One of the most controversial topics in genetics is genetic engineering. Organisms that have been modified genetically by introducing additional genes, often from other species, are referred to as transgenic organisms or genetically modified organisms (GMOs). The scientific objective of these gene transfers is to learn more about how genetics is expressed and how the genetic instructions are organized in organisms. The practical reason for producing transgenic organisms is to develop strains that have novel characteristics that often have economic value. Transgenic organisms have been produced in species that span the entire range of living organisms, including fishes. In this installment we will examine genetic engineering and how it can be done, the kinds of characters that can be altered, and some of the implications of developing transgenic organisms.
Genetically modified organisms (GMOs); genetic engineering! There, I’ve said it. Many people are extremely concerned about GMOs and regard them as somewhere between creations of Dr. Frankenstein and some evil mutant from outer space. They often envision creatures like the one in the movie *Alien*. The term GMO flips powerful emotional switches in many individuals. In this chapter, we consider the ways in which genetics can be used to alter characteristics (phenotypes: see Chapter 2. How Genes Vary in Fish Populations) of organisms. Clearly, there are mixed opinions about genetic engineering. Many opinions have some merit, but often the opinions are driven by emotion rather than fact, so we will also provide some facts as well as our opinions of the pros and cons. We will consider the pros first along with some of the underlying facts, but that does not mean that we are ignoring the cons because there are clearly serious issues that must be dealt with.

**The pros of genetic engineering**

Let’s step back and examine some facts. Genetic engineering in the broad sense involves manipulating the genetic composition of an organism to emphasize a trait that is in some way advantageous—to the population, society, industry, etc. Three common methods that are used for genetic engineering are genetic selection, ploidy manipulation, and gene transfer (also referred to as transgenics). For example, local adaptation, which we discussed previously in several different contexts, is “natural” genetic engineering. The genetic composition of a population changes in response to natural selection imposed by local environmental factors. Also, domestication selection (see Chapter 6. Genetics and Hatcheries) is usually inadvertent genetic engineering—the hatchery population changes in response to the conditions in which the fish are cultured.

**Genetic selection**

Genetic engineering has been practiced for tens of thousands of years. The term domestication that we used in the previous paragraph was not coined to describe hatchery fish; it describes the general process of taking a plant or animal from the wild, genetically (by breeding) removing many of the wild survival traits, and enhancing traits that we as humans think are useful or even aesthetically pleasing. Every agricultural crop, every breed of dog, cat, chicken—you name it—has been subjected to centuries and even millennia of genetic engineering. The principles of artificial selection, also known as selective breeding (see Chapter 2) work the same way in natural selection. When two individuals are mated, the phenotype of the offspring will tend to be more similar to the phenotypes of the parents than to those of other members of the population (on average) if there is a genetic basis for the trait. That means that if you breed larger, fluffier parents, the offspring will tend to be larger or fluffier, but only if there is a genetic basis for size and fluffiness. To see just how successful we have been, tune in a dog show on your television. Have you seen a hairless Chinese crested (Figure 1)? Clearly we have made substantial progress (sarcasm intended).

What we should not lose site of is that genetic engineering through selective breeding has improved lives all over the world and has successfully staved off hunger in many, but unfortunately not yet all, regions. Agriculture has developed crops that are resistant to many diseases, increased their production and efficiency, and altered many species to satisfy our tastes (both gustatory and aesthetic). Parallel progress has been achieved with animal breeds. For example...
in recent decades, the fat content of pork has been reduced (at our request) until it is now advertised truthfully as the other white meat (although many prefer the flavor of the older fattier varieties). All of these results come from selective breeding. Many of our domesticated animals and crops bear little resemblance to their wild ancestral sources.

**Ploidy manipulation**

“But,” you say, “that kind of engineering is ‘natural’ genetic engineering.” You are concerned by less “natural” engineering practices. Let’s take a look at another way in which we can genetically engineer an organism: ploidy manipulation. Most of the organisms we have considered so far are diploid; they carry two copies of information (alleles) for every gene (locus) (see Chapter 1. Even Fish Obey Mendel’s Laws). Diploid (2n) organisms are designed to produce haploid (n) gametes that restore the diploid number when fertilization occurred (i.e., the union of an egg and a sperm). Also, recall that the process of meiosis involves pairing of homologous chromosomes (chromosomes that carry the duplicates of the same alleles) during meiosis. It is part of the process that ensures that each gamete receives a complete haploid chromosome set.

