



THE QUEST TO DISCOVER HOW LIFE WORKS SEAN B. CARROLL AND WHY IT MATTERS

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Suppose it were perfectly certain that the life and fortune of every one of us would, one day or other, depend upon his winning or losing a game of chess. Don't you think that we should all consider it to be a primary duty to learn at least the names and the moves of the pieces? . . . Yet it is a very plain and elementary truth that the life, the fortune, and the happiness of every one of us, and, more or less, of those who are connected with us, do depend upon our knowing something of the rules of a game infinitely more difficult and complicated than chess. It is a game which has been played for untold ages. . . . The chessboard is the world, the pieces are the phenomena of the universe, the rules of the game are what we call the laws of Nature.

-THOMAS H. HUXLEY, A LIBERAL EDUCATION (1868)



FIGURE 1 The Naabi Entrance Gate, Serengeti National Park,

Photo courtesy of Patrick Carroll.

INTRODUCTION

MIRACLES AND WONDER

The corrugated gravel road known officially as Tanzania Route B144 provides a bone-jarring, teeth-rattling, bladder-testing connection between two of the great wonders of Africa.

At its eastern end stand the massive green slopes of Ngorogoro Crater, a giant, more than ten-mile-wide caldera formed by the collapse of one of the many extinct volcanoes of the Great Rift Valley, and home to more than 25,000 large mammals. To the west lie the vast plains of the Serengeti, our destination on this cloudless, postcard-perfect day.

The route in between is a stark contrast to the lush Ngorogoro highlands. There is no visible source of water; the Maasai herdsmen and boys we pass in their bright red shuka graze their livestock on whatever brown stubble they can find. But as we bounce our way through the first simply marked gate to Serengeti National Park, the landscape changes.

The Maasai vanish, and the nearly barren tracts they use are replaced by straw-colored grasslands, and instead of cattle and goats, sleek black-striped Thomson gazelles look up to see who or what is kicking up dust all over their breakfast.

The anticipation in our Land Cruiser rises. Where there are gazelles, there may be other creatures lurking in the tall grass. We pop open the top of the vehicle, stand up, and with the African rhythms of Paul Simon's *Graceland* playing in my head, I start to scan back

"endless plains." Joining me on my pilgrimage to this legendary wildlife sanctuary is my family: and forth. This is my first visit to what the Maasai call "Serengit" for

pilgrims with families and we are going to Graceland . . .

the dry season, but things look really dry. Can this place live up to its At first, I am a bit concerned. Where is all the wildlife? Yes, it is

eye is naturally drawn to these shapes. mounds projecting up to a few feet over the tops of the grass. One's ists) can scan around for miles. There are also gray or red termite rocky hills, or kopjes. From their granite boulders, animals (or tour-The continuous grass plain is broken only occasionally by small

"What is that over there?" asks a voice in the vehicle.

a couple of hundred yards away. A couple of us grab our binoculars and zero in on a lone mound

A golden lioness is standing on top, staring out over the surround-

Serengeti? OK, so they are here, I murmur to myself. But this is the famous

to do this for days on end. am the only biologist in my clan, I can't expect anyone else to want It is going to be really hard to spot things in this tall dry grass. I

a small rise, round a bend, and skid to a stop—zebra and wildebeest block the road and fill the entire view. ders through the green patches, and it has plenty of water. We go over iconic flat-topped acacia trees sprinkled about. A creek bed mean-As we drive on, some streaks of green grass appear, with a few

wildebeest, 200,000 zebras, and tens of thousands of other animals follow the rains north to greener grazing grounds. the greatest animal migration on the planet, when as many 1 million debeest seem to just mutter "huh?" These herds are stragglers from thing between a bark and a laugh: "kwa-ha, kwa-ha," while the wilnear a large waterhole, raising a ruckus. The zebras' calls are some-It is a sea of stripes. Perhaps 2,000 or more animals have gathered

> sters scurrying to keep up. The herds part to make way. left—the Dawn Patrol—a parade of elephants with several young-Coming next to the waterhole from over the small rise on our

and a cheetah posing just feet from the road. or three but at least nine species of antelope—the tiny dik-dik, the this first day, including several more lions, a leopard dozing in a tree backed jackals; towering Masai giraffe; and yes, all three big cats on the larger Grant's gazelles, and the ubiquitous wildebeest; black massive eland, impala, topi, waterbuck, hartebeest, Thomson's and hogs with tails standing straight up like our radio antenna; not two taining mammals of many sizes, shapes, and colors: small gray wart-From that point on, the Serengeti offers an unending canvas con-

scenery for the first time. pared me for, nor spoiled the thrill of, encountering this stunning Although I have seen many pictures and movies, nothing pre-

