Transition Pack

For

A-Level Biology

Mandatory Tasks

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Introduction and instructions READ CAREFULLY	1-3	
Writing processes	4-5	
Baseline Assessment	6-9	
Article Summation – Context Building	10	
Further Reading – Consolidating Ideas	11-47	

Optional Tasks

What did you read, see or do?

Year 11 Transition Task – A Level Biology

Biology is a broad subject that draws on multiple skills. The key aspect to its success is the ability to apply ideas/principles that have been learned to unfamiliar contexts and applications. Sometimes it's about what you know and can remember, but more often its about testing what you understand.

These tasks are about introducing some of these ideas and giving you an introduction to the key skills within a Biological context.

Task Instructions:

1. **Writing processes:** Lots of what you will learn involves processes - a series of steps start to finish. They appear in lots of contexts. You often must take a range of information types and then bring them together into one coherent series of steps. Use the provided information to produce processes for:
    a) What happens during breathing in and breathing out
    b) How to aseptically produce a bacterial culture on a petri dish of agar

2. **Baseline Assessment:** Complete and submit the baseline assessment. In this I would like you to attempt it **blind** (don't consult your notes as you attempt each question) in one colour of pen and **then** go back through the questions **open-book** (using your notes/support materials) and add to/complete answers in a different colour pen. I am not looking for perfection; just give it an honest go!

3. **Article Summation – Context Building:** Lots of questions in Biology are about applying your understanding of key principles to unseen contexts. The more contexts that your familiar with, the easier this task becomes. Reading around the modules you are studying is helpful in this regard. To practise this, choose **two** articles and summarise their content using **Cornell notes** (one page per article). Select things that **you** find interesting.

4. **Further Reading – Consolidating Ideas:** A key academic skill is reading academic literature such as books and being able to pull out the key ideas that the writer is trying to communicate. We can then use these ideas in our own writing by referencing the original author. What I want you to practice is the first bit – pulling out the key ideas. **Read one** of the book chapters that I have provided (pick the one that speaks most to your interests) and produce a summary (1 page max – Cornell notes will be helpful) of what is being communicated **and** the evidence used to support it. The chapters to choose from are:
    a. **Serengeti Rules (Sean B Carrol):** Stuck Accelerators and Broken Brakes (The interplay between regulation and cancer)
    b. **Gene Eating (Giles Yeo):** Are your genes to blame when your jeans don't fit? (Looking at the genetic components behind weight)
    c. **Furry Physics (Martin Durrani & Liz Kalaugher**): Electricity and Magnetism: Let the sparks Fly – Taser Eels (Looking at the Physics behind electric eels)
    d. **Serengeti Rules (Sean B Carrol):** The Economy of Nature (Why Ecosystems have the arrangements they do in terms of feeding relationships)

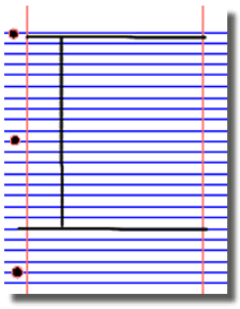
Optional Tasks

It's a long summer, and you may struggle to fill the time. You may also be genuinely enthused and interested – which would be amazing! To support this there are links to some TED talks, social media sites/feeds, and some Big Picture resources as well as book recommendations. Take a look at these, or go in a completely different direction that follows your own interests. The choice is yours, but it's good to read around the subject and it helps when it comes to personal statements for the next stage. Yes, we have this in mind all the way through. Enjoy.

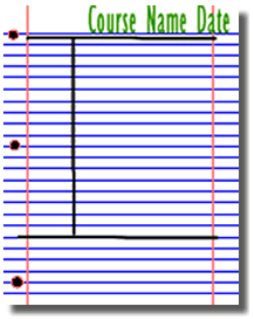
How to summarise ideas using Cornell Notes:

Research, reading and note making are essential skills for A level Biology study. For the following task you are going to produce 'Cornell Notes' to summarise your reading.

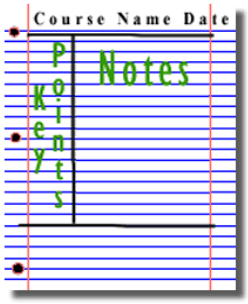
1. Divide your page into three sections like this



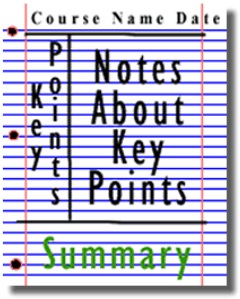
2. Write the name, date and topic at the top of the page



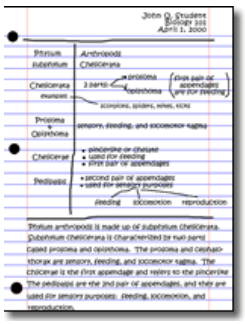
3. Use the large box to make notes. Leave a space between separate ideas. Abbreviate where possible.



4. Review and identify the key points in the left hand box



5. Write a summary of the main ideas in the bottom space



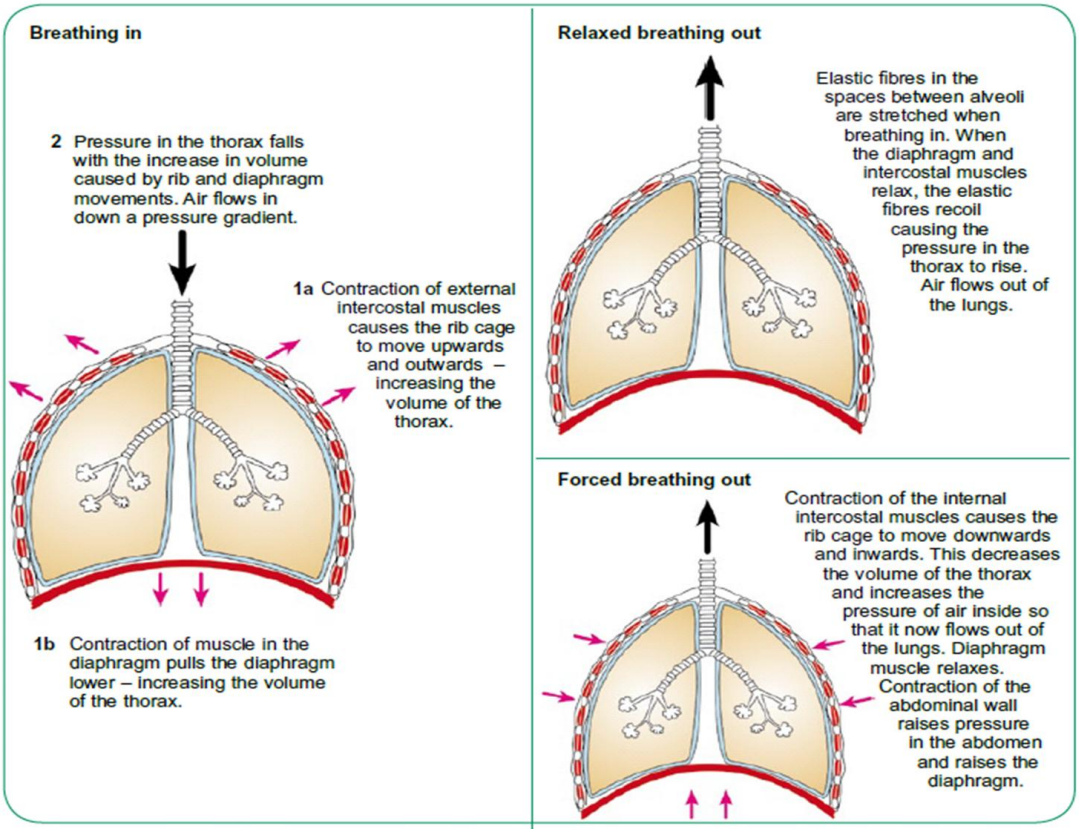
Images taken from http://coe.jmu.edu/learningtoolbox/cornellnotes.html

1. Task: Writing processes

Use the provided information to produce step by step processes for:

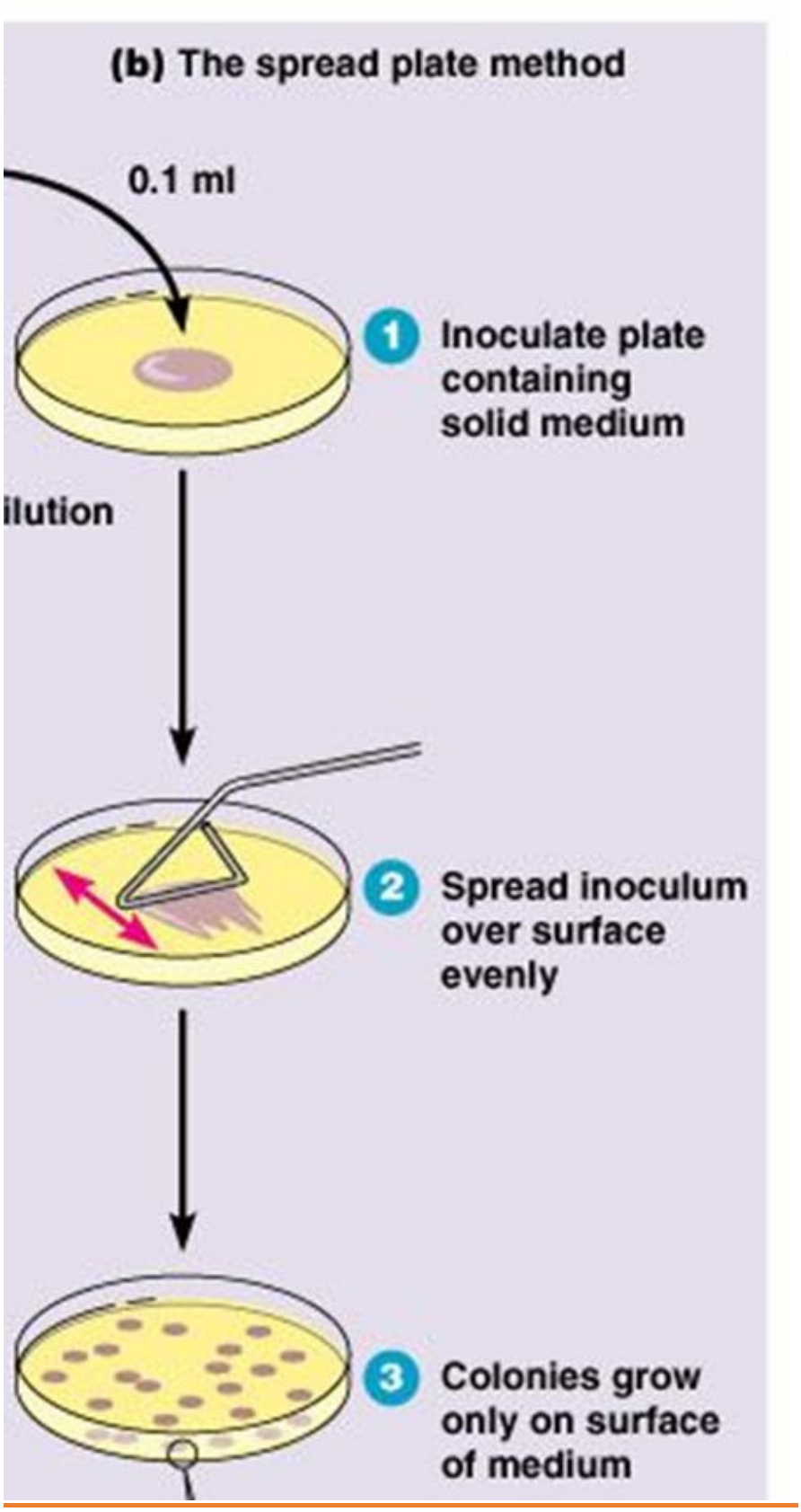
a) What happens during breathing in and breathing out

	Inspiration	Expiration
Diaphragm	Contracts, becomes flatter, and moves down	Relaxes, and is pushed up by pressure in abdomen
Rib Cage (ribs and intercostal muscles)	*External* intercostal muscles *contract* to move ribs up and out (internal intercostal muscles relax)	*External* intercostal muscles *relax* so that ribs fall with gravity (internal intercostal muscles contract during forced expiration)
Volume of thorax	Increase in size of chest cavity	Decrease in size of chest cavity
Pressure in lungs	Lower in chest cavity than atmospheric	Higher in chest cavity than atmospheric
Air movement	In	Out



b) How to aseptically produce a bacterial culture on a petri dish of agar

Watch this video to help: https://www.youtube.com/watch?v=1gs4JQ4B1TU



2. Task: Baseline Assessment

The following 40 minute test is designed to test your recall, analysis and evaluative skills and knowledge.
Remember to use your exam technique: look at the command words and the number of marks each question is worth.
A suggested mark scheme is provided for you to check your answers.

1. a) What are the four base pairs found in DNA?

.....

(2)

b) What does DNA code for?

.....

(1)

c) Which organelle in a cell carries out this function?

.....

(1)

2. a) What theory did Charles Darwin propose?

.....

(1)

b) Why did many people not believe Darwin at the time?

.....

(1)

c) Describe how fossils are formed.

.....

.....

.....

(3)

d) The fossil record shows us that there have been some species that have formed and some that have become extinct.
i) What is meant by the term 'species'?

.....

(2)

ii) Describe how a new species may arise:

.....

.....

.....(3)

3. Ecologists regularly study habitats to measure the species present and the effect of any changes.
One team of ecologists investigated the habitat shown in the picture below:

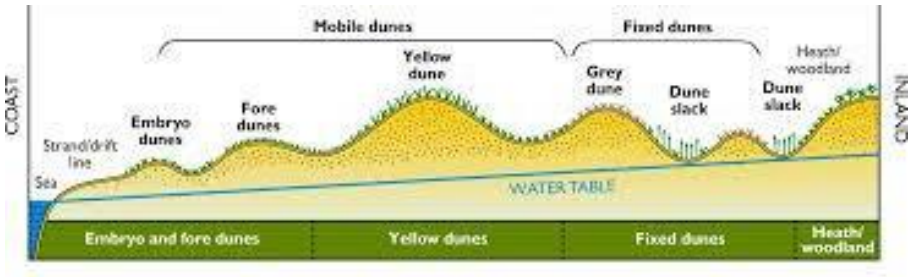


Image taken from http://www.macaulay.ac.uk/soilquality/Dune%20Succession.pdf

a) Define the following keywords:
i) Population

……

ii) Community

……

(2)

b) Give an example of one biotic factor and one abiotic factor that would be present in this habitat.

Biotic: ……

Abiotic: ……

(2)

c) Describe how the ecologists would go about measuring the species present between the coast and the inland.

……

……

……

……

……

……

(6)

4. Every living organism is made of cells.

Image taken from http://prestigebux.com/worksheet/label-an-animal-cell-worksheet

a) Label the following parts of the animal cell:

2 .....

5 .....

8 .....

(3)

b) Describe how the structure of the cell membrane is related to its function?

.....

.....

.....

(3)

5. A medical research team investigated how quickly the body deals with glucose after a meal. They studied the blood glucose concentration of people who exercised versus those who did not.
Here are their results:

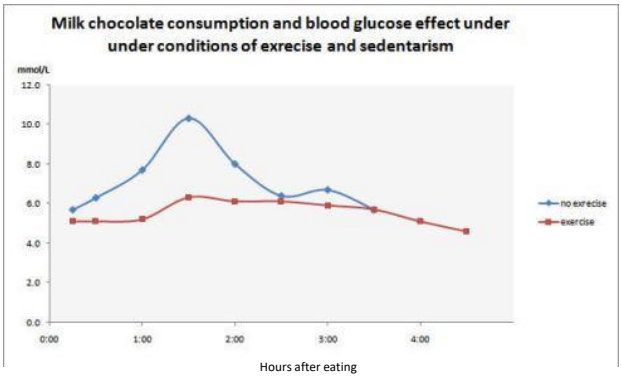


Image taken from https://memoirsofanamnesic.wordpress.com/category/blood-glucose/

a) What organ in the body regulates blood glucose concentration?

.....

(1)

b) Explain the stages that would bring about a return to normal blood glucose concentrations.

……

……

……

……

(4)

c) Name one variable the researchers will have controlled.

……

(1)

d) The researchers made the following conclusion:

"Blood glucose returns to normal values for all people after 4 hours"

To what extent do you agree with this conclusion.

……

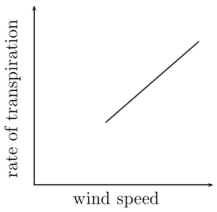
……

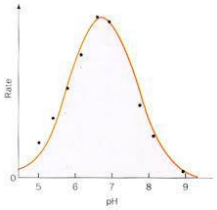
……

……

(3)

6. Scientists need to be able to interpret data in graphs to decide if there are trends in the results. For each graph below, describe the trend.





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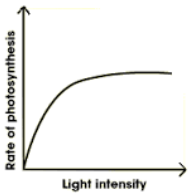
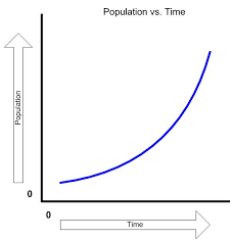




……

……(4)

Images taken from: http://www.everythingmaths.co.za/science/lifesciences/grade-10/05-support-and-transport-systems-in-plants/images/56aff2f9b6c5b041688f745ca928990c.png
http://www.bbc.co.uk/staticarchive/afa3f2b16b4d58d077943c96929c9a4020fea83a.gif
http://www.rpi.edu/dept/chem-eng/Biotech-Environ/Projects00/temph/enzyme.html
http://www.myearthwatchexperience.com/Essential%20Ecology.htm

3. Task: Article Summation – Context Building

Produced by the Wellcome Trust, the Big Picture magazine was aimed at post-16 students and explored contemporary issues within biology and medicine. Each contains accessible information, that is directly relevant to the curriculum, along with supporting resources such as stimulus materials, activity sheets and presentations. These can be used to illustrate how science works, science in society and also allow the issues to be tackled within the classroom. A wide range of topics are covered in this collection. For example, issues such as addiction, climate change, nanoscience, drug development, sex and gender, obesity and evolution.

