Chapter

5

The Developmental Systems Alternative

5.1 Gene Selectionism and Development

In chapter 3 we laid out the case for gene selection, and in the following chapter we discussed a composite "received view" reply. Here we turn to a radical alternative: a view that rejects the replicator/interactor framework itself. *Developmental systems* theorists claim that there is no privileged class of replicators among the many material causes that contribute to the development of an organism—that the entire replicator/interactor representation of evolution is refuted by the facts of developmental biology.

As we noted in section 3.2, Dawkins and Williams assume that genetic resemblances between parents and offspring have a significance that other resemblances do not. Dawkins tries to exclude nongenetic factors from evolutionary biology, as opposed to developmental biology, on these grounds:

> When we are talking about development it is appropriate to emphasize non-genetic as well as genetic factors. But when we are talking about units of selection a different emphasis is called for, an emphasis on the properties of replicators. . . . The special status of genetic factors is deserved for one reason only: genetic factors replicate themselves, blemishes and all, but non-genetic factors do not. (Dawkins 1982, 98–99)

We have already seen that the claim that nothing but genes are replicated in evolution is less obvious than it first seems (3.2). Developmental systems theorists argue that it is simply false.

The developmental systems critique is developed in two main stages. The first is to argue that the gene can be the unit of selection only if the gene plays some distinctive and privileged role in development. The second is to deny that genes play such a role. The main steps of the argument can be laid out as follows:

Step One: Organisms inherit a great deal more than their nuclear DNA. The epigenetic inheritance of nongenetic structures within the cell is a hot topic in current biology. Organisms also behave in ways that structure the broader environmental context of their successors. For instance, many birds inherit their songs through the interaction of their developing, species-specific neural structures with the adult songs to which they are exposed. So an organism inherits an entire *developmental matrix,* not just a genome.

Step Two: The orthodox view of development is that all traits develop through the interaction of genes with many other factors. So genes are neither the only things that are inherited nor the only things that help to build the organism. There is more to evolution than changes in gene frequencies. But genes might still be "privileged causes" of development, which control, direct, or act as an organizing center for everything else. If gene selectionism is to get off the ground, it must demonstrate that genes play some such privileged role.

Step Three: The notion of genetic information and its relatives cannot be made good in a way that singles out genes as privileged causes of development. Every reconstruction of the notion that genes contain information about the outcomes of development turns out to apply equally well to other causes of development.

Step Four: A range of further attempts to draw a distinction between the role of genes in development and the roles of other developmental factors fail. These attempts are either mistaken or overstated (for example, the idea that genes are copied "more directly").

Step Five: Developmental systems theorists conclude that for all their biological importance, genes do not form a special class of "master molecules" different in kind from any other developmental factor. Rather than replicators passing from one generation to the next and then building interactors, the entire developmental process reconstructs itself from one generation to the next via numerous interdependent causal pathways.

In this chapter we assess each step of this argument. We conclude that the argument as a whole has considerable force, and in the final sections we consider what this might mean for the debate over the units of selection.

5.2 Epigenetic Inheritance and Beyond

Developmental systems theorists agree with the normal emphasis on the cumulative nature of selection. But they point out that lineages of organisms

show repetition of many important elements from developmental cycle to developmental cycle. In many species of birds, for example, the juveniles acquire their songs, their preferences for nest sites and nesting materials, and many other aspects of their behavioral repertoires from their parents. Their experience in the egg, as nestlings, and as juveniles is critical to the acquisition of the skills that are normal for their species. In any species in which learning, broadly conceived, is important, there is likely to be this type of flow of information across the generations. It need not involve anything like explicit teaching. Parents structure the learning environment of their young and provide them with information just through their normal, species-specific activities of daily life. So "cultural transmission" in this sense is not restricted to cognitively fancy animals. Indeed, as we shall see, there is an important sense in which we find this phenomenon among the arthropods.

Moreover, the idea that nuclear genes are all an organism inherits in the cells carrying the gametes is simply out of date. To develop normally, the egg cell must contain a great array of complex biochemical machines. Any account of the molecular details of how these machines work would take us well beyond the scope of this book (and of our competence), but they include basal bodies and microtubule organizing centers, cytoplasmic chemical gradients, DNA methylation patterns, and membranes and organelles, as well as DNA. Changes in these mechanisms can cause heritable variation that appears in all the cells descended from that egg cell. These elements of the cell have been labeled *epigenetic* inheritance systems (Jablonka and Lamb 1995; Jablonka and Szathmary 1995). For example, the so-called *DNA methylation system* has excited a great deal of interest recently. It has even been suggested that some behavioral differences between human males and females are due not to genetic differences, but to the inheritance of a methylation pattern. DNA methylation is the attachment of a series of additional chemical groups to a DNA sequence in a sperm or egg by the parent organism. These methyl groups block transcription of any genes to which they are attached. The methylation pattern is replicated by a special methylation copying system in all the cells descended from that sperm or egg. Some recent research suggests that human females methylate a sequence of the X chromosome, so that individuals who get only one X chromosome and get it from their mothers cannot transcribe the genes in that region. Hence certain gene products are denied to all males. Males demethylate that sequence in their sperm cells, so that females get a working X chromosome from their fathers (Skuse et al. 1997).

Developmental systems thinkers extend the idea of inheritance still further. The characteristics of epigenetic inheritance systems within the cell are

shared by many extracellular structures. Some castes of the aphid *Colophina arma* require a growth spurt as part of their life cycle. These, and only these, castes inherit the microorganisms that make the chemicals on which this growth spurt depends (Morgan and Baumann 1994). The morphology of queens and the colony structures of the fire ant *Solenopsis invicta* differ radically between genetically similar lineages of the species because of stably replicated nest "cultures" mediated by pheromones (Keller and Ross 1993). Any queen raised in a colony with a particular culture will found a colony with the same culture, as can be demonstrated by moving eggs from one culture to another. Many parasites, both vertebrate and invertebrate, maintain associations with particular host species over evolutionary time through *host imprinting.* Thus insects of many kinds lay their eggs on the plant species whose leaves they tasted as larvae or caterpillars. Some parasitic finches lay their eggs in the nests of the host species that they imprinted on as chicks (Immelmann 1975). So *host switching* can occur when—once in a blue moon—something goes wrong and a moth, say, lays her eggs on a plant other than the one on which she fed. Usually those eggs are doomed, but occasionally they will survive (perhaps the plant is a new arrival in the region), and that same imprinting mechanism will then ensure that the moths that grow from those eggs return to the plant on which they, not their ancestors, fed. So parents pass on much to their offspring: genes, cellular chemistry, and other cell structures; features of their physical environment (burrow systems, nests, and the like); behavior patterns.

The developmental systems view argues that we should redefine *inheritance* so that every element of the developmental matrix that is replicated in each generation and which plays a role in the production of the evolved life cycle of the organism counts as something that is inherited (Gray 1992). Genes cannot be singled out as the unit of replication on the grounds that they, and they alone, persist through lineages long enough for cumulative selection to act upon them. Lineages can be selected for having good symbionts or being imprinted on a good host, and these features can persist for evolutionarily significant periods of time.

5.3 The Interactionist Consensus

Given that there are many different strands in inheritance, how do they combine to build a new organism? In section 1.4, we introduced the idea of genetic determinism. In its crudest form, genetic determinism is the view that a trait is genetically caused or innate; in contrast, other traits are environmentally caused or acquired. On this view, traits observed in all normal

members of a species, such as mating rituals, would be regarded as innate, while traits that differ widely between individuals, such as preferred foraging sites, are acquired. However, no one accepts this crude division between genetically caused and environmentally caused traits. All traits have both genetic and nongenetic causes. The development of any trait can be blocked by some genetic modification. Equally, barring mutation-induced disaster, nongenetic modifications can stop any trait from developing. Social deprivation of young rhesus monkeys will prevent them from displaying their "innate" sexual behaviors as adults. Yet a rat and a bird will emerge from an identical program of conditioning having learned very different behaviors: their genetic endowment affects what is "acquired."

So it is universally accepted that all biological traits develop as a result of the interaction of genetic and nongenetic factors. But perhaps some traits depend more on genes and less on the environment. It is now common to read that homosexuality, for example, is "substantially genetic," or that schizophrenia may be "partly genetic." Often actual figures are cited. One study might suggest that homosexuality is 30% genetic, another that schizophrenia is 10% genetic. These figures are produced by a statistical technique called *analysis of variance* or *ANOVA*. To perform an analysis of variance, we need a population of individuals, some of whom have the trait of interest and some of whom do not. Some individuals that differ with respect to the trait will also differ with respect to some genes. The more often this is true, the more of the *variance* in the trait can be correlated with that variation in the genes. If every individual with the trait has certain genes and every individual without the trait lacks those genes, then the proportion of the variance accounted for by those genes is 100%. If possession of the trait is random with respect to possession of those genes, then the proportion of the variance accounted for by those genes is 0%.

In many people's minds, the discovery that a trait is "substantially genetic" means that it is substantially genetically determined. The more "genes for" complex human behaviors are reported in the media, the more genetic determinism seems true. But this interpretation is simply wrong. Measuring the amount of variance accounted for by genetic factors does not measure the degree to which a trait is genetically caused or genetically determined (Lewontin 1974). A trait would be literally genetically *determined* if it could not be altered by changing nongenetic factors, a situation that we can be sure never arises. More realistically, a trait may be said to be genetically determined when altering it by changing nongenetic factors is difficult or impractical (if, for example, such changes would always kill or severely deform the embryo). But high scores for genetic factors in an analysis of variance do not

show that it is hard to alter the trait by nongenetic means, and hence do not show genetic determination. They show only that the actual environmental factors in the population under study do not alter the trait, not that no feasible set of environmental factors could alter the trait. One well-known example that illustrates this distinction is the disorder called phenylketonuria (PKU), which causes mental retardation. It is caused by a mutation that results in the bearer's inability to metabolize the amino acid phenylalanine. Under standard conditions, possession of the PKU mutation accounts for 100% of the variance between those who suffer PKU retardation and those who do not. However, PKU can be effectively treated by feeding people with the PKU mutation a special diet low in phenylalanine.

As we noted in discussing heritability in section 2.2, a uniform environment tends to increase the score of genetic factors in an analysis of variance. Conversely, genetic uniformity will increase the score of nongenetic factors (see box 2.2). Whenever a number of causal factors interact to produce an outcome, we should expect the effect of changing one factor to depend on what is happening to the other factors. To establish genetic determinism we would need high ANOVA scores for genetic factors across a wide range of values of all the other factors that typically play a role in development. Only if changes in those other factors had little effect on the relationship between genes and trait would it be proper to speak of the trait as genetically determined.

The points made so far are fairly uncontroversial—they make up the *interactionist consensus* in current biological thought. While nothing in the interactionist consensus makes genetic determinism (in the sense just described) impossible, there is plenty there that makes it unlikely. In the interactionist view, genes are "context-sensitive difference makers." They produce their effects by adding a physical product to a complex network of causes consisting of other genes and their immediate products, the other constituents of the initial cell, and all the inputs of materials and energy to the developing organism. The effect of one cause on the final outcome is mediated by all the others. Except in those cases in which having a nonfunctional gene is a disaster without remedy, it is unlikely that a change in an individual gene will produce the same effect no matter what changes occur in the other causes. The other causes, after all, include factors that affect *whether* the gene will be transcribed, *when* it will be transcribed, and *which* of the various possible final products will be made from its transcript (6.3, 6.4). In section 4.3 we saw that it is possible for a gene that is normally a "gene for" a trait to become a "gene for" its absence.

The argument so far creates a substantial challenge for gene selectionism.

Gene selectionism holds that evolution is nothing but the differential replication of genes. But genes are not the only things an organism inherits. Nor, as we have just seen, are they the only things that go into building an organism; on this, gene selectionists agree. So the gene selectionists need to show that the other elements that change over time through natural selection are somehow subordinated to the genes. They must demonstrate that, among the many inherited elements of the developmental matrix that combine to build an organism, the genes enjoy some special, privileged status. Otherwise, evolution will be the differential replication of the whole developmental matrix, not just the genes. The normal way of establishing this privileged status is to argue that while there are many *material causes* of development, genes are the only things that transmit *information* from one generation to the next.

5.4 Information in Development

In his later work, George C. Williams, the originator of the evolutionary gene concept, redefined evolutionary genes as units of pure information:

> DNA is the medium, not the message. A gene is not a DNA molecule; it is the transcribable information coded by the molecule. . . . the gene is a packet of information, not an object. (Williams 1992, 11)

This completes the drive to make the evolutionary gene concept independent of molecular biology, on which we commented in section 4.1. Williams's idea explains the sense in which it is widely thought that the organism gets nothing from its parents but its genes. The genes are the only things that contain information: they are the blueprint or program for building the organism. Genetic changes are changes in this plan and so constitute real evolutionary change. The other material causes of development are only building blocks, which are assembled according to the genetic plan (Lorenz 1965). Since changing the building blocks cannot alter the plan, nongenetic changes can only disrupt development by causing poor execution of the plan. Hence epigenetic inheritance is of no great evolutionary significance. The building blocks are not part of the evolving plan, so it is of no importance whether they are passed on by the parents or found in the wider environment.

Susan Oyama argues that the whole notion of developmental information that is transmitted from one generation to the next should be abandoned. Instead, she argues, the information manifested in an organism's life cycle is itself reconstructed in development; thus she speaks of the *ontogeny of information* (Oyama 1985). To understand Oyama's ideas, it is useful to see them

as analogous to the theory of memory according to which a rat that has learned to run a maze does not have in its brain a map of the maze with the route marked out. Instead, the rat has learned cues that, in conjunction with the maze itself, suffice to reconstruct the route as the rat passes through the maze. Just as the rat constructs its route using information from cues in the physical world and traces in its own memory, development in the embryo relies on cues in the developmental environment working with traces in the embryo itself. There is no developmental plan within the embryo.

However, a much weaker position than Oyama's would be strong enough to defeat the view that genes are privileged causes of development because they alone convey information. Developmental systems theorists argue that in any sense in which genes carry developmental information, nongenetic developmental factors carry developmental information too. If they are right, then gene selectionists will either have to come up with an alternative account of why the transmission of genes across the generations has special significance (we shall come to some suggestions shortly), or concede that both genes and other information carriers have this special significance.

