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Principles of Evolutionary Medicine

Second Edition

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TATJANA BUKLIJAS, FELICIA LOW, AND MARK HANSON

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Preface to the Second Edition

Since the first edition of *Principles of Evolutionary Medicine* was published in 2009, the field has grown considerably. An international society and new journals have been established, there has been a US taskforce on the teaching of evolutionary medicine, and many more medical, anthropology, and public health programs or courses on evolutionary medicine have been introduced. Research in the field has expanded greatly. This growing activity reflects a growing understanding of the value of applying an evolutionary approach to understanding human ecology, health, and disease. This edition reflects both this growth in the field and the continuing need for a summary of evolutionary principles appropriate to the distinct needs of health practitioners, educators, social scientists, and others interested in the human condition. With this in mind, this edition includes considerable revisions to each chapter.

The general structure of the book remains unchanged, with the first six chapters providing a summary of the evolutionary theory relevant to understanding human health and disease. The second part of the book describes how evolutionary principles can be used to understand behavior, metabolism, immunity, and reproduction, and, in an entirely new chapter, cancer. These two sections are bridged by a new chapter that details pathways by which evolutionary processes affect disease risk and symptoms, and how hypotheses in evolutionary medicine can be tested. The final two chapters are considerably expanded; they illustrate the application of evolutionary biology to medicine and public health, and consider the ethical and societal issues arising from an evolutionary perspective. A number of new clinical examples and historical illustrations are included.

With this expansion we have added two new authors who have been active in the field for many years: Dr. Tatjana Buklijas, who has a particular focus on historical and clinical perspectives, and Dr. Felicia Low, whose research has focused on molecular and developmental evolutionary biology. We thank the many readers who sent suggestions after the first edition, and the many colleagues who have helped develop the field and whose research is reflected in many places throughout this volume.

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August 2015

Preface to the First Edition

Evolutionary science can be viewed as the fundamental "organizing principle" of all biology. The biological and biomedical sciences can only be fully integrated with the aid of an evolutionary toolkit. Together with discovery of the nature of particulate inheritance (the gene) and the sciences of molecular and developmental biology, evolutionary biology provides the basis of our understanding both of the function of an organism and of its relationship with its physical, social, and biotic environment. Thus an effective comprehension of human biology, health, and disease requires knowledge of evolutionary principles and an appreciation of how they have shaped biological and biomedical processes at both an individual and a population level. Although this imperative is well appreciated in the other biological sciences, medicine has been slow to recognize evolutionary biology as a fundamental and underpinning science. However, advances in areas such as bacterial evolution, genomics, and epigenomics mean that evolutionary thinking has much to add to modern medicine.

There has been a growing list of books and edited volumes devoted to this topic following the publication in 1994 of the groundbreaking book by Randolph Nesse and George Williams entitled *Why We Get Sick: The New Science of Darwinian Medicine*. But it seemed to the authors of the present book that there was no integrated or comprehensive textbook which set out the basic principles of evolutionary biology for the medical reader and which focused on how medicine and public health can utilize these principles. Most members of the health professions have had little or no formal exposure to such principles—this volume aims to remedy that deficiency. We hope that it provides just such a toolkit which doctors, medical students, trainees and practitioners in allied health professions, biomedical scientists, and anthropologists interested in human health need in order to utilize evolutionary biology to gain a more complete understanding of the processes that shape the human condition.

Evolutionary biology emerged in the nineteenth century, although its acceptance and integration into modern biology was not without controversy and took many decades. The concept that species were not immutable emerged in Europe as a significant school of thought at the end of the eighteenth century, but it was not until Charles Darwin and Alfred Russell Wallace independently described natural selection in 1858, and thus provided an explanation of how species might change over time and how new species might evolve, that the field of evolutionary science was firmly established. But this science could not progress much further until the nature of inheritance was understood. Gregor Mendel had recognized the particulate nature of inheritance in the late nineteenth century, but the significance of his discovery was largely overlooked. It was not until his findings were rediscovered, the role of the nucleus in inheritance was determined, and chromosomal DNA was identified as the chemical basis of the gene, that there could be a fuller understanding of how evolutionary processes operate. It was the elucidation of the structure of DNA in 1953 which finally allowed evolutionary processes to be understood at a biochemical level. The subsequent explosion of knowledge in molecular and developmental biology has been informed by, and has also informed, progress in evolutionary science.

There are many dimensions to evolutionary biology and it has a number of sub-disciplines. It has to address many questions: how species have formed; how lineages respond to and adapt to

their environment and thus evolve to appear to be "designed" to match their environment; how environmental influences induce the development of a range of phenotypes from a single genotype; why different species even within the same taxa have very different physical, reproductive, and social characteristics; why species have particular life histories; and many more such issues. The answers to these questions inform our understanding of the origin of the particular characteristics of a species and the range of phenotypic variation seen between individual members of that species—in particular in their anatomy and their physiology, the characteristics of their life course, and the manner in which they respond to environmental challenge and opportunity. Thus evolutionary biology is very much concerned with the basis and the significance of individual variation.