One of the mechanisms that can isolate species is their chromosome complement. Most of the chromosomes carried by two closely related species have genes for the same traits and are very similar, if not identical. However, their genes may be arranged in different orders on their chromosomes, or the number of chromosomes may vary. For example, chum salmon carry 76 chromosomes (38 pairs), whereas pink salmon carry 52 (26 pairs). Natural hybrids between pink and chum salmon do occur. They are called chumpies, and carry 64 chromosomes (38 from the chum parent and 26 from the pink salmon parent). However, most chumpies are sterile because their chromosomes fail to find appropriate partners during meiosis (again refer to Chapter 1); and most of their gametes do not carry an intact haploid complement. As a result, mating hybrids to each other or to one of the parental species is usually unsuccessful. Just like a mule, the hybrid itself may be vigorous but it cannot produce offspring. Another example is a pink salmon egg fertilized by a chinook salmon sperm. The chinook-pink hybrids possess some characteristics that are advantageous for mass culture: they have early seawater tolerance like the pink salmon parent, carcass characteristics that are more similar its chinook salmon parent (most people would rather eat chinook salmon than pink salmon), and it is mostly sterile. In Alaska, the point is moot because pen-fish (intensive) farming is illegal, but in other areas that have numerous pink salmon and a few chinook salmon, the hybrid between chinook males and pink salmon females would be an attractive product. A few naturally occurring pink-chinook hybrids are found in the Great Lakes, but neither species is native there.

Induced polyploidy (see sidebar 1) can also be used to produce organisms that are usually sterile. Triploid females have been used in intensive (captive; see Chapter 6. Genetics and Hatcheries) trout culture because the females do not usually mature. This means that the energy ordinarily devoted to gamete production can be diverted to growth. Triploid fish have also been released to put-and-take fisheries. The idea is that they will not reproduce, but they will grow, so that the pond or lake will be populated by fish that grow to trophy size without contributing numerous small competitors that may prevent any fish from growing to appreciable size. Triploidy has been used extensively in the cultivated oyster industry. Triploid oysters provide a marketable product over most of the year, whereas diploid oysters undergo changes associated with reproduction that make them less palatable during summer months. Because of the triploid oyster, the industry in Washington state has grown tremendously since it was developed in the early 1980s.

What most people do not realize is that many of our agricultural crops are polyploids. The commercially cultivated banana is triploid (3n), has no fertile seeds, and is propagated from cuttings. Modern wheat is a hexaploid (6n) derived over thousands of years from hybrids that involved three different ancestral species. Most of our ornamental flowers and many of our cultivated crops are polyploids.

Polyploidy is a natural process. Salmonids (salmon and trout) and catostomids (suckers—the fish) descended from tetraploid ancestors. In fact, the entire vertebrate lineage was very probably made
THE WORLD OF POLYPLOIDS

There are many examples of organisms in which the entire chromosome set has been altered. Organisms that have multiple sets of chromosomes are called polyploids. On occasion, polyploids occur naturally. Of greatest relevance to us as vertebrates, are two chromosome doubling events that occurred during the emergence and evolution of the vertebrate lineage from invertebrates. There have been at least two events in which the entire complement of chromosomes doubled. The first event occurred at about the same time that craniate vertebrates (vertebrates with well defined heads) emerged. The additional genetic information may have provided the evolutionary fodder necessary to provide instructions for the new structures (head and gills) in lampreys and hagfish. A second doubling may have occurred at about the time that jawed vertebrates (cartilaginous and bony fish) emerged from the jawless vertebrates. It is likely that the extra information was modified to construct jaws and gill arches. After duplication, the genes and the chromosomes that carried them usually diverged until they became distinct—the tetraploid organisms became diploidized.

In addition to the duplications shared by all jawed vertebrates, some groups of species underwent a third duplication. Salmon and their relatives are descendants of a third duplication, and many of their genes retain a small amount of their tetraploid (4n) nature because the duplicated genes have not yet completely diverged. Members of the sucker family (Catostomidae) also arose through a ploidy event, but rather than a simple duplication of the chromosomes of an ancestral species, suckers arose from a hybrid ancestor in which the chromosome number doubled to include a complete set of chromosomes from each of the ancestral species.

