# The Emergence of Modularity in Biological Systems

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Abstract:

Modularity is a ubiquitous phenomenon in various biological systems, both in genotype and in phenotype. Biological modules, which consist of components relatively independent in functions as well as in morphologies, have facilitated daily performance of biological systems and their long time evolution in history. How did modularity emerge? A mechanism with horizontal gene transfer and a biological version of spin-glass model is addressed here. When the spontaneous symmetry is broken in an evolving environment, here comes modularity. Further improvement is also discussed at the end.

# Introduction

Modularity is an important concept with broad applications in computer science, especially in programming. A module, usually composed of various components, is a relatively independent entity in its operation with respect to other entities in the whole system. For a programmer, the employment of a module will increase the efficiency of coding, decrease the potential of errors, enhance the stability of the operation and facilitate the further improvement of the program. Coincidently, the nature thinks the same in its programming life: various biological systems are also in a modular fashion!

Let us take the model organism fruit fly *Drosophila melanogaster* as an example to sip the ubiquitous modularity in biological systems.

In view of morphology, *Drosophila* is a typical modular insect, whose adult is composed of an anterior head, followed by three thoracic segments, and eight abdominal segments at posterior[1](Fig. 1). Such a kind of segmentation is induced by a cascade of transcription factors in the embryo. First, maternal effect genes which are expressed in the mother's ovary cells distribute cytoplasmic determinants unevenly in fertilized eggs, which thus determines anterior-posterior and dorsal-ventral axis. Second, three classes of segmentation genes are induced in sequence, which locate every cell's position relative to the axes (Fig. 2). Finally, Hox (homeobox) genes set up the developmental task of every piece of segment (Fig. 1). Therefore, the hierarchical modularity of the phenotype originates from the corresponding modular genotype.
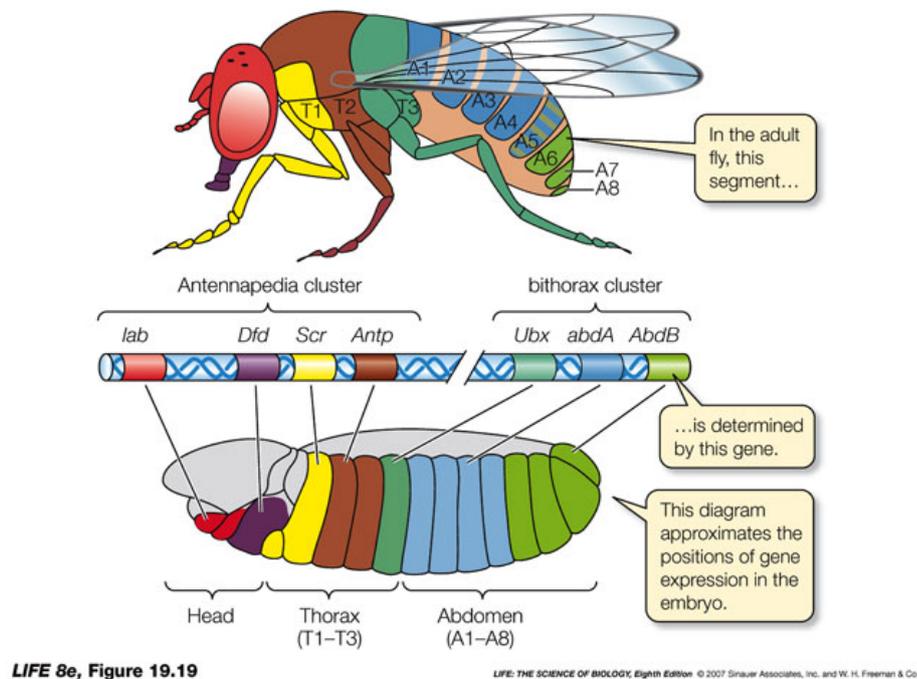


Fig. 1 Segmentation in *Drosophila*[1].

