

## Critical Review

# Systems Biology as a Research Program for Intelligent Design

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**Abstract**

Opponents of the intelligent design (ID) approach to biology have sometimes argued that the ID perspective discourages scientific investigation. To the contrary, it can be argued that the most productive new paradigm in systems biology is actually much more compatible with a belief in the intelligent design of life than with a belief in neo-Darwinian evolution. This new paradigm in system biology, which has arisen in the past ten years or so, analyzes living systems in terms of systems engineering concepts such as design, information processing, optimization, and other explicitly teleological concepts. This new paradigm offers a successful, quantitative, predictive theory for biology. Although the main practitioners of the field attribute the presence of such things to the outworking of natural selection, they cannot avoid using design language and design concepts in their research, and a straightforward look at the field indicates it is really a design approach altogether.

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## INTRODUCTION

Opponents of intelligent design (ID) theory have often argued that the ID approach is scientifically sterile—that it does not encourage scientific discovery. In response to this argument, which has appeared in many places over the years [1], in 2001 I wrote:

A theory of design can in principle be predictive and quantitative. For example, a computer chip manufacturer, which takes apart a chip made by a rival company, proceeds on the assumption that the circuits are well designed; this does not lead them to end their investigation, but rather, drives their study of the chip. The good-design assumption leads to specific predictions and applications, e.g., the prediction that it is unlikely to find wires which take up metal and space but serve no purpose, so that there should be few wires which are dead ends, with the application that studying any particular wire is likely to be useful. A bad-design assumption (e.g. that the chip maker made many random circuits and then just picked out the ones that worked) would give very different predictions. [2]

At that time, not being a biologist, I was not familiar with the field of systems biology, and did not know of the revolutionary new work that was beginning in this field. In the decade since then, systems biology has dramatically confirmed this picture of design-based research.

Before delving into the details of this new systems biology paradigm, it is worthwhile to look in more detail at what difference an intelligent design approach would make in doing biology. The intelligent design view makes the assumption that at some time in the past, one or more intelligently guided events took place that cannot be described by known physical laws and reasonable probabilities. How this happened is a secondary issue: some ID proponents invoke miraculous jumps within the history of the universe, at points like the Cambrian explosion [3], while others invoke no jumps, i.e., no discontinuities in physical law during the unfolding of the universe, but instead invoke extreme fine tuning at the beginning of the universe [4]. The Darwinist approach, by contrast, assumes that at some time in the past, random variation and natural selection led to existing biological systems with reasonable probabilities [5].

While the intelligent design approach and the neo-Darwinist approach make very different assumptions about the distant

past, both approaches are primarily concerned with the material processes that exist now in biological systems. The idea that ID implies giving up on looking for material causes altogether, invoking a miracle at every turn, is false. Rather, ID proponents base their arguments on material causation, arguing that the network of existing, known causes and effects in biology are best described as a product of past actions of an intelligent designer. In fact, they often criticize neo-Darwinians for invoking too many unknown and mysterious causes, such as de novo generation of genes [3]. Darwinist biology also largely focuses on presently operating causes and effects, for a much more mundane reason—the money in biology is in things that we can use and manipulate now, not in things that no longer exist.

If both viewpoints tend to focus on material causes and effects in presently existing systems, where do they diverge in their predictions? Consider the two cases mentioned above, namely a very good human designer and a very bad human designer. The bad designer may, for example, be a Darwinian designer who simply tries all kinds of things and throws out the attempts that don't work. How would we expect their products to differ?

To start, we would expect the good designer to produce products with few non-functional elements. This is related to the expectation that good design will have a high degree of optimization, or efficiency.

It is possible to imagine that a bad designer could also obtain some degree of optimization by simply trying many times, and always keeping the most efficient version. This is the Darwinian explanation of the efficiencies that may exist in biological systems. A bad designer could make random changes to existing designs, and toss away the less optimal versions each time. But even a short consideration tells us that such an approach would probably have *some* non-functional or non-optimal elements, and that we would expect *more* of them than we would in a truly well-designed system. Thus, proponents of Darwinism have historically argued for “junk” in living systems, such as “vestigial” organs or “junk” DNA [6,7].<sup>1</sup>

A good-design assumption also leads us to expect other attributes besides just the lack of non-functional elements. In well-designed systems we expect to find *subtle* and *elegant* methods. By contrast, in badly designed systems we expect to find “kludgy” and “brute force” methods, i.e., methods that involve gross inefficiencies but get the job done. Proponents of Darwinism have often argued that the kludgy, inelegant methods that exist in biology are evidence that biological systems are not designed by an intelligent agent [9].