So let's turn to the idea of the genome as a program. There are essentially two concepts of information, which we can label *causal* and *intentional*. *Causal* notions of information derive from the mathematical theory of communication, the discipline originally invented to design efficient telephone systems in the 1940s (Shannon and Weaver 1949). Mathematical information theory studies only the quantity of information in a physical system; it says nothing about what the information is about. The quantity of information in a system can be understood roughly as the amount of order in that system, or the inverse of the entropy (disorder) that all closed physical systems accumulate over time. However, there is a closely related causal notion of information content. Information flows over a *channel* connecting two systems: the *receiver,* the system that contains the information, and the *sender,* the system that the information is about. There is a channel between two systems when the state of one is systematically causally related to the state of the other—when we can infer the state of the sender from the state of the receiver. All scientific instrumentation is designed to ensure a reliable flow of information in this causal sense from sender to receiver. Thus there is a channel connecting a barometer to the state of the atmosphere because the state of the barometer is reliably caused by the state of the atmosphere.

When the states of two systems are reliably related, but not directly causally related, there is a *ghost channel* between them. There is a ghost channel between two copies of this book—you can reliably find out what is in our copy by reading your own. The channel between the barometer and the weather is also a ghost channel, because the barometer reading "rain" does

not cause rain, and the rain does not cause the barometer to read "rain." Instead of causing one another, both are caused by a drop in atmospheric pressure.

The existence of channels depends on the factors that connect the sender to the receiver: the *channel conditions.* There is a channel between the television studio and the television screen whose channel conditions include the machinery at the studio, the relay stations, the atmospheric conditions, the antennae, and your TV set. So what you see on the read-out device of an instrument causally depends on the state of the source and the states of the channel conditions. Think of a very simple instrument, a doorbell. The silence, as distinct from the buzz, of a doorbell depends on (1) whether the buzzer has been depressed, (2) whether the battery is charged, and (3) the condition of the wiring. We regard the buzzer as the source and (2) and (3) as channel conditions. But that is a fact about *us.* The sender/channel distinction is a fact about our interests, not a fact about the physical world.

Channels, whether real or ghost, can contain noise. The ratio between *noise* and *signal* is a measure of how reliably states of the receiver depend on states of the sender. So as noise increases, the amount of information at the receiver about the sender goes down. Cheap barometers are noisier than expensive ones: many of their readings are noise rather than signal.

The idea of information as systematic causal dependence can be used to explain how genes convey developmental information. The genome is the signal and the rest of the developmental matrix provides channel conditions under which the life cycle of the organism contains (receives) information about the genome. If we hold the developmental history of organisms constant, then their behavior carries information about their genes. We can tell if someone has the dyslexia mutation by whether they become dyslexic given a normal education. But if this is the sense in which genes convey information, it does not single them out from other developmental causes. It is a fundamental fact of information theory that the role of signal source and channel condition can be reversed. In this conception of information, information is just covariation. So if we hold the other developmental factors constant, genes covary with, and hence carry information about, the phenotype. But if we hold all developmental factors other than (say) nutrient quantity constant, the amount of nutrition available to the organism will also covary with, and hence also carry information about, its phenotype. Biologists exploit this fact when they use a clonal population of plants planted across a landscape to measure variation in some environmental factor. Natural selection exploits this fact when different castes are produced in different conditions. A clone of genetically identical aphids is not necessarily morphologically identical: in some species, some individuals will develop into warrior morphs that protect the others. A constant genetic channel is used to transmit information from nongenetic factors to the next generation of organisms. So genes have no distinctive role as bearers of causal information.

Another way to see the parity between genes and other developmental causes is to return to the ideas of noise and signal. So far, our examples have relied on holding every factor but one constant so as to get a pure signal. But typically, many factors are changing at once. What is noise and what is signal depends on what you are interested in. When you see a white dot passing across your television screen, it may be a tennis ball (signal) or it may be atmospheric interference or the cat sharpening its claws on the aerial (noise). But nothing in nature dictates that one dot is signal and the other is noise. Typically, we want desperately to know what happened at Wimbledon and care little about what the cat is doing on the roof. So to us, dots caused by balls are signal and dots caused by the cat are noise. A television engineer, however, will tune the television to receive a constant "test card" transmission, so that irrelevant noise from Wimbledon will not interfere with the important signals from the guts of the TV that are being received by the screen. Similarly, a geneticist may want to raise monkeys under constant conditions so as to detect genetic mutants, but a developmental biologist may want to raise cloned monkeys to detect the effects of different maternal care or social interactions. In causal terms, information is covariation, and all the factors with which development covaries are sources of developmental information.

The importance of channel conditions has been underscored by recent developments in molecular biology. The DNA sequence of a gene corresponds to the sequence of amino acids in the proteins made from that gene. This is the famous *genetic code.* But this code operates through an intermediate stage: the DNA is first used as a template for an RNA sequence, *messenger RNA.* RNA, not DNA, is directly involved in the assembly of amino acids into proteins. It is normal for much of the sequence of messenger RNA transcribed from the gene to be cut out and discarded as *introns* before the messenger RNA is translated into a protein. Different proteins can be made from one gene by cutting out different introns, a phenomenon that turns out to be very common. Which protein is made from a gene at a given time in a given part of the body depends on the overall chemical state of the cell, which can be influenced by many elements of the developmental matrix. So even the fundamental idea that the series of bases in DNA is a linear "code" for a protein needs to be stated carefully; even this depends on channel conditions. Only a DNA sequence plus just the right cellular context contains

enough information to specify the structure of a protein, let alone to specify a phenotypic trait (see 6.3, 6.4 for more detail).

The other concept of information is *intentional information* (sometimes called *semantic information*). Many of the thoughts possessed by intelligent beings like ourselves are about things with which they have only the most tenuous causal connection (e.g., thoughts about distant galaxies) or about things that do not exist (e.g., thoughts about phlogiston or Pope Joan). The relation between thoughts and things is called *intentionality* or *aboutness.* Thoughts contain intentional information *(intentional content)* about the objects of thought. Intentional information seems like a better candidate for the sense in which genes carry developmental information and nothing else does. If genes have intentional content, then they mean the same thing no matter what the state of the rest of the developmental matrix. When other conditions change, the content of the genes is merely misinterpreted. If other developmental causes do not contain intentional information and genes do, then genes do indeed play a unique role in development.

The idea that genes have meaning in something like the way that human thought and language have meaning is lurking in the background in many discussions of genetic information. For example, it is often said when an organism develops different phenotypes under different environmental conditions that the message of the genes is "Do this in circumstance A, do that in circumstance B" (a *disjunctive genetic program*). If genetic information is causal information, then this is just a quirky way of saying that changing the channel conditions changes the signal. A distinctive test of intentional or semantic information is that talk of error or misrepresentation makes sense. A map of Sydney carries semantic information about the layout of Sydney. Hence it makes sense to say of any putative map that it is wrong, or that it has been misread. Error and misrepresentation make no sense in the context of the purely causal notion of information. In the causal sense, a doorbell that rings because of corrosion in the wiring has not generated a false alarm. It is merely "reporting" a change in the channel conditions. Strikingly, genetic information is often described as if misinterpretation made sense. So no one says that the human genome encodes the instruction "when exposed to the drug thalidomide, grow only rudimentary limbs." This really would be the instruction if we were talking about causal information. When the channel is contaminated by thalidomide, human genes really do, sadly, contain this causal information.

To reiterate, according to the causal conception of information, there is no such thing as a channel that misinterprets the causal information in a signal sender. Any talk of the genes being misinterpreted, or of the information in the genes being ignored or unused, is a shift from the purely causal notion of information toward something like the intentional notion. So one way to make sense of the idea that some developmental pathways are programmed while others are misreadings of the program is to suppose that genes contain intentional information rather than causal information: information that remains the same when the channel conditions change.

Unfortunately, it is so hard to see how intentional information could be a property of physical systems that this has become one of the great stumbling blocks of contemporary philosophy of mind! The apparently magical nature of intentional information is one of the major objections to a materialistic account of thought. After all, how can a thought be about something that does not exist? Hence arguments for the special status of genes that rely on attributing intentionality to them face a very serious problem. The difficulties faced by attempts to "naturalize" intentional mental content form a vast and expanding literature, which is impossible to summarize here. But we will mention one such idea, for it shows that a successful attempt to remove the magic from intentionality might well restore the parity between genetic and other causes that the appeal to intentional information is being used to avoid.

One of the most popular attempts to explain intentional content in scientific terms appeals to the evolution of the mind. According to the *teleosemantic* theory of intentional content, a thought is about the things that evolution has designed it to be about. When a rabbit thinks PREDATOR, its thought may carry very little causal information about predators, because most such thoughts are false alarms caused by wind or shadows. The teleosemantic theory suggests that the thought PREDATOR has the intentional content that there is a predator here and now because it was produced by mental mechanisms selected for detecting predators. This theory can be applied to genes, yielding the conclusion that a gene contains information about the developmental outcomes that it was selected to produce. There are many possible objections to this idea. Many genes have important effects that they were not selected to produce. But these objections are not our concern here. We merely point out that many other means through which parents influence their offspring have selection histories too. These other elements of the developmental matrix have been selected for their developmental effects, hence they too can be said to contain information about the effects they were selected to produce. There seems to be a trade-off between defining a concept of information that is free of magic and defining one that applies to genes but not to other developmental causes. We return to this idea at the end of the chapter.

5.5 Other Grounds for Privileging Genes

Developmental systems theory argues for "parity" between genes and other developmental causes. It does not deny that nucleic acid sequences play a unique molecular role. It only denies that the differences between the role of DNA in development and the roles of other biological factors justify placing a distinction between genes and everything else at the heart of a theory of development. Nucleic acid sequences and phospholipid membranes both have distinctive and essential roles in the chemistry of life, and in both cases there seems no realistic substitute for them. However, the facts of development do not justify assigning DNA the role of information source and controller of development while inherited membrane templates, or methylation patterns, or pheromonal nest cultures get the role of "material support" for reading DNA.

Genes have been held to be unique on several grounds, the most important of which we considered in the last section. We cannot exhaustively survey the other possibilities, but here is a sketch of some of them, with brief indications of how developmental systems theory deals with them:

- *Genes are unique in their directness of replication.* Recent research casts doubt upon this claim. The accuracy of gene copying is purchased at the cost of a complex and mediated replication process. Now that the molecular process of gene replication is being described in detail, it seems at least as complex as many of the epigenetic inheritance mechanisms (Griesemer 1992a).
- *There is a causal asymmetry between the genes and other developmental factors.* The idea here is that every extragenetic element of the cell depends on the genes. There can be no membranes without genes for their constituents. Host imprinting events and maternal care also number gene products among their causes. So ultimately, everything depends on genes. This is one of the most popular responses to the idea of epigenetic inheritance. But the replication of the germ line genes is equally dependent on the reliable reproduction of a host of nongenetic factors. There can be no genes without membranes, for genes cannot exist without membranes, and gene products destined for membranes must be assembled using an existing membrane template. It is of no use to claim that all cellular conditions have genes among their causes, because every case of gene activation has cellular conditions among its causes. We cannot show that everything is in the genes by tracing the ramifying tree of causes back and stopping on each branch only if we reach a gene. We might equally arbitrarily decide to stop only at nongenetic causes and declare that developmental information is "in the environment"! It is possible, of course, that if we traced replicating DNA or RNA back far enough, its replication would be the sole lifelike process. But, first, this is by no means certain to be true (15.3), and second, even if it is, those early replicators would bear little resemblance to current ones.
- *Causal responsibility for variance distinguishes the role of the genes.* Genes can be selected by virtue of their effects. Relativized to typical background conditions, the substitution of one gene for a rival allele may yield a boldly striped organism. So that gene is the "gene for bold stripes." But the same comparison between variants, relativized to a normal background, gives us incubation temperatures for traits, cellular chemicals for traits, and so on.
- *Replicators must be reliably re-made, generation by generation.* Genetic replication is high-fidelity replication. But fidelity does not single out the genes, for they are not alone in reappearing with great reliability. It is also worth noting that the fidelity of genetic replication is overestimated by looking only at the intrinsic properties of genes—by considering only the preservation of the base sequences. Genes' relational properties are also of great causal importance, and these are not nearly so reliably copied to the next generation. Crossing-over in meiosis is a major source of evolutionary change, as are deletions, insertions, and translocations and inversions of the DNA sequence.

The search for facts about genes that distinguish them from all other systems of heredity and developmental causes continues. John Maynard Smith and Eos Szathmary have distinguished between "limited" and "unlimited" heredity systems (Maynard Smith and Szathmary 1995). They claim that only genes and memes (human ideas) display "unlimited" heredity: the possibility of limitless, open-ended evolution. Developmental systems theorists are unimpressed, citing pheromonal "cultural transmission" in eusocial insects as an inheritance system comparable to memes (and much better understood).

5.6 Developmental Systems and Extended Replicators

The developmental systems critique of gene selectionism concludes that nothing singles out genes as being sufficiently unique to justify the replicator/interactor distinction. Genes do not form a special class of "master molecules" different in kind from any other developmental factor. Hence genes are not the replicators. If anything, whole developmental systems are the replicators, but then the distinction between replicator and interactor is at best unclear. This argument is a most interesting and serious challenge to gene selectionism, and one of us (Griffiths) accepts it.

The positive proposal of the developmental systems theorists is that the

fundamental unit of evolution is the life cycle. A life cycle is a developmental process that is able to put together a whole range of resources in such a way that the cycle is reconstructed. The matrix of resources that create a life cycle is the "developmental system" from which the theory takes its name. Life cycles form a hierarchy of evolutionary units similar to that described by more conventional hierarchical views of evolution (2.3). A "selfish gene" like a transposon has its own life cycle, and variants on this life cycle compete with one another. Organisms have life cycles, and so do groups like ant colonies. Variants on these life cycles also compete with one another. In this respect, developmental systems theory offers a vision of evolution similar to the hierarchical views of Elliott Sober and David Sloan Wilson, which we will encounter in chapter 8.

