The Mathematics of Infectious Diseases

Cheat Sheet

SI-Model

Susceptible-Infectious Model: applicable to HIV.

S ----------> I
rβI/N

$dS/dt = -r\beta\,(I/N)\,S$
$dI/dt = r\beta\,(I/N)\,S$

S: Susceptible humans
I: Infectious humans
r: Number of contacts per unit time
β: Probability of disease transmission per contact
N: Total populationsize: N = S + I.

with solution for $I(0) = I_0$:

$$I(t) = \frac{I_0\,N}{(N - I_0)\exp[-r\beta t] + I_0} = \frac{N}{1 + (N/I_0 - 1)\exp[-r\beta t]}$$

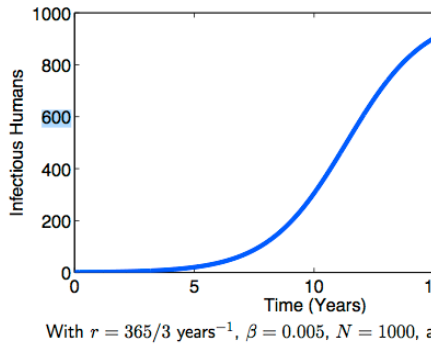
for $I_0 << N$ and with i = I / N

$$I(t) = \frac{I_0\,N}{N\exp[-r\beta t] + I_0} \Longrightarrow i(t) = \frac{1}{1 + N/I_0\exp[-r\beta t]}$$

for $t < 1/(r\beta)$

$$I(t) = \frac{I_0\,N}{N\exp[-r\beta t]} = I_0\exp[r\beta t] \Longrightarrow i(t) = i_0\exp[r\beta t]$$

SI-Model



With $r = 365/3$ years^{-1}, $\beta = 0.005$, $N = 1000$, a

$r\beta = 0.608$ years^{-1} ------> $T_{si} = \frac{\ln 2}{r\beta} = 1.15$ years

$r\beta = \frac{\ln 2}{T_{si}}$

SIS Model

Susceptible-Infectious-Susceptible Model: applicable to the common cold.

<----- γ --------
S I
---------->
rβI/N

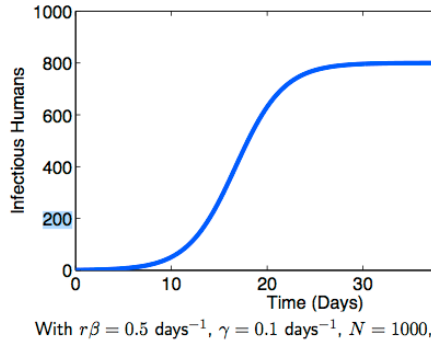
S: Susceptible humans
I: Infectious humans
r: Number of contacts per unit time
β: Probability of disease transmission per contact
γ: Per-capita recovery rate (1/γ = duration of infection)
N: Total populationsize: N = S + I.

$dS/dt = -r\beta\,(I/N)\,S + \gamma I$
$dI/dt = r\beta\,(I/N)\,S - \gamma I$

$$I(t) = I_0\frac{N\,((r\beta-\gamma)/r\beta)}{(N\,((r\beta-\gamma)/r\beta) - I_0)\exp[-(r\beta-\gamma)t] + I_0}$$

vgl. SI-Model

$$I(t) = I_0\frac{N}{(N - I_0)\exp[-r\beta t] + I_0}$$



With $r\beta = 0.5$ days^{-1}, $\gamma = 0.1$ days^{-1}, $N = 1000$,

$(r\beta-\gamma) = 0.4$ days^{-1} ----> $Tsis = \frac{\ln 2}{r\beta-\gamma} = 1.75$ days

$(r\beta-\gamma)/r\beta = 0.8$

SIR Model

Susceptible-Infectious-Recovered Model: applicable to measles, mumps, rubella

S ----- rβI/N----> I ----- γ --------> R

S = Susceptible humans
I = Infectious humans
R = Recovered humans
r = Number of contacts that one human has / time
β = Probability of disease transmission per contact that one human has

γ = Per-capita recovery rate (1/γ = duration of infection)
N = Total population size: N = S(t) + I(t) + R(t) = constant over time.

rβ = one human's probability of disease transmission per time
i / N = probability of meeting one infective in the population
rβ (I / N) = average number of significant contacts with infectives that one susceptible has per time

standard incidence
$dS/dt = -r\beta\,(I/N)\,S$
$dI/dt = r\beta\,(I/N)\,S - \gamma I$
$dR/dt = \gamma I$
R(t) = N - (S(t) + I(t))

s ----- β i ----> i ----- γ --------> r

s = S/N = Susceptible humans / total population (susceptible fraction)
i = I/N = Infectious humans / total population (infectious fraction)
r = R/N = Recovered humans / total population (recovered fraction)
r = ----------I ---> if β contains r, then
I ---> β = one human's probability of diseaase
transmission per time =
I ---> β = significant contact rate of one human
β: ----------I
γ: Per-capita recovery rate (1/γ = duration of infection)
N: Total population size: N = S + I + R ---> 1 = s + i + r

