' the system across the free energy landscape to a new stability pattern of the complex of enzyme and product.

## 6. Evolution as Creative Molecular Advance

Our final task is to place molecular change into the broader context of emergent chemical complexity and, ultimately, life. We need to understand that our new view, in which we see molecules as ecosystems and molecular change as environmentally responsive becoming, is fundamental to an understanding of how life can first come to be and how life is then able to develop, through the generations, into more and more complex forms. We will see that it is in the very nature of molecular change that life is allowed; evolution *is* creative advance driven by molecular change.

If we widen our view and reflect on the deep structure of nature, through space and time, we recognize evolutionary development as an overarching meta-process comprising processes within processes – the Grand Holoarchy of the Kosmos. In the evolution of life, in particular, we see "self-transcendence [and the] amazing capacity to go beyond what went before" (Wilber 2000, p. 20). Atoms bind into inorganic chemicals which rearrange and join to form organic molecules which polymerize into pre-biotic macromolecules which organize into supra-structures and the first proto-cellular forms. Life emerges from the Kosmos. But how is this possible? Why is it that life comes to be in this universe?

In Whitehead's philosophy of organism we have a starting point for the development of an answer. Whitehead wants us to understand that

[...] a thoroughgoing evolutionary philosophy is inconsistent with materialism. The aboriginal stuff, or material, from which a materialistic philosophy starts is incapable of evolution. [...] There is nothing to evolve, because one set of external relations is as good as any other set of external relations. There can merely be change, purposeless and unprogressive. [Evolution] requires an underlying activity – a substantial activity – expressing itself in individual embodiments." [Whitehead (1925) 1967, p. 107]

Evolution is the progressive advancement of subjects and reflects an underlying creativity that cannot be explained by an ontology of vacuous material substance. "Nuts and bolts cannot evolve! They can only be rearranged" (Birch 1988, p. 71). Evolution occurs by changes in the internal relations of the subject as they are influenced by the environment. The potentiality of self-transformation and self-transcendence that *is* evolution is actualized as teleological response, where, as we saw before, teleology is not the end determining the present, but the present, with the seeds of its future bound up in it, actualizing its potential. Teleology is "the process by which the immature becomes mature [is explicated] in terms of the



systematic whole that is being generated" (Harris 1993, pp. 70-71).

We now need to ask if this line of thinking, which views evolution in its broadest sense, can, in fact, find a coherent base in the process metaphysic of molecular change that we have been developing. While undertaking a comprehensive treatment of this problem is clearly beyond the scope of this paper, I would still like to consider molecular change, and catalysis in particular, in the context of two very different epochs in the history of life on this planet: a time more than 3.5 billion years ago when self-replicating, catalytic polymers of amino acids emerged as proto-types of our present enzymes and complex systems of biotemplate-based information propagation, and the contemporary world of the past 3.5 billion years in which point mutations in nucleotides of chromosomal DNA has led to proteins of altered functions and, ultimately, to adaptation-driven selection of favorable phenotypes.

"After almost 50 years of modern research, there is no paradigm of the origin of life." Thus begins a recent review by Noam Lahav and his colleagues at Hebrew University of Jerusalem on the chemical basis for the emergence of life on earth (Lahav *et al.* 2001). Notwithstanding Lahav's bleak assessment, this field has seen progress and workers within it generally agree that certain chemical features of the primal condition appear to have been an absolute necessity for organic life to arise. Among these features is the very early production of short, glycine- and alanine-rich polymers of  $\alpha$ -amino acids. Critically, a subpopulation of these peptides would need to have possessed autocatalytic ligation activity. That is, while covalent dimerization of amino acid X to form  $X_2$  would presumably be non-catalytic, formation of  $X_3$  from reaction of X and  $X_2$  and formation of all higher polymers would be subject to autocatalysis. In his analysis of this situation, Lahav remarks that "the catalytic activity of linear peptides cannot be accounted for by a simple combination of the relevant properties of their amino acids" (Lahav *et al.* 2001).

This is a most profound observation. In it, Lahav has expressed one of the central features of process ontology of chemistry: the essential nature of the compound subject transcends, and cannot be reduced to, the simples from which it is composed. These primal catalysts possessed unprecedented functionality, inherent only in the relational properties of the whole, that could be expressed only upon combination of certain amino acids. If we imagine these peptides embedded in a complex evolutionary oligarchy of biological catalysis, we see them transcending their constituent amino acids, which themselves have properties surpassing their atomic composition, and being subsumed by enzymes and then higher order biological catalysts and metabolic pathways. In this oligarchy, we also see a molecular teleology at work in which the potentiality possessed by amino acids to polymerize into forms with catalytic activity is actualized. We see then that the emergence of catalytic properties can be coherently incorporated into process-based metaphysics in which novelty emerges from the interplay of relation-creating and teleonomic complexification.

