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Chapter 7

Cavia porcellus: Mathematical guinea pigs

Within the seemingly innocuous dark blue covers of the twenty volumes of the *Oxford English Dictionary* lies a record of invasion and colonization. The story of English is one of wholesale theft – of countries, their animals, their plants and, most noticeably in this context, their words. The Latin roots of some English words are, in part, a record of the vocabulary the Romans imposed on the British, in an effort to educate and civilize them. When we do manual work for which we are remunerated, we are doubly commemorating our one-time Roman overlords – both 'manual' and 'remunerate' come from the Latin *manus*, a hand. And our salaries derive from the money paid to Roman soldiers to allow them to buy salt: from the Latin *salarius*, or 'salt-related'. Similarly, the fact that we call certain animals 'cows' when they are in a field, but 'beef' when they appear on our dinner plates, is a relic of 1066 and all that: the Norman lord called the animal *boeuf* when eating it, while the conquered Saxon peasant, who actually herded it, still referred to it by the old English word, *cú* (cow), which shares common Indo-European roots with a dozen similar words across northern Europe.

The kind of person who puts on jodhpurs (possibly khaki in colour) to go to a gymkhana and afterwards sit on the veranda of their bungalow is commemorating the impact on English of the British Raj: *khaki* is Urdu for dust; *Jodhpur* is a city in Rajasthan; gymkhana and bungalow both come from Hindustani – the first is a modification of Hindustani *gend-khna*, 'ball-house', a racquetcourt, while bungalow derives from *bangla*, meaning from Bengal. However, veranda, which is often thought to be an Indian word, is in fact one that travelled the other way: it comes from the Portuguese and older Spanish *varanda* (or *baranda*) meaning a railing or balcony; Europeans took it to India and it was then adopted into Hindi and Bengali.

Linguistic imperialism is also evident in the names of many of the plants and animals of the New World; as we have seen, most – like Oenothera – lost their indigenous names when Europeans renamed them, but a few native names survived. On occasion, the colonists simply failed to come up with names for the new species and borrowed the indigenous terms, which is why English has ended up with numerous borrowings from Quechua, the language of the Incas.

Quechua is still the most widely spoken Amerindian language and has given English dozens of words: guano, the once invaluable bird droppings used as fertilizer, comes from the Quechua word for dung, *huanu*. The beef 'jerky' that cowboys eat in movies derives its name from *ccharquini*, 'to prepare dried meat'. But perhaps the most important Quechua borrowing came from a tree which the indigenous people called *kina-kina*. Early Spanish explorers learned from the locals that the tree's bark had an almost miraculous ability to cure fever, even the lethal malarial fevers that defended the tropics from European invasion. In Europe, the mysterious bark became a Spanish monopoly, allowing them to successfully go where few white people had gone before. It thus became a key weapon for the invaders against the very people who had taught them its secrets. The British referred to the mysterious substance as 'Jesuit's bark', and put great effort into 'acquiring' seeds so that they could grow it in India and break the Spanish monopoly. The Spanish spelled the bark's name *quina-quina*, from which we get the drug's modern name, quinine.

Because there are often many indigenous terms for a species, or several species that bear the same name, native names are seldom retained as scientific ones, but the scientific name of the guinea pig is an exception. The genus's scientific name, *Cavia*, derives from

the Quechua *cui* or *cuy*, which may have echoed the squeaking *kwee-kwee* sound the animals make. The *cuy* is one of only four mammals to have been domesticated in the Americas – the alpaca, guanaco and llama being the others. The latter trio were domesticated for their wool or as beasts of burden, but *cuys* were mainly a source of meat. Several thousand years ago, perhaps as early as 7,000 BCE, the people of the Andes started to keep *cuys* as livestock. They were probably treated much as they are today; most rural families in the Andes have a dozen *cuys* living in their house – they usually live in hutches in the kitchen and feed on scraps. Once they are fat enough, they are killed and cooked. Among the Andean people they still have other uses, as gifts or as a form of pocket money for children. They play a part in traditional healing ceremonies, during which live *cuys* are sometimes still rubbed on the affected parts of people who are ill, and then sacrificed. *Cuys* are found at the heart of all kinds of Andean rituals, from birthdays to weddings; their ritual significance survived the transition to Christianity – on All Souls' Day, the dead are offered a portion of *cuy* meat.

As with any domesticated animal, the Incas began a haphazard kind of selective breeding of the *cuy*, almost without realizing it, as soon as they took an interest in the species. *Cuys* that were too fast to catch, too aggressive, or too skinny to eat simply did not find a home in Andean hutches. As with other domesticated species, features of the animal that would have been a distinct drawback in the wild became a plus in the domesticated breed; natural selection is unlikely to favour an animal that resembles a placid, slow-moving, substantial meal, but artificial selection favours precisely those traits. As the *cuy* changed its shape and behaviour to suit its new habitat, humans must have noticed what was happening and began to breed them deliberately, probably about 3,000 years ago. By the time the Spanish invaded South America in the sixteenth century, the *cuy* was fully domesticated and was used both for food and in Inca religious ceremonies. Mummified *cuys* have been found in Inca tombs, along with terracotta statues representing them. Modern guinea pigs have been steadily adapted to human needs ever since, so much so that they are now classed as a separate species, *Cavia porcellus*, whose precise relationship with the wild species of the Andes is no longer clear.

The *cuy* made its debut in print in 1547, when Gonzalo Fernández de Oviedo y Valdés (usually known simply as Oviedo) published his *Historia general y natural de las Indias* ('General and Natural History of the Indies'), the earliest illustrated natural history printed in Spain. Oviedo was an official imperial chronicler for the Spanish court, and accompanied the conquistador Francisco Pizarro to make an inventory of Spain's new possessions. The immensity of the New World's endless, nameless jungles threatened to make Oviedo's work impossible; he wrote that 'although it is visible, we ignore most of it, since we do not yet know either the names nor the properties of such trees'.[1] His interest in naming the contents of these new territories was very pragmatic; like most Europeans of the time, he saw the New World in terms of resources and named them so that they would be easier to exploit. When he preserved indigenous names it was for precision, to make the identity of a resource obvious. He saw his first *cuy* in Santo Domingo, but since they are not indigenous to any part of central America, these would have been domesticated ones the Spanish had brought there. Oviedo renamed them the '*chanchito de la India*', or little pig of the Indies. His decision to dub the animals 'pigs' may have been prompted by their squeaks and squeals, but the name seems more likely to refer to the fact that European pigs were often kept in much the same way: allowed to wander about the homestead, eating scraps until they were fat enough to eat.

As we have seen, Europe's naturalists were enthusiastically creating comprehensive catalogues of everything the world contained, often by copying and compiling each others' work, so once Oviedo described the *chanchito de la India* it became a feature of natural history books. The Swiss naturalist Konrad Gesner mentioned it in his *Icones animalium quadrupedum* (1553), giving it the name *Cuniculus indus*, or rabbit of the Indies – perhaps because of its size and habit of burrowing. It made its debut in English

in Edward Topsell's *The Historie of Foure-Footed Beastes*, which appeared in 1607. Topsell was a clergyman with no pretensions to be a naturalist – most of his animal stories served to illustrate moral points – and his book is largely a reworking of Gesner's. Topsell knew that the animal Gesner compared to a rabbit had also been likened to a pig, so he compromised by giving it the name 'Indian little pig coney', coney being a common word for a rabbit.

Sometime in the seventeenth century, English speakers started calling these animals guinea pigs. It remains unclear exactly when or why, but in 1664 the English natural philosopher Henry Power was confident that they were familiar enough to be used to provide a comparison for the distinctly unfamiliar cheese mites he had observed under his microscope, which he described as looking 'like so many Ginny-Pigs, munching and chewing the cud'.[2] The origins of 'guinea' remain a mystery. All kinds of implausible suggestions have been made, including the idea that these pets sold for a guinea (21 shillings, which would be £100 in today's money – rather a lot for a small pet). It has also been suggested that the ships bringing the animals from South America called in at Guinea in West Africa on their way to Europe, but there is no evidence for this, nor for the more plausible confusion of Guinea with the South American country of Guyana. It is more likely that the British used 'Guinea' in a very loose sense to mean any far-off, exotic country – somewhere so distant and foreign that no one knew (or perhaps cared) exactly where it was.

The animals were formally given the generic name *Cavia* by the German naturalist Peter Simon Pallas, in his *Miscellanea zoologica* (1766); *Cavia* being a Latinized version of *cuy*. The species name, *porcellus*, or 'little pig', was conferred by Linnaeus. The British naturalist Thomas Pennant seems – understandably – to have felt that the common English name 'guinea pig' was inappropriate for an animal that was neither a pig nor from Guinea, and so he added another Quechua name to the English dictionary, borrowing *cuy* via *cavia*, and re-christening Topsell's little pig coney as the 'restless cavy', in 1781.

However, 'restless' was a singularly inappropriate adjective for domesticated cavies, which had been selected over thousands of years for placid temperaments. Noticing that they rarely bit people, Dutch sailors were bringing them to Europe as pets for their children not long after Oviedo first described them. The English took to the guinea pig particularly enthusiastically and they soon became popular pets; even Queen Elizabeth I had one. Their good natures endeared them to the ladies of the Court, who were often to be seen accompanied by a servant carrying a pet guinea pig on a silk pillow. By Victorian times they were so popular that everyone in Britain could be assumed to know what a guinea pig looked and sounded like, to judge by the regularity with which they were used metaphorically. George Eliot mentions them several times; for example, describing a character in *Daniel Deronda* as possessing 'a pair of glistening eyes that suggested a miraculous guinea-pig'.[3] They also became part of the language in several common expressions: those who took company directorships only for the sake of the fees (paid in guineas) became known as 'guinea pigs', as did clergymen who were paid to give sermons on behalf of their wealthier, but more indolent, colleagues.

