Evolutionary Mismatch And What To Do About It: A Basic Tutorial

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Abstract

Evolutionary mismatch is a state of disequilibrium whereby a trait that evolved in one environment becomes maladaptive in another environment. Mismatch is an integral part of evolution in changing environments and is becoming increasingly common for all species living in human-altered environments. It is especially important to understand mismatch in relation to our own species, since humans have so radically altered their own environment and mismatches can occur for cultural evolution in addition to genetic evolution. This article provides a basic tutorial on evolutionary mismatch as part of a special issue of the journal *Evolutionary Applications*. Even professional evolutionists can benefit from our "back to basics" approach to one of the central concepts of evolutionary theory.

Introduction

Evolutionary mismatch is a state of disequilibrium between an organism and its environment. In a classic case of mismatch, adaptations that contributed to survival and reproduction in previous environments become relatively maladaptive in a changed environment, a situation that can only be addressed by a behavioral accommodation, subsequent evolution, or another environmental change.

The concept of mismatch is so central to evolutionary theory that a basic tutorial might seem unnecessary. On the contrary, a "back to basics" treatment is warranted for three reasons. First, human activities are changing the environments of other species at an unprecedented scale ({Grimm, 2008 #3; Smith, 2008 #1; Tseng, 2007 #2}). A basic tutorial on mismatch is needed for the general public and sectors of the academic and public policy communities that are not already well schooled in evolutionary science.

Second, mismatch is an exceptionally relevant concept for our own species. The modern human environment is radically different from the environments we experienced as hunter-gatherers in small-scale societies only ten to fifteen thousand years ago ({Barkow, 1992 #30}). Some genetic evolution has taken place during this period ({Cochran, 2009 #145}) and cultural change is itself an evolutionary process that adapts us to our environments ({Jablonka, 2006 #698}{Richerson, 2005 #407}). But cultural evolution also takes time, so cultural mismatch needs to be considered along with genetic mismatch.

Third, even professional evolutionists can benefit from a "back to basics" approach to fundamental concepts. Consider the landmark book *Natural Selection in the Wild*, published by John Endler in 1986. Despite the fact that natural selection is the centerpiece of Darwin's theory, evolutionists had not developed a clear set of guidelines for operationally defining it and standards of evidence for documenting it in natural populations. Endler's book performed this "back to basics" service for the concept of natural selection, and this article and special issue of *Evolutionary Applications* aim to perform the same service for the concept of mismatch.

Providing standards of evidence for cases of mismatch in our own species is especially important because some putative examples have acquired the reputation of "just-so stories" ({Gould, 1979 #27} {Coyne, 2009 #10}). Skeptical discussions often make it appear as if mismatch will forever remain a topic of idle speculation that is beyond the reach of serious scientific inquiry. This assessment is too pessimistic. As Endler and others have shown, hypotheses about adaptation and natural selection can be tested as thoroughly as other scientific hypotheses, and the same is true for hypotheses about mismatch. It is true that information about past environments can be difficult to obtain, but this is a problem for any historical science, and it is surprising how often hypotheses about the past can be strongly supported with enough ingenuity. Especially unhelpful is the suggestion that just because a mismatch hypothesis is difficult to test, it isn't worth the effort. A substantial proportion of human misery is probably due to genetic and cultural mismatch with our current environments. If mismatch hypotheses are difficult to test, then that's all the more reason to invest in the effort.

Finally, there is the question of what to do about cases of mismatch after they have been documented. An evolutionary mismatch is *a particular type of dysfunction* that results from evolution in changing environments. Evolution can result in dysfunctions for many other reasons. Consider atherosclerosis, the leading cause of cardiovascular disease in modern human populations ({Lindeberg, 2010 #17}). Is it caused by an infectious agent? Is it an inevitable consequence of aging that has become more common because we are living longer? Or is it caused by a mismatch between our evolved dietary adaptations and our current food environment? In the last case, what are the details of the mismatch? Is it an imbalance of macronutrients, such as too much fat and carbohydrates? Or is it a more subtle aspect of the modern dietary environment, such as particular compounds in grains or dairy products that are not digested and trigger an inappropriate response of the immune system? Clearly framing and testing mismatch hypotheses, along with other hypotheses informed by evolution, organizes the search for relevant information and possible solutions in ways that might not have occurred otherwise. As for atherosclerosis, so also for the myriad other maladies afflicting humans and other species in rapidly changing environments.

Defining Evolutionary Mismatch

An evolutionary mismatch can be defined as *a negative consequence that results from a trait that evolved in one environment being placed in another environment*. The typical example of mismatch was an adaptation in the prior environment, but traits that were originally neutral or even deleterious can potentially acquire new harmful consequences in an altered environment.

The most straightforward examples of mismatch have a clear temporal component. For example, species of birds on remote islands often evolve to become fearless of mammalian predators ({Blondel, 2000 #11}). Their fearlessness might have been adaptive, insofar as it allowed them to better conduct other activities. Alternatively, their fearlessness might have been a neutral trait, caused by the accumulation of mutations that are not removed by natural selection, similar to the loss of eyesight that evolves in cave-dwelling species ({Romero, 2005 #12}). Either way, fearlessness becomes highly maladaptive when the environment changes with the arrival of mammalian predators. In many cases, the native bird species cannot be trained to be fearful and the only way to prevent their extinction is to restore the earlier environment by removing the introduced mammalian predators, or by genetically selecting for more fearful strains of the native species ({Milberg, 1993 #13} {Zaveleta, 2001 #14}).

