Foreword

The 74th Cold Spring Harbor Laboratory Symposium on Quantitative Biology on *Evolution: The Molecular Landscape* was dedicated to Charles Darwin on the occasion of the bicentennial of his birth and the 150th anniversary of the publication of *On the Origin of Species.* The Laboratory celebrated the 100th anniversary in 1959 with its 24th Symposium on *Genetics and Twentieth Century Darwinism.* What was entirely absent from that Symposium and what dominated the Symposium 50 years later are the contributions molecular biology has made to our understanding of evolution. Even as the details of Darwin's ideas have been modified over the years, evidence from molecular studies has strengthened his fundamental thesis.

The 2009 Symposium set out to examine the current state of many of the ideas that Darwin developed in his four great books: *On the Origin of Species by Means of Natural Selection, The Variation of Animals and Plants Under Domestication, The Descent of Man and Selection in Relation to Sex,* and *The Expression of Emotions in Man and Animals*. Leading investigators were invited to present their latest research in a diversity of fields ranging from the origins of life (unicellular and multicellular) to speciation and domestication to the evolutionary basis of human attributes. An overarching theme of the meeting was the extent to which much of evolutionary biology can now be viewed in a molecular, and often genomic, framework and the extraordinary degree to which many of Darwin's insights remain profoundly relevant today.

The Symposium included two rather unusual sessions. Evolutionary concepts have had an impact far beyond the boundaries of science and there is hardly a field of human endeavor that has not been influenced by evolutionary thinking. To acknowledge this contribution of Darwin, there was a session on "Cultural Evolution" that included presentations on principles of natural selection applied to linguistics, ideas, and economics by, respectively, Daniel Dennett, Matt Ridley, and Niall Ferguson. In the second unusual session, "Evolution and the Public," Kevin Padian, Ken Miller, Barbara Forrest, and Eugenie Scott discussed so-called "intelligent design" and the threat such irrational and antiscientific attitudes pose to education in the United States and elsewhere.

In arranging this Symposium, the organizers were dependent on the guidance of a broad cadre of advisors including Drs. Nicholas Barton, Hans Ellegren, Claire Fraser-Liggett, David Haussler, Gerry Joyce, Susan McCouch, Sarah Otto, Svante Pääbo, Nipam Patel, Matt Ridley, James D. Watson, and Richard Wrangham. Opening night speakers included Janet Browne, Ed Wilson, David Kingsley, and Marc Hauser. Douglas Wallace presented the Reginald Harris Lecture on "Energetics in Eukaryotic and Human Origins." Kevin Padian enlightened a mixed audience of scientists and lay friends and neighbors with his Dorcas Cummings Lecture on "Darwin, Dover, & Intelligent Design," and Brian Charlesworth ended the meeting with a masterful and thought-provoking summary.

This Symposium was held May 27–June 1 and attended by 400 scientists from more than 25 countries. The program included 69 invited presentations and more than 175 poster presentations. For the first time, six Symposium fellows were selected from the submitted abstracts, and each of these young scientists gave a short research presentation.

We thank Val Pakaluk and Mary Smith in the Meetings and Courses Program Office for their assistance in organizing and running the meeting and John Inglis and his staff at Cold Spring Harbor Laboratory Press, particularly Joan Ebert, Rena Steuer, and Kathy Bubbeo, for publishing both the printed and online versions of the Symposium proceedings. Photographers Connie Brukin and Jan Witkowski captured candid snapshots throughout the Symposium, and artist Julia Kuhl sketched portraits of a number of the speakers.

Funds to support this meeting were obtained from the National Institutes of Health. Financial support from the corporate benefactors, sponsors, affiliates, and contributors of our meetings program is essential for these Symposia to remain a success and we are most grateful for their continued support.

Bruce Stillman
David Stewart
Jan Witkowski
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Summary

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Advances in molecular biology have revolutionized the study of evolution. Detailed comparative studies of genomes are facilitating the analysis of phylogenies and raising new questions such as the extent of lateral gene transfer. Evolutionary analyses of development show that innovations frequently involve the reuse of existing gene products and gene networks in new ways and that changes in gene expression are important in morphological evolution. Population genetic studies are shedding increasing light on the genetic basis of traits subject to both artificial and natural selection. Laboratory models of evolution are being applied to both molecular and whole-organism systems, yielding insights into the evolution of adaptations, which complement those arising from reconstructions of evolutionary paths using molecular sequence or paleontological data. Overall, the Symposium portrayed evolution as a field that, while retaining its Darwinian roots, is exploring ever-wider areas of biology as new techniques and ideas emerge.

