Modularity

Understanding the Development and Evolution of Natural Complex Systems

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4 Evolutionary Developmental Biology Meets Levels of Selection: Modular Integration or Competition, or Both?

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It is a truism that wholes are composed of parts. In recent years a number of biologists, particularly developmental biologists, have started a new field of inquiry into the parts of biological wholes, called "modules" (see, e.g., Wagner, 1996, 2001; R. A. Raff, 1996; Hartwell et al., 1999; von Dassow and Munro, 1999; Bolker, 2000; Winther, 2001a). In multicellular organisms, modules include repeated and conserved structures such as arthropod segments and developmental units such as germ layers, morphogenetic fields, and cell lineages. In social insect colonies, such as those of ants, modules include ant organisms with particular structures and distinct behaviors, such as reproductive ants (gynes, i.e., reproductive females, which, when they have established a colony, are called queens, and males) and potentially morphologically differentiated ant workers. When the colony is considered to be an individual (i.e., a superorganism), then the behavior of the ant organism can be thought of as a part of colony physiology. I use the term "individual" in a broad sense to include, for example, multicellular organisms and social insect colonies. I will focus on these because they are well-integrated modular individuals at two distinct and compositionally related levels of biological organization.

Do modules mechanistically interact or selectively compete, or both? Two perspectives answer this question differently. Investigations in the *integration* perspective are concerned with the interactive mechanisms among modules and with the patterns of evolutionary change of mechanisms and modules. Mechanisms of interest to this perspective can be roughly divided into two categories: (1) developmental, those involved in causing the dynamical path taken during the production of an individual, and (2) physiological, those processes occurring along every step of this path (tables 4.1 and 4.2). For example, in multicellular organisms, this perspective investigates both the different embryonic regions interacting with each other during development and the specialized physiological processes that ensure organismal functionality.

Research under the *competition* perspective explores the selective processes acting among units at different levels of the genealogical hierarchy (e.g., gene, organelle, cell, organism, superorganism, species, and even clade). Typically biologists and philosophers distinguish between (1) replicators, of which copies are made, and (2) interactors, which interact as a whole with their environment (Dawkins, 1976; Hull, 1980; Brandon, 1982; for a review, see Lloyd, 2000). Interactors at multiple levels (modules and individuals) compete directly and thereby lead to the differential survival of the particular replicators, which produce, or are at least statistically correlated with, them. Copies are then made of these

Table 4.1
Integration and competition perspectives at the organism level

	Integration Perspective	Competition Perspective
	What are the mechanisms among parts (modules) and parts–wholes (modules–individuals)? Physiology vs. development	Which selective forces among interactor modules *change* gene (replicator module) frequencies? Interactor vs. replicator
Partitioning Whole can be understood as an aggregate sum of parts	• Human Genome Project	• Selfish gene theory and game theory: Dawkins and Maynard Smith in 1970s and subsequently • Single-level kin selection: Maynard Smith and Szathmáry, 1995
Articulation *Organism as a legitimate individual* 1. Relations, not properties, of parts are important 2. Whole and parts provide mutual meaning 3. Constant interaction with environment	• Integrative mechanisms at multiple levels 1. Physiological approach 2. Developmental approach 3. Structural approach Gerhart and Kirschner (1) R.A. Raff (2) Wagner (3) • *Integratively defined* organism	• Two mechanisms 1. Group selection for cheater-suppression mechanisms 2. Multilevel kin selection Buss (1) Michod (1,2) • Multilevel selection theory employed • *Competitively defined* organism

Table 4.2
Integration and competition perspectives at the superorganism level

	Integration Perspective	Competition Perspective
	What are the mechanisms among parts (modules) and parts–wholes (modules–individuals)? Physiology vs. development	Which selective forces among interactor modules *change* gene (replicator) frequencies? Interactor vs. replicator
Partitioning Whole can be understood as an aggregate sum of parts	• E. O. Wilson in 1960s and subsequently	• Hamilton's inclusive fitness of the 1960s • Selfish gene theory and game theory: Dawkins and Maynard Smith in 1970s and subsequently
Articulation *Superorganism as a legitimate individual* 1. Relations, not properties, of parts are important 2. Whole and parts provide mutual meaning 3. Constant interaction with environment	• Gordon in 1980s and subsequently • *Integratively defined* superorganism	• Hamilton and Price hierarchical covariance approach of the 1970s • Multilevel selection theory: Wade and D. S. Wilson in 1970s and subsequently • *Competitively defined* superorganism

replicators. The competition perspective is fundamentally interested in the patterns and processes of changes in replicator (e.g., gene) frequencies, across generations, in populations of interactor modules and individuals (tables 4.1 and 4.2). For example, in social insect colonies, selection occurs at both the hymenopteran organism and the hymenopteran colony level. Rather than focus on the physiological and behavioral relations (i.e., integrative mechanisms) of colonies, this perspective explores, for example, the conditions necessary for the fixation of alleles for cooperation.

In short, work within the integration perspective focuses on how modules interact to form an individual and on the patterns of evolutionary change of mechanisms and modules, whereas research in the competition perspective emphasizes the selective dynamics, often at multiple levels of modules and individuals, that lead to changes in replicator frequencies. Although the replicator/interactor distinction could be employed in the integration perspective and mechanistic interactions could be investigated in the competition perspective, these are not the concerns guiding research in each perspective. As we shall see, the term "individual" is defined differently in each perspective. In this chapter, I will not further explore the abstract meaning of individuality, nor will I discuss individuals at levels higher than the superorganism, such as species and clades (for such discussion see, e.g., Eldredge, 1985, 1989; Ghiselin, 1974, 1997; Gould, 1995; Gould and Lloyd, 1999; Hull, 1978, 1980; Vrba and Eldredge, 1984).

Modular cooperation and defection are understood differently in each perspective. For the *integration* perspective, *modular cooperation* is understood not as a cooperative act, on the part of modules, to ultimately increase their inclusive fitness or their reciprocal fitness benefits, or both, but as a developmental and physiological process that establishes a functional integration of the whole. *Modular defection* is denied as a meaningful phenomenon. It is interpreted as mechanistic dysfunction; selection is understood as occurring among higher-level modular individuals.

For the *competition* perspective, *modular cooperation* is explained as a strategy, on the part of modules, to maximize their inclusive fitness or their reciprocal fitness benefits, or both, in a group context. Alternatively, modular cooperation can be enforced by various higher-level control methods subject to higher-level selection. *Modular defection* is accepted. It happens when a module gains short-term fitness benefits at the expense of other particular modules or the whole collection of modules (i.e., the individual), or both. Modular defection can occur whenever genetic relatedness among modules becomes too low, or when reciprocal fitness

benefits in mutualistic relationships become too low, or when the higher-level individual fails to control lower-level defector variant modules—or a combination of all three possibilities.

Addressing the issue of modular process—integration or competition—is distinct from the issue of whether the individual (whole) is greater than the sum of its modules (parts) (tables 4.1 and 4.2). This second issue is addressed by two distinct research strategies. The *partitioning* research strategy explains an individual as a relatively direct and linear aggregation of its modules (see Wimsatt, 1984, 1986; Gerson, 1998). Properties of modules, rather than interactions among modules, account for the dynamics and fitnesses of individuals. In contrast, the *articulation* research strategy emphasizes the dynamical and analytical relations among parts and wholes (tables 4.1 and 4.2).

I use the term "articulation" to stress the complex nonlinear interactions among parts—this is sometimes called "holism." Although my distinction is similar to the reductionism–holism distinction, I prefer my terms because I intend to classify rather than prescribe. I want to distance myself from the evaluative overtones of "reductionism" and "holism." With respect to articulation, biologists and philosophers make three classes of interrelated claims: (1) parts interact hierarchically—relations (i.e., interactions), and not context-independent additive properties, are of primary explanatory importance; (2) the whole provides meaning to the parts—parts can neither be defined nor be described independently of the whole; and (3) both parts and wholes interact with, and change in response to, their environment, which is hierarchical and also is defined by its interaction with the whole and its parts (e.g., Kauffman, 1971; Wimsatt, 1974, 1984, 1986; Levins and Lewontin, 1985; Lewontin and Levins, 1988; Gerson, 1995, and personal communication; Wade and Goodnight, 1998; Wade et al., 2001).

A research strategy consists of bets (commitments) that certain particular protocols and techniques will be more advantageous than others (see Gerson, 1998 on commitments). A perspective coordinates phenomena, methodologies (including research strategies), theories, and questions of interest into a general program of scientific investigative activity (e.g., Wimsatt, 1974; Griesemer, 2000a, and personal communication; Gerson, personal communication). Both research strategies are employed in both perspectives. For example, in studying the integration of ant colonies, Edward O. Wilson adopts a partitioning strategy when he argues that both chemical signals (pheromones) and ant organisms of distinct castes have context-independent properties that determine colony-level behavior in a linearly aggregative fashion. Deborah M. Gordon, who also adopts the integration perspective, adheres to an articulation strategy when she focuses on both context-dependent

interaction rates as communication mechanisms and the context-dependent task flexibility of workers.

