Acta Biotheoretica manuscript No.
(will be inserted by the editor)

The hybrid incidence susceptible-transmissible-removed model for pandemics

Scaling time to predict an epidemic's population density dependent temporal propagation

Ryan L. Benjamin

Received: date / Accepted: date

Abstract The susceptible-transmissible-removed (STR) model is a deterministic compartment model, based on the susceptible-infected-removed (SIR) prototype. The STR replaces 2 SIR assumptions. SIR assumes that the emigration rate (due to death or recovery) is directly proportional to the infected compartment's size. The STR replaces this assumption with the biologically appropriate assumption that the emigration rate is the same as the immigration rate one infected period ago. This results in a unique delay differential equation epidemic model with the delay equal to the infected period.

Hamer's mass action law for epidemiology is modified to resemble its chemistry precursor – the law of mass action. Constructing the model for an isolated population that exists on a surface bounded by the extent of the population's movements permits compartment density to replace compartment size.

The STR reduces to a SIR model in a timescale that negates the delay – the transmissible timescale. This establishes that the SIR model applies to an isolated population in the disease's transmissible timescale.

Cyclical social interactions will define a rhythmic timescale. It is demonstrated that the geometric mean maps transmissible timescale properties to their rhythmic timescale equivalents. This mapping defines the hybrid incidence (HI). The model validation demonstrates that the HI-STR can be constructed directly from the disease's transmission dynamics.

The basic reproduction number ($\mathcal{R}_0$) is an epidemic impact property. The HI-STR model predicts that $\mathcal{R}_0 \propto \sqrt[3]{\rho_n}$ where ρ_n is the population den-

R. Benjamin
Johannesburg, South Africa
Tel.: +27-(0)11-242-7268
E-mail: ryan.benjamin@lancet.co.za

sity, and $\mathfrak{B}$ is the ratio of time increments in the transmissible- and rhythmic timescales. The model is validated by experimentally verifying the relationship.

$\mathcal{R}_0$'s dependence on ρ_n is demonstrated for droplet-spread SARS in Asian cities, aerosol-spread measles in Europe and non-airborne Ebola in Africa.

Keywords susceptible-transmissible-removed (STR) · basic reproduction number · hybrid incidence · delay differential equation · rhythmic timescale · transmissible timescale

1 Introduction

The modelling of infectious disease dates from Bernoulli's 18^{th} century statistical model and En'ko's compartment-model in the 19^{th} century [1]. In this manuscript, the models will arbitrarily be introduced as deterministic or stochastic. The deterministic models will either be ordinary differential equation (ODE), partial differential equation (PDE) or delay differential equation (DDE) compartment models. These deterministic compartment models' numerical simulation will not be discussed. Under stochastic models, Cellular automata (CA) are introduced as a subcategory of stochastic models because the distinction between the model and the numerical method is not obvious.

The ODE deterministic theory describing the propagation of an infectious disease as presented by Kermack and McKendrick [2–5] is the convergence of the basic reproduction number ($\mathcal{R}_0$) concepts of Böckh [6, 7], Dublin and Lotka [8–10], and Kuczynski [11] in demography; Hamer's [5, 12, 13] mass action incidence from chemistry [14]; and the compartment models of Ross and Hudson [11,15], and En'ko [16,17]. The 2 ODE compartment model prototypes classify all individuals in a closed population as either susceptible, infected or removed. Removed can either mean recovered (assumed immune) or dead. In the susceptible-infected-removed (SIR) model, all three compartments are used and individuals move in one direction only – from susceptible to infected to removed. The susceptible-infected-susceptible (SIS) model only uses 2 of these compartments and individuals are able to return to the susceptible compartment upon resolution of infection. Since then, an analytic solution for the SIR model has been found [18], standard incidence introduced [19, 20] and pragmatic problems like herd immunity [21] and vaccination threshold [22] solved.

At least 2 layers of complexity have since been added. The basic ODE models assume an homogenous population – every infected-susceptible pair has the same probability of successful pathogen transmission over a fixed interaction period. Diekmann *et al* define a next generation matrix (NGM) on a heterogenous population [23–25]. This NGM predicts the secondary infections due to the current infected population. They then show that $\mathcal{R}_0$ is the dominant eigenvalue of this NGM. Van den Driessche *et al* propose that an

heterogenous population can be approximated as the superposition of N homogenous population compartments [26, 27]. The NGM calculates $\mathcal{R}_0$ for this system of equations.

Secondly, additional compartments allow more realistic simulation of the dynamics of each disease [19,28–32]. One such model is the susceptible-exposed-infective-removed (SEIR) model [33–35]. The incubation period effectively subdivides the infected compartment into an asymptomatic, non-infectious, exposed compartment and an infectious compartment [36].

Conventional DDE compartment models are an alternative to the exposed compartment of ODE models [37, 38]. These DDE compartment models simulate a biologically appropriate constant incubation period. In contrast, the exposed compartment in the SEIR and SEIRS models implies an exponential distribution of incubation time [37, 39]. The delay from infection to infectious is typically included with the force of infection term as $\beta I(t-\tau)S(t)$ or $\beta I(t)S(t-\tau)$. Hethcote *et al* introduced alternative delay models [39–44].

The homogenous mixing and large population assumptions reduce epidemic simulation to ODE models [25, 45]. The assumption that the rate at which migrants enter a compartment is directly proportional to the size of compartment they exit is inconsistent with the biology [46–49].

PDE models allow the simulation of spatial spread. The spatial spread model commonly used is diffusion [24, 27, 50, 51]. Although diffusions models are described for rabies in foxes [27, 52] and the mosquito-vector West Nile fever in birds [27, 53], the statistical mechanical derivation of Fick's law of diffusion requires random movement [54]. Given non-random human-vector movement [55–57], the conditions under which the diffusion model is appropriate are not obvious. Furthermore, the diffusion model is not the only spatial spread model [56, 58–61] nor the most general [25, 60, 62].

The large number of discrete events assumed by the deterministic models result in continuous differentiable functions [45]. Stochastic models are a complement able to simulate small populations (*e.g.* early in the epidemic) and assign probabilities to outlier events [20, 63–65]. In 1760, Bernoulli used a statistical model to predict the effect of vaccination [66, 67]. Farr fitted bell-shaped curves to epidemics – attempting to identify empiric laws that describe their episodic nature [67]. McKendrick constructed a spatial stochastic model on a two dimensional lattice [68, 69] but it was the Reed-Frost and Greenwood [70] binomial chain models that became popular [65, 67]. Both of these models assume long incubation periods with comparatively negligible infectious periods. A time increment equates to the incubation period and all infections occur at the end of this period. These assumptions result in asynchronous generations of pathogen hosts. Biologically, the model is consistent with seasonal procreation where the female dies after producing multiple off-

spring at that time (*e.g.* spawning salmon). The conditions under which these models simulate epidemics most appropriately are not obvious. Gani and Jerwood [71] recognised these binomial chain models as examples of discrete time Markov chains [72,73]. Continuous time Markov chains extrapolate the model to continuous time, discrete state variables [65, 73, 74]. This also represents a long latent period, branching process but the latent period is variable. Finally, continuous time, continuous state variables are simulated with stochastic differential equations [65,73–76] with the variance of a Gaussian distribution [77].

Cellular automata (CA) arose to study the complex phenomena that evolve when simple rules are applied on a regular lattice [78–82]. CA has been applied to computational fluid dynamics (CFD), economics, biology, ecology, physics and chemistry [83, 84]. Schneckenreither *et al* classify epidemic CA as lattice gas cellular automata (LGCA) or stochastic cellular automata (SCA) [59]. The terms LGCA and the lattice Boltzmann method (LBM) are from CFD [85, 86] where the appropriate 2-step rules of stream and redistribute are shown to simulate the macroscopic, incompressible Navier-Stokes (NS) equations [87, 88]. Similarly, Boccara and Cheong applied LGCA to epidemics by constructing a 2-step rule of streaming and redistribution of states S,I and R on a regular lattice [89–91]. Schneckenreither *et al* describe the LGCA spatial spread model as diffusion and classically simulates individuals occupying a cell. Mansilla and Gutierrez construct a spatial spread CA that can be tuned between the LGCA extreme of diffusion and perfect mixing [57].

In contrast, SCA redistributes cell states based on that cell's previous state and adjacent cells' proximity and previous states [92,93]. The simulation does not model migration between cells but is intended to allow individuals within a cell to make contact with individuals in adjacent cells. States are represented as a ratio. Schneckenreither *et al* refers to this spatial spread model as contact spread [59]. Redistribution of compartments is based on the probabilities of changing compartment upon contact. The probabilistic cellular automata (PCA) model combines the contact spread of the SCA model with the LGCA's integer cell occupants [94,95]. In the PCA model, the integer is 1. Holka *et al*'s PCA model simulates a whole country and superimposes daily commutes [96] – migration is a LGCA feature. The SCA model has been extended to include uncertainty using a Markov chain Monte Carlo method with coupled Beta and Dirichlet distributions [77, 97, 98].

Of note, in the CFD CA analogy, a Chapman-Enskog expansion is performed on the LGCA and LBM to derive the PDEs that describe the macroscopic phenomena [87, 88, 99]. In contrast, the mean field approximation used on epidemic CAs necessarily describe population level ODEs [89–91,100]. Thus the population level spatial spread models described by the epidemic CAs are not obvious. In the CFD analogy, the CAs' time- and space increments are tuned to achieve the appropriate viscocity – given that the viscocity in the CA-derived NS equations is a function of the time and space increments [87, 88].

Without epidemiology CA derived PDEs, it is not obvious whether similar constraints pertain to the discretisation of these CAs.

This manuscript derives a DDE model where the delay is not due to the incubation period and is not an alternative to the exposed compartment. The delay addresses the assumption that the rate at which individuals leave the infectious compartment is proportional to the size of that compartment.

The conventional, ODE model concepts and properties are explored before deriving the susceptible-transmissible-removed (STR) model. The deterministic SIR model [2–5] assumes that individuals move between three compartments – susceptible (S), infected-infectious (I) and removed-recovered (R) – during an epidemic. $S(t)$, $I(t)$ and $R(t)$ refer to the size of their respective compartments. There is no delay from infection to being infectious in the SIR model. R's individuals can either be dead or recovered (assumed immune). The ODE model describing the movement between these compartments is [64]

$$\begin{aligned}\dot{S}(t) &= -\frac{\xi(t)}{N}S(t)I(t)\\ \dot{I}(t) &= \frac{\xi(t)}{N}S(t)I(t) - \alpha I(t)\\ \dot{R}(t) &= \alpha I(t)\end{aligned} \tag{1}$$

where $S(t) + I(t) + R(t) = N$ – the constant population size. The rate of new infection is proportional to $S(t)I(t)$. This corresponds to the rate at which individuals leave S. The rate of recovery is directly proportional to $I(t)$.

In Model (1), the rate of recovery is directly proportional to $I(t)$. This has no biological interpretation. Biologically, an infection lasts for a fixed period (T_I). Individuals leave I at the same rate at which they entered it one T_I ago.

Hethcote [101], refers to $\xi(t)$ as the horizontal transmission incidence and it is usually treated as a constant (ξ). Epidemiologically, incidence is the number of new cases of a disease per unit time as a proportion of the susceptible population. At $t \gtrapprox t_0$, when $S \approx N$ and no individuals leave I,

$$\xi(t_0) = \frac{\dot{I}(t_0)}{S(t_0)} = -\frac{\dot{S}(t_0)}{S(t_0)} = \frac{\dot{I}(t_0)}{N}. \tag{2}$$

There are two ξs in epidemiology. The conventional mass action ξ assumes that interactions are completely random. Further, N is so large that, early in the epidemic, all interactions are with susceptible individuals. Here, $\xi = \beta N$.

