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SIR-based mathematical modeling of infectious diseases with vaccination and waning immunity

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ABSTRACT

In this paper we will derive an SIR model describing vaccination as well as waning immunity and propose a finite difference scheme for its solution together with some qualitative results. For the modeling of the waning immunity we assume a statistical distribution for the level of antibodies depending on the time lapsed since individual's full recovery or vaccination.

We arrive at a system of two ODEs and two PDEs that we reduce to a model of just two ODEs and a few algebraic equations. Next, we propose and implement an efficient numerical scheme to solve this reduced model, based on finite differences. To illustrate our findings we provide graphical results and discuss some qualitative properties of the solutions. Additionally, we derive formulas for the basic reproduction number $\mathcal{R}_0$ and the effective reproduction number $\mathcal{R}(t)$ of the reduced model and show the behavior of solutions for examples with $\mathcal{R}_0 > 1$ and $\mathcal{R}_0 < 1$.

1. Introduction

Susceptible-infectious-recovered (SIR) types of mathematical models are used to model the spread of an infectious disease. They are compartmental models, with the following standard compartments into which a population is divided: the group S of individuals who are susceptible to the disease and can become infected, the group I of individuals who are infectious and can infect other susceptible individuals during encounter, and the group R of recovered individuals who gained life-long immunity at recovery and cannot get infected anymore (this assumption can be relaxed). An SIR model was firstly proposed by Kermack and McKendrick [19] and it has been subject to various investigations, modifications and extensions since then. The basic homogeneous model can be extended for other compartments (SEIR, SEIS, MSIR, MSEIR, MSEIRS and other models), vaccination (e.g. [26,32]), regional, age or other heterogeneity of population (e.g. [34,27,8,28,35]), disease parameters heterogeneity (e.g. [16]).

Another option for extending SIR types of models is taking waning or boosting immunity into account. The duration of resistance against a disease after overcoming it naturally or after vaccination can differ for different diseases as well as over time. For infectious diseases like measles, one often assumes that immunity is long or even life-long after recovery or vaccination, but in reality it may be subject to waning with subsequent loss of immunity. There are a few different approaches to SIR models with waning immunity in the literature. Some authors utilized exponential waning profile/function [6], other authors used so-called renewal equations (e.g. [24]). Dafilis et al. [7] studied a SIRS model, in which one can transfer from the compartment of recovered back to susceptible and consequently oscillatory dynamics appear. Rouder et al. [25] considered optimal vaccination ages in one-dose and two-dose vaccination schedules, in regard to waning and boosting immunity. Barbarossa and Röst [2] provided an extensive theoretical study of a general model with waning and boosting immunity.

Estimating the real process of waning immunity is not easy, as it is hardly measurable. Mossong et al. [23] studied the decay in vaccine-induced immunity over time and assume that the level of antibodies has a log-normal distribution. Heffernan and Keeling [17] focused on investigating a mechanistic within-host model of the immune system, corresponding epidemiological transmission and the consequences of long-term vaccination. Some other authors have used delay differential equations to model waning immunity or other tools, see e.g. [1] or [3,18,29,30]. Vaccination

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coverage has been studied by Chladná and Moltchanová [4], asking questions if and how it can be modeled, from perspective of measles incidence in previous years.

A detailed overview of literature on this topic is provided in already mentioned paper [2] by Barbarossa and Röst. The authors also provide a general model for vaccination, waning as well as boosting immunity, in which individuals from the compartment of recovered or vaccinated are subject to waning (and boosting) immunity and after their immunity level drops below a certain critical threshold, they transfer back to a compartment of susceptibles. The authors cover a general case of an infectious disease model consisting of a system of ordinary differential equations (ODEs) coupled with two partial differential equations (PDEs) and investigate analytic properties of the solution like existence, uniqueness, non-negativity, equilibrium, stability, and they also discuss the connection of their general model to other models based on ODEs, PDEs or DDEs (delay DEs). Even though they provide an extensive theoretical study, they do not provide any suggestions for solving the dynamical system numerically. As far as analytic solutions are considered, the authors solve the system of two ODEs (for the compartments S, I) and one PDE (for the compartment of recovered) for three immunity levels only – high, intermediate, low – and do so by method of lines, which turns the PDE into a system of stiff ODEs.

In this paper, we will suggest an alternative model with vaccination as well as waning immunity and we shall also propose a numerical scheme for its solution together with providing some qualitative results. The difference to the general model of Barbarossa and Röst [2] is the modeling of waning immunity. While in [2], the authors considered a given function $g(z)$ describing the change of the immunity level, in our paper, we will adopt the approach of Mossong et al. [23] who assumed a statistical distribution for the level of antibodies depending on the time lapsed since individual's full immunity. We shall deal with a system of two ODEs (for S, I) and two PDEs (for recovered and vaccinated), which we shall reduce to just two ODEs and a few algebraic equations. Subsequently, we propose and implement an efficient numerical scheme to solve this reduced model, based on finite differences. We provide graphical results and discuss some properties of the solutions. We also derive formulas for the basic reproduction number $\mathcal{R}_0$ and the effective reproduction number $\mathcal{R}(t)$ implied by the reduced model and illustrate the behavior of solutions for examples with $\mathcal{R}_0 > 1$ and $\mathcal{R}_0 < 1$.

The paper is structured as follows. In Section 2, we recall the known basic SIR model and one with vaccination for the sake of readers' comfort. Section 3 summarizes the main points of modeling waning immunity, following Mossong et al. [23] and Zibolenová et al. [33]. We include this model of waning immunity into the SIR model in Section 4. Here we derive a system of ODEs and PDEs describing the dynamics of the system. Due to the complexity of the dynamics which cannot be "seen" right away, we start by evaluating the system balance in a discrete setting and then transfer it to a continuous model. Section 5 is dedicated to the reduction of the model from two ODEs and two families of PDEs to only two ODEs with a memory term and a few algebraic equations. We also derive formulas for the basic reproduction number and the effective reproduction number implied by this model. Finally, Section 6 contains the proposed numerical scheme and shows the results from two examples. We compare the results of our model with results of the known SIRS model in Section 7 and finally we conclude our work with a brief discussion.

2. Basic homogeneous SIR models

For the comfort of the readers, we recall the basic SIR model, firstly proposed by Kermack and McKendrick [19] and subsequently used, modified or investigated by many authors. The model's idea is to distinguish between three types of individuals with respect to their relationship to the disease: susceptible (S) who can get infected, infectious (I) who transmit the disease during encounters with susceptible individuals, and recovered (R) who are immune against the disease and cannot get infected. A *basic SIR model* describing the interactions between the compartments S, I and R reads

$$\begin{aligned} \frac{dS(t)}{dt} &= -\beta\frac{I(t)S(t)}{N} + \mu N - \mu S(t), \\ \frac{dI(t)}{dt} &= \beta\frac{I(t)S(t)}{N} - \gamma I(t) - \mu I(t), \\ \frac{dR(t)}{dt} &= \gamma I(t) - \mu R(t), \end{aligned} \tag{1}$$

where $S(t)$ is the number of susceptible individuals in the population at time t, $I(t)$ the number of infectious, $R(t)$ the number of recovered, $N = S(t) + I(t) + R(t)$ denotes the total (conserved) population, μ is the birth rate as well as mortality rate (the equality of these two rates ensures a constant size of population over time: $N(t) = N$), γ is the rate of recovery. The parameter β is the *transmission coefficient* reflecting the "strength" of disease in terms of probability that a susceptible individual becomes infected during an encounter with an infectious one on one hand, and the number of contacts of each individual on the other hand (we recall that in this simple model, the population is assumed to be homogeneous, i.e. all individuals have the same number of contacts as well as social habits and conditions). This model does not consider any age or spatial structure or vaccination or waning immunity.

