

Encyclopedia of Infection and Immunity (4 Volume set)

Type of mathematical model used for infectious diseases

Compartmental models are a very general modelling technique. They are often applied to the mathematical modelling of infectious diseases. The population is assigned to compartments with labels " for example, S, I, or R, (Susceptible, Infectious, or Recovered). People may progress between compartments. The order of the labels usually shows the flow patterns between the compartments; for example SEIS means susceptible, exposed, infectious, then susceptible again.

The origin of such models is the early 20th century, with important works being that of Ross[1] in 1916, Ross and Hudson in 1917,[2][3] Kermack and McKendrick in 1927[4] and Kendall in 1956.[5] The Reed-Frost model was also a significant and widely-overlooked ancestor of modern epidemiological modelling approaches.[6]

The models are most often run with ordinary differential equations (which are deterministic), but can also be used with a stochastic (random) framework, which is more realistic but much more complicated to analyze.

Models try to predict things such as how a disease spreads, or the total number infected, or the duration of an epidemic, and to estimate various epidemiological parameters such as the reproductive number. Such models can show how different public health interventions may affect the outcome of the epidemic, e.g., what the most efficient technique is for issuing a limited number of vaccines in a given population.

The SIR model [edit]

The SIR model[7][8][9][10] is one of the simplest compartmental models, and many models are derivatives of this basic form. The model consists of three compartments:-

S: The number of susceptible individuals. When a susceptible and an infectious individual come into "infectious contact", the susceptible individual contracts the disease and transitions to the infectious compartment. I: The number of infectious individuals. These are individuals who have been infected and are capable of infecting susceptible individuals. R for the number of removed (and immune) or deceased individuals. These are individuals who have been infected and have either recovered from the disease and entered the removed compartment, or died. It is assumed that the number of deaths is negligible with respect to the total population. This compartment may also be called "recovered" or "resistant".

This model is reasonably predictive[11] for infectious diseases that are transmitted from human to human, and where recovery confers lasting resistance, such as measles, mumps and rubella.

Spatial SIR model simulation. Each cell can infect its eight immediate neighbors.

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These variables (S, I, and R) represent the number of people in each compartment at a particular time. To represent that the number of susceptible, infectious and removed individuals may vary over time (even if the total population size remains constant), we make the precise numbers a function of t (time): S(t), I(t) and R(t). For a specific disease in a specific population, these functions may be worked out in order to predict possible outbreaks and bring them under control.[11]

As implied by the variable function of t, the model is dynamic in that the numbers in each compartment may fluctuate over time. The importance of this dynamic aspect is most obvious in an endemic disease with a short infectious period, such as measles in the UK prior to the introduction of a vaccine in 1968. Such diseases tend to occur in cycles of outbreaks due to the variation in number of susceptibles (S(t)) over time. During an epidemic, the number of susceptible individuals falls rapidly as more of them are infected and thus enter the infectious and removed compartments. The disease cannot break out again until the number of susceptibles has built back up, e.g. as a result of offspring being born into the susceptible compartment.

Each member of the population typically progresses from susceptible to infectious to recovered. This can be shown as a flow diagram in which the boxes represent the different compartments and the arrows the transition between compartments, i.e.

States in an SIR epidemic model and the rates at which individuals transition between them

Transition rates [edit]

For the full specification of the model, the arrows should be labeled with the transition rates between compartments. Between S and I, the transition rate is assumed to be $d(S/N)/dt = -\hat{I}^2 SI/N^2$, where N is the total population, \hat{I}^2 is the average number of contacts per person per time, multiplied by the probability of disease transmission in a contact between a susceptible and an infectious subject, and SI/N^2 is the fraction of those contacts between an infectious and susceptible individual which result in the susceptible person becoming infected. (This is mathematically similar to the law of mass action in chemistry in which random collisions between molecules result in a chemical reaction and the fractional rate is proportional to the concentration of the two reactants).

Between I and R, the transition rate is assumed to be proportional to the number of infectious individuals which is

$\hat{\nu}^3 I$. This is equivalent to assuming that the probability of an infectious individual recovering in any time interval dt is simply $\hat{\nu}^3 dt$. If an individual is infectious for an average time period D , then $\hat{\nu}^3 = 1/D$. This is also equivalent to the assumption that the length of time spent by an individual in the infectious state is a random variable with an exponential distribution. The "classical" SIR model may be modified by using more complex and realistic distributions for the I-R transition rate (e.g. the Erlang distribution[12]).

