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# Canalization, a central concept in biology

Canalization stands among the most elusive but also stimulating concepts in developmental and evolutionary biology. It was introduced by Waddington in the 1940 s to account, at the developmental level, for '*sharp differentiation of tissue types*', and at the genetic level, for the phenotypic '*consistency of the wild type*' [1]. *Phenotypic consistency in face of environmental and/or genetic perturbation*, could be a somewhat consensual definition. Note, however, that such a definition is imprecise: the '*and/or*' leaves open the distinction between the two sources of perturbation (environmental *vs.* genetic), and the term '*perturbation*' is also vague. A very controversial aspect of canalization is whether it is a mere property of the phenotype (invariance) or a developmental mechanism (the processes that allow such invariance). The second option – likely the most often used meaning – is by itself confusing, as it suggests that canalization is adaptive – which might not necessarily be the case (see [2,3] for discussions about definitions). Waddington used the term in a rather clearly adaptive sense: as argued in one contribution to this special issue [4] – canalization was inherently linked to *genetic assimilation*, the process by which environmentally induced phenotypes can become genetically fixed through selection.

Why is canalization so interesting – or at least, considered interesting by so many biologists (and also philosophers of science; e.g. [5,6])? There are many reasons for that. The most general one, in our opinion, is that, as the related concept of plasticity, it deals with one of the fundamental questions in philosophy and biology, which is the interplay and relative roles of internal vs. external forces in the making of living organisms (e.g. [7]). This opposition has taken many forms in the history of biology, but the debate over innate vs acquired traits is maybe the most obvious (the controversy around genetic assimilation is partly due to its Lamarckian flavor), with the gene centered vs. environment centered views of evolution – each with its dramatic extreme, i.e. eugenism and lysenkoism. The ongoing discussions on the need for a new evolutionary synthesis (e.g. [8]) are centered on this tension: to understand evolution one should account for the interplay between genes, development and environment – a complexity that was famously neglected in the modern synthesis, as stated by Leigh Van Valen: '*A plausible argument could be made that evolution is the control of development by ecology. Oddly, neither area has figured importantly in evolutionary theory since Darwin, who contributed much to each.*' [9]. This perfectly summarizes what is at stake in the study of canalization. Because natural selection screens phenotypic variation, all factors that modulate such variation are of central evolutionary importance [10].

Why is canalization elusive? There are also many reasons – some of which are also the reasons for its interest. Canalization is elusive because of definition problems as mentioned above (and Waddington certainly bears some responsibility in this). It has been elusive because of the long lack of an understanding of its molecular/genetic bases – in the first place: do canalizing genes exist at all? To be honest this is not fully specific to canalization, as for long the genetic and developmental basis of virtually any trait has been obscure, but it did not help not understanding the material basis of such phenotypic invariance. In that respect, a turn in the history of canalization is undeniably the publication in 1998 of Rutherford and Lindquist' study of Hsp90 [11]: highly debated (sometimes harshly criticized), it has deeply contributed to the renewal of the field, by proposing the first molecularly identified mechanism for canalization. Many papers have been published since (see Fig. 1) and much progress on the genetics of canalization have been achieved.

Another – and maybe more important – controversial aspect, is the evolutionary importance of canalization. As for plasticity, whether canalization might slow down evolution by shielding genetic variation, or rather speed it up when compromised by adverse, extreme environmental conditions or major mutations (decanalization) has been discussed (e.g. [12,13]). It has been proposed that canalization might be involved in the patterns of morphological stasis punctuated by fast evolution (e.g. [14]; see [15] for a discussion). Is genetic assimilation a common phenomenon or nothing more than an interesting curiosity with no general bearing on main evolutionary processes? Few data have been available to answer this question, although the situation is changing (e.g. [16,17]).

In this special issue, we intended to set up a collection of reviews on canalization by some of the most prominent actors of modern research on canalization, considered from various angles and at various scales. The opening contribution takes us at the historical origin of canalization: L. Loison [4] focuses his review on the link between canalization and genetic assimilation, an often overlooked aspect that is central to Waddington's contribution to evolutionary biology. This paper also aims at clarifying some of the terminological and conceptual confusion that has plagued the field since its origins.

