ORIGINAL PAPER

Application of Quantifier Elimination in Epidemiology

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ABSTRACT

Background:: An application of a novel method of a quantifier elimination in epidemiology was presented in this paper **Objective**: We investigated the existence of the endemic equilibrium for the SEIRS model by QE method and gave a short review of the epidemic prediction models for covid-19. **Methods**: A new method for quantifier elimination for the theory of real closed fields. **Results**: Obtained value of a reproduction number and endemic equilibrium for the SEIRS model by QEAnalysis of the SEIR model with the concrete values through the example of Severe Acute Respiratory Syndrome (SARS) (a critical value of a transmission rate is evaluated in the example). **Conclusion**: The main result of this paper is the obtained value of the endemic equilibrium for the SEIRS model (similar result is obtained for the SEIR model). Also, we have analysed the SEIR model through the examle of SARS and we reviewed several epidemic prediction models for covid-19.
Keywords: epidemic model, reproduction number, endemic equilibrium, quantifier elimination.

1. BACKGROUND

Numerous mathematical models have been formulated and applied in epidemiology. In the compartmental models, a population is divided into compartments and the certain assumptions about the nature and time rate of transfer from one compartment to another are specified. The basic model is the SIR model presented in [1]. The population is divided into three different groups, the Susceptible, the Infectious and Recovered in this model. Also, these assumptions are given: a population is closed and all the recovered individuals have complete immunity. The SIR model was used for modelling chickenpox, smallpox, rubella and mumps. The model that we analyse in this paper is the SEIR model; a population is divided into four different groups, Susceptible, Infectious, Exposed and Recovered [1]. Considering the SEIRS model, recovered individuals may become susceptible again in it.

The crucial question in epidemiology is if a disease currently present in a population will die out or will reach an endemic stage. More precisely, the question of the stability of a disease free equilibrium and of an endemic equilibrium has been posed. The notion of a basic reproduction number R_0 was introduced by Dietz in order to answer it [7]. R_0 is defined as the number of the secondary infections from each infected person in a population that consists only of susceptible persons. If a value of R_0 exceeds one then a disease will reach an endemic stage and will always be present in the population; if a value of R_0 is less than one the disease will die out.

The models that we have investigated and analysed in this paper are the SEIRS and SEIR. We have analysed the SEIR model using concrete values for the Severe Acute Respirator Syndrome (SARS), where the data were taken from [4]. Namely, the choice of the appropriate model for a certain disease is important in epidemiology. If we take SARS as the example, we cannot apply the classical SIR model on it. Although the SIR model provides the general framework to investigate a spread of a disease, it is too simple to accurately model the outbreak of SARS

and generally does not fit to a real data [14]. So, we have decided to use the SEIR model in our analysis. In this model a current number of people in the Infective class can be low while a number in the Exposed class is high; in this case the epidemic may seem stopped but it will be out of a control when the people from Exposed class migrate to Infective class and transmit a disease further (especially in case sanitary inspection is not good). Let us mention some other models that can be used in the analysis of a same disease, the SEIQR and SEIRP model. The SEIRP model was introduced in the paper [14]. A motivation for creating this new model was the fact that the SARS virus was less severe in the places with the poor hygiene conditions. So, there exists the possibility that a vaccination against another disease could protect the people against SARS. Another possibility is that a very similar disease spread before and immunized some of the people against SARS. A previously stated was the hypothesis in [14] and it was a base hypothesis for a new SEIRP model. So, a new class P was added to the SEIR model and it represented a group of people that already had some kind of a protection.

A global epidemiology of SARS was influenced by a phenomenon called superspreading. The largest outbreak of SARS occurred in Beijing in a year 2003 [15]. A statistical data showed that the most of the superspreading events occurred in the hospital environment. The superspreading was associated with the patients with a large number of contacts. After introducing the infection control measures in Beijing in response to the outbreak, the chances for events of superspreading were significantly reduced.

Both the SEIR and SEIRS model are used for the diseases with a long incubation duration. In the SEIRS model recovery does not confer permanent immunity so one application of this model can be application to malaria.

