Investigation of the efficient protection from Influenza pandemic using CARMS

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Abstract:The new influenza A virus,H1N1-pdm, is spreading out all over the world including Japan.Since almost all the people are non-immunized for this new influenza virus, it spreads all over the world quickly. Currently, we have two options for the disease prevention, i.e. vaccination and antiviral drags. And among them, vaccination is the best way for mass protection. However current system of vaccine production has limitation for production number and preparation time. To understand "the most efficient mass protection", we simulate the influenza spreading by using the Cellular Abstract Rewriting System on Multusets, CARMS**.**

Keywords: Influenza, pandemic, CARMS

I. INTRODUCTION

The new pandemic influenza virus, H1N1-pdm, is efficiently spreading out all over the world, because almost all the people in the world do not have antibody against this new influenza virus. Vaccination is a biological tool for acquisition of immunity to a particular disease. For the mass protection from influenza virus infection, vaccine has been developed and used. Vaccinated host's immune system can recognize the influenza virus as foreign material then destroy and "remember" it. The immunized host can be more resistant to the pathogen, because they easily and quickly exclude the virus after the exposure. Therefore a vaccinated person can reduce morbidity risk when the person contacts with infected persons. As a logical consequence, vaccination can decrease the chance of contact between contagious and susceptive persons. Vaccination creates "buffer" between infected and non-infected persons and therefore prevents epidemic.

However, as current problem, vaccine production takes long time; even when a new strain of influenza virus with epidemic potential is identified and isolated; it will take approximately five to six month for the first supplies of approved vaccine to become available. And once a new vaccine has been approved, the vaccine production process typically takes between 6 and 9 months.

Effectiveness of influenza vaccine to prevent infection is not perfect; there are multiple reasons behind in vaccine efficacy, the most common of which are the declining immunological function and frailty associated with advanced age [2],[4],[5].

It is no wonder that vaccination is the most effective method for preventing influenza virus infection, but we should consider that effectiveness of vaccine is not perfect, so even if all citizens have been vaccinated, we cannot prevent infection completely. And since it takes time to create and produce vaccines, it is not easy to deliver vaccines to all citizens quickly [3],[4].

In this study we investigate the effectiveness of strategies of prevention of pandemics;

 i.　how many persons should be vaccinated?
 ii.　how high effectiveness rates of vaccines are required?,
iii.　how effective is we take the priority for inoculation?

II. Method

We model the influenza infection process by using the cellular automata of Abstract Rewriting System on Multisets, CARMS..

ARMS [6] was proposed in 1996 as an abstract model of chemical reactions, *Artificial Chemistry* (AC), in the context of the Artificial Life. An ARMSis a construct Gamma Γ =(A,w,R), where A is an alphabet, w is a multiset present in the initialconfiguration of the system, and R is the set of multiset rewriting rules. Let A be an *alphabet* (a finite set of abstract symbols). A *multiset* over A is a mapping M: A$\rightarrow$**N**, where **N** is the set of natural numbers; 0, 1, 2,…. For each a_i $\in$A, M(a_i) is the *multiplicity* of a_i in M, we also denote M(a_i) as [a_i]. We denote by A$^{\#}$ the set of all multisets over A,with the empty multiset, emptyset, defined by emptyset (a)=0 $\forall$ a $\in$A.

A multiset M: A$\rightarrow$**N**, for A={a_1,…, a_n} is represented by the state vector w = (M(a_1), M(a_2), …, M(a_n)), w. The union of two multisets M_1, M_2: A $\rightarrow$o **N** is the addition of vectors w_1 and w_2 that represent the multisets M_1, M_2, respectively. If M_1(a) $\leq$ M_2(a) for all a $\in$ A, then we say that multiset $M_1$is included in multiset M_2 and we write M_1 $\subseteq$ M_2.A *reaction rule r* over A can be defined as a couple of multisets, (s_u), with s_u $\in$A$^{\#}$. A set of reaction rules is expressed as R. A rule r = (s, u) is also represented as r = s$\rightarrow$u. Given a multiset w$\subseteq$ s, the

application of a rule r=s→u to the multiset w produces a multiset w' such that w' = w - s + u.

In order to simulate pattern formation, we compose cellular automataby using the ARMS and call it Cellular Automata of Abstract Rewriting System on Multisets (CARMS) [2]. An n dimensional ARMS is called nD-CARMS. A periodic boundary condition is assumed. In the 2D-CARMS which we used, each molecule has three attributes: position in a field (2 dimensional spaces, 500 x 500), velocity and the condition of health. The condition of health is represented by following three states; health, infected and cured (vaccinated).