These kinds of rearrangements were important in our evolutionary history, but they did not occur frequently. In contrast, polyploidy is very common in plants. Many cultivated plants, including numerous ornamental flower species, are polyploids. Another example is modern wheat, which arose from three different ancestral species, first through an ancient hybridization and doubling (to 4n) followed more recently by a second hybridization and doubling to a hexaploid (6n) set of chromosomes; hexaploid wheat undergoes normal meiosis.

When polyploidy results in an odd number of chromosome complements (3n, 5n, 7n, etc.) meiosis is disrupted. Most triploids (3n), pentaploids (5n), etc., are sterile because most species with odd ploidy are unable to produce gametes that have a single intact set of chromosomes, so there is no way that their gametes that will restore ploidy in the fertilized egg. Many cultivated plants have odd ploidy and only regenerate vegetatively. Often female triploids fail to produce gametes. For example, the common banana and seedless watermelons are triploid and boysenberries are heptaploid (7n); all are sterile and reproduce vegetatively.

Above we saw that polyploids can occur naturally and we looked at some examples. It is also possible to manipulate entire chromosome complements and “create” polyploids. The technology is simple. Heat, cold, or pressure shocks applied to recently fertilized eggs can block the second meiotic division. The result is that the egg provides two chromosome sets and the sperm provides one, and the result is a triploid.
The Lowdown on Frankenfish  79

possible by two genome duplication events (see sidebar 1). The bottom line is that polyploidy is a natural phenomenon that has played an important role in the evolution of flora and fauna on earth.

Transgenics
The term “genetic engineering” often conjures up an image of mad scientists transplanting genes from one organism to another in exotic combinations that produce “monsters.” Although there is potential for abuse, there is also potential for societal benefits, such as enhanced world protein production and superior food quality. Because of the potential risks, transgenic research and product development in many countries are stringently regulated to prevent applications that might pose ecological, genetic, or health threats.

Although gene transfer is relatively easy to accomplish with plants, it is very difficult to do with animals. In principle, genetic selection accomplishes this slowly by aggregating the genes responsible for a desirable phenotype in a single population or lineage. Gene transfer, however, is more focused (sidebar 2). An authoritative source on the benefits and potential drawbacks of transgenic plants and world agriculture can be retrieved at http://books.nap.edu/html/transgenic/. The publication was produced by the Royal Society of London, U.S. National Academy of Sciences, Brazilian Academy of Sciences, Chinese Academy of Sciences, Indian National Science Academy, Mexican Academy of Sciences, and Third World Academy of Sciences.

Genes coding for growth hormones have been successfully introduced into fish, and expression of those genes has been documented. In many cases, faster growth has been observed. For example, a chinook salmon growth hormone gene was successfully introduced into chinook salmon, coho salmon, and rainbow trout; and an additional tilapia growth hormone was introduced into tilapia. The transgenic coho experienced a sevenfold increase in average size at 15 months of age, compared to controls. In all of these species, some of the fish were mosaics, which means that the gene was expressed in some tissues but not in others. However, some of the fish were transgenic; and in tilapia, the introduced genes were followed into the fourth generation. Much more work is required to ensure that there are not additional unexpected deleterious results such as sterility, lethargy, and weakness, which accompanied growth hormone gene transfer in swine. In another transgenic application, a gene for an antifreeze protein, which is synthesized by some species of arctic and Antarctic fishes, like the winter flounder, has been successfully introduced into Atlantic salmon (Salmo salar) with the hope that it might increase the survival of pen-reared fish in very cold waters.

Recently, some experiments have examined the interactions of coho salmon that are transgenic for a growth hormone gene with wild coho salmon. Under normal fish culture conditions, the transgenic coho grow very fast. They are voracious feeders and will eat the smaller wild fish, and eventually they dominate in the system. In experimental streams from which escape is not possible, the only food that is available is produced by the stream (e.g., insects). Under these conditions, relatively little food is available and the transgenic fish starved, which left only wild fish. This does not mean that releasing the transgenic fish poses no threat, but it does suggest that the threat may be less than we might imagine, at least in some instances. Obviously many more tests will need to be conducted before these fish would be considered safe for intrinsic culture applications.