β = one human's probability of disease transmission per time
i / N = probability of meeting one infective in the population
β (I / N) = β i = average number of significant contacts with infectives that one susceptible has per time

standard incidence (eq. 2.2)
ds/dt = - β i s dS/dt = - β (I / N) S. When mass action law is assumed: dS/dt = - eta N (I / N) S
di/dt = β i s - γ i
dr/dt = γ i
r(t) = 1 - (s(t) + i(t))

R_0 = Characteristic of the infectant = (Number of contacts / time) * (Probability of transmission / contact) * (Duration of infection)
$R_0 = r\,\beta / \gamma$

- The basic reproductive (or reproduction) number, R_0, is the number of secondary infections that one infected person would produce in a fully susceptible population through the entire duration of his infectious period.
- R_0 provides a threshold condition for the stability of the disease-free equilibrium point (for most models):
  - The disease-free equilibrium point is locally asymptotically stable when $R_0 < 1$: the disease dies out.
  - The disease-free equilibrium point is unstable when $R_0 > 1$: the disease establishes itself in the population or an epidemic occurs.
  - For a given model, R_0 is fixed over all time. This definition is only valid for simple homogeneous autonomous models.
- Can define similar threshold conditions for more complicated models that include heterogeneity and/or seasonality but the basic definition no longer holds.
- The (effective) reproductive number, R_e, is the number of secondary infections that one infected person would produce through the entire duration of his infectious period.
- Typically, but not always, R_e is the product of R_0 and the proportion of the population that is susceptible.

$R_e(t) = R_0 \times S(t) / N(t)$
$= r\,\beta / \gamma\ S(t) / N(t)$

- The control reproductive number, R_e, describes whether the infectious population increases or not.
  - It increases when $R_e > 1$;
  - it decreases when $R_e < 1$ and

- it is constant when $R_e = 1$.
- When $R_e = 1$, the disease is at equilibrium.

- R_e can change over time.
- R_c is the number of secondary infections that one infected person would produce through the entire duration of the infectious period, in the presence of control interventions.

- If $R_0 < 1$, introduced cases do not lead to an epidemic (the number of infectious individuals decreases towards 0).
- If $R_0 > 1$, introduced cases can lead to an epidemic (temporary increase in the number of infectious individuals).

vertical infection: I infection stemming from mother
V

horizontal infection: --> infection between MSEIR compartments

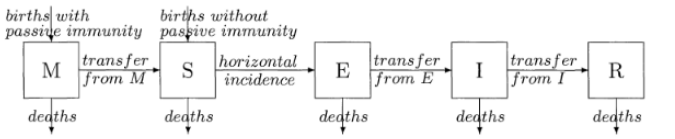


Fig. 1 *The general transfer diagram for the MSEIR model with the passively immune class M, the susceptible class S, the exposed class E, the infective class I, and the recovered class R.*

passive immune — Susceptible — Exposed — Infective (infectious) — Recovered

1/delta; period of passive immunity — 1/epsilon: latent period — 1/gamma: infectious period (waiting time)

measles: 6 - 9 months — 1 - 2 weeks — 1 week

Table 1 *Summary of notation.*

M	Passively immune infants
S	Susceptibles
E	Exposed people in the latent period
I	Infectives
R	Recovered people with immunity
m, s, e, i, r	Fractions of the population in the classes above
β	Contact rate
$1/\delta$	Average period of passive immunity
$1/\varepsilon$	Average latent period
$1/\gamma$	Average infectious period
R_0	Basic reproduction number
σ	Contact number
R	Replacement number

Ro =
- basic
  - reproduction number or
  - reproduction ratio or
  - reproductive rate
- average number of secondary infections that occur when one infective is introduced into a completely susceptible host population

R = replacement number = average number of secondary infections produced by a typical infective during his [infectious period i.e.] entire period of infectiousness
- R(t) = sigma s(t)
- R(t) < = Ro because, after the infection has invaded a population, not everyone is susceptible any longer

sigma = β / γ = contact number = average number of adequate contacts of a typical infective during his infectious period = contact rate (β) * average infectious period (1/ γ)
- sigma = Ro in most models, i.e. constant in time

At the beginning t = o of the spread of an infectious disease, the entire population (except the invader) is susceptible: s(t=0) = s_o = 1
- with R = sigma s(t) (Definition von sigma)
- @ t = 0, R = sigma = Ro

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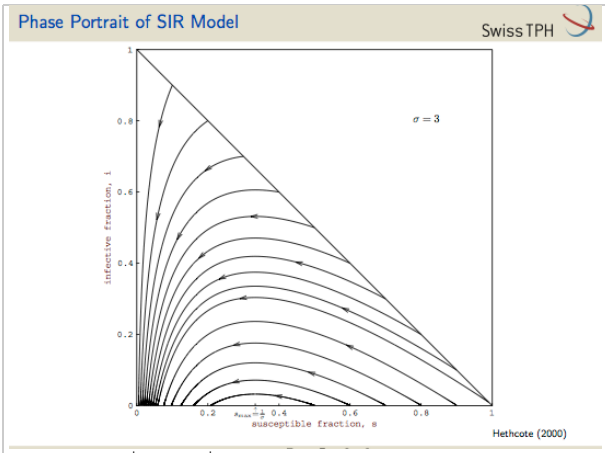