Besides the relative plain modular demonstration of genotype-phenotype mapping, the transcriptional regulation is also found to possess modularity. For

instance, the muscles of *Drosophila* are usually cataloged, according to their contractility and function, into dissected flight muscles, dissected jump muscles, hypodermic and visceral muscles. The genes encoding the corresponding muscle-specific proteins are regulated by enhancer-like elements. J. A. Mas *et al*[2] found that Upstream Regulatory Element (URE) and Intronic Regulatory Element (IRE), which cooperate to enhance the expression of Trophonin T (TnT) gene, both have a modular organization. URE contains a proximal region from -0.55 to -0.85 kb, related to embryo musculature, and visceral and hypodermic muscles, and a distal region from -2.5 to -1.6 kb, regulating the gene expressions for dissected flight muscles and dissected jump muscles (Fig. 3). Another two regulatory modules controlling TnT independently are found on IRE.



**Maternal effect genes** determine the anterior–posterior axis and induce three classes of segmentation genes.

**1** **Gap genes** define several broad areas and regulate…

**2** …**pair rule genes**, which refine the segment locations and regulate…

**3** …**segment polarity genes**, which determine the boundaries and anterior–posterior orientation of each segment.

Once segments are established, **Hox genes** define the role of each segment.

*LIFE 8e*, Figure 19.18

Fig. 2 Gene cascade in *Drosophila* embryos[1].

Although the illustration here is mainly based on the model *Drosophila*, modularity, in fact, is recognized as a ubiquitous phenomenon in various biological systems, both in genotype and in phenotype, from genomic level to whole organisms. Such a modular fashion of life organization has facilitated not only the daily performance of biological systems but their long time evolution in history as well.

For an individual, the ability to detect the change in its environment sensitively and respond appropriately and swiftly will acquire a selective advantage. Developmental plasticity is termed to describe the automatic adaptation of an organism to its environment in its morphological development. The larvae of moth

*Nemoria arizonaria*[1], which has two kinds of morphologies, can serve as a good example. In spring, the larvae, living on oak flowers, resemble the latter in appearance, while in summer, a new generation, feeding on oak leaves, protects themselves by camouflaging oak twigs. It is found that some chemical in oak leaves triggers the genetic switch which controls the module for camouflaging strategies. Hence, developmental plasticity, a non-unique mapping to phenotypes from one genotype, endowing the last word to environmental signals, enhances the adaptation of organisms.
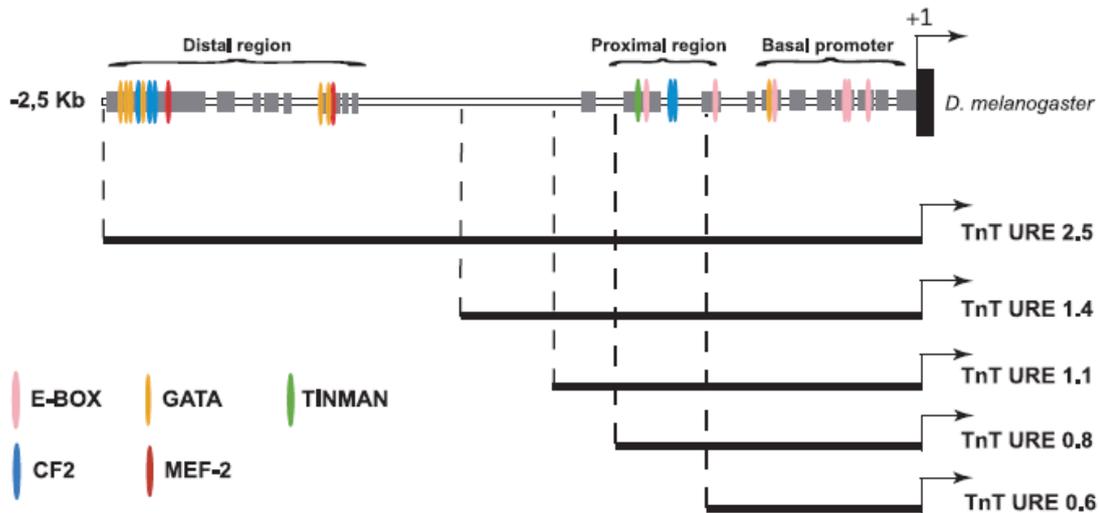


Fig. 3 URE element in *Drosophila melanogaster*[2].