For the ease of understanding the more complicated model presented in the next section easier, we first demonstrate incorporating vaccination in the basic model (1). If individuals get vaccinated right after birth as newborns and if x denotes the so called actual vaccination coverage (percentage of new vaccinated children per unit of time), and if we use different notation for birth rate (ν) and mortality rate (μ), the homogeneous model becomes

$$\begin{aligned} \frac{dS(t)}{dt} &= -\beta\frac{I(t)S(t)}{N(t)} + \nu(1-x)N(t) - \mu S(t), \\ \frac{dI(t)}{dt} &= \beta\frac{I(t)S(t)}{N(t)} - \gamma I(t) - \mu I(t), \\ \frac{dR(t)}{dt} &= \gamma I(t) + \nu x N(t) - \mu R(t), \end{aligned} \tag{2}$$

where $N(t) = S(t) + I(t) + R(t)$ denotes again the total size of population, which, in general, is non-constant if $\nu \neq \mu$. In this simple case, we assume that vaccines have 100% effectiveness, meaning they do not fail and they provide complete and life-long immunity, same as recovery from natural infection does. Alternatively, we could interpret x as the rate of successful (effective) vaccination.

3. Modeling waning immunity

Following the works [20,23,33], we denote by $SVF(\tau)$ (stands for *secondary vaccine failure*) the probability that the level of antibodies of an immune person with time τ since the last immunization (vaccination or recovery after natural infection) drops below a critical threshold C_{crit}. Next, we denote by

$$GMT(\tau) = GMT(0)e^{-w\tau},$$

the geometric mean of the level of antibodies, with w being the *waning rate*. We also assume that the concentration $C(\tau)$ of antibodies in each time τ since recovery or vaccination is a log-normally distributed random variable, that is, $x = \ln C(\tau)$ is a normally distributed random variable with mean $\ln GMT(\tau)$ and standard deviation σ. Then we can express the secondary vaccine

failure as

$$SVF(\tau) = P(x < \ln(C_{\text{crit}})) = \frac{1}{\sqrt{2\pi\sigma^2}} \int_{-\infty}^{\ln(C_{\text{crit}})} e^{-(x-\ln GMT(\tau))^2/2\sigma^2}\, dx. \quad (3)$$

In other words, *SVF* is the probability that the immunity of a host drops below a critical threshold and the individual becomes susceptible again. Data for this model is available from estimations in other research papers; we summarize the data as well as their sources in Table 1. We depict an example of the process of waning immunity in Fig. 1.

4. Model with vaccination and waning immunity

We shall now proceed to derive a model which utilizes the waning immunity concept introduced in the previous section. As it is not intuitively straightforward to write the continuous model right away, we shall start by the discrete consideration of the dynamics.

In a model with waning immunity, individuals who once have been immune (recovered or vaccinated), may lose their protection if the level of their antibodies decreases below a certain critical level C_{crit}. Individuals who have lost their immunity will enter back from R or V into the state S of being susceptible. The differential equation for S will therefore contain terms with the recovered R and the vaccinated V and so it is practical to start with deriving an equation for the dynamics of recovered and vaccinated yet before investigating the dynamics of S.

At the very beginning let us consider the simplest dynamics first, the one of I. There are no specific changes in the corresponding ODE compared to other known models also described in Section 2. Therefore, we just present it here without any further explanation:

$$\frac{dI(t)}{dt} = \beta \frac{I(t)S(t)}{N(t)} - \gamma I(t) - \mu I(t), \quad (4)$$

where we recall that γ is the rate of recovery, β is the transmission rate and μ is the yearly natural mortality rate. We allowed for a non-constant population size $N(t)$, as the birth and mortality rates will not have to be equal in the model, and hence the overall balance of the population might not be constant.

4.1. Equation for recovered individuals

We denoted by $S(t)$, $I(t)$ the number of susceptible and infectious individuals at time t. It is natural to define another unknown function as the number of recovered individuals at time t who recovered from the naturally gained disease τ time units before t. As we will see, a more suitable unknown function to work with is this number normalized to one time unit (year), which we shall denote by $R(t, \tau)$. We shall derive a differential equation governing the normalized number of recovered, $R(t, \tau)$.

First, we recall that $SVF(\tau)$ is the probability that individual loses immunity before time τ since recovery. Now, let $P(\tau) := 1 - SVF(\tau)$ denote the probability that an individual retains immunity at least up to time instance τ since recovery. During a small time interval from t to $t+\Delta t$, the number $\gamma I(t)\Delta t$ of infectious individuals get recovered, and out of them only $\gamma I(t)\Delta t\, P(0)$ gain a sufficient (and full) immunity for protection; the rest of them remain susceptible. The initial condition for normalized number of recovered will then be $R(t, 0) = \gamma I(t) P(0)$.

Let us denote for a moment the (not normalized) number of recovered at time t with time τ since recovery by $R^*(t, \tau)$. For the sake of simplicity, we now consider waning immunity as the only reason for individuals to leave the compartment of recovered. We do not take natural death into account at this point. Then it is obvious that $R^*(t, \tau) = R^*(t-\tau, 0)P(\tau)/P(0)$. Indeed, if $R^*(t-\tau, 0)$ is the number of individuals at time $t-\tau$ who are 0 time units since recovery and are immune, then $R^*(t-\tau, 0)/P(0)$ is the total number of individuals who just recovered at time $t-\tau$. Finally, $R^*(t-\tau, 0)P(\tau)/P(0)$ is the number of people who recovered at $t-\tau$ and are still immune at time t. Dividing both sides of this equation by Δt, we get the same equation for the normalized function R:

$$R(t, \tau) = R(t-\tau, 0)\frac{P(\tau)}{P(0)}. \quad (5)$$

Once knowing the profile $P(\tau)$ and the value of $R(t, 0)$ for a certain time t, values $R(t+h, h)$ are known for any time step $h > 0$. After a time step $\Delta t > 0$, the corresponding equation must hold as well:

$$R(t+\Delta t, \tau+\Delta t) = R(t-\tau, 0)\frac{P(\tau+\Delta t)}{P(0)}. \quad (6)$$

By dividing these two equations, we get

$$\frac{R(t, \tau)}{R(t+\Delta t, \tau+\Delta t)} = \frac{P(\tau)}{P(\tau+\Delta t)}. \quad (7)$$

In order for this operation to be legal, we need to secure nonzeroness of the terms in the denominators. It holds that $P(\tau) > 0$ for any τ. Positivity of $R(t, \tau)$ for any $t, \tau > 0$ will be a consequence of the following assumption:

$$\text{we assume that } I(0) = I_0 > 0. \quad (A1)$$

This assumption is meaningful and not restricting, as for $I(0) = 0$ there would be no relevant dynamics in the compartment R.