ettes of the surrounding foothills. Although it is the first time I have a wide green valley, with multitudes of creatures and acacia stretchever been to Tanzania, I feel at home. ing as far as I can see, and the sun beginning to set behind the silhou-A strange, but very pleasant feeling sweeps over me as I gaze across

of badlands. It was in its eroding hillsides (just three miles off of the ago. Thirty miles to the south at Laetoli, Mary and her team later discies of hominids that had lived in East Africa 1.5 to 1.8 million years current B144) that, after decades of searching, Mary and Louis Leakey ancestors' ancestors. Sandwiched between Ngorogoro Crater and but upright-walking ancestor Australopithecus afarensis. covered 3.6-million-year-old footprints made by our small-brained the Serengeti lies Olduvai Gorge, a thirty-mile-long twisting maze lay buried the bones of my and your ancestors, and those of our (and their sons) unearthed not one, not two, but three different spe-And indeed, this is home. For across the Rift Valley of East Africa

of grazing animals trying to stay out of the reach of a number of wily actors have changed, the drama we can still see today—of fleet herds haystack of other animal fossils that tell us that, although the specific predators—has been playing for thousands of millennia. Hoards of Those hard-earned hominid bones were precious needles in a

ancient stone tools found around Olduvai and butchery marks on those bones also tell us how our ancestors were not merely spectators but very much a part of the action.

Human life has changed immensely over the millennia, but never so much or so quickly as in the past century. For almost the entire 200,000-year existence of our species, *Homo sapiens*, biology controlled us. We gathered fruits, nuts, and plants; hunted and fished for the animals that were available; and like the wildebeest or zebra, we moved on when resources ran low. Even after the advent of farming and civilization, and the development of cities, we were still very vulnerable to the whims of the weather, and to famine and epidemics.

But in just the past hundred years or so, we have turned the tables and taken control of biology. Smallpox, a virus that killed as many as 300 *million* people in the first part of the twentieth century (far more than in all wars combined) has not merely been tamed but has been eradicated from the planet. Tuberculosis, caused by a bacterium that infected 70–90 percent of all urban residents in the nineteenth century and killed perhaps one in seven Americans, has nearly vanished from the developed world. More than two dozen other vaccines now prevent diseases that once infected, crippled, or killed millions, including polio, measles, and pertussis. Deadly diseases that did not exist in the nineteenth century, such as HIV/AIDS, have been stopped in their tracks by designer drugs.

Food production has been as radically transformed as medicine. While a Roman farmer would have recognized the implements on an American farm in 1900—the plow, hoe, harrow, and rake—he would not be able to fathom the revolution that subsequently transpired. In the course of just one hundred years, an average yield of corn more than quadrupled from about 32 to 145 bushels per acre. Similar gains occurred for wheat, rice, peanuts, potatoes, and other crops. Driven by biology, with the advent of new crop varieties, new livestock breeds, insecticides, herbicides, antibiotics, hormones, fertilizers, and mechanization, the same amount of farmland now feeds a population that is four times larger, but that is accomplished by less

than 2 percent of the national labor force compared to more than 40 percent a century ago.

The combined effects of the past century's advances in medicine and agriculture on human biology are enormous: the human population exploded from fewer than 2 billion to more than 7 billion people today. While it took 200,000 years for the human population to reach 1 billion (in 1804), we are now adding another billion people every twelve to fourteen years. And, whereas American men and women born in 1900 had a life expectancy of about forty-six and forty-eight years, respectively, those born in 2000 have expectancies of about seventy-four and eighty years. Compared to rates of change in nature, those greater than 50 percent increases in such a short timespan are astounding.

As Paul Simon put it so catchily, these are the days of miracles.

RULES AND REGULATIONS

Our mastery, our control over plants, animals, and the human body, comes from a still-exploding understanding about the control of life at the molecular level. And the most critical thing we have learned about human life at the molecular level is that *everything is regulated*. What I mean by that sweeping statement is:

- every kind of molecule in the body—from enzymes and hormones to lipids, salts, and other chemicals—is maintained in a specific range; in the blood, for example, some molecules are 10 billion times more abundant than other substances.
- every cell type in the body—red cells, white cells, skin cells, gut cells, and more than 200 other kinds of cell—is produced and maintained in certain numbers; and
- every process in the body—from cell multiplication to sugar metabolism, ovulation to sleep—is governed by a specific substance or set of substances.

Diseases, it turns out, are mostly abnormalities of regulation, where too little or too much of something is made. For example, when the pancreas produces too little insulin, the result is diabetes, or when the bloodstream contains too much "bad" cholesterol, the result can be

atherosclerosis and heart attacks. And when cells escape the controls that normally limit their multiplication and number, cancer may form.