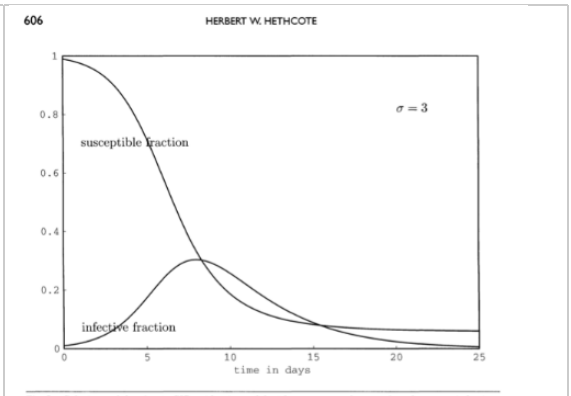
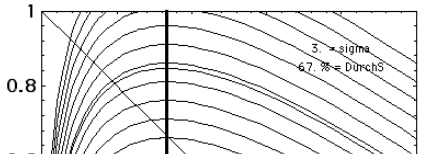


Fig. 3 *Solutions of the classic SIR epidemic model with contact number $\sigma = 3$ and average infectious period $1/\gamma = 3$ days.*

β = sigma γ = 1 day^{-1}



|----------|
| |
s_{inf} s_{max} = 1/sigma
Durchseuchung ?
|
|
bei s(t) < 1/sigma |
nimmt i(t) (mit fallendem s(t)) bei |
fortschreitender Zeit t ab |
| bei s(t) > 1/sigma
| nimmt i(t) (mit fallendem s(t)) bei

l fortschreitender Zeit t zu

Fig. 2: The epidemic dies out because, when the susceptible fraction s(t) goes below l/sigma, the replacement number R = sigma s(t) goes below 1. Observe that the threshold result here involves the initial replacement number R = sigma s, and does not involve the basic reproduction number Ro.

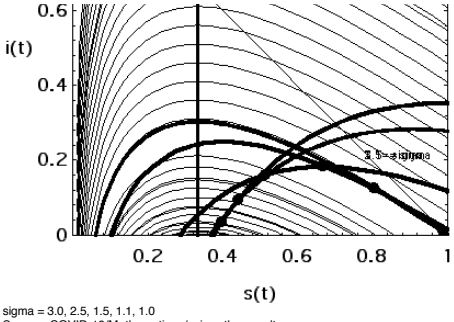
The solution paths are found from the quotient differential equation di/ds = -1 + l/(sigma s)
$i(t) + s(t) - \ln[s(t)] / \sigma = i_o + s_o - \ln[s_o] / \sigma$
If

- sigma $s_o < 1$, then i(t) decreases to zero as t --> t_{oo}.
- sigma $s_o > 1$, then
  - i(t)
    - first increases up to a maximum value
      - $i_{max} = i_o + s_o - 1/\text{sigma} (1 + \ln(\text{sigma } s_o)$ and
    - then decreases to zero as t -+ oo.
  - s(t)
    - is a decreasing function and
    - the limiting value s_{inf} is the unique root in (0, l/sigma) of the equation
      - $i_o + s_o - s_{inf} + \ln[s_{inf}/ s_o] / \sigma = 0$ (eq. 2.4)

Using (eq. 2.4) we can calculate the approximate contact number sigma for a specific disease with known

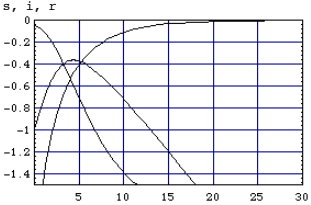
- s_o and s_{inf} and
- i_o beng infiniteley small:

$$\sigma = \frac{\ln[s_o / s_{inf}]}{s_o - s_{inf}} = \frac{\ln[s_o] - \ln[s_{inf}]}{s_o - s_{inf}}$$

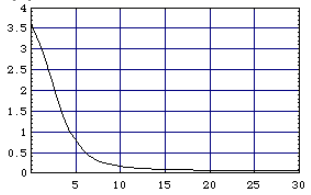


sigma = 3.0, 2.5, 1.5, 1.1, 1.0
Source: COVID-19/Mathematicae/seir-paths_results.ma

sigma = 4.0 (beta = 1.0, gammaG = 0.25)
s, i, r

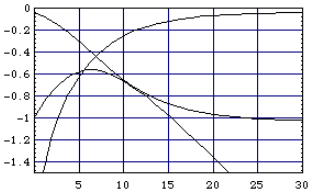


R[t]

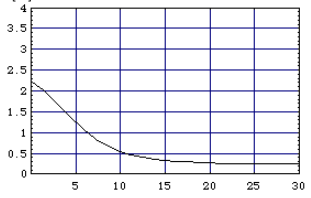


sigma = 2.5 (beta = 0.625, gammaG = 0.25)

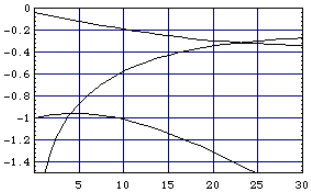
s, i, r



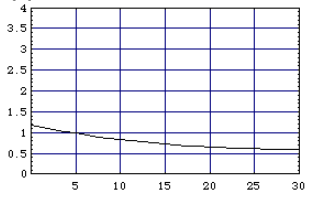
R[t]



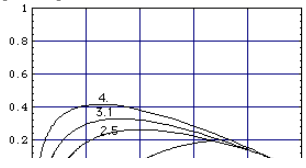
sigma = 1.3 (beta = 0.325, gammaG = 0.25)
s, i, r