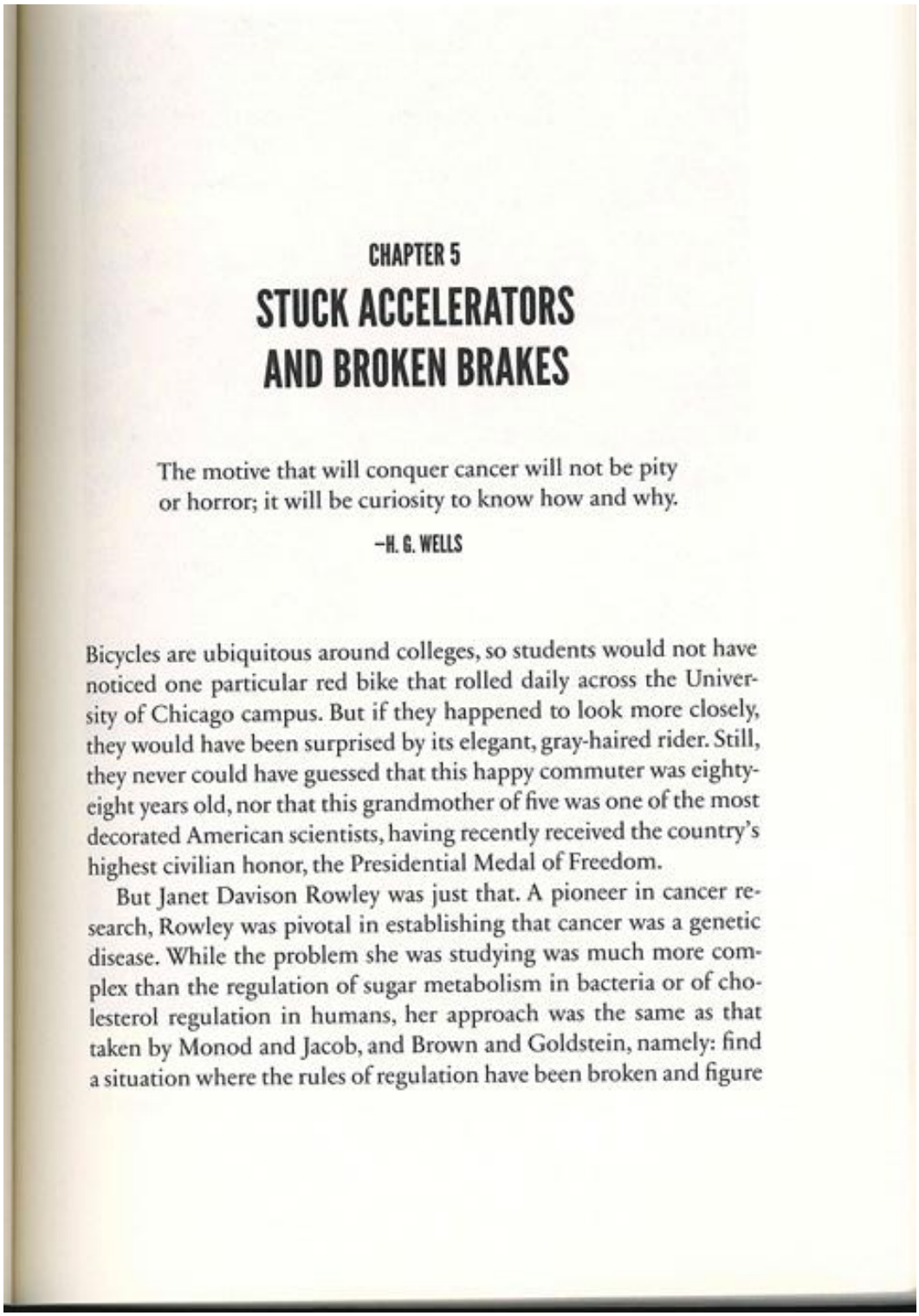
The Big Picture is no longer being published but STEM Learning has a database of articles and videos: | Resource Collection (https://www.stem.org.uk/resources/library/collection/2995/big-picture)

Task: Choose **two** articles and summarise their content using **Cornell notes** (one page per article). Chose something that **you** find interesting.

4. Task: Further Reading – Consolidating Ideas

Read one of the book chapters that I have provided (pick the one that speaks most to your interests) and produce a summary (1 page max – Cornell notes will be helpful) of what is being communicated **and** the evidence used to support it.

Serengeti Rules: Stuck Accelerators and Broken Brakes *(The interplay between regulation and cancer)*



CHAPTER 5

STUCK ACCELERATORS AND BROKEN BRAKES

The motive that will conquer cancer will not be pity or horror; it will be curiosity to know how and why.

—H. G. WELLS

Bicycles are ubiquitous around colleges, so students would not have noticed one particular red bike that rolled daily across the University of Chicago campus. But if they happened to look more closely, they would have been surprised by its elegant, gray-haired rider. Still, they never could have guessed that this happy commuter was eighty-eight years old, nor that this grandmother of five was one of the most decorated American scientists, having recently received the country's highest civilian honor, the Presidential Medal of Freedom.

But Janet Davison Rowley was just that. A pioneer in cancer research, Rowley was pivotal in establishing that cancer was a genetic disease. While the problem she was studying was much more complex than the regulation of sugar metabolism in bacteria or of cholesterol regulation in humans, her approach was the same as that taken by Monod and Jacob, and Brown and Goldstein, namely: find a situation where the rules of regulation have been broken and figure

FIGURE 5.1 Janet Rowley on her way to the laboratory.

Photograph by Dan Dry. Courtesy of the *University of Chicago Magazine*.

out what happened. Her breakthrough shaped a new view of cancer and ultimately led to a new kind of life-saving drug.

CHROMOSOMES AND PAPER DOLLS

Janet Davison grew up during the Depression in Chicago. Money was short, which required the family to move often from one neighborhood to another, and for young Janet to switch schools. The hard times precluded any luxuries or exotic hobbies. Her father introduced her to stamp collecting, and she became quite good at analyzing fine details. At an early age, she was able to pick out subtle differences among issues, such as whether there was a period or other distinguishing marks. She maintained the hobby well into adulthood, and the pattern recognition skills she acquired would turn out to serve her well.

After just two years of high school, Davison won a scholarship for a special program at the University of Chicago that enabled her to enroll at age fifteen and to complete both high school and a bachelor's degree. Davison thrived in the challenging but supportive atmosphere, and she developed a strong interest in biology and medicine. She then applied to and was accepted into the University's medical school. But in 1944, there was a quota for women, just three spots in a class of sixty-five students. The quota was filled, so Davison had to wait a year, which she did not see as a major setback, since she was still just twenty when she enrolled. She earned her medical degree in 1948, and the day after graduation married fellow medical student Donald Rowley.

While Davison (now Dr. Rowley) completed her education and training at an early age, she did not pursue a research career until much later. When she entered medical school, she looked forward to becoming a wife and mother, and she thought that being a physician would be an interesting, part-time profession. So, after completing their internships, she and Donald started their family. Rowley focused on raising four boys while working a few days a week at various clinics, first in Maryland and then back in Chicago.

One of those clinics served children with developmental disabilities. In 1959, only a couple of years after the correct total number of chromosomes in humans (forty-six) had been determined, it was

discovered that children with Down syndrome had an extra copy of chromosome 21. Although she had never taken a genetics class, Rowley became fascinated with the inheritance of genetic diseases. After having worked in the clinic for several years, she wanted to do something more challenging.

The opportunity soon came when Donald arranged to spend his sabbatical year at Oxford University with Howard Florey, Charles Elton's former tentmate and co-recipient of the 1945 Nobel Prize for the development of penicillin. Rowley figured that she could use the year in England to learn how to analyze chromosomes and then bring that expertise back to the Chicago clinic. The technique at the time involved taking blood cells and growing them in the presence of a radioactive precursor of DNA, then imaging the radioactive chromosomes with sensitive film. The procedure allowed an accurate count of chromosomes and could detect gross abnormalities, but it was hard to discern details that distinguished different chromosomes.

Rowley learned the procedure well enough to be a co-author on a paper that analyzed how chromosomes were copied as cells multiplied. On returning to Chicago, she decided that she did not want to continue at the clinic but to pursue research instead. With just one paper to her credit, she approached Dr. Leon Jacobson, director of the Argonne Cancer Research Hospital and former chief physician to the Manhattan Project research team at the University of Chicago.

"I have a research project started in England that I'd like to continue with. Could I work here part time[?]" Rowley explained. "All I need is a microscope and a darkroom. And by the way, will you pay me? I must earn enough for a baby sitter."

Jacobson agreed, and Rowley began looking at the chromosomes with various blood disorders. In some patients' cells, she could tell that there were extra or missing chromosomes, but she could not determine the specific chromosomes involved. It was not until a new banding technique was invented using a fluorescent dye that those details became discernible. Rowley learned that technique on another sabbatical in England. When she returned, she started looking at more samples from leukemia patients.

In early 1972, she noticed something unusual in cells from two acute myeloid leukemia patients: pieces of two different chromosomes (numbers 8 and 21) appeared to have broken off and swapped places. Known as a *translocation*, the fact that the same swap had taken place in two different patients with the same type of cancer was striking.

At the time, it was well known that cancer cells often had abnormal numbers or kinds of chromosomes. But on close inspection, many cancers often appeared to be quite heterogeneous. Because there did not appear to be any consistent pattern, the chromosomal aberrations were generally considered a later consequence, not a cause, of the cancer. Indeed, the idea that cancers had specific genetic causes was not widely accepted. When Peyton Rous received the 1966 Nobel Prize for his discovery of a virus that caused cancer in chickens, he stated, "A favorite explanation has been that oncogens [cancer-causing agents] cause alterations in the genes of the cells of the body. . . . But numerous facts, when taken together, decisively exclude this supposition."

Rowley was excited. Perhaps the specific change she observed in the chromosomes of two leukemia patients could be the cause of their disease? She wrote a short report and submitted it to the *New England Journal of Medicine*, the leading medical journal. It was rejected. When she called to ask why, she was told that the finding was deemed "unimportant." She sent the paper instead to the obscure French journal *Annales de Génétique*, which published it.

Shortly thereafter, Rowley began to look at the cells of patients with a different cancer called chronic myelogenous leukemia (CML). Working at home on her "off" days from the lab, she studied the details of their chromosomes. She took pictures of the stained preparations, cut out the individual chromosomes, attached them to scrap paper, and spread them out on the family dining room table. The chromosomes occurred in pairs, many joined near their centers with two long "arms" pointing up and down. The boys teased their mom about her playing with paper dolls.

Many years earlier, two Philadelphia researchers had discovered that some CML patients' cancer cells had one unusually small chromosome 22, dubbed the Philadelphia chromosome. When Rowley looked carefully at CML cells using the newer staining techniques, she detected that chromosome 9 was also longer than usual in three

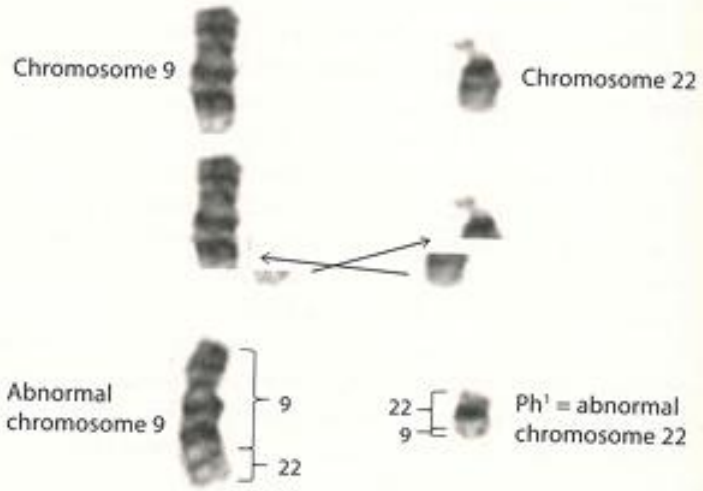


FIGURE 5.2 Chromosomal changes in a leukemia. Janet Davison Rowley noticed that not only was chromosome 22 abnormally small in chronic myelogenous leukemia cells (the Philadelphia chromosome), it had also exchanged ends with chromosome 9.

Reprinted by permission of Ruth MacKinnon.
http://scifundchallenge.org/firesidescience/2013/11/11/philadephia-the-birthplace-of-cancer-genetics/.

samples. In fact, the missing piece of chromosome 22 had been translocated to chromosome 9. This revealed that genetic information was not missing in CML cells, as previously thought: it had moved to a new location. [Figure 5.2]

With three independent cases of the chromosome 9;22 translocation in hand, she sent a report of her findings to *Nature*, the leading international science journal. The editors rejected the paper on the grounds that the translocation could just be a normal variation in the human population.

In the meantime, Rowley had examined the chromosomes of other cells in the patients' blood, which revealed forty-six normal chromosomes. The translocation was specific to the cancer cells. On top of that, she found several more independent cases of the same translocation among CML patients, nine in total. The anomaly

could not be a coincidence. With this additional data, *Nature* was convinced and published the paper in the summer of 1973.

Rowley's discoveries of specific but different chromosomal changes in two different types of leukemia was strong evidence that at least some cancers were caused by specific, perhaps unique, genetic mutations. The translocations she had observed raised all sorts of questions. Were there others? How did they trigger cancer? The questions began to consume Rowley. Suddenly, her part-time job had become the most exciting part of her life. Contrary to her longstanding plan, and to her own surprise, her career and research moved from being merely a sideline to, at age forty-eight, being the center of her life. She started biking to the lab five days a week.

Soon thereafter, Rowley identified another translocation between chromosomes 15 and 17 in acute promyelocytic leukemia, and another group discovered a translocation in Burkitt's lymphoma.

A translocation meant that two segments of DNA that were not previously neighbors had become joined. Rowley suspected that the new juxtaposition of two genes must be the critical event in the onset of the cancers. But in the mid- to late 1970s, the human genome (the DNA of all twenty-three chromosomes that contains all our genes) was *terra incognita*. Identifying which genes were involved, let alone understanding how their translocation caused cancer, seemed far out of reach. Until, that is, some startling insights emerged from an altogether different line of investigation.

FINDING THE GENES FOR CANCER

If there was skepticism about the role of chromosomal changes in the origin of cancer, and there was plenty, the role of viruses had been doubted even more. In 1910, Rockefeller Institute scientist Peyton Rous had identified a virus capable of producing sarcomas in chickens. However, there was so much skepticism about his finding, and so little he could do beyond asserting the existence of the virus responsible, that he himself gave up the line of work. It was not until decades later—when the virus could be seen in powerful electron microscopes, and additional tumor-causing viruses were isolated from other animals—that the concept of cancer-causing viruses was

firmly established. Hence, there was a fifty-six-year delay between Rous's discovery and his Nobel Prize. However, because no such viruses had been identified in humans, their role in human disease was at best unclear.

Still, the existence of tumor-causing viruses in animals offered potentially important clues to the rules for making cancer. One of the key advantages provided by studying a virus like the Rous sarcoma virus (RSV) was simplicity. RSV contained only a few genes, which raised the simple question: Which one(s) were involved in causing cancer?

The critical clue was discovered by Steve Martin, a graduate student at the University of California, Berkeley, who isolated a mutant RSV that was able to reproduce in cells but was unable to transform them into cancerous cells. The mutation responsible was in a single viral gene called *src* (pronounced "sark"), one of just four genes in the virus. Since an intact *src* gene was necessary for the virus to cause cancer, *src* was said to be a viral *oncogene* (a gene that induced cancer). But what could a chicken virus gene tell us about how cancer arose in general, particularly in humans?

The key insight from tumor viruses was obtained by another NIH-trained physician duo, Goldstein's and Brown's "classmate" Harold Varmus, and J. Michael Bishop. At NIH, Varmus studied the very enzyme regulation system pioneered by Monod and Jacob, while Bishop studied the polio virus. The two first teamed up when Varmus joined Bishop's laboratory at the University of California, San Francisco, in 1970 to study tumor viruses, RSV in particular; they later led a joint laboratory.

The discovery of the *src* gene provoked Varmus and Bishop to wonder about the origin of such a gene. The virus did not require it to infect or replicate in cells. If the virus did not need it to propagate itself, why did the gene exist, and where did it come from? Perhaps, they thought, it might be a cellular gene that the virus accidentally hijacked at some point in its history. If so, then one might find a *src* gene in normal chicken cells.

Looking for such a gene was much easier said than done in the era before the development of genetic engineering. It took nearly four

years before the critical experiment could be performed in which a radioactively labeled DNA "probe" representing the viral src gene was used to search for a similar gene in the DNA of normal cells. The first revealing results were obtained by postdoctoral fellow Dominique Stehelin in October 1974: chicken cells indeed had a similar *src* gene. They called it c-*src* (for cellular *src*) to distinguish it from v-*src*, the viral oncogene. C-*src* was soon found in other birds, including ducks and turkeys, even an emu.

But c-*src* was not just a bird gene. Varmus, Bishop, and their colleague Deborah Spector found the gene in mammals as well, including humans. Its presence in different animals revealed that c-*src* was an old gene that had existed for several hundred million years.

What could this mean? Varmus and Bishop pondered the exciting possibilities. First, the long evolutionary pedigree of c-*src* indicated that it had some job in normal cells. And, second, the close similarity between v-*src* and c-*src* suggested that the tumor-causing RSV could have acquired its v-*src* gene by hijacking a copy of the c-*src* gene, and in doing so, altered the gene so that it now caused cancerous growth.

Still, *src* was just one case. Were there other tumor virus oncogenes that had cellular counterparts? The race was on to find them. Very quickly, several viral oncogenes were discovered in different tumor viruses that infected chickens, mice, or rats, and their counterparts were found to exist not just in their host species, but in other animals, including humans. Genes named *myc*, *abl*, and *ras* extended the paradigm that viral oncogenes came from normal cellular genes, called proto-oncogenes.

By the late 1970s, there appeared to be two strong but unconnected bodies of evidence emerging as to the origin of cancer. The existence of viral oncogenes and cellular proto-oncogenes offered a powerful explanation of how viruses could cause cancers, but only in animals. The demonstration of consistent chromosomal changes in some human cancers was compelling but was limited to certain tumor types, and the genes involved were unknown. Was there any way to connect the two?

There was, and that connection would reveal how cancer was a disease of regulation.