To intervene in a disease, we need to know the "rules" of regulation. The task for molecular biologists (a general term I will use for anyone studying life at the molecular level) is to figure out—to borrow some sports terms—the players (molecules) involved in regulating a process and the rules that govern their play. Over the past fifty years or so, we have been learning the rules that govern the body's levels of many different hormones, blood sugar, cholesterol, neurochemicals, stomach acid, histamine, blood pressure, immunity to pathogens, the multiplication of various cell types, and much more. The Nobel Prizes in Physiology or Medicine have been dominated by the many discoverers of the players and rules of regulation.

Pharmacy shelves are now stocked with the practical fruit of this knowledge. Armed with a molecular understanding of regulation, a plethora of medicines has been developed to restore levels of critical molecules or cell types back to normal, healthy ranges. Indeed, the majority of the top fifty pharmaceutical products in the world (which altogether accounted for \$187 billion in sales in 2013) owe their existence directly to the revolution in molecular biology.

The tribe of molecular biologists, my tribe, is justifiably proud of their collective contributions to the quantity and quality of human life. And dramatic advances in deciphering information from human genomes are ushering in a new wave of medical breakthroughs by enabling the design of more specific and potent drugs. The revolution in understanding the rules that regulate our biology will continue. One aim of this book is to look back at how that revolution unfolded and to gaze ahead to where it is now heading.

But the molecular realm is not the only domain of life with rules, nor the only branch of biology to have undergone a transformation over the past half-century. Biology's quest is to understand the rules that regulate life on every scale. A parallel, but less conspicuous, revolution has been unfolding as a different tribe of biologists has discovered rules that govern nature on much larger scales. And these rules may have as much or more to do with our future welfare than all the molecular rules we may ever discover.

THE SERENGETI RULES

This second revolution began to flower when a few biologists began asking some simple, seemingly naïve questions: Why is the planet green? Why don't the animals eat all the food? And what happens when certain animals are removed from a place? These questions led to the discovery that, just as there are molecular rules that regulate the numbers of different kinds of molecules and cells in the body, there are ecological rules that regulate the numbers and plants in a given place.

I will call these ecological rules the "Serengeti Rules," because that is one place where they have been well documented through valiant, long-term studies, and because they determine, for example, how many lions or elephants live on an African savannah. They also help us understand, for example, what happens when lions disappear from their ranges.

But these rules apply much more widely than to the Serengeti, as they have been observed at work around the world and shown to operate in oceans and lakes, as well as on land. (I could just as easily call these the "Lake Erie Rules," but that just seems to lack a sense of majesty). These rules are both surprising and profound: surprising because they explain connections among creatures that are not obvious; profound because these rules determine nature's ability to produce the animals, plants, trees, and clean air and water on which we depend.

However, in contrast to the considerable care and expense we undertake in applying the molecular rules of human biology to medicine, we have done a very poor job in considering and applying these Serengeti Rules in human affairs. Before any drug is approved for human use, it must go through a series of rigorous clinical tests of its efficacy and safety. In addition to measuring a drug's ability to treat a medical condition, these studies monitor whether a drug may cause problematic side effects by interfering with other substances in the body or the regulation of other processes. The criteria for approval pose a high barrier; about 85 percent of candidate medicines fail clinical testing. That high rejection rate reflects, in part, a low tolerance on the part of doctors, patients, companies, and regulatory agencies for side effects that often accompany drugs.

But for most of the twentieth century and across much of the planet, humans have hunted, fished, farmed, forested, and burned whatever and settled wherever we pleased, with no or very little understanding or consideration of the side effects of altering the populations of various species or disturbing their habitats. As our population boomed to 7 billion, the side effects of our success are making disturbing headlines.

For example, the number of lions in the world has plummeted from about 450,000 just fifty years ago to 30,000 today. The King of the Beasts that once roamed all of Africa as well as the Indian subcontinent has disappeared from twenty-six countries. Tanzania now holds 40 percent of all of Africa's lions, with one of their largest remaining strongholds in the Serengeti.

There are similar stories in the oceans. Sharks have prowled the seas for more than 400 million years, but in just the past fifty years, populations of many species around the world have plunged by 90–99 percent. Now, 26 percent of all sharks, including the great hammerhead and whale shark, are at risk of extinction.

Some might say, "So what? We win, they lose. That is how nature works." But that it is not how nature works. Just as human health suffers when the level of some critical component is too low or too high, we now understand from the Serengeti Rules how and why entire ecosystems can get "sick" when the populations of certain members are too low or too high.

