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# Optimal control in models of virus propagation

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## Abstract

Based on the SEIRD model, we consider that when multiple viruses of different virulence coexist, the more virulent virus can reinfect nodes already infected by the less virulent virus, which we call here Superexposed. Based on the state transitions, the corresponding differential equations and cost functions are established, then building the corresponding optimal control problem, where the vaccine efficiency and drug efficiency are controlled variables. This nonlinear optimal control problem is solved by Pontryagin's maximum principle to finding the structure of the optimal control strategies. Based on the definition of the basic regeneration number, yielding the $R_0$ value for the model, then discussed the final epidemic size. In the numerical analysis section, we validate the accuracy of the structure, fitting the behavior of each state and the effect of different parameter values.

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## 1. Introduction

Research on epidemics, and how to prevent them, is a subject that has always existed and been conducted[1]. The epidemic model has been continuously refined from the basic SIS and SIR models[2, 3]. Considering the impact of patients in the COVID-19 incubation stage, [4] proposed a new epidemic model - the Susceptible Quarantined Exposed Infective Removed ($SQEIR$) model, to improve the accuracy of the model compared to traditional models. $SE_1E_2IQR$ model, which show the quarantine treatment plays a key role in controlling the epidemic disease and assessed the importance of the basic reproductive ratio $R_0$ is proposed in [5]. Mathematical models based on nonlinear differential equations have been developed and applied to a variety of basic epidemic modeling systems who are interested in controlling the evolution of states[6–8]. The model in this paper is a refinement of the underlying epidemic model, which involves the idea of multiple viruses coexisting and super-exposure, then analyzes and performs optimal control planning, and finally compares the impact of a general vaccine with that of a preemptive vaccine, which is the focus of this paper.

The first part presents the background of the study. In the part 2, we consider that when multiple viruses of different virulence coexist, the virulent virus will reinfect nodes already infected by the less. A new epidemic model is constructed on the simple SEIDR model[6]. This model can be extended to malwares attacks and information spreading models[7]. In the part 3, we establish the optimal control problem that minimizes the total cost in model and solve them. In the part 4, we introduce the preemptive vaccine, we will obtain the relationship between the final epidemic size and the fraction of preemptive vaccine. In the part 5, we verify the accuracy of the theorems, fitting the behavioral trajectories of the models with differences and the influence of each parameter. And compare general vaccinations and preemptive vaccinations, preemptive vaccines are effective in shortening the virus transmission cycle, which is the reason why all types of vaccines should now be administered at the early childhood stage.

## 2. Dynamics of the system model

First, the state evolution is determined, and then a system model is developed. A system consists of

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$N$ nodes with the number of susceptible, exposed, infected, recovered and dead states at time $t$ as $n_S(t), n_E(t), n_I(t), n_R(t)$ and $n_D(t)$, with the corresponding fractions $S(t) = n_S(t)/N, E(t) = n_E(t)/N, I(t) = n_I(t)/N, R(t) = n_R(t)/N, D(t) = n_D(t)/N$. So for all $t$, we have $S(t) + E(t) + I(t) + R(t) + D(t) = 1$. For type $i$, at time $t$, the fractions of exposure and infection are $E_i(t)$ and $I_i(t)$, respectively. In our model, we assume that the nodes of each type are stable and do not change over time.

A susceptible (S) node is a node that is vulnerable to virus attack but not infected; an exposed (E) node is a node that is infected but not capable of propagation; an infected (I) node is a node that has been contaminated with virus; a recovered (R) node is a node that is immune to virus; and a dead (D) node is a node that has no life[8].

Suppose a more virulent strain comes into contact with an individual of a less virulent strain, then the more virulent strain will completely replace the other strain in that individual. This is known as **Superexposure**[9]. That is, if a susceptible node is infected by a weakly virulent virus to become an exposed node and it is exposed to a more virulent virus, then the more virulent virus will replace the weakly virulent virus to infect the node again. Assume that there are $n$ classes of viruses with different virulence in the system, and that the virulence increases as the value of $i$ gets larger.

A pre-selected group of vaccine-filled nodes is called a vaccine group[10]. The vaccine group can distribute vaccines to susceptible nodes to make them immune to the virus. We assume that the number of vaccine groups is $NR_V^*$. A pre-selected set of nodes filled with medicines is called a medicine group. The medicine group can distribute medicines to the infected nodes to make them cured. We assume that the number of medicine groups is $NR_M^*$. The vaccine and medicine groups are not infected, so they recover themselves from the beginning.

In our model, we assume $\mu_i$ is contact rate of susceptible nodes to exposed nodes of type $i$, $\omega_i$ is contact rate of an exposed node of type $i$ and an infected node of type $i$, $\tau$ is the rate of superexposure that occurs, $\delta_i$ is the mortality rate of each infected node of type $i$, $u$ is the efficiency of the vaccine to cure a susceptible node, $v_i$ is the healing efficiency of $i$-type infected nodes by drug treatment, and $\bar{\omega}_i$ is the self-healing efficiency of $i$-type infected nodes, where all parameters belong to the set [0,1]. Figure 1 a). shows the system state transitions with three types viruses in the model with vaccination.