A good-design approach also leads us to think in terms of the designer's *goals*, i.e., to engage in *teleology*. With good design, we can see what purpose things serve, while with bad design, we must wonder, “What were they thinking?”, like a person discovering bad wiring schemes or bad plumbing in home repairs done by a previous owner. Good design makes sense to us because it accomplishes its purposes well. In contrast, Darwinism has historically rejected all teleological thinking [10].

Some may disagree with aspects of the characterizations I

have given here. But regardless of the details, it should not be hard to see that the two different accounts of the history of biological organisms will give very different expectations for what kinds of mechanisms will exist in biological organisms in the present. Given these different approaches and different expectations, what can current systems biology tell us? Which paradigm fits more naturally with the way that systems biology is actually being done?

## The Revolution in Systems Biology

In 2009, I attended the March Meeting of the American Physical Society (APS) in Pittsburgh, the largest annual physics conference in the United States. At this meeting, there were at least ten two-hour sessions on systems biology. The excitement about systems biology at that meeting was palpable. Speaker after speaker talked about how this field was, for the first time in history, allowing quantitative, mathematical predictions for biophysics that were being confirmed regularly by experiments.

This excitement has also been reflected in the literature. At least three new journals have been created in the past few years (*BMC Systems Biology*, *IET Systems Biology*, and *Systems and Synthetic Biology*). Bud Mishra of New York University writes in a review article for the Royal Society [11], “Systems biology, as a subject, has captured the imagination of both biologists and systems scientists alike.” Koepll and Setti [12] similarly write, “Systems and synthetic biology are two emerging disciplines that hold promise to revolutionize our understanding of biological systems and to herald a new era of programmable hardware, respectively.” Allarakha and Wensley declare [13], “Since the completion of the human genome project a new biological paradigm has emerged, namely systems biology.” Finally, Hiroaki Kitano [14] proclaims, “The application of systems biology to medical practice is the future of medicine.”

Given all this excitement, what is this new paradigm? Systems biology as a whole can be defined as the study of the “big picture” in cell biology, that is, looking at whole systems and how they function, rather than using a “bottom-up” approach that tries to deduce function from molecular interactions. The terms “holistic” or “emergent” are commonly used [15-17]. Systems biology researchers reject a reductionist view of biology, which says that adequate understanding can be obtained by starting with the physics of microscopic processes, and then working up to higher-level processes.

The new paradigm in the field that is gaining so much attention, however, is not just to pay attention to larger systems, but a new approach to looking at these systems. In particular, the new paradigm is to use the methods of systems *engineering* when looking at biological systems. R. Rushmer writes,

A new era of scientific research is set to produce a type of engineer unlike any other and take the UK into what experts claim will be the third industrial revolution after the one in information technology. Biology and engineering groups are converging to develop a new field known as systems biology. It borrows techniques and tools from systems engineering

<sup>1</sup> While the notion of “junk” DNA has decreased in popularity, it is still often promoted [8].

to build and test mathematical models of biological components, such as organs and cells. Experts predict that systems biology will revolutionise the medical sector. Discoveries in health and disease will lead to further research, which could boost the engineering industry with new materials, biofuels and manufacturing capabilities[18].

Biologists and biophysicists are now learning to think like engineers when approaching biological systems.

An important distinction must be made here. While to many people, engineering and physics are fundamentally similar, since engineering uses many physics principles, the approaches of the fields are quite different in practice. The world of physics has been dominated by bottom-up, first-principles thinking. In many cases this has meant starting with the microscopic elements of a system, but even in the fields of physics that look at macroscopic behavior, the focus has been on elementary, universal principles such as “scaling laws.” The overriding paradigm in physics has been that simple, non-teleological rules will eventually explain everything. Even emergent behavior in complex systems is assumed to be the result of simple interactions [19,20].

By contrast, engineering takes a top-down approach that is explicitly teleological. A goal is defined, and then the parts are arranged to bring about that goal. Basic physics principles may or may not be used, depending on whether they are helpful. Engineering principles are fundamentally *design* principles, not reductionist principles. Engineering students learn good ways of solving problems to achieve pre-defined goals in the same way that physics students learn universal physical laws.

The reductionist physics-like approach has been the dominant paradigm in biology since the Enlightenment, but systems biology researchers have argued that reductionism has arrived at the limits of its usefulness [21,22]. Even the type of reductionist physics that focuses on universal behaviors such as scaling laws has limited value in biology [23]. The new paradigm, by contrast, calls for an explicitly engineering-like approach in terms of design goals. While not everyone in the field agrees with the use of engineering terminology, even those who don't like the word engineering still use engineering-like teleological terms. For example, Wolkenhauer and Mesarovic, writing an essay against the use of engineering terms, say:

We first need to realize that in order to control, regulate or coordinate something, we mean to adapt, maintain, optimize. Thereby, implicitly, there must exist a *goal* or *objective* [24]. [Emphasis in original.]