The 100th anniversary of the publication of *On The Origin of Species* was celebrated by the 24th Cold Spring Harbor Symposium on Quantitative Biology "Genetics and Twentieth Century Darwinism." This was attended by many of the leading lights of the Modern Evolutionary Synthesis, including Theodosius Dobzhansky, Ernst Mayr, Bernhard Rensch, George Gaylord Simpson, G. Ledyard Stebbins, and Sewall Wright, all of whom have now departed from the scene. The Symposium was as much a celebration of the Modern Synthesis as of Charles Darwin. In his meeting summary, Stebbins (1960) remarked that the participants "have reached substantial agreement on concepts remarkably similar to those which Darwin himself held, not only about the existence of evolution and the course which it followed, but also about the basic processes responsible for it. The only major qualitative difference between our knowledge and that possessed by Darwin lies in our recognition of particulate Mendelian inheritance, determined by chromosomal genes, as the basis of nearly all of the hereditary variability upon which selection acts."

It is interesting to look back at the 24th Symposium to see how much the intellectual and methodological framework for studying evolution has changed during 50 years. There was very little mention of DNA, with the exception of Dobzhansky's impressively forward-looking paper (Dobzhansky 1960). He gave an estimate of the size of the human genome in terms of numbers of base pairs that was reasonably close to the current value. He recognized that this gives an enormous number of possible combinations of the four possible nucleotides at each site: "The four-letter 'genetic alphabet' is, to use Leonardo's words, a beautiful, economical and direct means to create an ample supply of genetic raw materials from which evolutionary changes can be constructed." Dobzhansky also compiled data on the genome sizes of different species and pointed out what is now known as the C-value paradox; there is little relationship between the perceived complexity of multicellular organisms and the sizes of their genomes. This has received essentially no recognition in the later literature on genome size evolution (see, e.g., Cavalier-Smith 1985). Dobzhansky went on to speculate about gene homology and sequence divergence in evolution, foreshadowing the subsequent rise of studies of molecular sequence evolution.

The contents of other papers presented at the 24th Symposium reveal astounding differences in the problems under consideration, and the methods used to solve them, from the papers in the 74th Symposium. Although few present at the latter event would probably dissent from the basic principles of the Modern Synthesis, the enormous advances in molecular biology since 1959 have revolutionized both the techniques used by evolutionary biologists and the questions that they ask. In addition, field and experimental studies at the whole-organism level have greatly advanced our understanding of phenotypic evolution. There have been substantial advances in the theoretical understanding of evolutionary processes, from models of molecular evolution and variation at one extreme to social behavior at the other. Modern methods of genome sequence comparisons and genome scans of variation within populations are using evolutionary methods to identify functional changes in the genome, so that there is now a two-way interplay between evolutionary and functional biology. All of these themes were represented at the 74th Symposium; as its title suggests, molecular aspects of evolution were especially emphasized.

The Symposium spanned an enormous range of topics, from the RNA world to human social behavior, making it an exceptionally challenging task to summarize coherently. I will begin by asking, What did it show us about the impact on evolutionary biology of the spectacular advances in

All authors cited here without dates refer to chapters in this volume.

molecular biology since 1959, culminating in whole-genome sequencing? One aspect of this revolution has been our ability to conduct ever-more detailed comparative studies of genomes and to relate these to changes in biological organization. This has greatly facilitated the analysis of phylogenies. For example, it now seems clear that the unicellular choanoflagellates are the sister group to metazoans (N King, pers. comm.). But as well as helping to settle old questions about evolutionary relationships, some challenging problems have emerged from sequence comparisons, particularly in prokaryotes. The evidence for lateral transfer of genetic information among archaebacteria and eubacteria, as well as among less distant prokaryote groups, is now overwhelming. One response to this is to abandon any concept of a classic Darwinian "Tree of Life" (WF Doolittle); another is to search for sets of genes with consistent phylogenies that shed light on the evolutionary histories of extant taxa (Koonin et al.). Although lateral gene transfer seems far less rampant in eukaryotes and poses few problems for phylogeny reconstruction, some surprising examples have nevertheless come to light, especially in the mitochondrial genomes of fungi and flowering plants (J Palmer, pers. comm.). A spectacular example is provided by the mitochondrial genome of *Amborella*, which has expanded in size to 4 Mb by incorporating pieces of DNA up to the size of whole mitochondrial genomes from other flowering plants, algae, and mosses.

