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Discrete-Event Systems Model of an Outbreak Response

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Abstract— **During an outbreak of an infectious disease the public health unit has several strategies which can be imposed to contain the spread of the disease. In order to do so it is necessary to evaluate the efficiency of different response policies according to the specific setting of the outbreak. In this work we present a new approach to model such infectious disease outbreaks using discrete-event systems. This approach allows us to adapt the system easily to specific settings or new diseases. Thus, using our model the health units would be able to determine an optimal response to a threatening outbreak.**

I. INTRODUCTION

In recent years the number of infectious disease outbreaks has increased significantly. Sudden epidemics like SARS and the threat of diseases capable of causing future epidemics like Avian flu have become a growing hazard in our societies.

Due to this increase in threatening outbreaks, much research on the detection of an outbreak in its early stage has been initiated. It can easily be verified that the delay in detecting an epidemic has a large impact on the size of the spread, i.e., the number of affected people. However, as soon as an outbreak is detected, the health unit has to decide which measures should be imposed to minimize the damage caused by the contagious agent. This damage may be of a personal as well as economical nature. Therefore, national and international experts are discussing sufficient actions which can be taken to control an outbreak, i.e., to contain the disease and stop its spreading. Knowledge about the efficiency of these outbreak responses is usually the result of studies relating to examinations of real outbreaks in history. However, this information might not be very useful to determine the effect of specific health care strategies related to an outbreak in today's world. In general, the specific setting of the location of an epidemic, i.e., population density, overall medical care system, cleanliness of accommodations, and of course the infrastructure might have a great influence on the course of a specific outbreak.

To evaluate the impact of response policies, different models have been developed, e.g., [1]. However, these models are usually very complicated and designed for a specific setting and a specific disease. Thus, only with effort it is possible to apply these models to a different setting or another disease.

In this paper, we are interested in modeling an infectious disease outbreak using a modification of standard discrete-event systems (DES) and specifically finite-state automata (FSA). This approach allows us to achieve a model which is simple, contains all the information necessary to model the outbreak, and offers possibilities to easily change the parameters according to the specific setting of the outbreak. Thus, using DES seems to be a very promising approach to model an infectious disease outbreak.

Through a simulation of the proposed system we are able to evaluate the impact of different health policy options. Therefore, it is possible to determine the different effects of implemented strategies in a defined but not fixed setting. In addition to that, we are able to compare different responses within the same setting to evaluate an optimal outbreak response.

II. BACKGROUND

As stated previously, we use a modified approach to standard discrete-event systems. The framework of standard DES was developed by Ramadge and Wonham [2], where processes and supervisors are modeled by automata. An automaton is represented by a five-tuple $G = (\Sigma, Q, \delta, q_0, Q_m)$ where Σ is a finite set of symbols, Q is a finite set of states, $\delta : Q \times \Sigma \rightarrow Q$ is the transition function between states, $q_0 \in Q$ is the initial state, and Q_m is the subset of states which are defined as marked (or final) states. For the case where Q is finite, G can be graphically represented by a finite-state machine whose nodes are states and whose edges are transitions defined by δ. On such a transition diagram, the initial state is indicated by an arrow entering it and marked states are identified by circles around the node. The set Σ is the set of all edge labels on the diagram.

A sequence of events is represented by a string of symbols from Σ. The notation Σ^* stands for all finite strings of symbols from Σ. The transition function can then be extended to Σ^*. The closed behavior of G is characterized by its associated language $L(G)$. It represents the set of all possible event sequences which the system may generate. Furthermore, the marked behavior of G, $L_m(G)$, represents completed tasks of the system.

In order to impose supervision on the system it is necessary to partition Σ into the disjoint sets Σ_c, the set of controllable events, and Σ_{uc}, the set of uncontrollable events. Controllable events are those which can be enabled or disabled by an external agent, while uncontrollable events cannot be prevented from occurring. Thus, uncontrollable

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events are considered to be permanently enabled. A supervisor is then an agent that observes the subsequences of strings generated by G and enables or disables controllable events in order to prevent the system from generating an undesirable string.