Humans, like all other living organisms, have individual characteristics, including the fact that we do not all suffer from the same diseases. This variation is defined in part by our evolutionary history and, conversely, without variation there could be no evolution. Indeed, understanding the significance of individual variation was one of Darwin's great insights. Thus to understand human biology and medicine fully we must have an understanding of evolutionary principles and how they apply to our species.

Much of medicine is focused on understanding disease causation, for this informs how to prevent disease and how to intervene when it does occur. Medical thinking has a tendency to dichotomize into normal or healthy and abnormal or pathological. But, as this book will make clear, such assessments are contextual—what is a successful adaptation in one context, and so normal under those conditions, may be highly abnormal in another.

The definition of what is health and what is disease when viewed through an evolutionary lens can therefore lead to helpful new perspectives on a potential patient. Variation is a fundamental attribute of biology, and it determines individual risk in response to an environmental challenge—whether this is a parasite like malaria, an environmental toxin like nicotine, or a lifestyle of excessive calorie intake, to name just a few examples. This textbook explains how individual risk is determined by our evolutionary history and how that history has given us a capacity to cope with many challenges but has also placed constraints on that capacity. The consequences of encountering challenges which exceed our adaptive capacity become manifest as disease.

Most medical training focuses on understanding the immediate pathways leading to disease—these are the so-called proximate causes. From this perspective, hypertension arises because of changes in peripheral vascular resistance or because of changes in the renin–angiotensin system secondary to renal disease; sickle cell anemia arises because of a mutation in the hemoglobin gene; appendicitis arises because of inflammation in a gastrointestinal diverticulum; and cerebral palsy can arise because of asphyxia at birth during an obstructed labor. It is this understanding of proximate cause that gives rise to most medical therapies: serotonin reuptake inhibitors to treat depression, antibiotics to treat bacterial pneumonia, angioplasty to improve blood flow through occluded coronary arteries, or cesarean section. But as we shall see, in each case there is a broader dimension.

The proximate explanations reveal *how* certain symptoms appear and provide the basis of a logical approach to intervention, but there is a further level of enquiry which is valuable. This concerns questions about *why* certain symptoms appear, *why* some individuals are at greater risk, *why* we cannot accommodate easily to certain situations healthily, *why* we have an appendix which gets inflamed, or *why* the day you are born was the most dangerous day of your life so far. This evolutionary level of interrogation seeks to understand the *ultimate* causes of health and disease. Through it, we discover that we get appendicitis because our evolutionary ancestors were leaf-eaters and had a large cecum to help digest cellulose-based foods; we now no longer need this large gastrointestinal organ, but the appendix remains as an evolutionary relic which can become inflamed. This ultimate perspective provides health professionals with better insights into their patient and must improve their management of the case. In many instances an evolutionary perspective leads to a better understanding of which approaches to prevention are more promising and why certain therapies are more likely to work.

Humans now live in very complex environments which are very different from those in which most of our ancestors lived and evolved. The consequent mismatches can challenge our health. We can never escape our biology or our biological past. Evolutionary processes operate to promote passage of genetic information from one generation to the next and evolutionary success is about successful passage of genes within a lineage to future generations. Thus the processes of evolution are focused on what drives reproductive success within a lineage, a concept termed "fitness." But fitness does not depend necessarily on longevity or health. It involves "trade-offs" which ensure reproductive success even if they incur other costs such as a shorter life. Evolutionary biology is a science that considers how an organism trades off one component of its biology against others to optimize its fitness. Because many modern humans live long lives and medicine is increasingly focused on promoting the quality of life, health professionals cannot ignore the constraints imposed by such evolutionary considerations.

Evolutionary medicine, therefore, is a growing and central discipline that applies evolutionary knowledge to the understanding of human biology, both normal and abnormal. It is an essential science, necessary for a holistic perception of how health and disease emerge. It has application in both individual healthcare and in public health. It adds much to understanding other basic disciplines of medicine, including physiology, anatomy, biochemistry, pathology, molecular biology, population health, and behavioral sciences. Indeed, a complete understanding of these more immediate disciplines is not possible without an understanding of evolutionary biology.

Evolutionary biology is a vibrant, if broad, domain of biomedical science. Some aspects of evolutionary knowledge are not essential or central to understanding the core principles of evolutionary medicine. For example, the subject of macroevolution—the process underpinning speciation and biodiversity—is not central to a medical perspective. Much of evolutionary biology involves quantitative approaches, for example for defining aspects of selection or genetic drift; again these are not essential for the medical reader. Many of the details of the dynamics of selective processes are technical and are not required in applying evolutionary principles in human medicine. We have therefore omitted them from this book, which is intended for the clinician, whether in training or in practice. Most textbooks in evolutionary biology focus on other species and only minimally refer to humans. In contrast, unless there is an essential comparative point to be made, we have tried to use only examples from human biology to illustrate key evolutionary principles.