For species, the forever change or relative frozen of timing or spatial patterns of gene expression, or even the turning off of certain expressions, results in biological bifurcation and parallel evolution. For example, the gremlin gene[1], whose protein inhibits the expression of BMP4 (bone morphogenetic protein 4) which will lead to the apoptosis of cells, is also expressed in the webbing cells of duck embryos (Fig. 4) besides on toe cells. Then an adult duck has a webbing foot in contrast to most of the other birds with clearly separated digits. By boxing the relatively independent gene expressions into modules, manipulating a small number of genetic switches enhances generic evolvability.

Therefore, modularity has played an essential role in life. No organism is built up in a non-modular design, which might be optimal for a fixed goal at a particular time point but is hard to evolve[3]. In other words, the changing environment favors modularity, which is relatively easy to adapt to new situations. Over the long history of evolution, the regulatory genes have not undergone much transformation. When transcription factors are compared between *Drosophila* embryos and mouse embryros (Fig. 5), which diverge very long time ago in phylogeny, the high similarity is striking. The conservation of regulatory genes stabilizes the coarse pattern of life. Over the millions of years, it is the various, hierarchical and nested modules that evolve continuously. New modules appear by assembling or modifying pre-existing modules. Pre-existing modules may also be recruited in novel circumstances. For example, the

hedgehog (hh) module[4], which functions in the segmentation of *Drosophila*, is found to be responsible for eyespot evolution in butterfly *Precis coenia* (Fig. 6). Balancing between redundancy[5], which offers insurance to the normal performance of key functions, and efficiency, the multifunction of a single module, evolution, as F. Jacob[6] put, goes on in a tinkering fashion.
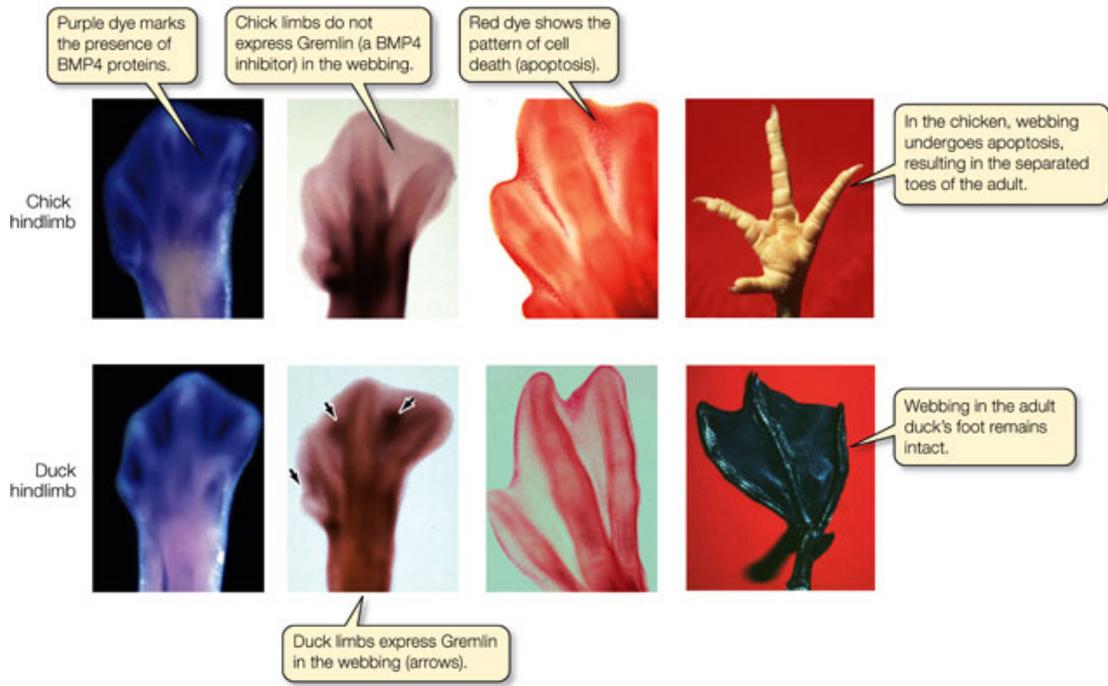