In nineteenth-century Britain, pet-keeping became an increasingly competitive business as dog shows and pigeon-fancying clubs became common. The guinea pig was soon attracting its own 'fancy', largely thanks to one man, Charles Cumberland, a writer and Fellow of the Zoological Society, who published *The Guinea Pig or Domestic Cavy* in 1886. Cumberland proffered his claim of having 'something new to tell' as 'my chief excuse for laying this brief treatise before the public', in the hope that its defects, 'of which I am conscious, may be atoned for by its novelty, and the value of its facts'.[4]

Cumberland's claim to novelty was not immediately apparent, since he began with a recapitulation of the relevant writings of Gesner, Topsell and the French naturalist, Buffon, but Cumberland claimed to write from first-hand experience, asserting that many of his predecessors had simply copied from other writers without checking their facts. As a result, basic

information, like the number of the animal's toes, had been continuously misreported for centuries. Yet despite his desire to sweep away misinformation with science, he added to the confusing legends about the animal's common name by suggesting that it probably came from the Spanish having first encountered them on sale in markets, prepared by 'scalding and scraping them in the same manner as we should treat a pig'; hence they looked rather like small suckling pigs. Cumberland lists their numerous European names – *Cochon d'Inde* (Indian pigs, in France); *Cochinillo das Indias* (Indian pigs again, in Spain); and *Meerschweinchen* ('little sea pigs' in Germany) – and suggests that they would be best known as domestic cavies, noting that 'cavy' is close to the Peruvian Indian words *Coüi* or *Coüy* (now spelt *cuy*).[5]

Cumberland relied on the libraries of the Zoological Society and the British Museum for the historical sections of his book, but felt that the days of compiling from other writers were over. Gripped by the prevailing spirit of empiricism, he proudly claimed that 'the observations upon the management of Cavies are based upon experiments, conducted by myself, on a considerable scale, during a period extending over more than five years'. Cumberland kept his guinea pigs much as the Andeans kept theirs; he describes how one of his males, 'Bobby', was allowed to run 'loose about a kitchen, and was much petted'. Once you got to know your cavy, Cumberland suggested, you would soon learn to recognize the 'little grumbling note, by which it appears to express satisfaction or affection' and to distinguish that sound from the call 'with which it greets the sound of the well-known step of its feeder or owner'. Those 'who are intimate with the animal, will . . . find many gratifying marks of intelligence and affection'.[6]

Cumberland's book was intended to promote fancy guinea pig shows, so he urged his readers to keep and breed cavies, to join or form cavy clubs, so as to exchange breeding stock and thus 'avoid the evil effects' of inbreeding. The would-be breeder nevertheless faced the problem of what to do with the 'weeds', the substandard members of any litter, which are useless for breeding and cannot be sold. 'This difficulty,' Cumberland wrote, 'may be removed by sending the useless Cavies to table, for which purpose they were, probably, in the first instance domesticated.' Indeed, not only does he present the eating of cavies as a necessary by-product of breeding them, but – as Cumberland acknowledged – persuading his readers to think of them as edible was 'the principal object I had in view when I began the cultivation of the cavy'. (His book, which went into several editions, bore the subtitle 'for Food, Fur and Fancy' – although he had to admit that their fur is not much use for anything.)

Cumberland gave detailed instructions on how to kill and clean your guinea pigs, but added that he looked forward 'to the time when Cavies will be bought up for market purposes by people who will make a business of fatting, killing, and preparing for cooking'. And just to ensure everyone got his point, Cumberland added a few recipes to his book, including curried cavy, *Cavy aux Fines Herbes* and '*Cavy en Gibelotte*' (sautéd cavy served with an eel in a white sauce, a few mushrooms, some white wine, 'and season with salt, pepper and, a bouquet of parsley, thyme, and little green onion'). Adding:

> I do not wish it to be supposed that I recommend Cavy as a cheap food, but rather for its delicious flavour and *recherché* quality. It may, no doubt, be sometimes grown at small cost; but I look upon it as being so excellent for the table as to be worthy both of trouble and expense in its cultivation. Think of its value in the game course when game is out of season.[7]

Into the lab

If being served sautéd with eel seems like a grim fate for a guinea pig, worse lay in store for *Cavia porcellus* when men of science started to take a serious interest in the poor creatures. Cumberland noted that the animals had first entered a lab in about 1780, when the pioneering French chemist Antoine Lavoisier used guinea pigs to measure the amount of oxygen consumed and carbon dioxide produced during respiration. The very qualities that made guinea pigs into ideal pets – their being small, docile and easy to look after – also made them ideal laboratory animals. And they bred comparatively rapidly; females can become pregnant when they are just three months old and are fertile every two to three months thereafter. They usually have two to four young at a time, but litters of up to eight are not uncommon.

By the time Cumberland was researching his book, guinea pigs were to be found in scientific laboratories all over Europe. In Germany, Robert Koch had used guinea pigs to persuade doctors of the truth of the still new 'germ theory', that diseases were spread by newly discovered minute creatures called microbes. Koch pioneered new techniques for identifying microbes under a microscope and proved that each disease was caused by a different germ; he and his co-workers identified the microbe that caused tuberculosis in 1882 and that for cholera in 1883. A few years later, an American journal was able to inform its readers of Koch's latest breakthrough: 'he had found the means of arresting the development of tuberculosis', as a result of experiments done on guinea pigs, which were 'even more sensitive than man' to the microbe that caused the disease.[8] A few years later, *Harper's* reported that each microbe had its own anti-toxin, and described experiments that concluded with one cage containing 'a dead guinea-pig, inoculated with diphtheritic poison, while its companion, inoculated . . . with the same poison and also with its correspondent antitoxine [*sic*], seemed to be a little ragged and under the weather, but otherwise in cheerful spirits and condition'.[9]

Among the many medical and scientific men who found guinea pigs invaluable for their research was the American-born physiologist Charles Édouard Brown-Séquard, who used them in his research on epilepsy, discovering that guinea pigs could be 'rendered epileptic in consequence of an injury to the spinal cord'.[10] Some of his contemporaries, including Charles Darwin, were intrigued by his results and defended animal experiments as vital to scientific progress, but others were deeply concerned by

Brown-Séquard's work. When he had referred to the guinea pig's having suffered 'certain injuries to the spinal cord' he was – perhaps not entirely accidentally – glossing over a significant point: he had caused those injuries. In an effort to discover what role the nerves and the signals they carried played in epilepsy, Brown-Séquard had deliberately severed the animal's major sciatic nerve, which joins the spinal cord to the leg and foot muscles. He had done the experiments for what he had felt were very good reasons: it had long been known that some human epileptics could be cured through having their toes flexed or immobilized.

Yet, however justified physiologists like Brown-Séquard felt they were in experimenting on animals, an increasingly vociferous and influential section of the public disagreed with them. Gradually, Brown-Séquard's fame took on a new quality: as an American doctor writing in the popular magazine *Scribner's* observed, he 'has probably inflicted more animal suffering than any other man in his time'. The article described a visit to Paris to observe Brown-Séquard at work: 'a Guinea-pig was produced – a little creature, about the size of a half- grown kitten – and the operation was effected, accompanied by a series of piercing little squeaks', after which the guinea pig ran in desperate circles, the injury to its brain leaving it unable to walk in a straight line. 'This experiment,' the writer argued, 'had not the slightest relation what-ever to the cure of disease.'[11] Why then were animals made to suffer? Partly as a result of such publicity, Brown-Séquard found that he was sometimes unable to get to scientific meetings because of the threat of demonstrations by anti-vivisectionists.

However, in the following issue of *Scribner's*, another doctor sprang to vivisection's defence, arguing that Brown-Séquard had not just induced epilepsy in guinea pigs, but had also discovered that 'if a certain region of the skin of the face is cut out, the animal gets well'. This had direct implications for human health:

> Some time since, a boy was struck on the head with a brick; epilepsy followed, and two years of complete wreck of health,

> threatening idiocy. A vivisector was at last called in consultation, and, bearing in mind Brown-Sequard's experiments, had the scar on the head cut out. Result – cure. A considerable gain, that, to one young life.[12]

For some doctors, such cures were sufficient to justify vivisection. They also argued that the pain they caused, which 'accomplishes so much for the human race', was 'inconceivably minute' when compared to that which nature inflicted through disease, predation and parasites. The clinching argument offered to the magazine's readers was that the regulation of vivisection would be expensive: the writer asked rhetorically if it was really appropriate 'that the population shall be taxed' even more heavily, simply 'to render more irksome and laborious that progress in the divine art of healing'?[13]

Because of their popularity as pets, guinea pigs were often prominent in these debates over vivisection and gradually 'guinea pig' came to be synonymous with 'experimental organism'. Cavies made one of their stranger cultural appearances in a short story, 'A Point in Morals', by the American novelist, Ellen Glasgow. In her tale, several characters discuss whether human life has become over-valued until everyone is being kept alive and 'the survival of the fittest is checkmated'. (Her story first appeared in 1895, just as interest in eugenics was beginning to revive on both sides of the Atlantic.) One of the characters, 'a well-known alienist [psychiatrist] on his way to a convention in Vienna', describes meeting a murderer on a train. The man admits his crime and claims to have no regrets: 'I was ridding the world of a damned traitor,' he argues. But he has decided to kill himself, so as to spare his wife and family the pain of seeing him tried and executed. He carries a vial of carbolic acid for the purpose, but has realized that the alienist can grant him a much less painful death – thanks to a large quantity of morphine the latter happens to have in his bag – and the murderer begs for it. The alienist hesitates over the morality of assisting a suicide and helping a murderer escape justice, but remembers 'that I had once seen a guinea-pig die from the effects of carbolic acid, and the remembrance sickened me suddenly'. Should he spare the guilty murderer the agony that the innocent animal suffered? He wonders what his favourite philosophers would advise him and imagines the man's 'broad-faced Irish wife and the two children' and the misery and disgrace they would otherwise face. And then 'I thought of the dying guinea-pig', and as the train pulls into the station where the alienist is to get out, 'I stooped, opened my bag, and laid the chemist's package upon the seat. Then I stepped out, closing the door after me.' When he reads of the man's death in the paper the following day, he admits that he feels like a murderer himself, but 'a conscientious murderer'.[14] By the end of the century, thanks to the anti-vivisectionists, guinea pigs were playing a rather different role in fiction from George Eliot's glistening eyes of twenty years earlier.

