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Article

Assembly Theory in Life Origin Models

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Abstract Any homeostatic protometabolism would have required orchestration of disparate biochemical pathways into integrated circuits. Extraordinarily specific moieties were also required. Assembly Theory conflated with its cousins—Complexity Theory, Chaos theory, Quantum Mechanics, Irreversible Nonequilibrium Thermodynamics and Molecular Evolution theory— collectively have great naturalistic appeal in hopes of their providing the needed exquisite steering and controls. They collectively offer the best hope of circumventing the need for active selection required to formally orchestrate bona fide formal organization (as opposed to the mere self-ordering of chaos theory) [1]. This paper focuses specifically on Assembly Theory's contribution to life-origin models.

Keywords: Life origin; molecular evolution; abiogenesis

Introduction

"Assembly Theory" explores the degree of causation difficulty and minimal requirements needed to produce a given molecular ensemble [2–9]. Lee Cronin and Sara Walker have probably taken the lead in promoting Assembly Theoy [10–13]. Sharma et al [14] published in Nature the most formally developed version of "Assembly Theory." Updates, clarifications, additions and defenses have been added mostly within YouTube URLs [6,7,9,15]. Assembly Theory could probably be viewed as a subset or outgrowth of complexity theory [3,16].

The Chaos Theory of self-ordering dissipative structures researched initially by Prigogine and Nicholis also plays a major role [17–30].

Behind Assembly Theory often lies the pre-assumption of impressive creativity producible by irreversible nonequilibrium thermodynamics [25,29,31]. Onsager's Nobel Prize winning work on "reciprocal relations" revealed these spontaneous paired reverse flux disequilibria [32,33]. Proponents of irreversible nonequilibrium thermodynamics contend that quanta dispersal over many degrees of microscopic freedom alone is sufficient to explain life origin) [34–42]. If so, this would obviate the need for any active selection required for molecular evolution. Nonequilibrium thermodynamics has been helpful in understanding protein folding [43,44] and molecular transport [45].Thus, irreversible nonequilibrium thermodynamic models, along with Assembly theory[34–41] become exceedingly appealing.

If there were any key to understanding "self-organization" and "emergence," it would come through a synthesis of Assembly Theory, Complexity Theory, Chaos Theory, Quantum Mechanics and Irreversible Non-equilibrium Thermodynamics. Molecular Evolution is added to the mix in hopes of providing the needed missing explanation for selection for "usefulness." But the focus of this paper is primarily on Assembly Theory.

Assembly Theory's Approach to Quantification

Proponents of Assembly Theory begin with what seems to be indistinguishable from Shannon's uncertainty measures of future possibility space. What is the phase space of physicodynamic *possibilities* [14]? What is the *history* of such possibilities having actually occurred?

Of particular interest to abiogenists is AT's proposed measurement of the *causation difficulty* of any molecular ensemble spontaneously arising that has sophisticated function. There would be no

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point to pursuing Assembly Theory if each ensemble did not possess some non-trivial utility. The spontaneous occurrence of any protometabolism would have required "useful" biomolecules.

Use of the words "challenge" and "difficulty" by AT theorists acknowledges that the formation of these useful molecular assemblies was not straightforward. That challenge is not just probabilistic. Determinative factors are involved. Physicochemical interactions with formal function require steering and control toward utility. Thus, the naturalistic goal of Assembly Theory (AT) ought to be the calculation of the formation challenges of *worthwhile* ensembles forming spontaneously. In abiogenesis research, only "usefulness" would contribute to naturalistic "self-organization" or "emergence" of protocells.

What in an Inanimate Environment Would Favor *Useful* Molecular Assemblies?

Given enough eons of time, laws, constraints, large phase spaces of possibilities, and thermodynamic fluxes are widely believed to produce formalistic physical entities and systems. Formalisms include sophisticated functions normally associated only with engineering. Evolution is claimed to polish the result of these non-evolutionary, purely thermodynamic and physicodynamic products. Yet physicodynamics itself provides no directionality toward the formation of useful assemblies or their holistic cooperation.

Perhaps the most fundamental question is, "How could sophisticated *functional* ensembles assemble in an inanimate environment without some basis for preference for function over nonfunction?"

Just being far from equilibrium does not necessarily produce functionality, let alone biofunction or homeostatic metabolism. And how could a prebiotic environment even identify functionality?

- Why would a prebiotic environment care whether anything functioned?
- What would have been the source of any motivation to prefer or pursue function?
- What were the means of such an achievement?
- Can chance and necessity produce sophisticated functions?
- Why would any accidental function have been preserved?
- What empirical evidence exists of nontrivial functionality ever having spontaneously occurred?

Few theorists believe that thermodynamics, chaos and complexity theories alone could have orchestrated homeostatic metabolism. "Systems biology" is just too formally orchestrated in its concepts, organization, pathways and methods. Sooner or later, molecular evolution and even neoDarwinian evolution has to be included in the measurement of causation of biologically useful ensembles. Thus, for AT to put a dent into the abiogenesis problem, it must ultimately quantify both physicodynamic and selection challenges in its measure of causation difficulty. And the selection challenge measured must be active selection challenge, not passive after-the-fact selection challenge.