Lemma 4.1. *Under Assumption (A1), it holds that $I(t) > 0$ for any $t > 0$.*

Proof. This statement is obvious from (4), the solution of which is

$$I(t) = I_0 e^{-\int_0^t (\beta S(s)/N(s) - \gamma - \mu)ds},$$

which means $I(t) > 0$ for all $t > 0$ if $I_0 > 0$. □

Remark 4.2. As a consequence of Lemma 4.1, it holds that $R(t, 0) := \gamma I(t) > 0$ for any $t > 0$. For now, let us make another assumption:

$$\text{we assume that } R(t, \tau) > 0 \text{ for any } t, \tau > 0. \quad (A2)$$

We shall show that this assumption is fulfilled later in Corollary 4.4. For now, it ensures that the denominator on the left-hand side of (7) is non-zero too.

Applying the logarithm to both sides of (7) yields

$$\ln(R(t, \tau)) - \ln(R(t+\Delta t, \tau+\Delta t)) = \ln(P(\tau)) - \ln(P(\tau+\Delta t)).$$

Adding a special zero on the left-hand side and dividing by Δt leads to:

$$\frac{\ln(R(t, \tau)) - \ln(R(t+\Delta t, \tau))}{\Delta t} + \frac{\ln(R(t+\Delta t, \tau)) - \ln(R(t+\Delta t, \tau+\Delta t))}{\Delta t} = \frac{\ln(P(\tau)) - \ln(P(\tau+\Delta t))}{\Delta t}.$$

Letting $\Delta t \to 0$, we arrive at the following differential equation:

$$\frac{\partial \ln((R(t, \tau)))}{\partial t} + \frac{\partial \ln(R(t, \tau))}{\partial \tau} = \frac{d \ln((P(\tau)))}{d\tau},$$

and hence, the PDE for the recovered individuals R reads

$$\frac{\partial R}{\partial t} + \frac{\partial R}{\partial \tau} = \frac{P'}{P} R. \quad (8)$$

Table 1
Measles: parameters entering the model of waning immunity. Scenario 1 without waning, more pessimistic scenarios 2 and 3, more optimistic scenarios 4 and 5.

	$GMT(0)$	σ	w (p.a.)	C_{crit}
Scenario 1	–	–	–	–
Scenario 2	1914 mIU/mL	0.92	0.069	150 mIU/mL (350 mIU/ml)
Scenario 3	1523 mIU/mL	0.97	0.078	120 mIU/mL
Scenario 4	2000 mIU/mL	0.9	0.05	150 mIU/mL (350 mIU/ml)
Scenario 5	2000 mIU/mL	0.9	0.03	150 mIU/mL (350 mIU/ml)

Source: [33,9,20].

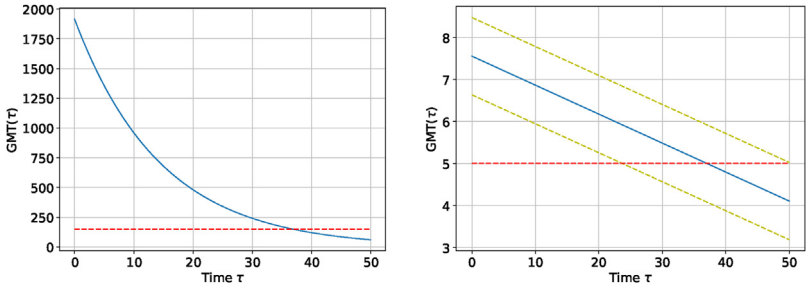

Fig. 1. Immunity waning scenario 2 (see Table 1). Left: $GMT(\tau)$. Right: $E(\ln C(\tau)) \pm \sigma$. The time τ since full immunity is in years. The red horizontal interrupted lines represent C_{crit} and $\ln C_{crit}$. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Next, let $R(t)$ denote the overall number of recovered individuals at time t. In the discrete setting, it is obvious that

$$R(t) = \sum_{i=0}^{\infty} R^*(t, \tau_i).$$

Recognizing that $\Delta t \equiv \Delta\tau$, because a shift in running time t is always the same like the shift in time since recovery τ for any individual, and multiplying the right-hand side of this equation by $\Delta\tau/\Delta t \equiv 1$, we get

$$R(t) = \sum_{i=0}^{\infty} \frac{R^*(t, \tau_i)}{\Delta t}\Delta\tau = \sum_{i=0}^{\infty} R(t, \tau_i)\Delta\tau,$$

which in the continuous limit $\Delta\tau \to 0$ becomes

$$R(t) = \int_0^{\infty} R(t, \tau)\, d\tau.$$

Now, to include the effect of natural death into our considerations, we look back at the relation (7) in another form:

$$R(t + \Delta t, \tau + \Delta t) = R(t, \tau)\frac{P(\tau + \Delta t)}{P(\tau)}.$$

Including natural death into this equation is now straightforward. If μ denotes the yearly natural mortality rate, then the probability that an individual does not die within an interval of length Δt is $1 - \mu\Delta t$. Since we consider natural mortality to be independent to waning immunity, we multiply these probabilities:

$$R(t + \Delta t, \tau + \Delta t) = R(t, \tau)\frac{P(\tau + \Delta t)}{P(\tau)}(1 - \mu\Delta t). \tag{9}$$

We again take analogous steps like previously: we divide the equation by $R(t, \tau)$, add a special zero, take logarithm, divide by Δt and arrive at

$$\frac{\ln(R(t + \Delta t, \tau + \Delta t)) - \ln(R(t, \tau))}{\Delta t} = \frac{\ln(P(\tau + \Delta t)) - \ln(P(\tau))}{\Delta t} + \frac{\ln(1 - \mu\Delta t)}{\Delta t}.$$

Letting $\Delta t \to 0$, we obtain

$$\frac{1}{R}\frac{\partial R}{\partial t} + \frac{1}{R}\frac{\partial R}{\partial \tau} = \frac{P'}{P} + \lim_{\Delta t \to 0} \ln\left((1 - \mu\Delta t)^{1/\Delta t}\right)$$

and subsequently

$$\frac{\partial R}{\partial t} + \frac{\partial R}{\partial \tau} = R\left(\frac{P'}{P} - \mu\right). \tag{10}$$

This is the PDE governing the evolution of the (normalized) number of recovered if waning immunity and natural deaths are considered.