Formally, a supervisor S consists of an automaton T which recognizes a language over the event set Σ and a feedback map ψ, i.e., a map from the event set Σ and states of T to the set $\{enable, disable\}$. By definition the feedback map ψ enables all uncontrollable events. According to the events generated by G, the automaton T changes its current state and determines whether an event is to be enabled or disabled at the corresponding state of G. The supervised system is then captured by an automaton S/G. Similar to the uncontrolled system the closed behavior is denoted by $L(S/G)$ and the supervised system's marked behavior is denoted by $L_m(S/G)$.

A problem that arises when modeling an outbreak of an infectious disease using DES is the issue of the dynamic (time-varying) properties of the system. Since standard DES theory is not capable of modeling such time-varying properties of systems, we use an approach called Dynamic Discrete-Event System (DDES), as proposed in [3]. Dynamic discrete-event systems are constituted of separate small DES modules, which are combined together to form a final system. The dynamic property of the system is captured by the appearance and disappearance of modules of which the system is assembled. Since neither the number of modules in the system nor the size of the different modules is restricted, the DDES may be as large as necessary.

Since the size of the DDES is not restricted, the issue of state-space explosion has to be addressed. The number of states in the overall system increases exponentially with respect to the number of modules. However, if a system is considered whose state space frequently changes without a basic change in the system's architecture, an approach called Parameterized Discrete-Event System (PDES) [4] can be used to avoid the phenomenon of state-space explosion. The basic idea of PDES is to append finite sets of parameters to finite-state automata, i.e., the system is modeled as a finite-state automaton equipped with a data collection. Using PDES, it is, in some cases, possible to avoid a huge state space. A parameter from the data collection can, for example, be used to count the elements in a buffer. This way it is not necessary to model the buffer as a finite-state automaton which, depending on the capacity of the buffer, can have a huge state space.

III. DES MODEL OF AN OUTBREAK RESPONSE

In order to model an epidemic we first want to introduce the basic possible actions a public health unit may take to contain a disease.

A. Possible Responses to an Outbreak

One of the most common, and in the course of an outbreak usually one of the first imposed, public health measures is isolation of symptomatic individuals. It allows for the focused delivery of specialized health care to people who are ill, and it protects healthy people from getting sick. The isolation strategy is especially likely to be successful if the infectious disease has a low transmission rate prior to symptoms, i.e., most infections from person to person take place after the onset of symptoms. However, if a disease is characterized by a high transmission rate in the prodromal period, isolation might not be sufficient in controlling the outbreak and spread of the disease. Thus, further control measures have to be implemented. Since the infection of an individual prior to symptoms is not recognizable, it is not possible to simply identify infected individuals. It is possible, though, to identify individuals who might have been exposed to the cause of the disease and therefore might be suspected of being infected.

The specific health action of identifying exposed individuals is called *contract tracing*. Contact tracing basically means that any identified symptomatic person gets his or her contacts traced. Trace individuals are people who have been in (close) contact with a confirmed case, e.g., family members. Once identified, there are several options for proceeding with traced individuals. One of the possible options is targeted surveillance. Traced individuals who are put under targeted surveillance are examined regularly but their everyday life does not change, i.e., they are not quarantined. Then, if a patient under surveillance becomes symptomatic, he or she will be isolated without (almost) any delay.

Another option for dealing with traced individuals is the implementation of quarantine. According to this strategy, a person who is identified as a close contact of a confirmed case will be quarantined whether or not the individual is infected at all. Note that quarantine refers to individuals who are suspected to be infected, while isolation refers to individuals who have a specific disease and have become symptomatic. Therefore, some quarantined patients may become symptomatic while others may stay asymptomatic and could be released after a certain period of time.