Comparative sequencing of whole genomes and parts of genomes is also shedding light on the evolution of the organization of the genome itself. One outcome of this work has been the discovery that transposable elements (TEs), and relics of TEs, comprise a large fraction of the genomes of many vertebrates (D Haussler, pers. comm.) and flowering plants (S Wessler, pers. comm.). There is increasing evidence that "domesticated" TEs have a significant functional role in gene regulation and contribute to conserved noncoding DNA. It is also clear from these studies, as well as from laboratory analyses of the rates of movement of TEs, that the numbers of copies of elements can expand very rapidly in evolutionary time when checks to their multiplication within the genome are removed, consistent with the idea that they are maintained in the genome primarily by their ability to self-replicate. Rapid progress has been made in understanding how TE activity is regulated by small interfering RNAs (Malone and Hannon; Cibrián-Jaramillo et al.), showing both how the host genome has evolved mechanisms to restrain TE activity and how TEs can evade these mechanisms.

Sex chromosome systems are another aspect of genome evolution whose understanding has recently advanced, with light being shed on their astonishing diversity within vertebrates alone. Mammals and birds are known to have diverged more than 300 million years ago; both groups have chromosomal sex determination, with male and female heterogamety, respectively. Sequencing of the chicken Z chromosome shows that it has homology with three different autosomes in humans, but not to the X chromosome (Bellott and Page). Despite the independent origin of the X and Z, they show interesting similarities in their organization, including an unusually low gene density and the acquisition of testis-expressed genes from elsewhere in the genome. These observations raise important questions concerning the evolutionary forces involved.

Genome evolution has long been known to involve a large amount of chromosomal rearrangements and changes in copy numbers. Modern technology allows much more detailed studies of these processes. Large segmental duplications of relatively recent origin form a significant portion of the human genome, and comparative studies of humans and other higher primates suggest an accelerated rate of occurrence of these in the common ancestor of humans, chimpanzees, and gorillas (Marques-Bonet and Eichler). This has resulted in the formation of new gene families, in some cases associated with signatures of positive selection. The presence of these duplications creates the opportunity for the generation of chromosome rearrangements by unequal exchanges, contributing to copy-number variation within the human population. Some regions of the human genome that contain unusual concentrations of duplications contain many different copy-number variants associated with genetic diseases, suggesting that the establishment of selectively advantageous duplications can result in an increased load of harmful variants (Dumas and Sikela). This illustrates the fact that Darwinian evolution is a process that lacks foresight, making use of whatever variants are currently selectively favorable or have a sufficiently weak disadvantage that they can be fixed by drift, without reference to long-term costs.

An objection to Darwinian evolution that is frequently made by the creationists is that it explains biological complexity by a random process. This of course ignores the fact that natural selection is decidedly nonrandom. Nevertheless, selection is impotent without the genetic variability that is thrown up by mutation, a much more random process. We now have a very detailed understanding of mutational mechanisms at the molecular level and of the elaborate cellular machinery that ensures the high accuracy of DNA replication and the correspondingly low rate of mutation (Kunkel). This accuracy reflects the fact that most mutations with any phenotypic effects are deleterious, because selection has had a long time to perfect most features of the biological machinery. But evolutionary change in response to a changing environment requires genetic variation on which selection can act, so that a zero mutation rate would bring evolution to a halt. Most evolutionists believe that the supply of mutational variability is rarely a rate-limiting factor in adaptive evolution (see, e.g., Muller 1949). Lindquist challenges this view, presenting evidence for special mechanisms that facilitate the production of novel phenotypes.