Lemma 4.3. *Eq. (10) with given initial profile $R(0, \tau)$ has the analytic solution*

$$R(t, \tau) = R(t - \tau, 0)\frac{P(\tau)}{P(0)}e^{-\mu\tau}. \tag{11}$$

Proof. First, we divide both sides of (10) by $R(t, \tau)$ and substitute $u(t, \tau) = \ln R(t, \tau)$ and arrive at

$$\frac{\partial u(t, \tau)}{\partial t} + \frac{\partial u(t, \tau)}{\partial \tau} = \frac{P'(\tau)}{P(\tau)} - \mu.$$

This is a first-order PDE with characteristic system

$$\frac{dt}{ds} = 1,$$
$$\frac{d\tau}{ds} = 1,$$
$$\frac{du}{ds} = \frac{P'(\tau(s))}{P(\tau(s))} - \mu.$$

Noticing that $\dot{t} - \dot{\tau} = 0$, we can identify the first characteristic $\Phi = t - \tau$. To get a second characteristic, we divide du/ds by $d\tau/ds$ and get

$$\frac{du}{d\tau} = \frac{P'(\tau)}{P(\tau)} - \mu,$$

which has a solution $u = \ln(P(\tau)) - \mu\tau + c_2$. Hence, the second characteristic is $\psi = u - \ln(P(\tau)) + \mu\tau$.

The general solution is then given by $F(\Phi, \psi) = 0$ with F being an arbitrary function. We choose $F(\Phi, \psi) = f(\Phi) - \psi$, where f will be determined later. We obtain

$$u = f(t - \tau) + \ln(P(\tau)) - \mu\tau.$$

By taking exponential from both sides, we get

$$R(t,\tau) = e^{f(t-\tau)}P(\tau)e^{-\mu\tau}.$$

If we choose $f(t-\tau) := \ln\left(R(t-\tau,0)/P_R(0)\right)$, it holds

$$R(t,\tau) = R(t-\tau,0)\frac{P_R(\tau)}{P_R(0)}e^{-\mu\tau}, \tag{12}$$

where we added the index R to the function P for the sake of distinguishing between the P function of recovered and vaccinated.

The final step is to show that there is no contradiction on boundary $R(t,0)$. The right-hand side of the above analytic expression (12) says that $R(t,0)$ should be equal to $R(t-0,0)P_R(0)e^{-\mu 0}/P_R(0)$, which is truly identical to $R(t,0)$. □

The following property justifies Assumption (A2) and follows directly from Lemma 4.3.

Corollary 4.4. *If $P(\tau)>0$ for all $\tau \in \mathbb{R}$, it holds that $R(t,\tau)>0$ for all $t,\tau \in \mathbb{R}$.*

Remark 4.5. If we want to solve (10) numerically, we would face a problem with convergence or numerical stability. Indeed, the term $R(t,\tau)P'(\tau)/P(\tau)$ contains two conflicting terms: $P'(\tau)/P(\tau)$ goes to $-\infty$ for $\tau\to\infty$, while $R(t,\tau)$ tends to zero for $\tau\to\infty$. Thus, we have a product of a term going to zero and of a term going to $-\infty$. One would have to prove that the speed of convergence to zero is faster than the one to $-\infty$, so we ensure that the number of recovered does not go to $-\infty$ (or is not negative at all). However, Eq. (10) can be reformulated using Lemma 4.3 into the form

$$\frac{\partial R(t,\tau)}{\partial t} + \frac{\partial R(t,\tau)}{\partial \tau} = R(t-\tau,0)\frac{P_R'(\tau)}{P_R(0)}e^{-\mu\tau} - R(t,\tau)\mu,$$

which avoids the problematic expressions. We do not need to solve Eq. (10) in this paper though, as we will reduce the model and get rid of this PDEs later.

Remark 4.6. We note that the derivation of a PDE for the population of vaccinated individuals is analogous to the one for recovered individuals, therefore we shall skip it in this paper and directly provide the corresponding PDE when presenting the complete model.

4.2. The effect of waning immunity on the susceptibles

To derive the waning immunity terms that should enter an equation for S, we again examine the discrete setting first. Let us start with making clear which part of R (or R^*) contributes to S. The following is true for all immune at time $t+\Delta t$:

$$\underbrace{\sum_{j=0}^{\infty} R^*(t+\Delta t, j\Delta t+\Delta t)}_{\text{Stillimmune}} = \underbrace{\sum_{j=0}^{\infty} R^*(t,j\Delta t)}_{\text{Immuneat } t} - \underbrace{\mu\Delta t\sum_{j=0}^{\infty} R^*(t,j\Delta t)}_{\text{Died}} - \underbrace{\Delta S(t)}_{\text{Lostimmunity}}.$$

Then

$$\Delta S(t) = \sum_{j=0}^{\infty}\left[R^*(t,j\Delta t)\left(1-\frac{P(j\Delta t+\Delta t)}{P(j\Delta t)}-\mu\Delta t\right)\right]$$

and finally we can write

$$S(t+\Delta t) = S(t) + \sum_{j=0}^{\infty} R^*(t,j\Delta t)\left(1-\frac{P(j\Delta t+\Delta t)}{P(j\Delta t)}-\mu\Delta t\right).$$

If we express $P(j\Delta t)$ and $P((j+1)\Delta t)$ from (5) and (6), we get

$$S(t+\Delta t) = S(t) + \sum_{j=0}^{\infty} R^*(t,j\Delta t)\left(\frac{R(t,j\Delta t)-R(t+\Delta t,j\Delta t+\Delta t)}{R(t,j\Delta t)}-\mu\Delta t\right)$$

and subsequently

$$S(t+\Delta t) = S(t) + \left(\sum_{j=0}^{\infty} R(t,j\Delta t) - R(t+\Delta t,j\Delta t+\Delta t) - R(t,j\Delta t)\mu\Delta t\right)\Delta t. \tag{13}$$

Now we can divide the entire equation by Δt and multiply the sum on the right-hand side by $\Delta t/\Delta t$. We get

$$\frac{S(t+\Delta t)-S(t)}{\Delta t} = \sum_{j=0}^{\infty}\left(\frac{R(t,j\Delta t)-R(t+\Delta t,j\Delta t+\Delta t)}{\Delta t} - R(t,j\Delta t)\mu\right)\Delta t.$$

Letting $\Delta t\to 0$, we arrive at:

$$\frac{dS(t)}{dt} = -\int_0^\infty\left(\frac{\partial R(t,\tau)}{\partial t}+\frac{\partial R(t,\tau)}{\partial \tau}\right)d\tau - \mu\int_0^\infty R(t,\tau)\,d\tau,$$

which by (10) is the same as

$$\frac{dS(t)}{dt} = -\int_0^\infty R(t,\tau)\left(\frac{P_R'(\tau)}{P_R(\tau)}-\mu\right)d\tau - \mu\int_0^\infty R(t,\tau)\,d\tau$$

and subsequently

$$\frac{dS(t)}{dt} = -\int_0^\infty R(t,\tau)\frac{P_R'(\tau)}{P_R(\tau)}\,d\tau.$$

Adding the standard terms into this equation, like the new infected, the newborn, and the naturally died, is now straightforward and we will present the complete equation when presenting the complete model.

