Review of "Biological Structuralism" by Stuart Pivar and colleagues

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<u>Introduction:</u> This review of *Biological Structuralism: A New Paradigm of Evolution and Development*, as well as numerous related e-mail messages and a manuscript entitled "The simulation of phyletic form by the deformation of a topological surface" by K. Y. Hall et al., is prepared in response to e-mail requests from November 2006 by Stuart Pivar. It is important to acknowledge that my fields of expertise include origin-of-life theory, mineralogy and crystallography, and a bit of history and philosophy of science. I am also studying (and still learning about) complexity theory, which treats transitions from simple to complex structure and behavior in systems of many interacting components. I am not an expert in developmental biology or cellular biology, which are more relevant to the underlying details of this study.

I have divided this review into two sections. The first section incorporates my reactions to the theory of biological structuralism as presented in the bound volume by Pivar, the manuscript by Hall et al., and some supporting e-mails from Pivar to Hazen. The second section addresses what I consider to be serious misunderstanding by Pivar about the process of science, the norms of scientific theory testing, and appropriate modes of advocacy for a new idea.

<u>Section 1. Review of "Biological Structuralism":</u> Pivar and colleagues propose a topological model of embryogenesis that is based on the properties of a toroidal surface. The principal evidence for this hypothesis consists of topological congruencies of a mechanical latex and polymer model (toroidal balloons) with observed embryological forms. The claim is made that this toroidal form arises during development from a process of self-organization.

Strengths: To me, the most intriguing and original aspects of this work are the design of the toroidal model and the closely-observed characterizations of the modes of its deformation (for example in the Hall et al. manuscript, pages 2-3 and Plate 1). I am not an expert in this area of topology and mechanics, but I'm sure there is a place for a more rigorous mathematical exploration of the relationships among such variables as length, width, viscosity, forces, and resultant segmented morphology. However, even the qualitative presentation is fascinating and seems worthy of publication.

The extension of the mechanical model to embryo morphogenesis is also intriguing and would seem to bear further study, perhaps with photographic documentation. As drawn in the many fine illustrations, there does appear to be a correspondence between the segmented model forms of Plate 1 of the article and volume to early stages of embryo development. Plate 10 is especially dramatic and has some of the gratifying aesthetic quality typified by the best 19th-century natural history illustration. It would be nice to see corresponding embryo photographs.

Finally, I am sympathetic to the references to "self-organized structures" as an underlying theme to aspects of embryo development. To me, that phrase implies that individual cells are responding to local (presumably chemical and mechanical) stimuli in their division, shape, apoptosis, etc. This idea makes a lot of sense, and it points to specific experiments that can be performed on developing embryos. After all, if an embryological form can be altered by specific chemical or mechanical stimuli, then we'll gain insight into development. In fact, I suspect that there's a significant literature on exactly this kind of experiment.

Taken together, these three aspects – the behavior of the mechanical toroid, the observations of early embryonic stages, and the concept of self-organization – might conceivably be woven together more tightly to produce a predictive model of the evolutionary sequence of embryo development.

Weaknesses: A significant and pervasive weakness of this model is the absence of new data or rigorous mathematical modeling. This hypothesis depends critically on details of the early stages of embryo development, but those details are presented only qualitatively in the form of artful drawings and pictorial analogies. There is also a lack of quantitative rigor in the description of deformational processes, and the exposition needs a much clearer and explicit explanation and experimental exploration of the role of self-organization.

In terms of the fascinating behavior of the bent toroidal balloon, I would like to see a much more quantitative approach. For example, how does changing viscosity or length-to-width ratio affect the segmentation? What is the relationship between applied force and number of segments? All of these experiments could be amplified with theoretical modeling as well.

In terms of the suggestive drawings of embryo development, these figures clearly relate the essence of the model, but there seems to be too much artistic license in essentially drawing the toroidal model in the first stages and then morphing into the embryo. I realize that's the point, so it would be more convincing to get actual photographs. There's a very contentious history of questionably-drawn embryo illustrations to advocate one position or another.

A second concern about this model of embryo development relates to what exactly is new here. It seems almost self-evident that any multicellular organism will need to be topologically toroidal. There needs to be a clearer statement of how this model leads to new insights. Specifically, what predictions arise from this model that would not follow from other models?

I also found the extension of this approach to the patterning of butterfly wings and zebra stripes unconvincing. I have observed such self-organizing patterning develop simply through local chemical signaling or diffusion-controlled reaction processes and there's a rich literature on the subject in the complexity literature. There's a huge conceptual jump required to go from primitive embryological structures to the surface expression of pigments and I see no need to bring toroids into such surface patterning.

Finally, the role of self-organization is important and, I think, widely recognized in the developmental biology community. Self-organization simply means that each element o agent of a system reacts to its local environment. Biological structuralism alludes to the idea that the mechanical stress of toroidal bending could, by itself, lead to segmentation by influencing the behavior of critical cells. That's an interesting idea but it needs a much more explicit description and some kind of experimental verification.

One additional comment has to do with the claim that this toroidal model is somehow a theory of life's origin. To me that's a misuse of the term "origin of life." The origin of life was a process of chemical evolution, perhaps involving some kind of vesicle, but equally likely a layer-like coating of self-replicating chemicals on a mineral surface. By claiming too much for the model, the issue is confuses and the case weakened. Stick to what the model does best, which is potentially to systematize the topologies of embryos.

In conclusion, I find the present exposition suggestive but weak in detail.

Section 2. On the Process of Science: Science, like any ongoing human endeavor, is a process with well-established norms of conduct and advocacy. In particular, the scientific community is organized to scrutinize and evaluate new ideas, and it does so constantly with rigor and (usually) objectivity. Nevertheless, occasionally a new theory will challenge conventional scientific thinking and may meet resistance simply because many established experts are invested in a rival theory. The microbe theory of disease, plate tectonics, and the idea of three domains of life all met with considerable resistance and took decades to be accepted. Given this history, it's instructive to examine how (and how not) to get new theories to become accepted.