For the special case in which there is no removal from the infectious compartment ($\hat{\nu}^3=0$), the SIR model reduces to a very simple SI model, which has a logistic solution, in which every individual eventually becomes infected.

The SIR model without vital dynamics [edit]

A single realization of the SIR epidemic as produced with an implementation of the Gillespie algorithm and the numerical solution of the ordinary differential equation system (dashed).

The dynamics of an epidemic, for example, the flu, are often much faster than the dynamics of birth and death, therefore, birth and death are often omitted in simple compartmental models. The SIR system without so-called vital dynamics (birth and death, sometimes called demography) described above can be expressed by the following system of ordinary differential equations:[8][13]

$$\left\{ \begin{aligned} \frac{dS}{dt} &= \hat{\nu}^2 I S N - \frac{\beta I S}{N}, \\ \frac{dI}{dt} &= \frac{\beta I S}{N} - \gamma I, \\ \frac{dR}{dt} &= \gamma I, \end{aligned} \right.$$

The SIR model.

where S is the stock of susceptible population, I is the stock of infected, R is the stock of removed population (either by death or recovery), and N is the sum of these three.

This model was for the first time proposed by William Ogilvy Kermack and Anderson Gray McKendrick as a special case of what we now call Kermack-McKendrick theory, and followed work McKendrick had done with Ronald Ross.

This system is non-linear, however it is possible to derive its analytic solution in implicit form.[7] Firstly note that from:

$$\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0, \quad \left\{ \text{displaystyle } \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0, \right\}$$

it follows that:

$$S(t) + I(t) + R(t) = \text{constant} = N, \quad \left\{ \text{displaystyle } S(t) + I(t) + R(t) = \text{constant} = N, \right\}$$

expressing in mathematical terms the constancy of population N $\left\{ \text{displaystyle } N \right\}$. Note that the above relationship implies that one need only study the equation for two of the three variables.

Secondly, we note that the dynamics of the infectious class depends on the following ratio:

$$R_0 = \frac{\beta}{\gamma}, \quad \left\{ \text{displaystyle } R_0 = \frac{\beta}{\gamma}, \right\}$$

the so-called basic reproduction number (also called basic reproduction ratio). This ratio is derived as the expected number of new infections (these new infections are sometimes called secondary infections) from a single infection in a population where all subjects are susceptible.[14][15] This idea can probably be more readily seen if we say that the typical time between contacts is $T_c = \beta^{-1}$ $\left\{ \text{displaystyle } T_c = \beta^{-1} \right\}$, and the typical time until removal is $T_r = \gamma^{-1}$ $\left\{ \text{displaystyle } T_r = \gamma^{-1} \right\}$. From here it follows that, on average, the number of contacts by an infectious individual with others before the infectious has been removed is: T_r / T_c . $\left\{ \text{displaystyle } T_r / T_c. \right\}$

By dividing the first differential equation by the third, separating the variables and integrating we get

$$S(t) = S(0) e^{-R_0 (R(t) - R(0)) / N}, \quad \left\{ \text{displaystyle } S(t) = S(0) e^{-R_0 (R(t) - R(0)) / N}, \right\}$$

where $S(0)$ $\left\{ \text{displaystyle } S(0) \right\}$ and $R(0)$ $\left\{ \text{displaystyle } R(0) \right\}$ are the initial numbers of, respectively, susceptible and removed subjects. Writing $s_0 = S(0) / N$ $\left\{ \text{displaystyle } s_0 = S(0) / N \right\}$ for the initial proportion of susceptible individuals, and $s_{\infty} = S(\infty) / N$ $\left\{ \text{displaystyle } s_{\infty} = S(\infty) / N \right\}$ and $r_{\infty} = R(\infty) / N$

$\{displaystyle r_{\infty }=R(\infty)/N\}$ for the proportion of susceptible and removed individuals respectively in the limit $t \rightarrow \infty$, $\{displaystyle t \rightarrow \infty ,\}$ one has

$$s_{\infty } = 1 - r_{\infty } = s_0 e^{-R_0 (r_{\infty } - r_0)} \quad \{displaystyle s_{\infty }=1-r_{\infty }=s_0 e^{-R_0 (r_{\infty }-r_0)}\}$$

