AGENT SIMULATION OF FUNCTIONAL DIFFERENTIATION-EFFECTS OF INFECTIOUS DISEASES ASSOCIATED WITH AMBIGUITY OF GENES

Masao Kubo\textsuperscript{1}, Saori Iwanaga\textsuperscript{2}, Hiroshi Sato\textsuperscript{1}

Abstract

In this paper, epidemic diseases are taken up as factors that contribute to “division of labor” and “functional differentiation”. We introduced an agent simulation with emphasis on reproduction. By this simulation we found that when genes have ambiguities and there are unique infectious diseases according to tasks and when not simultaneously suffering from multiple diseases, the occurrence of specialized sub-group is able to reproduce.

Index terms

Division of labor; functional differentiation; evolution; infectious disease.

1. Introduction

“Division of labor” and “functional differentiation” are key mechanisms for performing advanced tasks and are considered to be an important mechanism in forming an intelligent society. As an example of functional differentiation, leaf cutter ants carrying leaves to nests are unprotected so that parasite flies lay eggs on it. To prevent this, another ant on a leaf guards the carrier ant. Both ants have same gene but each ant has an unique shape that fits its own tasks.

Functional differentiation is a macroscopic strategy consisting of two different time scale dynamics. One is called division of labor in activity at task solving level and the other is a reproductive level activity, which is called “specialization”. Division of labor means that work performed by each individual varies according to changes in the environment, and specialization means that body and behavior of individuals are specialized in these roles.

Regarding division of labor, its dynamics has been attracting attention in the past, and many models have been proposed, including response threshold models\cite{1}, and there are many studies of speciation (for example, \textit{Rhagoletis}\cite{6}) that differentiate into different species and do not mate afterwards, but there are not many simulations

\textsuperscript{1}National Defense Academy of Japan, \textsuperscript{2}Japan Coast Guard Academy.
about specialization combined with the division of labor. Therefore, it becomes a divide in understanding functional differentiation seamlessly.

One of the doubts of the functional differentiation scenario is to elucidate the method of stably generating intraspecific species specialized for the task (hereinafter referred to as subspecies) by suppressing the occurrence of hybrids whose ability is not satisfactory. Fig. 1 illustrates this issue. If two tasks necessary for adaptation cannot be achieved with a single individual, there may be an approach based on the division of labor by generating subspecies that specialize in each. In speciation, these are specialized in different species and become unable to reproduce naturally and later, whereas in functional differentiation it is specialization in the same organization and mating between subspecies may be still possible. As a result, “hybrids” that cannot be done for both tasks will occur, making the growth of specialized subspecies unstable. As a method for avoiding this reproduction issue, a method such as polyphenism that generates a special individual by giving a unique food or stimulus to it in the growing process is known. In this study, we anticipate that there are other ways of functional differentiation, namely, generating and maintaining various subspecies, and we will examine the influence of infectious diseases here.

Infectious diseases are infected among members of the group (Fig. 2). The magnitude of the infection is determined by the threshold phenomenon determined by the number of susceptible ($S$), infection rate ($\beta$), recovery rate ($\gamma$). It has been expected that the evolution process of species will have a major influence because of the wide range of effects such as pandemic phenomenon that infects almost all the population. Meanwhile,
in the past 10 years, investigations on the insect mortality rate have progressed, and the relationship between the lifetime and illness has become clear. For example, it has been reported that the behavior that fellows who may be sick or ill within the ant nest are forced to be isolated can be seen. Brown [2] investigated the mortality rate of *Atta colombica* engaged in foraging and waste-heap work, and as a result. In ants engaged in this work, it was revealed that the death rate of ants touching waste is 60% higher. In addition, there is almost no change in work from worker who works in the back of the nest to work outside and little about waste-heap work on what was about the work of collection, It has been reported that it was not observed at all that waste-heap work was about the job of collecting. Waddington [5] investigated the body size of ant’s age for each role of foliar ants *Acromyrmex*. Waste contains pathogenic bacteria and toxic substances and it is said that division of labor has the effect of minimizing the risk of watching a group by dangerous substance contact among individuals. In this way, the disease and the infection of its members are a big issue in the leaf-cutter ant society, and it is expected that it affects the occurrence of roles and differentiation of functions.

