Why Study History?

George Santayana gave us the most powerful reason for studying history: "Those who cannot remember the past are condemned to repeat it " (Santayana, 1905-1906). This topic is treated in this and the subsequent chapter. The present chapter treats the scientific development of genetics. The subsequent chapter, Genes, Politics, and Society outlines the unhappy and disastrous social consequences of extrapolating "scientific genetic principles" into public policy before the science is well understood.

Prehistoric Genetics

We have good empirical evidence that humans had an implicit knowledge of genetics from at least 15,000 years BCE. Surprisingly as it may sound, the evidence resides in the remnants of the first attempts at genetic engineering. This engineering took the form of what today is called *artificial selection*—the deliberate breeding of plants and animals for desired characteristics. The best empirical evidence comes from the analysis of pollen in hermetically sealed ancient tombs and from the dog.

Current phylogenetic analyses[1] suggest that dogs evolved from wolves and were domesticated at least by 15,000 BCE in East Asia (Ostrander, Giger & Lindblad-Toh, 2008; Savolainen et al., 2002). The "at least" part of this temporal estimate derives from archeological and DNA evidence of North American dogs suggesting that they were brought into the continent from Asia by the new world's original discoverers. Artificial selection of the dog for behavioral traits like herding, guarding, hunting, and retrieving is some of he best evidence for genetic influences on mammalian behavior (Scott & Fuller, 1965)

Like many attempts to manipulate nature, early genetic engineering had unforeseen consequences. Merrill (1975) reports that the original progenitors for today's onions, lentils, ginger, and many other crops are extinct, probably because our human ancestors selected for fecundity. So called "wild onions" and "wild ginger" are really domestic varieties that "got loose" and outcompeted their wild type ancestors.

Early Historical Period

Having an implicit knowledge is very different from the explicit knowledge required of a science. You know how to tie your shoelaces. Think for a minute

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[1] Phylogenetics is a branch of genetics that explores the genetic origins of species and the genetic relationships among species.

about writing a professional article on how to tie a shoelace. The former is implicit knowledge. The latter is the explicit, scientific knowledge.

According to Stent (1971), the first known theory of inheritance in Western thought originated in Greece in the fifth century BCE and was taught (and probably developed) by Hippocrates. One could classify Hippocrates ideas as a "bricks and mortar" theory. That is, the hereditary material consists of physical material (as opposed to a blueprint). He postulated that elements from all parts of the body became concentrated in male semen and then formed into a human in the womb. He also believed in the inheritance of acquired characteristic. The large biceps of an Olympic weight lifter result in many "bicep parts" in the semen. Hence, his children would also have big biceps.

A generation later, Aristotle criticized this theory. His first objection was that mutilated and physically handicapped people can have normal children. If Kostas had lost his left arm in battle, then he has no "left arm parts." How come his children have perfectly formed left arms?

Aristotle's second objection was more subtle—people can transmit characteristics that they do not show at conception but develop at a later age. Think of gray hair or male pattern baldness. At the time of conception, most Greeks of the period would have brown to black hair and only a few would exhibit pattern baldness. Hence, there are no "gray hair parts" and few "baldness parts" although much later in life those "body parts" might be available. Still parents can transmit these traits to their offspring.

Aristotle went on to reject the bricks and mortar model of heredity transmission. Instead, he proposed that heredity involved the transmission of information—a "blueprint model." This remarkable insight was ignored until the middle of the 20th century. All subsequent theories were based on the bricks and mortar model.

Intellectual Background for Modern Genetics: The Four Ls

Genetics did not developed suddenly. Sure, there were very important contributions that radically changed the field. Think of Darwin or Mendel. But even Darwin's paradigm shift did not occur de novo. Instead, it evolved from the intellectual background of his time. Indeed, his grandfather, Erasmus Darwin, had written—albeit vaguely—about evolution. Here, we focus on "the four Ls" or four people whose surnames begin with the letter L that contributed to the intellectual climate that presaged genetics.

van Leeuwenhoek (1632 – 1723)

The first L is Anton van Leeuwenhoek. Many texts mistakenly credit van Leeuwenhoek with the invention of the microscope. Actually, that instrument was first developed around 1590, some 40 years before van Leeuwenhoek's birth, by two of his Dutch compatriots, the father and son team of spectacle makers, Zaccharis and Hans Janssen. Galileo further developed Janssens' invention into the telescope.