The holistic or emergent approach of systems biology is therefore not just a focus on larger systems or interactions of parts. The productive new paradigm is to look at those larger systems from the standpoint of an engineer seeking an objective. This is exactly the perspective I argued in 2001 should arise from a belief in intelligent design.

## ENGINEERING METHODS IN SYSTEMS BIOLOGY

It has become an extremely productive paradigm in biology to look for biological systems that exhibit the properties of sophisticated engineered systems, i.e ones that resemble methods developed by human engineers over the past few hundred years to accomplish complicated tasks. In what follows I describe examples of advanced engineering methods found in biological systems.

### Negative feedback for stable operation

Anyone who takes introductory electronics knows about the ubiquitous engineering tool of negative feedback. Suppose that we want to amplify a small input signal. For a system with large amplification, one can imagine that small changes of the amplifier, for example due to temperature fluctuations, could lead to large changes of the output. In a negative feedback system, a small amount of the output is taken and subtracted from the input. Thus, if the output swings too high, it immediately lessens the input, which reduces the output, and if it swings too low, this increases the input, pushing the output back up. The result is a stable amplification that is less sensitive to environmental fluctuations. There are numerous examples of this in biology [14,25,26].

### Thresholding and discrimination

On the other hand, another ubiquitous engineering method is to use positive feedback, in which the output is added to the input rather than subtracted. While this can lead to unwanted results in some cases (e.g. the familiar whistle when a microphone picks up too much of the output of the loudspeakers in a room), it is also very useful for systems to allow thresholding to discriminate signals from background noise. In this method, a threshold level is set, and signals above this level are amplified strongly, while signals below the threshold level are ignored. This allows systems to make decisions even in the presence of fuzzy, or noisy, inputs [27].

Many biological systems use a very sophisticated method of thresholding, in which the threshold level is not kept constant, but instead varies depending on the needs of the system at the time. For example, human eyes and many other detectors in living organisms become more sensitive in low-signal conditions, and less sensitive in high-signal conditions [28,29].

### Frequency filtering

One way to pull a signal out of a noisy background is to use amplitude filtering in a thresholding system, as described above. Another way is to use frequency filtering, in which only signals of a certain periodicity are amplified. Engineers are well familiar with this as “lock-in” detection. This also occurs in living systems [30-32].

### Control and signaling

All kinds of engineered systems have systems of control and regulation, by which conditions are detected and the system

reacts accordingly by sending signals to subsystems to act in response. Again, in biological systems there are many examples of all of these aspects of control: detection, decision, and signaling to other systems to induce a response [33,34]. Control mechanisms are quite often discussed in terms of “decision making” by the system, i.e., considered responses to accomplish a goal.

### Information storage

Control signals imply information. Biological systems also store information for use at much later times. In each case, the information “represents” a physical state that is not present [35,36].

It has sometimes been considered controversial to say that biological systems use information [37]. The systems biology revolution assumes that biological systems both use and store information in multiple contexts. Vincent, Bogatyreva, and Bogatyrev say [38], “Whereas technology uses energy as the main means of solving technical problems, biology uses information and structure.” Bill Bialek says [39], “The generation of physicists who turned to the phenomena of life in the 1930s realized that to understand these phenomena one would need to track not just the flow of energy (as in inanimate systems) but also the flow of information.” Allarakhia and Wensley say,

The pharmaceutical industry has gradually evolved from a purely chemistry-based paradigm to an information-based paradigm. With the completion of the human genome project, drug discovery knowledge is increasingly being viewed as part of systems biology. Systems biology does not focus on individual information bits one at a time, but considers the behavior and relationships of all units of information, in a particular biological system, from a functional perspective. [40]

and

This paradigm [of systems biology] is advancing the view that biology *is essentially an information science* with information operating on multiple hierarchical levels and in complex networks [13]. [Emphasis added.]

Kolch says,

What is systems biology, and more importantly what can it do for us? Here is the view of a biochemist who, while working on cellular signal transduction pathways, became increasingly astounded by a highly paradoxical observation. Signal transduction pathways collect numerous types of information in the form of hormones, growth factors or direct cues via contacts with neighbouring cells. These various types of information are transmitted, processed and integrated via the enzymes and their biochemical reactions that constitute the hardware of signalling pathways. In the end there is usually a specific and

reproducible biological response that is appropriate to the stimulus and also fitting the higher context of the tissue or organism. This is the Holy Grail that teases us: understanding the biochemical basis of biological decision making. [41]

There are so many similar quotes in the systems biology literature that it is simply out of touch to argue that information is not a valid concept in biological systems. Systems biology has benefited in particular from new paradigms obtained from information and computer engineering.