In particular, my interactions with Stuart Pivar have not been conducted according to established norms of scientific advocacy. I want to make some suggestions about how most effectively to approach other experts with these ideas.

1. Do Not Resort to Hyperbole: Nothing turns off the scientific community faster than claims of "proof," especially when coupled with attacks on prevailing paradigms. Consider the following quotes from the "Preface" of *Biological Structuralism*:

> "This is a mathematical construction theorem proven by the mere comparison …"
> "Illustrations offer proof of the predictive efficiency of the model …"

In e-mails I received:

> "No one has refuted any part of it."
> This is "The first [successful model] ever to be published"

This kind of rhetoric will not convince fellow scientists of the model. Scientific hypotheses of the sort you propose cannot be absolutely "proven." Rather they must make testable predictions and be subject to falsification if the predictions fail. The great strength of Darwin's theory of evolution by natural selection is that is makes countless predictions (for example, the postulated existence of many intermediate fossil forms), which have subsequently been substantiated through careful field observations. The successes of molecular phylogeny provide further strong, unanticipated support to the idea of common descent.

No matter how valid the hypothesis of biological structuralism might be, few scientists will read this material past the over-stated and hyperbolic Preface. I should note that the tone and content of the manuscript, "The simulation of phyletic form …" is much more reasoned. That should be the "first read" for other scientists.

2. Avoid Trying to Support the New Hypothesis by Denigrating Existing Paradigms: Most scientists work within established paradigms. They do not take kindly to blanket criticisms of well-established ideas. Pivar has written:

> "Darwin's over-arching theory … has yet to produce a model." (Preface)
>
> [The new model] "renders irrelevant natural selection and genetic inheritance" (e-mail to RMH)

When evaluating a new hypothesis, it's not always necessary to ask "What is it replacing?" Casually rejecting natural selection and genetic inheritance as important factors in evolution and development will alienate most of the mainstream community, and these attacks are really unnecessary. Why does the existence of a toroidal topology invalidate Darwin or genetic inheritance? It seems to me that such well-established theories can be easily coupled and that the central ideas of biological structuralism should be integrated with the existing framework.

3. New Ideas Require Time: During the past month I have received dozens of often pushy e-mails demanding that I quickly pass judgment on "Biological Structuralism." Pivar's e-mails typically contained phrases such as "discuss this properly without further delay," "awaiting your quick response," "a month should be sufficient time" and "urgent." This is the wrong tack. Science doesn't progress through snap decisions and uninformed opinions. Be patient. Carl Woese spent 20 years with numerous papers in PNAS before his ideas of three domains of life were widely accepted. One has to build a case step by step and have patience.

4. It Doesn't Matter What I (or any other individuals) Think: Perhaps the model of biological structuralism is correct, perhaps it isn't, or perhaps it requires some integration with existing ideas in developmental biology. Nevertheless, it doesn't matter who "endorses" the model and who doesn't. Early e-mails from Pivar insisted that Prof. Sasselov has endorsed these ideas: "Dimitar and others accept this model" (Nov. 14). Dimitar is an excellent astrophysicist, but his opinion of the work carries little weight in the scientific community because he is not an expert and he has not published anything on the subject. By the same token, I am not an expert in developmental biology and my opinions are irrelevant to the ultimate reception of this work. All I can say with any authority is that the ideas have no bearing on the processes of chemical evolution and mineral surface interactions that I study.

Far more important are opinions of the leading figures in developmental biology, including Lewis Wolpert, Peter Lawrence, Thomas Jessell, Elliot Meyerowitz, and others. (But please don't insult them by saying their ideas are all wrong!)

5. Avoid Confusing Nomenclature: A recurrent difficulty with the presentation is use of non-standard nomenclature or poorly-defined terms. Consider, for example, the phrase "the primordial germ-plasm is well known to be a streaming toroidal membrane." I have shown this phrase to several prominent biologists. Even in the context of the topological model, this language is baffling to most of us. First, "germ plasm" is not a widely used term in cellular biology, and it seems to refer to an aspect of a zygote's genetic material that doesn't obviously relate to this model of embryo development. Wikipedia says: "Germplasm is a term used to describe the genetic resources, or more precisely the DNA of an organism and collections of that material. Germ plasm (or polar plasm) is a zone found in the cytoplasm of the egg cells of some model organisms (such as *Caenorhabditis elegans*, *Drosophila melanogaster*, *Xenopus laevis*), which contains determinants that will give rise to the germ cell lineage. As the zygote undergoes mitotic divisions the germ plasm is ultimately restricted to a few cells of the embryo, these germ cells then migrate to the gonads. The term germ plasm was first used by the German biologist August Weismann (b.1834-d.1914) to describe a component of germ cells that he proposed were responsible for heredity, roughly equatable to our modern understanding of DNA." I clearly am NOT an expert in this subject, but it seems that "germ plasm" is at best a seldom used or obsolete term for genetic material and only adds confusion to the discussion. Second, it is unclear to most scientists what a "streaming toroid" is. At a minimum, some explicit definitions need to be included.

If one wants the mainstream community to consider a new idea, it is important to express that idea using conventional nomenclature. I notice that Peter Lawrence in *The Making of a Fly* (Blackwell, 1992) discusses early morphological changes and cellular differentiation that occurs during gastrulation, when two "germ layers" (mesoderm and ectoderm) form. He never mentions "germ plasma", nor does he discuss "streaming" (nor does the term appear in standard introductory textbooks on cellular biology). I would suggest sticking to standard nomenclature when discussing the topology of developing embryos.