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ORIGINAL RESEARCH ARTICLE

Quiescence Raises the Risk of Major Pandemic Outbreaks: Insights from Mathematical Modelling.

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ABSTRACT
The impact of quiescence or dormancy periods on the dynamics of infectious diseases and their possible involvement in significant pandemic outbreaks are investigated in this study. By using simulation and mathematical modelling, we show that quiescence greatly raises the likelihood of widespread pandemics. Quiescent people, who are infected but aren't actively spreading the disease, build up an undiscovered reservoir that can drive virulent epidemics when the conditions are right for them to change from passive to active infectious states. Insights from this study can help public health efforts to lessen the effects of transmissible diseases with quiescent phases on global health. It also advances our understanding of pandemic dynamics.

INTRODUCTION

A system or process that has active phases interspersed with periods of dormancy or inactivity is often described by a mathematical model involving a quiescence phase (Usman *et al.,* 2022; Lennon *et al.,* 2011; Jochen *et al.,* 2021). This idea is frequently utilised in many disciplines to investigate phenomena that show alternating periods of activity and rest (Jochen *et al.,* 2022; Cox, 2010; Nil *et al.,* 2018).The dynamics of disease transmission, including times of latent infection or carriers who are asymptomatic, can be studied using a mathematical model for treating infectious diseases with quiescence phases (Sorrel *et al.,* 2009). These kind of models are crucial for understanding disease transmission and developing potent preventative measures (Brauer *et al.,* 2008; Matt *et al.,* 2001).

SEIQR MODEL

The SEIR model studied in (Linda, 2015; Brauer *et al.,* 2008) which stands for Susceptible-Exposed-Infectious-Recovered, is one popular model that does not take quiescence phases into account. In this research we add a quiescent phase to the SEIR model to come up with SEIQR Model, which stands for Susceptible-Exposed-Infectious-Quiescence-Recovered:

We divide the population into five compartments for the SEIQR model, including:

$S(t)$: Susceptible individuals

$E(t)$: Exposed (infected but not yet infectious) individuals

$I(t)$: Infectious individuals

$Q(t)$: Quiescent individuals

$R(t)$: Recovered individuals

$$\begin{aligned}\frac{dS}{dt} &= -\beta\frac{SI}{N}\\ \frac{dE}{dt} &= \beta\frac{SI}{N} - \nu I\\ \frac{dI}{dt} &= \nu I - \rho I + \zeta Q - \sigma I\\ \frac{dQ}{dt} &= \rho I - \zeta Q,\\ \frac{dR}{dt} &= \sigma I\end{aligned} \qquad (1)$$

Where the total population size $N = S(t) + E(t) + I(t) + Q(t) + R(t)$ is kept constant and the β is the transmission rate, ν is the incubation rate, is the rate of latent people becoming infectious, the average incubation period is $\frac{1}{\nu}$, σ is recovery rate, ρ is the rate of entering quiescence phase and ζ is the rate of exiting quiescence phase. If the last equation of the model (1) is deleted one recovers the standard SEIQR model.

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The dynamics of an infectious disease in a population are captured by the SEIQR model with a quiescence phase, which accounts for both the active infectious period and a quiescent period. Let's dissect the biological interpretation of each model compartment. The model (1) accounts for how people go through the five stages of the disease—susceptible (S), exposed (E), infectious (I), quiescent (Q), and recovered (R)—as they get infected. For diseases having latent or asymptomatic phases, the quiescent phase (Q) reflects people who are infected but not actively contagious.

Numerical Solution of SEIQR Epidemic Model

We use MATLAB to obtain a numerical Solution of model 1, please observe that in Figure 1b the quiescence phase increases the time until the pandemic ends as compared with Figure 1a and the existence of exposed, infected and quiescent individual raises the probability of major outbreak.