If the total number of nodes ($N$) is large, then $S(t), E(t), I(t), R(t)$ and $D(t)$ converge to the solution of

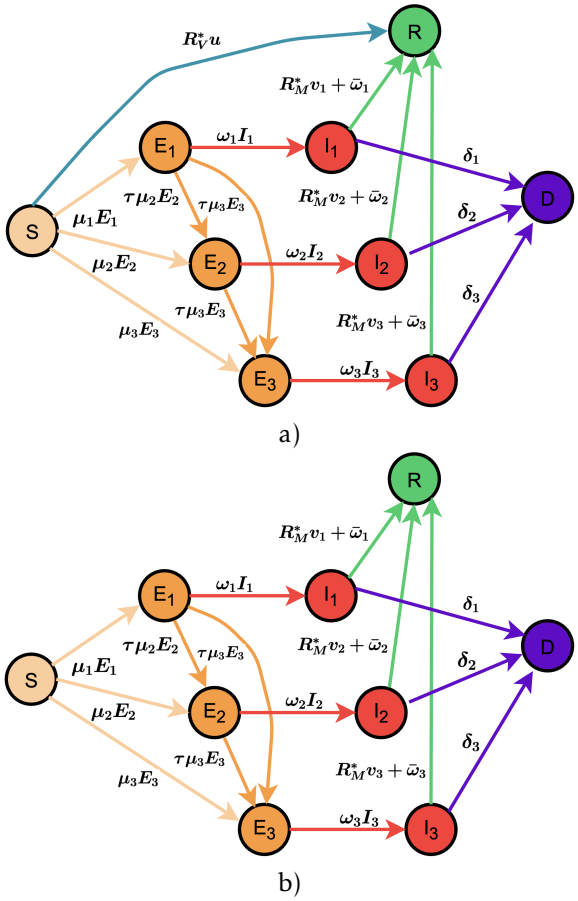



**Figure 1.** System state transitions with three types viruses. a) with vaccination; b) without vaccination.

the following system of differential equations[11]:

$$\begin{aligned}
\dot{S} =& -S\left(\sum_{i=1}^{n}\mu_i E_i + R_V^* u\right)\\
\dot{E}_i =& E_i\left(S\mu_i + \tau\mu_i\sum_{j=1}^{i-1}E_j - \tau\sum_{j=i+1}^{n}\mu_j E_j - \omega_i I_i\right)\\
\dot{I}_i =& I_i\left(E_i\omega_i - R_M^* v_i - \bar{\omega}_i - \delta_i\right)\\
\dot{R} =& R_V^* S u + R_M^*\sum_{i=1}^{n} I_i v_i + \sum_{i=1}^{n} I_i\bar{\omega}_i\\
\dot{D} =& \sum_{i=1}^{n}\delta_i I_i,
\end{aligned} \tag{1}$$

where $E(t) = \sum_{i=1}^{n} E_i(t), I(t) = \sum_{i=1}^{n} I_i(t)$.

The initial conditions and state constraints are given by

$$\begin{aligned}
&0 < S_0 < 1, 0 < E_0 < 1, 0 < I_0 < 1, D_0 = 0,\\
&S(t) \geq 0, E_i(t) \geq 0, I_i(t) \geq 0, R(t) \geq 0, D(t) \geq 0,\\
&S(t) + E(t) + I(t) + R(t) + D(t) = 1.
\end{aligned} \tag{2}$$

If $R_V^* u = 0$, it is a case where the corresponding system does not contain vaccination, and the virus transmission process is carried out according to b) of Figure 1.

## 3. Optimal control problem

We mimimize the aggregated system costs (3) for dynamic system (1) - (2) by properly adjusting $u(t)$ and $v_i(t)$ in the case that $t$ satisfies $0 \le u(t) \le 1, 0 \le v_i(t) \le 1$. Equation (3) covers the costs incurred by each state in the system[12]. Since the spread of the virus affects the evolution of the system, the system incurs a cost of $f(I(t)), g(E(t)), k(D(t))$ at each time $t$. The population also benefits at the rate of $L(R(t))$ because the vaccine eliminates state uncertainty. where $f(\cdot), g(\cdot), k(\cdot), L(\cdot)$ are all non-decreasing differentiable functions such that $f(0) = g(0) = k(0) = L(0) = 0$. We can assume that $f(\cdot), g(\cdot), k(\cdot)$ can be any function. Assume that each active group of immune zones consumes resources at time $t$ at a rate $h(u(t)) + \sum_{i=1}^{n} m_i(v_i(t))$, where $h(0) = m_i(0) = 0$ and $h(x) > 0, m_i(x) > 0$ if $x > 0$. The total cost is given by an expression of the following form, the constraints are given by equations (1) and (2).

$$J = \int_0^T (f(I) + g(E) + k(D) - L(R) + h(u) + \sum_{i=1}^{n} m_i(v_i))dt. \tag{3}$$

Consider the Hamiltonian $H$[13, 14], and the corresponding co-state or adjoint functions $\lambda^S, \lambda_i^E, \lambda_i^I, \lambda^R, \lambda^D$, defined as follows:

$$\begin{aligned} H(u(t)) = {} & f(I) + g(E) + k(D) - L(R) + h(u) + \sum_{i=1}^{n} m_i(v_i) \\ & - \lambda^S S\left(\sum_{i=1}^{n} \mu_i E_i + R_V^* u\right) + \sum_{i=1}^{n} \lambda_i^I I_i \left(E_i\omega_i - R_M^* v_i - \bar{\omega}_i - \delta_i\right) \\ & + \sum_{i=1}^{n} \lambda_i^E E_i \left(S\mu_i + \tau\mu_i \sum_{j=1}^{i-1} E_j - \tau \sum_{j=i+1}^{n} \mu_j E_j - \omega_i I_i\right) \\ & + \lambda^R \left(R_V^* S u + R_M^* \sum_{i=1}^{n} I_i v_i + \sum_{i=1}^{n} I_i \bar{\omega}_i\right) + \lambda^D \sum_{i=1}^{n} \delta_i I_i. \end{aligned} \tag{4}$$

