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Sympatric speciation: compliance with phenotype diversification from a single genotype

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A novel mechanism for sympatric speciation that takes into account complex bioprocesses within each individual organism is proposed. According to dynamical systems theory, organisms with identical genotypes can possess differentiated physiological states and may coexist 'symbiotically' through appropriate mutual interaction. With mutations, the phenotypically differentiated organisms gradually come to possess distinct genotypes while maintaining their symbiotic relationship. This symbiotic speciation is robust against sexual recombination, because offspring of mixed parentage with intermediate genotypes are less fit than their parents. This leads to sterility of the hybrid. Accordingly, a basis for mating preference also arises.

Keywords: sympatric speciation; differentiation; symbiosis; isologous diversification

1. INTRODUCTION

The question posed by Darwin (1859) of why organisms are separated into distinct groups rather than exhibiting a continuous range of characteristics has not yet been fully answered. In spite of several explanations involving sympatric speciation, according to Maynard Smith & Szathmáry (1995) 'we are not aware of any explicit model demonstrating the instability of a sexual continuum' (p. 167). The difficulty involving stable sympatric speciation is that it is not clear how two groups, which have just begun to separate, coexist while mutually interacting. Here, we propose a mechanism through which two groups with little (or no) difference in genotype form a 'symbiotic' relationship under competition. This mechanism is understood in terms of the 'isologous diversification theory' (Kaneko & Yomo 1997, 1999), according to which organisms with identical genotypes spontaneously split into distinct phenotypes and establish a relationship in which the existence of one group is mutually supported by the other. By considering genetic mutations and sexual recombinations, a sympatric speciation process follows, resulting in the formation of distinct genotypic groups exhibiting reproductive isolation. This process is robust with respect to fluctuations, due to the symbiotic relationship. The hybrid offspring of the two groups becomes sterile and also provides a basis for mating preference, which is a major mechanism in sympatric speciation (Maynard Smith 1966; Lande 1981; Futsuyma 1986; Turner & Burrows 1995; Howard & Berlocher 1998; Dieckmann & Doebeli 1999; Kondrashov & Kondrashov 1999).

In order to study phenotypic and genotypic diversification through interaction, we have to consider a developmental process that maps a genotype to a phenotype. As an illustrative model, we consider a dynamic process consisting of several interacting metabolic cycles. Each organism possesses such internal dynamics with several metabolic cycles, while it selectively consumes external resources, depending on its internal dynamics, and transforms them into some products. Through this process, organisms mature and eventually become ready for reproduction.

In most studies on population biology and evolution so far, it has been widely assumed that a phenotype is uniquely determined for a given genotype and environment. If this assumption were always true, population dynamics of only genotypes would be sufficient for studying the evolutionary process theoretically. However, there are cases where organisms of the same genotype may take distinct phenotypes through interaction.

First, some mutant genotypes related to malfunctions show various phenotypes, each of which appears at a low probability (Holmes 1979). This phenomenon is known as low or incomplete penetrance (Opitz 1981), which suggests plastic ontogenesis.

Although the origin of low penetrance in multicellular organisms may not be well clarified, differentiation of physiological states is already known in bacteria (Novick & Weiner 1957). Furthermore, one of the authors and his colleagues have found that specific mutants of *Escherichia coli* show (at least) two distinct types of enzyme activity, although they have identical genes. These different types coexist in the unstructured environment of a chemostat (Ko *et al*. 1994) and this coexistence is not due to spatial localization. Coexistence of each type is supported by each other. Indeed, when one type of *E. coli* is removed externally, the remaining type starts differentiation again in order to recover the coexistence of the two types. In addition, even at a molecular level, a mutant gene of xylanase was shown to produce various levels of enzyme activity (Ko *et al*. 1994). A mechanism for a single gene showing various levels of molecular function has also been elucidated in physicochemical terms (Kobayashi *et al*. 1997).

Such differentiation of a phenotype has also been discussed as a possibility for different inheritable states of the same genotype (see, for example, Landman 1991). Although we do not assume any epigenetic inheritance here since its relevance to evolution is still controversial, it should be noticed that the existence of different

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physiological states from a single genotype itself is demonstrated experimentally, even if one does not accept the inheritance of the states.

Note also that the differentiation of phenotypes from the same genotype is also supported theoretically, as will be mentioned later. Here we will study the relevance of such phenotypic diversification to evolution.

2. MODEL

In our theoretical model, the phenotype is represented by a set of variables corresponding to metabolic processes or some other biological processes. To be specific, each individual i has several (metabolic or other) cyclic processes and the state of the jth process at time n is given by $X_n^j(i)$. With k such processes, the state of an individual is given by the set $(X_n^1(i), X_n^2(i), \ldots, X_n^k(i))$, which defines the phenotype. This set of variables can be regarded as concentrations of chemicals, rates of metabolic processes or some quantity corresponding to a higher function. The state changes temporally according to a set of deterministic equations with some parameters.