Some transgenics may occur naturally. Dr. Peter Davies (Queen’s University, Ontario, Canada) reports that three distantly related species of very coldwater (–2ºC) fishes—herring, rainbow smelt, and sea ravens—naturally carry an antifreeze. Amazingly, the three antifreeze proteins are very similar and unlikely to have arisen independently in three parallel evolutionary lineages. Davies and his team speculate that the genes that specify the antifreeze proteins jumped from one species to another. Horizontal or lateral transfer (passing genes from one species to another) is common in bacteria, and occasionally viruses help genes move from one species to another. However, movement of genes from one animal to another has not been previously reported. The mechanism proposed by Davies might occur because most fishes have external fertilization. That is, males squirt sperm over eggs that have already been released or laid by females. If two fish are spawning at the same time and location, a sperm might stray and attach to the wrong egg. Ordinarily, a hybrid between two such
## Sidebar 2

### HOW IS GENE TRANSFER ACCOMPLISHED?

Gene transfer, or transgenics, provides another powerful tool with which favorable phenotypes can be developed. Of course, all tools should be used with care, but the development of molecular techniques has made genetic engineering possible and now provides exciting possibilities for developing aquacultural products. An entire industry has emerged that is based on genetically modified bacteria that produce valuable biochemicals. For example, the human insulin gene has been cloned into bacteria, which now produce insulin identical to that produced by humans for the treatment of diabetes. The process involves introducing a functional gene from another organism (a human in the case of human insulin) and getting the recipient organism to express that gene.

The technology for developing transgenic plants is quite advanced and relatively easy to accomplish, compared to animals. One of the reasons is that many plants (even sexual species) can reproduce vegetatively. The primary applications for transgenic crops at this time are herbicide tolerance and insect resistance. Transgenic crops that are grown in abundance worldwide are soybeans, cotton, corn, potatoes, rapeseed (canola oil), squash, and papayas. The United States, China, Argentina, and Canada are among the countries that grow these crops.

How is gene transfer done?
To accomplish the transfer, a gene (DNA) is introduced into the nucleus of a recipient cell; a successfully transferred gene becomes inserted into and becomes part of one of the recipient chromosomes. The gene transfer process is simple conceptually, but very difficult to accomplish in animals. Introduction is ordinarily done by microinjection (a miniature syringe-like instrument that punctures a single cell) or similar method to pass the gene across the cell membrane into the nucleus. Eggs or embryos are ordinarily used because there are only one or a few nuclei, the nuclei are accessible, and the tissue has not irreversibly differentiated into cell lines other than the germ line.

<table>
<thead>
<tr>
<th>What are the requirements for a “successful” transfer?</th>
</tr>
</thead>
<tbody>
<tr>
<td>First, a successful gene transfer is permanent and the recipient passes its transgene to its offspring. Second, the offspring express the gene. Unfortunately, there is little control over where the gene is actually inserted into a chromosome; but expression of the introduced gene depends to some degree on the location at which it inserts into the recipient’s genome. Also, insertion of the gene into the recipient’s chromosome is no guarantee that it will be expressed, because gene expression is usually switched on by sequences that signal the position of the gene and the circumstances under which it is to be expressed. These signal sequences, appropriately called promoters, are often part of the transgene package that is transferred into the recipient. Expression of many genes is also enhanced or hindered by complex interactions with a variety of DNA-binding proteins called enhancement factors.</td>
</tr>
</tbody>
</table>
different species would die. However, if the egg had already been fertilized by the right sperm, it might be possible for a small amount of the foreign DNA to be incorporated into the zygote. On rare occasions, the small amount of foreign DNA might include a useful gene, like the antifreeze gene. For more discussion see http://www.theelectronicconomist.com/science/displaystory.cfm?story_id=11703152.

And now the cons of genetic engineering

The promise of genetic manipulation is the ability to design organisms with characteristics not found in nature, and others with characters that have been enhanced. This promise of genetic engineering also raises serious concerns. Intentionally engineered organisms may have a competitive advantage over native species and displace them or even disrupt the ecosystem. Because of the unpredictability and the potential adverse impacts, extreme caution must be exercised in developing and evaluating engineered fish.