### Timing and synchronization

As in any computational system that executes actions in response to external inputs as well as internal stored information, timing and sequence are crucial. Thus biological systems have clocks and an exquisite structure for synchronization of different processes, with triggers, delays, and several different clock cycles operating simultaneously [42,43].

### Addressing

For signals to be useful, they must go to their intended target. Very rarely do biological signals simply float around until they hit their intended target by random motion. Instead, signals are typically labeled with addresses and carried to their targets, similar to the way that engineered systems such as the Federal Express delivery system efficiently get addressed objects to their intended goals [44-46]. While random thermal motion of molecules does occur and is an important factor in cells, this random motion is corralled and channeled into very specific uses by biological systems, such as thermal ratchets, which convert random motion into unidirectional motion, and portals, which only allow objects with certain configurations to pass through.

### Hierarchies of function

Every computer programmer and every electronics designer knows the virtue of modularity, that is, making devices that perform subtasks, which can then be bundled into higher-level structures that can themselves be bundled into even higher-level structures. Novice computer users are familiar with another version of this: the ability to store things in folders, which can then be put in other folders, allowing easy handling of large sets. This same type of structure is found in biological systems [47-49].

### Redundancy

Well-engineered systems have backup systems, or fail-safes, in case essential systems fail. The same occurs in biological systems, where it is often called “degeneracy” [50,51]. Redundancy occurs in biology at the obvious, organ level (two kidneys, two ovaries, etc.) as well as at the microscopic level. In many cases, it makes the most sense to turn on backup systems only when the main systems fail. This requires additional detection and triggering systems. There is a design balance involved with redundancy, because too much redundancy requires too large a cost to carry unused systems.

## Adaptation

Perhaps the most sophisticated type of engineering is adaptive engineering (e.g. “smart materials”), in which a system is programmed to change its overall configuration in response to changes in the environment.

This adaptive response may even extend to include processes long considered to be evolutionary processes. James Shapiro [52] of the University of Chicago, and Michael Deem of Rice University [53] have argued that much of the adaptation that we see in living systems today, such as bacterial immunity, is not due to random processes, but rather is due to very sophisticated problem-solving systems. These systems use randomization controlled by supersystems, just as the immune system uses randomization in a very controlled way. In bacterial immunity, as well as in the immune system and perhaps in many other systems, the system does not allow random changes and is quite stable (e.g., through error correction of genes), until certain outside stresses are detected. When external stress occurs, the system triggers a new process by which random solutions are generated. Only part of the system is allowed to vary randomly, while the rest is highly conserved. When a good solution is found by this highly parallel problem-solving method, a signal that detects success turns off the randomization. Deem suggests that this type of adaptive system, which now appears highly designed, is the product of much earlier, undetectable evolutionary processes. In engineering terms, however, such systems would be considered highly sophisticated adaptive engineering.

## GENERAL ENGINEERING ASSUMPTIONS IN SYSTEMS BIOLOGY

All of the above methods represent specific design elements that the field of systems biology has begun to tease out of the data. This progress has occurred as systems biologists start with basic engineering concepts and look for similar processes in biological systems. To do this involves several assumptions, or expectations, about the type of system one is looking at. These function as basic “laws” that make predictions about biological systems.

### Teleology

The entire paradigm of systems biology is to look at systems and figure out what they are “for.” This is the paradigm of “top-down” rather than “bottom-up” thinking—starting with a goal, and then working backwards to see what is needed and used to accomplish that goal.

The language of teleology has become explicit and common in systems biology. Even the word “teleology” is becoming more acceptable. Bud Mishra says, “teleological questions...are likely to take the centre stage as we grapple with ultimate causes in biology” [11]. Arthur Lander writes in his essay, “A Calculus of Purpose,” which is worth an extended quotation,

Why is the sky blue? Any scientist will answer this question with a statement of mechanism: Atmospheric gas scatters some wavelengths of light more than others. To answer with a statement of pur-

pose—e.g., to say the sky is blue in order to make people happy—would not cross the scientific mind. Yet in biology we often pose ‘why’ questions in which it is purpose, not mechanism, that interests us. The question ‘Why does the eye have a lens?’ most often calls for the answer that the lens is there to focus light rays, and only rarely for the answer that the lens is there because lens cells are induced by the retina from overlying ectoderm.

...As a group, molecular biologists shy away from teleological matters, perhaps because early attitudes in molecular biology were shaped by physicists and chemists. Even geneticists rigorously define function not in terms of the useful things a gene does, but by what happens when the gene is altered. Molecular biology and molecular genetics might continue to dodge teleological issues were it not for their fields’ remarkable recent successes. Mechanistic information about how a multitude of genes and gene products act and interact is now being gathered so rapidly that our inability to synthesize such information into a coherent whole is becoming more and more frustrating. Gene regulation, intracellular signaling pathways, metabolic networks, developmental programs—the current information deluge is revealing these systems to be so complex that molecular biologists are forced to wrestle with an overtly teleological question: What purpose does all this complexity serve?

