International Conference on Global Infectious Diseases and Clinical Vaccines（ICGDC-2025）

An Agent-Based Model of Infectious Diseases that Incorporate the Roles of immune Cells and Antibodies : An Application of Mechanism-Oriented Agent-Based Model

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Agenda

1. Mechanism-Oriented Agent-Based Modeling

・**Social requirements for understanding the causal mechanism.**

・**Principle and validation concept of mechanism-oriented ABM that enable rigorous validation and scientific understanding of causal mechanisms in social phenomena.**

・**Procedures to construct qualitative and quantitative models.**

・ **Applications to economic and other social phenomena.**

2. An Agent-Based Model of Infectious Diseases that Incorporates the Roles of Immune Cells and Antibodies

2.1 Introduction

2.2 Model Overview

2.3 Results

・**Validation** ・**Mechanisms of pandemic spread and convergence**

・**The role of fever as a critical factor in pandemic convergence**

2.4 Conclusions

Mechanism-Oriented Agent-Based Modeling (ABM)

Social problems requires the knowledge of the causality of social phenomena.

- Many social problems arises from a lack of understanding of causal mechanisms, unlike in natural sciences, leading to unscientific policy decision-making.
- The reason for this is that controlled experiments are hard to be done in social science and traditional methodology could not provide an alternative methodology.

Essential feature of ABM

- ABM is an only methodology that potentially fulfill this requirement because it is a bottom-up modeling approach with heterogeneous agents.

ABM so far developed cannot meet with this requirements.

- However, agent-based models so far reported are mainly abstract models or not fully bottom-up type that introduces macroscopic assumptions.
- As a result, validation is still a serious problem to overcome, and it is believed that there is no universally accepted validation approach.
- Thus, ABM so far developed is not enough to elucidate the causality.

Principles of Mechanism-Oriented Agent-Based Modeling

Since all social phenomena emerge from the actions and interactions of decision-makers (i.e., agents), the fundamental cause of a given social phenomenon lies in the set of behavioral rules, rather than in parameter values .

Therefore, mechanism-oriented agent-based modeling can be categorized into qualitative and quantitative models.

Qualitative Perspective:

The phenomenon results from a set of behavioral rules governing various types of heterogeneous agents.

There exists a particular set of behavioral rules that reproduces the qualitative features of the phenomenon.

Quantitative Perspective:

The phenomenon emerges from behavioral rules combined with numerical values assigned to relevant variables.

There exists a particular set of parameter values in addition to behavioral rules that reproduces the phenomenon quantitatively.

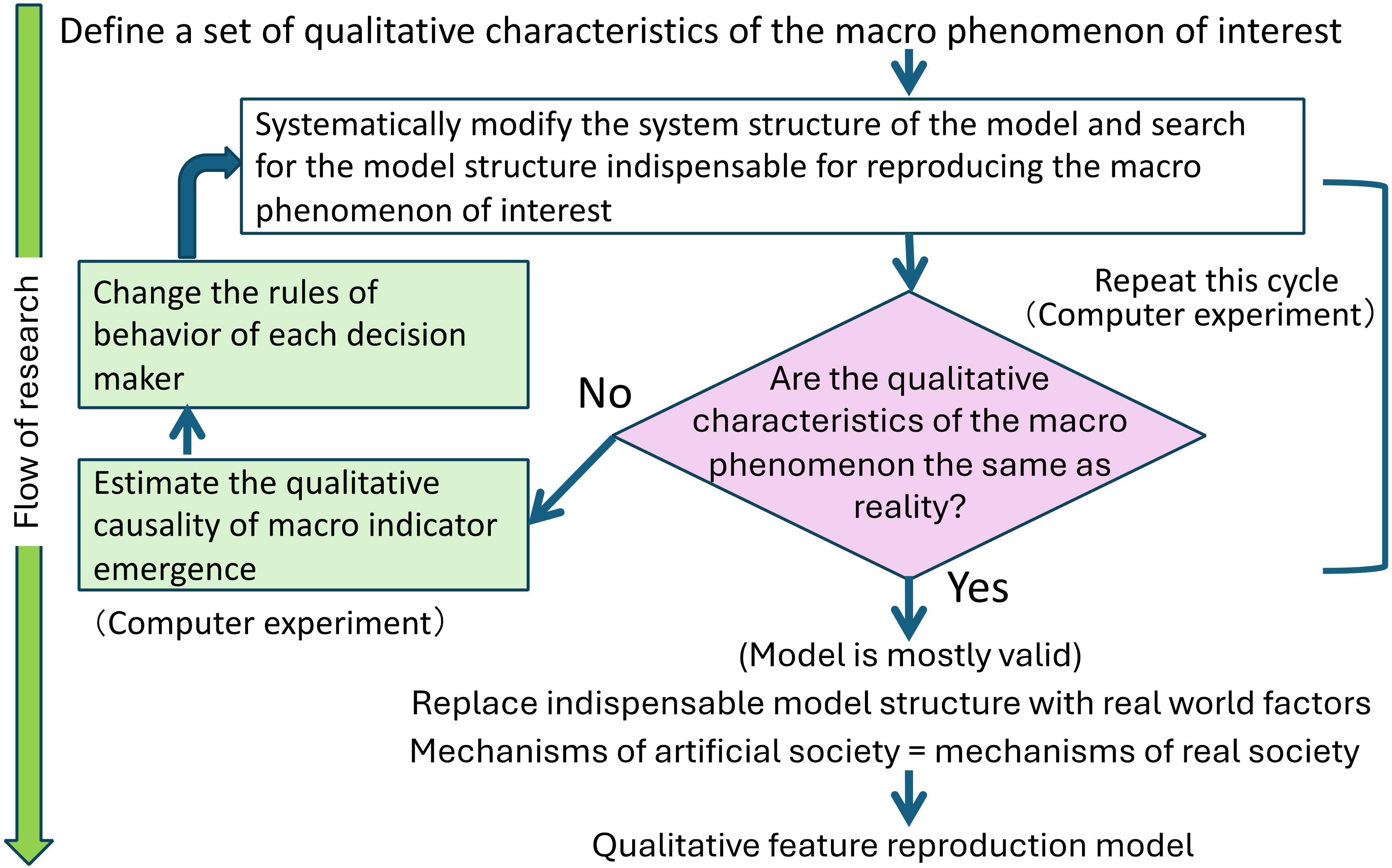
Procedure to construct a qualitatively validated model.

1. **Define the qualitative features** of the given phenomenon.
2. **Assume a set of behavioral rules that infer its causal mechanism, encode them in a program, and run simulations.**
   If the simulation results successfully reproduce the phenomenon's features the assumed set of behavioral rules is validated. Namely, it is an indispensable model structure for the emergence of the phenomenon. If not, refine the rules and repeat the process.
   Thus, we can elucidate an indispensable set of behavioral rules for the emergence of the phenomenon by a series of computer experiments.
3. **Analyze the reason why the set of obtained behavioral rules** is indispensable for the emergence of the phenomenon. Then, we can understand the causal mechanism of the phenomenon. This is feasible within artificial societies where complete data can be available.
4. **Apply the validated causal mechanism** to real-world social dynamics to gain scientific insights into the phenomenon.

This systematic approach allows for a **scientific understanding** of causal mechanisms in social phenomena.

A proposal for the approach of ABM research (Qualitative model building)

Qualitative modeling = causal mechanisms (qualitative level understanding)



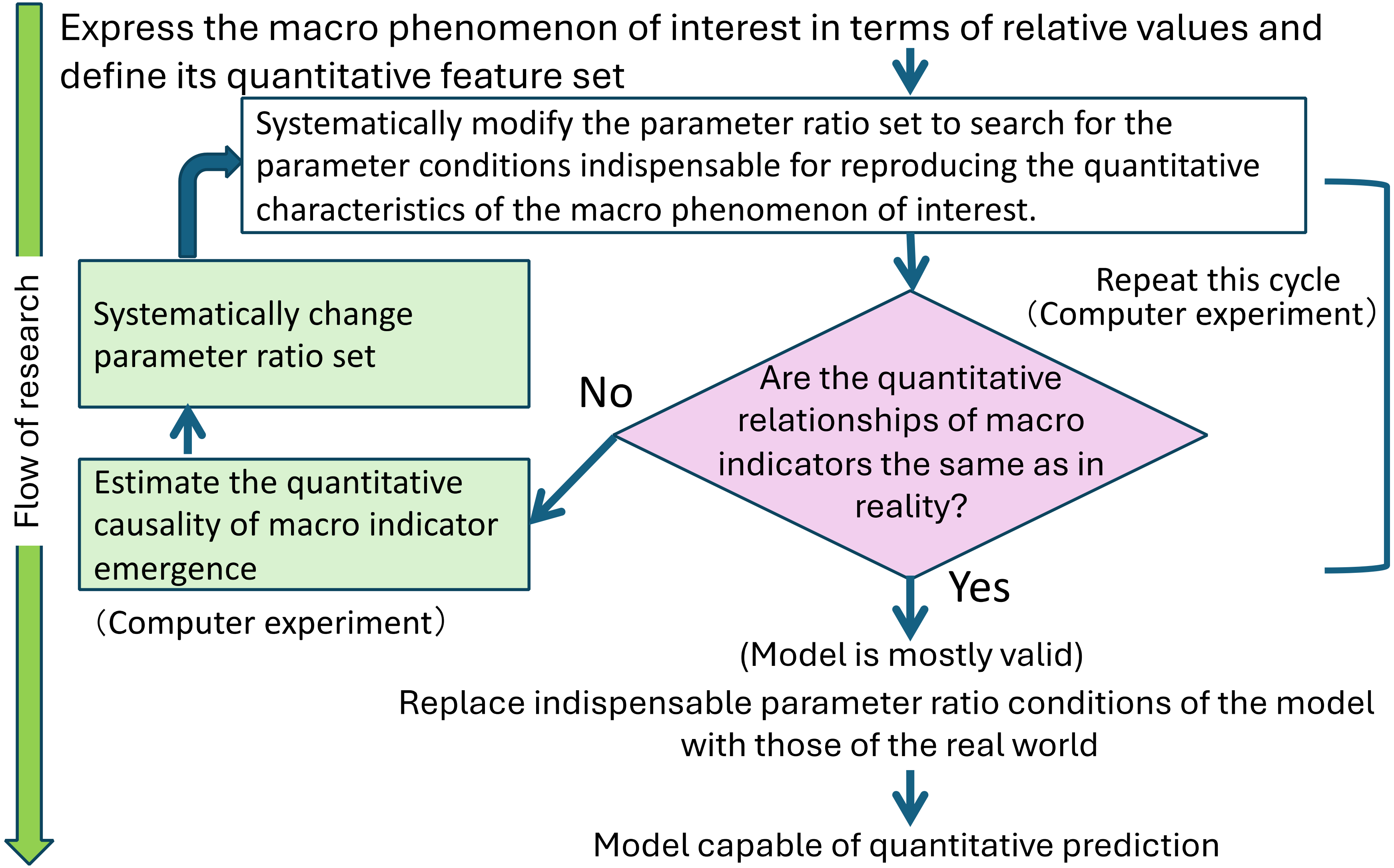
Procedure to construct a **quantitatively validated model(Future challenge)**

1. **Develop a qualitatively validated model** and construct a model that incorporates elucidated set of behavioral rules governing the social phenomenon.
2. **Express key variables in ratio-based forms**, such as non-dimensional variables or values normalized by representative quantities (e.g., total population or total money in the system).
3. **Assume a set of parameter values** for ratio-type variables that are expected to reproduce the quantitative features of the phenomenon.
4. **Implement these parameter values in the program** and run the simulation.
   - If the model **successfully reproduces** the quantitative characteristics of the phenomenon, it qualifies as a validated quantitative model.
   - If not, refine the parameter values and return to Step 3.
5. The **validated set of parameter values and behavioral rules** represent the indispensable model structure for accurately reproducing both **quantitative** and **qualitative** features of the phenomenon.

Using this validated model, we can **forecast** the potential effects of policies or countermeasures aimed at addressing the social issues under study.

A proposal for the approach of ABM resear (**Quantitative model building**)

Build a quantitative forecasting model (understanding at the quantitative level)



Phenomenon for which an indispensable set of behavioral rules has been elucidated.
(Qualitative models so far developed.)

1. Economic phenomenon

- **Price equilibrium**
- **Funds circulation**
- **Business cycles**
- **Effect of tax cut in income-tax systems**
- **Effect of tax cut in corporate-tax systems**

Once indispensable set of behavioral rules is elucidated, we can forecast the effect of public policies, using the obtained model structure.

Examples :

- **Effect of inefficient public expenditures. (Governments' waste of money)**
- **Effect of progressive taxation on GDP.**

2. Social phenomenon (Non-economic phenomenon)

- **Bullying phenomena**
- **Pandemic phenomena**

An Agent-Based Model that Incorporates the Roles of Immune Cells and Antibodies:

An Example of Mechanism-oriented Agent-Based modeling

1. Introduction

1） Although coronavirus pandemic has ended, various new sources of pandemics are emerging, necessitating effective countermeasures.

2) Many infection models, such as system dynamic model(e.g., SIR model) have been developed to understand infection disease dynamics. However, these models have failed to accurately reproduce key features of pandemic phenomena.

3) Agent-based modeling (ABM) is a promising methodology. However, previously developed model have focused solely on the infection process Consequently, they have also failed to reproduce the real characteristics of pandemics.

In this study, I have developed an agent-based model that accounts for both infection and recovery processes, incorporating the roles of immune cells and antibodies.

This results indicate that this model well reproduces detailed features of pandemic phenomena and enhances our understanding of the causal mechanisms and effective countermeasures.

2. The ABM model of present research

The ABM model of present study focuses on recovery processes, where behavioral rules relevant to the immunity response are assumed based on the well known medical knowledge.

【Main assumptions】

1. Initial Setup: 2000 agents are initially randomly placed in a two-dimensional space, with one agent initially assumed to be infected having a large number of viruses. Agents move randomly within a defined critical distance limit.
2. Neighbor Definition: Two agents are considered neighbors if they are within the critical distance limit.
3. Virus Exchange: Neighboring agents exchange viruses, infecting others or being infected.,
4. Virus Transmission: Among neighboring agents, viruses are released from an infected agent , with a portion being absorbed by the neighboring agents., The extent of virus transmission depends on the viruses release rate and absorbtion rate.
5. Immune response: When infected, innate immune cells first attack the viruses and if their effect is insufficient to counter virus replication, antibodies emerges depending on the agent-specific delay time after infection and the agent-specific threshold of virus count required for antibodies emrgence.

5. The number of viruses in agent (i) at time (t+1) is the sum of the following terms, which are divided into four , each of which is assumed to be proportional to the number of viruses at time (t):

1) Replication:

An increase in the number of viruses due to replication, where the replication rate is assumed to be constant.

$$\Delta N^{i}{}_{replicate} = r_{replicate} N^{i}(t)$$

2) Release from the body:

A decrease due to their release from the body via coughing, etc., where the release rate is an agent-specific constant defined by a uniform random number.

$$\Delta N^{i}{}_{released} = -r_{released} N^{i}(t)$$

3) Immune response:

A decrease due to attacks by immune cells and antibodies, is proportional to the total number of viruses, This assumption corresponds to the role of fever, because in the real system, if the effect of immunity cannot keep up with virus replication, body temperature rises to increase the immunity.

$$\Delta N^{i}{}_{atack} = -r_{attack} N^{i}(t),$$

$$r_{attack} = r_{attack\_immune\_cells} \ or \ r_{attack\_antibodies}, \quad r_{attack\_immune\_cells} < r_{attack\_antibodies}$$

4) New infection:

An increase in the number of viruses due to new infections via absorption of viruses released by infected neighboring agents. This increase is assumed to be proportional to the product of the release rate and the absorption rate, where the absorption rate is an agent-specific constant defined by a uniform random number.

$$\Delta N^{i}{}_{infected} = \sum_{j \in neighbor} r_{absorbed} r_{released} N^{j}(t)$$

Attribute variables shown in red are agent-specific uniform random numbers

Table　Attribute variables of agents and parameter values.

Variables	Initial value or definition
Number of agents	2000
Area of network system	1000×1000
Maximum Distance of agent's move	100
Critical distance for infection	5
Initial number of the infected	1
Number of virses hold by the infected initially	5000×100 (arbitrary unit)
Virus replication rate	1.4, 1.6, 1.8, 2.0
Virus attack rate by immune cells	0.3±0.1　uniform random number
Virus attack rate by antibodies	0.5±0.1　uniform random number
Elapsed period after infection for antibody emergence	7±2　uniform random number
Virus-count multiple for antibody emergence	0.5±0.2　uniform random number
Minimum-virus-count multiple for zero viruses	10^{-9}
Virus releasing rate	0.1±0.05　uniform random number
Virus absorbing rate	0.1±0.05　uniform random number
Position (x,y) in the 2 dimentional space	defined at every step for each agent
Distance of agent's move	[0, maximum distance] uniform random number
Direction of agent's move	[0, 2π] uniform random number
Agent as an object in the neighbour	defined at every step for each agent
Number of virses	calculated at every step for each agent
Infection-related state variables	calculated at every step for each agent

3. Experimental conditions.

1. Basic condition, only changing the virus replication rate.

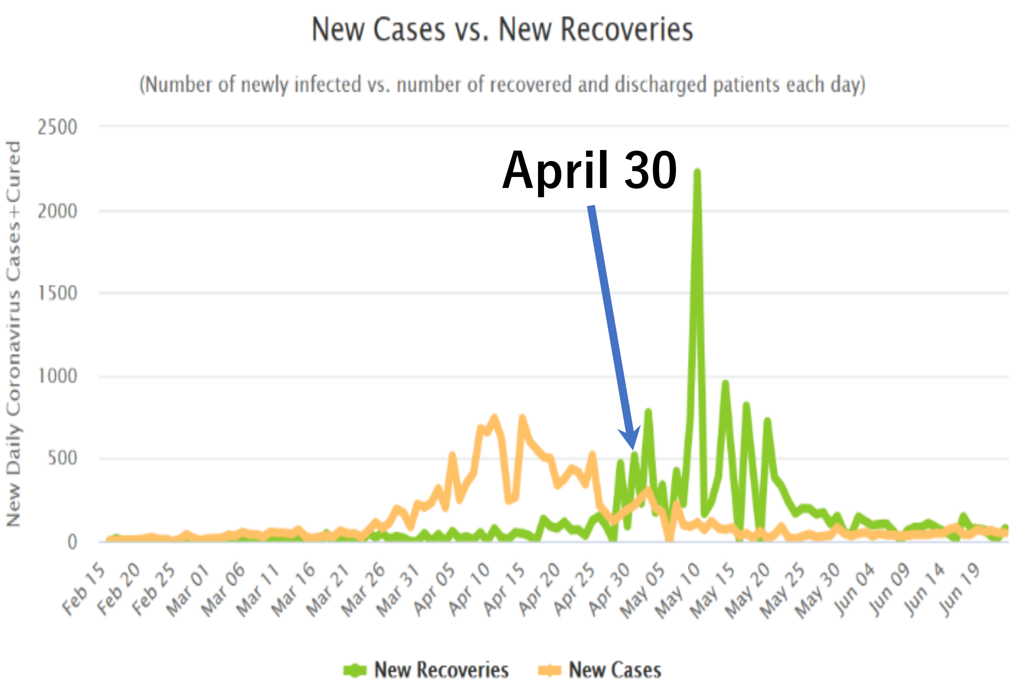
2. Experiments changing behavioral rules for immune cells and antibodies for elucidating the essential causal mechanism of the pandemic convergence..
   1) With or without antibodies emergence.
   2) With or without the effect of fever.
      In the present study, the former corresponds to the condition ,where the viruses release rate by immunity is proportional to the number of viruses and the latter corresponds to the condition where it is constant without depending on the number of viruses.

2. Experiments changing parameter values.
   1) Regulation of agent's movement
      during the whole period of time or temporary during the time 50-100.
      ,changing maximum moving distance.
   2) Regulation of wearing masks
      during the whole period of time or temporary during the time 50-100.
      , changing the virus-release rate and virus-absorb rate
   3) Temporary regulation in both the moving distance and wearing masks.