There is a spatial form of evolutionary mismatch that is closely related to the temporal form. Consider a species of aquatic insect that has always lived in a heterogeneous environment; sometimes the insects live in ponds that have fish in them (which is disastrous for the insects) while at other times they live in ponds that lack fish (in which case the insects thrive). Every generation, adults disperse from their natal pond and lay eggs in new ponds. These insects evolved adaptations that allow them to preferentially choose ponds without fish, but the adaptation is far from perfectly reliable. As a result, in every generation, some

larvae are deposited in bodies of water with fish and they are decimated. These individuals are as mismatched to their environment as the island birds encountering mammalian predators in the previous example. However, the species as a whole never experiences a change in environment, in that both kinds of pond are present at the same frequencies throughout the process ({McPeek, 2008 #15}).

Traits that evolved in one environment need not be dysfunctional in a second environment; they can be neutral or fortuitously beneficial, but these cases are excluded by the term "mismatch", which restricts our attention to the dysfunctional cases.

Evidence Required to Demonstrate a Case of Evolutionary Mismatch

In principle, the evidence required to demonstrate a case of evolutionary mismatch is straightforward. A given trait (T) must be shown to be adaptive, neutral, or deleterious in relation to its ancestral environment (E1) and relatively dysfunctional in relation to another environment (E2). "Dysfunctional" will usually be defined in terms of evolutionary fitness, but it can also refer to welfare in more general terms. For example, consider a human disease caused by evolutionary mismatch that does not manifest itself until late in life. The disease might have a negligible effect on evolutionary fitness but still be well worth curing to reduce human suffering.

Before dealing with problematic cases of mismatch that have earned the reputation of "just-so stories", it is important to stress that some cases of mismatch can be documented as thoroughly as any scientific fact. As one example, adult aquatic insects that fly in search of bodies of water are frequently attracted to manmade reflective surfaces such as solar panels or buildings with glass surfaces. Their attraction is fatal, and is therefore obviously dysfunctional in terms evolutionary fitness. Why does it occur? A plausible hypothesis is that the insects have evolved to rely on certain cues such as polarized light to find bodies of water and that reflective manmade surfaces provide the same cues. Horvath et al. (2010) tested this hypothesis by measuring the reflection-polarization characteristics of solar panels in relation to water, along with choice experiments by various species of aquatic insects. The authors showed that the solar panels were even more reflective than water and acted as super-stimuli for the insects, which not only preferred the panels but even completed their oviposition behavior.

Armed with this understanding of the proximate mechanism that causes the mismatch, Horvath et al. (2010) were able to solve the problem by adding white non-polarizing borders to the solar panels. This simple and inexpensive modification resulted in a 10- to 26-fold decrease in the attractiveness of the solar panels to the insects. Evidently, their perceptual machinery had evolved to find relatively large bodies of water and was not triggered by reflective surfaces enclosed by small non-reflective boundaries.

To formalize this example, the trait (T) is attraction to polarized reflective surfaces, (E1) are the surfaces of water that were present ancestrally, and the different environment (E2) is man-made polarized reflective surfaces. The adaptedness of T in relation to E1 can be documented as well as any scientific fact and need not remain in the category of "just-so story". The dysfunctional consequences of T in relation to E2

are also easy to document. Finally, understanding the nature of the adaptation and the mismatch in mechanistic detail leads to an elegant and simple solution that might never have been discovered otherwise. Other cases of mismatch might be more *difficult* to document and solve than this case, but the same degree of understanding might be *attainable* with enough hard work.

What makes a putative case of mismatch such as atherosclerosis in humans more difficult to study than the fatal attraction of aquatic insects to reflective surfaces? To begin, the trait (T) is harder to define. If we define the trait as "the disease atherosclerosis", then it might never have existed in the human ancestral environment. Instead, the disease should be regarded as a detrimental consequence of an interaction between a set of traits that evolved in an earlier environment and elements of the current environment. The set of traits, the earlier environment, the elements of the current environment, and their interactions all must be determined by scientific research.

The prospects for working out such a complex story might seem daunting, but consider the plight of biomedical scientists trying to understand the causes of atherosclerosis without the help of evolutionary theory. They are faced with the same problem of understanding a complex interaction between a set of traits in the organism and a set of traits in the current environment, leading to pathological consequences. Is their plight more or less daunting than the plight of the evolutionist?

We think that the problem faced by the evolutionist is more tractable, because evolutionary theory offers an abundance of testable hypotheses that might not occur otherwise. This raises an important point about the "just-so story" accusation that merits discussion in general terms, before returning to the subject of mismatch. "Just-so story" is just another term for "untested hypothesis". The purpose of any theory is to generate hypotheses, which always start out as untested. If hypotheses motivated by evolutionary theory were somehow less testable than other hypotheses, then they could be regarded as deficient, but there is no warrant for making this claim. Evolutionary theory's fecundity as a generator of testable hypotheses should therefore be regarded as an asset rather than a liability.

To see how this plays out for a disease such as atherosclerosis, an evolutionist would immediately think of reasons why a maladaptive outcome might exist for a given organism in a given environment. One possibility is that the outcome is caused by an infectious agent, initiating one line of inquiry ({Ewald, 2002 #18}). Another possibility is that the outcome is a negative byproduct of traits that are beneficial in other contexts, initiating another line of inquiry. A third possibility is that the outcome reflects a mismatch situation, initiating a third line of inquiry. As we stated earlier, a mismatch is a *particular type of dysfunction* that results from evolution in changing environments, and the utility of a mismatch hypothesis is the *specific testable predictions* that it makes.