There is mounting evidence that global ecosystems are sick, or at least very tired. One measure that ecologists have developed is the total ecological footprint of human activity from growing crops for food and materials, grazing animals, harvesting timber, fishing, infrastructure for housing and power, and burning fuels. Those figures can then be compared with the total production capacity of the planet. The result is one of the most simple but telling graphs I have encountered in the scientific literature (see Figure 2).

Fifty years ago, when the human population was about 3 billion, we were using about 70 percent of the Earth's annual capacity each year. That broke 100 percent by 1980 and stands at about 150 percent now, meaning that we need one and one-half Earths to regenerate

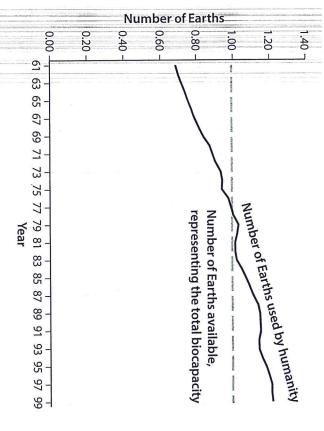


FIGURE 2 The trend in humanity's ecological demands relative to the Earth's production capacity. We are now overshooting what the planet can regenerate by about 50 percent.

Figure from Wackernagel, M., N. B. Schulz, D. Deumling, A. C. Linares et al. (2002) "Tracking the Ecological Overshoot of the Human Economy? *Proceedings of the National Academy of Sciences USA* 99: 9266–9271. © 2002

National Academy of Sciences.

what we use in a year. As the authors of this now annual study note, we have a total of just one Earth available.

We have taken control of biology, but not of ourselves

RULES TO LIVE BY

As biased it sounds, coming from a biologist, the impact of biology over the past century demonstrates that among all the natural sciences, biology is central to human affairs. There can be no doubt that in facing the challenges of providing food, medicine, water, energy, shelter, and livelihoods to a growing population, biology has a central role to play for the foreseeable future.

Every ecologically knowledgeable biologist I know is deeply concerned about the declining health of the planet and its ability to continue to provide what we need, let alone to support other creatures. Wouldn't it be terribly ironic if, while we race toward and discover more cures to all sorts of molecular and microscopic threats to human life, we continue to just sail on blissfully or willfully ignorant of the state of our common home and the greater threat from disregarding how life works on the larger scale? No doubt most passengers on the Titanic were also more concerned about the dinner menu than the speed and latitude at which they were steaming.

So, for our own sake, let's know all the rules, not just those that pertain to our bodies. Only through wider understanding and application of these ecological rules will we control and have a chance to reverse the side effects we are causing across the globe.

But my goals in this book are to offer much more than some rules, however practical and urgent they are. These rules are the hard-earned rewards of the long and still ongoing quest to understand how life works. One of my aims here is to bring that quest to life, as well as the pleasures that come from discovery. My premise is that science is far more enjoyable, understandable, and memorable when we follow scientists all over the world and into the lab, and share their struggles and triumphs. This book is composed entirely of the stories of people who tackled great mysteries and challenges, and accomplished extraordinary things.

As for what they discovered, there is more to gain here than just better operators' manuals for bodies or ecosystems. One of the beliefs that many people have about biology (no doubt the fault of biologists and biology exams) is that understanding life requires command of enormous numbers of facts. Life appears to present, as one biologist put it, "a near infinitude of particulars which have to be sorted out case by case." Another of my aims here is to show that is not the case.

When we ponder the workings of the human body or the scene I encountered on the Serengeti, the details would seem overwhelming, the parts too numerous, and their interactions too complex. The power of the small number of general rules that I will describe is their ability to reduce complex phenomena to a simpler logic of life.

That logic explains, for example, how our cells or bodies "know" to increase or decrease the production of some substance. The same logic explains why a population of elephants on the savanna is increasing or decreasing. So, even though the specific molecular and ecological rules differ, the overall logic is remarkably similar. I believe that understanding this logic greatly enhances one's appreciation for how life works at different levels: from molecules to humans, elephants to ecosystems.

What I hope everyone will find here, then, is fresh insight and inspiration: insight into the wonders of life at different scales; inspiration from the stories of exceptional people who tackled great mysteries and had these brilliant insights, and a few whose extraordinary efforts have changed our world for the better.

*

After five days in the Serengeti, we have seen all of the species of large mammals except one. As we drive back out through the straw-colored grasslands, as if on cue, a novel silhouette appears on the horizon with a prominent telltale horn—a black rhino. With just thirty-one rhinos remaining in the entire Serengeti, it is a rare and thrilling sight. But knowing that there was once more than 1,000 of the animals here, it is also a sober reminder of the challenges ahead. Although, thanks to knowing the molecular rules of human erections, we now have at least five different inexpensive pills that can do the job, rhino horns are still being poached for use as very expensive aphrodisiacs in the Orient.