Hethcote [19, 20] argues that individuals have regular close contacts that are of similar count whether in a tribe, a village or a metropolis. Furthermore, as a generalisation, interactions only occur with these close contacts.

This second ξ is the standard incidence. $\xi = \beta_{si}$ is a constant for standard incidence. Although standard incidence is usually used for sexually transmitted diseases; Anderson demonstrates experimentally that, for airborne diseases, $0.03 \leq \nu \leq 0.07$ in $\xi = \beta N^{\nu}$ [102, 103].

The basic reproduction number ($\mathcal{R}_0$) is a demographic concept [6, 7] that has been repurposed as an epidemic impact property. It represents the number of new infections produced by an infected individual directly. A straightforward $\mathcal{R}_0$ [20] derivation exists for the SIR model. Consider I of Model (1).

$$\dot{I}(t) = \left(\frac{\xi S(t)}{N} - \alpha\right) I(t) > 0 \iff \frac{\xi S(t)}{N} - \alpha > 0 \iff \frac{\xi}{\alpha}\frac{S(t)}{N} > 1.$$

Define

$$\mathcal{R}_0 \coloneqq \frac{\xi}{\alpha}. \tag{3}$$

For a completely susceptible population (at $t = 0$), $S(0) \approx N$. Then

$$\mathcal{R}_0 > 1 \iff \dot{I}(t) > 0 \tag{4}$$

implies that I grows indefinitely when $\mathcal{R}_0 > 1$. Biologically, α is interpreted as the infection frequency.

2 A boundaried, delayed differential equation, SIR-like model

Define a host as an individual harbouring a pathogen that has the capacity to cause a disease. If the pathogen can be transmitted to a new host, the disease is infectious. The disease can only be transmitted to a new host if the host makes sufficient contact with a susceptible individual or potential host.

There is a delay from becoming infected to being infectious. Thus the infectious period (T_i) is shorter than T_I. In the SIR model this delay is negligible. T_i and T_I are biologically defined and limited by either recovery or death. Interventions like vaccination or medication either shorten T_I or reduce the case fatality rate (CFR). The CFR is the ratio of those infected that die.

A host's ability to transmit a disease can also be limited behaviourally and technologically. An example of the former is isolation in chicken pox. When the vesicular rash appears, the diagnosis is obvious and the caregiver isolates the host. The pharmacological treatment of tuberculosis (TB) is an example of technological transmission restriction. TB treatment results in non-infectious hosts. The transmissible period ($\Delta\overline{\tau}$) will therefore be defined as the weighted average of the biological, behavioural and technological restrictions that limit the period during which a host has the opportunity to transmit a disease.

Define an isolated community as a subset of individuals that only interact with other members of that subset. The isolation can be due to a physical boundary like a mountain range or a wall; a cultural barrier like a tribal taboo or language; or a legal barrier prohibiting social interaction.

Let an isolated community of large population size ($N(\mathbf{x},t)$) exist on a boundaried surface $\delta A(\mathbf{x})$, where $\mathbf{x}$ is a central measure of δA, at time t. Natural births and deaths are neglected. Let the susceptible population in this community be $S(\mathbf{x},t)$. Let the density of susceptible individuals be $s(\mathbf{x},t) = \frac{S(\mathbf{x},t)}{\delta A}$. Similarly, let population density be $\rho_n(\mathbf{x}) = \frac{N(\mathbf{x})}{\delta A}$ at $\mathbf{x}$, $\forall\, t$. Then for $N(\mathbf{x}) = \int_{\delta A} \rho_n(\mathbf{x}) d\mathbf{A}$,

$$\begin{aligned} S(\mathbf{x},\mathbf{t}) &= \int_{\delta A} s(\mathbf{x},t) d\mathbf{A} \iff \frac{S(\mathbf{x},t)}{N(\mathbf{x},t)} = \frac{\int_{\delta A} s(\mathbf{x},t) d\mathbf{A}}{\int_{\delta A} \rho_n(\mathbf{x},t) d\mathbf{A}} \\ &\iff \int_{\delta A} s(\mathbf{x},t) d\mathbf{A} = S(\mathbf{x},t) \int_{\delta A} \frac{\rho_n(\mathbf{x},t)}{N(\mathbf{x},t)} d\mathbf{A} \end{aligned} \tag{5}$$

where $N(\mathbf{x},t)$ and $\rho_n(\mathbf{x},t)$ are assumed positive constants in time because natural births and deaths are not significant in this time frame. Let

$$\mathcal{M} := \frac{1}{N(\mathbf{x})} \int_{\delta A} \rho_n(\mathbf{x}) d\mathbf{A} = 1, \tag{6}$$

by the definition of properties of ρ_n and N above. For arbitrary scalar variable φ, (5) is

$$\int_{\delta A} s(\mathbf{x},t) d\mathbf{A} = \mathcal{M} S = \int \frac{\partial S}{\partial \varphi} \mathcal{M} d\varphi \tag{7}$$

because $\mathcal{M}$ is a constant. Substituting (6) back into (7),

$$\begin{aligned} \int_{\delta A} s(\mathbf{x},t) d\mathbf{A} &= \int \int_{\delta A} \frac{\partial S}{\partial \varphi} \frac{\rho_n}{N} d\mathbf{A}\, d\varphi = \int_{\delta A} \frac{\rho_n}{N} \int \frac{\partial S}{\partial \varphi} d\varphi\, d\mathbf{A} \\ &= \int_{\delta A} S(\mathbf{x},t) \frac{\rho_n(\mathbf{x})}{N(\mathbf{x})} d\mathbf{A} \end{aligned} \tag{8}$$

$$\iff s(\mathbf{x},t) = \frac{S(\mathbf{x},t)}{N(\mathbf{x},t)} \rho_n(\mathbf{x},t). \tag{9}$$

Similarly, for the transmissible compartment (T) and trasmission-capable host population density ($\tau(\mathbf{x},t)$),

$$T(\mathbf{x},t) = \int_{\delta A} \tau(\mathbf{x},t) d\mathbf{A} \iff \tau(\mathbf{x},t) = \frac{T(\mathbf{x},t)}{N(\mathbf{x})} \rho_n(\mathbf{x}). \tag{10}$$

Define sufficient contact between two individuals as sufficient proximity, and duration of that proximity, to allow pathogens to be transmitted from host to potential host within that period. An interaction is necessarily spatial and of sufficient contact.

The position vector will be omitted because only one community is considered further. Let the probability density function, $P(t)$, of an interaction at t be proportional to the product of the transmission-capable host density and the potential host density as for the law of mass action [104]. Then

$$P(t) = \eta\mu\kappa(\mathbf{x})\, s(t)\tau(t) \tag{11}$$

where η is an infectious disease-specific variable that reflects avidity (cumulative binding strength), μ is a function of mode of transmission (aerosol spread has a higher μ than droplet spread) and $\kappa(\mathbf{x})$ is a function of social behaviour (higher for a culture that greets by kissing compared to bowing). By definition,

$$0 \leq \int_{\Delta t} P(t)dt \leq 1.$$

An example of increased η resulting in higher probability of transmission has been demonstrated for the α and β variants of SARS-CoV2 in reference [105]. In coronavirus disease 2019 (COVID19), it is necessary that the SARS-CoV2 spike protein binds to the luminal angiotensin converting enzyme 2 (ACE2) receptor for transmission. The authors propose that the increased transmissibility of the α and β variants may be due to increased spike protein density, increased furin cleavage accessibility or increased spike protein-ACE2 receptor binding affinity. Affinity is the binding strength of one spike protein-ACE2 receptor combination. Avidity is the cumulative binding effect. In this case, avidity would be a function of the spike protein density, affinity and the concentration of virus particles. The authors demonstrate that the greater affinity of the α and β variants are consistent with the increased transmissibility (probability of transmission) of these variants.

The 4 recognised respiratory virus modes of transmission are direct contact, indirect contact (fomite), droplet and aerosol [106]. Although the distinction between droplet and aerosol spread is recognised, a consensus metric for distinguishing between them does not exist. In principle droplets are larger, heavier and travel a shorter distance. Aerosols form a suspension in the air and are displaced, dispersed and diluted by ventilation and convection currents [107]. Influenza is an airborne disease (droplet and aerosol). Nguyen-Van-Tam *et al* expose a control group and an intervention group to influenza. Droplet- and direct contact spread are negated in the intervention group. They demonstrate that, for influenza, droplet- and direct contact spread make negligible contributions to disease propogation. This and a proof of concept study were conducted in closed rooms. The infection rate (secondary attack rate) between this study and the proof of concept study differed significantly. The difference is ascribed to the ventilation rate of 4L/s per person confined to the rooms of the main study diluting the aerosol [108]. Given that both aerosol and droplet spread occur in influenza, they have demonstrated (at least for influenza and barring an additional mode of spread) that aerosol spread has a higher transmission probability than droplet spread. This is the effect of μ in (11).

It is assumed that cultures are location specific. $\kappa(\mathbf{x})$ can be interpreted as culture-specific, short-term, socially-acceptable, casual proximity – to distinguish it from population density. Casual contact is the collection of interaction types that exclude the intimate interactions typically occurring within families. For example, an acceptable distance from a stranger in Hong Kong is $\gtrapprox 1,1$m while in the USA this distance is $\lessapprox$ 1m [109]. Hong Kong has a much higher population density at 6677 per km^2 compared to the USA at 34 per km^2. Despite this difference in population density, $\mathcal{R}_0$ for 2009 influenza epidemic is consistently higher for the USA [110]. The difference in culturally acceptable personal space may explain part of the anomaly.

In a population of size N, the possible unique interactions are the sum of an arithmetic series $\left(\frac{N(N-1)}{2}\right)$. For $N \gg 1$, this approximates to $\frac{N^2}{2}$. Each interaction represents a transmission opportunity. Then the maximum transmission opportunities $\big(\psi(N)\big)$ approximate as

$$\psi(N) \lessapprox \frac{N^2}{2}. \tag{12}$$

The maximum possible direct secondary transmissions due to a single host is $N-1$ but this is limited by $\Delta\overline{\tau}$. Similarly, the maximum possible secondary transmissions over $\Delta\overline{\tau}$ are

$$\psi(N)\int_{\Delta\overline{\tau}} P(t)dt \lessapprox \frac{N^2}{2}\int_{\Delta\overline{\tau}} P(t)dt. \tag{13}$$

Substituting (9), (10) and (11) into (13), the transmissions produced over a primary host's $\Delta\overline{\tau}$ are

$$\begin{aligned}\int_{t_0}^{t_0+\Delta\overline{\tau}} \dot{T}(t_0)dt &= \int_{t_0}^{t_0+\Delta\overline{\tau}} \eta\mu\kappa\frac{N^2}{2}s(t_0)\tau(t_0)dt \\ &= \int_{t_0}^{t_0+\Delta\overline{\tau}} \frac{\eta\mu\kappa}{2}\rho_n^2 S(t_0)T(t_0)dt \\ &= \int_{t_0}^{t_0+\Delta\overline{\tau}} \beta_A\rho_n^2 S(t_0)T(t_0)dt\end{aligned} \tag{14}$$

where $\beta_A = \frac{1}{2}\eta\mu\kappa$.

For interval $\Delta t > \Delta\overline{\tau}$, the Heaviside step function is used and emphasises the discrete underlying processes. The equivalent of (14) over this Δt is

$$\int_{\Delta t} \dot{T}(t_0)\,dt = \int_{\Delta t} \left[u(t_0) - u(t_0+\Delta\overline{\tau})\right]\,\beta_A\rho_n^2\;S(t_0)\,T(t_0)\,dt. \tag{15}$$

Thus (14) is formulated over interval $\Delta\overline{\tau}$ or an arbitrary period $\Delta t > \Delta\overline{\tau}$ (15).