Is Chance and Necessity Sufficient?

Physicodynamics alone has never been observed to generate a single non-trivial formalism. Even a simple piece of physical wire is an instantiated formalism. The characteristics of this "molecular ensemble" and physical "object," as AT proponents would call it, have never been observed to spontaneously generate from the four know forces of physics, from law, from chance, or from irreversible nonequilibrium thermodynamics. Iron ore in the ground lacks the characteristics of a long piece of metal alloy with constant diameter and optimized tensile strength and malleability needed to make a simple paper clip. How many pieces of *any* kind of wire have ever spontaneously "self-organized," or "emerged" in the history of human observation? If a simple piece of wire has never "self-organized" or "emerged," what would make any reputable scientist believe so blindly in spontaneous generation of homeostatic metabolism?

The self-ordering phenomena of chaos theory are usually grossly overextended into wild imaginations of "self-organization" and "emergence" of formalisms. The self-orderings of chaos theory are not only blind to "usefulness," they usually destroy usefulness. Consider weather fronts, hurricanes and tornadoes. How much organization is produced by these self-ordered "dissipative structures"?

 doi:10.20944/preprints202407.1491.v1

Formalisms invariably require choice causation, as opposed to mere physicodynamic causation. Bona fide organization lies in the engineering domain, not the physical science domain. The great hope of Assembly Theory is that it could offer a solution to this physicalistic dilemma. Naturalistic science desperately wants to be able to explain exquisite biological engineering without formal choice, steering or controls.

No scientist has ever observed anything organize itself into existence "Self-organization" is a nonsense term. Nothing can possibly organize itself into existence. It would have to already exist to organize anything. If it already existed, it could not possibly organize itself into existence.

A piece of wire is an object that shows evidence of active selection in its formation. We do not attribute that selection to iron ore itself, or to the laws of physics and chemistry. An orchestrating, conceptualizing agent did the active selecting that brought this alloy "object" into existence. This "molecular ensemble" was "assembled" as an engineering project, not a mere physico-chemical sequence of spontaneous "possible" interactions. No empirical "history" of such "possibilities" actually occurring exists.

The Inadequacy of Physicodynamics

Efficacious active selections cannot be made by physicodynamics [46–49]. Sooner or later, molecular evolution has to be included in the causative mix. For Assembly theory to put a dent into the abiogenesis problem, it must ultimately quantify both physicodynamic and evolutionary challenge (causation difficulty).

But can physicodynamics, including irreversible nonequilibrium thermodynamics, actually orchestrate and organize formal function?

The proponents of irreversible nonequilibrium thermodynamics contend that thermal energy/mass conservation is maintained by reciprocal paired fluxes of reverse disequilibria. One flux is thermodynamically downhill, but drives another flux in close proximity uphill. Thermodynamic probabilism is viewed as an "imperative," as though it were a physicodynamic cause of creative physical effects. Irreversible far-from-equilibrium fluxes and states are imagined to spontaneously occur. This is viewed as the avenue to spontaneous abiogenic potential.

Empirical justification for this imagination, however, is grossly lacking. We simply do not see sophisticated functional players spontaneously occurring from mere irreversible nonequilibrium thermodynamics. Quantum mechanics doesn't even come close to explaining the engineering realities of subcellular life.

Evolution Requires Selection to Optimize Function

The passive selection of "natural selection" would not have existed in a prebiotic environment. But no known basis for active selection in pursuit of function exists in an inanimate naturalistic environment, either. Little else exists that could hopefully explain the spontaneous orchestration of any formal organization. The problem is that empirical evidence is painfully lacking of quanta dispersal over many degrees of microscopic freedom producing a single sophisticated protein [50,51], or orchestrating the slightest hint of formal function [1,46,48,49,52–70].

In any purely physicodynamic model of "self-organization" and "emergence," spontaneous function would always be after-the-fact of the assembly's formation and utility. Evolution has no goal. Final fitness of the ensemble would be happenstantial. Secondary preservation of already-optimized fitness would play no *causative* role in its formation.

NeoDarwinian selection is passive rather than active. The fittest already-programmed, already-cybernetically processed, already-living organisms differentially survive better in what we call "natural selection." Such "selection" is somewhat of a linguistic stretch of the meaning of "selection."

A more appropriate use of the term "selection" is "active selection." Choices must be made in the pursuit of utility that make the realization of that utility possible. In the absence of active selection, empirical evidence of any sophisticated function spontaneously arising from irreversible nonequilibrium thermodynamics is virtually nonexistent. Claims to the contrary can invariably be shown to have had "investigator involvement" in their experimental design.

