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Article *in* Journal of Experimental Zoology Part B Molecular and Developmental Evolution · February 2018

DOI: 10.1002/jez.b.22791

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Received: 11 September 2017 | Revised: 6 December 2017 | Accepted: 9 January 2018

DOI: 10.1002/jez.b.22791

COMMENTARY AND PERSPECTIVE

WILEY JEZ-B MOLECULAR AND DEVELOPMENTAL EVOLUTION

Where is, in 2017, the evo in evo-devo (evolutionary developmental biology)?

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Abstract

After the inaugural Pan-American-Evo-Devo meeting (2015, Berkeley), I showed how major concerns about evo-devo (Evolutionary Developmental Biology) research were demonstrated by a simple, non-biased quantitative analysis of the titles/abstracts of that meeting's talks. Here, I apply the same methodology to the titles/abstracts of the recent Pan-American-Evo-Devo meeting (2017, Calgary). The aim is to evaluate if the concerns raised by me in that paper and by other authors have been addressed and/or if there are other types of differences between the two meetings that may reflect trends within the field of evo-devo. This analysis shows that the proportion of presentations referring to "morphology", "organism", "selection", "adaptive", "phylogeny", and their derivatives was higher in the 2017 meeting, which therefore had a more "organismal" feel. However, there was a decrease in the use of "evolution"/its derivatives and of macroevolutionary terms related to the *tempo* and *mode* of evolution in the 2017 meeting. Moreover, the disproportionately high use of genetic/genomic terms clearly shows that evo-devo continues to be mainly focused on devo, and particularly on "Geno", that is, on molecular/genetic studies. Furthermore, the vast majority of animal evo-devo studies are focused only on hard tissues, which are just a small fraction of the whole organism—for example, only 15% of the tissue mass of the human body. The lack of an integrative approach is also evidenced by the lack of studies addressing conceptual/long-standing broader questions, including the links between ecology and particularly behavior and developmental/evolutionary variability and between evo-devo and evolutionary medicine.

KEYWORDS

developmental biology, evolutionary biology, genetics, genomics, genotype, molecular biology, organismal biology, phenotype

When? The main catalyst for the 2016 paper I wrote addressing the question "Where is the Evo in Evo-Devo?" was the inaugural meeting of the Pan-American Society for evo-devo, which took place at Berkeley in August 2015 (Diogo, 2016). The current paper is a follow-up of that paper, catalyzed by the second meeting of this Society that took place at Calgary in August 2017. As happened with the first meeting, I should already make it clear that this second meeting was very interesting and was also crucial to reinforce friendships and academic relationships and form new ones. Therefore, I am extremely thankful to its organizers, who did an extraordinary job.

Why? Hence, why write this paper? The major reason is obviously to contrast the observations and quantitative data compiled from the 2015 meeting to those I provide here about the second (2017) meeting. This allow us to check if at least some major criticisms that other authors and myself did about the status of evo-devo in the past years, which were clearly reflected in the 2015 meeting, still apply or not to the current works being done by evodevoists (for a detailed list of those criticisms, see Diogo, 2016, and below). The simple, unbiased quantitative analysis of the terms used in the abstracts of the 2015 meeting provided evidence for unevenness between the weight of devo—and more specifically of Geno (genetics/genomics)—versus that of evo, in evo-devo (Diogo, 2016). As it was stressed in that paper, I was not the first to raise the concern that evo-devo was becoming to be, in a way, basically devo with just some side-notes about evo (e.g., Minelli, 2003; Stern, 2003; Klingenberg, 2004; Groover & Cronk, 2007; Hoekstra & Coyne, 2007; Moczek, 2012; Murren, 2012; Winther, 2015). The problem is that the points raised by those researchers often quickly became centered on evolutionary versus developmental biologists and on their personal opinions and backgrounds, thus loosing their focus on objective, major problems. That is why I decided to undertake instead such a simple unbiased quantitative analysis of the words used in the titles and abstracts of the 2015 Berkeley meeting, in order to not fall in the trap of talking about just my own "impressions"—a methodology that I am thus applying in the present paper as well.

***How*?** Within the major reasons for writing the present paper (see above), a point that was crucial concerns the way *how* the general criticism of evo-devo made in my 2016 paper was received. This is because both the number and the status of the researchers that sympathized/agreed with that criticism far exceeded my own expectations. This agreement was stated in many different forms, from personal emails or conversations to scientific papers or meeting summaries, and from people that are consensually considered to be among the top scientists with a deep knowledge of both developmental and evolutionary biology. Just some illustrative examples of researchers that agreed with the general idea that evo-devo is currently to focus on devo are: Gerd Muller, Gunter Wagner, Frietson Galis, Raul Diaz, Alexander Vargas, and Brian Hall. I am mentioning these researchers among many others I could mention here because various of them were/are leaders of evo-devo societies and/or of journals that are mainly focused on evo-devo *per se*. This further illustrates the point, made in my 2016 paper, that in a way the factors driving the decrease of importance of evo within evo-devo resemble those driving a "monster without a head". That is, they are not driven by well-defined theoretical and conceptual ideas and broader questions, but rather by a combination of a number of other factors such as the current system of education and status of grant funding, and the atomistic view of science that is still prevalent in biological sciences.