As for the SIR model, the rate at which individuals leave S is the same as the rate at which they enter T. Restated, $\dot{S}(t) = -\dot{T}(t)$. Then from (14)

$$\dot{S}(t) = -\beta_A \rho_n^2 S(t) T(t). \tag{16}$$

For an interval greater than $\Delta\overline{\tau}$ (15), the Heaviside version of (14), is required.

Redefine the removed compartment as consisting of hosts no longer transmission capable by virtue of recovery, death, behavioural adaptation or technological intervention. An individual is infected at t_0. That host remains transmission-capable for $\Delta\overline{\tau}$. Thus the rate at which hosts enter R is the same as the rate at which they entered T one $\Delta\overline{\tau}$ ago [20]. Restated,

$$\dot{R}(t) = \dot{T}(t - \Delta\overline{\tau}). \tag{17}$$

The SIR model proposes that $\dot{I}(t)$ is the difference between S's rate of decrease and R's rate of increase. Similarly, substituting (16) and (17) to determine $\dot{T}(t)$, the system of DDEs describing the movement between compartments S, T and R are

$$\begin{aligned} \dot{S}(t) &= -\beta_A \rho_n^2(\mathbf{x})\; S(t)\, T(t) \\ \dot{T}(t) &= \beta_A \rho_n^2(\mathbf{x})\; S(t)\, T(t) - \dot{T}(t - \Delta\overline{\tau}) \\ \dot{R}(t) &= \dot{T}(t - \Delta\overline{\tau}). \end{aligned} \tag{18}$$

Model (18) is the boundaried DDE version of Model (1) and is designated the susceptible-transmissible-removed (STR) model. The derivation of this model on a surface has incorporated population density.

Assume that the homogenous solution to $T(\mathbf{x}, t)$ is exponential such that

$$T(\mathbf{x}, t) = A(\mathbf{x}) e^{r(\mathbf{x})t}. \tag{19}$$

Equation (19) is the real, homogenous solution to the linearised STR (18) [111](See Appendix). Substituting (19) into the delay term of Model (18)'s T,

$$\frac{\partial}{\partial t} T(\mathbf{x}, t - \Delta\overline{\tau}) = A(\mathbf{x}) r(\mathbf{x}) e^{-r(\mathbf{x})\Delta\overline{\tau}} e^{r(\mathbf{x})t} = \alpha T(\mathbf{x}, t) \tag{20}$$

where

$$\alpha(\mathbf{x}, t) = {}_{\tau}\alpha\, u(\Delta\overline{\tau}) \tag{21}$$

and ${}_{\tau}\alpha(\mathbf{x}) = r(\mathbf{x}) e^{-r(\mathbf{x})\Delta\overline{\tau}}$. The subscript τ is for transmissible. Substituting (20) into Model (18), reduces the latter to an ODE-like model,

$$\begin{aligned} \dot{S}(t) &= -\beta_A \rho_n^2(\mathbf{x})\; S(t)\, T(t) \\ \dot{T}(t) &= \beta_A \rho_n^2(\mathbf{x})\; S(t)\, T(t) - \alpha(\mathbf{x})\, T(t) \\ \dot{R}(t) &= \alpha(\mathbf{x})\, T(t). \end{aligned} \tag{22}$$

Comparing Models (22) and (1), the horizontal transmission incidence [101] is

$$\xi(\mathbf{x}) = \beta_A \rho_n^2(\mathbf{x})\, N(\mathbf{x}). \tag{23}$$

Applying the definition of $\mathcal{R}_0$ for the SIR model from Section 1's (3) [20], STR Model (22)'s basic reproduction number is

$$ {}_{\tau}\mathcal{R}_0(\mathbf{x}) = \frac{\xi(\mathbf{x})}{\alpha(\mathbf{x}, t \geq \Delta\overline{\tau})} \tag{24} $$

and undefined for $t < \Delta\overline{\tau}$.

ξ's derivation for Models (18) and (22) differs from Brauer *et al*'s [20] mass action ξ derivation. Brauer *et al* assume that a host has βN transmission-capable interaction per unit time. They then multiply this by the chance that such an interaction is with a susceptible individual $\left(\frac{S}{N}\right)$. This product is $\dot{S}(t)$. Consequently, $\xi = \beta N$ for mass action incidence. Thus only the potential direct secondary transmissions are considered. In contrast, (14)'s ξ calculates the average transmissions over all potential interactions on N over $\Delta\overline{\tau}$. This includes indirect secondary transmissions. Thus, in principle,

$$ \mathcal{R}_0 \leq {}_{\tau}\mathcal{R}_0. $$

Comparing the STR's ${}_{\tau}\mathcal{R}_0$ to $\mathcal{R}_0$ for mass action incidence ($\xi = \beta N$) and the standard incidence ($\xi = \beta_{si}$),

$$ \frac{\beta_A \rho_n^2(\mathbf{x}) N(\mathbf{x})}{\alpha(t > \Delta\overline{\tau})} = {}_{\tau}\mathcal{R}_0(\mathbf{x}) \geq \mathcal{R}_0 = \frac{\beta N}{\alpha} \text{ or } \frac{\beta_{is}}{\alpha}. \tag{25} $$

3 Biological derivation of a continuous basic reproduction number

A transmissible timescale is derived that converts the STR model (18) into an ODE model. A rhythmic timescale is then defined and mass action-, standard- and hybrid incidence derived in the rhythmic timescale.

3.1 Defining the transmissible timescale

STR Model (18)'s coefficients are derived, in part, from (14). Equation (14)'s Heaviside version (15) emphasises the finite transmissible period.

For timescale $1 : \Delta t < 1 : \Delta\overline{\tau}$, (15) should be used to derive a Heaviside version of (16). Thus timescale $1 : \Delta t < 1 : \Delta\overline{\tau}$ introduces a step function (15) in the STR Model (18)'s ξ. Conversely, $1 : \Delta t > 1 : \Delta\overline{\tau}$ introduces a step function in ODE-like Model (22)'s α.

Thus timescale

$$ 1 : \Delta t = 1 : \Delta\overline{\tau}. $$

transforms (22) into an ODE model similar to Model (1). This $\Delta\overline{\tau}$-based timescale is the transmissible timescale. ${}_{\tau}\alpha$ and ${}_{\tau}\mathcal{R}_0$ are then the transmissible timescale infection frequency and basic reproduction number, respectively.

3.2 Defining the rhythmic timescale

Consider a host infected by chickenpox (Varicella Zoster). The host becomes infectious after 14 days. There is an additional 2-3 days (the prodrome) before the vesicular rash appears, the diagnosis is obvious and the host is isolated.

This host's routine may include sleeping from 10 PM to 6 AM, public transport between 7:30 and 8AM, and from 5:30 to 6PM; classroom from 8AM to 5PM; a cafeteria at 1PM; and family time from 6PM to 10PM. Comparing this routine with (11), a diurnal variation exists to the probability of a successful interaction. Selecting a timescale of $1:1$ day masks this variation. Restated,

$$\int_{t_0+k\Delta t}^{t_0+(k+1)\Delta t} P(t)dt = p_{daily} \qquad \forall\ \Delta t = 1\,\text{day}, k \in \mathbb{N}$$

Similarly, weekly, monthly and annual activities are periodic. Thus multiple timescales may exist that result in constant integrals of (11) over a time unit in that timescale.

A rhythmic timescale

$$1 : \Delta t = 1 : \delta t$$

is defined for periodic host transmission opportunity. Assuming a periodic transmission opportunity, $\exists\ \delta t \in \mathbb{R}$ such that $\forall\, t_0 \in \mathbb{R}$

$$p = \int_{t_0}^{t_0+\delta t} P(t)dt = \int_{\delta t} P(t)dt. \tag{26}$$

The constant, p, represents the probability of an event on $\psi(N)$ over δt. Successful interactions are then independent events with probability p on $\psi(N)$.

3.3 The rhythmic timescale mass action-, standard- and hybrid incidence $\mathcal{R}_0$

Let the time increments in the transmissible timescale be an integer multiple of the increments in the rhythmic timescale. Then

$$\Delta\overline{\tau} \approx \mathfrak{B}\delta t \qquad \text{where} \qquad \mathfrak{B} \in \mathbb{N}. \tag{27}$$

$\mathfrak{B}$ is necessary to transform between the transmissible- and rhythmic timescales.

3.3.1 Mass action incidence, basic reproduction number in rhythmic timescale

The mass action incidence formulation assumes that all host interactions are random and that $S \approx N$ for several δt early in the epidemic. By definition, ${}_{\tau}\mathcal{R}_0$ is the number of secondary hosts produced by a primary host over $\Delta\overline{\tau}$.

At $t = t_0$ the only host is the primary host and the number of secondary hosts over $\Delta\overline{\tau}$ are necessarily ${}_{\tau}\mathcal{R}_0$. This can be restated as

$$ {}_{\tau}\mathcal{R}_0 = \int_{\Delta t = \Delta\overline{\tau}} \dot{T}(t_0)dt. \tag{28} $$

At the equivalent $t = \Delta\overline{\tau}$ in any timescale, (28) is true. From (2), in 1 time unit of the transmissible timescale,

$$ \xi(t_0) = \frac{{}_{\tau}\mathcal{R}_0}{N \times 1}. $$

From (26) the primary host will infect $pS \approx pN$ individuals over δt. Applying (2), over 1 time unit of the rhythmic timescale,

$$ {}_{\varrho}\xi(t_0) = \frac{pN}{N \times 1} $$

where ${}_{\varrho}\xi(t_0)$ is the rhythmic timescale ξ at t_0. Because mass action incidence assumes $S \approx N$ for several δt, there are $\mathfrak{B}pN$ transmissions over $\mathfrak{B}\delta t = \Delta\overline{\tau}$. From (28), $\mathfrak{B}pN = {}_{\tau}\mathcal{R}_0$. Therefore, after $\mathfrak{B}$ time units in the rhythmic timescale,

$$ \begin{aligned} \int_{t_0}^{t_0+\mathfrak{B}} {}_{\varrho}\xi(t)dt = \sum_{\mathfrak{B}} \frac{pN}{N \times 1} = \frac{\mathfrak{B}pN}{N} &= \mathfrak{B}\ {}_{\varrho}\xi(t_0) \\ &= \frac{{}_{\tau}\mathcal{R}_0}{N} \quad = \quad \xi(t_0). \end{aligned} $$

Therefore, the rhythmic timescale ξ is the arithmetic mean of the transmissible timescale ξ. Restated

$$ {}_{\varrho}\xi(t_0) = \frac{\xi(t_0)}{\mathfrak{B}}. \tag{29} $$

From (21), for $0 < t < \Delta\overline{\tau}$, $\alpha = 0$ and, consequently, ${}_{\varrho}\mathcal{R}_0$ is undefined. ${}_{\tau}\mathcal{R}_0$ is the number of secondary hosts originating over the primary host's $\Delta\overline{\tau}$ in a completely susceptible population. Therefore either $\mathcal{R}_0$ is timescale invariant or $\mathcal{R}_0 \geq 1$ or $\mathcal{R}_0 < 1$ (4) should be timescale invariant.

Define a non-zero rhythmic timescale α as

$$ {}_{\varrho}\alpha \coloneqq \frac{{}_{\tau}\alpha}{\mathfrak{B}}. \tag{30} $$

Then, from (3), one can use (29) and (30) to derive a rhythmic timescale $\mathcal{R}_0$:

$$ {}_{\varrho}\mathcal{R}_0 = \frac{{}_{\varrho}\xi(t_0)}{{}_{\varrho}\alpha} = \frac{\xi(t_0)}{{}_{\tau}\alpha} = {}_{\tau}\mathcal{R}_0 $$

that preserves $\mathcal{R}_0$ and the property $\mathcal{R}_0 \geq 1$ or $\mathcal{R}_0 < 1$. The resultant mass action incidence, STR model in the rhythmic timescale is then

$$\begin{aligned}\dot{S}(t) &= -\frac{\beta}{\mathfrak{B}}\, S(t)\, T(t)\\ \dot{T}(t) &= \frac{\beta}{\mathfrak{B}}\, S(t)\, T(t) - \frac{\tau\alpha}{\mathfrak{B}}\, T(t)\\ \dot{R}(t) &= \frac{\tau\alpha}{\mathfrak{B}}\, T(t).\end{aligned}$$

3.3.2 Standard incidence basic reproduction number in the rhythmic timescale

Hethcote's standard incidence assumes that interactions are non-random. One only interacts with close contacts, $N_c \ll N$ [101]. Anderson and May [19,102, 103] provide experimental evidence to support the argument.