In the case of a disease such as atherosclerosis, the mismatch hypothesis immediately directs attention to foods that are prominent in modern diets but rare or absent from ancestral diets. It encourages cross-cultural research and directs attention toward the few remaining human populations that still subsist on a pre-agricultural diet. It raises the possibility of genetic evolution adapting different human populations to different

diets over a range of time scales. It organizes the comparative study of nonhuman species. For example, what is the digestive physiology of grain-eating vs. non-grain-eating rodent species, and what happens when non-grain-eating species are fed grain? It suggests new ideas for human dietary trials that might not have been envisioned otherwise. All of these predictions start out *untested*, but they are just as *testable* as predictions that are formulated without the help of the mismatch hypothesis ({Lindeberg, 2010 #17}).

Since the plight of the evolutionist is still daunting, even if less daunting than the plight of the non-evolutionist, it is important to be as clear as possible about the information that is required to test a mismatch hypothesis and how it can be obtained. In the next section, we enumerate the types of information that are required to fully test a mismatch hypothesis. Optimally, when scientists offer evidence for a case of evolutionary mismatch, they should include all of these components in their case study ({Lloyd, 1987 #19}). At the beginning of an inquiry, a suggestive case of evolutionary mismatch would specify both a likely population and a current trait or traits (T), while also specifying and offering some evidence that the current trait(s) seems to be detrimental or badly fit to its present environment (E2). Some evidence may also be given that the trait existed in the past evolutionary environment (E1) and was also likely adaptive or neutral in that environment. These are the basics that are required to claim that a trait is an evolutionary mismatch. More well-established cases for mismatch require providing evidence for several of these components, and the more of them that receive empirical support, the better confirmed the mismatch hypothesis is ({Lloyd, 1987 #19}).

Information That Is Required To Test A Mismatch Hypothesis

In this section, we describe the components of a mismatch model, each of which can be supported with evidence by a variety of methods or techniques.

- **The population(s).** Any evolutionary scenario must specify the population that is evolving in relation to its old environment, (E1), and its new environment, (E2). One reason that our aquatic insect example seemed simple is because we assumed that the population is the entire species, which has been uniformly selected to be attracted to polarized reflective surfaces. In reality, most species are divided into subpopulations that experience different selection pressures and are connected by varying degrees of gene flow, so identifying the relevant population for a given case of mismatch is not necessarily straightforward. Clear membership criteria should be given in cases where the population is subdivided. Identifying the appropriate population for a case such as atherosclerosis in humans can be especially difficult. Is it the original small population that spread out of Africa approximately 70,000 years ago? Is it the population in a particular geographical area that has experienced a particular diet for 3,000, 20,000, or 40,000 years? These questions can only be answered by empirical research. Once again, if this kind of research appears daunting, consider the alternative. As a hypothetical example, suppose that atherosclerosis is caused in part by a substance in cow milk that is not digested by the adult human digestive system and triggers a maladaptive response of the immune system. Suppose that genetic evolution has taken place in human populations that have subsisted on cow milk during the last few thousand years, causing them to be less susceptible to this cause of atherosclerosis than other populations. How many decades would be required for

biomedical researchers to come to this conclusion without the guidance provided by the concept of evolutionary mismatch? To summarize, it is essential to determine the relevant population for a given case of mismatch, no matter how easy or hard it might be.

• **The phenotypic trait(s).** Evolutionists define phenotypic traits with great flexibility, as virtually any measurable property of an organism. Phenotypic traits that are subject to evolution must be heritable (see below), which means that they exhibit a correlation between parents and offspring.

Identifying the relevant phenotypic trait(s) in a mismatch scenario might seem straightforward, but it can become fraught with difficulties. We will describe two relatively straightforward cases before turning to more problematic cases. These examples will also introduce the method of phylogenetic inference, or "tree thinking", as a useful tool for studying evolutionary mismatch.

RuBisCO (for Ribulose-1,5-bisphosphate carboxylase oxygenase) is an enzyme that is responsible for the vast amount of carbon that is fixed into organic form. It is present in virtually all organisms (with the exception of some viruses that exploit the enzyme in their hosts), including the three major domains of Bacteria, Archaea, and Eucaryota, as shown by the phylogenetic tree in figure 1. Although it is theoretically possible that RuBisCO evolved independently in each domain, it is more plausible to hypothesize that it evolved very early in the history of life, before the domains branched off from each other, as indicated in the figure.

There is abundant evidence that the earth's atmosphere was originally anaerobic and that the accumulation of oxygen was a toxic byproduct of anaerobic metabolic activities. Aerobic metabolism evolved as a response to the new oxygenated environment (E2). It is also well known that oxygen reacts with RuBisCO in a way that is deleterious to organisms. Other adaptations are required to minimize the exposure of the enzyme to oxygen (e.g., the creation of a locally anaerobic environment) and to minimize damage when it occurs (e.g., by mopping up free radicals;({Nisbet, 2007 #20} {Tabita, 2007 #23})

This example contains several important lessons for the general study of evolutionary mismatch. First, it shows that a trait (T) can be identified that remains stable across species, environments, and time periods. The fitness associated with the trait varies, but the trait itself does not. Second, it shows that an earlier environment (E1), and the adaptedness of the trait to the earlier environment, can be ascertained with confidence, even when it occurred in the far distant past. Third, it illustrates the utility of "tree thinking" for drawing some of these inferences. When we are studying a particular case of mismatch in a particular species, it is helpful to broaden the analysis to include other species and their historical relationships with each other. Fourth, it shows that evolutionary mismatches are not necessarily transient, but can become permanent features of life. RuBisCO is a trait (T) that did not change when the environment changed, but rather remained static while other traits evolved to ameliorate the negative effects of the new environment. Human efforts to ameliorate mismatches to our current environment sometimes bear an intriguing resemblance to the traits that evolved to ameliorate the effects of oxygen on RuBisCO.