Determining whether a biologist or field of inquiry relies on partitioning or articulation strategies is not always easy. The conceptual contrast between the two extreme positions is clear, but much research is done somewhere in between them; a few researchers employ both of them, though they tend to use one more frequently. I will not attempt the difficult task of placing every discussed researcher somewhere along the continuum between the two extremes. It is also beyond the scope of this chapter to discuss the abstract question of the possibility of adopting both research strategies. However, for each of the four cases of perspective and biological level discussed, I will contrast two or more investigators who fall near either extreme (tables 4.1 and 4.2). The chapter first discusses the integration and competition perspectives, in that order, in multicellular organisms; it subsequently discusses these perspectives in social insect colonies.

This chapter sketches a map of the intellectual region where the material processes and scientific investigations of evolutionary developmental biology meet those of levels of selection. This area concerns both the evolutionary emergence of new levels of individuality and the evolutionary change of developmental patterns and processes of well-integrated individuals (see Winther, 2001a). Typically, proponents of the integration perspective, who are usually developmental biologists, are interested in describing the nature of, and evolutionary changes in, developmental mechanisms. Adherents of the competition perspective, who are usually evolutionary biologists, are often concerned with the selective processes affecting replicator frequencies or giving rise to new levels of individuality (e.g., multicellularity from unicellularity; see Buss, 1987). The correlation among perspectives, fields, and interests is high. I do not argue for the superiority of either perspective. Elsewhere, I have articulated how these perspectives relate with respect to the questions posed (Winther, 2001a).

In the conclusion, I will explore further the possible relations between the perspectives with respect to other components of a perspective (i.e., methodologies, which include research strategies, phenomena, and theories). I do not commit to any one interpretation of the relation between the integration and competition perspectives. Furthermore, although I think that the partitioning research strategy is more workable, the articulation research strategy is required in order to realistically describe the actual complexity of the world. Thus, each research strategy has strengths and weaknesses. My aim is diagnosis: I seek to make researchers in both perspectives aware of the other perspective and, furthermore, I invite them to consider the utility of the two research strategies of partitioning and articulation.

Integration Perspective on Multicellular Organisms

Kinds, Criteria, and Levels of Modules

Almost all the conceptual work on modularity stems from molecular and developmental biologists working on organisms and adhering to the integration perspective. Since discussion on modularity has focused on organisms and since the concept of modularity has been extensively reviewed elsewhere, here I will only briefly discuss some of the salient points (see, e.g., R. A. Raff, 1996; von Dassow and Munro, 1999; Bolker, 2000; Winther, 2001a). Because of the discussion available elsewhere, the first two sections, on multicellular organisms, will not be as detailed as the last two sections, on social insect colonies. I will, however, explore the concept of organismic modularity in the context of each perspective and will, in this first section on the integration perspective, relate it to other issues in the field of evolutionary development biology (sometimes called "evo-devo"). Evolutionary developmental biology is the study of how patterns and processes of development and heredity change during, and also influence, evolution (see R. A. Raff, 2000; Wagner et al., 2000).

There are various kinds of modules, and they differ among fields (Winther, 2001a). Systematics and comparative morphology study *structural* modules; developmental biology examines *developmental* modules; and physiology and functional morphology investigate *physiological* modules. Structural modules are the parts that compose an individual at a time slice of ontogeny; individualized vertebrate bones or arthropod segments are paradigmatic examples. Developmental modules can be of two subkinds—either parts that change over time or parts that induce other modules to change. Two examples of the latter kind are morphogenetic fields, which determine gradients that provide positional information for incipient structures (S. Gilbert et al., 1996; R. A. Raff, 1996; Wolpert, 1996), and *cis*-regulatory regions of the DNA, to which transcription factors bind (Arnone and Davidson, 1997). Physiological modules are individuated by their activity. For example, the production of insulin in the pancreatic islets of Langerhans uniquely distinguishes these clusters of cells as physiological modules. Any particular module may fulfill no, one, or multiple functional roles. It is important to distinguish physiological or developmental *processes* from abstract *functions*: these processes are activities, whereas functions are selective or analytic *reasons* for these processes. A process may not have a function (S. Gilbert and Bolker, 2001, p. 443; Winther, 2001a, pp. 117–118; on function, see Allen et al., 1998; Godfrey-Smith, 1993, 1996).

A number of criteria are employed to individuate structural, developmental, and physiological modules (R. A. Raff, 1996; Wagner and Altenberg, 1996; Gerhart and Kirschner, 1997; Bolker, 2000; Winther, 2001a). The more criteria a focal unit fulfills,

the more justified we are in deeming it a module; thus, there are degrees of modularity. Here I discuss four criteria. First, modules have differential genetic specifications. There is genetic overlap (e.g., pleiotropy) across modules, but on average each module is unique both in its set of expressed genes and in the way these genes interact among themselves and with their environment. Modules consisting *of genes* are also clearly genetically different from one another. Second, modules are often repeated and conserved (a) within or across taxa, (b) at or across hierarchical levels within individuals (e.g., molecular, cellular, and histological), and (c) in different and similar contexts. Repetition and conservation occur because modules are more likely to arise from the duplication of preexisting modules, followed by their co-option in new functional contexts, rather than from the development of new modules. Third, there is strong connectivity within, and weak connectivity among, modules. Different modules are semiautonomous during both development and evolution. Perhaps they can be thought of as "individuals" in some respects (Wagner, 1989, pp. 1160–1163; Bolker, 2000, p. 773), but I prefer to use that term to describe an independently existing whole. Fourth, modules vary and change over ontogenetic and phylogenetic time. Two of the main research goals of evolutionary developmental biology are to precisely map modular *variation* among, and within, taxa, and to describe modular *change* over time. These four criteria are used to individuate modules (Winther, 2001a).

Modules exist at a variety of levels. At the molecular level, they exist both in genes and in proteins. Arnone and Davidson (1997) use "modules" to refer to segments of *cis*-regulatory regions of DNA. The term could also be applied to exons. Although they do not use the term, Gerhart and Kirschner describe the 16 basic kinds of intercellular signaling systems (Gerhart and Kirschner, 1997, chap. 3). Each system, which is composed of transmembrane proteins, has a particular structure and engages in the process of transducing one kind of extracellular signal to another kind of intracellular one. Thus, each signaling system is a particular structural and physiological "module-kind" (on module-kinds versus module-variants-of-a-kind, see Winther, 2001a, p. 120). At the organismic level, modules exist as physiological adult structures, such as cells with limited behavioral repertoires (Larsen and McLaughlin, 1987; Larsen, 1992), internal organs, and segments in segmented taxa. Modules are also developing parts such as germ layers or morphogenetic fields in the developing limb buds of vertebrates (R. A. Raff, 1996, chap. 10).

Three Approaches to Modules and Modular Interaction

Gerhart and Kirschner, R. A. Raff, and Wagner each investigate the roles of modules in development and evolution. Although they share assumptions about the hierarchy and the criteria of modularity, they approach their study systems differently.

Here I argue that their approaches are primarily physiological, developmental, and structural, respectively (table 4.1). However, in what follows, I do not intend to suggest in any way that Raff, for example, is not interested in structure. However, Raff *focuses* on developmental modules rather than on physiological or structural ones.

Gerhart and Kirschner are, respectively, a biochemist and a cellular biologist; their investigations focus on these levels. Two important themes in their book (Gerhart and Kirschner, 1997) are the conservation of basic modular processes within and across taxa, and the intensity of interaction among modules. They explain the conservation of protein function and structure in terms of processes of connectivity among multiple intracellular metabolic and regulatory systems. This connectivity is "contingent" in that molecular and cellular networks require multiple inputs for proper functioning. For example, protein kinases, which change the conformation of other proteins by adding a phosphate group from ATP to them, quickly activate or inhibit the other proteins (Gerhart and Kirschner, 1997, pp. 80ff.). This is an example of contingent connectivity in that catalytic proteins *depend* on other catalytic proteins for their state of activation or inhibition. Contingent connectivity also indicates the importance of complex networks of processes—networks of biochemical modules, in Gerhart and Kirschner's approach. In their approach, biochemical physiological modules are crucial in explaining development and evolution (see also Kirschner and Gerhart, 1998).