From Section 3.2 and (26), the new transmisions over δt occur with probability p. Transmission occurring in subsequent δt are independent events. Early in the epidemic, the new entrants to T equate to $\dot{T}(t)$. Table 1 provides the

$\jmath : \jmath \in \mathbb{Z}$, $\jmath \leq \mathfrak{B}$	New $T = \dot{T}$	Cumulative T	S	N
< 0	0	0	N_c	N_c
0	1	1	N_c	$N_c + 1$
1	$N_c p$	$N_c p + 1$	$N_c(1-p)$	$N_c + 1$
2	$N_c(1-p)p$	$N_c p[(1-p)^0 + (1-p)^1] + 1$	$N_c(1-p)^2$	$N_c + 1$
3	$N_c(1-p)^2 p$	$N_c p \frac{1-(1-p)^3}{1-(1-p)} + 1$	$N_c(1-p)^3$	$N_c + 1$
$\jmath$	$N_c p(1-p)^{\jmath-1}$	$N_c p \frac{1-(1-p)^\jmath}{p} + 1$	$N_c(1-p)^\jmath$	$N_c + 1$

Table 1 Changes in the SI compartments per δt in the standard incidence model

compartment sizes, at δt intervals, before primary host removal ($\jmath \delta t \leq \Delta\overline{\tau}$).

From (2) and the definition of incidence,

$$\xi(t \approx t_0) = -\frac{\dot{S}(t)}{S(t)} = \frac{\dot{T}(t \approx t_0)}{S(t \approx t_0)}. \tag{31}$$

Substituting terms from Table 1 into (31), without loss of generality,

$$\xi(t \approx t_0) = -\frac{\dot{S}(t)}{S(t)} = \chi \qquad \text{where } \chi = p \text{ or } \frac{p}{1-p} \qquad \Longleftrightarrow\ S(t) = S_0 e^{-\chi t}.$$

In the rhythmic timescale ($1 : \delta t$), over one time unit,

$$_\varrho\xi = \frac{S_0 e^{-\chi} - S_0}{S_0 \times 1} \iff e^{-\chi} = {}_\varrho\xi + 1. \tag{32}$$

After $\mathfrak{B}$ time units in this rhythmic timescale, $S(t)$ is $S_0 e^{-\chi \mathfrak{B}}$. $\mathfrak{B}$ time units in the rhythmic timescale is only one time unit in the transmissible timescale. Substituting (32) at t_0 over $\Delta\overline{\tau}$ into the discrete version of (2),

$$ {}_{\tau}\xi = \frac{S_0 e^{-\chi \mathfrak{B}} - S_0}{S_0 \times 1} = ({}_{\varrho}\xi + 1)^{\mathfrak{B}} - 1 \iff \sqrt[\mathfrak{B}]{{}_{\tau}\xi + 1} = {}_{\varrho}\xi + 1. $$

Performing the binomial expansion,

$$ \sum_{k=0}^{\mathfrak{B}} \binom{\mathfrak{B}}{k} {}_{\varrho}\xi^k = {}_{\tau}\xi + 1 \iff {}_{\tau}\xi = \sum_{k=1}^{\mathfrak{B}} \binom{\mathfrak{B}}{k} {}_{\varrho}\xi^k. $$

For ${}_{\varrho}\xi \gg 1$ and ${}_{\tau}\xi \gg 1$,

$$ {}_{\varrho}\xi \lessapprox \sqrt[\mathfrak{B}]{{}_{\tau}\xi}. \tag{33} $$

As for the transmissible timescale mass action incidence in Section 3.3.1, from (21), $\alpha = 0$ in the rhythmic timescale. Consequently, $\mathcal{R}_0$ is undefined. Define

$$ {}_{\tau}\alpha \coloneqq \sum_{k=1}^{\mathfrak{B}} \binom{\mathfrak{B}}{k} {}_{\varrho}\alpha^k \Longrightarrow {}_{\varrho}\alpha \lessapprox \sqrt[\mathfrak{B}]{{}_{\tau}\alpha} = \sqrt[\frac{\Delta t}{\delta t}]{\alpha(t > \Delta\overline{\tau})} \quad 0 \leq t < \Delta\overline{\tau} \tag{34} $$

for ${}_{\varrho}\alpha \gg 1$ and ${}_{\tau}\alpha \gg 1$. Substituting (33) and (34) into (3),

$$ {}_{\varrho}\mathcal{R}_0 \lessapprox \sqrt[\mathfrak{B}]{\frac{{}_{\tau}\xi}{{}_{\tau}\alpha}} = \sqrt[\mathfrak{B}]{{}_{\tau}\mathcal{R}_0} \tag{35} $$

and the property of $\mathcal{R}_0 < 1$ or > 1 (4) is preserved across timescales.

The standard incidence, STR in the rhythmic timescale is approximately

$$ \begin{aligned} \dot{S}(t) &= -\sqrt[\mathfrak{B}]{\beta_{si}}\, \frac{S(t)\, T(t)}{N(\mathbf{x})} \\ \dot{T}(t) &= \sqrt[\mathfrak{B}]{\beta_{si}}\, \frac{S(t)\, T(t)}{N(\mathbf{x})} - \sqrt[\mathfrak{B}]{{}_{\tau}\alpha}\, T(t) \\ \dot{R}(t) &= \sqrt[\mathfrak{B}]{{}_{\tau}\alpha}\, I(t). \end{aligned} $$

3.3.3 Hybrid incidence basic reproduction number in the rhythmic timescale

Section 2 derives an N-dependent ξ (23). Substituting (23) into (33),

$$ {}_{\varrho}\xi = \sqrt[\mathfrak{B}]{\beta_A \rho_n^2 N} \tag{36} $$

ensures the geometric decrease in S. As in (34),

$$ {}_{\varrho}\alpha \coloneqq \frac{1}{\mathfrak{B}}\, \sqrt[\mathfrak{B}]{{}_{\tau}\alpha}. $$

From (35) and (25), the property $\mathcal{R}_0 < 1$ or $\mathcal{R}_0 > 1$ (4) is preserved by

$$ {}_{\varrho}\mathcal{R}_0(\mathbf{x}) \approx \sqrt[\mathfrak{B}]{{}_{\tau}\mathcal{R}_0} \geq \sqrt[\mathfrak{B}]{\mathcal{R}_0}. \tag{37} $$

The hybrid incidence, STR in the rhythmic timescale is then approximately

$$\begin{aligned}\dot{S}(t) &= -\sqrt[\mathfrak{B}]{\beta_A \rho_n^2 N}\,\frac{S(t)\,T(t)}{N(\mathbf{x})}\\ \dot{T}(t) &= \sqrt[\mathfrak{B}]{\beta_A \rho_n^2 N}\,\frac{S(t)\,T(t)}{N(\mathbf{x})} - \sqrt[\mathfrak{B}]{\tau\alpha}\,I(t)\\ \dot{R}(t) &= \sqrt[\mathfrak{B}]{\tau\alpha}\,I(t).\end{aligned}$$

4 Hybrid incidence, STR validation in the 1 : 1 day timescale

The HI-STR's predicted relationship between ${}_{\varrho}\mathcal{R}_0$ and ρ_n is demonstrated for a droplet spread, an aerosol spread and a non-airborne disease. Published central measures (mode, median or mean) will represent ${}_{\varrho}\mathcal{R}_0$ ranges.

4.1 SARS (SARS-CoV)

Severe acute respiratory syndrome (SARS) was caused by SARS Coronavirus (SARS-CoV) in the Far East Asia in 2002 [112,113]. Transmission was primarily droplet spread [113]. 22% may have required hospitalisation [114]. Symptom onset marked infectiousness [115]. The incubation mode was 4 days [116,117]. Symptom onset to self-isolation is unknown. Symptom onset to hospitalisation mode was 0.5 to 2.5 days [117,118]. This is summarised in Table 2. The

Group	Group proportion(%)	Incubation mode (days)	Time to removal mode (days)
hospitalised	22	4	1.5
non-hospitalised	78	4	N/A

Table 2 Transmission dynamics for SARS – removal refers to removal from society

unknown non-hospitalised $\Delta\overline{\tau}$ is assumed the same as for the hospitalised. $\Delta\overline{\tau} = 1.5$ days [118]. $\delta t = 1$ day. Substituting the resultant $\mathfrak{B} = 1.5$ into (37).

$$\begin{aligned}{}_{\varrho}\mathcal{R}_0 = \sqrt[\mathfrak{B}]{\tau\mathcal{R}_0} &= \sqrt[\mathfrak{B}]{\frac{\beta_A \rho_n^2 N}{\alpha(t > \Delta\overline{\tau})}} = \sqrt[\mathfrak{B}]{\frac{\beta_A N}{\tau\alpha}} \times \rho_n^{\frac{2.0}{1.5}}\\ \iff \qquad \ln({}_{\varrho}\mathcal{R}_0) &= \ln(\Gamma) + 1.3\ln(\rho_n) \qquad (38)\end{aligned}$$

(where $\Gamma = \sqrt[\mathfrak{B}]{\beta_A N/\tau\alpha}$). SARS' ${}_{\varrho}\mathcal{R}_0$'s theoretical dependence on ρ_n is (38).

Toronto and 4 Asian cities' experimental ${}_{\varrho}\mathcal{R}_0$ [120, 124, 126] and ρ_n [119, 121–123, 125] are presented in Table 3. The natural logarithms are plotted in Figure 1. The experimental gradient of 1.35 should be compared with (38).

The SARS-CoV validation uses retrospective ${}_{\varrho}\mathcal{R}_0$ on a cross-section of (mostly Asian) cities during the course of one droplet-spread epidemic.

City	Population density (ρ_n)	Median ${}_{\varrho}\mathcal{R}_0$	Year
Toronto	4334 [119]	0.58 [120]	2003
Hong Kong	6300 [121]	1.1 [120]	2003
Singapore	6186 [122]	1.17 [120]	2003
Hanoi	1926 [123]	0.2 [124]	2003
Taipei	9461 [125]	1.54 [126]	2003

Table 3 2002/2003 SARS epidemic's population density and basic reproduction number

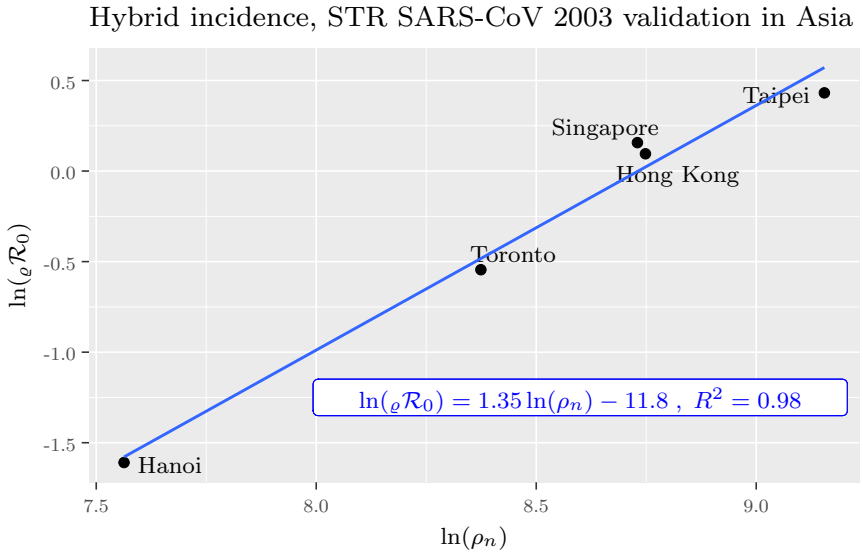

Fig. 1 Experimental depiction of the predicted linear $\ln({}_{\varrho}\mathcal{R}_0)$ to $\ln(\rho_n)$ relationship

4.2 Measles (Rubeola)

Measles incubates for 10-12 days [116]. The prodrome of non-specific [127], but debilitating, symptoms heralds the infectious [128] period. The pathognomic morbiliform rash ends the 2-4 day prodrome.

