13th Altenberg Workshop in Theoretical Biology 2005

ARRIVING AT A THEORETICAL BIOLOGY:
The Waddington Centennial

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organized by Manfred Laubichler and Brian K. Hall

Konrad Lorenz Institute
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Altenberg, Austria
&
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The topic

Starting in 1966, Conrad Hal Waddington convened a series of four meetings at the Villa Serbelloni in Bellagio, Italy, to explore questions related to Theoretical Biology. In the late 1960s molecular biology had reached its first peak – the structure of DNA, the genetic code, and the operon model had all been discovered in the previous 15 years. In this intellectual climate Waddington brought together biologists, physicists, and mathematicians in order to explore the concepts and methods around which a Theoretical Biology could grow. The resulting discussions raised many issues, identified relevant concepts and tools, and stimulated the further development of Theoretical Biology, but did not provide an organizing focus for a unified discipline. In the decades that followed centrifugal tendencies dominated the field, and only the recent explosion of molecular data, the increasing use of computational tools, and the integration of formerly separate research domains prompted a new demand for unifying theoretical concepts in biology. This workshop, honoring Waddington's 100th birthday, picks up the baton and explores the challenges of a Theoretical Biology at the beginning of the 21st century.

Program

WADDINGTON AT 100
AND THE HIOTORY OF THEORETICAL BIOLOGY

Manfred Laubichler Research Agendas in Theoretical Biology
Brian Goodwin, Jonathan Bard, Soraya da Chadarevian Roundtable: Waddington and his Place in 20th Century Biology

STRUCTURE OF THEORETICAL BIOLOGY:
UNIFIED OR DISCIPLINE ORIENTED

Jonathan Bard Position Statement: Development – Wad's Legacy I
Gerd Müller Position Statement: EvoDevo – Wad's Legacy II
Peter Hammerstein Is There a Theory of Biology?
Robert Brandon The Principle of Drift: Biology's 1st Law

PRINCIPLES OF BIOLOGICAL ORGANIZATION

Kurt Schwenk Biological Patterns
Graham Budd Functional Morphology as a High Level Control on the Emergence and Maintenance of Novelties

PRINCIPLES REALIZED

Adam Wilkins Waddington's Unfinished Critique of Evolutionary Genetics – Then and Now
Fred Nijhout Environment and Assimilation
Robert Page The Evolutionary Origins of Division of Labor in the Honey Bee

FORMALIZATION

Günter Wagner Measurement Theory in Evolutionary Biology
Ken Weiss The Phenogenetic Logic of Life: Fundamental Principles, or Just Decription?

Abstracts

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Development – Wad's Legacy I

This talk will consider how much of Waddington' s experimental and theoretical work in developmental biology is still germane today. While many of Wad's achievements have become so much part of our standard model of development to the extent that their source has been forgotten, he is still remembered for the novel terms that he introduced to the subject for to the metaphor of the epigenetic landscape. More important, however, is the intellectual approach that underpinned these concepts, and my intention is to show that this emerged from the experimental work on the genetic basis of development that Wad was doing in the '30s. This gave rise to a global view of development based on the integration of the behavior of sets of genes, and it is from this view that the terms and the metaphors emerge. Today, we would call this a systems biology approach to development – but Wad was doing it more than 60 years ago!

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The Principle of Drift: Biology's 1st Law

Drift is to evolution as inertia is to Newtonian mechanics. Both are the "natural" or default states of the systems to which they apply. The Principle of Inertia describes the zero-force condition in Newtonian mechanics. Many biologists treat the Hardy-Weinberg Law as if it were a zero-force law. It is not. It is neither a law nor does it describe a zero-force state. Failure to see this results in some serious misconceptions about the evolutionary process. In this paper the Principle of Drift is stated for the first time. It is the true analogue of Newton's 1st Law. It is the zero-force law of evolution. It supplies the appropri-ate null hypothesis for evolutionary scenarios.

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Functional Morphology as a High-Level Control on the Emergence and Maintenance of Novelties

Classical neo-Darwinian theorists tend not to see the problem at all. Developmental geneticists resolve it with the casual wave of an Eppendorf tube. Structuralists see it and then nothing else matters. Paleontologists pretend they don't notice it, but spend a lot of time secretly working on it. 'It' is of course the problem of how large scale structures originate and evolve in organisms. Despite the intense theoretical labors that have been expended on evolution in the last half-century, little of this effort has been directed at events taking place above the population level – they have just been assumed to be the natural working-out of lower-level events. Without denying this insight, the question remaining, then, is "could there be a general theory of how innov-ations like legs, eyes, flowers and nervous systems evolve"? And if so, what implications would this have for the genetics of the process? Taking up

examples from the fossil record, especially from the Cambrian, I will argue that the current obsession with genes, which also dominated the formative period of the neo-Darwinian synthesis, has resulted in only sporadic attempts to understand the controls on how morphology evolves. The unifying feature that is largely ignored is the importance of functional morphology, and how it erects a framework within with both the genome and morphology must be con-strained. If this "missing link" between population processes and the evidence of the fossil record could be supplied, then the exciting prospect of a truly unified theory of evolution lies ahead.Landscapes of Chreods and Catastrophes: How is Morphospace Organized?