BREAKING THE RULES OF REGULATION

Among the first handful of viral oncogenes and cellular proto-oncogenes discovered after *src* was the v-*abl* gene of the mouse Abelson leukemia virus and its cellular counterpart, the c-*abl* gene. Like c-*src* and the rest, c-*abl* also exists in the human genome. When researchers found that the c-*abl* gene mapped to human chromosome 9, the same chromosome implicated in the translocation Rowley described in CML, they wondered: Could there be some connection? Was the chromosome broken near the c-*abl* gene in CML patients?

It was a long shot. Chromsomes are very large, each containing an average of about 1,000 genes. C-*abl* could have been anywhere on the chromosome. A team of Dutch and British researchers probed cells containing the Philadelphia chromosome (number 22), and they were astonished to find that the c-*abl* gene from chromosome 9 had in fact moved to chromosome 22 (see Figure 5.3, left).

This discovery raised the exciting possibility that c-*abl* could be directly involved in the human cancer. To find out more about what happened to c-*abl* in CML cells, the researchers isolated the part of chromosome 22 that had been juxtaposed to the c-*abl* gene. Remarkably, it turned out that the c-*abl* gene had moved to almost the same place on chromosome 22 in seventeen different patients. So not only was the translocation from chromosome 9 to 22 a hallmark of the cancer, the chromosomes were joined at essentially the same location. This suggested that there was something very important about where c-*abl* was joined to chromosome 22. Further examination revealed that the c-*abl* gene was fused to another gene called *bcr* (for breakpoint cluster region). As a result, the fused gene produced an abnormal protein in which the "head" of the c-abl protein was fused to the "tail" of the bcr protein (see Figure 5.3, right).

Somehow, this fusion turned a normal proto-oncogene into a deadly oncogene. How it did so became clear when researchers compared the activities of the normal c-abl protein and the bcr/abl fusion protein. The c-abl protein is a member of class of enzymes called tyrosine kinases that work by adding phosphate groups to proteins. The addition and removal of phosphates is another common way

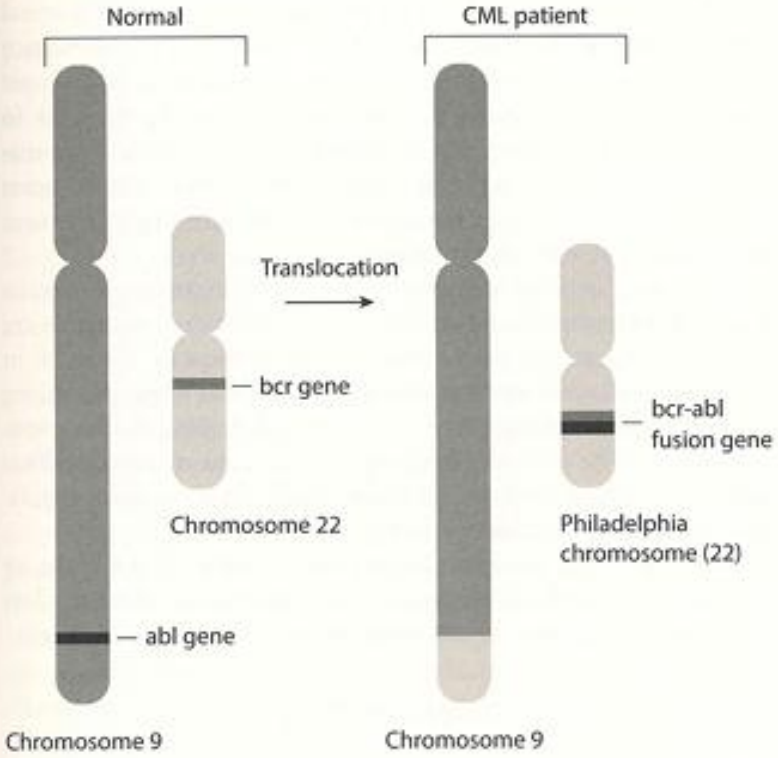


FIGURE 5.3 The fusion of two genes creates a cancer-causing oncogene. In chronic myelogenous leukemia cells the *abl* gene from chromosome 9 is fused to the *bcr* gene on chromosome 22; the hybrid gene produces a protein with abnormally elevated activity.

Illustration by Leanne Olds.

that protein activities are regulated, by flipping them between active and inactive states. Many kinases are parts of chemical relay systems that transfer information from outside cells to the internal machinery that determines whether the cell multiplies, differentiates, or dies. The activity of the c-abl tyrosine kinase activity is usually low in normal cells. But the activity of the bcr/abl fusion protein is much higher. The fusion created a mutant enzyme that, like the constitutive mutants studied by Monod and Jacob was always "on."

Leukemia, then, is a disease of regulation. In CML, the normal control of the multiplication of white cells is broken by the mutant bcr/abl protein. The hyperactive protein interferes with multiple relay systems in cells such that the signals to multiply are stuck in the "on" state, like a stuck accelerator in a car. As it turns out, mutations in several dozen other oncogenes implicated in myriad other cancers appear to have the same general effect, revealing that cancer in general is a disease of regulation.

While the discovery of oncogenes and their modes of action was a leap forward in understanding cancer, it turns out that oncogenes are just half of the genetic story of cancer. And perhaps by this point in this book, with what we have seen about regulatory logic, you might be able to guess the nature of the other half. A stuck accelerator is certainly not the only way for a car to careen out of control. What might be another mechanism? (Hint: think about negative regulation and double-negative regulatory logic.)

The same effect can result from a foot slipping off the brake, or cutting the brake lines. Researchers have found that indeed the loss of genetic "brakes" is a very common event in the genesis of cancer.

TUMOR SUPPRESSORS

The first genetic "brake" discovered involved a rare cancer of the eye called retinoblastoma. The disease usually develops in children at an early age and sometimes runs in families. The crucial clue to the genetic mystery of retinoblastoma was that in some cases, a portion of both copies of chromosome 13 was deleted, suggesting that the loss of both copies of some gene was the key event in the formation of retinoblastoma. This situation is in contrast to oncogenes, where the alteration of one copy of the gene (e.g., *bcr/abl*) was the key event in cancer formation.

In genetic parlance, we say that oncogene mutations are dominant, because they exert their effects even if the normal proto-oncogene is intact. In contrast, the retinoblastoma mutation is recessive, because both copies have to be altered for disease to form. It appears then that the normal function of the missing gene is necessary to prevent or suppress tumor formation, so this type of gene was dubbed a "tumor suppressor."

By zeroing in on the DNA that was missing in retinoblastoma patients, the retinoblastoma gene (dubbed *Rb*) was identified. *Rb*'s function, of course, is not to produce cancer, that is a consequence of its loss or alteration. Extensive studies of the Rb protein have revealed that its normal job is to control a critical decision in the life cycle of cells. For cells to multiply, they must copy their DNA and then divide into two. This process is highly regulated and progresses in phases. Rb acts at a major early checkpoint in this cycle by blocking the decision to replicate DNA. Loss of both copies of the *Rb* gene, then, allows cells to continue replicating in an uncontrolled way.

Rb is not the only tumor suppressor gene; about seventy such genes have now been identified. Nor are *Rb* mutations associated only with retinoblastoma; *Rb* mutations are found in other cancers, such as osteosarcoma and lung cancers.

Moreover, mutations are not the only way to inactivate Rb. The activity of the Rb protein is regulated by the addition of phosphate groups by protein kinases: Rb is most active when it is less phosphorylated, and inactivated by heavy phosphorylation. The direct or indirect effect of many oncogene proteins, including bcr/abl, is to increase the phosphorylation of Rb, which inhibits Rb activity and allows for continuous cell multiplication. Indeed, Rb is inactivated in some way in most, perhaps all, human cancers.

Here again is the sort of negative regulation and double-negative regulatory logic we have encountered before. Generally speaking, Rb is a repressor of cell multiplication. Cell growth, then, normally requires inhibition of this repressor to proceed. But inactivation (left) or loss (right) of Rb allows for constitutive growth:

Cancer via oncogene mutation	*Cancer via tumor suppressor mutation*
Oncoprotein (bcr-abl)	Oncoproteins
⊥	⊥
Rb protein inactive	Rb gene lost
⊥	⊥
DNA replication, Cell multiplication	**DNA replication, Cell multiplication**

The role of Rb fits remarkably well with Monod's and Jacob's speculation many decades ago about cancer resulting from the inactivation of a repressor of cell multiplication (see Chapter 3).

With this knowledge of how mutations in certain genes break the rules of the regulation of cell growth, the great challenge is to figure out how, if possible, to put the brakes back on in cancer cells.

LOGICAL THERAPY AND RATIONAL DRUGS

For many decades, cancer has been treated with surgery, irradiation, and cocktails of drugs that kill dividing cells. The latter are blunt instruments that do not target cancer cells specifically, so they are hampered by varying effectiveness, and cause many debilitating and dangerous side effects. The long-held hope of cancer research has been to design more effective, safer therapies that are tailored to a patient's specific cancer. That hope has become a reality. The pioneer in this new class of drugs, called Gleevec, targets the very mutation that Janet Rowley spotted on her dining room table.

But like many pioneers, Gleevec almost died several times before reaching its destination. Indeed, the parallels between the story of Gleevec and the development of the first statin are uncanny. But thanks again to a physician who saw the need and was tireless in encouraging drug development, there was spectacular clinical success that changed medical history.

The *bcr/abl* translocation creates a hyperactive protein kinase that causes the inactivation of the *Rb* repressor, allowing uncontrolled cell multiplication. What was needed was something that addressed the double-negative logic of CML—something that would inhibit *bcr/abl* and block the renegade enzyme from doing its harm.

Nick Lydon and Alex Matter, two scientists at the Ciba-Geigy pharmaceutical company in Basel, Switzerland, figured that since many oncogenes produced altered kinases, inhibitors of the enzymes might block cancer cell growth. Rather than searching through nature, as Endo did, or using the traditional trial and error methods of the pharmaceutical industry, they used a method called "rational design" to devise molecules that were to fit into and block the active site of kinases, so that the normal "key" can't fit into the "lock." After years of chemistry and testing, they had several candidate compounds, including a molecule that inhibited the normal c-abl kinase.

To find out whether any of their compounds could work on CML cells, Lydon offered them to a physician he knew. Brian Druker of the Oregon Health Sciences University in Portland was not only very interested in potential inhibitors of the bcr/abl kinase but, very importantly, he had access to CML patients' cells. Druker found that one particular compound Lydon gave him killed CML cells, but not normal cells, at very low concentrations.

While Druker, Lydon, and Matter were all excited by the results, the company did not think there was much of a market for a CML-specific drug. It took more than a year to convince them to advance to further testing in animals. Then, the first toxicology tests in dogs raised concerns that the drug was unsafe for intravenous use in humans. Soon thereafter, Ciba-Geigy merged with the Sandoz pharmaceutical company to create the new company Novartis. After the merger, the drug languished, and Lydon resigned.

Novartis scientists eventually put an oral formulation of the drug through animal testing, but the results again raised concerns. One toxicologist told Matter, "Not over my dead body will this compound go into man."

Druker, however, was not deterred. His patients' prognoses were grim—25 to 50 percent died in the first year after diagnosis—and the most he could do with available therapies was to buy time. Druker thought that any drug toxicity could be managed by monitoring patients and modifying the dosage. He urged Matter to "give the drug a chance," Matter kept pressing company management on the need for the drug. Finally, the new CEO of Novartis, Daniel Vasella, backed a clinical trial in humans. The study began in June 1998, almost five years after Druker had first tested the drug on CML cells in the laboratory.

Druker and two other physicians started administering the drug to a small number of CML patients, gradually increasing the dosage while monitoring both their disease and potential side effects. The main indicator of any benefit would be a drop in white cell count: normally there are about 4,000–10,000 cells per microliter of blood; in CML patients this can rocket to 100,000–500,000 cells per microliter. At low doses, they saw no effect. Then, as they administered larger doses, some patients' white cell counts dropped back toward normal. Inspection of their blood under the microscope revealed that the fraction of cells bearing the Philadelphia chromosome was also dropping. The drug was killing its target.

Novartis put its full resources behind the drug. The trial was expanded, the dosages were increased, and the patients followed for several months. Ninety-seven percent of patients who received the highest dose had their white blood counts return to normal, usually in just four to six weeks. In three-quarters of patients, the Philadelphia chromosome–containing cancer cells vanished. The results weren't good—they were great, unprecedented in the history of chemotherapy. The FDA gave the drug priority review and approved it in less than three months in May 2001.

Thanks to Gleevec, the prognosis for CML patients shifted dramatically. Long-term survival rates (longer than eight years) jumped to nearly 90 percent compared to about 45 percent before the introduction of the drug. Contrary to company forecasts, the drug turned out to be a blockbuster for Novartis, generating almost $28 billion in sales over ten years. In 2012, Lydon, Druker, and Rowley shared the prestigious Japan Prize for their respective contributions to the understanding and treatment of CML.

The rational approach to CML therapy was a spectacular success. But Gleevec is just one drug, *bcr/abl* is just one oncogene, and CML is just one type of cancer. What can we say or do about other cancers?

KNOW THY ENEMY—AND KILL IT

There are more than two hundred different cell types among the 37 trillion cells that make up the adult human body. Building and maintaining the right number of so many different kinds of cells requires a lot of regulation. It also requires the copying of many trillions of long molecules of DNA. Mistakes get made in the copying of DNA. Most of these mutations are harmless, but some create the potential for disaster. Understanding which specific mutations have occurred in an individual cancer is key to a more precise diagnosis and to targeted therapy.

The technology for analyzing cancers has come a long way since Janet Rowley cut out pictures of chromosomes and arranged them on her dining room table. Because of advances that have increased the speed and reduced the cost of DNA sequencing, it has become possible to peer into any tumor and assess the integrity of every gene.

By studying thousands of tumors of all sorts of tissues, researchers have built a catalog of gene mutations. By looking for genes that are frequently mutated (or lost) in each cancer, most of the genes that commonly contribute to cancer have been identified.

One major revelation from these surveys is that only a small fraction of all human genes are implicated in cancer. Of the roughly 20,000 genes in the human genome, about 140 have been found that are frequently mutated, with an almost even split between oncogenes and tumor suppressors. That figure can be seen as generally good news for researchers, doctors, and patients, as it narrows the number of players that we need to know about. And better still, we know a lot about the normal roles of these genes: virtually all of them are components of just a dozen well-studied relay systems or pathways that regulate cell differentiation or survival.

The surveys also reveal that most cancers contain mutations in two to eight of the 140 genes. Knowing which genes are altered in individual tumors provides a new way to classify them according to their genetic makeup, to relate the mutations to cancer behavior, and to target therapy against those mutations. In 1997, there were no approved drugs that specifically targeted mutations in any cancer; in 2015, there are more than three dozen drugs, with many more in the research pipeline. We are gaining ground, but it is far too early to declare victory.

In 2010, Janet Rowley was diagnosed with ovarian cancer. Throughout her treatment, she had biopsies and other samples of the tumor sent to her colleagues for study. But on December 17, 2013, she passed away from complications. She had pre-arranged her own autopsy, so that researchers could learn how her disease progressed.

I opened this chapter with a quote from H. G. Wells about the motives that would lead to the conquering of cancer. I omitted the preceding sentence of dialogue from the character in his novel *Meanwhile*: "The disease of cancer will be banished from life by calm, unhurrying, persistent men and women, working, with every shiver of feeling controlled and suppressed, in hospitals and laboratories."

The scientists who have made the greatest strides against cancer have neither been unhurrying, nor have they controlled or suppressed their feelings of urgency and compassion.

Gene Eating: Are your genes to blame when your jeans don't fit?
(Looking at the genetic components behind weight)

CHAPTER 1

Are your genes to blame when your jeans don't fit?

It has happened to us all.

You finally have a dinner date and you decide, in a fit of excitement, to call into service a pair of designer jeans you haven't worn in a little while. However, try as you may to pour yourself into the expensive denim, you find, to your horror, that the jeans now resemble a corset, requiring violent sucking in of your abdominal region, flirting with hypoxia, before the buttons can eventually meet the holes to perform their intended job.

Where can you ascribe blame for this scandalous state of affairs? Over-indulgence over the festive period? Your increasingly desk-bound job? Above-inflation increases in your gym membership fees? Bankers? Or can you, as is seemingly fashionable, place the blame squarely at the feet of genetics? Are your genes to blame when your jeans don't fit?

To answer this question, it is worthwhile considering some numbers:

a) an average-sized woman should consume around 2,000 calories a day in order to survive, and an average-sized man 2,500 calories; or around 750,000 – 900,000 calories a year;

b) while ageing from a youthful, exuberant twenty years to a middle-aged fifty, an average person will, depressingly, typically

gain 15kg (33lbs) in weight (some will of course gain little to no weight at all, while others will gain an awful lot more than 15kg);

c) if you or I were like a giant chocolate bar complete with nutritional information stamped on our collar labels, our caloric content would be around 5,000 calories per kg (give or take love handles/muffin-tops).

Because of c), the 15kg of weight gained over thirty years is worth about 75,000 calories, or 2,500 extra calories a year: a day's ration of calories if you're a man. If you did the necessary maths, you would find that an extra 7 calories a day for thirty years is all you would need to gain 15kg in weight!

Are you kidding me?

Other than it sounding like not an awful lot, what do 7 calories look like? Well, I rooted around my kitchen to see what I could find, and I came to the conclusion that nothing any of us would construe of as 'food' comes close to 7 calories. The nearest thing I could find was a 'serving' of ketchup. According to the nutritional information at the back of a half-empty squeezy bottle of ketchup that was purchased from a UK-based supermarket and languishing in my cupboard, a 'serving' of ketchup is 15g. Of course, to anyone who has ever introduced a bottle of ketchup to a burger or fries in anger, a 15g 'serving' of ketchup seems suspiciously austere. Even such a small amount of ketchup, however, would set back the energy storage account at the bank of your waistline a whole 15 calories. Using the same calculations as above, then the equivalent of an extra squeeze of ketchup, or even a heavy 'dip' with a chip or fry, every day for thirty years, would mean a weight gain of 30kgs!

The 'glass half empty' question that emerges from these numbers is: 'Why are we all not the size of houses?!' Good lord! We might all have to stop eating immediately, because of the imminent danger of exploding in a big red mess at the dining table! To the best of my knowledge, however, this is probably not happening out of sight in households up and down the country; at least certainly not on a regular basis.