The next contributions focus on the molecular bases of canalization, a long missing key element to Waddington's argument. K. Takahashi presents the various worked examples of individual genes and genetic systems contributing to canalization [18]. As

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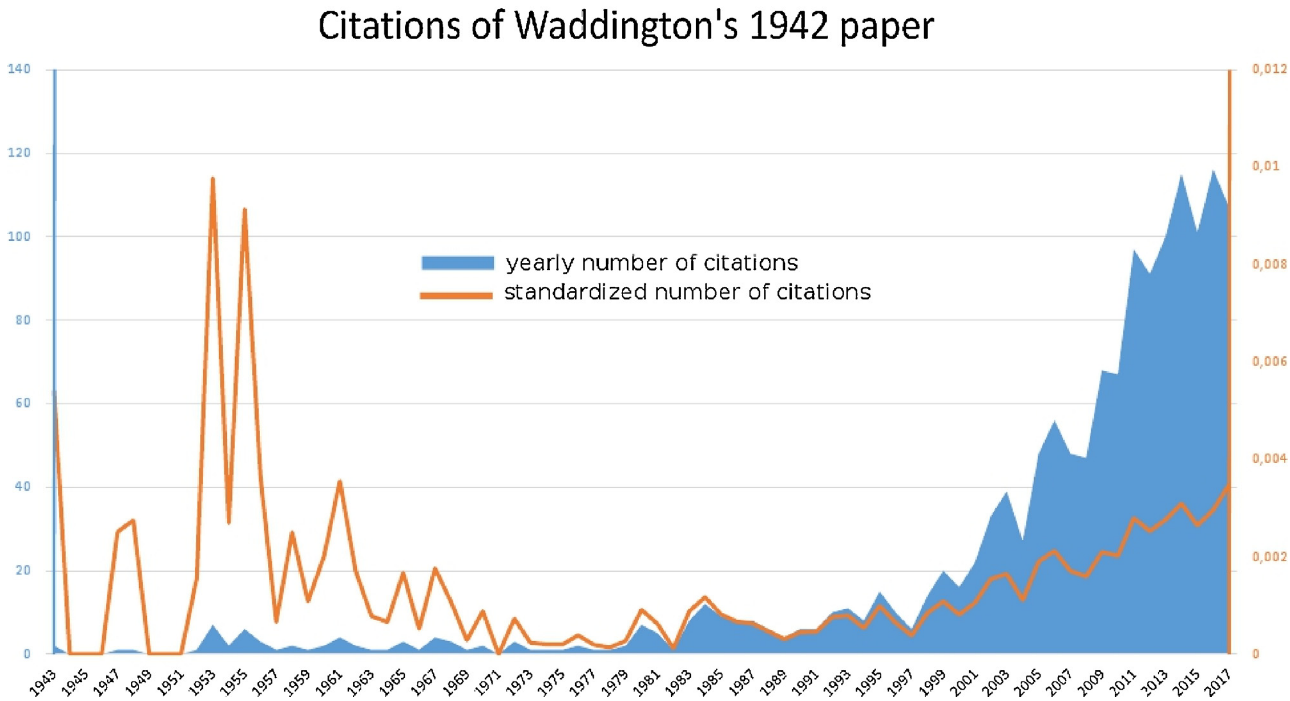


**Fig. 1.** A glimpse on the influence of Waddington's work from a bibliometric analysis of his 1942 Nature's paper "*Canalization of development and the inheritance of acquired characters*" [1], realized on Web of Science on february 2018. The blue area indicates the yearly number of citations, and the orange line the same value standardized by the number of publications in the field "Evolutionary biology" as defined by WOS research area. Note that before the 80′s the relative impact of the paper was high but erratic, an effect likely due to the very low number of publications in the field compared to more recent period. Both curves start climbing around 1998, which might partly reflect the publication of Rutherford and Lindquist [11]. The raise in relative number of citation suggests a sustained increased interest for canalization over the past 20 years.

mentioned earlier, Hsp90 occupies a particular place in the recent history of canalization. R. Zabinsky, G. Mason, C. Queitsch and D. Jarosz, in line with ideas developed by the late Susan Lindquist, provide a comprehensive review of this paradigmatic case [19], in relation with various phenomena, ranging from phenotypic evolution to cancer research. We then dive into the complexity of genetic and physiological interactions with the contribution of A. Badyaev on the evolution of metabolic networks and its role in phenotypic robustness [20]. An original contribution by J. Draghi investigates canalization in micro-organisms – i.e. in non-developing unicellulars [21]. K. Geiler-Samerotte, F Sartori and M. Siegal provide a thought-provoking overview on the emergence of canalization and potentiation from complex epistatic interactions in genetic networks [22].

B. Hallgrimsson and colleagues then propose a thoughful and sound synthesis of the recent research on the developmental genetics of canalization, while also discussing conceptual problems and advances [23].

The last two contributions consider the consequences of canalization (and decanalization) at the macro-evolutionary level. N. Levis and D. Pfennig review the literature on genetic assimilation and phenotypic accommodation, focusing on amphibians [24]. Finally, M. Webster investigates the challenges and opportunities for the investigation of canalization in the fossil record, linking developmental regulatory processes with deep time evolution [25].

By bringing together this panel of reviews, this special issue provides a comprenhensive picture of the ongoing research on canalization. After almost 80 years, Waddington's work – and singularly on canalization – continues to stimulate debates and generate new ideas. This is clearly because canalization stands at the cornerstone between ecology, developmental biology, genetics and evolutionary biology. Although rich of a history of controversy, canalization has been and will likely remain a central concept in biology.

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