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Since all known life is programmed and cybernetically processed by nanomachinery, Turing's halting problem is very relevant when AT purports to measure causation difficulty.

Configurable switches must be set in advance of realized integrated circuit efficaciousness. Decision node choices (e.g. nucleoside selection of which of four monomers to next polymerize to a forming nucleic acid strand) must be active, not passive or secondary. Such programming and computational processing is formal, not physical. If we are to measure the challenge or difficulty of achieving computation, we are going to need to measure the causative techniques of cybernetics, not mere thermodynamic probabilism.

What exactly are these magical "higher level constraints" that are just pre-supposed metaphysically to have so much formal capability? Choice causation is excluded in science until, that is, we award the Novel Prize for the wisest research choices. If those choices are ultimately purely physicodynamic, what's the purpose of awarding the Nobel Prize? Perhaps we should throw the entire field of creative research and engineering into the trash as superfluous and unnecessary. Neuroscience has failed miserably to explain "mind" with nothing but a physicalistic/naturalistic model of brain origin. In fact, it has not even come close to explaining the physical brain.

Constraints are not Controls [12]. Mere constraints cannot steer and control events toward conceptual, orchestrational, integrative, formal function. "The unreasonable effectiveness of mathematics in the natural sciences" [13,14] is only unreasonable for those who fanatically refuse to acknowledge the third fundamental category of reality: Choice Causation. No rational basis or empirical experience exists to justify attributing homeostatic metabolism to Chance and necessity.

AT Attempts to Redefine our Concepts of Objects (Molecular Assemblies)

Assembly Theory theorists modus operandi attempts to "redefine the concept of an 'object' on which laws act." Is "concept" inherent in a molecular object? Do physical molecules redefine the concept of themselves to make a naturalistic model "work for them"? What difference should it make to objective chemistry and physics how investigators "conceive" molecular assemblies? The approach hardly seems objective and naturalistic. It is more of a creative epistemological system in the minds of vivid imaginers who ascribe to matter and energy more than what physics alone can justify. Is this some kind of Gaia worldview where rocks can think? If inanimate objects cannot conceive, the model certainly falsifies itself as being naturalistically helpful. In a prebiotic environment, no agent exists yet to conceive anything.

AT Theorists claim that AT "enables us to incorporate novelty generation and selection into the physics of complex objects."

First, note the "us" involvement in what is supposed to be a stand-alone naturalistic model. They talk constantly about *their* "re-conceptualization" of physicality, as if that changed the physical entities objective properties and spontaneous reactions.

Second, does "novelty generation" necessarily embody functionality of any kind? Most novel ensembles totally lack usefulness. Any stochastic ensemble is "novel."

Third, the proponents talk of "selection" being introduced into "the physics of complex objects." Selection of what? Selection how? Selection why? Selection *by* what? Selection in pursuit of what? Does inanimate nature select for *utility* of any kind? Would a prebiotic environment even know what function was? Would it have any desire or purpose in identifying or preserving it?

"It explains how these objects can be characterized through a forward dynamical process."[14].

What is doing the characterizing? Is this "forward dynamical process" advancing with respect to programming, processing, steering, controlling toward increased sophistication of function? Exactly how? The forward functional process is just believed and hoped for by blind faith. It is just presupposed metaphysically, not established scientifically.

The only answer of what is doing the characterizing is the "who" of human agents writing the paper. They have very vivid imaginations. Physicodynamics doesn't envision or "characterize" anything. Molecular ensembles are what they objectively are.

The hypothesized processes of Assembly Theory have not been observed yet naturalistically, let alone repeatedly observed. Most any *sequence* of physicochemical interactions is possible. Physics can

 doi:10.20944/preprints202407.1491.v1

deal with spontaneous sequences of interactions. But physics knows nothing of conceptually steered cybernetic "*processes*." Physical interactions themselves know nothing of computational success. Physics knows nothing of integrated circuits. Physics cannot even operate the efficacious opening and closing of Maxwell's demon's trap door.

Agents can practice the scientific method. But their conceptualizations have no causative impact on physical interactions themselves.

Raw physicochemical reactions could not have conceived or generated "Systems Biology." Systems are formally engineered by Choice Causation and active selection. Active selection requires choice with intent. Meteorologists ere in referring to self-ordered weather fronts as formally organized "systems." This fact emphasizes the vast amount of confusion that prevails between the natural self-ordering of Chaos Theory and true formal orchestration of organization.

The proponents of AT argue:

"Combinatorial objects are important in chemistry, biology and technology, in which most objects of interest (if not all) are hierarchical modular structures." [14]

What generated these presupposed functional "modules"? We only consider them modules, and use them to construct more sophisticated programming modules, because they are *functional*. How did such modules get to be functional in an inanimate environment in the first place?

Shannon measured possibilities and uncertainty. He was unable to measure prescriptions of true information that generated meaningful messages or instructed non-trivial function. Only agents do that, not inanimate nature.