Anti-vivisectionists often protested that not only were animal experiments cruel, but nothing of value was learned from them. The increasing cost of modern science and the growing expectation that government should finance it brought guinea pigs into wider debates over who should pay for science. One magazine writer satirized the scientist's demands: 'Give me a thousand or fifteen hundred a year,' the fictitious physiologist asks the State, and 'In return I will give you some new facts about . . . the length of time a new poison takes to kill a guinea-pig.'[15]

Fortunately for the scientists – if not for the guinea pigs – cavies proved susceptible to scurvy, a fact that was to do much to redeem the public image of laboratory science. For centuries, scurvy had caused sailors more suffering than storms and pirates combined. After long voyages, mariners returned home covered in bruises, their mouths bleeding and their teeth falling out; left untreated, they eventually suffered internal bleeding and died of the disease. In the mid-eighteenth century a British doctor, James Lind, had discovered that fresh oranges prevented and cured scurvy. From then on, British navy ships always carried fruit, usually lemon or lime juice. After 1844 it became law for all British merchant vessels to do the same, so that British sailors and ships' passengers

became known in Australia and America as 'lime-juicers', or simply limeys. But, mysteriously, sometimes the lime juice failed and entire crews who had been drinking it regularly nevertheless became sick.

Doctors still did not know exactly what scurvy was, nor why lime juice sometimes cured it – and sometimes failed to. The disease's symptoms were similar to those of an even more painful disease, rickets, that regularly afflicted the children of Britain's seething slums in the late nineteenth century. In many cases, children moaning in agony were admitted to hospital and were found to be suffering from both diseases. Doctors found that, like scurvy, rickets could be cured if they were quick enough, by feeding children fresh milk, fruit and vegetables, which slum children rarely saw. Even children from prosperous homes suffered from the disease, because some misguided middle-class parents thought strongly flavoured foods, such as fruit and vegetables, were unsuitable for a child's diet. Another similar illness, known as 'ship's beriberi', seemed to afflict sailors on long voyages from the East, even though they had meat and vegetables on board. Some doctors wondered if the relatively new process of canning vegetables led to contamination and although no evidence of poisons could be found in the cans, it was clear that for some reason tinned or dried vegetables could not protect against scurvy-like diseases – fresh vegetables possessed some virtue that was lost when they were preserved.

Impressed by the success of microbe hunters like Koch, doctors turned to the new laboratories to try to work out exactly what caused the various scurvy-like diseases. Some assumed infectious microbes were at fault, others suspected poisons in the often badly-preserved foods on ships, while a third group assumed that diet alone was responsible. Initially, experiments were done with pigeons, but as it became clear that pigeons remained healthy on diets that made people sick, researchers started looking for a mammal to experiment on – in the hope that its reactions would be more comparable to human's. Guinea pigs, by this time common in laboratories, were an obvious candidate. Two

Norwegian doctors, Axel Holst (who had worked in Koch's lab) and Theodor Frölich, fed guinea pigs on a variety of diets and proved that while they remained healthy on fresh potatoes, they died if they were only fed dried ones. They also showed that well-known anti-scurvy treatments, like cabbage, became less effective or even worthless the longer they were cooked. When they published their results in 1907, they had found no evidence for either microbes or poisons – poor diet alone caused scurvy. Unfortunately, the chronic lack of funding for Norwegian scientific research at the time made it almost impossible for them to carry on with their work, which was largely ignored.

Despite the growing acceptance that the scurvy-like diseases (which, in addition to rickets and beriberi, also included pellagra) were all caused by dietary deficiencies, it was clear that the British Army had not learned the lessons their naval colleagues had long understood. During the First World War, scurvy became widespread among the troops; many of those evacuated from the disaster at Gallipoli were found to be suffering from diseases like beriberi and scurvy. More experiments, with more guinea pigs, were performed at London's Lister Institute, where a few years earlier a Polish chemist named Casimir Funk had demonstrated that an extract of rice could cure beriberi. Because the extract contained a chemical known as an amine (a derivative of ammonia), Funk decided he had discovered a new group of chemicals which he called 'vital amines', or vitamines.[16] By 1915, Funk had emigrated to America and nearly all the Lister Institute's other male scientists were away fighting in the war, so their colleagues Harriette Chick and Margaret Hume led a team of women who were given the task of identifying foods that could be easily transported to the troops to keep them healthy. They discovered that guinea pigs which were fed nothing but oats, bran and water quickly contracted scurvy, so they tried supplementing their diets, adding one extra food at a time, to discover what worked best to prevent the disease. Among other things, they discovered that not all limes are created equal: the West Indian sour lime, which had been the Royal Navy's main source of lime

juice since the late nineteenth century, turned out to be much less effective than the Mediterranean sweet lime it had replaced. Even worse, its effectiveness against scurvy fell rapidly when it was preserved in alcohol, as it had to be before shipboard refrigeration.

Meanwhile, on the other side of the Atlantic, rats were overcoming decades of prejudice to find their way into biology labs. They had, of course, long been regarded as aggressive, disease-carrying vermin, but were finally becoming common laboratory animals, as we saw with the Wistar rats in the previous chapter. Elmer V. McCollum, who led a research team at the University of Wisconsin, was particularly keen to promote the rat as a standard animal ('McCollum rats' are still in use laboratories today), not least because they bred much faster than guinea pigs. However, when he first suggested them to his boss, he was told that if anyone discovered his team were 'using federal and state funds to feed rats we should be in disgrace and could never live it down'.[17] Despite this reaction, McCollum's team managed to acquire some taxpayer-funded rats and used them to investigate dietary diseases. In the process, they discovered that each was caused by a different deficiency and christened the mystery factors 'A' (whose absence caused childhood blindness and reduced immunity to other illnesses) and 'B' (where deficiency caused beriberi). The Americans also repeated the British guinea-pig experiments, but found that fresh milk did not appear to prevent scurvy as the British had claimed. Since McCollum's team had been unable to link scurvy to either factor A or factor B, they suggested it might not be a deficiency disease at all. Back in Britain, Chick and Hume responded by repeating their initial experiment and finding that fresh milk *did* prevent scurvy.

Why did the experiments on opposite sides of the Atlantic have different outcomes? Was there something in British milk that its US equivalent lacked? A chemical analysis of the different diets eventually identified a third component, originally called 'accessory food factor C', a name that – not surprisingly – did not catch on. The public had grown used to talk of 'vitamines' so the scientists ended up adopting the name, despite the fact that amines turned out not to be important. As a concession to scientific accuracy, the final 'e' was dropped and vitamin C was born.

Fresh milk is a good source of vitamin C, so the failure of the US experiments was puzzling, but was explained by one of Chick and Hume's colleagues, who observed that 'the one thing which is fatal to nutritional work is, to send the animals away to an animal-house to be looked after by someone else', which is what the Americans had done. In the animal house, no one had checked to see whether or not the guinea pigs actually drank their milk; by contrast, Chick and Hume's guinea pigs 'have been tended and nursed and fed by the observers themselves'.[18] As long as the guinea pigs actually drank their milk, they stayed healthy, but another mystery remained, which was why guinea pigs developed scurvy on diets that were evidently adequate for rats. This confusion turned out to be a result of the fact that guinea pigs and humans cannot make vitamin C in their bodies and so have to consume it if they are to stay healthy; however, rats and pigeons produce their own vitamin C if their diets are deficient. Once it was clear that the guinea pig was the appropriate animal to work with, research began to find out exactly what vitamin C was and eventually – once the chemical structure was discovered – the first synthetic vitamin C was created in 1933 and successfully tested on guinea pigs.

The conquest of diseases like scurvy became one of the first big success stories for a new science, biochemistry, which used the vitamin story to promote the idea that it was a science of life, at a time when the older physical sciences were increasingly being used to create new and more dangerous weapons – bombs and poison gas. The massively influential and wealthy Rockefeller Foundation was persuaded by these arguments to switch much of its funding from physics to biological research in the 1930s. Thanks in part to guinea pigs, the newly wealthy life sciences began to attract bright young scientists who set to work to analyse the processes that sustain life, from fermentation and photosynthesis, to respiration and digestion. Understanding the chemistry of life was the first stage in a long boom for biology,

until it eventually threatened to displace physics as the queen of the sciences.

From agriculture to jazz

Ironically, the Norwegians Holst and Frölich were not the first to produce scurvy in guinea pigs: a group at the US Department of Agriculture's (USDA) Bureau of Animal Industry had accidentally done the same thing a decade earlier, when the supply of fresh grass ran out and the animal's keeper forgot to give the animals fresh vegetables instead. The Bureau's annual report related the details of the error rather apologetically and – unfortunately as it turned out – did not publicize their accident too widely; the story of vitamin C might have been very different had they done so.

The USDA had been established in 1862 by Abraham Lincoln. Coming from a farming background himself, Lincoln knew that the majority of his countrymen were farmers who needed the best seeds, crops and advice that science could provide. To head the new department, Lincoln appointed a man called Isaac Newton (no relation), a successful farmer from Pennsylvania who had previously been in charge of the agricultural section of the Patent Office. In his first report on the new department, Newton identified its main goals as: publishing useful agricultural information; introducing valuable plants and animals; responding to inquiries from farmers; and testing new agricultural machinery and inventions.

Guinea pig keeping was, unsurprisingly, not on Newton's list, yet within a few decades the USDA had a substantial colony, used to test vaccines. A dozen years later the guinea pigs were being bred on a large scale, as a substitute for traditional farm animals; but unlike Charles Cumberland, the Bureau was not breeding guinea pigs as a replacement for 'the game course when game is out of season', nor for their '*recherché*' flavour. The USDA wanted to investigate the breeding of livestock, but had no space for thousands of pigs or sheep. Since guinea pigs had proved a valuable alternative to humans in testing vaccines and vitamins, they were now becoming a substitute for farm animals in a large-scale investigation of the effects of inbreeding. In 1906, George M. Rommel, head of the Bureau's Division of Animal Husbandry, had decided to investigate inbreeding because it remained common – if controversial – among commercial animal breeders. As we have seen, some argued that this was the best way to 'fix' a desirable trait, while others argued that such incestuous couplings were invariably harmful. Rommel instituted controlled experiments to answer the question and, since the Bureau already had a colony of guinea pigs, he opted to use them.

A guinea pig's life at the Bureau's experimental farm in Maryland was more attractive than those of its colleagues in other labs; all the US government wanted of them was that they have lots of sex, albeit with their own siblings. The Bureau's researchers crossed brother and sister guinea pigs for more than two dozen generations, in order to create a number of heavily inbred families, but having done so, they had a problem. By 1915, they had accumulated data from tens of thousands of guinea pigs, but were unsure of the best approach to take in analysing it. Clearly, they needed a clever young geneticist who had learned the latest techniques, so Rommel approached his friend William E. Castle at Harvard to see if he could recommend one.