The book is presented in three parts. In the first we detail the basic principles of evolutionary biology: what biological evolution is, how it operates through the processes of selection, how evolution is reflected in our genome, the relationship between genotype and phenotype, how developmental and evolutionary processes interact, what determines the characteristics of the human life history, and how the evolution of our species has led to features which now become manifest in the doctor's office or on the hospital ward. An important evolved characteristic of our species is that we live in groups and our social environment and our capacity to develop and apply technology are essential components of our evolution. So it is not possible to discuss biological evolution without consideration of our cultural evolution, and this we do in the first part of the book.

In the second part of the book we describe how these principles can be applied to an understanding of human disease, using four illustrative axes: human reproduction; nutrition and metabolism; biological defense systems; and human behavior. We have intentionally restricted the discussion in this way so that these systems can be elucidated in sufficient detail to highlight how evolutionary approaches to the human condition can be applied in practice. This is not intended to be a comprehensive medical textbook—there are plenty of those—but is intended to give the reader a new understanding which can be applied generally in clinical medicine and which informs other domains of medical science.

In the third part of the book, we synthesize these various strands to provide a systematic evolutionary framework for understanding human health and disease. We propose that each person

presenting to a physician has three relevant histories: the history of the complaint itself; the developmental history of that individual; and his or her evolutionary history. All three histories are essential for a comprehensive understanding of the way an individual has responded to his or her environment. We detail the pathways by which individual risk can be influenced by evolutionary processes, pathways which should always be part of a health professional's reflection on the situation of the patient before him or her.

Evolutionary biology has an intimate relationship with the ecological sciences, and humans must also be understood in their ecological context. Consideration of how our lives progress in any environment, including our social environment, is greatly enhanced by understanding evolutionary biology. In turn, such understanding can contribute greatly to the development of effective public health strategies.

Evolutionary biology as a science has always had, and continues to have, an awkward and complex relationship with broader intellectual and philosophical concerns. For example, it is seen by some to be in conflict with their specific belief systems. Darwin's propositions when first put forward were clearly at odds with the prevailing concepts of natural theology and of an active creation, the dominant institutional explanations of the natural world in early nineteenth-century Britain. Yet today the majority of scientists find no need to see evolutionary biology as in conflict with their personal beliefs, and most religious authorities find no conflict between their theology and the science of evolution. Like modern astronomy, evolutionary science is a robust and mature science and, without it, human biology cannot be fully appreciated. The biology and the conceptual frameworks of evolutionary science are incontrovertible—but what they *mean* to individuals or particular faith groups is a quite distinct and in many ways unrelated issue. Many patients, and indeed many doctors, have a devout faith and this book does not set out to challenge that faith. Rather, it wishes to impart to those who have a responsibility for medical care and public health the principles of a biological science which is necessary for integrating the other basic and applied medical sciences. Without it, medicine cannot progress, any more than it could until the inaccurate anatomical teaching of Galen in the second century had been superseded.

Evolutionary concepts have been wrongly and inappropriately applied beyond biology, particularly in political contexts. In these circumstances a metaphorical understanding (or more often a misunderstanding) of evolutionary science has been applied in an inappropriate context. Anarchists on one hand and fascists on the other co-opted evolutionary thought to their political ideology. Because such abuses still occur today, health professionals will encounter them. In the final chapter of this book we will briefly discuss these issues.

Each of the authors has a long history of research in aspects of evolutionary biology and medicine. But none of us is an expert in all its aspects—it is a large field. We are grateful to the many colleagues who directly or indirectly have contributed to our understanding and thus to this volume. One person in particular, Dr. Chris Kuzawa (Northwestern University, Chicago), was critical to the book. Chris made major contributions to Chapters 5 [Life histories] and 8 [Nutrition] in the early stages. Unfortunately other commitments prevented him from playing the larger role which we, and he, had planned. We must also acknowledge colleagues who have read chapters, offered critiques and suggestions, and elucidated matters beyond our expertise. They include Professor Sir Patrick Bateson FRS (Cambridge), Professor Peter Ellison (Harvard), Professor Eva Jablonka (Tel Aviv), Professor Hamish Spencer (Dunedin), Professor Randolph Nesse (Michigan), Professor Paul Rainey (Massey), Professor Russell Gray (Auckland), Professor Wayne Cutfield (Auckland), Professor Murray Mitchell (Auckland), and Professor Des Gorman (Auckland). We thank Dr. Cinda Cupido (Auckland), Dr. Tatjana Buklijas (Auckland), Dr. Felicia Low (Auckland), and Ms. Amanda Calhoun (Yale) for assistance with research.

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PART 1

Fundamentals of Evolutionary Biology

CHAPTER 1

Introduction

Life expectancy in high-income societies has risen dramatically over the past 250 years, and more recently in many low- and middle-income countries, largely as a result of major technological changes, including improvements in public health and in the understanding of the biology of disease, and through concurrent societal changes which have brought a greater emphasis on the value of life. For example, the average life expectancy at birth in pre-revolutionary France was about 30 years—not so different from that of prehistoric (and in particular Paleolithic; Table 1.1) humans—yet now it is over 80 years.