Since a new virus covid-19 is similar to SARS, we will review prediction models appropriate for it. Several models were analysed in order to predict dynamic of the disease in [16]. The obtained results were compared to a real data. For example, the SEIR model was used to predict a number of covid-19 cases in Hubei. The SIRD model was used for the prediction in Italy, while the SEIRQ model was used for the data in China. The ARIMA model was used for prediction in three countries, Italy, Spain and France. When comparing the obtained values to a real data, the conclusion was that the two models, the SEIRQ and the ARIMA model, have the lowest difference between the obtained predicted values and the real data values. So, the SEIRQ and the ARIMA models are appropriate for covid-19. Let us mention here the SLIAR model that has been also used for the respiratory diseases. One variation of the SLIAR model was used for covid-19 in [17], where the parametrisation involves the same number of parameters as the basic model. We can point out that the simple models that can be fitted using the minimal number of parameters were very useful during the early stage of the covid-19 pandemic.

As a result in this paper for the SEIRS model, we obtained a value of the reproduction number and a value of endemic equilibrium by a novel method of QE. We also obtained these results for the SEIR model. When we compare our result to the result presented in paper [6], we can see that their algorithm returned only the formula for a reproduction number while a value of an endemic equilibrium was not calculated.

Considering the methods of mathematical logic used in this paper, we used a method for quantifier elimination first presented in [13]. The first real quantifier elimination procedure was presented by Tarski in [9]. Collins developed the first elementary recursive real quantifier elimination procedure [10,11], which was based on cylindrical algebraic decomposition (CAD).

In the other papers related to the application of QE, the completely different methods of QE were used. To be more precise, the approach that requires both quantifier elimination and simplification of a formula was used in [6]. QE based on virtual term substitution, Hermitian QE based on real roots counting and QE by cylindrical algebraic decomposition were used.

2. OBJECTIVE

The aim of this paper is to evaluate the endemic equilibrium of the SEIRS model and to analyse the SEIR model through the example of SARS.

3. MATERIAL AND METHODS

Quantifier Elimination

Let us introduce the basic definitions which are of importance for quantifier elimination.

The language L is recursive if the set of codes for symbols from L is recursive. The first order theory T is recursive if the set of codes for axioms for T is recursive. An L-theory T is complete if for every sentence in a language L the following holds:

$$\mathrm{T} \vdash \varphi \text{ or } \mathrm{T} \vdash \neg\varphi.$$

For each theory T arises question of its decidability, i.e. the existence of algorithm which for given $\varphi \in Sent_L$ gives an answer whether $\mathrm{T} \vdash \varphi$ or $\mathrm{T} \nvdash \varphi$In the case of recursive complete theory in a recursive language, the answer is affirmative.

A theory T of a language L admits quantifier elimination if for every formula $\varphi(\overline{\nu}) \in For_L$ there exist a quantifier free formula $\psi(\overline{\nu}) \in For_L$ such that:

$$\mathrm{T} \vdash \forall\nu\,(\varphi(\overline{\nu}) \leftrightarrow \psi(\overline{\nu}))$$

Every logic formula is equivalent to its following prenex normal form:

$$Q_1 x_1 \ldots Q_n x_n \varphi(x_1, \ldots, x_n, y_1, \ldots, y_m),$$

where $Q_i \in \{\forall, \exists\}$ and φ is a formula without quantifiers in DNF; formula of the form $\forall x\varphi$ is equivalent to $\neg\exists x\neg\varphi$; $\exists x\,(\varphi \vee \psi) \leftrightarrow \exists x\varphi \vee \exists x\psi$ is a valid formula. Using the previous we see that an L-theory T admits quantifier elimination if and only if for every L-formula of the form $\exists x\varphi(\overline{y}, x)$, where φ is a conjunction of atomic formulas and negations of atomic formulas, exists equivalent quantifier free formula $\psi(\overline{y})$.

The method used in this paper is the original general algorithm for QE for any theory T presented in [13]. This algorithm is applied to the theory of real closed fields (RCF).