As we have seen, Castle was also interested in inbreeding, which was why he had first brought fruit flies into his lab, but his real interest was in mammals. He had been born on a farm in Ohio and studied biology at Harvard in the early 1890s. Among his teachers was Charles Davenport, one of the pioneers of laboratory biology in America. Castle stayed on as Davenport's assistant, then taught zoology back in the Midwest for a couple of years before returning to Harvard, where he began rearing guinea pigs and mice for experiments. When the 'rediscovery' of Mendel's work was announced, Castle was intrigued and started using his mammal colonies for inheritance research, becoming one of the first mammalian Mendelians.

Within a few years of his return to Harvard, Castle had bred over 1,500 rabbits, 4,000 rats and 11,000 guinea pigs. He was

getting desperately short of space when he heard that Harvard's Bussey Institution – which had originally been founded to teach agriculture – was about to be closed down. Castle and others successfully lobbied to have it turned into a research facility for the biological sciences and persuaded the Carnegie Institution to contribute to the cost.

With the money and facilities secured to continue his mammal work, Castle set out to test de Vries's Mutation Theory. He had originally been largely convinced by it – and had been one of the scientists invited by Davenport to address the 1905 Philadelphia meeting of the American Society of Naturalists on the subject – but had since begun to have doubts. With the help of one of his students, Hansford MacCurdy, Castle set out to test the power of selection; he had told the Philadelphia meeting that 'the formation of new breeds begins with the discovery of an exceptional individual', and that 'such exceptional individuals are mutations'.[19] The question was whether, having found such an individual, it was possible through selective breeding to create not merely a new variety, but a new species. As Castle and MacCurdy put it in the published account of their experiments, a great deal had been written both for and against de Vries's theory, 'but discussion is at present less needed than experimental tests of the views outlined'.[20]

For their experiment, Castle and MacGurdy chose hooded rats (so called because they are white with black heads). The rats presented what looked like a classic case of continuous variation: some had very little black fur (giving small 'hoods') while others were predominantly black (large hoods), with most of the rats lying somewhere between these extremes. Since the amount of black varied smoothly, with no jumps or breaks in the sequence, it seemed unlikely that the pigmentation was controlled by a simple on/off Mendelian factor. Castle and MacCurdy mated large-hooded rats with each other, and did the same with the small-hooded rats. They expected to find, as plant breeders had done earlier, that selection could only shift a species so far; the amount of black could be increased or reduced up to a certain point, but eventually what was called a 'pure line' would be created and no further change would be possible unless a fresh mutation occurred.[21] They also assumed that once they stopped selecting, put their large- and small-hooded varieties back together and let them once more mate at will, later generations of rats would rapidly revert to type and show the original variation along a continuum.

To Castle and MacCurdy's surprise their rats did not revert; they appeared to have created some lasting genetic change. As they noted, these were results that 'support the Darwinian view rather than that of De Vries'.[22] Castle became a convinced Darwinian and argued that – despite appearances – there must indeed be a Mendelian factor for 'hoodedness', but that the factor was in some way altered by selection so as to produce discontinuous variations. However, his colleagues were unconvinced by this suggestion and argued that cases such as the hooded rats were better explained by assuming that several Mendelian factors were at work, which affected each other but did not actually change. There might, for example, be a basic pair of genes – large-hood and small-hood – but also several other 'modifier genes' that increased or reduced the effect of the basic pair. By removing the rats with intermediate amounts of black, Castle and MacGurdy had been removing the modifier genes from their breeding stock, until the animals that remained possessed only either the large-hood or small-hood gene. When these stocks were allowed to interbreed again, the original smoothly graduated range of blackness did not reappear, because no modifier genes remained. After several years of debate, it was this latter view that became widely accepted, largely because it was born out by the fly boys' work, which – as we have seen – showed that genes were not the simple switches they had originally been assumed to be. As a result, the long-standing distinction between continuous and discontinuous variation – and between blending and non-blending inheritance – began to be abandoned. 'It is impossible,' Castle said, 'to make a sharp distinction between continuous and discontinuous variation'; they were both controlled by genes.

Castle continued that it therefore seemed misleading 'to assign all evolutionary progress to one sort of variation or to one sort of inheritance'.[23] Between them, the rats and flies had finally persuaded most biologists that all inheritance was Mendelian – everything was in the genes.

Castle also had the rats to thank for the fact that he became one of the most influential of the early American geneticists. He travelled, lectured and wrote, explaining how the Mendelians were 'able to predict the production of new varieties, and to produce them'.[24] Prediction was one of the highest goals of any science: ideally, a scientific theory allows you to calculate the outcome of an experiment in advance – that way, actually performing the experiment allows you to test whether or not your theory was right. Castle's audiences would have grasped his implication: the biometricians – for all their complex mathematical tools – could not predict the outcome of a specific mating, while the Mendelians could. In the spring of 1912, Castle visited the University of Illinois to lecture on hooded rats and Mendelian genetics; in his audience was a young graduate student, Sewall Wright, who was excited by what he heard. Wright went up to Castle afterwards, to tell him 'that I was very much interested in genetics but that no course was given in it at Illinois', and asked if it might be possible to do research with Castle.[25] Wright had taught himself genetics from an article on Mendelism in the *Encyclopaedia Britannica*; its description of the simple mathematical rules that underpinned inheritance greatly appealed to him. Castle was impressed by the young man's intelligence and enthusiasm – he invited Wright to come and work with him.

When he arrived at Harvard, Wright found that he was not going to be working on flies or rats, but on guinea pigs. Castle was about to lose his existing guinea pig keeper, John Detlefsen, who had finished his graduate work; Wright was to be his replacement. Before he went off to start his first job, Detlefsen introduced Wright to the guinea pigs who, unbeknownst to the newcomer, were to be the focus of the rest of his working life. As well as teaching him the basics of guinea pig care and feeding, Detlefsen also showed Wright his data on six generations of guinea pigs; crosses between the common lab guinea pig *Cavia porcellus* and wild Peruvian cavies, *Cavia rufescens*, which Castle had collected a few years earlier. These crosses showed that while the first generation were almost all sterile, the population's fertility gradually recovered over successive generations, as the percentage of the other species' genes declined. However, Detlefsen could not produce a more precise analysis of his data. Wright took one look at it and did a quick calculation on the assumption that there might be several Mendelian factors operating (as with the hooded rats), each of which contributed equally to sterility. He immediately realized that if there were eight factors his calculation gave theoretical percentages that closely matched those Detlefsen had actually observed. The entire exercise took Wright only a few minutes and he was surprised by how impressed Detlefsen was; both the theory and the calculation had seemed quite obvious to him.

As the speed at which Wright had done his calculation suggests, he was fascinated by mathematics and had been from an early age. When he began school, just before his eighth birthday, he had been asked to demonstrate his mathematical skills, to enable his teachers to assign him to a grade. He remembers volunteering 'that I could extract square and cube roots', ruefully adding that, in retrospect, he would not have done so if he had had a little more experience of school life. He was taken down to the eighth grade's classroom and despite being almost unable to reach the blackboard, successfully extracted the cube root of a number. 'It must,' Wright later recalled, 'have been a most disgusting spectacle to the students.'[26] Being younger and shorter than most of his schoolfellows left Wright feeling 'much out of place', but his enthusiasm for maths was undiminished. He later wished that he had acquired a more thorough mathematical education, but nevertheless – as he modestly put it – he 'acquired some facility in translating questions into mathematical symbolism and solving [them] as best as I could'.[27]

Wright's modesty about his abilities was entirely characteristic: his contributions to the mathematical understanding of inheritance were to make him famous; he helped create a new mathematical approach to genetics that ended the long running battle between the Mendelians and biometricians. This mathematical treatment of evolution – along with his guinea pigs – also brought Wright into contact with one of the more extraordinary figures of early twentieth-century-British biology, John Burdon Sanderson Haldane.

Bombs, biochemistry and beanbags

Haldane and Wright could hardly have been more different: while Wright came from a fairly ordinary middle-class American family, Haldane was an aristocrat in two senses: his family could trace its lineage back to the ancient Scottish nobility, but – more relevantly – he was born into Britain's scientific aristocracy. His father was a distinguished physiology professor at Oxford, an expert on respiration who was frequently called in by the government to advise on such matters as safety issues in the mines. From the age of four, young JBS (as he was almost always known) was fascinated by what he referred to as his father's 'labertree' and the interesting game of 'experiments' that he played there. A precocious child, JBS could read by the time he was three; by the age of five he had learned enough German from his nurse to leave her little notes that read 'I hate you.'[28]

Haldane and Wright probably first heard of each other in 1915, when they each published papers demonstrating genetic linkage in mammals for the first time. Demonstrating that specific Mendelian factors were invariably inherited together in mammals – because they occurred on the same chromosome, as had been shown in Drosophila – was an important step to establishing that the connection between chromosomes and inheritance was universal; linkage had by now been found in plants too, so it seemed that every living thing shared the same machinery for passing on its variations. Wright's work grew out of his graduate studies at Harvard, which were in turn a continuation of Castle's rat work, but Haldane's had rather more unusual roots. In 1901 his father had taken his eight-year-old son to the Oxford Junior Scientific Club, to hear a lecture by Arthur Darbishire on the newly rediscovered principles of Mendelism. A few years later, his sister, Naomi (who would later become a celebrated novelist under her married name, Naomi Mitchison), developed an allergy to the horses she had loved and took up keeping guinea pigs instead. She loved the animals and knew many of them by name; she could impersonate their squeaks and grunts so well that they would answer her. When her elder brother came home from Eton for the school holidays and discovered her new pets, he 'suggested that we should try out what was then called Mendelism on them'. She agreed, deciding that 'Mendelism seemed quite within my intellectual grasp', and so her pet population began to expand. Well-known scientists, including pioneers of genetics, were familiar figures in the Haldane household – Naomi named one of her guinea pigs Bateson in honour of one of her father's visitors. One of JBS's friends remembered that in 1908 the lawn of the Haldanes' house was entirely free from the usual upper-class clutter of croquet hoops and tennis nets; instead, 'behind the wire fencing, were 300 guinea-pigs'. Naomi looked after them during term-time, and though five years younger than JBS, she became deeply interested in genetics, later recalling the 'the terrific thrill I got out of Morgan's great book [*The Mechanism of Mendelian Heredity*], reading it eagerly, curled up in a corner of the school room sofa, seeing it make sense of our puzzles'.[29]

