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No Age Limits: Can Mathematical Models of Fish Shed Light on Human Aging?

By Dana Mackenzie

The next time you sit down to a hearty plate of rockfish, you might want to approach it with a little respect. That fish may well be older than you are.

One of the longest-lived vertebrates, with ages as high as 205 years recorded for indivduals, the rockfish flourishes in the cool waters off the American and Canadian West Coast. It's a spectacular-looking fish, with dramatic spines and colorful stripes, which may account for its scientific name—*Sebastes*, from the Greek word for "magnificent." It can be found without much difficulty in grocery stores and restaurants on the West Coast, although it is usually mistakenly identified as red snapper. It's also a fish in trouble. Populations of some species of rockfish have been reduced to 2 percent of the levels reached before the 1960s, when intensive commercial fishing began. Because of their long life spans, they may take more than 50 years to return to their former abundance—if they ever do.

How Do You Tell a Fish's Age?

You don't ask a woman her age, and you can't ask a fish, either. Fortunately, for fish there is an alternative method. Fish have bones in their ears, called otoliths, that add a "growth ring" every year, just as a tree does. Because the otolith has a rather complicated shape, counting the rings is not an easy task, but it does provide a quick and dirty age estimate. Ichthyologists have compared otolith ages with more precise ages determined from radioisotopes, and found that the two match very well.

Competition-Inspired Diversity

The "magnificent" fish is also a magnificent puzzle to biologists. First and foremost, they would like to understand the secrets behind *Sebastes*' extraordinary life span. Differential equation models being developed by mathematical biologists like Marc Mangel, who is in the Applied Mathematics and Statistics Department at the University of California at Santa Cruz, may provide some answers.

"Rockfish are a wonderful system to study because they're really diverse," Mangel says. Indeed, the genus *Sebastes* comprises more than 100 species, which means that at least one new rockfish species emerges (on average) every 100,000 years. Much like Darwin's finches, they seem to be a genus for which biologists can watch speciation in action. "Another thing that's interesting about them," Mangel says, "is that within this one genus of *Sebastes*, the range of longevities is from a dozen years, for calico rockfish, to 200 years, for rougheye rockfish. These fish are more or less inhabiting the same environment, doing more or less the same kind of things. Why do they have such a range of life spans?"

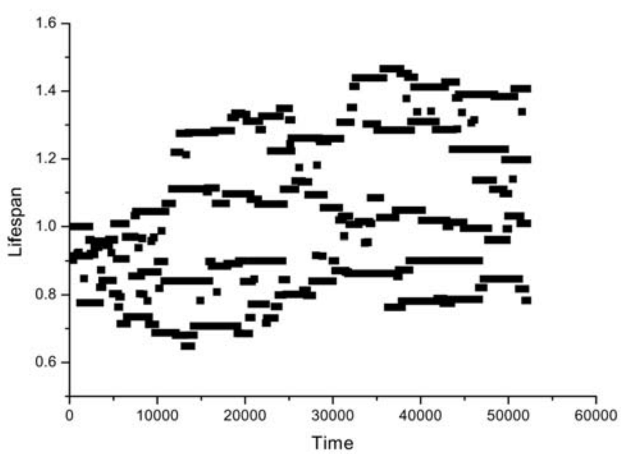


Figure 1. *Evolution of multiple species with different life spans from a single species with a life span of 1 time unit, in a simulation by Marc Mangel and Michael Bonsall. The model includes a set of differential equations that describe the population dynamics and competition between different species. It also includes a random mutation process that allows populations with different life spans to emerge (at a rate of roughly one mutation per 300 generations). Stable populations with diverse life spans emerge within 10,000 generations and persist for at least 40,000 more generations. The average life span of all the species increases gradually during this time. Reprinted with permission from "Life History Trade-offs and Ecological Dynamics in the Evolution of Longevity,"* Proceedings of the Royal Society of London B, *271 (2004), pages 1143–1150, Figure 4b.*

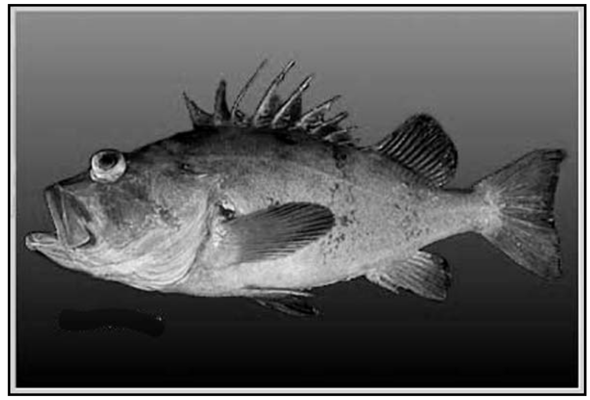
In a paper published last year in the *Proceedings of the Royal Society of London B*, Mangel argued that the rockfish's rapid speciation and long life have the same evolutionary cause, which he calls "competition-inspired diversity." Mangel and biologist Michael Bonsall of Imperial College London studied what happens when an established population of fish is invaded by a mutant species that's just getting started. If the mutant population cannot outcompete the established one for food, it will have to gain an evolutionary foothold in some other way. A decrease in its natural mortality rate (and therefore an increase in its life span) could do the trick. "If you go through the math, the invader can increase its numbers if its longevity is long enough," Mangel says. "So just this process of having to compete with another species selects for greater longevity."