(note that the infectious compartment empties in this limit). This transcendental equation has a solution in terms of the Lambert W function,[16] namely

$$s_{\infty } = 1 - r_{\infty } = \hat{r}_0^{-1} W(\hat{r}_0^{-1} s_0 R_0 e^{\hat{r}_0^{-1} R_0 (1 - r_0)}) \quad \{displaystyle s_{\infty }=1-r_{\infty }=-R_0^{-1} W(-s_0 R_0 e^{-R_0 (1-r_0)})\}.$$

This shows that at the end of an epidemic that conforms to the simple assumptions of the SIR model, unless $s_0 = 0$ $\{displaystyle s_0=0\}$, not all individuals of the population have been removed, so some must remain susceptible. A driving force leading to the end of an epidemic is a decline in the number of infectious individuals. The epidemic does not typically end because of a complete lack of susceptible individuals.

The role of both the basic reproduction number and the initial susceptibility are extremely important. In fact, upon rewriting the equation for infectious individuals as follows:

$$\frac{dI}{dt} = (R_0 \frac{S}{N} - 1) \gamma I, \quad \{displaystyle \frac{dI}{dt}=\left(R_0 \frac{S}{N}-1\right)\gamma I,\}$$

it yields that if:

$$R_0 \frac{S(0)}{N} > 1, \quad \{displaystyle R_0 \cdot S(0)/N>1,\}$$

then:

$$\frac{dI}{dt}(0) > 0, \quad \{displaystyle \frac{dI}{dt}(0)>0,\}$$

i.e., there will be a proper epidemic outbreak with an increase of the number of the infectious (which can reach a

considerable fraction of the population). On the contrary, if

$R_0 < 1$, the spreading accelerates, and when $R_0 > 1$, $\lim_{t \rightarrow \infty} (S(t), I(t), R(t)) = EE = (\hat{I}^3 + \hat{I}^2, \hat{I}^2, \hat{I}^3)$. $\{displaystyle R_0 > 1, I(0) > 0 \rightarrow \lim_{t \rightarrow \infty} (S(t), I(t), R(t)) = \text{term } \{EE\} = \left(\frac{\gamma + \mu}{\beta}, \frac{\mu}{\beta} (R_0 - 1), \frac{\gamma}{\beta} (R_0 - 1) \right).$

The point EE is called the Endemic Equilibrium (the disease is not totally eradicated and remains in the population). With heuristic arguments, one may show that R_0 $\{displaystyle R_0\}$ may be read as the average number of infections caused by a single infectious subject in a wholly susceptible population, the above relationship biologically means that if this number is less than or equal to one the disease goes extinct, whereas if this number is greater than one the disease will remain permanently endemic in the population.

The SIR model [edit]

$S(0) = 997, I(0) = 3, R(0) = 0$ $\{textstyle S(0)=997, I(0)=3, R(0)=0\}$ $\hat{I}^2 = 0.4$ $\{textstyle \beta = 0.4\}$ $\hat{I}^3 = 0.04$ $\{textstyle \gamma = 0.04\}$ Diagram of the SIR model with initial values, and rates for infection and for recovery

$S(0) = 997, I(0) = 3, R(0) = 0$ $\{textstyle S(0)=997, I(0)=3, R(0)=0\}$ $\hat{I}^3 = 0.04$ $\{textstyle \gamma = 0.04\}$ $\hat{I}^2 = 0.5$ $\{textstyle \beta = 0.5\}$ $\hat{I}^2 = 0.12$ $\{textstyle \beta = 0.12\}$ Animation of the SIR model with initial values, and rate of recovery. The animation shows the effect of reducing the rate of infection from 0.4 to 0.12. If there is no medicine or vaccination available, it is only possible to reduce the infection rate (often referred to as "flattening the curve") by appropriate measures such as social distancing.