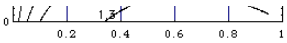


R[t]



phase space



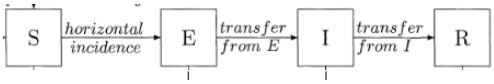


SEIR Model

by Gabriela Gomes et al. 21 May 2020
https://www.medrxiv.org/content/10.1101/2020.04.27.20081893v3.full.pdf
https://www.medrxiv.org/content/10.1101/2020.04.27.20081893v3.supplementary-material

Individual variation in susceptibility or exposure to SARS-CoV-2 lowers the herd immunity threshold

medRxiv, 21 May 2020
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7239079/
https://www.medrxiv.org/content/10.1101/2020.04.27.20081893v3.full.pdf



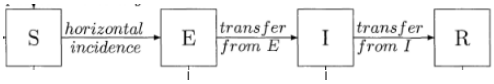
x lambda E(x) delta I(x) gamma

dS(x) / dt = - lambda x S(x)
dE(x) / dt = lambda x S(x) - delta E(x)
dI(x) / dt = delta E(x) - gamma I(x)

- x = susceptibility of individuals S(x) and I(x)
- <x> = mean susceptibility factor at epidemic onset.
- lambda = $(\beta/N)\int[\rho E(x) + I(x)]\,dx$
  - is the average force of infection upon susceptible individuals in a population of size
  - rho is a factor measuring the infectivity of individuals in compartment E in relation to those in I
- q(x): prior to the epidemic, susceptibility is described by a probability density function q(x) with
  - mean q(x) = 1 and
  - CV = $\langle (x-1)^2 \rangle$ explored as a parameter.
- $R_0 = \langle x \rangle(\beta/N)(\rho/\delta + 1/\gamma)$,
- $R_{eff}(t)$ (effective reproduction number, also denoted by R_e or R_t) is a time-dependent quantity obtained by multiplying R_o by the susceptibility of the population over time.

Abstract:
Abstract: As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spreads, the susceptible subpopulation is depleted causing the incidence of new cases to decline. Variation in individual susceptibility or exposure to infection exacerbates this effect. Individuals that are more susceptible or more exposed tend to be infected earlier, depleting the susceptible subpopulation of those who are at higher risk of infection. This selective depletion of susceptibles intensifies the deceleration in incidence. Eventually, susceptible numbers become low enough to prevent epidemic growth or, in other words, the herd immunity threshold (HIT) is reached.
Although estimates vary, simple calculations suggest that herd immunity to SARS- CoV-2 requires 60-70% of the population to be immune.
By fitting epidemiological models that allow for heterogeneity to SARS-CoV-2 outbreaks across the globe, we show that variation in susceptibility or exposure to infection reduces these estimates.
Accurate measurements of heterogeneity are therefore of paramount importance in controlling the COVID-19 pandemic.

We integrate continuous distributions of susceptibility or connectivity in otherwise basic epidemic models for COVID-19 and show that as the coefficient of variation (CV) increases from 0 to 4, the herd immunity threshold declines from over 60% to less than 10%.



x lambda E(x) delta I(x) gamma
β

S: Susceptible individuals (S) become exposed (E) at a rate dependent on
- their susceptibility x,
- the number of potentially infectious contacts β/N they engage in, and
- the total number of infectious people in the population (Integral([rho E(x) + I(x)] dx) per time unit.

E: Upon exposure, individuals (E) enter an asymptomatic incubation phase, during which they slowly become infectious.
- Thus, infectivity of exposed individuals is made to be 1/2 of that of infectious ones (rho = 0.5).

I: After a few days, individuals develop symptoms – on average, 4 days after the exposure to the virus (delta = 1/4 per day) – and become fully infectious.
R: They recover, i.e., they lose their infectiousness 4 days after that on average (gamma = 1/4 per day).

We have assumed that no reinfection can occur after recovery, which means absolute long-lasting immunity.

Once containment measures are put in place in each country,
- we postulate it takes 14 days until the maximum effectiveness of social distancing measures is reached.
- In the simulations presented throughout we have held this condition (maximum "lockdown" efficacy) for 30 days,
- after which period, social distancing measured are progressively relaxed, slowly returning to its original value (normality) after 1-year.
- Both the implementation and relaxing of the social distancing measures are imposed to be linear in this model.

We would need to estimate
- when local transmission started to occur (to), and
- the pace at which individuals infected each other in the very early stages of the epidemic (Ro).

To fully understand the interplay between herd immunity and the impact of NP interventions, we then set out to estimate
- the time at which social distancing measures started to have an impact on daily incidence (t_o^d), and
- what is their maximum effectiveness (d), for each country.

