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An Analysis of Organizing Process of R&D Projects:
Multi-agent Simulation and Case Study

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Abstract: The purpose of this paper is to analyze the organizing process of research projects, which affect the performance of research and development (R&D) crucially, by using agent-based simulation and case study. We develop a multi-agent simulation model that contains two types of R&D style: Japanese pharmaceutical companies' style and Merck's style. Simulation result proves that the senior managers observed in Merck possessing strong communication capabilities, whom we call "HWCM (Heavy-Weight Communication Manager)" in this paper, enhance initial start-up of projects. Furthermore, we study the case of Merck again and try to show the effect of HWCM on high R&D performance of Merck.

Keywords: R&D, multi-agent simulation, HWCM

1. Introduction

This paper employs multi-agent simulation and case study for the purpose of analyzing the organizing process of research projects, which affect the performance of research and development (R&D) crucially. Multi-agent simulation is a relatively new

method, which came to gather attention in the 1990s, yet has already been applied in various fields of studies (e.g., Epstein & Axtell, 1996; Thomas & Seibel, 1999, 2000). From existing studies up to this date, we may say that there are two types of opposite approaches in multi-agent simulation method.

(a) Build a relatively abstract model, such as artificial society, and extract various findings from there

(b) Build a model on the most specific individual example and use the model literally for calculation

For instance, Epstein and Axtell (1996) is a typical example of approach (a); they built an artificial society model called Sugarscape where food (sugar) is placed here and there for the agents (ants) to eat. They analyzed the model and extracted various implications as mating, culture, war, and epidemic. On the other hand, as an example of approach (b), Thomas and Seibel (1999, 2000) have successfully improved cargo operations at Southwest Airlines by putting the multi-agent simulation method into practice.

While the two approaches are thus quite opposite, this paper will follow approach (a). We build a multi-agent model from different R&D styles at Japanese pharmaceutical companies and one of the world's largest pharmaceutical company, Merck. We further go through the different organizational performances which the different R&D styles lead to.

In conclusion, a senior manager as HWCM (Heavy-Weight Communication Manager) at Merck who have strong communication capability enhances start-up speed of projects. Based on simulation results, this paper compares again the cases of Merck and Japanese pharmaceutical companies to confirm the possibilities that HWCM practically contributes to the high R&D performances at Merck.

2. Communication Competition Model

2.1. Pharmaceutical R&D Process and Heavy-Weight Communication Manager

Pharmaceutical industry in general is said to be determined much of their corporate performances by R&D achievements. Placing a new innovative drug on the market will yield enormous profit, on the other hand pharmaceutical product development costs nearly 20 years of time and 10 to 20 billion yen; 30 to 50 billion yen including failed projects. Therefore, at pharmaceutical companies, release of a new drug has become of great managerial goal (Kuwashima & Takahashi, 2001).

In typical cases at Japanese pharmaceutical companies, first a research theme is set then chemists and biologists start working in development teams of one to several personnel. Ideas are brought up within these small teams and if a potential chemical compound is discovered, chemists and biologists are added to examine various derivatives synthesized from the leading compound to attain stronger activity. Accordingly, research at individual level is launched as an official project.

As an example, we would like to investigate a

R&D case of a carbapenem antibiotic Carbenin; nonproprietary name panipenem (Kuwashima, 1998). Carbenin has been released from Sankyo in 1993 as the first domestic carbapanem antibiotic product, which is one of the company's core products selling 12.3 billion yen in 2000. Research which lead to Carbenin started in 1977 where two themes were set simultaneously: search for carbapenem compound and synthesis of related penem compound. Initially though, according to differences in approaches, there were in total four research teams, one carbapenem team and three penem teams. Since 1978, various penem compounds were synthesized yet none proved effective displaying acute toxicity or insufficient *in vivo* activity. On the other hand, carbapenem showed stronger antibacterial activity. At this, penem research teams shifted to carbapenem research and applied penem compound synthesis methods to carbapenem. Various derivatives were synthesized such as pyrrolidine derivative and other cyclic amine derivatives. In 1981, panipenem, the sought after substance, has been discovered. Thereafter, yet many problems stood before them from pre-clinical test to actual market release, we would like to point out two aspects in the R&D process hitherto.