In the initial state, each molecule is located randomly in the field and is given a random speed, v=1.0~2.0, and a random angle, Θ=0~2π. The size of an molecule is 12 in diameter. And the periodic boundary condition has been taken. Each molecule updates velocity (speed and angle) at the every collision, while an molecule does not collide, its velocity and angle do not change. When a health molecule collides with an infected molecule, its condition of health is changed to "infected"; while other types of collisions do not change the condition of health. An infected molecule changes the condition of health from "infected" to "vaccinated" after 200 time steps from when it has been collided with an "infected" molecule. In the initial state of every simulation, we set the number of infected molecule is one.
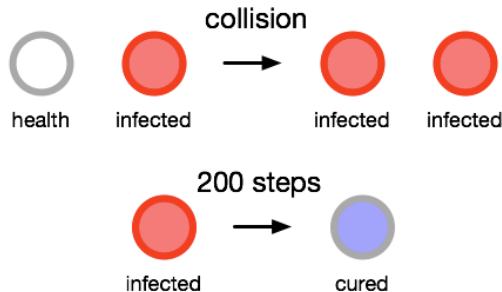

Fig.1 Reaction rules of molecule s actions

II. Experiments

Experiment1: how many parsons should be vaccinated?;
We set the p for immunization rate for vaccines of a group, where we assume that the vaccine efficacy rate is 100% so every person gains anti-body by an inoculation. We increase p from 0.1 to 0.9 by 0.1 and examine the temporal development of the number of infected persons, the number of step until the termination epidemic and the number of not infected persons until the epidemic terminates.

Experiment2: how high effectiveness rates of vaccines are required?
In order to express the effectiveness rate of a vaccine, we set the threshold value for applying reaction rules; in case an molecule has a low effective vaccine then the

molecule will be infected when it will collide infected molecule s few times, where the threshold value, Θ set to small, and the reaction rule of "health + infected → infected, infected" (Fig.1 upper) will not be fired within Θ times of collisions with infected molecule s, while in case the effectiveness is high, Θ is set to large and the reaction rule will not be applied within many times of collisions . We examine the change of temporal development of the number of infected persons, when Θ is 1, 2, 5 and 10.

Experiment3: how effective if we take the priority for inoculation?
We simulate the case when we take priority of inoculating for high risk of infection possessed molecule s. In order to express the degree of the risk of infection, we use the velocity of moving of an molecule ; when the velocity is slow then the molecule will not collide against many infected molecule s so the probability of infection will be low, while the velocity is fast then the molecule will collide against many infected molecule s and the probability of infection will be high. We classify molecule s into three groups with according to its risk of infection as low, middle and high. In this experiment, the total number of molecule s is 300 and they are classified into three groups equally (100 molecule s each). We examine the case when the all molecule s in one of these groups take priority for inoculation and the change of temporal development of the number of infected persons are examined.

III. Results

All of the results of simulations are the average of 100 trials.

Experiment 1
When the immunization rate for vaccines $p = 50\%$, the peak of the number of infected molecule s was suppressed around 75% low compared to the case when $p = 0\%$; however, the duration of epidemic was prolonged and all molecule s is infected, after all (Fig.2).
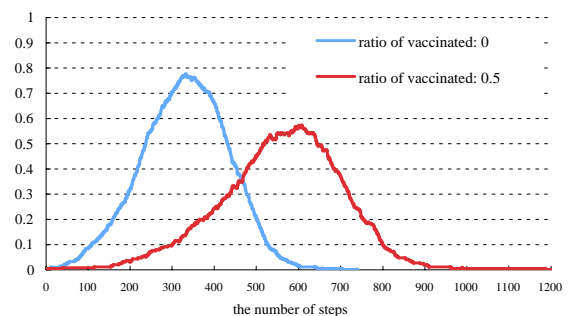

Fig.2 temporal development of the number of infected molecule , where the blue line illustrates the case when $p = 0\%$ and the red line illustrates when $p = 50\%$.