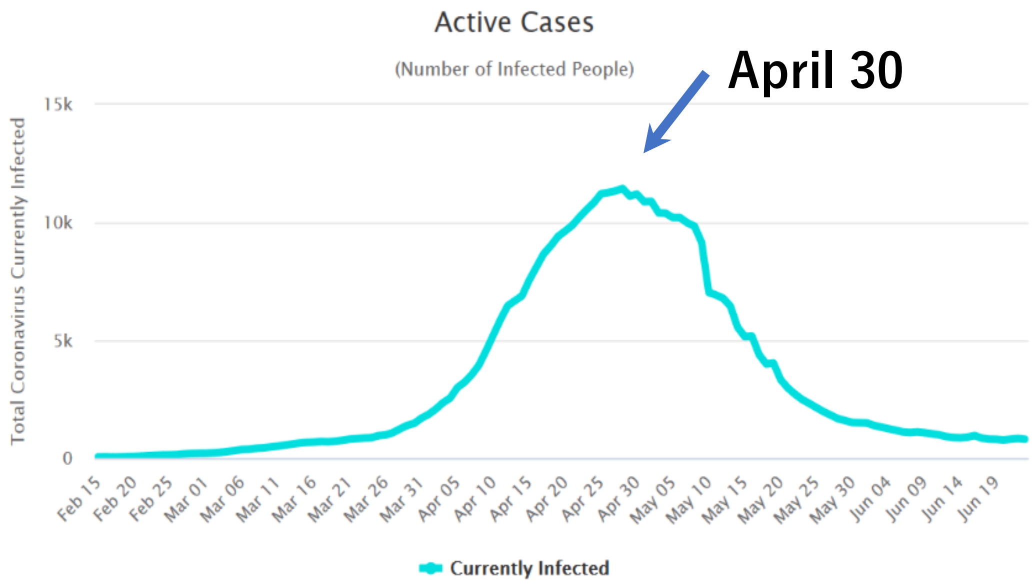
4. Actual feature of the pandemic phenomenon that should be reproduced by the model.

1. The number of newly recovered agents exceeds the number of infected agents, at some point, at which total number of infected agents shows its peak value.

Newly Infected vs. Newly Recovered in Japan



Active Cases in Japan



2. A regulation of the movement of people and wearing masks are effective for quick convergence of the pandemic.
3. Despite of historically encountering multiple times of severe pandemics, due to the viral particles of various replication rate, human being survived without been perished.

5.1 Fundamental behavior during infection and recovery.

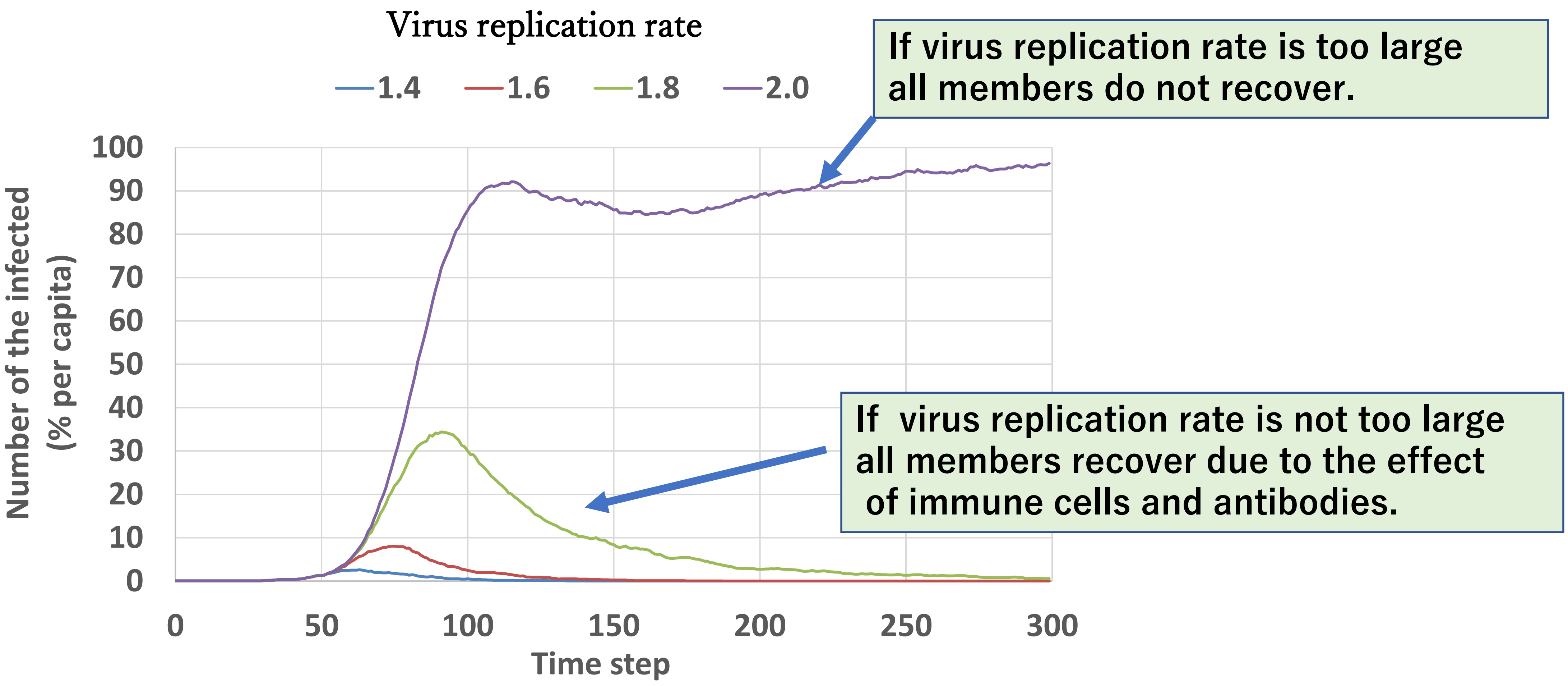


Fig. Effect of the virus replication rate on the number of infected agents.

Relationship between the pattern of the change in the number of newly infected, newly recovered and currently infected agents.

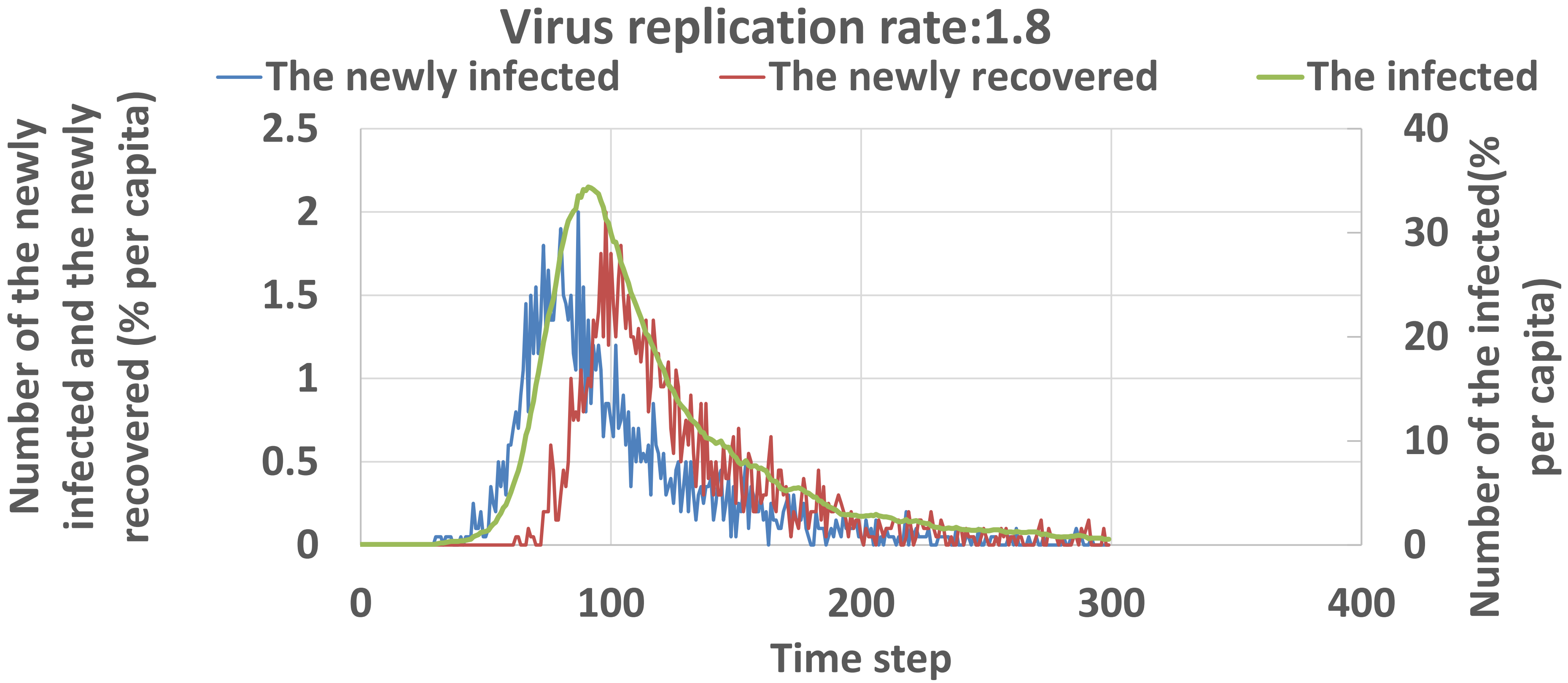


Fig. Changes in the numbers of newly infected, newly recovered, and total infected agents.

Number of total infected agent peaks
when the number of newly infected equals the number of recovered.

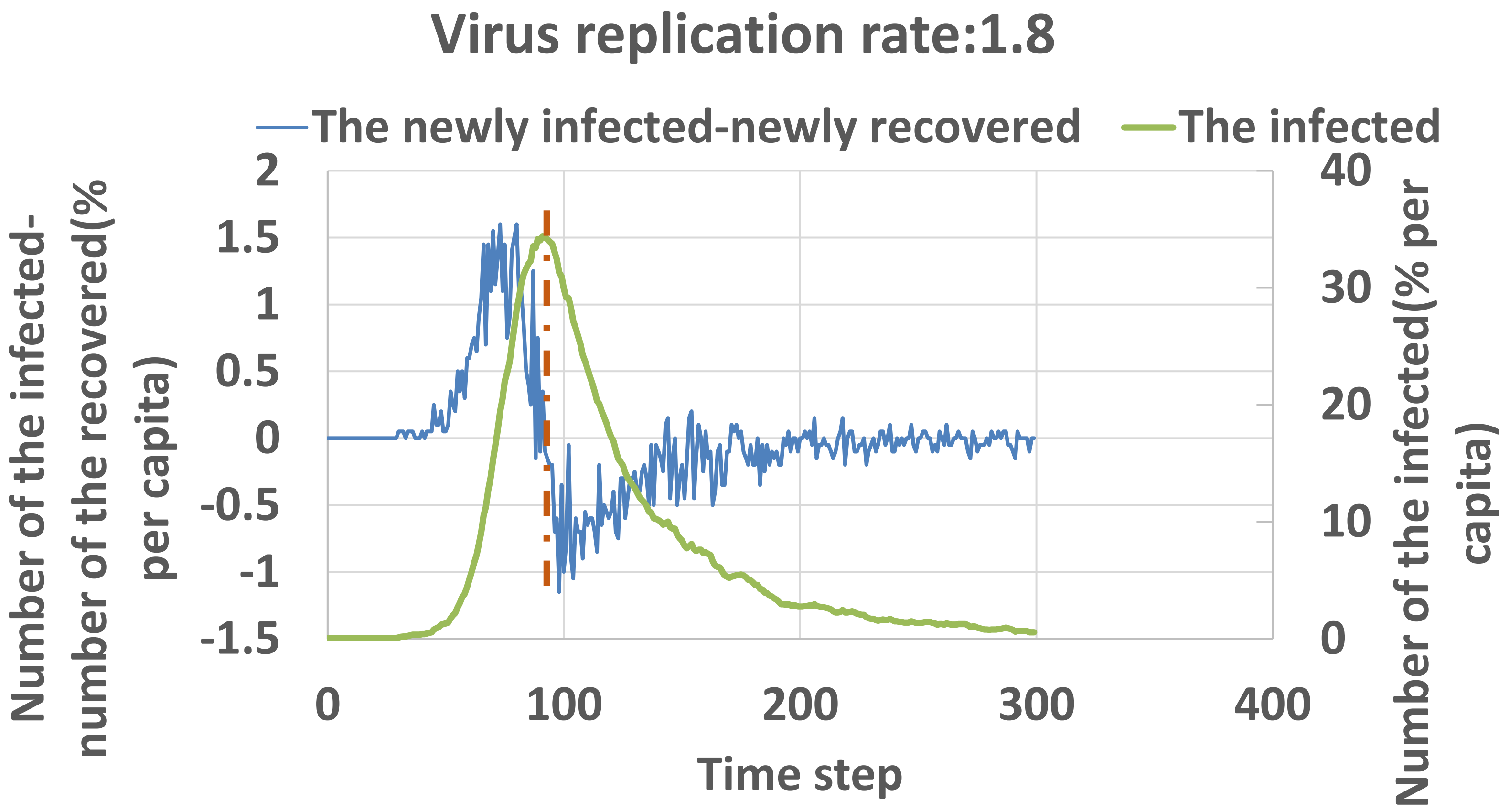
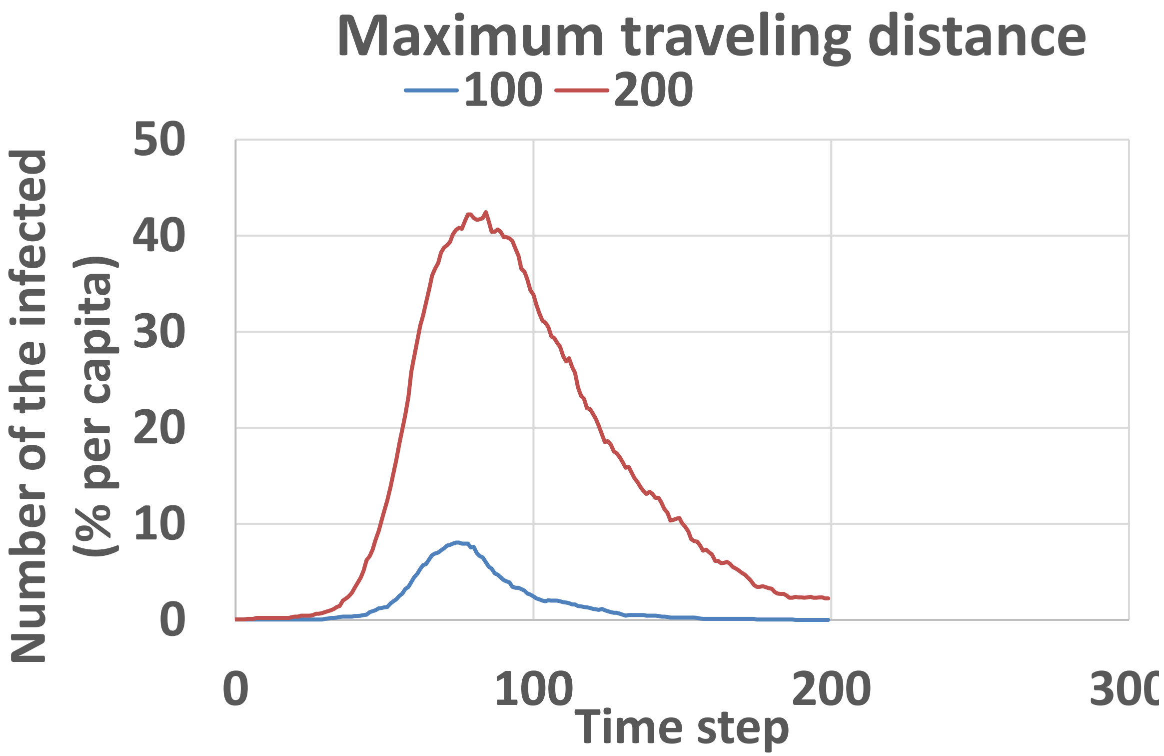
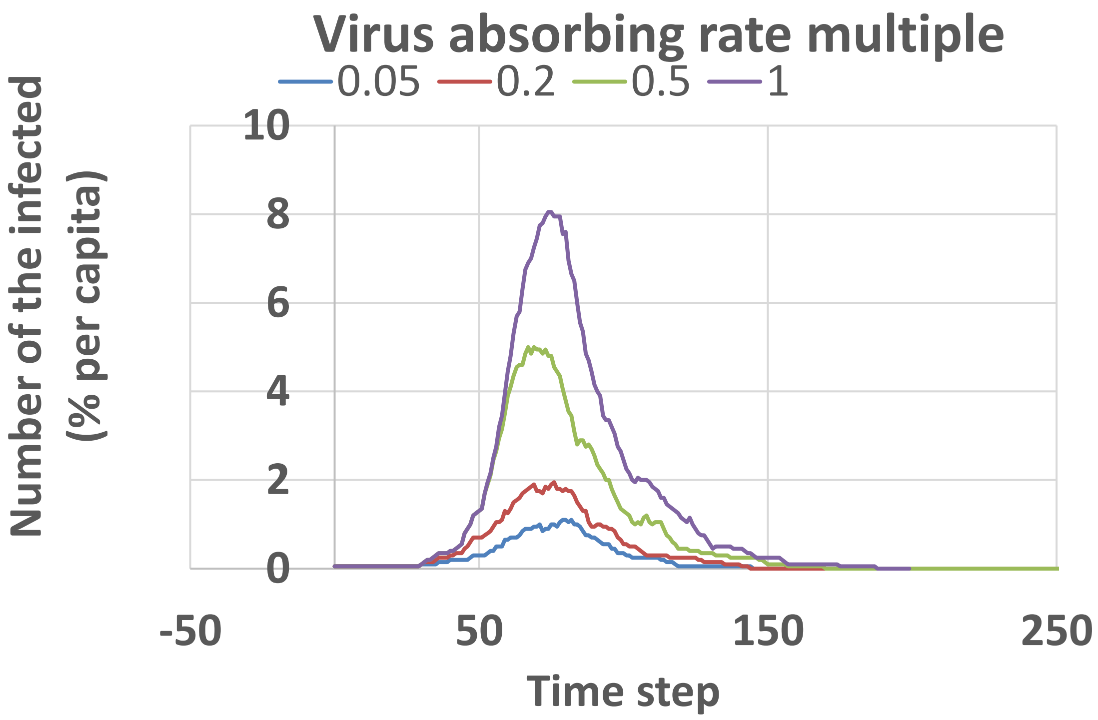


Fig. Change in the total number of infected agents and the difference between the numbers of newly infected and newly recovered agents.

5.2 Effect of the regulation of movement and wearing a mask.



Effect of the regulation of movement.



Effect of wearing a mask.

5.3 Mechanism of the pandemic convergence.

In this model, we can track every detail of infection propagation as well as changes in the number of viruses within each agent.

