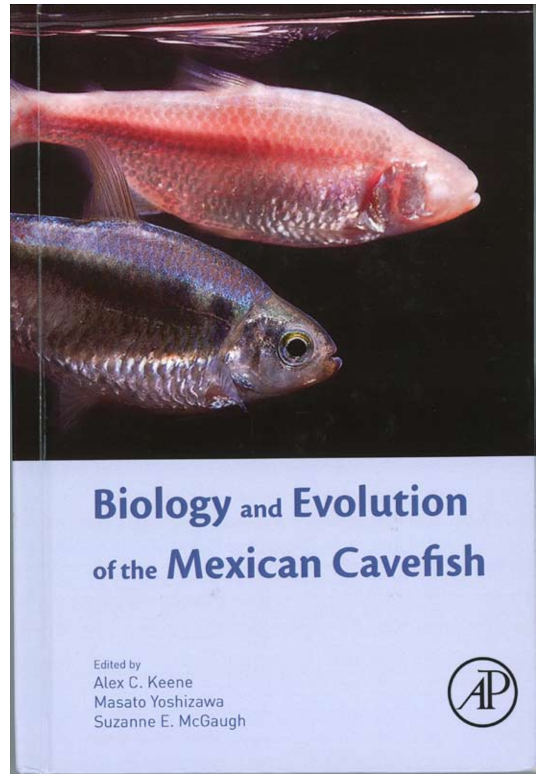
BOOK REVIEW:
THE BIOLOGY AND EVOLUTION OF THE MEXICAN CAVEFISH

Alex C. Keene, Masato Yoshizawa, and Suzanne E. McGaugh, editors, 2016, Elsevier/Academic Press, The Netherlands, 403 p., 6.1 X 9 inches, hardbound, $99.95, ISBN 978-0-12-802148.



The Mexican cavefish, *Astyanax mexicanus,* was first discovered and collected by Salvador Coronado in Cueva Chica in Mexico in 1936 and brought to the United States by steamer from Tampico by C. Basil Jordan. It is probably the best known cave animal, especially because it is commonly used in biomedical research as a model of eye development and because it is widely available in aquarium stores. Easy to raise in the lab, it also has the advantage, from an experimental point of view, of hybridizing with its surface ancestors, now placed in the same species as the cave populations.

Its reputation as a model for the evolution of adaptation to cave life is decidedly mixed. At first glance, Mexican cavefish look like their surface relatives except for the lack of eyes and pigment. Relative to other fish in caves, such as the North American amblyopsid fish and the Chinese cyprinid fish, the Mexican cavefish is pedestrian in appearance. First impressions can be deceiving. Sylvie Rétaux and her colleagues, in a chapter in the volume under review, point out that "anyone . . . who has a good sense of observation will at first have a hard time believing that they [surface and cave animals] belong to the same species." The pioneering study of ecology and distribution of the Mexican cave fish (Mitchell et al. 1977) suggested, based on geological, distributional, and hydrological evidence that the populations had been isolated in caves less than 100,000 years, a short time compared to the millions of years of isolation of amblyopsid cavefish. These observations all suggested that the Mexican cavefish was in very early stages of adaptation to cave life. This view was reinforced by the work of Horst Wilkens and his colleagues, beginning in the early 1970s and continuing to the present. Wilkens has championed the view that eye and pigment loss, the most visible of changes in the Mexican cavefish, was entirely due to the accumulation of mutations that reduced eye and pigment, and that these mutations had no advantage or disadvantage with respect to natural selection. The Mexican cavefish became a model for what is often called neutral mutation, but not for adaptation.

All this has changed, beginning in the early 2000s with the work of William Jeffery and his graduate students and post-docs (e.g., Jeffery 2001, Strickler et al. 2001). They showed that eye reduction was associated with changes in the jaw and in taste buds, and that not all proteins involved in eye development actually decreased in function in cavefish but, on the contrary, some increased. Taken together, their studies and many later studies reviewed in this volume make it impossible to sustain the view that the Mexican cavefish is a recent colonist of caves and that the changes are largely non-adaptive. The development of genomics, especially the ability to rapidly sequence genes, together with the ability to do eye transplants from surface to cave individuals, has established the Mexican cavefish as a model, not only of adaptation to caves, but of adaptation in general.