The opportunistic nature of evolutionary change was brought out by several contributions, at a variety of levels of biological organization. One major insight that has emerged from our advancing understanding of the functions of genes and the genetic control of development, is that evolutionary innovations frequently involve the reuse of existing gene products and gene networks, rather than the emergence of completely new genes and pathways. This was strikingly brought out by analyses of the genomes of choanoflagellates mentioned above and sponges. The choanoflagellates are unicellular, but some species form

colonies by cell division. They possess genes that code for proteins involved in both cell adhesion and signaling between cells. The latter appear to be used in sensing and responding to the environment in the choanoflagellates. The genome sequence of the demosponge *Amphimedon queenslandica* (Richards and Degnan) reveals that, despite lacking nerve cells, this organism possesses many of the components needed for synapses. In addition, most of genes that code are present for the major components of the signaling systems used in the major developmental pathways of more complex animals. At a lower taxonomic level, the unusual mode of embryonic development of sea urchins is associated with a remodeling of a regulatory circuit present in other echinoderms (Davidson and Erwin). Evidence from bacteria for the evolution of the control of different regulatory circuits by the same upstream regulator is described by Goley et al. Yet another example of a shift in the role of a developmental regulator is provided by the regulation of apoptosis in horned beetles (where is it is involved in the remodeling of tissues used for horn development) by the *Scr* homeobox gene (Moczek). In insects, the product of the *Dorsal* gene binds to numerous other genes, whose pattern of activity depends on the identity of activation proteins that bind close to Dorsal protein-binding sites in their enhancers (Perry et al.). Comparisons of different insect species suggest that changes in enhancer sequences, not the evolution of new enhancers, are responsible for changes in expression of genes regulated by *Dorsal*.

Nevertheless, there are cases where novel genes with important functional roles have emerged during evolution, other than by the mechanism of gene duplication and divergence mentioned earlier. For example, the snaR family of small noncoding RNA genes is restricted to humans and the African great apes and has evolved from TEs in a complex series of steps, which have been reconstructed in detail (Parrott and Mathews). In other cases, the details remain obscure, as in the case of *nodal* (Grande and Patel). This gene is involved in the control of left/right asymmetry in chordates; it is now known to be present in molluscs but absent from ecdysozoa, which include insects and nematodes.

There is increasing evidence concerning the role of changes in gene expression in morphological evolution, a topic that was well represented at the Symposium. S Carroll (pers. comm.) argued that changes in *cis*-regulatory elements allow tissue-specific changes in gene expression to occur, without the harmful pleiotropic effects that may be caused by mutational changes in widely expressed, *trans*-acting regulatory proteins. He presented evidence for this thesis from several studies of the evolution of *Drosophila* pigmentation and pattern differences. In one example, the intraspecific evolution of darker abdominal pigmentation in *D. melanogaster* populations is associated with the spread of a haplotype surrounding an enhancer of *ebony*, with a total of five mutations that confer the new phenotype. Examples of this kind are relevant to the old controversies concerning micromutations versus macromutations in morphological evolution (see, e.g., Sheppard 1960). There are now several cases in which multiple changes in a small regulatory region are required for the full development of a novel phenotype, yet classical genetic analyses would have suggested that the phenotypic difference is under major gene control. Stepwise Darwinian evolution at the sequence level is thus likely to be pervasive at the level of changes in gene expression.

Linnen and Hoekstra described a somewhat contrasting genetic scenario for the adaptation of the deermouse *Peromyscus polionotus* to the beach environment of the Florida Gulf and Atlantic coast, a classic example of natural selection for cryptic coloration that protects against predation. Here, the white coat coloration associated with the beach environment involves mutations affecting three different genes, one of which (in *Mc1r*) is a single-amino-acid mutation; the two others involve regulators of gene expression. Examination of the genotype–phenotype relationships enabled reconstruction of the most likely route to the evolution of the complete phenotype, by a stepwise path in which each change increases fitness, in accordance with Darwin's views on the evolution of adaptations.