Furthermore, there are two options regarding the treatment of quarantined individuals. Medication could be administrated to everyone, i.e., everyone who is quarantined will be treated. This is a prophylactic measure also called *chemoprophylaxis*. Although this strategy is highly efficient in preventing the disease from spreading, chemoprophylaxis is limited by two factors. First of all, the probability of medications causing side effects has to be considered. Chemoprophylaxis should be imposed only if the benefits of treatment outweigh the risks involved. The second factor limiting the use of this strategy is associated with the possibility of prohibitive costs. When the costs of treatment are high or the transmission rate of the disease is low, chemoprophylaxis might not be cost-effective. In such cases, the second policy on treatment of quarantined patients should be considered. Using this strategy, the treatment process is delayed until the actual onset of symptoms in individuals. Thus, it is ensured that only infected patients will be treated and healthy patients will be prevented from adverse drug reactions.

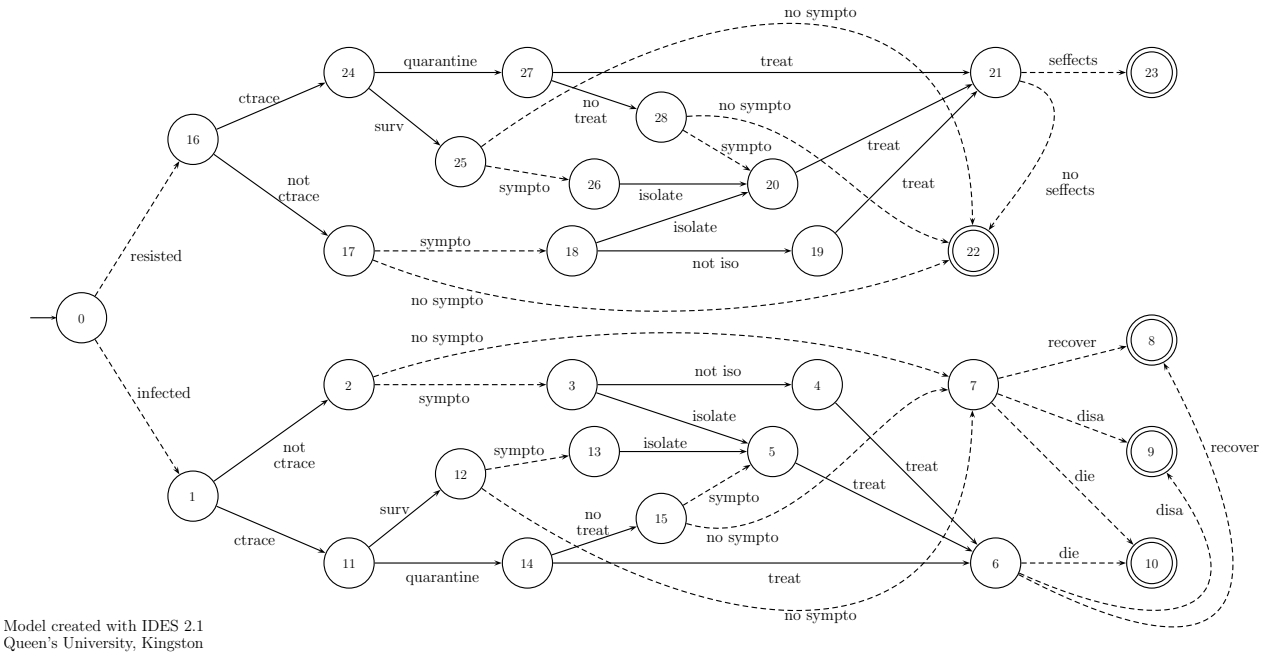

Fig. 1. Finite-State Automaton of an Exposed Individual

B. Characteristic Properties of Diseases

As mentioned before, the efficiency of all health care strategies is always dependent on the specific disease. Thus, it is necessary to find parameters to characterize and differentiate diseases.

One of the most important factors of an infectious disease is the infection rate, ξ_I. Although this rate is a characteristic feature of the pathogen, it is not fixed but depends on certain circumstances. For example, the infection rate of a disease causing an outbreak in a home for the elderly might be different from the infection rate of the same disease in a student residence. In addition, the vaccination status of the population has an influence on ξ_I.

