

Homology is dead! Long live homology! A review of *Deep Homology?*

DEEP HOMOMOLOGY?: UNCANNY SIMILARITIES OF HUMANS AND FLIES UNCOVERED BY EVO-DEVO

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Deep Homology?: Uncanny Similarities of Humans and Flies Uncovered by Evo-Devo is Lewis Held's final act in a three-part series discussing developmental evolution. Part one of the series – *Quirks of Human Anatomy: An Evo-Devo Look at the Human Body* — journeyed through the oddities of our own human form. Part two — *How the Snake Lost its Legs* — ventured away from the idiosyncrasies of our own anatomy to examine the most fascinating morphological features of other metazoans. In *Deep homology?* Held now unites human and fly, placing them side by side to address the concept of deep homology, arguably one of the most important concepts to emerge from the field of evolutionary developmental biology (Shubin, Tabin, & Carroll, 2009). Specifically, deep homology describes situations in which homologous genes and pathways inherited from a common ancestor underlie seemingly disparate morphological features, features that lack strict homology by traditional criteria such as relative position or intermediate forms (Remane, 1952). *Deep homology?* explores this concept in detail by embarking on a quest across a variety of human and fly body regions. It begins broadly with body axes and progresses through the nervous system, vision, touch/hearing, smell/taste, limbs, and concludes (appropriately, we like to think) with the heart. The development and genetics of each organ and sense are compared between the two species as Held guides us through a review of the evidence for deep homology. This is a well written, easily accessible, and effective book that is appropriate for a wide audience ranging from undergrads to experts in the field. Held, through his trilogy of books, has perfected his eloquent and entertaining writing style, his creative figures, and his ability to generate a piece of writing that can stand as a guidebook for future “evo-devotees.”

THE VITRUVIAN MAN-FLY MODEL

Held has utilized a beautiful figure theme to visually depict his points within *Deep homology?*, which is based off Leonardo da Vinci's Vitruvian Man. Inspired by this classic piece, Held has paired “man” with a wonderfully drawn “Vitruvian fly.” The two “models” are compared and contrasted in various figures set up as amorphous Venn diagrams. Parallels between fly and man are outlined in the middle of each figure, and the so-called quirks, or unique developmental aspects flank the sides. The theme runs continuously through the text, and offers a quick, easily understood visual reference for the text and includes extensive figure descriptions. Five centuries ago da Vinci created the Vitruvian Man to convey ordered, standardizable ratios superimposable onto the human body to illustrate what he saw as the “ideal” shape. It is thus fitting that in *Deep homology?* Held has redeployed the Vitruvian Man to discuss how the genes and pathways that help instruct this “perfect” shape, and various organ systems within it, are the same even in what many consider to be a most alien, certainly unhuman, creature: the fruit fly.

FUNNY BOOK?

Science is a serious endeavor, and this seriousness pervades, and sometimes paralyzes, scientific writing. Here, *Deep homology?* surprises, with a poetic balance between academically informative and snort-ingly funny. The evidence for this refreshing disposition is sitting, subtly, even in the very title of the work – *Deep Homology* “?”. To explain: homology is a seemingly simple concept (“the *same* organ in different animals under every variety of form and function”; Owen & Cooper, 1843), however, since the advent of *evo devo* this definition has had to undergo significant revision, causing some to consider homology a concept that has lost its value to evolutionary biologists (Wake, 2003). Others have kept it alive by invoking partial homology (Abouheif, 1997), or by separating homology as it may apply differentially to character identity and character state (Wagner, 2007), or by emphasizing deep homology: the existence of tool kits and

their equivalents on the levels of genes, pathways, cell types, neural circuitry, etc., whose continuous redeployment over and over again may both facilitate and bias developmental evolution (Moczek, in press). Clearly, the debate regarding homology is far from settled, and Held adeptly acknowledges this issue with a simple question mark trailing the title; a creative catchall to criticism of an emerging concept.

THE GUIDEBOOK FOR OUR GENERATION: PUZZLE BOXES AND AN EPIC REFERENCE LIST

Along with the colorful writing and lovely figures, two additional features of *Deep Homology?* establish the text as an effective guidebook for the up and coming evo-devotees. The first is Held's use of "puzzle boxes." There are endless questions to be explored in *evo devo*, and acknowledging this Held has conveniently delineated these questions in the form of puzzle boxes, which outline prominent questions and supply the interested reader with enough references to aid in the further, independent exploration of the posited questions.

This leads directly into the second guidebook-like aspect of *Deep Homology?*: the references. Congruent with his previous works, Held unleashes the full, epic spectrum of his reference library. While amazing for background follow-up and a pocket(ish) sized catalog of nearly every high impact evo-devo paper in the previous decades, the epic in-text references can, at times, distract a bit from the flow of the read. Never the less, it is a small price to pay for such an extensive catalog of organized literature and, in summary, an overall positive feature to the book.

VITRUVIAN BEETLE, BEE, FLATWORM?


The fly and the mouse (the surrogate for humans) have always been among the most genetically tractable model systems. Thus, understandably, both are the focus of Held's book and often the key players of deep homology discussions over the past decades. However, as we move deeper into the genomics era, this focus may prove to be too narrow. Additional sequencing information (genome/RNA sequencing) from a spectrum of metazoans is arriving concurrently with technologies facilitating reverse genetics, such as RNA interference (RNAi) and CRISPR-Cas systems. Combined, this information is rapidly broadening our view of genes and, more slowly, gene functions, across the tree of life. And each wave of genomic information, for each new emerging model, has the potential to reveal additional examples of deep homology, which otherwise would have remained hidden in the fly-human microcosm.

