COMPUTATIONAL BIOLOGY/EVOLUTION/COMPLEX SYSTEMS

Modularity

Understanding the Development and Evolution of Natural Complex Systems

edited by Werner Callebaut and Diego Rasskin-Gutman

foreword by Herbert A. Simon

Modularity—the attempt to understand systems as integrations of partially independent and interacting units—is today a dominant theme in the life sciences, cognitive science, and computer science. The concept goes back at least implicitly to the Scientific (or Copernican) Revolution, and can be found behind later theories of phrenology, physiology, and genetics; moreover, art, engineering, and mathematics rely on modular design principles. This collection broadens the scientific discussion of modularity by bringing together experts from a variety of disciplines, including artificial life, cognitive science, economics, evolutionary computation, developmental and evolutionary biology, linguistics, mathematics, morphology, paleontology, physics, theoretical chemistry, philosophy, and the arts.

The contributors debate and compare the uses of modularity, discussing the different disciplinary contexts of "modular thinking" in general (including hierarchical organization, near-decomposability, quasi-independence, and recursion) or of more specialized concepts (including character complex, gene family, encapsulation, and mosaic evolution); what modules are, why and how they develop and evolve, and the implication for the research agenda in the disciplines involved; and how to bring about useful cross-disciplinary knowledge transfer on the topic. The book includes a foreword by the late Herbert A. Simon addressing the role of near-decomposability in understanding complex systems.

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all units of evolution need to be modules. Most important, Schlosser suggests both empirical and experimental procedures to analyze this two-step test for modularity.

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2 Natural Selection and the Origin of Modules

Günter P. Wagner, Jason Mezey, and Raffaele Calabretta

There is an emerging consensus about the existence of developmental and evolutionary modules and their importance for understanding the evolution of morphological phenotypes (Bolker, 2000; Raff, 1996; Wagner and Altenberg, 1996). Modules are considered important for the evolvability of complex organisms (Bonner, 1988; Wagner and Altenberg, 1996) and for the identification of independent characters (Houle, 2001; Kim and Kim, 2001; Wagner, 1995) and necessary for heterochrony (Gould, 1977). Methods to recognize and test for modularity have been developed (Cheverud et al., 1997; Mezey et al., 2000) and comparative developmental data have been reinterpreted in the context of the modularity concept (Nagy and Williams, 2001; Schlosser, chapter 7 in this volume; Stock, 2001). In contrast to the progress made in these areas, there has been very little research on the origin of modules, and the few results published about models for the origin of modules point in widely different directions (Altenberg, 1994; Ancel and Fontana, 2000; Calabretta et al., 2000; Rice, 2000). As of 2004 no unitary explanation has emerged for the evolution of modularity. This is surprising, since modularity seems to be so common among higher organisms that one might expect a robust and unitary mechanism behind its origin.

In this chapter we want to review the current models and ideas for the evolutionary origin of modules. The majority of the models discussed below were published in 2000 or 2001, and we thus feel that an overview might be useful. Another goal of this chapter is to identify the range of open problems we face in explaining the ultimate causes of modularity.

Kinds of Modules

While the intuitive idea of modularity is pretty simple, the distinction between different types of modularity and their operational definition stimulates ongoing conceptual development (Brandon, 1999; von Dassow and Munro, 1999; Nagy and Williams, 2001; Sterelny, 2000; and chapters 4, 7, and 8 in this volume). In this chapter, however, we do not want to enter the discussion about the more subtle aspects of the modularity concept but, rather, use a few fairly simple and perhaps robust distinctions and definitions sufficient to communicate about models for the origin of modularity.

The biological modularity concept has several largely independent roots. In developmental biology the modularity concept is based on the discovery of

semiautonomous units of embryonic development (Raff, 1996). The empirical basis for *developmental modules* is the observation that certain parts of the embryo can develop largely independent of the context in which they occur. Examples are limb buds and tooth germs (Raff, 1996), developmental fields (Gilbert et al., 1996), and clusters of interacting molecular reactions (Abouheif, 1999; Gilbert and Bolker, 2001; Wray 1999). On the other hand, *evolutionary modules* are defined by their variational independence from each other and the integration among their parts, either in interspecific variation or in mutational variation (Wagner and Altenberg, 1996).