Advances in nutrition, infection control and treatment, trauma care, and maternity and neonatal services have addressed many of the extrinsic causes of death that led to the short lifespan of our Paleolithic forebears. These causes were major contributors to what in our not-so-distant ancestors we would now call "premature" death (Figure 1.1). But as we live for longer, diseases which were previously unimportant become more so; many, such as cardiovascular disease, appear in middle age—by which time the majority of our forebears were already dead. Other morbidities, such as mental disorders, have become more dominant as a result of the pressures of living in the much more complex societies that urbanization and changes in modes of communication have brought.

In addition, our ambitions as organisms have changed: advances in medical care, improved access to knowledge, and individual empowerment have brought a changed individual and societal focus on longevity and quality of life. Modern medicine is increasingly faced with patients' expectations of being able to live well into their ninth decade and to expect highly interventional medicine, if needed, to maintain quality of life throughout. Increasingly we face disabilities that do not arise from extrinsic causes but instead result from intrinsic ageing of the body's cells, as reflected in degenerative diseases. Thus, while medicine is now dominated by a population-wide expectation of good health into old age this is, to a large extent, in conflict with the evolutionary processes that have molded our species. This textbook is about the principles underlying those processes and how many disease states can be understood in terms of this conflict. While health and longevity are the primary concern of our patients, neither of these, with caveats to be discussed later, are the primary drivers of evolutionary processes.

Briefly stated, evolution of a species (*macroevolution*) and evolutionary change within a species (*microevolution*) operate to produce an organism that is matched or adapted to its environment. That match is not primarily defined by a particularly long or comfortable life for an individual, but rather by the successful passage of that individual's genes to successive generations. Indeed it is a truism that all organisms on the planet today are here because their ancestors reproduced successfully. Lineages that did not do so are now extinct. This is the core concept of *fitness*, which is fundamental to evolutionary biology.

Evolution is the process whereby a population changes over time to optimize the fitness of its individual members within a particular environment. Thus *Homo sapiens* largely evolved by adaptations that maximized its fitness in the environments of eastern Africa, the region in which our species first emerged. Biological fitness for a human was—and

Table 1.1 Approximate human and geological timescales expressed in thousands of years before present (kya). Definitions for human timescales can vary depending on region

Human timescale			Geological epoch
Period		**kya**	
Paleolithic	Lower	2500–100/200	Pliocene (5300–1800 kya) and Pleistocene (1800–10 kya)
	Middle	300–30	
	Upper	50–10	
Mesolithic		10–6	Holocene (10 kya–present)
Neolithic		10–4	
Bronze Age		5.3–2.4	
Iron Age		3.3–1.6	

still is—achieved by a strategy of supporting a small number of progeny to grow successfully to adulthood, reproduce, and live long enough to support their own offspring in becoming reproductively competent. Evolutionary pressures on our lineage operated to ensure this; there were few, if any, drivers of health beyond the reproductive period in the life course, or generally of longevity beyond the period necessary to support offspring into adulthood.

The term *environment* occurs frequently throughout this book, and a definition here is thus appropriate. Evolutionary and developmental biologists use the term in a wider sense than in common popular usage, where it relates to issues such as global warming or threatened biodiversity. We define the environment of an organism as the sum of all the external conditions and stimuli that it experiences, including climate, nutrient supply, social structure resulting from cooperation with or competition from other members of its own species, symbiotic relationships with other species, particularly microbiota, and threats from other species in the form of predation, parasitism, or infection. If the environment changes for the worse, the lineage may be able to cope, but at a cost; or it may go extinct; or individuals may adapt to their new environment or, if mobile, migrate to a more suitable environment. Some species can ensure relative constancy of their environment by constructing it themselves, a process called *niche construction*—examples include the temperature-controlling mounds of termites or the dams constructed by beavers. The human species is a niche constructor *par excellence* through its use of technologies ranging from fire and clothing to urban design and, as described in numerous places in this book, this capability has both positive and negative consequences for our health.

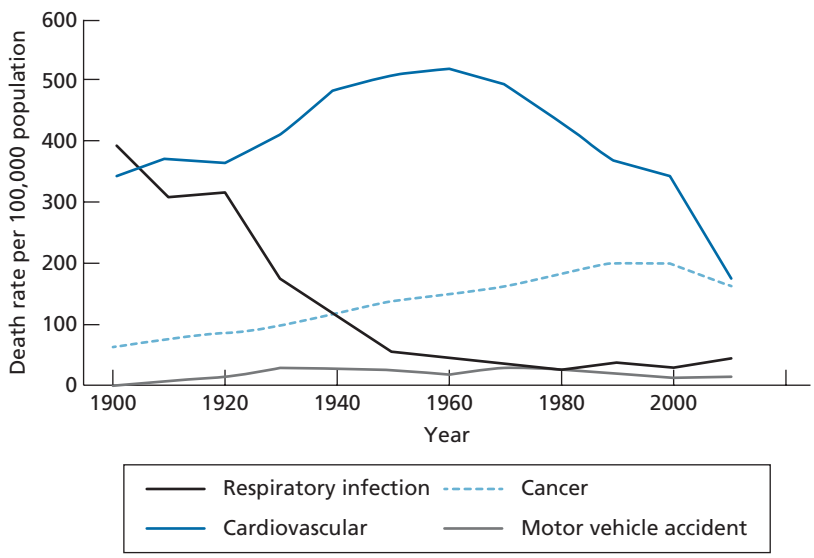

Figure 1.1 Causes of death in the United States have changed in the twentieth century. Data plotted from Hoyert (2012).