Since genes are simply chemicals contained in DNA, they could in principle be included in the set of variables. However, according to the 'central dogma of molecular biology' (Alberts *et al.* 1994, ch. 3 & 6), the gene has a special role among such variables. Genes can affect phenotypes, i.e. the set of variables, but the phenotypes cannot directly change the code of genes. Over the course of one generation changes in genes are negligible compared with those of the phenotypic variables they control. Hence, in our model, the set corresponding to genes is represented by parameters that govern the dynamics of phenotypes, since the parameters in an equation are not changed while they control the dynamics of the variables.

Our model consists of the following procedures.

(i) Dynamics of the phenotypic state. The dynamics of the variables $X_n^j(i)$ consist of mutual influence of cyclic processes $(X_n^l(i))$ and interaction with other organisms $(X_n^j(i'))$.

(ii) Growth and death. Each individual splits into two when a given condition for growth is satisfied. Taking into account the fact that the cyclic process corresponds to a metabolic, genetic or other process that is required for reproduction, we assume that the unit replicates when the accumulated number of cyclic processes goes beyond some threshold. To introduce competition for survival, death is included by both random removal of organisms at some rate as well as by a given death condition based on their state.

(iii) Genetic parameter and mutation. Following the above argument, genes are represented as parameters in the model. With reproduction, the genes slowly mutate. The set of parameters in the model changes slightly through mutation when an offspring is reproduced.

To be specific we consider the following model. First, the state variable $X_n^j(i)$ is split into its integer part $R_n^l(i)$ and fractional part $x_n^l(i) = \mathrm{mod}[X_n^l(i)]$. The integer part $(R_n^j(i))$ is assumed to give the number of times the cyclic process has occurred since the individual's birth, while the fractional part $(x_n^l(i))$ gives the phase of oscillation in the process. As a simple example, the internal dynamics of the cyclic process is assumed to be given by $\Sigma_m\{a^{lm}/2\}\sin(2\pi x_n^m(i))$, while the interaction among organisms is given by the competition for resources among the $\mathcal{N}_n$ organisms existing at the time, which is given by

$$I^l(i) = p\sin(2\pi x_n^l(i)) + \frac{s^l - \sum_j p\sin 2\pi(x_n^l(j))}{\mathcal{N}_n}. \qquad (1)$$

(The second term comes from the constraint $\Sigma_i I^l(i) = s^l$, i.e. the condition that $\mathcal{N}$ individuals compete for a given resource s^l at each time-step. The first term represents the ability to secure the resource, depending on the state.) Our model is given by

$$\begin{aligned} X_{n+1}^l(i) = X_n^l(i) &+ \sum_m \frac{a^{lm}(i)}{2}\sin(2\pi x_n^m(i)) \\ &- \sum_m \frac{a^{ml}(i)}{2}\sin(2\pi x_n^l(i)) + p\sin(2\pi x_n^l(i)) \\ &+ \frac{s^l - \sum_j p\sin 2\pi(x_n^l(j))}{\mathcal{N}_n}. \end{aligned} \qquad (2)$$

Then, as a specific example, the condition for reproduction is given by $\Sigma_l R_n^l(i) \geqslant$ Thr. The rotation number $R_n^l(i)$ is reset to zero when the corresponding individual splits. On the other hand, with the death condition, an individual with $R_n^l(i) < -10$ (i.e. with a reverse process) is removed.

Next, genotypes are given by a set of parameters $a^{ml}(i)$, which represent the relationship between the two cyclic processes l and m ($1 \leqslant l$ and $m \leqslant k$). With each division, the parameters a^{ml} are changed to $a^{ml} + \delta$ with δ, a random number over $[-\varepsilon, \varepsilon]$, with small ε, corresponding to the mutation rate. Although the results in the figure adopt the mutation rate $\varepsilon = 0.001$, a change in mutation rate is responsible only for the speed of the separation of the parameters and the conclusions are independent of its specific value.

Let us make some comments about our model. Each term $a^{lm}\sin(x_n^m(i))$ shows how a process x^m influences x^l. For example, in a metabolic process, one cycle influences some other through catalytic reactions, depending on the activity of the enzyme corresponding to it. With the change of genes, the activities of enzymes can change, which leads to the change of the parameter values of a^{lm} accordingly. Following this argument, genotypes are regarded as being represented by a set of parameters a^{lm}. Indeed, we have also studied a specific biochemical reaction network model with its catalytic efficiency as a genetic parameter and the results, which will be presented, were observed.

The interaction term $p\sin(2\pi x_n^l(i))$ represents the influence on the cyclic process between individuals through the exchange of chemicals (or by other means). Since this term can change its sign, chemicals can be secreted to the environment from each individual. Then, the resources that are taken from one individual may be used by some other. Through this ecological interaction, individuals may keep some relationship if they are differentiated.