R. A. Raff and Wagner both focus on the organismic level, but Raff concentrates on developmental modules, whereas Wagner emphasizes structural modules. Raff and coworkers have studied the genetic and developmental differences between two sister species of sea urchins (e.g., R. A. Raff, 1996; R. A. Raff and Sly, 2000), *Heliocidaris erythrogramma* and *H. tuberculata*. The former species is a direct developer, whereas the latter is an indirect developer; it has a pluteus larval stage (R. A. Raff, 1996, 2000). In the direct developer, all of the early cells of the morula are the same size. In contrast, in the indirect developer, morula cells have significantly different sizes. Furthermore, in direct developers "cell types homologous to those of indirect developers have different precursors" (R. A. Raff, 1996, p. 231). The splitting of these lineages occurred only 4–5 million years ago (personal communication to Rudolf Raff by Kirk Zigler, who used calibration data of Lessios et al., 1999), which makes the evolution of their radical developmental differences remarkable. In addition to investigating differences in developmental patterns, Raff and coworkers successfully hybridized the two species to explore genetic and developmental patterns and processes in the hybrids (E. C. Raff et al., 1999; Nielsen et al., 2000). This research, as well as his theoretical discussion of morphogenetic fields (S. Gilbert

et al., 1996; R. A. Raff, 1996, chap. 10), indicates Raff's emphasis on developmental modules.

Wagner studies morphology, developmental biology, systematics, and theoretical population genetics. For Wagner, modules and homologues are deeply connected: all modules of a particular kind are homologues and vice versa (Wagner, 1996, and personal communication). Unlike Raff and many others, Wagner prefers a structural rather than a phylogenetic definition of homology (Wagner, 1994, 1995, 1996). Modules are character complexes determined by unique sets of expressed genes (Wagner, 1996; Wagner and Altenberg, 1996; Mezey et al., 2000). Wagner also describes modules or "building blocks" as structures (homologues) that are stabilized and constrained during development and evolution (Wagner, 1994, 1995; see also Roth, 1994). In this sense, modules are structures that are conserved across taxa, not only because of descent from a common ancestor but also because of developmental constraints ("generative" and "morphostatic" constraints; Wagner, 1994).

Wagner is clearly interested in development as well as structure; this can be gleaned from his studies on bottom-dwelling blenny fish (Wagner, 1989, 1994). I consider his approach to modularity and homology to be primarily structural, however, because although he considers developmental mechanisms and constraints to be explanatory, what he seeks *to* explain is the structural identity and individualization of morphological sets of characters during development and evolution (Wagner, 1994, 1995).

These four investigators all explore mechanisms of modular integration at various levels. However, each approaches modules and modular interaction differently.

Partitioning and Articulation: How Powerful Are Genes?
Genes are often considered to be the agents of development. The four investigators discussed in the previous section, however, are aware of the complex hierarchical environment in which genes, proteins, and other molecules interact nonlinearly during development. They endorse an articulation strategy. Other adherents of the integration perspective employ a partitioning strategy by focusing on the context-independent power of genes (table 4.1).

Because the Human Genome Project (HGP), as described by key advocates, ultimately seeks to investigate genes as mechanistic prime movers of the development of morphology, physiology, behavior, and disease, it employs partitioning within the integration perspective. Proponents of the HGP claim that "the genetic messages encoded within our DNA molecules will provide the ultimate answers to the chemical underpinnings of human existence" (Watson, 1990, p. 44). Since we are "dictated by our genetic information," the HGP will allow us to "find sets of genes for such

conditions as heart disease, susceptibility to cancer, or high blood pressure" (W. Gilbert, 1992, pp. 96, 94). Although the publication in *Science* presenting the human genome warns of the "fallacies of determinism and reductionism" (Venter et al., 2001, p. 1348), it is clear that the HGP adheres to a partitioning strategy which is premised on determinism and reductionism. A number of authors have discussed the weaknesses of this strategy (Lewontin, 1991; E. F. Keller, 1992; Griesemer, 1994; Lloyd, 1994; Oyama, 2000a, 2000b; Oyama et al., 2001).

The integration perspective on organisms focuses on the mechanisms of organismic development and physiology. This contrasts with the competition perspective, which I will now explore.

Competition Perspective on Multicellular Organisms

Selective Processes, Replicator Modules, and Interactor Modules

The competition perspective focuses on the competitive dynamics within multicellular organisms. In a typical selection scenario, units replicate *differentially* because they have heritable differences *and* also because they vie for a common pool of limited resources, such as food or mates, or are subject to differential predation or parasitism, or a combination of any of these factors. The competition perspective analyzes the origin and maintenance of multicellularity as a case of selection at, potentially, multiple levels (e.g., genes, cells, organisms, and even groups of organisms as well as species and clades; in this chapter I do not discuss species or clade selection).

The distinction between replicators and interactors highlights a *functional* difference of biological units (Griesemer, 2000b, in press). Some units, the interactors, interact with their environment and with other units. Interactors have a hierarchical structure. They are (1) parts of either higher-level parts or wholes, or (2) wholes themselves (i.e., interactors are either modules or individuals). Replicators are units of which copies are made, and they are statistically correlated with—or, more contentiously, cause—the development of the interactors (Dawkins, 1976; Hull, 1980). The higher the correlation, the more efficient the selection process—where efficiency is the realized heritability (Michael Wade, personal communication). Replicators also have a hierarchical structure (Brandon, 1982, 1990). Sometimes they are independent genes with context-independent, additive phenotypic or fitness effects, or both, but they can also be genes in linkage disequilibrium due to, for example, epistasis for fitness. Replicators can even be groups of organisms or species.

Here I will be concerned with genes, potentially in linkage disequilibrium, as replicators. Selection of interactors leads to the differential reproductive success of replicators involved in producing interactors (see Lloyd, 2000 for a review). Modules

exist both in an interactor and in a replicator hierarchy. Since I will mainly analyze those selective processes among interactors that biologists have suggested for the origin and maintenance of multicellularity, the term "modules" will refer to interactor modules unless otherwise stated.

Suborganismic modules pertinent to the competition perspective include both genes that function as interactors (e.g., selfish transposons; Werren et al., 1988) and cell lineages. Because most work has been done on cell lineages, I will focus on them. The key question for the competition perspective is: Why did, and do, cell lineages in organisms cooperate rather than defect? Defection appears to be favored at the cell level; cell lineages leaving more cell offspring have a higher fitness, at that level, than those that do not. Cooperation seems to be disadvantageous at that level; somatic specialization and curtailed reproduction lower the immediate fitness of a particular cell. I divide my discussion into investigators who claim that cell-lineage defection is mainly absent in well-integrated organisms and those who claim that it is prevalent.

Cell-Lineage Defectors Are Mostly Absent in Well-Integrated Organisms

The Evolution of Individuality: Higher-Level Control Methods and Kin Selection
The locus classicus for discussion of the evolution of multicellularity is Buss's *The Evolution of Individuality* (1987; see also Buss, 1983, 1985, 1999). Buss notes that an organism is actually not a "genetically homogeneous unit" (1987, p. 19), although it does consist of "clonal lineages" (1987, p. 77). An organism is an environment "populated by normal and variant cells" (1987, p. 76). Cell developmental modules, which are interactors, compete within this "somatic ecology" (1987, p. 139). Variant (i.e., defector) cell lineages divide in an uncontrolled fashion and contribute little to *somatic* cell function. They are often detrimental to the whole organism. There is also strong cell-lineage selection for variant cell lineages to enter into the areas, or be part of the lineages, that fulfill the *reproductive* functions. Defector cell lineages can therefore disrupt both somatic and reproductive organismic functions, according to Buss.

Since organismal stability, early in the evolution of multicellularity, was threatened by defector cell lineages, methods of controlling defection were strongly favored at the organismic level. For example, (1) the evolution of a sequestered germ-line eliminated the possibility that a variant developmental module could be heritable *across* organismic generations. Furthermore, since germ cells undergo significantly fewer cell divisions than somatic cells, there is a smaller likelihood of mutation occurring in them, given an approximately constant mutation rate per cell

division. Buss also considers (2) maternal control of early development and (3) inductive interactions as control methods. If maternally derived egg cytoplasmic mRNA and proteins determine division patterns and cell fate, then a cell-lineage variant, with its own genotypic and phenotypic properties, cannot arise until maternal control stops (1987, pp. 54ff.).

Similarly, inductive interactions between cell lineages "restrain [ ] or direct [ ] the activities of neighboring cells, . . . [thereby] enhanc[ing] their own replication and the survivorship of the individual harboring them" (1987, p. 78). This last control method is the only one in which the direction of selection is the *same* at both the cellular and the individual levels. Note that all these methods of control are considered higher-level adaptations at the organismic level.

Sometimes these methods of control fail, as when mammalian cancers occur (1987, p. 51). Less dramatic somatic mutations can also occur. Thus, Buss implies that defection by developmental somatic modules does occur in well-integrated organisms, despite numerous control methods. Germ-line mutational variants are, however, rare because there are "overlapping periods of maternal direction and germ-line sequestration" (1987, p. 116). The generation of germ-line variation is mainly a consequence of meiosis and recombination.