Where the adjoint functions $\dot{\lambda}^S = -\frac{\partial H}{\partial S}, \dot{\lambda}_i^E = -\frac{\partial H}{\partial E_i}, \dot{\lambda}_i^I = -\frac{\partial H}{\partial I_i}, \dot{\lambda}^R = -\frac{\partial H}{\partial R}$ and $\dot{\lambda}^D = -\frac{\partial H}{\partial D}$ are continuous functions, we have differential equation,

$$\begin{aligned} \dot{\lambda}^S = {} & \lambda^S \left(\sum_{i=1}^{n} \mu_i E_i + R_V^* u\right) - \sum_{i=1}^{n} \lambda_i^E E_i \mu_i - \lambda^R R_V^* u \\ \dot{\lambda}_i^E = {} & -\frac{\partial g(E)}{\partial E_i} + \lambda^S S\mu_i - \lambda_i^E \Bigg(S\mu_i + \tau\mu_i \sum_{j=1}^{i-1} E_j - \tau \sum_{j=i+1}^{n} \mu_j E_j \\ & - \omega_i I_i\Bigg) - \tau \sum_{j=i+1}^{n} \lambda_j^E E_j \mu_j + \tau\mu_i \sum_{j=1}^{i-1} \lambda_j^E E_j - \lambda_i^I I_i \omega_i \\ \dot{\lambda}_i^I = {} & -\frac{\partial f(I)}{\partial I_i} + \lambda_i^E E_i \omega_i - \lambda_i^I (E_i\omega_i - R_M^* v_i - \bar{\omega}_i - \delta_i) \\ & - \lambda^R (R_M^* v_i + \bar{\omega}_i) - \lambda^D \delta_i \\ \dot{\lambda}^R = {} & \frac{\partial L(R)}{\partial R} \\ \dot{\lambda}^D = {} & -\frac{\partial k(D)}{\partial D}, \end{aligned} \tag{5}$$

along with the final conditions

$$\lambda^S(T) = 0, \lambda_i^E(T) = 0, \lambda_i^I(T) = 0, \lambda^R(T) = 0, \lambda^D(T) = 0. \tag{6}$$

Then the PMP shows that the optimal control at time $t$ satisfies the following conditions:

$$\begin{cases} u \in \underset{\xi}{argmin} H(\xi) \\ v_i \in \underset{\eta_i}{argmin} H(\eta_i), \end{cases} \tag{7}$$

where the minimization is over the space of admissible controls.

Vector minimization can be expressed as scalar minimization:

$$\begin{cases} u(t) \in \underset{0 \le x \le 1}{argmin} \gamma(x, t) \\ v_i(t) \in \underset{0 \le y_i \le 1}{argmin} \varepsilon_i(y_i, t), \end{cases} \tag{8}$$

where, to highlight the impact of $u(t)$ and $v_i(t)$ on the total cost, we define

$$\begin{cases} \gamma(x,t) = h(x) - R_V^* \phi(t) x \\ \varepsilon_i(y_i,t) = m_i(y_i) - R_M^* \psi_i(t) y_i, \end{cases} \text{ and } \begin{cases} \phi(t) = S(\lambda^S - \lambda^R) \\ \psi_i(t) = I_i(\lambda_i^I - \lambda^R). \end{cases} \tag{9}$$

**Theorem 1.** Assuming the existence of an optimal control[12]:

- If $h(\cdot)$ (or $m_i(\cdot)$) is concave, then the optimal control has the following structure:
  - $u^*(t) = 1$ for $0 \le t < t^1$ (or $v_i^*(t) = 1$ for $0 \le t < t_i^1$),
  - $u^*(t) = 0$ for $t^1 \le t \le T$ (or $v_i^*(t) = 0$ for $t_i^1 \le t \le T$), where $t^1 \in (0, T)$ (or $t_i^1 \in (0, T)$).

- If $h(\cdot)$ (or $m_i(\cdot)$) is strictly convex, then the optimal control has the following structure:
  - $u^*(t) = 1$ for $0 \le t \le t^1$ (or $v_i^*(t) = 1$ for $0 \le t \le t_i^1$),
  - $u^*(t) = 0$ for $t^2 \le t \le T$ (or $v_i^*(t) = 0$ for $t_i^2 \le t \le T$),
  - $u^*(t)$ (or $v_i^*(t)$) strictly decreases in the interval $(t^1, t^2)$ (or $(t_i^1, t_i^2)$), where $0 < t^1 < t^2 < T$ (or $0 < t_i^1 < t_i^2 < T$).

*Proof.* According to equations (4) and (9), this time the Hamiltonian is

$$\begin{aligned} H(u(t)) =& f(I) + g(E) + k(D) - L(R) - \lambda^S S \sum_{i=1}^{n} \mu_i E_i \\ &+ \sum_{i=1}^{n} \lambda_i^E E_i \left( S\mu_i + \tau\mu_i \sum_{j=1}^{i-1} E_j - \tau \sum_{j=i+1}^{n} \mu_j E_j - \omega_i I_i \right) \\ &+ \sum_{i=1}^{n} \lambda_i^I I_i (E_i\omega_i - \bar{\omega}_i - \delta_i) + \lambda^R \sum_{i=1}^{n} I_i\bar{\omega}_i \\ &+ \lambda^D \sum_{i=1}^{n} \delta_i I_i + h(u) - R_V^* \phi(t) u \\ &+ \sum_{i=1}^{n} (m_i(v_i) - R_M^* \psi_i(t) v_i). \end{aligned} \tag{10}$$

1) Let $h(\cdot)$ (or $m_i(\cdot)$) be a concave function, i.e., $h''(\cdot) < 0$ (or $m_i''(\cdot) < 0$), then the Hamiltonian is a concave function of $u$ (or $v_i, i = 1, 2, ..., n$). There are two different possibilities (see Fig.2) for $u \in [0, 1]$ (or $v_i \in [0, 1]$) that minimize the Hamiltonian[15],