Another example of the successful genetic dissection of the evolution of novel phenotypes in a new environment with respect to predator pressure is provided by sticklebacks, which have repeatedly invaded freshwater habitats (D Kingsley, pers. comm.). Here, the adaptive phenotypes involve loss of function, an evolutionary phenomenon also discussed by Cronk. Loss of the hindfin is a repeatable characteristic of these populations; a major (but not sole) contributor to this phenotype is a reduction in the expression of the *Pitx1* gene in the hindlimb, due to deletions of portions of the enhancer that evolved independently in different populations. In contrast to this use of new mutations, the loss of the lateral armour plate, which has also evolved in freshwater populations, appears to have involved the repeated spread of the same mutation at a locus controlling expression of the ectodysplasin signaling molecule. The evidence for this comes from the fact that the same haplotype with respect to sequence variants surrounding this locus is found in different populations and is also found at low frequencies in ocean populations.

This population-genetic approach of searching for signatures of selection from the effects of the spread of a selectively favorable variant on patterns of variation at linked sites is an increasingly used tool for identifying both targets of selection at sites with unknown phenotypic effects and the sites associated with changes in a specific phenotype. This provides a paradigm for integrating molecular and developmental approaches with evolutionary genetics methods, and it is likely that we will see an explosive growth in studies of this kind with the advent of new technologies. The theoretical basis for this approach was worked out long ago by Maynard Smith and Haigh (1974), well before the advent of modern methods for screening populations for large numbers of polymorphic markers. This method is being widely used in human evolutionary genetic studies (C Bustamante, pers. comm.) and (complemented by more traditional genetic mapping) in studies of the genetic basis of traits that have evolved during animal and plant domestication, as exemplified by dogs (Quignon et al.; C Bustamante, pers. comm.) chickens (Andersson), maize (J Doebley, pers. comm.), and forest trees (Sederoff et al.).

The joint effects of linkage and selection have long been studied theoretically by evolutionary geneticists interested in the evolutionary origin and maintenance of genetic recombination and sexual reproduction. Barton reviewed the population-genetic processes that are thought to be involved, especially the "Hill–Robertson effect," a probable major player in creating an evolutionary advantage to recombination. This involves the fact that two mutations at different loci which increase fitness are likely to be present in different haplotypes, given the finite sizes of natural populations. In the absence of recombination, the spread of a favorable mutation to a high frequency may be hindered by the presence of one or more harmful mutations in the same genetic background. Similarly, an absence of recombination makes it easier for deleterious mutations scattered across the genome to increase in frequency as a result of genetic drift. A new model of this process makes predictions about levels of variability in nonrecombining genomic regions that appear to be consistent with observations on DNA sequence variation in *Drosophila* (Charlesworth et al.).

The evolutionary interactions between parasites and their hosts are an important source of ongoing selection pressures that are thought by many to provide an advantage to genetic recombination. The importance for medicine and agriculture of understanding the biology of pathogens is another reason for the increasing interest in studies of their evolutionary biology. This topic was covered by several contributors. Plant bacterial pathogens such as *Pseudomonas syringae* use the same type III effectors as many animal pathogens for attacking host cells, and their distribution among different strains provides an excellent system for the study of host–pathogen evolution (J Dangl, pers. comm.). The water flea *Daphnia*, with its recently sequenced genome and facility for clonal reproduction, is an unusually favorable system for the dissection of the genetics and evolution of host–parasite interaction, providing strong evidence for interactions between host and parasite genotypes (Allen and Little). The fact that pathogens are often exceedingly specialized with respect to the hosts that they can infect raises important practical and evolutionary questions. These are being tackled using the evolution of RNA viruses on alternative hosts as a model system (Ogbunugafor et al.).

Experimental models of evolution in the laboratory have long been used to test hypotheses in evolutionary biology, dating back to experiments on artificial selection experiments in mice and *Drosophila* (Greenspan). A spectacular example of this is provided by the 48,000 generation experiment on 12 replicate lines of *Escherichia coli*, started from a single isogenic strain (Barrick and Lenski). This experiment has shown how the fitness of a population in a new environment steadily increases, eventually approaching an asymptotic value as the supply of new mutations that cause adaptations to the environment runs out. Because ancestral populations can be kept as frozen samples, these populations provide a unique window on the time course of evolutionary change that is now being explored with next-generation sequencing technology. This allows the tracking of individual mutations that spread through the population and reveals others that rise to high frequencies and then disappear, probably because of Hill–Robertson interference from the other, more successful mutations. Theoretical studies of "adaptive walks" of this kind, which extend Fisher's classic model of adaptive evolution in a multidimensional phenotype space (Fisher 1930), predict that mutations of relatively large effect are likely to be the main players in the first few hundred generations from the start, and this is being confirmed by genetic analyses of several different evolutionary experiments (Bell).