1.1 What is Disease?

Whereas modern medicine focuses on the concept of health, evolutionary biology focuses on the determinants of optimal fitness. Importantly, fitness can only be defined in relationship to a particular environment: for example, polar bears have evolved with a physiology suited to the Arctic but not appropriate for a temperate world. This conceptual difference between health and fitness is critical for understanding the human condition and in defining normality and the disease process.

Consider a young man who presents with abdominal pain, bloating, and diarrhoea. He is a recent immigrant from Southeast Asia with no history of these symptoms. He reports that yesterday he shared lunch with work colleagues during which he consumed a couple of glasses of milk and had a plate of ice cream. This was unusual for him, but his colleagues, who are of European ethnicity, were unaffected. Why is this young man made ill by ingesting a normal foodstuff?

Cows' milk, like the milk of most mammals, is rich in the disaccharide lactose. The sugar transporters in the human gastrointestinal tract cannot move intact lactose across the gut wall, but babies can digest lactose because of the presence of the enzyme lactase, which breaks down lactose into easily absorbable glucose and galactose. In most humans, lactase expression in the intestine disappears after weaning, but human populations with a history of pastoralism—mostly people of northern European or East African origin—have a high prevalence of mutations in the promoter region of the lactase gene, causing the enzyme to be expressed within the intestinal tract throughout life. This enables them to consume milk throughout their lives.

But this young man of Asian origin does not carry the persistence mutation and therefore does not express lactase in his duodenum. The discomfort that he experiences after drinking milk is caused by the osmotic load of the unabsorbed lactose, and by the gas produced by fermentation of the sugar by intestinal bacteria. Regardless of the molecular details, his symptoms arise from a *mismatch* between his genetic origin—from a population where, historically, consumption of milk after weaning was unknown and lactase persistence is rare—and his current environment where milk is easily available and widely consumed.

His friends could drink milk freely because their forebears inherited the lactase persistence allele which was selected for in populations that herded cows. Because the ability to absorb milk had a nutritional advantage, and allowed individuals to grow, survive, and reproduce more successfully, the mutant form had become the most common allele in their forebears. This example is central to the purpose of this book, because Western medical textbooks often define the inability to absorb lactose as a metabolic *disorder*—adult hypolactasia—but from an evolutionary point of view this man's inability to digest lactose is *normal* and is shared with 70% of the world's population. It has only become manifest in an environment distinct from that to which he is adapted.

Parenthetically, very rarely there are mutations in the expressed sequence of the lactase gene which means that even the infant cannot digest its mother's milk. Such congenital hypolactasia is a severe disorder that requires urgent attention and lactose-free nutritional support. Congenital hypolactasia would have been fatal in the past when milk, human or otherwise, was the sole source of infant nutrition, and thus remains a rare autosomally recessive condition.

There are several lessons to be learned here. The first is that our understanding of an individual's health status may depend on our knowledge of their evolutionary origin and how that interacts with the place where they now live. This concept of an organism *matched* or *mismatched* with its environment is fundamental to both evolutionary biology and evolutionary medicine, where mismatch—that is, failure to adapt because of temporal or structural constraints—may lead to pathology.

The second lesson from this case is broader: it is not always easy to define disease. Disease may be caused by an external agent such as trauma or infection, but it can also arise from a mismatch between the physiology of an individual and the environment in which they live. The physiology of an individual is influenced by their evolutionary history. Thus can we really say that the majority of humans have a disease because they do not carry a single nucleotide polymorphism which emerged in a subpopulation

and that causes lactase to persist into adulthood—a deficiency that is of no consequence for their health or fitness in the context of an environment free from cows' milk? Rather, should we label the species-atypical state of lactase persistence in people of northern European origin as the *abnormal* condition, and then reflect on the context-sensitive dichotomy between abnormality and ill-health?

The third lesson relates to the impact of novel environments on human health, and how the capacity to cope with a range of environmental exposures is in turn determined in large part by our evolutionary history. Exposure to milk after infancy represents a novel environment for people of Asian lineage and thus they have not evolved the capacity to cope with it (Box 1.1).

Box 1.1 The Genetics of Drinking Milk

For most adults of northern European or East African origin, milk is a normal part of the diet. But for the majority of the world's population, drinking milk would be the precursor to some unpleasant gastrointestinal symptoms. The reason for this is that most adult humans cannot digest the disaccharide lactose, which is a major constituent of milk. The World Health Organization classifies such "lactose intolerance" as a metabolic disorder, although in fact this trait represents the normal and ancestral human condition.