Our second relatively straightforward example is the genetic evolution of lactose tolerance in human adults in some populations but not others ({Swallow, 2003 #25} {Cochran, 2009 #5}). Most mammals are lactose tolerant as infants but lose the ability to digest lactose as adults. It is not obvious that this should be the case from an evolutionary perspective. It is perfectly possible for a trait that is useful early in life to be retained later in life, but natural selection has been sufficiently economical in this case to "turn off" the ability to digest lactose after it is no longer useful.

Humans are an exception, but only in some geographical regions and not others, at least prior to recent worldwide dispersal, as shown by the tree diagram in figure 2. Unlike the tree for RuBisCO, where the trait is clearly ancestral, the trait of lactose tolerance in adult humans is clearly derived. Enough research has been conducted to be confident that the phenotypic trait evolved not once but at least twice, in Europe and Africa, and that the genetic basis of the phenotypic trait is different in these two cases ({Ingram, 2007 #24} {Cochran, 2009 #5}). What appears to be a single trait in functional terms is at least two traits in mechanistic and historical terms. The mechanistic difference is likely to be important when it comes to the exact physiological response to lactose, and therefore of relevance to the question of "what to do about it" in a practical sense.

This example is one of the best documented cases of recent genetic evolution in humans—and an evolutionary mismatch for adult humans who are lactose-intolerant in a world where milk products are a common part of the dietary environment. It also contains some complexities that are instructive for the study of evolutionary mismatch as a whole. First, what seems like a straightforward phenotypic trait becomes two traits when studied in more detail. This is likely to be common, because whenever the same phenotypic trait evolves independently in different populations, the exact mutations that arise and are selected typically are often not the same (refs).

Second, the fitness consequences of an environmental change (E2) on a given trait (T) are likely to be complex and need to be considered on a component-by-component basis. When dairy practices first evolved by cultural evolution, the net benefit was positive despite the fact that most adults lacked the genetic ability to digest lactose.
Milk products might still have deleterious health consequences in some respects, even in populations that have genetically adapted in other respects. In general, many more generations are required to adapt to deleterious consequences that are expressed late in life, compared to those that are expressed during the peak reproductive years of the life cycle. Thus, milk products are implicated in late-onset diseases such as atherosclerosis, even in populations that have genetically evolved to digest lactose ({Lindeberg, 2010 #17}).

The fact that a disease such as atherosclerosis might have been virtually nonexistent in humans prior to the advent of agriculture ({Lindeberg, 2010 #17}) challenges conventional thinking on the stability of phenotypic traits. In the classic mismatch scenario, a new environment (E2) changes the fitness consequences of a trait (T) but does not change the trait. This can be true for traits with a strong genetic basis, such as RuBisCO or a particular genetic change that enables adults to digest lactose, but other phenotypic traits are caused by a more complex gene-environment interaction. For these traits, a change in the environment can change the trait, not just the fitness consequences associated with the trait. The hardening of the arteries associated with

atherosclerosis provides an example. It is a genetically heritable phenotypic trait in most modern human populations, but it came into being not by genetic mutation, but by a change in the gene-environment interactions caused by a change in the environment. Similar examples are likely to be common whenever phenotypic traits are caused by gene-environment interactions. In the atherosclerosis example, the phenotypic trait is absent in (E1) and suddenly appears in (E2). It is also possible for a phenotypic trait to be present in (E1) and (E2) but to have a completely different mechanistic basis, in which case the phenotypic continuity is misleading. Who can say whether the phenotypic trait of homosexuality is caused by the same gene-environment interactions in modern populations as in ancient populations, for example?

In problematic cases such as these, the phenotypic traits are a composite of lower-level traits that are interacting with each other and the environment. By focusing on the component traits, we can potentially identify cases where the trait remains constant and only the fitness consequences are altered by the environmental change—more like RuBisCO than like atherosclerosis.

An environmental change can even change the nature of phenotypic traits that are species-typical and have remained stable for eons. The vertebrate eye, for example, is a product of a complex gene-environment interaction during development (need ref). The reason that eyes develop so reliably is because the elements of the environment involved in the gene-environment interaction are so reliably present. If these previously reliable elements of the ancestral environment (E1) change, then even adaptations that have been species-typical for eons can become maladaptive. In the case of vision, eye development has taken place outdoors with a wide range of focal distances for eons. In modern human populations, the large proportion of time spent indoors focusing at short distances has resulted in an epidemic of vision disorders requiring an environmental intervention (glasses) to fix (refs). Even more severe disorders result when the vertebrate immune system develops in modern environments (E2) lacking elements that were reliably present in the past (E1). The most important general point is that the trait (T) cannot necessarily be defined independently of the environments (E1 and E2) when gene-environment interactions in the development of traits are taken into account.

• **Inheritance.** Traits must be heritable to evolve, but the raw fact of heritability says remarkably little about a trait in the absence of other information ({Sesardic, 2005 #26}). For example, a trait that is under strong directional selection evolves until heritable variation is exhausted. The absence of heritability at this point says nothing about the presence of heritability during its evolution. Heritable individual differences can be either adaptive (e.g., personality differences maintained by balancing selection) or nonadaptive (e.g., products of recombination). A given trait such as height might have high heritability in a uniform environment (such as when everyone is well fed), and low heritability in a variable environment (such as when some individuals have more access to food than others).

Increasingly, evolutionists are studying genetic polymorphisms as traits that can be measured directly as DNA sequences, such as the long and short repeat regions of the dopamine receptor gene DRD4 ({Cochran, 2009 #5}). It might seem that such traits can be studied more rigorously than phenotypic traits whose genetic basis is

unknown, but this is not always the case. Very few genetic polymorphisms result in a single phenotypic trait whose fitness consequences can be measured. In most cases, a genetically polymorphic locus plays a role in the expression of many phenotypic traits through a web of gene-gene and gene-environment interactions. Studying a single genetic polymorphism that affects many phenotypic traits can be as difficult as studying a single phenotypic trait that is influenced by many genes.