A developmental system is a very complex entity, raising the question of how a biologist could actually study such an object. Opponents of the developmental systems view see it as unmanageably holistic. If no element within the developmental system is more important than any other, then perhaps to understand the role of *any* element we have to understand the role of *every* element. But that seems to undercut the standard methodological strategy in science of understanding a system one element at a time. Defenders of the developmental systems view point out that in actual research, a biologist usually chooses to assume that many elements of a developmental system stay constant over time and studies the change over time in a few chosen elements. This approach simplifies a reality in which change over time in any one element is coupled to change over time in many others. Such research strategies are familiar from traditional evolutionary studies, in which biologists try to study change over time in a phenotypic trait without considering how all the other traits on which its fitness depends are changing. The success of such "atomistic" approaches depends on the actual degree to which the fitness of alternative forms is constant across contexts.

One proposed advantage of the developmental systems approach is that it allows the biologist to study change over time in elements of the developmental matrix or the life cycle that are not parts of the traditional phenotype—for which there is no gene. She can model, for example, the evolution of competing alternative pheromonal nest cultures or competing alternative methylation patterns. Another proposed advantage is that as a theoretical framework, the developmental systems approach continually draws attention to the interdependence of elements of the system, whereas gene selectionism deliberately thrusts it into the background. This, of course, is the flip side of the heuristic argument for gene selectionism: that it draws attention to the fact that the integration of biological organizations may break down due to competition between their parts (3.4).

There is at least one possible response to the developmental systems challenge, which is endorsed by one of us (Sterelny), but it involves a considerable revision of the gene selectionist idea. This response is the so-called *extended replicator* theory. The idea is to rescue the notion of genetic information in something like the way outlined at the end of section 5.4. The genome really can be said to *represent* developmental outcomes because representation depends not on correlation, but on function. The plans of a building are not the primary cause of a building. The relationship between plan and building is indirect. But plans do play a distinctive functional role in the construction of a building. The role of the plan is to make sure that the building comes out as planned. That is not the function of a bag of cement. Similarly, replicators are designed mechanisms: their biofunction is to contribute to the process through which phenotypes and genotypes reproduce themselves. Replicators play a privileged role in the developmental matrix because they are designed copying mechanisms. Some parent/offspring similarities result from elements of the developmental matrix that have been selected to produce those similarities: those elements are replicators. Replicators exist because they produce those similarities; that is what they are for (Agar 1996; Sterelny, Smith, and Dickison 1996). That is why they have the function of producing that phenotype, and hence why they represent that phenotype. So an informational idea of a replicator can be preserved. A consequence of this argument is an extension of the class of replicators. In this view, the full suite of developmental adaptations emerge as replicators. The genes are paradigmatic replicators, but not the only ones. Most of the extragenetic copying mechanisms that we have mentioned in this chapter are also replicators.

5.7 One True Story?

The debates over gene selection and its alternatives raise a difficult overarching problem. Most of the participants agree that each of these views can give some account of almost every feature of evolutionary history. There is no very marked empirical difference among them, as there was, for example, between Darwin's theory and its predecessors, or between the "modern synthesis" of Darwin and Mendel and older non-Mendelian versions of Darwinism. Heterozygote superiority does not refute gene selection in favor of the organism as the unit of selection (3.3), and extended phenotype examples do not turn the tables on the received view (3.4). We have just seen that nongenetic replication does not straightforwardly refute gene selection, but rather forces it to take more seriously its own formal definition of a replicator. If this is true, then what is the status of these disagreements? At times,

gene selectionists seem to be claiming that their view is the only right view of evolution. But many of the arguments for gene selection (and other rivals of the received view) are heuristic. They allow us to see certain similarities more easily, help us to avoid errors we could easily make, and make us less likely to overlook important phenomena. These arguments suggest an alternative conception of gene selectionism. There are a number of more or less adequate descriptions of evolution, but the gene's eye view offers methodological advantages over its rivals, at least for some evolutionary questions. This question of whether disputes are factual or heuristic will arise as well about other rivals of the received view.

Further Reading

5.1 Developmental systems theory grew, not surprisingly, out of developmental biology and developmental psychology, perhaps beginning with Daniel S. Lehrman's critique of the ethological notion of instinct (1953) and continuing in, for example, Lehrman 1970, Gottlieb 1981, and Stent 1981. The work of Patrick Bateson (1976, 1983, 1991) has been important in this tradition. Lickliter and Berry (1990) have written a useful paper explaining why developmental biologists have always been frustrated with the genetic program concept. Susan Oyama's *The Ontogeny of Information* (1985) is regarded by many as *the* book of the developmental systems tradition. A new edition has just been published by Duke University Press, along with a volume of Oyama's collected papers. Griffiths and Gray (1994) attempt to state systematically the implications of the developmental systems approach for evolutionary theory. Their paper is reprinted in Hull and Ruse 1998, which has a good selection on developmental biology as well as units of selection. Gray 1992 is an excellent general introduction to the developmental systems approach, and Gray 1997 discusses further implications of these ideas. Schaffner's paper (in press) is an important attempt to assess the validity of the developmental systems critique of "gene-centered biology." It is accompanied by a number of useful peer commentaries.

5.2 The mechanisms of epigenetic inheritance are reviewed by Jablonka and Lamb (1995) and Jablonka and Szathmary (1995). These papers put a radical spin on these discoveries, while Maynard Smith and Szathmary (1995) play down their radical implications.

5.3 Lewontin (1974) makes a classic presentation of the pitfalls of partitioning traits into genetic and environmental components. A similar view is presented by Sober (1988a). Lewontin's more radical views can be found in

Lewontin 1982b, 1983, and 1991. Kitcher (in press) has written an important paper rejecting Lewontin's later views and defending the interactionist consensus. The defense of the "gene for a trait" locution by Sterelny and Kitcher (1988) is relevant here, and is attacked from a developmental systems perspective by Gray (1992).

5.4 In addition to Oyama, Griffiths, and Gray in the works cited above, Johnston (1987) rejects the notion of genetic information, as does Sarkar in two very substantial and important papers (1996, 1997). Maclaurin (1998) mounts a defense of genetic information. Nijhout (1990) has written a useful paper on the lack of fit between the program metaphor and actual molecular processes. Fox-Keller (1995) provides an extended but very readable discussion of the same topic. Moss (1992) also focuses on whether the idea of a genetic program has any basis in molecular reality. Chadarevian (1998) traces the growing disillusionment with the program concept in one field of molecular biology.

The literature on naturalizing intentional content is enormous. A quick introduction to the various alternatives is chapter 6 of Sterelny 1990. The first attempt to analyze intentional content in terms of causal information was made by Dretske (1981). Dretske 1983 is a useful summary of his theory together with peer commentary. The problems facing Dretske's theory are surveyed by Godfrey-Smith (1989, 1992). Millikan 1989a is a brief introduction to "teleosemantics"; its problems are surveyed in Godfrey-Smith 1994a, Neander 1995, and Godfrey-Smith 1996.

5.5, 5.6 For a good introduction to the complexity of the gene, and the indirectness of genetic copying, see Fogle 1990. The idea that genes are copied more "directly" is critiqued by Griesemer (1992b). Sterelny, Smith, and Dickison (1996) accept much of the critical case made by developmental systems theorists, but argue for the retention of the replicator concept in a revised and more general form. Griffiths and Gray (1997) reply to this paper; the ideas in it are developed further by Godfrey-Smith (in press-a).

5.7 Dawkins appears to change his mind, quite frequently, on whether gene selectionism is first among equals, or the only right view. In Dawkins 1982 he is pluralist, but both Dawkins 1976 and Dawkins 1989b seem less concessive. The pluralist position is defended by Sterelny and Kitcher (1988), Dugatkin and Reeve (1994), and Waters (1994a). Pluralism in philosophy of biology in general is defended with gusto by Dupré (1993) and attacked with equal vigor by Hull (1997; in press).

Box 6.1 What Is an Allele?

Mendelian genetics defines genes, and hence variants of the same gene, through their effects on phenotypes rather than by appeal to their intrinsic physical structures. So when do we have two genes, each of which may exist in a variety of forms? When do we have different alleles of one gene? Since genes can affect more than one trait, we cannot assume that a gene that affects, say, antenna structure in fruit flies is distinct from one that affects their wing length.

Genetic complementation was a central technique in answering this question. Suppose we have two mutant flies: one with short wings, and another with wrinkled antennae. We wish to know whether we have two different mutated alleles of the same gene or mutant forms of two different genes. Mutant forms of different genes (typically) *complement* one another. That is, if we cross the short-winged fly with the wrinkled-antenna fly, and the result is phenotypically normal offspring, we can infer that the mutations are of distinct genes at different loci. We have discovered that the genes are *complementary*. The phenotypically normal offspring result because the gametes from the parent with wrinkled antennae have an unmutated, *wild-type* allele for wing length, and the gametes from the short-winged parent have an unmutated, wild-type allele for antenna form. So the offspring get one unmutated allele for each gene, and are hence phenotypically normal. The offspring are heterozygotes at both loci, with the normal (wild-type) allele dominant over the mutant allele. Clearly, this explanation of why the offspring are normal assumes that the mutations were of separate genes, hence the inference from complementation to alleles of distinct genes. On the other hand, if the hybrid generation is phenotypically unusual, we can infer that we have two mutations of the same gene, and hence two different alleles of the one gene.

patterns of parent/offspring similarity manifested in an organism's phenotype. This program is sometimes known as *transmission genetics*. The debate about human intelligence is one particularly controversial example of such studies.

Shortly after the rediscovery of Mendel's work, a second closely related program developed: an investigation into first the cellular and then the molecular basis of heredity. While the molecular basis of hereditary factors—protein versus nucleic acid—remained in dispute until the mid-twentieth century, their cellular basis in chromosomes was soon discovered. As early as 1903, Walter Sutton showed that meiosis explains our second principle, Mendel's *law of segregation*. For meiosis results in each gamete receiving just one of a homologous pair of chromosomes. Somewhat later, in T. H. Morgan's famous fly lab, the discovery of the physical location of genes on chromosomes undercut principle 5, the *law of independent assortment*. When genes are located on the same chromosome, the inheritance of one is not independent of the inheritance of the other. Further on down the track it was discovered that nucleic acids were the critical molecules making up the genes. Then, in 1953, James D. Watson and Francis Crick developed the famous double helix model of the structure of DNA. Since then, discoveries have come thick and fast.

How, then, might these theoretical programs be related? One possibility is the *displacement* of one program by another—that is, one program can show that another is simply mistaken. The geological program of plate tectonics displaced the conception of earth history in which the position of the continents was taken to be fixed. Much more controversially, Paul and Patti Churchland argue that folk psychology is being displaced by the neurosciences. It was once expected that folk psychological explanations of behavior could be "reduced" to neurophysiological explanations. The idea was to define the concepts of folk psychology—moods, emotions, and cognitive states—in neurophysiological terms. Fear, for example, might turn out to be a specific form of arousal of the autonomic nervous system. Most philosophers of mind are physicalists and think that there is nothing to the mind except the physical brain and the wider physical context it inhabits. However, it is now generally accepted that though the emotions do depend on the physiology of the nervous system, they do so in complex ways that vary from individual to individual and over time. So there is wide agreement that psychological concepts like belief and desire cannot be defined in neuroscientific terms. The Churchlands take this to be a symptom that there is something wrong with folk psychology. In their view, the failure of reduction suggests that the neurosciences should displace folk psychology (P. Churchland 1986; P. M. Churchland 1989).

A second possibility is that one program *incorporates* or absorbs the other—that the first is shown to be just a special case of the second. Planetary motions in the solar system are well described by Kepler's three laws of planetary motion:

1. The orbits of the planets are ellipses with the sun at a common focus.

2. The line joining a planet to the sun sweeps out equal areas in equal periods of time.

3. The squares of the periods of any two planets' orbits are proportional to the cubes of their mean distance from the sun.

Reduction takes place when such laws are shown to be a special case of a more general system of laws. Thus Kepler's laws were shown (with minor corrections) to be a special case of Newton's laws of motion. They can be deduced from, and hence are reduced to, those more general laws. As we shall see, "reduction" is an ambiguous notion, but construed this way, it explains why nothing is lost in the move from the old theoretical framework to the new one. The first theoretical framework is shown to have limited validity by its successor framework; it is incorporated within its successor.

Displacement and incorporation should probably be seen as two ends of a continuum rather than two sharply distinct fates. The fate of Newton's theory is often seen as intermediate between incorporation and displacement. Newton's theory correctly predicts how objects move in space and time at low speeds. At these speeds, the predictions of a theory in which an object has an absolute location in space and time are almost exactly the same as those of a theory in which an object's location is relative to the observer's frame of reference. Relativistic physics is both more accurate and covers a wider array of cases than Newtonian mechanics, but Newton's framework is shown to have some partial validity by its successor.

A third possibility is that two programs can be *integrated*. The classic theory of gases describes the lawlike relationships between observable quantities such as pressure, volume, and temperature. The kinetic theory of gases explains these relationships as the effect of random movements of large ensembles of molecules, each with a quantity of kinetic energy, which it can transfer by impact to other molecules. The explanation of the laws in terms of molecular motion supports the claim that gases are "nothing but" ensembles of molecules in motion. The ontology of the first theory—gases, heat, and pressure—is reduced to the ontology of the second theory—molecules and kinetic energy. We have here a second concept of "reduction": the objects described by one theory are "reduced to" the apparently very different entities postulated by another theory. The classic theory of gases relating pressure, volume, and temperature is sometimes called the *phenomenological* theory of gases because the properties it deals with are observable phenomena. A reduction in this second sense explains the regularities among these observable properties by appeal to the properties of their unobservable constituents.

The distinction between incorporation and integration is not sharp. If the ontological reduction is simple—if there are definitions or bridge laws linking the concepts of a reduced theory to the concepts of a reducing theory—then integration can turn into incorporation. The chemical property of valency, which measures the capacity of an element to form compounds with other elements, turns out to have a straightforward physical basis in an atom's configuration of electrons. Valency is definable in physical terms. So some chemical generalizations about the combinatory power of atoms will turn out to be special cases of physical principles about electron bonds. They can be deduced from physical generalizations via these bridge laws or definitions. Usually, however, it is at least practically necessary to continue to use phenomenological theories. Trying to calculate the efficiency of a heat pump in a freezer by tracking individual molecules would be a thankless task. And, as we shall see, there can be more fundamental reasons that block incorporation.