The major contributions of van Leeuwenhoek were his significant improvements to the microscope that enabled him to observe what he termed *animalcules*, today called microbes or microorganisms. Many consider van Leeuwenhoek the father of microbiology. Even if one were to dispute this, there is no doubt that he was the first to report on single cell organisms. Scientists of the day greeted his finding with suspicion and resistance. It was not until a team of impartial observers replicated van Leeuwenhoek's observations that microbes were accepted as a real phenomenon.

Hence, his major contribution was to initiate a whole field of science that eventually led to the development of cell theory and the identification of chromosomes.

Linnaeus (1707 – 1778)

Carl von Linné, better known by his Latinized surname, Linnaeus, was a Swedish physician and biologist, concerned with the classification of biological entities, a scientific enterprise of great popularity at the time. In 1735, he published the first edition of *Systema Naturae* that, in its brief 11 pages, provided the seeds for modern biological classification. His major contribution was not the organisms that Linnaeus classified. Rather, he established a *set of rules* for classification that gradually became universally accepted.

There are several salient aspects of the Linnaean system. First, it is *binomial* (two names). In this system, an organism is referred to by two names—its genus and species—using Latin (but sometimes Greek) roots. Hence, we humans are *Homo sapiens* (wise man) and your pet cat is a member of *Felis catus* (cunning cat). Second, the system was based largely on external morphology. Third, the system was hierarchical. That is, species X is more closely related to species Y than to species Z if it looks more like Y than Z. An ant and a termite will be classified closer in the hierarchy than either would be with an elephant.

Along with the biologists of his time, Linnaeus believed in the biblical account of creation. Hence, he viewed species as being created and then remaining fixed and immutable. The idea of evolution was developed by our third L.

Lamarck (1744 – 1829)

Lamarck, formally named Jean-Baptiste Pierre Antoine de Monet, Chevalier de Lamarck, is usually associated with the inheritance of acquired characteristics, a phenomenon that modern biology terms (in a somewhat derogatory sense) as *Lamarckism*. Sadly, this heritage overshadows his major contribution to the intellectual background of genetics—Lamarck was the first to propose a comprehensive theory of evolution.

Lamarck's theory was not the first to challenge the literal biblical account of creation and its implication that species are fixed and immutable. In the 1700s, the Scottish scholar James Burnett (Lord Monboddo), known today as one of the founders of linguistics, speculated that modern chimps and humans originated from a common ancestor. Just before the dawn of the nineteenth century, Erasmus

Darwin's *Zoömania* also contained hints about evolution. Why have Monboddo and E. Darwin not been credited with "discovering evolution?" The answer is instructive to every student of science—the laurels often go not to the person who originates an important idea, but to the person who develops that idea into a comprehensive theory and/or the person that popularizes that idea. Let's spend a moment exploring a specific case about evolution. Consider the following quote from Erasmus Darwin:

> Would it be too bold to imagine that, in the great length of time since the earth began to exist, perhaps millions of ages before the commencement of the history of mankind would it be too bold to imagine that all warm-blooded animals have arisen from one living filament, which the great First Cause endued with animality, with the power of acquiring new parts, attended with new propensities, directed by irritations, sensations, volitions and associations, and thus possessing the faculty of continuing to improve by its own inherent activity, and of delivering down these improvements by generation to its posterity, world without end!

The implication for biology is clear. The term "First Cause" derives from one of the arguments made by the medieval scholar Thomas Aquinas for the existence of God. God's initial creation may not have resulted in a large number of immutable species. Instead, there was one "living filament" bequeathed with the traits that allow it to change in different directions over time. Changes to this single living filament (and its offspring) resulted in the myriad of species we observe today.

This is clearly a statement about evolution. Lamarck, however, is credited as the "first modern evolutionist" because he developed a comprehensive theory about the process of evolution. Erasmus Darwin speculated that a camel and a giraffe may be contemporary manifestations of "one living filament." Lamarck took this a step further. Camels and giraffes have a common ancestor, but they differentiated in terms of their adaptations to different environments. In lush environments, the primordial ancestor of the camel and giraffe first ate the lower leaves of a tree and then stretched its neck to reach the higher leaves. This "stretched neck" was then transmitted to its offspring, and after a large numbers of generations, viola—we have a large number of animals with very long necks, members of a species that we now call the giraffe.