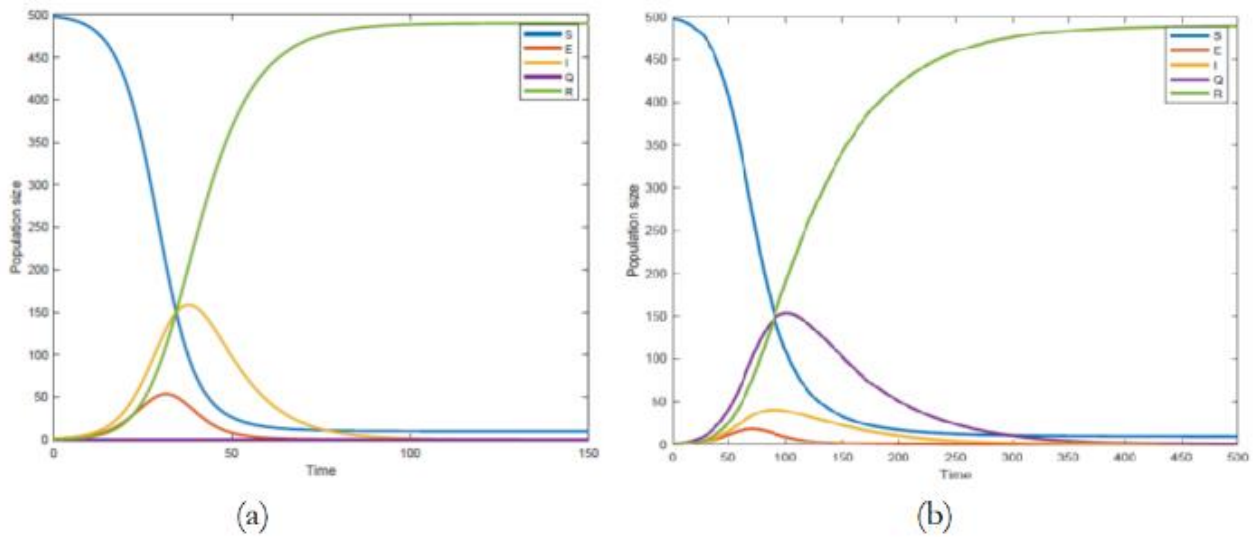

Figure 1: (a) Numerical solution of model 1 $\beta = 0.4$, $\nu = 0.4$, $\sigma = 0.1$, $\rho = \zeta = 0$, the initial population sizes are $S(0) = 498$, $E(0) = I(0) = 1$, $Q(0) = R(0) = 0$, $N = 500$, one gets the solution of SEIR model b) Numerical solution of model 1 $N = 500$, $\beta = 0.4$, $\nu = 0.4$, $\sigma = 0.1$, $\rho = 0.4$, $\zeta = 0.1$, the initial population sizes are $S(0) = 498$, $E(0) = I(0) = 1$, $Q(0) = R(0) = 0$, total population size $N = 500$. Please observe that in Figure 1b the quiescence phase increases the time until the pandemic ends as compared with Figure 1a.

Transition Probabilities

Our main aim is to study the probability of an outbreak of an epidemic, thus, it is paramount to transform the deterministic model (1) into a stochastic (birth and death) process. Therefore, we have to find the transition probabilities of each event. The following table describes the probabilities of moving from one state to the other within a small time interval $o\Delta(t)$. Here, the states are exposed, infection, recovery, entering and exiting quiescence.

Table 1: Transitions rates for the SEIQR model

Type	Transition	Probability
Latency period	$(S_t, E_t, I_t, Q_t, R_t) \rightarrow (S_t - 1, E_t, I_t + 1, Q_t, R_t)$	$\beta \frac{SI}{N} \Delta t + o(\Delta t)$
Infection I	$(S_t, E_t, I_t, Q_t, R_t) \rightarrow (S_t, E_t - 1, I_t + 1, Q_t, R_t)$	$\nu I \Delta t + o(\Delta t)$
Recovery of I	$(S_t, E_t, I_t, Q_t, R_t) \rightarrow (S_t, E_t, I_t - 1, Q_t, R_t + 1)$	$\sigma I \Delta t + o(\Delta t)$
Go quiescent of I	$(S_t, E_t, I_t, Q_t, R_t) \rightarrow (S_t, E_t - 1, I_t - 1, Q_t + 1, R_t)$	$\rho I \Delta t + o(\Delta t)$
Wake-up of Q	$(S_t, E_t, I_t, Q_t, R_t) \rightarrow (S_t, E_t, I_t + 1, Q_t - 1, R_t)$	$\zeta Q \Delta t + o(\Delta t)$