Another important point is that there is more to inheritance than genetic inheritance. Epigenetic mechanisms, familial and social learning (in many species), and symbolic systems of thought (largely restricted to humans) also result in traits that are transmitted across generations with a correlation between parents and offspring or their equivalents ({Jablonka, 2006 #698}). A good example of cultural mismatch was documented by the political scientist Robert Putnam in his book *Making Democracy Work* ({Putnam, 1992 #5}). When Italy decentralized its government during the 1970's, the provinces varied greatly in how well they produced efficient governments of their own. The variation ran largely along a north-south axis and was due to differences in social organization that had been in place for a millennium. Northern provinces had a "horizontal" social organization, originally based upon trade guilds that encourage cooperation among peers. Southern provinces had a "vertical" social organization, originally based upon a military empire, that caused peers to compete with each other to curry the support of social superiors. These cultural adaptations to past environments had a large impact on the capacity for efficient governance in the current environment. Although Putnam did not explicitly frame his analysis in terms of cultural evolution and mismatch, he provided an excellent case study and future research can probably benefit from a more explicitly evolutionary approach.

To summarize, inheritance is required for evolution to occur, and the more information that can be obtained about inheritance the better, but it must also be appropriately interpreted. Evidential support of this type can be gained through breeding experiments (e.g., {Reznick, 1996 #21}), heritability studies, analysis of consecutive generations, and pedigree analysis. Once again, if this seems dauntingly complex, consider the alternative of facing the same degree of complexity without the guidance provided by evolutionary theory. Moreover, a strong case for mismatch can be built without much detailed knowledge about heritability. In our aquatic insect example, the attraction of adults to reflective surfaces clearly counts as an adaptation because it is a complex trait essential for reproduction. This is the kind of evidence that enabled Darwin to build a compelling case for his theory of natural selection without any mechanistic knowledge about inheritance, which also can be used to produce a strong case for mismatch.

Selection pressures and fitness consequences of the trait(s) in the ancestral environment (E1). All adaptations evolve in the context of selective pressures that operated in the past, which can be called the "adaptively relevant past environment" or "environment of evolutionary adaptedness", a term coined by the pioneering evolutionary psychologist John Bowlby ({Bowlby, 1969 #321}). We will use the term "ancestral environment" (E1) for simplicity, knowing that it needs to be appropriately interpreted. Evidence for a description of the ancestral environment may include geological information (for example, about an ice age or aspects of the savannah environment), information about the availability of different foods or supplies, or evidence concerning aspects of the local fauna or human social groups

that may be deemed relevant to fitness. Some ancestral environments are easy to infer, in part because they still exist in the present. In our aquatic insect example, the ancestral environment was, and remains, bodies of water with their polarized reflective surfaces. For the human eye, the ancestral environment was the outdoor environment with its range of focal distances.

Because the ancestral environment is defined in terms of relevant selection pressures, it must be defined separately for each trait. The appropriate spatial and temporal scale can be hugely variable, as can be seen from the examples described in previous sections--everything from RuBisCO, which became entrenched early in the history of life, to social organizations that became entrenched in current-day Italy a mere millennium ago. Some genes that affect human appetite evolved so long ago that they are also present in nematodes ({Ashrafi, 2003 #33}). Some aspects of our dietary physiology might reflect the largely vegetarian diets of the primate order, the diets of our more recent chimp-like ancestors that might have included meat, the diets of our still more recent hominid ancestors that might have included more meat and foods made edible by cooking, the diets associated with different regions of the world inhabited during the last 50,000 years, or the diets associated with domestication of plants and animals during the last few thousand years. Research is required to determine the appropriate spatial and temporal scale for any particular case, and to verify that the ancestral environment really did display the hypothesized selective forces. Once again, evolutionary theory makes this formidable task easier by asking the appropriate questions.

The term “ancestral environment” does not imply that the relevant selection pressures were homogenous. A given trait could have been positively selected at some times or locations but not others, evolving on the strength of its net effect. Patterns of spatial and temporal heterogeneity in the ancestral environment are especially important for understanding patterns of phenotypic plasticity in modern environments. As a straightforward example, the trait of human skin pigmentation reflects patterns of spatial and temporal heterogeneity in the ancestral environment ({Jablonski, 2004 #30}). Sunlight is important for the skin to manufacture vitamin D but also causes cancer. In sunny equatorial regions, constant exposure to the sun led to the evolution of relatively dark skin as a fixed trait. In the temperate zones, seasonal variation in exposure to the sun led to the evolution of skin pigmentation as a phenotypically plastic trait—sun tanning. Dark skinned people who move to temperate regions suffer from an inability to manufacture vitamin D, a clear case of mismatch that luckily can be easily corrected with dietary supplements. People capable of skin tanning can also experience mismatch in a variety of ways, because their phenotypically plastic adaptation is calibrated to the particular pattern of variation that existed in their ancestral environment. A person from England who moves to Australia will never become as dark as the aborigines who have inhabited Australia for 40,000 years. Anyone capable of tanning who spends a lot of time indoors or covered with clothing will experience sunburn when their skin is suddenly exposed to the sun, a pattern of variation that seldom, if ever, occurred in their ancestral environment. In general, phenotypically plastic traits are as vulnerable to mismatch as phenotypically fixed traits, whenever the patterns of environmental variation of the new environment (E2) depart from those of the ancestral environment (E1).