4.3. The complete model with waning immunity

We can now summarize the complete model when waning immunity and vaccination at the moment of birth are considered:

$$\begin{aligned}\frac{dS(t)}{dt} &= -\beta\frac{S(t)I(t)}{N(t)} + \nu N(t)(1-x) - \mu S(t)\\ &\quad - \int_0^\infty R(t,\tau)\frac{P_R'(\tau)}{P_R(\tau)}\,d\tau - \int_0^\infty V(t,\xi)\frac{P_V'(\xi)}{P_V(\xi)}\,d\xi\\ &\quad + (1-P_R(0))\gamma I(t) + (1-P_V(0))\nu N(t)x\end{aligned} \tag{14}$$

$$\frac{dI(t)}{dt} = \beta\frac{S(t)I(t)}{N(t)} - \gamma I(t) - \mu I(t) \tag{15}$$

$$\frac{\partial R(t,\tau)}{\partial t}+\frac{\partial R(t,\tau)}{\partial \tau} = R(t,\tau)\left(\frac{P_R'(\tau)}{P_R(\tau)}-\mu\right) \tag{16}$$

$$\frac{\partial V(t,\xi)}{\partial t}+\frac{\partial V(t,\xi)}{\partial \xi} = V(t,\xi)\left(\frac{P_V'(\xi)}{P_V(\xi)}-\mu\right) \tag{17}$$

with initial conditions

$$R(t,0) = \gamma I(t)P_R(0), \quad V(t,0) = \nu N(t)xP_V(0). \tag{18}$$

We denoted by x the portion of newborn individuals who are vaccinated at the moment of birth. We also distinguish between

$$P_R(\tau) := 1 - SVF_R(\tau) \quad \text{and} \quad P_V(\xi) := 1 - SVF_V(\xi)$$

as these may in general have different parameters, and so these two functions might differ. The variable ξ represents the time of an individual since their vaccination. The last two terms in the equation for S are terms containing individuals who got vaccinated or recovered, but lost their protection right away.

Remark 4.7. Eqs. (16) and (17) as well as the integral terms in (14) can be rewritten by means of Lemma 4.3. We did not do it here because we are not going to solve this system numerically.

5. A reduced model

In this section We shall solve the PDEs for R and V analytically, which will allow us to reduce the model (14)–(17) into just two ODEs.

Preposition 5.1. Analytic solutions to (16) and (17) are as follows:

$$R(t,\tau) = \gamma I(t-\tau) P_R(\tau) e^{-\mu\tau}, \tag{19}$$

$$V(t,\xi) = \nu N(t-\xi) x P_V(\xi) e^{-\mu\xi}. \tag{20}$$

Proof. The statement follows directly from the interpretation of the function P. Starting from new recovered (or vaccinated), $R(t-\tau, 0)$ (or $V(t-\xi, 0)$), the number of individuals who still retain protection, i.e. who did not lose immunity and who did not die, is

$$\begin{aligned} R(t,\tau) &= R(t-\tau,0)\frac{P_R(\tau)}{P_R(0)} e^{-\mu\tau}, \\ V(t,\xi) &= V(t-\xi,0)\frac{P_V(\xi)}{P_V(0)} e^{-\mu\xi}. \end{aligned}$$

The rest follows easily from plugging in the boundary conditions (18). □

Next we substitute $R(t,\tau)$ from (19) and $V(t,\xi)$ from (20) into (15). We arrive at a system of two ordinary-integral differential equations with one-dimensional time variable:

$$\begin{aligned} \frac{dS(t)}{dt} &= -\beta\frac{S(t)I(t)}{N(t)} + \nu N(t)(1-x) - \mu S(t) \\ &\quad + \int_0^\infty \gamma I(t-\tau) e^{-\mu\tau} P_R'(\tau)\, d\tau \\ &\quad + \int_0^\infty \nu N(t-\xi) x e^{-\mu\xi} P_V'(\xi)\, d\xi \\ &\quad + (1-P_R(0))\,\gamma I(t) + (1-P_V(0))\,\nu N(t) x. \end{aligned} \tag{21}$$

$$\frac{dI(t)}{dt} = \beta\frac{S(t)I(t)}{N(t)} - \gamma I(t) - \mu I(t), \tag{22}$$

supplemented by relationships for total recovered and vaccinated at time t, reading

$$R(t) = \int_0^\infty R(t,\tau)\, d\tau = \int_0^\infty \gamma I(t-\tau) P_R(\tau) e^{-\mu\tau}\, d\tau \tag{23}$$

and

$$V(t) = \int_0^\infty V(t,\xi)\, d\xi = \int_0^\infty \nu N(t-\xi) x P_V(\xi) e^{-\mu\xi}\, d\xi. \tag{24}$$

Finally, we have

$$N(t) = S(t) + I(t) + R(t) + V(t). \tag{25}$$

Moreover, one can notice that Eq. (22) can be solved analytically as well. To do so, we use the formula of variation of constants and obtain

$$I(t) = I_0 \exp\left(\beta \int_0^t \frac{S(a)}{N(a)}\, da - (\gamma+\mu)t\right). \tag{26}$$

That means, to compute $I(t)$ analytically, we would need to integrate the ratio $S(a)/N(a)$ over all $a \in [0,t]$. It is not really possible to do this analytically, though, as we can only calculate $S(t)$ from the nonlinear ODE (21) numerically and using $I(t)$ itself.

Remark 5.2. The model (21) and (22) can be re-written in terms of relative subpopulations $s(t) := S(t)/N(t)$, $i(t) := I(t)/N(t)$. If the population has a constant size ($\nu = \mu$), i.e. $N(t) \equiv N = \text{const.}$, then it is easy to re-write the system to the following one:

$$\begin{aligned} \frac{ds(t)}{dt} &= -\beta s(t) i(t) + \nu(1-x) - \mu s(t) \\ &\quad + \int_0^\infty \gamma i(t-\tau) e^{-\mu\tau} P_R'(\tau)\, d\tau + \int_0^\infty \nu x e^{-\mu\xi} P_V'(\xi)\, d\xi \\ &\quad + (1-P_R(0))\,\gamma i(t) + (1-P_V(0))\,\nu x \end{aligned} \tag{27}$$

$$\frac{di(t)}{dt} = \beta s(t) i(t) - \gamma i(t) - \mu i(t). \tag{28}$$

For the numbers of recovered and vaccinated, we get

$$r(t) = \frac{R(t)}{N} = \int_0^\infty \gamma i(t-\tau) P_R(\tau) e^{-\mu\tau}\, d\tau, \tag{29}$$

and

$$v(t) = \frac{V(t)}{N} = \int_0^\infty \nu x P_V(\xi) e^{-\mu\xi}\, d\xi. \tag{30}$$

We note that for a nonconstant population size $N(t)$, it is rather difficult to re-write the equations in this way.