The preliminary definition of an evolutionary module used in this chapter is a set of phenotypic features that are highly integrated by pleiotropic effects of the underlying genes and are relatively isolated from other such sets by a paucity of pleiotropic effects (figure 2.1). This preliminary definition is also the basis for attempts to measure and test for modularity in genetic data (Cheverud et al., 1997; Mezey et al., 2000). *Functional modules*, on the other hand, are parts of organisms that are independent units of physiological regulation (Mittenthal et al., 1992), such as biomechanical units (Schwenk, 2001), or an isolated part of the metabolic network (Rohwer et al., 1996). The precise definition of all these concepts is somewhat difficult and still controversial. The real challenge, however, is to determine how these different kinds of modules relate to each other. For instance, are evolutionary and developmental modules the same? If not, why and in what respects are they different?

Intuitively, developmental and evolutionary modules should be very closely related. The developmental process determines how a gene influences the

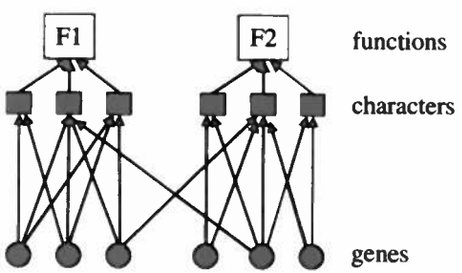

Figure 2.1
Variational modularity of a set of phenotypic characteristics is defined as integration due to the presence of many pleiotropic effects of genes and relative independence from other phenotypic characters due to a relative lack of pleiotropic effects. It is also often the case that a phenotypic module also is dedicated primarily to a specific function. In this case the variational module is also an adaptive character, or an evolutionary module.

phenotype, and hence the existence of developmental modules should influence the structure of the genotype–phenotype map. This is a largely correct argument, but it fails to show that developmental modules map one-to-one to evolutionary modules. One of the reasons is that developmental modules can be deployed repeatedly, as in the case of the left and right forelimb buds. Each of the two forelimb buds is an independent developmental module because each is a self-contained developmental unit with its own capacity for self-differentiation. From a variational point of view, however, the left and right forelimbs are not independent, because they express the same genetic information. Mutations are thus expected to affect both forelimbs simultaneously, and the genetic variation is correlated. Hence the two forelimbs indeed are two *different developmental modules* of the organism, and also are parts of the *same evolutionary module*.

The distinction between developmental and evolutionary modules may be critical for the question of how evolutionary modules originate. One of the most common modes for the origin of evolutionary modules (i.e., phenotypic units of variation) is the differentiation of repeated developmental modules (Raff, 1996; Riedl, 1978; Weiss, 1990). One example is the evolutionary differentiation of teeth. Each individual tooth germ is a developmental module, but each differentiated tooth class is an evolutionary module (Stock, 2001). Another example is arthropod segments, which are potential developmental modules, and tagmata like thorax and abdomen as the evolutionary modules derived from the differentiation of a set of segments (Nagy and Williams, 2001). This fact may be relevant for the origin of evolutionary modules. The main problem is to explain the suppression of pleiotropic effects among genetically coupled parts of the body (i.e., the evolution of individuality of primitively integrated units). The implications of this fact have not been explored systematically, but may hold the key to one of the problems in the origin of modules discussed in the next section.

Mechanisms for the Origin of Modules

In this section we review models for the evolutionary origin of modules. The objective is to understand how natural selection may have acted on the phenotype so as to produce evolutionary modules. As defined above, evolutionary modularity is a statement about the statistical structure of the genotype–phenotype map (Mezey et al., 2000). It implies that certain sets of phenotypic features are affected by the same set of genes, and thus are highly integrated, but these genes have few pleiotropic effects affecting other parts of the body. An evolutionary model for the origin of

modules has to explain how natural selection could produce this distribution of genetic effects. Hence the origin of modules is a special case of the evolution of genetic architecture. So far we recognize two classes of models. In one class of models there is a more or less direct selective advantage associated with evolutionary modularity. Within this class, different models differ with respect to the kind of connection assumed between modularity and fitness. In the second class there is no direct selection for modularity, which arises more indirectly through the dynamics of evolution (Calabretta et al., 2000; Force et al., 2004).