Conjecturing isolation at day 3 of the prodrome, $\Delta\overline{\tau}$ is 3 days; $\delta t = 1$ day and $\mathfrak{B} = 3$. Substituting the latter into (37), for measles:

$$\ln({}_{\varrho}\mathcal{R}_0) = \ln(\Gamma) + 0.66\ln(\rho_n). \tag{39}$$

Table 4 documents the experimental ${}_{\varrho}\mathcal{R}_0$ for 5 countries at 8 historical periods [130]. Figure 2 demonstrates the linear relationship predicted by (39).

Several experimental ${}_{\varrho}\mathcal{R}_0$ methods across multiple, historical, European measles epidemics have validated the STR for aerosol-spread infections. The

Country	Population density (ρ_n) [129]	Middle ${}_{\varrho}\mathcal{R}_0$ [130]	Year
Germany	70 [131]	9	1861
Italy	110 [132]	13	1901
Denmark	65 [133]	6	1911
Denmark	101 [133]	16	1948
Netherlands	443 [134]	23	1990
Luxembourg	161 [135]	7	1996
Germany	236 [136]	30	2006

Table 4 Population density and historical measles ${}_{p}\mathcal{R}_0$ for Measles in Europe

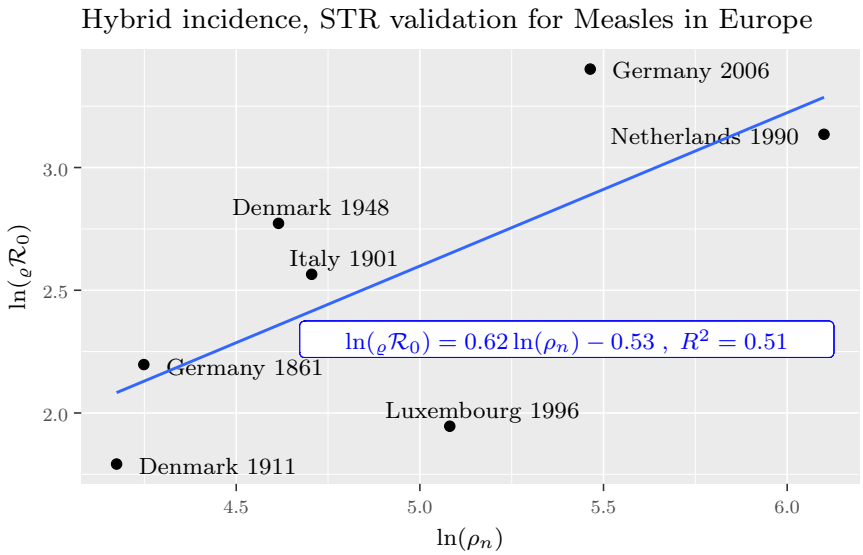

Fig. 2 Predicted linear relationship between $\ln({}_{\varrho}\mathcal{R}_0)$ and $\ln(\rho_n)$for measles in Europe

increased R^2 is likely due to the several methods used by several investigators to calculate $\mathcal{R}_0$ for measles. The STR model applies to isolated communities. Although regions within countries may be treated as sufficiently isolated, it may be that countries are insufficiently isolated in Europe.

4.3 Ebola (EBOV)

Ebola disease is caused by 1 of 7 Ebola virus species in the genus *Ebolavirus* of the family *filoviridae* [137–139]. Ebola disease has a high CFR [140–143] and is not airborne. Bodily fluid transmission is by blood, urine, faeces, vomit, breast milk, saliva and sexual contact [139].

Ebola virus disease is the ebola disease caused by the Zaire species (EVOD). CFR is 43-89% [139–141] and δt is 1 day. The infected are categorised as

– asymptomatic,
– symptomatic and quarantined (hospital or an ebola treatment unit) [139],
– symptomatic and isolated at home [138, 141].

The median incubation period– 6-12 days [137–139, 141–145].

Country	Population density (ρ_n) [146]	${}_{\varrho}\mathcal{R}_0$	Year
Uganda	118	2.7 [147]	2000
Guinea	45	1.51 [142]	2014
Sierra Leone	97	2.53 [142]	2014
Liberia	33	1.59 [142]	2014

Table 5 Population density and Ebola ${}_{\varrho}\mathcal{R}_0$ for African countries

Kerkhove *et al*'s median time from symptom onset to hospitalisation is 4 days [145]. Hospitalisation has been demonstrated to reduce transmission [148].

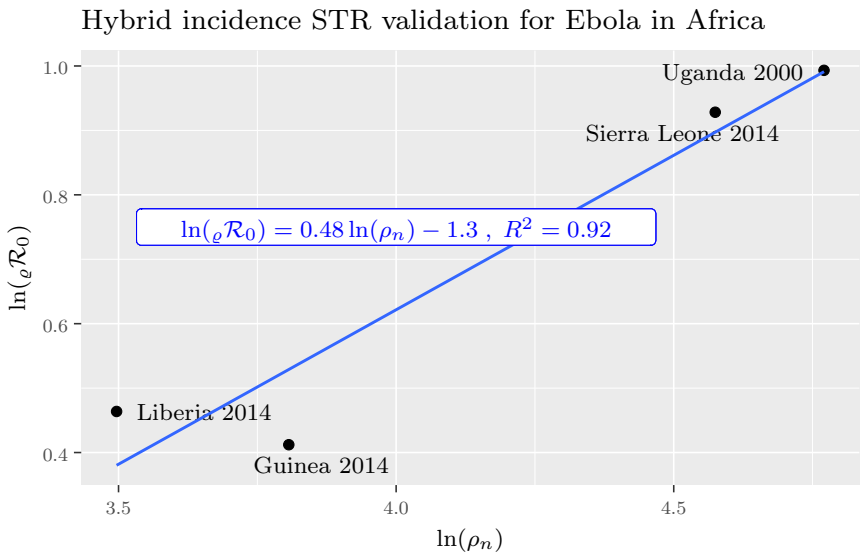

Fig. 3 Experimental linear relationship between $\ln({}_{\varrho}\mathcal{R}_0)$ and $\ln(\rho_n)$ for Ebola in Africa

The end of $\Delta\overline{\tau}$ is the weighted average of the time to hospitalisation and the time to isolation. These periods are assumed the same. The median time

to hospitalisation is $\Delta\overline{\tau} = 4$ days [145]. Substituting δt and $\Delta\overline{\tau}$ into (37),

$$\ln({}_{\varrho}\mathcal{R}_0) = \ln(\Gamma) + 0.50\ln(\rho_n). \tag{40}$$

The Democratic Republic of Congo (DRC) outbreak in 1995 differs from the 2000 Uganda outbreak and the 2014 outbreak [147,149]. Chowell [149] shows a shortened infectious period and Legrand [147] demonstrates more transmission at funerals in the DRC. The DRC outbreak is omitted. Table 5 summarises ${}_{\varrho}\mathcal{R}_0$ for Guinea, Sierra Leone, Liberia [142] and Uganda [147] . Equation (40)'s predicted linear relationship is demonstrated experimentally in Figure 3.

The non-airborne Ebola validation has been performed using retrospective ${}_{\varrho}\mathcal{R}_0$ data for multiple African countries.

5 Discussion

The transmissible timescale is based on the period that a host is able to transmit disease. This period ends with either host demise, recovery, behavioural modification or technological intervention.

The rhythmic timescale is a consequence of the host's cyclical transmission opportunity. The sleep-wake cycle is the origin of the periodic transmission opportunity of the childhood infectious diseases. For childhood infectious diseases the diurnal periodicity corresponds to the period of experimental data collection.

Hybrid incidence (HI) lies between the extremum of completely random interactions (mass action incidence) and completely non-random interactions (standard incidence). The geometric mean converts the basic reproduction number, infection frequency and horizontal transmission incidence between the transmissible- and rhythmic timescales under special circumstances.

The HI-STR model can predict the basic reproduction number for sufficiently isolated communities. The prediction is based on transmission dynamics, population-size and -density. It reduces to an ODE model in the transmissible timescale. The resultant localised basic reproductive numbers facilitate differentiated control measures and resource allocation. The isolated community idealisation has imposed a significant constraint on the discretisation of a surface. Experiential construction of isolated communities is necessary until an objective measure of sufficient isolation is derived.

The geographical constraints of the SIR model were not obvious. The HI-STR has established that the SIR model applies to sufficiently isolated populations. The HI-STR model effectively recognises a pandemic as a collection of epidemics of the same kind at multiple locations and stages of temporal propagation.

6 Conclusion

A boundaried, DDE SIR-like model – the susceptible-transmissible-removed (STR) model – is constructed. The hybrid incidence (HI) STR model in the rhythmic timescale predicts the basic reproduction number ($\mathcal{R}_0$)'s dependence on population density. The model has been validated for multiple transmission modes where one host-vector predominates. The HI-STR allows *a priori* determination of localised $\mathcal{R}_0$s by adjusting for local population-size and -density. This permits localised mitigation strategies, resource allocation and temporal resource redistribution. Cultural similarity is required to transfer adjusted $\mathcal{R}_0$s.

For models simulating only one host type transmitting a disease, the transmissible timescale masks the HI-STR model's delays. The geometric mean converts the horizontal transmission incidence and infection frequency between the transmissible- and rhythmic timescales.

7 Recommendation

The HI-STR allows geographical risk stratification based on population-size and -density. The impact is not obvious. It is conceivable that a high $\mathfrak{B}$ diminishes the significance of geographical stratification.

The isolated community idealisation simplifies the reduction of the HI-STR model to an ODE model. The resultant ODEs prohibit the modelling of spatial spread. A surface STR model with partial differential equations will simplify surface discretisation, simulate population mobility and predict a pandemic's wave-like spatial propagation.

The model has been validated for infectious diseases with a diurnal variation in transmission opportunity. The sexually transmitted diseases' (STDs') cyclical transmission opportunities have a low frequency. The STDs thus provide an opportunity to validate the model in (non-diurnal) timescales that mask their longer transmission opportunity period.

Appendix: Solution for linearised STR model

A real solution to the linearised STR model is derived. Smith [111] and Diekman *et al* [150] provide comprehensive coverage.