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Is There a Theory of Biology?

Biology as a field is not a ‘monolithic block’ but rather a collection of specialized subdisciplines, such as genetics and neuroscience. The recent ‘molecular revolution’ has offered powerful tools to all these subdisciplines, but it also led to more specialization and disintegration of the life sciences. Tools alone are of no value, however, unless they are used for an interesting pur-pose. In biology, the goal is to understand how life in its various forms is organized, what kinds of functionality exist, and how these functionalities are generated on different time scales, such as that of evolution, development, or of fast chemical reactions. This goal unites all subdisciplines of biology and forces them, in principle, to interact. Since ‘organization’ and ‘functionality’ are abstract concepts, this interaction needs to be guided by theory and mathe-matical attempts to ‘capture’ the principles of ‘organismic design’. Perhaps the most important step in the search for biological principles is the identification of fruitful questions. Current theoretical biology has made major progress with asking questions that demonstrate its role as the ‘backbone’ of the life sciences.

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Research Agendas in Theoretical Biology

Theoretical Biology, either as Theoretical Biology per se, or in form of related concepts, such as Systems Biology, is gaining prominence in 21st century biology. Theoretical issues in biology, however, are as old as biology itself, and even Theoretical Biology as a recognizable filed of inquiry within the Life Sciences dates back to the late 19th century. Throughout the 20th century research agendas within Theoretical Biology have changed considerably and many of those have spun off self-sustaining areas of biological inquiry. As a consequence the integrative function of Theoretical Biology has often been neglected. Waddington’s famous attempt at conceptual integration in “Towards a Theoretical Biology” is a notably exception to this general trend. In this paper I will argue that knowing the multiple research agendas within Theoretical Biology puts us in a better position to accomplish the integrative goals of Theoretical Biology today. I will sketch the main developments in the history of 20th century Theoretical Biology and demonstrate how they contribute to the conceptual and theoretical integration of the Life Sciences.

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EvoDevo – Wad's Legacy II

C.H. Waddington criticized neo-Darwinism for its neglect of the phenotype and called for an inclusion of the rules of development into evolutionary theory. The gene binge that prevailed in biology during much of the second half of the 20th century largely stifled this program, but the recent rise of Evolutionary Developmental Biology takes up many of the themes Waddington had seen at the core of such an endeavor. In this presentation I will sketch the present conceptual structure of EvoDevo and discuss its commonalities and differ-ences with Waddington's ideas. In particular I will concentrate on the problem of morphological novelty and emphasize the requirement of a concept for genetic integration as foreseen by Waddington. Finally, I will discuss the consequences of the EvoDevo agenda, and I will argue that EvoDevo can develop the necessary tools for formalizing the processes of developmental organization as required for a theory of the phenotype.

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Environment and Assimilation

Waddington´s experiments on genetic assimilation showed that selection on environmentally induced phenotypic variants can cause inherited evolutionary changes in the phenotype. We have recently extended this work by de-monstrating that it is possible to select for a polyphenism (alternative phenotypes in two different environments) in a monophenic species (with the same phenotype in those two environments). We found that the mechanisms that regulate the levels of developmental hormones can mask genetic variation. These homeostatic mechanisms, like heat-shock proteins, can act as capacitators for evolutionary change. A sensitizing mutation that alters the hormone titer can, in certain environments, reveal previously masked genetic variation. Selection on this variation can result in the genetic accommodation of a discontinuous norm by coupling a physiological mechanism of homeo-static regulation with developmental thresholds.

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The Evolutionary Origins of Divisions of Labor in the Honey Bee

Honey bee workers undergo changes in their behavior as they age that result in a division of labor among nest mates. A major transition occurs when the bees change from performing tasks with the nest to foraging. As foragers, individuals tend to specialize on collecting nectar or pollen. Research performed in my lab over the past 15 years has demonstrated a suite of behavioral, physiological, and biochemical traits that correlate with collecting pollen or nectar. This "syndrome" is a consequence of genetic pleiotropy, which we have demonstrated with genetic mapping, and reveals that the evolutionary origin of division of labor among worker honey bees is derived from a reproductive regulatory network that evolved in solitary insects.