Direct Selection for Modularity

For natural selection to cause modularity, there has to be a connection between a selective advantage and modularity. One of the most frequently noted effects of modularity is its potential impact on evolvability (Altenberg, 1995; Galis, 1999, 2001; Gerhart and Kirschner, 1997; Holland, 1992; Liem, 1973; Riedl, 1978; Vermeij, 1970; Wagner and Altenberg, 1996). Hence it is tempting to suggest that modularity evolves as a result of selection for evolvability (Gerhart and Kirschner, 1997; Riedl, 1978). We will explore this possibility first. The other possibility is that modularity is a result of mutations that break developmental constraints due to nonadaptive linkages between characters (Leroi, 2000).

Selection for Evolvability The question of whether modularity can be explained as an adaptation for evolvability has to be discussed in the broader context of whether selection for evolvability can be a factor in the evolution of genetic architecture. This question is unresolved. In principle, selection for evolvability is possible, particularly in asexual species. The mechanism is a simple Darwinian selection process based on a difference in mean fitness caused by differences in the rate of adaptation among clones (Wagner, 1981). Experimentally it has been shown that alleles that increase the mutation rate get selected in bacterial populations if the population faces a new environment, a situation which is consistent with models for the selection for evolvability (Cox and Gibson, 1974).

However, the mechanism works well only if there is either no recombination or there is a strong linkage disequilibrium between, say, the mutator locus and the genes which mutate to advantageous alleles. With recombination, the mutator gene can no longer ride to fixation on the coattails of the other genes, a process that has been called "hitchhiking" (Maynard-Smith and Haigh, 1974). The reason is that recombination will separate the mutator from the advantageous mutations. The same argument holds for any other mechanism that may influence the rate of adaptation, such as differential epistasis that may suppress deleterious pleiotropic effects

(see below). Consequently, with recombination, selection for evolvability becomes a very weak force.

At this point, we want to report the results of a study that aimed at modeling the evolution of pleiotropic effects (Mezey, 2000). Let us consider two characters, one under directional selection and one under stabilizing selection. This model represents a fairly generic scenario for a complex organism. Whenever natural selection acts to change a character, many other characters of the same organism will remain under stabilizing selection. It has been shown that pleiotropic effects among these two characters decrease the rate of evolution of the character under directional selection (Baatz and Wagner, 1997). Pleiotropic effects decrease evolvability. The question then is whether natural selection could fix a modifier allele which suppresses the pleiotropic, and thus increases evolvability (figure 2.2). We used an individual-based model to investigate this question and estimated the selection coefficients of the modifier allele by measuring the time to fixation. The result was that there was quite a strong selection for the modifier (a sample of the results is given in table 2.1).

However, the selection coefficient alone does not tell us whether we are dealing with selection for evolvability. The mean fitness of genotypes with different modifier alleles is influenced by at least two factors: (1) the amount of variation in the character under stabilizing selection, and (2) the relative location of the genotypes along the direction of directional selection (figure 2.3). Only the second factor can be called selection for evolvability, since it derives from differential rates of adaptation. We determined the relative contributions of these two factors to the selection coefficient of the modifier and found that in all cases where we checked, the

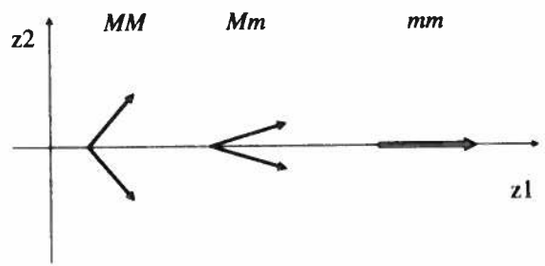

Figure 2.2
A modifier model in which the genotype at a modifier locus determines the relative size of pleiotropic effects between two characters. With MM the effects on the two characters of a mutation are of the same magnitude; with Mm the effects on z2 are smaller than the effects on z1; and with mm the mutations have no effect on z2. The modifier allele m suppresses the pleiotropic effects on the character that is under stabilizing selection. Selection of this allele increases evolvability (Baatz and Wagner, 1997).