As a result of these back-garden experiments, JBS and Naomi found they had, as she put it, 'tumbled onto what was then called linkage' (it was in fact often called 'reduplication' at the time, but 'linkage' became the accepted term soon after). JBS read all the papers on Mendelism then available to try to make sense of their results. In a recent scientific paper by Darbishire, Haldane noticed evidence of linkage, which the paper's author had overlooked; he and Naomi tried to prove that it existed using their pets. 'The guinea pigs were a mine of information,' Naomi recalled, 'we had to arrange marriages, which sometimes went

against the apparent inclinations of the partners, though I rather enjoyed exercising power over them.'[30] But tragedy intervened. One of JBS's school friends, Cedric Davidson, recollected that the experiments 'necessitated the breeding of many generations of guinea-pigs, and our wretched little fox terrier . . . Billy . . . crawled over your front gate . . . goodness only knows how . . . promptly jumped on the cages in which were your g-pigs and they one and all died of fright', a double tragedy since 'they were the penultimate generation which were to prove your theory!!' Davidson was appalled; forty years later he could still remember how upset the Haldanes' mother had been as she waited for JBS to return from Eton that afternoon and discover what had happened. But Davidson recalled that when JBS got back, 'you came up to see us & told us not to worry, that you yourself were quite satisfied that your theory was correct, but admitted it only required one further generation for you to submit as a scientific fact'. Long afterwards, when Davidson wrote to his now famous friend to remind him of the disaster, he observed that 'I thought then and still think you lied and lied most nobly. I have never forgotten it and never shall.'[31] Nor, it seemed, had Haldane: his reply to Davidson's long, chatty letter was noticeably terse.

Thanks to Billy the fox terrier, Haldane's announcement of linkage in mammals had to wait until 1912, when he presented his analysis of Darbishire's mouse data to an undergraduate seminar at Oxford, where he studied first mathematics and then classics. He was advised to gather his own data before publishing and opted to work with mice, perhaps still mourning the fate of the original guinea pigs. Naomi and another friend, A.D. Sprunt, helped with the work, but before it could be published the First World War had broken out – by the time the paper appeared in 1915, Sprunt was already dead and Haldane was in the trenches.

Haldane had joined up immediately and served with considerable courage (and not a little foolhardiness) as a bombardier in the Black Watch. He briefly left the front after the first German poison gas attacks of the war: his father had been asked to help devise defences against the gas and had requested his son's assistance. As with many earlier experiments, the Haldanes, father and son, used themselves as guinea pigs (the Haldane family motto was the single word, 'Suffer'). They tested gas masks by entering a sealed chamber full of hazardous gases and then seeing how well they could walk, run or recite poetry, with and without the masks. Their work resulted in improved respirators that saved thousands of lives. Once it was done, JBS went back to fight, to discover that most of his fellow officers in the Third Battalion of the Black Watch had been killed during his absence.

After the war Haldane returned to Oxford, where he started teaching physiology, despite having no qualifications in the subject other than his famous father (JBS never in fact took a science degree of any kind); all he had, he claimed, was 'about six weeks' start on my future pupils' – but it proved to be enough. He was still interested in genetics, however, and discovering that Wright and Castle had published a paper on linkage in mammals, Haldane sent Wright a copy of his own paper on mice. He worried that 'it is not very intelligible', but explained that 'I was wounded at the time I wrote it, and thought I had better publish as quickly as possible'.[32]

The two geneticists must have rapidly discovered their common interest in guinea pigs. Wright's doctoral work had involved searching for a Mendelian explanation of the guinea pig's continuously varying coat colour. So when George Rommel from the USDA approached Castle for a Mendelian with expertise in guinea pigs, Wright – who had just completed his PhD – was the obvious choice and he became 'senior animal husbandman' for the Animal Husbandry Division of the Bureau of Animal Industry.

As well as doing research, Wright was still expected to keep up the long-standing tradition of the USDA and answer questions from farmers, amateur and professional breeders and, indeed, any random crackpot who felt like writing to him, including the secretary of the Illinois Vigilance Association. The Association, as its letterhead proclaimed, was 'organized for the purpose of suppressing the traffic in women and girls and the conditions which make that traffic possible'. Among other things it

campaigned against the evil effects of Chicago's flourishing jazz scene. 'Moral disaster is coming to hundreds of young American girls,' wrote a journalist in the *New York American,* 'through the pathological, nerve-irritating, sex-exciting music of jazz orchestras.' He added that 'according to the Illinois Vigilance Association, in Chicago alone the association's representatives have traced the fall of 1,000 girls in the last two years to jazz music'.[33] The Association's secretary wrote to ask Wright if suppressing the 'sex instinct' could be scientifically proven to benefit the species. Wright's characteristically polite and careful reply simply observed that he knew of no evidence of ill effects from 'infrequent breeding of domestic or wild animals' apart from 'temporary sterility in the male'. The Association's secretary requested that Wright provide him with any future evidence on 'the benefits of the restraint of the sex instinct', if he should come across any.[34] Wright was exceptionally generous with his time and knowledge, feeling that as a public servant he was duty bound to answer every question as fully as he could. It was a habit that never left him; the immense influence he would eventually have in the scientific world was, in part, due to his generosity in answering his colleagues' questions.

Wright was too modest and shy to enjoy publicity, but Haldane revelled in it. He wrote a regular column for the British Communist Party's paper, the *Daily Worker*, as well as numerous popular books and a collection of children's stories, *My Friend Mr Leakey*, which remains in print almost eighty years after it first appeared. He also broadcast regularly for the BBC and proved to be an editor's dream, invariably available whenever an opinion, preferably a controversial one, was needed on any scientific topic. Haldane shared Wright's willingness to answer letters from the public, so while Wright was patiently answering questions about prize bulls and fallen women, Haldane's letters covered everything from the advisability of cousin marriage to the possibility of life on other planets; from offers to send him interesting cats to invitations to address student socialist societies; and explanations of original proofs of the mathematical Four-colour-map theorem.[35]

Haldane's knowledge of genetics inevitably also led to discreet enquiries about eugenic matters, especially whether it was advisable to have children if either spouse suffered from a particular illness or disability. On one occasion, a correspondent who 'suffered considerably from defects which I would rather not risk transmitting' asked JBS to help him locate a sperm donor, preferably 'an "allrounder" mentally and physically' – someone like JBS himself, the writer seemed to be hinting. Haldane pencilled 'really can't' in the margin of the letter and left it to his secretary to break the bad news.[36]

In 1923 Haldane defected twice: from Oxford to Cambridge and from physiology to biochemistry. Attracted by the power and promise of the new science of life, he accepted a new job working alongside Gowland Hopkins, another of the discoverers of vitamins (for which the latter won the Nobel Prize in 1929 – one of twenty-three that guinea pigs have helped win). Ten years after that, Haldane moved again – to University College London – initially as a professor of genetics and then of biometrics. These changes of location, specialization and interests were not as unusual then as they would be now – biology had not yet become quite as specialized as it now is – but they were nevertheless an indication of Haldane's restless intellectual energy, as well as his enormous talent for quarrelling with those around him. His contributions to any conversation were 'frequently caustic, at times vehement, but always profoundly human'.[37] Again, the contrast with Wright is striking: the American worked quietly, checking and rechecking his results before publishing them. Unusually for a geneticist of his generation he said little, in public at least, about eugenics, a subject – like most subjects – on which Haldane, over the course of his life, had numerous opinions, each of which was liable to be loudly discarded in favour of an equally strenuously maintained, but entirely contradictory, position within a few years.

While Haldane was busy shifting his stances and sciences, Wright stuck to his guinea pigs. He arrived in Washington to discover the USDA had kept meticulous, detailed records of over

34,000 matings; the results of each cross having been carefully recorded using a rubber stamp outline of a guinea pig, coloured in to show what the offspring looked like. Impressed by the accuracy of the records, Wright began analysing them with the techniques he had devised at Harvard. He discovered that, despite twenty generations of brother-sister matings, there were no signs of major problems, such as deformities. However, closer inspection showed that litters were becoming smaller and less frequent, the guinea pigs' birth weight was down, as was their disease resistance, and they were dying sooner. Inbreeding was clearly not good for them, a result that Wright must have felt some personal interest in, since his parents – like Charles and Emma Darwin – were first cousins.

Wright also found that the inbred guinea pig families looked very different from one another, despite having all descended from the same original stock. Just as Sergei Chetverikov had found with his wild Drosophila, there could be a lot of variation hidden in a population that only became visible slowly over several generations of inbreeding; this was the effect of recessive genes, which only became visible when an animal had two copies of them. Inbreeding made what were normally rare combinations – many of which were bad for the animal's health – much more common. However, it was also noticeable that when the inbred families were crossed with each other, much healthier, more vigorous animals immediately resulted, a phenomenon that became known as hybrid vigour (and which we will return to). Wright concluded that the best way to improve a breed was not continued selection within the breed as a whole, but the production of heavily inbred lines which might show up rare but useful traits. These could then be crossed to combine the desirable traits while restoring the breed's lost vigour.