Preliminaries. Theories of ACF and RCF

The notion of the algebraically closed fields and real closed

field is well known in mathematical logic.

In order to know how to eliminate quantifiers in a theory of algebraically closed fields, it is sufficient to know how to eliminate the existential quantifier in the formula of the form:

$$\exists x \left(t_1 = 0 \wedge \cdots \wedge t_k = 0 \wedge t \neq 0\right),$$

where t_i represent an atomic formula of a language L. So, every t_i is polinomial by x whose coefficients are polynomials by the other variables with coefficients in **Z**.

In order to know how to eliminate quantifiers in a theory of real closed fields, it is sufficient to know how to eliminate the existential quantifier in the formula of the form:

$$\exists x \left(p_1 = 0 \wedge \cdots \wedge p_k = 0 \wedge q_1 > 0 \wedge \cdots \wedge q_m > 0\right),$$

where p_i, q_j are polinomials by x whose coefficients are polynomials by the other variables with coefficients in **Z**.

4. RESULTS

Application of QE in Epidemiology

In this paper we will investigate the SEIRS and the SEIR model that are presented in [3]. Note that the recovered individuals may be susceptible again in the SEIRS model. So, a population is divided into the following classes: the Susceptible (S), the Exposed (E), the Infectious (I) and the Recovered (R). The Susceptible class contains the individuals who are at risk of become infected. The Exposed class represent the individuals who may or may not develop the disease. The Infectious class contains the individuals who have been infected. The Recovered class represent the individuals who have been recovered. Mathematical models consist of the systems of differential equations that describe the dynamics in each class.

SEIRS model

The SEIRS model has been investigated by the quantifier elimination methods in [6]. The methods for QE in this paper completely differ from the methods used in [6]. Additionally, we obtained a value of the endemic equilibrium as a ne w result directly by QE.

The SEIRS model for the transmission of infectious diseases is presented by the system of four differential equations

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}S &= \mu + \gamma R - \mu S - \beta IS \\
\frac{\mathrm{d}}{\mathrm{d}t}E &= \beta IS - (\mu + \sigma)\, E \\
\frac{\mathrm{d}}{\mathrm{d}t}I &= \sigma E - (\nu + \mu)\, I \\
\frac{\mathrm{d}}{\mathrm{d}t}R &= \nu I - (\mu + \gamma)\, R,
\end{aligned}$$

where the meaning of the variables and parameters is the following:

S susceptibles
E exposed
I infectious
R recovered
β transmission parameter
μ birth rate = mortality rate
σ rate of change from exposed to infectious
γ rate of loss of immunity
ν rate of loss of infectiousness

The birth rate is equal to the mortality rate in this model.

A point in SEIR-space is an equilibrium point if

$$\mu + \gamma R - \mu S - \beta IS = 0 \wedge \beta IS - (\mu + \sigma)\, E = 0 \wedge$$
$$\wedge \sigma E - (\nu + \mu)\, I = 0 \wedge \nu I - (\mu + \gamma)\, R = 0,$$

(it holds: $I + S + E + R = 1$) and represents an endemic state if

$$S > 0 \wedge E > 0 \wedge I > 0 \wedge R > 0.$$

(a disease free equilibrium, obtained by setting $I = 0$, always exist and has a value (1, 0, 0, 0))

There exists an endemic equilibrium for the SEIRS model if the following formula holds:

$$(\exists E)\,(\exists R)\,(\exists I)\,(\exists S)\,(\mu + \gamma R - \mu S - \beta IS = 0 \wedge$$
$$\beta IS - (\mu + \sigma)\, E = 0 \wedge \sigma E - (\nu + \mu)\, I = 0 \wedge \nu I -$$
$$(\mu + \gamma)\, R = 0 \wedge S > 0 \wedge E > 0 \wedge I > 0 \wedge R > 0)$$
$$I + S + E + R = 1 \qquad (1)$$