(1) At the initial stage, four teams of different approaches existed under two research themes.

(2) Since penem research team shifted to carbapenem research, synthesis methods from penem teams were brought to the joint research team.

In such major Japanese pharmaceutical companies as to rank in the top ten, generally various research themes are studied at the laboratories. In addition, multiple research teams are organized for a single theme according to different approaches. Typically, when a certain theme or approach turns out to be promising, researchers on other themes and approaches join the hopeful one, thus an official project is launched. Relocation of researchers from theme or approach is basically agreed upon talks between researchers and locale supervisor of general manager rank.

In complete contrast, when we turn our eyes from the typical project start-up process in Japan to that of overseas companies as Merck in US, we would notice an aspect outstandingly dynamic; that is the presence of senior managers with strong communication capability and their commitment to corporate performance. At Merck, ideas from research centers worldwide are gathered and launched as official projects. During the process, managers at the research centers play a vital role. In many cases, these managers are world authorities on a specific field of illness, who is a medical doctor at the same time a researcher of medicine. For example, at Banyu Pharmaceutical in Japan, which is affiliated to Merck, the head of Tsukuba Research Institute is a world authority on cancer, who has been picked out from a national laboratory. Merck lay emphasis that these managers play a crucial role upon project launch.

This paper aims to examine what benefit is brought to R&D process, in particular, organizing

process of research projects, when a senior manager with strong communication capability (HWCM: Heavy-Weight Communication Manager) is in presence. We intend to utilize multi-agent simulation method for our purpose.

2.2. Outline of Model

As we can see from the Carbenin case in section 2.1, "ideas" are significant at the organizing stage of pharmaceutical research projects. Therefore, we will build an multi-agent simulation model assuming that the organizing process of a research project is a "cluster formation process by agents (researchers) who possess ideas."

First, we picture the R&D process in the Carbenin case at a Japanese pharmaceutical company. For simplification, we assume that there were two themes in presence, Red and Blue, and researchers are initially involved in either. Next, as it is hard to give external criteria to the potential of themes or approaches, we simply grant that the more the ideas are in presence, the more promising the theme or approach is. Then we hypothesize that

(1) agents possess ideas and move towards positions where they are more able to communicate with other ideas and agents possessing ideas;

(2) when multiple clusters (research teams) exist, agents choose a cluster where they are able to communicate with more ideas.

We thus describe the rules by which agents form clusters seeking more promising research themes and approaches. We shall depict the ways that agents flow into promising clusters, thus effecting research themes and approaches to merge.

Our interest is to see what happens when HWCM as found in Merck is introduced to above Japanese company model. How are the start-up processes in Red and Blue research projects influenced by this? In the simulation model, "ideas" are in a sense treated as "bait" for which agents compete, thus, hereafter we shall call this model Communication Competition Model, for short, ComCom Model. Below, we will describe the model by specific rules presuming that we use KK-Multi Agent Simulator for multi-agent simulation.

(1) Path Length: L

Path length is defined as following 1 to 3 and determined as in the example of Figure 1.

Figure 1. Determination of Path Length L
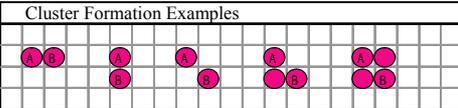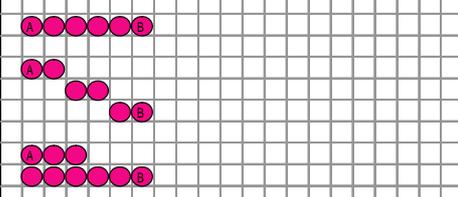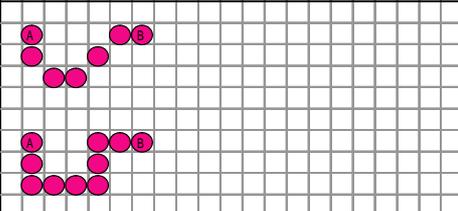
1. A path is formed between agents A and B when A and B are the same color and all agents aligned in between A and B are also the same color. A and B are able to communicate.