Wright must have known of Haldane's interest in guinea pigs, since he offered to send him some of the USDA's stock. Haldane thanked him, but suggested that 'if you are testing this linkage on a big scale, there is no need for me to butt in. So please do not send them – if it is of any great trouble to you.' JBS had already taken on some rabbits from a co-worker and 'In consequence of this I shall have less space than I thought, so I should not be able to keep as many guinea pigs as I had hoped.'[38] A lack of space may have prevented Haldane from working regularly on guinea pigs, but so did his intellectual restlessness; he simply was not temperamentally suited to years of patient attention to detail in the way that Wright was. The practical side of biology also required other skills that JBS lacked; one of his former students remembered that 'he was not himself a good observer – and he was a terrifyingly bad experimenter'.[39]

However, one area in which Haldane and Wright were well matched was mathematics. Haldane had won a mathematical scholarship to Oxford, where he had achieved a First in the subject. In 1924, just after he had switched from physiology to biochemistry, Haldane published his first major genetics paper. Just as Wright had turned his mathematical mind to guinea pigs, Haldane turned his to moths, particularly the peppered moth (then known as *Amphidasys betularia*, now renamed as *Biston betularia*). This was a famous case of natural selection in action: in the mid-nineteenth century, as industrial pollution started to turn much of Britain's landscape black, entomologists noticed that among these greyish-white moths there were increasing numbers of the normally very rare dark form of the insect. The moths usually rested on the pale bark of birch trees, where the occasional dark moth stuck out and soon fell prey to hungry birds. However, in some areas of the country, industrial soot and smoke had darkened the tree bark so much that it was the more common pale moths who were the more exposed to predation, while the dark ones were camouflaged. In polluted areas, the dark moths gradually became more common as the numbers of light ones declined. This was widely accepted in Haldane's day, but he was interested in trying to calculate exactly how much of an advantage the 'dark' version of the moth colour gene would have to have over the 'light' one, in order for the populations to change in the way naturalists were observing. The dark-coloured form had first been recorded in 1848 and fifty years later had become dominant in polluted areas: using his unusual combination of mathematical

and genetic expertise, Haldane calculated that the dark form must be producing 50 per cent more surviving offspring than its pale-coloured rivals.

Such topics filled Haldane and Wright's correspondence for many decades; their letters were often covered in calculations and formulae, clarifying and criticizing each other's ideas, but while Haldane had moved from mice and guinea pigs – via moths and horses – to newts, Wright had never taken his eyes away from his guinea pigs. He wrote to Haldane to say that he would not be able to meet him at that summer's major international genetics congress because he needed to use his summer vacation 'to analyze a mass of accumulated data on my guinea pig colony', while his graduate students were out of his way.[40]

Haldane and Wright were not alone in attempting to solve biological problems mathematically. Forty miles from Cambridge were Britain's oldest agricultural research centre, the Rothamsted Experimental Station, and Ronald Aylmer Fisher, whose Cambridge-trained mathematical mind dwarfed even Wright's and Haldane's. His job at Rothamsted involved analysing the results of the station's plant-breeding experiments, such as trials of the effectiveness of different chemical fertilizers, to calculate precisely how much of the difference in yield between two crops was caused by the growing conditions and how much was due to the genetic superiority of one variety over another. The mathematical analysis of the relative contributions of nature and nurture was a subject that was important to Fisher; he was a committed eugenicist. He had helped found the Cambridge University Eugenic Society as a student and had become a close friend of Charles Darwin's son Leonard, president of the Eugenics Education Society.

Nevertheless, it was statistics rather than biology that had brought Fisher into contact with biometrics and Karl Pearson. Even after Fisher became convinced by Mendelism (which led to a falling out with Pearson), he remained interested in the biometrician's techniques. Fisher created a mathematical model of a population of hypothetical organisms, which used subtle and complex mathematical techniques to demonstrate how favourable genes spread through the population. He also showed that while the incidence of unfavourable mutations would decline, they would not necessarily be eliminated if they were recessive, but would survive, as Chetverikov had found among his wild flies. Fisher's mathematical demonstration was important, since some interpreted the biometricians' arguments as implying that natural selection must eventually use up all the variation in a population. If the fittest survived and the unfit died out, would not every organism in time simply have the best possible genes? The resulting genetically homogenous population would be perfectly adapted to its environment, but if and when that environment changed, it would be unable to adapt. It seemed as though perfection must guarantee extinction for every species, including our own. This was an especially worrying prospect for eugenicists, since their selective breeding programmes were intended to achieve perfection even faster than natural selection could. But Fisher showed how the genetic diversity of a population was maintained, in part because organisms with two different versions of a gene (heterozygotes) were sometimes fitter than either of the homozygous forms. The classic example of this process is sickle cell anaemia: one copy of the sickle cell gene confers some resistance to malaria, but two copies cause the painful and sometimes life-threatening disease. Nevertheless, the benefit conferred by the gene, the malaria resistance, has been enough to ensure that natural selection did not eliminate it from the population. To biologists, Fisher's calculations, if they were able to follow his complex maths (which many could not), revealed a picture of continuous, gradual evolution – and of evolution without end.

Despite their many differences (political as well as scientific), Wright, Haldane and Fisher had independently arrived at Chetverikov's idea of studying evolution mathematically. Each had recognized the predictive power of Mendelian genetics while realizing that it could not be applied to wild populations using the standard technique of controlled experiments, given the impossibility of recording each wild organism's pedigree. Ironically, it

was the Mendelians' scientific opponents, the biometricians, who had supplied the solution: their statistical tools made it possible to take a sample, assess its genes experimentally, and extrapolate the results to a whole population. Equations revealed the genes of thousands of wild plants or animals to the laboratory scientist; plotted on graph paper, changes in the genes of an entire population could be observed. They made it possible to extend the power of genetics from the laboratory into nature.

'Just another geneticist'

In 1920 Wright had spent his thirty days' annual leave at Cold Spring Harbor Laboratory, using his summer holiday to do more guinea pig experiments. There he had met a young woman called Louise Williams, a fellow biologist who was at the lab to take care of some rabbits that were being studied by her former teacher. The animal caretaker who had been cleaning her rabbits' cages had recently quit; when Wright arrived she had hoped he was the new animal caretaker. He later recalled that 'the first thing that she had said to me . . . was how badly she had been disappointed in me' when he proved to be 'just another geneticist'. Both chagrined and charmed, Wright immediately offered to help her with the cages. They began to take walks together after dinner and were always seen sitting with each other at the lab's regular picnics. Wright later wrote that 'I was so much in love with her at the end of my vacation and so dubious about merely starting a correspondence that I proposed on the last evening. She demurred at first because of the shortness of our acquaintance and because I had not met her parents or she mine but finally agreed to consider us engaged.' They were married the following year.[41]

A couple of years later, Wright was discreetly approached by the University of Chicago and offered an academic job. Although he and Louise Wright, as she now was, would have preferred to raise their children nearer to open countryside, the prospect of better facilities, a community of other geneticists (Wright felt somewhat isolated in Washington) and a salary increase finally persuaded him to accept the job and the couple moved. Wright briefly considered switching to another experimental animal, but realized that he had invested too much time and energy in guinea pigs to abandon them now; one of his conditions for the new job was that Chicago build him 120 custom-built pens to house the guinea pigs he brought with him from Washington.

At Chicago Wright discovered that he was not a natural teacher, too shy and nervous to make off-the-cuff remarks or banter with the students. Instead, he prepared every class in great detail and always gave formal lectures, even to the smallest groups. Teaching forced Wright to be unfaithful to his guinea pigs – they bred much too slowly to be used for experiments in a ten-week course – so he acquired Drosophila stocks from Morgan's lab at Columbia. One of his students remembered Wright as 'a very mild mannered gentleman who would stand there looking hurt and blinking when his students would not come to the obvious conclusions – obvious to him from the analysis that he put on the blackboard'. Wright would scribble continuously as he talked; 'he would cover the entire blackboard of a 30 foot wide classroom, 3 times a lecture'. Despite the necessity of using Drosophila in experiments, Wright would bring guinea pigs into the classroom whenever he could justify doing so; on one occasion he brought one in to show his class some interesting variations in its coat colour. 'This particular guinea pig was somewhat more fractious than usual and was scurrying around on the desk and was not about to be quiet,' a student recalled, so Wright picked up the restless cavy and tucked it under his armpit, where he usually kept his blackboard eraser. A few minutes later, running out of space for the next equation, he reached for his eraser 'and started to erase the blackboard with a squeaking guinea pig'.[42]

With the (sometimes reluctant) help of his guinea pigs, Wright had devised mathematical tools for making sense of biological problems. Fisher and Haldane had come up with similar techniques for addressing comparable problems; in the process, the three of them found they had invented a new science – population genetics. But there were important differences between them: Haldane and Fisher's work was more mathematically sophisticated

than Wright's, but also more abstract. They were forced to treat each gene separately, assigning it an adaptive value and then predicting how it would spread through a hypothetical population. This abstract modelling of the way isolated genes behaved became known, not always politely, as 'bean-bag' genetics, because genes were treated as if they were picked randomly and independently out of a bag, rather than existing alongside each other – and interacting with each other – as in living organisms.

Haldane and Fisher understood that to make their calculations possible (especially in the days before electronic computers) they had to simplify their models, to reduce the number of variables they had to calculate. This led to what they realized were unrealistic assumptions: for example, in a real population of moths – or any other organism – mating is never completely random; apart from anything else, moths (like the rest of us) are much more likely to find potential mates close by. In a small population of moths, it is possible that there might be more dark than light moths purely by chance, so the number of dark offspring could increase without natural selection having anything to do with it. Castle's hooded rats had demonstrated a similar effect – that continued selection within a small population created unusual genetic combinations that might never exist in a larger population; paradoxically, that meant that a small inbred population might actually vary more than a large, freely interbreeding one. To avoid having to calculate the effects of this kind of random factor, Fisher and Haldane assumed that each of their mathematical species had an infinitely large population; all the potential complications that might arise in small isolated groups were simply ignored. Wright's work was subtly different; partly because of his abiding affection for his guinea pigs, his maths also accounted for factors like inbreeding.

One result of the mathematical trio's work was to persuade biologists of the power of natural selection – that it alone was enough to achieve changes such as had been observed in the peppered moth. As a result, some older ideas about inheritance, especially the possibility of Lamarckian inheritance, were finally abandoned. Haldane had never believed in Lamarckian inheritance, but – in one of history's more bitter ironies – he ended up defending it for political reasons, because the inheritance of acquired characteristics was at the heart of the style of genetics being promoted in the Soviet Union by Lysenko. Lamarckian ideas had often attracted those on the political left, because they seemed to suggest that better living conditions would produce better people. By contrast, many felt that the growing Mendelian orthodoxy, that genes were a stable given, was a reactionary view, suggesting that the poor were poor because they were biologically inferior and only eugenics could cure poverty, by getting rid of the genes that that 'caused' poverty – and those that carried them. Certainly many right-wing eugenicists chose to interpret Mendelism this way, including the Nazis, a fact that Lysenko seized on to accuse Soviet Mendelians of being in league with fascism.

