Modelling to Contain Pandemic Influenza A (H1N1) with Stochastic Membrane Systems: A Work-in-Progress Paper

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Abstract. Pandemic influenza A (H1N1) has spread rapidly across the globe. In the event of pandemic influenza A (H1N1), decision-makers are required to act in the face of substantial uncertainties. Simulation models can be used to project the effectiveness of mitigation strategies. Since nature is very complex, the perfect model that explains it will be complex too. Membrane system (P system) can be a perfect model modelling ecological system. This paper briefly describes stochastic membrane systems for modelling spread of pandemic influenza A (H1N1) in an isolated geographical region. The model is based on a discrete and stochastic modelling framework in the area of Membrane Computing. This model can be a useful tool for the prediction of infectious diseases within predefined areas, and the evaluation of intervention strategies.

Keywords: pandemic influenza A (H1N1), pandemic spread modelling, stochastic membrane systems, membrane computing.

1 Introduction

Cases of pandemic influenza A (H1N1) were first reported in Mexico in April 2009 in [1]. Subsequently, the virus spread rapidly across the United States and Canada, and then became a global concern [2]. The influenza A (H1N1) virus is highly transmissible. Urgent implementation of measures against pandemic influenza A (H1N1) is required. Modelling the spread and control of pandemic influenza A (H1N1) can help to predict the spread tendency of pandemic influenza A (H1N1), thus help to choose the effective measures to control the pandemic.

The application of mathematical modelling to the spread of epidemics was initiated by Daniel Bernoulli's work on the effect of cowpox inoculation on the spread of smallpox. Classical epidemic modeling was built on differential equations. These models revealed the threshold nature of epidemics and explained herd immunity, where the immunity of a subpopulation can stifle epidemics' outbreaks to protect the entire herd. But such models are ill-suited to capture the direct contacts between individuals and complex virus spreading social networks.

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P systems, or membrane systems, were introduced in [3] as a class of unconventional computing devices of distributed, parallel and nondeterministic type, inspired by the compartmental structure and the functioning of living cells. P systems are based on a hierarchical structure of nested membranes, inspired by the structure of living cells. Each region can contain objects, mimicking the presence of molecules, proteins, etc. in the compartments of living cells. Moreover, each region has an associated set of multiset rewriting rules. These rules are motivated by chemical reactions that occur inside the regions of living cells. We can refer to [3,13] for details on Membrane Computing.

Although most research in P systems concentrates on the computational power of the devices involved, lately they have been used to model biological phenomena within the framework of computational systems biology. In this case P systems are not used as a computing paradigm, but rather as a formalism for describing the behavior of the system to be modelled. In this respect, several P systems models have been proposed to describe oscillatory systems [4], signal transduction [5], gene regulation control [6] and quorum sensing [7]. These models differ in the type of the rewriting rules, membrane structure and the strategy applied to run the rules in the compartments defined by membranes.

Recently, P systems have been applied in modelling complex systems. In particular, P systems are used to model cellular processes and biochemical or cellular systems to analyze the complex behaviors [8,9]. They are feasible also for the investigation of biological systems at a higher scale order, such as the ecological systems, where the interactions between individuals are analyzed [10].

As P systems are inspired from the structure and functioning of the living cell, it is natural to consider them as modelling tools for biological systems, within the framework of systems biology, being an alternative to more classical approaches like ordinary differential equations (ODEs) and to some recent approaches like Petri nets and π-calculus.

Simulating natural phenomena using membrane systems can keep the most important natural factors and overcome some limitations of classical mathematical models. The complex social networks and interaction between individuals can be expressed by the complex structure and rules of membranes. There are enormous cells and chemical substances even in a limited space. Chemical substances in membrane are natural agents, and they quite differ from cyber agents where chemical reactions inside membrane systems are obedient to the nature's law. What is more, the chemical reactions in membrane systems are highly parallel. In this respect, using membrane systems to model the spread of pandemic may be more advantageous than classical mathematical modelling such as ordinary differential equations modelling.

Modelling pandemics with P systems is a novel way to use the concept of agent-based model to model pandemics spreading. P systems show their power of modelling and investigating ecological systems. Modelling pandemics with P systems can capture the direct contacts between individuals and complex virus spreading social networks. It also overcomes the shortcomings of classical mathematical modelling.

2 Objectives

We extend the stochastic modelling framework of dynamic probabilistic P (DPP) systems, initially introduced in [9]. The goal is to construct a model of dynamic probabilistic P systems to simulate and investigate the spread and control of pandemic influenza A (H1N1) in an isolated geographical region.

3 Modelling Framework

Dynamical probabilistic P systems are membrane systems where probabilities are associated with the rules, and such values vary during the evolution of the system according to a prescribed strategy. Each membrane identifies a *region*, delimited by it (if any) immediately inside it. The number of membranes in a membrane structure is called the *degree* of the P system. The number of hierarchical levels in a membrane structure is called the *depth* of the P system. The whole space outside the skin membrane is called the *environment*. Different from the DPP systems introduced in [10], the probabilities are given instead of been evaluated in our model and our construct of DPP systems is a little different from construct in [10]. More details about DPP systems and examples of simulated systems can be found in [12].