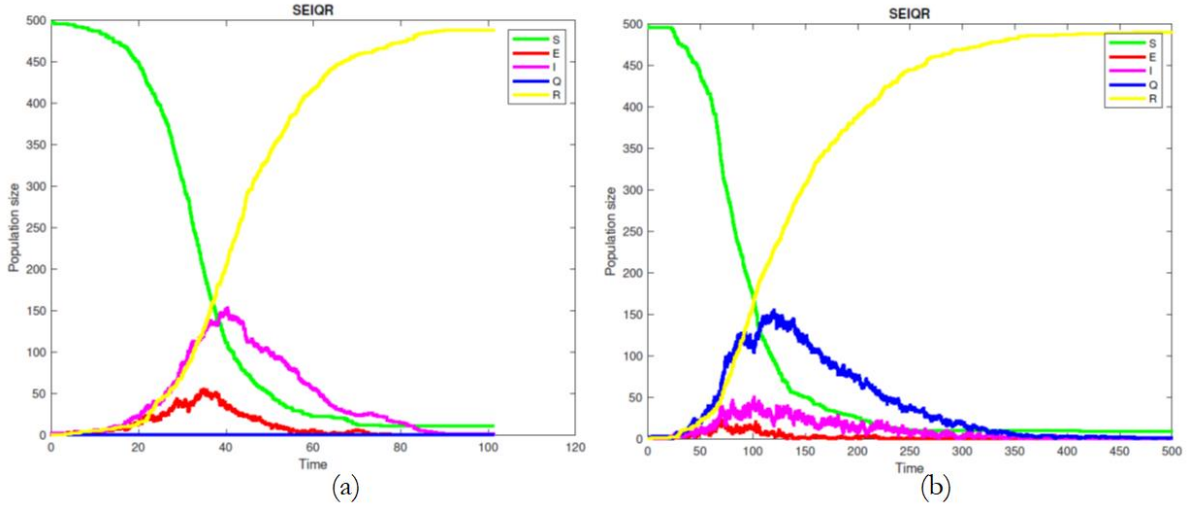

Figure 2: (a) Stochastic simulation of SEIQR CTMC with the parameter values $\beta = 0.4$, $\nu = 4.0$, $\sigma = 0.1$, $\rho = \zeta = 0$, the initial population sizes are $S(0) = 497$, $E(0) = I(0) = Q(0) = 1$, $R(0) = 0$, $N = 500$, one gets the solution of SEIR model (b) Stochastic simulation of CTMC with the parameter values $\beta = 0.4$, $\nu = 0.4$, $\sigma = 0.1$, $\rho = 0.4$, $\zeta = 0.1$, the initial population sizes are $S(0) = 498$, $E(0) = I(0) = Q(0) = 1$, $R(0) = 0$, total population size $N = 500$.

Probability of an Outbreak

Basic reproductive number of the model (1) is given by

$$R_0 = \frac{\beta}{\nu}$$

Probability of no major outbreak (extinction of the pandemics) for the continuous Time Markov chain of SEIQR epidemic model is given as

$$P_0(e_0, i_0, q_0) = \begin{cases} 1, & \text{if } R_0 \leq 1 \\ (1/R_0)^{e_0+i_0+q_0} & \text{if } R_0 > 1 \end{cases} \quad (2)$$

Thus , the probability of an outbreak is

$$P_0(e_0, i_0, q_0) = \begin{cases} 0, & \text{if } R_0 \leq 1 \\ 1-(1/R_0)^{e_0+i_0+q_0} & \text{if } R_0 > 1 \end{cases} \quad (3)$$

For the origin of these formulas see (Linda, 2013; Norman, 1990; RB, 1999).

RESULTS

Figure 3 shows that the probability of an outbreak increases with the increase of Basic Reproduction number. Figure 4 shows that the probability of an outbreak is zero when the Reproductive number is less that one. Figure 5 and 6 show that in all the values of eo,i0,q0 tested, the probability of major outbreak is greater than 85% when the basic reproduction number is 2 and above.

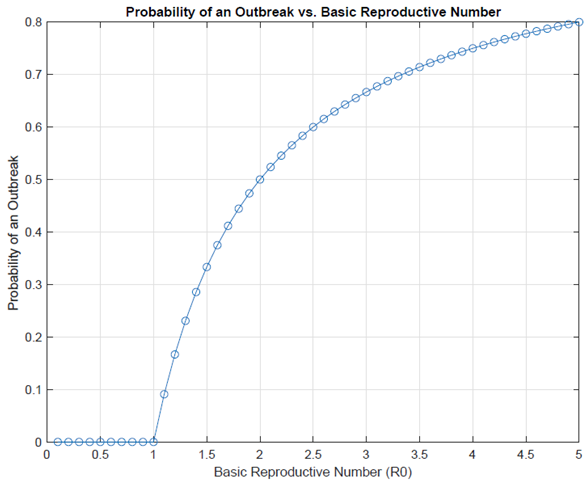

Figure 3: Probability of Outbreak against the Basic reproductive number

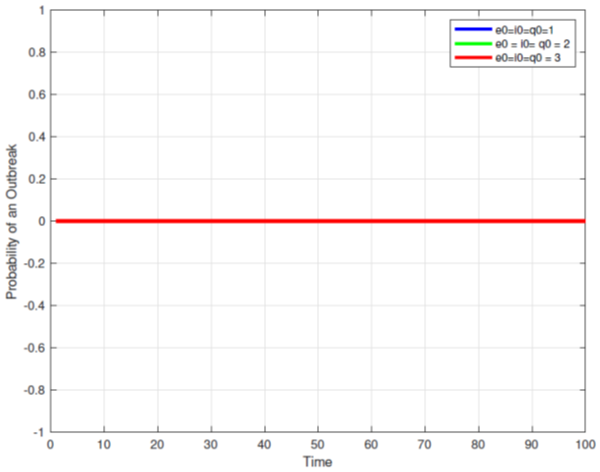

Figure 4: Probability of an Outbreak vs. Time for Different e_0, i_0, q_0 values with $R_0 = 0.8 < 1$