Infection Propagation		Number of Viruses at infection
Agent 1	at t=0	10^5
Agent 13	at t=4	10^4
Agent 1373	at t=6	10^2
Agent 1019	at t=7	10^1
Agent 1911	at t=13	10^{-1}

Agent 155 at t=25

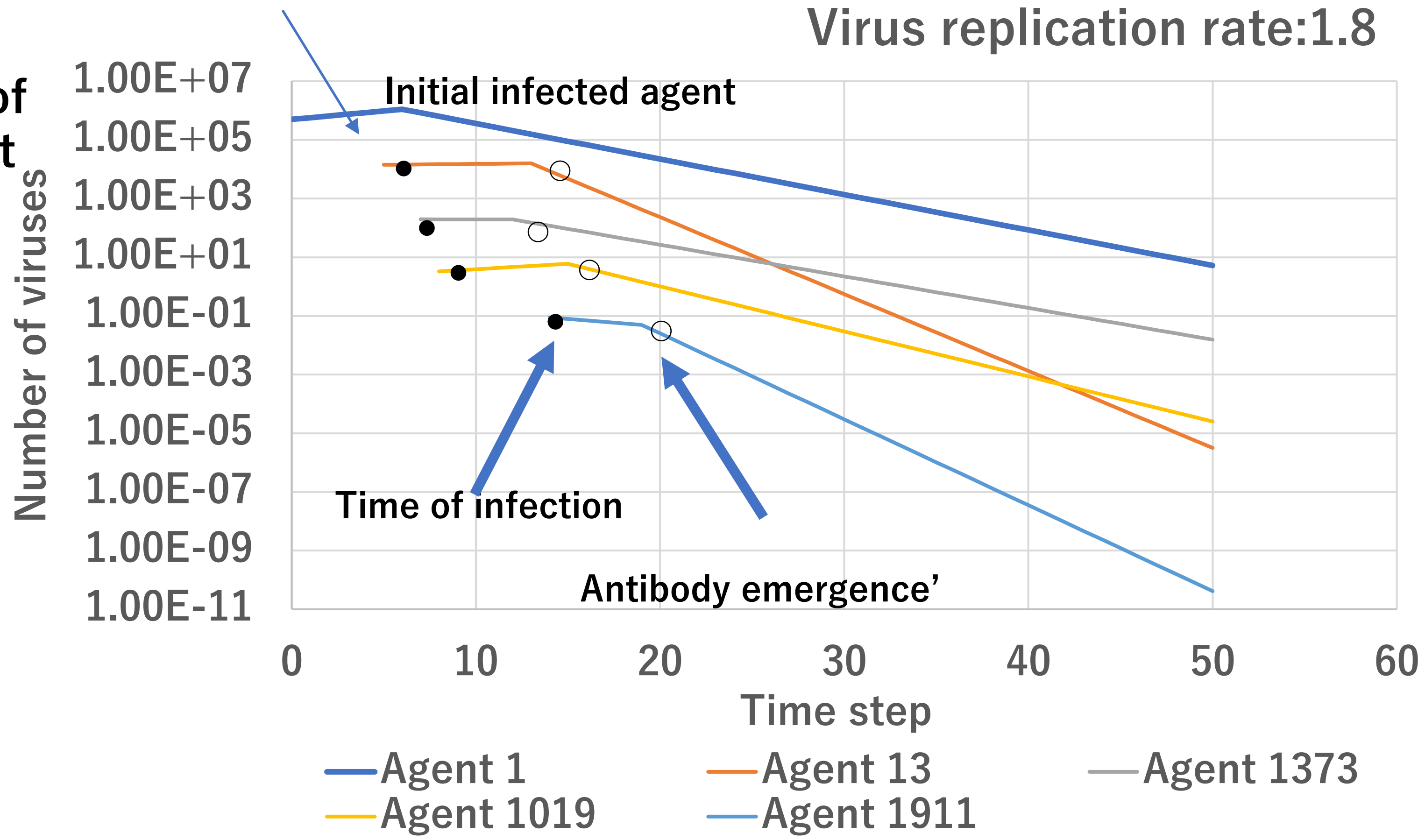
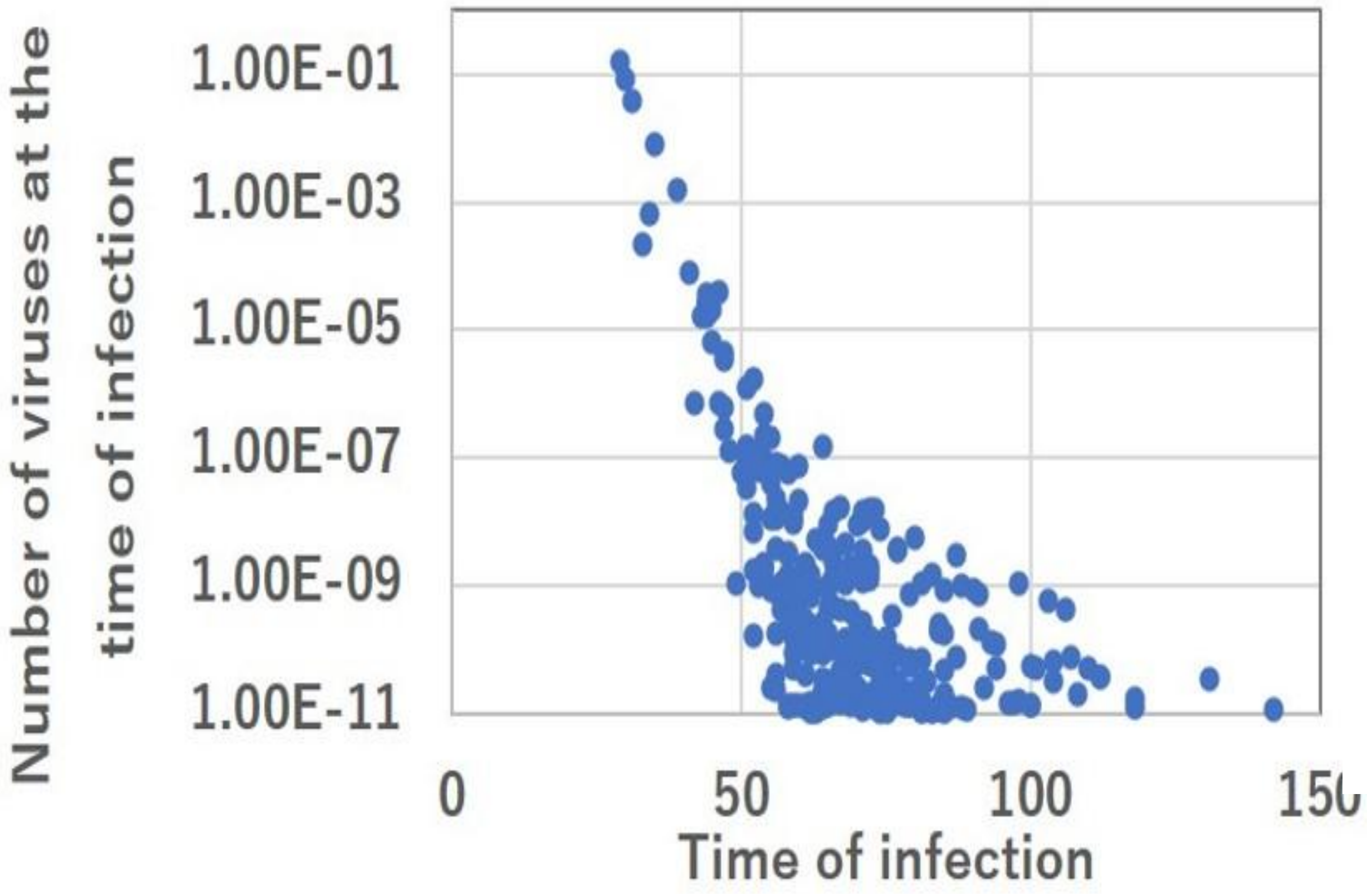
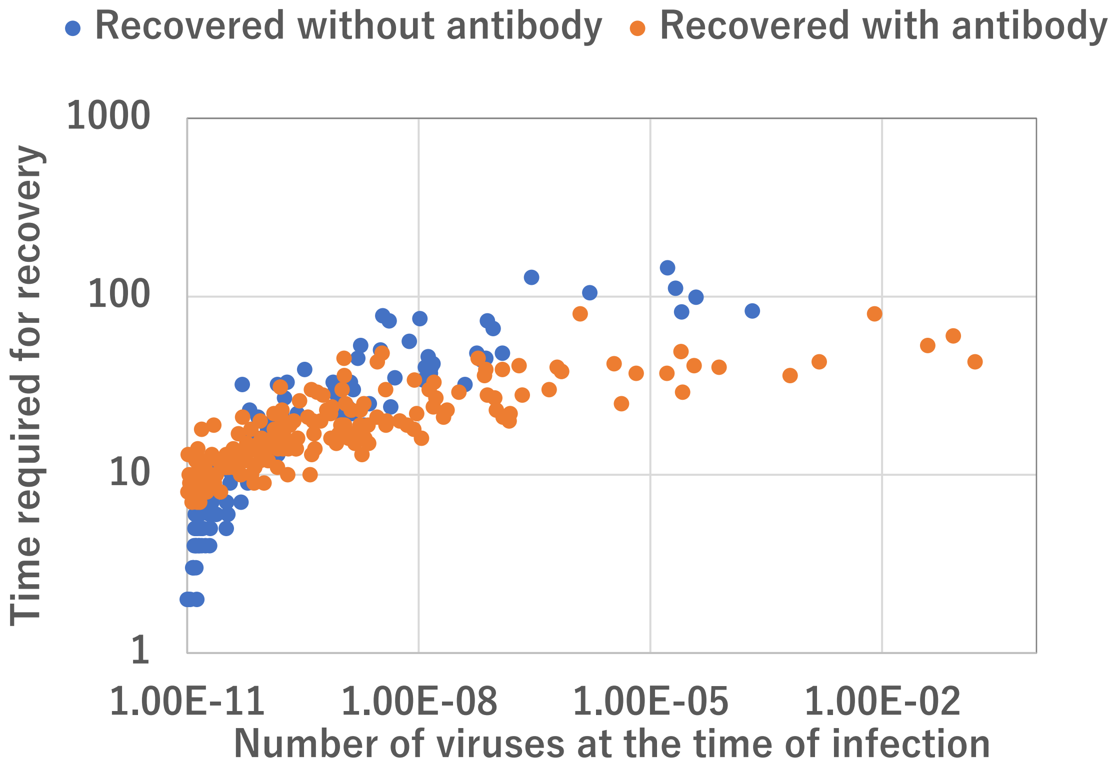


Fig. Change in the number of viruses of each agent during the beginning of infection spread.

Mechanism of the pandemic emergence and convergence.

At the initial stage, the number of infected individuals rapidly increases due to transmission chains. As the virus count within the system decreases and the amount of virus entering the body upon infection sharply declines, recovery is more likely to surge, leading to the pandemic convergence.

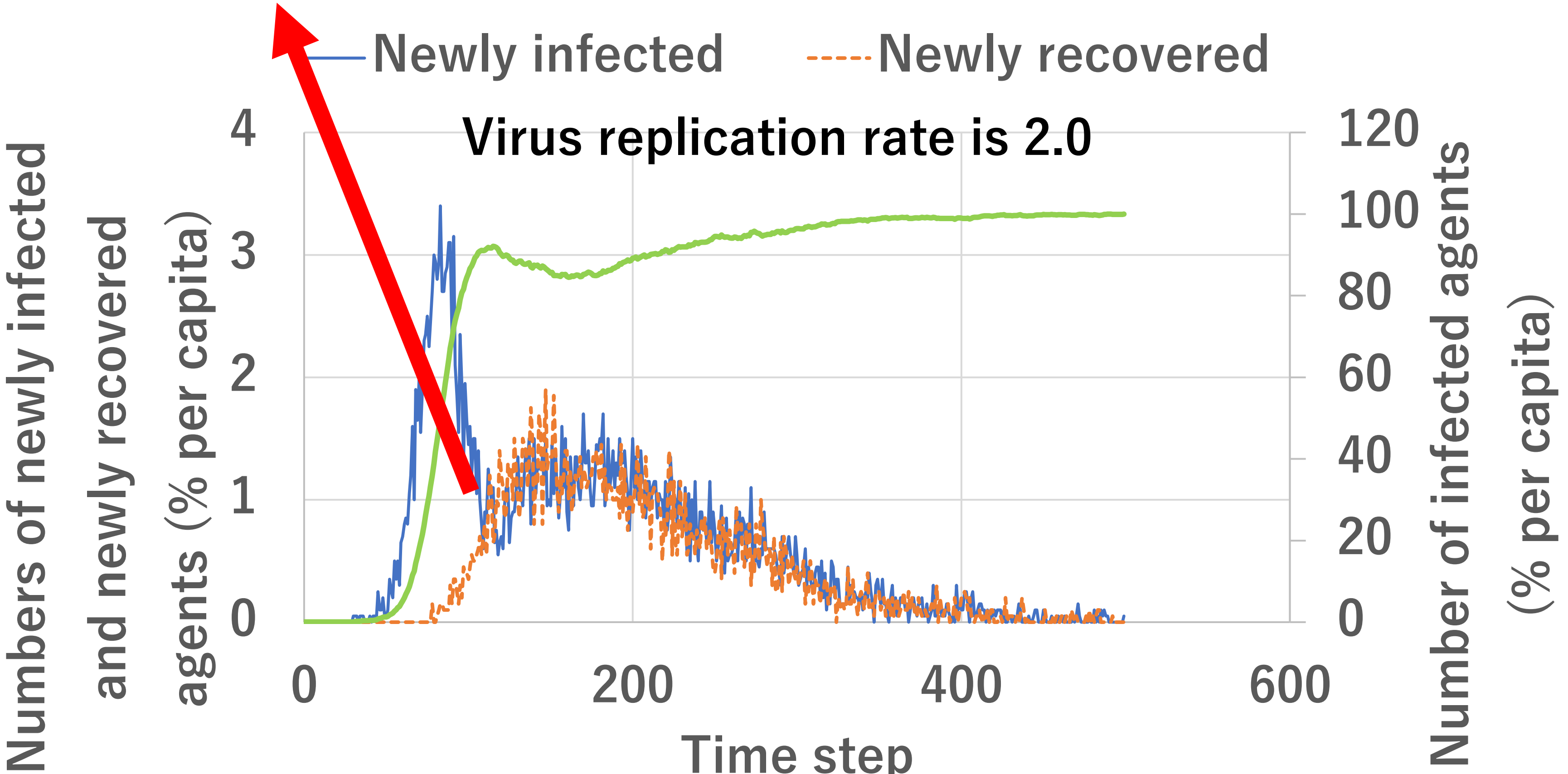




5.4 Mechanism behind a pandemic that does not converge. What happens?

When an agent with weak immunity is infected(agent 71), the number of viruses increases, indefinitely, leading to a resurgence of viruses.

Isolating severely infected individuals is essential for the pandemic convergence.



Virus replication rate 2.0

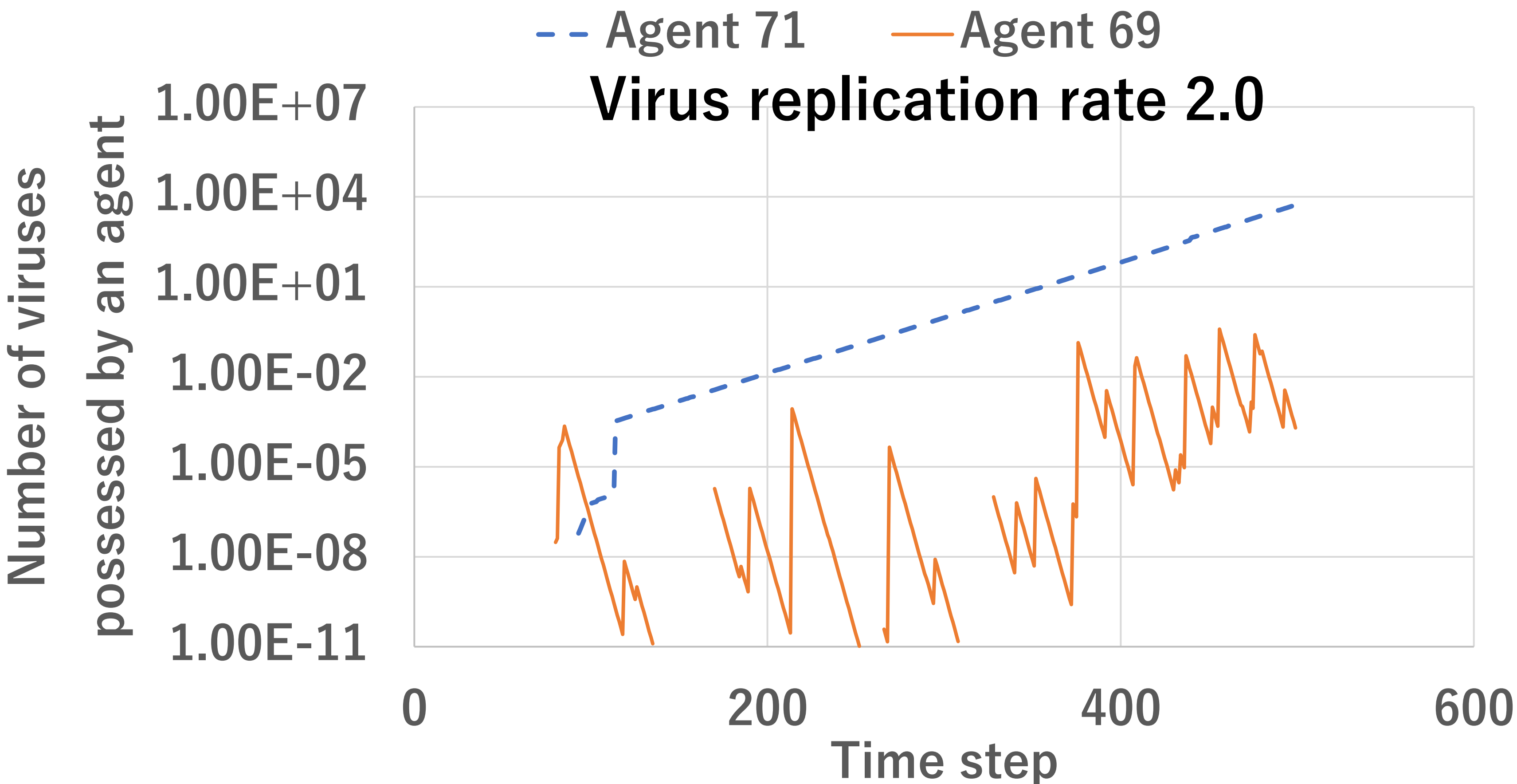
Change in the virus count of agents with weak immunity and normal immunity.

Agent71(Weak immunity) : Infected at t=92, and at t=113.

The number of viruses increases indefinitely due to viral replication.

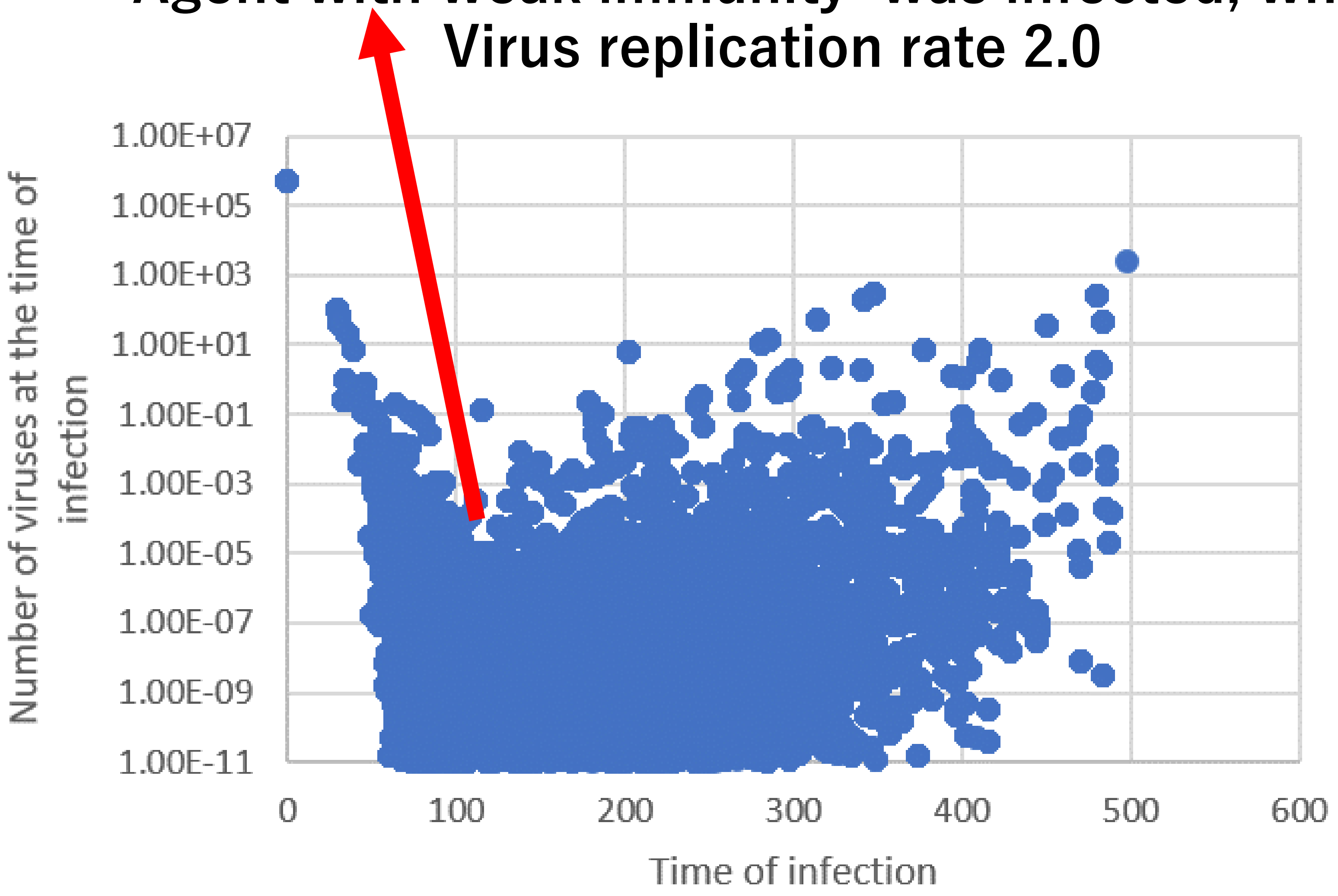
Agent 69(Normal agent) : Infected multiple times.