Table 2.1
Selection coefficient of a modifier that suppresses pleiotropic effects and the percentage of the selection coefficient explained by selection for evolvability

	s	% explained by evolvability
Vs = 2	0.08	2.0%
Vs = 10	0.08	4.5%

Note that the selection coefficient is quite high with 8%, but only 2%–5% of that can be attributed to selection for evolvability. Vs is the strength of stabilizing selection; the directional selection was 0.1; and the population size was 100.

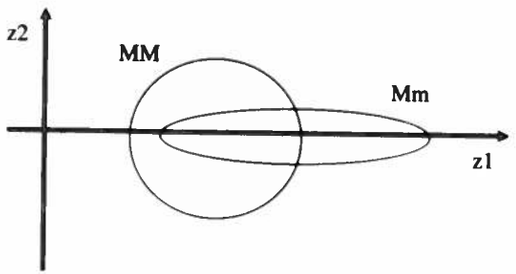

Figure 2.3
Comparison of the distribution of genotypic values of two classes of genotypes. The MM genotypes have equal mutational effects on the two characters, and the distribution is thus circular in this model. The other class of genotypes, Mm, has smaller effects on the second character, and the distribution of genotypic values is thus more extended along the axis of the first character. If the first character is under directional selection for larger character values and the second is under directional selection, the relative mean fitness of these two classes of genotypes is influenced by two factors. The first is the relative location of the genotype distribution along the z1 axis. The more the distribution is to the right, the higher is the mean fitness. The second is the amount of variation in the second character. Since z2 is under stabilizing selection, the fitness is higher the smaller the variance for the second character. In this case the Mm distribution has higher fitness, but only the component of this fitness advantage that is due to the location along the axis of the first character can be said to be selection for Mm caused by selection for evolvability. As seen in table 2.1, this contribution is in fact very small, less than 5% in most cases tested.

fraction of the selection advantage due to selection for evolvability was much less than 10%. In other words, more than 90% of the selective advantage of suppressing pleiotropic effects was due to direct selective advantages rather than advantages related to evolvability per se. Hence, we concluded that even if natural selection can be effective in removing pleiotropic effects, the resulting increase in evolvability is not explained by direct selection for the rate of evolution.

Another study on the evolution of evolvability had a similar result (Turney, 2000). The model considered mutations which increased the dimensionality of the phenotype and thus the number of degrees of freedom for adaptive variation. It was shown that evolvability increases during the simulation runs. The evolutionary mechanism was a direct selective advantage to the mutations that increased evolutionary versatility. Mutations that increased versatility led directly to higher fitness phenotypes that were previously inaccessible.

Hence evolvability can evolve and even improve, but evolvability per se is perhaps not the target of selection. From that we conclude that evolution of modularity is unlikely to result from direct selection in favor of evolvability. One caveat in this argument, however, is that we are not aware of any work on selection for evolvability in populations with spatial structure. Spatial structure may make selection for evolvability more likely than selection in panmictic populations.

These results suggest two possible mechanisms for the origin of modules. One is that the genotype–phenotype map has a direct impact on mean fitness, in particular if the population is far from equilibrium (see also Rice, 1990). Hence it is conceivable that modularity results from the fact that pleiotropic effects can decrease the mean fitness of a population if the population experiences directional selection. The other possibility is that mutations that produce modularity break genetic constraints on adaptation and thus would be selected because they make advantageous phenotypes accessible.