Experimental evolution also is being extensively applied to the evolution of protein molecules. This is especially relevant to the problem of "irreducible complexity" raised by critics of neo-Darwinism such as Michael Behe (pers. comm.), a participant in the Symposium. How can a polypeptide that performs a function requiring a specific combination of amino acids evolve from a sequence that lacks all of them? This question was beautifully answered by experiments challenging cytochrome P450 from *Bacillus megaterium* to perform new functions (Arnold). By gradually increasing the severity of the challenge, and selecting for induced mutations that meet it, it was possible to evolve a fatty acid hydroxylase into a protein that acted as an efficient propane hydroxylase, involving a stepwise accumulation of 23 mutations. Darwin and Fisher would have been delighted!

Another approach to this problem is to use phylogenetic comparisons to reconstruct an "ancestral sequence" of a protein, synthesize it, and express the protein in an experimental system that permits tests of its functional efficiency (J Thornton, pers. comm.). This has allowed reconstructions of the pathways of functional evolution of steroid hormone receptors. More traditional methods for studying molecular evolution have long been applied to the very complex pathway involved in vertebrate blood coagulation, showing that there has been a progressive increase in complexity from early vertebrates to mammals, often involving gene duplications (RF Doolittle).

Again, this work shows that biological complexity can be built up in a series of graded steps, which was also brought out by the paleontological studies described by Kevin Padian (unpubl.) in his Dorcas Cummings Lecture to the public. The human fossil record has been uncovered by discoveries made since Darwin's time, and it provides further evidence of graded evolution, especially for cranial capacity (White). Genetic studies of human populations are yielding increasing insights into population histories, as well as signatures of selection in relation to local environments, from both mitochondrial (Wallace) and nuclear gene (Lambert and Tishkoff) markers. The genetic and paleontological evidence for an African origin of modern humans is now overwhelming, confirming Darwin's insights of 150 years ago. The sequencing of the genome of Neanderthal humans is in progress and will undoubtedly shed further light on many questions in human evolution at the genetic level (S Pääbo, pers. comm.).

The advent of large-scale genome resequencing projects on populations of humans and other species will increase the amount of data on within-species variability

and species differences by several orders of magnitude over the next few years. This presents the new generation of evolutionary biologists with a set of huge challenges: How to organize these data in an accessible fashion, how to interpret them by means of sensible models of the evolutionary processes involved, and how to integrate the results of inferences from model-fitting exercises into programs of experimental work designed to test them. We have in our grasp the potential to answer a large number of questions that have long concerned evolutionary geneticists, especially the interplay among mutation, genetic drift, and natural selection in shaping natural variability and evolutionary divergence at both the genomic and phenotypic levels. The impressive set of posters presented at the meeting, and the talks by the Symposium Fellows, give one great confidence that this challenge will be met.

Evolution is probably the area of biology that probably attracts the most attention outside of the scientific community, and the question of the public understanding of evolution was also well represented at the Symposium. The idea that we are ourselves simply exceedingly complex machines, produced by impersonal evolutionary forces acting over billions of years, is still repugnant to many people, especially in the United States and the Islamic world, where fundamentalist religious beliefs are widely held. It is one of the paradoxes of our time that the country with the greatest concentration of scientific talent in the world is the only developed nation where a large fraction of the population espouses creationism, a doctrine that is tantamount to rejecting the scientific exploration of nature. A series of contributions to the Symposium presented the background to the "Intelligent Design" movement, and the Dover trial that represented a major setback to this attempt to introduce creationism into the U.S. public school curriculum by the back door (Forrest; Miller; E Scott, pers. comm.).