The number of viruses increases due to the rising viral count in the system, which is caused by the agent with weak immunity.



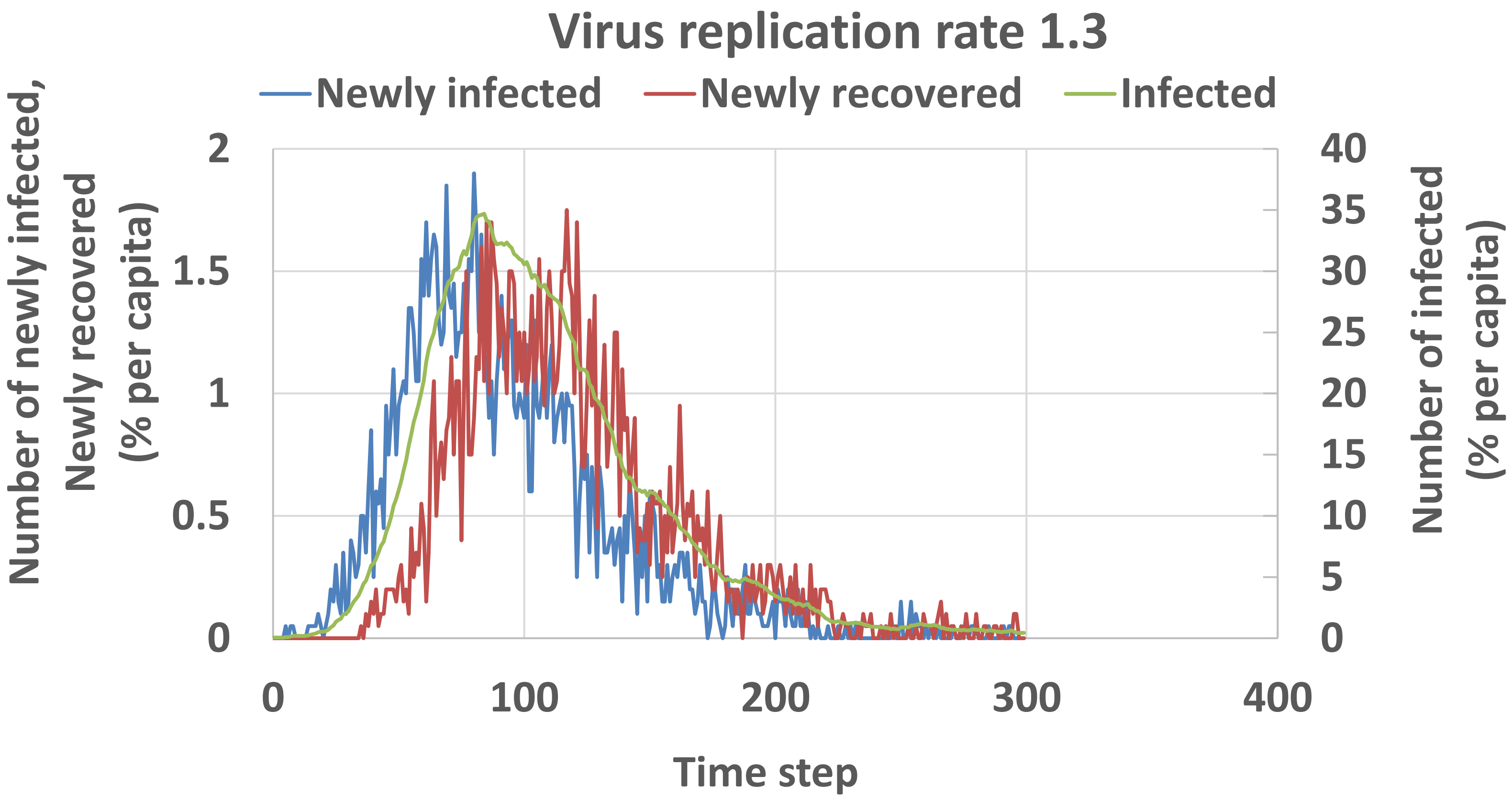
Resurgence of viruses following the infection of an agent with weak immunity.

Agent with weak immunity was infected, who is agent 71.
Virus replication rate 2.0

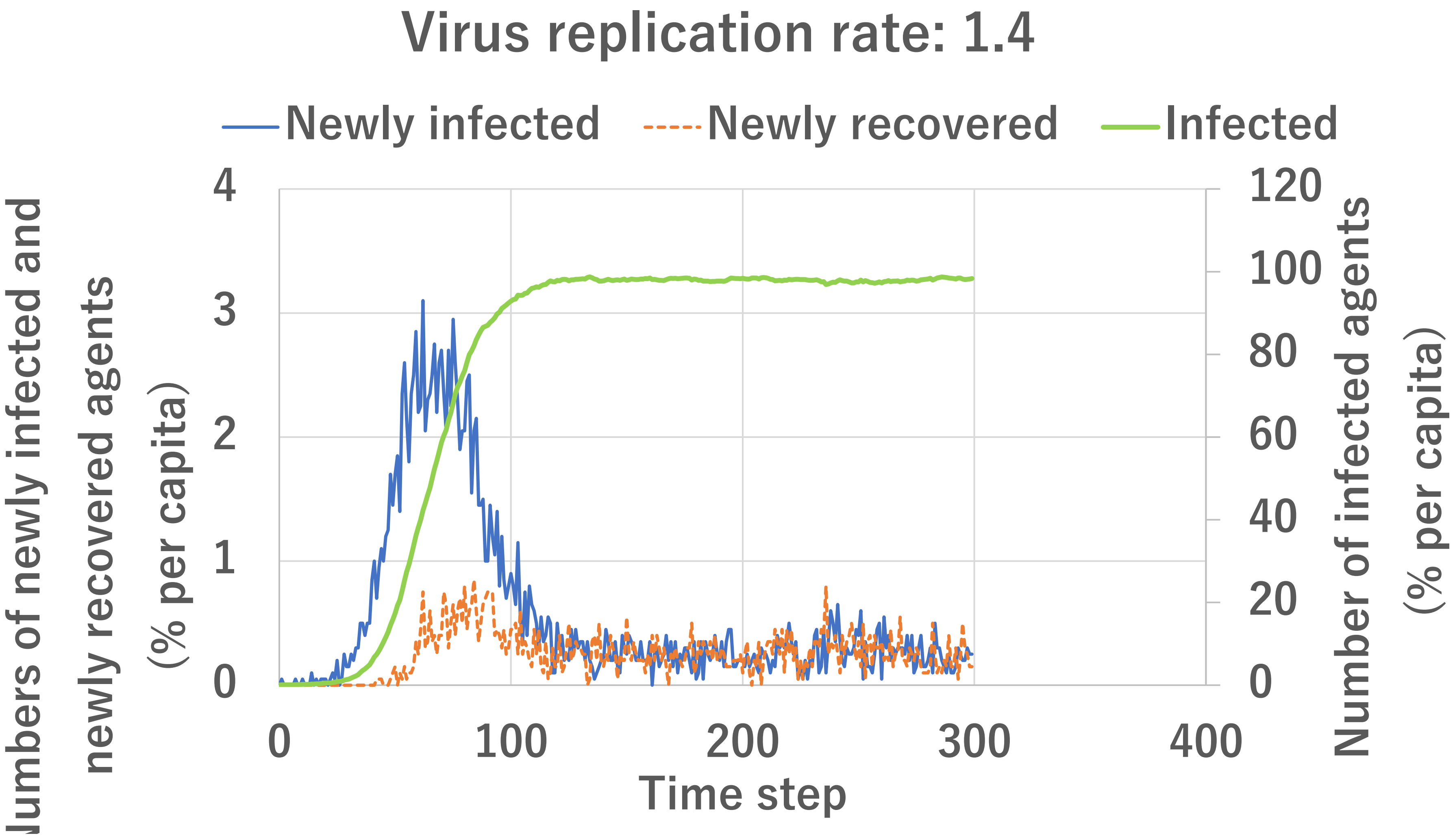


3.5 Effect of antibodies on the pandemic behavior.

Without antibodies, the upper limit of the virus replication rate for pandemic convergence becomes much smaller, from 1.8 to 1.3, but fundamental pattern of the pandemic is unchanged, indicating that antibodies are not essential factor for the pandemic convergence.



Calculated result in the case without antibodies.


Virus replication rate: 1.4
Newly infected
Newly recovered
Infected
4
3
2
1
0
120
100
80
60
40
20
0
0
100
200
300
400
Time step
Numbers of newly infected and newly recovered agents (% per capita)
Number of infected agents (% per capita)

3.6 Effect of the role of fever on the pandemic behavior

Without the effect of fever, a pandemic either does not occur or does not subside depending on the virus replication rate, making stable convergence across various rates unexplainable

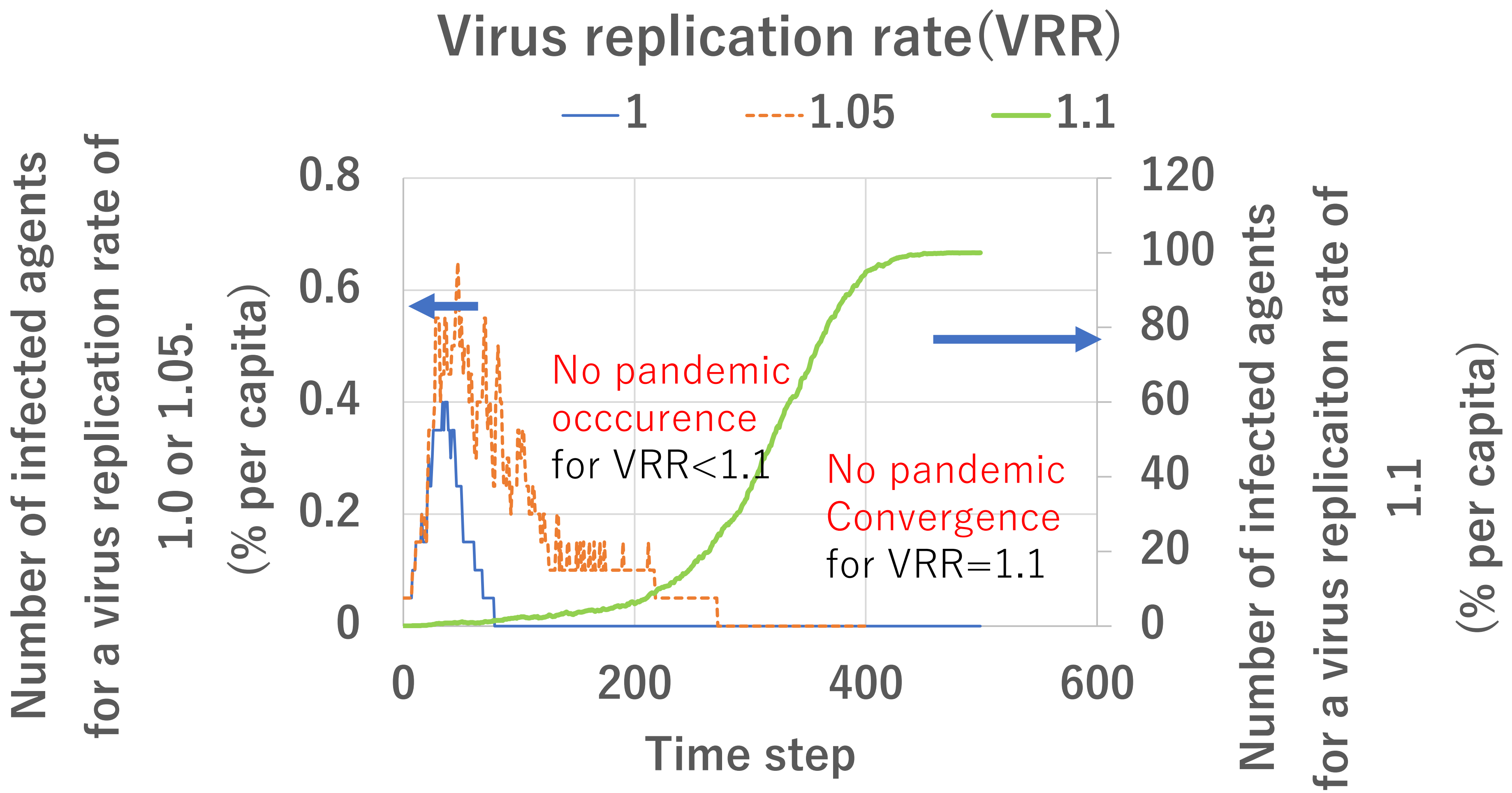
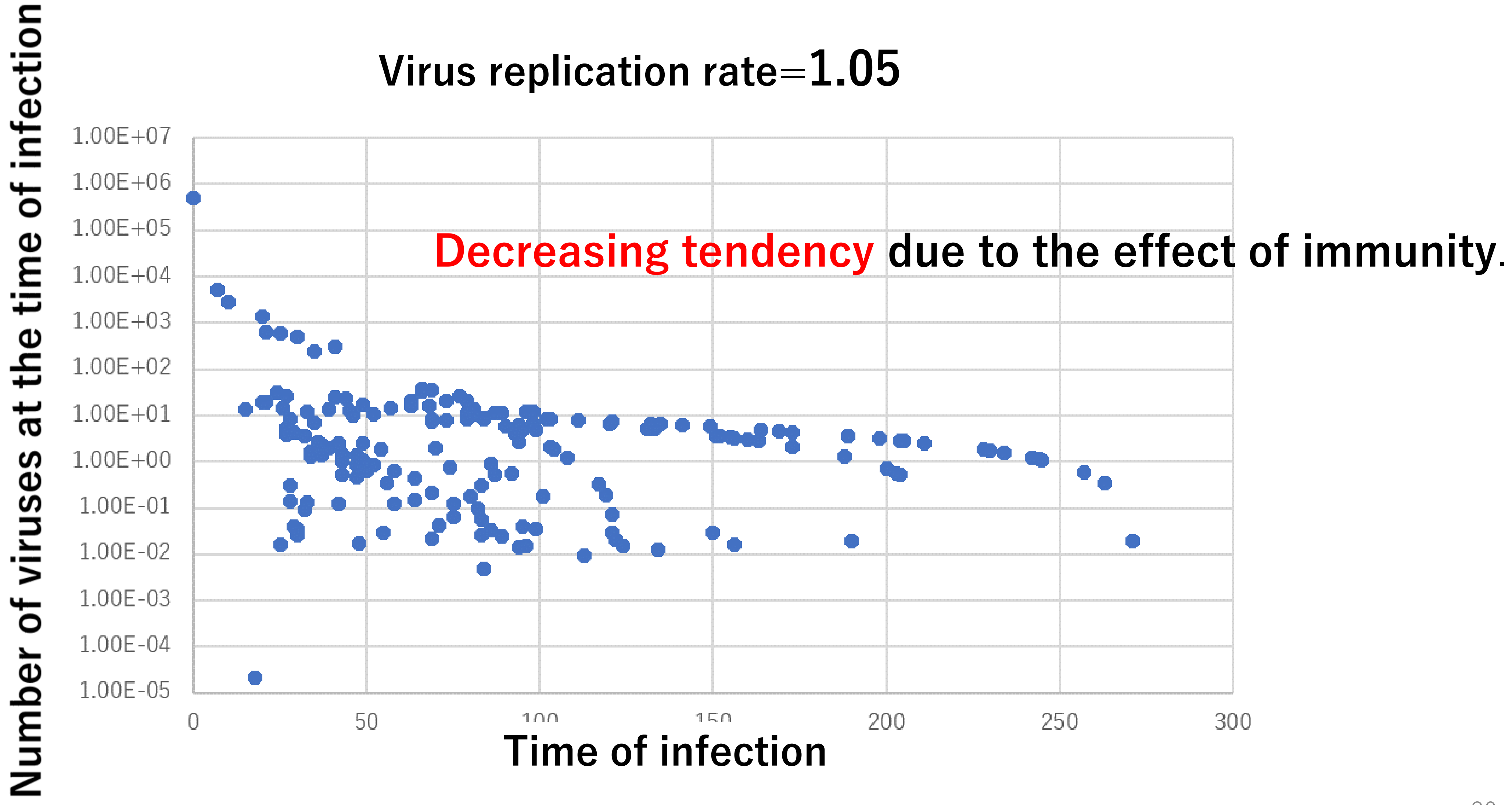


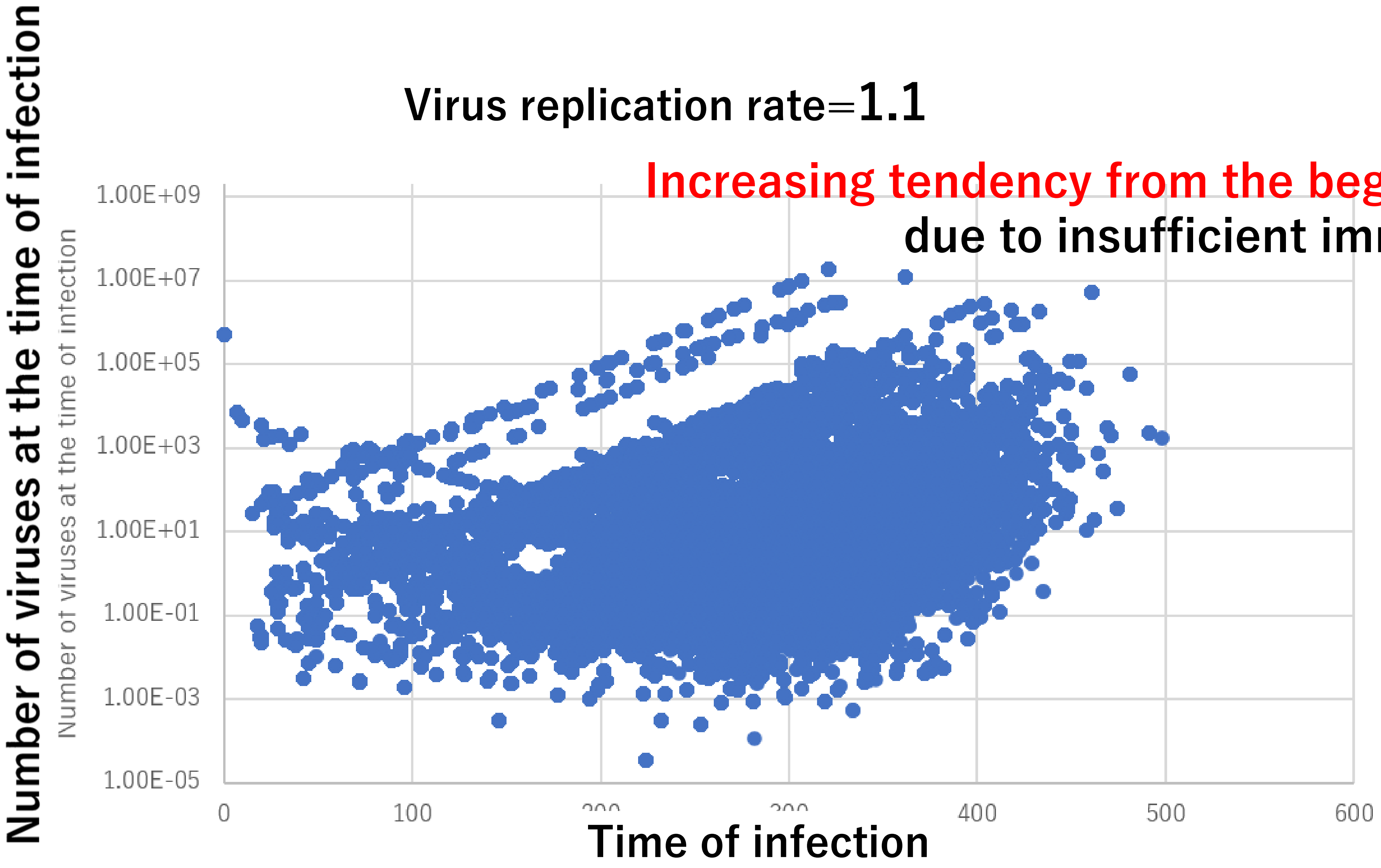
Fig. The behavior of the pandemic when the role of fever is not present.