2. Path length L is determined by the number of agents between agents A and B. However, agent B is counted as well, thus when A and B is next to each other, it is L=1.

3. If multiple choices of paths exist, the shortest should be determined as path length L.

(2) Amount of Effective Idea

We define the amount of an agent's effective idea as the sum of the total number of same colored agents whom the agent is able to communicate with weighted by 1/L. A typical calculation is shown in Figure 2(A). It is weighted by 1/L because we assume that where path length L is greater, the impact of a idea weakens and communication of the idea takes time.

As shown in Figure 2(A), agents belonging to a same cluster have different amounts of effective idea according to where the agent stands within the cluster. In Figure 2(A), the amount of effective idea for A is larger than B, and that for C is larger than A. In general, agents posted nearer the center of the cluster have larger amount of effective idea. We shall describe as follows the rules of ComCom Model by the amount of effective idea.

1. An agent moves towards larger amount of effective idea.

2. An agent moves the distance of either 0 or 1 in one period.

3. An agent searches other agents within distance 1. In other words, an agent cannot perceive agents beyond distance 2.

4. An agent in contact with a cluster of other colored agents will switch sides (i.e., change color) when by doing so the amount of effective
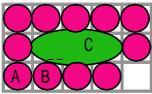
Figure 2. Calculation of the Amount of Effective Idea

(A) Determining Amount of Effective Idea
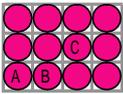
	calculation of corresponding number of agents and amount of effective idea					
	A		B		C	
L=1	3	3×1=3.0	5	5×1=5.0	8	8×1=8.0
L=2	5	5×(1/2)=2.5	6	6×(1/2)=3.0	3	3×(1/2)=1.5
L=3	3	3×(1/3)=1.0				
total	11	6.5	11	8.0	11	9.5

(B) Change in Amount of Effective Idea after Big Agent Input

	calculation of corresponding number of agents and amount of effective idea			
	A		B	
L=1	3	3×1=3.0	4	4×1=4.0
L=2	8	8×(1/2)=4.0	7	7×(1/2)=3.5
L=3				
total	11	7.0	11	7.5

idea of the agent becomes larger.

Under above rule, an agent will prefer belonging to a cluster, and possibly a larger cluster, than staying alone.

(3) Big Agent

Big agent is a concept created with HWCM at Merck in mind, who is literally a "big" agent capable to contact and communicate directly with greater number of agents. In particular, for example, in Figure 2(A), suppose agent C has become the size of three cells. Given that the number of agents composing a cluster does not alter, it should become as in Figure 2(B). Accordingly, 1) a big agent has more surfaces potentially in contact with other agents, and 2) however big the agent is, path length is still measured as 1. Therefore, as in Figure 2(B) the amount of effective idea changes.

Still, casting in a big agent does not necessarily mean that all other agents in the cluster will gain more amount of effective idea as well. In fact, comparing Figure 2(A) and Figure 2(B), we can see that the amount of effective idea of agent A has increased from 6.5 to 7.0, on the other hand, the amount of effective idea of agent B has dropped from 8.0 to 7.5.

(4) Index

In our model, the following three indexes are indicated in numeric value and map.

    1. Activity rate: This shows the number of agents that move in each period. The activity rate for period $t+1$ represents the amount of activity which occurred between the state in the map of time period t and $t+1$.

    2. Total amount of effective idea: This is the total sum of the amount of effective idea of all agents belonging to the same cluster. From the lattice model in Figure 1, we treat agents joint at a corner of a cluster as members of the cluster as well.

    3. Mean cluster scale: The number of agents consisting a cluster is called cluster scale. Mean cluster scale is attained by dividing the total number of agents by the number of clusters.

2.3. Simulation Results

2.3.1. Competition between Research Themes for Agents

In the present model, we presumed that every agent is involved in either Red or Blue research theme. Here, for the purpose of investigating the effect of big agents, we would input big agents to theme Red and see if this will avail theme Red in acquiring more agents.