I have further discussed each of these points, particularly the latter one about the prevalence of such an atomistic view in a book "*Evolution driven by organismal behavior: a unifying view of life, function, form, mismatches and trends*" that also includes a general criticism about the almost complete exclusion of behavioral studies from current evo-devo research. A similar criticism about the way behavior is often neglected in both developmental and evolutionary studies was recently made in a series of papers of the special issue "*New trends in evolutionary biology - biological, philosophical and social science perspectives*" (e.g., Whiten, 2017). That special issue is focused on the extended evolutionary synthesis, and is therefore crucial for broader conceptual discussions within the field of evo-devo. Many authors of the papers published in that special issue did stress the lack of a more integrative, comprehensive organismal view within biological sciences in general and within evolutionary and developmental studies in particular, as well as within evolutionary medicine. For instance, within that special issue, Noble (2017: 7) noted that evolutionary medicine, and medicine in general, are examples of other fields "of science where focusing on the molecular level has blinded us to functional processes of higher levels". As noted by him, an editorial in *Nature* in 2010 stated: "but for all the intellectural ferment of the past decade, has human health truly benefited from the sequencing of the human genome? (as) a startlingly honest response .. the leaders of the public and private efforts, Francis Collins and Craig Venter, both say 'not much'". As further noted by Noble, "the problem does not therefore lie in the absence of knowledge about the sequences; the problem is that we neglected to do the relevant physiology at the higher levels". According to him, "the consequence of diverting large-scale funding towards the search for new drugs via genomics has been that .. the pharmaceutical industry is producing fewer new medications at vastly greater cost".

This point thus further allows us to understand part of a problem that is likely also affecting evo-devo, the funding and its sources, and leading it to be driven like "a monster without a head" as noted above, and as medicine in general also seems to be. That is, the problem is that more funding is being given to devo, and particularly to geno, studies without a true comprehensive intellectual and conceptual effort to make sure that such funding actually makes sense and can really produce the best answers to the major evolutionary and developmental questions that remain to be satisfactorily addressed. I strongly recommend the readers to read in much detail that whole special issue of Interface Focus, because the extended evolutionary synthesis received major contributions from evo-devo (e.g., about the importance of constraints in evolution) but also takes into account many other crucial aspects that are paradoxically often neglected by evo-devoists (e.g., the importance of behavior and of niche construction, and a more organismal and integrative pespective).

I will refer here to just two illustrative examples of agreement with the main ideas expressed in the paper about the 2015 Pan-Evo-Devo meeeting (Diogo, 2016), which that were presented in papers or scientific meetings by other authors. One is a paper entitled "*Morphomechanics and Developmental Constraints in the Evolution of Ammonites Shell Form*" (Erlich, Moulton, Goriely, & Chirat, 2016). The authors cited the quantitative data compiled in my 2016 paper to state that "evo-devo is now often perceived as synonymous with comparative developmental genetics" (Erlich et al., 2016: 438). They subsequently noted that "the exploration of the relationships between the processes of individual development and phenotypic changes during evolution actually" should involve instead "a more diversified set of conceptual and methodological approaches, including theoretical modeling of developmental processes and the study of generic physical and self-organizing properties of developmental systems". They correctly noted that crucial evo-devo pioneers such as Pere Alberch drew their "inspiration, in part, from the complex behavior of dynamical systems and was also interested in the mechanics of morphogenesis", which they "saw as key in addressing the central issue of the genotype–phenotype relationships and in uncovering the rules that channel morphological evolution".

The other illustrative example concerns a summary of the "*37th New Phytologist Symposium - Plant Developmental Evolution*" that took place in May 2016 in Beijing, China. The summary was done by Liau et al. (2016), who stated in their page 827 that the symposium was "a forum for leading scientists from around the world to share current work and knowledge in the field and to discuss the main questions and motivations that drive the field of plant evodevo". Specifically, they wrote: "as with the recent Pan-American meeting, many presentations at this symposium were biased toward comparative developmental genetics in a macro-evolutionary context (Diogo, 2016); one of the challenges of evodevo is to address questions of how developmental genetic processes evolve in a micro-evolutionary context". They referred in particular to one of the main criticisms done by other colleagues and myself about evo-devo in general: the lack of studies on variability. They stated: "few studies have attempted to ascertain whether and how variation in developmental processes may produce fitness variation, which then could lead to selection and adaptation;

this approach provides the missing link to understanding how developmental processes have evolved over different timescales". One of the major aims of the present paper is therefore to analyze whether the criticisms of evo-devo done by other researchers and by me in the past years also apply to the 2017 Pan-Evo-Devo meeting of Calgary, or whether they might have contributed to change, at least in some way, the field towards a more organismal, evolutionary, holistic and/or conceptual approach.