These peptides were, of course, the very early, evolutionary precursors of the first cellular life that arose on earth about 3.5 billion years ago. Across these billions of years, increasingly complex forms of life have evolved, a process that most certainly continues even now. To understand evolution, to grasp the driving force beneath this continual complexification, we must view it at the molecular level because it is at the level of chromosomal DNA that evolutionary changes have their origin. Either through mutation of individual nucleotides or through genetic recombination, rearrangement, or swapping, new protein products are generated that possess properties that differ from those of their immediate progenitor. And it is through increased survival ability imparted by some of these new proteins that novelty enters the world; first at the macromolecular level, but ultimately at level of the organism.

But how is it that a mutated protein can assume the role of native protein in cellular physiology? More perplexing still, how can such an altered protein occasionally increase survival odds of the organism? The answers to these questions, of course, lie in the fact that proteins have a degree of structural plasticity that allows them to tolerate certain changes and still maintain functional integrity. Techniques of molecular biology that are now common place allow a single amino acid in a protein to be changed to any other amino acid, with consequences for the new protein that range from the innocuous to modified function to

loss of function. In isolation, this is nothing more than protein tinkering and cannot serve as a base for evolution. Evolutionary change occurs when new proteins respond to their cellular environments in new ways. Such is not the case for machines, where altered parts cannot be 'swapped-in'. This speaks for the relational nature of the cell which comprises a holoarchy of functionality of which the protein is but a part. The cell as vital actuality is subsumed in this holoarchy which extends into the biosphere, luring all towards greater complexity. Processes within processes, the holoarchy of functionality deepens with greater complexification until self-consciousness emerges from the Kosmos.

## 7. Conclusions – New Metaphysical Theories Allow New Scientific Understanding

Ivor Leclerc, in the preface to *The Nature of Physical Existence*, tells us that only through the development of new metaphysical theories will new ways emerge for understanding the reality that is revealed by science:

Indispensable in the future will be the formulation of alternative theories of nature as bases for alternative interpretations of scientific evidence. Through such interpretations the philosophical theories will be tested, and the scientific evidence understood." [Leclerc 1972, pp. 15-16]

One such 'alternative theory' originates from process thought. As we have seen, this comprehensive metaphysical system stresses becoming over being and environmentally responsive transformation. These concepts that emerge from process metaphysics fit well the intuition of many chemists, especially those of us whose day-to-day business is chemical kinetics, dynamics, and catalysis. For us, the molecules that capture our attention are not static, unchanging substances, but rather are dynamic entities that negotiate complex energy landscapes. Process thought, and its powerful metaphor of molecule-as-ecosystem, gives us the language to express what we believe to be the case when we think about molecules and molecular change.

## Notes

[1] To say that molecular change has a 'deep structure' is to say that there may be an aspect of molecular change that cannot be probed by experimentation. Such deep structural features would be in the realm of Kant's *noumena* (Kant 1997 [1783]): things in themselves and unavailable to sensible experience, which in this case means standard chemical experimentation that merely explores *phaenomena*; appearances apprehended from sensible experience. The principle view of this paper is that without deep structure, molecular change does not give rise to complexity and, ultimately, to life.

[2] Pre-Socratic speculative philosophy about nature clearly owes a debt to Egyptian and Babylonian influences. Miletus, the home of the early Presocratics, was an active center of trade and cultural exchange on the Aegean coast. Its citizens were thus exposed to the many and varied religious and cosmological ideas of Egypt and Babylonia.

[3] It must be mentioned that process thinking is not unique to the Western mind. In fact, it could rightfully be argued that such thinking in Buddhist philosophy predates a fully articulated Western process philosophy by many centuries. In Buddhism, nothing in the physical universe escapes the operation of the Law of Becoming. "Change, flux, or becoming is the Absolute. What we ordinarily call a thing is itself a process, a ceaseless coming to be and passing away" (Singh 1987, p. 10). It is in this ceaseless process of coming to be and passing away that Buddhism recognizes the universal Law of Momentariness (*kshanika-vada*). "The world [...] is not one of trees, plants, mountains, tables books or persons – it is a world of momentary events or *dharmas* [primary level of reality]. [...] What we conventionally refer to

as a 'person' therefore, is really a continually changing continuum of moments of experience – a stream of evanescent *dharmas* following each other in such quick succession that the illusion of persistence is maintained so long as one observes with an uncritical and untrained mind." (King 1999, pp. 116-117) For Buddhists, like Whitehead, the primary level of reality is not objects or entities but momentary events that, on a fundamental level, constitute such phenomena.