All young mammals rely on their mother's milk, which is high in the disaccharide lactose, for early nutrition. They can tolerate the lactose because their small intestine contains the enzyme lactase, which breaks down lactose into the two easily absorbed sugars glucose and galactose. But after weaning, production of the enzyme is largely switched off: most animals will never encounter large amounts of lactose again, so why waste resources synthesizing the enzyme? In most human populations, lactase is lost between the ages of 2 and 5 years. Without lactase in the intestine, lactose in the diet cannot be absorbed and causes gastrointestinal upset, both because of its osmotic activity, causing water to be drawn into the gut, and because intestinal bacteria ferment the sugar, leading to gas production, bloating, and cramps.

Yet only a minority of the world's population continues to express lactase and is able to drink fresh milk in adulthood—that is, they show "lactase persistence." This ability is genetically transmitted as a dominant trait, and in general lactase persistence in a population correlates with that population's history of domestication of cattle. Although milk can be used by people who lack the enzyme—the lactose content of milk can be decreased by processes that encourage the growth of lactose-hungry micro-organisms such as by allowing it to sour or by making cheese—individuals who can digest fresh milk benefit from the additional energy obtained from the lactose. Thus, in the absence of major costs of maintaining expression of lactase it is easy to see how strong selection pressure for lactase persistence would have favored the retention of this capacity into adulthood in cultures that domesticated cattle (Figure 1.2).

The genetic basis for lactase persistence in populations of northern European origin has been traced to a single nucleotide polymorphism, C/T(–13910), in a regulatory element upstream of the lactase gene, with the T allele completely associating with lactase persistence (Figure 1.2). Estimates from modern populations for the age of this allele center on about 10,500 years before present, roughly in line with estimates of the introduction of domestic cattle to Europe some 8000–9000 years before present. Furthermore, there is evidence from Neolithic and Mesolithic remains that the allele was not widespread in Europe before that time, suggesting that selection for the allele occurred after the introduction of dairying rather than supporting the competing hypothesis that dairying was only adopted in populations that already carried high levels of the allele.

Europeans are by no means the world's only cattle herders, and there are pastoralist populations in East Africa who also show lactase persistence (Tishkoff et al. 2007). Those populations do not carry the C/T(–13910) allele, but instead carry several other genetic changes in the same regulatory region upstream of the lactase gene, of which G/C(–14010) is the most common and the most tightly linked to lactase persistence. That allele appears to have spread to its present high frequency in Kenyan and Tanzanian populations within the past 3000–7000 years, one of the strongest examples of recent positive selection in the human genome. The later appearance of the G/C(–14010) allele in East Africa compared with the C/T(–13910) allele in Europeans is consistent with archeological evidence dating the spread of cattle domestication into those areas. Yet another lactase-persistence allele appears to have arisen in Arab populations, possibly associated with consumption of camels' milk (Enattah et al. 2008). These independent origins of lactase persistence are examples of evolutionary convergence, wherein natural selection arrives at a similar functional trait in different populations owing to similar selection pressures.