What? So what is the evidence obtained from the simple, objective, neutral quantitative analysis of the number of times that certain key devo and evo terms were used in the titles *and* abstracts of *all* the 59 talks (see Table 1) and 117 posters of the 2017 Calgary meeting for which abstracts were made available in the meeting booklet? Again, and as explained in more detail in the 2016 paper, the main reason for using this simple methodology is that it cannot be said that there was "cherry picking" of only certain abstracts to support *a priori* assumptions or confirm a particular position.

In the 2016 paper on the 2015 meeting, I reported that terms with, or derived from, "gene" (i.e., gene/tic, geno-type/me/mic) were present 204 times in the talk abstracts of that meeting, while "phenotype/phenotypic" were only present 33 times, that is, about one out of seven (16%) times as often as the "gene" terms. Within the 2017 talk abstracts there are 228 "gene" terms versus 45 times in which the terms "phenotype/phenotypic" are mentioned. That is, these latter terms are mentioned 20% of the times that the "gene" terms are, a very slight increase in comparison with 2015. What about the numbers concerning the 2017 poster abstracts? There are 357 "gene" terms versus 77 "phenotype/phenotypic" terms, that is, the latter are mentioned about 21% as often as the "gene" terms, indicating that in this sense there was no apparent bias towards choosing presentations more focused on genes than on phenotypes for the talks versus posters.

As I noted in the 2016 paper, some could argue that the marked difference between the use of "gene" versus "phenotype" terms in the abstracts could be because researchers might be using terms such as morphology, or anatomy, or other similar terms instead. However, that was not the case in the 2015 meeting, as the term "morphology" and all its derivatives were used only 37 times, "anatomy/anatomical" only two times, and "Bauplan/Bauplans" 0 times. What about the 2017 meeting? Within the poster abstracts and talk abstracts the numbers are respectively: "morphology"/its derivatives 62 and 51 times, that is, 17% and 22% the number of times "genes"/its derivatives were mentioned; "anatomy/anatomical" eight and one times, and "Bauplan/Bauplans" one and four times. In the overall, there was therefore a slight increase in the proportion in which the terms "morphology"/its derivatives were cited in the 2017 meeting, as the overall rate was only 18% in the 2015 meeting. Moreover in the 2017 meeting the committee chose—consciently or not—presentations that focused more on morphology for the meetings talks, as these terms were cited almost one out of four times less in the poster abstracts than in the talk abstracts. The same applied to "Bauplan"/its derivatives, and in a way also to "anatomy"/its derivatives in the sense that these terms were more cited in the 2017 abstracts. That is, in overall the proportion of presentations referring to morphology and/or anatomy was higher than in 2015, what is encouraging, although the disproportion between the focus given to genes/genomes *vs.* the phenotype continues to be striking.

However, as explained in the 2016 paper, one could also argue that the focus should not be on the phenotype, or specifically on morphology/anatomy, because there is much more to organismal evolution than the study of form. In the case of the 2015 meeting, this assumption unfortunately did not apply: "evolution"/its derivatives were used only 137 times, that is, only 67% of the times that "gene"/derivatives were used, demonstrating the shrinking of evo, and even of non-molecular (e.g., organismal; embryology) devo within the field at that moment. In the 2017 poster and talk abstracts the numbers were respectively 190 and 132, that is, 53% and 57% the times that "gene" terms were cited. That is, in the overall there was actually a clear decrease in the use of "evolution"/its derivatives in the 2017 meeting.

Another way of discussing this subject is to count the number of times the terms "organism/organismal", "selection/selective", "adaptive/adaptation/adapted", and "phylogenetic/phylogeny/phylogenetically", which are at the core of evolutionary biology, were used. In the 2015 meeting they were only used 13, 14, 13, and 7 times, respectively. Those numbers were particularly remarkable because molecular/developmental terms such as "patterning" and its derivatives (in the context of, e.g., gene expression) were used 67 times, "expression" in this context was used 82 times, "enhancer/enhancers" 22 times, "signaling" 28 times, and "transcript" and its derivatives 31 times. So what about the 2017 meeting? In the poster versus talk abstracts, the terms "organism/organismal", "selection/selective", "adaptive/adaptation/adapted", and "phylogenetic/phylogeny/phylogenetically" were used respectively 25 versus 27 times, 18 versus 16 times, 29 versus 29 times, and 23 versus 10 times. These numbers clearly show an increase of the use of evo-related terms in the abstracts of the 2017 meeting in general, as well as a higher proportion of the use of such terms in the talk abstracts *vs.* poster abstracts. This is because in the 2017 meeting booklet there were 117 abstracts for posters and 59 abstracts for talks, as noted above; so in terms of percentages of use of these terms per each poster versus talk abstract the numbers are 21% versus 46%, 15% versus 27%, 25% versus 49%, and 20% versus 17%. That is, apart from "phylogenetic/phylogeny/phylogenetically", which use was proportionally slightly higher in the posters, all the other terms were cited almost twice, or even more than twice, as much in the talk abstracts than in the poster abstracts.