Yet, when we reach for that extra chip, or helping of mayonnaise, or ketchup, or gravy, or wafer-thin mint, or a zillion other things which might be pleasant accompaniments to our meals but we don't even consider as real food, I guarantee that its energy content will be nearer to 70 calories than 7. So the 'glass half full' question is actually still, 'Why are we all not the size of houses?'

THE SET POINT

What is clear from data stretching back many decades is that mammals will robustly defend their bodyweight. The first data of this came not from humans, but from lab rats. Experiments done in the 1940s, which I have illustrated in the graph below, found that if a rat was left in a cage to its own devices and with sufficient food, it would grow at a certain rate. (Rodents, incidentally, never stop growing; they will keep growing until the day they die.) If the amount of food provided to the rat was reduced (i.e. if the rat was placed on a 'diet'), the rat would lose weight, which was unsurprising. Once the amount of food that was provided went back to normal however, the rats rapidly began to gain back the weight, but interestingly, only back to the growth rate they were on before the 'diet', and then they carried on like the diet never happened. When the food provided to the rats was changed to something very palatable, say high in sugar and fat, then the opposite was true, with their weight rapidly increasing. Once their food source was back to normal, the rats' weight drifted back down to the previous trajectory. These experiments led to the so-called 'set point' hypothesis, which proposed that all mammals in a stable environment will achieve a genetically determined trajectory of

growth. Any deviation from this trajectory, as with the dieting rats above, will be defended.

Data collected since those initial experiments shows that the same phenomenon occurs in humans. Despite all the holiday periods, the resulting diets, illnesses, pregnancies and life's many other little surprises, only very unusually will anyone deviate more than 20 per cent in their adult bodyweight over a lifetime. This is why when you see someone often, on a daily or weekly basis for instance, you can rarely tell if they have lost or gained any weight. Yet we do tend to gain weight as we age. Why?

There are two major reasons. First, as we clear our twenties and go through our thirties and beyond, we begin to accumulate inefficiencies in our various organ systems, such that our metabolism begins to slow down. Sadly, while this slow-down occurs at different rates in different people, it will happen in all of us. Second, on average, we move less as we get older; for example, perhaps with seniority in our jobs, we end up with more paperwork, and we have less time to get to the gym. Yet we don't tend to eat that much less (if at all) as we age. So when you head back for your

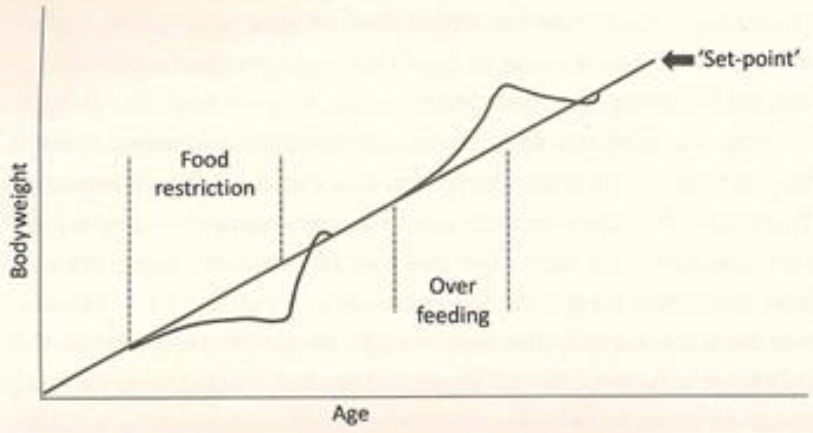


FIGURE 1 The 'set-point'

25th school reunion, you suddenly find it difficult to control your facial expression as you barely recognise anyone through all the increased fleshiness (I'm not trying to be a pot calling any kettle black as I would be unrecognisable as well).

The strategy used by our brain to defend our bodyweight is straightforward, even while the underlying mechanisms are complex (this will be a constant theme that runs through this book); that is, to influence food intake and energy expenditure. What I am not talking about here is the executive decision to go on a diet or to go to the gym. Those are conscious choices with their own distinct mechanistic and sociological underpinnings. Rather, the bodyweight defence strategy deployed by our brain is subconscious.

Let me give you an example. Imagine a typical festive season or some other vacation period, where there may have been a certain amount of overindulgence. Bacon and eggs every morning for breakfast you say? Sure! Desserts during both lunch and dinner? Why not! Eventually, and reluctantly, you have to get back to the real world and your normal day-to-day routine. Then comes that time in the day when you have to interact with food. Peering at a refrigerated supermarket shelf or perusing a menu in a restaurant, you may say, 'gosh, I don't feel so hungry tonight, I might just have a salad', thus eliciting a state of shock from your dinner companion.

I don't feel so hungry tonight.

Why not? Did you have a sudden attack of 'will-power'? Did a rod of steel just get shoved up your vertebral column, stiffening your back? No, the signals in your brain are simply making you feel 'not hungry'. 'Why can't I feel like that a little more often?' many of you will undoubtedly be thinking.

More than almost anything however, your brain absolutely hates it when you lose any weight. How much fat you are carrying is essentially how long you would last without food, so your brain equates weight loss to a reduced chance of survival. So when you

lose even a few pounds, your body begins to fight back, making it rapidly more and more difficult (or so it seems) to shift each additional gram. Your body reduces its energy expenditure; it is with little consequence, for instance, that the energy efficiency of your metabolically most active organs, such as your liver or skeletal muscles, can be reduced by a few per cent. Your body also makes you feel more hungry, driving you to eat more. Keeping in mind that just a pesky 7 extra calories a day makes such a surprisingly large impact over a lifetime, the depressing phenomenon familiar to dieters the world over occurs; where after a couple of months, all of the weight you fought to lose has somehow grimly clawed its way back. This is, of course, what most will be familiar with as 'yo-yo' dieting, where you lose weight (yay!) then you regain the weight (boo!) and the cycle, depressingly, repeats itself interminably. Although it might seem as if you are gaining more weight than you had lost, this is seldom the case, and your weight will typically go back to where it was before you began your diet, i.e. your set point. Considering at any given point in time, nearly 20 per cent of you reading this book will be on some sort of 'diet', there are a lot of depressed people about due to this pattern.

BODY MASS INDEX

In fact, while 20 per cent of us are desperately trying to diet, the reality is that nearly 60 per cent of us in the UK and US are either overweight or obese.[1] Obesity is measured by Body Mass Index (BMI). This is a ratio of bodyweight in kilograms divided by the square of one's height in metres, and hence is represented as kg/m^2. A 'normal' BMI is 20–25kg/m^2. Anything below a BMI of 18 would be considered underweight, a BMI of 25–30kg/m^2 is considered 'overweight,' and if you have a BMI north of 30kg/m^2, you would then be classed as obese. However, it is important to know that ubiquitous as it is, BMI as a measure of 'fatness' is inherently imperfect because it is derived using purely your weight and your height. It cannot, for instance, differentiate between a rugby or American football player and a Joe Public of similar height and weight but carrying substantially less muscle mass. Crucially, it is the percentage of fat that one carries and where it sits in the body, rather than one's weight *per se*, that is strongly linked to disease.

There are any number of ways to measure fat percentage. The 'gold-standard' method of measuring fat-mass is by use of a technique called Dual-energy X-ray absorptiometry or DEXA. This is where two low-power X-ray beams, with different energy levels, are used to scan your body. X-Rays work by differentiating tissue density, which is why it is traditionally used to look at your bones, which are the densest part of the body. At a lower power however, it is also able to detect the difference between muscle (which has a higher density) and fat (which has a lower density), and therefore be used to calculate fat-percentage.

Another approach, that will be more familiar to many of you, will be the use of body-fat scales. These are available in countless models, and use a technology called 'bioelectrical impedance' to estimate how much body fat you have. The most popular models are integrated into traditional bathroom scales. When you step, barefoot, on to sensors on the scale, an imperceptible electrical current passes up one leg, across the pelvis and then down the other leg. There are also larger versions of these, typically built into weighing machines found in drug-stores or pharmacies, which get you to grip two handle-bars, and a current is passed through one arm, across your torso and through the other arm. The underlying principal in both these types of scales is identical. Because it contains much more water, muscle conducts electricity better than fat does, so the greater the electrical resistance, the more body fat you have.

But yet, in spite these available tools, the use of the BMI still dominates. Why is that?

DEXA is certainly both very accurate and precise. It is however, also expensive, requiring specialist equipment and technicians to run, so is just not logistically suitable for use in population-wide studies. The body-fat scales, while widely available, are notoriously inaccurate. There are too many variables, including how hydrated you are, when you last ate and exercised, and even whether your feet are particularly calloused or dirty, that can influence the calculated fat percentage from measurement to measurement. There is also the type and quality of the product itself, ranging in price from less than £30 to nearly £2,000, which precludes truly comparative measurements across different instruments.

In contrast, your BMI is free to calculate, assuming you have a way of weighing yourself and measuring your height, so is suitable for large population studies. And critically, despite being imperfect for measuring fatness in particularly athletic individuals, the sad fact is that the VAST majority of the population do not fall into this category. As a result, for most of us, the higher our BMI, the more fat we do tend to carry. So the use of the BMI as a proxy for 'fatness' continues to dominate.

IN AND OUT, IT'S PHYSICS!

Today, 60 per cent of us are carrying too much fat, making obesity one of the greatest public health challenges of the 21st century. It is a modern problem, with the prevalence of obesity having tripled in many countries in the world since the 1980s. According to the latest health report from the Organisation for Economic Co-operation and Development,[2] more than 30 per cent of adults in the US, New Zealand and Mexico, and more that 25 per cent in the UK, Australia, Canada, Chile, and South Africa, are obese. Within the European Union nearly 150 million adults and 15 million children are considered obese. The problem is not with obesity itself, but with the accompanying increased risk to a whole host of nasty diseases, including type 2 diabetes, heart-disease, high blood pressure and certain types of cancer. Unfortunately, we don't really have to gain that much weight before we are in the same frame as these 'co-morbidities'.

So how can we explain this rapid worldwide increase of bodyweight? Have our genes changed? Have we suddenly evolved? Clearly not. These dramatic changes have occurred over the past thirty years, against a constant gene pool and well within the lifetime of many of you reading this book. This would put the smoking gun in the guilty hands of 'environmental changes', an all-encompassing term used to describe changes in lifestyle, diet and working practices. Sadly, no matter how much one doth protest, the ONLY way you can gain weight, is if you eat MORE than you burn. It is simple physics.

Let me say this very clearly: the reason we have become more obese as a species is because we eat too much and don't move enough. Therefore, the only way to become less obese is to eat less and move more. There we have the cause and cure for the obesity epidemic. We all know this.

That being said, hidden in this simple statement is an oft-overlooked complexity that is well worth further exploration. Have a look at the two graphs below. Both indicate the real-world increase in average BMI, as charted by the US Centre for Disease Control or CDC, within the US population from 1985 (23kg/m^2) to 2014 (27kg/m^2).[3] The upper and lower graphs then plot two different possible distributions of BMI within the population in 2014 as compared to 1985. The upper panel models what the data would look like IF the environment was the ONLY influence on our bodyweight. In this scenario, everyone should respond to the environment in the same way, and everyone should therefore gain

the same amount of weight. Thus the BMI distribution within the population should remain the same shape, but simply be shifted to the right, revealing a shape reminiscent of the Golden Gate Bridge.

The real data, however, shown in the bottom graph, reveals something very different. While the average BMI within the population has indeed increased, the shape of the 2014 curve has changed. This has happened because some people have gained lots of weight in the current environment, some not so much and some have not gained a single gram. In other words, everyone responds differently to the change in environment.

What all this means is that the environment cannot be the only thing that is influencing our BMI. There must be biological variation in our response to a changing environment. Put another way, the question of HOW we have become obese is one of physics. The question of WHY we have become obese requires examination of why some people eat more than others, why some people are more metabolically efficient and why some people burn more energy. It is in these latter questions that the biological variation lies.

Our biology, how we are put together, how our organs work, how the cells that characterise our organs function, how the molecules and proteins that form our cells interact, begins with our genes. So to understand biological variation, it is inescapable that we first need to understand variation in genetic heritability. The past twenty years of my life have been spent studying the genetic heritability of bodyweight and how it varies throughout the population.

THE POWER OF TWINS

One of the most invaluable tools in determining the genetic heritability of specific traits is the study of twins. Identical twins are genetic 'clones', while fraternal (or non-identical) twins share 50

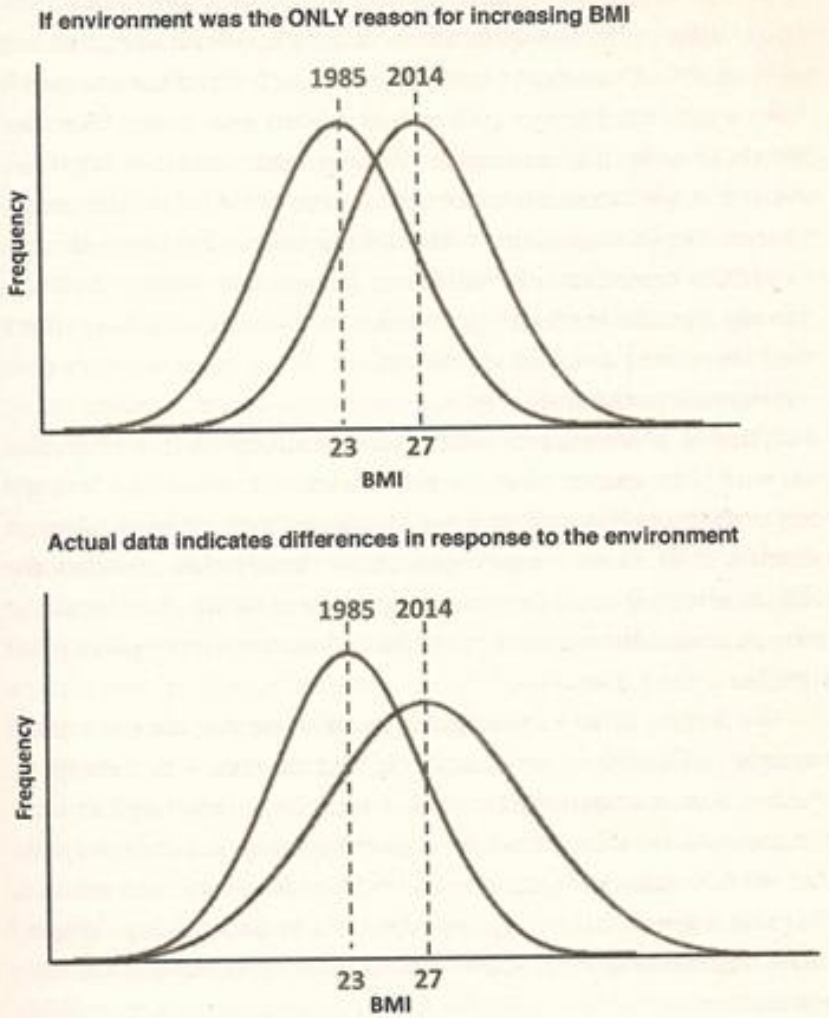


FIGURE 2 Two possible models to explain the increase in average BMI from 1985 to 2014

per cent of genetic material, as you would with any of your siblings. Thus, with the study of enough twins, both identical and non-identical, one could look at any trait that could conceivably have a genetic element, such as eye colour, hair colour, foot size, height or weight, and calculate how heritable each trait might be. As you might imagine, traits such as eye colour and hair colour (peroxide aside) are almost entirely genetically determined, with very little environmental influence. In contrast, while a trait like having freckles is clearly genetically influenced, whether, where and how many freckles appear will be down to how much time one spends in the sun.

There is, however, one valid argument against twin studies; that is, while the genetic power is self-evident, twins are still brought up in the same household, thus possessing a shared environment during their most formative of years. Surely this muddies the water when it comes to measuring the heritability of traits where the environment wields a powerful influence? A very good point indeed.

We do live in an unpredictable world where sometimes awful things can happen; one of which is that siblings, a percentage of whom will of course be twins, are sometimes separated at birth and raised in different adoptive homes, often in completely different countries and cultures. So you may have one twin raised as a carnivorous Catholic and another as a vegetarian Jew. When I first began my career, I did wonder how often could this situation possibly have occurred? While accurate numbers are not available, the answer is most certainly in the thousands – more often than any of us could ever imagine.

One, but by no means the only, driving force has been China's one-child policy, which has since been toned down somewhat. This led to the abandonment of tens of thousands of infants, amongst which were many hundreds of twin-pairs adopted and raised separately. Recently, there was a documentary by Norwegian filmmaker Mona Friis Bertheussen called *Twin Sisters*, telling the story of just such a pair of identical Chinese twin girls.[4] After being found abandoned in a cardboard box, Mia was adopted by a Californian couple and Alexandra by a couple from the north of Norway. Mia was raised as an 'all-American' girl, playing soccer, selling girl-scout cookies and going to the mall, while Alexandra led an outdoor life in the quiet solitude of a tiny village close to the Arctic circle. Just imagine the difference in diet and culture, in temperature and availability of sunlight, in education system and types of daily activity. Yet at ten years old when they eventually meet, aside from the expected language barrier, they are alike in character and temperament, and almost identical in height and weight. This same story has been reported many times over, with twins of other ethnicities and raised apart in other countries. Of course, the older the twins are when they are eventually reunited, the larger the influence of the environment, and consequently, the greater the variance in their weight. Time and time again, however, the power of genetics even in the face of such environmental differences is quite literally jaw-dropping.

What surprises most people is that the heritability of weight is actually close to that of height. No one would dispute the fact that height is genetically determined: tall parents = tall children. It is also well known that skeletons and written records show that human beings today are inches taller than humans just a century or two ago. For example, soldiers around the age of twenty who enlisted in the army during World War I were on average 168cm (5'6"), while today's average for young men is 178cm (5'10").[5] Why have we become taller as a species? Because of changes in diet, environment, and lifestyle.