In 1927, W. O. Kermack and A. G. McKendrick created a model in which they considered a fixed population with only three compartments: susceptible, $S(t)$ $\{displaystyle S(t)\}$; infected, $I(t)$ $\{displaystyle I(t)\}$; and recovered, $R(t)$ $\{displaystyle R(t)\}$. The compartments used for this model consist of three classes:[4]

$S(t)$ $\{displaystyle S(t)\}$

$I(t)$ $\{displaystyle I(t)\}$

$R(t)$

The flow of this model may be considered as follows:

$S \hat{\rightarrow} I \hat{\rightarrow} R$

Using a fixed population, $N = S(t) + I(t) + R(t)$ in the three functions resolves that the value N should remain constant within the simulation, if a simulation is used to solve the SIR model. Alternatively, the analytic approximant[9] can be used without performing a simulation. The model is started with values of $S(t=0)$, $I(t=0)$ and $R(t=0)$. These are the number of people in the susceptible, infected and removed categories at time equals zero. If the SIR model is assumed to hold at all times, these initial conditions are not independent.[9] Subsequently, the flow model updates the three variables for every time point with set values for $\hat{\beta}$ and $\hat{\gamma}$. The simulation first updates the infected from the susceptible and then the removed category is updated from the infected category for the next time point ($t=1$). This describes the flow persons between the three categories. During an epidemic the susceptible category is not shifted with this model, $\hat{\beta}$ changes over the course of the epidemic and so does $\hat{\gamma}$. These variables determine the length of the epidemic and would have to be updated with each cycle.

$\frac{dS}{dt} = \hat{\beta} \frac{SI}{N}$

$\frac{dI}{dt} = \hat{\beta} \frac{SI}{N} - \hat{\gamma} I$

$\frac{dR}{dt} = \hat{\gamma} I$

Several assumptions were made in the formulation of these equations: First, an individual in the population must be considered as having an equal probability as every other individual of contracting the disease with a rate of a and an equal fraction b of people that an individual makes contact with per unit time. Then, let $\hat{\beta}$ be the multiplication of a and b . This is the transmission probability times the contact rate. Besides, an infected individual makes contact with b persons per unit time whereas only a fraction, S/N of them are susceptible. Thus,

we have every infective can infect a $\beta S = \hat{\beta}^2 S$ susceptible persons, and therefore, the whole number of susceptibles infected by infectives per unit time is $\hat{\beta}^2 S I$. For the second and third equations, consider the population leaving the susceptible class as equal to the number entering the infected class. However, a number equal to the fraction $\hat{\gamma}$ (which represents the mean recovery/death rate, or $1 / \hat{\gamma}$ the mean infective period) of infectives are leaving this class per unit time to enter the removed class. These processes which occur simultaneously are referred to as the Law of Mass Action, a widely accepted idea that the rate of contact between two groups in a population is proportional to the size of each of the groups concerned. Finally, it is assumed that the rate of infection and recovery is much faster than the time scale of births and deaths and therefore, these factors are ignored in this model.[22]

Steady-state solutions [edit]

The expected duration of susceptibility will be $E[\min(T_L, T_S)]$ where T_L reflects the time alive (life expectancy) and T_S reflects the time in the susceptible state before becoming infected, which can be simplified[23] to:

$$E[\min(T_L, T_S)] = \int_0^{\infty} e^{-(\mu + \lambda)x} dx = \frac{1}{\mu + \lambda},$$

such that the number of susceptible persons is the number entering the susceptible compartment μN times the duration of susceptibility:

$$S = \frac{\mu N}{\mu + \lambda}.$$

Analogously, the steady-state number of infected persons is the number entering the infected state from the susceptible state (number susceptible, times rate of infection) $\lambda S = \frac{\beta I N}{\mu + \nu}$ times the duration of infectiousness $1 / (\mu + \nu)$:

$$I = \frac{\beta I N}{\mu + \lambda} \frac{1}{\mu + \nu}.$$

Other compartmental models [edit]

There are many modifications of the SIR model, including those that include births and deaths, where upon recovery there is no immunity (SIS model), where immunity lasts only for a short period of time (SIRS), where there is a latent period of the disease where the person is not infectious (SEIS and SEIR), and where infants can be born with immunity (MSIR).

Variations on the basic SIR model [edit]

The SIS model [edit]

Some infections, for example, those from the common cold and influenza, do not confer any long-lasting immunity. Such infections may give temporary resistance but do not give long-term immunity upon recovery from infection, and individuals become susceptible again.