Therefore, focusing on the ambiguity of genes, we would like to investigate infectious diseases and functional differentiation. If the infection is irrelevant to the task solving capacity of the member, it gives influence uniformly to each individual of the subspecies. This seems to be a kind of *genetic drift*. On the other hand, it is known that some genes have ambiguity which affects the functions having different effects of decoded proteins. For example, it is known that resistance to malaria is genetically strongly related to blood diseases even in humans. In this case it is expected that the infection of a certain
disease will work more intensely and complicately to increase or decrease the specific task solving capability. In particular, as shown in Fig. 3 infectious diseases are expected to be effective as a method to prevent hybrids caused by reproductive development with partners with significantly different genes, pointed out in Fig. 1. When a patch has a contagious endemic disease X, creatures in the patch are adapted to this and the occurrence of endemic disease is suppressed. Let’s assume that a creature without immunity to endemic attacks invades through the aisle. Because this creature infects endemic disease X and loses energy, even though it is reproduced by an indigenous individual, it is inferior to the number of descendants due to crossbreeding of indigenous creatures. Therefore, it does not prevent adaptation of indigenous creatures to this patch. Based on the above expectations, we will study the relationship between infectious disease and functional differentiation using simulation in this paper. Conventionally, there are few cases where this route was verified using a computer, and it is tried in this paper.

This paper is the extended work of our past research [4]. In [4], we introduced the simulation tool for this research and the capability of this tool was investigated by bringing out an example of division of labor. Here with the idea of infectious disease as a key to occurrence functional differentiation is examined by a wide-ranging computer simulation. As a result, we found that immigration of creatures greatly affects adaptation and function differentiation.

2. The proposed method

It is believed that social organisms typified by ants have an information structure called micro-macro loop. It seems that the micro behavior of each individual produces macroscopic characteristics and the macroscopic characteristics behave like a living thing as a whole by defining individual actions.

Normally, the relationship between this micro-level behavior and macroscopic dynamics is nonlinear, it is not easy to clarify this relationship analytically. For that reason, agent simulation which reproduces such aggregates first and investigates constructively is widely used. The agent decides its own behavior (corresponding to micro action) based on its point of view and investigates the relation with the macroscopic characteristic to emerge. In this paper, unlike strict agent simulation, we perform agent simulation more simplified than some macroscopic characteristics are predefined.

2.1. Overview of creature

Here, an agent equivalent to ant is called a creature. The creature’s algorithm is shown in Fig.5. Creatures live together with other creatures in a living environment called a patch. Creatures acquire the food in the patch and use the energy gained by consuming it. If energy runs out, it dies and it is quickly removed from the system. As shown in Fig. 4, multiple patches are connected in a grid pattern by passage, and if agent’s living environment is uncomfortable, the agent can immigrate to one of adjacent
patches. We suppose agents of this paper perform sexual reproduction and have gender. The behavior of the both sexual types of agents is exactly the same algorithm except that female agents with a given condition is satisfied can make offsprings.

2.2. Amount of foods the creature obtains

The food each creature gets is determined with the attributes of other creatures living in the same patch. Assuming that the number of creatures living on patch $i$ is $N(i)$, the amount of food acquired by creature $j$ is

$$C_fN(i)\alpha S_j^\beta/(\Sigma S^\beta).$$

(1)

$S_j$ is the strength of agent $j$, $C_f$ is a constant that determines the total amount of food, $\alpha$ is a parameter representing the macroscopic effect on the number of people, if $\alpha \geq 0$, food increases according to the number of creatures living in the patch, $\alpha = 0$, it means that a constant food occurs in the patch regardless of the number of people. $\beta$ represents the relationship between the strength of individuals and the amount of acquisition when competing for foods in patches against other creatures.
With these $\alpha$ and $\beta$ parameters, it is possible to avoid carrying out a complicated simulation on food acquisition, and it is possible to improve the prospect of simulation on function differentiation. In the following, we set $\alpha \geq 0.0, \beta = 0.0$ to get more foods by collective effect and evenly distribute that food among the members in the patch.