Prima facie, the relationship between molecular and Mendelian genetics includes elements of both incorporation and integration. Molecular mechanisms, we might suppose, explain the regularities in parent/offspring similarity revealed in Mendelian genetics. Molecular genetics seems to be a superior and more general successor to Mendelian genetics. Mendel's original laws are reasonably accurate in a limited range of cases because some of the DNA segments described by modern molecular biology are passed on from one generation to another in roughly the way Mendel postulated. When Mendel's laws are not honored, the new theory can explain what is happening instead. These considerations suggest partial incorporation. Molecular genetics also seems to reduce earlier genetic theories ontologically. Surely there is nothing more to genes than the DNA studied by molecular biologists? Classic Mendelian genetics is a phenomenological theory, for it involves observable patterns in the inheritance of phenotypic characteristics. Just as the phenomenological theory of gases, relating the observable quantities of heat, pressure, and volume, is explained by features of their microscopic constituents, so too are the generalizations of classic Mendelian genetics explained by microscopic constituents of genes. Yet for the same reasons that the phenomenological theory of gases remains useful in practice, transmission genetics retains some practical value.

No one doubts that there is something right about this picture of the relationship between Mendelian and molecular genetics. Everyone agrees that the genetic material is made up of DNA and associated molecular structures, and that the behavior of these molecular structures underlies the regularities observed by earlier geneticists. However, there is an influential group

of philosophers of biology, starting with Hull (1974), who think that the relationship between classic genetics and molecular biology is vastly more complicated than the parallels with heat, valency, or planetary motion suggest. Over this chapter and the next we shall focus on the relations between molecular and Mendelian genetics. In this discussion, the following themes will all be prominent:

1. To what extent does molecular biology vindicate the central ideas of Mendelian genetics, explaining the molecular mechanisms that underlie the patterns of similarity and difference among relatives? To what extent does molecular biology require a revision of these ideas?

2. To what extent can transmission genetics and molecular genetics be developed independently of each other? The chemical property of valency is linked via a bridge law or definition to the configuration of an atom's electrons. According to the antireductionists, the concepts of transmission genetics are not definable in any comparable way. Molecular biology illuminates many aspects of earlier genetic theory, but in complex and indirect ways. Mendelian genetics contains theoretical concepts, such as the idea that one allele is "dominant" to another, whose explanation in molecular biology varies case by case. The idea of dominance has no single, natural correlate at the molecular level. Furthermore, molecular biological explanations often refer to the wider cellular context in which molecular events occur. This seems to run counter to the idea that the behavior of larger entities is being explained in terms of their smaller constituents. So, although the transmission of similarity from parent to offspring depends on molecular mechanisms and their context, these patterns can be studied in relative independence from molecular biology. The two theories are linked by the fact that in any given case, we can explain the observable similarity between parent and offspring in molecular terms, but since these explanations vary from case to case, their integration is not tight.

3. Entwined with these specifically biological themes are more general ones about the right way to conceive of the relationship between scientific programs. Here the general issue of *reduction* looms large. As we have already noted, "reduction" is a many ways ambiguous notion. Three ideas, at least, are in play:

   a. An idea that historically has been very prominent in the discussion of reduction is the idea of *theoretical unification*. According to this conception, the aim of science is to develop systems of laws or generalizations. Particular branches of science are characterized by the laws or generalizations that they discover. We have already seen an example in planetary science, Kepler's three laws of motion. Theoretical unification was achieved when these laws were shown to be, with minor corrections, a special case of Newton's laws of motion. More controversially, and with much more correction, Newton's laws are seen as a special case of relativistic laws. Many philosophers of science interpret the relations between the generalizations of chemistry and those of physics in the same way. The generalizations of chemistry are shown to be special cases of those of physics with the aid of various bridge laws defining chemical properties in physical terms. A definition of valency in terms of electron shells is an example of such a bridge law. So theoretical unification involves the incorporation of the laws of a reduced theory into those of the reducing theory, either directly or via the aid of bridge laws. Thus one aspect of scientific progress is the construction of an increasingly general, unified conception of nature's laws.

As we shall see, it is this sense of reduction that is most under the gun in the antireductionist consensus. Hull and the other antireductionists have raised doubts about the existence of suitable bridge laws. But as we shall see in section 15.2, it is not at all clear that we should think of the branches of biology as being in the business of formulating laws or generalizations. This whole conception of reduction and the nature of science, based as it is on physics and chemistry, may not fit biology well.

   b. An important "reductive" research strategy in contemporary science is explanation by *decomposition*. How do we work out what is going on in some domain? By taking it apart and studying the components in isolation. If the system cannot be decomposed physically, we can decompose it methodologically. We do this by keeping every component but one constant, and studying the behavior of the system when that one component changes. For instance, we can establish a *norm of reaction* for a genotype by studying how a clone of plants grows when we vary different aspects of the environment, one by one. Variation in the system as a whole is studied by controlling potential sources of variation and allowing only one focal component to vary.

Those who argue for the importance of *holistic* approaches to science and against reductionism often have this conception of reduction in mind. They oppose it by arguing for the importance of *emergent* phenomena. For example, it is common to suggest that ecosystems cannot be understood by decompositional methods because crucial ecological phenomena arise only out of the interaction of many components of a system. Whatever the merits of this idea,

it is important to realize that it is quite different from the view that Hull and his allies put forward. There are, however, echoes of this idea in the view that the cellular context in which a gene acts is so important that the strategy of explanation by decomposition is undermined (7.3).

c. A third sense of reduction is the idea that a scientific explanation must include an identifiable mechanism—it cannot depend on "miracles." One reason why the proponents of continental drift remained in the minority in the period between the two world wars was that it was impossible to see how the continents *could* shift. The mechanisms proposed were unworkable. So continental drift was unpopular as a scientific theory because it depended on a spooky mechanism, a process that could not be understood as a concatenation of ordinary physical and chemical processes. The objects, mechanisms, and processes of a scientific theory must involve nothing spooky: no additions to the standard mechanical processes of the world.

We take this third idea to be an uncontroversial version of reductionism. For instance, a standard puzzle about memory is posed by the fact that humans are very good at recognizing human faces in their normal orientation, but not if the face is inverted. Explaining this phenomenon by detailing the physical changes in the parts of the brain involved in memory is in this sense a reductive process, however complex the relation between a psychological description of what we can remember and a neuroscientific description of changes in neural connectivity might be, for an account of the neural substrate would show that memory involves nothing spooky or occult. In this sense, molecular explanations of dominance or of the independent assortment of traits are reductive explanations, however complex they are, for they show that nothing spooky is in play.

So one sense of reduction clearly involves the incorporation of the reduced theory into the reducing theory. But the two other senses may not: they are compatible with the two theories being integrated without one being incorporated within the other. Consider, for example, the fact that genes are often *pleiotropic;* that is, they have effects on more than one trait. Explanation by decomposition may be an effective strategy for studying this phenomenon even if the relationship between pleiotropy and the molecular mechanisms that explain it is too complex and varied for there to be a bridge law defining it in molecular terms.

We have no interest in haggling over which of these various ideas deserves to be called "reduction." The important point is to recognize their differences, and the fact that the relationship between real theories in science will

rarely fit exactly one of these definitions cleanly. So the reader is warned: in this and the next chapter, a number of balls are in the air. We first sketch the empirical background of this controversy, and then proceed to the theoretical upshot.

6.2 What Is Mendelian Genetics?

Mendelian genetics is the theory that grew by elaboration and development of the laws of segregation and independent assortment after these were rediscovered at the beginning of the twentieth century. The first Mendelians realized that the pattern of inheritance of some biological traits could be explained by postulating a pair of factors underlying each trait—a pair of *alleles* occupying a *locus* on a chromosome. The law of segregation says that the two alleles are separated in the formation of the gametes (sex cells), with each gamete receiving only one allele. Although the alleles from two gametes are united in the *zygote* (the fertilized egg), they do not mix together, and they are separated again to form the next generation. The law of independent assortment says that the probability of a gamete receiving a particular allele at one locus is independent of which allele it receives at another locus. This second "law" was subsequently discovered to be widely violated. There are *linkages* of varying strength between loci: the stronger the linkage, the more likely the alleles are to be inherited together.

Both the original Mendelian "laws" and the exceptions to them were discovered through breeding experiments. In his seminal presentation of the antireductionist consensus, Hull followed the geneticist Theodosius Dobzhansky in using this methodological fact to distinguish the new molecular genetics. Molecular genetics is concerned with the intrinsic nature of the hereditary material; it proceeds by looking inside the cell. In contrast, "genetics is concerned with gene differences; the operation employed to discover a gene is hybridization: parents differing in some trait are crossed and the distribution of the trait in hybrid progeny is observed" (Dobzhansky 1970, 167; quoted in Hull 1974, 23).

The outcomes of breeding experiments, however, were very quickly related to *cytology*—the study of the structure and activity of cells. The discovery of chromosomes provided an explanation for the phenomenon of gene linkage. The genetic material in the cell nucleus consists of several chromosomes. If we assume that genes occur in a line along each chromosome, then genes on different chromosomes will assort independently, while those on the same chromosome will be linked together. A further cytological observation explains the fact that the links between genes can differ in strength. Chromosomes come in homologous pairs, and one of the pair is passed on

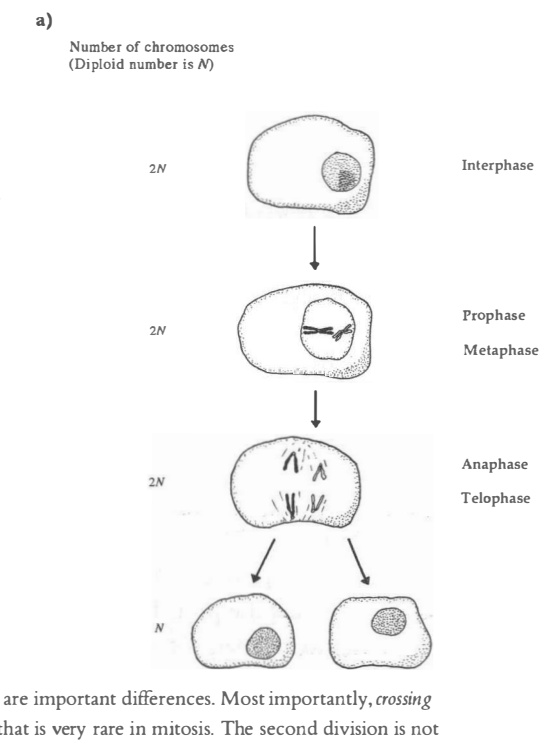


Figure 6.1 Mitosis, meiosis, and crossing-over. (a) Mitosis is the process by which cells multiply and organisms grow. It is represented here for one pair of homologous chromosomes (the two copies of the same chromosome contributed by the organism's two parents). During *interphase* the cell's DNA is replicated, so that when the chromosomes become condensed and visible in *prophase,* each consists of two *chromatids* connected by a *centromere.* During *metaphase* the nuclear membrane disintegrates, and microtubules from the centromeres join to those of the *spindle.* During *anaphase,* the chromatids are drawn apart by the spindle. During *telophase,* two new nuclear membranes form. The cell can then split into two. (b) Meiosis, or reduction division, forms four haploid sex cells by two successive divisions of one diploid cell. The process is represented here for two pairs of homologous chromosomes. The first division resembles mitosis, although there are important differences. Most importantly, *crossing over* occurs during prophase I, something that is very rare in mitosis. The second division is not preceded by DNA replication, and so produces haploid cells with half the diploid chromosome number. (c) (Adapted from Alberts et al. 1994, 100.) Crossing-over is a process in which pairs of homologous chromosomes line up with one another and exchange segments. Where the mother and father were not genetically identical, this can create new gene combinations.

to each gamete. During meiosis, homologous chromosomes cross over and recombine, so that a part of each chromosome is exchanged with the other (see figure 6.1c). The probability of two linked genes being separated by *crossing-over,* thus breaking the link between them, can be greater or smaller depending on how close together they are on a chromosome.

Two other important elements of Mendelian genetics are its account of the relations between genes and phenotypes and its account of the relations between the pairs of alleles that occupy a locus. It was natural for early Mendelians to adopt the hypothesis that there is a single gene for each phenotypic trait. It soon became clear, however, that this hypothesis could not be defended in the face of pleiotropic genes and polygenic traits. *Pleiotropy* refers to the phenomenon of one gene having many effects. Hull gives the nice example of an allele that affects both the eye color of *Drosophila* (fruit flies) and the shape of the spermatheca (an organ in females for storing sperm). *Polygenic* traits, such as human height, are affected by many different genes. Furthermore, some genes interact *epistatically:* the effect of an allelic substitution at one locus depends on which alleles are present at one or more other loci. The relation between genes and phenotypes is thus not one-to-one, but many-to-many.

The way in which the two alleles at a single locus interact to create their distinctive effect is similarly complex. An allele can be characterized as *dominant* or *recessive* relative to some other allele that can occupy the same locus. When two different alleles occur together, if the heterozygote, *Aa,* has a phenotype identical to that of an organism with two copies of one of the alleles—say, *AA*—then *A* is dominant and *a* is recessive. Numerous other categories of dominance were defined by classic geneticists. When the heterozygote expresses a trait more extremely than either homozygote, the alleles are said to be *overdominant.* When the heterozygote expresses the traits of both homozygotes, the alleles are said to be *codominant.* An allele of a pleiotropic gene may be dominant with respect to some of its effects and recessive with respect to others.

Box 6.2 Genetic Atomism

In the growth of theories of heredity and development, the gene has been pressed into service to play a number of distinct biological roles. One is transmission: the production of offspring/parent similarity. But another is mutation: the creation of an unheralded phenotypic form in offspring. Yet a third is recombination: the reshuffling of traits in the phenotype of the next generation that occurred separately in the last, and vice versa. Recombination thus defines the "grain" of inheritance. Finally, genes must somehow function in the development of the organisms that carry them.