Another important factor of a disease is the proportion of transmission prior to symptoms. The higher the proportion of asymptomatic transmissions, the harder it is to control the outbreak. The human immunodeficiency virus (HIV), for example, is more than 90 per cent of the time transmitted by individuals who are not aware of the fact that they carry the virus. Since its first appearance 25 years ago, there is still no strategy to control the spread of HIV once it is contracted.

Of importance for the strategy to control an outbreak is also the mortality rate and the rate of permanent damage due to an infection. Similar to the infection rate, these rates are usually highly dependent on the specific setting of the outbreak.

C. Model of an Exposed Individual

We consider a fictitious (or nonspecific) disease and explore how DES can be used to model a response to an outbreak. The idea of our model is to create small modules representing single individuals and combine them to form a final system of an outbreak response. To model an individual, it is necessary to consider the different "paths" a person can take, i.e., the different events that can occur in the module of a person. In addition, one has to decide which events are necessary in order to capture all possibilities that may occur in an outbreak.

The individuals modeled have all been exposed to the contagious pathogen at some point. After the exposure they might either get infected or they might resist an infection. The complete module of an exposed individual is shown in Fig. 1. In this graph an exposed individual is initially in state 0. At that state either the event *infected* or the event *resisted* can occur. Thus, the individual can either enter state 1 or state 16, respectively. According to the state a person is in different events can occur and their occurrence then changes the state of the individual. While most of the event names are self-explanatory others are not as obvious. For example, the event *ctrace* refers to contract tracing, *surv* refers to targeted surveillance, *disa* refers to a person suffering from permanent physical harm, and *seffects* refers to side effects due to medication. The lower part of the module represents an infected individual while the upper part of the module represents an exposed but uninfected person.

Assuming that no public health measures are imposed yet, the medical condition of an infected person will most probably result in symptoms of some sort, depending on the disease. Since each disease has different intrinsic symptoms that can appear, it is a priori necessary to define these symptoms, e.g., the typical symptom of smallpox would be the development of a rash. Nonetheless, in some abnormal cases it is possible that an infected person will never show symptoms or that the symptoms are very subtle and misin-

terpreted.

If an individual becomes symptomatic, he or she will probably go to a doctor and will receive some sort of treatment. What kind of treatment is prescribed is not important at this point, although it does have an influence on the probabilities of the future path of the patient. More specifically, depending on the infectious disease and on the prescribed medication of the patient, the individual will, with certain probabilities, either recover, die, or suffer from some permanent handicap due to the infection. Note that the specific probabilities capture the risks of the disease as well as possible risks due to adverse drug reactions. An example of a disease capable of causing permanent handicaps is poliomyelitis. Usually, an infection of poliomyelitis results in only temporary paralysis and recovery is complete within six to eight months but, in some cases, paralysis will be permanent.

An asymptomatic infected individual will also recover, die or suffer from permanent consequences of the disease but, since he or she never got medication, the probabilities of the aftermath of the disease might be different.

Once the public health unit detects an outbreak, the strategy of isolation might be considered and imposed. This would change the path of the symptomatic patient. Instead of just getting treatment after symptoms develop, he or she will be isolated first and then get medication. After isolated individuals are treated, they enter the same state as those not isolated and may either recover, die or suffer from permanent consequences. At first sight it might not be clear why, independent from the strategy, a patient who has not been isolated would have the same chance to recover as a patient who has been isolated. The reason for that, though, is simple: isolation does not interfere with the recovery process. Moreover, isolation is not imposed on the infected individual to ensure his or her health but to prevent transmission of the pathogen to other people.

Given that simple isolation of infected cases is not sufficient to prevent a vast spread of the disease, the next strategy would be contact tracing combined with targeted surveillance. The path of an infected individual would change in this case. Before the person develops symptoms, he or she will be contact traced and put under surveillance. As soon as the patient becomes symptomatic, isolation and treatment start. After that, the person is in the same state as the people that have just been isolated and will face the consequences of the infection. Of course, individuals under targeted surveillance may also stay asymptomatic although they are actually infected. These patients will face the aftermath with the same probabilities as asymptomatic cases who were not traced.