We have the model:

$$\begin{aligned} \frac{dS}{dt} &= \lambda - \beta \frac{SI}{N} + \gamma I \\ \frac{dI}{dt} &= \beta \frac{SI}{N} - \gamma I \end{aligned}$$

Note that denoting with N the total population it holds that:

$$\frac{dS}{dt} + \frac{dI}{dt} = 0 \quad \hat{=} \quad S(t) + I(t) = N$$

It follows that:

$$\frac{dI}{dt} = (\beta - \gamma) I - \frac{\beta}{N} I^2$$

i.e. the dynamics of infectious is ruled by a logistic function, so that $\forall I(0) > 0$:

$$\begin{aligned} \beta < \gamma & \hat{=} \lim_{t \rightarrow +\infty} I(t) = 0, \quad \beta > \gamma & \hat{=} \lim_{t \rightarrow +\infty} I(t) = \left(1 - \frac{\gamma}{\beta}\right) N. \end{aligned}$$

$$\{\gamma\} > 1 \rightarrow \lim_{t \rightarrow \infty} I(t) = \left(1 - \frac{\{\gamma\}}{\{\beta\}}\right) N.$$

It is possible to find an analytical solution to this model (by making a transformation of variables: $I = y^{-1}$ and substituting this into the mean-field equations), [24] such that the basic reproduction rate is greater than unity. The solution is given as

$$I(t) = \frac{I_{\infty}}{1 + V e^{-\chi t}}$$

where $I_{\infty} = \left(1 - \frac{\gamma}{\beta}\right) N$ is the endemic infectious population, $\chi = \beta - \gamma$, and $V = \frac{I_{\infty}}{I_0 - 1}$. As the system is assumed to be closed, the susceptible population is then $S(t) = N - I(t)$.

As a special case, one obtains the usual logistic function by assuming $\gamma = 0$. This can be also considered in the SIR model with $R = 0$, i.e. no removal will take place. That is the SI model. [25] The differential equation system using $S = N - I$ thus reduces to:

$$\frac{dI}{dt} = I(N - I).$$

In the long run, in the SI model, all individuals will become infected.

The SIRD model [edit]

$S(0) = 997$, $I(0) = 3$, $R(0) = 0$, $\beta = 0.4$, $\gamma = 0.035$, $\mu = 0.005$. Diagram of the SIRD model with initial values and the rates of infection, recovery and mortality

$S(0) = 997$, $I(0) = 3$, $R(0) = 0$, $\gamma = 0.035$, $\mu = 0.005$, $\beta = 0.5$, $\delta = 0.12$. Animation of the SIRD model with initial values, and rates of recovery and mortality. The animation shows the effect of reducing the rate of infection from 0.4 to 0.12. If there is no medicine or vaccination available, it is only possible to reduce the infection rate

(often referred to as "flattening the curve") by measures such as "social distancing".

The Susceptible-Infectious-Recovered-Deceased model differentiates between Recovered (meaning specifically individuals having survived the disease and now immune) and Deceased.[14] This model uses the following system of differential equations:

$$\begin{aligned} \frac{dS}{dt} &= \hat{\alpha}' - \hat{\beta}^2 I S N, \quad \frac{dI}{dt} = \hat{\beta}^2 I S N - \hat{\alpha}' - \hat{\beta}^3 I, \quad \frac{dR}{dt} = \hat{\beta}^3 I, \quad \frac{dD}{dt} = \hat{\mu} I, \end{aligned}$$

where $\hat{\beta}^2$, $\hat{\beta}^3$, $\hat{\mu}$ are the rates of infection, recovery, and mortality, respectively.[26]

The SIRV model [edit]

The Susceptible-Infectious-Recovered-Vaccinated model is an extended SIR model that accounts for vaccination of the susceptible population.[27] This model uses the following system of differential equations:

$$\begin{aligned} \frac{dS}{dt} &= \hat{\alpha}' - \hat{\beta}^2(t) I S N - v(t) S, \quad \frac{dI}{dt} = \hat{\beta}^2(t) I S N - \hat{\alpha}' - \hat{\beta}^3(t) I, \quad \frac{dR}{dt} = \hat{\beta}^3(t) I, \quad \frac{dV}{dt} \\ &= v(t) S, \end{aligned}$$