Creatures live until their energy has become zero. The initial energy is 10, which consumes $e_c = 0.1$ per unit time. One energy is obtained when one food is acquired.

2.3. Reproduction of creature

A female individual can make an offspring once if its energy exceeds 20. 20 is the twice of the initial energy. We set this value on the assumption that parents and adult children can coexist. At that time, it randomly selects a male from within the same patch and inherits the strength and resources of both as follows. Resources are personal characteristics described later.
Fig. 6. Infection probability

\[ S_{\text{offspring}} = \max(S_{\text{parents}}) + \epsilon \cdot N(0, 1) \]  \hspace{1cm} (2)

\[ r_{\text{offspring}} = \text{random}(r_{\text{parents}}) + \lambda \cdot N(0, 1) \]  \hspace{1cm} (3)

Here, \( N(0, 1) \) is a random number that follows the Gaussian distribution with mean 0 variance 1.

2.4. Migration of creature

Migration of creatures is done by comparing their own energy levels and nearby patches. Compare its own energy with the average of the energies of creatures in each of the 4 neighboring patches (i.e. von Neumann neighborhood) and move to the highest average patch with probability \( C_i \).

However, in the following experiments, we deal with not only criteria related to this profit, but also conditions on the morbid status. A creature that does not migrate if it is in a diseased state is called H type (Healthy), and a creature attempting to migrate even if it is affected is called N type (Negligent), because the movement of the ant in the disease is restricted within the nest It reflects which reports ([3], [5]) are inspired.

2.5. The ambiguity of Gene: Characteristics required for each patch and its Endemic disease

Each patch shall have characteristics that creatures living in the patch should have. Creatures without this are susceptible to patch-specific infectious diseases. Now the disease \( D_j \) is characterized by the following four items.

\[ D_j = \{ \text{stress vector } d_j, \beta_j, \gamma_j, e_{d,j} \}. \]  \hspace{1cm} (4)
\( \beta_j, \gamma_j \) is the probability of infection and recovery rate when contacting an individual infected with \( D_j \). \( e_{d,j} \) is the extra energy consumed during infection. Stress vector \( d_j \) is equivalent to resistance to this disease, and if an individual has a resource vector similar to this vector, the probability of infection will be low as the patch has the characteristics sought. On the other hand, individuals with resource vectors different from stress vector \( d_j \) tend to be infected. The probability that creatures \( c_i \) will now infect \( D_j \) is

\[
\frac{1 - r_i \cdot d_j}{2}
\]

(5)

Fig. 6 illustrates this relations among \( r_i, d_j \).

The ambiguity of the gene is expressed by the relation between the stress vector of this disease and the resource vector of the agent.

2.6. Infection and healing of disease

When infected, it consumes \( e_d \) extra energy per unit step. Also it cures with probability \( \gamma \) per unit time. On the other hand, creatures living in the same patch are contacted with everyone each time, and if they come in contact with sick creatures that creature may become infected diseases. The probability of creatures \( i \) being infected is

\[
\frac{1 - r_i \cdot d}{2}.
\]

(6)

The \( d \) is a stress vector of diseases infected by some other creature. However, for the sake of simplicity, it is assumed that a creature will not infect multiple diseases at the same time.

3. Computer simulation

Three experiments are conducted below. First of all, we verify whether creatures can adapt if all the patches have the same endemic disease. Next, we examine the case where
endemic disease differs locally. Finally, we examine the case where different infectious diseases occur for each patch according to the achievement degree of the task. In the all cases, we use two kinds of agents: creatures that do not migrate in case of disease (H type) and creatures that migrate even with disease (N type).