Linnaeus' hierarchical classification implies that certain species are closely related while others are distantly associated. It is natural for biologists to ask the question "why are ants and termites more closely related than either is to an elephant?" Lamarck's theory provides an answer—ants and termites diverged more recently than either did from the ancestor of the elephant. In short, what Lamarck got right was the concept of change as a function of heritable transmission and adaptation to the environment. What he got wrong, and for which he has been disparaged ever since, was the mechanism of such change, his concept of the inheritance of acquired characteristics.

Lyell (1797 – 1875)

The last L is Charles Lyell, a Scottish lawyer turned geologist. Lyell's contributions to pre genetic thought are much less attributable to him as an individual than they are to his overall field. He is given credit here because his surname begins with the letter L (making it easier to remember) and because he authored one of the classic books of the day—one that greatly influenced the young Charles Darwin—the *Principles of Geology*, published in several volumes from 1830 to 1833.

Lyell's major importance resides in the fact that he compiled and systematized the thought that became the origins of modern geology (to which he, himself, made important contributions). The prevailing opinion about the origins of earth and biological species was taken from the two accounts of creation in Genesis, the first book of the bible. Around 1600, Bishop James Ussher used temporal estimates of the genealogies in Genesis and other biblical texts to conclude that creation occurred on October 23, 4004 BCE.

The modern geology summarized in Lyell's text seriously challenged that view. It proposed that contemporary geological formations (e.g., the Rocky Mountains, the Sahara desert, the white cliffs of Dover) were the result of natural, physical process occurring over millions of years. At this point many of you might infer that Lyell's greatest contribution was his (as well as other geologists of the time) contention over the timing of the earth. Interesting enough, Lyell attributes this challenge to Lamarck: "That the earth is quite as old as he [Lamarck] supposes, has long been my creed" (Lyell, 1881, Vol. 1, p. 168).

The concept in modern geology of an old versus young earth is undoubtedly a major contribution to science, but it should not overshadow another (and arguably more important) contribution—namely, that changes over time are the result of natural processes and not divine intervention. Why does the Thames twist and turn in serpentine fashion? According to modern geology, this is the result of differential erosion, the undercutting of riverbanks in soft versus hard strata, and other physical and identifiable processes. The task of science is to identify and explicate these physical processes.

In his voyage on the Beagle, Charles Darwin had a copy of Lyell's *Principles of Geology*. Hence, he was familiar with the concepts of the age of the planet being much longer than that implied by the bible and that things change gradually over time according to physical principles.

Fertilization and Gestation of Modern Genetics

It took well over 50 years for genetics to emerge as a unified field. If we consider that time as the birth of genetics, then its fertilization and gestation began with three disparate developments during the nineteenth century. Two of the three are associated with individuals—Charles Darwin and Gregor Mendel. The third is early cell biology. We consider each in turn.

Charles Darwin (1809 -1882) and his Heritage

Charles Darwin was the son of a prosperous country physician. His recent biographer, Janet Browne (1993, 2003), reports that he was a rather ordinary child not noted for the brilliance he exhibited later in life. Like his father and elder brother, Darwin attended medical school in Edinburgh. His passion for collecting biological specimens in the Scottish countryside, however, far exceeded his interest in human anatomy and physiology, so he dropped out and went to Cambridge to undertake preparatory studies for becoming an Anglican priest.

At Cambridge, Darwin was initially an indifferent scholar. Over time, however, his zeal for "naturalism" (observational biology) took hold. He became a protégé of the botanist John Henslow and spent so much time with him that the Cambridge dons referred to Darwin as "the man who walks with Henslow." That friendship led to one of the most famous "accidents" in history. After his exams, Darwin was planning a trip to Tenerife to study the biology of the tropics when Henslow recommended him for the position of naturalist on HMS Beagle, a ship commissioned to chart the waters along South America's coast. The "accident" here is that Darwin was not nominated because of his prowess as an established and respected naturalist. Rather he was chosen mainly for his pleasant disposition and conversational skills. One could argue that a major reason for the development of the theory of natural selection was the fact that Charles Darwin was a nice guy.