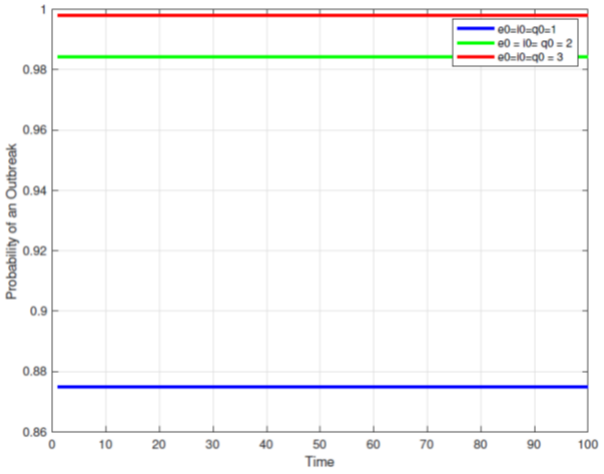

Figure 5: Probability of an Outbreak vs. Time for Different e_0, i_0, q_0 values with $R_0 = 2 > 1$

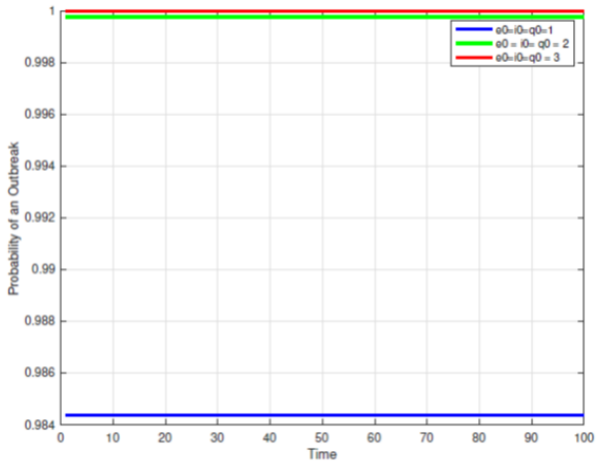

Figure 6: Probability of an Outbreak vs. Time for Different e_0, i_0, q_0 values with $R_0 = 4 > 1$, Probability of major outbreak as calculated analytically is 0.984375 when e_0, $= i_0 = q_0 = 1$ which is consistent with the result obtained by using simulation as shown in the graph above

We have seen in Figure 3 that the probability of an outbreak increases with the increase of Basic Reproduction number. We also learnt in Figure 4 above that the probability of an outbreak is zero when the Reproductive number is less that one. We have seen also in Figure 5 and 6 that in all the values of eo,i0,q0 tested the probability of major outbreak is greater than 85% when the basic reproduction number is 2 and above.

DISCUSSION

The likelihood of a severe pandemic breakout can be significantly increased by the presence of quiescence, or latent periods, within the dynamics of an infectious disease. This conclusion emphasises the significance of quiescent phase in disease transmission models and emphasises their potential function as important triggers of widespread outbreaks. Relevant implications may include

1) Early Detection and action: Early detection and prompt action depend on an understanding of the quiescent phases of disease transmission. Although it might be difficult, keeping track of and identifying individuals at these stages is essential for stopping serious epidemics.

2) Enhanced Preparedness: When diseases with quiescence are discovered, public health institutions and policy-makers must be ready to react quickly. To stop epidemics from getting worse, strategies should include efficient testing, contact tracing, and isolation techniques. The possibility of quiescent carriers should be taken into consideration while planning vaccination campaigns. The likelihood of a significant outbreak can be decreased by making an effort to immunise not just persons with current illnesses but also those who are in quiescent stages of the disease.

3) Behavioural Interventions: Even in those who seem healthy, behavioural interventions and public health messaging should stress the value of hygiene, mask use, and social isolation. When dealing with diseases that have asymptomatic or dormant carriers, this is very pertinent.

In the final analysis, reducing the danger of catastrophic pandemic breakouts requires understanding and addressing the significance of quiescent stages in disease transmission. Management and effect reduction of infectious diseases in quiescent phases require a comprehensive strategy that integrates surveillance, early detection, immunisation, and behavioural interventions

CONCLUSION AND FUTURE WORK

The result of this research indicates that quiescence considerably increases the likelihood of severe pandemic breakouts, so it is obvious that current pandemic preparedness and control tactics must take this hidden component into consideration. A significant and sometimes ignored threat to the security of the global health system is the presence of people who are in quiescent stages of the disease, diseased but not actively spreading it. Developing infectious disease transmission models to properly take into consideration quiescent stages should be the main goal of future research. This will make it easier to anticipate and manage outbreaks.

In a nutshell, it is crucial for the control of pandemics to take into account the importance of quiescent stages in the spread of diseases.

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