These are the days of miracle and wonder, And don't cry baby, don't cry Don't cry

And like the specific molecular rules that govern our health, these ecological rules are also rules to live by. For as we shall see next, when they are broken, bad things happen in *our* world. And just as with molecular rules, understanding these rules of ecological regulation enable us to diagnose what is ailing ecosystems, and potentially, to cure them.

CHAPTER 8

ANOTHER KIND OF CANCER

It is failures in regulation of numbers of animals which form by far the biggest part of present-day economic problems in the field.

-CHARLES ELTON

At 1:20 a.m. on Saturday, August 1, 2014, the city of Toledo, Ohio, issued an urgent alert to all residents:

DO NOT DRINK THE WATER DO NOT BOIL THE WATER

Chemists at the city's water treatment plant had detected dangerous levels of a nasty toxin in the water supply, a toxin that could not be destroyed by boiling, but instead would only become more concentrated.

The metropolitan area of one-half million people was brought to a standstill. Restaurants, public buildings, and even the city zoo closed. People quickly bought up whatever bottled water was on store shelves. The governor of Ohio declared a state of emergency. The National Guard was enlisted to truck in water and portable water treatment plants. The national and international news media covered the story of a modern American city without the 80 million gallons of water it needed daily. It was not the sort of attention the long-struggling, rust-belt city wanted.

I was paying extra attention. It is a city, and water, that I know very well. I was born and raised in Toledo, which is situated on the southwest shore of massive Lake Erie. My friend Tom Sandy and I often went snake hunting near the edge of the lake, and the thrill of those catches played a large part in my desire to become a biologist. But never in my entire childhood did I dip one toe in the lake's waters. Nor would I eat anything anyone caught in it.

The lake was notorious for its level of pollution while I was growing up in the 1960s and early 1970s, so notorious that Dr. Seuss singled it out in his environmental fable *The Lorax* (1971):

You're glumping the pond where the Humming-fish hummed!
No more can they hum, for their gills are all gummed.
So I am sending them off. Oh, their future is dreary.
They'll walk on their fins and get woefully weary
In search of some water that isn't so smeary.
I hear things are just as bad up in Lake Erie.

Spurred by the dire condition of Erie and other lakes, the US Congress passed the 1972 Clean Water Act that authorized the Environmental Protection Agency to regulate the discharge of pollutants into waterways and to set the acceptable limits for water quality for humans and aquatic life. In 1972, the United States and Canada also signed the Great Lakes Water Agreement, which promoted a coordinated effort to reduce the loads of chemicals that were being dumped and washed into the Great Lakes.

Algal populations dropped, fish populations grew. The recovery of Lake Erie was so dramatic that in 1986, Dr. Seuss even agreed to remove its mention from later editions of *The Lorax*.

But Lake Erie is again getting glumped. The immediate culprit is a 'tiny, single-celled, blue-green algae called *Microcystis* that forms thick mats that can cover many miles of lake surface. In 2011, the lake experienced its largest bloom in history, a green carpet up to four inches thick stretched for 120 miles along the southern shore, from Toledo to Cleveland. In 2014, the thick pea soup formed right on top of the Toledo water treatment plant's main intake pipe. [Figure 8.1]

The blooms contain astronomical numbers of algae. Under typical conditions, there may be just a few hundred algal cells in a lite.

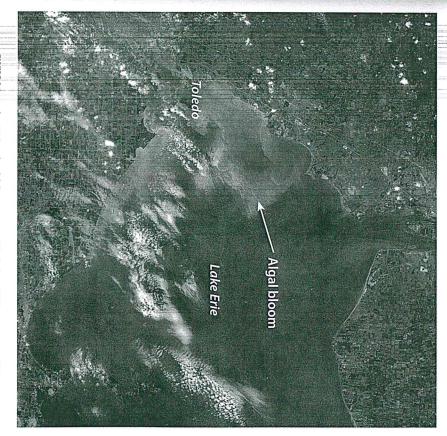


FIGURE 8.1 Lake Erie algal bloom near Toledo, Ohio, August 2014.

NASA satellite photograph taken on August 1, 2014.

of lake water. In a bloom, this can rocket to more than 100 million cells per liter. The 2011 bloom may have contained as many as 1 quadrillion (1 million trillion) to 1 quintillion (1 billion trillion) toxin-producing cells in all.

Like a tumor metastasizing through the human body, the mass of algae sows destruction as it spreads through the body of the lake. The massive overgrowth of algae is indeed an ecological cancer.

