Profile

Pere Alberch: Originator of EvoDevo

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In September 2008, 10 years after the untimely death of Pere Alberch (1954–1998), the 20th Altenberg Workshop in Theoretical Biology gathered a group of Pere's students, collaborators, and colleagues (Figure 1) to celebrate his contributions to the origins of EvoDevo. Hosted by the Konrad Lorenz Institute for Evolution and Cognition Research (KLI) outside Vienna, the group met for two days of discussion. The meeting was organized in tandem with a congress held in May 2008 at the Cavanilles Institute for Biodiversity and Evolutionary

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Figure 1.
Participants in the Altenberg Workshop, from left to right. Front row: Arantza Etxeberría, Ann Burke, Gerd Müller, Laura Nuño de la Rosa Garcia, and Charles Archer. Back row: Hernán Dopazo, Miquel De Renzi, Chris Rose, Diego Rasskin-Gutman, John Reiss, Richard Hinchliffe, and Emily Gale.

Biology (ICBiBE) in Valencia, Spain. The talks at the KLI were equal parts: nostalgic remembrance, excitement over new ways of thinking about old problems, and an unrepressed vitriol against the resurgence of reductionist thinking in EvoDevo. Here we highlight some of the key aspects of Pere's life and work that informed and infused the talks.

Life

Pere Alberch was born in Badalona, Barcelona Province, Spain, on November 2, 1954. He developed his interest in herpetology early, publishing his first paper in the field when he was only 19. He moved to the University of Kansas in the same year, where he completed a bachelor's degree with a double major in philosophy, and systematics and ecology in 1976. From here his path led to the University of California, Berkeley, where he studied under David Wake and George Oster. It was apparently the reading of Stephen J. Gould's *Ontogeny and Phylogeny* (1977) that ignited his lasting interest in the interrelationship of development and evolution. He pursued this interest with remarkable vigor, publishing a series of papers in the early 1980s in which he explored this relationship in empirical studies of salamanders, in mathematical models of development, and in a theoretical framework for the analysis of ontogenetic evolution. In so doing he developed concepts that have been central to EvoDevo ever since, including heterochrony and ontogenetic trajectories, developmental constraints, and generative rules.

Pere Alberch (1954–1998)

Pere moved to Harvard in 1980 as an assistant professor and began an ambitious experimental program in evolution and development, including his now classic work with Emily Gale on parallels between experimentally induced and natural patterns of digital reduction in salamanders and frogs as well as experimental and theoretical studies on amphibian metamorphosis. Together with Neil Shubin, a graduate student in paleontology, he developed a conceptual model for limb development based on the branching and segmentation of precartilaginous mesenchymal condensations. At the same time, he pursued a long-standing interest in teratology and the evidence that "monsters" provide about underlying generative rules of form.

Harvard was not quite sure what to do with Pere and declined to tenure him, to the shock of most of the community. Thus, in 1989, he moved closer to his native Catalunya to take up a position as the director of the *Museo Nacional de Ciencias Naturales* in Madrid. Here he immersed himself in the logistics and politics of rebuilding the museum while continuing his theoretical exploration of evolution and development as time permitted. He died in his sleep on March 13, 1998, at the age of 43. At the time, he was preparing to take up a new position at the ICBiBE, back at the Mediterranean coast, not far from his native Barcelona.

Holes in the Modern Synthesis

Central to Pere's early work was his perception that the Modern Synthesis was incomplete; it provided an understanding of adaptation, but had little to say on classic issues of morphological evolution such as parallelism, convergence, and long-term "orthogenetic" trends. It was here that he saw a crucial role for development in the evolutionary process. As he stated in what might be called his opening manifesto, the morphological expression of mutation is not random even though mutation at the molecular level may be: "epigenetic interactions drastically constrain the universe of possible morphological novelties and impose directionality in morphological transformations through phylogeny" (Alberch 1980: 654).

Heterochrony and Ontogenetic Trajectories

Gould's work on *Ontogeny and Phylogeny* (1977) presented a "clock model" for the description of heterochrony, or evolutionary changes in developmental timing. Pere found this model stimulating but inadequate, and together with Wake, Oster, and Gould developed a more quantitative and dynamic method of describing "ontogenetic trajectories" and the temporal relationship between them, resulting in a classification of modes of possible change in developmental timing based on changes in the rate and relative onset and offset times of developmental processes (Alberch et al. 1979). The underlying assumption of this work was that phenotypic changes in developmental timing obey relatively simple rules, because they are based on quantitative modifications of underlying processes. Later on, Pere moved to an even more dynamic and mechanistic view of ontogeny. He considered development not as a series of stages, as assumed in earlier models of heterochrony, but as a process of developmental events governed by basic construction rules (Alberch 1985).