Genetic selection

Natural selection is a normal process that occurs during local adaptation and evolution. The process is essential for the long-term persistence of most species. Both directed and domestication selection, however, result in phenotypes that may not be “in harmony with nature.” In captive culture, the selected traits may increase economic value as a result of improved product or easier culture, such as fryer hens that are ready to market in six weeks. The phenotypes produced by directed selection may or may not be maladaptive in the wild, although chances are they will be, or else wild populations would evolve in the same direction. The cultivated fryer hens would not have survived long in my grandparent’s farm, where chickens roamed at will, because the fryer hens have adapted to being fed high quality (to chickens anyway) food and inoculated for disease. They are ill suited for making it in the nature of the chicken yard. There are other concerns with directed selection. One is that over many generations, genetic variation is generally reduced both by the selection process and by the relatively smaller numbers of breeders that are practical to maintain (see Chapter 6. Genetics and Hatcheries). A second concern is that a trait chosen for selection is often correlated to other traits that are also inadvertently selected for. For example, early growth rate in coho salmon is often correlated with early returning precocious males—jacks. This means that many stocks selected for rapid growth during their early lives will mature in a short time as very small individuals. It is well known that these precocious males are excluded from hatchery brood stock and have little economic value. Consequently, directed or inadvertent selection for early growth rate may be counterproductive in culture operations.

In defense of these little guys, jacks often play an important role in maintaining genetic variation in populations. Obviously, they contribute genes that influence growth and maturity that may be less abundant in the rest of the population; but of more importance, they genetically tie together different brood years. For example, in many areas most coho salmon mature at three years. If the two-year-old jacks were not allowed to contribute genes, the populations would become three genetically isolated lineages (analogous to the two brood lines of pink salmon). Because the two-year-old coho jacks carry genes between what would otherwise be three genetically isolated lineages, they increase the genetic resources to all three, and help to stabilize the species genetically.

Most directed selection is designed for organisms produced by intensive culture; that is, pen culture or artificial culture systems that isolate the cultured organisms from wild organisms. Escapees from the culture facility may interbreed with wild fish, which can result in gene flow. As we saw in Chapter 6, occasional cultured strays may be genetically tolerated in a wild system because their few maladaptive genes will be removed by natural selection. However, persistent gene flow from the cultured stock will change the genetic composition of the recipient wild population. Note that pathology risks are a separate issue. Fish ranching operations (see Chapter 6), however, will probably produce persistent straying that can modify local wild populations. If domestication selection occurs in the culture environment, the genetic changes in the wild population are probably for the worst.
Ploidy manipulation

Clearly, there are some polyploids and hybrids that possess characteristics that may be useful or beneficial in a variety of fisheries management or cultural settings. Where a sterile or nearly sterile organism is advantageous—such as for a put-and-take fishery—they are ideal, particularly if the system is isolated (a pond or barrier lake) and the possibility of a very small amount of fertility is tolerable. Unfortunately, some interspecies hybrids are not completely sterile, and even offspring of hybrids like chumpies have a low survival (about 1%).

Under many circumstances where ploidy-manipulated organisms are cultured or even stocked, they pose little or no genetic threat in isolation. However, other species such as Asian oysters are often introduced for commercial culture outside their native range. One of the problems is that the process that produces triploids may not be 100% efficient and residual diploids may be present. Also, some triploids can undergo a bizarre meiosis that results in a few viable diploid gametes. Under such circumstances, the species may have sufficient fertility to establish self-perpetuating diploid populations, thereby resulting in an exotic introduction. Exotic introductions such as the rabbit to Australia or lampreys into the Great Lakes often cause severe ecological repercussions, but the extent and nature of their effects cannot be predicted in advance. The Chesapeake Bay oyster industry has suffered severely from disease problems. The nonnative oyster from Asia, however, appears to do well there and is resistant to some of the diseases. The dilemma has been how to proceed—keep working with the disease-susceptible native species, culture triploid Asian oysters with a small risk of permanent introduction, or culture diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area. The conclusion reached by the National Academies committee (http://dels.nas.edu/dels/rpt_briefs/oyster_brief_final.pdf) was to cultivate triploid Asian oysters because introduction of the nonnative diploid Asian oysters that surely will take hold in the area.

