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Cellular struggle at heart of variety

David Krakauer
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BIOLOGICAL SCIENCE

Title: **The Plausibility of Life: Resolving Darwin's Dilemma**
Author: Marc W. Kirschner and John C. Gerhart
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The central interests of Marc Kirschner and John Gerhart, explored in depth in their fascinating book *The Plausibility of Life*, are the many connections between evolution and development. It will be recalled that Charles Darwin knew nothing of genetics and very little about development. Nevertheless, he articulated clearly a process whereby locally random variation in heritable traits serendipitously improving function, when imperfectly replicated over many generations lead to morphologies and behaviours of great sophistication. His explanation, natural selection - a plurality of feedbacks that increase or decrease the probability of organisms leaving offspring - has proven to be an essential mechanism of cross-generational ordering. What Darwin could not know was where this local variation came from. Why do the offspring of lions not look like lemurs, and how is it that an overgrown jaw can survive centuries of breeding - the mandibular prognathism of the Habsburgs? These variational properties, which make natural selection possible, are not explained by the theory of evolution alone but require consilience with developmental genetics.

Kirschner and Gerhart refer to Darwin's silence on the origin of heritable variation as "Darwin's dilemma" and in this book present a range of important new ideas, under the general heading of facilitated variation, all of which attempt to explain interlocked developmental mechanisms able to compensate for, or enhance, the effects of random genetic variation. What makes Kirschner and Gerhart's position novel is that they have recognised that multicellular organisms are hierarchical structures made up from smaller elements (cells, organs, tissues), all of which engage in a struggle for existence within the larger body they constitute and on which they depend. One is reminded of Abraham Bosse's frontispiece illustration to Hobbe's *Leviathan*, which represents the state as monarch constructed from the bodies of countless individuals. Unlike William Paley's analogy of the organism as a well-designed clock, in which every part must be harmoniously pre-co-ordinated into the whole, the body more resembles a mini-ecosystem or economy, with many parts engaged in the generation of novelty in the pursuit of local competitive superiority, out of which comes the mutual facilitation of adaptive function and variation.

It is as if Adam Smith's invisible hand had reached down inside the organism, operating within a carefully regulated arena, promoting structures of increasing diversity, durability and complexity.

Readers will be introduced to the concepts of "weak regulatory linkage", whereby clusters of genes or cells are organised into modules that can be permuted like organic Lego blocks into structures of incredible diversity.

Like Lego blocks, the "atomic" biological components are conserved, but their constructions can be as various as Lego buildings, Lego aircraft and Lego robots.

The way the blocks come together is through processes of "exploratory behaviour" in which cells or tissues seek contact through signals released into the environment and that serve to stabilise the resulting associations. One of the great mysteries of evolution is how intricate structures survive a change in some part of their organisation. Kirschner and Gerhart show that in the economics of development, this perturbation can be compensated for through competition promoting reorganisation, much like a diverse economy recovering from the loss of a large firm. In addition to showing us the facilitated accessibility of morphologies, this book elegantly refutes the "intelligent design" contention that highly co-ordinated systems could not have evolved.

David C. Krakauer is research professor, Santa Fe Institute, US.

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