When cancer spreads in a person, it can invade and cripple the organs that maintain the body's homeostasis. When it hits the bone marrow or lungs, the body can starve for oxygen; when it invades

the digestive organs, the body is starved for nutrients; and when it infiltrates the liver and bone, it can throw off the delicate balance of key chemicals in the bloodstream. Similarly, the algal mass kills by blocking vital functions in the lake. The toxin(s) it produces is highly toxic to fish and other wildlife, wreaking havoc on the food chain. And as the algae die off, they sink to the lake bottom, where bacteria that decompose them use up the lake's supply of oxygen—suffocating fish and other creatures, and creating an uninhabitable dead zone with altered water chemistry.

Lake Erie is not the only large body of water that is in critical condition. It has plenty of company, including Lake Winnipeg in Canada, Lake Taihu in China, and Lake Nieuwe Meer in the Netherlands. Nor are these the only ecosystems suffering from the overgrowth of some creature. Cancer takes various forms in different parts of the biosphere. I will look at a few more cases before asking what sorts of rules have been broken that can make lakes, fields, bays, and the savannah sick, and in Chapters 9 and 10 I will show how that knowledge can be used to heal them.

PESTILENCE

Fly over or visit any of the sixteen countries of tropical Asia, and it is clear what the people are eating. From India to Indonesia, mile after mile of rice fields sprawl across valleys and up and down terraced hillsides. In Cambodia, for example, rice production alone occupies over 90 percent of the total agricultural area. The grain is a critical staple now for almost half of humanity. Over 30 percent of all calories consumed in Asia come from rice, and in some countries, such as Bangladesh, Vietnam, and Cambodia, the grain provides over 60 percent of daily intake.

Rice has been cultivated in Asia for more than 6,000 years, but today's lush fields are the products of the Green Revolution of the 1960s. Facing the possibility of massive famine due to drought, crop failures, and a booming population, new genetically improved rice varieties were developed, and more productive farming methods were introduced, including the routine application of fertilizers and pesticides. Within ten years, more than a quarter of all farms were

using new rice strains, and many farmers across Asia saw their rice yields per acre nearly double.

But in the mid-1970s, many bright green paddies in the Philippines, India, Sri Lanka, and elsewhere across tropical Asia were turning orange-yellow, then brown. In 1976, disaster struck Indonesia. More than 1 million acres of crops were afflicted. In a region where farmers rely on their crops to feed their families for the year, or for most of their annual income, the situation was dire.

The culprit was a tiny insect called the brown planthopper. Although just a few millimeters long, individual females that land on a plant may lay up to several hundred eggs that then hatch into hungry nymphs that feed on the growing rice plants. [Figure 8.2] The little bugs suck the sap; then the plants leaves turn yellow, dry out, and die, producing a characteristic "hopperburn." With a rapid generation time in the warm, moist tropics, the bug population can go through three generations in the time it takes the rice plant to mature. The number of bugs can explode and overwhelm a field, going from less than one insect per plant to 500–1,000.

Naturally, the first instinct of farmers at the sight of planthoppers in their fields was to bombard them with pesticides. The Indonesians sprayed from the air and from the ground, but the outbreak continued. Over 350,000 tons of rice was lost, enough to feed 3 million people for a year. Many farmers lost nearly everything. Indonesia was forced to become the largest rice importer in the world.

The insect was considered only a minor rice pest prior to the 1970s. What happened that made the brown planthopper a menace? And how did it resist the assault of tons of insecticides?

Careful study of insect growth on farmers' and experimental rice fields revealed an astounding surprise: it was not that plants treated with insecticides had as many eggs, nymphs, and insects on them as untreated plants—they had more! Indeed, insecticide treatment caused up to an 800-fold increase in insect density. This meant that insecticides weren't preventing hopperburn, they were largely responsible for causing it.

How the hell could that happen?

It turns out that many factors were at work. First, the insects had evolved resistance to commonly applied insecticides, such as



FIGURE 8.2 Brown planthoppers on rice plants.

Photo courtesy of IRRI/Sylvia Villareal.

diazinon. But that would only render the insecticide useless. There had to be more to the outbreak, and there was. A second, much more surprising, discovery was that the pesticide actually increased the rate of egg-laying, by about 2.5-fold. And the third factor, well, I am not going to tell you yet the third reason the populations exploded. I am going to save that revelation until after a couple more examples of ecological cancers, for the general rule of regulation that was broken in the rice fields has also been broken elsewhere. Some fields in West Africa are stalked by a much larger pest.

A BABOONIC PLAGUE

In the village of Larabanga, in the savannah of northwestern Ghana, nightfall puts its residents on edge. The rural community of 3,800 is situated just a few kilometers from Mole National Park, home to a diverse array of mammals including hippos, elephants, buffalo, a slew of antelopes and primates, and a variety of cats, from servals to leopards and lions. Villagers commonly encounter wild animals, but it is not the lions that keep them up at night.