A cartoon for the SIRV model.

where $\hat{\beta}^2$, $\hat{\beta}^3$, v are the rates of infection, recovery, and vaccination, respectively. For the semi-time initial conditions $S(0) = (1 - \hat{\alpha}' / \hat{\beta}^2) N$, $I(0) = \hat{\alpha}' / \hat{\beta}^2$, $R(0) = V(0) = 0$ and constant ratios $k = \hat{\beta}^3(t) / \hat{\beta}^2(t)$ and $b = v(t) / \hat{\beta}^2(t)$ the model had been solved approximately.[27] The occurrence of a pandemic outburst requires $k + b > 0 \rightarrow \lim_{t \rightarrow \infty} (S(t), E(t), I(t), R(t)) = EE$.

In case of periodically varying contact rate $\hat{\beta}^2(t)$ the condition for the global attractiveness of DFE is that the following linear system with periodic coefficients:

$$\frac{dE_1}{dt} = \hat{\beta}^2(t) I_1 - (\gamma + a) E_1 \quad \frac{dI_1}{dt} = a E_1 - (\gamma + \mu) I_1$$

is stable (i.e. it has its Floquet's eigenvalues inside the unit circle in the complex plane).

The SEIS model [edit]

The SEIS model is like the SEIR model (above) except that no immunity is acquired at the end.

$$S \rightarrow E \rightarrow I \rightarrow S$$

In this model an infection does not leave any immunity thus individuals that have recovered return to being susceptible, moving back into the S(t) compartment. The following differential equations describe this model:

$$\frac{dS}{dt} = \lambda - \beta \frac{SI}{N} - \mu S \quad \frac{dE}{dt} = \beta \frac{SI}{N} - (\epsilon + \mu) E \quad \frac{dI}{dt} = \epsilon E - (\gamma + \mu) I$$

The MSEIR model [edit]

For the case of a disease, with the factors of passive immunity, and a latency period there is the MSEIR model.

$$M \rightarrow S \rightarrow E \rightarrow I \rightarrow R$$

$$\frac{dM}{dt} = \lambda - \mu M - \beta \frac{SI}{N} \quad \frac{dS}{dt} = \beta \frac{SI}{N} - (\epsilon + \mu) S \quad \frac{dE}{dt} = \epsilon S - (\gamma + \mu) E \quad \frac{dI}{dt} = \epsilon E - (\gamma + \mu) I \quad \frac{dR}{dt} = \gamma I - \mu R$$

The MSEIRS model [edit]

An MSEIRS model is similar to the MSEIR, but the immunity in the R class would be temporary, so that individuals would regain their susceptibility when the temporary immunity ended.

$$M \rightarrow S \rightarrow E \rightarrow I \rightarrow R \rightarrow S \rightarrow I \rightarrow R \rightarrow S$$

It is well known that the probability of getting a disease is not constant in time. As a pandemic progresses, reactions to the pandemic may change the contact rates which are assumed constant in the simpler models. Counter-measures such as masks, social distancing and lockdown will alter the contact rate in a way to reduce the speed of the pandemic.

In addition, Some diseases are seasonal, such as the common cold viruses, which are more prevalent during winter. With childhood diseases, such as measles, mumps, and rubella, there is a strong correlation with the school calendar, so that during the school holidays the probability of getting such a disease dramatically decreases. As a consequence, for many classes of diseases, one should consider a force of infection with periodically ('seasonal') varying contact rate

$$F = \hat{\beta}^2 (t) \frac{I}{N}, \quad \hat{\beta}^2 (t + T) = \hat{\beta}^2 (t) \quad \left\{ \text{displaystyle } F = \beta(t) \frac{I}{N}, \text{quad } \beta(t+T) = \beta(t) \right\}$$

with period T equal to one year.