Definition 1. *A dynamical probabilistic P system of degree n is a construct*

$\Pi = (O, \mu, M_0, \ldots, M_{n-1}, R_0, \ldots, R_{n-1}, I)$ *where:*

- O *is an alphabet, and its elements are called objects.*
- μ *is a membrane structure consisting of n membranes labeled with the numbers $0, \ldots, n-1$. The skin membrane is labelled with 0.*
- $M_i, i = 0, \ldots, n-1$, *is the initial multiset over O inside membrane i.*
- $R_i, i = 0, \ldots, n-1$, *is a finite set of evolution rules associated with membrane i. An evolution rule is of the form $r : u \xrightarrow{P} v$, where u is a multiset over O, v is a string over $O \times (\{here, out\} \cup \{in_j | 1 \leq j \leq n-1\})$ and $P \in \mathbb{R}^+$ is a constant between 0 and 1 associated with the rule.*
- $I \subseteq \{0, \ldots, n-1\}$ *is the set of labels of the analyzed regions.*

A DPP system works as follows: A fixed initial configuration of Π is given according to the simulation design, hence it consists of the multisets initially present inside the membrane structure, rules and corresponding probability of each rule.

At each step of the evolution, all applicable rules are simultaneously applied and all occurrences of the lefthand sides of the rules are consumed. We assume that the system evolves according to a universal clock, that is, all membranes and the application of all rules are synchronized. The applied rules are chosen according to the probability values assigned to them; the rules with the highest normalized probability value will be more frequently tossed. If some rules compete for objects and have the same probability values, then objects are nondeterministically assigned to them.

4 Method

Based on the framework of dynamical probabilistic P systems, a model is constructed to reveal and simulate the spread and control of pandemic influenza A (H1N1) in an isolated geographical region. It is believed that the model and parameters are based on reasonable estimates of what could happen, and these results are assisting the planning of a response.

Membranes can be agents representing different regions in our socity. For example, we can make some membranes represent schools and some represent workplaces and others represent households, etc. The different substances in and out of membranes can be agents representing different individuals (susceptible, infected, recovered) in our society. The activities of human beings can be modeled by some regulated application rules of substances. The quantity of regions and people can be enormously large because of the large quantity of membranes and substances. The model can be described as Fig. 1.

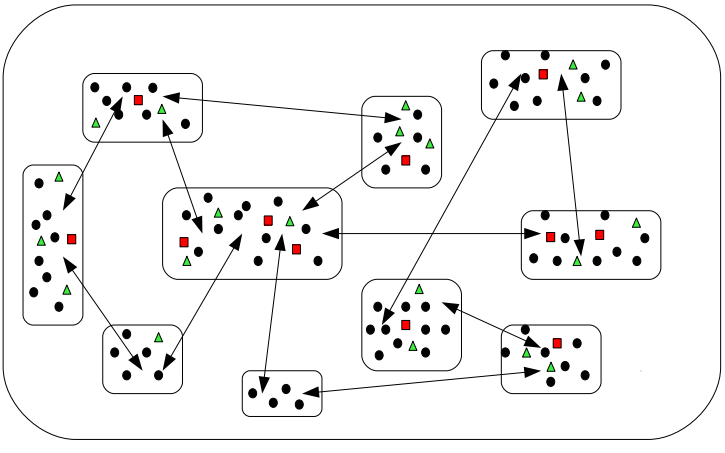

Fig. 1. Membrane system modelling spread of pandemic

The rectangle regions mean the hierarchical membranes. The shapes with different colors represent different individuals in each region: the black circles represent the susceptible individuals; the red squares represent the infected individuals; the green triangles means the recovered individuals. The arrows in the model describe the movements of individuals between different regions.

Based on [11], some assumptions about the spread of pandemic influenza A (H1N1) are made to construct the dynamical probabilistic P system model:

1. Each infected individual is equally infectious, and the infectiousness of an infected individual remains changeless during the course of symptomatic period.
2. The virulence of the pandemic influenza A (H1N1) virus remains changeless during the course of spreading.

3. The immunity and susceptibility of each individual is identical regardless of his/her age.
4. Recovered individuals get immunized and are excluded from the infection. The death incidents which are insignificant compared to the whole population in reality are ignored.

The scheme of DPP systems model for simulation of pandemic influenza A (H1N1) is:

$\Pi = (O, \mu, M_0, M_1, M_2, M_3, \ldots, M_{n-1}, R_0, R_1, R_2, R_3, \ldots, R_{n-1}, I)$ where:

• $O = \{S, I, R\}$. S, I, R stand for a susceptible, a infected and a recovered individual respectively.

• $\mu = [[\,]_1[\,]_2[\,]_3 \cdots [\,]_{n-1}]_0$.

• $M_0 = \lambda$ (λ means no objects), $M_1, M_2, M_3, \ldots, M_{n-1}$ contains different numbers of S, I, R respectively, which means the initial population in each region.