Direct Selection on Pleiotropic Effects Based on the results reported above, we attempted to evolve modularity in a quantitative genetic model by alternating directional selection and differential epistasis (figure 2.4). The rationale was that directional selection on a single character selects against pleiotropic effects on other characters. If two characters never experience directional selection simultaneously, a modular genetic architecture for the two characters may arise (i.e., one set of genes with most of their effects focused on one character and another set of genes with most of their effects focused on the other character). The results, however, showed that alternating selection does not lead to a separation of genes into two

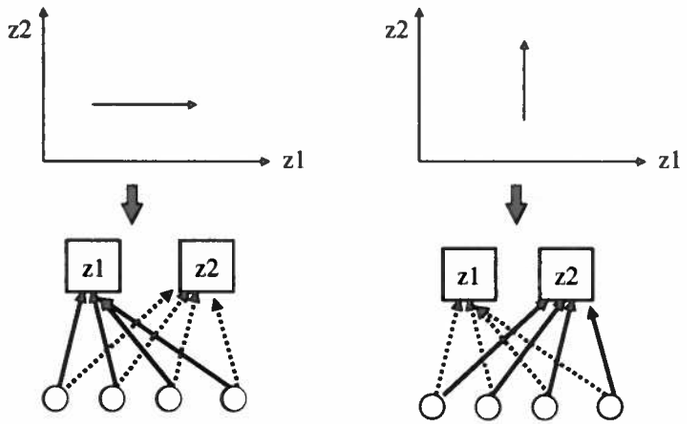

Figure 2.4
The effect of directional selection on one character on the genetic architecture of a two-character phenotype. Whenever there is directional selection on any one character, all the genes increase their contribution to this character. Even directional selection strictly alternating between the two characters does not lead to a segregation of genes into a modular pattern.

character-specific sets, one with effects on one character and the other with effects on the other character. The distribution of gene effects did not settle into a modular pattern; rather, any episode of directional selection tended to recruit genes into the selected character (Mezey, 2000). From this we concluded that alternating selection alone cannot account for the origin of evolutionary modularity.

Modularity as an Escape from Adaptive Constraints The second alternative mentioned above is that modularity may result from mutations which overcome constraints among adaptive traits. This idea is related to the fact that structural and functional decoupling can facilitate adaptation (Galis, 2001; Liem, 1973) and was proposed as a mechanisms for the origin of modularity by Leroi (2000), but to our knowledge it has not been explicitly modeled, and thus is hard to evaluate at this time. Perhaps the most relevant, but still limited, model is that of Turney (2000) on the evolution of evolutionary versatility discussed above.

Constructional Selection The oldest model for the origin of modularity that in fact works is constructional selection, proposed by Altenberg (1994; see also chapter 5 in this volume). It is based on the assumption that genes with fewer pleiotropic effects have a higher probability of establishing duplicated copies of themselves in the genome. This model is thus based on intragenomic competition among genes

with different degrees of pleiotropy. It predicts the evolution of lower and lower average degrees of pleiotropy. The problematic aspect of this model, however, is the assumption that the degree of pleiotropy is heritable among copies of genes, in particular if the genes acquire new functions. In fact there is evidence for lower pleiotropy among duplicated gene copies, but this fact is better explained by subspecialization of the gene copies due to degeneration of and complementation among modular enhancer elements (Force et al., 1999).

Phenotypic Stability In an important computational study on the evolution of RNA secondary structure, Ancel and Fontana (2000) found that selection for phenotypic stability also leads to modularity (see also chapter 6 in this volume). Ancel and Fontana found that in RNA there is a three-way correlation among phenotypic stability in the sense of robustness against thermal noise, mutational robustness, and modularity of the molecule. Of these three properties, phenotypic stability is most effectively selected, that is, is best "seen" by natural selection (Wagner et al., 1997). The evolution of mutational robustness and modularity is a correlated response to selection on phenotypic robustness. Since the correlations are not coincidental, but are intrinsic to the biophysics of RNA, Ancel and Fontana call this phenomenon "plasto-genetic congruence."