Developmental Constraints and Generative Rules

In parallel with this work on the description of ontogenetic trajectories, Pere considered the relation of developmental systems to the distribution of form in morphospace. In opposition to those who would ascribe all limitation of organic form to natural selection, Pere argued that the nature of developmental systems imposes constraints on form, limiting the morphologies that can evolve to restricted regions of morphospace: "the role of selection is basically stabilizing, being responsible for 'pruning out' the nonfunctional morphologies . . . the realm of possible morphologies is basically determined by the internal structure of the system" (Alberch 1982a: 318–319). Drawing on Waddington's concept of the "epigenetic landscape," Pere argued that because development is a dynamic process, with a complex, hierarchical organization, there is only a limited number of stable states that the system can achieve (Alberch 1982b). These states impose directionality on the evolutionary process. Thus, developmental constraints (in spite of the name) are not merely a limiting but also a facilitating factor in evolution.

This clear conception perhaps explains Pere's disappointment with the joint statement that emerged from the Mountain Lake Conference on Development and Evolution (Maynard Smith et al. 1985), in which constraints were defined to include a hodgepodge of all factors that could limit changes in form, including selection for developmental stability, functional constraints on development, and lack of genetic variation. For Pere, constraints were not mere biases or limits to variation that restrict the power of directional selection. Instead, they were reflections of the "epigenetic properties" of developmental systems, or the "morphogenetic" or "generative" rules of development that act—together with selection—to direct the course of evolution. This is why in his later papers he paid particular attention to the concept of "evolvability." The ability of developmental systems to change in certain directions illustrated the constrained creativity of development.

In Pere's view, the basic variational properties of ontogenetic systems were established in the Cambrian, a period of creative exploration of developmental rules. Selection acts "not on the phenotype nor on the genotype, but rather on the emergent properties of developmental systems" (Alberch 1991: 10), a source of variation that allowed groups to evolve quickly. Then, developmental variation comprises the alteration of certain rules, while the structure of interactions at the gene and cell levels remains constant. This is why, Pere argued, our experimental perturbations are "only able to explore the potentialities of the [fixed] developmental system and consequently reiterating, for the most part, forms that had already been realized during the past 500 million years of evolution."

Modeling and Experimental Approaches to EvoDevo

What made Pere's work groundbreaking is that he took the general view that evolution is controlled by internal organismic mechanisms, a view which—as he was well aware—was common in the European literature (e.g., Riedl 1978), and he attempted to turn it into a theoretical and empirical research program. On the theoretical side, his work with George Oster and colleagues explored the variational properties of developmental systems using mathematical models. A key early model dealt with epithelia as a sheet of cells with certain viscoelastic properties of the apical microfilaments (Odell et al. 1981). Not only was this model able to reproduce many of the characteristic folding patterns seen in animal morphogenesis, but small modifications of the input parameters often produced great variation in the morphogenetic outcome. This variation could be ascribed to "bifurcations" in the morphological domains of the outcome space (Oster and Alberch 1982). The discreteness of the resulting morphospace was not only an empirical reality, but also a necessity coming from the processes inherent in dynamical systems. This view was a central theme in Pere's work, used again and again to elaborate a concept of evolutionary dynamics that would bring together the central tenet of punctuated equilibria (that morphospace is discrete) with the generative properties of developmental systems to account for these bounded domains.

On the empirical side, Pere's work with Emily Gale on digital reduction in amphibians remains classic (Alberch and Gale 1983, 1985). Here the morphological effect of a particular developmental constraint is studied experimentally. Experimental reductions in cell number in frog and salamander limb buds through the use of mitotic inhibitors led to loss of digits and phalanges, suggesting that the size of the limb bud during initial stages of pattern formation was critical in determining digit and phalanx number. Moreover, they showed that experimental digit loss started with digit 1 in frogs, but digit 5 in salamanders, precisely mirroring the patterns of digital reduction in natural species.