Two simplifying assumptions:
I. the fraction of infectious individuals reported as COVID-19 cases (reporting fraction) is 10%;
II. local transmission starts (t_o) when countries report
  - 1 case per 30 10^6 population in one day
  - i.e. when there are 10 infections per 30 10^6 population in one day

$\frac{dS(x)}{dt} = -x\frac{\beta}{N}\int_0^\infty [\rho E(x) + I(x)]\,dx\; S(x) = -x\,\lambda\,S(x)$ ..... (susceptibles)
$\frac{dE(x)}{dt} = -x\,\lambda\,S(x) - \delta E(x)$ ..... (infected normally called "exposed" who originally had susceptibility x) ..... (eq. 1)
$\frac{dI(x)}{dt} = \delta E(x) - \gamma I(x)$ ..... (infectives who originally had susceptibility x, i.e. with susceptibility x?)
$\frac{dR(x)}{dt} = \gamma I(x)$ ..... (recovereds)

notation
- S(x) = number of individuals with susceptibility x
- E(x) = number of individuals ("exposeds") who originally
  - had susceptibility x,
  - became exposed & infected but
  - are neither symptomatic nor infectious
- I(x) = number of individuals who originally had susceptibility x and became infectious
- **x = susceptibility**
  - <x> = mean susceptibility factor at epidemic onset.
  - lambda = $(\beta/N)\int[\rho E(x) + I(x)]\,dx$
    - is the average force of infection upon susceptible individuals in a population of size N,
    - corresponds to β / N I in homogeneous SIR model above.
  - rho is a factor measuring the infectivity of individuals in compartment E in relation to those in I .....(rho = 0.5)
  - $R_0 = \langle x \rangle(\beta/N)(\rho/\delta + 1/\gamma)$ = basic reproduction number ..... (eq. 2)
  - 1/delta = latency period .....(4 days)
  - 1/gamma = average recovery time .....(4 days)
  - q(x): **prior** to the epidemic (@ t = t_o), susceptibility x(t_o) is described by a probability density function q(x) with
    - mean q(x) = 1 and

- CV = $\langle (x-1)^2 \rangle$ explored as a parameter.

- **x = connectivity** = exposure to infection (dependent on social distancing) of individuals S(x) and I(x)
  - connectivity: variation in exposure to infection is primarily governed by patterns of connectivity among individuals. We incorporate this in the system (eq. 1) by adding variation in infectivity and assuming a positive correlation between susceptibility and infectivity
  - $\lambda = (\beta/N)(\int x[\rho E(x) + I(x)]\, dx / \int x q(x)\, dx)$
  - $R_0 = (\langle x^2 \rangle / \langle x \rangle)(\beta/N)(\rho/\delta + 1/\gamma)$ ..... (eq. 3)
  - where $\langle x \rangle$ and $\langle x^2 \rangle$ are the first and second moments of the distribution q(x) prior to the epidemic

- $R_{eff}(t)$ (also called R_e or R_t) = x(t) R_o (i.e. R_o multiplied by the susceptibility of the population over time, i.e. R_o S(t)/N = sigma s(t) ?)
  - [when $R_{eff}(t) = R_o$ (i.e. x(t) = 1) the model is called homogeneous ?]
- Once containment measures are put in place in each country,
  - we postulate it takes 14 days until the maximum effectiveness of social distancing measures is reached.
  - In the simulations presented throughout we have held this condition (maximum "lockdown" efficacy) for 30 days, after which period, social distancing measures are progressively relaxed, slowly returning to its original value (normality) after 1 year.
  - Both the implementation and relaxing of the social distancing measures are imposed to be linear in this model.
- t_o = estimate of the start of local disease transmission = time when 1 reported case per (3 10^6people day)
- t_o^d = estimate of the time at which social distancing measures started to have an impact on daily incidence
- d = maximum effectiveness of social distancing measures for each country
- y(k, theta) = simulated COVID-19 cases at day k after t_o
- theta = set of parameters Ro, t_o^d , d
- n = 91 = total number of days included in the analysis (day 91 = 30 April)
  - 1 = 1 February
  - 29 = 29 February
  - 30 = 1 March
  - 46 = 17 March
  - 48 = 19 March
  - 60 = 30 March, 62 = 1 April
  - 80 = 19 April

Probability Density Function of the gamma distribution ("Gamma Distribution")

$$q(x) = \frac{(\frac{x-\mu}{\beta})^{\gamma-1} \exp(-\frac{x-\mu}{\beta})}{\beta\, \Gamma(\gamma)} \quad \text{for } x >= \mu \text{ and } \gamma, \beta > 0$$

with
- gamma being the shape,
- mu the location,
- beta the scale parameter,
- the gamma function

$$\Gamma(\gamma) = \int_0^{\infty} t^{\gamma-1} e^{-t}\, dt$$

- the coefficient of variation

$$CV = \frac{1}{\sqrt{\gamma}}$$

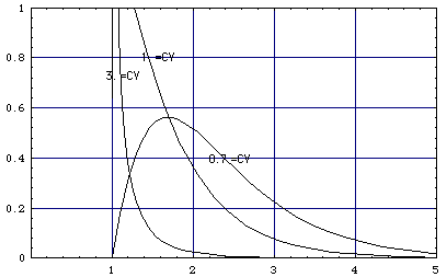
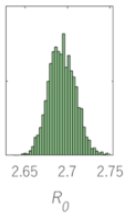


Fig. J1: q[x] = probability density function of the gamma distribution. Abscissa = x, ordinate = q(x), mu = 1, beta = 1,
- gamma =
  - 0.111 (CV = 3)
  - 1 (CV = 1)
  - 2.111 (CV = 0.7)

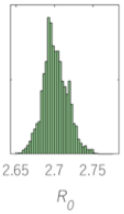
Gamma distributions with
- mu = 0, beta = 1 (standard distribution),
  - gamma = 0.1, 1.1, 2.1 (corresponding to CV = 3.2, 1, 0.7)