Similar principles have been found to hold for protein structure (Bornberg-Bauer and Chan, 1999). These results suggest the intriguing possibility that modularity and other properties of the genetic architecture may evolve as a side effect of the evolution of phenotypic robustness against environmental perturbations. It is thus of greatest importance to investigate whether similar congruence principles may hold for organismal characters as well.

In the older literature about genetic and environmental canalization, the question of whether there might be a correlation between these two forms of robustness was addressed (reviewed in Scharloo, 1991). In general, however, the conclusion was negative. There is no simple relationship between genetic and environmental canalization of a character. The methods available at the time, however, were quite limited, and the question requires new studies with better experimental techniques. One set of papers which supports the notion of a correlation between genetic and environmental robustness for organismal characters consists of the studies on the canalization of life history characters of *Drosophila melanogaster* (Stearns et al., 1995; Stearns and Kawecki, 1994). Stearns and his collaborators found a three-way correlation among fitness sensitivity and mutational and environmental robustness. The results, however, do not address the question of whether genetic and environmental robustness are two independent characters or are variationally correlated.

Modularity Facilitates Physiological Adaptation Another intriguing model is one with which Calabretta and collaborators simulated the evolution of an artificial neural network dedicated to two functional tasks, the "where and what" task (Di Ferdinando et al., 2001; see also chapter 14 in this volume). The network was expected to produce two kinds of outputs. One indicated the location of an object and the other, its identity. The model led to the evolution of a modular neural architecture and had two components. The neural architecture (i.e., the question of which neurons are connected with each other) was genetically determined, and evolved by mutation and selection. On the other hand, the strength of the neural connection was determined by a learning algorithm based on back propagation (i.e., was acquired by each individual during its ontogeny).

This model, but none of the others investigated by Calabretta and his colleagues, led to the evolution of modularity. The reason is that the effectiveness of the learning algorithm depended on the neuronal architecture. Only a modular architecture provides the basis for successful learning. Hence modularity, which was genetically determined, had a direct fitness advantage mediated through its influence on the effectiveness of individual learning. In addition, the modular neural architectures are also genetically modular with respect to certain mutations. However, the genetic modularity quite evidently did not evolve in this model because of its variational (genetic) consequences. All attempts to evolve modularity without learning (i.e., only with genetic mutations) failed.

This scenario is similar to the one described by Ancel and Fontana (2000) in that there is an interaction between genetic modularity and plasticity or learning, but the selective mechanism is quite different. In the study of Di Ferdinando and collaborators (2001), the highest fitness phenotype could not develop without modular architecture. In the RNA example the highest fitness phenotype was attainable, but at a lower frequency than with modularity. In addition, in the RNA example it was not clear whether there was any causality from modularity to phenotypic robustness at all, while in the Di Ferdinando model there was a clear causal connection from neuronal modularity to high fitness phenotypes due to plasticity.

Modularity from "Frustration" In a study on the general mathematical theory of gene interactions, Sean Rice (2000) discovered an unexpected mechanism for the origin of modules. Rice found that positive correlations are expected to evolve if the effects of two characters on fitness are synergistic (i.e., if the increase of one character value increases directional selection on the other character). On the other hand, the evolution of a negative correlation is predicted if the characters are antagonistic with respect to fitness. If we consider more than two characters with pairwise antagonistic interactions on fitness, however, something unexpected happens. It is impossible to have negative correlations among three or more characters simultaneously. The evolution of negative correlations is said to be "frustrated."

The only stable solution is that the characters evolve variational independence. It is surprisingly simple to find a scenario for this phenomenon. For instance, assume that three characters contribute to a composite of characters $C = x + y + z$, and in addition assume that the composite character C is under stabilizing selection. Then there is antagonism among all three characters, and Rice's theory predicts selection for independence among the characters. Hence, modularity (i.e., character independence) can result from antagonistic fitness interaction among three or more characters.

Modularity as a Dynamical Side Effect

In all the models discussed above, modularity is assumed to be connected to some sort of selective advantage. In a study on the evolution of functional modularity using an artificial life model, Calabretta and collaborators (2000) discovered a mechanism which cannot be classified as direct or indirect selection for modularity per se. Functional modularity arises from subspecialization of duplicated structural modules without any intrinsic benefit in terms of level of performance or rate of advantage. Modularity arises entirely as a side effect of the evolutionary dynamics.