During the five-year voyage, Darwin regularly sent specimens and notes on his observations to Cambridge. His collection and meticulous documentation made such an impression on the scientific community that when he returned to England in 1836, he was already a minor celebrity. His reputation was enhanced as he traveled through scientific circles giving presentations and soliciting feedback about his collections. His travels exposed him to English fossil collections of extinct species that showed striking similarities with existing species. Also, the theory of "transmutation" (the term used at the time for the change of one species into another) was a topic of strident debate in the intellectual circles that Darwin joined. Along the way, he was impressed with Thomas Malthus' *Essay on the Principle of Population*. Within two years, he had connected the dots of these disparate observations and ideas and developed—at least in an incipient stage—his theory of natural selection.

Darwin did not "discover" evolution. Even before Darwin went to sea, scientists were publishing papers on evolution, mostly from a Lamarckian perspective. What Darwin did discover was a major mechanism (probably *the* major mechanism) for evolution—natural selection. Genetic contributions to individual differences fuel natural selection. Environmental demands steer the direction of evolution. Those organisms best adapted to the environmental contingencies reproduce more than other, less well-adapted organisms. Hence, the subsequent generation has more copies of the "best adapted" genes than their parents. Over time, a new species arises.

At the time, Darwin major occupation was his commission to write several volumes describing his voyage on the Beagle. That, along with his ill health and almost obsessional propensity to find empirical examples for every aspect of natural selection, led to a slow pace of development for his theory. It took him four years to put pen to paper (in 1842), and even that was not a formal, scientific article. Instead, it was a letter to Charles Lyell, who had become Darwin's close colleague. This letter evolved into a "sketch" and later an "essay," both unpublished but read by a few colleagues. Interestingly, almost all the feedback was negative.

It was not until 1854 that Darwin devoted full time work to his theory. By then, "transmutation" had become a popular topic of conversation for the general public. Within scientific circles, debate about transmutation became acerbic. Darwin took no part in the academic pillorying of believers in transmutation, although he did try to spark amicable debate over evolution itself, ignoring the mechanisms that drove it. Then, in 1855, Alfred Wallace published a paper on evolution.

Alfred Wallace (1823 – 1913)

An early believer of transmutation, Wallace was inspired by the accounts of travelling naturalists, including Darwin, to undertake an expedition to the Amazon, partly to explore and partly to collect species, hoping to find evidence for transmutation. Wallace was ever a target for bad luck. His return ship sank along with the majority of his collection and notes. He was rescued, returned to England, and, undaunted by his lost notes, within a year and a half published two books and several papers. While in England, he established associations with notable naturalists, among them Charles Darwin.

In 1854, he left for what is known today as Malaysia and Indonesia and within a year was developing his own version of natural selection. His 1855 paper on evolution was read by none other than Charles Lyell, who immediately brought it to Darwin's attention. Lyell urged Darwin to publish his thoughts. Darwin took that advice and started work on a book.

Three years later, Wallace refined his thoughts and sent his paper to Darwin, with whom he had established a correspondence, asking him to see if it could get published. That paper, "On the Tendency of Varieties to Depart Indefinitely From the Original Type", outlined a theory very similar to (or, as some argue, identical to) Darwin's. Always the gentleman, Darwin responded and offered to send it to any journal.

Darwin's chums, recognizing that he had devoted twenty years developing his theory and cataloging the evidence for it, arranged for Wallace and Darwin to give a joint presentation to London's Linnean Society. Wallace gleefully accepted. He lacked Darwin's eminence and was pleased to share the stage with the scholar. On July 1, 1958, Wallace presented his paper. Darwin was unable to attend because of his son's recent death, but several of his notes and letters were read.

Apathy with hints of negativity characterized the response to Wallace's paper. It was not until the publication of Darwin's *Origin of Species* a year later that his contributions were recognized.

According to Browne (2003), Darwin and Wallace met only once. Nevertheless, they became friends and enjoyed regular and stimulating correspondence, with each soliciting advice and feedback from the other. Although historians debate about differences in the two theories, Darwin himself regarded them as equivalent and considered Wallace a leading thinker on evolution. For his part, Wallace championed Darwin's *Origin* and in 1889 titled his book defending natural selection *Darwinism*.

Today, Wallace is often treated as a footnote—someone who motivated Darwin to publish his tome. That he certainly did, but he must also be recognized as a co-founder of modern evolutionary theory. The principle of natural selection should really be termed the Darwin-Wallace theory of natural selection.