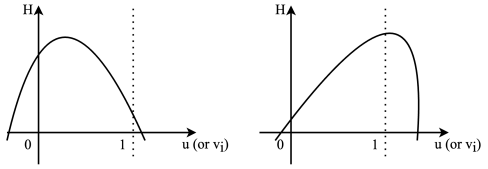



**Figure 2.** The case of concave function - $h''(\cdot) < 0$ (or $m_i''(\cdot) < 0$)

If at the time $t$

$$H(0) > H(1)$$

$$0 > h(1) - R_V^* \phi(t) \quad (\text{or} \quad 0 > m_i(1) - R_M^* \psi_i(t))$$

that is, $\phi(t) > \frac{h(1)}{R_V^*}$ $\left(\text{or } \psi_i(t) > \frac{m_i(1)}{R_M^*}\right)$, then the optimal control is $u^* = 1$ (or $v_i^* = 1$); otherwise $u^* = 0$ (or $v_i^* = 0$).

$\phi(t)$ (or $\psi_i(t)$) is a decreasing function of $t$, and Lemmas will prove this. Define $\phi(t^1) = \frac{h(1)}{R_V^*}$ $\left(\text{or } \psi_i(t_i^1) = \frac{m_i(1)}{R_M^*}\right)$. We have

$$\begin{cases} \phi(t) > \frac{h(1)}{R_V^*}, t \in [0, t^1) \\ \phi(t) < \frac{h(1)}{R_V^*}, t \in [t^1, T]. \end{cases}$$

$$\left( \text{or} \quad \begin{cases} \psi_i(t) > \frac{m_i(1)}{R_M^*}, t \in [0, t_i^1) \\ \psi_i(t) < \frac{m_i(1)}{R_M^*}, t \in [t_i^1, T]. \end{cases} \right) \tag{11}$$

So,

$$\begin{cases} u^* = 1, t \in [0, t^1) \\ u^* = 0, t \in [t^1, T]. \end{cases}$$

$$\left( \text{or} \quad \begin{cases} v_i^* = 1, t \in [0, t_i^1) \\ v_i^* = 0, t \in [t_i^1, T]. \end{cases} \right) \tag{12}$$

2) Let $h(\cdot)$ (or $m_i(\cdot)$) be a strictly convex function, i.e., $h''(\cdot) > 0$ (or $m_i''(\cdot) > 0$), then the Hamiltonian is a convex function of $u$ (or $v_i$). There are three different possibilities (see Fig.3) for $u \in [0, 1]$ (or $v_i \in [0, 1]$) that minimize the Hamiltonian,

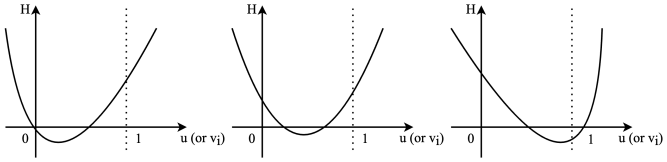



**Figure 3.** The case of convex function - $h''(\cdot) > 0$ (or $m_i''(\cdot) > 0$)

If at time $t$,

$$\frac{\partial(h(u) - R_V^* \phi(t) u)}{\partial u}|_{u=0} = h'(0) - R_V^* \phi(t) \ge 0,$$

$$\left( \text{or} \quad \frac{\partial(m_i(v_i) - R_M^* \psi_i(t) v_i)}{\partial v_i}|_{v_i=0} = m_i'(0) - R_M^* \psi_i(t) \ge 0, \right)$$

then the optimal control is $u^* = 0$ (or $v_i^* = 0$).

If

$$\frac{\partial(h(u) - R_V^* \phi(t) u)}{\partial u}|_{u=1} = h'(1) - R_V^* \phi(t) \le 0,$$

$$\left( \text{or} \quad \frac{\partial(m_i(v_i) - R_M^* \psi_i(t) v_i)}{\partial v_i}|_{v_i=1} = m_i'(1) - R_M^* \psi_i(t) \le 0, \right)$$

then the optimal control is $u^* = 1$ (or $v_i^* = 1$).

Otherwise,

$$\frac{\partial(h(u) - R_V^* \phi(t) u)}{\partial u}|_{u=u^*} = 0.$$

$$\left( \text{or} \quad \frac{\partial(m_i(v_i) - R_M^* \psi_i(t) v_i)}{\partial v_i}|_{v_i=v_i^*} = 0. \right)$$

we can find such a value $u^* \in (0, 1)$ (or $v_i^* \in (0, 1)$).

$\phi(t)$ (or $\psi_i(t)$) is a decreasing function of $t$. Define $\phi(t^1) = \frac{h'(1)}{R_V^*}, \phi(t^2) = \frac{h'(0)}{R_V^*}$ $\left(\text{or} \quad \psi_i(t_i^1) = \frac{m_i'(1)}{R_M^*}, \psi_i(t_i^2) = \frac{m_i'(0)}{R_M^*}\right)$. We have

$$\begin{cases} \phi(t) \geq \frac{h'(1)}{R_V^*}, t \in [0, t^1] \\ \frac{h'(0)}{R_V^*} < \phi(t) < \frac{h'(1)}{R_V^*}, t \in (t^1, t^2) \\ \phi(t) \leq \frac{h'(0)}{R_V^*}, t \in [t^2, T]. \end{cases}$$

$$\left( \text{or} \quad \begin{cases} \psi_i(t) \geq \frac{m_i'(1)}{R_M^*}, t \in [0, t_i^1] \\ \frac{m_i'(0)}{R_M^*} < \psi_i(t) < \frac{m_i'(1)}{R_M^*}, t \in (t_i^1, t_i^2) \\ \psi_i(t) \leq \frac{m_i'(0)}{R_M^*}, t \in [t_i^2, T]. \end{cases} \right) \tag{13}$$