5.1. The reproduction number

In the theory of infectious disease modeling and epidemiology the notion of the reproduction number is a central quantity. The *basic reproduction number* [5] is defined as the number of secondary infections caused by a single infectious introduced into a fully susceptible population over the course of the infection of this single infectious individual. The *effective reproduction number* [10] is the instantaneous reproduction number at calendar time t. If the reproduction number of a disease is greater than 1, the disease breaks out into epidemics; if it is less than 1, the disease dies out quickly. This characterization can be expressed in terms of the sign of the derivative of the number of infectious individuals: if $dI(t)/dt > 0$, the disease spreads out, if $dI(t)/dt < 0$, the disease dies out.

This allows to derive from (15) the formula for the reproduction number:

$$\begin{aligned} &\frac{dI(t)}{dt} = \beta\frac{S(t)}{N(t)} I(t) - (\gamma+\mu) I(t) \overset{!}{<} 0, \\ &\text{i.e.} \quad \frac{S(t)}{N(t)}\frac{\beta}{\gamma+\mu} < 1, \end{aligned}$$

hence the (constant) basic reproduction number (for $S(t) = N(t)$) reads

$$\mathcal{R}_0 = \frac{\beta}{\gamma+\mu}, \tag{31}$$

and the effective reproduction number at time t is defined as

$$\mathcal{R}(t) = \frac{S(t)}{N(t)}\frac{\beta}{\gamma+\mu}. \tag{32}$$

We can observe that none of these reproduction numbers depend on the size of the vaccinated, infectious or recovered subpopulation. Moreover, it is reasonable that the formula for the basic reproduction number $\mathcal{R}_0$ is identical to the one in the standard SIR model. This is due to the fact that in our model, the ODE for I was not modified compared to the standard model.

Remark 5.3. The formula for the effective reproduction number can be re-written in terms of relative population of susceptibles introduced in Remark 5.2 as

$$\mathcal{R}(t) = s(t)\frac{\beta}{\gamma+\mu},$$

from which we can see that the chance of the disease to break out in intermediate time t depends (besides the parameters of the disease) on the percentage of susceptible individuals in the current population.

The obvious relation $\mathcal{R}(t) \leq \mathcal{R}_0$ naturally implies an upper bound on the size of the epidemics: the epidemic size is maximal if the population is virgin.

6. Numerical implementation and results

In this section we shall propose a numerical scheme for solving system (21)–(25). The first two equations are ODEs, for which we will use forward Euler method (except of the integral terms, which we treated as explained below in (33)). The latter three equations are not differential equations. We note that the equations for S, R, V use information about the complete history of I or N.

To stay consistent with the rest of the text in this paper, we shall adopt the Δt notation for the numerical scheme too, instead of indexed time instances t like it is standard in most literature. Hence, let $\Delta t > 0$ be an equidistant time discretization step, $\tau_{\max}$ the maximal possible value of time since recovery considered for numerical computations (instead of infinity), similarly $\xi_{\max}$ the maximal considered time since vaccination.

Before we proceed to specifying a complete numerical scheme, we first take a look at the discretization of the integral terms in Eq. (21):

$$\int_0^\infty \gamma I(t-\tau)P_R'(\tau)e^{-\mu\tau}d\tau. \tag{33}$$

This integral represents immunity waning of recovered individuals. To find a discrete version of this term, we will use the balance equation (13):

$$\begin{aligned}
\Delta S(t) &= \left(\sum_{j=0}^{\infty} R(t,j\Delta t) - R(t+\Delta t, j\Delta t+\Delta t) - R(t,j\Delta t)\mu\Delta t\right)\Delta t\\
&= \left(\sum_{j=0}^{\infty}(1-\mu\Delta t)R(t,j\Delta t) - R(t+\Delta t, j\Delta t+\Delta t)\right)\Delta t\\
&= \left(\sum_{j=0}^{\infty}(1-\mu\Delta t)R(t,j\Delta t)\right)\Delta t - \left(\sum_{j=0}^{\infty}R(t+\Delta t, j\Delta t+\Delta t)\right)\Delta t\\
&= \left(\sum_{j=0}^{\infty}(1-\mu\Delta t)R(t,j\Delta t)\right)\Delta t - \left(\sum_{j=0}^{\infty}R(t+\Delta t, j\Delta t+\Delta t)\right)\Delta t\\
&\quad - R(t+\Delta t,0)\Delta t + R(t+\Delta t,0)\Delta t\\
&= \left(\sum_{j=0}^{\infty}(1-\mu\Delta t)R(t,j\Delta t)\right)\Delta t - \left(\sum_{j=0}^{\infty}R(t+\Delta t, j\Delta t)\right)\Delta t\\
&\quad + R(t+\Delta t,0)\Delta t\\
&= (1-\mu\Delta t)R(t) - R(t+\Delta t) + \gamma I(t)P_R(0)\Delta t.
\end{aligned}$$

The same procedure can be applied to the waning term for the vaccinated individuals, arriving at:

$$V(t)(1-\mu\Delta t) - V(t+\Delta t) + \nu N(t)xP_V(0)\Delta t.$$

In order to get more consistent results as $\Delta t \to 0$, we chose dying factor from equations (23) and (24) to keep in continuous form of $e^{-\mu\tau}$ and $e^{-\mu\xi}$, not coming back to discrete $(1-\mu\Delta t)^{\tau/\Delta t}$ and $(1-\mu\Delta t)^{\xi/\Delta t}$.

To improve computational efficiency, one can replace element-wise multiplication and summing by calculating inner products and working with vectors. All constants can be taken out before the product, which also speeds up the calculations. Let us note that the factors $e^{-\mu\tau}P_R(\tau)$, $e^{-\mu\xi}P_V(\xi)$ as well as $\mu\Delta t$ and $\nu\Delta t$ can be pre-calculated, so they do not need to be calculated in every iteration.

Ordering the discrete equations in the order in which they will be needed in the computation, we can write

$$I(t+\Delta t) = I(t) + I(t)\left(\beta\frac{S(t)}{N(t)} - \gamma - \mu\right)\Delta t, \tag{34}$$

$$R(t+\Delta t) = \sum_{j=0}^{\tau_{\max}/\Delta t} P_R(j\Delta t)e^{-\mu j\Delta t}\gamma I(t-j\Delta t)\Delta t, \tag{35}$$

$$V(t+\Delta t) = \sum_{j=0}^{\xi_{\max}/\Delta t} P_V(j\Delta t)e^{-\mu j\Delta t}\nu N(t-j\Delta t)x\Delta t, \tag{36}$$

$$\begin{aligned}
S(t+\Delta t) &= S(t) + \nu N(t)(1-x)\Delta t\\
&\quad + \nu N(t)x\left(1-P_V(0)\right)\Delta t - \mu S(t)\Delta t\\
&\quad - \beta\frac{S(t)I(t)}{N(t)}\Delta t + \left(1-P_R(0)\right)\gamma I(t)\Delta t\\
&\quad + R(t)(1-\mu\Delta t) - R(t+\Delta t) + \gamma I(t)P_R(0)\Delta t\\
&\quad + V(t)(1-\mu\Delta t) - V(t+\Delta t) + \nu N(t)xP_V(0),
\end{aligned} \tag{37}$$

$$N(t+\Delta t) = N(t) + N(t)(\nu-\mu)\Delta t \tag{38}$$

In Eqs. (34) and (37) we used forward differences to approximate the derivatives.