We expect the first scenario to show the capability of adaptation of our agents. We suppose that the second scenario represents a static environment where agents have to adapt their naive disease corresponding to their task. The third example supposes a dynamic environment similar to the leaf caring ant and its guard ant.

3.1. Adaptation of creatures for single stress vector

Here we show the ability of creatures to adapt to the environment. The role of agent required corresponds to the stress vector of each patch, and it corresponds to adaptation that the resources of creatures almost agree with this. In this first experiment, all patches have the same stress vector.

First 80 patches connected in a lattice pattern of $10 \times 8$ were prepared and the stress vector of all patches was set to $(x, y) = (0, 1)$. $\alpha = 0.1, \beta = 0, e_c = 0.1, C_i = 0.1, \beta_s = 0.01, \gamma_s = 0.1, e_d = 0.5$. 2000 creatures were randomly deployed to the patches in the initial stage and tried 10000 steps.

In starting all the experiments below, the initial value of the initial strength of the creature is a uniform random number of $[0, 1]$, and the resource is an angle of $[-2\pi, 2\pi]$ It was generated with a uniform random number.

The agent simulation is executed by Processing 2.2.1. The interface of this simulation tool is shown by Fig. 7. The map F shows the number of each creature of the $10 \times 8$ patches in the size of a circle. The G represents its cumulative probability density distribution. The H represents the time progress graph of the average number of creatures with inhabited patches and it turned out that 240.2 creatures survived per patch.

Fig. 8. The case when the stress vector is changed to $(x, y) = (0, -1)$
The graph E is the average strength of the creature, which is 0.5 at the initial value, whereas it is found that it increases as the trial progresses. The graph A is the number of creatures that moved, which shows that an average of 17.5 (=1400/80) creatures per patch are moving to a neighboring patch every step. The graph B is the number of creatures in being infected. There are 61 infected and 4 recovered at the end. The graph C is the average of the absolute values of the difference between the stress vector and the resource vector of the creatures of the patch, which is 0.5 in the initial value and 0.019 in the final state. The graph D indicates the angle between the average of resource vectors for each patch and the x axis. The horizontal axis is a patch. This shows resource vectors of almost all patch are about 90 degrees. From the results of C and D, we can see that creatures are adapting to the environment and acquiring appropriate functions.

Next, the same experiment was conducted by substituting stress vector for another. Fig. 8 shows C, D when the stress vector of all patches is (x, y) = (0, -1). In this case as well, the creatures did not have the resources suitable for their patches at the initial stage, but at the end, the average difference was 0.02, which turned out to be -90 degrees.

From these experiments it was found that if all the creatures are required to have the same function, the function can be acquired.

### 3.2. Typical adaptation examples when there are endemic diseases different from region to region

Next, experiments were conducted on cases where different functions were required locally. Fig. 9 (s) shows the patch setting. Here, the stress vector of 40 patches (1 ≤ x ≤ 5) in half of the patch is (x, y) = (0, 1), the stress vector of the other half patch is (x, y) = (0, -1), the experiment was carried out with the same setting as in the experiment described above. In this case, creatures that require 3 ≤ x ≤ 5 patch and creators that need 6 ≤ x ≤ 10 patch must acquire different functions and different adaptation
is required. Ideally a stepwise (D) like that shown in Fig. 9 (I) should be obtained when creatures of a patch succeed in adaptation to their environment.