Many families meet their needs by farming maize, yams, cassava, and small livestock on shared lands. But in recent years, some very bold four-legged thieves have been working together to slip into the fields under the cover of darkness to raid the crops—olive baboons. In a matter of minutes, a group of a dozen or more animals can strip stands of plants and severely damage many others before slinking away or being chased off by angry farmers.

The baboons have become so brazen that they also scout and attempt to raid the fields during the day. Constant vigilance is required on the part of farmers, who have resorted to using children to guard the precious crops—children who would otherwise be in school. The combined economic and social impact of the marauding primates has precipitated a serious crisis.

Humans and baboons have long lived in close proximity through-

Humans and baboons have long lived in close proximity throughout Africa, so when and why did the baboons become such a problem in Ghana?

Part of the answer is found in the handful of protected reserves and parks that have been set aside in different parts of the country. To

keep tabs on the wildlife, the Ghana Wildlife Division started keeping a careful census of forty-one species of mammals in 1968. Every month, rangers at sixty-three posts in six different reserves walked six-to nine-mile-long stretches and counted sightings or other signs of each animal. The several-decades-long census is a remarkably detailed accounting of the changes in mammal populations in different sized-reserves ranging from the smallest, Shai Hills Resource Reserve (fifty-eight square kilometers), to the largest, Mole National Park (4,840 square kilometers).

The census reveals that of the forty-one species, all but one declined in sightings across the six reserves over the thirty-six-year period from 1968 to 2004, including many species that became locally extinct, especially in the smallest reserves. The one exception? You guessed it—olive baboons, which increased by 365 percent. Moreover, the animals expanded their range in the parks by 500 percent.

I am going to hold off on the question of why the baboons flourished until after describing one more example of an ecological cancer, one that closed a valuable fishery on the Atlantic Coast of the United States.

FAMINE

Bay scallops have long been part of North American culture. Before European settlement, Native Americans along the East Coast harvested the mollusks for their inch-long, white adductor muscles. From the mid-1870s to the mid-1980s, large commercial scallop fisheries operated in Massachusetts, New York, and North Carolina. In 1928, North Carolina led the nation with a harvest of 1.4 million pounds of scallop meat. For many of the state's fishermen, an early winter harvest was an important source of income between other fishing seasons.

But in 2004, the total scallop harvest was less than 150 pounds. The century-old fishery was declared "depleted" and closed for most of the following years, including 2014. Fishermen, state authorities, and scientists asked: What happened?

It was the fishermen who first noticed the clues in their trawl and pound nets, which were pulling up large numbers of cownose rays.

The three-feet-wide fish migrate down the East Coast during the fall and were getting entangled in and damaging the nets. With their poisonous barbs, and no commercial market for the rays, they were becoming a nuisance to the fishermen.

The fishermen complained to University of North Carolina marine biologist Charles "Peter" Peterson, who had been studying the impact of cownose ray predation on bay scallops along the Carolina coast. Peterson teamed up with colleagues at the University of North Carolina and Dalhousie University to study the problem. They found that cownose ray populations had expanded by at least tenfold along the Atlantic coast over the previous sixteen to thirty-five years, to a population of perhaps 40 million animals. Peterson had previously observed how cownose rays wipe out entire populations of scallops at certain locations along the coast. The explosion in cownose rays seemed to explain the absence of scallops from most locations In North Carolina waters. But what explained the greater numbers of cownose rays?

It is time to unravel the mysteries of these cancers.

MISSING LINKS

Microcystis, planthoppers, baboons, cownose rays. What rule or rules of regulation have been broken that enabled these organisms to explode in numbers?

To answer that, we first have to ponder: What could regulate these populations? Elton stressed that if one wants understand the workings of a community of creatures, one should trace the food chain. Could the populations have increased because there is more food available?

For *Microcystis*, that appears to be a good part of the explanation. The element phosphorus is a limiting nutrient for algal growth. The immediate catalyst to algal blooms is the surge of phosphorus (in the form of inorganic phosphate) that enters Lake Erie from farms and other sources in the spring and summer. In the structure of the lake's food chain, the phosphorus exerts a bottom-up effect on algal populations.

But more food does not appear to explain the other cancers. There are plenty of rice plants for planthoppers to feed on in every field,

but the bugs usually don't affect very many. And more food would not explain why they boom in the presence of pesticides. Similarly food would not explain why only baboons increased while all other mammals decreased in Ghanian parks, nor did cownose rays increase because there were more scallops. So, if not food, what else could regulate the numbers of these animals?

Maybe we should look up, not down the food chain from these animals.