Fig. 4 Gremlin expression in chick and duck embryos[1].
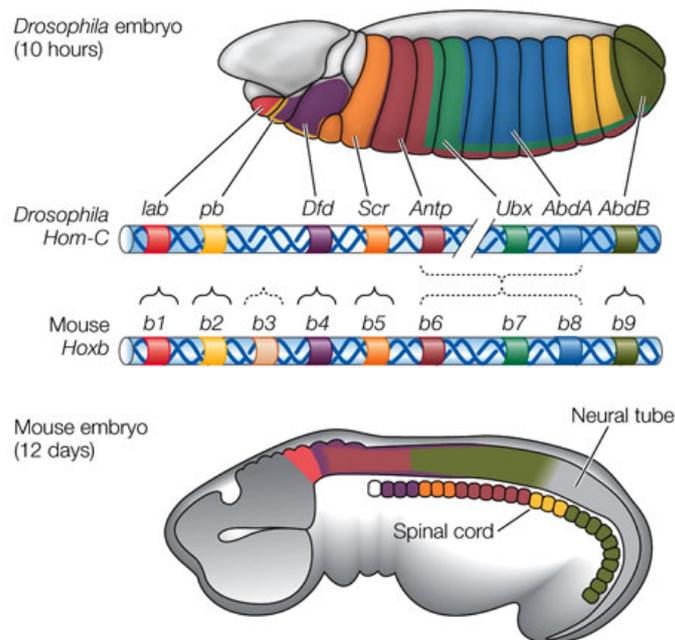


Fig. 5 Comparison of regulation genes in Drosophila and mouse embryos[1].

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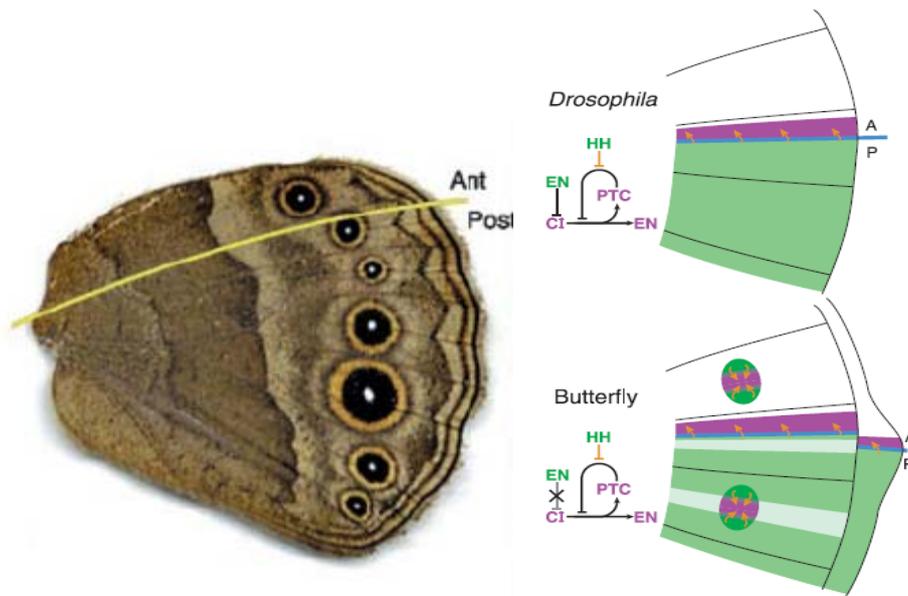
Fig. 6 Hedgehog module in *Drosophila* segmentation controls
eyespot evolution in *P. coenia.*

Next, we will explore the emergence of modularity by computer simulation and see the nail down the mechanisms that propel modularity.