Thus, our model becomes

$$\frac{dS}{dt} = \hat{\beta}^2 (t) \frac{I}{N} S - \hat{\beta}^2 (t) \frac{I}{N} S - (\gamma + \mu) S \quad \left\{ \text{displaystyle } \begin{aligned} \frac{dS}{dt} &= \hat{\beta}^2 (t) \frac{I}{N} S - \hat{\beta}^2 (t) \frac{I}{N} S - (\gamma + \mu) S \\ \frac{dI}{dt} &= \hat{\beta}^2 (t) \frac{I}{N} S - (\gamma + \mu) I \end{aligned} \right\}$$

(the dynamics of recovered easily follows from $R = N - S - I$), i.e. a nonlinear set of differential equations with periodically varying parameters. It is well known that this class of dynamical systems may

undergo very interesting and complex phenomena of nonlinear parametric resonance. It is easy to see that if:

$$1 - T \hat{\alpha} \ll 0 \quad T \hat{I}^2 (t) \hat{I}^{1/4} + \hat{I}^3 \frac{d}{dt} 0.$$

In such a case the eradication condition becomes:

$$P(0) \hat{\alpha} \geq P^*, \quad \left\{ \text{displaystyle } P(0) \geq P^*, \right\}$$

i.e. the baseline vaccination rate should be greater than the "mandatory vaccination" threshold, which, in case of exemption, cannot hold. Thus, "rational" exemption might be myopic since it is based only on the current low incidence due to high vaccine coverage, instead taking into account future resurgence of infection due to coverage decline.

Vaccination of non-newborns [edit]

In case there also are vaccinations of non newborns at a rate $\hat{\rho}$ the equation for the susceptible and vaccinated subject has to be modified as follows:

$$\frac{dS}{dt} = \hat{I}^{1/4} N (1 - \hat{\alpha} P) \hat{\alpha}' - \hat{I}^{1/4} S \hat{\alpha}' - \hat{\rho} S \hat{\alpha}' - \hat{I}^2 \frac{I}{N} S \frac{dV}{dt} = \hat{I}^{1/4} N P + \hat{\rho} S \hat{\alpha}' - \hat{I}^{1/4} V \quad \left\{ \text{displaystyle } \begin{aligned} \frac{dS}{dt} &= \mu N(1-P) - \mu S - \rho S - \beta \frac{I}{N} S \\ \frac{dV}{dt} &= \mu NP + \rho S - \mu V \end{aligned} \right\}$$

leading to the following eradication condition:

$$P \hat{\alpha} \geq 1 - \hat{\alpha}' \left(1 + \hat{\rho} \hat{I}^{1/4} \right) \frac{1}{R_0} \quad \left\{ \text{displaystyle } P \geq 1 - \left(1 + \frac{\rho}{\mu} \right) \frac{1}{R_0} \right\}$$

Pulse vaccination strategy [edit]

This strategy repeatedly vaccinates a defined age-cohort (such as young children or the elderly) in a susceptible population over time. Using this strategy, the block of susceptible individuals is then immediately removed, making it possible to eliminate an infectious disease, (such as measles), from the entire population. Every T time units a constant fraction p of susceptible subjects is vaccinated in a relatively short (with respect to the dynamics of the

disease) time. This leads to the following impulsive differential equations for the susceptible and vaccinated subjects:

$$\begin{aligned} \frac{dS}{dt} &= \hat{\mu} N - \hat{\mu} S - \beta \frac{I}{N} S, \quad S(nT^+) = (1-p)S(nT^-), \quad n = 0, 1, 2, \dots \\ \frac{dV}{dt} &= \hat{\mu} V, \quad V(nT^+) = V(nT^-) + pS(nT^-), \quad n = 0, 1, 2, \dots \end{aligned}$$

It is easy to see that by setting $I = 0$ one obtains that the dynamics of the susceptible subjects is given by:

$$S^*(t) = (1-p)^{\lfloor t/T \rfloor} (1-p)^{-\mu t} E^{-\mu \text{MOD}(t, T)} \quad \{displaystyle S^*(t) = 1 - \frac{p}{1 - (1-p)E^{-\mu T}} E^{-\mu \text{MOD}(t, T)}\}$$

and that the eradication condition is:

$$R_0 = \int_0^T S^*(t) dt < 1 \quad \{displaystyle R_0 = \int_0^T S^*(t) dt\}$$

Reference

[Essentials of Biostatistics for Public Health \(Essential Public Health\)](#)

[Evaluating Research in Communication Disorders \(Pearson Communication Sciences and Disorders\)](#)