Transgenics

Gene transfers have the advantage that only one or a very few genes are introduced and need to be monitored. The disadvantage is that it is difficult or impossible to predict in which chromosome and at what location on the chromosome the gene will be inserted. Unfortunately, the site of insertion can influence the extent to which the introduced gene and genes near the insertion site are expressed. In addition, the promoters (see sidebar 2) that turn on expression of the transgenes require subcellular-level signals that will promote their expression. Questions that can result include, “Is the transgene expressed at appropriate times?” and, “Is the transgene expressed in a tissue that will make it useful?”

For plants, the issue is the effect of the transgenic product designed to ward off insects; in humans, it is the possibility of “shedding” genes; and in general the worry is the potential change in the ecological role of the transgenic organism. The most troubling issue for transgenic animals is the ecological effect they might have in the wild. It is difficult to foresee the possible negative results that might occur, but that does not mean there will not be any; and the possibility that a transgenic organism will behave like an introduced exotic cannot be ruled out without extensive evaluations. One modeling study suggests that a trait like size, which could increase mating success, might give the transgene an advantage in a wild system. The problem is that even if the progeny of the transgenic line were less viable, the transgene (which was referred to as a “Trojan” gene) might flourish in the population because of sexual selection, but ultimately erode the fitness of the population if the new phenotype (size for example) is maladaptive.

Fact can be stranger than fiction, or Monsters of the Deep (and not so deep)

Mother Nature is the ultimate genetic engineer. Some of her results would chill the most enthusiastic monster film aficionado and her products even serve as models for film producers. Examples include human flesh-eaters, species that have absolutely disgusting habits, hideous looking creatures, and incredibly venomous fish.
The man-eaters
Of course, sharks immediately come to mind when we think of man-eaters. The most attacks on humans have been great white, tiger, and bull sharks (http://www.flnmh.ufl.edu/fish/sharks/statistics/species2.htm), although most of the Internet sources stress that the majority of attacks resulted from provocation or carelessness. Many sharks are indiscriminant about what goes into their mouths. A variety of weird (and indigestible) items have been found in the stomachs of tiger sharks that includes ladies’ pajamas, a roll of chicken wire, rubber tires, shoes, rags, a bag of potatoes, bottles, tar paper, a sack of coal, and a spam can (http://www.tiger-shark.info/). Clearly, they are not too discriminating, so a wiggling appendage or two would not be ignored. At the voracious “killer Pomeranian” end of the spectrum is the notorious piranha. As you have doubtless seen many times on the screen, these fish attack in packs and can strip the meat from the bones of a large mammal in very short order. One of my friends kept an aquarium for pirhanas—at the head of his bed. One morning he awoke to a piranha lying next to him staring him in the face. I guess it miscalculated its jump.

The ugly
There are some frighteningly ugly fish out there that range from sort of cute to absolutely hideous. My favorite ugly cute fish is the spiny lumpsucker (Figure 2). These little guys are nearly spherical and move around rocks like little helicopters. I could watch one (and have, in an aquarium) for hours.

On the scarier side are the viperfishes (Figure 3). These fish live in very deep water and have bioluminescent structures on their bodies that probably attract food organisms and mates. Its fangs would make Dracula jealous, and are so long that they curve back along the side of its head. The hinged jaw opens very wide to trap unsuspecting prey. Their stomachs are large and expandable, so they can take advantage of prey when it is abundant.

The gross
Some species have disgusting personal habits. One is the South American candiru (Figure 4) or, as the locals call it, the willy fish. It is a small catfish. Candiru ordinarily parasitize the gills of larger fishes. They lurk in the mud at the bottom of the river and “sniff” out currents of nitrogenous wastes that flow from fish gills. Then they dart out, follow the stream, attach to the gills of the prey by lodging in place with its spines, and feed on the blood flowing through the gills. Occasionally they make a mistake and follow a current of human urine or other material, which also carries nitrogenous waste products, into a genital or other orifice where they are stuck because their spines prevent them from going backward. The consequences are bad for both the fish, which die, and the person they attacked, who suffer shock.
and infection. The fish must be removed surgically. Candiru can be surprisingly large—the largest grow to more than six inches. I would presume that the smaller ones are more dangerous to most humans.

Another misleadingly named fish is the pearlfish. Some pearlfish back into sea cumbers, tail first, and live on the cucumber’s internal organs. There is no getting around it; this must be uncomfortable for the host. The good news, however, is that some sea cumbers expel their innards when threatened and then regenerate them. So, at least the host can replace its devoured parts.