[4] The term 'holoarchy' is part of a useful descriptive apparatus developed by Ken Wilber (2000) in which particular elements of reality are seen as constituting parts of a relational set of 'nested' or 'concentric' elements. While Wilber traces the idea to Arthur Koestler who coined the term 'holon' to refer to an entity that is simultaneously a whole and a part of some other whole (Wilber 2000, p. 17), similar thinking appears in the work of Leclerc (1972, p. 311) and process thought, in general (Rescher 2000, pp. 30-32).

[5] The claim that molecules have a 'subjective nature' is a restatement of a basic doctrine of process thought that all things that exist possess a subjective nature that can experience. John Cobb explains that this sort of view of nature requires that we adopt a "double view of every real individual. Each such individual exists for my objectifying thought and experience. But each exists also as its own center of experience. In most cases this experience is not *conscious* experience. But it is an activity of taking account of its world and thereby constituting itself out of its relations" (Cobb 1988, p. 108). Thus, subjective experience need not imply consciousness. Whitehead reminds us: "Consciousness presupposes experience, and not experience consciousness" (Whitehead 1978 [1929], p. 53).

[6] Nonetheless, we chemists often fall victim to the "fallacy of misplaced concreteness" (Whitehead 1967 [1925], chap. III) and ascribe stability where there is none. The reason for our erroneous beliefs is easy to understand. The relative durations of the reactions we study lead us to characterize some of them as 'slow' and to say that the molecular reactants in these systems are 'stable'. We are astounded to hear, for example, that the half-time for decarboxylation of amino acids is upwards of  $10^9$  years (Snider & Wolfenden 2000). Surely *this* is a slow process! But such designations are radically conditioned by the durations of the chemists themselves, relative to the world around them. It is our human existential concerns that bring forth our subjective characterizations of reaction rates.

[7] Perhaps the most striking example of enzymatic catalysis is the decarboxylation of amino acids (Snider & Wolfenden 2000). In the absence of enzyme, these reactions proceed with half-lives of about a billion years (*i.e.*,  $k_{obs} \sim 10^{-17} \text{ sec}^{-1}$ ), while in the presence of enzyme these half-lives are reduced to less than a millisecond (*i.e.*,  $k_{cat} \sim 10^3 \text{ sec}^{-1}$ )!

[8] For reviews of the concept of energy transduction in enzymology, see the collection of essays in *The Fluctuating Enzyme* (Welch 1986).

## References

Bergson, H.: 1998 [1907], *Creative Evolution*, Dover Publications, New York, NY.

Birch, C.: 1988, 'The Postmodern Challenge to Biology', in: D.R. Griffin (ed.), *The Reenchantment of Science*, State University of New York Press, Albany, NY, pp. 57-68.

Bogaard, P.A.: 1993, 'The Philosophical Content of Quantum Chemistry', in: P.A. Bogaard & G. Treash (eds.), *Metaphysics as Foundation – Essays in Honor of Ivor Leclerc*, State University of New York Press, Albany, NY, pp. 252-71.

Cobb, J.B., Jr.; Griffin, D.R.: 1976, *Process Theology – An Introductory Exposition*, Westminster

Press, Philadelphia, PA

Cobb, J.B.: 1988, 'Ecology, Science, and Religion: Toward a Postmodern Worldview', in: D.R. Griffin (ed.), *The Reenchantment of Science*, State University of New York Press, Albany, NY, pp. 99-114.

Cunningham, M.A.; Bash, P.A.: 1997, 'Computational Enzymology', *Biochimie*, **79**, 687-9.

Dirac, P.: 1929, 'Quantum Mechanics of Many-Electron Systems', *Proceedings of the Royal Society*, **A123**, 714-33.

Harris, E.E.: 1993, 'Leibniz and Modern Science', in: P.A. Bogaard & G. Treash (eds.), *Metaphysics as Foundation – Essays in Honor of Ivor Leclerc*, State University of New York Press, Albany, NY, pp. 59-72.

Hirsch, J.A.: 1974, *Concepts in Theoretical Organic Chemistry*. Allyn and Bacon, Inc. Boston, MA.

Jencks, W.P.: 1969, *Catalysis in Chemistry and Enzymology*, McGraw-Hill, New York, NY.