The simplest hypothesis is that the gene is the fundamental unit of all four processes. This hypothesis was developed by Morgan and his school in the 1920s. One way of interpreting the further developments in both transmission genetics and molecular genetics since that time is that these roles have been separated. For example, the fundamental unit of mutation (the single base) is distinct from that of function (the codon, a three-base sequence), and that is different again from the unit of recombination (Portin 1993, 781).

Mendelian genetics discovers phenomena that are revealed through breeding experiments, so the explanation of dominance, overdominance, codominance, and similar effects lies outside its scope. Genes interact with one another to determine the norm of reaction of a genotype, and this interacts with environmental variables to determine a phenotype. Mendelian genetics can describe the differences made to this process when one allele is substituted for another at a particular locus on a chromosome, but it does not explain the mechanical bases of these differences. It is part of the role of molecular genetics to uncover these underlying mechanisms. The theorists who expected to reduce Mendelian genetics to molecular biology expected to find one or a few molecular mechanisms that would explain how gene substitutions cause phenotypic differences. This would have allowed them, for example, to identify the phenomenon of dominance with one or a few specific molecular mechanisms. The antireductionist consensus is generated by the fact that expectations of this sort have not been fulfilled.

6.3 Molecular Genetics: Transcription and Translation

The phrase *molecular genetics* refers to the study of the chemical nature of the hereditary material and its molecular surroundings. Chromosomes had long

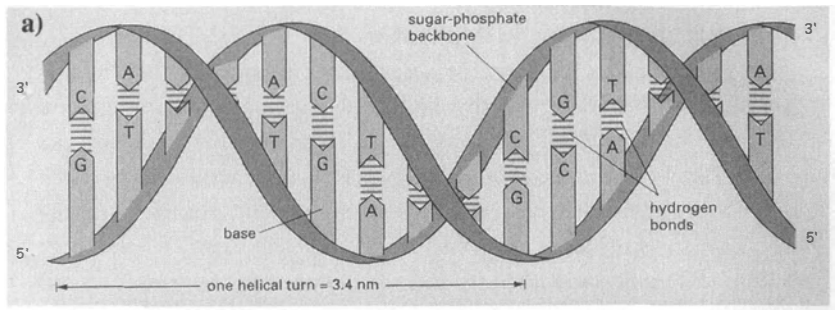


Figure 6.2 (a) The double-stranded helical structure of DNA. (b) The single-stranded structure of RNA, which is the genetic material in viruses and some bacteria. (Adapted from Alberts et al. 1994, 101.)

been known to contain nucleic acids, such as DNA, and proteins, such as histones. It finally became clear at the beginning of the 1950s that DNA was the critical ingredient of the genes. In 1953 Watson and Crick produced a successful model of the molecular structure of DNA. Since then, much has been discovered about its molecular machinery. In this context, these discoveries all contribute to a common theme: they highlight the critical role of the cellular environment in structuring the effect of DNA sequences on an organism's phenotype. The causal chain between DNA and phenotype is indirect and complex not just in having many links; it also has many branches. As we shall see, different cellular environments link identical DNA sequences to quite different phenotypic outcomes.

It was clear as soon as the structure of DNA was elucidated that this structure explains some of the phenomena observed by transmission geneticists. DNA plays its central role in life because it can be both replicated and read.

Box 6.3 DNA as Code and Replicator

DNA can be reliably replicated because guanine and adenine form hydrogen bonds with cytosine and thymine, respectively, and only with them. When the double helix is split apart, each half specifies how to reconstruct the other by forming G-C and A-T bonds. Later research has revealed how DNA functions in the formation of the proteins that make up the structural and functional elements of cells. A single strand of messenger RNA (mRNA) is transcribed by *RNA polymerase enzymes* from one half of the double strand of DNA. The DNA sequence specifies the mRNA transcript by means of the same complementary pairing that allows DNA replication (except that in the mRNA transcript, the base uracil replaces thymine). Within the DNA sequence there is a region beginning with a start and ending with a stop signal. These signals form a *reading frame.* Within the reading frame, the bases divide into three-base sequences, counting from the start signal. Each of these triples is a codon. Hence *frameshift mutations* can cause transcription of the sequence to begin at a new point by redefining the reading frame. A sequence that had been segmented into the codons, say, __/AAG/AGG/GUU/_ can become redivided into __A/AGA/GGG/UU_/.

The critical feature underlying its replicability is its *complementarity*—the fact that when the double helix splits into two single strands, each uniquely specifies the other. Each base in the sequence will pair with only one other base.

DNA reading depends on two main mechanisms, *transcription* and *translation.* First, DNA specifies *messenger RNA (mRNA)* by the same unique pairing mechanism involved in its replication. The resulting mRNA transcript, like its DNA template, is organized into three-base sequences called *codons.* This *primary transcript* plays a central role in protein synthesis, as the codons specify particular amino acids. These amino acids, in turn, are the constituents of proteins. However, it would be wrong to suppose that DNA specifies proteins in the sense of uniquely determining a particular protein. Different primary RNA transcripts can be transcribed from the same DNA sequences. It is also possible for sequences transcribed as different mRNAs to overlap one another (see box 6.3). So the relation between a given DNA sequence and the mRNA input to the protein-making system is one-to-many. When we consider the reading mechanisms of eukaryotic cells, this basic message gets further support.

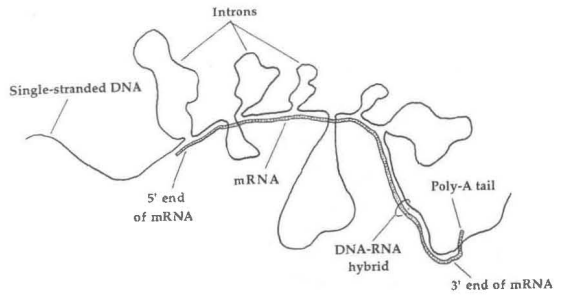


Figure 6.3 Introns can be located by artificially inducing an edited mRNA transcript to bind to a single strand of the DNA from which it was transcribed. Each section of the mRNA *hybridizes* with the section of the DNA from which it was transcribed. The leftover loops of DNA are the introns; the corresponding sections of the mRNA were spliced out during posttranscriptional processing. (Redrawn from Arms and Camp 1987, 205.)

In eukaryotic cells, such as those of plants, animals, and fungi, the primary transcript of mRNA is further processed by the enzymatic machinery of the cell. "Tails" and "caps" are added to the mRNA transcript, and extensive portions are cut out and discarded. These discarded segments are referred to as *introns.* The segments that are retained and spliced together to form the final mRNA are known as *exons.* Alternative splicing patterns, of which there are many examples, make it possible to produce several final mRNA transcripts from the same DNA sequence. Finally, it has recently been discovered that some primary mRNA transcripts may be edited in detail, one base at a time, before proceeding to the translation phase. Some mRNAs are edited (by converting a C into a U) so as to produce a *stop codon* in the middle of the transcript so that it codes for a different, shorter protein. Notice, already, the complex, indirect, and equivocal nature of the relationship between the DNA sequences in chromosomes and their phenotypic consequences. In what follows, this message gets yet more support.

Translation from mRNA to protein occurs with the help of devices called *ribosomes* and a second form of RNA, *transfer RNA (tRNA),* which acts as a physical link between the amino acids that are the constituents of proteins and the final mRNA transcript. The ribosome moves along the mRNA, creating chains of amino acids that are then folded into proteins. The genetic code is *degenerate*—different codons specify the same amino acid—but it is never *ambiguous:* the same codon is never linked via its various intermediaries to more than one amino acid.

Even in the accompanying technical boxes we have barely scratched the surface of the complex machinery that mediates between DNA and protein construction. But the take-home message is simple: One DNA sequence can

Box 6.4 The Genetic Code

In a rather dubious metaphor, the genome of an organism is often regarded as a coded description of the organism as a whole. But there is a sense in which it really is a code for the proteins in the organism. Proteins are made from a stock of twenty different amino acids. So the basic function of the genetic code is to specify those amino acids in the right sequence. Each amino acid is specified by a three-base sequence drawn from the mRNA bases uracil, adenine, guanine, and cytosine. But since there are sixty-four ($4 \times 4 \times 4$) possible three-base sequences, there are sixty-four different codons, and hence there is *degeneracy* in the coding system. That is, more than one three-base sequence can code for the same amino acid. AUG codes for the amino acid methionine, and since all newly synthesized proteins start with methionine, AUG functions as the *start codon.* But there are three *stop codons* (UGA, UAA, and UAG), and sixty-one codons that code for amino acids. The degree of redundancy ranges from leucine, coded by six sequences (UUA, UUG, CUU, CUC, CUA, CUG) to tryptophan, coded only by UGG. An additional source of degeneracy is the differences between the coding mechanism of the genes in the cell nucleus and those in the mitochondria. UGA is not a stop codon for mitochondrial DNA. But though the code is degenerate, it is never *ambiguous:* one codon is always mapped onto one, and only one, amino acid.

be input to mechanisms that yield different protein sequences. So though the RNA codon/tRNA anticodon/amino acid system is not ambiguous in that anticodons always attach to the same codon and are always attached to the same amino acid, this is merely an unambiguous subsystem within a system fraught with ambiguity. It is a system that maps the same DNA sequences onto different proteins and, further, to different phenotypic outcomes. The one-to-many character of the DNA/phenotype relationship is even more apparent when we consider the regulation of genes—the mechanisms that turn them on and off.

6.4 Gene Regulation

A skin cell and a brain cell are very different from each other—and they and their descendants will probably remain that way. Tissue differentiation is often a one-way street. Once a cell lineage has become a lineage of one particular tissue type, it usually does not revert to some earlier, more plastic form. Early cell biologists took very seriously indeed the idea that the hereditary material was divided up between the different tissue types, so that the hereditary material for skin went to skin cells and the hereditary material for nerves went to nerve cells, and only the sex cells retained a full copy (the *mosaic theory*). But this hypothesis was disproved. In fact, most cells have the complete genome. The differences between them are due to mechanisms of gene regulation and cell line heredity. These mechanisms are being discovered at an impressive rate, and any attempt to summarize them here would be quickly out of date. Furthermore, even the mechanisms already known are far too varied and complex to describe in a text of this kind. So we offer here some very general observations about these mechanisms, which will play a role in the arguments over reductionism.

Box 6.5 Reading the Code

Only one strand of the DNA double helix is read, since DNA can be read from only one end, the 5′ end. From this strand, an mRNA strand is constructed as each base in the 5′ strand is paired with its complementary base. The codons of the genetic code are sequences in this mRNA strand.

Actual protein synthesis takes place at structures called *ribosomes* in the cell cytoplasm. Transfer RNAs (tRNA) are chunks of RNA in the cell cytoplasm, each consisting of three bases. Each tRNA binds at one end to a specific amino acid and at the other, again via the base pairing mechanism in which each base has a unique partner, to the mRNA at the ribosomes. So each codon of the mRNA is recognized by a tRNA *anticodon* with an amino acid attached. As the amino acids are lined up and attached by tRNA to mRNA at the ribosome, they form bonds with their neighbors, and a sequence of amino acids is built. This sequential order, in the right molecular context, specifies the protein.

As we have noted, the genetic code is degenerate. Where it is degenerate, it is usually so at the third position in a codon. So mutations that affect the third position are often *silent:* they have no effect on the amino acid being made. But they can affect the rate at which it is made. For the rate at which the code is read depends on the stock of available reading chemicals. The building of a protein depends on the supply of tRNA in the cell cytoplasm. The range of tRNAs that a cell synthesizes helps to determine the assembly of amino acids into proteins.

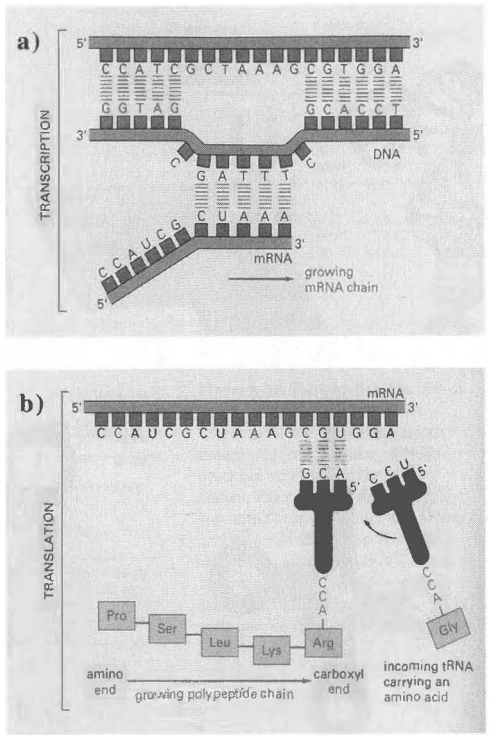


Figure 6.4 Transcription and translation. (a) Each base of DNA is transcribed into the corresponding RNA base, producing a strand of messenger RNA. (b) Each codon of the mRNA transcript matches the anticodon on one end of a transfer RNA. The other end of each tRNA carries a specific amino acid. Ribosomes (not illustrated) move along the mRNA, translating it into a chain of amino acids—one of the polypeptide chains of which proteins are composed. (Adapted from Alberts et al. 1994, 108.)

The expression of a DNA sequence can be controlled at almost every stage of the process between the sequence itself and the functional protein it produces. Various posttranscriptional mechanisms operate on the mRNA transcript, as we have already described. Each of these offers a point of intervention affecting the final protein. Splicing and editing affect the type of protein translated, and other processes affect the quantity translated. Since two forms of RNA play an essential role in this process, the rate of translation of mRNA to protein is affected by the availability of tRNAs (which are synthesized from other regions of the genome) and by the rate at which mRNAs are degraded so that they become unavailable for translation.

Gene regulation through control of transcription has been known for much longer than these posttranscriptional processes. The most intensively studied and best understood form of gene regulation involves *regulatory sequences,* short stretches of DNA that bind to certain characteristic classes of *regulatory proteins.* Transcription of DNA depends on an enzyme called *RNA polymerase,* which splits the double helix and begins the transcription process.

Regulatory proteins affect the ability of RNA polymerase to bind to the regulatory sequences and initiate transcription.