The number of viruses shows decreasing tendency with time when VRR is 1.05, but increasing tendency with time when VRR is 1.1.



Virus replication rate=1.1

Increasing tendency from the beginning due to insufficient immunity.



6. Conclusions

1) Many social problems arises from a lack of understanding of causal mechanisms . To overcome social problems , piling up the knowledge regarding causality is indispensable. I have been proposing mechanism-oriented agent-based modeling that can elucidate the causal mechanism of various social phenomena through a series of systematic computer experiments.
2) As an example of this methodology, an agent-based infection model incorporating the roles of immune cells and antibodies was constructed and pandemic phenomenon was analyzed taking into account the effect of immunity on the number of viral particles.
3) Calculated results well agree with the actual phenomena helps us understand the causal mechanism of pandemic phenomenon as well as effective countermeasures.
4) The most essential factor for the pandemic convergence is the role of fever, rather than antibodies. Based on this finding, the most essential individual level countermeasure is self-monitoring body temperature to recognize the state of infection at an earlier stage.

Thank you for your attention!

6. Conclusions

1) **An agent-based infection model incorporating the roles of immune cells and antibodies was constructed and aggregate phenomena were analyzed based on the behavior of viral particles during the infection and recovery processes.**

2) **The calculated trend in the number of infected shows good agreement with the actual data. Effect of movement restriction and wearing a mask is also reproduced**

3) **The most essential factor for accurately reproducing the characteristics of pandemic phenomena is the role of fever, rather than antibodies. Based on this finding, an effective individual level countermeasure is self-monitoring body temperature to recognize his state of infection at an early stage, followed by self-restriction of movement if necessary . If a large number of individuals adopt this measure, it will contribute to the rapid containment of the pandemic.**

4) **I have proposed a new methodology for elucidating the causal mechanisms behind the emergence of social and economic phenomena using ABM and this research is an example of such an approach. I believe this methodology can be also applied to biological systems, as many phenomena emerge from bottom-up interactions.**

The ratio of the number of recovered agents with antibodies.

The number of agents who are recovered with antibodies increases with increasing virus replication rate.

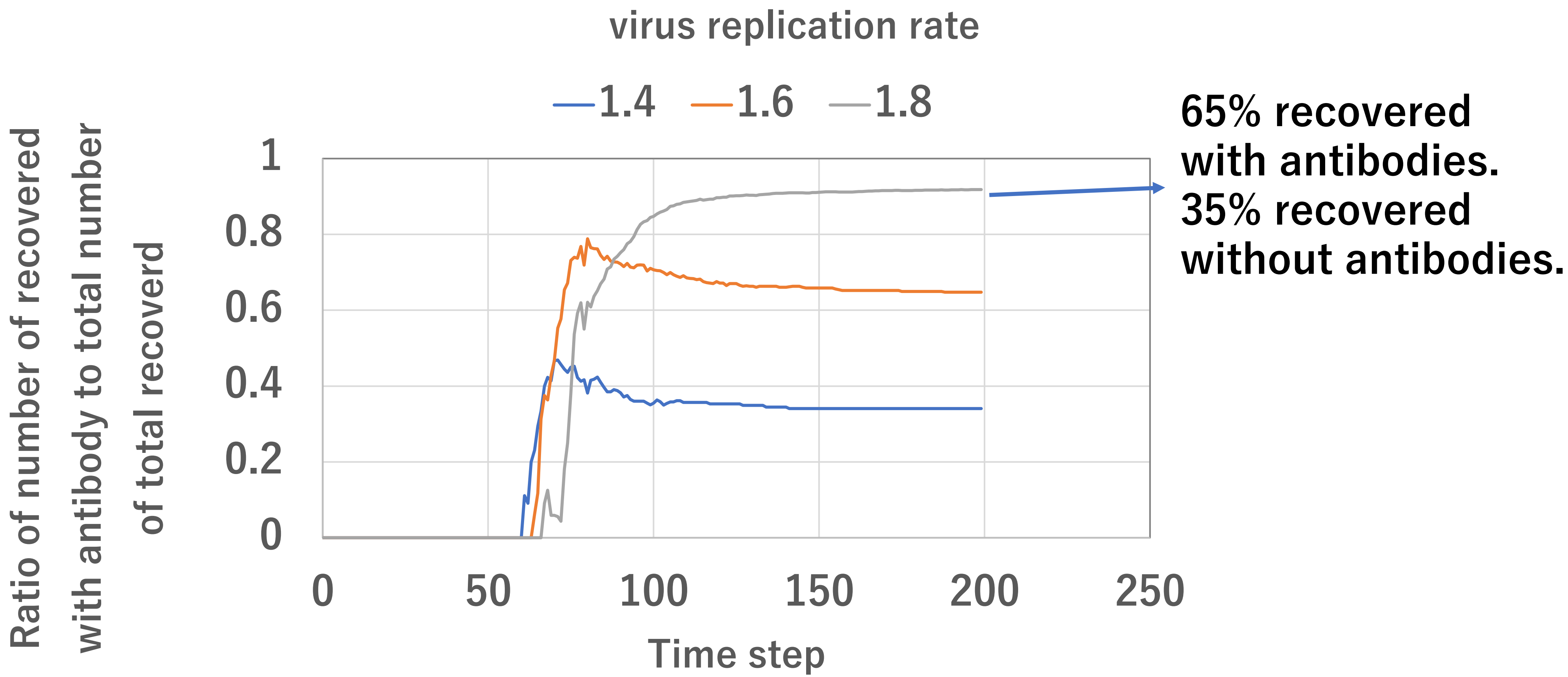


Fig. Effect of virus replication rate on the ratio of the number of recovered agents with antibodies to the total number of recovered agents.

3.3 Temporal regulation of movement followed by temporal mitigation

- It decreases the peak value of the number of infected agents.
- Resultant second wage is not remarkable,
  if the new infected person does not enter into the system from outside.

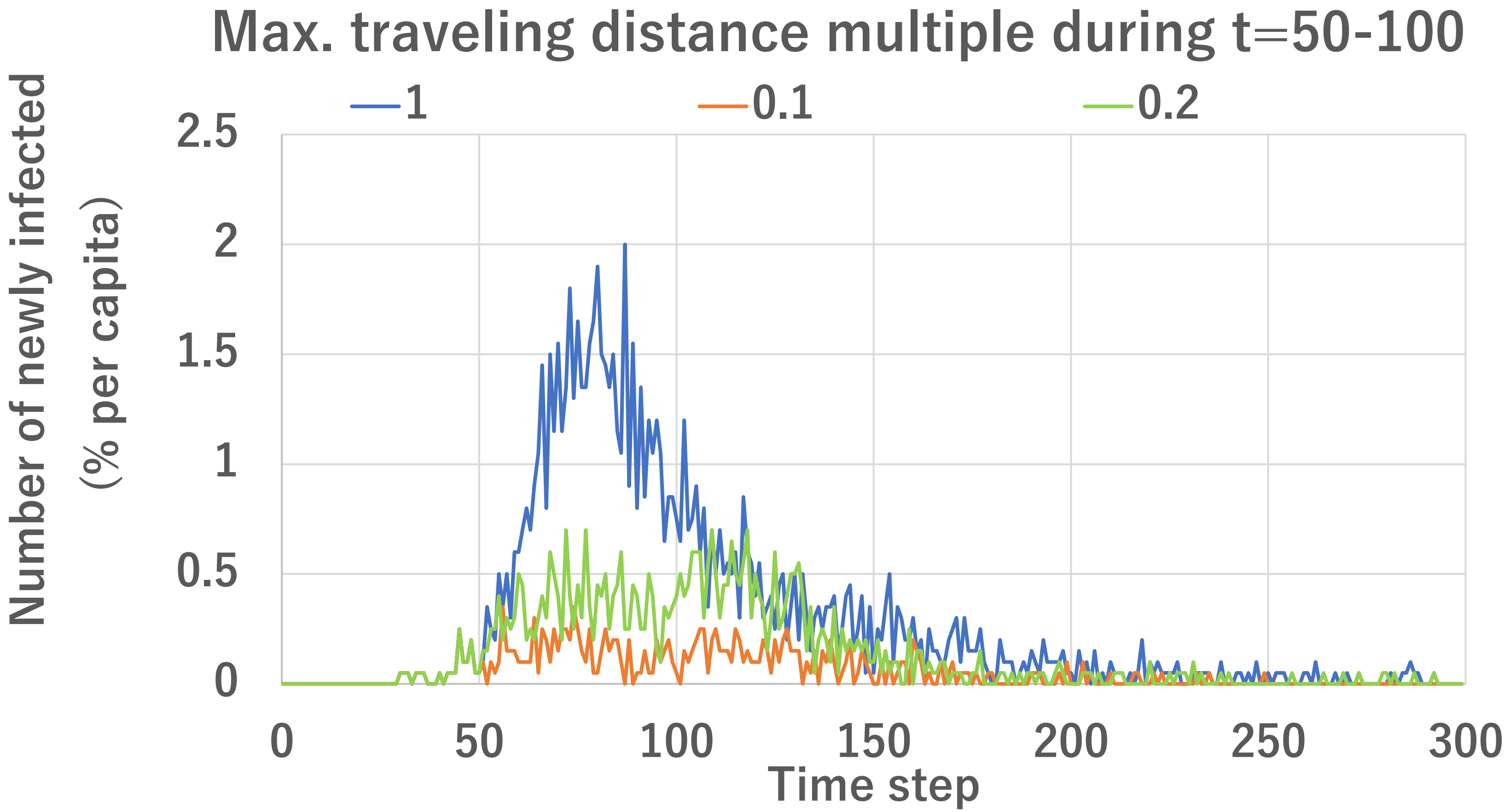


Fig. Effect of temporary regulation of traveling distance and its release on the number of infected neighbors (virus growth rate: 1.8).

3.2.2 Effect of virus absorbing rate on the infection behavior during the regulation and mitigation of movement.

Decreasing the virus absorbing rate by wearing masks is effective for preventing the second wave occurrence.

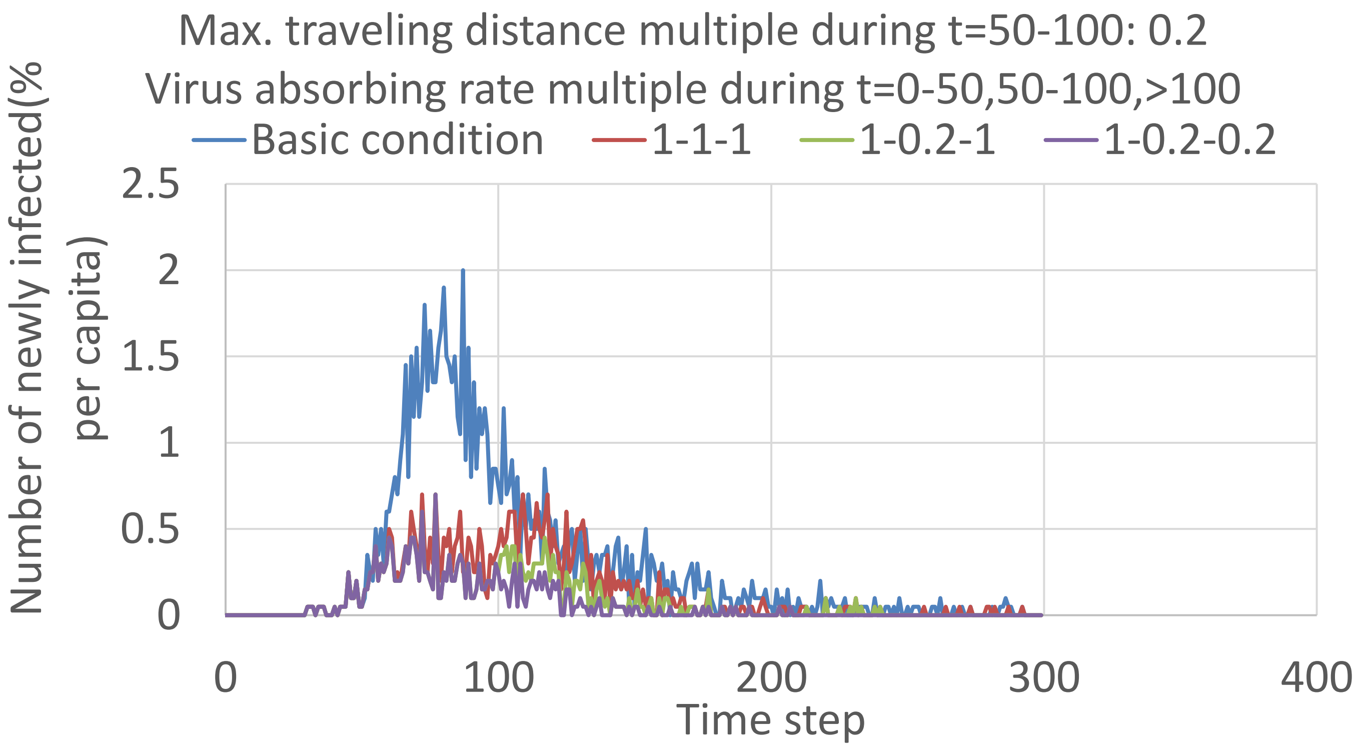


Fig. 24. Effect of the virus absorbing rate on the number of newly infected agents when movement regulation is applied.

What is Agent-Based-Modeling(ABM)?

ABM is a bottom-up modeling method in which an artificial society is constructed on a computer and causal mechanism of the phenomenon under concern can be elucidated by a series of computer experiments.

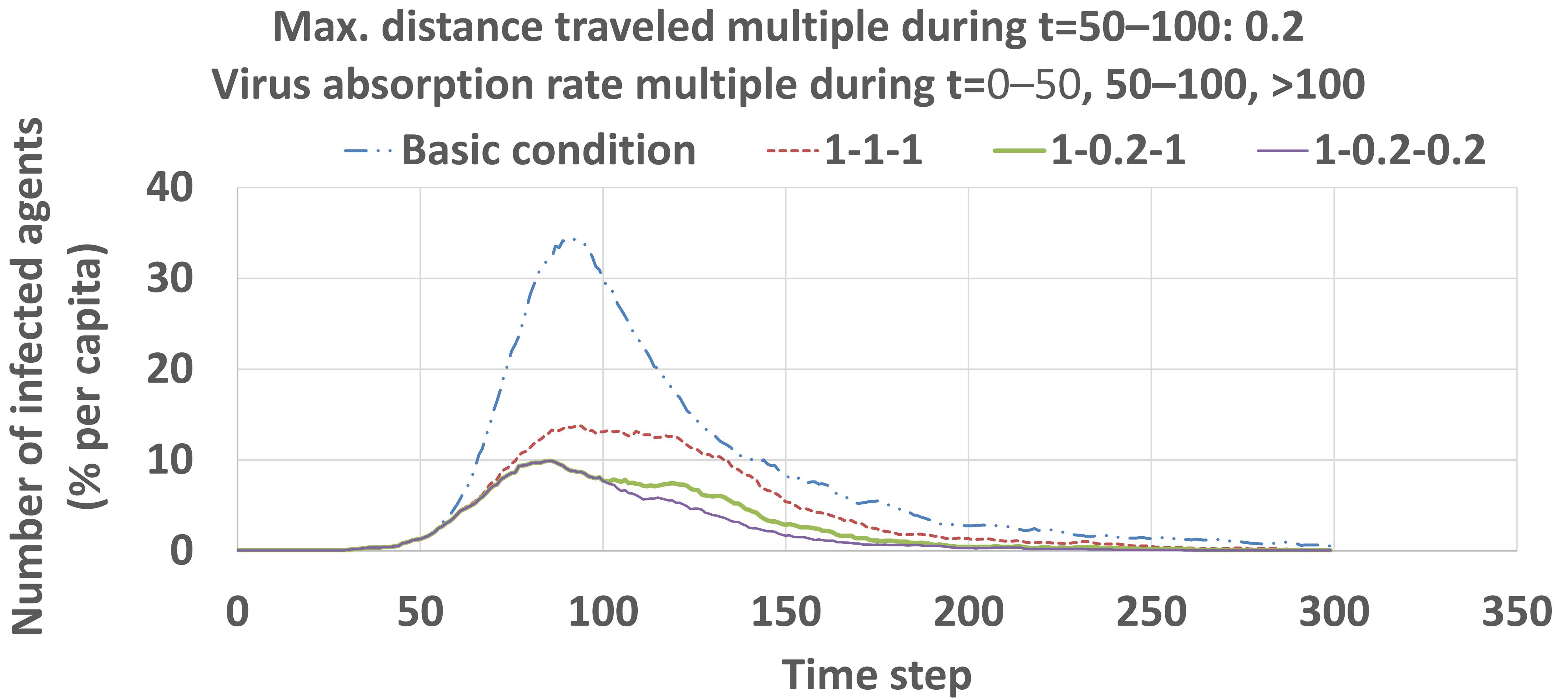
The principle of this methodology is as follows:

1. Every aggregate phenomenon in the society is caused by the heterogeneous agents' behaviors and interactions.
2. Using ABM, we can construct an artificial society on a computer which works in the same principle of the actual society.
3 . The model must incorporates a set of behavioral rules that is indispensable to reproduce actual phenomenon, which is a cause of the phenomenon and can be elucidated by a series of computer experiments.
4. Then, we can elucidate the causal mechanisms of the phenomenon by considering the reason why those factors are indispensable.