The simulation results are summarized in Fig. 10, and the vertical axis shows the average of the absolute values of the difference between the stress vector and the resource vector $\bar{Er} = \text{average}(|d - r|)$. The horizontal axis is the migration rate $C$. H-type creature with marker graph, and N-type creature adaptation degree in graph without marker. Roughly speaking, we found that if $\bar{Er} < 0.2$, creatures can adapt to the environment and gains different functions locally similar to Fig. 9 (I). On the other hand, when $\bar{Er} > 0.3$, it turns out that resource vectors are almost random as shown in Fig. 10 upper left figure. In this experiment, we used infectious diseases $(\beta, \gamma) = \{(0.01, 0.1), (0.01, 0.01), (0.1, 0.1)\}$, which have three different characteristics. In the case of H type creatures, if the migration rate is $C < 0.05$, we can see that in this parameter range creatures are adaptable to the environment. On the other hand, in the case of N-type creatures, it is found that it cannot adapt unless it is $C < 0.0001$. From this result, it supposes that diseases could be transmitted to creatures already adapted their own patches. We think that immigrating to another patch while suffering from the disease makes creatures as a whole difficult to adapt.

### 3.3. When the infectious diseases that occur depending on the achievement rate of the task are different

Next, we simulated a case where infectious diseases occur according to the degree of achievement of the task for each patch. There is no geographically predetermined endemic disease. In leaf cutter ants, carrying leaves to the nest is a very important task in obtaining food. Therefore, if all the ants carry leaves it is expected that the
efficiency will be the maximum, but in this case, the ants cannot protect themselves from parasitic fly and parasitic flies grow in the ants’ nest. In this case, if the amount of leaves carried into the nest is small, problems of food shortage occur, and if there are too many, there is a problem that the number of members decreases if parasitoid flies occur. This may be considered as a case where the disease occurs according to the degree of accomplishment of the task.

So, here we suppose that there are multiple diseases (D1 and D2), disease D1 ((x, y) = (0, -1)) occurs if the achievement rate of task1 is low and the achievement rate of task1 is If it is too high, a disease D2 ((x, y) = (1, 0)) occurs. Conditions of disease occurrence are

\[
\text{(Rule 1)} \quad D_1 \text{ occurs when } (r \cdot D_1) < 0.5 \\
\text{(Rule 2)} \quad D_2 \text{ occurs when } (r \cdot D_1) > 0.8.
\]

The both infection rate and cure rate are equal, and \( \beta = 0.1, \gamma = 0.01 \), respectively.

Examples of results of the simulation (H type) and (N type) are shown in Fig. 11 and Fig. 13, respectively. In any of the experiments, the resource vector of the creature is random in the initial state. Fig. 12 illustrates the transition of behavior of creatures (H). This figure shows the number of infected individuals of each disease and the distribution of resource vectors for each patch at four time points, t = 100, 300, 1000, and 2500. Since the resource vector of the creature is random in the initial state, infectious disease D1 (occurrence condition rule 7) occurs in all patches (t = 100). Infections to D1 occurred in each patch and creatures resistant to D1 increased (t = 300). At this time, a patch with too high resistance to D1 appeared, accompanied by the occurrence of epidemic disease D2 it was. Increasing number of patches whose tolerance to D1 is increasing
too much, and with this the number of infected people to D2 increases \((t = 1000)\), after that, each patch will continue to adapt to either D1 or D2 epidemic diseases \((t = 2500)\). Sometimes, transitions from D1 to D2 and vice versa can be seen but none of the intermediate resource vectors were kept for a long time. On the other hand, in case of N type, resistance to D1 is obtained, but there is no patch adapted to D2 after that. Contagious diseases D2 has been infected with many continuously.

On the assumption that there is a genetic association between epidemic diseases
and tasks, simulation was conducted in cases where different geographically different functions are required and different functions are required depending on the achievement degree of the task. Based on the above experimental results, it was found that there were cases where sub-species occurred depending on the environment and it was possible to maintain this for a long time if not immigrated when the individual is in sick.