The most disgusting of all fish, however, may be the hagfishes (slime eels) (Figure 5). These jawless marine fish lurk in the mud and wait for sick, dead, or hooked fish to sink near them. Hags then enter the fish through whatever opening may be available, even the eye socket, and eat the fish from the inside. Occasionally, their prey are hooked by fishermen. Just imagine on the deck of the boat a fish from which several “alien-like” creatures emerge. And just to be sure they retain the title of grossest conceivable fish, they secrete a slime that can turn a bucket of water into jelly in no time. So how do they unslime themselves? They tie themselves into a simple (overhand) knot and pass the knot from one end to the other to remove the slime in a single glob. After one had slimed me and a laboratory sink, I was forbidden by a senior laboratory technician ever to bring a hag into her lab again. And she was tolerant of (although not an admirer of) lampreys!

**The venomous/poisonous**

A **venomous** organism delivers venom by injection or piercing. **Poisonous** organisms are harmful when eaten or touched. Many fishes use venoms or poisons as a defense. The poison tetrodotoxin shows up in Ian Fleming’s James Bond thriller, *From Russia with Love*. That novel ends in a cliffhanger. Bond was kicked by a spike-tipped shoe laced with tetrodotoxin, and we had to await the next book in the series to learn his fate. The neurotoxin is produced by symbiotic bacteria in the pufferfish (fugu) (Figure 6), which is the second most toxic animal in the world after the golden poison frog. Tetrodotoxin blocks nerve function. Tetrodotoxin is also concentrated from...
bacteria in the blue ring octopus, whose bite can be terminal. Tetrodotoxin is concentrated on the skin, liver, ovary, and other structures of the puffer. So how do puffers and other species that carry tetrodotoxin avoid poisoning themselves? Of course the answer is genetics! They have an alteration of a single nucleotide in the gene that encodes the structures (ion channel in nerve endings) that are blocked by tetrodotoxin.

Fugu meat and other parts are a delicacy in Japan, even though there are a number of deaths each year from fugu poisoning. Fugu chefs are licensed after they have received extensive training (10 years). The chefs are also expected to kill themselves if one of their customers dies from fugu poisoning. Raw fugu (sashimi) is very delicate and tasty. Yes, I survived several servings, but I did not experience the buzz that some say accompanies eating fugu. An interesting overview of fugu can be seen at http://www.thingasian.com/stories-photos/3048.

The stonefish (Figure 7) is the most venomous fish in the world. Its dorsal fin includes numerous spines that release venom from two sacs attached to each spine. The venom is a mixture of proteins, which include hemolytic, neurotoxic, and cardioactive toxins. Typically, surviving victims suffer localized nerve damage that occasionally leads to atrophy of nearby muscles. The venom causes severe pain with possible shock, paralysis, and tissue death depending on the depth of the penetration. The pain has been called the worst pain known to man and victims often plead to have the affected limb amputated. A stonefish sting can be fatal to humans if they are not given medical attention within a couple of hours.

It should be clear from these examples and your own worldly experience that Mother Nature is an awesome genetic engineer.

Summary

Geneticists and culturists have an obligation to thoroughly evaluate potential genetic and ecological effects of introducing genetically engineered fish into natural systems or culturing them where they may escape. One of the fears many people have is that regulatory agencies will not be sufficiently stringent in their oversight. That is an issue that cannot be disregarded out-of-hand. But that particular fear pervades many areas of government oversight and is a political problem rather than a biological problem. Obviously, clear communication is part of the solution to such problems.

In spite of those and other caveats and issues, genetic engineering has the potential to increase protein and food production, which is badly needed to meet the world’s growing demand in face of dwindling resources. That fact alone will keep the genetic technologies in the foreground. Given that reality and the enormous economic potentials of
transgenic organisms, we will need to apply our knowledge cautiously and wisely, during the next few decades. If we can accomplish that, we should be able to benefit from natural production and also take advantage of benefits that genetic engineering may provide, without compromising our natural resources.

Finally, it should be recognized that genetic engineering occurs naturally. Not only does Mother Nature produce some exciting and bizarre creatures, but some of the methods she uses might even involve transgenics, moving genes from one organism to another.