Let us rewrite the system first. We combine a substitution method and QE method. We express the values of E and R from the third and fourth equation, respectively:

$$E = \frac{(\nu + \mu)\, I}{\delta},\ R = \frac{\nu I}{\mu + \gamma} \qquad (2)$$

The next step is to substitute the previous values into the second equation and a formula (1). So, we get the following system:

$$\beta IS - (\nu + \sigma)\, \frac{(\nu + \mu)\, I}{\sigma} = 0$$
$$I + S + \frac{(\nu + \mu)\, I}{\sigma} + \frac{\nu I}{\mu + \gamma} = 1$$

or equivalently

$$\beta IS - (\nu + \sigma)\, \frac{(\nu + \mu)\, I}{\sigma} = 0$$
$$I + S + \frac{(\nu + \mu)\, I}{\sigma} + \frac{\nu I}{\mu + \gamma} - 1 = 0$$

Now we apply QE algorithm to the inner quantified subformula of a formula:

$$(\exists I)\,(\exists S)\left(\beta IS - (\mu + \sigma)\, \frac{(\nu + \mu)\, I}{\sigma} = 0 \wedge I + S + \right.$$
$$\left. + \frac{(\nu + \mu)\, I}{\sigma} + \frac{\nu I}{\mu + \gamma} - 1 = 0 \wedge S > 0 \wedge I > 0\right)$$

More precisely, we apply the algorithm to the formula:

$$(\exists S)\left(\beta IS - (\mu + \sigma)\, \frac{(\nu + \mu)\, I}{\sigma} = 0 \wedge I + S + \right.$$

$$+\frac{(\nu+\mu)I}{\sigma}+\frac{\nu I}{\mu+\gamma}-1=0\wedge S>0\wedge I>0\Bigg)$$

By the QE method we have

$$T_1 = A_2 t_1 - A_1 t_2$$

where $t_1 \equiv \beta IS - (\mu+\sigma)\frac{(\nu+\mu)I}{\sigma}$, $t_2 \equiv I + S + \frac{(\nu+\mu)I}{\sigma} + \frac{\nu I}{\mu+\sigma} - 1$ and the coefficients are equal $A_1 = \beta I,\ A_2 = 1$. Our formula is equivalent to:

$$A_2 \neq 0 \wedge (\exists S)\,(T_1 = 0 \wedge t_2 = 0 \wedge S > 0 \wedge I > 0)\,.$$

When we rewrite the equality $T_1 = 0$ we get the following one:

$$(\mu+\sigma)\frac{\nu+\mu}{\sigma}+\beta I+\beta\frac{(\nu+\mu)I}{\sigma}+\frac{\beta\nu I}{\mu+\gamma}-\beta=0$$

Now we substitute values from (2) into the previous formula. A formula is equivalent to:

$$(\mu+\sigma)\frac{\nu+\mu}{\sigma}+\beta I+\beta E+\beta R-\beta=0$$

When we express a value of *S* from (1) and substitute it into the previous formula we get:

$$(\mu+\sigma)\frac{\nu+\mu}{\sigma}+\beta-\beta S-\beta=0$$

So, we can express a value of *S* as a function of parameters:

$$S=\frac{(\mu+\sigma)(\nu+\mu)}{\sigma\beta} \tag{3}$$

Now we use the second equality $t_2 = 0$ and substitute a value of *S* into it. It follows:

$$I+\frac{(\mu+\sigma)(\nu+\mu)}{\sigma\beta}+\frac{(\nu+\mu)I}{\sigma}+\frac{\nu I}{\mu+\sigma}-1=0$$

We can see that the previous equality has only one unknown *I* and we can express a value of *I* as a function of parameters. When we combine it with a condition *I* >0 we get the following:

$$\frac{(\mu+\sigma)(\nu+\mu)}{\sigma\beta}<1 \tag{4}$$

Notice that a resulting formula represents a condition for a reproduction number in the epidemiological literature. The identical formula (4) was obtained in [6], but the method for QE was different. More precisely, REDLOG was used in [6] and it computes a quantifier free equivalent formula that consists of 25 atomic formulas. So, their result needed to be simplified in order to transform the obtained formula into a formula (4).