But what happens next? Why doesn't the invader species drive out the established one? The answer is that if their life spans are different, the individuals of the two species will not necessarily compete throughout their lifetimes. They may have different metabolic needs at different times. Mangel and Bonsall assumed that the more distinct the life spans, the less the two species would compete for resources. They incorporated these life span-dependent competition rates into a standard differential equation model (the "Levins metapopulation model," named after Richard Levins, a biomathematician in the Harvard School of Public Health), and added in a reasonable rate of random mutations. What emerged on their computer screen was virtual speciation (see Figure 1). Within 10,000 generations, four distinct populations had emerged, each with a different life span. Over the next 40,000 generations, the number of species hovered between three and five, and the average life span of each slowly increased with time. "So we have a mechanism that generates diversity *and* longevity," Mangel says. "I think that's pretty impressive."

Boom-and-Bust Cycles

Competition-inspired diversity, however, is not the only possible explanation for the rockfish's unusual longevity. Depending on how you look at it, it's either a blessing or a curse that no one really understands the cause of aging. It means that mathematical biologists have many different ideas to play with.

Many biologists think, for example, that the long life span of *Sebastes* has evolved in response to the wide range of climatic conditions in which rockfish live, which translates into wide swings in reproductive success. El Niño events bring warm water to the north Pacific roughly every seven years, and the Pacific Decadal Oscillation causes temperature fluctuations on an even longer scale. Even without these fluctuations, the Pacific Coast is a tough place for a newly spawned fish to grow up. "You have the California Current flowing along the coast, and for a fish it's like living next to a freeway," says Alec MacCall of the National Marine Fisheries Center's Santa Cruz lab. Many larvae simply get swept out to sea and are never heard from again.



Sebastes levis, *the cowcod rockfish. Is* any *harvest rate for this fish too high? Some researchers think the answer is "yes." In 2001, a no-fishing zone was established off the coast of southern California; if this effort can reduce the cowcod catch to zero, the numbers of cowcod might reach pre-1960 levels in about 59 years. Photo by Milton Love.*

For all these reasons, rockfish are prone to boom-and-bust cycles. The number of juvenile rockfish can vary by a factor of 20 from one year to the next, and the bust cycles can last a very long time. According to MacCall, who keeps a census of ten rockfish species, the whole period from the late 1990s to the early 2000s was a demographic disaster.

As an evolutionary strategy, therefore, it makes sense for rockfish to live a long time and to spawn repeatedly, in order to "hedge their bets" against the lean years. But does it make sense mathematically?

From a Darwinian viewpoint, natural selection is not concerned with the life spans of individuals. It acts only to maximize the reproductive fitness of individuals. This can be measured by the natural rate of growth of the population—in other words, the birth rate minus the death rate. One of the oldest equations in biology, called the Euler–Lotka equation, relates this rate of growth (r) to the age structure of the population:

$$\sum l_x m_x e^{-rx} = 1,$$

where l_x represents the probability of survival from birth to age x, and m_x represents the number of offspring per female at age x. If you know the life history of a species—that is, the way it allocates its resources toward survival (l_x) or reproduction (m_x) at each age x—you can use this equation to compute its reproductive fitness.

There's one problem: The Euler–Lotka equation assumes a steady environment and a stable age distribution. Rockfish populations, with their boom-and-bust cycles, are anything but stable. Therefore, Mangel applied a stochastic model to simulate the variation in the environment, and replaced the constant growth rate r with a geometric mean of the growth rates in good years and bad years. As expected, he found that short-lived fish had fitnesses that were near zero or even negative. "They might spend their entire life in a bad world and never be able to reproduce," Mangel says. "The longer-lived fish are able to persist in this environment because they're able to wait for opportunities."

If rockfish need to live 50 years or more to ensure survival of the species, the consequences for fishery managers are very troubling. "It's been known for forty years that overfishing shortens life span," MacCall says. Fishermen tend to catch the largest fish, which are also the oldest. Over time, fish more than 50 years old practically disappear. In terms of absolute numbers, a particular species may not seem to be threatened, but it will not be able to weather a prolonged series of bad spawning years. According to Stephen Ralston of the National Marine Fisheries Center, that is exactly how the rockfish got into their current predicament. "We applied conventional thinking from other species," Ralston says. "Our harvest rates have been too high."

Some biologists, like Steven Berkeley of UC Santa Cruz and Milton Love of UC Santa Barbara, argue that *any* harvest rate is too high. The only way to keep the longer-lived species intact, they say, is to create marine reserves. Because most rockfish are relatively sedentary (they like to congregate around rocks or oil platforms), a no-fishing zone would allow some individuals to live to a ripe old age. In fact, such a zone was established for the cowcod rockfish in 2001 off southern California. If it succeeds in reducing the cowcod catch to zero, Berkeley and Love estimate that cowcod would take 59 years to return to their former numbers.

Fountain of Youth?

If we can only keep them around long enough, we might learn something from rockfish about prolonging our own life spans. For humans, it may be just a polite joke to say, "You're not getting older—you're getting better!" For *Sebastes*, it actually seems to be true. Seventy-year-old rockfish seem to be no more vulnerable to disease than ten-year-olds; in fact, the older fish produce more and healthier offspring, and are less vulnerable to predation. Biologists are currently studying the livers, brains, proteins, and DNA of rockfish to see if they can find clues about how they grow old without aging.

Even if biologists fail to discover a Fountain of Youth in the rockfish's genes, Mangel's mathematical models may still give us some ideas. His most recent project is a differential equation model of another type (called a "linear chain" or the "method of stages," depending on which book you learned it from) that describes the delayed effects of free oxygen radicals on an organism. Given enough data on the growth rate and metabolism of rockfish, Mangel hopes to use the equations to figure out how they apportion their energy between prevention and repair of oxidative damage. That, in turn, might suggest an anti-aging strategy for humans, whether it is limiting caloric intake (to slow the metabolism) or taking antioxidants.

"Having an overall evolutionary framework for the way organisms respond to oxidative damage will help us think about how humans respond to interventions," Mangel says. "Although I tend to think of these equations as characterizing fish, clearly with modifications they can characterize people."

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