That is just what Peterson and colleagues did for cownose rays. Sharks eat the rays, and when the scientists examined records of shark populations along the eastern seaboard, they saw dramatic declines in five species since 1972 including: an 87 percent decline in sandbar sharks; a 93 percent decline in blacktip sharks; and 97–99 percent declines in hammerhead, bull, and dusky sharks. Sharks prey on other animals as well. If the shark declines were responsible for the boom in cownose populations, one would also expect other shark prey to increase in numbers. Sure enough, the researchers found that in addition to the cownose ray, thirteen other prey species, including various small rays, skates, and small sharks increased dramatically in numbers.

A similar explanation accounts for the baboon plague in Ghana. Lions and leopards prey on baboons, and their numbers have plummeted in Ghana's parks, having disappeared completely from three of the six parks by 1986. As the lions and leopards vanished from those parks, the baboons flourished. [Figure 8.3]

Turning to the planthoppers, why did they explode upon treatment of rice fields with pesticide? It turns out that spiders and a few insects are natural enemies of the planthoppers. Wolf spiders and their young spiderlings, for example, are able to consume significant numbers of brown planthoppers and their nymphs, respectively. The pesticide killed off spiders (and other enemies) that keep the insect population under control. In pesticide-treated fields, the predators are reduced, and the pesticide-resistant prey flourishes.

The discovery from these three very different cancers is one simple, common observation: kill the predators, and the prey run amoke The logic of these ecological cancers is familiar. The predators are negative regulators of population growth. Just like a tumor suppressor, they act as brakes on proliferation. Remove these critical links

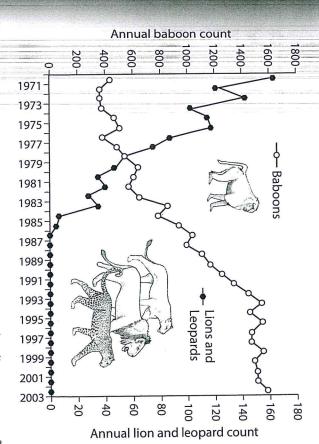


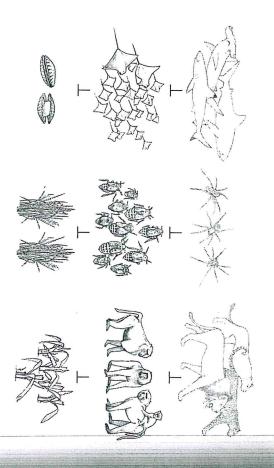
FIGURE 8.3 The increase in olive baboons accompanying the disappearance of lions and leopards in areas of Ghana.

Illustration based on Brashares et al. (2010), redrawn by Leanne Olds

in the food chain, and the growth of their prey is unchecked, with downstream trophic effects. Each cancer results from the cascading effects of the decapitation of the top trophic level of predators, the reduction of three-level cascades to two. [Figure 8.4]

From the viewpoint of the scallop fisherman, the rice farmer, or a Ghanian family (and in the light of the double-negative logic of the intact cascades), sharks, spiders, and lions should be viewed as allies and not persecuted. In each case, the ancient proverb "the enemy of my enemy is my friend" rings true.

The elimination of trophic levels has probably also contributed to the situation in Lake Erie. In healthy freshwater lakes, algal growth is also controlled from the top down by plankton, such as small crustaceans, which graze on them. In algal blooms, this regulation is overwhelmed or killed off by algal toxins. The algal cancer then is a combination of too much bottom-up input (a stuck accelerator) and too little top-down control (weak brakes).



FIBURE 8.4 Cascading effects of the loss of sharks, spiders, and large cats. The loss of control of cownose rays, planthoppers, and baboons has led to a decline in scallops, and loss of rice and other key crops, respectively.

Illustration by Leanne Olds.

TOO MANY, TOO FEW, AND TOO MUCH

Graeme Caughley, who co-wrote a leading textbook on wildlife ecology and management with Tony Sinclair, sorted all the problems of wildlife populations into just three simple categories: too many, too few, and too much. The examples here of too many planthoppers, baboons, and rays are the result of too few spiders, lions, and sharks, respectively.

But the ultimate causes of these cancers are not the missing predators, they are a matter of humans doing too much: too much phosphorus on our farms, too much pesticide on our fields, too much poaching of lions and leopards and their prey, and too much fishing for sharks. It is becoming ever clearer from the kinds of indirect, inadvertent, unanticipated side effects I have described that we are doing these things against our own long-term interest. For many decades, one could say we did not know any better, that we were ignorant of the rules of regulation in nature. But not any longer.

Now that we do know better, can we use our understanding of these rules to fix any of these problem? Some bold attempts have been and are being made on surprisingly large scales. To quote Cannon when he addressed Boston doctors on the rules of physiological regulation, there are "reasons for optimism in the care of the sick."