In practice, we compare the following two cases.

Case 1: ten L=1 Red agents; and ten L=1 Blue agents.

Case 2: eight L=1 Red agents and two L=3 Red agents, in total ten Red agents; and ten L=1 Blue agents.

Cluster formation is significantly influenced by the initial posting of agents, therefore prior to a simulation we specified a random number seed value

for KK-MAS execution configuration. Particularly, in each case, random number seed value takes 1 to 30, increased by 1 in 30 trial runs. "Mean cluster scale" and "total amount of effective idea" are kept record up to period 300 in each trial run.

First we compare the results at period 300 in the standard Case 1. The average number of agents in theme Red was 10.07 while average number of agents in theme Blue was 9.93, thus in both cases

result was approximately 10. Next we proceed to Case 2 where big agents were input in theme Red alone, replacing two regular agents with two big agents. In result, we could not see any advantage gained by theme Red against Blue in gathering agents. Comparing results at period 300, the average number of Red theme agents is reduced to 7.70 from 10.07 in Case 1. Mean difference is not significant (t =1.633; p =0.108), nevertheless, theme Red proves

Figure 3. Average Mean Cluster Scale
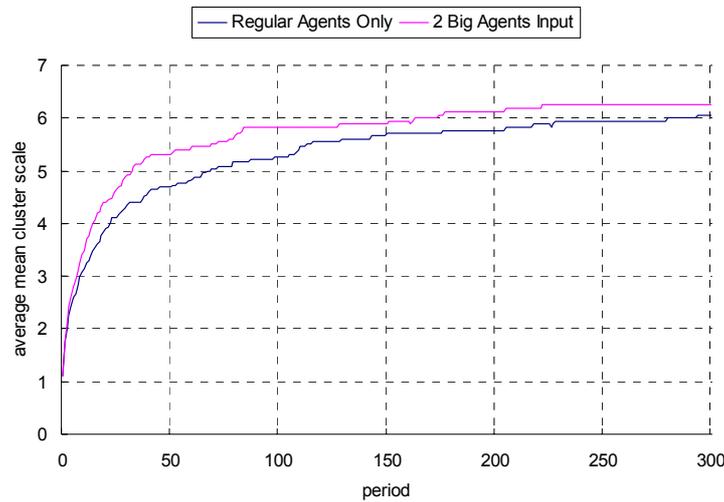
Figure 4. Average Total Amount of Effective Idea

15
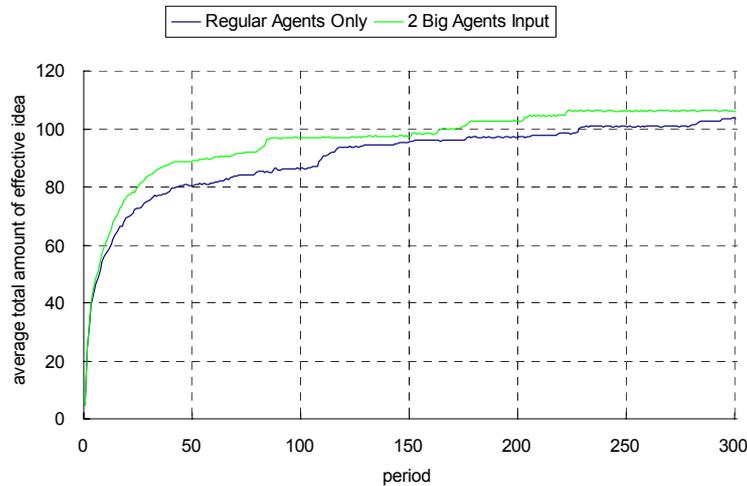
weaker. From observation of simulation process, it revealed that the reason for this was that the big agents have switched to theme Blue at an early stage. Thus, big agents choose between themes as well as regular agents. In other words, the theme big agents are assigned to at an initial stage is not critical when research themes compete to acquire more agents, in other words, when they compete for research resources.