Last but not least, the combination of contact tracing and quarantine is considered. It differs only slightly from the surveillance strategy. Instead of being put under surveillance, the infected individual is quarantined as soon as he or she is identified. If treatment is delayed until the symptoms show, the patient's path will be very similar to the path of people under surveillance. In this case, an infected person might be asymptomatic again and will not be treated.

If quarantine is imposed in combination with chemoprophylaxis, all persons will be treated. The development of symptoms is not required to start the treatment process and, therefore, even possible infected but asymptomatic cases will have the same chances to recover.

The different paths for exposed but uninfected individuals are similar to the ones of infected persons. Since the infection itself is not observable, it is unknown whether an exposed person is infected or not. This is an issue especially when contact tracing is imposed because, given an infection rate of $\xi_I = 0.2$, about 80 per cent of the traced individuals will be uninfected. Due to the fact that the actions of surveillance and quarantine are imposed on every traced individual, the upper part of the module of an exposed person is an almost identical copy of the lower part. Only the last few nodes are different because, in general, uninfected persons will not suffer any harm directly related to the disease. However, if medication is administered either to symptomatic but uninfected cases or to individuals under quarantine, these (uninfected) persons might suffer from adverse drug reactions.

In addition to these few differences in the composition of the two parts of the module, there are some more differences within the system that are not visible in the structure of the model. These differences refer to the probabilistic values on the occurrences of events. For example, if one considers one infected and one uninfected person being in state 2 and state 17, respectively, the individuals will either show symptoms or not. The infected person will most likely show symptoms and move to state 3 while the uninfected person will not be very likely to develop symptoms. Thus, this person will most probably move to state 22. Therefore, although both individuals could go either way, the probability of the occurrence of the events is different.

Formally, the module of an exposed individual can be described by the finite-state automaton $G = (\Sigma, Q, \delta, q_0, Q_m)$ where Σ is the set of events as described above and the set of states, Q, and the transition function, δ, can be determined from Fig. 1. The initial state is $q_0 = 0$, and Q_m is the set of marked states ($Q_m = \{8, 9, 10, 22, 23\}$). The set of uncontrollable events can be determined by examining Fig. 1, where all uncontrollable events are indicated by dashed lines.

D. Parameters of the Model

As mentioned before, the infection rate ξ_I determines the probability of the event *infected* occurring. In addition to that, there are a few more parameters within the model. It is necessary to associate a probability to each occurrence of the events *ctrace* and *isolate*, e.g., it might not be possible to trace every contact of an infected individual. These probabilities are denoted by ξ_c and ξ_{iso}, respectively. Furthermore, the probability of becoming symptomatic has to be defined on order to capture abnormal cases of asymptomatic infected, and symptomatic uninfected individuals. Thus, infected individuals will develop symptoms with a probability of ξ_s^i, while uninfected persons will develop symptoms with a probability of ξ_s^u. The mortality rate and the rate of infected people suffering from permanent physical

harm are denoted by ξ_d^t, ξ_p^t, ξ_d^n, and ξ_p^n, where the superscript t refers to individuals who have been treated, n refers to infected persons who have not been treated, d refers to mortality and p refers to permanent physical harm. Last but not least, the probability of adverse drug reactions for uninfected individuals is denoted by ξ_a and refers to the event *seffects*.

As the disease spreads, an increasing number of people will get exposed to the disease by infected individuals. In other words, there will be new people getting into the system and persons who have recovered from the infection will leave the system. This dynamic character is captured by the appearance of modules of infected individuals and the disappearance of modules of individuals entering a marked state. The appearance of new modules is triggered by certain events in the modules within the system, and thus models how the disease is passed from one person to another. For example, if the event *sympto* occurs, a certain number of people will get exposed and enter the system as new modules. The specific number of people getting exposed is drawn from a Poisson distribution of mean λ [1]. The events triggering the entry of new modules into the system are *infected*, *quara*, *not iso*, *sympto*, and *no sympto*. For the last two events, the value of λ is also dependent on when *sympto* or *no sympto* occurs. If, for example, an individual becomes symptomatic prior to isolation, he or she might expose a different number of contacts than a person who develops symptoms while quarantined.