In his book's last chapter, aptly titled "The Evolution of Hierarchical Organization," Buss argues that "The history of life is a history of transitions between different units of selection" (1987, p. 171). This is because "Any given unit of selection, once established, can come to follow the same progression of elaboration of a yet higher organization, followed by stabilization of the novel organization" (1987, p. 172). Thus, stabilization of individuals through control methods occurs after transitions to *that* level of individuality. Buss's book is an exploration of the transition to, and stabilization of, the multicellular level. In his conclusion he notes that there are many other levels requiring investigation. I will consider the social insect level in the last two sections of this chapter.

Buss explored one explanation for the evolution of cellular cooperation—higher-level control methods. Another crucial explanation investigated subsequently to Buss is kin selection, which Hamilton first developed in a mathematically rigorous fashion. The basic idea of kin selection is that an allele that is correlated with, or causes, a behavior lowering the immediate fitness of the benefactor may actually increase in frequency (i.e., be selected) when the recipients of the behavior are close kin who have a high probability of carrying the same allele. Some proponents of kin selection propose that it operates at only a single level—the gene or the organism (Dawkins, 1976; Maynard Smith, 1976); others argue that kin selection has components at multiple levels (e.g., Price, 1970, 1995; Hamilton, 1975; Uyenoyama and

Feldman, 1980; Wade, 1980, 1985; Queller, 1992a, 1992b; Sober and Wilson, 1998). I will develop the logic of kin selection in more detail in the section on the competition perspective on social insects.

Michod and coworkers provide detailed models that employ both multilevel kin selection and higher-level control methods to explain the origin and maintenance of multicellularity (Michod and Roze, 1997; Michod, 1999a, 1999b). Michod has both cell-level and organism-level fitness parameters in his models (e.g., replication rate of defector versus cooperator cells; organism-level fitness as a function of cooperator cell frequency). If higher-level (i.e., organismic) selection is sufficiently strong, alleles for cooperation will increase in frequency in the population. However, a number of parameters need to be considered to determine whether cooperation can reach fixation[1]: total number of cell divisions in an individual, mutation rate, and relative benefit to a defector cell (which can be less than 1; in this case mutations are deleterious at both the cell and the organism levels).

In most of the parameter space Michod explores, alleles for cooperation do *not* reach fixation even though interactor cell modules are related by common descent (Michod, 1999a, chap. 5). Kin selection is not sufficient for the origin of organismic individuality; higher-level control methods such as germ-line sequestration and defection-policing mechanisms (e.g., immune systems) are necessary (Michod, 1999a, chap. 6). Questions about how kin selection, control methods, and mutualism—cooperation through expected long-term reciprocal benefits—are related still require investigation. As we will see in the section on the competition perspective on social insects, these questions have been addressed in more detail in social insects, where an important control method is parental manipulation and reciprocal mutualistic benefits among organisms are easily conceptualized.

Partitioning and Articulation: Interactors and Replicators By employing an explicitly multilevel selection framework and emphasizing the importance of higher-level control methods, Buss and Michod employ an articulation research strategy (table 4.1). They stress the relations among parts at, and across, hierarchical levels and among parts and wholes, as well as the importance of higher-level mechanisms. In their book on transitions, Maynard Smith and Szathmáry argue that control methods are not required for the stabilization, during evolution, of higher-level organisms (Maynard Smith and Szathmáry, 1995; see also Szathmáry and Maynard Smith, 1995). Genetic similarity among modules of an organism is sufficient to arrest any potential conflicts (Maynard Smith and Szathmáry, 1995, pp. 8, 244). Alleles for cooperation can reach fixation given such high degrees of relatedness ($r \approx 1$) between modules. With this argument, these authors ignore the potentiality, and reality, of

mutation and they do not consider the full range of selective parameters (e.g., when defection benefit is high). If mutation occurs, and the selective differential is sufficiently high, cooperation will not reach fixation despite generally high relatedness (Michod, 1999a).

Regarding kin selection, Maynard Smith has argued that it should be understood as happening at the level of the individual—the organism (Maynard Smith, 1976, 1982). But when he and Szathmáry discuss cell (*sensu* individual) versus organism (*sensu* group) selection, it is unclear whether they argue that kin selection has only a cell-level component or whether it also has an organism-level component (see, e.g., their analogy between the "stochastic corrector model" and kin selection in Szathmáry and Maynard Smith, 1995, pp. 227–229). They do, however, state their allegiance to the "gene-centered approach" of Williams (1966) and Dawkins (1976), and they do not cite any of the literature on multilevel kin selection theory. Both of these actions imply that Maynard Smith and Szathmáry believe that cellular kin selection occurs only at the cell level. By denying the importance of higher-level control methods and by implying that kin selection operates at a single low level, Maynard Smith and Szathmáry reveal partitioning research strategies (table 4.1). Thus, with respect to interactors, Buss and Michod adopt an articulation strategy, whereas Maynard Smith and Szathmáry endorse a partitioning strategy.

The articulation versus partitioning research strategy distinction has thus far been applied to interactors. I will how briefly discuss this distinction in light of the replicator question (Lloyd, 2000). Dawkins argues that the replicator in evolution is the individual selfish gene, which has context-independent additive effects (Dawkins, 1976, 1982). Linkage disequilibrium (which Dawkins mentions only in passing) due to, for example, epistasis for fitness "*simply* increases the size of the chunk of the genome that we can usefully treat as a replicator" (Dawkins, 1982, p. 89; emphasis added). Dawkins's position is partly based on Williams's partitioning argument for the universal validity of calculating additive genetic effects by averaging the effect of a gene across all genetic backgrounds in a population; this is justified, according to Williams, "no matter how functionally dependent a gene may be, and no matter how complicated its interactions with other genes and environmental factors" (Williams, 1966, p. 57; for critical discussion that emphasizes considerations such as small natural population sizes and nonrandom distributions of genetic backgrounds, see Wimsatt, 1984; Lloyd, 1988, chaps. 5 and 7, and 2000; Wade, 1992; Wade and Goodnight, 1998; Wade et al., 2001). Dawkins's partitioning strategy can be clearly gleaned from the concluding sentences of *The Extended Phenotype*: "The integrated multicellular organism is a phenomenon which has emerged as a result of natural selection on primitively independent selfish replicators. It has paid replicators to

behave gregariously.... In practice the organism has arisen as a partially bounded local concentration, a shared knot of replicator power" (Dawkins, 1982, p. 264).

On the other hand, views which utilize articulation strategies in investigating replicators include (1) those that emphasize the importance and ubiquity of interactions among genes, that is, epistasis which cannot be removed by averaging across genetic backgrounds (e.g., Avery and Wasserman, 1992; Wade and Goodnight, 1998; Wolf et al., 2000; Wade et al., 2001), as well as (2) the "reproducer" and "developmental systems" views developed, respectively, by Griesemer and Oyama (Griesemer, 2000a, 2000b, in press; Oyama, 2000a, 2000b; Oyama et al. 2001). These last two authors, however, are attempting to dismantle the replicator versus interactor distinction.

Cell-Lineage Defectors Are Common in Well-Integrated Organisms

A number of authors who endorse the competition perspective claim that cell-lineage selection occurs with substantial frequency in well-integrated organisms. Otto and coworkers have investigated germ-line cell-lineage selection in contemporary organisms (Otto and Orive, 1995; Otto and Hastings, 1998). They argue that the number of cell divisions from zygote to zygote is sufficiently large to consider their mutations and mutation rate evolutionarily important (e.g., 50 in corn, 25 for *Drosophila*, 25 for female mice, and 23 for human females, per generation; Otto and Hastings, 1998, p. 510). The models of Otto and coworkers indicate that, depending on the hierarchical (i.e., cell-level and individual-level) costs and benefits of mutations, intraorganismal selection can increase or reduce the mutation rate. Furthermore, selection between germ-line developmental modules can also decrease the mutation load in a population because deleterious mutations in such modules will tend to be eliminated as they compete.

These selective scenarios differ crucially from Buss's, Michod's, and Maynard Smith and Szathmáry's in that selection is interpreted as often acting in the *same* direction at both levels. Most loss-of-function mutations that are deleterious at the individual level are also deleterious at the cellular level. Furthermore, "mutations that improve the efficiency of metabolic pathways may often be beneficial at both levels" (Otto and Hastings, 1998, p. 520). Insofar as selection operates in the same direction at both levels, control methods are not necessary. However, if a fraction of mutations have beneficial cell-level effects, but deleterious individual-level effects, control methods will be necessary. An interesting research project investigating the relative frequency of this case of opposing directions of selection at the two levels, and the evolution of control methods as a function of its increased frequency, awaits exploration (Sarah Otto, personal communication).