Spontaneous cybernetic halting would correspond to successful naturalistic computation. Once we had a history proving the possibility of successful spontaneous computation, we might be able to reduce Shannon's Uncertainty measure (of "possibilities") with the observed computational steps and time requirements needed to calculate Reduced Uncertainty. But nobody has ever observed an inanimate successful computation. That "concept" is called Cybernetic "halting," not a physicodynamic interaction sequence.

The Problem of Active Selection

Selection comes into play much earlier than initially envisioned by proponents of the all-sufficiency of irreversible nonequilibrium thermodynamics, Complexity Theory, Chaos Theory and AT. Even if spontaneous physicodynamic formation is presupposed, one ensemble needs to be preferred over others to isolate and promote the continued existence of worthwhile ensembles. The components of formation must react in the right order and in the right quantities under the right conditions to produce anything other than useless tar [71–73]. Not only formation difficulty and assembly difficulty become an issue, but also *half-lives*.

Spontaneous formation of innumerable needed life-origin players is statistically prohibitive [50,51]. Not only that, but the spontaneous formation of many needed moieties have Universal Plausibility Metrics of ξ <1.0. The Universal Plausibility Principle requires peer-review rejection of any model proposing the spontaneous formation and collection of these moieties into the same place at the same time [74–76].

Life is the ultimate in algorithmic optimization. Algorithms cannot be optimized without active selection. Selections must be made "in order to . . . " Such choices cannot be attributed to evolution. Choices at true decision nodes must be made prior to the realization of any function.

Active selection cannot be circumvented. The secondary after-the-fact selection of neo-Darwinism is irrelevant to the abiogenesis problem. Prebiotically, active selection is required to generate ensembles with sophisticated functionality. Tertiary molecular function is determined largely by primary and secondary structure. Genetic instruction and control is determined by specific monomeric sequencing in linear digital prescriptions [77]. These monomeric programming selections have to be made during molecular construction (polymerization with all the same 3′5′ phosphodiester bonds). This takes place prior to any evolutionary model, molecular or Darwinian. That selection has to be active, not passive, since no life or even function exists yet for the environment

 doi:10.20944/preprints202407.1491.v1

to prefer. So, the fundamental question is, "Can AT explain or quantify this *active selection process difficulty*?"

Molecular Evolution

Molecular evolution theory has no basis for selection other than greater molecular stability and self-catalysis of massive quantities of one entity.

Molecular stability has nothing to do with utility. Some of the most toxic molecules to life are the most stable molecules (e.g. heavy metals).

Massive self-replication of one RNA analog would deplete the environment of the resources for hundreds of other needed molecular entities to form.

Crude catalytic agents would have to be legion and all-too-specific for many essential protometabolic moieties to form. Even if they all formed, they would have to be carefully sequenced in their reactions at the right times and under the required conditions. Reaction sequences would have to be selectively interrupted just at the right time to preclude biochemical catastrophe. Any protometabolism would have to be formally orchestrated, not merely self-ordered [1], to achieve the slightest hope of homeostasis.

What Could Have Been the Source of the Needed Active Selection?

AT authors state that, "The assembly is defined as "the total amount of selection necessary to produce an ensemble of observed objects."

Since the object or ensemble of objects forming does not exist yet in completed form, the selection required to achieve it is active, not passive. Evolution is only passive selection. It favors by differential survival and reproduction the fittest already-living organisms after-the-fact of their being alive and fittest. Therefore, evolution is always secondary, passive selection.

Active selection is performed "in order to . . . ." (to realize some goal). That is called Engineering, not "natural" science!

Quantum mechanics could be appealed to here. But quantum mechanics is inseparable from extensive epistemological confusion and misrepresentations of pseudo-engineering prowess.

Physics and chemistry are simply not capable of active selection in pursuit of functional ensembles. Function is no better than non-function to an inanimate environment. Laws and constraints could care less whether anything functions.

What exactly is AT's "assembly space?" How does it differ from a physical phase space? Is it not the sum of all possible physicodynamic outcomes? Is this not directly analogous to Shannon Uncertainty?

What does it have to do with active selection at bona fide decision nodes?

Is not the "assembly pool" with its minimal steps to computational success the essence of an empirically-known halting program? But how did the laws of physics ascertain in an inanimate environment what the optimized "assembly pool" steps should be? How did nature overcome Turing's halting problem?

Says AT proponents, "Once a pathway to assemble an object is discovered, the object can be reproduced." [14] How was this pathway (justifiably called a "program" or "optimized algorithm") "discovered"? The replication of DNA by PCR does not explain the origin of that DNA's sequencing and instruction sets. Did AT proponents really discover a truly naturalistic pathway to the programming of that gene? Forensic technicians "discover" people's DNA codes every day. That doesn't mean they understand how that prescriptive information was programmed into each prescriptive strand.

