On "Growth and Form" and ASAPbio reform

On 18th–22nd June 2017, University Cultural Centre of the National University of Singapore hosted the 18th Congress of the International Society of Developmental Biologists. Having no opportunity for a more detailed specialist-directed report on this noticeable scientific event, I am going to stop just on two moments deserving a broader enlightening and discussion. They, no doubt, go far beyond the field of developmental biology and have close relation to the journal issue of *Biological Communications* you keep now in hand. Namely, they are D'Arcy Thompson Symposium of plenary lectures celebrating 100th anniversary of his classical "Growth and Form" (see figure), and brief announcement made by Martin Chalfie before his lecture on neuronal fate in *C. elegans*, inviting colleagues to join the movement of pre-press archiving of biological papers. Those interested in these or other materials of the Congress, I propose further to visit the congress' official site at http://isdb2017.com/ and look through commemorative edition of *Mechanisms of Development* (volume 145, p. 1–37), and the abstracts of talks (volume 145, Supplement, pages S1-S176) published earlier this year.

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D'Arcy Weintworth Thompson (1860–1948), Scottish bio-mathematician, has published his most influential work "Growth and Form" in Cambridge University Press in 1917. This book inspired many scientists (anthropologists, developmental and evolutionary biologists), artists, and architectures over the subsequent century. Scientific work and creation by Stephen Jay Gould, Conrad Waddington, John Maynard Smith, Alan Turing, Paul Jackson Pollock, Eduardo Paolozzi, and others may serve as examples. This seems to be especially true regarding the most striking Thompson's theory of transformed coordinates (Briscoe and Kicheva, 2017; Durston and Zhu, 2017; De Robertis, Moriyama, and Colozza, 2017). According to the theory, different biological forms can be explained through Cartesian coordinate transformations of another form. For example, the body form of the sunfish (*Mola mola*), which would be better called like in Russian, "Luna-ryba" ("moonfish", bearing in mind the form of the growing, but yet not full Moon), can be easily imagined as a consequence of coordinate transformations of tail end of a closely related fish species with a more drop-like form of the body. Remarkably, this idea was expressed at the time when the mechanisms coordinating these transformations were entirely unknown and no data on molecular gradients of morphogens were available or even expected. The state of science nowadays helps approaching to understanding the developmental and evolutionary mechanisms of form change.

Most recent elegant experiments with depletion of Tolloid and Sizzled in the ventral side by injecting antisense morpholinos (MOs) just it two ventral blastomeres of a four-cell stage *Xenopus* embryo provide a hint on an underlying mechanism of body form transformations (De Robertis, Moriyama, and Colozza, 2017). Sizzled is a part of Chordin/Tolloid/BMP biochemical network and regulates the level of Chordin and BMP by competitive inhibition of Tolloid. Reducing the level of Sizzled by application of the corresponding MOs reduced Chordin protein levels and increased BMP signaling through an increase in Tolloid enzyme activity. When the application of Sizzled MOs were restricted to ventral blastomeres, it promoted an enlargement of the ventro-posterior part of the embryo and shaped it in a fashion resembling much the sunfish appearance, i.e. with the tail shortened and the posterior part of the embryo enlarged dorso-ventrally, but left the most anterior part of the embryo unaffected. The similar ventral depletion of Tolloid had, correspondingly, the opposite effect (De Robertis, Moriyama, and Colozza, 2017). The reported experiments have explicitly shown the real possibility to change the body form along the lines of transformed coordinates suggested by D'Arcy Thompson by modifying the gradient of Chordin/Tolloid/BMP. The Chordin/Tolloid/BMP pathway patterns the embryos of many organisms, including prebilaterian diploblasts such as the sea anemone *Nematostella vectensis*, in which Chordin and Tolloid, like in *Xenopus*, maintain stable BMP gradient, suggesting this pathway is an ancestral network allowing modification of the animal form in evolution, as well (Genikhovich et al., 2015).

The above example is only one of many possible applications of Thompson's work. The book also covers topics as diverse as growth of trees and shells, temperature regulation, and cell and organ shape, particularly hollow structures. Turning to this classical thoughtful masterpiece, no doubt, may further inspire amateur and more experienced researchers providing the source of ideas for experimentation. The biomechanical paper by Valentin Borkhvardt (see pages 103–155) that we publish in this issue of *Biological Communications* (Borkhvardt, 2017) is also written as a wide theoretical generalization and might be compared in style and the widths to Thompson's book; hence it is a seamless addition to the theoretical disputes so numerous in this commemorative year. Borkhvardt's hydromechanical theory was initially based on empirical observations on the growth of vertebrate limb buds (Borkhvardt, 2000) providing a convincing hypothesis of how interactions of the mesenchymal inner cell mass within the limb bud, its ectodermal sheath and the collagen fibers that link the opposite walls of the bud produce its final form. Although somewhat similar thoughts on a possible mechanical role of the ectoderm have been put forward in early reports on chick limb bud growth and morphogenesis (e.g., Hornbruch and Wolpert, 1970), they were not that clearly formulated and were not integrated to other biomechanical issues; hence, rejected (probably prematurely) by later experimenters (see Boehm et al., 2010 for discussion). The current work by Borkhvardt represents the fullest and the latest version of his theory of mechanical transformations of all living cavitary bodies and besides limb bud formation discusses issues as diverse as plant and animal cell outgrowths, endocytosis, cell division, gastrulation, amoeboid movement, and even muscle contraction, all considered from a single hydromechanical point of view. As in case of the limb buds, the theory of muscle contraction before actin-myosin era was represented by alternative hypotheses including one considering osmotic pressure as a factor of contraction, which was also published like Thompson's book nearly 100 years ago (Roaf, 1914). Although such ideas may look severely outdated in the beginning of the 21st century having mainly a historical interest, we took the risk to publish a contemporary remake.