It is the same argument with bodyweight, except that the changes have happened over a far shorter period of time. We are now more obese as a species compared to thirty years ago because of changes to our diet, environment and lifestyle. But it does not

change the fact that if our parents are overweight and/or a certain shape, we are very much more likely to be overweight and/or be that shape. The studies demonstrated that the genetic heritability of bodyweight and shape in twins is approximately 70 per cent.[6]

The next time you have an opportunity to people watch, while you are at the airport or a coffee-shop for instance (please do be discreet), have a look at just how heritable body-shape in particular is. Your shape is largely determined by where fat sits in your body. This is not meant to depress you, but close your eyes for just one moment and reflect upon the shape of your parents. Does your mum have a big bum and a skinny upper body? Does your dad have a big tummy and skinny legs? Who do you look like? Who do your siblings look like? While the absolute amount of fat may differ – you may have a bigger bum or a smaller tummy, say – the chances are very high indeed that you will have the shape of one of your parents.

In truth, everything about us – our looks, our shape and size, our character, our intelligence, our athleticism, our risk of mental illness, even our risk of getting into a car accident, along with a million other traits – all have a genetic and an environmental component. It is very rarely, if at all, 100 per cent genetic or 100 per cent environmental. The real difficulty is in determining the relative contribution of each and, crucially, how they interact with each other.

DESERTS OF THE AMERICAN SOUTHWEST AND THE ISLANDS OF THE SOUTH PACIFIC

Yet another fact that has revealed the role of genetics in bodyweight is the observation that certain ethnic groups are more likely to become obese than others. Two examples from the more severe end of the spectrum have proven to be particularly informative.

The first are the Pima Indians, who are not South Asian Indians, but rather are indigenous or native Americans that live in the deserts of Arizona in the American Southwest. They are, infamously, one of the heaviest peoples in the world.[7] Nearly all Pimas, some from a frighteningly early age, become obese, with more than 50 per cent of Pimas suffering from type 2 diabetes.[8] This prevalence of type 2 diabetes is nearly five times higher than in the rest of the United States, a country of course deep in the grip of its own modern obesity crises. The Pimas, however, have been suffering from obesity and their related diseases for more than 50 years! And yet another group of Pimas, those living up in the Sierra Madre mountains of Mexico, display no proclivity to obesity at all. By all accounts, the Pima people were all initially from the Arizona region, but a contingent, at some point in the past and for some unknown reason, moved to the Sierra Madre. These two groups of Pima Indians remain genetically indistinguishable. Why, then, do they possess such vastly different bodyweights and rates of metabolic disease? The answer lies in the environment. The Arizona Pimas enjoy (is this the right word?) the American lifestyle, together with all of its conveniences and its excesses. The Sierra Madre Pimas however, still live like their ancestors. They are a farming community that still works with animals, with hard physical labour very much a part of everyday life, and who, of course, subsist on a very different diet from their American cousins. This is almost like having a time machine, allowing us to glimpse what the Arizona Pimas would have looked like living in the desert, prior to the arrival of European settlers.

The second example comes not from one singular ethnic group, but rather the multiple different peoples of the Pacific Island nations of Polynesia. The small island of Nauru for instance (and most of the Pacific Island nations are by and large small islands), is one of the most obese countries in the world, with nearly 95 per cent of its inhabitants being overweight and more than 45

per cent classed as obese. In fact, according to the World Health Organization (WHO), nine of the ten most obese countries or territories globally are Polynesian Pacific Islands.[9] The Cook Islands top this deadly leader board, with more than 50 per cent of their population classed as obese. Nauru, Palau, Samoa, Tonga and the Marshall Islands are all not far behind. This is, certainly when it comes to percentages, the fattest region in the world. Why is this the case?

On the face of it, the explanations that emerge when one takes a peek at Wikipedia or Google seem to make sense. One argument is that on these paradise islands, perhaps more than anywhere else in the world, there is wide cultural acceptance that bigger is more beautiful. Another argument, echoing the lifestyle issues faced by the Arizona Pimas, is that the life of the typical Polynesian is based upon consumption of imported, highly processed food, very little exercise and remote access to healthcare. These answers, however, are just too pat, too simplistic. Many cultures, for instance, embrace the 'big is beautiful' mantra, and a love of cheap processed food is hardly unique to the American Southwest and the South Pacific. But yet in an increasingly overfed world, these two groups of people stand out. What, then, are the root causes of these problems, and why have the results been so extreme for the Pimas and Polynesians in particular?

While the details differ, the underlying reasons are actually the same. In both regions, there have been millennia of adaptation to fluctuations of food availability in a harsh (for the Pimas) or geographically isolated (Pacific Islanders) environment and the necessity therefore of hard physical labour to secure food. Then quite abruptly, because of events completely out of their control, there was a very rapid and very dramatic change in the diet and lifestyle of both peoples.

The Pimas have lived on the banks of the Gila and Salt Rivers since long before European contact, which provided an important lifeline in the deserts of the Southwest. Life would have been very harsh, and a genetic premium would have been placed on those individuals better adapted to the episodic 'feast or famine' food environment. Those individuals who were better able to eat more and store fat during times of plenty and then be more efficient with energy usage in times of famine would have been more likely to survive. In turn, the genes which determined these survival characteristics were more likely to be passed on to their children. This is, in essence, evolution at play, with many generations of Pimas undergoing this extreme genetic selection, resulting in a population finely adapted to living in that particular environment. In the 1920s, however, the US government began a water irrigation project that necessitated the construction of a water storage dam on the Gila River upstream from Pima native lands, stopping its flow almost overnight. With the loss of their water (and thus food) supply, the Pimas became reliant on government food handouts. These tended to be processed, higher in sugar and refined flour and therefore much more calorically dense, and critically, a world away from their traditional diet. This mix of Pima genes with the new diet resulted in a rapid increase in levels of obesity.

Colonisation of the Polynesian Islands took place over nearly three millennia, beginning in the Philippines and New Guinea in around 1500 BC, Samoa in 800 BC, Hawaii and Easter Island not until 900 AD, with New Zealand the last to be colonised in 1200 AD. Given the geographic isolation of these tiny islands in an absolutely enormous area of the South Pacific, their colonisation is really a testament to human endeavour. The early Polynesians would first have had to survive canoe journeys of many weeks, and then, having arrived on small Pacific islands (atolls even), they would have to live and thrive. In this context, to be big meant certainly much more than being beautiful; it meant being much more likely to survive. The islanders formed – unsurprising given

their geographic location – traditional fishing communities. The arrival of US and British airbases during World War II, as well as the proliferation of mining in some islands, drove globalisation, including the importation of western foods. These were brought in initially for the allied airmen and the miners. However, as is true the world over, imported food (highly processed in order to survive the journey) was very cheap and energy dense, and was rapidly embraced by the Polynesians. As with the example of the Pimas, the environment changed dramatically and rapidly for the Polynesians.

But why did both the Pimas and the Polynesians respond in such an extreme fashion to the change in environment? Many people, after all, you and me included, eat these same foods without tipping into extreme obesity. The difference is that the vast majority of us have adapted to live on continental plains. If our ancestors encountered a famine or drought, they could have mitigated against this 'selection pressure' and moved somewhere else. If, however, you were tied to one specific area like the Pimas, or were geographically isolated like the Polynesians, and therefore wouldn't or couldn't move, you either adapted quickly, or you died. Imagine, for a moment, if there was a sudden extreme change to our cosy situation that required us to be able to run really quickly, otherwise we would, say, be eaten by some rapidly reproducing carnivores with long legs and very pointy teeth. Well, we would very quickly end up with a population enriched with very fast runners, who would then pass on their genes to their offspring and so on and so forth. The fact that the Pima and Polynesian populations are still around meant that enough extraordinary individuals were able to adapt quickly, eating enough and storing enough fat during times of plenty, and being efficient during famines or paddling for weeks across the ocean, thereby surviving to pass those genes on. After just a few generations, those 'extraordinary' genes then became the norm within that population. The problem is that while those genes were advantageous and enabled survival in a 'feast–famine' environment, they have become deadly in today's 'feast–feast' environment.

All living creatures live by the golden rule to be as energy efficient as possible, in order to conserve calories for times of food austerity, and to make sure to eat as much as possible when the opportunity presents itself. So if a cheaper and more energy-dense food source suddenly appears, why would you continue wasting energy going out fishing or farming? That obviously had the deadly double result of increasing intake of highly calorific available foods (more about this later on in the book) and reducing physical activity in both the Pimas and Polynesians, thus driving the severe obesity problems in both communities.

THE HIGHLY EVOLVED RESPONSE

While the examples of the Pimas and Polynesians might seem extreme, the issues that arise are relevant to all of us. The concept of being as efficient with our energy expenditure and calorie usage as possible is true for us all. It is easy to forget that not so long ago, all our physical activity was gained from daily living. Working on the farms and in the mines; fishing and hunting; hand-washing everything (clothes and dishes); hand-sewing everything etc., etc. The whole concept of 'exercise' as a leisure activity would have been alien until just a few decades ago. Why would you do anything other than eat and sleep in your spare time, if you've spent all day in hard physical labour? If you think about it, is it not a weird thing for a significant chunk of the population to drive to a gym, maybe take an escalator or elevator up (or down) a couple of floors, only to get on a treadmill or stationary bike?

Then there is the current food environment we live in. One clear

case in point is the phenomenon of 'fast food', which is, as we are all too familiar with, pervasive in our society. The vast majority of this food is calorically dense, highly processed, very cheap and often delivered straight to your door after a brief interaction with a smartphone.

What the data tells us is that, in effect, some of us simply feel a little more hungry all of the time. Not eating when you are not hungry is easy. Whatever the press, beauty/fashion/health/fitness magazines, Hollywood and 'inspirational I-did-so-you-can-too' speakers say, thin people are not morally superior, with the willpower of forged steel. They just feel a little less hungry, so get full up more easily. It requires no effort.

Have you, however, tried to stop eating when you are still hungry? It's difficult, even for one meal, because it's just not what we are designed to do. We have evolved to eat when we are hungry and when there is food, not to stop. Now imagine feeling slightly more hungry in this food environment and trying to halt the eating process every single day, for every single meal, for your whole life. This is what overweight and obese folk go through.

Obese people are not morally bereft, lazy or bad. They are fighting their biology. In fact, you could argue that being obese is the natural, highly evolved even, response to our 21st-century environment! We are simply preparing ourselves for a famine . . . that is never ever going to arrive.

But here is the rub. Not everyone has become obese in this environment. This is in contrast to our response to starvation, which is reassuringly uniform, across not only humankind but pretty much across the entire animal kingdom; that is, to find enough food as quickly as possible and eat it before you die. The dying bit ensured that only animals with the required drive and tools to find and eat food survived.

FROM GENETIC CODE TO FUNCTION

If you will indulge me, a brief genetics 'primer'. The complete set of our genetic material, our DNA, is called the genome. It is composed of three billion nucleotides, each coming in one of four different flavours; adenine or 'A,' thymine or 'T', guanine or 'G' and cytosine or 'C'. Two complete sets of this genome (one from mum and one from dad) are present in every single cell in our body (the two exceptions being, depending if we are male or female, our sperm or eggs, which only contain one copy of the genome; and our red blood cells, which don't contain any DNA at all). DNA is literally a very long, thin thread of these three billion A, T, G and C nucleotides strung together. If it were possible to stretch out the DNA from a single cell, you would find it to be, incredibly, nearly two metres (six feet) long! This enormous length of DNA is tightly and neatly origamied into two sets of 23 different chromosomes (one set for each copy of the genome, so 46 chromosomes in total), each containing around 25,000 different genes. However, only 1–2 per cent of our three billion nucleotides in our genome actually code for genes. A significant but small percentage of the 98 per cent of 'non-coding' DNA are regulatory elements that control whether and how these genes are turned on or off. How much exactly we still don't know is the subject of ongoing and cutting-edge research. The vast majority of the remaining 'non-coding' DNA, what we used to call 'junk' DNA, remains 'dark' to us, and is largely a mystery. Much of this dark DNA may well turn out to be junk, but equally, there are almost certainly untold hidden treasures of functional significance yet to be uncovered.

The genes themselves do not confer function *per se*. Rather, they carry the information required to assemble the proteins that actually confer structure and function, the biology of life. Our genes

are therefore an instruction manual for all of the different proteins that enable life.

ARE OUR GENES TO BLAME WHEN OUR JEANS DON'T FIT?

Mutations within our DNA happen randomly and at a low background level all of the time. Because the vast majority of our DNA has no known function, mostly these changes have no measurable effect. Rarely, a mutation may occur in a segment of DNA that regulates gene expression; meaning whether it is 'turned on', transcribed into RNA and translated into protein. Even more rarely, it could change the actual gene sequence, thus altering the function of the resulting protein. If the change in gene expression or sequence is severe enough to either disrupt translation or dramatically alter the function of its corresponding protein, it manifests as a disease, or at its most severe, death. At other times, however, genetic changes might simply modulate the function of the protein, either positively or negatively, depending on the environment.

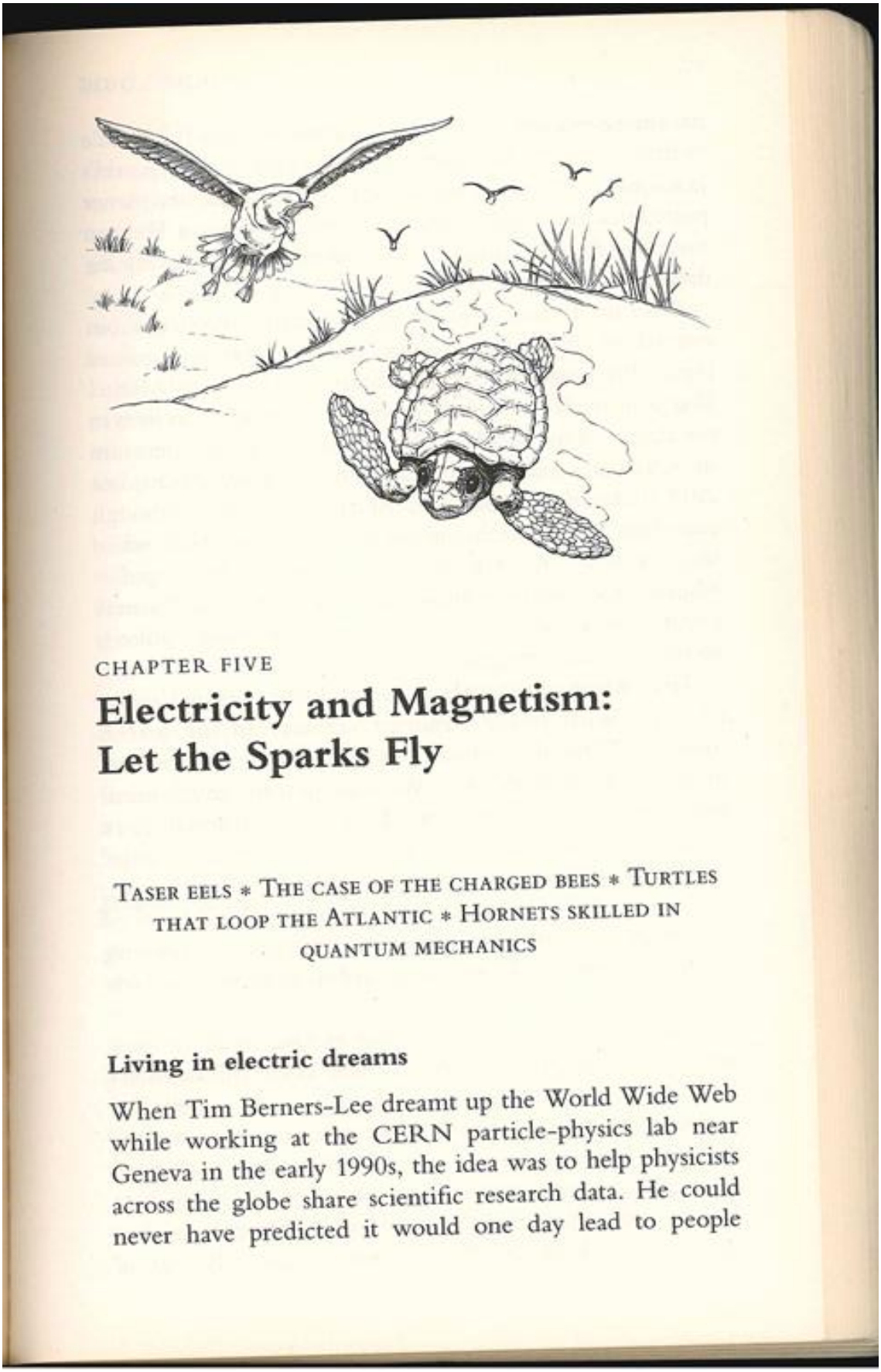
If a genetic change is not desirable in a certain environment, then it is 'selected against' and not passed on. If a genetic change increases your chances of survival, then it is 'selected for' and that change is then passed on and integrates itself into the population. Take the response to starvation, for example. Any genetic change that increased your likelihood of finding enough food would mean that you could get bigger or faster or stronger, which would in turn increase your chances of finding a mate to reproduce and passing those genetic changes to your offspring.

Then there are genetic changes that in one environment have a neutral effect, but in another environment suddenly have a huge positive or negative effect. So, for example, in our current cosy situation, someone like Usain Bolt clearly runs very quickly and therefore can have a career in athletics, whereas while I cannot run quickly, I can make my living as a geneticist. Our proclivity to run has a neutral effect on our ability to survive in our current environment. But when the environment changes and long-legged pointy-toothed bitey carnivores begin to rapidly reproduce, Mr Bolt's fast twitch muscle genes suddenly have a positive effect on his ability to survive and are therefore selected for. In contrast, my ability as a geneticist has a neutral effect in the new environment, while my inability to run quickly has a negative effect on my likelihood of outrunning the carnivore.

Having too much food, coupled with not moving enough, is a contemporary problem, and would not have been a 'selection pressure' during evolution. With the rapid changes over the past few decades, accumulated genetic changes, which would have varied across the population and had a neutral effect when there was not enough food, were suddenly unmasked in our modern food and living environment. So while the average weight of the population has increased because everyone is exposed to more food and moving around less, some people, because of their repertoire of genetic variation, have become more obese than others in this environment.

So, to bring it back to my original question: are your genes to blame when your jeans don't fit? In many ways, yes. While the changing environment has undoubtedly driven the rapid increase in the prevalence of obesity, it is now becoming clear that our genes have influenced our response to this change. Where there are genes, there are molecules to identify and biology to study. That is what I am interested in studying; the pathways and mechanisms that control food intake, and how these vary between lean and obese individuals.