So,

$$\begin{cases} u^* = 1, t \in [0, t^1] \\ u^* = h'^{-1}(\phi(t)), t \in (t^1, t^2) \\ u^* = 0, t \in [t^2, T]. \end{cases}$$

$$\left( \text{or} \quad \begin{cases} v_i^* = 1, t \in [0, t_i^1] \\ v_i^* = m_i'^{-1}(\psi_i(t)), t \in (t_i^1, t_i^2) \\ v_i^* = 0, t \in [t_i^2, T]. \end{cases} \right) \tag{14}$$

□

**Lemma 1.** $\phi(t)$ and $\psi_i(t)$ is a decreasing function of $t$ [1].

**Lemma 2.** The positivity constraints $\lambda_i^E(t) - \lambda^R(t) \geq 0$ and $\lambda^D(t) - \lambda^R(t) \geq 0$ hold for all $i = 1, ..., M$ and all $t \in [0, T)$.

## 4. Basic reproduction number

### 4.1. Calculation of $R_0$

The basic reproduction number, denoted $R_0$, it refers to the average number of individuals infected by an initial individual infected with an infectious virus without the involvement of any vaccination measures, while all individuals are not immune[16]. Studies have shown that if $R_0 < 1$, then the disease free equilibrium is locally asymptotically stable; whereas if $R_0 > 1$, then it is unstable.

In both models, progression from $E_i$ to $E_j$ $(i \neq j)$ or from $E_i$ to $I_i$ is not considered a new infection, but a progression between infected nodes.

$$\mathcal{F} = \begin{cases} S\mu_i E_i, & i = j \\ 0, & otherwise, \end{cases} \tag{15}$$

and

$$\mathcal{V} = \begin{cases} -E_i\tau(\mu_i \sum_{j=1}^{i-1} E_j - \sum_{j=i+1}^{n} \mu_j E_j) \\ \quad +I_i(R_M^* v_i + \bar{\omega}_i + \delta_i), & i = j \\ 0, & otherwise. \end{cases} \tag{16}$$

Giving $m = n$, an equilibrium solution with $E = I = 0$ has the form $x_0 = (S_0, 0, 0, 0, 0)^t$. Without loss of generality, assume $S_0 = 1$ is a disease free equilibrium (DFE). Then,

$$F = \begin{pmatrix} \mu_1 & 0 & 0 & ... & 0 \\ 0 & \mu_2 & 0 & ... & 0 \\ 0 & 0 & \mu_3 & ... & 0 \\ ... & & & & \\ 0 & 0 & 0 & ... & \mu_n \end{pmatrix} = \begin{cases} \mu_i, & i = j \\ 0, & otherwise, \end{cases} \tag{17}$$

and

$$V = \begin{pmatrix} R_M^* v_1 + \bar{\omega}_1 + \delta_1 & ... & 0 \\ 0 & ... & 0 \\ 0 & ... & 0 \\ ... & & \\ 0 & ... & R_M^* v_n + \bar{\omega}_n + \delta_n \end{pmatrix} \tag{18}$$

$$= \begin{cases} R_M^* v_i + \bar{\omega}_i + \delta_i, & i = j \\ 0, & otherwise. \end{cases}$$

with $FV^{-1}$ non-singular as required. Giving

$$|V| = \prod_{i=1}^{n} (R_M^* v_i + \bar{\omega}_i + \delta_i), \tag{19}$$

$$V^* = \begin{cases} \prod_{k=1}^{i-1} (R_M^* v_k + \bar{\omega}_k + \delta_k) \\ \cdot \prod_{k=i+1}^{n} (R_M^* v_k + \bar{\omega}_k + \delta_k), & i = j \\ 0, & otherwise, \end{cases} \tag{20}$$

and

$$V^{-1} = \frac{V^*}{|V|} = \begin{cases} \frac{1}{R_M^* v_i + \bar{\omega}_i + \delta_i}, & i = j \\ 0, & otherwise. \end{cases} \tag{21}$$

Then,

$$FV^{-1} = \begin{cases} \frac{\mu_i}{R_M^* v_i + \bar{\omega}_i + \delta_i}, & i = j \\ 0, & otherwise. \end{cases} \tag{22}$$

$FV^{-1}$ has the $n$ eigenvalues[17],

$$R_{0,i} = \frac{\mu_i}{R_M^* v_i + \bar{\omega}_i + \delta_i}. \tag{23}$$

The $n$ eigenvalues correspond to the reproduction numbers for each strain. The basic reproduction number for the system is the maximum of them. That is,

$$R_0 = \rho(FV^{-1}) = \max_{i \in \{1,2,3,...,n\}} R_{0,i}. \tag{24}$$

[1] The proofs of the two lemmas follow the ideas of [M. H. R. Khouzani, 2011] [Elena Gubar, 2018] [Gubar Elena, 2021] [Xiuxiu Liu, 2023].

### 4.2. Final epidemic size for model without vaccination

In epidemiological models containing vaccines, we assume that the vaccine is administered after the virus. Here, we will introduce a pre-emptive vaccine in an epidemic model that does not contain vaccine. If $R_V^* u = 0$, according to the corresponding differential equation, we get

$$\frac{dS}{d(R+D)} = -S \sum_{i=1}^{n} \left( \frac{E_i}{I_i} R_{0,i} \right) \tag{25}$$

Integrating the above equation from time 0 to $\infty$, we obtain the equation for the final epidemic size $R(\infty) + D(\infty)$[12]:

$$S(\infty) = S(0) e^{-\sum_{i=1}^{n} (\frac{E_i}{I_i} R_{0,i})[R(\infty)+D(\infty)-R(0)-D(0)]} \tag{26}$$

Using the initial condition $S(0) \approx 1$ and $R(0) = D(0) = 0$, and the final state $I(\infty) = E(\infty) = 0$ and $S(\infty) = 1 - R(\infty) - D(\infty)$, we obtain:

$$\begin{aligned} R(\infty) + D(\infty) &= 1 - S(\infty) \\ &= 1 - e^{-\sum_{i=1}^{n} (\frac{E_i}{I_i} R_{0,i})(R(\infty)+D(\infty))} \end{aligned} \tag{27}$$

$R(\infty) + D(\infty)$ is the final epidemic size, it's the final fraction of individuals infected during the epidemic outbreak, which can be calculated numerically from the above equation. We can see that the final size is positive when and only when $R_{0,i} > 1$, and if $R_{0,i} < 1$, the disease does not spread.