Although Haldane had no sympathy for the idea of the inheritance of acquired characteristics, he had plenty for Marxism, first supporting and then eventually joining the British Communist Party during exactly the period – from the mid-1930s to the late 1940s – when Lysenko's views were becoming the Soviet biological orthodoxy. As the nature of Nazism became clearer during the 1930s, even non-communists began to see the USSR as the only barrier to the rise of fascism, not least because democratic governments stood by and did nothing while republican Spain fought for its survival against fascist forces backed by Hitler and Mussolini. Haldane was one of hundreds of British communists who went to Spain to fight fascism; he offered his scientific expertise and made several visits to Madrid to help the republican government plan for air raids and possible poison gas attacks. The threat of fascism made support for the USSR an even more pressing duty for British communists; in these circumstances, any criticism of Soviet policy was seen as disloyal.

An additional factor that shaped Haldane's views was that, as we have seen, he had visited the USSR and – like Hermann Muller before him – had been impressed by the level of state

funding for science, which dwarfed the meagre funds made available to scientists by the British government. Haldane was one of many scientists who were drifting to the left in the 1930s, and the British Communist Party actively and successfully recruited them, promising them a future in which science would be unconstrained by limits on either money or freedom. Such promises began to look increasingly unconvincing as in the Soviet Union, Lysenko manoeuvred to ensure that those who disagreed with him lost their jobs, were arrested or simply disappeared. As we have seen, Chetverikov, his friends and colleagues were all victims of Stalin and Lysenko's terror, but Haldane – who had done so much to publicize and promote Chetverikov's work in the West – stood by and watched, unable or unwilling to speak out in defence of his Russian colleagues. For many years Haldane maintained an uneasy silence, unwilling to say anything that could be useful to anti-communist propagandists. In private, especially at the British party's scientific debates, he was critical of many of Lysenko's claims, recognizing them as unscientific nonsense. But gradually his political loyalties forced him to defend Lysenko and the party line in terms that, if they did not involve outright lies, certainly fell far short of the truth. In the late 1940s, he even began to suggest that there might be some scientific evidence for Lamarckian inheritance, but eventually found he could not live with his divided loyalties any longer. In 1950 he quit the Communist Party, feeling unable to reconcile his political loyalties with his obligation as a scientist to pursue the truth as he saw it. A belated recognition, but he was virtually the only leading British Communist scientist to quit the party over Lysenkoism.

From Russia with flies

Perhaps the only positive product of Lysenko's reign was Theodosius Dobzhansky, possibly the most brilliant biologist of the twentieth century, who was to complete the rapprochement between the Mendelians and biometricians that Haldane, Fisher and Wright had begun. Dobzhansky came to the United States in 1927, to work with Morgan's group at Columbia. He had originally planned to return to Russia after his studies, but when he realized how hostile the political climate in the Soviet Union had become to Mendelians, he decided to stay in America, eventually becoming a US citizen.

Dobzhansky had arrived steeped in the Russian tradition of field work, used to working with wild flies. Although he had not been one of Chetverikov's students, Dobzhansky knew all about his statistical methods and how to apply them to understanding evolution outside the lab. At Columbia, he learned all the lab techniques of Morgan's fly boys and decided to try and combine the Soviet and American approaches; he took his lab on the road. In the late 1930s, he began to drive up into southern California's San Jacinto mountains, his car packed with bottles, microscopes and – most important of all – lab-bred flies. Over the following years, Dobzhansky travelled all over the southern USA, from California to Texas, catching wild Drosophila. Early each morning or late in the evening, he would put some fermenting mashed banana into a half pint milk bottle and wait for the flies to catch the scent and enter the bottle; then he and his students would trap them. Once caught, the flies were crossed with the cleaned-up lab flies, whose genetic make-up was by now well known. Breeding experiments allowed Dobzhansky to use the lab flies as Chetverikov had done – as a probe to reveal the unknown genes of wild Drosophila.

Dobzhansky discovered that the genetics of the wild populations consisted of several distinctive sets of genes, or genotypes, and – more unexpectedly – he found that the percentage of each genotype varied according to the season. One type dominated in the summer, but was much rarer in winter-caught flies. Like most biologists, he had always assumed that natural selection was much too slow for humans to observe in a lifetime, but as he trapped and bred his flies, Dobzhansky realized that only natural selection could account for the changing frequencies of the different genotypes. One type was better adapted to cold weather, another to drought, and so on. He tested this idea by raising mixed populations in large cages, built from fine mesh screens. Some

cages were kept wet and cold, others hot and dry, to simulate the seasons; he found that one particular type of fly became dominant in each cage: in one case, a genotype that made up just 10 per cent of the initial population had increased to 70 per cent in just ten months. Thanks to Drosophila's rapid breeding, he was watching evolution in action.

By cross-breeding his lab flies with wild ones, Dobzhansky was completing the transformation Chetverikov had begun; bringing together lab and field. As he proudly wrote, 'Controlled experiments can now take the place of speculation as to what natural selection is or is not able to accomplish.' For the first time in the history of biology, the raw material of evolution, the endless variability of living things, 'now lies within the reach of the experimental method'.[43]

Dobzhansky met Wright in 1932 at an international genetics congress, where – in Dobzhansky's words – he 'fell in love' with Wright; it was the beginning of a long and highly productive friendship. Despite knowing little maths, Dobzhansky absorbed all of Wright's papers by carefully reading their introductions, skimming the central mathematical problems, and carefully reading the conclusions. When he needed help analysing his results, it was Wright to whom he turned, and they collaborated closely on Dobzhansky's enormously influential series of papers that described and analysed his work with the wild flies. Dobzhansky got into the habit of consulting Wright when planning new experiments, and Wright often checked and commented on Dobzhansky's work before it was published.

Dobzhansky and Wright's work was the last, decisive step in one of the most momentous achievements of twentieth-century biology: the creation of the modern theory of evolution. It has become known as the modern synthesis, because – as biologists still like to present it – it combined Darwin's ideas and Mendel's. But describing the synthesis in this way omits all the practical detail of how the story actually happened: the hours Weldon spent counting shrimp, which helped transform Darwinism into biometrics; or the patient fly breeding that turned Mendel's mysterious *Anlagen* into genes on chromosomes. Despite the failure of the Mutation Theory, Oenothera established that evolution could be investigated in laboratories, a point Castle acknowledged when he described his use of rats to test natural selection: 'to De Vries we owe much for showing that such tests are possible'.[44] Though the modern synthesis is often described as the marriage of Darwin and Mendel, it really involved cross-breeding Soviet and American flies with guinea pigs, hybridizing scientific practices and disciplines and forcing biometricians to work with Mendelians so that they could mate maths with moths, to give birth to genes on graph paper.

Wright never really chose to work with guinea pigs; in a sense, they chose him, since his position at Harvard was dependent on his looking after the existing colony. There were good reasons why he might have wanted to work on another species: they were much harder to keep than Drosophila; they bred much slower; they were prone to disease; they have far more chromosomes than the flies (thirty-two, compared to four, although the guinea pigs' number was not even known until long after Wright graduated); and guinea pig chromosomes are small and hard to identify under a microscope. While Morgan's fly team had hundreds of mutations to work with, hardly any were known in guinea pigs (since only two examples of linkage in guinea pigs had been demonstrated, Wright once complained that 'everything in the guinea pig seems to be independent of everything else'), so chromosome mapping was impossible.[45] Worst of all, there was no guinea pig community for Wright to share ideas with; at the time, there were only a couple of other scientists using them for genetic research. Yet Wright seems to have taken to guinea pigs from the outset and never regretted the fact that they chose him. Although few guinea pig genes were known at the time, there were about 3.5 million possible combinations of the genes that were known, so Wright studied the problem of gene interactions – how the genes affected each other – for his entire career.

Because they forced Wright to concentrate on the interaction between genes, the guinea pigs prevented him making some of the

elegant but unrealistic simplifications that Haldane and Fisher's work relied on. As a result, his work was more accessible – and more useful – to working field biologists than theirs. Thanks, in part, to Castle's influence, but also through working with the inbred colony in Washington, Wright had to develop mathematical tools with which to analyse the effects of inbreeding. As he struggled to understand the odd-looking inbred families that had been produced from the USDA's single original stock, he was constantly reminded that genes interacted with each other to produce variation, the raw material of evolution. As the organism's original hand of genes was shuffled and redealt with each new mating, new combinations arose, giving the offspring new strengths – or weaknesses. He concluded that evolution was most likely to take place in small, isolated populations – populations that were nothing like the infinitely large ones hypothesized by Haldane and Fisher.

Given the comparative ease with which Wright's insights could be applied to real population studies, it is no surprise that, of the three great mathematical population geneticists, he was the one who most influenced Dobzhansky, as he did many other field biologists, not many of whom could follow the complex mathematics used by the pioneers of population genetics. Wright's ideas were the easiest and most useful for them to apply to their own work, particularly because the importance of treating a species as a series of small, largely isolated sub-populations had emerged quite independently from field studies of wild populations. Thanks in large measure to Dobzhansky's book *Genetics and the Origin of Species* (1937), Wright's work became vital to successive generations of biologists.

Yet despite the huge affection and respect in which Wright was held by his colleagues, his guinea pig work at Chicago produced one major disappointment. He had hoped to connect genetics with development, to show how genes actually turned a fertilized egg into an adult guinea pig. Like many of his contemporaries, Wright suspected a chemical connection, that specific genes produced specific chemicals, probably the enzymes whose workings were then being unravelled by the biochemists (Haldane had played a useful part in this work before he defected to genetics). Yet despite years of hard work, Wright never made any real headway with this problem. Understanding how genes actually worked in practice would require a new science, molecular biology, which was to be built on work with an organism that could not have been more different from the guinea pig – a virus called bacteriophage.