Furry Physics: Electricity and Magnetism: Let the sparks Fly – Taser Eels *(Looking at the Physics behind electric eels)*



CHAPTER FIVE

Electricity and Magnetism: Let the Sparks Fly

TASER EELS * THE CASE OF THE CHARGED BEES * TURTLES THAT LOOP THE ATLANTIC * HORNETS SKILLED IN QUANTUM MECHANICS

Living in electric dreams

When Tim Berners-Lee dreamt up the World Wide Web while working at the CERN particle-physics lab near Geneva in the early 1990s, the idea was to help physicists across the globe share scientific research data. He could never have predicted it would one day lead to people

streaming endless cute animal videos on YouTube. One online sensation has been Tardar Sauce – 'the world's grumpiest cat' – who went viral in 2012 after her owner posted footage of this miserable-looking sourpuss. You can even buy mugs, T-shirts, books and calendars featuring the discontented feline.

Over on Twitter, you'll find enthusiasts tweeting about everything from ducks and dogs to parrots and guinea pigs. Our favourite tweeting animal, though, is Miguel Wattson, an electric eel (*Electrophorus electricus*), who lives in the Rivers of the World gallery at the Tennessee Aquarium in Chattanooga, US. He sent his first tweet in late 2014 under the handle @EelectricMiguel and although aquarium staff write his messages, Miguel controls when the tweets go out. Gadgets pick up the electrical pulses Miguel emits while roaming around his tank and a new tweet from a pre-written list hits social media if a pulse is above a certain strength.

The tweets are mostly groan-inducing animal jokes, such as 'What is the strongest creature in the sea? A mussel!', 'What do you call it when it rains chickens and ducks? Fowl weather!' and 'Why do hummingbirds hum? Because they can't remember the words!' Meanwhile, an amplifier converts Miguel's pulses into a stream of 'pops' that visitors hear as they wander through the aquarium. Each pop also triggers a light bulb, the brightness of which depends on the strength of the pulse – turning Miguel's otherwise silent electrical emissions into a *son-et-lumière* feast.

Terrible puns aside, the project does have an educational side: to raise the profile of electric eels. These animals don't have the best reputation. Their electric pulses, which they use to stun and kill crabs and other prey, are strong enough to injure humans. So if you're planning to visit Miguel Wattson, do keep your hands out of his tank. That said, as long as you keep your distance, electric eels are the perfect candidate to kick off this chapter on animals' use of

electricity and magnetism. Back in the late eighteenth century, these creatures inspired some of the earliest research into this branch of physics. What's more, researchers recently discovered that electric eels stun their prey in a similar way to the Taser weapons used by police. These 'guns' were invented by NASA physicist Jack Cover, who coined the name in honour of a character from a children's book: it's an acronym of Thomas A. Swift's Electric Rifle.

We should point out that, despite appearances, electric eels aren't eels at all. They're bony, freshwater fish that mooch about at the bottom of murky swamps and creeks along the Amazon and Orinoco rivers in South America (eels are fish too but from a different grouping). Grey-brown on the back and yellow-orange on the belly, electric eels are up to 2.5m (8ft) long, with a flat head and wide mouth. Their eyesight is terrible, and they're mostly out and about at night, swimming by wobbling the single, long fin that runs down their underside. The river waters contain so little oxygen that electric eels can't get enough through their gills; they rise to the surface every 10 minutes to breathe air before sinking back to the river bed. They have strange reproductive habits too: the female lays her eggs in a nest the male makes from saliva.

R-eel-y scary

But it's their ability to create electrical pulses for which electric eels are most famous – and feared. News of these mysterious creatures first reached Europe during the sixteenth and seventeenth centuries. French astronomer Jean Richer (1630–96), for example, reported seeing an eel-like fish on an expedition in 1670 that was 'as fat as a leg' and had numbed his arm for 15 minutes when he touched it with his finger. Intrigued by these 'trembling eels', European travellers carried out some unscrupulous experiments that today would be banned on ethical and health-and-safety grounds. They'd 'invite' local people to

stick their arms into a tank containing one of these fish and touch it with their bare hands or a metal stick. It was incredibly dangerous – we now know that a fully grown adult eel can create an electric shock of over 600 volts (V) – and few wanted to repeat the test. When an English surgeon called Dale Ingram tried to pat an electric eel with an iron hoop from a Madeira barrel in 1745, the fish's strike was so strong it knocked the entire metal object from his hand, like an invisible opponent disarming a fencer.

As historian William Turkel describes in his book *Spark from the Deep*, such accounts caught the ear of eighteenth-century scientists such as America's Benjamin Franklin and Britain's Joseph Priestley, who were seeking to uncover the mysterious phenomenon of electricity. The stories persuaded these investigators that the trembling eel's shock was electric in origin – a suspicion confirmed in 1775 by British scientist John Walsh, who found that an eel, imported to London from South America, could create a spark of electricity through the air. The sighting convinced doubters that the shock from the animal was linked to more familiar forms of electricity such as lightning.

With our laptops and light bulbs, these days we take electricity for granted. But back in the eighteenth century it was a strange phenomenon, with public displays of electrical effects being hugely popular. German professor Johann Heinrich Winckler, for example, electrified a servant before offering him a glass of brandy. 'Sparks from the servant's tongue ignited the brandy to the amusement of everyone present, probably excepting the servant,' writes Turkel in *Spark from the Deep*. Such demonstrations had a more sinister side too. Swiss medic Jean Jallabert used a Leyden jar – a device for storing electric charge – to stimulate involuntary contractions in the muscles of his own arm, triggering a craze for 'electrotherapy'. Doctors wanted to find out if electricity could cure patients of everything from epilepsy and lockjaw to rheumatism and

toothache. Turkel tells the horrific story of an official in the Dutch colony of Essequibo (in present-day Guyana), who every day would throw a slave boy who had crooked arms and legs into a tub containing an electric eel. The fish shocked the boy so powerfully that he had to crawl out or be yanked free by an assistant, who received a shock too. Far from being cured, the youngster was instead left with permanently deformed shin-bones.

Those early studies were unsavoury, but electric eels had a huge scientific impact. News of John Walsh's proof that eels make electric sparks spread quickly across Europe, inspiring Italian scientist Luigi Galvani (1737–98) to use frogs to show that electricity helps nerves and muscles to work. Electric eels, it's fair to say, triggered the birth of modern neuroscience. Walsh's work also motivated another Italian researcher, Alessandro Volta (1745–1827), to press the ends of a wire made from two different metals into the nerve of a frog, which caused its muscles to contract. When Volta put one of these bimetallic wires into his own mouth, he noticed an acid sensation and suspected the wire was electrically stimulating his tongue's taste sensors. The experience led him to build a device for creating electricity by stacking discs of silver and zinc on top of each other, separated by thin bits of paper soaked in a salt solution. This 'voltaic pile', inspired by the electric eel, was the world's first battery. Volta's device had so many parallels with this fish that when he wrote up his findings in a paper for the Royal Society in 1800, he called it 'an artificial electric organ'. We now know that an electric eel has several thousand thin, disc-like cells stacked on top of each other, like a giant version of Volta's primitive battery. Known as electrocytes, these discs sit in three dedicated organs that make up two-thirds of the eel's body, while its heart, intestines and liver are crammed into a narrow region at the front. But how do these cells generate electricity? And while we're at it, what is electricity anyway?

Current thinking

Electricity takes its name from the Greek for amber: *electrum*. If you rub amber with animal fur, this yellow, fossilised tree sap becomes electrically charged. Rubbing transfers electrons – negatively charged particles found in any atom – from the fur to the amber. You can now use the negatively charged amber to pick up bits of paper (the amber repels electrons in the paper, making it positive on the surface and so attracted to the negatively charged lump in your hand). The same happens if you rub a balloon against your jumper. By shifting electrons to the balloon, you can amuse yourself by sticking it to the wall or making your hair stand on end (perfect for livening up children's parties). This triboelectric effect (from *tribo*, the Greek for 'I rub') can also charge you up by several thousand volts if you walk across a nylon carpet. Reach for a metal door handle and the build-up of electrons on your hand may spark through the air to the metal. Ouch!

Fur-rubbed amber or your nylon-charged body are examples of static electricity; their surfaces have more (or fewer) electrons than they ought. The charge stays where it is – it's static – unless it can flow away as an electric current, as it does between you and the door handle. Static electricity is vital for photocopiers, but in everyday life we mostly experience electricity as electrons flowing in a current down metal wires and cables or through transistors (powering your screen if you're reading *Furry Logic* as an e-book). That's what electricity is – a flow of electric charge. If the charge is in the form of electrons, we're talking big numbers. An electric current of 1 ampere (A) has more than 6 billion billion electrons passing any point in 1 second. The unit is named after French physicist André-Marie Ampère (1775–1836), who showed that two current-carrying parallel wires attract each other if the currents flow in the same direction and push apart when the currents flow in opposite directions. Like Pierre-Simon Laplace (see Chapter 4), Monsieur Ampère has

his name engraved on the Eiffel Tower. As does another French physicist with a double-barrelled first name: Charles-Augustin de Coulomb (1736–1806), whose surname is given to the amount of charge transported by a current of 1 ampere in 1 second. It's crowded up there.

The French don't have a monopoly on electrical units. Italy's Signor Volta gave his name to the volt, which is a measure of electrical 'potential'. In a battery, electrons have the *potential* to flow from the negative to the positive terminal, but they'll only do so if you wire the two ends together, say via your bike light. Current is like water flowing in a mountain stream: it will flow only if you've spent energy transporting it to the top, with the height of the mountain equivalent to the voltage. If the mountain's tall, the voltage is big and water will cascade down. If it's small, so is the voltage, and the flow is slow. Stack two mountains on top of each other (if you can imagine such a thing) and you'll

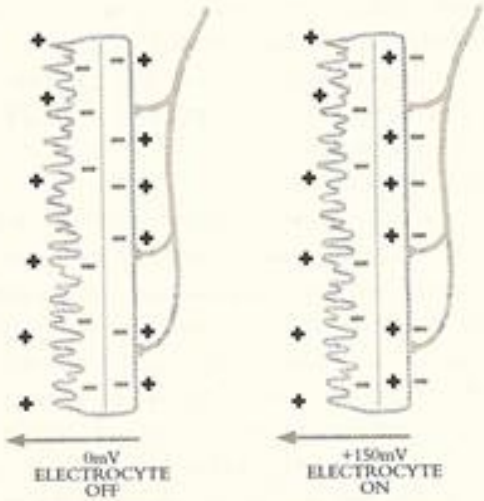


Figure 5.1 ***Switched on****. An electric eel has thousands of electrocyte cells stacked together, with nerves (curly lines) connecting one side of each cell to the brain. The voltage is zero when the cells are off, but +0.15V when on. (Based on illustrations from askanaturalist.com)*

double the voltage, like wiring up two 1.5V batteries back to back to get 3V. Multiply the current by the voltage and you get the amount of electrical power measured in watts, a unit named after Birmingham-based engineer James Watt (which is why the Tennessee electric eel is called Miguel Wattson).

An electric current doesn't have to involve flowing electrons, however. It can also consist of atoms that have lost electrons (making them positively charged ions) or gained electrons (resulting in negatively charged ions). That's what happens in an electric eel, which makes currents from positive sodium, calcium and potassium ions. These move through the surface of each electrocyte cell until they're clinging to the outside, which becomes positively charged. The inside surface of the cell – with a shortfall of positive ions – becomes negatively charged. Each side of the cell is like a tiny battery with plus and minus terminals, and a voltage of 0.085V. Not huge, given that an ordinary AA battery is rated 1.5V and you need two to power a bike light. There's another problem too: as both the left and right sides of the electrocyte are positive on the outside and negative inside, it's like having two batteries with the negative terminals touching (+ − − +). The overall voltage is zero and no current flows. But wait ... the electric eel has a trick up its sleeve.

Each electrocyte isn't symmetrical: one side is knobbly, while the other is smooth and connected by nerve fibres to the eel's brain. When the eel thinks electric thoughts, tiny pores on the smooth side open, allowing the positive ions clinging to the outside of the electrocyte to stream back into the cell. The smooth side is now positive on its inner surface and negative outside, creating a voltage of 0.065V on that side of the cell. The knobbly side is still at 0.085V, positive on the outside and negative inside, so the cell is + − + −. Add the two numbers and you get 0.15V, which is much more powerful.

Eventually the pores close and the cell loses its voltage, but the electric eel's no fool and it synchronises its

electrocytes so they're all 'on' at the same time. With as many as 6,000 cells, an eel can generate a voltage of 6,000 × 0.15V = 900V. The fish is, in other words, like a giant 900V battery with a positive terminal in its head and a negative terminal in its tail. Current flows from its front end, through the water, and back to its tail. It's hard to say how big the current is because it flows through the whole space around the eel. Any animal that crosses the fish's path, however, will be in for a shock.

Zap! Pow!

That's how an electric eel generates electricity, but how does it use these currents to stun its prey? Despite countless studies of these fish over the centuries, it's a question that remained unanswered until 2014, when Kenneth Catania from Vanderbilt University in Tennessee took up an interest. Anyone wanting to experiment on an electric eel first needs to get their hands on one of these slippery customers. Catching them is hard because you must make the fish discharge their electricity until they're worn out. Instead, Catania bought four eels from a commercial supplier and housed them in a plastic aquarium the size of a supermarket trolley. To make the fish at home, he added gravel, plastic branches and plants, while ensuring the water was a cosy 25–26°C. Ernie, Ellie and his two other eels (who remained nameless) were fed earthworms and crayfish.

Keen to watch his quartet in slow motion, Catania rigged up a high-speed video camera and installed electrical sensors in the water to measure the electric currents the fish produce. Catania noticed, as others have done, that electric eels are no slouches. These fish can spot suspicious changes in the flow of water around them barely three-hundredths of a second after they've occurred. 'Even if they're asleep and you stir the water ever so slightly they'll immediately wake up,' Catania explains. Electric eels know

what's around them thanks to small, pit-shaped sensors on their faces that constantly monitor the electric field in the surrounding water. If you're mad enough to dunk your hand in next to one of these eels, you'll distort the field, which changes the amount of current flowing across the eel's skin. It's a tiny effect, but the eel's sensors are super-sharp, making these fish masters of 'electrolocation' (not to be confused with echolocation – that was bats in Chapter 4). When they sense a tasty victim, electric eels don't hang about – they can strike and swallow their dinner in a tenth of a second.

Electric eels don't just wait for changes in the electric field. Except when they're having a nap, these fish are always on active duty, navigating through murky river waters, sending out low-voltage pulses themselves. When an eel suspects there's something tasty moving through the water or lurking in nearby vegetation, it fires bursts of two or three pulses at a much higher voltage. If that something is an animal, its muscles will twitch, inadvertently creating tiny ripples in the water. Thanks to those sensors on its face, the eel knows if the object is edible; a bit of wood, for

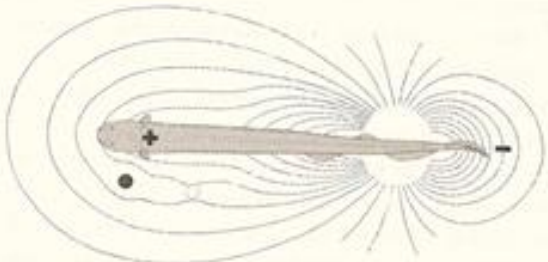


Figure 5.2 ***Detecting trick****. An electrically conducting object (black dot) moves the electric-field lines right at the surface of an electric eel closer together, boosting the electric current across its skin, while an insulating object (white dot) spaces the lines apart, lowering the current. (Adapted from Henning Scheich)*

example, wouldn't move a muscle and wouldn't disturb the water in response to the eel's test shock.

Roughly 20–40 milliseconds after sussing out that its target is alive, and with dinner firmly in its sights, the electric eel now blasts out a machine-gun-like volley of high-voltage electrical pulses at 400 times a second. At up to 500V, these pulses aren't much fun for the eel's target; within milliseconds of being hit by the first one, the animal can't move. The pulses act on the prey's motor-neurone nerves, making the animal involuntarily contract its muscles. With its prey unable to escape, the eel can start snacking; it's as if it has a remote control over its victim's muscles. The same happens if a police officer fires a Taser at you. The weapon embeds two metal barbs into your body and gives off almost 20 pulses of high voltage per second, which will have you lying flat on your face before you know what's hit you. Unlike the eel's victims, you won't be eaten but will be carted off in a police van for questioning. Just like the effects of a Taser, the paralysis in the prey is only temporary. If it doesn't immediately get eaten, the target animal regains its power of movement and can head off to safety. Sending a couple of test pulses before the main volley is, however, 'a really clever way of saving energy', according to Catania. 'Firing off round after round of high-voltage pulses is energy intensive and the eel will only want to do this if it's sure the prey is alive,' he says.

The eel has a couple of other tricks too. Catania discovered that the eel not only uses low-voltage pulses for electrolocation, which biologists had known since the 1950s, but it deploys its high-voltage volleys for the same purpose too. In other words, the eel uses its high-voltage blasts for two purposes: to stun prey, as we saw above, and to zero in on a paralysed victim that's not stationary but floating through the water. What's more, when an electric eel attacks a large animal, such as a crayfish, it has yet another tactic. The eel bites its prey before curling its tail round the victim that it almost touches its own head.

By sandwiching its victim between its positive and negative poles (its head and tail), the eel more than doubles the strength of the electric field from its high-voltage pulses. The increased power coupled with the high pulse rate drive its prey's muscles so hard and fast that they become exhausted. With the prey worn out, the eel can swallow its entire victim in peace.

We have to admit to developing a peculiar fascination with electric eels while writing *Furry Logic*, and Catania has too. He became interested in these fish after winning a Guggenheim Foundation fellowship to write his own book about the sensory systems in a range of animals. 'I originally thought that electric eels would be a kind of break from my main work but I soon discovered that they are the most interesting animal ever – despite having been studied for centuries,' he says. 'I got totally sidetracked.' Even the naturalist Charles Darwin found electric eels a mystery, placing their electric organs under a heading 'special difficulties of the theory of natural selection' in his masterwork *On the Origin of Species*. The great man found it 'impossible to conceive by what steps these wondrous organs have been produced'. Darwin would surely have been interested to learn that electric eels aren't the unsophisticated, one-trick ponies that biologists once thought, simply bludgeoning their prey to death with high voltages. Instead, these fish are masters of manipulating their electric fields.