(a) What cared about successful assembly in an inanimate environment?
(b) What did the "discovering" (the active selection programming)?
(c) What took notes and recorded all of the successfully halting decision-node choices?
(d) How did Inanimacy select for function over non function?
(e) Did the four known forces of physics care whether the "assembly" highly integrative homeostatic metabolic function rather than useless tar?

 doi:10.20944/preprints202407.1491.v1

(f) How does the Assembly Index take the accomplishment of these tasks into consideration?
(g) What is the difference in quantification between formal success or failure?

The Problem of Measuring Active Selections

Say AT authors, "The 'assembly index' is the number of steps on a shortest path producing the object."[5]

- How is the shortest path chosen?
- Did the *object* do the choosing?
- Did randomness actively "select" the shortest path to success?
- Did constraints or the laws of physics choose the shortest path to success?

Measurements of physicodynamic interactions cannot quantify cybernetic/computational/engineering function. All known life is programmed and cybernetically computed. Computations have never been observed to arise spontaneously from constraints, laws or natural processes. Computational success originates only from the far side of the Cybernetic Cut, not the near physicodynamic side [66,78,79]. Laws and constraints are incapable of pursuing Choice Causation in pursuit of formal function (active selection from among real physicodynamic and thermodynamic options).

Says Sharma et al, "We introduce a measure called assembly (A), capturing **the degree of causation** required to produce a given ensemble of objects."[14]

Thus, the authors are proposing to *measure* the degree of causation difficulty of molecular ensembles. Is it fair to ask for clarification of the nature of these ensembles? Are these molecular ensembles all-inclusive? Do they include highly improbable and highly functional proteins, for example? Axe found that the overall prevalence of protein sequences performing a specific function by any domain-sized fold may be as low as 1 in 10^{77}, adding to the body of evidence that functional folds require highly extraordinary sequences.[50,51]. Do they include molecular ensembles like genes with all of their instantiated linear digital nonphysical Prescriptive Information [80]? Do they include the location of methyl groups at just certain positions to effect epigenetic controls?

Thus, we first need to know:

a. Are these ensembles purely physicodynamic and spontaneous, or is any selection, steering or control required in the causation of these assemblies?
b. Might this "degree of causation" measurement be related to the degree of cybernetic/computational difficulty associated with the assembly's causation?

Useful peptides, co-enzymes, proteins, and polynucleotide genes could be considered functional "assemblies." Are these unique assemblies going to be included in AT's measurements? If so, the needed utility, and how it was achieved, should also be included in the measurement of causation difficulty.

a. Might Turing's halting problem be inherent in this degree of difficulty?

Can the laws of physics and chemistry outsmart Turing's halting problem? Intelligent programmers can't.

So, the bottom line of what we are addressing here is: "Does Assembly Theory really address and measure whether an ensemble of objects does anything useful?" Suppose the contention is that it does. Is the usefulness non-trivial—something at least as unlikely to spontaneously form as a piece of wire from iron ore in the ground?

Shannon realized much to his chagrin that it was impossible to measure purposeful choices. Every choice involved in algorithmic optimization is unique and highly contextual. Each choice has a different weight of importance and criticality to the success of the formal process. Thus, specific positive choices cannot be measured with fixed units. He was forced to settle for measuring Uncertainty, not Prescriptive Information (instructions or controls) [81–83]. Not even passive, after-the-fact mutation value can be measured with fixed units. Nearly all mutations are either deleterious or neutral. But how could the value of the very few and questionable "good" mutations be measured? Some mutations have major effects. Others have minor or seemingly no effects. That being the case,

 doi:10.20944/preprints202407.1491.v1

it is impossible to assign a particular programming choice (e.g. nucleoside polymerization in a certain sequence) a fixed unit of helpful measurement or causation challenge (difficulty).

All nucleosides are polymerized with the same 3′5′ phospho-diester bond forming difficulty. This has nothing to do with the difficulty of prescribing polyamino acid sequencing so as to instruct a functional protein. And we are not even addressing the problem of multidimension coding's such as the superimposed translational pausing coding needed for proper protein folding. A sextet code prescription is superimposed on the triplet coded prescription, providing a completely different class and set of instructions in a different language. That's a formalism.

Abiogenists' queries of Assembly Theory proponents

The first questions abiogenists should pursue relevant to Assembly Theory are:

Does assembly theory differentiate between functional vs. nonfunctional molecular assemblies? Potential function matters a great deal in abiogenic theory. Sara Walker would probably agree. She is an abiogenist herself.