Darwin Redux

In 1859, one year after Wallace's presentation, Darwin published his masterpiece, *On the Origin of Species by Means of Natural Selection, or The Preservation of Favoured Races in the Struggle for Life*, usually referred to as *On the Origin of Species* or simply *The Origin of Species*. Eagerly awaited, the first printing sold out before it was distributed to the bookstores.

Reaction was immediate, international, and intense but also mixed. Scientific reviews ranged from the negative to the positive, and even some of Darwin's close friends and scientific colleagues, including Lyell, expressed reservations. Some clergy considered the book heretical. Others adopted natural selection as a mechanism of God's will. Interestingly the debate was less over natural selection (Darwin's major contribution to science) than about evolution itself. Were species fixed and immutable or could one species diverge into one (or more) species?

Darwin was not prone to sit on his laurels. He continued publishing for the rest of his life. Two of his works are highly relevant for the social sciences. In 1871, Darwin published *The Descent of Man, and Selection in Relation to Sex*. In *Origin*, he deliberately refused to touch on human evolution. Now, he turned his sights directly on the topic, which at the time was highly debated. The book was largely a reaction to this debate. Darwin argues that many traits considered uniquely human—e.g., empathy, morality—can be seen in some animal species, albeit in different degrees. Departing from prevailing opinion of the time, he strongly defended what contemporary anthropologists called *monogenism*—that all human races were members of the same species. Darwin also argued that the differences among races are largely superficial. He also developed the concept of *sexual selection*—that species can evolve because of interspecies competition and mate preferences.

The second book, *The Expression of the Emotions in Man and Animals*, was published one year later. Here, he argued for the universality of facial expressions of mood and affect. Together with *The Descent of Man*, this work is among the first—if not the first—explorations of the field today known as *evolutionary psychology*.

An Historical Footnote: Pangenesis and Blending Inheritance

Darwin had one problem with this theory of evolution—he had no mechanism of inheritance. In 1868, he developed such a theory, terming it *pangenesis*. His concept was a modern update of Hippocrates' bricks and mortar approach. Darwin proposed that cells in the body excreted what he called *gemmules* that were then collected and concentrated in the reproductive organs. Father's gemmules and mother's gemmules then blended to form an embryo.

The problem with the theory is the blending part. Recall that genetic variation fuels natural selection. If all organisms are genetically identical for a trait, then selection will have no effect on the next generation. In childhood, we have all engaged in an "experiment" that demonstrates the effect of blending. Our parents gave us a set of watercolors. When we first opened the container we were met with great color variation—an array of bright and vivid differences in color. At some point, we started mixing blue with red and then the result of that with yellow and so on. At the end of the day, what did we have? A uniform mucky brown. The effect of blending is to reduce variation and to eventually remove it entirely.

In his review of a later edition of *Origins*, the Scotsman Fleeming Jenkin pointed this out. If inheritance blends, then after several generations natural selection would have no effect and evolution by that mechanism would be stopped in its tracks. Darwin took it as a serious challenge to his theory. To recapture variation, he proposed the inheritance of acquired characteristics.

The interesting part is that had Darwin read his mail, he would not have had to concoct an ad hoc solution to the problem. After Darwins' death, an uncut reprint of Gregor Mendel's pioneering work was found in Darwin's library (Henig, 2000) Mendel demonstrated that inheritance was discrete and particulate and did not involve blending.

Francis Galton (1822 – 1911)

Francis Galton was Darwin's second cousin and a major contributor to the social sciences and genetics. He was the first to establish a lab expressly intended to study *differential psychology*, the analysis of individual differences. He was the first to apply statistical methods to analyze human individual differences, along the way developing the concepts of regression and correlation. He was also the first to report on the phenomenon of regression toward the mean.

Stimulated by his cousin Charles, in 1965, he published the first empirical work on the genetics of individual differences in behavior, later elaborating on it in his 1869 book *Hereditary Genius*. Because of this achievement, some regard Galton as the father of behavioral genetics. There are important lessons from this book, so let us spend a moment discussing it.

This was a family study starting with men eminent in a number of different fields ranging from politics, law, science, music, the arts, clergy and even the "physically gifted" (oarsmen and wrestlers). Galton then traced their family histories and reported the percent who were also eminent or illustrious (just short of eminence). Table X.X shows his results across all groups.