Germany

- susceptibility - 1



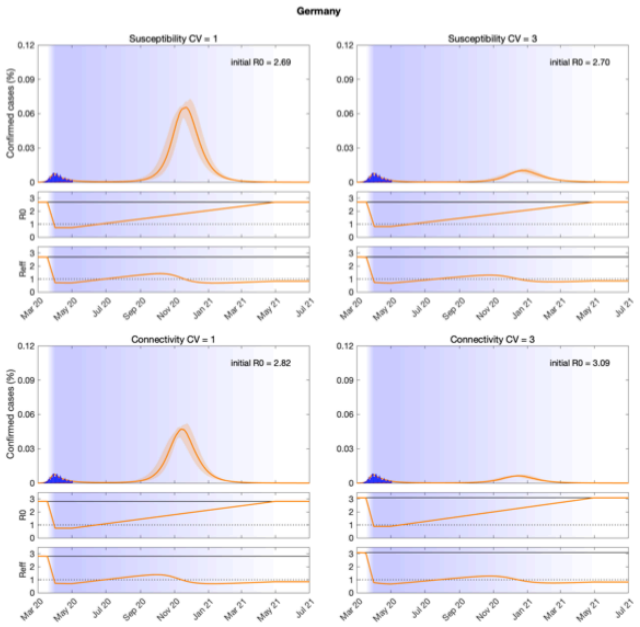
- susceptibility - 3



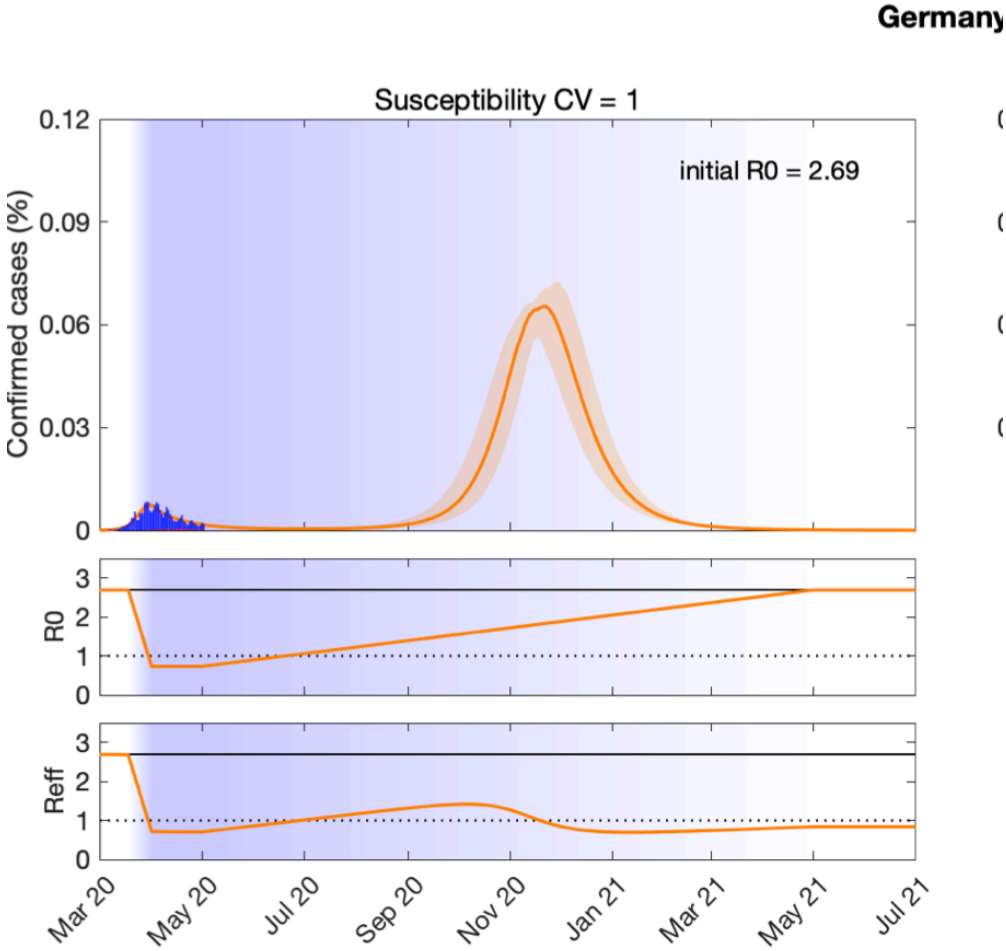
R_o for
- homogeneous model (5 percentile, median, 95 percentile) ..... CV=1: 2.662, 2.692, 2.722, CV=3: 2.663, 2.692, 2.723
- heterogeneous susceptibility model ..... CV=1: 2.664, 2.694, 2.725, CV=3: 2.671, 2.700, 2.735

- heterogeneous contacts model ..... CV=1: 2.781, 2.816, 2.847, CV=3: 3.045, 3.089, 3.129