These numbers therefore result from a choice for talks versus posters by the meeting committee that does not seem to have been completely unconscious. This choice might thus have been related to recent criticisms to the lack of evo in evo-devo, including about the 2015 meeting (see Diogo, 2016, and above) and/or to the fact that the president of Pan-Evo-Devo in 2017, as well as for example the main local organizers of the 2017 meeting, came from the "Evo"/organismal side of evo-devo (Karen Sears and Campbell Rolian/Heather Jamniczky, respectively). In fact, these numbers can explain the fact that although "evolution"/its derivatives were actually proportionally less cited than in the 2015 meeting, many colleagues with whom I talked during the 2017 meeting stated that this meeting had a more "Evo"/organismal feel. This aspect thus clearly needs to be applauded,

TABLE 1 List of talks of the calgary 2007 Pan-American Evo-Devo meeting, following the order given in the talks abstract document provided in the meeting (by alphabetic order of their presenting authors)

- Obligate endosymbiosis in ants reveals evolutionary developmental steps to conflict resolution and integration
- The genetic basis of jaw shape and plasticity in cichlid fishes
- Evolution of the hypoxia-sensitive cells involved in amniote respiratory reflexes
- Cell differentiation and pattern formation in the transition to aggregative multicellularity
- Adjusting the valves: plant stomatal development in space and time
- Sharks did it first: where our muscle development comes from
- Coloniality in marine chordates: eco-evo-devo approaches to understand different levels of biological organization
- Functional and molecular evolutionary analysis of polyphenism-specific transcription in the nematode model *Pristionchus pacificus*
- The Thrill of Discovery: Pioneer Stories
- Regulation of nutrition-responsive growth and scaling in the horned beetle *Onthophagus taurus*
- What does ontogenetic integration tell us about how integration patterns arise in *Schizanthus*?
- Evo-Devo of feathers
- Dissecting the genetic basis of morphology and evolution in *Nasonia*
- Developing an ancient epithelial appendage: FGF signalling regulates shark denticle formation
- The Hox code and the identity of the teleostean fish caudal fin
- The ABC model of flower development in non-core eudicots: a functional synthesis in a ranunculid
- The evolution of insect eggs and cellular development across eight orders of magnitude
- Are sex differences in size and shape the same? Insights with the *Drosophila* wing
- Genome of the Tasmanian Tiger Provides Insights into the Genetic Basis of Convergent Evolution
- Using Machine Learning to reconstruct evolution of segmentation
- Limb development and regeneration in fossil amphibians and extant salamanders
- Developmental Nonlinearity Drives Phenotypic Robustness
- Evolution of enteric neural crest cells in the vertebrates
- Non-genomic actions of thyroid hormones as a potential regulator of larval skeletogenesis in sea urchins
- The genetic basis of mimetic color diversity in bumble bees
- A genome-wide assessment of the ancestral neural crest gene regulatory network
- Evo-Devo: Crossing genomes and phenomes
- Embryonic patterning of airway cartilage and the avian vocal organ
- Why snakes are so unique? Some insights from developmental pathways
- Use of experimental atavisms to estimate soft tissue reconstructions of the earliest tetrapod limbs
- Sex Change in Slipper Limpets
- Why don't elephants get cancer? Developmental constraints and evolutionary tradeoffs in the resolution of Peto's paradox
- The Wnt beneath my wings: exploring butterfly pattern formation in the CRISPR era
- The development and evolution of morphological scaling relationships
- Exploring Ecological Sexual Dimorphism through Morphometrics, Genetics and Biomechanics
- Sweet genes are made of STYLISH – Members of the STYLISH gene family control both style and nectary development in *Aquilegia* (Ranunculaceae)
- Evolutionary origins of the endoskeletal joint in vertebrates
- The gradual molecular and developmental evolution of butterfly wing eyespots
- Digits and fin rays share common developmental histories
- Evaluating the molecular basis for diet-induced phenotypic plasticity in teleosts
- Interspecies gene transfer reveals a distribution of size effects underlying the morphological divergence between species
- Genetic complexity and the evolution of quantitative traits
- Genomic Red Queen and the evolution of limb genetic architecture
- Genetic and environmental decanalization are not correlated among altitudinal varying populations of *Drosophila melanogaster*
- Identifying cis-regulatory enhancers associated with cichlid craniofacial evolution
- Cell-Cycle-Coupled Oscillations in Apical Polarity and Intercellular Contact Maintain Order in Embryonic Epithelia
- Reproductive constraint: a developmental mechanism regulating social cohesion in ant societies
- Deciphering genomic and developmental mechanisms that underlie vision adaptations in noctilionoid bats
- How can complex gene networks build complex bodies in development and evolution
- Homology of process: petals and petaloidy in the tropical gingers (Zingiberales)
- On the wings of love: pigment patterning and the checkered past of rock pigeons
- Genetic mechanisms and macroevolution of flower color in the tomato family
- Metabolic evolution in cave fish
- Patterns of transcriptional parallelism and variation in the developing olfactory system of Drosophila species
- The Evolutionary Biology of Cell Types: the next frontier of Devo-Evo