Percent of illustrious or eminent men as a function of genetic relatedness.

Degree of		

Relationship	Relationship	Percent
First Degree	Fathers	31
	Brothers	27
	Sons	48
Second Degree	Grandfathers	8
	Uncles	5
	Nephews	5
	Grandsons	7
Third Degree	Great-grandfathers	1
	Great-uncles	2
	First cousin	1
	Great-nephew	1
	Great-grandson	1

Many of you examining the design and the data note that only males are included. If Galton was the first behavioral geneticist was he also the first sexist behavioral geneticist? He was, but probably no more sexist than his contemporaries. Indeed, he attributes the surplus of eminent sons to talented mothers.

A second issue is his conclusion that the familial aggregation is genetic in nature. Galton spares no words. The first sentence of the text starts with "I propose to show in this book that a man's natural abilities are derived from inheritance … ." In fact, family studies confound the effects of genetic transmission with the effects of family environment. In different words, familial resemblance can be due to: (1) shared genes; (2) shared family environments; or (3) both shared genes and shared family environment. In *Hereditary Genius* we find the first methodological mistake in behavioral genetics. To his credit, Galton later realized this and became a proponent of the use of twins to separate the effect of genes from the effect of family environment.

In 1883, Galton coined the term *eugenics* and became a strong proponent of the offering monetary incentives to talented people for marrying young and having large families. Eugenics evolved into an academic field and eventually the Galton Chair of Eugenics was established at University College in London.

Darwin's Legacy

The Darwinian-Galtonian tradition evolved into a school that often called *English biometry*. This field was characterized by mathematical and statistical explorations into inheritance and evolution. A major player was Karl Pearson who elaborated Galton's ideas on regression and correlation, (giving us the Pearson product-moment correlation), developed theories on statistical distributions, invented a chi-square test, and gave us an important formula that examined the simultaneous effects of natural selection on several traits. Pearson also established the first department of statistics.

A second noteworthy biometrician was Ronald A. Fisher. Exposed to genetics at Cambridge, Fisher came enthralled with eugenics and devoted his considerable talent in mathematics to genetic problems. In 1918, he published a classic paper (Fisher, 1918) demonstrating that Mendelian inheritance could account for the transmission of continuous traits, thus resolving a strident academic debate of the time. In that paper in a footnote on the first page, he briefly sketched the logic of the analysis of variance (ANOVA). He invented a crucial method of statistical estimation—maximum likelihood—and developed discriminant function analysis. He also did pioneering work in the fields of evolution.

If you have taken a course in statistics, you should recognize that problems in genetics sparked the development of many of the statistical tests taught in that course and used in the social sciences.

Gregor Mendel (1822 – 1884)

Gregor Mendel was an Austrian monk living in an Augustinian monastery in Brüun (or Brno) in what is now the Czech Republic but at the time called Moravia. He was fortunate in having an abbot who encouraged intellectual and research pursuits, and spent his early years mastering mathematics, physics and chemistry. Later, he became particularly interested in the study of hybrids, a "hot topic" in biology at the time.

Another historical accident: the regional bishop regarded Mendel's monastery as something of a rogue institution emphasizing scholarship over prayer. At the time, Mendel was breeding albino with pigmented mice and caging the mice in his own room. The bishop noted the strong smell and suspected that watching mice have sex was an unnecessary temptation. As one of the compromises between the bishop and the abbot, Mendel's mice had to go, leaving him free to devote more time to his plants.

Mendel later quipped, "I turned from animal breeding to plant breeding. You see, the bishop did not understand that plants also have sex" (Henig, 2000, pp 15-16).

Mendel began breeding common garden peas (*Pisum sativum*) in the mid 1850s, the same time that Darwin decided to write his book. In 1865, Mendel presented his work to the Brüun Natural History Society and published a paper ("Experiments in plant hybridization") in the Society's proceedings. The presentation and paper were largely overlooked and remained unappreciated until 1900. Why?

Mendel's presentation probably bored his audience and his paper was easily overlooked. The real importance of his research was to demonstrate the inadequacy of blending inheritance and propose a new model involving the transmission of discrete units. The headline should have been "Inheritance does not blend. It is particulate and discrete!"

