1 Bilaterian evolution re-considered: aligning theory with fact

2 James Graham^a

3 **Abstract**

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author points out that Bilaterian evolution thus involved unbroken chains of virtually perfect development in every single breeder. This precision had to entail highly-efficient developmental mitosis throughout all ~550 years of

Reasoning from the tautology that no ancestral animal died as a juvenile, the

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transformational evolution; such efficiency must be

explained—mechanistically—by theory. He proposes that his previously-published

idea that lethal juvenile cancer imposed an imperative of precision in the produc-

tion of somatic cells provides a mechanism essential to understanding those un-

12 broken chains.

Keywords

14 feedback loops; cancer selection; evo-devo; pediatric cancer; unbroken chains

Introduction

Not a single ancestor of any Bilaterian that ever existed died as a juvenile. That is

a tautological certainty: because only adults breed we know that all actual breed-

ers survived pre-adult life. One can then infer, with confidence, that every 18 breeder was the beneficiary of "perfect" development. (Convinced that reproduc-19 tion by significantly mal-developed animals was as rare in the past as it is at pres-20 ent, I place "perfect" in quotes merely to discourage unwarranted skepticism.) 21 Here is another tautological certainty: every Bilaterian breeder possessed 22 correctly-constructed organs and organ systems. No juvenile with fatally mal-23 developed vital organs ever achieved sexual maturity; every breeder possessed 24 adequate essential organs, the product of meticulous development. Those chains 25 of precise organ construction never broke, even as cumulatively enormous 26 changes in specific organs were mandated by actual evolution. The powerful 27 hearts of elephants (which may weigh more than 20 kilograms) [1] were preceded 28 by organs of smaller size and simpler structure; the earliest circulatory systems in 29 that lineage probably propelled fluids not with actual hearts but, not unlike 30 modern earthworms [2], with thick muscles that lined segments of blood vessels 31 and which, by contracting, functioned as pumps. The essential point is that all 32 modifications of all organs were expressed with utmost precision in every 33 breeding animal. 34

Perfect mitosis

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Perfect organs in perfect bodies consisted of individual somatic cells and, with the
exception of insects (see below), every cell was the product of a process seldom
mentioned by writers on animal evolution: mitosis.

I do not assert that every act of cell division in every developing breeder was perfectly executed. Nor do I ignore the likelihood that corrective mechanisms such as post-mitotic cell repair, apoptosis or autectomy of mal-formed cells played essential roles in some lineages. What I do assert is that all acts of developmental mitosis needed to produce every actual ancestral animal were of an order of precision sufficient to ensure exact construction of the entire organism, complete with functioning organs and organ systems.

To my knowledge no one else has attempted to provide a mechanistic explanation for the meticulous efficiency of the uncountable number of cell divisions required for the construction of all Bilaterian breeders over the past ~550 million years. But the fact of animal evolution informs us that those feats of precise mitosis actually occurred. In my opinion, a theory of Bilaterian evolution is not complete unless it offers a mechanistic explanation for that record of spectacular efficiency.

It is perhaps useful to ponder the enormous number of somatic cell divisions that were required to produce, during ~550 million years, in millions of lineages all the actual breeders beginning with Ur-Bilaterians and ending with extant animals. Did it exceed trillions of trillions of trillions? What matters is that although the number was unimaginatively large, it is not fantasy: those breeders existed and each was the product of precise developmental mitosis.

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There are other numbers of significance: those of the different cell types in the adult breeders. Among living Bilaterians the number ranges upward from less than 20 in nematodes to about 55 in annelids, 120 in bony fish and in humans, about 200 [3]. In the non-Bilaterian jellyfish the number is about 10 [3]. It is obvious that development is several orders of magnitude more complex if it begins with a zygote and ends with a ten-trillion-cell organism containing 200 different kinds of cells than if it ends, as in the case of smallish jellyfish, with a trillion-cell organism having ten cell types. That's because in each somatic cell that possesses a full complement of the organism's DNA (in humans, most of them) in order to produce a particular cell type any action performed by genes exclusively in the construction of any of the other 199 types must be neutralized. Nonetheless, because I am considering only actual ancestral animals we know that the gene pools managed to accomplish those feats in unbroken chains of perfectly developed animals and that they could not have done it without meticulous control over developmental mitosis.