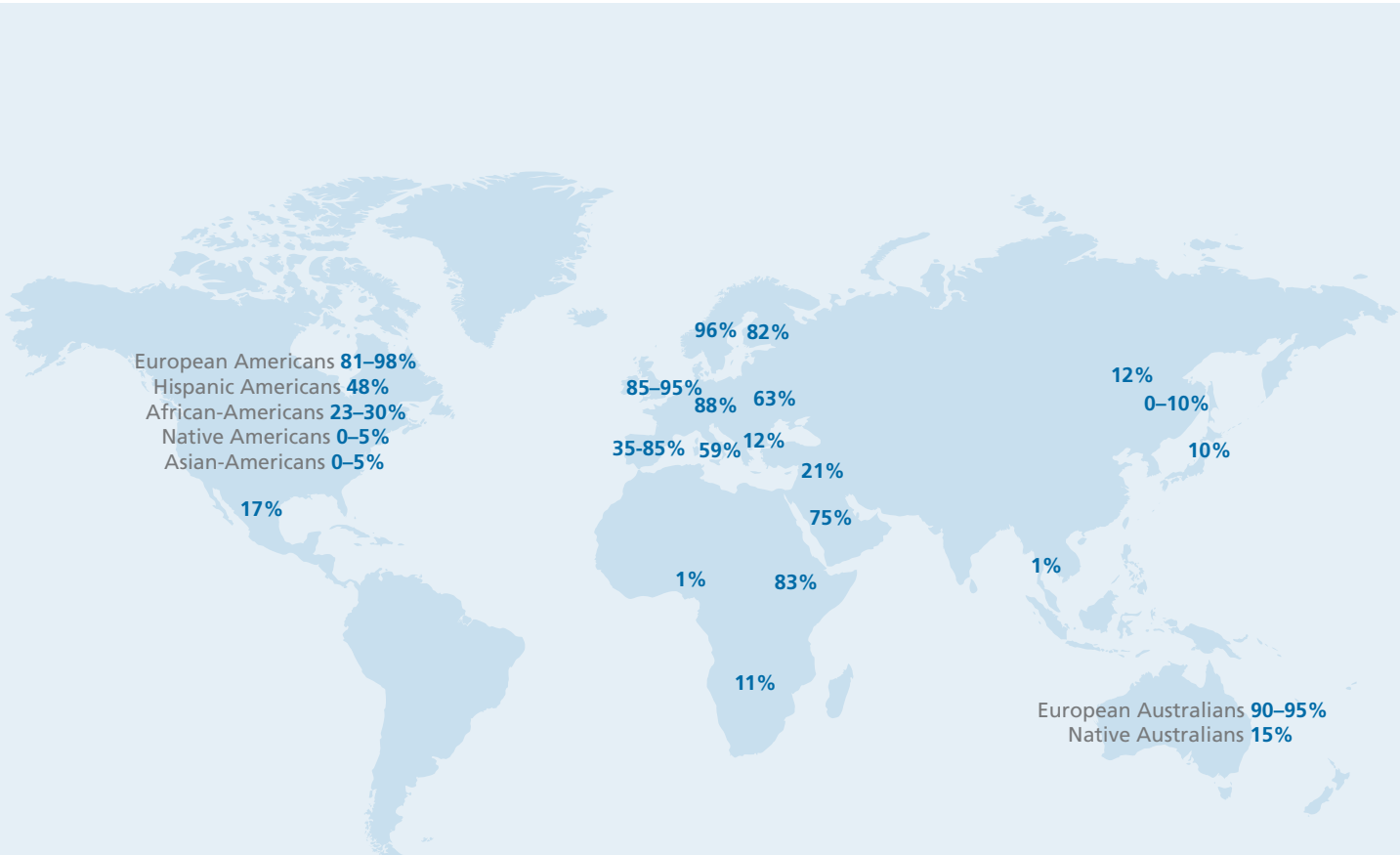

Figure 1.2 Worldwide distribution of lactase persistence.

Physiological systems can generally maintain homeostasis in the presence of a degree of environmental variation, but there are limits to that capacity. When those limits are exceeded, disease can occur. The range of environments to which a lineage has been exposed in its evolutionary history will influence that range of adaptability, and human health can be compromised by living in marginal environments beyond our homeostatic capacity. For example, humans cannot live in an iodine-deficient region because of the importance of iodine for metabolism and brain growth. The Sherpa population of the Himalayan foothills lives in a permanent state of iodine insufficiency, and this is reflected in both developmental disruption (impaired cognition because of poor brain growth) and compensatory plasticity in the form of goiter, in which the thyroid gland is enlarged in an attempt to maintain adequate production of thyroid hormone.

The fourth lesson is that the environments inhabited by humans are not constant, and much of this environmental change comes from the activities of humans themselves. The young man's discomfort after drinking milk can be linked to two environmental changes caused by human activity. The first is the historical domestication of cattle and the concomitant selective pressure for lactase persistence, together resulting in widespread use of cows' milk as a component of the adult diet of certain populations. The second is the recent social and technological changes that have encouraged large-scale migration and mixing of individuals from different cultures and evolutionary backgrounds.

Another change in the social environment, discussed in more detail in Chapter 11, is the increasing size of social networks. In Paleolithic times it is thought that an individual would only have interacted with about 150 other humans over his or her lifetime, as our ancestors lived in small, isolated social groups. The invention and adoption of agriculture (see Sections 6.3.10 and 9.3.2) committed humans to living in an increasingly complex and dense social network. This became progressively more complex following the Industrial Revolution, and has of course been magnified still further by modern technologies. The Nobel prize-winning economist Robert Fogel has proposed that the improvements in health and knowledge over the past few centuries are mutually reinforcing, a process he calls techno-physiological evolution, leading to an accelerating rate of technical change and population growth (Figure 1.3). Nevertheless, as we will discuss in Chapter 11, there is growing evidence that the mismatch between the social environment in which we evolved and that in which most humans now live has consequences for mental health. Throughout this book we will see many examples of rapid environmental change leading to pathological consequences because of constraints on our speed or capacity to adapt.

1.2 What Evolution Is: Fundamental Principles

Evolutionary biology is fundamentally concerned with the various processes that have determined the "design" of the human body at all levels, from how we interact as whole organisms with other members of our species to every component and level of our internal biological organization. *Design* is a frequently used term in the evolutionary literature. It is a metaphor, used as shorthand to describe the various processes by which a species evolves, such that its characteristics—anatomical, physiological, biochemical, maturational, and behavioral—fit the environment in which the population lives. It does *not* in any way imply the existence of a designer; it just happens that it is much easier to describe processes using this metaphor, but we must always remember that it is a metaphor and no more.

Each evolved characteristic of a person is often described as an adaptation, although strictly *adaptation* as used in evolutionary biology refers to those evolved elements (or *traits*) that can be shown to have promoted fitness. A further commonly used metaphor is *strategy*, which allows us to describe the functional significance of these adaptations. We will expand on these concepts in Chapter 2.