2.3.2. Mean Cluster Scale and Total Amount of Effective Idea

Based on above finding, next we shall give the statistics on cluster scale and total amount of effective idea on the whole disregarding themes Red and Blue. Figure 3 shows the average mean cluster scale for 30 trial runs concerning Case 1 and Case 2. Accordingly, Case 2 where big agents are cast in, reveals a tendency to experience a growth of mean cluster scale at an earlier stage. Nevertheless, at period 300, mean cluster scales are slightly more than 6 in either case, thus the gap is narrowed. Therefore, big agents do not commit to the size of clusters but to the earlier formation of clusters.

Likewise, in Figure 4, total amount of effective idea for each period in 30 trial runs are averaged out. As the figure indicates, total amount of effective idea increases at an earlier stage in Case 2 where big agents are cast in, similar to the analysis of mean cluster scale. However, at period 300, total amount of effective idea in either case are slightly more than 100; again the gap between Case 1 and Case 2 are

narrowed.

In sum, 1) input of big agents as a whole enhance the formation of clusters and total amount of effective idea at an earlier stage. 2) Though speed is enhanced, neither mean cluster scale nor total amount of effective idea take lager values in the end.

3. HWCM in Practice and R&D Performances

3.1. Case Study: Merck and Japanese Companies

As have been described, the effect of big agent (HWCM)'s presence were proved in the simulation, that is, initial rise in (1) number of cluster formation, and (2) amount of effective idea. What kind of observation can we make from this simulation result in actual R&D process? Here, based on simulation results, we shall compare again the case at Merck and Japanese pharmaceutical companies.

First, we will go over result (1). As we have briefed in 2.1, at Merck, HWCM, who is a medical doctor knowledgeable of biological mechanism at the same time engaging in pharmaceutical studies, play a vital role in R&D process. As an example, we would like to investigate the case of an anti-cancer drug which has been at initial clinical testing stage at West Point in 1999. When biologists and chemists at West Point were discussing the improvement of existing drugs, a researcher invited from National Cancer Institute reviewed the idea of an anti-cancer drug among their discussions. Then a cancer expert invited to Tsukuba Research Institute of Banyu

Pharmaceutical, one of Merck affiliates, at once participated in strategic councils and research reviews at Merck. This lead to collaborative cancer studies between Banyu Tsukuba Research Institute and West Point. Cluster formation was thus swift and HWCM acted much alike big agents as in a simulation model. We can see that the presence of HWCM contributes significantly to such quick cluster formation. In fact, a person in charge of Worldwide Strategic & Capital Planning at Merck remarked that "the secret of Merck's strength lie in the fact that people who are both medical doctor and pharmaceutical researcher (HWCM) held responsible posts for the past 25 years." Being familiar with both human biological mechanism (medical science) and pharmaceutical drugs (pharmaceutical science) will allow, for example, to enhance multilingual communication (Clark & Fujimoto, 1991) between two different groups of knowledge system or influence review competence of samples and projects. This presumably contributes to earlier formation of clusters. On the contrary, when compared to cases in Europe and US, Japanese pharmaceutical companies have much few numbers of medical doctors, and such senior manager as HWCM in Merck practically do not seem to exist.

Next, we will consider Result (2). We would like to investigate whether in fact at Merck amount of ideas build up as quickly as in the simulation result. To prove this, we need to know that at Merck, in comparison with Japanese pharmaceutical companies, there are more ideas in the upstream stage of R&D process, that is, there are more different and varying ideas which become the sources of new drugs. Concerning this issue, there is collateral evidence. From the latter half of 1980's to the 1990's, a new technology called HTS (High Throughput Screening) became popular for reviewing various samples of new drugs at high velocities. HTS review large quantities of samples automatically at one time by processing a microplate with numerous (generally 96) holes. It is frequently used together as a set with a massive synthesis technology called CC (Combinatorial Chemistry). Lately, by far powerful UTS (Ultra Throughput Screening) have appeared, which claims capable of reviewing 3000 samples at a time and 500 thousand samples in a week. The most crucial key to success utilizing such high-velocity screening machine is to provide massive amounts of samples of various structures. Theoretically, given that as long as there are ideas infinite numbers of samples can be synthesized with CC, the crucial point is to have distinct and various ideas sufficient to run the machine at capacity. In regard of this fact, at leading Japanese pharmaceutical companies HTS operates far below their capacity, though almost 80% of them introduce HTS (Nihon Seiyaku Kogyo Kyokai, 1998). In contrast, UTS is open for 24 hours and operates most of the time at Merck West Point. Can we not say from this example that quantity and quality of ideas differ between Merck and Japanese firms?

