20th Altenberg Workshop in Theoretical Biology 2008

Origins of Evo-Devo:
A Tribute to Pere Alberch

18-21 September 2008

organized by Gerd B. Müller and Diego Rasskin-Gutman

Konrad Lorenz Institute
for Evolution and Cognition Research
Altenberg, Austria

The topic

Pere Alberch has been one of the most gifted and inspirational figures in developmental and evolutionary biology. In particular, he had been one of the founding proponents of the research endeavor that has come to be known as EvoDevo, the study of how the processes of individual development interact with the processes that cause evolutionary change. Whereas much of today's EvoDevo is focused on developmental genetics, the field had been triggered by the desire to understand the evolution of organismal phenotypes, a topic much sidelined by the Modern Synthesis framework of evolutionary theory.

Pere's main interest was the generation and transformation of animal form. The depth and breadth of his integrative approach was such that he was willing to transcend the purely scientific enquiry by bridging the world of biological objects with the way artists create new worlds. This workshop is an occasion to celebrate Pere's life and work by bringing together those who had the occasion to work with him as well as those who have been inspired by his intellectual legacy. Thus, this workshop is a second occasion to honor Pere, after the first meeting that was hosted at the Institute Cavanilles for Biodiversity and Evolution, were Pere was going to continue his research activities, a plan that had reached an advanced stage when he tragically passed away in 1998.

We have divided this workshop into four sessions in a rather idiosyncratic way: no manner of reductionism can be imposed on the scientific legacy of such an exuberant mind!

The session on ORIGINS highlights Pere's influence on the nascent field of EvoDevo, from historical and conceptual perspectives, and its evolution from the pre-HOX times to today's understanding of the links between development and evolution. The session on EXPERIMENTS commemorates Pere's work on amphibian life histories and limb development, some of the finest examples of early morphological EvoDevo that inspired a whole generation of subsequent researchers. Pere's theoretical insights will be discussed in session three, INTERNALISM, a title that characterizes his strong opinion that internal causes are fundamental for any understanding of evolutionary dynamics, because of the constraints imposed by the developmental programs of organismal lineages. The final session, CONNECTIONS, shall build bridges with the future, exploring the ways in which the legacy of Pere's work connects with today's research in the biosciences. Theoretical biology, genomics, and stem cell research will be discussed before the final lecture will bring back glimpses of the atmosphere in those Harvard days.

Program

ORIGINS

Gerd B. Müller Origin and diversification of EvoDevo
John Reiss Origins of EvoDevo: Gould and Alberch, Raff and Kauffman
Laura Nuño de la Rosa Patterns, processes, and mechanisms in the early stages of EvoDevo

EXPERIMENTS

Richard Hinchliffe Making very long larval limbs: Heterochronic modulation of skeletogenesis in the pelagic larvae of the S. Crested Newt
John Archer Evolution of synovial joints
Ann Burke Journey to the lateral somitic frontier

INTERNALISM

Chris Rose Pere Alberch, the internalist viewpoint of morphological evolution, and amphibian metamorphosis
Miquel De Renzi Development and paleobiology: a fruitful feedback
Arantza Etxeberría A world of opportunity within constraint: Pere Alberch's early EvoDevo

CONNECTIONS

Diego Rasskin-Gutman What's the (new) story with heterochrony and developmental constraints?
Hernán Dopazo Adaptation at the genome scale: A gene or a function centered concept?
Emily Gale "Show me the gene for remorse."

Abstracts

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Evolution of synovial joints

In my presentation, I will discuss the early evolution of synovial joints, the initial effects this allowed in terms of prey selection and on mobility during the occupation of land. Further refinements increased the range of mobility on both land and water and the conquest of the skies. Mention will be made of the molecular bases of joint formation and the use of highly conserved matrix molecules such as hyaluronan. Lastly, the importance of hyperphalangy will be addressed in relation to understanding the mechanisms of joint formation.

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Journey to the lateral somitic frontier

I recently had cause to reread the first chapter of Hans Meinhardt's 1982 book, Models of Biological Pattern Formation. I must have borrowed the original from Pere, as the margins of my faded photocopy include notes in his surprisingly neat hand. Meinhardt's third paragraph begins "As in any other branch of science, attempts have been made to explain the observed details [of development] through the invention of hypothetical mechanisms - models- which account for the observed as well as the possible. A criteria of a good model is that several seemingly unrelated observations appear as the expression of a single underlying mechanism." Pere's marginalia reads: " •agreement •simplicity •compatibility". It certainly seems simple enough. In reflection, what I learned from Pere was that the motivation to search for these things can be championed even in the face of everything we know which confounds a simple solution. I had only a vague, if exhilarating idea at the time that what I was learning was how to walk the razor line between imagination and data, between the observed and the possible, a place that allows for an occasional intellectual acceleration that makes it all worthwhile. Pere legitimized this place for me, and I will discuss how it propelled me to the lateral somitic frontier.