This procedure is a new validation method of ABM that I have been proposing ,

3.3 Temporal regulation of movement with temporal regulation of wearing masks

- It drastically decreases the peak value of the number of infected agents.
- Resultant second wage is not remarkable, if the new infected person does not enter into the system from outside



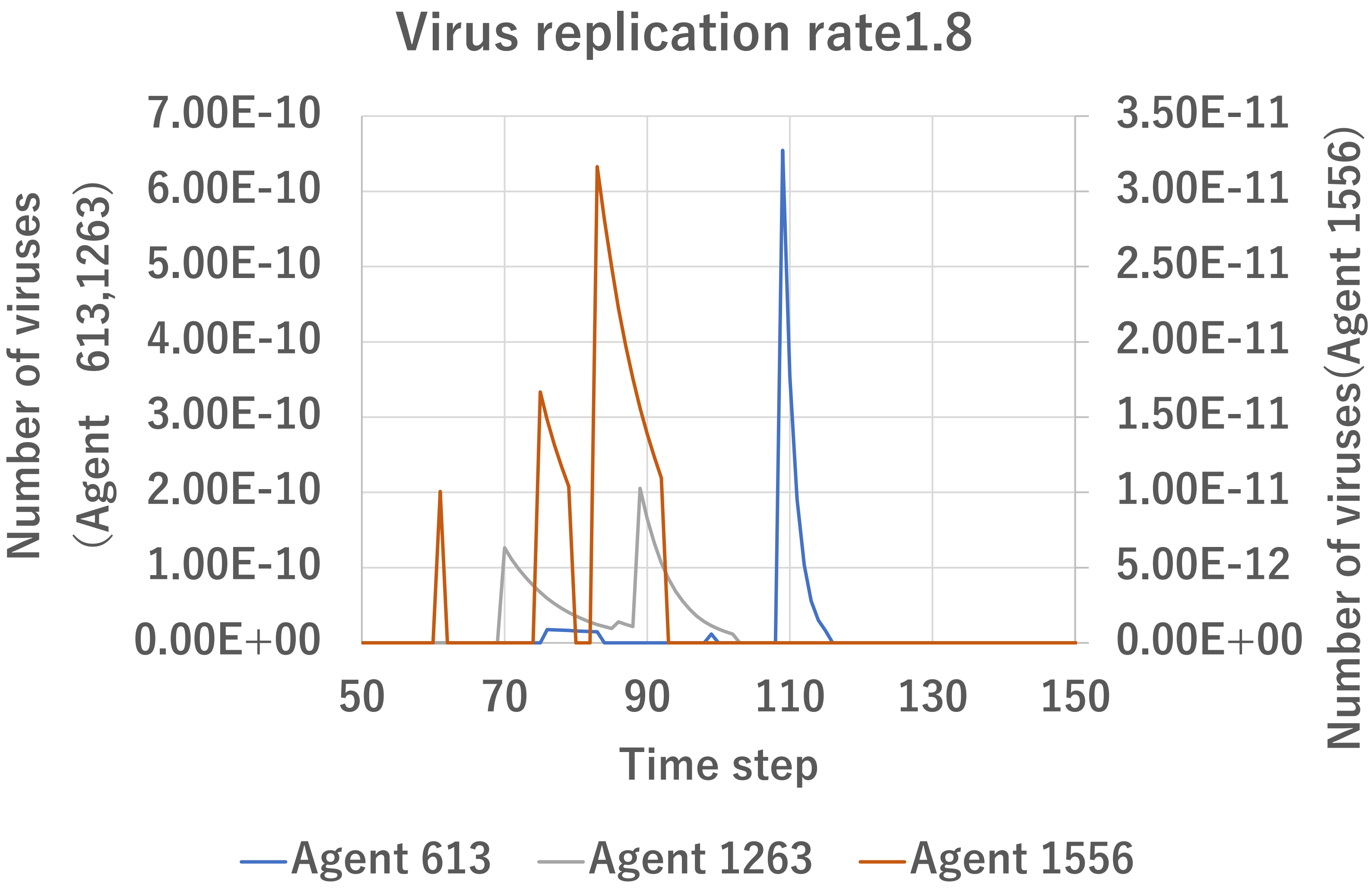


Fig.　Examples of cases of multiple infections

6. The decrease in the number of viruses discharged every time step by the attack of immune cells and antibodies are assumed as proportional to the number of viruses.
This assumption corresponds to the role of fever, associated with immunity.
The proportional constant are defined as virus attack rate, specified by agent-specific random number.
The viruses multiplies at a virus replication rate which is assumed constant.

8 The number of viruses is redefined every time step as shown below.

$$N^i{}_{VP}(t+1) = \left(1 - R^i{}_{release} - R^i{}_{attack}\right) \cdot N^i{}_{VP}(t) \cdot Rate_{replication} + \Delta N^i{}_{infected}(t) \qquad (4)$$

$$\Delta N^i{}_{infected}(t) = \sum_{j \in neigbours} N^j{}_{VP}(t) \cdot R^j{}_{released} R^i{}_{absorbed} \qquad (5)$$

where, $R^j{}_{released}$: *Virus releasing ratio of agent j*

$R^i{}_{absorbed}$: *Virus absorbing ratio of agent i*

$R^i{}_{attack}$: *Virus attack rate of agent i*

$Rate_{replication}$: *Virus replication rate defined as a constant value*

$\Delta N^i{}_{infected}(t)$: *Increasing increment of the number of virses at the time t*

1. Introduction

1) Although coronavirus pandemic has been calmed down, various new sources of the pandemic are showing up worldwide, and effective countermeasures are required.

2) Many infection models have been so far developed for understanding the infection problems, but they do not model the recovery process .

■ System dynamic model (SIR model, SIER model etc.)
An equation-based model which assumes the set of constant parameters Thus, heterogeneity of agents ,regarding both infection and recovery processes is not implemented in the model.

■ Agent-based model (ABM model)
Most of the previous infectious-diseases-related ABM models deal with the infection process in detail using geographical data, but the recovery process is not modeled from bottom-up, i.e. heterogeneity of agents' immunity is not implemented in the model.

1. Introduction

1) Mechanism-oriented agent-based modeling.

■ All social phenomena ,including infectious diseases pandemic , emerge as a result of heterogeneous human behaviors of various type and their interactions.

■ As agent-based modeling (ABM) is a bottom-up modeling method, using ABM we can construct an artificial society in which various phenomena emerge in the same principle in a real world, where the set of behavioral rules is the cause of the phenomenon in this artificial society.

■ By systematically changing the behavioral rules, and observing if the qualitative feature of the emerged phenomenon is the same as that of real world, we can determine an indispensable set of behavioral rules to reproduce the phenomenon .

■ The reason why the set of behavioral rules is indispensable, helps us to get better understanding of the causal mechanism of the phenomenon.

This procedure is a new validation method of ABM that I have been proposing , providing us a scientific methodology to understand the causal mechanism of social phenomena. The present study is one of such works.

Actual data observed during the early stage of corona pandemic in Japan.

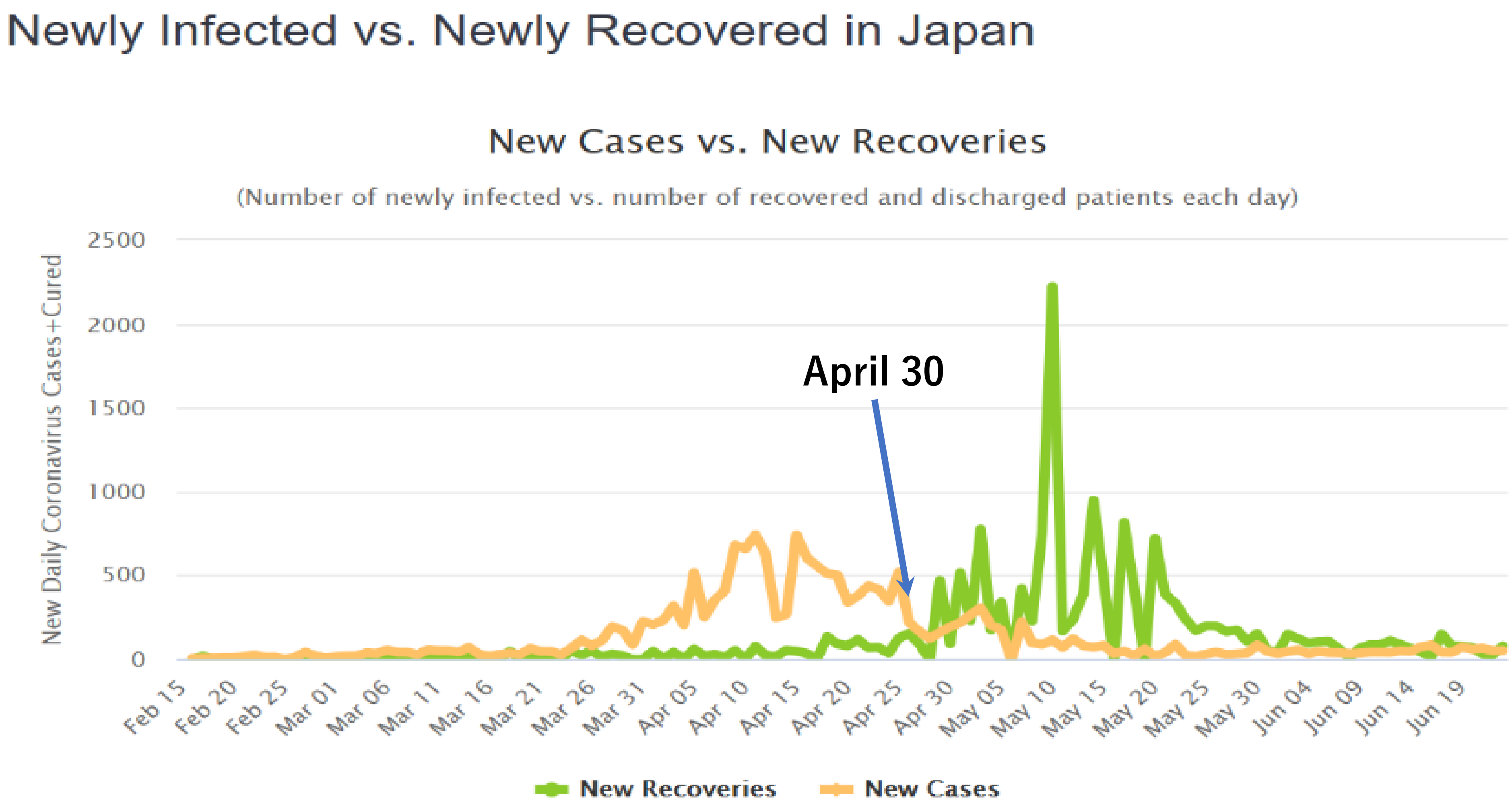


Figure 17. Changes in the numbers of newly infected and recovered people in Japan as of June 20, 2020.[17)]

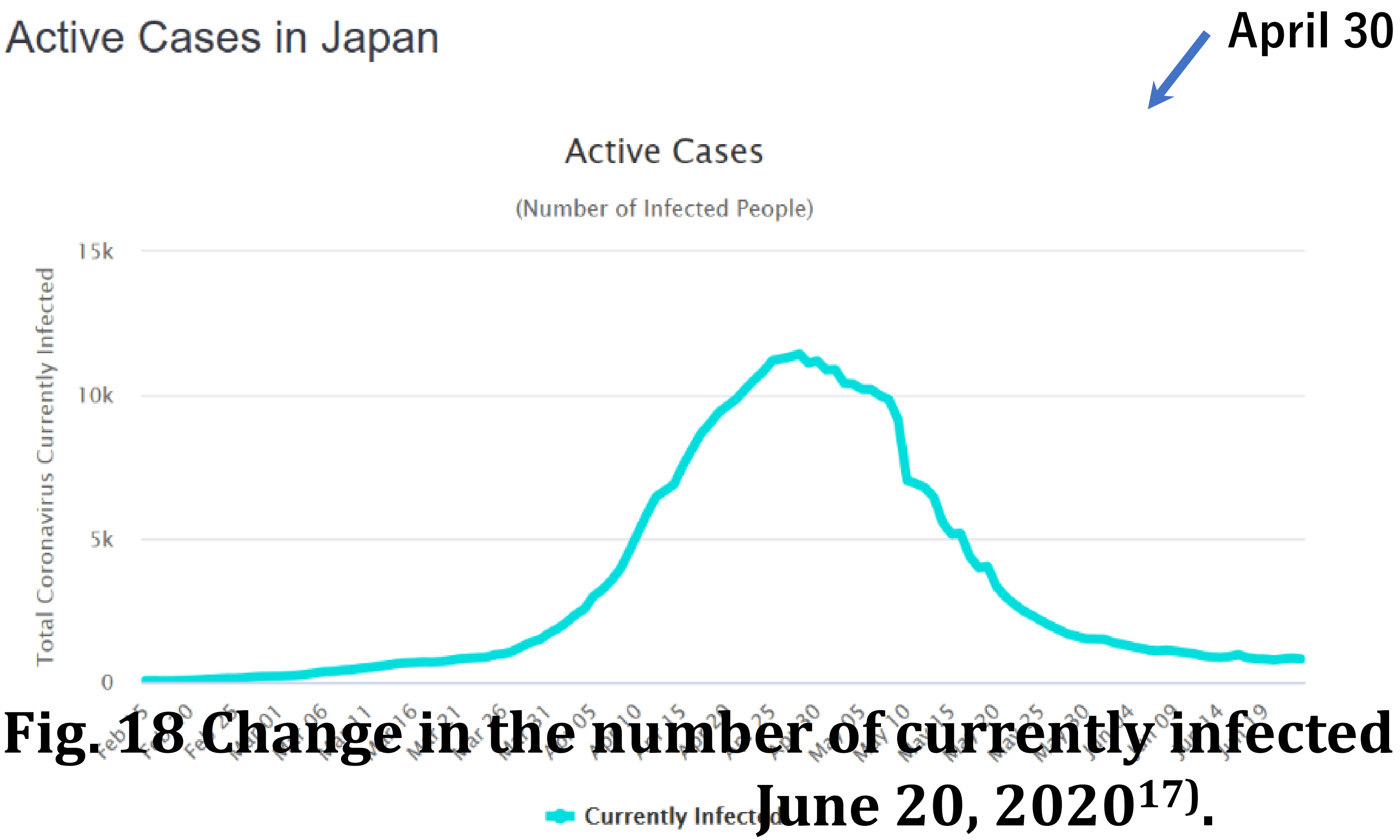
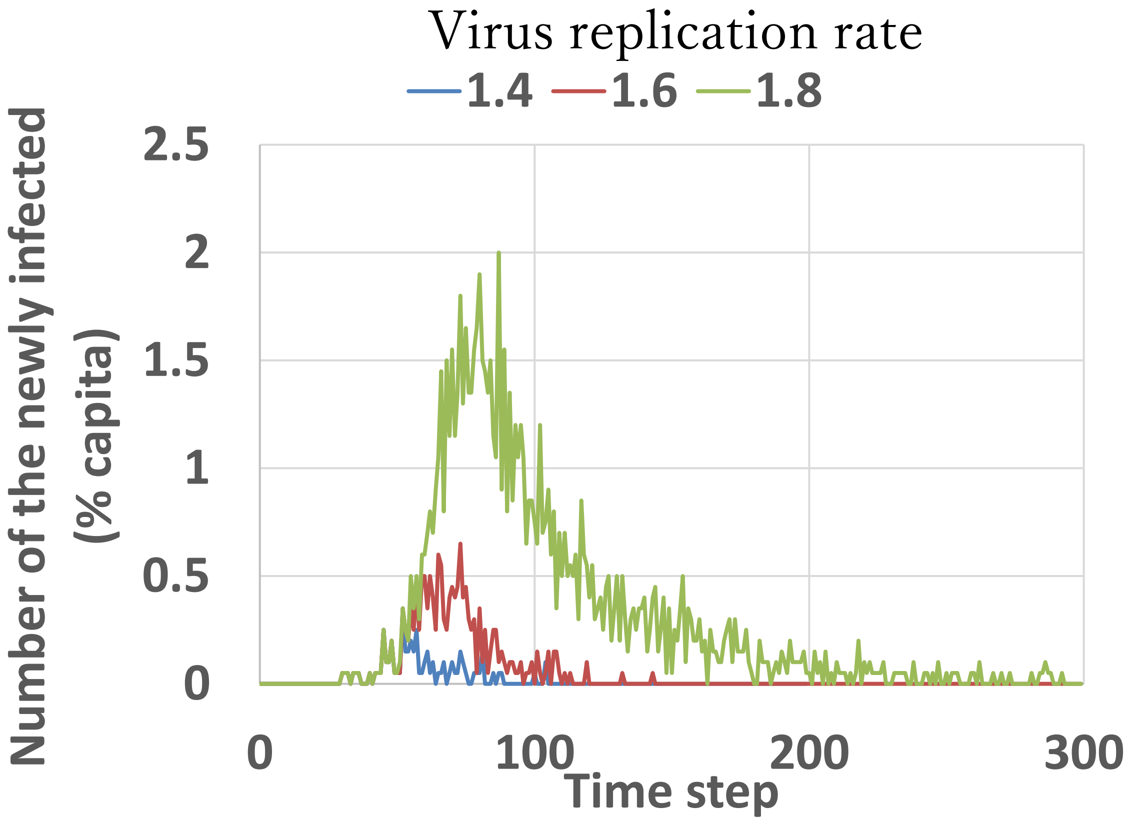


Fig. 18 Change in the number of currently infected people in Japan as of June 20, 2020[17).

Newly infected agents



Newly recovered agents

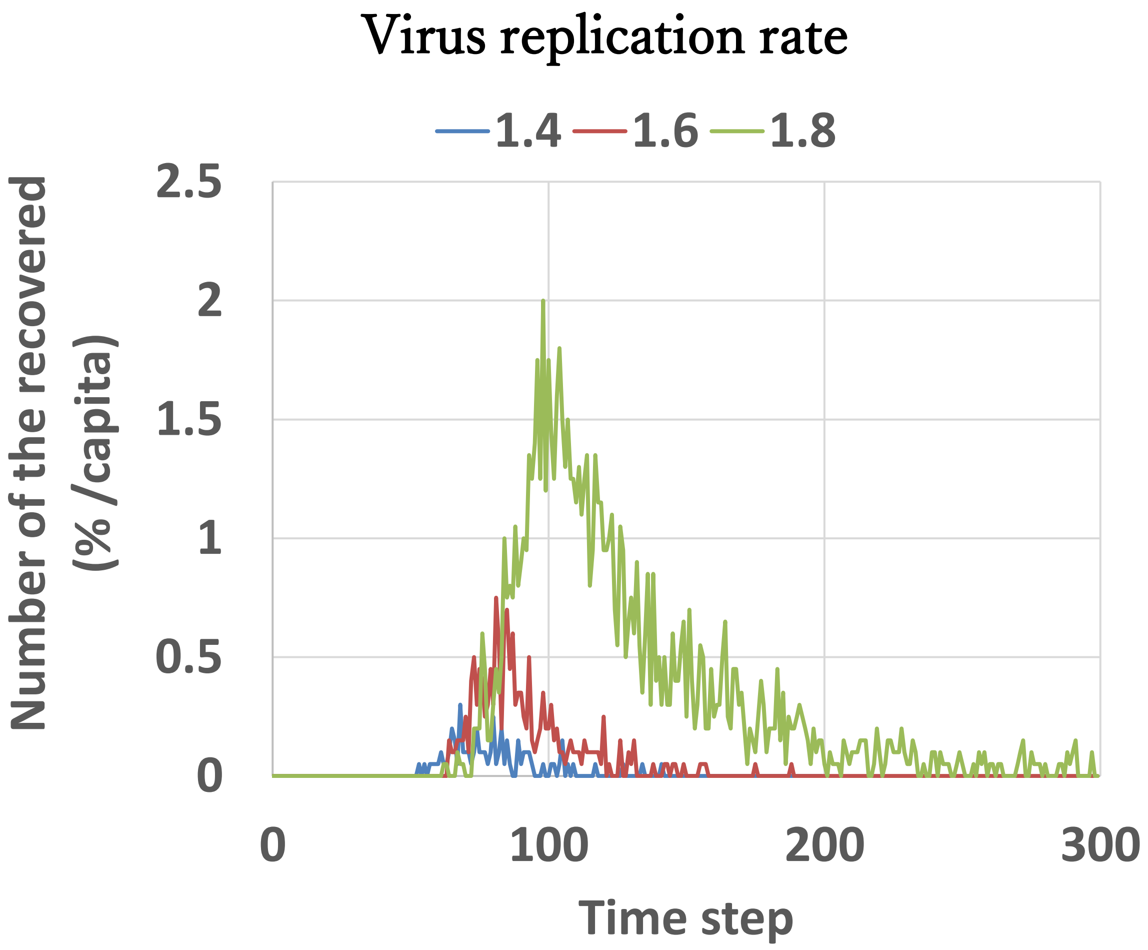


Fig. Effect of virus replication rate on the number of newly infected agents. And the number of newly recovered agents.

3.4 Effect of countermeasures on the pandemic behavior.

3.3.1Regulation of the movement

It is effective throughout the whole stage of the pandemic.