Blending inheritance implies that if mother is a strawberry milkshake and father a vanilla one, then an offspring will be half strawberry and half vanilla—an intermediate shade of pink—and transmit this intermediate pinkness to the next generation. Mendel implies that mother transmits a strawberry colored marble and father contributes a vanilla colored one. The offspring transmits one of these two marbles—totally intact—to the next generation.

Instead of emphasizing the paradigm shift about genetic transmission, Mendel wrote about his laws and how his data agree with these principles. In short, Mendel may have lost sight of the forest for the trees.

A second issue is the context in which Mendel worked. Compare Mendel and Darwin. Darwin was deeply tied into the most prestigious body of scientists in the world—the Royal Society of London. Most of these members were acquainted with Darwin's work before it was published, so they, along with all those within whom they communicated, chomped at the bit to obtain his book. There is no surprise here that it was a bestseller.

How many academic libraries subscribed to the *Proceedings of the Natural History Society of Brüun*? Mendel also had about 40 reprints of his work which he sent to biologists throughout Europe, one of them being Darwin. How many of these recipients opened the envelope, looked at the title and author, noted that the article was published in the *Proceedings of the Natural History Society of Brüun*, and said, "WOW! This must be important!" Many, like Darwin, probably looked at the return address or the title of the folio and then threw it into a pile with good intentions of getting to it "when I have time" but, realistically, he never had the time.

This is not a universal view. Other historians of science attribute the inattention to Mendel as due to the novelty of his approach. Vorzimmer (1968. P 82) writes "That recognition and appreciation of his discoveries was delayed for thirty-five years was not so much a problem of promulgation within the scientific community as it was an incapacity for members of that community to comprehend what he was saying because of the novelty of the method and presentation which he had employed."

In 1868, three years after he published his seminal work, Mendel became abbot of the monastery. Despite administrative duties, he carried on with his research, but never presented his results or wrote them up. After he died in 1884, the monastery burned all of his papers. Mendel may have uncovered many other genetic principles, but we will never know.

Early Cell Biology

Unlike Darwin and Mendel, no single individual can be credited with the development of early cell biology and its contributions to genetics. Like many scientific breakthroughs, early cell biology began with the development of a measurement instrument, the microscope, that permitted observation of micro phenomena that could not be visually resolved using the magnifying lens, a tool available since Roman times.

In 1665, the Englishman Robert Hooke used the term "cell" to describe the compartments of cork and other plants because they reminded him of *cellula*, the small single-room dwellings of monks. At the same time, Antony van Leewenhoek, reported on single cell organisms. Curiously, medical science of that time regarded the microscope with deep suspicion and sometimes outright hostility, leading to a dearth of observations in the ensuing 18th century.

Discoveries in early cell biology went hand-in-hand with the slow perfection of the light microscope in the 1800s. The role of cells was a hotly debated topic until the development (and, later, gradual acceptance) of "cell theory" by German botanist Mathias Schleiden and German physiologist Theodor Schwann in 1838-1839. This theory held that all life is composed of cells and that the only origin of cells was from other cells. Previously, biologists believed that cells arose spontaneously and de novo from their parts.

A major advance was the detection of chromosomes and the unraveling of cell division. These "colored bodies" (from the Greek χρομοσ, meaning color, and σομα, meaning body) were first reported in the early 1840s by Karl Wilhelm von Nägeli in plants and Edouard Van Beneden in animals, although the actual word "chromosome" was coined several decades later. Painstaking work by Walther Flemming, Anton Schneider, Eduard Strasburger and others in the late 1879s and 1880s led to observations that are almost intuitively evident to us today—(1) chromosomes were duplicated during cell division; (2) each daughter cell received the same number of chromosomes; (3) gametes contained half the number of chromosomes as an adult cell; (4) fertilization involved the fusion of the nuclei of sperm and egg; (5) the resulting zygote had the full chromosome complement.

It was quite natural then to speculate—as Oscar Hertwig did in 1876 and Wilhelm Roux did in 1883—that chromosomes were involved in the transmission of hereditary information. August Weissmann soon developed "germ plasm" theory—germ cells transmit the hereditary information through the chromosomes while somatic cells underlie bodily functions.

