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## NEWS AND COMMENTARY

Modularity and adaptation

# Genetic and functional modularity: how does an organism solve a nearly infinite genetic/environmental problem space?

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Modularity, the concept that a group of items function together and they are less connected to items within other groups, has been a key concept underpinning numerous research fields from quantitative genetics to computational biology. In genetic terms, a variational module is made of traits that vary together and are independent of other modules (Wagner and Altenberg, 1996). In molecular biological terms, a functional module is composed of genes/proteins that coordinate to perform a function that is semiautonomous from other functions (Wagner *et al*., 2007). In this issue, floral and vegetative developments are shown to have hallmarks of genetic modularity (Edwards and Weinig, 2011). Interestingly, unexpected links between the two tissue variational modules are identified and the authors show that the module shows differential susceptibility to two environmental perturbations.

Modularity and genetics is probably most studied and discussed within the evo-devo field with significant research showing that natural variation in the complex shape of the mouse mandible involves numerous quantitative trait loci that function in concert, as a module, to shift the shape of the mandible (Klingenberg, 2008). This was extended to show that mammalian limbs show modular variation across most species except bats, where the limbs have evolved for a new function (Young and Hallgrimsson, 2005).

Plant developmental variation also shows modular characteristics both within and between species with most of this work focused on modularity of flower shape. In this issue, the authors begin to identify links between flower and leaf modules suggesting pleiotropy between loci controlling variation in floral characters and leaf characters (Edwards and Weinig, 2011). Interestingly, molecular analyses of plant development are identifying functional modules in which some genes within the module function in multiple tissues and other components are tissue specific (Brady *et al*., 2007). Often, the tissue-specific components are the products of whole-genome duplications whereas the non-tissue-specific components return to single copy status by loss of a duplicate (Freeling, 2009). This molecular work, in combination with the genetic modularity work in this issue, begins to lay the foundation for testing the links between functional and variational modularity (Edwards and Weinig, 2011). For instance, does variation in duplicated regulatory genes within a functional module explain the observed tissue-specific variational modules? Conversely, does variation in their non-duplicated colleagues provide the variational links between tissue modules?

The presence of, and repeated identification of, modularity within genetic systems raises the question of why modularity exists? Given the potential philosophical underpinnings of this question, there are two possibilities that Edwards and Weinig (2011) begin to address. One theory for the presence of modularity is that variational modules and the modular genotypes contained therein may facilitate evolvability in response to a variable environment. Recent modeling work provided support for this theory (Kashtan and Alon, 2005). Interestingly, with the authors' observation that the variational modularity in plant development is not universally sensitive to environmental perturbation, with temperature having more influence than photoperiod, it would appear that not all environmental perturbations are equal (Edwards and Weinig, 2011). Future work to understand what differentiates these perturbations will be essential to understanding how the environment interacts with modularity. For instance, is the difference between photoperiod and temperature due to the difference in annual variance of these environmental parameters at a local level?

Another possible benefit of modularity may arise from the simple combinatorial aspect of genetic variation within a large genome. Twenty-six genes (similar to the number of independent loci found; Edwards and Weinig, 2011), each with two functionally discrete alleles within a diploid species can generate approximately 2.5 trillion possible combinations. This is more possible combination than there likely have ever been human individuals. With genomics studies showing that most organisms likely have thousands of genes with functionally discrete alleles (Clark *et al*., 2007; Buckler *et al*., 2009), this creates a potential genotype/phenotype universe that can never be fully sampled given the typical effective population size for a single species, even prokaryotic. If every gene were functionally connected to every other gene, this would establish a level of interconnectivity that might generate significant secondary constraints on phenotypic adaptation. It would never be possible for an organism to fully test if a new allele was beneficial or detrimental in all possible contexts. However, modularity may alleviate this problem by allowing the system to function as a set of independent groups of genes, allowing a species to better sample its potential phenotypic and genotypic diversity (Leroi, 2000).

Answering the above questions and theories about modularity has been largely facilitated by the analysis of quantitative genetic variation or modeling. However, recent advances in the systematic analysis of quantitative trait loci are beginning to enable the rapid identification of the causal genes underpinning this genetic variation. It is likely that in the near future studies will begin to identify all the causal loci controlling modular genetic networks, as in the case highlighted here (Edwards and Weinig, 2011). The identification of these causal genes will allow the bridge between variational and functional modules to be crossed and lead to significant advances in our understanding of modularity. This will likely answer the known questions and may possibly lead to the identification of new questions. For instance, is modularity solely a positive process or are there genes that function as insulators to prevent links between modules? Finally, the availability of large stable populations phenotyped

by a myriad of laboratories may allow the development of massive phenotypic databases that could enable the extension of modularity to test how all phenotypes within a species are coordinated (Atwell *et al*., 2010). Thus, the topic of modularity in genetics may be just beginning to flex its muscles.

## Conflict of interest

The author declares no conflict of interest.

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