If we consider preemption by assuming that the proportion of nodes initially vaccinated is $x$, then equation (27) can be rewritten as

$$\begin{aligned} R(\infty) + D(\infty) &= 1 - S(\infty) \\ &= (1-x)(1 - e^{-\sum_{i=1}^{n} (\frac{E_i}{I_i} R_{0,i})(R(\infty)+D(\infty))}) \end{aligned} \tag{28}$$

Increasing vaccination will reduce final epidemic size. If $x > x' = 1 - \frac{1}{R_{0,i}}$, then $R(\infty) = 0$. The threshold $x'$ is called the "population immunity threshold". When $x$ is above this threshold, the virus does not spread. Thus, for vaccine-preventable diseases, herd immunity can indirectly protect unvaccinated nodes.

## 5. Numerical investigations

In this section, to verify the theorem, we simulate the case where three virulent viruses of different virulence are present in the system. The optimal control of the **Superexposure** model with vaccination (when all states are present and all cost functions are basis functions) is depicted in Figure 4, where a) is related to the concave function $h(u)$, b) is related to the convex function $h(u)$, c) is related to the concave function $m_i(v_i)$, and d) is related to the convex function $m_i(v_i)$. The relevant parameters are $\mu_1 = 0.52, \mu_2 = 0.52, \mu_3 = 0.52, \omega_1 = 0.85, \omega_2 = 0.9, \omega_3 = 0.95, \bar{\omega}_1 = 0.5, \bar{\omega}_2 = 0.4, \bar{\omega}_3 = 0.3, v_1 = 0.25, v_2 = 0.24, v_3 = 0.23, \delta_1 = 0.02, \delta_2 = 0.025, \delta_3 = 0.027, \tau = 0.1, u = 0.05, R_V^* = 0.1, R_M^* = 0.1, f(I) = 5\sum_{i=1}^{3} I_i, g(E) = 6\sum_{i=1}^{3} E_i, k(D) = 10D, L(R) = 5R$.

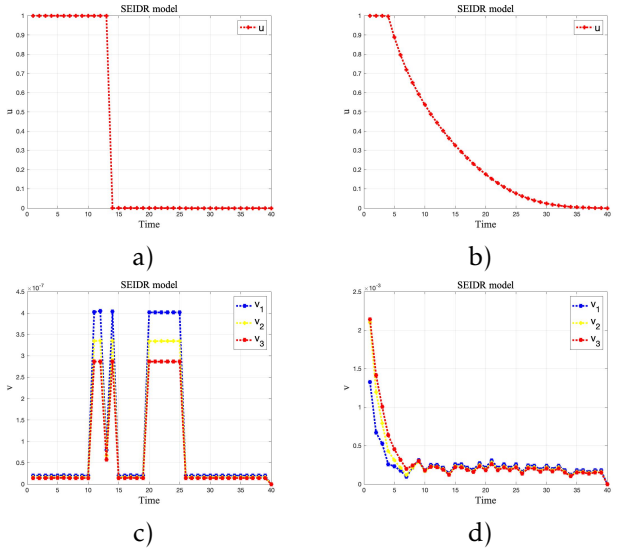



**Figure 4.** Verification of Theorem. a) $h(u)$ is concave; b) $h(u)$ is convex; c) $m_i(v_i)$ are concave; d) $m_i(v_i)$ are convex. For concave $h(u)$ and $m_i(v_i)$ we have used $h(u) = 10u$ , $m_1(v_1) = 5v_1$, $m_2(v_2) = 6v_2$, and $m_3(v_3) = 7v_3$, and for convex $h(u)$ and $m_i(v_i)$ we have used $h(u) = 10u^2$, $m_1(v_1) = 5v_1^2$, $m_2(v_2) = 6v_2^2$, and $m_3(v_3) = 7v_3^2$.

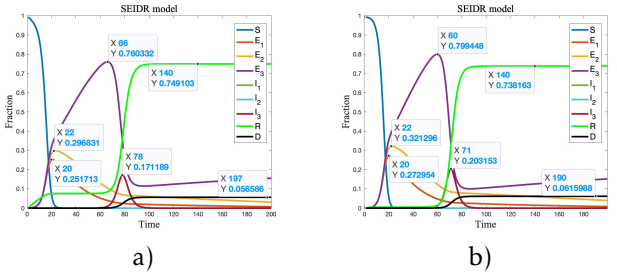
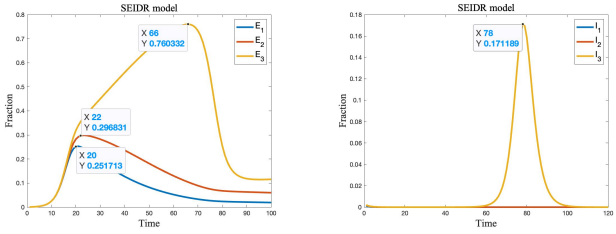