E. Complete System

In order to capture the overall system, a custom version of parameterized discrete-event systems is introduced. In this approach, parameters are used to describe the different modules. More specifically, each module is represented by one parameter in the overall system. The value of the parameter is equal to the current state of the corresponding module. Therefore, the system's state can be represented by a vector of parameters, denoted by M. The length of this vector will be equal to the number of modules currently in the system.

In addition to the vector of parameterized modules, the overall system requires a prototype module to be able to determine the next possible set of parameters. If a module enters a final state, it will disappear from the vector M. Similarly, a new parameter will be attached with the appearance of every new module, i.e., every new exposed individual. Due to the identical structure of all the modules, this is sufficient to obtain the complete model. Thus, the final model of the uncontrolled system is defined as $R := \{G, M\}$, where G represents a prototype of the FSA structure of a module and M represents the vector of parameters.

Supervision of the uncontrolled system amounts to disabling some of the controllable events throughout the evolution of R. Any strategy that the health unit imposes can be thought of a supervisor. For instance, one such strategy could involve always isolating a symptomatic person (which, in effect means disabling *not iso* at state 3 of Fig. 1). In the next section, we examine the effects of various supervisors, i.e., various health unit strategies.

IV. SIMULATION & RESULTS

A simulation was performed to show the functionality of the proposed system. The algorithm we developed was implemented in Matlab 7.4.0. The software has access to the set of parameters specifying the disease, the initial state of the scenario, a vector of parameters representing the current states of the modules, the basic structure of the finite-state automaton model of an exposed individual, and the supervisor models of the different health care strategies. The software has also information about the probabilistic distributions associated with specific events and is equipped with a random number generator. The computer used was running the Microsoft Windows XP operating system on a AMD Athlon 64 3200+ 1.99 GHz processor. The machine was equipped with 960 MB of RAM.

The setup of the simulation is as follows. It is assumed that the outbreak has been detected in its early stage. The disease causing the outbreak is a highly transmissible disease similar to a form of influenza. The initial state of the system consists of a small number of symptomatic individuals and a number of exposed individuals. The algorithm then moves stepwise across the elements of the vector M and determines the events which lead out of the specific state of each module. At each "time step" one event will occur in every module. When the algorithm reaches the last element of the vector, it will move back to the top and start over again. This loop is repeated either until M is an empty vector or until the outbreak is considered to be uncontrollable with respect to the chosen health care strategy. An outbreak is considered uncontrollable if there are more than 10,000 infected individuals in the system at the end of a loop.

When the simulation has to choose between events with associated probabilities, the software will generate a random number from a uniform distribution in the interval 0 to 1. By means of this random number the algorithm decides which event will occur. For example, the event *infected* will occur if the generated random number is smaller than the infection rate ξ_I. In this way, the larger the ξ_I (which means the higher the infection rate), the more likely that a random number will be smaller than it (and hence the more likely that the event *infected* will occur).

When an event which initiates the exposure of new individuals occurs, the software will generate a random number from the Poisson distribution which is related to the event. The vector M is then expanded according to the number of newly exposed individuals. A module is removed from the vector M as soon as it enters a marked state.

In our simulation the parameters of the disease were set to:

$$\xi_I = 0.05, \quad \xi_c = 0.99, \quad \xi_s^i = 0.999, \quad \xi_s^u = 0.0001,$$
$$\xi_d^t = 0.001, \quad \xi_p^t = 0.001, \quad \xi_d^n = 0.001, \quad \xi_p^n = 0.001,$$
$$\xi_{iso} = 0.99, \quad \xi_a = 0.01.$$

Initially, there were 15 symptomatic cases and 200 exposed individuals. Dozens of simulations were run and after

