doi:10.1111/j.1558-5646.2009.00799.x

ADAPTIONISM—30 YEARS AFTER GOULD AND LEWONTIN

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Received July 16, 2009
Accepted July 16, 2009

Gould and Lewontin's 30-year-old critique of adaptionism fundamentally changed the discourse of evolutionary biology. However, with the influx of new ideas and scientific traditions from genomics into evolutionary biology, the old adaptionist controversies are being recycled in a new context. The insight gained by evolutionary biologists, that functional differences cannot be equated to adaptive changes, has at times not been appreciated by the genomics community. In this comment, I argue that even in the presence of both functional data and evidence for selection from DNA sequence data, it is still difficult to construct strong arguments in favor of adaptation. However, despite the difficulties in establishing scientific arguments in favor of specific historic evolutionary events, there is still much to learn about evolution from genomic data.

The Spandrels of San Marco

In 1979, Stephen Jay Gould and Richard C. Lewontin (Gould and Lewontin 1979), published their highly influential paper on adaptionism entitled "The Spandrels of San Marco and the Panglossian Paradigm: A Critique of the Adaptationist Programme." In this paper, Gould and Lewontin warned against confusing function with adaptation. Functional observations may not always have adaptive explanations—existence of form does not prove purpose. If one observes the spandrels (spaces that exist between arches) of the San Marco church in Venice—the mosaic designs are, in the words of Gould and Lewontin, "so elaborate, harmonious, and purposeful that we are tempted to view it as the starting point of any analysis, as the cause in some sense of the surrounding architecture." There is in evolutionary biology a similar "failure to distinguish current utility from reasons for origin," they argued. Functional observations (e.g., short front legs of a tyrannosaurus) are often followed by adaptive stories (the use of the front legs to titillate female partners) even if such stories are purely speculative and cannot be tested.

Gould and Lewontin's arguments were by no means embraced by all biological researchers. Their critique of the "adaptionist programme" was embedded in a more general critique of reductionism that did not appeal to many scientists, especially geneticists. However, now 30 years later it is clear that, although Gould and Lewontin's paper did not spell the end to adaptionist storytelling, it radically increased the awareness among evolutionary biologists about the pitfalls of adaptionism. Evolutionary biologists are today, arguably, much more reluctant to invent adaptive stories without direct evidence for natural selection acting on the traits in question. We still regularly encounter very naïve adaptive stories, particularly about human behavior, but rarely in journals such as *Evolution* or other related journals with high standards of peer review, and rarely from researchers with a background in evolutionary biology.

There is also another fundamental difference between evolutionary biology in 1979 and in 2009: the current availability of cheap DNA sequence data used to test hypotheses of selection, the evolutionary force behind adaptation. Hypotheses regarding past selection acting on a gene can be tested directly using comparative or population genetic methods. Although many of the statistical methods used to detect selection at times have been controversial, the field has matured to a state in which it often

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is possible to make definitive statements about past selection. A good example is the *Lactase* gene in humans, where even the most skeptical neutralist must be convinced by the overwhelming evidence in favor of selection based on allele frequencies, haplotype structure, and levels of population differentiation (Cavalli-Sforza 1973; Bersaglieri et al. 2004; Coelho et al. 2005; Voight et al. 2006). Another example is the evolution of certain viruses such as HIV (Bonhoeffer et al. 1995; Nielsen and Yang 1998; Ross and Rodrigo 2002) and Influenza (Bush et al. 1999; Yang 2000), where the rate ratio of nonsynonymous to synonymous mutations (d_N/d_S) is so extreme in certain regions, that only selection acting in favor of new mutations can provide an adequate explanation.

Selection and Adaptation

We now have the ability to detect past selection. The question that remains is if that ultimately helps us establish evidence in favor of adaptation. In some cases it clearly does. The difference in lactose intolerance among human geographic groups, is caused by a difference in allele frequencies in and around the *lactase* gene (Harvey et al. 1998; Hollox et al. 2001; Enattah et al. 2002; Poulter et al. 2003). The cause for the difference in allele frequencies is primarily natural selection emerging about the same time as dairy farming evolved culturally (Bersaglieri et al. 2004). Together, these observations lead to a compelling adaptive story of natural selection favoring alleles causing lactose tolerance. But even in this case we have not directly shown that the cause for the selection is differential survival due to an ability/inability to digest lactose. We must acknowledge that there could have been other factors, unknown to us, causing the selection acting on the region around the *Lactase* gene. Even if we can argue that selection acted on a specific mutation, and functionally that this mutation has a certain effect on the ability to digest lactose, we cannot, strictly speaking, exclude the possibility that selection acted on some other pleiotropic effect of the mutation. This argument is not erected to dispute the adaptive story regarding the *lactase* gene, the total evidence in favor of adaptation and selection related to lactose tolerance is overwhelming in this case, but rather to argue that the combination of a functional effect and selection does not demonstrate that selection acted on the specific trait in question.

The example of selection on viruses is somewhat different. We can here observe selection in action, as the viruses evolve at a rate that allows for direct observation and manipulation. We can repeat the experimental evolution of phages in the laboratory, and demonstrate that the same mutations go to fixation in repeated experiments conducted under the same conditions (Bull et al. 1997; Wichman et al. 2005). We can change environmental conditions to determine which factors cause the selection and measure fitness of specific haplotypes (Crill et al. 2000; Holder and Bull 2001). In the HIV, we can observe that the d_N/d_S ratio changes when the selective pressure imposed by the hosts defense/immune system weakens (Bonhoeffer et al. 1995; Ross and Rodrigo 2002). By observing the same process multiple times, and by laboratory manipulation, we can directly test hypotheses and more rigorously establish claims of adaptation. However, this possibility is usually not available to us in higher organisms. In humans, we must rely on inferences regarding past events by observing scant fossil evidence and the current pattern of genetic and phenotypic variation. We may be able to detect selection, but we may never be able to directly determine which traits selection acted on.