Nunney also emphasizes the reality of modular competition, in the form of cancer, in well-integrated organisms (Nunney, 1999a, 1999b). Growth-controlling genes that suppress the defector consequences of mutations in other growth-controlling genes would be selectively advantageous at the organism level. Despite such controls, cancers are almost inevitable in modules with high replication and turnover rates (e.g., epithelial cells in the skin, hemopoietic cells in bone marrow and lymphatic tissue). Like Michod and Buss, Nunney emphasizes the case of multilevel selection operating in opposite directions. However, he differs from them in believing that modular defection is ubiquitous.

Investigations on multicellular organisms differ significantly, depending on the perspective employed. The integration perspective attempts to understand the integrative mechanisms occurring among modules within organisms. Adherents of this perspective do not deny selection, but they generally argue that it does not occur *within* organisms. Selection occurs as a consequence of the ecological context in which whole organisms are found. Conversely, proponents of the competition perspective agree that myriad kinds of mechanisms occur within organisms. But they are interested in the ones directly pertinent to fitness, particularly those concerning cell-lineage defection and those pertinent to the control of lower-level module defection. They are typically concerned with hierarchical selective dynamics. The two perspectives thus guide distinct kinds of research on multicellular organisms.

Integration Perspective on Social Insects

Modularity in Social Insects

The better-integrated a hymenopteran colony is, the more it can be interpreted as a superorganism (i.e., an individual) with component parts. These parts, the hymenopteran organisms, as well as various symbiotic organisms and structures such as the nest, can be usefully interpreted as modules. In particular, the hymenopteran organisms can be viewed as structural, developmental, and physiological modules. Hymenopteran organisms serve as the structural modules that compose the reproductive and somatic task force of the colony. They also develop over time, as developmental modules, through egg, larval, pupal, and adult stages. Depending on species and conditions, they can take distinct morphological courses during development. Hymenopteran organisms and labor groups (e.g., foragers) are also physiological modules—they engage in particular processes that maintain the colony. In the next two sections, I will explore the two perspectives with regard to the relations among hymenopteran modules.

Early Twentieth-Century Work on Superorganismic Integration
In addition to being the first to clearly and explicitly state that the ant colony was analogous to an organism, William M. Wheeler was also a pioneer in suggesting explanations for the origin of eusociality. He saw hymenopteran social organization as a special case of the "sociogenic" "tendencies of life" (1939 [1911], p. 26). In 1918 he suggested that "trophallaxis" (i.e., the sharing of nutrition among adults and larvae) caused potentially reproductive females, in the phylogenetic past, to stay in their mother's colony and help her rear more offspring, which were sisters to the worker ants. Although this explanation is not incompatible with Hamilton's subsequent kin selection explanation, Wheeler was focused on interorganismal physiological mechanisms, rather than on genetic selective dynamics, for both the origin and the maintenance of eusociality.

The termite expert Alfred Emerson and his collaborators further articulated a superorganismic perspective on hymenopteran and termite integrative mechanisms. They did this at the University of Chicago from the 1930s to the 1950s. In his thorough review of the superorganism concept, Emerson notes, "We find that the important ecological principle of natural selection acts upon the integrated organism, superorganism or population" (Emerson, 1939, p. 197). But his brief remark on hierarchical levels of selection is hidden among a swarm of examples and citations concerning hierarchical integrative mechanisms. Listing the section headings in his 1939 article provides a feeling for its colony-level developmental and physiological emphasis: "Division of Labor"; "Ontogenetic Coordination and Integration," which is divided into five sections—"Chromosomal Foundations of Integration," "Activity Gradients and Symmetry," "Chemical Integration," "Nervous Integration," and "Rhythmic Periodicity"; and "Superorganismic Phylogeny." Emerson also developed the idea of superorganismic homeostasis with negative feedback loops (Emerson, 1956).

Emerson's colleague at Chicago, the population geneticist Sewall Wright, was working on hierarchical selection in developing his Shifting Balance Theory. Thomas Park, Emerson's ecological colleague, viewed his own work on competition as a study in the physiology of populations (Michael Wade, personal communication). Furthermore, it was partly in reaction to Emerson's research program that George C. Williams, a figure instrumental in the history of the competition perspective, developed his criticisms of group-level integration and adaptation (Williams, 1966; see also Sober and Wilson, 1998, p. 36, which recounts Williams's critical response to a lecture by Emerson while Williams was a postdoctoral student at Chicago in the 1950s). The University of Chicago is thus a fascinating locus for investigating the theoretical and experimental cooperation and conflict between the two

perspectives analyzed in this chapter. Historical research investigating this university would be useful for exploring the possibilities of synthesis between the two perspectives (see Mitman, 1992; Gerson, 1998).

Partitioning and Articulation in the Behavioral Ecology of Ants: Edward O. Wilson and Deborah M. Gordon

Two important researchers in the behavioral ecology of ants, Edward O. Wilson and Deborah M. Gordon, both study the behaviors and communication systems of ant organisms and ant colonies from an integration perspective. But whereas Wilson adopts the partitioning strategy, Gordon employs the articulation strategy (table 4.2).

The myrmecologist, and later sociobiologist, E. O. Wilson started working on the behavioral ecology, systematics, and communication systems of ants in the 1950s. One of his first conceptual pieces was a strong criticism of the superorganism concept (Wilson, 1967). He writes, "There is . . . a shared faith that characterizes the reductionist spirit in biology generally, that in time all the piecemeal analyses will permit the reconstruction of the full system *in vitro*. In this case an *in vitro* reconstruction would mean the full explanation of social behavior by means of integrative mechanisms experimentally demonstrated and the proof of that explanation by the artificial induction of the complete repertory of social responses on the *part of isolated members of insect colonies*" (p. 36; emphasis added). Note that he is interested in integrative mechanisms, for example, pheromonal communication signals. Note also that Wilson believes a comprehensive understanding of the whole can be achieved through the manipulation of the parts. Each part (i.e., module) has particular social responses, which are context-independent. The implicit idea is that social behavior is a linear extension of individual behavior. The employment of partitioning is further evidenced in his autobiography, written three decades later, in which he notes, "This reductionism [partitioning], as Lewontin expressed and rejected it, is precisely my view of how the world works" (Wilson, 1994, p. 346).

Wilson's adoption of partitioning can be best understood by analyzing two particular cases: caste membership as a determiner of tasks performed, and context-independent meaning of chemical signals. A minority of ant species have workers of different sizes and allometric proportions (the relative dimensions of their body parts are not scaled equally). For example, leaf cutter ants of the genus *Atta* often have four castes. Wilson and others argue that tasks performed are highly correlated with caste membership; ants of different castes specialize in different tasks (e.g., E. O. Wilson, 1968, 1971; Oster and Wilson, 1978; Hölldobler and Wilson, 1990).

Therefore, colony-level productivity is correlated with caste distribution, and there should be optimal caste distributions if selection can act on the colony, a

premise Wilson accepted as early as a 1968 article. However, he does not explicitly argue for the utility of the superorganism concept, which includes the idea of colony-level selection, until the 1990 book written with Hölldobler (E. O. Wilson, 1968; Hölldobler and Wilson, 1990); in both Oster and Wilson (1978) and Wilson (1985), Wilson is implicitly sympathetic to some aspects of the superorganism concept. Wilson thus understands colony-level productivity as an aggregative function of caste membership, which is an ant organismal (i.e., modular) property.

Wilson also argues for the context-invariant meaning of chemical signals. In the chapter titled "Communication," Hölldobler and Wilson present a table in which they attribute context-invariant responses to particular chemical emissions from glands (1990, p. 228). In his autobiography, Wilson recounts his first discovery of an ant pheromone. He interprets the function of this ant pheromone as follows: "The pheromone in the gland is . . . both the command and the instruction during the search for food. The chemical was everything" (E. O. Wilson, 1994, p. 291). The meaning of the pheromone (i.e., the action it elicits) does not, for Wilson, depend on other pheromones simultaneously employed, the quantity of pheromone present, the state the perceiving ant is in, or any other factor. The meaning is context-independent. Furthermore, Wilson postulates that "mass communication" occurs through the aggregation of pheromones by workers walking along the same food trail (Wilson, 1994, p. 291; Wilson and Hölldobler, 1988). Thus, according to Wilson, communication among ants is a linearly aggregative function of context-invariant chemical signals. Wilson's partitioning strategy can be seen in how he (1) argues for the context-independent properties of both ant organisms and chemical signals, and (2) suggests that colony-level behavior is a linear aggregation of these properties.