In evolutionary thought it is important to avoid the trap of describing an evolutionary process, or evolution itself, as having a purpose or direction: to do so is a form of *teleology*. One of the dangers of the design and strategy metaphors, or of speaking about higher or lower species, is that they can encourage

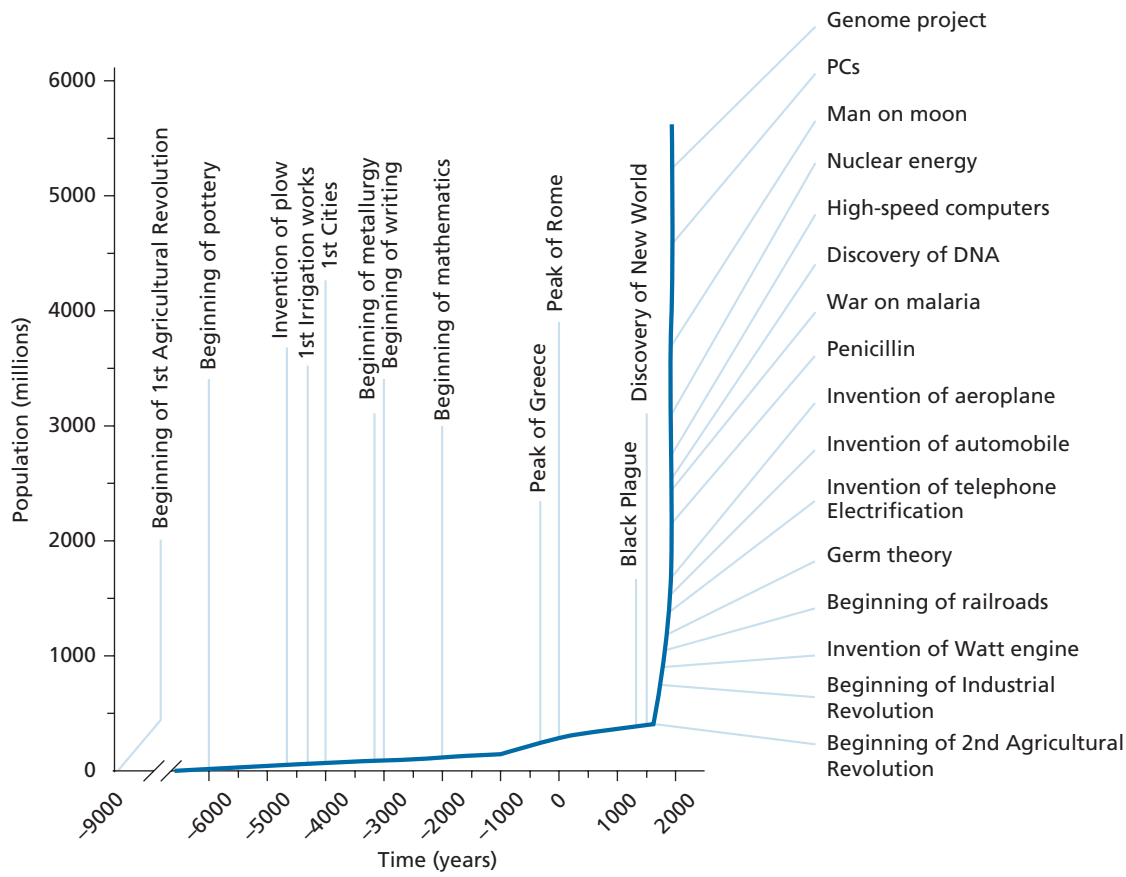

Figure 1.3 Anthropogenic changes in the human environment. From Fogel (2004), with permission.

such thinking. There is a major difference in the thought processes underlying the statement that "limbs evolved for walking," which is teleological, and the evolutionary statement that "there was progressive selection over time on the traits associated with the ancestral fin, and the adaptive advantage associated with effective terrestrial movement led to cumulative selective change resulting in the formation of the limb." But we can see how clumsy the second statement is, so it is easy to be sloppy and say that a process or a structure "evolved for …." It is an almost unavoidable temptation, but when we use such language we must also remember that it does not imply purpose.

The beginning of modern evolutionary theory in the late eighteenth century was based in the growing acceptance of two fundamental concepts. The first was gradualism, the idea that the geological features of the planet are the result of slow processes operating over "deep time." The second concept was that biological species are not immutable but that, with time, new species could emerge, evolve into other species, or become extinct, and that in biology, as well as geology, deep time provides a setting for such gradual change. Although macroevolution is a large component of evolutionary biology, it is not a major focus of this book beyond a brief consideration of the evolutionary history of the hominin clade since the last common ancestor that humans and their direct ancestors shared with chimpanzees (Box 1.2; Chapter 6). But Charles Darwin recognized that species could change their characteristics over time, and we call this within-species change *microevolution*. Importantly, macroevolution and