Many questions about the evolution of humans concern mental qualities that seem to divide us sharply even from our nearest primate relatives, especially the use of language and symbolic reasoning. These problems were discussed by several participants (Dennett; M Hauser; S Pinker; both pers. comm.), as well as some provocative extensions of Darwinism to social questions (Ridley; Ferguson). There is an inherent difficulty in studying evolutionary processes when there is no replication of the events involved across independent lineages, as is the case for human language and cognition. There is also no possibility of major experimental manipulations of humans to investigate the genetic control of behavior, in contrast with what can now be done with model organisms (Grant). Ingenious and (sometimes) convincing hypotheses can be proposed, but rigorous tests are problematic. This should not be taken as a reason for questioning the proposition that these aspects of humans have evolved in the same way as other traits, but merely that the nature of the case makes scientific investigation especially difficult. There is, however, hope that the use of genome-wide scans to detect genetic variants associated with individual differences in human behavior and cognition will provide insights into their genetics and the mechanisms involved.

There is a similar lack of evolutionary replication in the origin and early evolution of life itself, but here, laboratory experiments can illuminate the probable nature of the processes involved, with increasing success in providing models of the origins of self-replicating informational molecules, cell membranes, and the translational machinery (Cech; Joyce; Ramakrishnan; Mansy and Szostak).

One aspect of humans that has commonalities with other organisms is our social behavior, in particular "altruism," whereby individual fitness is sacrificed with benefits to others in the social group (this is perhaps less prevalent in human society than we would like to think). The most spectacular examples are found in social insects, where sterile workers comprise most of the members of a colony. The molecular developmental basis of differences among workers in bee colonies is starting to be understood (Toth and Robinson), which should greatly aid in understanding the evolution of these traits. Darwin himself proposed that the adaptations of different types of workers to their roles in the colony, which often reach bizarre extremes (Wilson), are the result of what animal breeders call "family selection": The worker phenotypes enhance the reproductive success of the breeding individuals in the colony, to whom they are usually closely related. This interpretation represents a special case of "kin selection," a process whose importance in social evolution was vigorously defended by Foster. In contrast, Wilson dismissed kin selection and argued that social insects represent superorganisms that have evolved by a form of group selection based on colony-level characteristics. This disagreement probably left the audience somewhat bemused and showed that modern advances have not completely eliminated the ability of evolutionary questions to generate controversy.

Darwin's work went well beyond the evolutionary ideas presented in *Origin*, including a large body of experimental work on plants (Browne). Nevertheless, *The Origin of Species* is his book that captured most public attention. It has, however, frequently been pointed out that Darwin's concept of what constitutes a species was very different from current views. He never arrived at a satisfactory theory of the origin of reproductive isolation, regarded by most modern evolutionary biologists as the primary criterion for speciation in sexual organisms. The species problem was covered by several contributors to the Symposium, although there was regrettably no mention of the spectacular work that has recently been done in *Drosophila* in establishing the molecular genetic basis of reproductive isolation among closely related species and the important role of natural selection in this process (see, e.g., Tang and Presgraves 2009). We are likely to see much more work of this kind, in a wider range of taxa, as more genome sequences become available.

Work toward establishing a systematic database of species identified by "bar coding" using short mitochondrial DNA sequences was described by P Hebert (pers. comm.). Soltis discussed the important role of hybridization followed by polyploidy in plant speciation and documented examples of rapid genomic alterations following very recent events of this kind. Ehrenreich et al. described

the remarkable genetic system in *Caenorhabditis elegans*, where two different haplotypes at a pair of tightly linked genes are present in natural populations. Crosses between strains with different haplotypes result in lethality of one-quarter of the F_2 embryos, as a result of a toxic interaction between the two loci. This represents a type of "Dobzhansky–Muller" incompatibility that is normally associated with divergence between two geographically isolated populations that are on the way toward speciation.

I hope that this summary brings out some of the amazing advances in evolutionary biology that have been made since 1959, which are nevertheless consistent with much of what Darwin proposed in 1859. These advances owe much to molecular biology. But what Ernst Mayr said in introducing the 24th Symposium remains true today (Mayr 1960): "We live in an age that places great value on molecular biology. Let me emphasize the equal importance of evolutionary biology. The very survival of man on this globe depends on a correct understanding of the evolutionary forces and their application to man."

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