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Development and palaeobiology: a fruitful feedback

Pere Alberch had important contributions to modern evolutionary palaeobiology. He emphasized the causal internal role of development in evolutionary processes, in contrast with the common ideas about evolution of his time. Since development determines preferential directions of morphological transformation from discrete morphological domains, Pere was directionalist and punctualist. Heterochrony and its quantification were his early topics. Two contemporary achievements of palaeobiology were supported by his ideas: punctuated equilibria and constructional morphology. Alberch's viewpoints suggest new ways of palaeobiological research. Studies on heterochrony receive

good support from sclerochronology. Thus, an interesting field arises in order to relate the geometric parameters of theoretical morphology to the timing parameters associated with heterochrony. Last but not least: Pere paid attention to the feedback of the genetic-epigenetic pair. Skeletal morphogenesis and biomineralization processes provide an interesting field of study since they involve gene expression and self-organization (epigenetic) of gene products.

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Adaptation at the genome scale: A gene or a function centered concept?

Large or complete genome analyses of adaptation are based on concepts and methods developed for single gene analysis. Statistical methods to test for neutrality are equally used today for genes working independently or associated by functional demands. The main outcome of this gene centered view is interesting, few evidences of adaptive divergence seems to be found between major clusters of mammals. Looking through the complete genome of human, chimpanzee, mouse, rat and dog we demonstrate that in protein coding genes selective pressures not necessarily indicating positive selection are functionally associated to a many different classes of biological functions. Moreover, we found that proteins changing at faster rates of dN are physically closer in chromosomes and many of them associated to different metabolic pathways. All these evidences points out that adaptive evolution at genomic level seems to work through a high number of slightly correlated non-synonymous changes affecting functionally related genes rather than a few major single changes produced by positively selected genes.

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A world of opportunity within constraint: Pere Alberch's early EvoDevo

This presentation will report an overview (prepared in collaboration with Laura Nuño de la Rosa) of Pere Alberch´s work as an exponent of early EvoDevo. It takes into account a selection of his best papers, and the main theoretical issues stemming from them: the discrete morphospace, the peculiarities of the morphogenetic level, developmental constraints and evolutionary opportunities. Alberch explored internal developmental order from different perspectives. Some of the questions arising in his papers are: How does development influence evolution? Is development an active evolutionary force? How can restrictions (of possible variation) and opportunities (for novelty) interact? Does development provide rules of general validity? Does it direct evolution? We comment on some consequences of his work for three important debates in EvoDevo, namely: the nature of developmental constraints, the issue of typology, and the role of dynamical systems theory in evolutionary biology.

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„Show me the gene for remorse." (Pere Alberch)

Pere Alberch was an exuberant mind. His campaign against reductionism in biology and championing the cause of developmental constraints were carried out with equal parts of artistic flair and intellectual

rigor. He directed these and all his energies towards understanding creation of form: the crossroads of development and evolution. The work I shared with Pere focused on the limitations of plasticity in development that reflected constraints in evolution. This included exploring potentialities in limb formation and in cell dedifferentiation or respecification. My fascination with the possible pathways of development has continued with work on neural tube segmentation and pluripotency of embryonic stem cells. Sadly, Pere's fight against reductionism currently brings to mind Don Quixote rather than El Cid but that is slowly changing. On the other hand, the study of gene cascades is revealing both mechanism for and examples of developmental constraints.

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Making very long larval limbs: heterochronic modulation of skeletogenesis in the pelagic larvae of the Southern Crested Newt, *Triturus karelinii*

Pere Alberch highlighted the role of heterochrony generally in evolution and development. Urodeles provided much evidence for him. Here I report its role in generating long larval limbs.
Generally urodeles have larvae adapted to bottom living with relatively short developing limbs (the 'standard' pattern). But the Southern Crested Newt has early larvae with a pelagic lifestyle and relatively very long forelimbs (approximately 50% of snout/vent length compared with the 'standard' 25%). Examination of development of their radius/ulna and metacarpals/phalanges (digit 2) aimed to identify possible modification of the 'standard' development programmes. Initial prechondrogenic condensations appear only marginally longer than the 'standard'. The remarkable rapid elongation of the long thin cartilage 'models' is achieved mainly by early extensive cartilage hypertrophy, accompanied by early diaphysis ossification.
The most unusual of these cartilage models is the very long and thin terminal phalange (only 1-3 cells thick), in which only the proximal part ossifies, with the terminal part of the cartilage being lost during its metamorphosis to the short definitive element. The remarkable morphology of these terminal phalanges probably represents a larval adaptation to swimming.
Overall key features of these larval limbs appear to involve heterochronic changes in the relative timing and positioning of developmental processes.