Of course, the above explanation is just one example of the correspondence of our model to a real biological process.

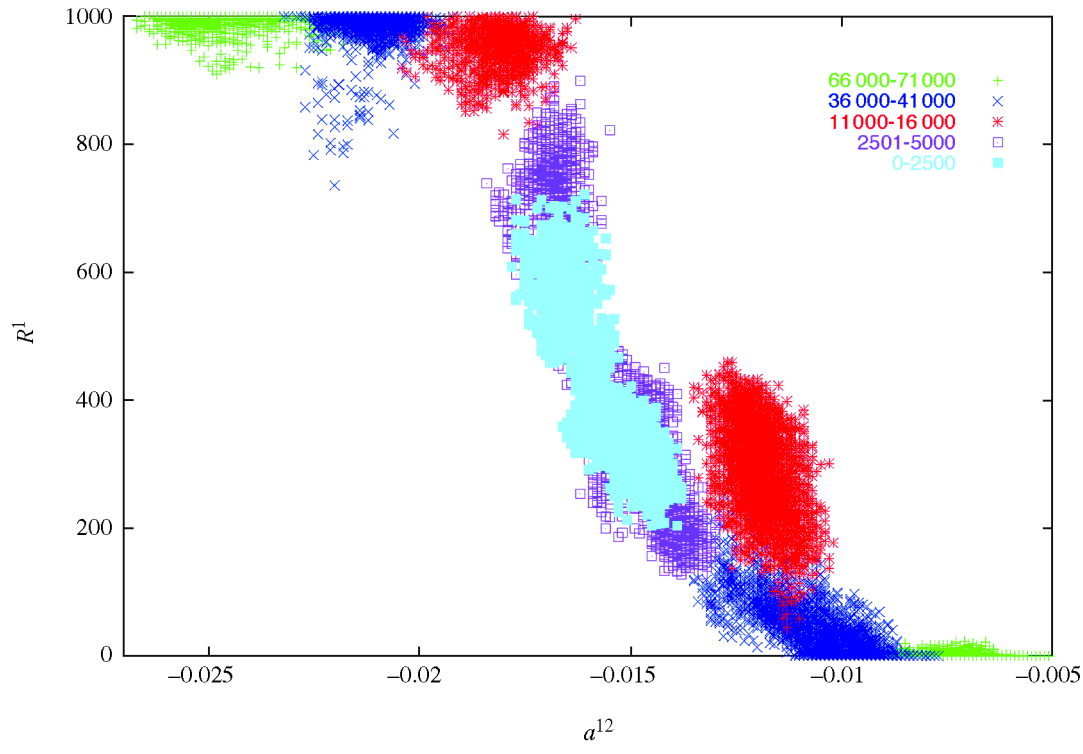

Figure 1. Evolution of genotype–phenotype relationship. In the present model, due to the nonlinear nature of the dynamics, x_n^l often oscillates chaotically or periodically in time. Hence, it is natural to use the integer part $(R^l(j))$ as a representation of the phenotype, since it represents the number of cyclic processes used for reproduction. Here (R^1, a^{12}) is plotted for every division of individuals. The first 2500 divisions are plotted in light blue, divisions 2501–5000 in pink, 11 000–16 000 in red, 36 000–41 000 in blue and 66 000–71 000 in green. Initially, phenotypes are separated, even though the genotypes are identical (or only differ slightly), as shown in light blue. Later, the genotypes are also separated according to the difference in phenotypes. In the simulation, the population size fluctuates around 300 after an initial transient. (Hence, the generation number is given approximately by dividing this division number by 300.) In the figures in the model, we adopt the following parameter values and initial conditions. The threshold number (Thr) for the reproduction is 1000 and the mutation rate of the parameters (ε) is 0.001. Initially, the genotype parameters are set as $a^{ij} = -0.1/(2\pi)$. The parameter values for figures 1 and 2 are set at $p_k = 1.8/(2\pi)$, $s^1 = 8$, $s^2 = 7$, $s^3 = 2$.

As long as its mathematical structure is common, the validity of our model is not restricted to the above example and the results, to be presented, can generally be applied.

3. SCENARIO FOR SYMBIOTIC SYMPATRIC SPECIATION

The above model is one of the simplest for discussing loose developmental processes. We have also carried out simulations of several models of this type, for example those consisting of a metabolic process of autocatalytic networks. Through the simulations and theoretical considerations of several models the following mechanism for speciation is proposed. Since the characteristic features for speciation, which are to be presented in the following, are common, we adopt the simplest model above in order to illustrate the scenario here. Note, of course, that the scenario for speciation is expected to work in a more realistic model including much more complicated processes for development and interaction.