We implemented the above numerical scheme in `Python 3.7` using `numpy 1.15.4` and `scipy 1.1.0`[1] with the following parameters: $\Delta t = 0.001$, modeled time horizon $t_{\max} = 100$ years, maximal time since recovery $\tau_{\max} = 100$ years, maximal time since vaccination $\xi_{\max} = 100$ years, transmission parameter for disease outbreak $\beta = 50$ and for disease elimination $\beta = 40$, vaccination rate $x = 0.2$, natural natality and mortality rates $\nu = \mu = 0.02$, recovery rate $\gamma = 36$. We emphasize that all these parameters are academic, not real-life values.

Our aim was to illustrate the behavior of the system on a sample population of size $N(0) = 10^5$ and for suitably chosen parameters so that we get $\mathcal{R}_0 > 1$ in one case and $\mathcal{R}_0 < 1$ in the other case. Specifically, we have $\mathcal{R}_0 \approx 1.23$ for $\beta = 50$ and $\mathcal{R}_0 \approx 0.98$ for $\beta = 40$. We note that case studies using real data is a subject of our future work.

The parameters for modeling the waning immunity (*SVF*) were taken from Scenario 2 from Table 1, i.e. $GMT(0) = 1914$, $w_\tau = 0.069$, $w_\xi = 0.069$, $\sigma = 0.92$ and $C_{\text{crit}} = 150$.

We present the results of the model in Figs. 2 and 3 . We can see that for $\beta = 40$, which is corresponding to $\mathcal{R}_0 < 1$, the number of infectious decreases from the initial value $I_0 = 1$ to zero and no epidemic occurs. On the other hand, for $\beta = 50$ (corresponding to $\mathcal{R}_0 > 1$, epidemic outbreaks repeat over time, while we can

[1] The source codes can be found online on https://github.com/gasper6/SIRS-model.

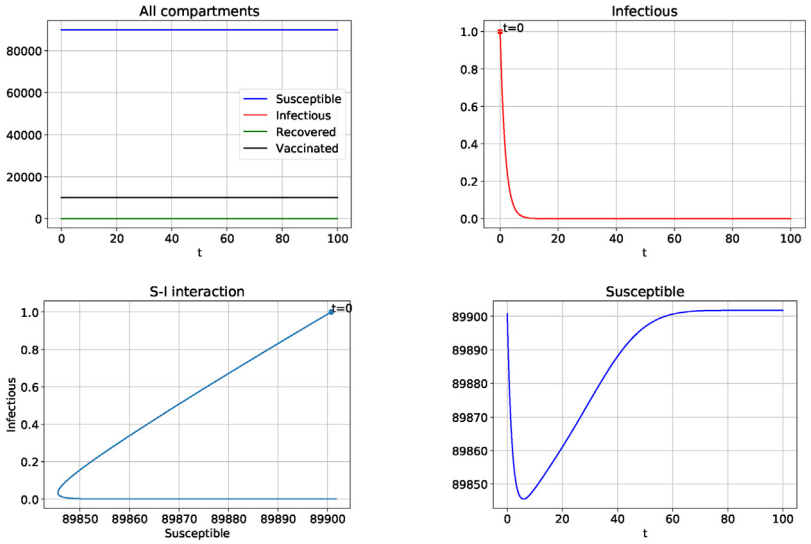

Fig. 2. Solution of our model for $\beta = 40$, disease dies out without breaking out into epidemics.

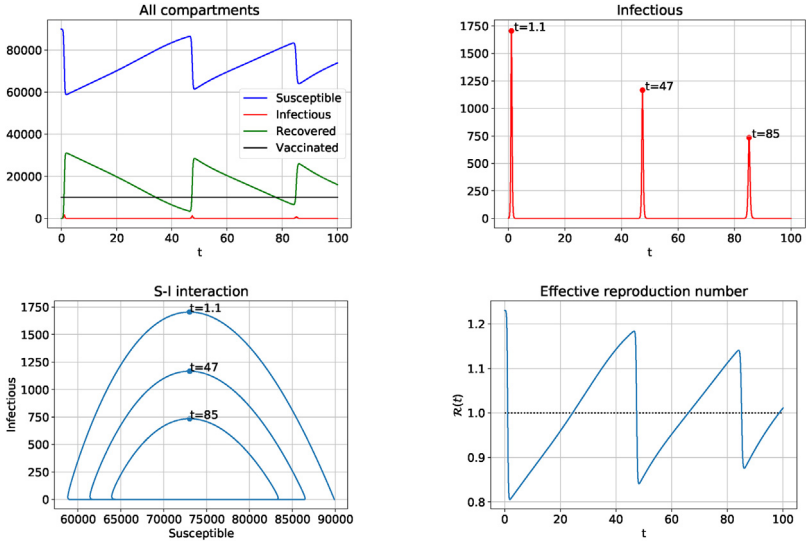

Fig. 3. Solution of our model for $\beta = 50$, disease returns in repeated epidemics with its size becoming smaller with each cycle.

observe a diminishing size of epidemic, with peaks of the number of infected being lower each time. We can also observe cycling dynamics between S and I. The model parameters in both examples were chosen to ensure a constant population N. These two examples illustrate two possible behaviors of the systems, depending on the estimate of the reproduction number. For future work, we can study the situation for real world data of Germany and Slovakia. However, this model is continuous and homogeneous, therefore its results will never correspond to reality. One can obtain qualitative insights into the dynamics, though.

7. Comparison to the SIRS model

In order to verify the qualitative behavior of our results (repeating epidemics with their size decreasing over time), we now compare our model to the classical SIRS model with population dynamics, given by the following set of equations [21]:

$$\frac{dS(t)}{dt} = \nu(1-x)N(t) + \theta R(t) - \beta\frac{S(t)I(t)}{N(t)} - \mu S(t), \tag{39}$$

$$\frac{dI(t)}{dt} = \beta\frac{S(t)I(t)}{N(t)} - \gamma I(t) - \mu I(t), \tag{40}$$

$$\frac{dR(t)}{dt} = \nu x N(t) + \gamma I(t) - \theta R(t) - \mu R(t), \tag{41}$$

The immunity waning in this model is modeled by the term $\theta R(t)$ in Eqs. (39) and (41). If we neglect all other terms in (41), we find that the dynamics of the waning immunity has an exponential form $R^{\text{waning}}(t) = c\exp(-\theta t)$, where c is a constant. Therefore, to compare the results of our model with the results from a SIRS model, we replace the *SVF* waning profile by an exponential one; see Fig. 4.

We chose the parameter $\theta = 0.03602$, because this value ensures that $\int_0^\infty P_R(\tau)\,d\tau$ does not change. We computed this integral numerically on a bounded domain from 0 to 250 with a discretization step 0.001 using the rectangular rule. The parameters $\tau_{max} = \xi_{max} = 250$, $\beta \in \{50, 35\}$, and all other parameters are unchanged, see Section 6. We solved the SIRS model numerically by the Runge-Kutta method of 4th order and depict the results in Figs. 5 and 6 .