The myrmecologist Deborah M. Gordon started her investigations on ant behavioral ecology and communication systems during the 1980s (Gordon, 1989, 1996, 1999). She investigates the ecology and the behavior of a species of desert seed harvester ant, *Pogonomyrmex barbatus*. This species, like most ant species, lacks morphologically distinct castes. Furthermore, particular ants switch between different tasks: foraging, patrolling, colony maintenance, midden work, and resting. Task-switching by ant organisms depends on circadian and seasonal rhythms, weather conditions, colony age, food availability, and presence of neighbors. Thus, the behavior of an individual ant is extremely sensitive to surrounding conditions. Gordon has not found any particular organismal property that may correlate with task proclivities. In collaboration with others, she has developed models that capture the flexibility of individual ants (Gordon et al., 1992). Gordon opposes Wilson's caste perspective and instead emphasizes the interactive context dependency of ant

organism and ant colony behavior. She employs an articulation research strategy, which endorses—even requires—a superorganism view of ant colonies.

Gordon also emphasizes the role of interactions in ant communication. She distinguishes between two kinds of relations: interactions and interaction *rates* (see Winther, 2001b). Antennal contact between two ants is an example of an interaction. The number of different ants a particular ant interacts with in such a manner per unit time is an example of an interaction rate. Gordon's experiments and models indicate that ants change behavior in different contexts as a consequence of interaction rate, rather than due to any message carried in the interaction itself. Response to interaction rate may also occur in "brains, immune systems, or any place where the rate of flow of a certain type of unit, or the activity level of a certain type of unit, is related to the need for a change in the rate of flow" (Gordon, 1999, p. 169). Interaction rate, rather than interaction per se, explains temporal behavioral variance of complex dynamical systems: "the interaction pattern may be more important than the message" (Gordon, 1999, p. 156). Furthermore, information concerning ecological conditions surrounding the system can be transmitted through interaction rate. Interaction rates of pheromonal transmission and reception could also be modeled.

Note that focusing on either the message (e.g., pheromone) or the interaction rate is, strictly speaking, distinct from adhering to either context dependence or independence (i.e., pheromonal meanings could be context-dependent and a particular interaction rate could have a context-independent meaning). However, in this case, Wilson focuses on messages with context-independent meanings, whereas Gordon emphasizes the context-sensitive interaction rates of pheromonal, tactile, and nutritional communication as the ways that modules of an ant colony communicate.

The contrast between Wilson and Gordon with respect to their views on caste and communication in ants exemplifies how partitioning and articulation strategies are employed. Their common interest in understanding behavior as a consequence of physiological and ecological processes indicates their shared employment of an integration perspective.

Is an Evolutionary Developmental Biology of Social Insects Possible?
An evolutionary biologist once claimed that "evolution is the control of development by ecology" (van Valen, 1973). A significant amount of work has been done on the behavioral ecology of social insects (see West-Eberhard, 1987; Franks, 1989; Bourke and Franks, 1995; Gordon and Wilson references above). Thus, we have significant data on the ecological context in which social insect evolution occurs. The competition perspective has also provided voluminous information on evolutionary

genetic aspects of insect societies. However, there is much less work on the development of insect societies considered as physiologically integrated wholes in an ecological context. In other words, we know relatively little about the patterns and processes of differential gene expression, and the developmental pathways, of social insect modules and colonies. An evolutionary developmental biology of social insects requires that we investigate this.

Schneirla (1971) performed an early set of investigations into development of army ant colonies. Army ant colonies have two discrete stages: nomadic and statary. The 15-day nomadic stage of *Eciton burchelli* starts when a cohort of adults has just emerged from their pupal case and a distinct cohort of eggs has just hatched into numerous hungry larvae (on the order of hundreds of thousands) requiring large amounts of food. The 20-day statary phase commences when these larvae pupate. Ten days into the statary phase, the queen starts laying eggs again. The timing of this 35-day cycle, with the synchronized timing of the development of the two generations, is the result of multiple reciprocal chemical, tactile, and nutritive interactions among queens, workers, and brood. Schneirla, following Wheeler, called these interactions "trophallaxis" (Schneirla, 1971; see Hölldobler and Wilson, 1990, pp. 577–579 for a note of skepticism).

More detailed research on developmental integration of social insect colonies has appeared subsequently (e.g., E. O. Wilson, 1985; D. E. Wheeler, 1986, 1991; Hölldobler and Wilson, 1990; Robinson et al., 1997; Hartfelder and Engels, 1998; Evans and Wheeler, 1999, 2001; Robinson, 1999). In her review of the different mechanisms involved in reproductive-somatic caste determination, Diana Wheeler discusses queen effects (parental manipulation) on (1) worker behavior, (2) larval development, and (3) egg production and/or quality (Wheeler, 1986). In bees and wasps, a queen pheromone affects the building of gyne wax cells; the pheromone usually suppresses its construction. Larvae in gyne wax cells receive more food from workers. As a consequence, they have higher levels of juvenile hormone (JH), which is necessary to develop into a reproductive female. The production of JH being contingent on nutrition quantity is called a "nutritional switch." Further elaboration of organism and colony physiology leading to reproductive caste differentiation in honeybees (*Apis mellifera*) can be found in Hartfelder and Engels (1998).

Similar mechanisms involving pheromones, nutrition, and JH are found in ants despite the absence of brood cells. A queen pheromone acts during a critical period of ant larval development to induce the loss of the capacity of larvae to develop as gynes. This inhibition occurs before the nutritional switch. Regarding egg production and quality, the ant queen can control how many eggs she lays—which is, of course, a function of how much nutrition she ingests, the temperature to which she

is exposed, and other factors. More important, the queen can allocate different amounts of nutrition, mRNA, or hormones, or a combination of all three, to different eggs. In *Formica polycenta*, for example, large eggs with relatively large amounts of maternal mRNA develop into gynes (D. E. Wheeler, 1986). There are multiple strategies available to hymenopteran queens and workers for reproductive caste determination of the developing brood.

The hymenopteran colony can be interpreted as an individual with mechanisms of developmental differentiation and an internal physiology. When evolutionary developmental biology investigators study module differentiation in organisms, they study patterns and processes of differential gene expression. An evolutionary developmental biology of social insect superorganisms requires a search for such patterns and processes in hymenopterans. Evans and Wheeler (1999, 2001) found reliable differences in patterns of gene expression between honeybee workers and queens. They also found that "several genes with caste-biased expression in honey bees show sequence similarity to genes whose expression is affected by hormones in *Drosophila*" (Evans and Wheeler, 2001, p. 64). Thus, hormones such as JH may be involved in differentially activating genes correlated with morphological and physiological differences between workers and queens. Thus, the hymenopteran colony has an internal physiology that induces differential gene expression of its modules.

Behavior is a crucial factor in colony development and physiology. Although Evans and Wheeler do not ignore behavior, their focus is at the molecular and organism-physiological level. Gene Robinson and coworkers have explicitly called for the study of "the molecular genetics of social behaviour in ecologically relevant contexts" (Robinson, 1999, p. 204; see also Robinson et al., 1997). Their research program seeks to synthesize processes involving gene expression, hormones, pheromones, neurophysiology, behaviors, and ecology. They want to do this because "focusing on genes provides a common language and convergent research themes" (Robinson et al., 1997, p. 1099). Whether a synthetic theory of colony integration requires a genetic focus merits further discussion.

Since about 1990, several biologists have investigated the developmental and physiological mechanisms of social insect colonies. This application of the integration perspective has similarities to the evolutionary developmental biology synthesis that has been occurring at the organism level. Is an evolutionary developmental biology of social insect colonies possible? Clearly, differential gene expression of colony modules has been found. But this does not necessarily imply that we can consider social insect colonies as individuals when it comes to assessing module homologies, establishing ancestral and derived colony-level developmental patterns, describing the origin of colony-level innovations, and linking colony-level microevo-

lutionary with colony-level macroevolutionary change (see R. A. Raff, 2000, p. 75; Wagner et al., 2000, p. 820).

Progress has been made, however, on some of these aspects of individuality as applied to social insect colonies. Colony-level properties such as nest morphology have been used in determining robust phylogenetic trees in wasps (Wenzel, 1993); some superorganismic modules can therefore be used for establishing homologies. Furthermore, Anderson and McShea (2001) argue that organs or "intermediate-scale structures," such as teams (workers adopting different subtasks in order to perform a task, e.g., carrying a prey item) and nests, exist in social insect colonies. These results, in combination with the work discussed in this section, indicate that an evolutionary developmental biology of social insect colonies is possible. We should embark on such a project, which would also involve an investigation of the individuality of social insect colonies.

Competition Perspective on Social Insects

Kin Selection, Inclusive Fitness, and Multilevel Selection, 1964–1975: The Work of Hamilton and Price

Why do some organisms, such as hymenopteran workers, become sterile? The origin and maintenance of cooperation, which is often called altruism, was a problem that Darwin wrestled with in his *Origin of Species* (Darwin, 1964 [1859], chap. 7). His prescient answer appealed to family-level selection of "fertile parents which produced most neuters with ... profitable modification[s]" (Darwin, 1964 [1859], p. 239).