Calabretta et al. (2000) investigated an artificial life model in which a genetic algorithm had the task of developing both the architecture and the connection weights for a population of neural networks controlling the behavior of a mobile robot. Each robot lived in a walled arena and had the task of exploring the arena and picking up objects and dropping them outside the arena. The robot had infrared sensors that informed it of the presence of objects and walls. It had two wheels for moving forward and backward and for turning in the environment, and a gripper for picking up one object at a time and transporting it outside the environment. The task of the robot was to move in the environment by differentially rotating the two wheels, to find an object, to pick up the object with the gripper and transport it near one of the walls, and finally to release the gripper in such a way that the object was placed outside the environment. To do this, the robot had four motor systems: the two wheels, the motor that controlled the opening and rising of the gripper, and the motor controlling the lowering and opening of the gripper.

As one can easily see, this was a difficult task to learn. The neural network must be able to control the correct sequence of subbehaviors: to explore the environment, to find an object by discriminating it from the wall, to pick up the object by lowering and then raising the gripper, to find the wall while avoiding the other

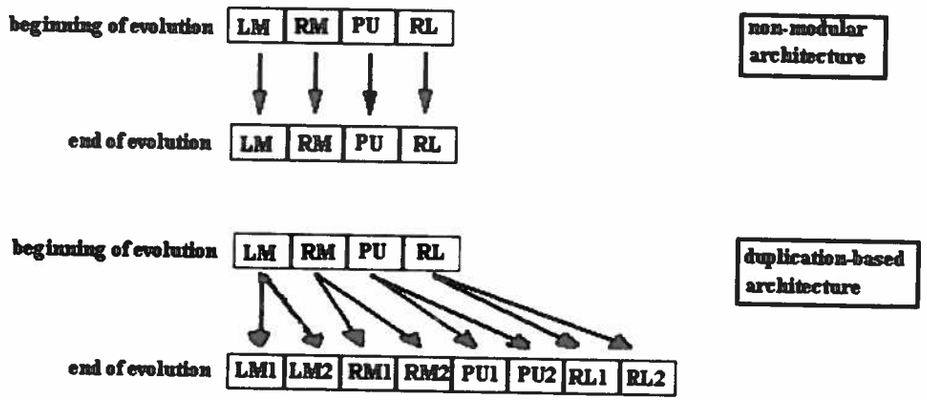

Figure 2.5
Schematic representation of the genomes of the nonmodular and duplication-based modular architectures. LM, genetic encoding for the connection weights of the left motor; RM, right motor; PU, pickup motor; RL, release motor. (Modified from Calabretta et al., 2000).

objects, and to release the object correctly outside the wall. Hence there were a number of behavioral tasks that required different neuronal control over the motor output. Basically there were two types of behavior: searching for a new object and removing the object from the arena. The absence of an object in the gripper should lead to searching and pickup behavior, and the presence of an object in the gripper should lead to a behavioral sequence resulting in the removal of the object from the arena. The question is whether these two behavioral sequences were represented by different neuronal substrates (i.e., functional modularity).

In a study by Nolfi and collaborators (Nolfi 1997) it was shown that functional modularity is not necessary for solving this adaptation problem. Nolfi provided the robot with duplicated neuronal elements to control the output to the motor units of the robot. He found that the genetic algorithm could solve the problem but that the behaviors were not represented by different neuronal elements. No functional modularity evolved. This result shows that functional modularity is not necessary for solving a complex adaptive challenge consisting of a number of different tasks.

Calabretta and colleagues conducted slightly modified simulations. The robots started out with only one neuronal control element per output unit (i.e., motor). During the evolution of the neuronal network, however, a new form of mutation was allowed, the duplication of these control units (figure 2.5).