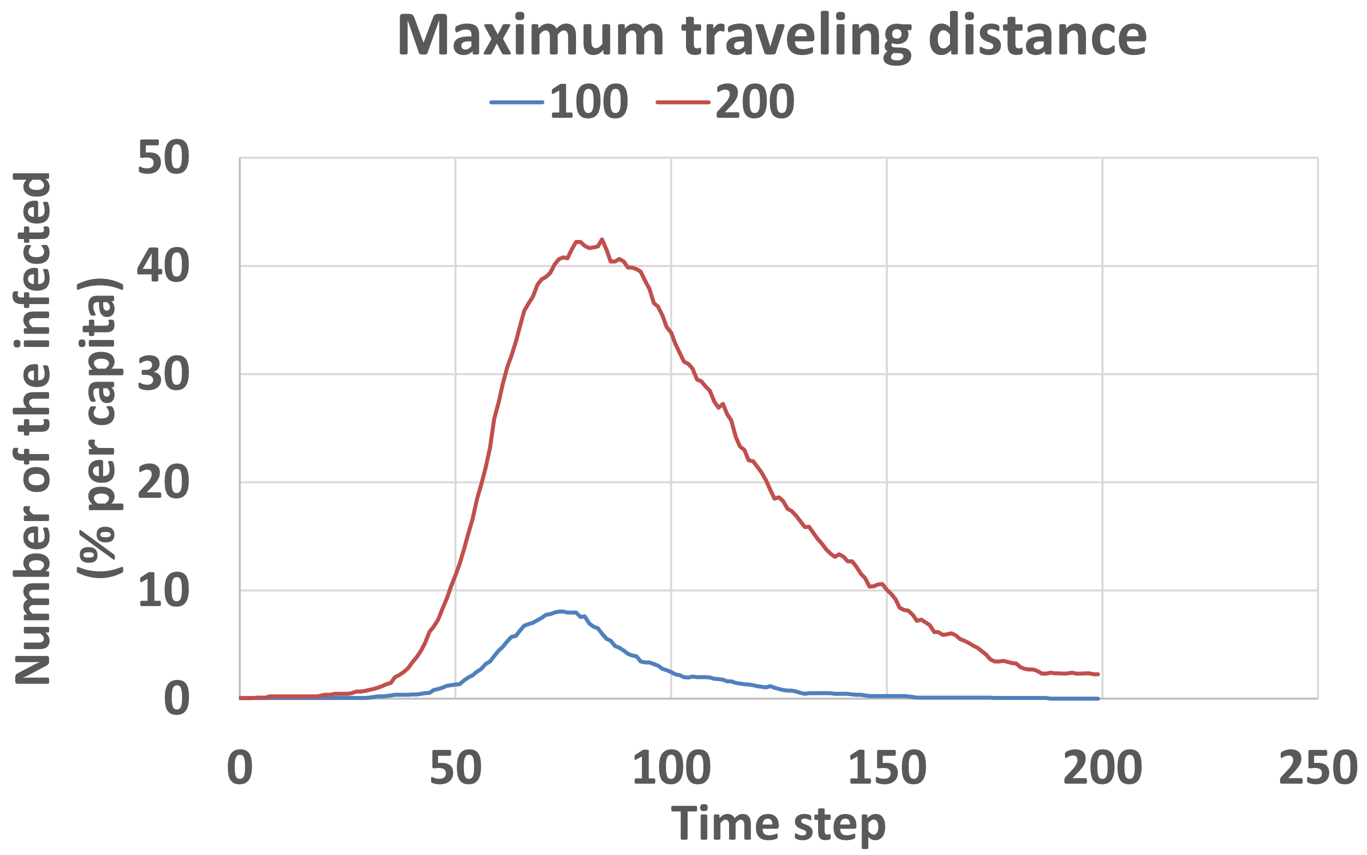


Fig. Effect of the maximum traveling distance on the total number of infected agents (virus replication rate: 1.6).

Effect of virus absorbing rate, which corresponds to the effect of wearing a mask.

Decreasing the virus absorbing rate by wearing masks decreases the number of infected persons, , meaning that wearing masks is effective for preventing the infection.

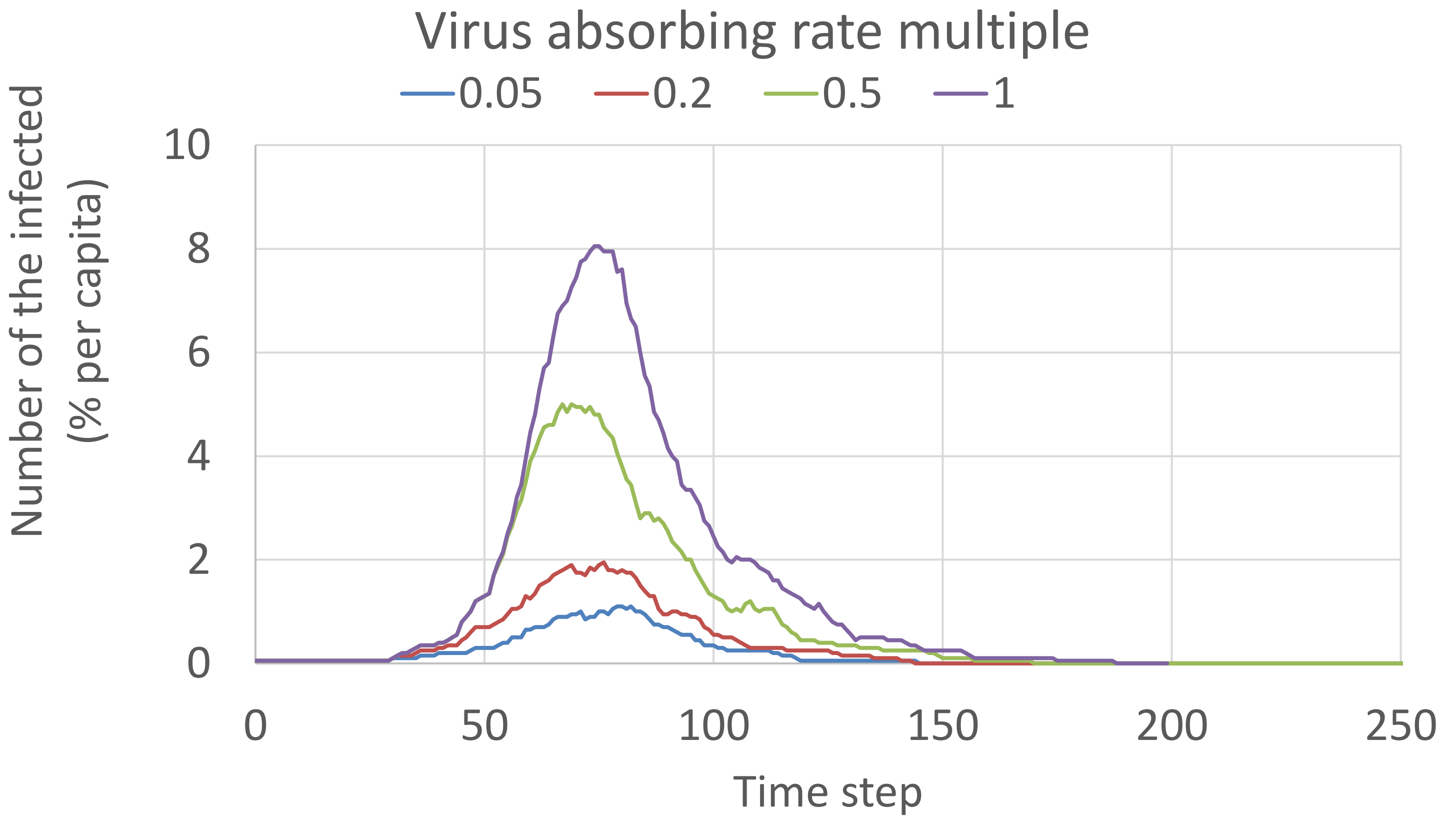
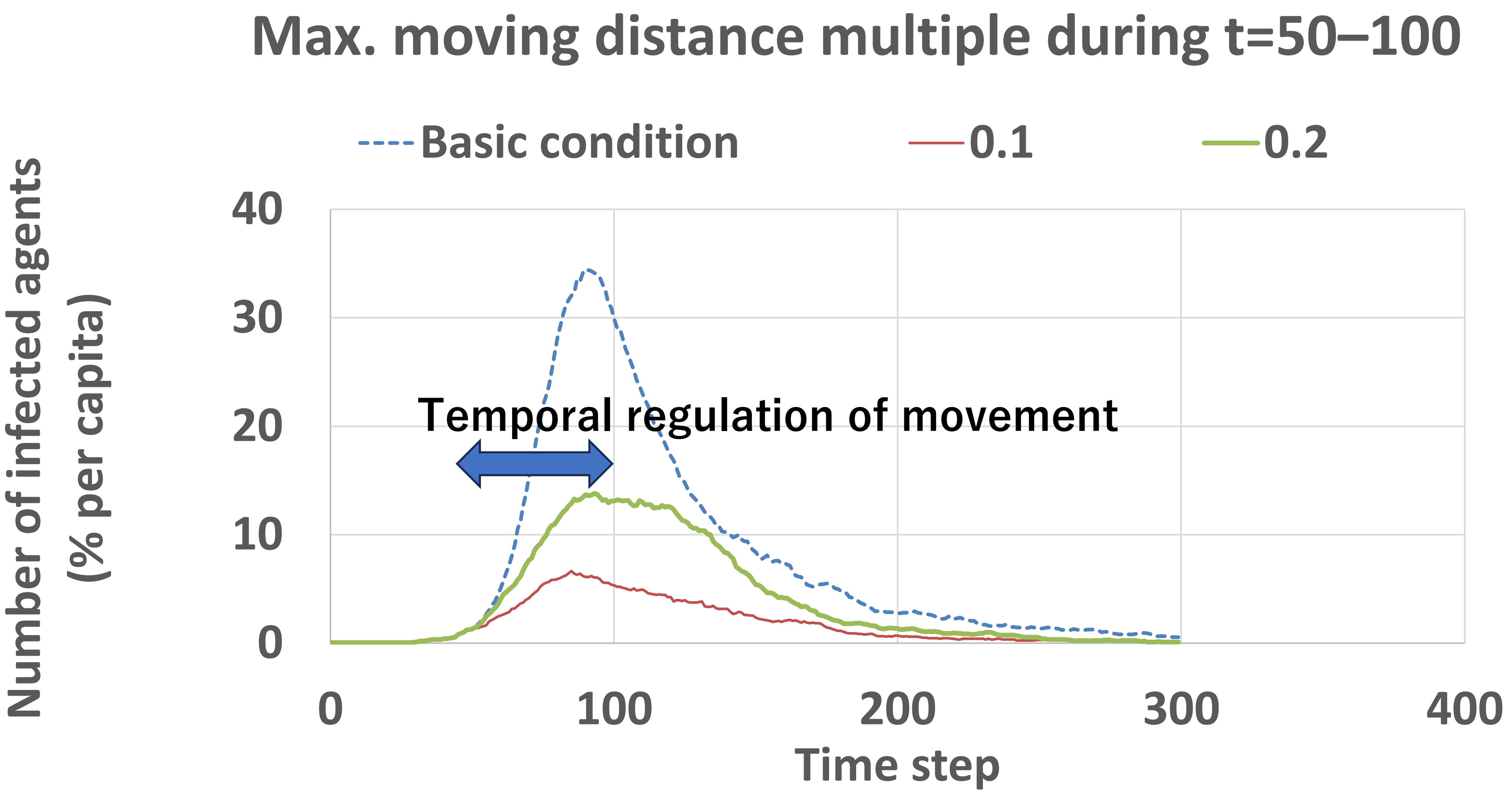


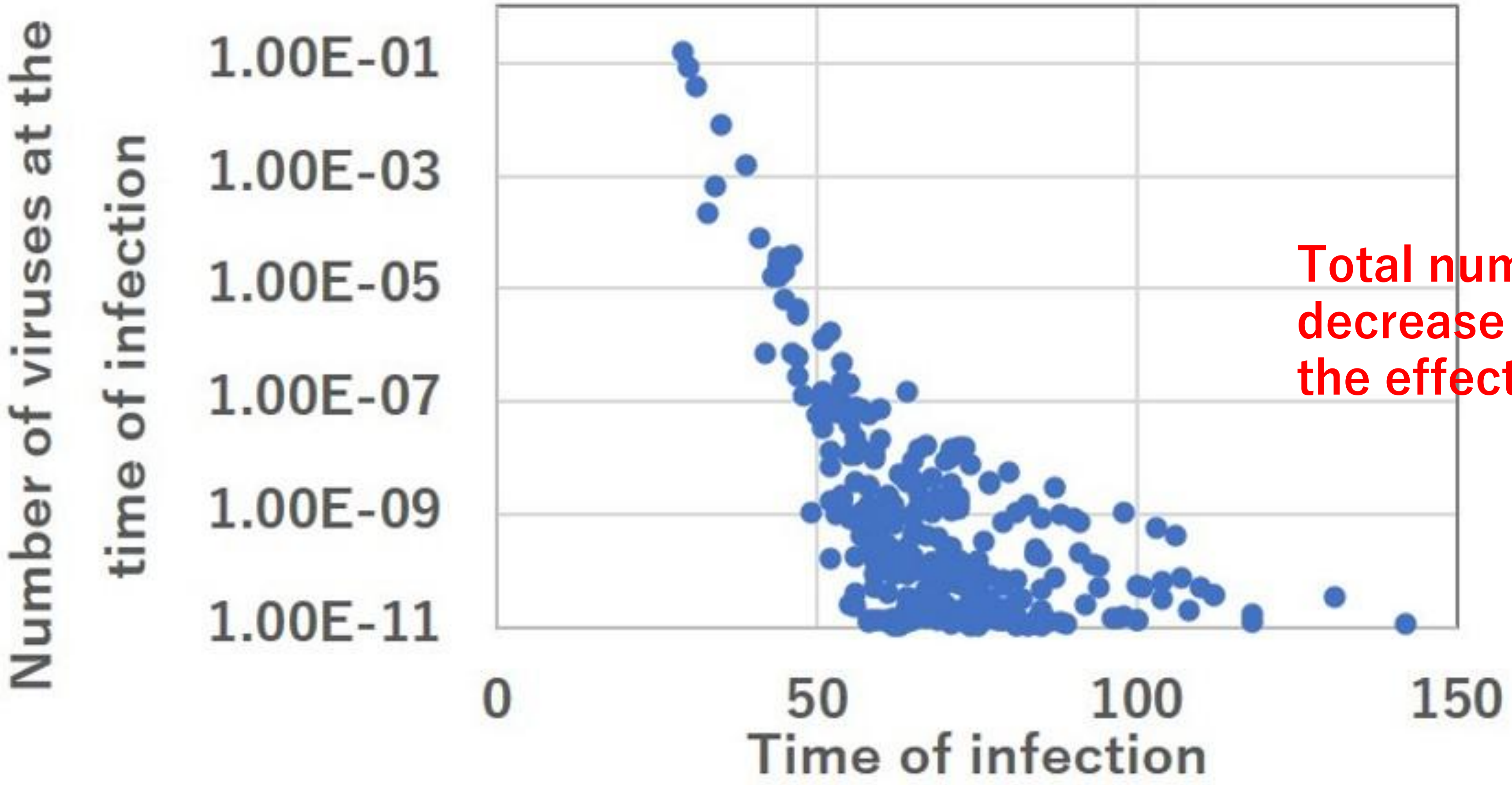
Fig. 16 Effect of the virus absorbing rate on the number of infected agents.

Temporal regulation of movement

- It drastically decreases the peak value of the number of infected agents.
- Resultant second wave, i.e., re-increase in the number, does not occur, if the new infected person does not enter into the system from outside.

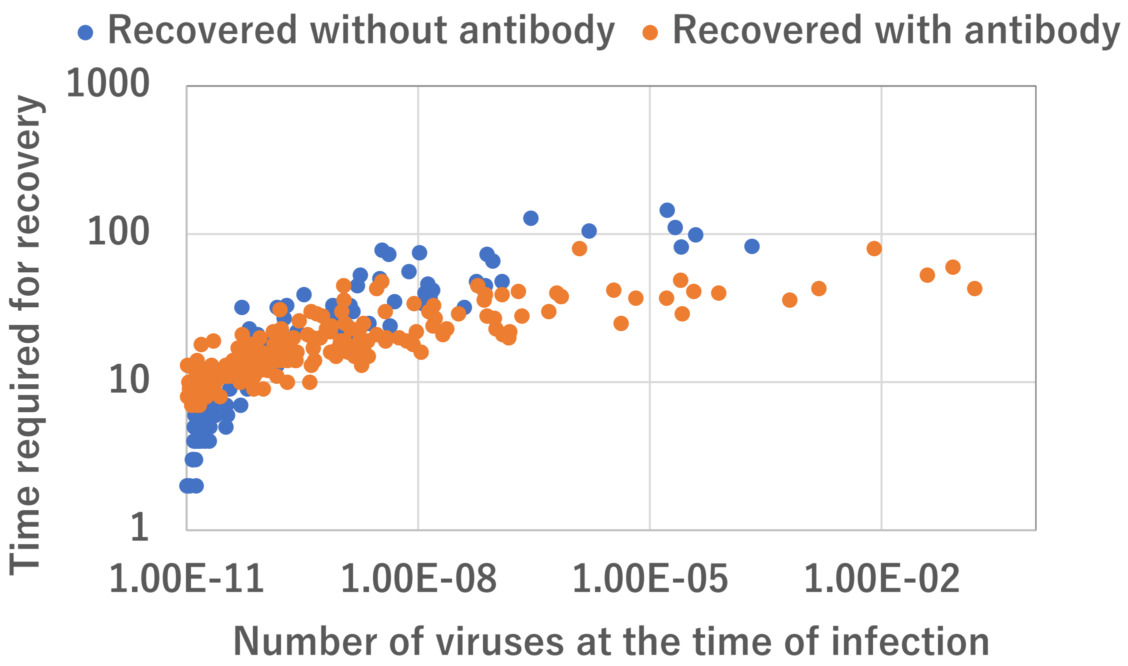


One of the important features that characterize the pandemic convergence is that the number of viruses at the time of infection decreases with time.



Total number of viruses decrease with time due to the effect of immunity.

Fig. Change in the number of viruses at the time of infection during infection spread and convergence.



Recovered without antibody
Recovered with antibody
Time required for recovery
1000
100
10
1
1.00E-11
1.00E-08
1.00E-05
1.00E-02
Number of viruses at the time of infection

Effect of virus replication rate on the number of infected neighbors.

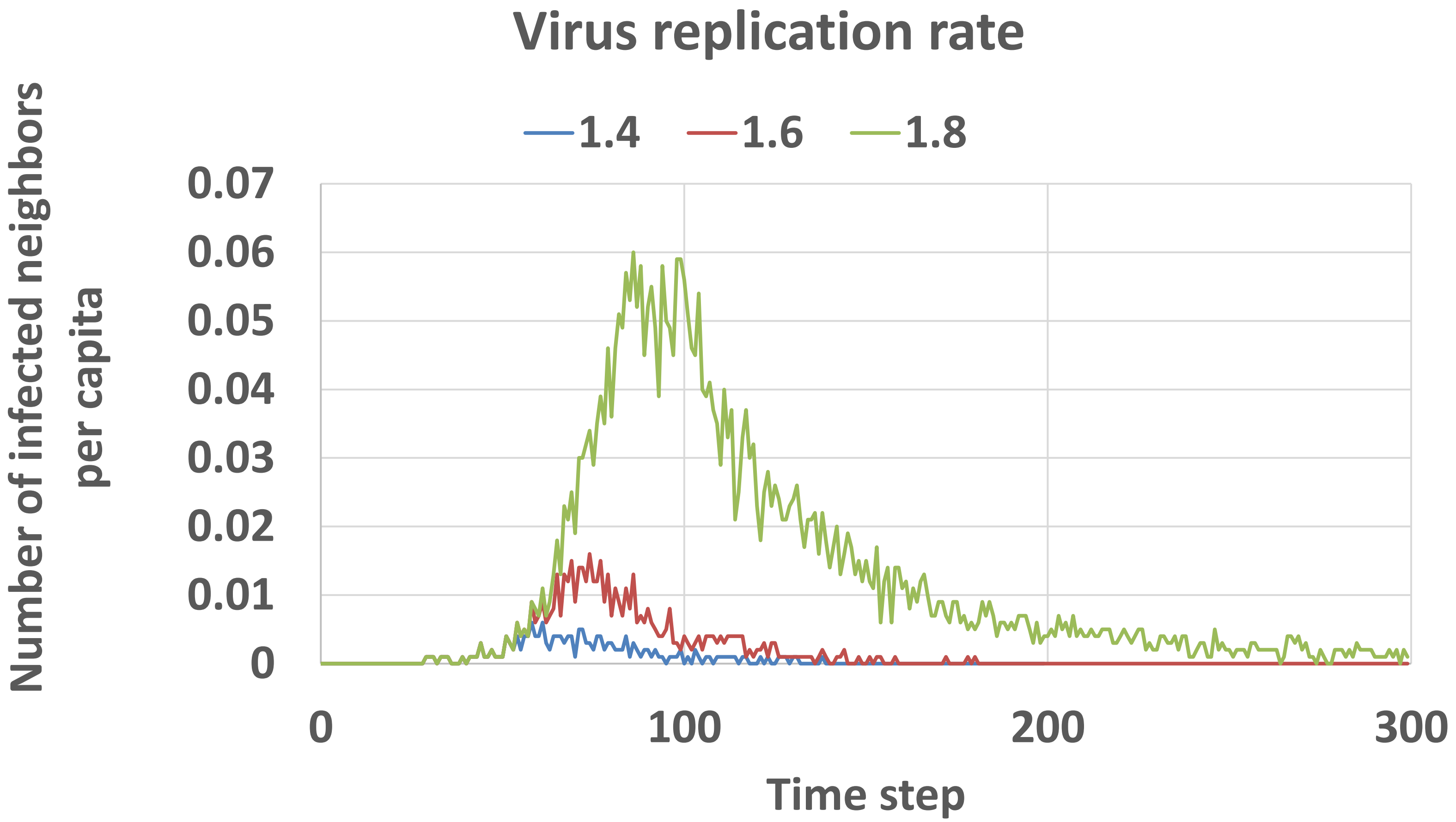


Fig. Effect of virus replication rate on the average number of infected neighbors.