Kant, I.: 1997 [1783], *Prolegomena to Any Future Metaphysics*, trans. and ed. by G. Hartfield, Cambridge UP, Cambridge, UK.

King, R.: 1999, *Indian Philosophy – An Introduction to Hindu and Buddhist Thought*, Georgetown UP, Washington, D.C.

Lahav, N.; Nir, S.; Elitzur, A.C.: 2001, 'The Emergence of Life on Earth', *Progress in Biophysics and Molecular Biology*, **75**, 75-120.

Leclerc, I.: 1972, *The Nature of Physical Existence*, George Allen & Unwin, London.

Lumry, R.: 1986, 'Free-Energy Management in Protein Reactions: Concepts, Complications, and Compensation', in: G.R. Welch (ed.), *The Fluctuating Enzyme*, Wiley, New York, NY, pp. 3-190.

Marcus Aurelius: 2002 [ca. 170], *Meditations*, trans. by G. Hays, Random House, New York, NY.

Ma, B.; Kumar, S.; Tsai, C.-J.; Hu, Z.; Nussinov, R.: 2000, 'Transition-State Ensemble In Enzyme Catalysis: Possibility, Reality, or Necessity?', *Journal of Theoretical Biology*, **203**, 383-397.

Matthews, J.M.; Fersht, A.R.: 1995, 'Exploring the Energy Surface of Protein Folding by Structure-Reactivity Relationships and Engineered Proteins: Observation of Hammond Behavior for the Gross Structure of the Transition State and Anti-Hammond Behavior for Structural Elements for Unfolding/Folding of Barnase', *Biochemistry*, **34**, 6805-14.

Monard, G.; Merz, K.M.: 1999, 'Combined Quantum Mechanical/Molecular Mechanical Methodologies Applied to Biomolecular Systems', *Accounts of Chemical Research*, **32**, 904-11.

Rescher, N.: 1996, *Process Metaphysics – An Introduction to Process Philosophy*, State University of New York Press, Albany, NY.

Rescher, N. 2000: *Process Philosophy – A Survey of Basic Issues*, University of Pittsburgh Press, Pittsburgh, PA.

Singh, B.: 1987, *Indian Metaphysics*, Humanities Press, Atlantic Highlands, NJ.

Snider, M.J.; Wolfenden, R.: 2000, 'The Rate of Spontaneous Decarboxylation of Amino Acids', *Journal of the American Chemical Society*, **122**, 11507-8.

Stein, R.L.: 1981, 'Analysis of Kinetic Isotope Effects on Complex Reactions Utilizing the Concept of the Virtual Transition State', *Journal of Organic Chemistry*, **46**, 3328-9.

Stein, R.L.: 2002, 'Enzymatic Hydrolysis of p-Nitroacetanilide: Mechanistic Studies of the Aryl Acylamidase from *Pseudomonas fluorescens*', *Biochemistry*, **41**, 991-1000.

Stein, R.L.; Fujihara, H.; Quinn, D.M.; Fascher, G.; Barth, A.; Schowen, R.L.: 1984, 'Transition-State Structural Features for Anilide Hydrolysis from  $\beta$ -Deuterium Isotope Effects', *Journal of the American Chemical Society*, **106**, 1457-61.

Welch, G.R.: 1986, *The Fluctuating Enzyme*, Wiley, New York, NY.

Welch, G.R.; Somogyi, B.; Damjanovich, S.: 1982, 'The Role of Protein Fluctuations in Enzyme Action: A Review', *Progress in Biophysics and Molecular Biology*, **39**, 109-146.

Whitehead, A.N.: 1967 [1925], *Science and the Modern World*, Macmillan, New York, NY.

Whitehead, A.N.: 1978 [1929], *Process and Reality*, corr edn. by D.R. Griffin and D.W. Sherburne, Macmillan, New York, NY.

Wilber, K.: 2000, *A Brief History of Everything*, rev. edn, Shambhala, Boston, MA.

Woolley, R.G.: 1978, 'Must a Molecule Have a Shape?', *Journal of the American Chemical Society*, **100**, 1073-8.

Zeidler, P.: 2000, 'The Epistemological Status of Theoretical Models of Molecular Structure', *Hyle*, **6**, 17-34.

---

*Ross L. Stein:*

*Laboratory for Drug Discovery in Neurodegeneration, Harvard Center for  
Neurodegeneration and Repair, 65 Landsdowne Street, Cambridge, MA 02139, USA;  
[rstein@rics.bwh.harvard.edu](mailto:rstein@rics.bwh.harvard.edu)*

---

*Copyright © 2004 by HYLE and Ross L. Stein*