**Figure 5.** Behavioral trajectory of SEIDR & Superexposure model: a) With vaccination, b) Without vaccination.

Then we confirm our results with some numerical simulations, The focus of this section is to study the behavior of the modified model. From Figure 5, we can see that the number of susceptible nodes decreases extremely rapidly at the beginning of virus propagation and has reached a stable state at $t = 20$. Recovery nodes and dead nodes will rise steadily in the middle and late stages of virus transmission and reach a steady state near $t = 100$. Exposed and infected nodes behave similarly, rising to a certain value and then beginning

to gradually decline until there is no virus transmission in the population, at which point exposed and infected nodes are approximately equal to zero. We can clearly see that the order in which the apparent behaviors appear in each state is susceptible, exposed, infected, dead, and cured, consistent with the order of successive transitions between states. Comparing a) and b), it can be seen that the presence or absence of a vaccine during virus transmission affects whether the number of cured nodes increases significantly during the initial phase of virus transmission ($0 < t < 60$).




a) b)

**Figure 6.** Exposed and Infected fractions

In Figure 6, a) shows the behavioral trajectories of exposed nodes under three different virulence forces, and b) shows the behavioral trajectories of infected nodes under three different virulence forces. Among them, blue, red and yellow indicate the cases of the 1st, 2nd and 3rd viruses, respectively, and the virulence is gradually strengthened. It can be seen that the higher the number of exposures, the higher the number of corresponding infections.

$\tau = 0$ means that there is no repeated exposure, i.e., a node that has been infected by one virus will not be infected by other viruses. $\tau = 1$ means that when a node that has been infected by a less virulent virus is exposed to a more virulent virus, the more virulent virus will replace the less virulent virus and be infected again. As can be seen in Figure 7, $\tau = 0$ corresponds to

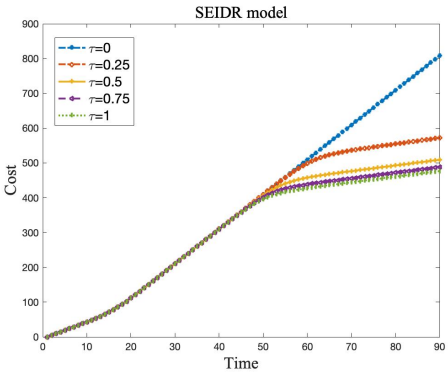
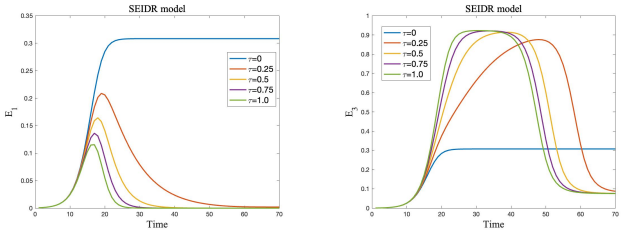



**Figure 7.** Cost-$\tau$ relationship diagram

**Table 1.** Effect of vaccine efficacy on final epidemic size

| u | 0 | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 |
|---|---|---|---|---|---|---|
| $R(\infty)$ | 0.738 | 0.497 | 0.225 | 0.005 | 0.005 | 0.005 |
| $D(\infty)$ | 0.062 | 0.041 | 0.019 | 0 | 0 | 0 |
| Final epidemic size | 0.800 | 0.538 | 0.244 | 0.005 | 0.005 | 0.005 |

higher resource consumption, while $\tau = 1$ corresponds to lower resource consumption.




a) b)

**Figure 8.** Exposed fractions-$\tau$ relationship diagram

The larger the value of $\tau$, the more nodes with weak virulent infection are converted to strong virulent infection. In Figure 8, a) shows that as the $\tau$ value increases, the number of nodes exposed by the 1st virus (i.e., weakly virulent) decreases. b) shows that as the $\tau$ value increases, the number of nodes exposed by the 3rd virus (i.e., strongly virulent) increases.

In Figure 9, a) explains the virus propagation process of the model with vaccine, where a vaccine and medicine are introduced as soon as the virus appears. All three affect the state transitions of all nodes simultaneously throughout the virus propagation process. b) explains the virus propagation process of the model without vaccine, where a preemptive vaccine is introduced before the virus emerges to make some nodes immune. When some nodes are infected, we will use medicine to make them recovered.

Table 1 show the variation of the final epidemic size in the model with vaccination when $u$ takes different

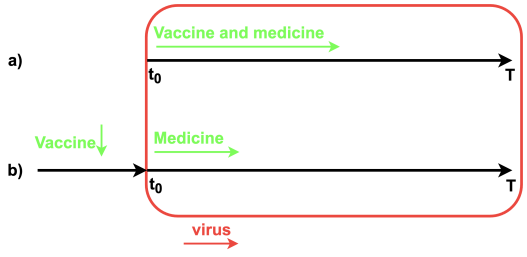
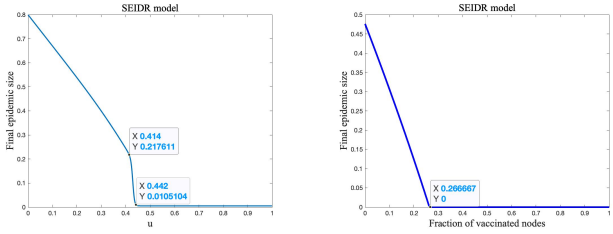



**Figure 9.** In the two models, the vaccines appear at different times and have different impacts.




a) b)

**Figure 10.** Final epidemic size. a) general vaccination; b) preemptive vaccination.

**Table 2.** Effect of preemptive vaccines on the final epidemic size

| Preemptive vaccines | No | Yes |
|---|---|---|
| The moment when The Final Epidemic Size = 0 | t=0.442 | t=0.267 |

values. The larger the value of $u$, the more susceptible nodes will be immune to the virus, and the number of infected nodes will be reduced significantly, and the final epidemic size will be reduced accordingly. a) of Fig. 10 shows that in the model with vaccination, when the vaccine and virus act synchronously, the final epidemic size is equal to 0 when $x > 0.442$.