Evolutionary inferences often have a historic nature to them. Hypotheses regarding the underlying causes of past selection or changes in gene frequencies usually focus on single unique historical events. This does not imply that evolutionary theory does not produce falsifiable predictions—it clearly does (e.g., Williams 1973). But specific historical evolutionary hypotheses, such as just-so stories of why the giraffe got its long neck, or why humans have less body hair than other apes, might not be falsifiable or simple to investigate within any epistemological framework. This has not changed with the presence of molecular data. Although the presence of selection acting on genes underlying a phenotypic trait of interest does help support adaptive stories, it does not establish that selection acted directly on the specific trait of interest.

Microcephalin and ASPM

The fallacy that functional effects combined with evidence for selection provides evidence that selection is acting on the specific traits has lead to a number of dubious claims in human genomics. The most famous and maligned example is the selection acting on *Microcephalin* (Dorus et al. 2004; Evans et al. 2004a, 2005) and *ASPM* (Zhang 2003; Evans et al. 2004b; Mekel-Bobrov et al. 2005). *ASPM* and *Microcephalin* both code for centrosomal proteins involved in cell cycle regulation. Individuals who are homozygous for certain mutations in either of these genes have a complex disease phenotype with microcephaly—a decreased brain size—as its primary feature. Both of these genes also show some evidence of positive selection. *ASPM* has a very high d_N/d_S ratio in the human lineage (Zhang 2003), and *microcephalin* has an increased d_N/d_S ratio in the ancestral lineages leading to apes (Evans et al. 2004a). Based on these observations it was proposed that the two genes were involved in the evolution of increased brain size in humans and human ancestors. The argument was further refined with back-to-back papers in *Science* (Evans et al. 2005; Mekel-Bobrov et al. 2005) arguing in favor of ongoing selection in these genes in humans occurring within the last 5800 (*ASPM*) and 3700 years (*Microcephalin*). It was pointed out that the allelic variant supposedly under positive selection in *Microcephalin* (haplogroup D), has the lowest frequency in sub-Saharan

Africa and highest frequency in Europeans. Not surprisingly, the popular press had a field day with this story. However, the particular mutations of interest cannot be shown to correlate with cognitive abilities (Mekel-Bobrov et al. 2007; Timpson et al. 2007). Furthermore, fossil evidence shows that human brain size has not increased over at least the last 35,000 years. It seems that there has been substantial selection acting on *ASPM* and *microcephalin*, possibly also within the last few tens of thousand of years (consult Currat et al. 2006 for an alternative view). But there is no evidence that this selection has anything to do with human intelligence. Deleterious mutations in *ASPM* and *microcephalin* may lead to reduced brain size, presumably because these genes are cell-cycle regulators and very fast cell division is required for normal development of the fetal brain. Mutations in many different genes might cause microcephaly, but changes in these genes may not have been the underlying molecular cause for the increased brain size occurring during the evolution of man.

The *Microcephalin* and *ASPM* story is just one of a number of adaptive stories told recently relating to human evolution and motivated by the analyses of DNA sequence data. Although it is clearly within normal scientific praxis to propose hypotheses regarding the underlying causes of specific observations, publishing such hypotheses can be particularly problematic when the adaptive stories being told relate to human behavior and cognitive functions. In a country where there are vast differences in average income and expected educational outcome between ethnic groups, even indirect suggestions from scientists that these differences might have genetic causes may affect public opinion and policy making. This should make any responsible scientist hesitate when publishing results relating to adaptive differences between ethnic groups—even if the stories are well supported. And it should certainly prevent us from publishing such stories when they have only little or no support.

Whither?

The *Microcephalin* and *ASPM* stories illustrate that evidence of selection, and knowledge of the function of a gene, does not constitute evidence of adaptation. The same will be true even if we know the phenotypic effects of specific mutations under selection—which we rarely will in humans. Most genes have pleiotropic effects and establishing the direct cause of selection in an organism such as humans might in most cases be difficult or impossible.

The evolutionary genomics community has to an increasing degree come to expect and require functional evidence in support of claims of selection (MacCallum and Hill 2006). However, the functional information does not "validate" claims of selection. It mostly serves to provide a more interesting and entertaining story. In humans, where controlled experiments and measurements of fitness are difficult or impossible to obtain, the evidence for selection must come directly from the genetic data.

So should we give up making claims about selection and adaptation in humans and other similar organisms? Yes and no. We can certainly identify selection in the human genome and learn a tremendous amount about evolutionary processes from that. We can also use inferences regarding selection to propose functional hypotheses, which can be tested. We may even, recognizing evolutionary science as partly a historical science, speculate on specific historical events and causalities in human evolution. But the latter must be done acknowledging that no simple experiment or functional data can falsify or "validate" historical adaptive hypotheses. And in communicating with our peers, and with the popular press in particular, we may individually, and as a scientific field, benefit from understanding the societal impact of the statements we make.

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Associate Editor: M. Rausher