(a) *Stage 1: interaction-induced phenotypic differentiation*

When there are many individuals interacting for finite resources, the phenotypic dynamics begin to differentiate even though the genotypes are identical or differ only slightly (see the light blue points in figure 1). This differentiation generally appears if nonlinearity is involved in the internal dynamics of some phenotypic variables (Kaneko & Yomo 1997, 1999; Furusawa & Kaneko 1998). Then slight phenotypic differences between individuals are amplified by the internal dynamics (e.g. metabolic reaction dynamics). Through interaction between organisms, the different phenotypic dynamics tend to be grouped into two (or more) types, despite the fact that all have identical (or only slightly different) genotypes. In the example in figure 1, the phenotype splits into two groups, which we refer to as the 'upper' and 'lower' groups.

This differentiation process has recently been clarified as isologous diversification (Kaneko & Yomo 1997, 1999), in which two groups with distinct phenotypes even appear in a group with a single genotype. This interaction-induced phenotype diversification is a general consequence when the developmental process with interactions between organisms is considered as a nonlinear dynamics process (Kaneko 1990, 1994). When there is instability in the dynamics, the temporal evolution of individuals in phenotype space begins to diverge. Then, through interactions, these dynamics are stabilized through the formation of distinct groups with differentiated states in the phenotype space. The existence of the two (or more)

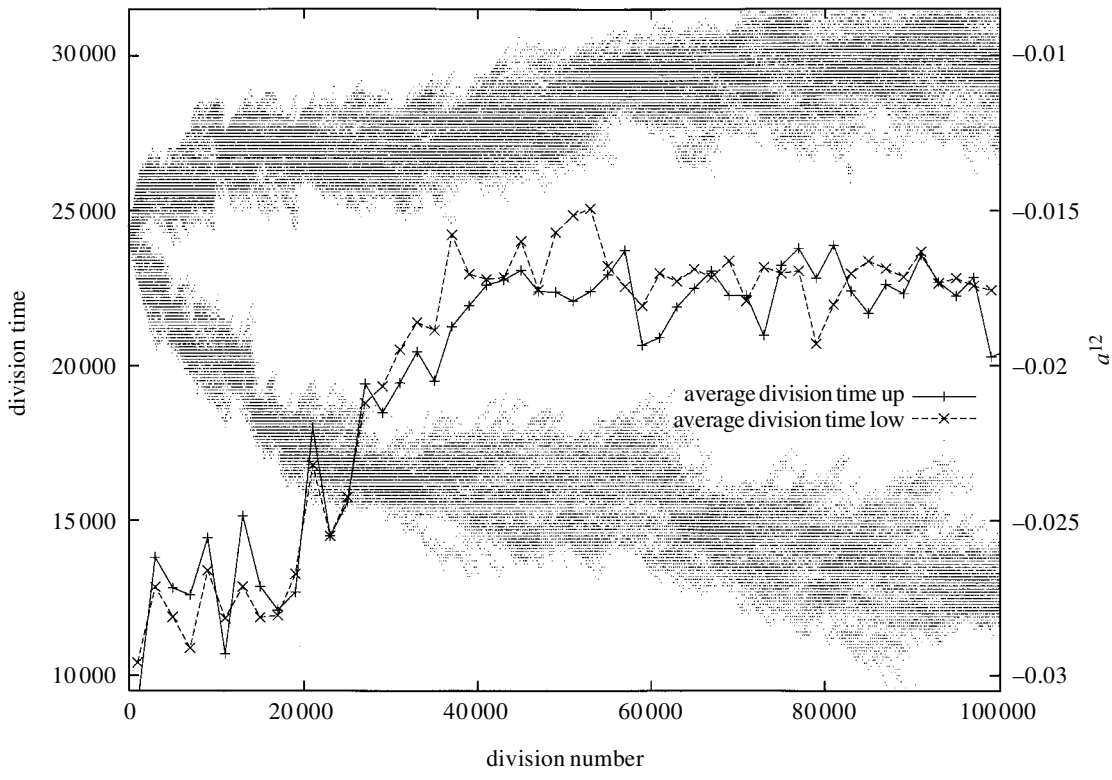

Figure 2. The evolution of the genotypic parameter. (*a*) The parameter $a^{12}(i)$ is plotted as a dot at every division (reproduction) event with the abscissa as the division number. The average time necessary for division (reproduction) is plotted for the upper and lower groups, where the average is taken over 2000 division events (sixth to eighth generations). As the two groups are formed around the two-thousandth division event, the population size becomes twice the initial size and each division time is also approximately doubled. Note that the two average division speeds of the two groups remain of the same order, even when the genetic parameter evolves in time.

groups eliminates the instability in the dynamic (metabolic) process that exists when one of the groups is isolated. Hence, the existence of all groups is required for the survival of each. For example, if a group of one type is removed, then the phenotype of individuals of another type changes in compensation for the missing type.