The DNA sequences that are transcribed into mRNA are preceded by *promoter* sequences, to which RNA polymerase attaches itself. In prokaryotic cells, such as the bacterium *E. coli,* regulation is relatively simple. Regulatory sequences lie adjacent to the promoters. Some of these bind *repressors,* negative regulatory proteins that interfere with RNA polymerase binding. Others bind *transcription factors,* positive regulatory proteins that facilitate RNA polymerase binding. In eukaryotic cells, such as those of plants and animals, things are much more complex. The RNA polymerases that transcribe eukaryotic genes typically require a whole complex of transcription factors to be present for them to initiate transcription. This complex machinery enables the overall rate of transcription to be influenced by many different factors, contributing to the ability of eukaryotic cells to create many different cell types from the differential activation of a single genome.

Transcription in eukaryotes is also affected by the organization of DNA into chromosomes. Chromosomes are composed of a material called *chromatin,* which consists mainly of DNA and structural molecules called *histones.* The long DNA molecule can be condensed in various ways in chromatin structures. The most compressed forms are known as *heterochromatin,* and DNA in these forms cannot usually be transcribed into mRNA. This form of gene regulation plays a well-known role in female mammals. Females have two X chromosomes, one of which is rendered inactive by being compressed into a dense, heterochromatic *Barr body.*

A cell's pattern of gene activity is frequently passed on to descendant cells that originate from it by mitosis. Some cells pass on to their descendants not only the genome, but a complex of extragenomic factors that they have acquired during the process of tissue differentiation and which cause them to express those genes, and only those genes, needed in that tissue. The inactivation of the second X chromosome just described is a case in point. One or the other X chromosome is randomly chosen to become a dense, inactive Barr body in the founding cells of certain cell lineages. All cells in the lineage inherit the same pattern of inactivation. So female organisms are genetic mosaics, with different sets of X chromosome genes acting in different tissues.

Another mechanism of cell line heredity is *DNA methylation,* in which parents attach methyl groups to the DNA of their sperm or eggs. In vertebrates and some invertebrates, additional methyl groups can be attached to the bases cytosine or guanine. Heavily methylated sequences are not transcribed. An enzyme called *DNA methyltransferase* copies the methylation

pattern when DNA is replicated. A gene that was turned off by methylation in the parent cell is thus turned off in daughter cells.

Overall, then, the same lesson as before applies: the connection between DNA sequence and phenotype is not just indirect, it's many-to-many. The effect of DNA sequences on phenotype is modulated by mechanisms that turn genes on and off, mechanisms that affect the rate at which "on" genes are transcribed and translated, and mechanisms that determine which proteins are eventually built from a transcribed sequence. So the relationship between DNA sequence and phenotype is many-to-many with a vengeance.

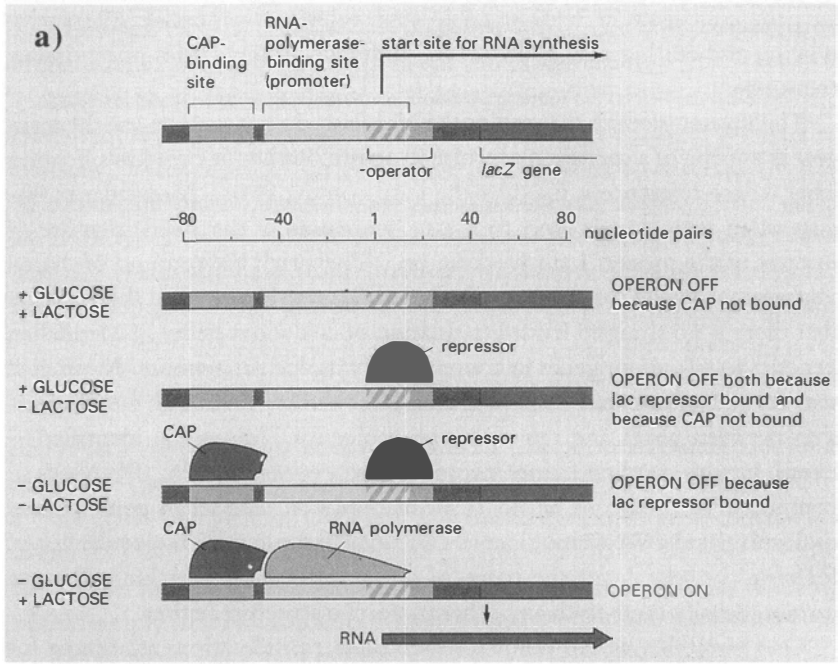
6.5 Are Genes Protein Makers?

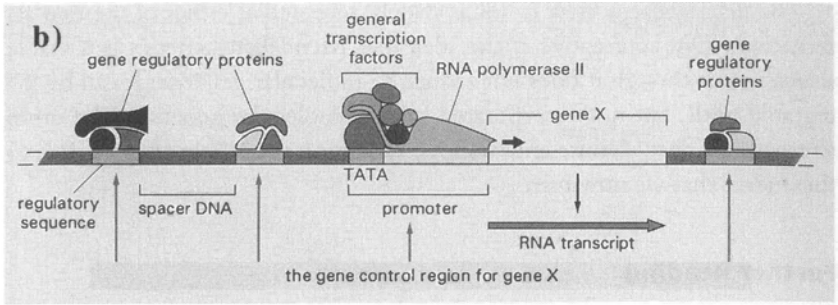
Just as early research in genetics was guided by the ultimately untenable "one gene–one trait" concept, early research in molecular genetics was guided by a "one gene–one protein" concept. The classic molecular gene concept is a stretch of DNA that codes for a single polypeptide chain. We have not tied any of the foregoing discussion to this important gene concept, referring instead simply to DNA sequences. That is because the classic molecular gene is a highly problematic unit in light of the very processes of transcription and translation that we have just described. The original intent of the classic molecular gene concept was to identify a gene with the DNA sequence from which a particular protein is transcribed, via mRNA. But even ignoring the fact that reading frames may overlap, the relationship between DNA sequences and protein chains is many-to-many, not one-to-one. To see this, consider the role of regulatory sequences. These sequences do not themselves code for a protein (so, if they are independent genes, the classic molecular gene concept is already in trouble). But unless at least some noncoding regulatory machinery is included along with the transcribed sequence, the presence of a gene does not explain the presence of the relevant protein. If all regulatory and promoter sequences were adjacent to the transcribed sequences they regulate, we could regard the whole sequence as a single gene. Bacterial genetics more or less works this way. The *operon* of bacterial genetics consists of one or more transcribed sequences and their immediately adjacent promoter and regulatory sequences (see figure 6.5a). In eukaryote gene regulation, however, regulatory sequences may be distant from the sequences they regulate and may be involved in regulating many sequences. Genes coding for transcription factors may be arbitrarily distant from the genes transcribed, perhaps because eukaryote DNA can loop around to bring transcription factors bound to distant regulatory sites close to a gene being transcribed (see figure 6.5b,c). Other problems for the classic molecular gene concept arise because of posttranscriptional processes. Alternative splicing and editing may make several different proteins from one primary transcript.

The upshot, then, is that molecular biologists do not seem to use the term *gene* as a name of a specific molecular structure. Rather, it's used as a floating label whose reference is fixed by the local context of use. Molecular biologists often seem to use *genes* to mean "sequences of the sort(s) that are of interest in the process I am working on." Their rich background of shared assumptions makes this usage perfectly satisfactory. However, it then follows that there is no straightforward translation of talk about genes in Mendelian genetics to talk about genes in contemporary molecular genetics. As we shall see, the antireductionist consensus makes the further point that the relationship between genes and the structures molecular biology has identified—exons, introns, reading frames, promoters, repressors, mRNA, tRNA—is so complex that there can be no clean mapping of Mendelian genes to *any* molecular kinds. We cannot identify Mendelian genes with molecular genes, for *molecular gene* is not the name of one specific molecular kind. But we cannot identify them with any other molecular structure, either.

One possibility at this point is to see these considerations as arguing for the displacement of Mendelian genetics by molecular biology. Contemporary geneticists have proposed, for example, that the dominant/recessive distinction be replaced by a gain of function/loss of function distinction. Recessive phenotypes, according to this idea, are typically the result of an organism being saddled with two copies of a defective gene. The recessive phenotype develops because something does *not* happen. Moreover, though genes can lose function for more than one reason, this would still be a more cohesive molecular-level explanation than the dominant/recessive one. One problem with this revisionary idea is that the gain of function/loss of function distinction depends on how wild-type gene functions are defined. *Oncogenes,* for example, are dominant and represent an inappropriate (from the organism's point of view) gain of function leading to cancer. However, it might be argued that the true "function" of an oncogene is to remain silent in certain cell types, and it is a *loss* of function in its control system that leads to its *gaining* the ability to be expressed at the wrong time (Chambers, personal communication). A more straightforward problem is that some loss of function mutations are dominant; for example, in cases in which the loss of one allele lowers protein production below a critical threshold level.

Classic accounts of reduction acknowledged that the old theory would often have to be "corrected" before it could be reduced. The old theory might contain elements unconnected with its explanatory successes (but





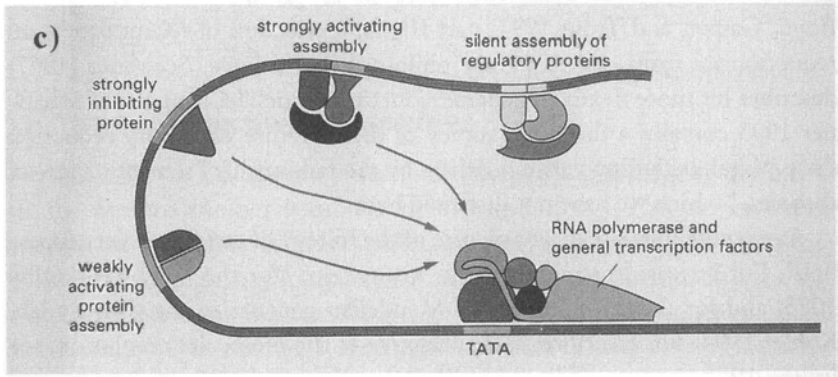


Figure 6.5. Gene regulation. (a) The *lac* operon in the bacterium *E.coli* was the first gene regulatory mechanism to be understood. The operon consists of a transcribed sequence plus one *promoter* site and one *repressor* site adjacent to the start site for mRNA transcription. The regulatory proteins bound at these sites respond to glucose and lactose concentrations. The regulatory factor CAP (catabolite activator protein) helps the enzyme RNA polymerase to open the double helix and initiate transcription of the DNA. The repressor protein stops this process from proceeding. This causes RNA polymerase to be bound and transcription to commence only when there is a low concentration of glucose and a high concentration of lactose. The resulting gene product metabolizes lactose into glucose. (b) Gene regulation in eukaryotes is much more complicated than in bacteria. The TATA box is a sequence of T-A and A-T base pairs close to the start site for mRNA transcription. This sequence binds a collection of general transcription factors (involved in the same process for many other genes). Regulatory regions specific to the particular gene may exist far upstream of the TATA box, or even downstream of the transcribed sequence. (c) The regulatory proteins bound to these distant regulatory regions are thought to be brought into contact with those bound to the TATA box by looping of the DNA. (Adapted from Alberts et al. 1994, 420, 424, 429.)

perhaps responsible for its explanatory failings) that could not be derived from the new theory and the bridge principles. However, if too much correction were required to effect a reduction, this process would no longer be one of theory reduction, but of theory replacement—that is, of displacement rather than incorporation or integration. No one would dream of "correcting" the phlogiston theory of combustion to say that phlogiston is taken up in combustion rather than lost in combustion and then claiming to reduce the phlogiston theory to the oxygen theory. The phlogiston theory was just wrong, and the oxygen theory displaced it. In one view, the "corrections" in Mendelian genetics that would be required in order to reduce it to molecular genetics are so large that this project resembles the frivolous proposal to "reduce" phlogiston to oxygen. So, just as the Churchlands take the irreducibility of psychological kinds to neural kinds to show that there really are no such things as beliefs, Rosenberg takes the irreducibility of classic genes to molecular genes to show that molecular genetics displaces Mendelian genetics:

> Molecular genetics reveals that there is no one single kind of thing that in fact does what Classical genetics tells us (classical) genes do. In this respect of course molecular genetics replaces classical Mendelian genetics. (Rosenberg 1997, 447)

One of the best current texts offers a summary review of "classical genetics," beginning with the claim that in classic genetics a gene is "a functional unit of inheritance usually corresponding to the segment of DNA coding for a single protein product" (Alberts et al. 1994, 1072). This, of course, is the classic *molecular* gene concept; Mendelian genes have disappeared from the map altogether.

The displacement view is not as widely accepted as either of the two alternatives. One alternative is the idea that Mendelian genetics is a viable science even though it does not reduce to molecular genetics: it can be integrated with, but not incorporated within, molecular genetics. The other alternative is that, despite appearances, reduction is possible after all. It is to these ideas that we now turn.

Further Reading

6.1 The classic account of theory reduction is given by Nagel (1961). See Boyd, Gasper, and Trout 1991, part III, for a selection of recent papers on reductionism from contemporary philosophy of science. Schaffner (1967) describes his more flexible "general reduction model." Chapter 9 of Schaffner 1993 contains a thorough survey of the literature on theory reduction since Nagel, including versions driven by the fashionable "semantic view of theories," which we have not discussed here.

As we note in the text, our picture of the history of genetics is very superficial. For serious treatments of this history, see (for the early days) Olby 1985, and for the development of Mendelian genetics in the fruit fly lab, Kohler 1994. For a very readable narrative of the molecular revolution, see Judson 1997. A more philosophically focused account of the history is given by Depew and Weber (1995). Mayr wears a historian's hat too: part III of Mayr 1982a is his account of the development of genetics. Dupré (1993) and Rosenberg (1994) present an interesting contrast. They essentially agree in thinking that the classic accounts of theoretical unification fail to fit biology. But whereas Dupré develops a case for thinking that the program of unification and the metaphysics that underlies it is wrong-headed, Rosenberg argues that unreduced biology cannot be regarded as an objective account of the way the world is. So their work is relevant throughout this and the next chapter.

6.2–6.5 The history of the gene concept is complex and controversial. Falk (1984, 1986) discusses its many transformations. Portin (1993) presents a good recent treatment. As usual, Keller and Lloyd (1992) provide a good entrée into the literature; Maienschein overviews the history of the concept, and Kitcher surveys its current uses. An authoritative source on modern molecular biology is Alberts et al. 1994. For accessible introductions to these difficult issues, see Moore 1993 or Mayr 1982a.