Evidence for past selection pressures and fitness consequences can sometimes be obtained by experiments that attempt to reproduce the hypothesized adaptively relevant ancestral environment, (E1), while placing organisms that exhibit the relevant trait in that environment: the consequences for fitness are then obtained through the usual means ({Endler, 1986 #8}, {Reznick, 1996 #21}). In this fashion, the trait can be correlated with fitness gains in the hypothesized past environment, (E1), thus supporting the claim that in the ancestral condition, the trait was adaptive. Sometimes the experiment can't be carried out (either because of biological or ethical considerations). For example, we can't manufacture an organism that doesn't use RuBISCo, or a human being who doesn't like to eat sugar and fat.

Alternatively, there may be "natural experiments" available in living populations in various present-day environments. For example, current human hunter-gatherer societies have often provided information about the correlations between various traits and fitness values that are used in evolutionary inferences (e.g. {Boehm, 1993 #31} {Lee, 2004 #32}). Such inferences must be made with due caution ({Boehm, 1993 #31}), but the information is still highly useful. For example, a few human populations still subsist on diets that are largely pre-agricultural . Not only do these populations differ from populations subsisting on a modern western diet, but sometimes the frequency distributions barely overlap. Virtually everyone who subsists on a modern western diet has at least some fatty deposits in their veins, which is the cause of atherosclerosis. People at the extreme low end of the continuum for this trait are at the extreme high end of the continuum for the same trait on the Pacific island of xx. Making use of "natural experiments" such as these is an important precursor to conducting real experiments, such as dietary trials in which elements of the diet are systematically varied.

• Integrating ultimate and proximate explanations for the study of the trait(s) in relation to E1. One of the most important distinctions in evolutionary theory is between ultimate and proximate causation. Ultimate causation explains why a given trait exists, compared to many other traits that could exist, often (but not always) due to the winnowing action of selection. Proximate causation explains the mechanistic basis of the trait. These explanations mutually inform each other and both are required to fully understand the evolution of any particular trait.

Our aquatic insect example nicely illustrates how ultimate and proximate explanations both play an essential role in documenting a case of mismatch. The example begins with the phenomenon of aquatic insects attracted to manmade polarized reflective surfaces. Ultimate causation plays a role at the beginning of the inquiry by providing a hypothetical functional explanation: these insects evolved to be attracted to water, which is mimicked by manmade polarized reflective surfaces. Proximate causation plays an increasingly large role as the inquiry continues: not only are the insects attracted to shiny surfaces, but the particular cue is polarized light unbounded by non-reflective borders. Knowledge about proximate causation is especially important for devising a solution to the problem: adding non-reflective borders to manmade reflective surfaces. Most cases of mismatch can benefit from a similar interplay of ultimate and proximate explanation.

In an influential paper titled "The Methods and Aims of Ethology", Nobel laureate Nikko Tinbergen ({Tinbergen, 1963 #555}) stressed the need for four separate

explanations for any particular trait, including 1) its functional basis; 2) its mechanistic basis; 3) how it develops during the lifetime of the organism; and 4) how it evolved during the history of the lineage. "Tinbergen's four questions" as they are often called, are an elaboration of the ultimate/proximate distinction and serve as well for the study of mismatch as for the study of ethology or any other topic that is approached from an evolutionary perspective. We have already emphasized the importance of understanding development, which reveals the interdependence of the foundational concepts "trait" and "environment".

• **Selection pressures and fitness consequences of the trait(s) in E2.** Cases of mismatch typically present themselves in the form of obvious dysfunctions that demand an explanation, such as insects attracted to solar panels or humans dying of heart disease. As the inquiry continues, it is necessary to identify the relevant aspects of E2 that cause the dysfunction, just as it is necessary to identify the adaptively relevant aspects of E1. In our aquatic insect example, it is the polarized light reflected by manmade surfaces and not any other aspect. In the case of human eye development, it is the contracted range of focal distances experienced in indoor environments.

There are a variety of ways to measure the dysfunction occurring in cases of mismatch. In cases involving diminishment of actual evolutionary fitness, there are surrogate measures or performance measures for fitness, in addition to standard reproductive success. In general, there is some negative consequence associated with the trait(s), whether it is fitness, well-being, or other measures of desirability or health. This is the point at which the notion of evolutionary mismatch offers real insight: this negative outcome is interpreted as the result of an old, adaptive or neutral trait thrust into a new environment, rather than on the pathology of the trait itself. Evidence of a present selection pressure (E2), can be found in various cases; for example elements of the modern western diet, including foods rich in fats and sugars. In this case, the presence of an environment with large quantities and easy access to high fat and high sugar foods creates a selection pressure new to our species, and one, combined with our previously evolved preferences for such foods, detrimental to our health.

In cases of mismatch involving phenotypic plasticity, the relevant aspects of E2 that cause the dysfunction can be subtle and seemingly distantly related to the dysfunction itself. Toward the end of World War II, the Germans imposed a famine upon the Dutch that lasted for seven months. Decades later, adults who were fetuses during this period developed diet-related diseases at a greater rate than those born earlier or later. Until then, no one had imagined that adult-onset diseases could be influenced by events taking place so early in life. Although the effect could have been due to a disruption of development, subsequent research has implicated a form of phenotypic plasticity called Predictive Adaptive Response (PAR), whereby environmental cues experienced early in life direct pathways of development that are manifested throughout life ({Gluckman, 2004 #656}). Evidently, food-poor and food-rich environments require different metabolic adaptations, just as sun-rich and sun-poor environments require different degrees of skin pigmentation. In the ancestral environment of humans and many other mammals (E1), the amount of available food varied, but the pattern of spatial and temporal variation was such that the amount of

food experienced early in life reliably predicted the amount of food available throughout life. This particular pattern of environmental variation resulted in a particular pattern of phenotypic plasticity in which the environmental cue determining the adult phenotype is experienced during an early stage of development, even before birth. In the case of the Dutch famine, the pattern of environmental variation in the modern environment (E2) was altered, such that individuals experiencing a food-poor environment as fetuses were born into a food-rich environment, resulting in a host of diet-related diseases later in life.