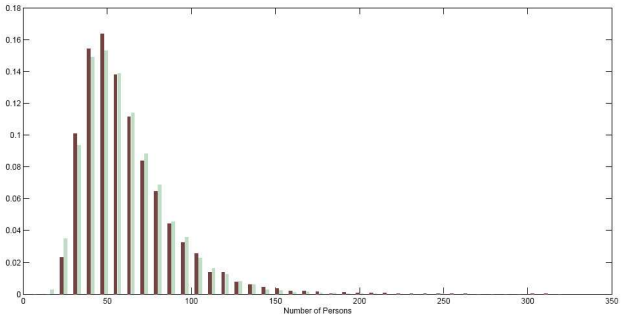

Fig. 2. Number of infected individuals under the quarantine strategy with immediate treatment (dark red) combined with a synthetically generated log-normal distribution (light blue)

every run, the data obtained was stored. Among this data is the number of infected individuals and the number of imposed treatments.

Due to the large variations in the number of affected people in each simulation, each scenario was simulated 10,000 times. This enables us to analyze the data obtained. First of all, the simulations made clear that neither the isolation nor the targeted surveillance strategy is sufficient to control the outbreak of this specific disease. However, by imposing either one of the quarantine policies, it is possible to contain and finally stop the epidemic.

Furthermore, the analysis of the obtained data showed that the number of people affected by an outbreak obeys a log-normal distribution. Thus, using the obtained data it is possible to determine the corresponding distribution parameters which are necessary to calculate values for the expected number of affected individuals and the variance.

For this specific setting combined with the quarantine strategy with delayed treatment, the values calculated using Matlab are: $E = 67.69$ and $Var = 1.878 \cdot 10^3$, where E is the expected number of infected individuals and Var is the variance. For the same setting with immediate treatment, $E = 56.70$ and $Var = 651.80$.

Thus, it is possible to determine the expected number of infected individuals for a specific setting. Furthermore, the variance provides a measure of the statistical dispersion, i.e., how the possible numbers are spread around the expected number. Since the variances are high the number of infected individuals is subject to large variations. Fig. 2 shows the distribution of the number of infected people under the quarantine strategy with immediate treatment combined with a synthetically generated log-normal distribution.

In addition to the analysis of the effectiveness of strategies, it is possible to apply a cost-benefit analysis. Such an analysis might be very useful, since the number of occurrences of events, connected to some costs, could differ. If we consider the aforementioned example, using the strategy with delayed treatment, a total number of 1,049 individuals were quarantined compared to only 830 when immediate treatment was administrated. However, in the first scenario, only 68 patients were treated, while in the second scenario about 845 patients received treatment. Consequently, if we presume that there is a cost to treatment and a cost (e.g., loss of livelihood) to quarantine, then the determination of a suitable response policy is more complex when costs must be taken into account.

Yet another analysis which could be performed using the simulation is the study of the impact of variations of different parameters. If, for example, the rate of contact tracing is reduced to 80 per cent (80 per cent of the close contacts of a confirmed case are traced), in our case the expected number of infected individuals increases to 161.61 with delayed treatment and to 110.12 with immediate treatment, respectively. Similarly, other parameter combinations can be considered and their impact can be evaluated by simulating the system with the "new" setting.

V. Discussion

We have shown that discrete-event systems are promising in modeling infectious disease outbreaks. Using a simulation it is easy to change the parameters of the specific setting and to evaluate the impact of different outbreak policies.

The results obtained by the simulation appear to be reasonable but further testing is necessary. A discrete-event systems model of an outbreak response requires slightly different parameters than a continuous-time model. Since this work is only a first attempt using DES, it was not possible to obtain accurate values for these parameters. Therefore, approximations of parameters previously used in continuous-time models have been taken to model the disease. Due to these approximations, the simulation does not guarantee that the calculated numbers of infected individuals coincides with the numbers of a real outbreak.

Once accurate parameters have been obtained for specific diseases, it will be possible to simulate "real" outbreaks. The results might then help the public health units to determine optimal response policies. In addition, DES control theory could be explored as a tool for generating the response policies.

VI. Acknowledgments

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