Continues

TABLE 1 Continued

- Ontogenetic tooth reduction in theropod dinosaurs and the macroevolution of avian beaks
- Endless Networks Most Beautiful: connecting diversity to alterations in a gene regulatory network
- Origin and evolution of the WUSCHEL-RELATED (WOX) homeobox transcription factors in plants
- Somite Compartmentalization in Amphioxus: on the Evolutionary Origin of Vertebrate Skeletons
- The genetic basis of evolutionary transitions in early development using a polychaete model

and hopefully one will continue to see this trend in the talks of the upcoming 2019 meeting and of other evo-devo meetings organized by other societies. In fact, from the beginning the 2017 meeting started with a more "Evo", organismal, integrative feel. For instance, one of the inaugural talks was given by the same person that gave one of the 2015 inaugural talks, but it had a completely different feel and scope. While Sean Carroll's 2015 talk was entitled "*Gene co-option and the evolution of novelties*", his 2017 talk was entitled "*The Thrill of Discovery: Pioneer Stories*" and was based on literature review that he did for his book "*The Serengeti Rules*", which mainly focus on evolution and ecology.

Going now back to the way evo-devo was described in the two main reference papers chosen for Diogo's (2016) paper—that is, Organ et al.'s (2015) and Mozcek et al.'s (2015) papers—let us now focus on their emphasis that evo-devo should ideally also help to uncover macroevolutionary processes and patterns. According to those two papers, this should therefore apply to both modern and extinct species, for instance discussing terms such as heterochrony, constraint, extinctions, or mosaic evolution. As noted in my 2016 paper, such statements on evo-devo and macroevolution did not match at all what was seen in the 2015 meeting. For instance, the term "macroevolution" and all its derivatives were only mentioned three times in the abstracts of that meeting, "pattern" and its derivatives were used only 11 times in an evolutionary sense, "allometry/allometries" only four times, "homology" only nine times, and "polarity", "direction", and "mosaic" and all their derivatives were not used at all in a macroevolutionary context in the abstracts of that meeting. As a reminder, in those abstracts the term "gene" and its derivatives were used 204 times, "expression" 82 times, "enhancer/enhancers" 22 times, "signaling" 28 times, and "transcript" (and its derivatives) 31 times, clearly reflecting the gene/molecular-centric aspect of evo-devo displayed at that meeting.

So, what happened in the talk versus poster abstracts of the 2017 meeting? The numbers are: the term "macroevolution" and all its derivatives were only mentioned nine versus three times, "pattern" and its derivatives were used 39 versus 47 times in an evolutionary sense, "allometry/allometries" three versus three times, "homology" five versus four times, and "polarity", and "direction", and "mosaic" and all their derivatives were used in a macroevolutionary context 0 versus 0, 2 versus 1, and 1 versus 0 times. These numbers—except the decrease of the use of "homology"—indicate again that the "Evo" side of evo-devo was more prominent in general in the 2017 meeting than it had been in the 2015 meeting, and particularly in the 2017 talks, because the total numbers of poster abstracts was about twice the number of talk abstracts as noted above. This indicates once more that more "Evo" abstracts tended to be more often chosen to be delivered as talks than as posters. However, this does not mean that there is no more unbalance between evo and devo, as this unevenness is evident when one compares these numbers with the use of devo terms in the 2017 talk and poster abstracts. "Expression", "enhancer/enhancers", "signaling", and "transcript" (and its derivatives) were respectively used in a strictly devo context 39 and 128 times, 15 and 5 times, 12 and 25 times, and 29 and 52 times, respectively. The fact that, for instance, just in the poster abstracts the term (gene) "expression" was mentioned more times than were all the evolutionary terms related to "pattern", "allometry/allometries", "homology", "polarity", "direction", "mosaic", and all their derivatives in both the talk and poster abstracts is a clear, disturbing, reminder of the current power of devo within evo-devo.