Chapter

7

Reduction: For and Against

7.1 The Antireductionist Consensus

The classic account of theory reduction underpinning the incorporation of one theory into another is quite simple (Nagel 1961). The old and new theories are first made commensurable by providing translations from the vocabulary of one theory to that of the other. Then the old theory is shown to be deducible from the new theory, given these translations, and perhaps some restrictions on the range of systems for which the old theory is reasonably accurate. The translations from the vocabulary of the old theory to that of the new theory are known as *bridge principles* or *bridge laws*. In the case of classic and molecular genetics, the bridge principles would specify which molecular structures count as genes, how to recognize the dominance of one allele over another in molecular biology, and so forth. In the restricted range of cases in which classic genetics is accurate, it should be deducible from molecular genetics via these bridge principles.

The logical empiricist philosophers who originally developed this account of reduction supposed that bridge principles would always be available. They believed that the theoretical terms of a genuine scientific theory gained their meaning from the way the theory related them to observation and experiment. Hence it should always be possible to compare the vocabularies of two theories by translating them into a common vocabulary of observations. This view was challenged in the 1960s when Kuhn and Feyerabend argued that there is no theory-neutral observational vocabulary in which to state bridge principles (Feyerabend 1962; Kuhn 1970). Although this challenge has been extremely important in philosophy of science, it has never been one of the reasons for denying the reducibility of classic to molecular genetics, and so we will pass over it here. It has always been assumed by both sides in the debate that molecular biologists could determine how their theories would

translate to the preferred vocabulary of genetics: the ratios of observable phenotypes produced by cross-breeding.

The antireductionists' most fundamental claim is that any number of different molecular arrangements could correspond to a single category in classic genetics. Bridge principles for the terms *gene, locus, allele, dominant,* and so forth would relate each of these Mendelian kinds to many different molecular kinds. Molecular genes coding for different mRNA transcripts function as alleles, but so do noncoding regulatory regions that affect transcription, and so do various forms of a sequence coding for a product involved in alternative splicings of some other gene product. A similar situation exists with the family of terms associated with the dominance relation between alleles. In Mendelian genetics, an allele is dominant if its characteristic effect is seen in the heterozygote. There are at least as many molecular ways to be dominant as there are ways for an allele to have a phenotypic effect, and as we have seen, there are many ways for an allele to have a phenotypic effect.

The fact that the bridge principles between Mendelian and molecular genetics have this one-to-many form means that the different instances of a single Mendelian kind may have no distinctive molecular property in common. Therefore the bridge principles are not lawlike. They do not connect a natural kind identified by hybridization and observation with a natural kind independently identified by molecular biology. What properties do the molecular structures that count as alleles all share? They have some effect on the phenotype, perhaps through their epistatic effect on the expression of alleles at other loci, and they occupy chromosomal locations that cause them to assort and recombine so that those phenotypic effects are expressed in Mendelian ratios. These properties are precisely those that Mendelian genetics ascribes to alleles. Molecular structures are recognized as alleles for no other reason than that they obey the principles of the old theory. The fact that alleles obey these principles cannot then be explained by the fact that molecular correlates of alleles obey them, since that is true by definition. The molecular ensembles that correspond to the Mendelian kinds do not emerge from molecular biology, but are constructed by grouping together diverse molecular events that look the same when viewed using the experimental techniques typical of classic genetics. The reduction relationship this generates is not one in which the new theory explains the old, but one in which the new and old theories represent complementary and mutually illuminating ways of viewing the same physical processes.

We do not see this as a troubling conclusion. There is nothing here to undercut the uncontroversial but important sense of reduction we identified in section 6.1, the ban on miracles. This idea of reduction has played, and continues to play, an important regulative role in scientific debate. As we

noted in section 6.1, the evidence for continental drift was quite impressive even before World War II. But continental drift remained marginalized among geologists, in part because the mechanisms they proposed to shift continents were implausible. The "drifters" of the thirties conceived of continents as plowing through the ocean floor rather as a concrete slab might be pushed half through, half over the top of, a layer of earth. The proposed forces were too weak, and the stresses on the continental crusts would be far too great for them to survive the passage. Until drift could be backed up with a plausible physical mechanism, driftist explanations of continental movement were hard to accept (Le Grand 1988). Scientific theories cannot traffic in apparently miraculous mechanisms. There is a tree of explanatory dependence that links together all the different causal mechanisms postulated in science. That tree is rooted in fundamental physical processes. Through various different branchings, all scientific kinds depend on that root. The light molecular biology sheds on classic genetics is quite adequate show that inheritance in classic genetics is not mysterious or spooky in any way.

7.2 Reduction by Degrees?

When a macrolevel object, property, or process can be built in many different ways out of its microlevel constituents, we speak of that property (or object or process) being *multiply realized.* It is realized (made real) by different microlevel configurations. The claim that the theoretical entities of classic genetics are multiply realized at the molecular level is the core of the antireductionist consensus. Perhaps this argument looks so powerful only because we have supposed that the key kinds of Mendelian genetics are to be directly reduced to DNA sequences. But there is an important reductionist alternative. First, Mendelian kinds are reduced to gross features of cytology and development. Something is an allele just because it has a chromosomal location. Allele *A* dominates allele *a* because, for some complex developmental reason, the *Aa* heterozygote resembles the *AA* homozygote. Alleles on homologous chromosomes assort independently because there are two chromosomes that separate in meiosis, carrying one allele to each gametic cell. Second, these gross features of cytology—assortment, crossing-over, and the like—are explained by molecular biology. Molecular biology has shown that chromosomes are structures of histones and DNA, and is starting to explain how the cell moves these structures about in meiosis. The law of independent assortment is reduced to the molecular mechanisms of chromosome structure and meiosis. So Mendelian genetics is reduced to molecular biology in a two-stage rather than a one-stage process.

Kitcher has responded to this version of reductionism by arguing that the

explanatory power of cytological features does not depend on their molecular implementation (Kitcher 1984). As Waters puts it in his critical response, according to Kitcher, the "gory details" of molecular mechanisms are irrelevant to the explanatory power of Mendelian principles (Waters 1994c). The gory details of the chromosome and its dance are not important in explaining the law of independent assortment. That law is fully explained when we know that there are two chromosomes and that one goes to each gamete. This "gory details" argument is a variant of the multiple realization thesis. Kitcher compares the situation to knowing why a round peg won't fit into a square hole, which is fully explained by the shapes of the two items, however they are physically realized. An explanation that specifies the molecular configurations of the peg and the hole is *too* detailed (Putnam 1978, 42). Any molecular configuration of the same shape would produce the same effect. Similarly, Kitcher argues, the generalization that explains independent assortment is an abstract statistical generalization about the effect of randomly dividing pairs of entities.

At this point we need to avoid becoming enmeshed in pointless squabbles about what counts as reduction and explanation. For, as we noted in discussing gene selection (4.2), there is a place for explanations that abstract away from the details of an event's causal history, but also for explanations that are rich in detail. A geometric explanation of why a round peg fails to fit into a square hole is a robust process explanation. Any variation in circumstances that preserves the gross geometry of peg and hole will yield the same outcome. An explanation of a particular peg's failing to fit a particular hole in terms of their precise physiochemical composition is an actual sequence explanation, for it gives the detailed, close-grained explanation of this particular event. These two explanatory strategies are compatible because they answer different questions. So the argument that Mendelian genetics can always ignore the gory details of its link with the molecular world is gratuitously strong. We might well want an actual sequence explanation of why, say, the sex chromosome and the sickle-cell gene sort independently. After all, some genetic diseases are sex-linked. However, there would remain a robust process explanation of independent segregation, one independent of the actual sequence explanation, just because there may be many molecular mechanisms that determine the placement of genes on particular chromosomes.

Robust process explanations are important when, and to the extent that, macroscopic processes are invariant over changes in the microscopic processes on which they depend in each particular case. If the antireductionist view that Mendelian categories and molecular ones are related in highly complex many-to-many ways is right, then Mendelian genetics is integrated with, and causally explained by, molecular biology, but it is methodologically

and conceptually independent of that discipline. But that is not to deny the significance of individual, close-grained actual sequence explanations. Moreover, a sense of reduction is involved here too: the ban on miracles. The molecular explanation of meiosis shows that the law of independent assortment is mechanical; no spooky mechanism is involved.

7.3 Are Genes DNA Sequences Plus Contexts?

We have just considered the idea that the concepts of classic genetics can be reduced to molecular structures indirectly, via developmental biology. But perhaps the problem isn't with reduction as such, but with the proposal that classic genes reduce to DNA sequences alone. As we saw in sections 6.3 and 6.4, many molecular elements in addition to DNA play a role in the phenotypic effect of a DNA sequence. So perhaps classic fruit fly genes such as *wingless, white eye color,* and the like are DNA stretches *plus* the molecular machinery that uses them. In his seminal presentation of antireductionism, Hull remarked "The only plausible molecular correlate for a dominant gene is a highly specified molecular mechanism, not an isolated stretch of DNA" (Hull 1974, 24).

This idea gets off the ground because, as Hull notes, Mendelian geneticists have always been on the lookout for some concrete, structural object that they can identify as a gene. It was in this way, for example, that they made sense of the "position effects" first discovered in the 1920s, in which the same gene has a different effect on the phenotype when it is moved to a new location. If genes were actually *defined* by their position and function, the very idea of a position effect would have made no sense. Yet any structurally defined segment of DNA has the properties of an allele only because it is embedded in a much broader molecular context. So if we are to identify an allele with a specific molecular structure, the allele has to be the DNA plus this context.

The idea of identifying genes as DNA sequences in their context poses two problems. Hull himself thought there would be a serious problem because the bridge principles from the genes of classic genetics would have to specify unmanageably large chunks of the molecular context. Moreover, the relationship would still be one-to-many. Many different DNA sequences in different contexts would count as instances of the same allele. Second, this identification of a gene poses a problem for the decompositional strategy we identified in section 6.1 as one strand of reductionist thinking. The guiding assumption of this strategy is that the constituents' causal powers are relatively independent of their environment, so that the system can be taken apart and each part understood in isolation. If molecular biology had vindicated "bean-bag genetics," the idea that each trait of an organism is explained by the

separate action of a particular gene for that trait, the decompositional strategy would have triumphed spectacularly (Kitcher 1984). But, on the contrary, this explanatory strategy may well be undercut by developments in cell biology. In addition to large-scale cytological events being explained by the action of their molecular constituents, molecular events are being explained in the context of the broader cellular milieu in which they occur. The large multinucleate cell that constitutes the early fruit fly embryo expresses different genes in different parts of its cytoplasm, and processes these gene products differently, because of the uneven distribution of chemicals in the cytoplasm. Hence large-scale developmental biology explains the action of individual genes just as much as the action of individual genes explains development.

So identifying genes with DNA sequences in their cellular milieu might not be a reductionist strategy at all, in one important sense of reduction. But reductionist or not, it is certainly a viable option. It has been recently defended by Neumann-Held (1998), whose takeoff point is the impossibility (in her view) of identifying genes with DNA sequences alone. We have already described how the effect of a gene depends on the broader molecular context of the cell (6.4). Neumann-Held argues that even whether a DNA sequence counts as a gene depends on the context in which it occurs. This context depends in turn on the processes by which cells differentiate and become part of larger units of biological organization. Neumann-Held suggests that a gene is a *process* that regularly results, at some stage in development, in the production of a particular protein. With rare exceptions, this process centrally involves a linear sequence of DNA, some parts of which correspond to the protein via the genetic code. But it also involves all the elements of the developmental matrix, inside and outside the cell, that regularly coincide at this stage in development to cause expression of the protein. Perhaps the most radical feature of Neumann-Held's proposal is that it makes genes themselves include environmental causes in development! Despite this feature, and the fact that she seems to "reduce" genetics to developmental biology rather than the other way around, Neumann-Held's radical proposal has some analogies with the reductionist views we are about to consider. The classic geneticists proposed that a gene was a unit underlying a given hereditary characteristic. Neumann-Held's proposal retains this property of genes at the expense of making genes simple sequences of DNA.

7.4 The Reductionist Anticonsensus

The antireductionist consensus depends on the complexity of the relationship between the genes identified by transmission genetics and molecular structures. As we have just seen, that consensus has been challenged. The

inspiration of the reductionist anticonsensus can be summed up in a quote from the eminent geneticist Gunther Stent:

> What geneticist could take seriously any explication of "reductionism" which leads to the conclusion that molecular genetics does *not* amount to successful reduction of classical genetics? (Stent 1994, 501; italics in original)

Several philosophers of biology agree with Stent that if current philosophical accounts of reduction do not yield the desired conclusion, then it is the accounts of reduction that are at fault. Obviously, classic genetics was not just some horrible mistake, and we should not say about it what we say about phlogiston. So there must be some relation between the factors of inheritance identified by classic genetics and the molecular machinery discovered later on: a relation that explains the very considerable theoretical and predictive achievements of the classic tradition. In our view, the reductionist anticonsensus can be seen as raising, though not settling, the following questions:

1. Is the relationship between molecular and classic genetics strikingly different from, because it is more complex than, say, the relationship between heat, pressure, and volume and the kinetic properties of particle aggregates? If so, is it misleading to label both "reductions"?

2. As we have noted, the idea of reduction comes with a load of theoretical and ideological baggage. It is partly a legacy of sophisticated versions of positivist philosophy of science, a view of science that is dominated by models from physics and chemistry. So, if the relationship between more and less fundamental domains is typically complex, should classic theories of reduction, together with their attachments, be abandoned and replaced rather than updated?

3. Even if in some interesting sense classic genetics does reduce to molecular genetics, there may be an important sense in which macroscopic explanations remain independent of reducing explanations. As we have noted, actual sequence explanations do not exclude robust process explanations. So might not Mendelian genetics remain an independent theory more or less integrated with molecular genetics, rather than being incorporated by it?