By analyzing the behavior exhibited by the robots, the authors showed that duplication-based modular networks possess a high degree of specialization

(Calabretta et al., 2000). Some neural modules are specialized for some subtasks (e.g., controlling the robot's movements when the robot is exploring the environment in search of objects), and other neural modules are specialized for other subtasks (e.g., picking up an object). It is important to note that the populations which evolved functional modularity reached the same level of performance as the populations which did not. Furthermore, modular neural networks did not reach the solution faster than others. Hence there was no intrinsic adaptive benefit to functional modularity.

But what was the mechanism that produced functional modularity in these simulations? Various observations point to an evolutionary scenario like the following. First, the duplication of a neuronal control unit. This step was neutral in this model, since the two duplicates were identical. Second, the acquisition of a neutral change in the regulation of the duplicated modules which made one unit more likely to be deployed in one situation—for instance, while searching for another object rather than in object removal. Finally, the accumulation of mutations that adapt the neuronal control unit to the functional context in which it is employed more frequently. This step led to a coadaptation between the regulatory and the functional parts of the control units that locked the system into the functionally specialized state.

From a population genetic point of view, the evolution of functional specialization in this model was caused by epistatic interactions among genes that influence in what situation a control unit is active and genes which control the motor output that is produced. There was a ratchet between a bias in deployment of a control unit and the specialization of the output to the behavioral context in which it was used. One can think of this process as being like a dynamical bifurcation which leads to increasing specialization between control units.

Conclusions

The above overview of possible mechanisms for the origin of modularity identified eight different evolutionary mechanisms, each mechanistically independent from all the others. The majority of them have been proposed since about 2000, and none is understood well enough to be excluded as a candidate. A massive amount of research is necessary to sort out these various possibilities and perhaps even discover additional ones. In our understanding of the situation, there are a number of pressing research questions that need to be addressed to make progress in this area.

Evolution of Evolvability

As summarized above, the results on the possibility of direct selection for evolvability are mixed, but we still lack important results for it to be dismissed entirely.

The most glaring gap in our knowledge is a lack of studies including subdivided populations. There is the possibility that in structured populations, selection of genetic traits influencing the rate of adaptation is more likely than in unstructured populations (Joshua Mitteldorf, pers. communication, 2000).

Congruence Principles

Many of the models that have been shown to create modularity imply some sort of congruence between modularity and some directly selectable property. The best example is the study on modularity in RNA secondary structure by Ancel and Fontana (2000), in which a correlation exists between the degree of modularity and phenotypic stability against environmental noise. But other models can be understood along similar lines. For instance, the model of Di Ferdinando and collaborators on the "where and what" task points to a congruence between physiological and genetic modularities that leads to a selective advantage. Constructional selection assumes a congruence between variational pleiotropy and probability of fixation of a duplicated gene. And the simulations regarding the evolution of pleiotropic effects point to a congruence between evolvability and mean fitness in nonequilibrium populations.

We think that there are sufficient grounds to consider congruence principles as an important component of many scenarios for the evolution of modularity, and that they should therefore be the focus of future investigations. Congruence principles have been discovered in models of molecular dynamics and neuronal networks rather than being modeled themselves. We think that it is time to develop abstract models of congruence principles in order to incorporate them into population genetic theory. In addition, it will be important to find new examples of congruence principles in models of physiology or development and in empirical research. Empirical research is not mentioned first here because it is expensive and should be done only for good reasons. For instance, measuring the mutational variability of a trait is a serious effort, and comparing it to phenotypic stability is even more so.

Mechanistic Plurality Is a Real Possibility

It would be a mistake to assume that we will discover one and only one mechanism that explains the origin of modularity in all circumstances. It is clear that for the origin of species there are many population biological and genetic mechanisms that can lead to the origin of a new species (Otte and Endler, 1989). There is no unitary "speciation mechanism." Similarly, there might be a multitude of mechanisms acting in nature to produce modular genetic architectures. Hence, it might not be productive to try to identify one mechanism among proposed models as "the Solution." Each model needs to be judged on its own merits, and it may be that we end up with an array of mechanisms, each of which may play a role in a variety of different circumstances.

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