We can observe in Figs. 5 and 6 that the solutions obtained by our model and but the standard SIRS model coincide. The green curve in

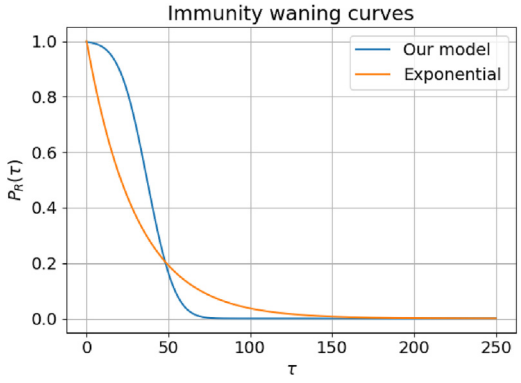

Fig. 4. Comparison of the waning curves in our model (probabilistic distribution) and SIRS model (exponential curve).

the graph of the recovered compartment in the SIRS model contains all individuals from the recovered and vaccinated compartment of our model, therefore the quantitative values of recovered compartments differ. Other than that, the results from the two models coincide, which justifies the correctness of our model as well as the numerical scheme we proposed.

There is one important observation to be made from this comparison. We can notice that changing the character of the waning curve has changed the solution significantly. Indeed, with probabilistic distribution considered in Definition (3) of SVF, only 3 epidemics occur during the 100 years of the simulation period. Changing the waning curve to the exponential one, with faster immunity waning at the beginning, leads to 8 epidemics during the 100 years. This indicates that, in future work when studying the model on real data, it will be of crucial importance to calibrate or estimate the waning curve as realistically as possible.

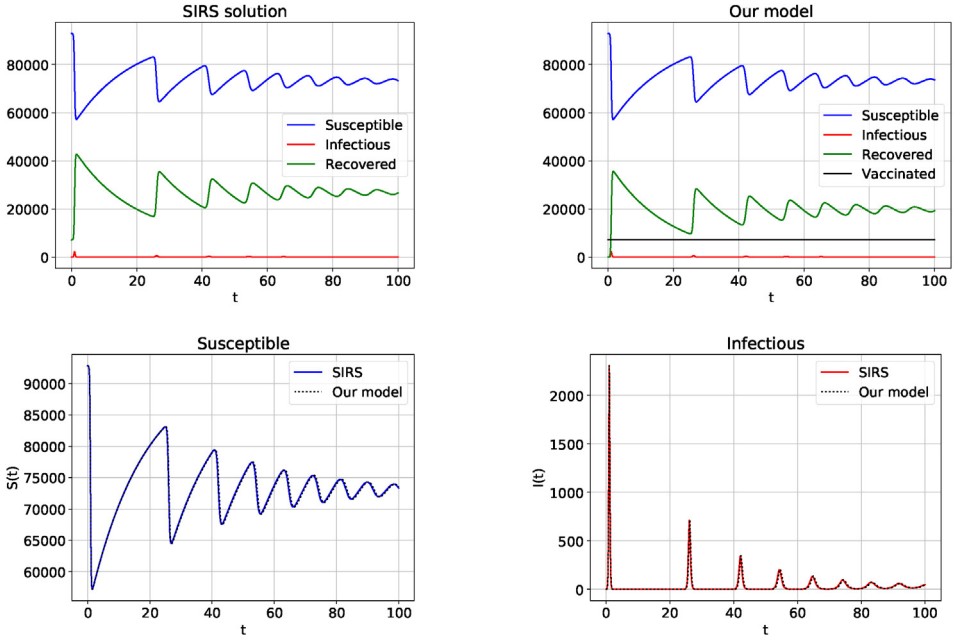

Fig. 5. SIRS model (top left) and our model (top right) results for $\beta = 50$. We note that the number of recovered in the SIRS model (green curve) corresponds to the sum of recovered and vaccinated (green and black curves) in our model. The number of susceptible and infectious individuals coincides for both models (bottom graphs). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

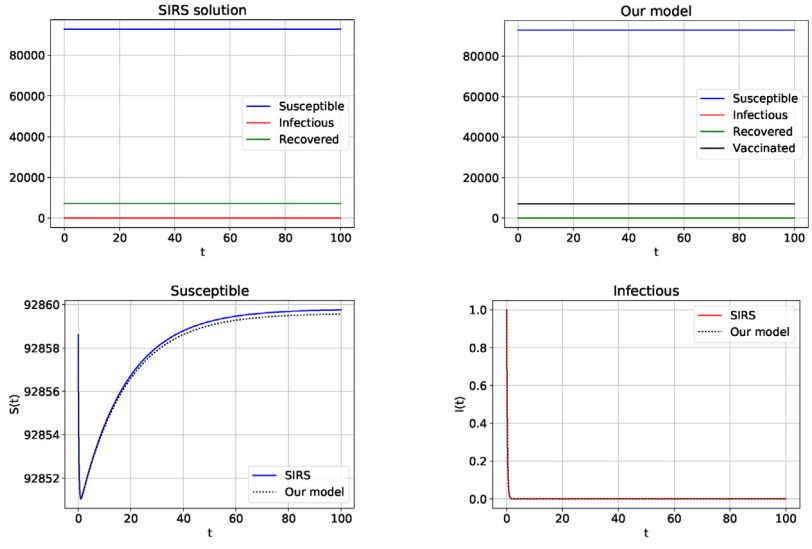

Fig. 6. SIRS model and our model with $\beta = 35$.

8. Conclusions

In this work we proposed and analyzed an SIR model with vaccination and waning immunity. Following the work of Mossong et al. [23], we assumed that the level of antibodies is driven by a normal distribution. We derived a system of two ODEs (for susceptible and infectious) and two PDEs (for recovered and vaccinated). Then we reduced this model to just one ordinary-integral differential equation and one ODE and derived expressions for the basic and the effective reproduction numbers. Next, we proposed a numerical scheme based on finite differences.

We illustrated two types of system behavior: a case with epidemic recurrence, and a case when the disease dies out soon after it was initially brought to the population. We also compared the results of our model with the exponential waning curve with a standard SIRS model, which showed that our model is correct and the chosen numerical scheme appropriate.

Our future work will consider the dynamics of infectious diseases with boosting of immunity (by exposure to the pathogen) and also allowing for stochastic terms that reflects the uncertainty in the used parameters. We will also perform a calibration of the parameters using real data for measles in Germany and Slovakia. Also we will, following the ideas of Georgescu and Zhang [15] and Elazzouzi et al. [12], consider an extension to a SIRI-type epidemic model describing that recovered individuals may encounter a relapse of the disease (due to a reactivation of a latent infection or due to an incomplete treatment of the disease) and again enter the compartment of the infectious individuals.

Finally, it will be the goal of our future work to calibrate our model parameters with respect to real data, e.g. taken from [14,22,31].

Conflict of interest

None declared.

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