Consider the system of DDEs (18). Early in the disease, one can make the approximation $N \approx S$ reducing the system to the linear DDE system

$$\begin{pmatrix} \dot{S} \\ \dot{T} \\ \dot{R} \end{pmatrix} = \begin{bmatrix} 0 & -\xi & 0 \\ 0 & \xi & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{pmatrix} S(t) \\ T(t) \\ R(t) \end{pmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & -1 & 0 \\ 0 & 1 & 0 \end{bmatrix} \begin{pmatrix} \dot{S}(t-\Delta\overline{\tau}) \\ \dot{T}(t-\Delta\overline{\tau}) \\ \dot{R}(t-\Delta\overline{\tau}) \end{pmatrix}$$

which (for $\mathbf{z} \in \mathbb{R}^3$) is of the form

$$\dot{\mathbf{z}} = A\mathbf{z}(t) + B\dot{\mathbf{z}}(t-\tau). \tag{41}$$

Refer to Kuang for analysis of this first order real scalar linear neutral delay equation [151]. Only the transmissible compartment is considered further. For

$$\dot{z}_2 = \xi z_2(t) - \dot{z}_2(t-\tau) \tag{42}$$

Let $z_2(t) = e^{\lambda t}$ where $\lambda \in \mathbb{C}$. Substituting this into (42),

$$\lambda e^{\lambda t} = \xi e^{\lambda t} - \lambda e^{\lambda(t-\tau)} = \xi e^{\lambda t} - \lambda e^{\lambda t} e^{-\lambda\tau} \iff e^{\lambda t}(\xi - \lambda - \lambda e^{-\lambda\tau}) = 0 \tag{43}$$

and the roots of the characteristic equation

$$\xi - \lambda(1 + e^{-\lambda\tau}) = 0$$

are the solutions to λ. Let the real part of λ be x and the imaginary part be y then on the complex plane,

$$\begin{aligned} \xi &= x + xe^{-x\tau}\cos(y\tau) - ye^{-x}\sin(y\tau) \\ 0 &= y + xe^{-x\tau}\sin(y\tau) + ye^{-x}\cos(y\tau) \\ \begin{pmatrix} \xi \\ 0 \end{pmatrix} &= \left[I + e^{-\tau x} R(\tau y) \right] \begin{pmatrix} x \\ y \end{pmatrix} \end{aligned} \tag{44}$$

where I is the identity matrix $\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$ and $R(\tau y) = \begin{bmatrix} \cos(\tau y) & -\sin(\tau y) \\ \sin(\tau y) & \cos(\tau y) \end{bmatrix}$ is the rotation matrix. Note that a positive real solutions exist. At $y = 0$, for $x > 0$. $0 < e^{-x} < 1$ and therefore $\frac{\xi}{2} < x < \xi$. Given that (biologically) $\xi > 0$, for $y = 0$, all the terms in $R(\tau y) > 0$ and $e^{-\tau x} > 0 \Rightarrow x \not\leq 0$.

Declaration

Funding Not applicable
Conflicts of interest/Competing interests Not applicable
Availability of data and material Not applicable
Code availability Not applicable
Ethics approval Not applicable

Acknowledgements I wish to thank my colleague Dr Steven Miller for his encouragement and my former supervisor, Professor Batmanathan Dayanand (Daya) Reddy for his advice.

References

1. Foppa IM. A Historical Introduction to Mathematical Modeling of Infectious Diseases. Foppa IM, editor. Boston: Academic Press; 2017.
2. Kermack WO, McKendrick AG. Contributions to the mathematical theory of epidemics–I. 1927. Bull Math Biol. 1991;53(1-2):33–55.
3. Kermack WO, McKendrick AG. Contributions to the mathematical theory of epidemics–II. The problem of endemicity.1932. Bull Math Biol. 1991;53(1-2):57–87.
4. Kermack WO, McKendrick AG. Contributions to the mathematical theory of epidemics–III. Further studies of the problem of endemicity. 1933. Bull Math Biol. 1991;53(1-2):89–118.
5. Kermack WO, McKendrick AG, Walker GT. A contribution to the mathematical theory of epidemics. Proceedings of the Royal Society of London Series A, Containing Papers of a Mathematical and Physical Character. 1927;115(772):700–721. Available from: https://royalsocietypublishing.org/doi/abs/10.1098/rspa.1927.0118.
6. Dietz K. The estimation of the basic reproduction number for infectious diseases. Statistical Methods in Medical Research. 1993;2(1):23–41. PMID: 8261248. Available from: https://doi.org/10.1177/096228029300200103.
7. Heesterbeek JAP. A Brief History of R0 and a Recipe for its Calculation. Acta Biotheoretica. 2002 Sep;50(3):189–204. Available from: https://doi.org/10.1023/A:1016599411804.
8. Dublin LI, Lotka AJ. On the True Rate of Natural Increase. Journal of the American Statistical Association. 1925 2020/09/20/;20(151):305–339. Full publication date: Sep., 1925. Available from: http://www.jstor.org/stable/2965517.
9. Lotka AJ. The measure of net fertility. Journal of the Washington Academy of Sciences. 1925;15(21):469–472. Available from: http://www.jstor.org/stable/24527482.
10. Perasso A. An Introduction to The Basic Reproduction Number in Mathematical Epidemiology. ESAIM: ProcS. 2018;62:123–138. Available from: https://doi.org/10.1051/proc/201862123.
11. Heesterbeek JAP, Dietz K. The concept of RO in epidemic theory. Statistica Neerlandica 50: 89-110. 1993 01;.
12. Hamer WH. The Milroy Lectures ON EPIDEMIC DISEASE IN ENGLAND—THE EVIDENCE OF VARIABILITY AND OF PERSISTENCY OF TYPE. The Lancet. 1906;167(4305):569 – 574. Originally published as Volume 1, Issue 4305. Available from: http://www.sciencedirect.com/science/article/pii/S0140673601801872.
13. Heesterbeek H. 5 - THE LAW OF MASS-ACTION IN EPIDEMIOLOGY: A HISTORICAL PERSPECTIVE. In: Cuddington K, Beisner BE, editors. Ecological Paradigms Lost. Theoretical Ecology Series. Burlington: Academic Press; 2005. p. 81–105. Available from: https://www.sciencedirect.com/science/article/pii/B9780120884599500078.
14. Waage P, Gulberg CM. Studies concerning affinity. Journal of Chemical Education. 1986 Dec;63(12):1044. Available from: https://doi.org/10.1021/ed063p1044.
15. Ross R, Hudson HP. An application of the theory of probabilities to the study of a priori pathometry.—Part III. Proceedings of the Royal Society of London Series A, Containing Papers of a Mathematical and Physical Character. 1917;93(650):225–240. Available from: https://royalsocietypublishing.org/doi/abs/10.1098/rspa.1917.0015.
16. En'ko PD. On the Course of Epidemics of Some Infectious Diseases. International Journal of Epidemiology. 1989 12;18(4):749–755. Available from: https://doi.org/10.1093/ije/18.4.749.
17. Dietz K. The first epidemic model: A historical note P.D. En'ko. Australian Journal of Statistics. 1988;30A(1):56–65. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1467-842X.1988.tb00464.x.
18. Harko T, Lobo FSN, Mak MK. Exact analytical solutions of the Susceptible-Infected-Recovered (SIR) epidemic model and of the SIR model with equal death and birth rates. Applied Mathematics and Computation. 2014;236:184 – 194. Available from: http://www.sciencedirect.com/science/article/pii/S009630031400383X.

19. Hethcote HW. The Mathematics of Infectious Diseases. SIAM Review. 2000;42(4):599–653. Available from: https://doi.org/10.1137/S0036144500371907.
20. Brauer F, Castillo-Chávez C, Feng Z. Mathematical Models in Epidemiology. Springer Netherlands; 2019.
21. Thompson RN, Hollingsworth TD, Isham V, Arribas-Bel D, Ashby B, Britton T, et al. Key questions for modelling COVID-19 exit strategies. Proceedings of the Royal Society B: Biological Sciences. 2020;287(1932):20201405. Available from: https://royalsocietypublishing.org/doi/abs/10.1098/rspb.2020.1405.
22. Tuite AR, Fisman DN. Number-needed-to-vaccinate calculations: Fallacies associated with exclusion of transmission. Vaccine. 2013;31(6):973 – 978. Available from: http://www.sciencedirect.com/science/article/pii/S0264410X12017495.
23. Diekmann O, Heesterbeek JAP, Metz JAJ. On the definition and the computation of the basic reproduction ratio R0 in models for infectious diseases in heterogeneous populations. Journal of Mathematical Biology. 1990 Jun;28(4):365–382. Available from: https://doi.org/10.1007/BF00178324.
24. Diekmann Ov, Heesterbeek JAP. Mathematical epidemiology of infectious diseases : model building, analysis, and interpretation. Chichester : Wiley; 2000. Available from: http://lib.ugent.be/catalog/rug01:000897478.
25. Diekmann O, Heesterbeek H, Britton T. Mathematical Tools for Understanding Infectious Disease Dynamics. Princeton Series in Theoretical and Computational Biology. Princeton; 2013.
26. van den Driessche P, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical Biosciences. 2002;180(1):29–48. Available from: https://www.sciencedirect.com/science/article/pii/S0025556402001086.
27. Brauer vdDP F, Wu JH. Mathematical Epidemiology. Springer-Verlag, Berlin; 2008.
28. Ivorra B, Ferrández MR, Vela-Pérez M, Ramos AM. Mathematical modeling of the spread of the coronavirus disease 2019 (COVID-19) taking into account the undetected infections. The case of China. Communications in nonlinear science & numerical simulation. 2020 Sep;88:105303–105303. S1007-5704(20)30135-0[PII]. Available from: https://doi.org/10.1016/j.cnsns.2020.105303.
29. Baccini M, Cereda G, Viscardi C. The first wave of the SARS-CoV-2 epidemic in Tuscany (Italy): A SI2R2D compartmental model with uncertainty evaluation. PLOS ONE. 2021 04;16(4):1–23. Available from: https://doi.org/10.1371/journal.pone.0250029.
30. Leontitsis A, Senok A, Alsheikh-Ali A, Al Nasser Y, Loney T, Alshamsi A. SEAHIR: A Specialized Compartmental Model for COVID-19. Int J Environ Res Public Health. 2021 Mar;18(5).
31. Rădulescu A, Williams C, Cavanagh K. Management strategies in a SEIR-type model of COVID 19 community spread. Scientific Reports. 2020;10(1):21256. Available from: https://doi.org/10.1038/s41598-020-77628-4.
32. Giordano G, Blanchini F, Bruno R, Colaneri P, Di Filippo A, Di Matteo A, et al. Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. Nature Medicine. 2020;26(6):855–860. Available from: https://doi.org/10.1038/s41591-020-0883-7.
33. Liu WM. Dose-dependent latent period and periodicity of infectious diseases. J Math Biol. 1993;31(5):487–494.
34. Greenhalgh D. Hopf bifurcation in epidemic models with a latent period and nonpermanent immunity. Mathematical and Computer Modelling. 1997;25(2):85–107. Available from: https://www.sciencedirect.com/science/article/pii/S0895717797000095.
35. Korobeinikov A, Maini PK. Non-linear incidence and stability of infectious disease models. Math Med Biol. 2005 Jun;22(2):113–128.
36. van den Driessche P. Reproduction numbers of infectious disease models. Infect Dis Model. 2017 Aug;2(3):288–303.
37. Huang G, Takeuchi Y, Ma W, Wei D. Global Stability for Delay SIR and SEIR Epidemic Models with Nonlinear Incidence Rate. Bulletin of Mathematical Biology. 2010;72(5):1192–1207. Available from: https://doi.org/10.1007/s11538-009-9487-6.