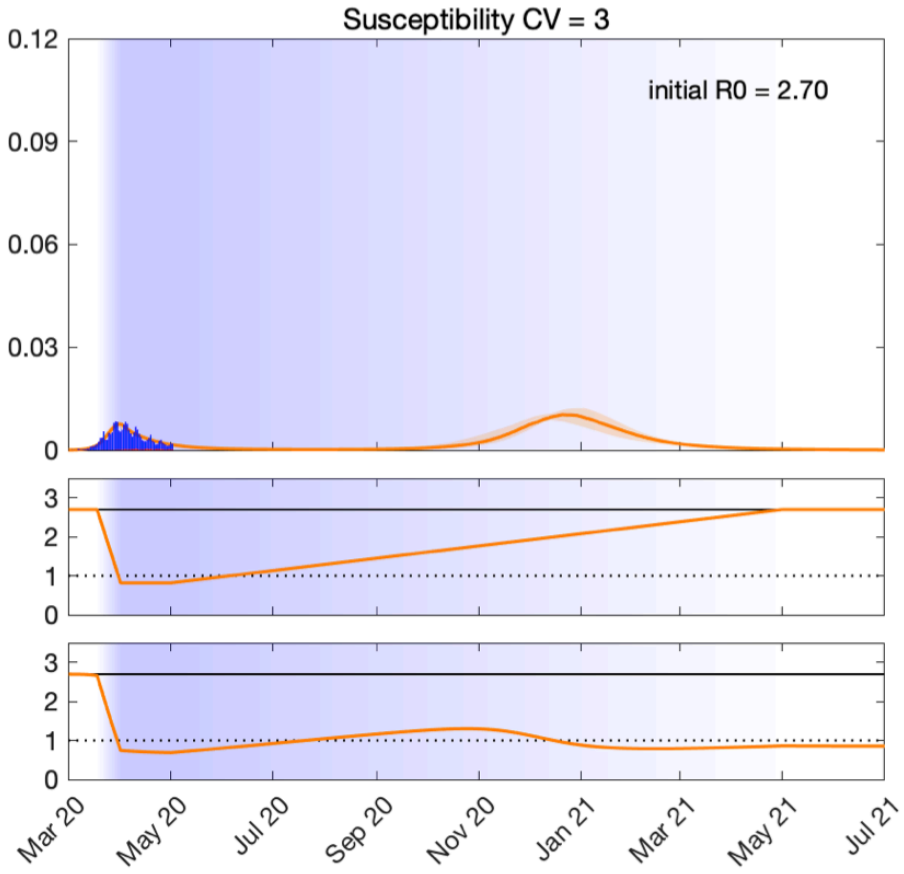
Figure S15



Supressed wave and subsequent dynamics in Germany. Blue bars are confirmed new cases and overlaid red bars represent deaths. Basic (R_0) and effective (R_{eff}) reproduction numbers are displayed on bottom panels. Blue shades represent social distancing periods. Curves represent median model predictions from 10^4 posterior samples. Orange shades represent 95% credible intervals.



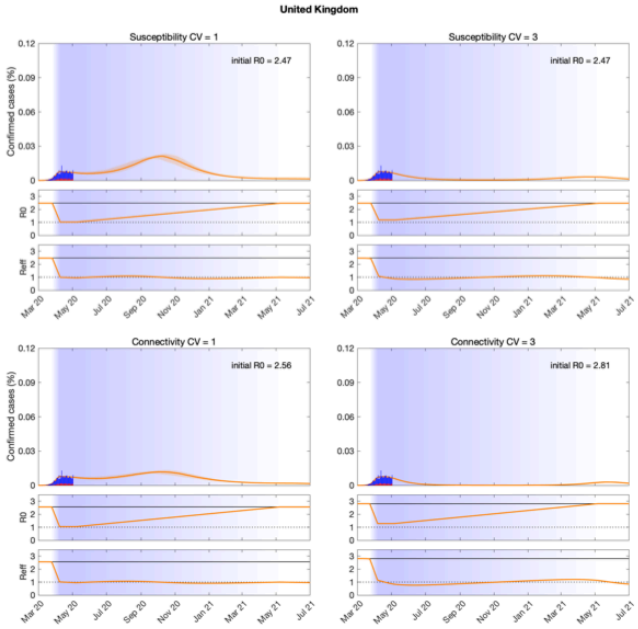
nany



connectivity = exposure

0.01% = 0.8 10^6, 0.12 % = 9.6 10^6

Figure S20



Supressed wave and subsequent dynamics in United Kingdom. Blue bars are confirmed new cases and overlaid red bars represent deaths. Basic (R_0) and effective (R_{eff}) reproduction numbers are displayed on bottom panels. Blue shades represent social distancing periods. Curves represent median model predictions from 10^4 posterior samples. Orange shades represent 95% credible intervals.