Perfection must be explained by natural selection

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In addressing actual evolution it is unfortunate that some biologists are 75 apparently taught to consider death of juveniles from mal-developed organs as 76 examples of "negative," "purifying" or "stabilizing" selection. Experimenters 77 working with small, laboratory-controlled populations for brief periods may find it 78 helpful to classify mortality in mal-formed juveniles as something other than what 79 it certainly was—death caused by imperfect development; however, in 80 considering the entire history of Bilaterian life such gratuitous characterizations 81 obscure the obvious fact: natural selection imposed an imperative of perfect 82 development. Populations were propagated exclusively by perfectly-formed 83 adults. 84

But what explains the uncountable numbers of perfect somatic cells formed by perfect mitosis in all those ancestral Bilaterians? How was the power of natural selection imposed on mitosis?

Although conventional theory identifies no evolutionary mechanism that was exclusive to Bilaterians, it has already been proposed that lethal juvenile cancer

played an essential role in the origin and evolution of the Bilaterians and no role whatsoever in other multicells. [4] The occurrence of lethal cancer in prereproductive animals—in numbers sufficient to produce strong selection pressure—would provide a mechanistic explanation for perfect developmental mitosis. Such deaths would have initiated a feedback loop between somatic cells under construction and the controlling gene pool; the lethalization of imperfect mitosis would have produced selection pressure favoring perfect mitosis.

Evolutionarily significant characteristics of cancer

In order to appreciate lethal juvenile cancer's power to originate and enforce an imperative of perfect mitosis, evolution theorists need know only a few basic cancer facts and accept two postulates. 100

These are the facts:

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Carcinogens are mutagens [5]. 102

Cancer begins in somatic cells that divide [6].

Lethal cancer has been found only in Bilateria. [See Note]

Cancer has been observed in juveniles as distantly related as humans and Drosophila [7].

Once initiated, cancer can kill developing animals.

And these are the postulates:

All Bilaterians—and no other multicells—possessed in every somatic cell, cancer-triggering mechanisms embedded in oncogenes [4] [8].

Every Bilaterian lineage experienced, in evolutionarily significant numbers, lethal juvenile cancer. [4]

Minimization of mitosis as a cancer defense

If every act of developmental mitosis risked cancer initiation then reduction of mitosis lowered that risk. That may explain why in some animals—most notably, the insects—not equipped with immune systems capable of destroying transformed cells developmental mitosis was minimized by producing small animals with brief pre-reproductive lives. Other means of minimizing mitosis in insects noted by Gateff and Schneiderman include growth without cell division (polyploidy and polyteny), construction during metamorphosis from imaginal discs and, in adults, the nearly complete absence of mitosis [7].

Cancer defenses enabled perfect development

It is proposed that early Bilaterian populations experienced "cancer selection," the extermination of young animals (and their genotypes) that did not avoid imperfect mitosis leading to cancer. Because carcinogens are mutagens, anticancer mechanisms are also anti-mutation mechanisms; selection pressure to avoid juvenile death from cancer was also selection pressure for precise developmental mitosis.

The idea that early Bilaterian gene pools acquired masterful control over developmental mitosis is evident in their descendants' accomplishment: construction in unbroken chains of precise development, in millions of highly diverse forms and in uncountable trillions of individual breeders, the most complex, precisely-constructed things known to exist in the universe.