• $R_0 = \lambda$ (λ means no rules), $R_1, R_2, R_3, \ldots, R_{n-1}$ contains different rules respectively reflecting the transmission and control of pandemic influenza A (H1N1).

• $I = \{1, 2, 3, \ldots, n-1\}$ indicates the analyzed regions.

In modeling the spread and control of pandemic influenza A (H1N1), the membrane system model can incorporate the underlying mechanism of transmission and recovery dynamics and can be able to account for experimental data in a number of cases. In this regime, a probabilistic description must be used. Schematically, the stochastic infection and recovery dynamics is given by

$$SI \xrightarrow{\alpha} (II, here),$$

$$I \xrightarrow{\beta} (R, here).$$

The first reaction reflects the fact that an encounter of an infected individual with a susceptible results in two infecteds at a probability α; the second indicates that an infected individual gets recovered at a probability β.

The stochastic movement dynamics is given by

$$S \xrightarrow{\gamma} (S, in_j | 1 \leq j \leq n-1),$$

$$I \xrightarrow{\delta} (I, in_j | 1 \leq j \leq n-1),$$

$$R \xrightarrow{\theta} (R, in_j | 1 \leq j \leq n-1).$$

The three rules reflect the fact that a susceptible, a infected and a recovered individual moves into one region at probabilities γ, δ, and θ respectively.

We assume that a global clock exists, marking the time for the whole system (for all cells of the system); that is, all application of all the substance rules are synchronized. The rules are also applied in a *maximal consistent parallelism*; that is, all those rules must be applied simultaneously in a maximal way.

5 Future Work

In the next step, the specific DPP systems modelling spread and control of pandemic influenza A (H1N1) should be constructed. The social places can be categorized into five categories: school, household, workplace, community and quarantine. The model is depicted in Fig. 2. In the model, both free movement (depicted with green arrows) and forced quarantine (depicted with red arrows) are considered.

In a future work, transmission probabilities and realistic interactions between people through which transmissions arise should be also investigated. Once we get the real sample data of the spread of pandemic influenza A (H1N1), we can build the initial model according to the sample data, and set the related rules and probabilities. Then the model is modified until it can reveal the real situation of pandemic's spread. The simulation can run thousands of times to forecast the spread of pandemic influenza A (H1N1). Moreover, different measures to be implemented can be simulated in the model so that the impact of these measures can be correctly estimated.

Before we construct the model, it is necessary to perform simulations of the model. We will perform simulations by means of a dedicated program written in Matlab language. In the simulations, the stochastic and parallel application of the rules is done by splitting each parallel step into several sequential sub-steps. Each single parallel step is separated into three stages: in the first one, a random number (between 0 and 1) generator is used to generate a probability. The probability generated is compared with the given probability of the specific rule. If the probability generated is less than the given one, the rule associated with the probability will be applied. Otherwise, the rule will not be applied in this step. So the rule is chosen to be applied according to the comparing result; in

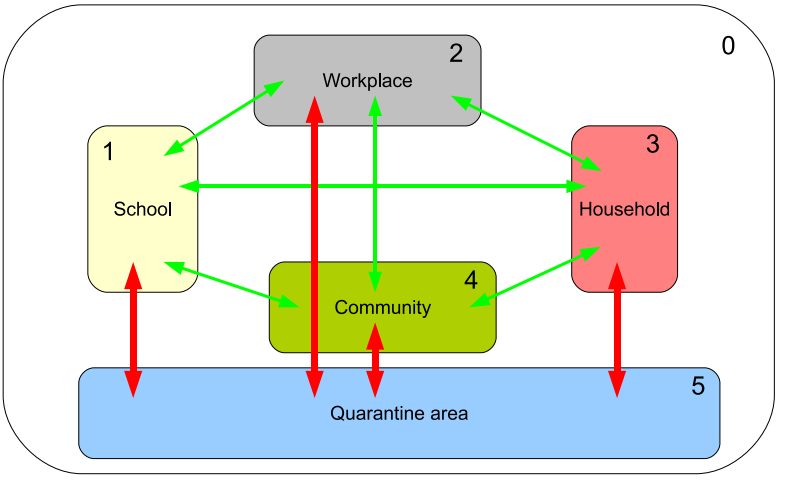

Fig. 2. Social networks of pandemic influenza A (H1N1) spreading

the second one, rule is applied to correspondingly consume the objects appearing in its left-hand side; in the third one, the multisets are updated using a stored trace of the rules previously tossed. Each stage starts only when the previous one has been applied to all the membranes in the DPP system, and the same process is repeated for all evolution steps. A detailed description of the way the simulation algorithm works and of its complexity can be found in [12].

6 Conclusions

Simulation of pandemic's spread using membrane systems is a novel way to forecast the spread of pandemic. Membrane system is a natural tool with a lot of advantages like the large quantity, the high parallelism and the natural behavior based on rules. As pandemic influenza A (H1N1) progresses, and new health challenges emerge, such novel agent-based model will show tremendous advantages in simulation. Once the model is considered to be experimentally validated, it is possible to provide hypotheses about the possible spread of pandemic influenza A (H1N1).

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