Hamilton developed the mathematics of this group selection argument more than 100 years later. Initially, however, he argued against group selection and felt that inclusive fitness made kin selection an extension of individual selection (Hamilton, 1963, 1964a, 1964b). Hamilton was interested in why organisms would reduce their fitness, for the benefit of other organisms, through behaviors such as defending the other organism or helping it to reproduce. Qualitatively, he argued that an allele that caused a behavior detrimental to a particular individual would increase in frequency when the recipients of the behavior were close kin who, with a high probability, carried the same allele (Hamilton, 1963, 1964a, 1964b). Quantitatively, he noted the conditions under which alleles for cooperation could increase in frequency: $(rB - C) > 0$, or $r > (C/B)$. In this equation, r is the coefficient of relatedness (e.g., in diplo-diploids such as mammals, organism-to-sibling $r = 0.5$; organism-to-first cousin $r = 0.125$); B is the fitness benefit the given behavior provides to the

recipient; and C is the fitness cost to the benefactor (particular individual) of performing the behavior. This equation is known as Hamilton's rule.

What Hamilton noted was that in hymenopterans, females are more closely related to their sisters ($r = 0.75$) than to their offspring of either sex ($r = 0.5$), provided that the females have the same father. This high relatedness occurs because hymenopterans are haplo-diploid: males have only one chromosome of each pair of chromosomes, whereas females have both chromosomes of each pair. Thus, on relatedness grounds alone, a female should choose to help her mother rear offspring, which are her sisters: "Our principle tells us that even if this new adult had a nest ready constructed and vacant for her use she would prefer, other things being equal, returning to her mother's and provisioning a cell for the rearing of an extra sister to provisioning a cell for a daughter of her own" (Hamilton, 1996 [1964b], p. 58).

There are complications to this simple theory, however. Hamilton noted, as others subsequently have, that multiply mated queens produce female offspring with a relatedness coefficient smaller than 0.75. If the queen has mated with two males, and assuming equal contribution from the two males and no sperm competition, among-sibling relatedness is 0.5. If the queen has mated with more than two males, the relatedness coefficient is smaller than 0.5 and converges to 0.25 as the number of males gets very large, given the assumptions stated above (Hamilton, 1996 [1964b], p. 62; Hamilton did not explicitly mention sperm competition). Hamilton noted that despite this, cooperation would still be favored, given appropriate B and C parameters. Furthermore, in some genera (e.g., worker fire ants of the genus *Solenopsis*, which lack ovaries), reproduction is not a possibility. Thus, other parameters and conditions besides r, B, and C need to be considered.

Another complication that Hamilton discussed, but did not suggest an explanation for in his early articles, is that a worker is related by only 0.25 to her brothers, whereas she would be related by 0.5 to a son. Trivers and Hare (1976) subsequently suggested that workers would still prefer to raise sisters rather than offspring if they could skew the sex ratio of sibling reproductives toward a 3 : 1 gyne : male ratio (see also Crozier and Pamilo, 1996). Complications such as these have convinced investigators that Hamilton's rule is a shorthand for more complex quantitative and population genetic models.

Investigators in the competition perspective employ Hamilton's rule. Their focus is on the reproductive dynamics of social insect colonies leading to gene frequency change. Furthermore, they have tended only to estimate r (see Gadagkar, 1991; Bourke and Franks, 1995; Queller and Strassman, 1998). This is in part because it remains conceptually unclear how to estimate B and C, which both depend on eco-

logical conditions. For example, which metric could we use to compare alternative worker strategies of egg-laying and foraging in estimating B and C? (Deborah Gordon, personal communication).

Hamilton initially emphasized that kin selection was an extension of individual selection; he used the term "inclusive fitness" (e.g., Hamilton, 1996 [1964a]; table 4.2). Price's covariance approach to selection radically changed Hamilton's view on kin selection. (Covariance is a probabilistic and statistical measure of the *correlation* between two variables.) Price sought to develop a "general selection theory" (Price, 1995, p. 389; Price, 1970). He realized that selection could be thought of as a covariance between the fitness of the units under study and their properties. These properties could be genotypic or phenotypic. Price, and others, have shown mathematically that this covariance can be decomposed into two components, each of which describes selection at one of two levels—one *within* the interactor unit and one *among* interactor units (Price, 1970, 1995; Wade, 1980, 1985; Frank, 1995). A hierarchical selection process causes gene frequency change.

In social insects, a nonzero first component representing within-colony selection could be caused by workers altering the colony sex ratio and thereby altering the normal Mendelian ratios (i.e., underrepresenting maternal genes by destroying males, overrepresenting paternal genes by not destroying gynes). This is analogous to meiotic drive in organisms (see Werren et al., 1988; Hurst et al., 1996). In social insects, a nonzero second component indicating among-colony selection would occur whenever some colonies left more offspring colonies than other colonies. Such selection is also part of some sex-ratio evolution models (Michael Wade, personal communication). Among-colony selection is analogous to organismal selection in organisms. Price's multilevel selection equation, which decomposes the causes of gene frequency change, can be further expanded to any number of levels so that we can have, for example, among-colony, among-organism (i.e., among-ant-organism module), and within-organism (i.e., within-ant-organism module, such as meiotic drive in queen ants) selection in social insects.

Hamilton employed Price's equation in an article in which he argued that kin selection was, indeed, a multilevel selection process (Hamilton, 1996 [1975]; table 4.2). Cooperation could evolve (i.e., alleles for cooperation increase in frequency) if among-colony selection for such alleles was stronger than within-colony selection against such alleles. One way to increase among-colony additive genetic fitness variance was precisely to have colonies with only one or a few queens mated with only one or a few males. This is analogous to unicellular bottleneck reproduction of sexual organisms (see Michod, 1999a). In these cases most additive genetic fitness variance would be among colonies rather then within them.

Kin selection, whether conceptualized as a single-level or a multilevel process, describes the selective dynamics among interactor modules, such as ant organisms, of social insect colonies. Furthermore, replicator modules, such as alleles for cooperative behavior, can increase in frequency as a consequence of these dynamics.

Other Mechanisms for the Origin and the Maintenance of Cooperation: Parental Manipulation and Mutualism

Two other explanations for the evolution of cooperation in social insects have been suggested. The first is a kind of control method, parental manipulation: offspring are inhibited during ontogeny so that they become sterile and help their mother (Michener and Brothers, 1974; Alexander, 1974). Parental manipulation can occur through pheromones, physical force, or limited nutrition. We encountered these mechanisms, as integrative mechanisms, in the section on the integration perspective on social insects. The second explanation is mutualism: social cooperative interactions between two organisms, each of which can reproduce, are beneficial to each organism in the long run, even if they are, on occasion, detrimental in the short run (Trivers, 1971; Axelrod and Hamilton, 1981; Maynard Smith, 1982, chap. 13, "The Evolution of Cooperation"). Evolutionary game theory has been used to model this mechanism. Both of these mechanisms can be interpreted as pertaining to modules of social insect colonies that have, respectively, (1) asymmetric power relationships or (2) long-term fitness benefits.

Some authors have presented the three mechanisms for the evolution of cooperation as *distinct* alternatives (Hölldobler and Wilson, 1990; Seger, 1991). Hölldobler and Wilson consider kin selection and parental manipulation to be distinct explanations for the origin of sterile castes (1990, p. 182). Other investigators, however, imply that it is meaningless to attribute relative importance to each of these mechanisms because they operate simultaneously and actually influence one another. Instead, these researchers have developed models that explicitly incorporate all of these mechanisms (e.g., L. Keller and Reeve, 1999; Crespi and Ragsdale, 2000; Timothy Linksvayer, personal communication).

Partitioning and Articulation: Kin Selection, Inclusive Fitness, and Multilevel Selection, 1976–2001

Subsequent to the development of Price's equation, multilevel selection theory was expanded by a number of investigators (Uyenoyama and Feldman, 1980; Wade, 1980, 1985, 1996; D. S. Wilson, 1980; D. S. Wilson and Colwell, 1981; Queller, 1992a, 1992b; for historical and philosophical reviews, see Lloyd, 1988, 2000; Sober and Wilson, 1998). Broadly stated, these investigators found that most cases of selection

can be understood as hierarchical selection processes with hierarchical selective components. All cases of selection in populations with social interactions can be decomposed into at least two components: group and individual selection. Thus all cases of kin selection are hierarchical (see Wade, 1980). Not all cases of hierarchical selection need involve kin, however: consider selection on symbiotic relations such as lichens.

There are few cases in nature to which a hierarchical approach could not be applied. Those cases that approach the Fisherian idealization of extremely large, randomly mating, unstructured populations are candidates. The hierarchical selection approach, which implies an articulation research strategy (table 4.2), has been applied to social insects (e.g., Bourke and Franks, 1995). It can be used to understand the selective dynamics occurring among and within social insect colonies.