...The study of such networks focuses not on the exact values of outputs, but rather on qualitative behavior, e.g., whether the network acts as a ‘switch,’ ‘filter,’ ‘oscillator,’ ‘dynamic range adjuster,’ ‘producer of stripes,’ etc. By investigating how such behaviors change for different parameter sets—an exercise referred to as “exploring the parameter space”—one starts to assemble a comprehensive picture of all the kinds of behaviors a network can produce. If one such behavior seems useful (to the organism), it becomes a candidate for explaining why the network itself was selected, i.e., it is seen as a potential purpose for the network. If experiments subsequently support assignments of actual parameter values to the range of parameter space that produces such behavior, then the potential purpose becomes a likely one.

...From these and many other examples in the literature, one can begin to discern several of the elements that, when present together, elevate investigations in computational biology to a level at which ordinary biologists take serious notice. Such elements include network topologies anchored in experimental data, fine-grained explorations of large parameter spaces, identification of “useful” network behaviors, and

hypothesis driven analyses of the mathematical or statistical bases for such behaviors. These elements can be seen as the foundations of a new calculus of purpose, enabling biologists to take on the much-neglected teleological side of molecular biology. ‘What purpose does all this complexity serve?’ may soon go from a question few biologists dare to pose, to one on everyone’s lips. [54]

Systems biology makes it an empirical fact that it is a useful paradigm for research to ask what things are “for,” and then work backwards to see how it is done.

## Optimization

That we expect living things to have a purpose is part of a broader assumption, namely that living systems are nearly optimized for their expected modes of operation. In other words, in looking at any given part or unknown operation, one assumes that it has some purpose. This presumes that just about everything in the cell does indeed have a role, i.e., that there is very little “junk.”

Some systems biologists go further than just assuming that every little thing has a purpose. Some argue that each item is fulfilling its purpose *as well as is physically possible*.

Princeton biophysicist Bill Bialek has been an evangelistic promoter of this view in public talks around the country. Using examples such as the bat hearing (which has nanosecond resolution, as good as it possibly can be, given the physical constraints of sound waves in air) or embryo segmentation signaling (which has single-molecule detection capability), he argues that nearly all biological systems are operating nearly the best they can. If there are multiple functional goals, optimization exists as the best possible compromise of tradeoffs, and if there are no competing goals, then only the physical constraints of natural law limit the optimization. He argues this is not just bare conjecture, but experimentally confirmed by numerous successful quantitative predictions; it is a “real” theory of biology:

Although sometimes submerged under concerns about particular systems, the idea that information flow is optimized provides us with a candidate for a real theory of biological networks, rather than just a collection of parameterized models. [39]

Realizing ... optimal information capacity would require that the dynamic range of TF [transcription factor] concentrations used by the cell, the input/output relation of the regulatory module, and the noise in gene expression satisfy certain matching relations, which we derive. These results provide parameter-free, quantitative predictions connecting independently measurable quantities. Although we have considered only the simplified problem of a single gene responding to a single TF, we find that these predictions are in surprisingly good agreement with recent experiments. [55]

The assumption of optimization allows for quantitative,

predictive modeling of biological systems as never before because it allows all of the systems engineering methods of constrained optimization to be used [56,57]. One can define the constraints, make a guess at the functional goal (teleology), and then run a numerical model to achieve that goal within the constraints. In mathematical terms, it allows one to set first derivatives equal to zero. When there is more than one goal, the relative cost of tradeoffs between different goals can be calculated. As J.R. Banga puts it in his article, “Optimization in computational systems biology,”

The key elements of mathematical optimization problems are the decision variables (those which can be varied during the search of the best solution), the objective function (the performance index which quantifies the quality of a solution defined by a set of decision variables, and which can be maximized or minimized), and the constraints (requirements that must be met, usually expressed as equalities and inequalities) [58].

Another way to put it is that the exceedingly complex systems of biology are assumed to be complex because that is the best way to achieve the purposes of the organism. The systems are not assumed to have many useless or dysfunctional parts.

Many, of course, such as Avise [59], have argued strongly that biological systems are not generally optimized, and that this is evidence against intelligent design. As I have argued previously [60], some degree of sub-optimality is to be expected in any engineered system; we may conclude that a system has less than optimal design either 1) because we do not know what all the design goals were (e.g., the hubcaps of a Mercedes Benz may not be as aerodynamic as we would like, but may be designed to look pretty), or 2) because systems have partially decayed over time. The question of optimality is still under debate, but the trend of systems biology is toward ever more respect for the near-optimality of living systems.