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8. William Graham Sumner, quoted in D.R. Oldroyd, *Darwinian Impacts: an introduction to the Darwinian Revolution*: 214.
9. Lord Roseberry, quoted in D. Trotter, 'Modernism and Empire: Reading The Waste Land', in *Futures for English* (Manchester University Press): 143–153: 150.
10. K. Pearson, *The Groundwork of Eugenics* (1909), quoted in W.H. Tucker, *The Science and Politics of Racial Research* (University of Illinois Press, 1994): 59.
11. Quoted in R.E. Kohler, *Lords of the Fly: Drosophila Genetics and the Experimental Life* (University of Chicago Press, 1994): 26.
12. Fernandus Payne to A.H. Sturtevant, [16 October 1947]. Sturtevant Papers. Quoted in G.E. Allen, 'The introduction of *Drosophila* into the study of heredity and evolution, 1900–1910', *Isis*, 1975: 322–33: 330.
13. R.E. Kohler, *Lords of the Fly: Drosophila Genetics and the Experimental Life*: 33–4.
14. W.S. Sutton, 'On the morphology of the chromosome group in *Bracystola magna*', *Biological Bulletin* 1902, 4: 24–39, and W.S. Sutton, 'The chromosomes in heredity', *Biological Bulletin*, 1903, 4,: 231–51. See E.W. Crow and J.F. Crow, 'Walter Sutton and the Chromosome Theory of Heredity', *Genetics*, 2002: 1–4: 1.
15. Morgan, *Evolution and Adaptation*, (London: Macmillan and Co. 1903): 286–287. Quoted in G.E. Allen, *Thomas Hunt Morgan: the man and his science* (Princeton University Press, 1978): 111.
16. X-rays were originally known as Röntgen rays in honour of their German discoverer, Wilhelm Conrad Röntgen.
17. G.E. Allen, *Thomas Hunt Morgan: the man and his science*: 152–3. Lilian Morgan's recollection was that it was *white* that

Morgan discussed so enthusiastically when their first child was born on 5 January 1910, but as Kohler has pointed out, she must have been mistaken: it could only have been *with* Morgan was talking about, as *white* did not turn up until May. R.E. Kohler, *Lords of the Fly: Drosophila Genetics and the Experimental Life*: 46.

18. F.W. Taylor, *The Principles of Scientific Management* (1911; Routledge/Thoemmes, 1993).
19. Quoted in B.T. Clause, 'The Wistar Rat as a Right Choice: Establishing Mammalian Standards and the Ideal of a Standardized Animal', *Journal of the History of Biology*, 1993: 329–49: 343.
20. T.H. Morgan, 'Random Segregation Versus Coupling in Mendelian Inheritance', *Science*, 1911: 384; G.E. Allen, *Thomas Hunt Morgan: the man and his science*: 160–1.
21. By J.B.S. Haldane, see: R.E. Kohler, *Lords of the Fly: Drosophila Genetics and the Experimental Life*: 47–8, 79–80.
22. G.E. Allen, *Thomas Hunt Morgan: the man and his science*: 191.
23. M.B. Adams, 'Sergei Chetverikov, the Kol'tsov Institute, and the Evolutionary Synthesis', in *The Evolutionary Synthesis: Perspectives on the Unification of Biology* (Harvard University Press): 262–4.
24. T.H. Morgan to H. de Vries, [5 January 1918]. Archives of the Biological Laboratory, Vrije Universsiteit, Netherlands. My thanks to Elliot Meyerowitz for showing me this letter and to Tom Gerats for permission to quote from it.
25. R.J. Greenspan, *Fly Pushing: The theory and practice of Drosophila genetics* (Cold Spring Harbor Press, 1997): 125.
26. T.H. Morgan, 'A critique of the theory of evolution', Princeton; Princeton University Press, 1916.

Chapter 7: *Cavia porcellus*: Mathematical guinea pigs

The **primary sources** were: C.É. Brown-Séquard, 'Hereditary Transmission of an Epileptiform Affection Accidentally

Produced', *Proceedings of the Royal Society of London*, 1859–60: 297–8; W.E. Castle and H. MacCurdy, *Selection and Cross-breeding in Relation to the Inheritance of Coat-pigments in Rats and Guinea-Pigs* (Carnegie Institution of Washington, 1907); W.E. Castle, 'An expedition to the home of the guinea-pig and some breeding experiments with material there obtained', in *Studies of Inheritance in Guinea-Pigs and Rats* (Carnegie Institution of Washington, 1916); and T. Dobzhansky, 'Genetics of natural populations. XIV. A response of certain gene arrangements in the third chromosome of *Drosophila pseudoobscura* to natural selection', *Genetics*, 1947: 142–60.

For the **history of the guinea pig**, see: C. Cumberland, *The Guinea Pig or Domestic Cavy for Food , Fur and Fancy* (L. Upcott Gill, 1897); B.J. Weir, 'Notes on the origin of the domestic guinea-pig', in *The Biology of Hystricomorph Rodents* (Zoological Society of London, 1974); B. Müller-Haye, 'Guinea-pig or cuy', in *Evolution of domesticated animals* (Longman, 1984); E. Morales, *The Guinea Pig: healing, food, and ritual in the Andes* (University of Arizona Press, 1995); S. Pritt, 'The history of the guinea pig (*Cavia porcellus*) in society and veterinary medicine', *Veterinary Heritage*, 1998: 12–16; J. Clutton-Brock, *A Natural History of Domesticated Mammals* (Cambridge University Press, 1999); and J.C. Castillo, 'Naming Difference: The Politics of Naming in Fernández de Oviedo's *Historia general y natural de las Indias*', *Science in Context*, 2003: 489–504.

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For **J.B.S. Haldane's life and work**, I used: his archives at University College London; his own publications, especially: *Possible worlds and other essays* (Chatto & Windus, 1940); and *Science advances* (G. Allen & Unwin, 1947). Also invaluable were: R. Clark, *J.B.S.: The Life and Work of J.B.S. Haldane* (Hodder & Stoughton, 1968); A. Lacassagne, 'Recollections of Haldane', in *Haldane and modern biology* (Johns Hopkins University Press, 1968); N. Mitchison, 'Beginnings', in *Haldane and modern biology* (Johns

Hopkins University Press, 1968); N. Mitchison, 'The Haldanes: Personal notes and historical lessons', *Proceedings of the Royal Institution of Great Britain*, 1974: 1–21; D.B. Paul, 'A War on Two Fronts: J.B.S. Haldane and the Response to Lysenkoism in Britain', *Journal of the History of Biology*, 1983: 1–37; M.B. Adams, 'Last Judgment: The visionary biology of J.B.S. Haldane', *Journal of the History of Biology*, 2001: 457–91.

For **Sewall Wright's life and work**, I am greatly indebted to William Provine's publications: 'The Role of Mathematical Population Geneticists in the Evolutionary Synthesis of the 1930s and 1940s', *Studies in the History of Biology* (1978); *Sewall Wright and Evolutionary Biology* (University of Chicago Press, 1986). Provine has deposited all his research materials for his biography of Wright with the American Philosophical Society, whose archives I also consulted. I also made use of: J.F. Crow, 'Sewall Wright's place in twentieth-century biology', *Journal of the History of Biology*, 1990: 57–89.

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Notes

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2. Power, *Experimental philosophy* (1664), I: 16.
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4. C. Cumberland, *The Guinea Pig or Domestic Cavy for Food, Fur and Fancy* (L. Upcott Gill, 1897): 2.
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6. ibid.: 7–8.
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9. R. Wheatley, 'Hygeia in Manhattan', *Harper's New Monthly Magazine*, 1897: 384–401: 386.
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12. H.C. Wood, 'The Value of Vivisection', *Scribners Monthly, an illustrated magazine for the people*, 1880: 766–71: 768.
13. ibid.: 770.
14. E. Glasgow, 'A Point In Morals', *Harper's New Monthly Magazine*, 1895: 976–82.
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16. L.G. Wilson, 'The clinical definition of scurvy and the discovery of Vitamin C', *Journal of the History of Medicine and Allied Sciences*, 1975: 40–60: 47–51; C. Funk, *The Vitamines* (1st English edition, 1922).
17. E.V. McCollum. Quoted in H.E. Smith, et al., 'Architecture and science associated with the Dairy Barn at the University of Wisconsin-Madison' (Department of Landscape Architecture University of Wisconsin-Madison, 2000).
18. L.G. Wilson, 'The clinical definition of scurvy and the discovery of Vitamin C': 56–7.
19. W.E. Castle, 'The Mutation Theory of Organic Evolution, from the Standpoint of Animal Breeding', *Science*; 1905, 21 (536): 524.
20. W.E. Castle and H. MacCurdy, *Selection and Cross-breeding in Relation to the Inheritance of Coat-pigments in Rats and Guinea-Pigs* (Carnegie Institution of Washington, 1907): 3.
21. As we'll see in Chapter 9, the Danish botanist, Wilhelm Johannsen, had done the first pure line experiments with edible beans, Phaseolus.
22. W.E. Castle and H. MacCurdy, *Selection and Cross-breeding in Relation to the Inheritance of Coat-pigments in Rats and Guinea-Pigs*: 3–4.

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25. S. Wright, 'Birth and Family (Series III: Biographical and autobiographical materials)' (Sewall Wright Papers, American Philosophical Society, Philadelphia).
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28. N. Mitchison, 'The Haldanes: Personal notes and historical lessons', *Proceedings of the Royal Institution of Great Britain*, 1974: 1–21: 3; R. Clark, *J.B.S.: The Life and Work of J.B.S. Haldane* (Hodder & Stoughton, 1968): 17.
29. N. Mitchison 'Beginnings', in *Haldane and modern biology* (Johns Hopkins University Press): 302–3; N. Mitchison, 'The Haldanes: Personal notes and historical lessons': 8–9; R. Clark, *J.B.S.: The Life and Work of J.B.S. Haldane*: 29–30.
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43. Dobzhansky, 1947. Quoted in G. Allen, *Life Science in the Twentieth Century* (Cambridge University Press, 1978): 142.
44. W.E. Castle and H. MacCurdy, *Selection and Cross-breeding in Relation to the Inheritance of Coat-pigments in Rats and Guinea-Pigs*: 3.
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Chapter 8: Bacteriophage: The virus that revealed DNA

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My account of **Felix d'Hérelle** and **the history of bacteriophage** relies on the work of William Summers, in particular: 'From culture as organism to organism as cell: Historical origins of bacterial genetics', *Journal of the History of Biology*, 1991: 171–90; 'How Bacteriophage Came to Be Used by the Phage Group', *Journal of the History of Biology*, 1993: 255–67;

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