Now comes one of the most interesting epochs in the history of science. For the better part of 20 years, the cytologists could actually see the genetic material. Yet they still could not deduce the basic laws of segregation and independent assortment! Mendel, who to the best of our knowledge never saw a chromosome, was able to work these out because the implications of a mathematical model—the expansion of a binomial—so nicely fitted his data. The icing on this cake of irony comes from correspondence between von Nägeli (one of those who first described chromosomes) and Mendel. Mendel sent von Nägeli a reprint, a long letter of explanation, and even packets of his seeds with notes on how to breed them. Still von Nägeli was unable to (or, perhaps disinclined to) take the results seriously.

Sturtevant (1965) obliquely faults the great attention given to Weissmann's theory for the inability of the cytologists to grasp the principles of segregation and independent assortment. In trying to explain why an organism can resemble several different ancestors, Weissmann postulated that each chromosome carried all the hereditary information. Because Mendel's peas had 14 chromosomes, they carried 14 copies of an hereditary factor, not two as Mendel held. Sturtevant recounts a little-known German biologist, Haacke, whose paper, published in a very influential journal, came very close to independently formulating Mendel's laws of segregation and independent assortment for coat color (albino versus pigmented) and waltzing (waltzing versus nonwaltzing) in mice. Haacke, however, "was unaware of the 1:1 segregation in heterozygotes and, in fact, apparently visualized various kinds of heterozygotes, at least for color" (Sturvevant, 1965, p. 23).

Whatever the causes of this failure, it took a completely different line of research to unite the observations about chromosomes with Mendel's laws.

Birth of Genetics as a Unified Field

In 1900, Mendel's results were independently replicated by three people: the Dutch botanist Hugo de Vries, the Austrian Erich von Tschermak (whose grandfather, ironically, was Mendel's botany professor), and the German Carl Correns (ironically again, the student of Nägeli, one of the discoverers of chromosomes and Mendel's correspondent). It is often stated that they "rediscovered" Mendel, but that is misnomer. What they did is to expose modern science to Mendel. Mendel's work had been sporadically cited between its date of publication and 1900, but nobody seriously considered its implications. It is more correct to say that 1900 was the year in which Mendel was finally appreciated.

Around the same time, the English biologist William Bateson read Mendel and became an enthusiastic advocate. He translated Mendel into English and dubbed the new field "genetics," a term already in use but in the vague sense as something pertaining to origins. He also introduced the terms *allele*, *zygote*, *heterozygote*, and *homozygote*. In 1904, he along with Reginald Punnett (who gave us the eponymous square) described genetic linkage, but got the mechanism wrong. He did not believe that chromosomes had anything to do with Mendelian inheritance.

The work in Thomas Hunt Morgan's lab from 1910 through 1914 firmly united the Mendelian and Early Cell Biology lines of inquiry. Using fruit flies (*Drosophila*), Morgan and his collaborators proposed that genes[2] were linearly arranged on the chromosome, giving us the "beads on a string" model of the genome. They also demonstrated sex linkage and identified the sex chromosomes. In Morgan's lab, Alfred Sturtevant produced the first genetic map. Because of Morgan's contributions, the unit of distance along chromosomes was called a Morgan and one hundredth of that unit a centiMorgan (cM).

Things did not go so smoothly with the Darwinian trend. Two heirs of the Darwinian-Galtonian trend, Karl Pearson and his colleague Raphael Weldon, held that Mendel's theory is fine for qualitative/discrete traits like yellow versus green pea seed color but could not account for continuous variation. Continuous variation involved traits like height—we all have height but we all possess different amounts of it. They suspected that there were other mechanisms involved in hereditary transmission besides Mendel's units. The Mendelists, especially the aforementioned William Bateson, vigorously disagreed, some going to far as to claim that obvious

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[2] The word *gene* along with the terms *genotype* and *phenotype* were coined in by the Danish scientist Wilhelm Johannsen in 1909. Mendel referred to genes as *hereditary factors*.

continuous traits like bristle number on a fly actually fell into two categories, few and many.

The situation was finally resolved in 1918 when Ronald Fisher published a classic paper, *The correlation between relatives in the supposition of Mendelian inheritance*. Here, Fisher demonstrated that a Mendelian inheritance could account for continuous variation when a number of genes contributed to a trait and the effect of each individual gene was small.

Hence, one can make an argument that genetics as a unified field was "born" in 1918, the year in which the first World War ended.

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