As previously proposed [9, 10], throughout Bilaterian evolution some changes in physiology precipitated temporary increases in the incidence of lethal juvenile cancer; the gene pools required time to achieve precision in expressing the latest modifications. Significantly, human pediatric cancers most frequently originate at sites that have experienced recent evolutionary change: the brain, leg and arm bones, the retina and—because of the need to meet threats from constantly-evolving pathogens—the immune system [10, 11, 12]. Those cancers imply that

~550 million years after its postulated origin, lethal juvenile cancer continues to exert selection pressure favoring precise developmental mitosis.

Jellyfish: a *de facto* "control" in a ~550 million year "experiment"?

In addition to functioning as Nature's masterful problem-solvers, gene pools may also serve as historians; cursory examination of the organisms they now produce may help to identify major challenges their gene pools overcame in the past or they may strongly suggest that certain problems had never been encountered.

Both present-day jellyfish and fossils from the mid-Cambrian [13] are consistent

Both present-day jellyfish and fossils from the mid-Cambrian [13] are consistent with the idea that those naked, un-pigmented, soft-bodied sunbathers—so different from the earliest Bilaterians which, according to fossils, burrowed in the sea bottom, or their crawling, heavily-armored early descendants [14]—had no compelling reason to avoid exposing somatic cells to mutagenic UV and other environmental radiation. I infer that in order to survive the early jellyfish gene pools had no need to acquire that perfect defense against cancer: hyper-efficient control over developmental mitosis. And, consistent with the proposal that cancer defenses enabled Bilaterian-level complexity [4], those putatively cancer-free gene pools devoted ~500 million years to the production of jellyfish. Nothing but jellyfish.

Suggested falsifications

Although it is not possible to subject an entire theory of evolution, or its proposed major amendment, to confirmatory testing, essential components of this proposal could be falsified [10]:

- 1. Using a mutagen, initiate lethal cancer in a plant, jellyfish, sponge or other non-Bilaterian multicell.
- 2. Initiate lethal cancer in a Bilaterian without using either a mutagen or a mitogen. (Asbestos and other non-mutagenic mitogens cause excessive cell division, permitting the subsequent occurrence of carcinogenic mutations.)
 - 3. Identify a morpho-physiological character in any Bilaterian that would protect it from cancer initiation but which would not also enhance mitotic precision during development.
 - 4. Discover a complex animal (one possessing at least 50 different somatic cell types) with no apparent defenses against mutagenic radiation or cancer.

Conclusion

Neo-Darwinism is insufficiently Darwinian. It is most unlikely that multicellular life could have progressed beyond the level of cell colonies unless natural selection

mandated that the Ur-Bilaterian gene pools acquired ultra-precise control over the construction of somatic cells. Juvenile cancer deaths triggered by imperfect mitosis seem to be the only observable phenomenon capable of imposing such an imperative.

There are two alternatives to this proposal. Either some other (unobserved and unidentified) events, unique to Bilaterians, initiated powerful feedback loops from misformed somatic cells in pre-reproductive animals to the controlling gene pool, or, as is implicit in the accepted theory, although Bilaterian gene pools produced the most complex organisms, no evolutionarily significant feedback loops from such cells to gene pools occurred; the origin and evolution of all complex animals is adequately explained by phenomena observed in plants, sponges, jellyfish and other cell colonies.

Significance

If the unbroken chains of perfect development in all Bilaterian breeders cannot be explained mechanistically by a theory of transformational evolution then that theory cannot explain the existence of a single complex animal.

Note

Before describing their initial finding in 1969 of *lethal* cancer in *Drosophila*, Gateff and Schneiderman [7] commented on earlier research: "More than a hundred papers have been published describing abnormal lesions in insects which have been called 'tumors' or 'neoplasms,' [but none of those tumors were] ... lethal to their hosts." More than forty years later, it is possible to read in contemporary literature *non-lethal* lesions described as "tumors" and "cancer" [15, 16]. Inasmuch as my published theory says *lethal* juvenile cancer occurred only in Bilaterians, the findings of *non-lethal* lesions in the referenced report do not refute that assertion.

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- ²³⁸ a Current address: Mr. James Graham, 101 Lee Avenue #142, Lexington, VA 24450,
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