This example nicely illustrates some general themes about mismatch, in addition to the particular points that we are making about discovering the relevant aspects of E2. As we stated earlier, mismatch is *a particular type of dysfunction* that results from evolution, which needs to be distinguished from *other types of dysfunction*. In the case of the Dutch famine, the adult-onset diseases resulting from food deprivation during gestation could potentially be explained in two very different ways: 1) as a disruption of normal development; and 2) as the normal operation of a phenotypically plastic mechanism that is mismatched to the current environment. These two hypotheses make very different predictions that can be used to guide empirical research. It is extremely unlikely that the kind of research motivated by the mismatch hypothesis would be conducted by biomedical researchers who do not have the possibility of mismatch in mind.

Many other examples can be cited in which obvious physiological, behavioral, and social dysfunctions are interpreted as disruptions of normal development, ignoring the possibility of adaptive mechanisms of phenotypic plasticity that have become mismatched to the current environment (e.g., {Ellis, 2011 #35} for risky adolescent behavior).

• Integrating ultimate and proximate explanations for the study of the trait(s) in relation to E2. Taking both ultimate and proximate causation into account is as important for studying the trait in relation to E2 as to E1. In cases where the trait was an adaptation in E1, its functional design in relation to E1 needs to be understood to appreciate how it is misfiring in E2. Optimality models can be used to formulate testable hypotheses, and we can do experiments on mechanisms in present-day organisms to explore the present-day effects of traits evolved in E1 on fitness, well-being, or other measures of desirability. Continuing the example of the previous section, a PAR is a strategy in terms of ultimate causation, requiring the fetus to make a decision on the basis of available information. The fact that the fetus might still lack a brain is irrelevant. Bacteria and plants also lack brains, but they also make many "decisions" (i.e., adaptively changing their behavior on the basis of environmental information) as far as ultimate causation is concerned.

Of course, to make further progress, we must know the proximate mechanisms whereby the decision is made. In the case of human fetuses "deciding" which metabolic strategy to employ, the information takes the form of certain substances derived from the environment that trigger different patterns of gene expression, and so on. The more the mismatch is understood from both an ultimate and proximate evolutionary perspective, the more likely solutions will be found to prevent dysfunction from taking place in the current environment. For these purposes, we need information about actual mechanisms linking the trait(s) and fitness or other

measures arising out of the experiments mentioned in the above section, as well as the studies of past and present selection pressures.

In sum, a well-established case of evolutionary mismatch would specify both a population and a current trait or traits, (T), while also specifying and offering evidence that the current trait(s) is correlated with detrimental outcomes or evidence that it is badly fit to its present environment (E2). Some evidence supporting the inheritance or genetic basis of the trait should also ideally be offered. A mechanism linking this trait(s) to the detrimental outcome should also be provided. Evidence should also be given that the trait existed in the past environment of evolutionary adaptation (E1). If the claim is not that the trait was neutral in the evolutionary past, but was, in fact, adaptive, then evidence needs to be offered that there was a correlation in the past environment of evolutionary adaptation between the trait and fitness. If the claim is that the trait was an evolutionary adaptation in the past, then evidence concerning a mechanism linking the trait to evolutionary fitness in the past also needs to be provided.

• Why Do Cases of Mismatch Persist? Mismatch is typically regarded as a transient condition, in which the trait that has become maladaptive in E2 is gradually modified by natural selection. The amount of time required depends upon factors such as the intensity of selection, the heritability of the trait, and the availability of more adaptive variants. Deleterious effects expressed toward the end of the life cycle will be removed more slowly than those that are exhibited during peak years of reproductive value, as we have seen in the case of dietary mismatch. In addition, some cases of mismatch can become permanently entrenched, as we saw in the case of RuBisCO, in which the cost of the trait (T) in the new environment is ameliorated by the evolution of other traits, rather than via a modification of the original trait.

Even strong selection on the trait (T) in the new environment (E2) can require too many generations to solve problems of mismatch in a practical sense. In one classic example, baby sea turtles that hatch on the beach have evolved to make their way toward the sea by being attracted to light reflected on the water surface (E1). They become disoriented by lights from beach houses (E2), causing them to head inland, which is fatal. Very strong selection is operating on the phenotypic trait of orienting toward the sea (T), but there is no guarantee that the population will respond to selection before going extinct. An environmental intervention is required, such as shielding the lights from beach houses or collecting the turtles and carrying them to the sea ({Schlaepfer, 2002 #5}).

It is important to remember that some cases of mismatch involve traits that are nearly neutral with respect to genetic fitness but nevertheless important for human or animal welfare, such as diseases expressed very late in life. These cases of mismatch will persist for a very long time unless an environmental intervention is found.

Discussion

Mismatch is an integral part of evolution in changing environments. It is not a problem that requires a solution in any general sense. Specific cases of mismatch do

pose problems for human, animal, and environmental welfare, however, typically requiring solutions that are faster than letting evolution run its course.

This article is intended as a tutorial for a wide variety of people who need to know about mismatch in order to effectively deal with it. The other articles in this special issue of *Evolutionary Applications* show how the general principles that we have outlined can be applied to specific case studies in both humans and nonhuman species.

As we stated at the beginning of this article, a "back to basics" approach is needed for professional evolutionists, as well as for people who are learning about mismatch for the first time. Evolutionists benefitted enormously from the "back to basics" approach of John Endler ({Endler, 1986 #8}) and others for the subject of natural selection. We hope that this article and special issue will perform a similar service for the subject of mismatch.