Suppose $\frac{E_1}{I_1} = \frac{E_1(0)}{I_1(0)} = \frac{1}{2}, \frac{E_2}{I_2} = \frac{E_2(0)}{I_2(0)} = \frac{1}{3}, \frac{E_3}{I_3} = \frac{E_3(0)}{I_3(0)} = \frac{1}{3}$, and from (28), we have $R(\infty) + D(\infty) = (1-x)(1 - e^{-1.358(R(\infty)+D(\infty)}$). b) of Fig. 10 shows that when $x > 0.267$, a preemptive vaccine immunizes all susceptible nodes against the virus, making the sum of nodes that die due to infection and those that are cured by drug treatment 0. Table 2 illustrates that former delays the epidemic from reaching a steady state. Thus, for vaccine-preventable diseases, preemptive vaccine can effectively protect unvaccinated nodes.

## 6. Conclusion

Based on the SEIRD model, we add the ideas of multiple virus coexistence and super-exposure to refine the model even more. Then the optimal control problem is analyzed, and proved and verified the structure. Finally, based on the final epidemic size, the general vaccine and preemptive vaccine are compared, and the results show that preemptive vaccine can effectively protect unvaccinated nodes.

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## References

[1] Principles of Epidemiology (PDF) (Third ed.). Atlanta, Georgia: Centers for Disease Control and Prevention. 2012.

[2] Pastor-Satorras Romualdo, Castellano Claudio, Mieghem Piet and Vespignani Alessandro. (2014). Epidemic processes in complex networks. Reviews of Modern Physics. 87. 10.1103/RevModPhys.87.925.

[3] Elena Gubar, Vladislav Taynitskiy and Quanyan Zhu. 2018. "Optimal Control of Heterogeneous Mutating Viruses" Games 9, no. 4: 103. https://doi.org/10.3390/g9040103

[4] Wu Y, Sun Y, Lin M. SQEIR: An epidemic virus spread analysis and prediction model. Comput Electr Eng. 2022 Sep; 102:108230. doi: 10.1016/j.compeleceng.2022.108230. Epub 2022 Aug 10. PMID: 35965689; PMCID: PMC9364756.

[5] Dong, N. P., Long, H. V., and Son, N. T. K., "The dynamical behaviors of fractional-order $SE_1E_2IQR$ epidemic model for malware propagation on Wireless Sensor Network", Communications in Nonlinear Science and Numerical Simulations, vol. 111, 2022. doi:10.1016/j.cnsns.2022.106428.

[6] Xiuxiu L., Gubar E. (2023). Optimal Control in the Network Model of Bi-virus Propagation. Contributions to Game Theory and Management, 15, 265-286. https://doi.org/10.21638/11701/spbu31.2022.20

[7] Vladislav Taynitskiy, Elena Gubar, Denis Fedyanin, Ilya Petrov, Quanyan Zhu, Optimal Control of Joint Multi-Virus Infection and Information Spreading, IFAC-PapersOnLine, Volume 53, Issue 2, 2020, Pages 6650-6655, ISSN 2405-8963, https://doi.org/10.1016/j.ifacol.2020.12.086.

[8] S. Eshghi, M. H. R. Khouzani, S. Sarkar and S. S. Venkatesh, "Optimal Patching in Clustered Malware Epidemics," in IEEE/ACM Transactions on Networking, vol. 24, no. 1, pp. 283-298, Feb. 2016, doi: 10.1109/TNET.2014.2364034.

[9] Broom, M. and Rychtář, J. (2022). Game-Theoretical Models in Biology (2nd ed.). Chapman and Hall/CRC. https://doi.org/10.1201/9781003024682

[10] Fu Feng, Rosenbloom Daniel I., Wang Long and Nowak Martin A. 2011Imitation dynamics of vaccination behaviour on social networksProc. R. Soc. B.27842–49 http://doi.org/10.1098/rspb.2010.1107

[11] Kamien, M. I., and Schwartz, N. L. (1991). Dynamic Optimization: The Calculus of Variations and Optimal Control in Economics and Management. Amsterdam: North-Holland.

[12] M. H. R. Khouzani, S. Sarkar and E. Altman, "Optimal control of epidemic evolution," 2011 Proceedings IEEE INFOCOM, Shanghai, China, 2011, pp. 1683-1691, doi: 10.1109/INFCOM.2011.5934963.

[13] Boltyanski, V.; Martini, H.; Soltan, V. (1998). "The Maximum Principle – How it came to be?". Geometric Methods and Optimization Problems. New York: Springer. pp. 204–227. ISBN 0-7923-5454-0.

[14] Gamkrelidze, R. V. (1999). "Discovery of the Maximum Principle". Journal of Dynamical and Control Systems. 5 (4): 437–451. doi:10.1023/A:1021783020548. S2CID

122690986. Reprinted in Bolibruch, A. A.; et al., eds. (2006). Mathematical Events of the Twentieth Century. Berlin: Springer. pp. 85–99. ISBN 3-540-23235-4.

[15] Gubar Elena, Policardo Laura, Carrera Edgar and Taynitskiy Vladislav. (2021). Optimal Lockdown Policies driven by Socioeconomic Costs.

[16] van den Driessche P, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math Biosci. 2002 Nov-Dec; 180:29-48. doi: 10.1016/s0025-5564(02)00108-6. PMID: 12387915.

[17] Marcus, M. and Minc, H. Introduction to Linear Algebra. New York: Dover, p. 145, 1988.