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Origins and diversification of EvoDevo

In the late 1970s and early 1980s, critique of adaptationism highlighted the inability of neo-Darwinian theory to account for essential phenomena of phenotypic evolution, such as biases in the variation of morphological traits, rapid changes of form, the origin of non-adaptive traits, and the establishment of complex body plans. These explanatory deficits of neo-Darwinism were primarily attributed to the absence in its formal framework of the generative rules that relate between genotype and phenotype. Pere Alberch and his coworkers were among the first to show that it was possible to formulate meaningful mechanistic concepts about the relationship between developmental and evolutionary processes and that these issues could be addressed experimentally. Since these experimental beginnings the field has grown into what is now known as EvoDevo, but at the same time its agenda has diversified into several distinct strands of research. The conceptual foundation of EvoDevo has also expanded. Whereas heterochrony and constraint were the major contributions to evolutionary theory in the early days, evolvability, modularity, and innovation have become leading themes of EvoDevo today, contributing to an extended evolutionary synthesis.

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Patterns, processes and mechanisms in the early stages of evodevo

Due to the current widespread identification of EvoDevo with evolutionary developmental genetics, the origins of the discipline are usually traced back to the discovery of new molecular techniques in the 1990's. However, the work of Pere Alberch, developed from the late 1970's to the late 1990's, does not fit in such an approach to development and evolution. The 'morphogenetic school' to which Alberch belonged thought of development and evolution in a very different way. However, the history of the early stages of this other EvoDevo remains still to be done. Starting from a previous work in collaboration with Arantza Etxeberria, my presentation aims to be a contribution to this open historiographical enterprise, focusing on the theoretical debates that took place among the supporters of the morphogenetic approach to evolution from the late 70's to the late 90's. In particular, I will pay attention to the different conceptual approaches to the relationship between patterns, processes and mechanisms in development and evolution.

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What's the (new) story with heterochrony and developmental constraints?

Heterochrony as a "mechanism" underlying allometry, that is, as differential growth rates of anatomical parts, has been a central focus of the EvoDevo agenda in embryology, anatomy, paleontology, and systematics. The other hot topic, developmental constraints, typical of the early days of EvoDevo, was concerned with possible internal processes driving directionality on evolutionary change. Pere Alberch was a main actor in working out and spreading these issues. Thus, three seminal articles carry his mark: "Size and shape in ontogeny and phylogeny" (Alberch, Gould, Oster, and Wake 1979); "Developmental constraints in Evolutionary Processes, (Alberch, 1982); and "Problems with the interpretation of developmental sequences" (Alberch, 1985). They all had a long lasting influence in those fields, inspiring a whole generation of research that, in general (and contra Alberch's own recommendations), avoided any encounter with molecular mechanisms. Meanwhile, Developmental Genetics EvoDevo has been flourishing on its own, largely ignoring the rich empirical and conceptual literature that has accompanied heterochrony and developmental constraints throughout the years. Can both approaches be reconciled? Is the time finally ripe for the long awaited Gene-Pop-Devo-Eco->Morpho-Evo?

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Origins of EvoDevo: Gould and Alberch, Raff and Kauffman

In 1983, as a senior at the University of California, Santa Cruz, I enrolled in a grad seminar on Evolution and Development. Our text was Rudy Raff and Tom Kauffman's Embryos, Genes, and Evolution; we also read papers by a young professor at Harvard, Pere Alberch. What excited me about EvoDevo in general, and Pere's work in particular, was the prospect of finding developmentally determined laws of form, laws controlling the path of morphological evolution. Today, this vision has been marginalized within the field, to be replaced by the neo-Darwinian orthodoxy of workers such as

Sean Carroll and Hopi Hoekstra. Why has this happened? I argue that the fundamental problem lies in the teleological structure of selectionist explanations. The realization of Pere's vision of a broader evolutionary theory requires a reconciliation of selectionist and developmentalist accounts. This can come only through a reformation of the theory of natural selection itself.

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Pere Alberch, the internalist viewpoint of morphological evolution and amphibian metamorphosis

Alberch's contributions to the theory and practice of modern EvoDevo research are remarkable for their timing, breadth and impact. The two contributions that attracted me to his lab and have most influenced my research are his promotion of an internalist approach to the evolution of form, and his work on amphibian metamorphosis.

Alberch's internalist thinking focused on the discontinuous nature of morphological variation and the epigenetic nature of developmental systems. He predicted that the complex relationships between gene expression and cell behaviors could be reduced into a set of pattern-generating rules that govern the outcome of morphogenetic processes. He also emphasized the importance of epigenetic interactions as a buffer against intrinsic changes and as a focal point for evolutionary change. This largely nongenetic viewpoint has since been sidelined by the mainstream explosion of developmental genetics, which attributes cell fate and tissue form primarily to the actions of selector genes, gene cascades and cell signaling. This deterministic view of gene function and the claim that morphology evolves by mutations in cis-regulatory elements conflicts with the evidence that morphology is shaped by rule-bound cell behaviors. Interestingly, molecular studies of regulation and regeneration are uncovering patterns of gene expression and regulatory interactions that serve holistic purposes and reinforce the epigenetic nature of developmental systems.

Alberch's work on the throat cartilages of metamorphosing salamanders pioneered the developmental analysis of evolutionary differences in skeletal anatomy. While recent research on amphibian metamorphosis has focused on the regulatory role of thyroid hormone receptors, I am following in Alberch's path to understand the cellular bases of larval growth and shape change in amphibian cartilages.