Two of the most consistent advocates of reduction have been Kenneth Waters and Kenneth Schaffner. Schaffner was the philosopher who first suggested that classic genetics was being reduced to molecular biology (Schaffner 1967, 1969). The antireductionist consensus developed in response to this suggestion. In the thirty years since he first proposed this idea, Schaffner has

developed a series of increasingly sophisticated and "data-driven" models of how theory reduction actually proceeds in the biological sciences (Schaffner 1993, 1996). Waters, too, has argued that the relation between Mendelian and molecular biology is at least in the spirit of the classic account of theory reduction, and has produced replies to many of the antireductionists' arguments (Waters 1994a,c).

Waters's reply to the multiple realization thesis has two elements. First, he argues that it depends on treating genes as causes of traits rather than causes of trait differences. Second, he doubts that there is an interesting, autonomous explanation of Mendelian facts through cell cytology. So if we are to explain Mendelian principles at all, the explanations will be molecular, and the "gory details" will matter. We start with multiple realizability. His reply begins with the observation that Mendelian genetics never claimed that there were genes for traits, only that there were genes for trait *differences*. A *red eye* allele in *Drosophila* does not really cause the production of red eyes. Instead, it makes the difference, in the presence of many other causes, between red eyes and eyes of some other color. If we think of genes as entities that code for phenotypic traits, we will reach the antireductionist conclusion that for any trait, many complex molecular arrangements can constitute the gene for that trait. However, if we concentrate on the idea of genes as difference makers, Waters claims that the entities that make such differences all turn out to have something in common: "The gene can be specified in molecular biology as a relatively short segment of DNA that functions as a biochemical unit" (Waters 1994c, 407). The phrase "functions as a biochemical unit" seems to nicely bring under one heading both coding regions and regulatory sequences of various kinds. This approach also fits well with the idea that genes are not self-sufficient causes, but difference makers in a larger causal process (a view developed most fully in Sterelny and Kitcher 1988). Clearly, alternative promoter or regulatory sequences that occupy allelic positions on the chromosomes could be difference makers in this sense, and thus genes in the sense of classic genetics.

In practice, though, Waters interprets his proposal as something like the classic molecular gene concept. This concept, he suggests, "is that of a gene for a linear sequence in a product at some stage of gene expression" (Waters 1994a, 178). So *gene* means "coding sequence," and regulatory sequences are really only parts of the coding-sequence genes that they regulate. There is an obvious problem with this proposal, which is that for some purposes, molecular biologists clearly do not regard some regulatory sequences as parts of the genes they identify. This is not surprising. In eukaryotes, transcription factors can bind to sites distant from the gene they regulate, and hence regulatory regions can assort independently of the gene they regulate. Waters suggests that the conversational context indicates to the molecular biologist which stage of gene expression is of interest, and hence whether to adopt a wider or narrower conception of the gene. While this explains how molecular biologists understand one another's usage, it hardly defends the view that *gene* names a single molecular unit.

Neumann-Held (1998) has expressed considerable skepticism about Waters's definition of *gene*. She suggests that it adds no more than a verbal unity to the diverse molecular units that geneticists refer to as genes. According to Waters's proposal, we must rely on the conversational context to determine whether to include introns, adjacent regulatory regions, distant regulatory regions, coding regions for transcription factors that bind to the regulatory regions, or coding sequences for factors involved in splicing or editing in "the gene." This suggests that *gene* does not really name a unit of molecular biology, but is shorthand for any of several different units. As we noted in section 6.5, *gene* is used in molecular biology as a shifting tag rather than as a name for a specific molecular kind. A few examples from the literature will illustrate the diversity of its actual use. First, *gene* means "coding region": "In this chapter we use *gene* to refer only to the DNA that is transcribed into RNA . . . , although the classic view of a gene would include the gene control region as well" (Alberts et al. 1994, 423). Second, Alberts et al. use *gene* to name the unit of function in transcription: "This definition [of gene] includes the entire functional unit, encompassing coding DNA sequences, noncoding regulatory DNA sequences, and introns" (Alberts et al. 1994, G-10). Biologists also use *gene* to mean a sequence of exons. There are further alternatives, which will become more important as posttranscriptional processing becomes better understood. So Waters's defense of reductionism against the multiple realization argument is at best problematic. The shifting use of *gene* undercuts the first stage of Waters's argument, which identifies genes as difference makers and hence suggests that they are identifiable molecular kinds.

Second, Waters doubts that there is any decent explanation of Mendelian principles in terms of cytology. This charge looks very plausible when leveled at some of Kitcher's examples. For instance, Kitcher suggests that the law of independent assortment is explained by the fact that pairs of alleles are situated on pairs of chromosomes, one of which goes to each daughter cell. Stripped of any details explaining *why* chromosomes separate—stripping that is necessary because these details vary case by case—this is a pretty thin explanation, and Waters's skepticism looks justified. However, other findings in developmental biology suggest that there really is a robust and interesting

level of structure between Mendelian patterns and molecular structure. For example, one important and much reinterpreted concept in developmental biology is that of the *morphogenetic field* (for the most recent interpretation, see Gilbert, Opitz, and Raff 1996). A morphogenetic field is a region of the developing embryo that acts as a unit. A developing embryo, in this view, is a mosaic of such three-dimensional regions. Within each region, cells interact strongly with one another; between regions, there are relatively weak interactions. The precursors of the segments in the body of an arthropod emerge in this fashion long before they develop the physical boundaries that mark segments in the adult. Morphogenetic fields are set up by the action of genes in combination with environmental influences and the existing cytoplasm. The action of the genes is significantly influenced by the different chemical milieu of each field. For example—and very roughly—the initial distribution of chemical traces in the arthropod egg determines the differential gene expression in various areas of the egg that sets up the first fields. Differences in the fields lead to further differential gene expression, which further differentiates the fields from one another and creates fields within fields, and so forth.

The morphogenetic field concept provides an example of the sort of large-scale explanation that might not be illuminated by a case-by-case reduction to molecular processes. Developmental biologists and geneticists have long considered it a real possibility that such large-scale patterns in development *canalize* development toward certain outcomes (Waddington 1959; Kauffman 1993; Goodwin 1994; Wagner 1996; Wagner, Booth, and Homayoun 1997). Development compensates for minor changes in the genome in just the same way that it compensates for minor changes in environmental inputs, protecting important developmental outcomes against interference from such variation. Across a wide range of parameters, developmental outcomes will be invariant, and a robust process explanation identifies the space within which development is or is not canalized. An example of this phenomenon may be provided by the reversion of the bithorax mutation in *Drosophila.* This mutation in the important homeobox regulatory genes converts a segment of the fly into a copy of the segment carrying the wings, yielding a four-winged mutant fly in place of the usual two-winged wild type. However, bithorax strains need continuing selection to maintain the mutant form. Left to itself, the lineage will revert to the wild type (H. F. Nijhout, personal communication).

The idea that developmental outcomes can be stable in the face of underlying genetic variation has two implications. First, it makes the generalizations of developmental biology multiply realizable at the molecular level, creating the kind of theoretical independence for these generalizations that the antireductionists claimed to identify. Second, it creates the possibility of explaining gene action in terms of biological processes at a larger scale, and thus undermines the basic intuitions concerning the direction of explanation in science that motivate reductionism in the decompositional sense. There will, of course, be a close-grained actual sequence explanation for any particular developmental outcome. But the fact that that developmental sequence gives rise to, say, a two-winged rather than a four-winged fruit fly is itself explained by biological processes at a broader scale. Hence the existence and importance of actual sequence explanations does not undercut the explanatory importance of larger-scale explanations.

Schaffner has given the contrast between general robust process explanations and case-by-case explanations his own distinctive twist. He argues that the role of actual sequence explanations is filled in a special way through work on model organisms. Their role is both to exhibit and hence demystify the actual causal mechanisms involved in particular biological processes—say, the expression of segmentation genes in a fruit fly embryo's development—and to serve as a rough, partial template for similar explanations of the same process in other organisms. Thus theories in the biomedical sciences are characterized by a mixture of broad and narrow causal generalizations. The broad generalizations resemble traditional scientific laws, but the narrow ones elucidate the workings of particular model systems and are not expected to be applicable in any unmodified form to other cases. Model systems, which may be individual gene systems such as the *lac* operon in the bacterium *E. coli* or whole organisms such as the nematode *C. elegans,* act as exemplars (roughly, inspirational case studies) for work on less well studied systems of a similar type.

Our conclusion after reviewing both the "antireductionist consensus" and the "reductionist anticonsensus" is that nobody wins. Rather, considerable progress in understanding the relationship between molecular biology and classic genetics has been made under both headings. It has become clear that the reducing theory is not really independent from the theory it is supposed to reduce. Molecular genetics did not emerge cleanly as a new discipline with categories and laws that explained the successes of its predecessor. Instead, molecular biology has subsumed and enriched classic genetics, turning it into the modern transmission genetics that still plays a crucial role in determining the actual functions of stretches of DNA. In part this is because molecular biology, or molecular genetics, is misnamed. It is not a simple extension of biochemistry, but rather the study of how biochemical and other physical laws operate in the complex and varied cellular contexts that evolution has produced. The concepts of classic genetics, most notably *gene* itself, continue to play a role in molecular biology, although perhaps as little more

Chapter

6

Mendel and Molecules

6.1 How Theories Relate: Displacement, Incorporation, and Integration

One problem in philosophy of science concerns the relationship between apparently different theories of the same domain. For example, in psychology, we have three apparently different ways of explaining human behavior. Cognitive psychology explains human behavior by seeing it as the result of information processing. Its program is to explain, say, our ability to predict others' behavior by characterizing the information about others we possess, the form in which that information is stored, and the techniques we use to process and deploy that information. But the neurosciences are also in the business of explaining human behavior. Those disciplines are gradually developing an account of the physiological mechanisms on which our behavioral abilities depend. Furthermore, we were not wholly incapable of explaining human behavior before the scientific developments of the twentieth century. For thousands of years we have had at our disposal a "folk psychology" through which we have explained the behavior of others. These explanations are couched in terms of beliefs, goals, emotions, moods, and the like. How do the explanations of folk psychology relate to those developed in the natural sciences? How do the two scientific programs relate to each other?

This general problem arises in biology as well. As we saw in section 2.2, heredity—parent/offspring similarity—is central to evolution. Unless offspring tend to resemble their parents more than they resemble some randomly chosen member of their parents' generation, natural selection is powerless to change the character of a population over time. But there seem to be two different theoretical programs through which this central phenomenon can be studied. The first of these dates back to Gregor Mendel's

work in the mid-nineteenth century; the second began when the rediscovery of his work at the beginning of the twentieth century prompted a search for its cellular and molecular basis. What follows is a cartoon version of these programs; we go into more detail in section 6.2.

It was Mendel who hit on the idea of genes as discrete units of inheritance while studying the results of pea breeding experiments in the 1860s. When he focused on two states of a single character, round versus wrinkled seeds in true-breeding pea lineages, he noted that first-generation hybrids were all round, but that second-generation hybrids were not. Some—about ¾—were round, but ¼ were not. When he considered not just one, but two traits, seed texture and flower color, once again the first-generation hybrids were uniformly round-seeded, yellow-flowered peas. But the second-generation hybrids were not. Roughly 9/16 of the second generation were like the first-generation hybrids. But about 3/16 were yellow-flowered, wrinkled-seeded peas; about 3/16 were green-flowered, round-seeded peas; and about 1/16 were both green-flowered and wrinkle-seeded.

Mendel realized that these results fell into place with the following assumptions:

1. Phenotypic traits such as color and texture are determined by a unitary hereditary factor. These factors can exist in alternative forms, or *alleles*.

2. The gametes of an organism (the pollen or the ova) carry just one of the alternate character states of these traits (one of the factors for yellow or green; round or wrinkled).

3. When an organism is formed from two gametes that carry rival factors for one trait, one dominates the other. In this case, the factor for round is *dominant* over the factor for wrinkled. In other words, the factor for wrinkled is *recessive*.

4. When a first-generation hybrid organism (the *first filial* or F_1 generation) forms gametes, about 50% of the gametes carry one factor, and about 50% carry the other.

5. The factors for traits that are not alternatives to one another—in this case, flower color and seed shape—are inherited independently of one another. From the fact that a gamete carries the *wrinkled* factor, we can tell nothing about whether it carries the *yellow* factor, and vice versa.

As we shall see in section 6.2, after the rediscovery of Mendel's work around 1900, much was added to this picture, and it was altered in important ways. But biologists have continued to investigate heredity by studying the

than shorthand for the various DNA sequences and collections of interacting DNA sequences used in molecular biological explanations of organisms and their traits.

Further Reading

7.1–7.3 An extended treatment of the debate over genetics and reductionism has recently been given by Sahotra Sarkar (1998). Hull's original presentation of antireductionism in his *Philosophy of Biological Science* (1974) is still an excellent introduction to this debate. Other important presentations are those of William C. Wimsatt (1974, 1976, 1994, in press); Phillip Kitcher (1984); Alexander Rosenberg (1985), and Dupré (1993). Kitcher's account is developed further in Kitcher 1989 and Culp and Kitcher 1989.The parallels between these issues in biology and psychology are especially evident in Jerry Fodor's presentation (1974, 1975). Neumann-Held (1998) outlines her concept of the contextualized or constructionist gene. There is a brief note in *Nature* objecting to ideas along these lines as conflating the distinction between what a gene is and how it is used (Epp 1997). Griffiths and Neumann-Held (in press) reply to this objection.

7.4 Waters defends reductionism in a number of papers (1994a,c). Schaffner's views are developed in Schaffner 1969, 1993, 1996, with a good concise summary in Schaffner 1993. Gilbert, Opitz, and Raff 1996 is a good, not overly technical account of the morphogenetic field concept and its importance within developmental biology. The relationship between developmental and molecular biology, with special reference to that concept, is explored in a recent paper by Richard Burian (1997). Rosenberg (1997) argues against the idea that developmental biology has any macrolevel explanatory generalizations; in his view, the morphogenetic field concept and its ilk are descriptive, but not explanatory. So his paper is a critique of antireductionism from the perspective of developmental biology. But he interprets the antireductionist position as having a commitment to "top-down" causal explanations, so the antireductionism under Rosenberg's gun is a stronger position than the "antireductionist consensus" that we outline here. It is, however, relevant to Neumann-Held's identification of a gene. Some of Rosenberg's ideas take off from an interesting paper on these issues by Wolpert (1995).