The infection spread and convergence are essentially governed by the probability of a healthy person encountering the infected person.
The essential cause of recovery is that the number of viruses in the system decreases with time due to the effect of immunity, which progressively shorten the time for recovery.

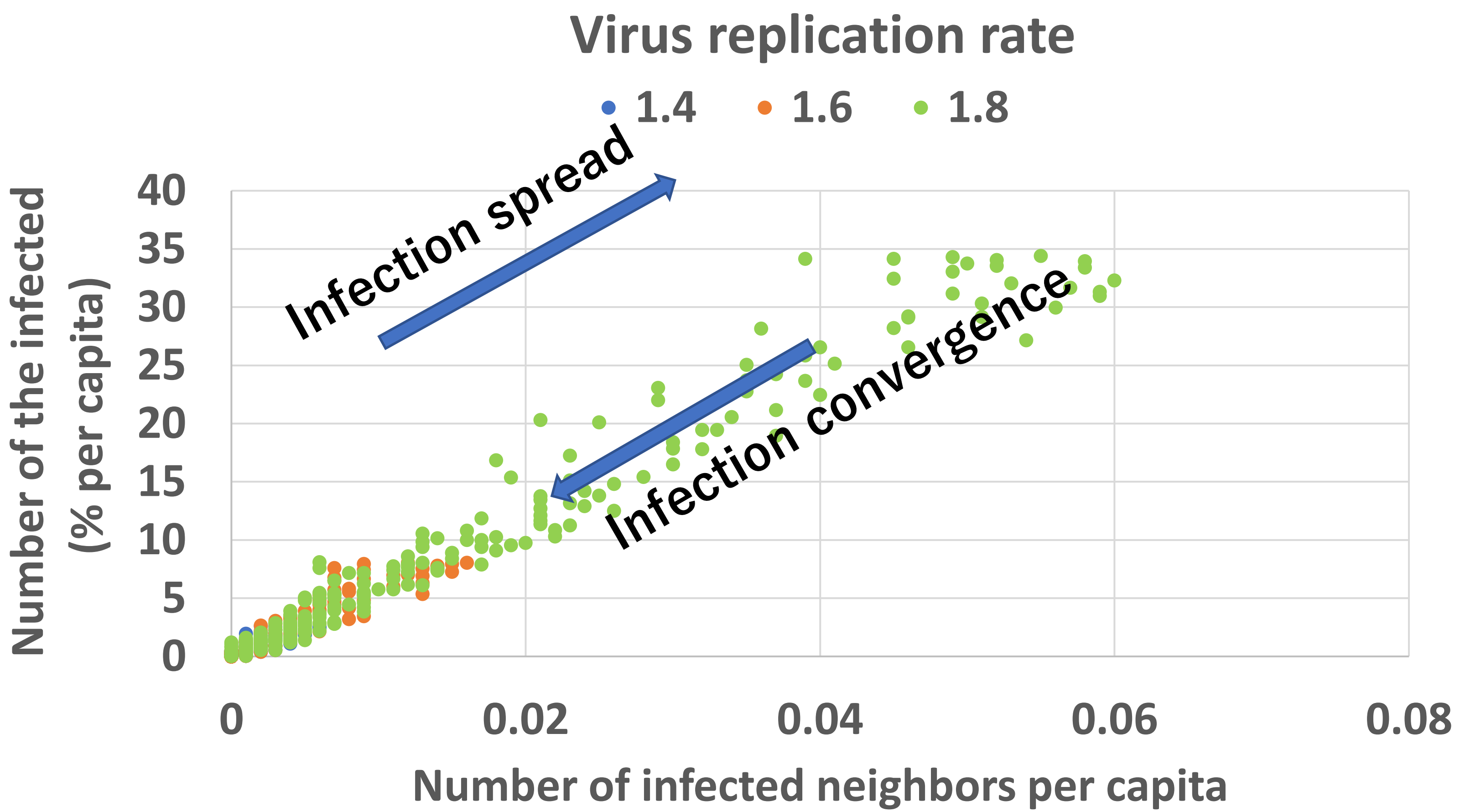


Fig. Relationship between the number of infected agents and the average number of infected neighbors.

4. Summary of the calculated results.
Fundamental mechanism of infection spread and convergence

1) Fundamental mechanism of infection spread and convergence is the progressive increase and decrease in the probability of a healthy person or a recovered person meeting with infected people.

2) Fundamental mechanism of the recovery is that total number of viruses in the system decreases with time due to the effect of immunity overcoming the virus replication effect.

3) The pandemic never converges if there exists a person whose immunity response is too small compared to the virus replication effect unless completely isolated, because of the infinitely increase in the total number of viruses in the system .

4) The most essential factor for the pandemic convergence is the role of fever associated with immunity. Without the effect of fever, the actual fact that the pandemic converges for the wide variety of virus replication rate cannot be reproduced.

5) The role of antibodies is to increase the discharging rate of viruses, thereby enlarging the upper limit of the virus replication rate for the pandemic convergence.

Principle of Mechanism-Oriented ABM

- Social phenomena emerge from heterogeneous human behaviors and interactions.
- Since ABM operates bottom-up with heterogeneous agent behaviors, phenomena in artificial societies can, in principle, emerge through the same underlying mechanisms as in the real world.
- By systematically changing behavioral rules and observing whether the model reproduces qualitative features of the phenomenon in the real world we can identify the essential behavioral rules necessary for its emergence.
- Considering the reason why specific rules are indispensable provides insights into the phenomenon’s causal mechanisms.

Agenda

1. Mechanism-Oriented Agent-Based Modeling

・Social problems requires understanding the causal mechanisms behind various social phenomena.

1.2 Properly validated agent-based modeling can fulfill this requirement.
Proposal of a new validation methodology in agent-based modeling.

1.3 Principles of mechanism-oriented agent-based modeling that enable rigorous validation and scientific understanding of causal mechanisms in social phenomena.

1.4 Applications to economic and other social phenomena.

2. An Agent-Based Model of Infectious Diseases that Incorporates the Roles of Immune Cells and Antibodies

2.1 Introduction

2.2 Model Overview

2.3 Results

・Validation ・Mechanisms of pandemic spread and convergence

・The role of fever as a critical factor in pandemic convergence

2.4 Conclusions

Qualitative and Quantitative Validation

- **Qualitative Validation:**
    1. **Define the qualitative characteristics of the phenomenon.**
    2. **Implement behavioral rules in simulations.**
    3. **Validate rules if the artificial society reproduces the real-world phenomenon; refine otherwise.**
    4. **Analyze indispensable behavioral rules to understand causality.**
    5. **Apply findings to real-world social dynamics.**

•Quantitative Validation:

1. **Develop a model incorporating validated behavioral rules.**
2. **Express key variables in ratio-based forms (e.g., non-dimensional variables).**
3. **Assign expected values for these variables and run simulations.**
4. **If the model quantitatively reproduces the phenomenon, it is validated; otherwise, refine parameters.**
5. **The validated rules and parameters allow forecasting of policy impacts and potential interventions.**

This methodology ensures scientific rigor without relying on ad hoc assumptions, offering a structured approach to understanding and predicting complex social phenomena.

Outline

1. What is the mechanism-oriented agent-based modeling
   1.1 Solving social problems requires an understanding of causal mechanism of various social phenomena.
   1.2 Agent-based modeling can meet this requirement if it is properly validated.
   1.3 A principle of mechanism-oriented agent-based modeling that allows us properly validate a model, scientifically understanding the causal mechanism of social phenomena.
   1.4 Application to economic phenomena and other social phenomena.
2. An agent-based model of infectious diseases that incorporates the roles of immune cells and antibodies: An application of mechanism-oriented agent-based modeling.
   2.1 Introduction
   2.2 The model
   2.4 Results
      ・Validation, ・Mechanism of pandemic spread and convergence
      ・ The role of fever is the most essential for pandemic convergence.
   2.5 Conclusions.

1.**Develop a model** incorporating the elucidated set of behavioral rules governing the social phenomenon.
2.**Express key variables in ratio-based forms**, such as non-dimensional variables or values normalized by represen
2.**Determine a set of parameter values** for ratio-type variables that are expected to reproduce the quantitative featur
3.**Implement these parameter values in program code** and run the simulation.
- If the model **successfully reproduces** the quantitative characteristics of the phenomenon, it qualifies as a valida
- If not, refine the parameter values and return to Step 3.

4.The **validated set of parameter values and behavioral rules** represent the indispensable model structure for accu

Using this validated model, we can **forecast** the potential effects of policies or countermeasures aimed at addressing the social issues under study.

This version enhances clarity and logical flow while keeping your original intent intact. Let me know if you'd like any further refinements!

Mechanism Oriented Agent-Based-Modeling(ABM)

ABM is a bottom-up modeling approach in which an artificial society is constructed on a computer and causal mechanism of a given phenomenon can be elucidated thorough a series of computer experiments.

I have proposed a new validation method for agent-based modeling, which I refer to as mechanism-oriented agent-based modeling.

The principle of this methodology is as follows:

- ■ All social phenomena ,including pandemics, emerge as a result of heterogeneous human behaviors of various types and interactions.
- ■ Since ABM is a bottom-up modeling approach, phenomena within the artificial society could , in principle, emerge under the same mechanism as in a real world, where the set of behavioral rules is the cause of the phenomenon.
- ■ By systematically changing the behavioral rules, and observing if the qualitative feature of the emerged phenomenon is the same as that of real world, we can determine an indispensable set of behavioral rules for accurately reproducing the phenomenon through a series of systematic computer experiments.
- ■ Then , we can elucidate the causal mechanism of the phenomenon by analyzing the reason why those factors are indispensable.

This procedure is scientifically rigorous without depending on the modeler’s ad hoc factors.

1. Introduction

1.1 Knowledge of the causality is required in social science.

■ Various social problems stem from the lack of understanding of causal mechanism of various phenomenon, in contrast to the development of natural science, resulting in unscientific policy decision-making based on inferences, which are primarily derived from the theories and statistical data, but the they differ among peoples, even among academic experts.

■ Agent-based modeling（ABM) is a promising methodology in social science, because it is a bottom-up modeling method. Therefore, in ABM, social phenomenon emerges in an artificial society due to the behaviors of and interaction among each heterogenous decision-makers (i.e. agents). This implies that an essential cause of a given social phenomena lies in the set of behavioral rules of agents of various types, not in the parameter values.

1.1 The Importance of Understanding Causality in Social Science

- **Many social problems arise from a lack of understanding of causal mechanisms, unlike in natural sciences, leading to unscientific policy decisions based on differing interpretations of theories and statistical data—even among experts.**
- **Agent-Based Modeling (ABM) is a promising bottom-up approach in social science. In ABM, social phenomena emerge within an artificial society through the behaviors and interactions of heterogeneous decision-makers (i.e., agents).**
- **This suggests that the fundamental cause of a given social phenomenon lies in the set of behavioral rules governing agents of various types, rather than in parameter values alone.**

1.2 Current status of validation in ABM in the literatures.

Since the pioneering work of "Models of Segregation"(T.C. Shelling,1969) and "Growing Artificial Societies"(R.L. Axtell et.al and J.M. Epstein, 1996), the type of ABM models are divided into "Abstract Model", "Middle Range Model", and "Facsimile Model"(N. Gilbert, 2007) .

As a result, even in the latest literature, it seems believed that there is no universally accepted approach for assessing a simulation, ("Method That Support the Validation of Agent-Based Models: An Overview and Discussion"(A.J. Collins, et.al., 2024).

This is due to the classification of agent-based models.

The type of models in ABM should be divided into qualitative and quantitative models. The validation should be assessed by the reproducibility of the qualitative or quantitative features of the phenomenon.

For this purpose, the model in ABM should be constructed as real as possible. For instance, in order to model the economic phenomena, the model should be able to calculate the flow of money and GDP.

Otherwise, no one can assess the reproducibility of the phenomenon.

1.3.2 Mathematical representation of the causality of social phenomenon and the validation of ABM.

Since all social phenomena emerges as a result of decision makers' action and interactions, the causal relationship is expressed as the followings.

$$S_T \rightarrow M_T \qquad (1)$$

$$S_T = \{V_1 \times V_2 \times \cdots \times V_n\} : A\ set\ of\ actions\ of\ decision\ makers\ interacting\ with\ each\ other$$

$$V_i : Various\ types\ of\ decision-making\ agents$$

$$V_i = \{A_i, B_i, C_i\}$$

$$A_i : A\ set\ of\ rules\ of\ behavior\ of\ agent\ i$$

$$B_i : A\ set\ of\ variables\ included\ in\ decision-making\ rules$$

$$C_i : A\ set\ of\ values\ of\ variables\ including\ attribute\ \mathrm{variables}\ and\ system\ state\ \mathrm{var}iables$$

$$M_T = \{Mq, q = 1, \cdots, p\}\ A\ set\ of\ social\ phenomena$$

$$M_q = \{m_k, k = 1, \cdots, s\}\ A\ set\ of\ qualitatively\ same\ phenomena$$

$$m_k : A\ quantitatively\ different\ social Phenomennon$$

As every phenomenon emerges as a result of decision-makers' actions and interactions, the quantitative cause of the phenomenon is $\{A_i, B_i\}$, and quantitative characteristics depends on $\{C_i\}$ which is changed by the input conditions.

Therefore, the model in ABM is classified
into qualitative model and quantitative model,.

■Qualitatively different phenomena are those that vary in the set of behavioral rules, $\{A_i, B_i\}$

■Quantitatively different phenomena are those that vary in the values of their input conditions that changes $\{C_i\}$.

This distinction is best understood through the following equation.

$$S_E \rightarrow M_E \qquad S_E \subset S_T, M_E \in M_T$$

$$S_E = \{V_1 \times V_2 \times \cdots \times \mathrm{V}_m\} : A\,set\,of\;actions\;of\;decision\,makers\,interacting\,with\,each\,other$$

$$V_i = \{A_i, B_i, C_i\} : Various\,types\,of\;decision - making\;agents\;i$$

$$A_i : A\,set\,of\;\;rules\,of\;behavior\,of\;agent\,i$$

$$B_i : A\,set\,of\;variables\,included\,in\,decision - making\,rules$$

$$C_i : A\,set\,of\;values\,of\;variables\,including\;attribute\,\mathrm{variables}\,and\;system\;\;state\,\mathrm{var}\,iables$$

$$M_T = \{Mq, q = 1, \cdots, p\}\;A\,set\,of\;\;social\;\;phenomena$$

$$M_E = \{m_k, k = 1, \cdots, s\}\;A\;particular\,social\;\;phenomenon\,that\,are\;qualitatively\,same$$

$$m_k : A\,quantitatively\,different\;socialPhenomennon$$

$$\Phi_E = \{\phi_i, i = 1, ...s\} : A\,set\,of\;qualitative\;\;features\;of\;\;the\;\;phenomenon$$

When replacing the particular social phenomenon M_E with a set of qualitative features of the phenomenon Φ_E , the causal relationship is expressed as follows.

$$S_E = \{A_E, B_E\} \rightarrow \Phi_E$$

Conditions for a model to be qualitatively valid

The causal relationship in the real system : $S_E = \{A_E, B_E\} \rightarrow \Phi_E$

The causal relationship in the model system: $S_M = \{A_M, B_M\} \rightarrow \Phi_M$

The following proposition holds.

(1) If $\Phi_M = \Phi_E$, **then,** $\{A_M, B_M\} \supseteq \{A_E, B_E\}$

$(\because A_E, B_E \textit{ is an indispensable element for emergence of } \Phi_E)$

(1) If $\Phi_M = \Phi_E$, then $\{A_M, B_M\} \supseteq \{A_E, B_E\}$ ($\because \{A_E, B_E\}$ is an indispensable element for emergence, if the above relationship does not hold, then $\Phi_M \neq \Phi_E$ is assumed, which contradicts the assumption.

(2) In (1) above, if V_S is the set of system state variables included in B_E, Φ_{VS} is the set of characteristics of the phenomenon that affect the determination of the variables, and $\{A_{VSE}, B_{VSE}\}$ is the indispensable factor that causes the variable, then $\{A_{VSE}, B_{VSE}\} \subset \{A_E, B_E\}$, $\{A_{VSM}, B_{VSM}\} \subset \{A_M, B_M\}$.

(3) When $\Phi_M = \Phi_E$, the model is a quasi-isomorphic mapping of the real system, and the emergence mechanism of the phenomenon in the model is equal to that in the real system.

1.3.2 The procedure of building a qualitatively valid agent-based model.

Step 1: Define qualitative features of a given real phenomenon.
In this case, all of the features could be reproduced by one set of behavioral rules , but there could be the case in which additional feature requires additional behavioral rules.

Step 2: Assume the set of behavioral rules that could be the cause of the features of the phenomenon.

Step 3: Write a program that represents the set of behavioral rules.

Step 4: Run the program and check whether the model reproduced the features of the phenomenon which is defined at Step 1.

Step 5: If the model reproduces the features of the phenomenon, go to next step. Otherwise, go to Step 2 to consider another set f behavioral rules.

Step 6: Analyze the reason why those set of behavioral rules are indispensable go reproduces the features of the phenomenon. Then, consider the causal mechanism of the phenomenon in the artificial society.

Step 7: Replace the causal mechanism in the artificial society to that in the real society.

1.3.2 The procedure of building a quantitatively valid agent-based model.

Step 1: Define the quantitative data of the phenomenon that should be reproduced by the model.
Step 2: Chose the set of behavioral rules that are indispensable to reproduce the qualitative feature of the phenomenon.
Step 3: Modify the set of variables in the model to a nondimensional variables or a ratio of the variable to a representative variable
Step 4: Set the parameter variables to the modified variables.
Step 5: Run the program and check if the program quantitatively reproduces the phenomena.
If the program quantitatively reproduces the phenomenon, go to step 6, otherwise, go to step 4.
Step 6: The model is the quantitative model that reproduces the same result with the phenomenon in the actual phenomena

5. A proposed strategy for controlling the pandemic while saving the economy

1) To identify the infected people and isolate the severly infected individuals or refuse their entry at the national border or at the comertial establishment.

Body temperature measurement followed by PCR test if necessary is the most reasonable, because

a fever is a sign of being infected ,showing the severity of infection ,highly infected individuals are characterized by high fever who are the minority and body temperature measurement requires the least cost , while PCR test provides ON/OFF information and requires much time and cost.

2) Each individual's self-monitoring body temperature and self-regulating his movemen on the bases of this information.

Each person should recognize his own normal temperature, and self-identify his state of infection by monitoring body temperature and self-regulate his movement if necessary. If many of the individuals employ this measure, the number of newly infected persons will drastically reduce and the pandemic will converge much faster.

3) Wearing masks and ventilation at the densely populated closed area

4) Temporary regulation of the movement of people followed by its mitigation for the short period is also effective for the pandemic convergence with small extent of the deterioration of the economy if the temporal period is short and the item 1) is perfectly conducted.

The pandemic phenomenon in the real world that should be reproduced by the model.

1. **The number of newly infected agents first increases and decreases .**
   Then the number of newly recovered agents increases and exceeds the number of newly infected agents at some point.

2. **When the number of recovered agents exceeds the number of infected agents.**
   The total number of infected agents shows its peak value.

3. **A regulation of the movement of people and wearing masks are effective for quick convergence of the pandemic.**

4. **Human being historically encountered various types of the pandemics, such as cholera, tropical infectious diseases , etc. that features viral particles with wide range of replication rates .**
   However, human being has overcome those pandemics and survived without being perished.