To put the above explanation in biological terms, consider a given group of organisms faced with a new environment and not yet specialized for the processing of certain specific resources. Each organism has metabolic (or other) processes with a biochemical network. As the number of organisms increases, they compete for resources. The interaction, for example, results from the use of some by-product of one organism by others. As this interaction becomes stronger, the phenotypes become diversified in order to allow for different uses of metabolic cycles and they split into two (or several) groups. Each group is specialized in some metabolic cycles and also in the processing of some resources. Here the by-product of the metabolic processes of one group is necessary for allowing another group to specialize in some particular metabolic cycle. Resources secreted from one group can be used as a resource for the other group and vice versa. Hence, the two groups realize a differentiation of roles and form a symbiotic relationship. Each group is regarded as specialized in a different niche, which is provided by another group.

As an extreme case, this differentiation can occur even when a single resource is supplied externally (i.e. $s^j = 0$ for $2 \leqslant j \leqslant k = 3$). In this case, the temporal average of $p \sin(x_n^2(i))$ is positive for one group and negative for the other, while that of $p \sin(x_n^3(i))$ has the opposite sign. With this differentiation of phenotypes, one group uses x^2 as a resource for growth provided by the other, which in turn uses x^3 as a resource.

It should be pointed out that the progeny of a reproducing individual belonging to one group may belong to the other group at this stage, since all groups still have almost identical gene sets.

(b) *Stage 2: coevolution of the two groups in order to amplify the difference of genotypes*

Now we discuss the evolutionary process of genotypes. After the phenotype is differentiated into two groups, the genotype (parameter) of each group begins to evolve in a different direction, as shown in figures 1 and 2. This evolution occurs because, for the upper (lower) group, those individuals with a smaller (larger) parameter value reproduce faster. In our numerical simulations, there always exists (at least one) such parameter. As a simple illustration, assume that the two groups use certain metabolic processes differently. If the upper group uses one metabolic cycle more, then a mutational change of the relevant parameter in order to enhance this cycle is favoured for the upper group, while a change to reducing it (and enhancing some others) may be favoured for the lower group. In other words, each organism begins to adapt in one of the niches formed by another (or others).

Note that R^2 also takes a different value between the two groups in the opposite direction, since $\Sigma_j R^j = \mathrm{Thr}$ for each division. As for the parameter change, the values of a^{12} and a^{21} split first in this example, but then a^{23} and, later, other parameter values also start to split into the two groups. Several genes start to be responsible for the differentiation.

As the genetic separation progresses, phenotypic differences between the two groups also become amplified (see figure 1). With the increase in the split in genotypes, it begins to become the case that offspring of members of a given group certainly keep the phenotype of this group. Since the phenotype of one group stabilizes the other, the evolutions of the two groups are interdependent. Hence, the tempo of the genetic evolution in one group is related to that of the other. The two groups coevolve, maintaining the 'symbiotic' relationship established in the previous stage. Indeed, as shown in figure 2, the growth speeds of the two groups remain of the same order, even if each genotype and phenotype change with time.

With the coevolutionary process described above, the phenotype differentiation is fixed to the genotype. In much later generations, this fixation is complete. In this case, even if one group is isolated, offspring with the phenotype of the other group are no longer produced. Offspring of each group keep their phenotype (and genotype) on their own.

(c) *Reproductive isolation with respect to sexual recombination*

The importance of the present scenario lies in the robustness of the speciation process. Even if one group happens to disappear through some fluctuations in the initial stage of the speciation process, coexistence of the two distinct phenotypic groups is recovered. Hence, the present process is also expected to be stable against sexual recombination, which mixes the two genotypes and may bring about a hybrid between the two genotypes. In order to demonstrate this stability, we have extended the previous model to include this mixing of genotypes by sexual recombination.

Here, we have modified our model so that sexual recombination occurs and mixes genes. To be specific, reproduction occurs when two individuals i_1 and i_2 satisfy the threshold condition ($\Sigma_l R^l_{\mu}(i_k) > \mathrm{Thr}$) and the two genotypes are then mixed. As an example, we have produced two offspring, $j = j_1$ and j_2, from individuals i_1 and i_2 as

$$a^{lm}(j) = a^{lm}(i_1) r_j^{lm} + a^{lm}(i_2)(1 - r_j^{lm}) + \delta, \qquad (3)$$

with a random number $0 < r_j^{lm} < 1$ for mixing the parents' genotypes, besides the random mutation term by δ. Even if two separated groups may start to form according to our scenario, the above recombination forms 'hybrid' offspring with intermediate parameter values a^{lm} when two organisms from different groups mate. In addition, depending on the random number, for some offspring the parameter value a^{lm} may be closer to one of the parents, but that of $a^{l'm'}$ may be closer to that of the other of the parents. Accordingly, recombinations of the two groups can lead to a different combination of alleles, since the two groups take different combinations of the parameter values $\{a^{lm}\}$.