Quite what he'd have made of Miguel Wattson and his tweets, though, is something we'll never know.

Let the field be with you

The beauty of electric eels is that they eased us into some key electrical concepts, such as charge, voltage and current. But when discussing how these fish navigate, we slyly slipped in one term without explanation: the electric field.

The field is a concept we touched on in Chapter 3 when looking at the Navier–Stokes equation, that chunky mathematical formula that says how fast and in which direction every point in a fluid moves. That's what a field is: a quantity you can quantify at every point in space. Solve the Navier–Stokes equation with a computer and you'd get a map with thousands of arrows showing the direction the fluid's flowing in at each point, with the length of the arrow indicating its speed. Join all the arrows up and you get imaginary lines that are a handy way of visualising the fluid field, like the lines representing wind on a TV weather map. In the same way, the electric field shows the strength and direction of the electric force between objects, such as the positively charged head and the negative tail of an electric eel, and you can visualise that field with a stream of lines flowing from one end of the animal to the other.

In one way, the electric force is similar to gravity (see Chapter 2). Just as the gravitational force between two objects weakens fourfold every time you double their separation, so the electric force between two charges follows the same inverse-square rule. But there are two huge differences. First, the electric force is about a billion, billion, billion, billion times stronger than gravity. You only feel gravity's effects for massive objects, like when your mobile phone slips out of your fingers and, attracted by the gravitational pull of planet Earth, hits the tarmac and smashes its screen. Grrr. The other big difference is that gravity always pulls objects together, whereas for the electric force, it's a case of opposites attract, but likes dislike. Electrons push electrons away. Protons – positively charged particles that skulk in the nucleus of an atom – repel other protons, but woo electrons. Now if you thought electric fields were strange, let's enter another field that's odder still. It's time to talk about an animal we met in Chapter 3 that has yet more secrets to behold.

CHAPTER 2

THE ECONOMY OF NATURE

[T]he study of the regulation of animal numbers forms about half the subject of ecology, although it has hitherto been almost untouched.

—CHARLES ELTON

The charge was a bluff. The elephant took only a few steps, just enough to let us know which mammal was boss of that hilltop.

Once our heartbeats returned to normal, and after he worked his way down the slope, we ventured back outside to survey the aftermath of the night's raid. There was a wake of broken trees, naked branches, and the lingering aroma of dung (theirs, not ours). Elephants are prodigious producers of the latter: their hundred-foot-long intestines manufacture up to 200 pounds of manure per day to keep up with the more than 200 pounds of food and fifty gallons of water they consume.

Given the absence of any natural predators, and their enormous appetites, one might ask why East Africa is not overrun with, or stripped bare by, elephants? Perhaps it is because African elephants, the largest of all land animals, reproduce very slowly? Females do not mature until their teens, they give birth to just a few young in their lifetimes, and it takes twenty-two months of gestation for a 250-pound baby elephant to develop.

It was Charles Darwin who famously dispelled that explanation in *On the Origin of Species*:

> The elephant is reckoned the slowest breeder of all known animals, and I have taken some pains to estimate its probable minimum rate of natural increase; it will be safest to assume that it begins breeding when thirty years old, and goes on breeding till ninety years old, bringing forth six young in the interval, and surviving till one hundred years old; if this be so, after a period of from 740 to 750 years there would be nearly nineteen million elephants alive, descended from the first pair. Indeed, in fewer than 50 generations or about 2500 years, the total *volume* of elephants would exceed that of the planet.

That figure is ridiculous. But consider the other end of the size spectrum. A typical bacterium, such as the *Escherichia coli* that populates our intestines, weighs about one-trillionth of a gram (one trillion bacteria weigh one gram; an elephant weighs about four million grams). Based on a maximum doubling time of twenty minutes, one can calculate how long it would take for one bacterium to give rise to enough bacteria to equal the weight of the Earth. The answer: just two days.

But the world is not made of solid elephants or bacteria.

Why? Because there are limits to the growth and numbers of all creatures.

Darwin recognized that. And he understood it because Reverend Thomas Malthus stated it long before in his landmark *Essay on the Principle of Populations* (1798):

> Population, when unchecked, increases in a geometrical ratio. . . . The germs of existence contained in this spot of earth, with ample food, and ample room to expand in, would fill millions of worlds in the course of a few thousand years. Necessity, that imperious all pervading law of nature, restrains them within the prescribed bounds. The race of plants and the race of animals shrink under this great restrictive law.

But just how are these "bounds" set? And how are they set differently for different creatures? Darwin did not know. These questions were

not pursued in earnest until another young English naturalist went on an expedition to some other remote islands, also encountered an odd assortment of creatures, became gripped by a mystery, had an epiphany (or several) during his adventures, wrote a great book, and founded a new field of science. Charles Elton is nowhere near as famous as Darwin or Malthus, but he is known to biologists as the founder of modern ecology, and the central mystery that gripped him was how the numbers of animals are regulated.

A JOURNEY TO THE ARCTIC

The *Terningen* pitched and rolled on the heaving, icy Barents Sea, and twenty-one-year-old Oxford University zoology student Charles Elton heaved right along with it. The two-masted schooner had left Tromsø two days earlier under the June midnight sun, bound for Bear Island, a desolate, rocky island well above the Arctic Circle, whose most prominent feature was aptly named Mount Misery.

Elton was part of a small advance party of the first so-called Oxford University Expedition to Spitsbergen, a team of twenty students and faculty from various disciplines—ornithology, botany, geology, and zoology—who aimed to carry out an extensive geographic and biological survey of the largest island in the Arctic archipelago northwest of mainland Norway. It was a bold and ambitious undertaking to venture far into storm-tossed and ice-strewn waters, to go ashore and traverse largely uninhabited and partly snow- and ice-covered islands, while risking the whims of some of the most intense weather on the planet; not to mention the fact that none of the team had any prior experience in the Arctic. But it was just the sort of adventure, and personal test, that the select group of Oxford men sought.

The voyage to Bear Island was a bit less than 300 miles and a severe test for Elton, who had never even left England before. The ship was a converted sealing boat whose sleeping quarters previously served to hold blubber, the smell of which could not be removed. That combined with the rough seas spelled utter misery.

From an early age, Elton had been captivated by wildlife. He spent countless days walking through the English countryside, watching birds, catching insects, collecting pond animals, and examining

FIGURE 2.1 The First Oxford University Spitsbergen Expedition team, 1921. Charles Elton is fifth from the right in the turtleneck sweater, Vincent Summerhayes is to the immediate left of Elton.

Photo from account by C. S. Elton written in 1978–1983. Courtesy of Norsk Polarinstitutts Library, Tromsö, Norway.

flowers. He began a diary of all of his wanderings and observations at age thirteen. Elton had been invited on the expedition by his tutor, the eminent zoologist and writer Julian Huxley (grandson of close Darwin ally Thomas Huxley), who was impressed with his student's passion for and command of natural history. He had relatively little time to prepare, as his slot on the expedition was confirmed just one month before sailing. His father provided some money, his brother lent him his Army boots and other gear, and his mother helped him put together clothes for the two-month voyage. Elton was, by his own account "very inexperienced, very raw indeed," and had only previously done some rough camping. Huxley encouraged Elton and reassured his parents, "Please assume that there is no danger in the expedition further than that involved, say, in elementary Swiss climbing, certainly much less than difficult mountaineering and indeed negligible."

By just the third day of the voyage, that pledge had crumbled. Forty-six-year-old medical officer and accomplished mountaineer

Tom Longstaff was the most seasoned voyager aboard. Seeing Elton suffering, he said, "I must do something for that poor boy," and proceeded to medicate him with large doses of brandy. With nothing in his stomach, Elton was so drunk when the landing party of seven finally went ashore at Walrus Bay on the island's southeast coast that he arrived sitting on top of a load of baggage in the whale boat, singing at the top of his lungs.

Once sober, Elton set up camp with his companions inside the ruins of an old whaling station near the shore, where the ground outside was littered with whale bones, walrus skeletons, a polar bear's skull, and a couple of arctic fox skulls. The plan was for the party to spend a week exploring the southern portion of the twelve-mile-long island before rejoining the full team and sailing on to Spitsbergen, about 120 miles to the north. The four ornithologists in the group were to focus on the birdlife, while Elton and botanist Vincent Summerhayes would survey all plants and other animals.

The birders were a bit zealous about their mission, especially F.C.R. Jourdain, the leader of the expedition. At 2:30 a.m. of the first "night" on shore (there were twenty-four hours of daylight), Jourdain awakened Elton, Summerhayes, and Longstaff with the command to get up and get to work, as there was no time to lose. Longstaff replied, "I must have my eight hours sleep," and the veteran explorer whispered to Elton and Summerhayes, "Don't take any notice." Elton soon appreciated Longstaff's wisdom, as the birders were completely exhausted by evening. Elton learned to pay close attention to Longstaff's sage advice whenever offered.

After a good night's rest, Elton and Summerhayes went out to explore and collect. Elton dreamed of one day knowing what animals "are doing behind the curtain of cover." Now he would have a chance to peer into an alien world that few had ever visited, let alone studied.

Situated where the cold polar current meets the Gulf Stream from the west, the island was constantly shrouded in fog, when it was not pounded by sleet or blizzards. Largely flat and dotted with dozens of lakes throughout its interior, and marked by a barren almost moon-like landscape in the north, the island was not without its wonders. On the southern end stood several tall cliffs overlooking the sea, populated by hundreds of thousands of seabirds. Among

the most numerous were black and white Common and Brunnich's guillemots, black-legged kittiwakes, and gray fulmar petrels; Elton also saw little auks, Norwegian puffins, and glaucous gulls.

Elton and Summerhayes started their surveys near the camp, then eventually fanned out to various lakes and other features. Elton quickly discovered that he had an excellent, determined partner in the small, slightly-built botanist. Just three years older, Summerhayes had seen more of the world, including fighting in the battle of the Somme (1916). Summerhayes was as keen to identify all the Arctic plants as Elton was to discover the animals, and in the course of their wanderings he taught Elton a great deal of botany.

Despite the weather and the shortness of time, the two men were able to survey all the island's various habitats for plant and animal life. The task was made easier by the relative sparsity of species. For instance, throughout the island, there were no butterflies, moths, beetles, ants, bees, or wasps whatsoever; the insect life consisted mostly of flies and primitive bugs known as springtails.

Elton had brought various means for collecting and preserving such treasures. He caught flying insects in a butterfly net, and shook other bugs out of plants and leaves onto a white sheet, or uncovered them by flipping over stones. The insects were killed with cyanide, and Elton put them inside tissue paper with labels and packed them into cigar boxes. For aquatic creatures Elton used a series of nets with different mesh sizes. He preserved some aquatic animals inside glass tubes containing alcohol or formalin, which he then corked and sealed with wax.

Elton paid particular notice to what enabled each species to survive in the generally barren and harsh conditions. For example, it was obvious that the seabirds lived off the sea and that the vast quantities of manure they dropped from the cliffs fertilized the lush vegetation growing below. Other birds Elton found inland, such as the snow bunting, dined on sawflies, while the arctic skua lived off other birds, stealing their food and eggs.

As the days wore on and food supplies began to dwindle, the skua weren't the only creatures living off the birds. The ornithologists collected many eggs and birds. The egg shells were preserved by blowing out their contents (Jourdain once blew so many that he fainted),

which were then made into omelettes. And after skinning, the bird carcasses were put in cooking pots. Elton and the team were surprised at how many species were edible, and he jovially wrote home about having guillemot eggs for breakfast and "stew of fulmar, eider duck, long-tailed duck, purple sandpiper, snow bunting, vegetables & rice!"

Toward the end of their planned week on the island, a gale blew in that would make it impossible for the ship to approach the island safely. Longstaff realized that they would have to stay longer and needed to get a message to the *Terningen*, which was waiting in Tromsø. He asked Elton to walk with him to the northeastern corner of the island (an expeditionary rule was to always go out in pairs for safety) to a coal mine with a wireless station. It was a brutal seven-mile, four-hour hike in driving snow and sleet to reach the mine, and then another four hours back again across knife-edge stones and slushy ground.

Despite the storms, running low on bread, being out of margarine for cooking, and having nearly worn through his Army boots in just a week, Elton declared that life on Bear Island "is rather fun."

After four days of battling strong gales, the ship was able to return to Bear Island and to retrieve Elton and his comrades just a few days behind schedule. The entire expedition team then headed farther north toward Spitsbergen—and straight into another gale that pushed "growlers" (chunks of dangerous, greenish sea ice) into their path.

Once that storm subsided, the *Terningen* made its way up the west coast of Spitsbergen. About halfway up the 280-mile-long island, the ship turned toward the azure waters of Ice Fjord, and the clouds parted. The team was treated to a stunning panorama of jagged, snow-capped mountain peaks and shimmering glaciers that crept down pure white valleys to the sea. A whale's spout and then a pod of porpoises broke the glassy surface, while strings of petrels and auks darted just above the water.

More than 200 miles wide, Spitsbergen presented a vast opportunity, and challenge, for exploration. Elton landed first on a smaller island west of the main island called Prince Charles Foreland, where he would spend about ten days surveying with Summerhayes. Longstaff helped Elton establish a campsite on the scrabble near a large, several-mile-long lagoon that was half covered with ice, on which many seals lounged. Before returning to the ship, Longstaff cautioned

Elton not to walk across the lagoon ice. Elton had learned that Longstaff only gave advice once, and if one forgot it, well, that was one's own mistake.

After nine fruitful days on the island collecting and observing the animals, Elton made that mistake. He was out walking with geologist R. W. Segnit on the ice attached to the shoreline of the lagoon. He stepped on a weak spot created by runoff from the shore and broke through into the frigid water. He was saved from going under only by his ruck-sack, which held him up a bit, and was able to climb carefully back up on the ice. However, freezing cold, momentarily stunned, and wearing sun-goggles, Elton did not realize that he had been turned around and almost stepped right back into the hole. Only a shout from Segnit stopped him from another misstep that would have likely drowned him. Shivering with hypothermia, Elton was able to return to camp to dry out; he left the island two days later for a longer stay at Klaas Billen Bay in the interior of the main island.

FIGURE 2.2 Charles Elton studying pond life at Bruce City, Spitsbergen, 1921.

Photo from account by C. S. Elton written in 1978–1983. Courtesy of Norsk Polarinstitutts Library, Tromsö, Norway.

Despite being farther north, and more snow- and ice-covered than Bear Island, the summer temperatures on Spitsbergen were much warmer (some days over fifty degrees Fahrenheit) and more comfortable, at least when it was not snowing. Elton took advantage of the conditions to conduct some actual experiments on the adaptations of Arctic animals. To learn more about how they survived in the climate and which habitats they could live in, he tested the tolerance of crustaceans and their eggs to freezing and thawing, and to different concentrations of sea water. [Figure 2.2]

Elton found very similar birdlife, vegetation, and insect life on Spitsbergen as on Bear Island but saw more evidence of larger mammals, including two species of arctic foxes, reindeer (in the form of shed horns), and seals. Then, one morning while the breakfast bacon was frying, a shout came up from below the campsite: "Polar bear!"

No one knew how the unwelcome visitor had reached the bay over the glaciers and valleys. But now that it had found their camp, there was sadly no alternative but to shoot it. Elton, ever the zoologist, did a very thorough inspection of the body, both outside and in, and was disappointed not to find any hitchhiking parasites for his collections.

After more than two months of collecting and living on the tundra, the now-veteran Arctic explorer assembled his thirty-three boxes and bundles of gear and specimens, loaded them all onto the ship himself, and sailed home.

UP AND DOWN AN ARCTIC FOOD CHAIN

Once safely back at Oxford, Elton and Summerhayes assembled the data they had gathered from their surveys. Many naturalists, especially those with a collector's bent, might have been disappointed at the meager pickings on the Arctic islands. But Elton realized that the relative scarcity of species presented a rare opportunity to describe all the transactions and relationships among an entire community of organisms—to peel back the curtain on animal life.

While previous naturalists had seen a community as one entity, or as a collection of species, Elton took a novel, functional approach. It was obvious to Elton that in the economy of Arctic islands, the precious commodity was food. So he traced where every creature's food came from.

Food was extremely scarce on land, but it was plentiful in the sea, so he started there. He knew that marine animals (plankton, fish) were eaten by the seabirds and by the seals. The seabirds were eaten in turn by the arctic fox (as well as by the skua and glaucous gull), while the seals were eaten by polar bears. These relationships formed what he dubbed "food chains."

But the connections among the inhabitants of the tundra extended far beyond a few animals. The droppings from the seabirds

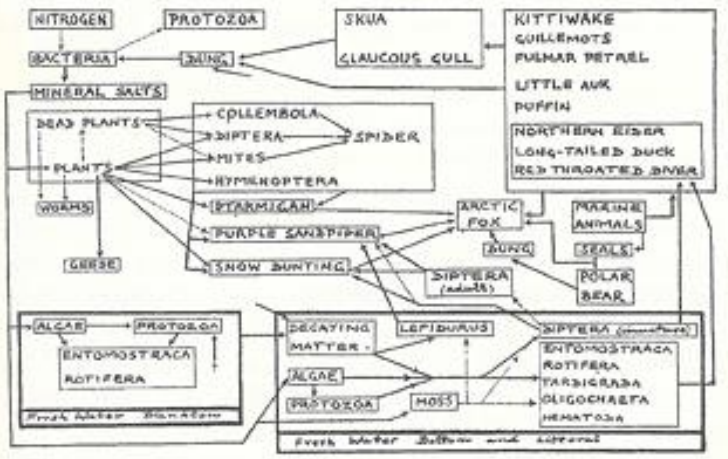


FIGURE 2.3 The food chain on Bear Island. The first food web drawn by Charles Elton. To follow the food chain on land, start with the nitrogen and bacteria at upper left and trace the links all the way to the arctic fox.

From Summerhayes and Elton (1923).

contained nitrogen, which was used by bacteria, which nourished plants, which produced food for insects, both of which were consumed by land birds (ptarmigan, sandpiper), which in turn were food for the arctic fox. In this manner, the food chains in a community were connected into larger networks that Elton dubbed "food-cycles," later called food "webs." Elton drew a schematic of these chains and webs, the first of its kind, in a paper published with Summerhayes in 1923. [Figure 2.3]

LEMMINGS AND LYNX

Elton himself moved quickly up the academic food chain, as well as the ranks of the Oxford University Expeditions. After receiving his undergraduate degree in 1922, he was appointed to a departmental lectureship in 1923, and named chief scientist for a new expedition to Spitsbergen.