## Emergence of Modularity

### (1) Model

As stated above, biological systems in a modular fashion are not only robust to small perturbations, but also evolvable to better adapt to the mainstream changes in the environment. J. Sun and M. Deem[7] studied in an evolutionary environment, the spontaneous emergence of modularity in a population with horizontal gene transfer[8] by a biological version of spin glass model[9, 10].

The spin glass model has an undetermined ground state which yields frustration. Its biological version yielding hierarchical structure has been widely applied to RNA and protein evolution, protein-folding, immune systems[9] etc. D. J. Earl and M. W. Deem[10] have also used it to demonstrate that the dramatic environmental change favors larger evolvability, which is consistent with part of the result that will be illustrated later.

In the model here[7], there are three different time scales that need explicit description. The first, and fastest as well, is a generation of the individuals. Mutation, gene swapping, replication and individual updating all occur on this scale. The rates for mutation and gene swapping, which accounts for horizontal gene transfer, are both fixed throughout. Replication and individual updating are performed by duplicating the better fitted 50% sequences to the whole population, thus conserving the total number of individuals in the system. The second scale is the flow of environmental change. This is the macroscopic flow where environmental fluctuation has already been evened out. The evolving environment is described by the change, with some

probability called rapidity, of matrix elements which denote environmental coupling. The larger the rapidity, the more dramatic the environment will evolve. The slowest time scale is the change of structure in the population's protein, where modularity is expected to emerge. Modularity is delineated by the non-homogenous connection between different sites on the sequence. Since a random distribution will also yield a non-zero absolute value for modularity, it is the excess modularity by subtraction of the initial value which accounts for the concept of modularity in our usual sense. In addition, some artificial emergence which may result from the increase in the total number of connections is intentionally inhibited.

## (2) Discussion

Figure 7 shows the emergence of modularity, where $T_2$ and $T_3$ are the time scale for environmental change and protein structure change, respectively. The initial modularity is 22, so from a random state, the curve shows an approximate linear increase in modularity. The excess modularity, whose increase is due to the broken symmetry, is the order parameter in the system.
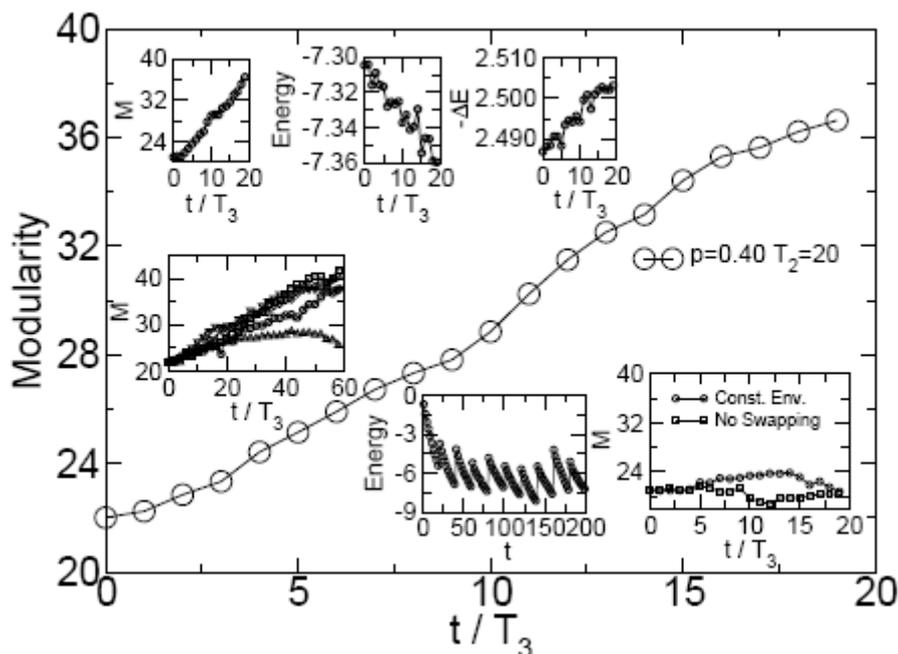


Fig. 7 Emergence of modularity[7].