Finally, we investigated the relationship between the migration rate of H type creatures \( C \) and their functional differentiation capability. While repeating experiments on H-type creatures, we found some relation between patches adapting to D2 and the migration rate \( C \). So, behavior with \( C = 0.75, 0.0 \) have been simulated repeatedly and the relation between the infection rate \( \beta_{D2} \) and the ratio of patches specialized for D2 is illustrated in Fig. 14 and Fig. 15, respectively. In the case of \( C = 0.75 \), as the infection rate of D2 increases, the number of patches adapting to D2 increases, whereas in the case of \( C = 0.0 \) it is hardly affected by the infection rate of D2. In addition, the number of patches dedicated to D2 is relatively small. From the above, it can be expected that functional differentiation is difficult to proceed if there is no migration at all.

Fig. 14. Rate of patches specialized to D2 when migration rate \( C = 0.75 \).
4. Conclusion

In this paper, we have constructed a simulator for investigating the influence of infectious diseases concerning the division of labor and functional differentiation. Creatures live in finely divided residential environments, patches, and they get food acquisition and reproduction in patch units, but they can migrate to good patches. Experiments using computer simulation were performed, and the differentiation of functions could be reproduced. Especially, we found that immigration of creatures greatly affects adaptation and function differentiation. Emigration while suffering from the disease disturbs the adaptation in other patches and as a result could be expected to make adaptation more difficult. On the other hand, in systems that do not emigrate at all, it could be expected that the differentiation of functions would be difficult to progress.

Acknowledgment

This work was supported by JSPS KAKENHI Grant Number JP15K00433.

References

Masao Kubo is Associate Professor of Department of Computer Science at National Defense Academy in Japan. He graduated from the precision engineering department, Hokkaido University, in 1991. He received his Ph.D. degree in Computer Science from the Hokkaido University in 1996 (multi-agent system). He had been the research assistant of the chaotic engineering Lab, Hokkaido university. He was a visiting research fellow of Intelligent Autonomous Lab, university of the west of England (2005). He is the associate professor of information system lab, Dep. of Computer Science, National Defense Academy, Japan. His research interest is Multi agent system.

Saori Iwanaga is Professor of Department of Maritime Safety Technology at Japan Coast Guard Academy (JCGA) since 2012. She received her B.E. degree in applied chemistry engineering from Utsunomiya University, Japan in 1994 and her M.S. and her Ph.D. degree in computer science from National Defense Academy, Japan, in 2001 and 2004, respectively. She has worked at JCGA since 2006. She is interested in complex theory, evolutionary games. She is a member of Information Processing Society of Japan and Japan Society for Safety Engineering.

Hiroshi Sato is Associate Professor of Department of Computer Science at National Defense Academy in Japan. He was previously Research Associate at Department of Mathematics and Information Sciences at Osaka Prefecture University in Japan. He holds the degrees of Physics from Keio University in Japan, and Master and Doctor of Engineering from Tokyo Institute of Technology in Japan. His research interests include agent-based simulation, evolutionary computation, and artificial intelligence. He is a member of Japanese Society for Artificial Intelligence, and Society for Economic Science with Heterogeneous Interacting Agents. He is an editor of IEICE transactions on Fundamentals of Electronics, Communications and Computer Sciences.

MÔ PHỎNG TÁC TỬ CÁC TÁC ĐỘNG CHỨC NĂNG CỦA BỆNH TRUYỀN NHỊỆM LIÊN QUAN ĐẾN TÌNH NHẬP NHẰNG CỦA GIEN

Tóm tắt
Trong bài báo này, các bệnh truyền nhiễm được sử dụng là nhân tố đóng góp vào "phân chia lao động" và "phân biệt chức năng". Chúng tôi đề xuất mô phỏng tác tử với tập trung vào khả năng tái sinh sản. Bằng cách mô phỏng, chúng tôi nhận thấy khi gien có tính nhập nhằng và có duy nhất một bệnh truyền nhiễm gắn với mỗi tác vụ và đồng thời không có nhiều bệnh khác, sự xuất hiện của một nhóm con có thể dẫn đến khả năng tái sinh sản.