Although the hybrid is formed in this random mating with some proportion (0.5 if the two groups have equal population), it turns out that this hybrid, irrespective of which phenotype it realizes, has a lower reproduction rate than the other two groups which have a 'matched' genotype–phenotype correspondence with a higher reproduction rate. We have plotted the average offspring number for given genotype parameters in figure 3 (to be precise, the average over a given range of parameters). As shown, a drop at the intermediate value in the offspring number starts to appear through generations. Within a few dozen generations, as certain genotypic parameters are apart, there is little or no chance of a hybrid reproducing and F_1 sterility results.

Note that this conclusion is drawn even without assuming a mating preference. Rather, it is natural, according to the present scenario, that mating preference in favour of similar phenotypes evolves, since it is disadvantageous for individuals to produce a sterile hybrid. In other words, the present mechanism also provides a basis for the evolution of sexual isolation through mating preference. Note, however, that, in sympatric speciation starting from only the mating preference, one of the groups may disappear due to fluctuations when its population is not sufficiently large. In contrast, according to our scenario, the coexistence of the two groups is restored even under disturbances. Hence, it is concluded that our mechanism yields robust sympatric speciation, i.e. differentiation of genotypes and phenotypes and sexual reproductive isolation (Dobzhansky 1951), even in the situation in which all individuals interact with all others equally.

(d) *Importance of phenotypic differentiation*

Evolution according to our scenario often leads to specialization with regard to resources through competition. Indeed, the coexistence of two (or more) species after the completion of the speciation is also supported by the resource competition theory of Tilman (1976, 1981). However, in order to realize the speciation process, phenotype differentiation from a single genotype is essential. As long as a phenotype is uniquely determined by a genotype, two individuals with a slight genotype difference can only have a slight phenotype difference also. Since competition is strong between individuals with similar phenotypes, they cannot coexist as a different group. Hence, two groups cannot be differentiated from a group of single (or similar) genotypes. In contrast, in our scenario, even if the genotypes of two individuals are the same or only slightly different, their phenotypes need not be similar and can in fact be of quite different types, as shown in figure 1. Accordingly, these two groups can coexist.

In order to check the importance of this phenotypic differentiation from a single genotype, we also performed several numerical experiments with our model by choosing parameters such that differentiation into two distinct phenotype groups does not occur initially. In this case, separation into two (or more) groups with distinct phenotypes or genotypes is not observed, even if the initial variance in the genotypes is large or even if a large