This work on limb development led to the formalization of patterns of formation of cartilage elements in the limb in the work he did with Neil Shubin. On the basis of detailed examinations of the early stages of limb development, they built a conceptual model in which the basic structure of the limb skeleton is laid down by a process of segmentation, branching ("bifurcation" in another sense), and de novo formation of precartilaginous mesenchymal condensations (Shubin and Alberch 1986). This model and its heterochronic variations could account for most of the diversity in limb morphology seen among tetrapods (e.g., Burke and Alberch 1985; Müller and Alberch 1990; Blanco and Alberch 1992). A key concept emerging from this model is that the central metapterygial axis of the fish fin has been bent into a "digital arch" in tetrapods. Moreover, fundamental features of this conceptual model were consistent with mathematical models of limb condensation patterning.

Finally, Pere examined the remodeling associated with amphibian metamorphosis, in particular the remodeling of the hyobranchial apparatus in the salamander *Eurycea bislineata*. Alberch and Gale (1986) were able to show that rather than simply converting the larval form into the adult, larval elements are destroyed, and adult elements form from undifferentiated "set-aside" cells adjacent to the larval elements. The underlying conceptual framework here is that the evolution of a new developmental pathway, using "set-aside" cells to make an adult cartilage, released the animal from constraints imposed by the larval morphology and allowed the evolution of an altogether new, more specialized feeding morphology (Alberch 1987).

Monsters

In the search for internal rules governing form, Pere was naturally led to teratology. The study of the logic of monsters has a long history from the internalist side of the perennial form/function debate, stretching back to the work of Étienne and Isidore Geoffroy Saint Hilaire in the early 19th century. Pere became interested in the evidence that monsters provide for internal control of form, precisely because such monstrous forms, obviously nonadvantageous from a selective point of view, recur again and again (Alberch 1989). If order appears even in monsters, such order cannot be ascribed to external selection, but instead must reflect internal variational properties of the developmental system. A classic example of such internal control of variation is the "cosmobiotic series" from cyclopia to axial duplication described by Wilder (1908), which Pere was able to relate to the underlying mechanisms of head development. An important point was that many different developmental perturbations, from genetic to environmental to experimental, could give the same morphological outcome: irrespective of the precise cause of the anomaly, "a cyclops will always have the nostrils above the single eye" (Alberch 1989: 46).

Art and Science

Pere was an exuberant, rich personality, and his interests extended from science to art, music, and philosophy. This led him to examine the limits of form as exhibited not only by organic processes, but also by artifacts and products of the artistic imagination, from prehistoric cave paintings to modern art. In this he followed the lead of another eminent developmental biologist, C. H. Waddington, for whom human knowledge required a multiverse of perspectives to account for the single reality, science itself not being a cyclops with a single eye: "man is Argus with innumerable eyes, all yielding their overlapping insights to his one being, that struggles to accept them in all their variety and richness" (Waddington 1969: 243). In considering form, Pere thought that the romantic tradition in art, which compares the organic process of development with the process of artistic creation, constituted an interesting source of ideas to understand form in a nonmechanistic way. Whereas in artifacts forms depend on functions established before the system is assembled, he intended to explore the realm of *forms without function*, that is, of forms not attending to external functional demands. In his last published work, written for the popular Spanish science magazine *Mundo Científico*, Pere considered what was probably a project for an encompassing theory of possible forms (including organic forms), artifacts, and compositions such as creatures of mythological stories or science fiction (Alberch 1998). In his view, the latter, although fictional and separated from reality, reflect the structure of the mind and the way we perceive the world. He speculated that we should not expect imaginary creations with parts not reminiscent of forms existing in nature, even though Joan Miró, one of his favorite artists, in his later years attempted to paint them. Pere called Miró's claim of having "liberated himself from reality" into question, because without some "hook" to reality, forms may not be conceived by the imagination, and even if they could, others looking at them would require some personal frame of reference to understand them: "it must be concluded that a universe of nameless objects could not exist in our brain" (1998: 23). Even the artist is constrained by the internal structure of the mind. In a joint experiment, the participants of the KLI workshop tested this proposition and found it supported by the results (Figure 2).