In my 2016 comment to the 2015 meeting, I noted that one of the most striking facts observed in that meeting was the lack of studies and discussions on the *tempo* of evolution. As an example, in the abstracts of that meeting the terms "fossil/fossilized/fossils" were only used nine times, "extinct" three times, temporal terms such as "years" (e.g., in millions of years) only four times, "punctuated" one time, and "gradual/gradualism", "cladogenesis", and "anagenesis" were not used at all. Let us now compare these numbers with those for talk versus poster abstracts in the 2017 meeting: "fossil/fossilized/fossils" were used seven versus six times, "extinct" one versus one times, "years" three versus two times, "punctuated" 0 versus 0 times, "gradual/gradualism" two versus 0 times, "cladogenesis" 0 versus 0 times, and "anagenesis" 0 versus 0 times. These numbers are not encouraging at all.

Let's now thus analyze, as done in the 2016 paper, if these data might mean that evo may still be strongly represented in evo-devo, but be more focused on microevolution than on macroevolution. As noted in that paper, this was clearly not the case in the 2015 meeting, as reflected by the numbers compiled from the titles and abstracts of the 56 talks at the 2015 meeting: "selection/selective/selected" and "adaptive/adaptation/adapted" were only used 14 and 13 times, respectively, "speciation" three times, "fitness" four times, and "allopatry", "sympatry", and even "geographic" (e.g., in geographic isolation) and all their derivatives were not used at all. As explained above, in the talk versus poster abstracts of the 2017 meeting the terms "selection/selective" and "adaptive/adaptation/adapted" were used respectively 27 versus 25 times, and 16 versus 18 times. What about the more specific microevolutionary terms "speciation", "fitness", "allopatry", "sympatry", and "geographic"? Remarkably, none of these terms was referred a single time in the 87 pages containing all the talk and poster abstracts of the 2017 meeting, with the exception of the related term "sympatrically", which was used only once in the poster abstracts. So, while there seems to be a slight increase in the proportional use of some evo terms in the 2017 meeting abstracts, namely in the talk ones, including some referring to, for example, the direction or patterns of macroevolution, the reality is that there was even a decrease of the

use of terms regarding the tempo of evolution as well as concerning microevolution.

As noted in my 2016 review, it is unfortunately not so surprising to find that evo-devo is not paying as much attention as it should to, for instance, geographic and environmental factors in general, as authors often stress that this is one aspect where evo-devo urgently needs to improve (Abouheif et al., 2014). For instance, some researchers have been stressing the scarce use of ecological data in evo-devo and the need of laboratory experiments to include variable conditions and not minimize "noise"—for example, variation—in order to more accurately replicate the true natural conditions in which organisms live (Ledon-Rettig and Pfennig, 2011). What these new numbers from the 2017 meeting show is that despite the desperate calls of these authors, there has been no real improvement since the 2015 meeting, well on the contrary. As noted above, in the 2017′s book "*Evolution Driven By Organismal Behavior*" I provide an extensive, updated criticism about the lack of not only ecological and behavioral studies but also of works on phenotypic plasticity and variation within the field of evo-devo. Interestingly, another book, published just one month before that book, discusses very similar ideas and also criticizes current evo-devo for its lack of focus on behavior and on the key, active evolutionary role of organisms themselves (Bateson, 2017).

The last numbers I will refer to, in this Section, relate to the question on whether current evo-devo is or not interested in addressing major conceptual evolutionary questions/theories from a more developmental—but still organismal—perspective. This is because, as noted in Diogo (2016), one of the main forces leading to the development of evo-devo was the integration—by, for example, Gould (1977, 2002) and Alberch (see Rasskin and De Renzi, 2009)—between evolutionary patterns observed in studies of adults with developmental processes such as heterochrony. Notably, in that review I showed that even "heterochrony", a key term that refers exclusively to changes of *developmental* timing, was used just two times within all the abstracts of the 2015 meeting. Moreover, a related term such as "acceleration" (both in a evo and even in a devo context) was used only one time, while "peramorphosis", "deceleration", "paedomorphism", "vestigial", "atavism", "phylotypic" (stage), "hourglass" (in a devo context), and "neoteny" were not used at all in those abstracts. What about the 2017 meeting? For the talk *vs.* poster abstracts, "heterochrony" was cited 0 versus two times, "vestigial" two versus three times, "atavism" three versus 0 times, while "acceleration", "peramorphosis", "deceleration", "paedomorphism", "phylotypic", "hourglass", and "neoteny" were not mentioned at all. What does this mean? That the problem reflected in the 2015 meeting continues to be even deeper than the evo shrinking in evo-devo: the devo itself remains in reality mainly "Geno", focusing essentially on genetics/genomics/molecular biology and neglecting embryology and organismal devo per se.