3.2. Influence on R&D Performances

From above discussion, it is confirmed by both simulation and case analysis that presumably the presence of HWCM enhances the speed of initial cluster formation and building up of ideas. Then, we would like to investigate how the actual R&D performances at pharmaceutical companies are influenced by the two "speeds" achieved by the presence of HWCM. In general, R&D speed (development lead time) is considered to be extremely crucial to the competitive advantage of a firm (Clark & Fujimoto, 1991). Speedier R&D result in shorter time required for a project, thus more projects could be undertaken in a given period. In pharmaceutical companies as well, assuming that success rate is fixed, a firm which has gained R&D speed should be able to develop more new drugs.

Moreover, in the case of pharmaceutical industry, when two companies of different R&D-product development speed compete, there would be a wider gap in the number of new drug release between the two than the number of new drug development successes. This is because in pharmaceutical industry, "first-mover advantage" is particularly strong. There is said to be no market for latecomers who could not rank within the first few in a particular area of medicinal properties. Therefore, release is canceled when a costly project turns out be almost a success in product development itself, nevertheless, a good many number of competing products already exist in the market. Development speed decisively effects the number of new drug release.

Actually, Merck with HWCM system shows extraordinary performance in placing new products on the market. Some of Japanese top ten pharmaceutical companies seem to have none or few self-developed product in the past ten years. In contrast, Merck released Mevacor (lipid-lowering agent, released 1983), Vasotec (antihypertensive drug, released 1986), Pepcid (anti-gastric ulcer drug, released 1986), Zocor (lipid-lowering agent, released 1992), and Cozaar (antihypertensive drug, released 1998), naming merely the big hits selling over one hundred million dollars a year. As a result, Merck kept a profit increase rate over 10% per year throughout the 1990s, and in 2000, sales reached approximately 39 billion dollars. In the pharmaceutical industry where M&A mammoths keep growing, Merck walks its unique path while maintaining world best standing.

4. Conclusion

This paper built multi-agent simulation model from the different R&D styles at Japanese pharmaceutical companies and one of the world largest pharmaceutical company, Merck. We reviewed how the differences influence the R&D processes and performances. Simulation result showed that a senior manager as HWCM in Merck, who has strong communication capabilities, shorten organizing time of R&D projects. Furthermore, we compared again Merck and Japanese pharmaceutical companies by case analysis to prove the possibility that HWCM

does in fact contribute to strong R&D performances of Merck.

The reason that our study conducted case analysis in addition to simulation analysis was to provide complementary investigation to the result drawn from the "rather abstract simulation model (Section 1, Approach (a))"; that is, to see how the influences of HWCM on organizing processes are observed in actual pharmaceutical product development. While typically such products as automobiles are produced under highly successful routine R&D and product development, pharmaceutical product R&D projects, which is the object of our analysis, operates under such sparing success rate of thousands to ten thousands to one: Projects literally emerge from a single idea. When we analyze such cases as this one, empirical measurement and analysis of a certain variable (in this paper the presence of HWCM), given that other conditions are fixed, is unreliable. We believe that combining simulation and case analysis, as we have done in this paper, proves as a useful research approach when analyzing an innovation of low success rate.

Besides, it is possible to regard this kind of research method, combining simulation and case analysis, as a stepping stone from simulation to further empirical study. Our procedure was to build a simulation model inspired by the case at Merck, then based on the simulation result, go back to the case to analyze the HWCM effect. From the results of this paper, our future object is to put more emphasis on case analysis; We aim to measure HWCM by manipulated profiles and behavioral patterns along with more systematic analysis of the relation between HWCM and R&D performances.

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