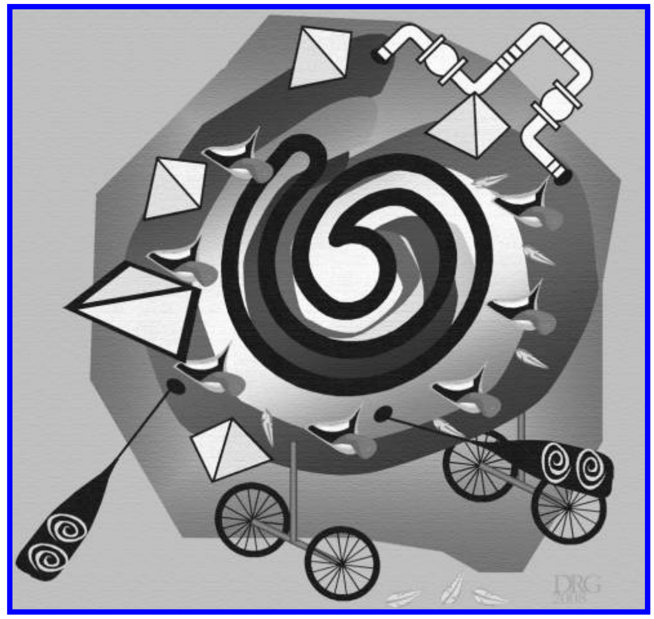

Figure 2.
Morphus alberchi resulting from the experiment by the workshop group. Redrawn by Diego Rasskin-Gutman from the original white board version.

Epigenesis, Genetic Reductionism, and EvoDevo Today

One of the most pervasive themes at the KLI workshop was the extent to which Pere's vision for the relevance of development to evolution conflicts with the predominant paradigm of today's EvoDevo, which for many is synonymous with evolutionary developmental genetics (even the term "epigenetics" is now mostly restricted to patterns of DNA methylation). Although quite cognizant of the role of genes in development, Pere insisted that the genetic level was not necessarily the most critical one for understanding how developmental systems can be modified in evolution. At the base of this argument was the conception of the developmental epigenetic system as a physiological one, one which could be perturbed by many factors. He was much influenced by the phenomena of phenocopies and genetic assimilation (Waddington 1957), in which experimental perturbations can result in phenotypic changes that mimic those caused by genes. As he put it:

> The internalist approach focuses on the determination of the "tracks" available for the railroad car to move on rather than on the forces that fuel the movement. From an evolutionary point of view, only perturbations based on genetic mutation are inherited—an argument often used to base the study of morphological evolution at the level of genes to the exclusion of any other levels of interaction. However, if we want to understand the organization of the generative system, we can gain insights by studying the results of perturbations at any of the levels of interaction. (Alberch 1989: 46)

Genes can affect morphology only by affecting cellular behavior. As the number of genes known to be involved in any developmental process increases, the role of each one is minimized. Whereas subsequent work in developmental genetics has emphasized the roles of selector or master regulatory genes, cell signaling, and gene cascades in specifying cell fate and tissue form, Pere's belief that the morphogenetic level is fundamental for the understanding of evolution is still germane, since morphogenesis is the only bridge that can give us full access to the logic of living forms. Only the convergence of the morphological, the theoretical, and the experimental approaches that Pere put into practice can bring a complete picture of developmental evolution. It may be that the scientific quest for understanding evolution will yet return to something like Pere's view.

Possible Peres

If he had lived, what would Pere be doing today? This question engaged several participants in the KLI workshop. Upon taking up the position in Valencia, would he have returned to a pursuit of theoretical modeling approaches to development, as one participant suggested? Or would he have become a fan of genomics, or systems biology, and delved into the gene regulatory networks involved in development, as another participant suggested? Or would he have returned to his fieldwork with salamanders, his first love? Unfortunately, we will never know. But it is clear that he would have continued to be fascinated by the problems of organic form, attempting to grasp the conditions for their establishment in biological as well as cultural evolution.

Participants at the workshop highlighted many of the themes of Pere's work, including the limits of the reductionist approach and of adaptationist explanations, the search for generative rules, the creation of possible monsters, and the development of an extended evolutionary synthesis, historically and beyond. They also presented new data on extant developmental pathways, and on conceptually matching the natural experiments of phylogeny with the results of experimental perturbations in the lab. Work on limbs and branchial arches continues, heterochrony goes on to mature, and generative rules and pattern formation remain a focus, with both paleontological endeavors and the new-found riches of molecular techniques.

The flavor of the meeting was classically Alberchian, exuberantly mixing data with theory, experiments with philosophy, and science with art. Interspersed talks from scientists and philosophers are not for the overly focused. A sandstorm of "isms" swirled around: reductionism, holism, internalism, externalism, selectionism, neutralism, determinism, emergentism, and interactionism. But above all, out of the swirl of terminology and jargon, debates, and diagrams arose a powerful sense of affection, wonder, and gratitude for the importance of Pere's vision.

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