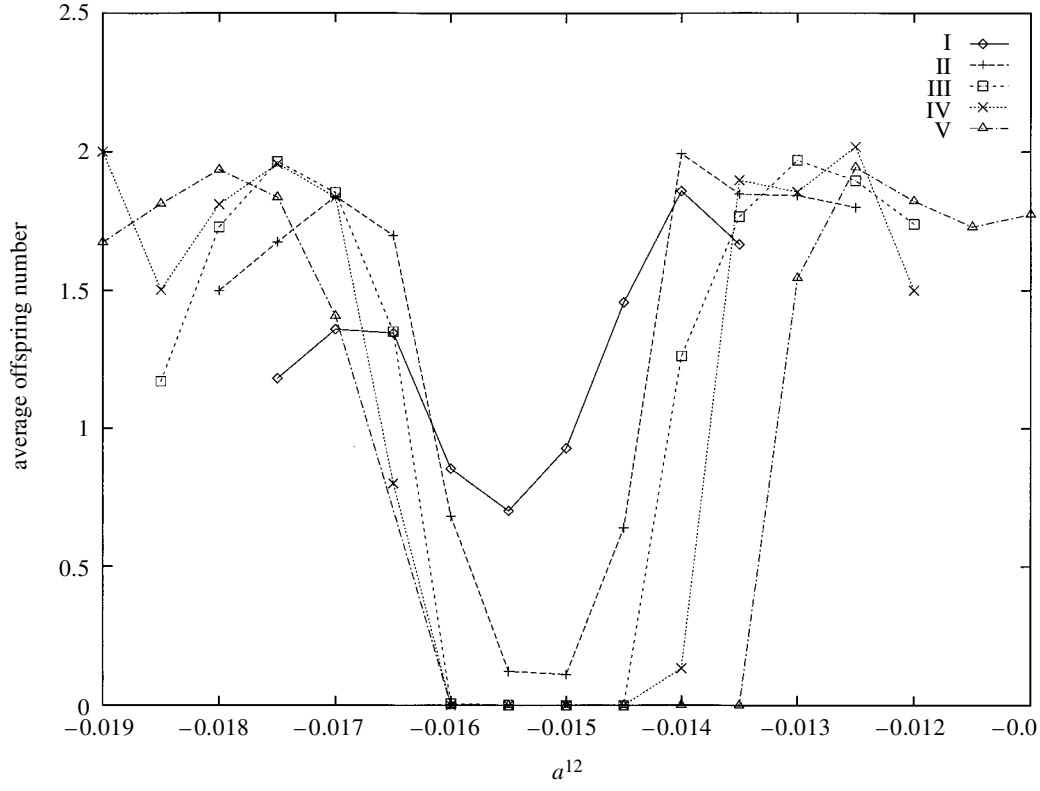

Figure 3. The average offspring number before death is plotted as a function of the parameter (genotype) for simulations with sexual recombination. As an extension for including sexual recombination, we have also studied a model in which two organisms satisfying the above threshold condition mate to reproduce two offspring. When they mate, the offspring have parameter values that are the randomly weighted averages of those of the parents, as given in the text. We measured the number of offspring for each individual during its life span. By taking a bin width of 0.005 for the genotype parameter a^{12}, the average offspring number over a given time-span is measured to produce a histogram. The histogram over the first 7500 divisions (*ca.* 20 generations) is plotted by solid line I and the histogram for later divisions is overlaid with a different line, as given by lines II (over 7500–15000 divisions), III ($1.5–2.25\times10^4$), IV ($2.25–3.0\times10^4$) and V ($3.75–4.5\times10^4$). As shown, a hybrid offspring will be sterile after some generations. Here we have used the same model and initial condition as in figure 1 and imposed recombination with the parameters $p_k = 1.5/(2\pi)$ and $s^1 = s^2 = s^3 = 2$. The population fluctuates around 340 in the run.

mutation rate is adopted. This clearly demonstrates the relevance of phenotypic differentiation.

On the other hand, genetic differentiation always occurs when the phenotype differentiates into two (or more) groups. To be specific, in our model, the condition for the differentiation is as follows. First, the parameter p should be larger than some value. For example, for $k = 3$ with $s^1 = 2$, $s^2 = 4$ and $s^3 = 6$ and with the initial parameters $a^{lm}(i) \approx -0.2/(2\pi)$, the differentiation appears for $p \gtrapprox 1.8$. Second, the resource term per unit $(\Sigma_j s^j/N)$ should be smaller than some threshold value. For example, the threshold resource is $s_{\mathrm{thr}} \approx 10$ for $s^1 = s^2 = s^3$, $p = 1.5/(2\pi)$ and $N \approx 300$ and the initial parameters $a^{lm}(i) \approx -0.1/(2\pi)$. Note that these conditions imply strong interaction in competing for resources and are easier to satisfy, as the number of individuals competing for given resources increases.

4. DISCUSSION

In the symbiotic speciation process, the potential for a single genotype producing several phenotypes declines. After the phenotypic diversification of a single genotype, each genotype again appears through mutation and assumes one of the diversified phenotypes in the population. Thus, the one-to-many correspondence between the original genotype and phenotypes eventually ceases to exist. As a result, one may see a single genotype expressing small numbers of phenotypes in nature, since most organisms at the present time have gone through several speciation processes. One can also expect that mutant genotypes tend to have a higher potential than the wild-type genotype for producing various phenotypes. Indeed, this expectation is consistent with the observation that low or incomplete penetrance (Holmes 1979; Opitz 1981) is more frequently observed in mutants than in a wild-type.

Taking our results and experimental facts into account, one can predict that new species or organisms emerging as a species have a high potential for producing a variety of phenotypes, while 'living fossils', such as *Latimeria chalumnae* and *Limulus*, have a stable expression of a small number of phenotypes. The relationship between evolvability and plasticity in ontogenesis is an important topic to be pursued.

Since the speciation discussed in this paper is triggered by interaction and not merely by mutation, the process is not so much random as deterministic. In fact, the speciation process occurs irrespective of the adopted random number in the simulation. Some of the phenotypic

explosions in nature that have been recorded as occurring within short geologic periods may have followed the deterministic and relatively fast process of interaction-induced speciation. Hence, our scenario may shed some light on the variation in time-scales on which evolution proceeds, e.g. punctuated equilibrium (Gould & Eldredge 1977). Here it should be noted that the change in phenotypes occurs in a few generations. The speed of genetic change, of course, depends on the mutation rate, but the present mechanism is found to work even for any smaller mutation rate (say $\varepsilon = 10^{-6}$).

In the present paper, we have mostly reported the case with only three processes ($k = 3$), but we have numerically confirmed that the present speciation process also works for $k > 3$ (e.g. $k = 10$). By choosing a model with many cyclic processes, we have also found successive speciation of genotypes into several groups from a single genotype. With evolution, the phenotypes begin to be separated into two groups, each of which is specialized in some processes and depends on the by-products of the other. Later, the species diverge into further specialized groups, which are fixed into genotypes. This process is relevant when considering adaptive radiation.