It was extraordinary responsibility for a 23-year-old, but it was par for the Oxford enterprise. Polar exploration was largely a young man's game, and Elton was in what proved to be remarkable company, as many expedition members subsequently distinguished themselves in other endeavors or perished trying. The organizer of the first expedition was George Binney, who was just a twenty-year-old undergraduate at the time. Binney would also organize the 1923 expedition and a much more ambitious and complex 1924 expedition. He was later knighted for his exploits during World War II, in which he organized operations to run through the German blockade of Sweden. The 1923 expedition added twenty-one-year-old Sandy Irvine, who would attempt to climb Mount Everest the next year and disappeared with George Mallory just a few hundred meters from its summit. Medical officer Longstaff was the first person to summit a mountain over 7,000 meters and would later climb peaks all over the world. The medical officer on the 1924 expedition, and Elton's sometimes tent-mate, was twenty-five-year-old Australian Rhodes Scholar Howard Florey, who would develop penicillin into a drug during World War II and share the 1945 Nobel Prize in Physiology or Medicine.

The 1923 expedition had a new make-up and destination. Binney sought a leaner, more efficient enterprise and trimmed the team to fourteen: seven scientists and seven "henchmen" who were able hunters, rowers, and mechanics. The *Terningen* steered this time for Spitsbergen's little-explored sister island North East Land (Nordaustlandet). Despite its proximity to Spitsbergen, the island proved much less accessible. The ship was thwarted by thick belts of ice that surrounded the island and broke its propeller while trying to force its way through a strait. Partially crippled, the ship was pushed about by the ice floes, and the plans to explore the island had to be abandoned.

But for Elton, the journey was not a bust. On the way back to England, the ship stopped as usual at Tromsø. Elton went browsing in a bookstore and happened across a large tome on Norwegian mammals titled *Norges Pattedyr* by a Robert Collett. Although Elton did not read Norwegian, he was intrigued enough to plunk down one of the remaining three British pounds he had left in his pocket for the journey home for a book that Elton later declared "changed my whole life."

Back in Oxford, Elton obtained a Norwegian dictionary and laboriously worked out a word-by-word translation of one part of the book. There were fifty or so pages on lemmings that, although he had never seen one of the small guinea pig–like animals, enthralled Elton. He was captivated by Collett's descriptions of so-called lemming years, when the rodents swarmed out of Scandinavian mountainsides and tundra in such massive numbers in the autumn that citizens had taken note of the extraordinary phenomenon for centuries.

Elton drew up charts of the reported events and found that they occurred with a fairly regular periodicity of three to four years. He made maps and noticed that migrations involving different lemming species in different parts of Scandinavia seemed to occur mostly in the same years. He stared for hours at the maps spread around the floor of his cubicle in an old building at Oxford, thinking there must be something important he was missing. Then, sitting on a seat in the lavatory, it came to him "in a flash." Like Archimedes in his bathtub, Elton on his toilet got the idea that the lemmings were the "overflowing" of a periodically increasing population. At the time, zoologists had assumed that animal numbers largely remained steady. But Elton now realized that they could fluctuate dramatically.

Digging further, Elton wondered how general the phenomenon was. Even though there were no direct reports of lemming migrations in Canada, Elton was able to infer those events by thinking about food chains. He had previously read a book by a Canadian naturalist that described fluctuations in the populations of other mammals, including the arctic fox. Knowing that the foxes eat Canadian lemmings, Elton located a table of the number of fox skins taken by the fur-trading Hudson Bay Company and, sure enough, found a good correlation between a spike in the number of fox skins and the timing of lemming years in Norway.

The implications for Elton's food chain concept multiplied. Lemmings were also preyed on by birds. Elton noted that short-eared owls gathered in numbers in lemming years in southern Norway, as did peregrine falcons that preyed on the owls.

Lemmings were not the only prey whose numbers fluctuated wildly. Elton learned that the populations of Canadian rabbit (or "varying hare") also oscillated, spiking enormously about every ten

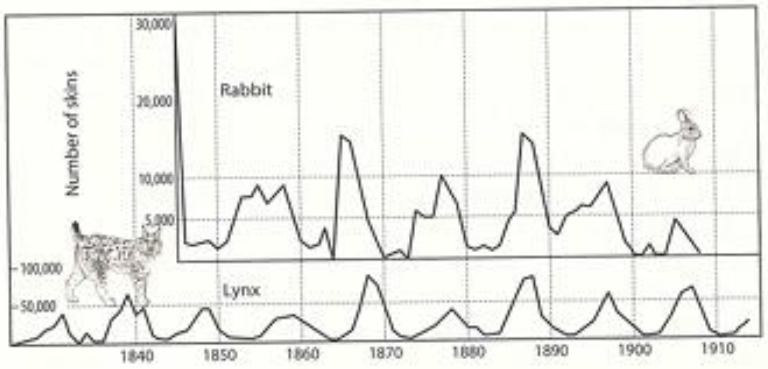


FIGURE 2.4 The ten-year cycles of lynx and rabbits in the Canadian north. Elton studied the records of the Hudson Bay company to determine that the populations of lynx and rabbits surge and crash with a ten-year periodicity.

From Elton (1924).

years before plummeting. The rabbits are the favorite prey of the Canadian lynx. "It lives on Rabbits, follows the Rabbits, thinks Rabbits, tastes like Rabbits, increases with them, and on their failure dies of starvation in the unrabbited woods," wrote one naturalist. The cat's fur meanwhile was the favorite quarry of fur trappers for the Hudson Bay Company. The company, it turned out, kept careful records of furs taken every year from about 1821 on. When plotted, the number of furs taken also showed a striking ten-year cycle that correlated with the rabbit cycle. [Figure 2.4]

Elton thought these cycles offered valuable glimpses into the workings of animal communities. They demonstrated the remarkable power of populations to increase dramatically, particularly if unchecked. By the same token, the abrupt crash in lemmings and rabbits showed that there were also forces, such as epidemic disease, that could rapidly eliminate a large proportion of animals. And these cycles showed how the numbers of one species can influence the numbers of other species through food chains.

In short, the cycles demonstrated that the numbers of animals are regulated in a variety of ways. Elton documented these "Periodic Fluctuations in Numbers of Animals" in a forty-five-page paper he

crafted in 1924. He did not know it at the time, but he was laying a cornerstone of the new science of ecology. The young naturalist would next lay the foundation.

LIFE IS ALL ABOUT FOOD

In 1926, Elton's former tutor Julian Huxley was putting together a series of short books on biology. He was keen to have each one written by leading thinkers that would focus on new and emerging principles. Although Elton was just twenty-six, Huxley respected his extensive Arctic experience (three expeditions by that time) and admired the original thinking evident in his published work. Huxley proposed, and Elton accepted to write, a short book on animal ecology.

Elton hurled himself into the project. He wrote like a fiend, most every night from 10 p.m. to 1 a.m. in his flat near Oxford's University Museum and completed the book in just eighty-five days! Despite the breakneck pace, the resulting *Animal Ecology* was a classic in terms of both style and substance. The 200-page book had an engaging, conversational tone, with many handy analogies. Its chapters were logically organized around key ideas that introduced and set the agenda for major facets of what Elton saw as the new science of ecology.

Elton explained that his book was "chiefly concerned with what may be called the sociology and economics of animals." The analogy to human society and economics was deliberate. "It is clear that animals are organized into a complex society, as complex and as fascinating to study as human society," and "subject to economic laws," Elton wrote. The analogy had deep roots in biology. The concept of an "economy of nature" had been embraced by the great naturalist Carl Linnaeus in the eighteenth and by Darwin in the nineteenth century. The connotation was that like human society, animal communities were composed of interacting creatures with different places and roles.

"At first sight we might despair of discovering any general principles regarding animal communities, " Elton said. "But careful study of simple communities," as he had performed in the Arctic, "shows that there are several principles which enable us to analyse an animal community into its parts, and in the light of which much of the apparent complication disappears."

Those principles emerged from the central importance Elton placed on food and food chains. He saw food as the "currency" of animal economies. "The primary driving force of all animals is the necessity of finding the right kind of food and enough of it. Food is the burning question in animal society, and the whole structure and activities of the community are dependent on questions of food-supply," he asserted. Elton encapsulated each principle that flowed from this basic premise with a charming and apt Chinese proverb:

Food Chains

"The large fish eat the small fish; the small fish eat the water insects; the water insects eat plants and mud."

Food chains formed the "economic" connections among the various members of a community. Chains of animals were linked together by food, and all were ultimately dependent on plants. In Elton's scheme, plant-eating herbivores were "the basic class in animal society," the carnivores that preyed upon them were the next class, and the carnivores that preyed upon them the next class and so on, until one reaches an animal "which has no enemies" at the terminus of the food chain.

According to Elton, the structure of these food chains was related to the sizes of creatures at different levels.

Size of Food

"Large fowl cannot eat small grain."

Elton argued that size is the main determinant in the structure of the food chain. Things that were too big to subdue or too small to support an animal were off the menu: "the size of the prey of carnivorous animals is limited in the upward direction by its strength and ability to catch the prey, and in the downward direction by the feasibility of getting enough of the smaller food to satisfy its needs."

These size parameters in turn had important consequences for the numbers of the different kinds of animals in populations and food chains.

The Pyramid of Numbers

"One hill cannot shelter two tigers."

Elton noted that the animals at the base of a food chain are typically abundant, while those at the end, such as tigers, were relatively few in number. There was generally a progressive decrease in numbers between the two extremes. Elton called this pattern the *pyramid of numbers*.

One example he cited was an English oak wood, where one finds "vast numbers of small herbivorous insects like aphids, a large number of spiders and carnivorous ground beetles, a fair number of small warblers, and only one or two hawks." Another example he had documented first-hand was in the Arctic, where copious numbers of crustacea are eaten by fish, the fish eaten by seals, and the seals by a smaller number of polar bears. Elton asserted that such pyramids existed in animal communities "all over the world."

The pyramids of numbers implied that normally there was some balance of animal numbers in a given area. A fundamental question then was how such densities were maintained: How did animals regulate their numbers so that they avoided overpopulation on one hand, and extinction on the other? Elton suggested that, in general, increases in numbers were held in check by predators, pathogens, parasites, and food supply. Extinction was avoided, he explained because as a prey became scarce, predators would switch to other quarry, allowing numbers to recover.

Elton's picture of the regulation of animal numbers, then, was somewhat akin to Cannon's idea of homeostasis—that levels were kept within ranges by counterbalancing factors. (Elton did not use this term, for Cannon had not yet popularized it, but some later ecologists did).

Elton considered the regulation of animal numbers to be of enormous fundamental as well as practical significance, and devoted almost one-quarter of his book to the subject. But, he admitted, "It has been necessary to speak in generalities, since so little is known at present about the rules governing the regulation of animal numbers."

Indeed, ecologists were spurred by Elton's book to search for those rules of the regulation of animal numbers, just as physiologists were motivated by Cannon to search for the rules that regulated processes within humans and other creatures.

And that is where we will head next.

But just before we do, there is one more impact of Elton's book to mention—in fostering the myth of suicidal lemmings. According to Elton's reading of Collett's book, a lemming year occurred "when a whole lot of lemmings apparently went crazy and walked downhill." He wrote in *Animal Ecology*: "The lemmings march chiefly at night, and may traverse more than a hundred miles of country before reaching the sea, into which they plunge unhesitatingly, and continue to swim until they die." This description, however, was based on yarns collected in Collett's book. Elton had never seen a lemming, nor a migration, let alone a mass suicide.

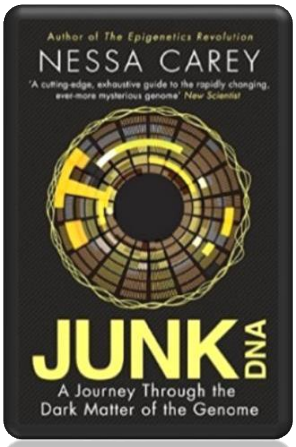
The myth of lemming suicide received a considerable boost from the 1958 Walt Disney film *White Wilderness*, which depicted lemmings leaping to their demise. After the narrator explained, "A kind of compulsion seizes each tiny rodent and, carried along by an unreasoning hysteria," viewers saw lemmings leaping into the water from a high cliff. The scene was faked; the animals were flung off the cliffs by the filmmakers.

The movie won an Academy Award.

Optional Extras

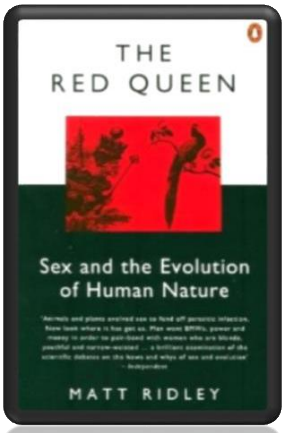
Book Recommendations

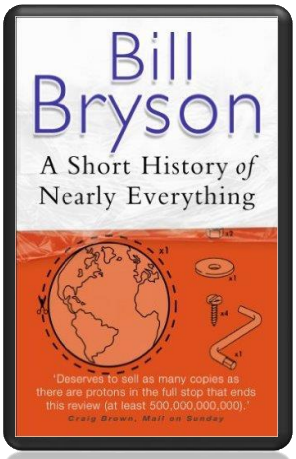
Kick back this summer with a good read. The books below are all popular science books and great for extending your understanding of Biology.



Junk DNA
Our DNA is so much more complex than you probably realize, this book will really deepen your understanding of all the work you will do on genetics. Available at amazon.co.uk

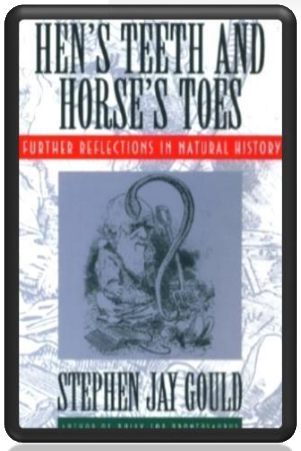
The Red Queen
Its all about sex. Or sexual selection at least. This book will really help your understanding of evolution and particularly the fascinating role of sex in evolution. Available at amazon.co.uk

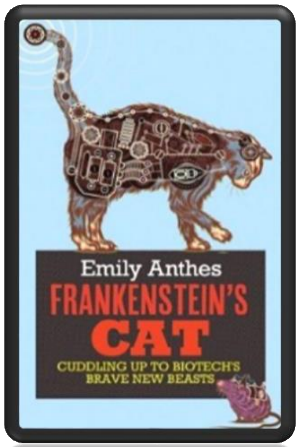




A Short History of Nearly Everything
A whistle-stop tour through many aspects of history from the Big Bang to now. This is a really accessible read that will re-familiarise you with common concepts and introduce you to some of the more colourful characters from the history of science! Available at amazon.co.uk

Studying Geography as well?
Hen's Teeth and Horse's Toes
Stephen Jay Gould is a great evolution writer and this book discusses lots of fascinating stories about geology and evolution. Available at amazon.co.uk





An easy read..
Frankenstein's Cat
Discover how glow in the dark fish are made and more great biotechnology breakthroughs. Available at amazon.co.uk

Movie Recommendations

If you have 30 minutes to spare, here are some great presentations (and free!) from world leading scientists and researchers on a variety of topics. They provide some interesting answers and ask some thought-provoking questions. Use the link or scan the QR code to view:

A New Superweapon in the Fight Against Cancer
Available at :
http://www.ted.com/talks/paula_hammond_a_new_superweapon_in_the_fight_against_cancer?language=en
Cancer is a very clever, adaptable disease. To defeat it, says medical researcher and educator Paula Hammond, we need a new and powerful mode of attack.

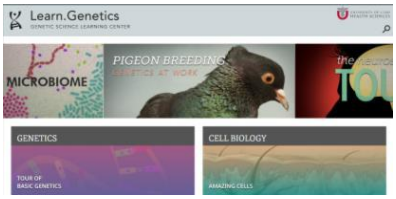
Why Bees are Disappearing
Available at :
http://www.ted.com/talks/marla_spivak_why_bees_are_disappearing?language=en
Honeybees have thrived for 50 million years, each colony 40 to 50,000 individuals coordinated in amazing harmony. So why, seven years ago, did colonies start dying en-masse?

What Doctors Don't Know About the Drugs They Prescribe
Available at :
http://www.ted.com/talks/ben_goldacre_what_doctors_don_t_know_about_the_drugs_they_prescribe?language=en
When a new drug gets tested, the results of the trials should be published for the rest of the medical world — except much of the time, negative or inconclusive findings go unreported, leaving doctors and researchers in the dark.

Growing New Organs
Available at :
http://www.ted.com/talks/anthony_atala_growing_organs_engineering_tissue?language=en
Anthony Atalla's state-of-the-art lab grows human organs — from muscles to blood vessels to bladders, and more.

Science Websites

These websites all offer an amazing collection of resources that you should use again and again throughout your course.



Probably the best website on biology….
'Learn Genetics' from Utah University has so much that is pitched at an appropriate level for you and has lots of interactive resources to explore, everything from why some people can taste bitter berries to how we clone mice or make glow in the dark jelly fish.
http://learn.genetics.utah.edu/

ZSL
LIVING CONSERVATION

In the summer you will most likely start to learn about biodiversity and evolution. Many Zoos have great websites, especially London Zoo. Read about some of the case studies on conservation, such as the Giant Pangolin, the only mammal with scales.
https://www.zsl.org/conservation

At GCSE you learnt how genetic diseases are inherited. In this virtual fly lab you get to breed fruit flies to investigate how different features are passed on.
http://sciencecourseware.org/vcise/drosophila/

'DNA from the Beginning' is full of interactive animations that tell the story of DNA from its discovery through to advanced year 13 concepts. One to book mark!
http://www.dnaftb.org/

Ok, so not a website, but a video you definitely want to watch. One of the first topics you will learn about is the amazing structure of the cell. This BBC film shows the fascinating workings of a cell… a touch more detailed than the "fried egg" model you might have seen.
http://www.dailymotion.com/video/xzh0kb_the-hidden-life-of-the-cell_shortfilms
If this link expires – google "BBC hidden life of the cell"