The average rate of the number of not infected and

infected molecule s until the epidemic terminates (we will denote this rate as γ) increased exponentially when $p = 0.8$; so when p is equal or larger than 0.8 almost no one was infected. In such cases, infected molecule s were likely to be disappeared until 200 simulation steps so the value of γ increased rapidly; when p = 0.8 and 0.9, the number of cases when no epidemic emerges was 25 and 42 for 100 times of trials of simulations (Fig.3).
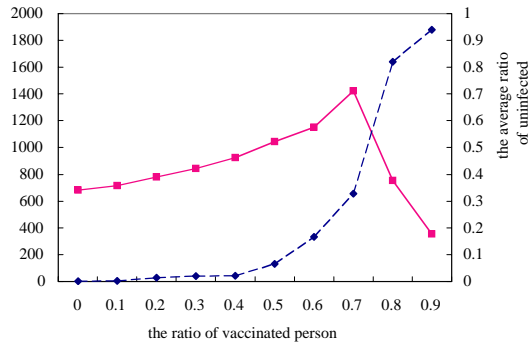

Fig.3 the immunization rate for vaccines p and the average of the number of not infected molecule s until epidemic terminates.

Experiment 2

We examined temporal development of the number of infected molecule s when the effectiveness rate of vaccinated, Θ is 1, 2, 5 and 10. When $\Theta = 5$, the peak of the number of infected molecule s were largely suppressed, compared to the case when $\Theta = 1$ or 2. When $\Theta =1$, 2, and 5, the ratio of the number of infected molecule s for the total number of molecule s were 0.88, 0.78 and 0.48, respectively. And when $\Theta = 10$, no epidemic emerges and infections were terminated (Fig.4).
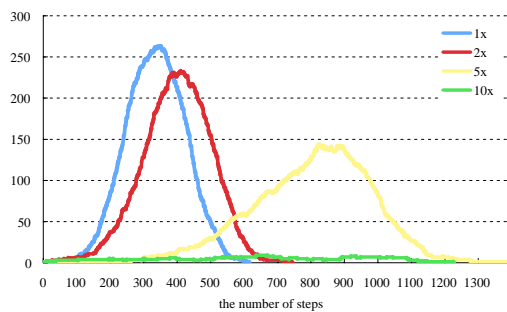

Fig. 4 temporal development of the number of infected molecule s, where blue line illustrates the case when $\Theta =1$, red line, $\Theta =3$, yellow line, $\Theta =5$ and green line, $\Theta =10$.

Experiment 3

When only the low risk infection molecule s were vaccinated, the ratio of the number of infected molecule s at the peak of epidemic is 0.83 (=165/200), it was

lesser than the case when no molecule was vaccinated (276/300 = 0.92). When only the middle risk infection molecule s were vaccinated, the number of infected molecule s at the peak was 0.75 (150/200), while only the high risk molecule s were vaccinated, the number of infected molecule at the peak was 0.45 (=89/200) (Fig.5).
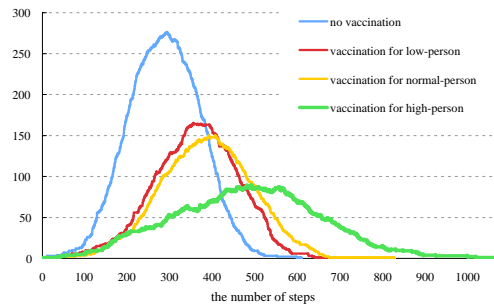

Fig.5 temporal development of the number of infected molecule s when the priority for vaccination is taken; where the red line illustrates when low risk infection molecule s are vaccinated, the yellow line, middle risk molecule s are vaccinated and the green line, high risk molecule s are vaccinated (the blue line illustrates the case when no molecule is vaccinated).

IV. Discussion

It is no wonder that vaccination is effective method for preventing infection; throughout simulations it has shown that vaccination creates "buffer" between infected and non-infected persons and prevents epidemic.

The result of experiment 1 shows that vaccination suppresses the number of infected molecule s at the peak of pandemic; it is important for controlling the pandemic, because the high peak of the infected people's number causes break down of social and medical structures. However, the result of experiments shows that large scale vaccination (more than 80% in the experiment) will be required for preventing pandemic, otherwise vaccination cannot completely prevent spreading of the infection and it will be smoldering until almost all the persons are infected, even if it can suppress the peak number of infected persons during pandemic.

It has been reported that effectiveness of influenza vaccine to protect form the infection is not perfect; because of the declining immunological function and frailty associated with advanced age [1]. However the result of experiment 2 shows that even if the quality of vaccine is not perfectly good, it can prevent the pandemic.

The result of experiment 3 indicates that the priority for vaccination for high risk infection molecule s, such as medical experts, will be effective for preventing epidemic. Hence, in case we cannot take large scale vaccination, we can suppress the pandemic by the priority for vaccination; this policy has been proposed

by the Ministry of Health and Welfare of Japan and this result supports its effectiveness.

In this study, we modeled temporal development of the number of infected / non-infected persons; to expand this simple model including diffusions in the space [1] is our future work.

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