Discussion of the mechanism involved in evolution often consists of mere speculation. In contrast, most important in our scenario is its experimental verifiability. Isologous diversification has already been observed in the differentiation of enzyme activity in *E. coli* with identical genes (Ko *et al*. 1994). In observing the evolution of *E. coli* in the laboratory (Xu *et al*. 1996; Kashiwagi *et al*. 2000), by controlling the strength of the interaction through the population density one can check whether evolution at a genetic level is accelerated through interaction-induced phenotypic diversification. Our isologous symbiotic speciation, which was based on dynamical systems theory and which was numerically confirmed and biologically plausible, can be verified experimentally.

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REFERENCES

Alberts, B., Bray, D., Lewis, J., Raff, M., Roberts, K. & Watson, J. D. 1994 *The molecular biology of the cell*, 3rd edn. New York: Garland.

Darwin, C. 1859 *On the origin of species by means of natural selection or the preservation of favored races in the struggle for life*. London: Murray.

Dieckmann, U. & Doebeli, M. 1999 On the origin of species by sympatric speciation. *Nature* **400**, 354.

Dobzhansky, T. 1951 *Genetics and the origin of species*, 2nd edn. New York: Columbia University Press.

Furusawa, C. & Kaneko, K. 1998 Emergence of rules in cell society: differentiation, hierarchy, and stability. *Bull. Math. Biol.* **60**, 659.

Futsuyma, D. J. 1986 *Evolutionary biology*, 2nd edn. Sunderland, MA: Sinauer Associates, Inc.

Gould, S. J. & Eldredge, N. 1977 Punctuated equilibria: the tempo and mode of evolution reconsidered. *Paleobiology* **3**, 115.

Holmes, L. B. 1979 Penetrance and expressivity of limb malformations. *Birth Defects* **15**, 321.

Howard, D. J. & Berlocher, S. H. (ed.) 1998 *Endless form: species and speciation*. Oxford University Press.

Kaneko, K. 1990 Clustering, coding, switching, hierarchical ordering, and control in a network of chaotic elements. *Physica* D **41**, 137.

Kaneko, K. 1994 Relevance of clustering to biological networks. *Physica* D **75**, 55.

Kaneko, K. & Yomo, T. 1997 Isologous diversification: a theory of cell differentiation. *Bull. Math. Biol.* **59**, 139.

Kaneko, K. & Yomo, T. 1999 Isologous diversification for robust development of cell society. *J. Theor. Biol.* **199**, 243.

Kashiwagi, A., Kanaya, T., Yomo, T. & Urabe, I. 1998 How small can the difference among competitors be for coexistence to occur. *Res. Popul. Ecol.* **40**, 223.

Ko, E., Yomo, T. & Urabe, I. 1994 Dynamic clustering of bacterial population. *Physica* D **75**, 81.

Kobayashi, C., Suga, Y., Yamamoto, K., Yomo, T., Ogasahara, K., Yutani, K. & Urabe, I. 1997 Thermal conversion from low- to high-activity forms of catalase I from *Bacillus stearothermophilus* *J. Biol. Chem.* **272**, 23 011.

Kondrashov, A. S. & Kondrashov, A. F. 1999 Interactions among quantitative traits in the course of sympatric speciation. *Nature* **400**, 351.

Lande, R. 1981 Models of speciation by sexual selection on phylogenic traits. *Proc. Natl Acad. Sci. USA* **78**, 3721.

Landman, O. E. 1991 The inheritance of acquired characteristics. *A. Rev. Genet.* **25**, 1.

Maynard Smith, J. 1966 Sympatric speciation. *Am. Nat.* **100**, 637.

Maynard Smith, J. & Szathmáry, E. 1995 *The major transitions in evolution*. Oxford, UK: W. H. Freeman.

Novick, A. & Weiner, M. 1957 Enzyme induction as an all-or-none phenomenon. *Biochemistry* **43**, 553.

Opitz, J. M. 1981 Some comments on penetrance and related subjects. *Am. J. Med. Genet.* **8**, 265.

Tilman, D. 1976 Ecological competition between algae: experimental confirmation of resource-based competition theory. *Science* **192**, 463.

Tilman, D. 1981 Test of resource competition theory using four species of Lake Michigan algae. *Ecology* **62**, 802.

Turner, G. F. & Burrows, M. T. 1995 A model for sympatric speciation by sexual selection. *Proc. R. Soc. Lond.* B **260**, 287.

Xu, W.-Z., Kashiwagi, A., Yomo, T. & Urabe, I. 1996 Fate of a mutant emerging at the initial stage of evolution. *Res. Popul. Ecol.* **38**, 231.

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