Is there any natural process directionality toward the formation of *useful* assemblies? Or is the usefulness of any assembly purely happenstantial?

a. How would a prebiotic environment have recognized or made use of "usefulness"?
b. Does an inanimate environment "value" function over non-function?
c. Will Assembly Theory elucidate the purely physicodynamic causative *route* to useful assemblies as opposed to non-useful assemblies?
d. Would any spontaneous usefulness be preserved and expanded upon by an inanimate environment?
e. How many molecular assemblies with happenstantial sophisticated function would AT proponents expect to spontaneously form in the same place at the same time?
f. What about the fact that many potential players in abiogenesis models have very short half-lives?
g. What about the homochirality problem? Yes, Sharma [84] has recently published a very interesting paper on homochirality origin. But this model is quite limited in scope.
h. What about the spin-polarized electron problem [85]?
i. Does mere molecular stability equal molecular function?
j. Wouldn't a self-replicating RNA-peptide assembly tend to consume all the resources needed for the formation of many other assemblies required for protolife to "self-organize"?
k. Does Assembly Theory address any engineering-like *steering or controls* that might be needed to generate function, as opposed to mere mindless constraints [63]?
l. Are any *active selections* at all required to generate assemblies with sophisticated functions? The entire engineering field might tend to question whether natural science could address such active selections in pursuit of utility.
m. Is the measurable causation *difficulty* equal for functional vs. non-functional assemblies?
n. If the causation difficulty for functional molecular assemblies is greater than for non-functional ones, can the *specific* steering and controls needed to orchestrate protometabolic function be measured with fixed units?
o. Wouldn't some active selections be more consequential than others?
p. Wouldn't some selections be harder to make than others?
q. Ultimately, abiogenists wonder how useful Assembly Theory quantifications will be in measuring the challenge of achieving formal organization, decision-node selections, integration of circuits, quality control, minimization of required steps to computational success, orchestration of disparate biochemical pathways into homeostatic protometabolism and metabolism, the molecular machinery needed to process the prescriptive information of programming and cybernetic controls, the difficulty inherent in Turing's "Halting Problem" [86]. Even "trial and error" quests presuppose intent, purpose and goal. Neither molecular nor neoDarwinian evolution has any goal.

 doi:10.20944/preprints202407.1491.v1

The problem of Prescription

Prescription of non-trivial function is a different modality altogether from the prescribed physical product itself [87,88]. The same is true of the physical objects (the tokens or physical symbol vehicles) containing that prescription's instantiation [77]. A triplet codon is a physical symbol vehicle used to prescribe formal meaning and function [70,89]. So are the multidimensional translational-pausing sextet codes superimposed on the amino acid sequencing coding [90]. This research paper may be recorded into cyberspace or recorded with paper and ink molecules, but its content is abstract, conceptual, non-physical and formal. DNA, RNA, chaperones and other useful polypeptides may be physical, but the formal Prescriptive Information instantiated into these molecules is the real issue. How were their primary structures sequenced so as to produce instructive value in a completely different language of polyamino acid primary structure sequencing? How were secondary and tertiary structures anticipated when primary structure formed? Efficacious prescriptive sequencing was required upon pre-function polymerization. That required active selection, not passive after-the-fact selection.

Causation of active selection cannot be physical [60]. It arises from the far side of the Cybernetic Cut [66,78,79]. The Cybernetic Cut is the great divide between Physicodynamic Causation ("necessity") and formal Choice Causation. The decision-node programming choices of coded genetic prescription can arise only from the far side of the Cybernetic Cut. Physicodynamics has no ability to program computation or to orchestrate formal organization.

The quest turns more cybernetic, as acknowledged by AT theorists themselves, when they introduce the question of "What would be the fewest steps needed to accomplish the goal?" [14] AT theorists also ask the purely formal, cybernetic question, "What possible pathway would require the shortest processing time?" [14] These are cybernetic questions, not natural science questions. The problem is that cybernetics by definition pertains to control. Controls are not constraints [63]. Controls require choices. Controls steer interactions toward formal success. Systems biology is impossible without controls. We are shooting ourselves in the foot by disallowing discussion of steering and the needed formal controls when trying to elucidate the origins of Systems Biology. We are looking in the wrong place. We are looking to fixed laws when we should be looking at programming rules.

AT "reimagines the concept of matter within assembly spaces," [14]

a. What exactly is doing the imagining? The physical "object," or the AT agent imaginers *about* the object? What does agent imagining have to do with physicodynamic abiogenesis in an inanimate environment?
b. Is this imagining a physical cause of purely physicodynamic events?
c. Is this truly a naturalistic model?

The object of AT doesn't exist yet. It is being manufactured not by possibilities, but by purposeful choices of possibilities made in pursuit of utility.

How exactly are the required purposeful choices being measured?

Randomness has never programmed any non-trivial computation. And if programming were done by law, there would be no contingency. Programming is impossible when law precludes contingency. Not just contingency, but purposeful choice contingency is the key to cybernetics and the engineering of nontrivial function.

AT authors contend that, "For the shortest path to success, "the assembly space captures the *minimal memory*, in terms of the minimal number of operations necessary to construct an object based on objects that could have existed in its past."[14]

What determined the minimal number of operations necessary? Some law of physics? One of the four known forces? Thermodynamic possibilities?