Let us find a value of the endemic equilibrium. We have already evaluated a value of S^* by the method of QE directly and that is obtained in (3):

$$S^*=\frac{(\mu+\sigma)(\nu+\mu)}{\sigma\beta}$$

We can substitute the previous value into the system in which derivatives are equal to zero and evaluate the endemic equilibrium. Since it holds:

$$S^*=\frac{1}{R_0},$$

we present the obtained value as a function of R_0:

$$(S^*,E^*,I^*,R^*)=\Bigg(\frac{1}{R_0},\frac{\mu+\nu}{\sigma}I^*,$$

$$\frac{(\mu+\gamma)\mu}{R_0(\beta(\mu+\gamma)-\gamma\nu)}(R_0-1),\frac{\nu}{\mu+\gamma}I^*\Bigg).$$

Since in the paper [6] a value of endemic equilibrium was not obtained, we can point out this value as a new result obtained by QE method.

Numerical analysis of the SEIR model for SARS

The SEIR model has been presented in [3]. We have obtained the values of a reproduction number and an endemic equilibrium by QE method described in 4.1. In order to analyse the SEIR model we have taken the data for Severe Acute Respiratory Syndrome (SARS) from [4]. The numerical data are the following:

transmission rate	$\beta = 0.75$
rate of natural mortality	$\mu = 0.000034$
rate of change from exposed to infectious	$\sigma = 0.33$
recovery rate of infected individuals	$\gamma_1 = 0.125$
recovery rate of diagnosed individuals	$\gamma_2 = 0.2$

When we use a formula for a basic reproduction number:

$$R_0=\frac{\beta\sigma}{(\mu+\gamma)(\mu+\sigma)},$$

and substitute values from a table into it, we get R_0 = 3.75. Note that we have used the second value $\gamma_2 = 0.2$ for a value of γ. Since it holds($R_0 = 3.75$)>1, the endemic equilibrium is stable.

Let us analyse the sensitivity of endemic equilibrium of the SEIR model. We suppose that the values of mortality rate, expose rate and recovery rate are considered to be fixed in this analysis. While the values of three parameters μ, σ, γ are fixed, the corresponding value of a transmission rate has been changing. We have calculated the value of the reproduction number R_0 for every combination of parameters and represented the results in the Table 1. We can notice that in cases when a value of transmission rate β decreases (0.75 → 0.15) while the values of the other three parameters are fixed, then a value of R_0 decreases. In cases when a value of R_0 becomes less than one, the endemic equilibrium becomes unstable.

Now let us find the critical value of a transmission rate. In order to find this value, we set up the equality $R_0 = 1$, where the values of the other parameters are fixed. So, we get a resulting value $\beta^* = 0.2$. We can conclude that in a case we set up the values of three parameters to be constant, a disease will spread out if a value of a transmission rate is bigger than a critical value $\beta^* = 0.2$; the disease will be controlled if a value of β

μ	β	σ	γ	R_0	Nature of EE state
0.000034	0.75	0.33	0.2	3.75	Stable
0.000034	0.7	0.33	0.2	3.5	Stable
0.000034	0.5	0.33	0.2	2.5	Stable
0.000034	0.3	0.33	0.2	1.5	Stable
0.000034	0.2	0.33	0.2	1	Critical value
0.000034	0.18	0.33	0.2	0.9	Unstable
0.000034	0.15	0.33	0.2	0.75	Unstable

Table 1. Sensitivity analysis of the Endemic Equilibrium state

is less than $\beta^* = 0.2$.

Before the vaccine against SARS was invented, the quarantine and the isolation were the only control measures. The aim of these measures was to decrease a value of a transmission rate and control a disease. However, in a practice a disease did not die out because of the phenomenon called superspreading. Namely, the superspreading is the transmission of an infectious disease to a very large number of uninfected persons by the relatively small number of highly contagious persons. Beijing experienced the largest outbreak of SARS, with more than 2500 cases reported between March and June 2003 [15]. The superspreading mostly depends on the environment (the hospitals have a crucial role) and the age of a patient. This phenomenon also played major role in a transmission of SARS in Singapore and Toronto. After introducing the measures decided by WHO and relayed by governments a situation approved significantly.