Hypotheses that invoke both natural selection and mismatch are frequently criticized as speculative "just-so stories". We think that this critique itself deserves to be critiqued. A less pejorative term for "just-so story" is "untested hypothesis". Scientific inquiry on all subjects involves the framing and testing of hypotheses. If a given hypothesis is prematurely accepted without being sufficiently tested, then that particular case deserves to be critiqued. Critiquing an entire field of inquiry, such as all adaptationist or mismatch hypotheses, is another matter. There is no principled reason why hypotheses that invoke adaptation or mismatch are less testable than other hypotheses. The examples that we have provided in this article, and the case studies in the special issue, demonstrate that adaptation and mismatch hypotheses can be tested as well as any other kind of scientific hypothesis.

Some topics, such as the causes of diet-related human diseases, are enormously complex from *any* perspective. We think that the disciplined application of evolutionary concepts, including but not restricted to mismatch, makes difficult topics easier by suggesting hypotheses that might not have occurred otherwise.

Especially unhelpful is the suggestion that if a hypothesis is difficult to test, it isn't worth testing. This reasoning is absurd in general terms and should be recognized as such for the topic of evolutionary mismatch. The merits of testing a given hypothesis must be based on a comparison of benefits and costs. Understanding and ameliorating genetic and cultural mismatches can result in enormous benefits for human and planetary welfare. If the challenges are daunting, then all the more reason to mount the necessary effort.

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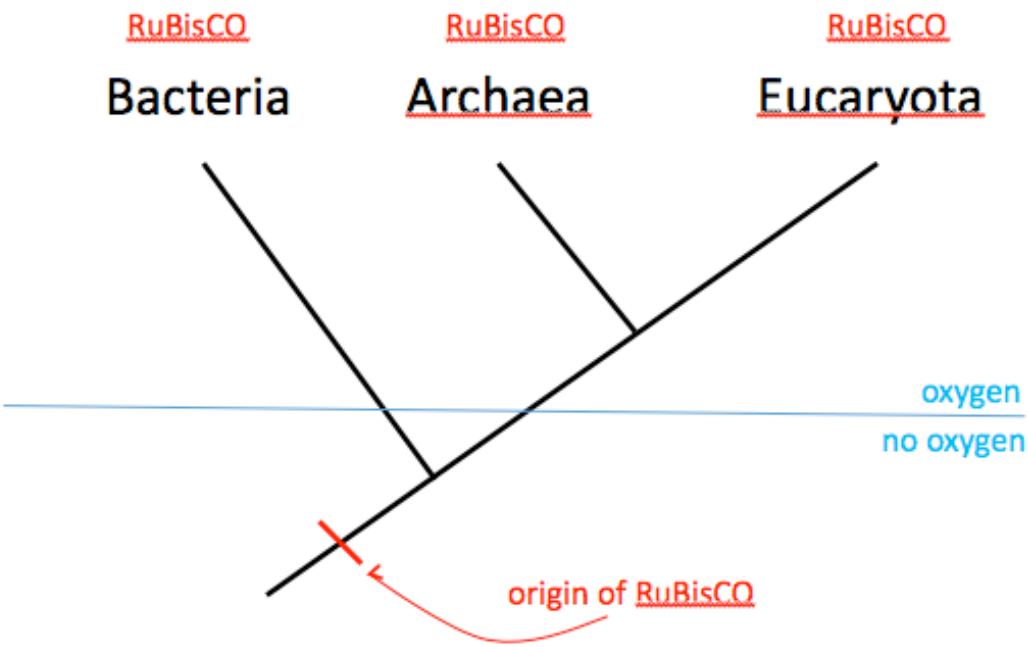

Figure 1. RuBisCO evolved early in the history of life and is present in virtually all current-day organisms, despite negative effects in oxygenated environments.

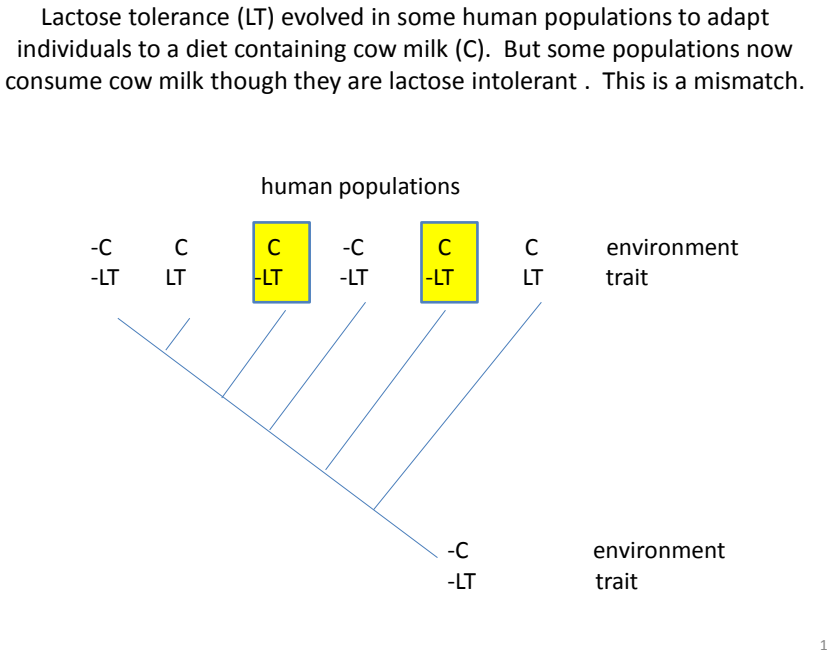

Figure 2. Lactose tolerance (LT) evolved in some human populations to adapt individuals to a diet containing cow milk (C). But some populations now consume cow mile thought they are lactose intolerant. This is a mismatch.