Shannon theory (itself conducted only by human agents) gives us the total number of binary options (possibilities) from which an ideal path *could be* chosen. Shannon's measure of Uncertainty does not measure the optimal choices that get us to the destination the fastest, or with the greatest

 doi:10.20944/preprints202407.1491.v1

computational efficiency. Shannon theory tells us nothing about how an algorithm got optimized. The AT measurement is bogus.

This supposedly naturalistic model is not naturalistic.

Shannon's "reduced uncertainty" measurements are calculated after-the-fact of having achieved computational halting through wise programming choices by agents. It represents the difference between all possible "steps" and the specific steps that produced the history of successful computation. Assembly theory is blind to which happenstantial "choices" from among real computational options will halt. Again, that requires formal cybernetics, not inanimate physical law and constraint measurements.

We can measure Shannon's Uncertainty to measure probability space. But that has nothing to do with function. An agent must use Reduced Uncertainty which first requires known halting Prescriptive Information to subtract from the statistical phase space. Even then, the measurement is only a measure of reduced uncertainty, not a measure of the specific Prescriptive Information that instructs halting success.

An agent must also apply Shannon's measure of Reduced Uncertainty relating to the solution of *a specific problem of interest*. All of this requires agency, not just physicodynamic interactions.

Only agents care about achieving a goal with the fewest number of operations. That is called cybernetics, not natural science! Laws and constraints can do no such thing.

The bottom line is that what is being appealed to is really nothing more than a mere phase/probability space, not a cybernetic (steered toward utility) space. What is actually being sold is a supposedly naturalistic "algorithmic optimization" that in reality does not exist. A mere probability space cannot achieve sophisticated assemblies, meaningful messages, or computation.

The only thing preventing the production of chemical "tar" is precise prescription of many synthetic steps and factors detailed in great detail by Prof. James Tour at Rice University [71–73]. No "history" of "possibilities" is provided wherein spontaneous generation of even protolife is produced. Nothing is more functional than homeostatic metabolism far from equilibrium. The only thing emerging here is the vivid imagination of the AT agents' wish fulfilment.

History doesn't even include the spontaneous emergence of a simple piece of wire from iron ore in the forest floor. Spontaneous wire formation may be a theoretical extreme "possibility," but spontaneous formation of a piece of wire alloy of constant diameter would not constitute a plausible scientific hypothesis [57,74–76].

AT theorists acknowledge that "Molecules with a high assembly index are very unlikely to form abiotically, and the probability of abiotic formation goes down as the value of the assembly index increases." [57,74–76]Their Universal Plausibility Metric $\xi < 1.0$. The reason "laws do not predict emergence," as the authors admit, is that laws cannot produce Choice Causation in pursuit of formal function (Active Selection from among real physicodynamic options).

Assembly theory is little more than the same embarrassing boondoggle of Richard Dawkin's 1986 *Blind Watchmaker* model of supposed evolution of a linguistically functional phrase [91]. The model was altogether dependent upon agent active selections. Dawkins chose which phrase to keep building on in the step-wise construction of a message meaning. Dawkins was blind to his own investigator involvement in his experimental design. So are Sharma et al.

Agent Choice Causation and agent concept are being snuck in through the back door of AT's supposedly naturalistic model. Imagination is being conveniently confused with "history" and "possibilities" in "conceiving" computational success without any basis for active selection. AT ignores Turing's cybernetic halting problem.

Already Published Critiques of Assembly Theory

Multiple researchers have already criticized Assembly Theory. Hector Zenil [92,93] cites multiple fallacies, both conceptual and methodological. Zenil claims that AT's algorithms are really no different from Shannon's Uncertainty measures and Kolmogorov Compression Theory.

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Hazen et al [94] disagree with the contention that only life can generate molecular structures with an MA index (Molecular Assembly measure) ≥ 15. Both Hazen et al and Zenil take issue with AT's ability to differentiate between living and nonliving systems using single scalar values.

Chemist Steven Benner [95] contends that AT has not solved "the wickedly complex problem central to organic chemistry: The problem of reactivity." Renowned synthetic organic chemist James Tour certainly agrees. [71–73]

In a 2024 paper in the Journal of Molecular Evolution entitled "Assembly Theory: What It Does and What It Does Not Do" [96], Johannes Jaeger asserts that Assembly Theory "certainly does not provide any new explanation of biological evolution or natural selection, or a new grounding of biology in physics." Jaeger goes on to say, "the paper is starkly distorted by hype, which may explain some of the outrage it created." But in criticizing Assembly theory, Jaeger [96] reveals his own confusion in his phrase, "higher level emergent causal constraints in computational worlds made of basic objects and their combinations." Constraints cannot cause computation. Only the controls requiring active selections can generate formal function. Objects and their combinations do not program or compute. Mere spontaneous molecular assemblies ("combinations") do not constitute programs or Turing machines, let alone ribosomes. Since these selections would have to be made prior to the existence of the functional entity, those selections would have to have been made actively rather than passively. Evolution would not have existed yet in an inanimate environment. Nothing was alive yet to differentially survive and reproduce.