The mechanism of broken symmetry is the changing of the environment, which can be seen from Figure 8. In an initial state of relatively high modularity, the lack of environmental change (rapidity p=0) will decrease excess modularity, while its presence (p=0.10, 0.25, 0.40) continually promotes the level of modularity. Thus, the result is coherent with the conclusion of preference for greater evolvability from [10], and the better adaptation ability that modularity is supposed to confer to its possessor. The inset displays the faster development of excess modularity with the increase of environmental rapidity.

However, the change of environment should not be too frequent to leave far

behind the adaptation of individuals, which is shown in Figure 9. When $1/T_2 > 1/5$, which indicates fast environmental update, the population will lose its track and the modularity will decay. Thus it can be inferred that the time it needs for the system to adapt to the environment is related to the reformation or modification of modules. The minimal time in need is related to the severity the environment is changed and the modification velocity of the modules. If environmental changes are triggered as long as novel modules are mature, the modularity will increase fastest.
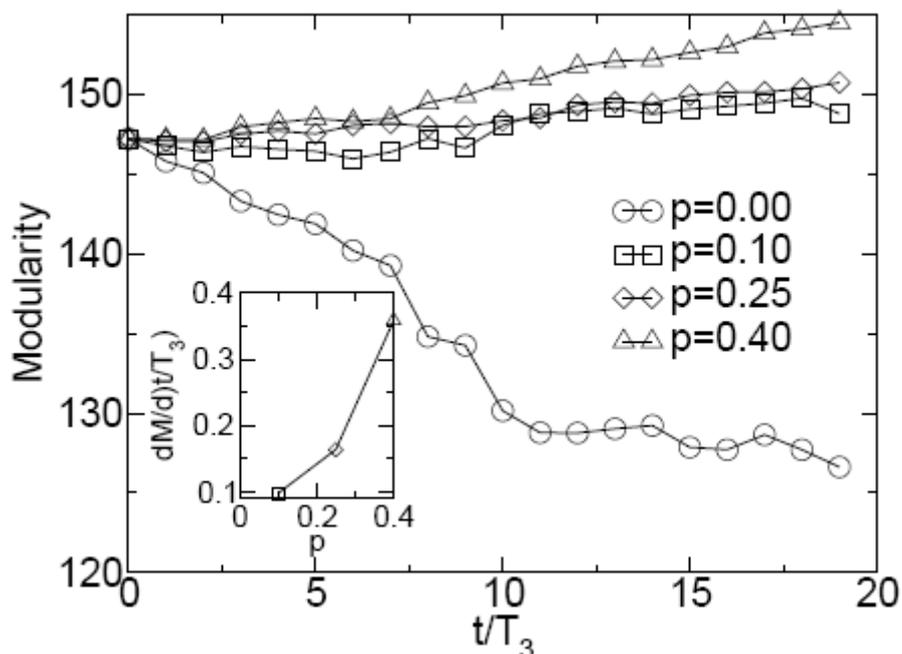


Fig. 8 Change of modularity with time for different rapidities[7].

Furthermore, there is a saturation point of steady excess modularity which is usually smaller that the total number of connectivity. At first glance, Figure 10 may appear strange since the modularity degrades even when rapidity and environmental update period is properly chosen. The decay is due to the fact that the states shown exceed the steady excess modularity, i.e. they are oversaturated. This can be better elucidated by taking thermodynamics as a reference. The adaptation to the environment which increases modularity can be mapped to the minimization of system energy, while the random mutation is correspondent to the maximization of entropy. The steady excess modularity is determined by the compromise of the contradictory mechanisms.

**(3) Conclusion**

Using a biological version of the spin glass model, we see that the evolutionary environment breaks the symmetry. When the different time scales are properly chosen, modularity will emerge spontaneously and enhance toward some saturation value. The emergence of modularity promotes evolvability of the system. In other words, evolution selects the modular fashion.