5. CONCLUSION

We successfully applied a method of mathematical logic, quantifier elimination, in epidemiology. We presented the application of QE for the SEIRS model in this paper. We obtained the values of a reproduction number and an endemic equilibrium as a result. Considering the methods used in the other papers related to the application of QE, the methods for QE were completely different. A resulting quantifier free equivalent formula consists of 25 atomic formulas for the SEIRS model, while the value of endemic equilibrium was not evaluated in [6].

In this paper, we also analysed one concrete example for SARS. The SEIR model was applied in the analysis. A main problem in a practice was the phenomenon called superspreading, but measures decided by WHO were effective in preventing superspreading. Considering the SEIRS model, it is applicable to the diseases with a long incubation period and temporary immunity of recovered persons. One example of its application is an application to malaria.

In the introductory part we reviewed the prediction models for covid-19. When comparing the predictions of several models with the real data, it was concluded that the SEIRQ and the ARIMA model were appropriate for analysis of covid-19 [16].

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REFERENCES

1. Brauer F, Castillo-Chavez C. Mathematical Models in Population Biology and Epidemiology, New York: Springer, 2012.
2. Brauer F, van den Driessche P, Wu J. Mathematical Epidemiology, Berlin: Springer Science and Bussines Media, 2008.
3. Liu WM, van den Driessche P. Epidemiological models with varying population size and dose-dependent latent period, Mathematical Biosciences. 1995; 128: 57-69.
4. Naheed A, Singh M, Lucy D. Numerical study of SARS epidemic model with the inclusion of diffusion in the system, Applied Mathematics and Computation. 2014; 229: 480-498.
5. Hethcote HW. The mathematics of infectious disease, SIAM Review. 2000; 42(4): 599-653.
6. Brown CW, El Kahoui M, Novotni D, Weber A, Algorithmic methods for investigating equilibria in epidemic modeling, J. of Symbolic Computation. 2006; 41: 1157-1173.
7. Dietz K. Transmission and control of arbovirus diseases, Epidemiology, pages. SIAM. 1975: 104-121
8. El Kahoui M, Weber A. Deciding Hopf bifurcations by quantifier elimination in a software-component architecture, J. of Symbolic Computation. 2000; 30(2): 161-179.
9. Tarski A. A decision method for elementary algebra and geometry, 2nd Edition, RAND (1957)
10. Collins GE. Quantifier elimination for real closed fields by cylindrical algebraic decomposition-preliminary report. ACM SIGSAM Bull. 1974; 8(3): 80-90. Proc. EUROSAM 74
11. Collins GE. Quantifier elimination for the elementary theory of real closed fields by cylindrical algebraic decomposition. In: Automata Theory for Formal Languages, 2nd GI Conference, volume 33 of LNCS, pp. 134-183, Springer, 1975.
12. Marker D. Model theory-an introduction, Springer-Verlag, 2002.
13. Udovičić M. Quantifier Elimination in fields and application in Geometry, Advanced Technologies, Systems and Applications. 2020; 142(V): 375-396.
14. Wai Ng T, Turinici G, Danchin A. A double epidemic model for the SARS propagation, BMC Infectious diseases. 2003; 3: 19.
15. Shen, F. Ning, W. Zhou, X. He, C. Lin, D. P. Chin, Z. Zhu, Z, Schuchat A. Superspreading SARS events, Beijing. Emerg Infect Dis.. 2003; 10(2): 256-260.
16. Anirudh A. Mathematical modeling and the transmission dynamics in predicting the Covid-19- What next in combating the pandemic, Infectious Disease Modelling. 2020; 5: 366-374.
17. Arino J, Portet S. A simple model for COVID-19, Infectious Disease Modelling. 2020; 5: 309-315.