But the hierarchical approach has been met with resistance from investigators adopting a partitioning strategy regarding kin selection (table 4.2). A number of behavioral ecologists still interpret inclusive fitness and kin selection as an organism- (or gene-) level process or property, as Hamilton originally did in his articles from the 1960s (e.g., Dawkins, 1976; Grafen, 1984; Krebs and Davies, 1993). For these investigators, complete models can be built using inclusive fitness defined only at the single level of the organism or gene.

But perhaps the difference between articulation and partitioning research strategies is not significant. A number of modelers have cogently shown that single-level inclusive fitness is equivalent to hierarchical selection if the former is defined, modeled, and estimated correctly (Queller, 1992b; Dugatkin and Reeve, 1994; Bourke and Franks, 1995; Kerr and Godfrey-Smith, 2002). Two points should be made in response to this. First, hierarchical selection models still reveal articulation strategies in that they make the investigator aware of *all* the selection processes actually occurring in nature. A problem with individual-level inclusive fitness models is that they require that fitness parameters be averaged from the hierarchical selective parameters; a loss of theoretical and empirical information regarding selective dynamics occurs as a consequence of this averaging (Lloyd, 1988; Wade, 1992; Wade and Goodnight, 1998; Wade et al., 2001; Sober and Wilson, 1998). Second, claims about the equivalence of models should be assessed on a case-by-case basis.

In concluding this section I want to return to the superorganism, which I described in the section on the integration perspective on social insects. In the integration perspective the superorganism, as well as the multicellular organism, is defined in terms of developmental and physiological integration mechanisms. Although such mechanisms are not denied in the competition perspective, this perspective defines the

superorganism, and the multicellular organism, in terms of the strength of selection at multiple levels (D. S. Wilson and Sober, 1989; Ratnieks and Reeve, 1992). Wilson and Sober state the definition succinctly: "When between-unit selection overwhelms within-unit [between-module] selection, the unit itself becomes an organism [individual] in the formal sense of the word" (1989, p. 343). According to the competition perspective, an increase in any of three factors will increase the among-unit component of total additive genetic fitness variance: relatedness, control methods, and the benefits from mutualism. If the among-unit component is greater than (i.e., "overwhelms") the within-unit component, an individual will have been "formally" identified. Each perspective employs its own definition of individuality. A further discussion of overlaps and tensions in these definitions is necessary for a synthesis of the two perspectives.

On Material Nature and Theoretical Perspectives: Modular Integration or Competition, or Both?

In this chapter, I have explored two perspectives on modular processes. Since I have been interested in exploring two distinct levels of individuality, I have focused on cells and social insect (particularly hymenopteran) organisms as parts of a whole. Under the integration view, these parts are intermediate-level modules involved mainly in mechanistic processes. Under the competition view, these parts are interactor modules engaged primarily in selective processes. But genes have also been important modules in my analysis. Genes are important mechanistic modules in the integration view and are, generally, replicator modules in the competition view. Partitioning research strategies in *both* perspectives tend to focus on the context-independent properties, and powers, of genes.

An apt distinction between gene-P (phenotypic gene) and gene-D (developmental gene) serves to contrast the two perspectives (Moss, 2001). Moss defines a gene-P in terms of "its relationship to a phenotype albeit with no requirements as regards specific molecular sequence nor with respect to the biology involved in producing the phenotype" (Moss, 2001, p. 87). A gene-D, in contrast, "*is defined by its molecular sequence. A Gene-D is a developmental resource (hence the "D") which in itself is indeterminate* with respect to phenotype" (Moss, 2001, p. 87). Whereas the integration perspective's goal is to unravel the mechanisms involving genes-D, the competition perspective is concerned with the change in frequencies of genes-P. The integration view seeks to unpack the molecular activities of genes-D. The competition view is not concerned with developmental mechanisms; statistical correlations, produced by genes-P, between genotype and phenotype are sufficient.

In either perspective, genes are undoubtedly crucial. However, in both perspectives, articulation research strategies go beyond the partitioning assumption of invariant monadic properties of genes by articulating the complex, nonlinear mechanistic and selective relationships that hierarchical modules, including genes, have (1) among themselves both at and across levels, (2) with respect to the whole in which they exist, and (3) with respect to the hierarchical environment in which they exist.

The historical origins of these two perspectives are worth noting. The field of evolutionary developmental biology, which is the primary territory of the integration perspective, first investigated organisms. This had started with Darwin's, Haeckel's, and Weismann's nineteenth-century syntheses of evolution, development, and heredity (e.g., Churchill, 1987; Gerson, 1998; Winther, 2000, 2001c). Investigators studying organisms also have developed the concept of modularity. Only very recently has the possibility of an evolutionary developmental biology research program of social insect colonies become real. Conversely, the field of levels of selection, which is the main territory of the competition perspective, first investigated groups of individual organisms, in particular social insect colonies. This started with Darwin's worries about the evolution of sterility in the Hymenoptera. It is not surprising that levels of selection theory started with the Hymenoptera; after all, it is here that the drastic reduction of immediate organism (or gene) fitness in favor of a higher-level group of related organisms is most obvious. Only recently has a levels of selection research program been applied to multicellular organisms and modularity.

In this chapter, I have presented the two perspectives without explicitly discussing how they are related or whether they are even different. A detailed analysis of the relationships between the perspectives would require a separate article. Therefore, in concluding this chapter I will merely sketch some of the relationships.

Perspectives coordinate scientific activity (Wimsatt, 1974; Griesemer, 2000a and personal communication; Gerson, personal communication). Phenomena, methodologies (including research strategies), theories, and questions of interest are all involved in scientific activity. Thus, perspectives coordinate relations among these aspects of science.

When considering these aspects it becomes clear that the integration and competition perspectives are distinct. For example, they are committed to different *methodologies*. Developing a detailed narrative of gene expression patterns or morphogenesis, or both, requires elaborate molecular techniques, whereas investigating gene frequency changes in hierarchically structured populations involves detailed quantitative genetic and population mathematical genetic models and simulations.

Work in the integration perspective could, and does, involve mathematical models, and simulations, whereas work in the competition perspective could, and does, involve molecular techniques. But the overall pattern of commitment to techniques, and the ways the techniques are used, are distinct in the two perspectives.

When considering the conclusions arrived at from abstract mathematical *models*, there can be a significant overlap between the two perspectives. A family of models constitutes a theory. Some modelers have used the Price multilevel selection equation to model the evolution of integration (Sahotra Sarkar, personal communication). But there is still a difference between the model types generally employed in the two perspectives: mechanistic narrative models in the integration perspective, as opposed to abstract mathematical models in the competition perspective. Furthermore, even when the integration perspective uses mathematical models, it tends to employ models that do not explicitly consider selection but, instead, describe interactions among modules and the effect of such processes on the whole (e.g., Gordon et al., 1992; von Dassow et al., 2000). When selection is considered in the mathematical models of the integration perspective, the models are different from the prevalent ones in quantitative and population genetics. Investigators in the integration perspective conceive of selection as acting on the whole individual; that is, modules do not compete (e.g., Oster and Wilson, 1978; Kauffman, 1993). Thus, by considering techniques and theories, which are families of models, it becomes clear that the integration and competition perspectives are distinct.

Elsewhere I have articulated how the two perspectives relate with respect to the *questions* posed: (1) the questions are different—this is the *different questions* interpretation (What are the mechanisms among parts and among parts and higher-level wholes? versus How do gene frequencies change as a consequence of competition among parts?); (2) the questions are the same, but concern different episodes in the history of life—integrative mechanisms work within stable individuals, whereas competitive dynamics are crucial during transitions to higher levels of individuality; this is the *nonoverlapping* interpretation (What developmental and evolutionary forces shape stable individuals? versus What developmental and evolutionary forces act during transitions?); (3) the questions are the same and explanations, integrative or competitive, are in conflict—this is the *irreconcilable* interpretation (What developmental and evolutionary forces shape stable individuals? The integration perspective would emphasize integrative mechanisms and would interpret apparent modular competition simply as mechanistic dysfunction; the competition perspective would emphasize competitive mechanisms and would tend to see the whole as a population with competing parts rather than as an integrated individual.) (Winther, 2001a). Only under the last interpretation are the perspectives in conflict.

Further work is required to express the multiple relationships between these two perspectives in terms of the phenomena, methodologies (including research strategies), theories, and questions of interest that they coordinate and employ. These perspectives guide the work in the scientific fields investigating the processes of evolutionary development biology and levels of selection. We need to understand the differences, similarities, conflicts, and complementarities between these perspectives in order to develop a complete contemporary synthesis of scientific fields pertinent to evolution, development, and genetics.

Acknowledgments

Note

1. As any of these three parameters increases, the equilibrium frequency of cooperation diminishes (Richard Michod, personal communication). Note that by "fixation" I mean an extremely high frequency of alleles for cooperation: recurrent mutation ensures that no allele is ever fixed, strictly speaking.

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