**(4) Improvement**

There is experimental evidence which suggests that in certain species, where sexual and asexual reproduction are both probable, such as yeasts[11], sexual reproduction has a selective advantage. It will be interesting to explore further the interplay of recombination and modularity.
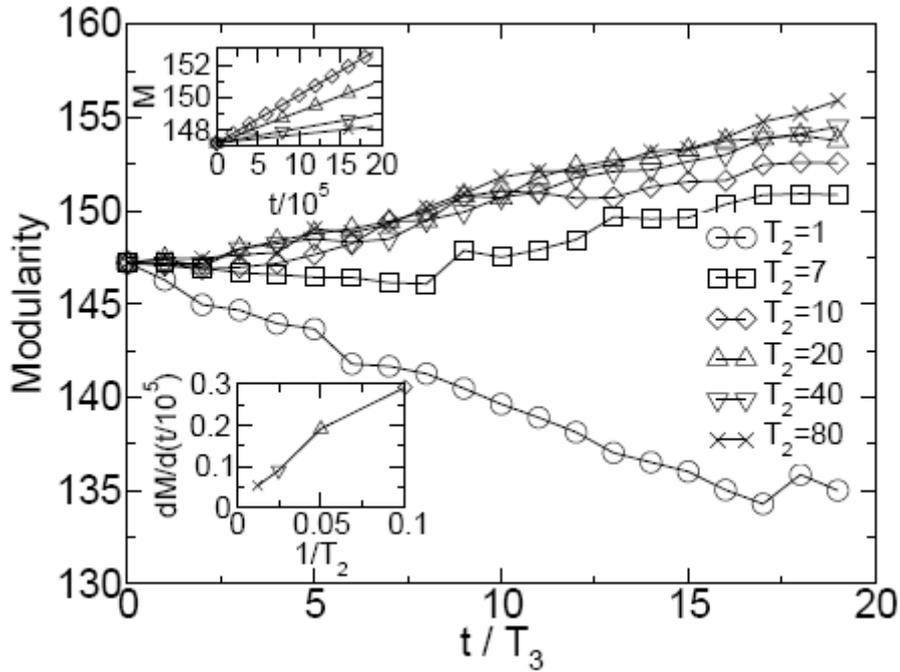


Fig. 9 Change of modularity with time for different period of environmental change[7].
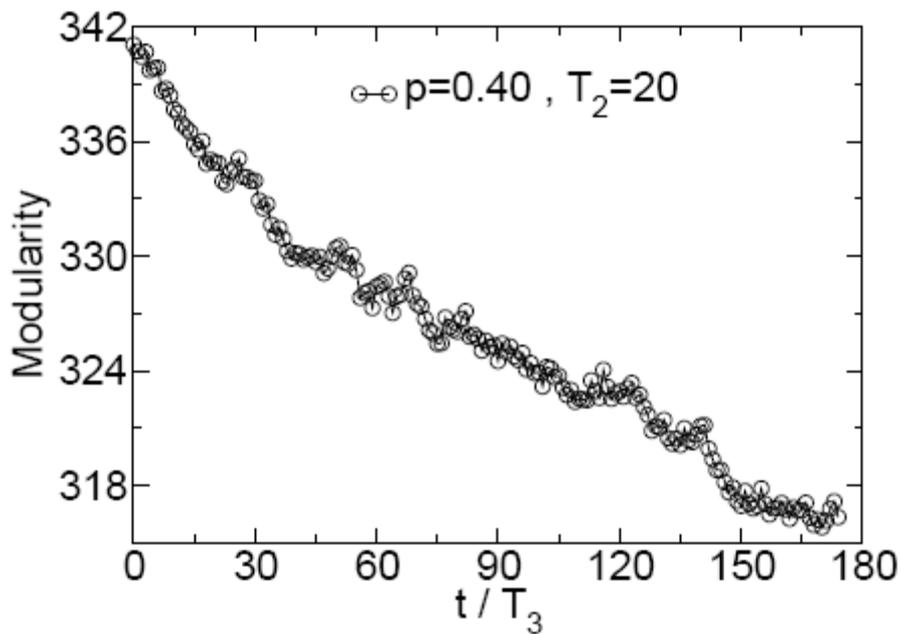


Fig. 10 Decrease in modularity when it is oversaturated[7].

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