## Robustness

A corollary of good design is robustness: the ability of a system to withstand changes in its environment and operate stably. This is also an assumption of systems biology. As Lander writes,

Because real organisms face changing parameter values constantly—whether as a result of unstable environmental conditions, or mutations leading to the inactivation of a single allele of a gene—robustness is an extremely valuable feature of biological networks, so much so that some have elevated it to a sort of *sine qua non*. Indeed, the major message of the von Dassow article was that the authors had uncovered a ‘robust developmental module,’ which could ensure the formation of an appropriate pattern even across distantly related insect species whose earliest steps of embryogenesis are quite different from one another. [54]

Robustness is observed not only in the ability of a single organism to operate in a changing environment, but in the

ability of a type of organism to endure in multiple forms and different ecosystems. This is dramatically seen, for example, in certain types of insects that have very similar body plans even though they are very different sizes (by orders of magnitude). This may not seem too surprising, but is actually quite tricky to accomplish. Each egg starts as an undifferentiated globule, and becomes differentiated into segments of the insect body by a chemical signal that starts from one end of the egg and triggers certain cells to differentiate when the signal drops below a preset concentration. If the egg is bigger, and if the chemical signal stays the same, it will diffuse the same distance along the egg, which will be proportionally less of its length. This would imply that the size of the segments will not scale with the size of the egg, unless the chemical signal is altered to also scale with the size of the egg. This, of course, is what happens, although the chemical signal is produced by a different mechanism in the body of the mother, another example of apparent fine-tuning.

Closely related to the concept of robustness is the concept of “overdesign.” Some systems may be designed to continue to operate under conditions far from the expected normal operating conditions. Typically the subsystems that are overdesigned are those that are essential for the operation of the whole system. This occurs at all levels in biological systems.

### **Reverse Engineering**

All of these engineering paradigms applied to biology have the characteristics of “reverse engineering,” a major goal in systems biology, as evidenced by the frequent explicit use of this term [38,58,61-65].<sup>2</sup> Reverse engineering is the process, often done in industry, of taking a system designed by someone else and trying to figure out how it works. In the context of biology, reverse engineering of living systems has the potential payoff of leading to new designs of systems based on the designs discovered in biology. Thus systems biology is strongly coupled to the field of synthetic biology, in which new variations of biological systems are created for specific human goals.

Reverse engineering assumes not only that biological systems are as good as ones designed by humans, but may actually be better in many cases, so that we can learn new tricks for good design by studying existing biological systems.

### **The Language of Design**

All of the above can be classed under the heading of “design language,” and authors in the field are not reticent to use the word “design.” For example, Braillard writes

“I present an example of what can be called design explanation and show how it differs from classical mechanistic explanations. First, it is a non-causal kind of explanation that does not show how a function is produced by a mechanism but illustrates how a system’s function determines its structure. Second, it points to general design principles that do not depend much on evolutionary contingency... Although some aspects of systems biology fit the

mechanistic framework, explanations used by working scientists do not always correspond to the traditional definitions of mechanistic explanations provided by philosophers.... I refer to this kind of explanation as *design explanation*” [66]. [Emphasis in original]

Soyer goes beyond this, asking,

Can we employ understanding from specific cases to decipher “design principles” applicable to all biological systems? Providing an affirmative answer to this question is one of the key prospects of systems biology [67].

An older generation sometimes used the language of design, but felt it could be treated as a merely aesthetic concept without scientific impact. Francis Crick said, “Biologists must constantly keep in mind that what they see was not designed, but rather evolved” [68]. Dawkins famously said, “Biology is the study of complicated things that give the appearance of having been designed for a purpose” [69]. The above survey of recent systems biology, however, shows that the concepts of design are not merely colorful language, but deeply impactful paradigms.

## **CAN WE COUNT THE NEW PARADIGM IN SYSTEMS BIOLOGY AS A SUCCESSFUL PREDICTION OF ID?**

It goes without saying that a paradigm in which biologists think like engineers, that is, by looking for design when approaching living systems, is consistent with a belief that a creator designed the processes in living systems and instituted them, whether by miraculous intervention or by fine-tuning in the structure of physical law. “Reverse engineering” would seem to imply that there was “engineering” in the first place. Systems designed by intelligent humans are characterized by the property that their parts are there for a purpose; the more well-designed something is, the more we find that each little part has some function. It is reasonable to expect that the creator’s intelligence is like ours, and even better than ours, and so every little part of the systems should play an important role in some function.