Despite the considerable increase in our knowledge on molecular interactions and molecular motors in the last decades, and incredible developments of the research technologies, simple observations and logics remain generally the key for understanding the mechanisms underlying biological processes. The accepted theories may cause in wearing blinkers for ages; hence regular attempts to get rid of them with fresh thoughts going down to the basics are scientific necessity. The universal hydromechanical model proposed by Borkhvardt considering the biomechanical bases of so many biological processes is one such a good attempt (Borkhvardt, 2017).

Yet another important aspect of the passed Congress and, more generally, communications of researchers in the first place, is the appeal of Martin Chalfie (one of five nobelists who have given talks) to join the recently established movement for a wider use of preprints in biology. This may need a brief history note. In 1991, Paul Ginsparg, a high energy particle theorist at the Los Alamos National Laboratory wrote a program allowing researchers in his field to post, archive, and therefore freely distribute their manuscripts in the internet with further plans for a formal electronic peer review process (Hayes, 1995). Hayes further speculated only four years later that with that level of electronic transactions, which had Ginsparg's server, the *Nuclear Physics B* should be the first journal to collapse. However, 22 years after this prediction we only see a drop down of the impact factor from 4.5–5.0 in late 90s to ca. 3.5 in recent years, what is a tendency for many journals in this period; hence it is still in Q1 rank. But what is probably more important, the journal indeed experienced the decrease in annual institutional subscription rate from US$ 10,775.00 to just US$ 954.00 although one can only guess what were the reasons, and whether the open pre-print server of Paul Ginsparg played a role. At least, the researchers got an alternative for their publications, which we know nowadays as arXive (https://arxiv.org/). It covers topics of physics, mathematics, computer science, and, to a lesser extent, quantitative biology. For Russian broad auditorium, including most biologists, this preprint server has become famous due to solution by Grigory Perelman the Puincare conjecture in a series of three papers published at arXiv and widely announced by mass media in early 2000s.

So, now back to biology. On 16–17 February 2016 the ASAPbio (Accelerating Science and Publication in biology) meeting took place at the Howard Hughes Medical Institute in Chevy Chase, Maryland to discuss ways in which "preprints" might facilitate the communication of particularly biological research (Berg et al., 2016). This was a scientist-driven initiative based on the fact of relatively low level of preprint use in life sciences. Both at that meeting and in the talk of Martin Chalfie at ISDB2017 in Singapore the following arguments were put forward, showing the advantages of preprints over the routine peer review publication. First, the publication is very fast and does not include several rounds of submission-rejection-resubmission to several journals. Second, the posting of the preprint at the online preprint server like arXiv.org immediately exposes the research to many scientists and provides an opportunity for authors to obtain feedback, sometimes less biased and more detailed and constructive than they have from few reviewers in a journal. The advanced and corrected version of the preprint can be posted again. Third, the preprints give an opportunity to see in real time the reactions from the community and the author's responds. This may be helpful not only for the researchers themselves, but also for reviewers in the journal, where the manuscript is later submitted, and for reviewers from funding agencies to better assess the applicant's (the preprint author's) ideas and most recent findings (note, a researcher who is under pressure to submit a grant proposal have usually no time to wait for the printed edition of his article). Preprints also offer more opportunity for early-career scientists to get peer feedback (Berg et al., 2016). Finally, already many journals have a policy to consider manuscripts already published as preprints at a recognized preprint server; see for example a List of academic journals by preprint policy in Wikipedia (List of…, 2017). *Biological Communications* also appreciates author's posting the manuscript at a biological preprint server, like bioRxiv.org, arXiv q-bio, F1000Research and others, which are indexed in Prepubmed (http://www.prepubmed.org/) and encourages parallel submission to our journal. The final printed journal version can be later uploaded as the final version at the preprint server or elsewhere (see https://biocomm.spbu.ru/about/editorialPolicy for the journal policy). In turn, we will keep the link to the earliest version of the manuscript published in bioRxiv.org in the final publication in *Biological Communications*. We do believe that this way may help authors to improve substantially the manuscripts and to provide faster feedback to authors and acquire more citations to the published research. Although some skeptics suggested that the preprint servers will be overloaded with weak papers just to assert priority, the real practice shows that authors do not publish openly poor-quality work due to potential impact on their own reputation (Berg et al., 2017). Generally, it is the author's decision whether to submit a manuscript just to a journal or to a preprint server as well.

The last but not least. Some biological journals encourage scientists for post-press discussions of the published research at the web pages of the articles or in blogs. This however does not seem to work well, probably, because post-press discus-

sions cannot improve the published article anymore and the critics at this stage is not so vividly accepted by the authors. Therefore, the preprint discussions are potentially more fruitful. What Martin Chalfie stressed further in his talk, is a specific way on how we, readers, could further help authors in their hard work on improvement of their manuscripts and, at the same time, help younger members of our own labs to discuss recent scientific discoveries and critically evaluate them. Many laboratories in the field of life sciences, and especially in biomedical institutions, run so called "journal clubs", where members of the lab regularly report on a specific subject or observe most recent papers in the field. Why not then to concentrate the journal club discussions specifically on manuscripts published at pre-print servers, like bioRxiv.org and others and later summarize the ideas and concerns and send as a feedback to the authors? I fully agree with Chalfie that this way would be certainly helpful both to the laboratory members and the authors. This would be a step towards a new culture of biological communications.

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