38. Li M, Liu X. An SIR Epidemic Model with Time Delay and General Nonlinear Incidence Rate. Abstract and Applied Analysis. 2014 02;2014:Article ID 131257, 7 pages.
39. Arino J, van den Driessche P. Time delays in epidemic models Modeling and Numerical Considerations. In: Arino O, Hbid M, Dads E, editors. Delay Differential Equations and Applications.. vol. 205 of Nato Science Series (II. Mathematics, Physics and Chemistry). Springer, Dordrecht; 2006. p. 539–578.
40. Hethcote HW, Tudor DW. Integral equation models for endemic infectious diseases. Journal of Mathematical Biology. 1980;9(1):37–47. Available from: https://doi.org/10.1007/BF00276034.
41. Hethcote HW, Stech HW, van den Driessche P. Stability analysis for models of diseases without immunity. Journal of Mathematical Biology. 1981;13(2):185–198. Available from: https://doi.org/10.1007/BF00275213.
42. Hethcote HW, Lewis MA, van den Driessche P. An epidemiological model with a delay and a nonlinear incidence rate. Journal of Mathematical Biology. 1989;27(1):49–64. Available from: https://doi.org/10.1007/BF00276080.
43. Hethcote HW, van den Driessche P. An SIS epidemic model with variable population size and a delay. Journal of Mathematical Biology. 1995;34(2):177–194. Available from: https://doi.org/10.1007/BF00178772.
44. Hethcote H, Stech H, Driessche P. NONLINEAR OSCILLATIONS IN EPIDEMIC MODELS. Siam Journal on Applied Mathematics. 1981;40:1–9.
45. Nåsell I. Stochastic models of some endemic infections. Math Biosci. 2002 Jul-Aug;179(1):1–19.
46. Bailey NTJ. On Estimating the Latent and Infectious Periods of Measles: I. Families with Two Susceptibles Only. Biometrika. 1956;43(1/2):15–22. Available from: http://www.jstor.org/stable/2333574.
47. Bailey NTJ. On Estimating the Latent and Infectious Periods of Measles: II. Families with Three or More Susceptibles. Biometrika. 1956;43(3/4):322–331. Available from: http://www.jstor.org/stable/2332910.
48. Lloyd AL. Realistic Distributions of Infectious Periods in Epidemic Models: Changing Patterns of Persistence and Dynamics. Theoretical Population Biology. 2001;60(1):59–71. Available from: https://www.sciencedirect.com/science/article/pii/S0040580901915254.
49. Krylova O, Earn DJD. Effects of the infectious period distribution on predicted transitions in childhood disease dynamics. Journal of The Royal Society Interface. 2013;10(84):20130098. Available from: https://royalsocietypublishing.org/doi/abs/10.1098/rsif.2013.0098.
50. Plank JDSSBD M. 16. In: Differential Equations and Mathematical Biology. 2nd ed. Chapman and Hall/CRC; 2009. p. 418–424.
51. Chalub FACC, Souza MO. The SIR epidemic model from a PDE point of view. Mathematical and Computer Modelling. 2011;53(7):1568–1574. Mathematical Methods and Modelling of Biophysical Phenomena. Available from: https://www.sciencedirect.com/science/article/pii/S0895717710002906.
52. Källén A, Arcuri P, Murray J. A simple model for the spatial spread and control of rabies. Journal of theoretical biology. 1985;116 3:377–93.
53. Lin Z, Zhu H. Spatial spreading model and dynamics of West Nile virus in birds and mosquitoes with free boundary. Journal of Mathematical Biology. 2017;75(6):1381–1409. Available from: https://doi.org/10.1007/s00285-017-1124-7.
54. Gillespie D, Seitaridou E. Simple Brownian Diffusion: An Introduction to the Standard Theoretical Models. Oxford University Press; 2012.
55. Kurashima T, Althoff T, Leskovec J. Modeling Interdependent and Periodic Real-World Action Sequences. Proc Int World Wide Web Conf. 2018 Apr;2018:803–812.
56. Mollison D. Spatial contact models for ecological and epidemic spread (with Discussion). J Roy Stat Soc. 1977 01;39:283–326.
57. Mansilla R, Gutierrez J. Deterministic site exchange cellular automata model for the spread of diseases in human settlements. Complex Systems. 2001;13(2):143–159.
58. Chen D, Moulin B, Wu J. Analyzing and Modeling Spatial and Temporal Dynamics of Infectious Diseases; 2014.

59. Schneckenreither G, Popper N, Zauner G, Breitenecker F. Modelling SIR-type epidemics by ODEs, PDEs, difference equations and cellular automata – A comparative study. Simulation Modelling Practice and Theory. 2008;16(8):1014–1023. EUROSIM 2007. Available from: https://www.sciencedirect.com/science/article/pii/S1569190X08001160.
60. Diekmann O. Thresholds and travelling waves for the geographical spread of infection. J Math Biol. 1978 Jul;6(2):109–130.
61. Bosch F, Metz J, Diekmann O. The velocity of spatial population expansion. Journal of Mathematical Biology. 1988;28:529–565.
62. Mollison D. Dependence of epidemic and population velocities on basic parameters. Mathematical Biosciences. 1991;107(2):255–287. Available from: https://www.sciencedirect.com/science/article/pii/0025556491900098.
63. Bartlett MS. The Relevance of Stochastic Models for Large-Scale Epidemiological Phenomena. Journal of the Royal Statistical Society Series C (Applied Statistics). 1964;13(1):2–8. Available from: http://www.jstor.org/stable/2985217.
64. Chowell G, Hyman J, Bettencourt L, Castillo-Chavez C. Mathematical and statistical estimation approaches in epidemiology. Springer Netherlands; 2009.
65. Allen LJS. An Introduction to Stochastic Processes with Applications to Biology. 2nd ed. Chapman and Hall/CRC; 2010.
66. Dietz K, Heesterbeek JAP. Daniel Bernoulli's epidemiological model revisited. Mathematical Biosciences. 2002;180(1):1 – 21. Available from: http://www.sciencedirect.com/science/article/pii/S0025556402001220.
67. Bailey NTJ. The mathematical theory of infectious diseases and its applications. 2nd ed. Hafner Press; 1975.
68. M'Kendrick A. Applications of Mathematics to Medical Problems. In: Proceedings of the Edinburg Mathematical Society. vol. 44; 1925. p. 98–130.
69. Andersson H, Britton T. Stochastic Epidemic Models and Their Statistical Analysis; 2000. .
70. Greenwood M. On the Statistical Measure of Infectiousness. Journal of Hygiene. 1931;31(3):336–351.
71. Gani J, Jerwood D. Markov Chain Methods in Chain Binomial Epidemic Models. Biometrics. 1971 September;27(2):591–603.
72. Gagniuc P. Markov Chains: From Theory to Implementation and Experimentation; 2017.
73. Allen LJS, Burgin AM. Comparison of deterministic and stochastic SIS and SIR models in discrete time. Mathematical Biosciences. 2000;163(1):1–33. Available from: https://www.sciencedirect.com/science/article/pii/S0025556499000474.
74. Allen LJS. A primer on stochastic epidemic models: Formulation, numerical simulation, and analysis. Infectious Disease Modelling. 2017;2(2):128 – 142. Available from: http://www.sciencedirect.com/science/article/pii/S2468042716300495.
75. Cai S, Cai Y, Mao X. A stochastic differential equation SIS epidemic model with two correlated Brownian motions. Nonlinear Dynamics. 2019;97(4):2175–2187. Available from: https://doi.org/10.1007/s11071-019-05114-2.
76. Gray A, Greenhalgh D, Hu L, Mao X, Pan J. A Stochastic Differential Equation SIS Epidemic Model. SIAM Journal of Applied Mathematics. 2011 01;71:876–902.
77. Osthus D, Hickmann KS, Caragea PC, Higdon D, Del Valle SY. Forecasting seasonal influenza with a state-space SIR model. Ann Appl Stat. 2017 Mar;11(1):202–224.
78. Neumann J. Theory Of Self Reproducing Automata. Burks A, editor. Urbana and London: University of Illinois Press; 1966.
79. Codd EF. Cellular Automata. New York: Academic Press; 1968.
80. Sarkar P. A Brief History of Cellular Automata. ACM Comput Surv. 2000 Mar;32(1):80–107. Available from: https://doi.org/10.1145/349194.349202.
81. Toffoli T, Margolus N. Cellular Automata Machines: A New Environment for Modeling. The MIT Press; 1987. Available from: https://doi.org/10.7551/mitpress/1763.001.0001.
82. Wolfram S. Statistical mechanics of cellular automata. Reviews of Modern Physics. 1983;55:601–644.
83. Li X, Wu J, Li XY. Theory of Practical Cellular Automaton. Springer Singapore; 2018.

84. Menshutina NV, Kolnoochenko AV, Lebedev EA. Cellular Automata in Chemistry and Chemical Engineering. Annual Review of Chemical and Biomolecular Engineering. 2020;11(1):87–108. PMID: 32513081. Available from: https://doi.org/10.1146/annurev-chembioeng-093019-075250.
85. Frisch U, Hasslacher B, Pomeau Y. Lattice-Gas Automata for the Navier-Stokes Equation. Phys Rev Lett. 1986 Apr;56:1505–1508. Available from: https://link.aps.org/doi/10.1103/PhysRevLett.56.1505.
86. Wolf-Gladrow D. Lattice-Gas Cellular Automata and Lattice Boltzmann Models - An Introduction. Springer-Verlag Berlin Heidelberg; 2000.
87. Guo Z, Shi B, Wang N. Lattice BGK Model for Incompressible Navier–Stokes Equation. Journal of Computational Physics. 2000;165(1):288–306. Available from: https://www.sciencedirect.com/science/article/pii/S0021999100966166.
88. He X, Luo LS. Lattice Boltzmann Model for the Incompressible Navier–Stokes Equation. Journal of Statistical Physics. 1997 08;88:927–944.
89. Boccara N, Cheong K. Automata network SIR models for the spread of infectious diseases in populations of moving individuals. Journal of Physics A: Mathematical and General. 1992 may;25(9):2447–2461. Available from: https://doi.org/10.1088/0305-4470/25/9/018.
90. Boccara N, Cheong K. Critical behaviour of a probabilistic automata network SIS model for the spread of an infectious disease in a population of moving individuals. Journal of Physics A: Mathematical and General. 1993 aug;26(15):3707–3717. Available from: https://doi.org/10.1088/0305-4470/26/15/020.
91. Boccara N, Cheong K, Oram M. A probabilistic automata network epidemic model with births and deaths exhibiting cyclic behaviour. Journal of Physics A: Mathematical and General. 1994 mar;27(5):1585–1597. Available from: https://doi.org/10.1088/0305-4470/27/5/022.
92. White SH, del Rey AM, Sánchez GR. Modeling epidemics using cellular automata. Applied Mathematics and Computation. 2007;186(1):193–202. Available from: https://www.sciencedirect.com/science/article/pii/S0096300306009295.
93. White S, Rey Á, Sánchez G. Using Cellular Automata to Simulate Epidemic Diseases. Applied Mathematical Sciences. 2009 01;3:959–968.
94. Schimit PHT, Monteiro LHA. On the basic reproduction number and the topological properties of the contact network: An epidemiological study in mainly locally connected cellular automata. Ecological Modelling. 2009;220(7):1034–1042. Available from: https://www.sciencedirect.com/science/article/pii/S0304380009000386.
95. Pereira FMM, Schimit PHT. Dengue fever spreading based on probabilistic cellular automata with two lattices. Physica A: Statistical Mechanics and its Applications. 2018;499:75–87. Available from: https://www.sciencedirect.com/science/article/pii/S0378437118300499.
96. Holko A, Mędrek M, Pastuszak Z, Phusavat K. Epidemiological modeling with a population density map-based cellular automata simulation system. Expert Systems with Applications. 2016;48:1–8. Available from: https://www.sciencedirect.com/science/article/pii/S0957417415005631.
97. Lili Wang JHBZFWLTMKDBMCE Yiwang Zhou, Song PXK. An epidemiological forecast model and software assessing interventions on COVID-19 epidemic in China. Journal of Data Science. 2020;18(3):409–432.
98. Zhou Y, Wang L, Zhang L, Shi L, Yang K, He J, et al. A Spatiotemporal Epidemiological Prediction Model to Inform County-Level COVID-19 Risk in the United States. Harvard Data Science Review. 2020 8;Https://hdsr.mitpress.mit.edu/pub/qqg19a0r. Available from: https://hdsr.mitpress.mit.edu/pub/qqg19a0r.
99. Chapman S, Cowling TG, Burnett D, Cercignani C. The Mathematical Theory of Nonuniform Gases: An Account of the Kinetic Theory of Viscosity, Thermal Conduction and Diffusion in Gases. Cambridge Mathematical Library. Cambridge University Press; 1990. Available from: https://books.google.co.za/books?id=Cbp5JP2OTrwC.
100. Berec L. Techniques of spatially explicit individual-based models: construction, simulation, and mean-field analysis. Ecological Modelling. 2002;150(1):55–81. Available from: https://www.sciencedirect.com/science/article/pii/S030438000100463X.