The new systems biology movement did not grow out of the intelligent design (ID) community, however. Its major players have explicitly Darwinist commitments, in the main, and the field has remained relatively uncontroversial, from a political and social standpoint, because almost all the authors in the field attribute the good design to undirected evolution. The degree to which some authors go to remove any reference to a creating designer from the appearance of design is sometimes almost comical, as in the following quote:

Metabolic networks, which have been extensively studied for decades, are emblematic of how evolution has sculpted biologic systems for optimal function...Biochemistry textbooks describe metabolism as having evolved to be ‘highly integrated’ with the

<sup>2</sup> A literature search on the term “reverse engineering” gives dozens of references in addition to these references.

*appearance of a ‘coherent design.’* Here we explore both important ‘design’ (*with no implication of a ‘designer’*) features of metabolism and the sense in which stoichiometry itself has highly organised and optimised tolerances and tradeoffs (HOT) for functional requirements such as flexibility, efficiency, robustness and evolvability, constrained by conservation of energy, redox and small moieties” [70]. [Emphasis added.]

Biological systems are called “smart,” [38] “sophisticated,” [71] and “clever” [72] but all this cleverness is assumed to arise from random causes and natural selection.

There are two main reasons why the systems biology movement has arisen. The first one is that biology remains firmly an empirical field, and the data increasingly demand a design approach. While Darwinist presuppositions might have led many scientists to expect to see a lot more “junk” in living systems, most biologists are more committed to going where the data leads than they are to particular evolutionary models. The systems biology approach is advancing because it has led to successful, quantitative predictions, and that is enough for most biologists, even though some have expressed discomfort with its teleological language.

The second reason why the good design paradigm in systems biology has flowered is that there is a long history in biology and medicine of expecting each part of living systems to have a function. This expectation, or paradigm, goes back at least as far as William Harvey, considered the father of modern medicine, who described his discovery of the system of circulation in the body as follows:

So Provident a Cause as Nature had not so placed so many Valves without design; and no Design seemed more probable than that, since the Blood could not well, because of the interposing Valves, be sent by the Veins to the Limbs; it should be sent through the Arteries, and Return through the Veins, whose Valves did not oppose its course that way [73].

The examination of the bodies of animals has always been my delight; and I have thought that we might thence not only obtain an insight into the lighter mysteries of Nature, but there perceive a kind of image or reflex of the omnipotent Creator himself [74].

Although there have been many claims of “vestigial,” i.e. non-functioning or non-optimal organs, by and large medicine has not proceeded under the assumption that much of the body is vestigial. Medicine and biology have maintained the working hypothesis of Harvey that if there is something there, it probably has a purpose and is not junk. This assumption came originally from an explicitly theistic design paradigm. Systems biology, and biology in general, can be seen as a longstanding successful outworking of this original explicit good-design hypothesis of Harvey and other Christians like him. Biology research, especially human biology in medicine, preceded Darwin and owes a

debt to many others besides him.

One can ask, on first principles, if there had not been this long history of empirical success in looking for the purpose of unknown parts of living systems (starting with Harvey), one would expect a random-evolution theory to predict a high degree of optimization and systems integration. To find everything so extremely well-optimized and integrated seems antithetical to the expectation that evolution progresses by many blind stabs in the dark that are only weeded out over time.

As discussed in the introduction, there are mechanisms within the standard Darwinist evolutionary scenario that can increase optimality and efficiency. For example, if an organism carries around inefficient and useless stuff, it will be less fit and more likely to die, allowing more efficient organisms to gain more of a fraction of the population. However, most evolutionists over the past 150 years have tended to argue that evolution leads us to expect “bad design” of one type or another, with lots of “junk,” “vestigial” organs, or other useless stuff [75,76], and elements which seemed to be useless have been used as evidence of undirected evolution. Only recently has the term “junk DNA” begun to be disfavored, as functions for noncoding DNA have been found in more and more cases [77]. (The final nail in the coffin has probably been given by the ENCODE project [78-80], although some still argue strongly that much DNA is “junk,” based on the observation that some small organisms have very little of it [8,81].) Some have tried to argue that biologists did not really view junk DNA as “junk,” but I have attended biophysics and biology talks for 30 years, and I can attest that in the 1980s many speakers really did make the argument that the existence of junk DNA proves that living systems are messy and not optimized and therefore do not reflect the work of a creator. Avise’s recent book [59], while more sophisticated, makes essentially the same point.<sup>3</sup>

The reason for this expectation, from a Darwinist standpoint, is that although the standard model of evolution does have some pressure toward optimization, there is a “catch-22” which should prevent a high degree of optimality. If the energy cost of carrying useless or suboptimal structures is too great, then no novel structures will ever be generated. Assuming that new structures with novel function must be generated from several separate parts, each of which is not by itself beneficial to survival, a species must carry around various useless or suboptimal parts for some time, until all the parts are in place for the new, optimized function. In addition, natural selection would seem to reward the first success more than the most efficient success. Any change which decreases the efficiency of function, even if it is a step toward an ultimately more optimal solution, will be selected against.