The editors have assembled not only many of the titans in the field, especially William R. Elliott, William R. Jeffery, Sylvie Rétaux, and Clifford J. Tabin, but also a new generation of biologists at the forefront of the emerging studies of the Mexican cavefish. The book is organized into five parts, with twenty chapters:

I. Ecology and Evolution
II. Genetic Diversity and Quantitative Genetics
III. Morphology and Development
IV. Behavior
V. Future Applications

There are opening and closing chapters by Tabin and Jeffery. Tabin, in whose Harvard laboratory many of the authors trained and who discovered the most fundamental genes of animal development, outlines the advantages of the Mexican cave fish as a model system, including its morphological variability and the ease of maintaining reproductive populations in the laboratory. Jeffery, whose pioneering work on the pathways of eye degeneration served as an impetus for many of the studies, closes the book with a review of the research groups involved with the Mexican cavefish, beginning in the 1940s and 1950s with José Álvarez, Charles Breder, and Perihan Şadoðlu.

Part I, on ecology and evolution, is especially welcome because relatively little has been written previously about what the ecologist G. Evelyn Hutchinson called the "ecological theater" of Mexican cavefish, compared to the "evolutionary play." There are two chapters by Elliott, who provides detailed descriptions of both the 29 caves with cavefish and the community of organisms that occupies the caves. One message from these chapters is that there is a wide variety of subterranean habitats occupied by the cavefish. One interesting point he makes is that the aquarium fish from Cueva Chica are atypical, both because they are from a hybrid population and because they have been subjected to many generations of artificial selection in aquaria. Espinasa and Epinasa provide a fascinating chapter on the hydrologic context and point out that many of the caves with cavefish, such as Cueva Chica and Cueva de El Pachón, are much younger than the likely age of the cavefish populations, so that it is a mistake to think current conditions are those under which the population evolved. Ornelas-García and Padraza-Lara review the taxonomic history, back to the time when each cave population was thought to be a separate species in the troglomorphic genus *Anoptichthys.* They hold that too much emphasis has been placed on hybridization in taxonomic considerations, that genetic evidence suggests that there are four or five separate cave invasions and species, and that these species may even have had different surface ancestral species in the genus *Astyanax.* While they do not formally describe these species, they set the stage for a reconsideration of the taxonomy of what we currently call *Astyanax mexicanus.*

Part II focuses on population genetics. Borowsky focuses on the decades-long debate about the relative importance of selection versus genetic drift (neutral mutation) in eye and pigment loss. He takes a statistical approach, rather than focusing on an individual pathway, and argues that eyes are lost through the direct (energy economy) and indirect effects (pleiotropy) of selection and that pigment is lost through drift. As more evidence becomes available, it remains to be seen whether his predictions will hold. O'Quin and McGaugh examine the genetic basis of troglomorphy (those traits convergent in cave populations) using quantitative trait loci that link genotype to phenotype. The technique, still in its beginning phases with respect to Mexican cavefish, offers considerable promise in the analysis of adaptation, especially the linkages between traits such as eye loss and taste bud number. They point out that except for albinism and the "brown" phenotype, all traits examined, morphological and behavioral, are polygenic. Rohner looks at natural selection even more directly. He examines the hypothesis, originally due to C.H. Waddington, that much genetic variation is canalized (i.e., silenced with respect to phenotype) and can be released by environment perturbation. He shows that such variation exists in surface populations and is released in cave populations, and it may be the important driver of adaptation. His suggestion that the environmental perturbation responsible is a drop in conductivity in cave streams cannot be generally true, since conductivity is typically higher in cave streams because water in contact with limestone rock increases in concentration of calcium ions. Nevertheless, this is really a quibble, because there are many candidates for the environmental perturbation of cave water, starting with darkness itself.