A case-study for this effect emerges when we examine perhaps the second most well-studied insect model, *Tribolium castaneum* (the red flour beetle), belonging to an order – Coleoptera – often credited with being a "more representative" holometabolous insect than *Drosophila*. In the *Tribolium* genome, originally sequenced in 2008, we find ~700 genes that are conserved between beetle and human but, importantly, are absent in the fly (see Figure 3 in *Tribolium* Genome Sequencing Consortium, 2008). Currently, the functional role of the majority of these genes is unknown, however, examination of the *Tribolium*/human overlapping gene list reveals a variety of genes with the potential to instruct diverse and possibly disease-related roles. We will need to wait for more detailed functional analyses (such as genome-wide RNAi screens; Schmitt-Engel et al., 2015), but it is not difficult to imagine how this handful of genes, enigmatic during the previous decades of fly-dominated research, could expand our view of the deep homologies that exist among bilaterians. This rabbit hole may grow even deeper when we consider that each emerging model will likely produce the same effect. For example, both *Drosophila* and *Tribolium* lack a complete methylation machinery, initially raising the possibility that this may be true for all insects, until work in the aphids, social hymenoptera (reviewed in Glastad, Hunt, Yi, & Goodisman, 2011) and in fact other beetles (e.g. Snell-Rood, Troth, & Moczek, 2013) demonstrated the opposite: a complete methylation machinery exists in diverse insects just like it does broadly across all three domains of life, and in at least some insects it plays critical roles in postembryonic development (Kucharski, Maleszka, Foret, & Maleszka, 2008). Such discoveries are bound to continue, thus, perhaps in the coming years, Held can draw us a Vitruvian beetle, or a Vitruvian flatworm?

CONCLUSION

Held is an honest, excited, and entertaining writer. His ode to the odd similarities between humans and flies, *Deep Homology?* ruminates on a topic that is still so new it can not hope to provide final answers. Held says it best, "for those of us who happen to like Swiss cheese with our ham, we can still savor the taste in spite of the holes". Never the less, Held has delivered an essay that can be a valuable tool for future evo-devotees seeking to probe the deepest dark depths of deep homology. His work has cataloged and organized the key works of the field and the brains that were behind them. It has outlined the questions that still perplex us – and some of the directions we must go to refine our answers. His Vitruvian-based figures are lovely, and creative. And along with all this, Held writes with a humor and epigrammatic wit that turns pages with ease.

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REFERENCES

- Abouheif, E. 1997. Developmental genetics and homology: A hierarchical approach. *Trends in Ecology & Evolution*, 12(10), 405–408.
- Glastad, K. M., Hunt, B. G., Yi, S. V., & Goodisman, M. A. D. 2011. DNA methylation in insects: On the brink of the epigenomic era. *Insect Molecular Biology*, 20(5), 553–565, <https://doi.org/10.1111/j.1365-2583.2011.01092.x>
- Kucharski, R., Maleszka, J., Foret, S., & Maleszka, R. 2008. Nutritional control of reproductive status in honeybees via DNA methylation. *Science (New York, N.Y.)*, 319(5871), 1827–1830, <https://doi.org/10.1126/science.1153069>
- Moczek, A. P. (in press). The shape of things to come: Evo devo perspectives on causes and consequences in evolution. In L. K & U. T (Eds.), *Vienna series in Theoretical Biology: cause and process in evolution*. Cambridge, MA, MIT Press.
- Owen, R., & Cooper, W. (1843). Lectures on the comparative anatomy and physiology of the invertebrate animals: delivered at the Royal College of Surgeons, in 1843. London: Longman, Brown, Green, and Longmans. Retrieved from <http://www.biodiversitylibrary.org/item/29826>
- Remane, A. (1952). Die Grundlagen des natürlichen Systems der vergleichenden Anatomie und der Phylogenetik. Leipzig: Geest und Portig.
- Schmitt-Engel, C., Schultheis, D., Schwirz, J., Ströhlein, N., Troelenberg, N., Majumdar, U., & Bucher, G. 2015. The iBeetle large-scale RNAi screen reveals gene functions for insect development and physiology. *Nature Communications* 6, 7822, <https://doi.org/10.1038/ncomms8822>
- Shubin, N., Tabin, C., & Carroll, S. 2009. Deep homology and the origins of evolutionary novelty. *Nature*, 457(7231), 818–823, <https://doi.org/10.1038/nature07891>
- Snell-Rood, E. C., Troth, A., & Moczek, A. P. 2013. DNA methylation as a mechanism of nutritional plasticity: Limited support from horned beetles. *Journal of Experimental Zoology Part B, Molecular and Developmental Evolution*, 320(1), 22–34, <https://doi.org/10.1002/jez.b.22479>
- Tribolium* Genome Sequencing Consortium 2008. The genome of the model beetle and pest *Tribolium castaneum*. *Nature*, 452, 949–955, <https://doi.org/10.1038/nature06784>
- Wagner, G. P. 2007. The developmental genetics of homology. *Nature Reviews Genetics*, 8(6), 473–479, <https://doi.org/10.1038/nrg2099>
- Wake, D. (2003) Keywords and concepts in evolutionary and developmental biology. *Homology and homoplasy*. Cambridge, MA: Harvard University Press, pp. 191–200).