101. Hethcote HW. 1. In: The basic epidemiology model: Models, expressions for $\mathcal{R}_0$, parameter estimation, and applications. World Scientific Publishing Co (Pty) Ltd; 2008. p. 1–61. Available from: https://www.worldscientific.com/doi/abs/10.1142/9789812834836_0001.
102. Anderson RM, May R, editors. Population Biology of Infectious Diseases. 1st ed. Springer-Verlag Berlin Heidelberg; 1982.
103. Anderson RM, May R, editors. Infectious Diseases of Humans: Dynamics and Control. Oxford University Press; 1992.
104. Ferner RE, Aronson JK. Cato Guldberg and Peter Waage, the history of the Law of Mass Action, and its relevance to clinical pharmacology. Br J Clin Pharmacol. 2016 Jan;81(1):52–55.
105. Ramanathan M, Ferguson ID, Miao W, Khavari PA. SARS-CoV-2 B.1.1.7 and B.1.351 spike variants bind human ACE2 with increased affinity. Lancet Infect Dis. 2021 May;.
106. Leung NHL. Transmissibility and transmission of respiratory viruses. Nat Rev Microbiol. 2021 Aug;19(8):528–545.
107. WELLS WF. ON AIR-BORNE INFECTION*: STUDY II. DROPLETS AND DROPLET NUCLEI. American Journal of Epidemiology. 1934 11;20(3):611–618. Available from: https://doi.org/10.1093/oxfordjournals.aje.a118097.
108. Nguyen-Van-Tam JS, Killingley B, Enstone J, Hewitt M, Pantelic J, Grantham ML, et al. Minimal transmission in an influenza A (H3N2) human challenge-transmission model within a controlled exposure environment. PLOS Pathogens. 2020 07;16(7):1–16. Available from: https://doi.org/10.1371/journal.ppat.1008704.
109. Sorokowska A, Sorokowski P, Hilpert P, Cantarero K, Frackowiak T, Ahmadi K, et al. Preferred interpersonal distances : a global comparison. Journal of Cross-Cultural Psychology. 2017;48(4):577–592. Available from: http://wrap.warwick.ac.uk/100226/.
110. Biggerstaff M, Cauchemez S, Reed C, Gambhir M, Finelli L. Estimates of the reproduction number for seasonal, pandemic, and zoonotic influenza: a systematic review of the literature. BMC Infect Dis. 2014 Sep;14:480.
111. Smith H. An Introduction to Delay Differential Equations with Applications to the Life Sciences. vol. 57. Springer, Mew York, NY; 2010.
112. Cheng VCC, Lau SKP, Woo PCY, Yuen KY. Severe Acute Respiratory Syndrome Coronavirus as an Agent of Emerging and Reemerging Infection. Clinical Microbiology Reviews. 2007;20(4):660–694. Available from: https://cmr.asm.org/content/20/4/660.
113. Christian MD, Poutanen SM, Loutfy MR, Muller MP, Low DE. Severe Acute Respiratory Syndrome. Clinical Infectious Diseases. 2004 05;38(10):1420–1427. Available from: https://doi.org/10.1086/420743.
114. Lau J WTea Fung KS. SARS Transmission among Hospital Workers in Hong Kong. Emerging Infectious Diseases. 2004;10(2):280–286.
115. Zeng G, Xie SY, Li Q, Ou JM. Infectivity of severe acute respiratory syndrome during its incubation period. Biomed Environ Sci. 2009 Dec;22(6):502–510.
116. Lessler J, Reich NG, Brookmeyer R, Perl TM, Nelson KE, Cummings DAT. Incubation periods of acute respiratory viral infections: a systematic review. Lancet Infect Dis. 2009 May;9(5):291–300.
117. Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. Lancet. 2003 May;361(9371):1761–1766.
118. Anderson RM, Fraser C, Ghani AC, Donnelly CA, Riley S, Ferguson NM, et al. Epidemiology, transmission dynamics and control of SARS: the 2002-2003 epidemic. Philos Trans R Soc Lond B Biol Sci. 2004 Jul;359(1447):1091–1105.
119. Statistics Canada 2017. Toronto, C [Census subdivision], Ontario and Canada [Country] (table). Census Profile. 2016 Census. Statistics Canada Catalogue no. 98-316-X2016001. Ottawa. Released November 29, 2017.;. https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/prof/index.cfm?Lang=E(accessedAugust29, 2020). Available from: https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/prof/index.cfm?Lang=E(accessedAugust29,2020). [cited 29/08/2020].
120. Chowell G, Castillo-Chavez C, Fenimore PW, Kribs-Zaleta CM, Arriola L, Hyman JM. Model parameters and outbreak control for SARS. Emerg Infect Dis. 2004 Jul;10(7):1258–1263.

121. Hong Kong Government. Hong Kong 2003: The facts;. https://www.yearbook.gov.hk/2003/english/hkfact/hkfact.html. Available from: https://www.yearbook.gov.hk/2003/english/hkfact/hkfact.html [cited 30/08/2020].
122. World Bank. Population density Singapore;. https://data.worldbank.org/indicator/EN.POP.DNST?end=2004&locations=SG&start=1992&view=chart. Available from: https://data.worldbank.org/indicator/EN.POP.DNST?end=2004&locations=SG&start=1992&view=chart [cited 30/08/2020].
123. Central Population and Housing Census Steering Committee. The 2009 Vietnam population and Housing Census Major Findings; 2010. https://unstats.un.org/unsd/demographic/sources/census/wphc/Viet%20Nam/Vietnam-Findings.pdf.
124. Tuan PA, Horby P, Dinh PN, Mai LTQ, Zambon M, Shah J, et al. SARS transmission in Vietnam outside of the health-care setting. Epidemiol Infect. 2007 Apr;135(3):392–401.
125. Taipei City Government. Resident Population, Sex Ratio and Population Density in Taipei City;. hhttps://www-ws.gov.taipei/Download.ashx?u=LzAwMS9VcGxvYWQvMzYxL3JlbGZpbGUvMTY4NzEvMTE2OTMyLzAwMzFmNjQ1LTc1M2MtNDFhYy04OGZkLTFlZDc5NjUyZWYxMS5wZGY%3D&n=6Ie65YyX5biC6K2m5YuZ57Wx6KiI5bm05aCx6Iux5paH54mI5YWo5paH44CQcGRm44CRLnBkZg%3D%3D&icon=..pdf.
126. Zhang Z, Sheng C, Ma Z, Li D. The outbreak pattern of the SARS cases in Asia. Chin Sci Bull. 2004;49(17):1819–1823.
127. Moss WJ, Griffin DE. Measles. Lancet. 2012 Jan;379(9811):153–164.
128. Klinkenberg D, Nishiura H. The correlation between infectivity and incubation period of measles, estimated from households with two cases. J Theor Biol. 2011 Sep;284(1):52–60.
129. Mitchell BR. International historical statistics : Europe, 1750-1993. 4th ed. London : Macmillan Reference ; New York, N.Y. : Stockton Press, 1998.; 1998.
130. Guerra FM, Bolotin S, Lim G, Heffernan J, Deeks SL, Li Y, et al. The basic reproduction number (R(0)) of measles: a systematic review. Lancet Infect Dis. 2017 Dec;17(12):e420–e428.
131. Wikipedia contributors. Census in Germany — Wikipedia, The Free Encyclopedia; 2020. [Online; accessed 31-August-2020]. https://en.wikipedia.org/w/index.php?title=Census_in_Germany&oldid=967955707.
132. World Bank. Italian Land area;. https://data.worldbank.org/indicator/AG.LND.TOTL.K2?end=1969&locations=IT&start=1961.
133. World Bank. Danish Land Area;. https://data.worldbank.org/indicator/AG.LND.TOTL.K2?end=1969&locations=DK&start=1961.
134. World Bank. Netherlands land area;. https://data.worldbank.org/indicator/AG.LND.TOTL.K2?end=1969&locations=NL&start=1961.
135. Grand-Duché de Luxembourg. "Population totale 1821 - 2016". Le portail des statistiques;. https://statistiques.public.lu/stat/TableViewer/tableView.aspx.
136. World bank. European population Densities;. https://data.worldbank.org/indicator/EN.POP.DNST?end=2009&locations=NL-DE-IT-DK-LU&start=2000.
137. Feldmann H, Sprecher A, Geisbert TW. Ebola. New England Journal of Medicine. 2020 May;382(19):1832–42.
138. Weppelmann TA, Donewell B, Haque U, Hu W, Magalhaes RJS, Lubogo M, et al. Determinants of patient survival during the 2014 Ebola Virus Disease outbreak in Bong County, Liberia. Global Health Research and Policy. 2016;1(1):5. Available from: https://doi.org/10.1186/s41256-016-0005-8.
139. Jacob ST, Crozier I, Fischer WA, Hewlett A, Kraft CS, Vega MAdL, et al. Ebola virus disease. Nature Reviews Disease Primers. 2020;6(1):13. Available from: https://doi.org/10.1038/s41572-020-0147-3.
140. Colebunders R, Borchert M. Ebola haemorrhagic fever–a review. J Infect. 2000 Jan;40(1):16–20.
141. Chowell G, Nishiura H. Transmission dynamics and control of Ebola virus disease (EVD): a review. BMC Med. 2014 Oct;12:196.
142. Althaus CL. Estimating the Reproduction Number of Ebola Virus (EBOV) During the 2014 Outbreak in West Africa. PLoS Curr. 2014 Sep;6.

143. Feldmann H, Jones S, Klenk HD, Schnittler HJ. Ebola virus: from discovery to vaccine. Nature Reviews Immunology. 2003;3(8):677–685. Available from: https://doi.org/10.1038/nri1154.
144. Velásquez GE, Aibana O, Ling EJ, Diakite I, Mooring EQ, Murray MB. Time From Infection to Disease and Infectiousness for Ebola Virus Disease, a Systematic Review. Clin Infect Dis. 2015 Oct;61(7):1135–1140.
145. Van Kerkhove MD, Bento AI, Mills HL, Ferguson NM, Donnelly CA. A review of epidemiological parameters from Ebola outbreaks to inform early public health decision-making. Scientific Data. 2015;2(1):150019. Available from: https://doi.org/10.1038/sdata.2015.19.
146. Bank W. African Population densities;. https://data.worldbank.org/indicator/EN.POP.DNST?end=2018&locations=CD-GN-LR-SL-UG&start=1990.
147. Legrand J, Grais RF, Boelle PY, Valleron AJ, Flahault A. Understanding the dynamics of Ebola epidemics. Epidemiol Infect. 2007 May;135(4):610–621.
148. Agua-Agum J, Ariyarajah A, Aylward B, Bawo L, Bilivogui P, Blake IM, et al. Exposure Patterns Driving Ebola Transmission in West Africa: A Retrospective Observational Study. PLoS Med. 2016 Nov;13(11):e1002170.
149. Chowell G, Hengartner NW, Castillo-Chavez C, Fenimore PW, Hyman JM. The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda. J Theor Biol. 2004 Jul;229(1):119–126.
150. Diekmann O, van Gils S, Lunel S, Walter HO. Delay Equations : Functional-, Complex-, and Nonlinear Analysis. 1st ed. Springer-Verlag New York; 1995.
151. Kuang Y. In: Delay Differential Equations: With Applications in Population Dynamics. ISSN. Elsevier Science; 1993. p. 67–72. Available from: https://books.google.co.za/books?id=YWsz1IXkvy0C.