Who? In the 2016 paper, I addressed the question: who's to blame for the imbalance between the huge weight given to devo—and in particular to geno (genetics/genomics)—in evo-evo? My answer was, simply: nobody specifically, and surely not the organizers of the 2015 meeting at Berkeley. As noted above, the organizers of the 2017 meeting probably did an even more active effort to choose, particularly for the talks, abstracts that in general had a more "Evo", or organismal feel, in general. They also continued the tradition from the 2015 meeting of trying to provide a fair balance between the different backgrounds of taxa studied, including a wide variety of both animal and plant taxa covered in this 2017 meeting. This is also reflected by the excellent idea of having, every night, two panel discussions—open to everybody—that clearly had the aim of making researchers with very different backgrounds and personalities feel at home within evo-devo. There were panels about "People of color in science", about "Women in science", about "LGBTQ in Science", about "EvoDevo Education" and about "EvoDevo in Latin America".

Therefore, we come back again to the "monster without a head". Surely the intellectual leaders within the field of evo-devo, or the leaders of the evo-devo societies that organize such meetings or of the journals that are mainly focused on evo-devo are not to blame, because many of them actually subscribed to at least some of the main criticisms raised in my 2016 paper, as explained above. The "monster without a head" seems, unfortunately—and thus more worryingly—to be driven by other factors such as the current system of education and of funding in most Western countries, including the overwhelming — and often misdirected as noted above — interest of pharmaceutical and/or industrial companies, and many other players within the medical field, about genes and genomes. It cannot be ignored, for instance, that numerous evodevoists doing research in the USA are funded by the NIH (National Institute of Health): this provides an healthy connection to medicine as will be discussed below, but results in a huge stress to evodevoists to focus on genetics/genomics on their grant proposals. As I addressed such topics in Diogo (2016) I will not repeat them here, and will instead just briefly refer to some of the issues that, in my personal opinion and in no particular order, should ideally be integrated in future evo-devo studies.

For instance, I should of course stress again that there were various talks at the 2017 meeting concerning what are, in my opinion, truly integrative evo-devo studies. To give just some illustrative examples, Ehab Abouheif's talk on ants included evolution, ecology, development, genetics, anatomy, phylogeny and even some behavioral notes, a remarkable case of an eco-evo-devo study that moreover addressed broader conceptual and theoretical topics, e.g. about major evolutionary transitions. Another example was Maria Pesevski's talk on *Drosophila*, in which she combined development, genetics, ecology and anatomical variation, in an integrative, multidisciplinary context. However, these are major exceptions to the rule, as demonstrated by the numbers given in the Section above. Therefore, I should emphasize that, in my opinion, integrating ecology, and above all behavior, in evo-devo studies is one of the most crucial needs for the field as a whole.

I should note that there were also a few presentations dealing with soft tissues of animals, such as Daniel Smith's poster on the development of limb muscles of crocodilians and birds. Also, Tetsuto Miyashita's talk on early vertebrates included some notes about muscles and other soft tissues. Similarly, Alexa Sadier's talk on bat vision referred to some soft tissues of the eyes, and Craig Albertson's talk on cichlids mentioned jaw soft tissues. Another examples are Evan Kingsley's talk on the avian vocal organ, which included notes on the evolution of some soft tissues of this organ, and Hans Larsson's superb talk

on atavisms that mainly focused on the muscles and other soft tissues of tetrapod limbs.

But again, as shown by the results of the quantitative analysis presented in the Section above, these examples are clearly just the exception to the rule. Apart from being mainly devo, and particularly geno, one might say that animal evo-devo is mainly "Hard"-evo-devo, as soft tissues are often neglected. This is actually a curious aspect of evo-devo. In paleontology, or evolutionary biology in general, the skeleton is often more studied because for the vast majority of fossils that is the only information we can extract from them. But if evo-devo is unfortunately mainly devo, and particularly geno, as noted above, why are most evodevoists focusing only in the hard tissues of animals, and ignoring their soft tissues? It is not particularly more difficult to analyze soft tissues than hard-tissues in evo-devo studies, and obviously hard tissues are just a small fraction of their whole bodies. For instance, in humans the skeleton makes up only about 15% of the total weight of the body. So why is the vast majority of evodevoists concerned with that very specific, minor part of the animal body? How can evo-devo aim to be an integrative, comprehensive field contributing to address major broad and conceptual developmental, evolutionary and medical questions, when most works of evodevoists focus on a system that makes less than even one out of six of our own bodies, and that is only directly involved in/affected by a very small fraction of the most damaging birth defects and diseases that are prevalent in our species? Particularly at a time when systems biology and a more holistic view of the whole body and thus the network connections between its parts should ideally become more relevant in biological sciences, and therefore in evo-devo, focusing just on bones and cartilages does not really seem to make sense.