In Part III, on morphology and development, individual traits are considered. In general, the debate on selection and neutrality recedes a bit, and the focus becomes whether the hypothesis that a particular trait is adaptive. With the exception of eyes, pigment is the best-studied trait in Mexican cavefish, and while there is an emerging consensus about the involvement of natural selection in eye loss, there is no consensus about pigment. Jeffery and his colleagues provide an exceptionally clear description of pigment development in cavefish. They convincingly argue that while the number of pigment producing cells (melanophores) may be controlled by drift, melanin production is affected by natural selection, since the blockage of the conversion of L-tyrosine to L-DOPA allows L-tyrosine to increase activity levels in cavefish, an adaptation to low food. While they may ultimately be wrong, they very clearly lay out the evidence and the steps involved. Yamamoto lays out in detail the development of the eye and its degeneration in adult cavefish, pointing out the critical role of an increase in the activity level of the sonic hedgehog (*shh)* gene in cavefish. The increase in *shh* and other genes was one of the key findings that led biologists to look to natural selection as a cause of eye degeneration. Curiously, Yamamoto takes an agnostic view with respect to the selection-versus-drift controversy at the end of his chapter. Gross and Powers examine and document the changes in the craniofacial complex in cavefish, a topic deserving further attention. They document the differences between surface and cavefish and between different cavefish populations. Some of the changes are the consequence of eye loss and reduction in the size of the orbit, and many changes are difficult to characterize as adaptive or not. Atukorala and Franz-Odendaal look closely at the lower jaw and taste buds on the lower jaw. Their chapter is very much in the context of hypothesizing how the changes in jaw and taste buds are an adaptation and how they are linked to eye reduction. They make the point that taste buds and eyes are linked by the *shh* gene pathways. The final chapter in this section is by Rétaux and colleagues. They look at brain neuroanatomy and neurochemistry, documenting changes in the brain associated with loss of vision, such as an increase in olfactory components. It is a clear demonstration that there is more to Mexican cavefish than loss of eyes and pigment.

Part IV concerns behavior. Yoshizawa reviews sensory adaptation, emphasizing vibration-attraction behavior (VAB).

Occasionally found in surface fish and ubiquitous in cavefish, the lateral line system allows the fish to detect vibrations in the water. He carefully builds the case that VAB is an adaptation and connects behavior and morphology by showing that the quantitative trait loci for VAB and eye size overlap and that the position of taste buds in the lower jaw is connected to the 45° feeding angle. As Yoshisawa and collaborators have shown, the genetic bases of these two traits are entirely different, and thus are convergent in different cavefish populations. Perhaps more than any other system, the work on VAB, taste buds, and feeding angle is the closest to a complete adaptationist hypothesis. Volkoff also looks at feeding behavior, but focuses on the peptide regulation of feeding. She points to potentially interesting peptides like orexin, but comparisons between surface and cavefish have not been done. What she does is point out an interesting research agenda for future researchers. The same can be said for Duboue and Keene's study of sleep and Beale and Whitmore's study of circadian clocks. They point out the utility of these systems not only as models of adaptation, but also as models of study for the phenomena of sleep and rhythmicity itself. Hinaux and colleagues review social behavior and aggressiveness in cavefish. As they point out, schooling behavior is unimportant in a cave environment that lacks predators and may even be maladaptive in that it reduces foraging success. They are firmly in the adaptationist camp and propose the loss of territorial behavior and aggressiveness may be adaptive. In the final chapter of this section, Santacruz and colleagues pose the basic question of how the brain makes sense of space, especially in blind cavefish. This chapter also poses a research agenda, and proposes an expansion of the work that has been done on spatial orientation in Mexican cavefish.

Part V, on future applications, consists of a single chapter by Tabor and Burgess, who urge the Mexican cavefish research community to take up the techniques and procedures of transgenetics to understand more fully the biology of Mexican cavefish.

Anyone with an appreciation of cave life will find this book interesting. The earlier chapters are perhaps of more general interest and are the least technical in nature. However, all readers should find the final chapter by Jeffery on the social history of Mexican cavefish research interesting. As is the case for nearly all edited volumes, there is no one clear voice. For example, a number of authors mention the pigmentation system in Mexican cavefish and the gene responsible for albinism—*oca2*—but they do not all come to the same conclusion as to whether it has been subject to natural selection. Overall, the decades-long debate on selection versus drift is receding, and a number of the chapters ignore the role of genetic drift or only give it lip service. This is due in part to the success investigators have had in finding evidence that is hard to explain by genetic drift, such as the increased expression of the *shh* gene in cavefish, and in part, because it is easier to design an experiment to test the hypothesis of natural selection than it is to test the hypothesis of neutral mutation and genetic drift. Nonetheless, the issue is certainly not resolved, and what the book represents is a snapshot of the state of the field, clearly a very active and exciting one. While the authors represent the range of researchers working on Mexican cavefish, I find it a pity that two authors were not included. One is the great champion of neutral mutation and genetic drift Horst Wilkens, who is still active after five decades of research in the field. The other is a young researcher who is a leader in integrating behavior, morphology, and their genetic mapping, Johanna Kowalko. Her work is very much in evidence in a number of chapters.

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Reviewed by:
David Culver
Department of Environmental Science
American University Washington DC, USA