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Biological Patterns

Pattern can be defined as 'non-randomness' relative to a null model. Patterns are ubiquitous and diverse in biological systems. Hierarchical structures and networks are especially common. Nonetheless, biological patterns are of little use in generating fundamental principles because they are contingent and therefore lack universality. The contingency of biological patterns results from lineage independence, or clade specificity. Clade specificity means that prin-ciples derived from shared (ancestral) attributes of life are of diminishing general value as one proceeds towards the tips of a clade because at any given time, an independently evolving lineage represents a unique interaction of environment, phenotype, genetic, and epigenetic background. The unique-ness of phenotypic "solutions" to identical environments among different lineages shows that biological systems fail to behave in predictable or "law-like" ways. Important as they are in a local context, biological patterns fail to support the idea of a foundational theoretical biology.

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Measurement Theory in Evolutionary Biology

Measurement theory is a branch of applied mathematics that provides numerical representations of empirical relationships. Such numerical representations play a fundamental role in all mathematical branches of science, where they are known as quantitative variables, such as weight, temperature, and distance, for instance. Biology is perhaps the only major science in which the fundamental quantitative concepts are not grounded in a sound measurement theoretical basis. Here I will argue that this is to the detriment of theory development because measurement theory functions as a critical link between empirical information and theoretical structures. At the one hand the structure of mathematical theories depends to a large extent on the mathematical properties of the basic variables, which in turn are determined by measurement theory. On the other hand the empirical meaning of a quan-titative variable is also defined in the measurement theory of the variable. As a historical aside one can discuss the role measurement theory may have had in the revolution in theoretical physics at the beginning of the 20th century (relativity and quantum theory). I will propose that many conceptual issues associated with quantitative variables can be turned into technical questions, and thus made solvable in principle, once they are understood as problems of measurement theory. This approach will be exemplified with a proposal to define fitness as a measure of competitive ability. It will be shown that the measurement theoretical properties of the fitness measure are necessary to explain "downstream" concepts such as gene interaction, and epistasis.

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The Phenogenetic Logic of Life: Fundamental Principles, or Just Description?

Across the spectrum of life from simpler to more complex organisms, a few generalizations appear to apply both to the organization of genomes and to phenogenetics, that is, the ways genomes are used to assemble organisms. These facts can be viewed as simply descriptive generalizations about genomes and organisms, or as reflections of an underlying phenogenetic logic, or relational principles somehow built into the nature of life. There are both analogs and homologs between Darwinian descent with modification during evolution, and phenogenetic duplication with variation during development, which relate to homologous and underlying phenomena. This provides a basis for "EvoDevo". But there are also important differences, not least of which is the "Lamarckian" nature of phenogenetic logic as compared to the "random" nature of evolutionary processes. In some ways phenogenetic logic resembles computer algorithms, but whether this is superficial is less clear; unlike programs, phenogenetic logic is implicit rather than explicit in genomes. For-malizing a minimal sufficient set of phenogentetic logic, and testing the degree to which these principles are fundamental to the nature of life, rather than simply being common facts, is a potentially important area for theoretical biology for three reasons. A valid set of principles can provide a program for research as Darwinian postulates do for evolutionary biology, can provide an overview of life that is not vulnerable to the next finding to be revealed by new technologies such as high-throughput genomics, and could more formally unify evolution and development as a single phenomenon.

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Waddington's Unfinished Critique of Evolutionary Genetics – Then and Now

Though C.H. Waddington is remembered not least as a critic of the genetic foundations of 20th century evolutionary theory, his specific criticisms tend to be given far less attention today than to his proposed solutions to the gaps, namely the phenomena of "canalization" and "genetic assimilation". Yet, while at least one of his criticisms of neo-Darwinian evolution now seems mistaken, others look prescient. In particular, he questioned the implicit emphasis of population genetics on additive gene effects and, following Mivart's critique of Darwinism 60-70 years earlier, argued that the neo-Darwinian theory neg-lected the inherent degrees of order that can be evoked by simple mutational changes. Given the state of knowledge of genes and gene action during the '50s and '60s when Waddington was producing his last significant papers, it is perhaps not surprising that he could not take these insights further than he did. Yet, with a growing body of recent knowledge about both the genetic networks that underlie the development of various morphological traits and the evolution of such networks, we can begin to see how his critique could be fleshed out today. A central conclusion of this talk is that evolutionary genetics is still largely in thrall to a class of formal models proposed long before there was any actual knowledge of genes or gene action and that its intellectual edifice is in urgent need of major repair, if not wholesale renov-ation.