It is beyond the scope of this paper to survey the various

<sup>3</sup> Avise lists “fallibility” (the fact that the systems can break down), “baroqueness” (unnecessary extra complexity), and waste (redundancy) as his key evidences that life cannot be designed. Clearly, no system designed by humans has any of these three properties! As pointed out by C.G. Hunter [82], those opposed to the inference of intelligent design of life frequently invoke theological assumptions about how God would act; these assumptions raise the bar significantly above the simple concept of design to a notion of near-perfect, ideal design. Apologists who embrace intelligent design generally accept that decay and “devolution” occur, that baroque life, like baroque art, may be pleasing to God, and that absolutely maximizing efficiency may not be the only design goal.

pathways to optimization and good design available to evolution; for example, there have been various proposals of how to cross the “fitness valleys” between different local fitness maxima, including “annealing” (random shake-ups of the environment) and fortuitous combination of two or more separate functions [83]. It is a historical fact, however, that evolutionary theory has tended to lead to the expectation of bad design, junk, and sub-optimality, while those following the intelligent design perspective of Harvey have tended to look for a purpose for every little element of living things.

The fact that the design paradigm in systems biology did not come directly from researchers associated publicly with the ID movement is not surprising. At present, the ID research effort is tiny: literally half a dozen or less researchers, none of whom has public funding; at present they can produce about 2-3 papers per year using private funding. The secular systems biology effort, by contrast, has thousands of well-funded researchers and labs. Yet despite the political incorrectness of the intelligent design movement, “design” has become a successful paradigm within the secular biology world, as long as “intelligent” is not added.

## CONCLUSION

For many who oppose the ID movement, saying that living systems “look designed” is a vacuous statement, amounting to saying “I don’t understand it; therefore I will leap to invoking a miracle.” The systems biology field shows, however, that saying things “look designed” is a meaningful statement with quantitative, predictive implications. Even if one is not comfortable with the metaphysics of saying that what looks designed, is designed, it is time to put to rest the objection that saying life “looks designed” is an empty statement.

It has become clear in the past ten years that the concept of design is not merely an add-on meta-description of biological systems, of no scientific consequence, but is in fact a driver of science. A whole cohort of young scientists is being trained to “think like engineers” when looking at biological systems, using terms explicitly related to engineering design concepts: design, purpose, optimal tradeoffs for multiple goals, information, control, decision making, etc. This approach is widely seen as a successful, predictive, quantitative theory of biology.

Perhaps just as striking is the fact that the new systems biologists by and large *make almost no reference to the history* of the organisms. In many cases of “bad design” we are familiar with, the history matters quite a bit. For example, the “evolution” of Windows operating systems through many versions is widely

considered bad, or at least highly suboptimal, design. To understand Windows properly, a good computer technician must understand all the “legacy” issues—such-and-such was done to allow for backwards compatibility with software running under previous versions, some sections of code were copied wholesale from previous versions and aren’t really optimized for new elements, etc. In the same way, a person encountering bad home repairs often must sort through the history—this layer of wiring was put on top of old wiring without pulling the old stuff out, etc. It stands to reason that a theory that insists on the relevance of a history of variations, namely Darwinism, would have at least as much need to understand previous stages. Yet in modern systems biology, this type of analysis is almost completely absent, except in small variations that occur at the lowest level. We thus have a program in which the concepts of good design are quite useful, and the concepts of historical previous versions are largely irrelevant to the task at hand.<sup>4</sup>

This paradigm is clearly consistent with a belief in intelligent design. The question is whether it is also consistent with a belief in Darwinian evolution, given the optimization mechanisms that are known to exist in that framework. We can say generally that the distinction between the two is not an all-or-nothing difference. The good-design paradigm (ID) allows for mechanisms that give suboptimality, and the Darwinian paradigm includes forces that lead to increase of optimality. But as discussed in the introduction, the *degree* of optimality, or good design, which we expect to occur depends quite a bit on which model we adopt. Historically, Darwinians have argued that suboptimality and “junk” are evidence for their view.

Our assessment of which paradigm better describes biological systems will depend in large part on whether we view biological systems as mostly kludgy and full of junk, with a few optimized parts, or whether we view them as highly designed and optimized, with a few sub-optimal parts. The systems biology community is rapidly trending toward the latter view, largely because it has proven useful.

Many have demanded that the intelligent design paradigm must come up with a successful, predictive, quantitative program for biology, but it seems that such a program already exists right under our noses.

<sup>4</sup> As discussed above, J.A. Shapiro and M. Deem argue that adaptations seen today, such as bacterial immunity and other adaptations to environmental stress, are the product of a non-changing system that uses controlled randomization as a solution method. Deem has argued [53] that previous structures that gave rise to this system no longer exist and therefore cannot be studied.

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