"Assembly Theory" does not appear to be a naturalistic, bench-science, cause-and-effect model that will benefit abiogenesis research. Present-day reconceptualization's of physicality in the minds of scientist agents have little relevance to what actually happened physicodynamically in a prebiotic environment. Abiogenists need stand-alone models of self-organization and emergence that can be empirically verified without investigator involvement in experimental design.

AT cannot measure the orchestrational challenge of even a theoretical protometabolism. Life is not just a molecular assembly. Life is highly integrated innumerable cybernetic computational haltings that repeat through time far from equilibrium. Though instantiated into physicality, life is fundamentally formal rather than physicodynamic. Life originates from the far side of the Cybernetic Cut [66,78,79].

Physico-chemically, assembly is not as likely as disassembly. Neither would spontaneously generate sophisticated function.

Discussion

Time, including four billion years of time, is not a cause of any effect! Lee Cronin says the mechanism was four billion years of "technology"— "four billion years of search, destroy and survive."[6] Are "search" and "technology" natural science terms? Do they have naturalistic meaning, or formal engineering/cybernetic meaning? How exactly did an inanimate, prebiotic environment "search" for or achieve "technology"? Can we not see how utterly fallacious is the entire presupposition of the spontaneous generation of life? Even "trial and error" constitutes *a search mechanism* of which an inanimate environment is incapable.

A prebiotic environment would have been oblivious to generating or preserving formal function. The most fundamental need of life-origin research is to elucidate the source of orchestrational prowess needed to prescribe and formally organize even the simplest imaginable homeostatic proto-metabolism [52,54,56,59–62,78]. This requires explaining the source of particular nucleoside sequencing that programs functional polyamino acid sequencing. It requires explaining the mechanisms of generating the eventual cybernetic processing of that programming by sophisticated machinery. In addition, biochemical pathways must not only be prescribed; they must be formally processed by subcellular nanocomputers. Molecular machine utility must be orchestrated into highly conceptual integrated circuits. Only then does the myriad of synthetic biochemical problems begin [71–73] Successful measurement of the challenge of functional assembly of each and every physico-chemical moiety, and the difficulty of orchestrational integration, should not be naively expected or proclaimed.

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Few theorists honestly believe that thermodynamics, chaos, complexity, Assembly theory and molecular evolution alone could have collectively orchestrated homeostatic metabolism. But to admit this would threaten their metaphysically-mandated physicalistic careers. Physicalists own the stadium, the playing field and the ball. You either play by their rules, or you don't play at all. The result is the greatest Kuhnian paradigm rut in the history of science.

Does AT really measure the steering and control needed to craft the primary, secondary and tertiary structure of highly efficacious enzymes? If AT pre-assumes nothing more than chance and necessity, ignoring the third fundamental category of reality (Active Selection) [61], it is guaranteed that it's measurements of difficulty will be bogus.

Conclusions

How much empirical evidence have we observed through the centuries of sophisticated function spontaneously arising out of physicodynamics alone? Have spontaneous molecular assemblies, for example, ever produced a single simple piece of wire from iron ore in the ground? If not, why not?

The paraphrased bottom-line of AT hype is that "AT enables us to conceptualize and ascribe engineering prowess into ordinary molecular assemblies. We can then call this mentation a naturalistic model and measurement of purely physicodynamic 'self-organization' and 'emergence.'"

The "measurers" are intelligent choosing agents who imagine "novelty" and conflate that with biofunction in their minds. The organizational active selection required is artificial, not natural. Neither the physical "objects" (the spontaneous molecular ensembles) nor the fixed laws and constraints of physics and chemistry can account for the hundreds of highly specific essential players needed for abiogenesis. No basis for orchestration of any bona fide formal organization is presented. Spontaneous homeostatic metabolism is just religiously and blindly believed to have occurred in accord with the purely metaphysical Kuhnian paradigm rut that pre-assumes axiomatically that "physicodynamics did it."

Irreversible nonequilibrium thermodynamics has not lived up to its hype. Neither have Complexity, Chaos and Assembly Theories. Molecular evolution is impossible without *active* selection. If Assembly Theory, Complexity Theory, Chaos Theory, Irreversible Non-equilibrium Thermodynamics, Quantum Mechanics and Molecular Evolution Theory are collectively so capable of explaining abiogenesis, why have we not seen scores of instances of spontaneous generation over the last few centuries? If we have never witnessed the spontaneous formation of a simple long piece of metal alloy of constant diameter, what would ever make us think we could explain the emergence of homeostatic metabolism from nothing but chance and necessity?

Science, biology especially, must stop excluding the third repeatedly observable fundamental category of reality—Choice Causation [61]—from its study. It must at least be willing to acknowledge the reality of subcellular biological engineering when it sees it. Science requires self-honesty, not obfuscation. All known life is formally programmed with formal material symbol systems. It is cybernetically processed with some very sophisticated nanocomputers. These are simply not the effects of "natural process" causation.

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