Similarly, it should be recognized that some talks in the 2017 meeting directly addressed the connection between evo-devo and human pathologies and thus medicine, that is, they could be considered as part of evo-devo-path :(Evolutionary Developmental Pathology: Diogo et al., 2015a,b, 2017; Diogo, 2017) research. An emblematic example was Cliff Tabin's talk on metabolic evolution in cave fish, in which he directly made connections with pathological human conditions such as diabetes. Another clear example was Vincent Lynch's talk on why elephants do not get cancer as often as they could be expected to, which obviously has implications for a major issue within human medicine. But, again, these are very rare exceptions to the rule, and evo-devo-path studies are extremely scarce within current evo-devo. This is surprising because in decades and even centuries ago there were numerous authors trying to connect evolution, developmental, and pathology. This trend was unfortunately mainly lost during the second half of the 20st century, and begun to be mainly recovered in the beginning of the 21st century by authors such as Galis and her colleagues (e.g., Galis, van der Sluijs, van Dooren, Metz, & Nussbaumer, 2007; Van Dongen, Ten Broek, Wijnaendts, & Galis, 2009; Bots et al., 2014; see recent reviews by e.g. Guinard, 2015; Diogo, 2017; Diogo, Guinard, & Diaz, 2017; see also, e.g., Laubicher and Maienschein, 2007). But there is clearly still much to do at this level, and one of the aspects that should be taken further in consideration is the study of phenotypic variation in general and of variations and pathologies of not only the hard tissues, but also of the soft tissues, of humans in particular.

Lastly, as the quantitative analysis provided in the above section shows, although in some ways this 2017 meeting had in general a more "organismal" feel then the 2015 meeting, in many ways it was not completely so. In particular, it is clear that in the overall many of its and posters were not focused on an integrative approach that could help addressing and hopefully solving some of the major broader, conceptual questions within the fields of evolutionary and developmental biology. Therefore, one needs to continue to stress that a major effort needs imperatively to be done, by evodevoists, to integrate the new developmental data they are obtaining into broader discussions of major evolutionary theories and long-standing conceptual questions.

A clear example of this lack of broader conceptual definitions and theories behind current evo-devo thinking is the confusion about the term homology, which is central to both evolutionary and developmental biology. This confusion was evident in the presentation that Linda Holland did of Gunter Wagner's completely deserved award, in the end of this 2017 meeting. Linda criticized the common use of terms such as "functional homology" by saying that Gunter had fortunately defended in his book on homology that the only correct definition of homology was when it referred to a feature that is acquired from a common ancestor. This subject is related to the huge problem, mainly due precisely to the importance of evo, and particularly geno, in evo-devo, of confusing "deep homology", which is part of homoplasy (namely mainly corresponding to evolutionary parallelism), with true homology (see Diogo, 2017, for an updated, extensive discussion of this subject).

I completely agree with both the homology definition given by Linda and with her criticism of how the term homology is wrongly used in most current evo-devo works. However, to show the gravity of this problem and particularly of the communication problems and misunderstandings that it creates, it is not completely true that Gunter defends the strict evolutionary definition of homology used by Linda, and by me. This is because Gunter explains in his book and subsequent works that for him there can be homology at many levels, that is, historical—with matches with our definition—but also morphological, and developmental definitions (e.g., Wagner, 2007, 2014). The latter one matches with the way homology is used by most evodevoists today, that is, with "deep homology", when they state that a structure is homologous in two taxa *because* its ontogeny in those two taxa involves similar developmental mechanisms, even if that structure was not present in the last common ancestor of those taxa (thus contradicting the historical/evolutionary definition).

In summary, it is hoped that the present paper stresses some of the topics that, in the opinion of many authors and myself, are not being addressed in an appropriate way within current evo-devo, by providing a simple, unbiased quantitative analysis of the abstracts of the recent 2017 Pan-Evo-Devo meeting in Calgary. Again, the point is not to criticize anybody in particular, but instead to try to contribute to a more integrative, organismal, evo-devo that focus not only in more body parts (e.g., soft tissues) and their variations as well as in a wider range—and more relevant—taxa (including fossils), but also in a plurality of aspects other than evo and particularly geno, such as comparative anatomy, ecology, behavior, systems biology, and evolutionary medicine.

ACKNOWLEDGMENTS

I thank above all the organizers of the excellent Calgary meeting, and the Pan-American Society for evo-devo in general. I am also particularly thankful to all the numerous colleagues with whom I have discussed the subjects addressed here, as well as to two anonymous reviewers.

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How to cite this article: Diogo R. Where is, in 2017, the evo in evo-devo (evolutionary developmental biology)? *J Exp Zool (Mol Dev Evol)*. 2018;1–8. https://doi.org/10.1002/jez.b.22791