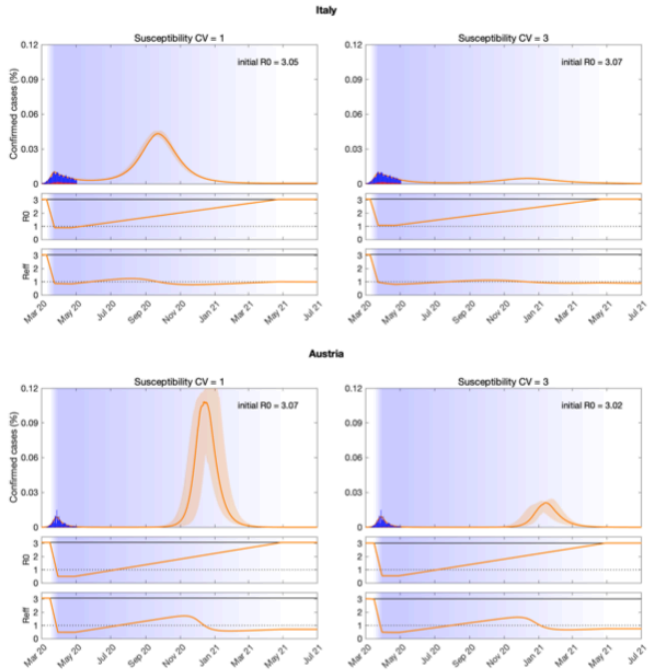


Figure 1: The effect of variation in susceptibility to infection on the size of epidemics. Suppressed wave and subsequent dynamics in Italy and Austria. Blue bars are confirmed new cases and overlaid red bars represent deaths. Basic (R_0) and effective (R_{eff}) reproduction numbers are displayed on bottom panels. Blue shades represent social distancing (intensity reflected in R_0 trends and shade density). Susceptibility factors were implemented as gamma distributions. Consensus parameter values (Materials and Methods): $\delta = 1/4$ per day; $\gamma = 1/4$ per day; and $\rho = 0.5$. Fraction of infected individuals identified as positive (reporting fraction): $p = 0.1$. R_0 and social distancing parameters were estimated by Bayesian inference as described in Supplementary Materials. Curves represent median model predictions from 10^4 posterior samples. Orange shades represent 95% credible intervals.

Result

Individual variation in susceptibility or exposure (connectivity) accelerates the acquisition of immunity in populations due to selection by the force of infection. More susceptible and more connected individuals have a higher propensity to be infected and thus are likely to become immune earlier. Due to this selective immunization, heterogeneous populations require less infections to cross their herd immunity thresholds (HITs) than homogeneous (or not sufficiently heterogeneous) models would suggest.

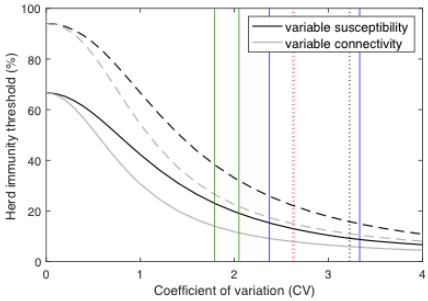
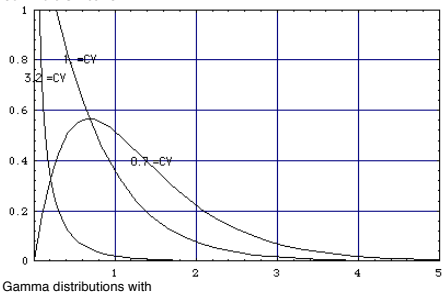


Figure 3: Herd immunity threshold with variation in susceptibility and exposure to infection. Curves generated with the model (Equation 1) with gamma distributed susceptibility (black) or connectivity (gray) assuming $R_0 = 3$: (solid) herd immunity threshold; (dashed) final size of uncontrolled epidemic. Vertical lines indicate coefficients of individual variation for several infectious diseases according to literature: (solid green) susceptibility or exposure to malaria [Amazon 1.79 (*6*), Africa 2.05 (*7*)]; (solid blue) susceptibility or exposure to tuberculosis [Portugal 2.37, Brazil 3.33 (*8*)]; (dotted red) infectiousness for SARS-CoV-1 [Singapore 2.62, Beijing 2.64 (*9*)]; (dotted black) infectiousness for SARS-CoV-2 [3.22 (*10*)].

Gamma distribution



Gamma distributions with

- mu = 0, beta = 1 (standard distribution),
- gamma = 0.1, 1.1, 2.1 (corresponding to $\text{CV} = \frac{1}{\sqrt{\gamma}}$ = 3.2, 1, 0.7, CV being independent from mu and beta)

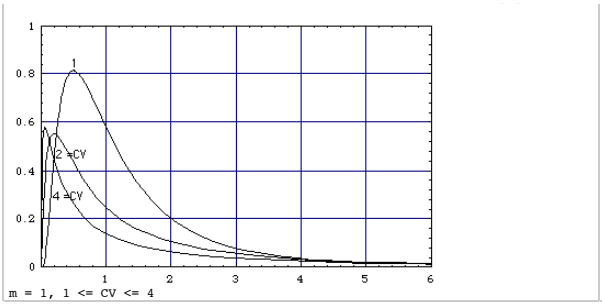
Log-normal distribution

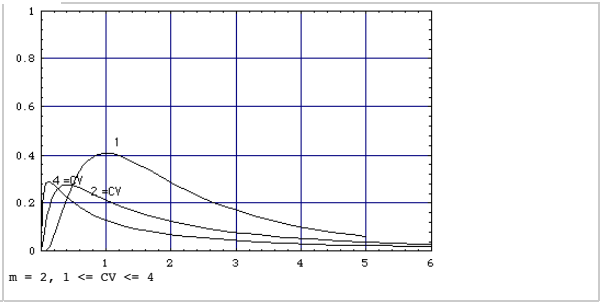
- LogNormal1(μ,σ) with mean, μ, and standard deviation, σ, both on the log-scale [23]

$$P(x;\boldsymbol{\mu},\boldsymbol{\sigma}) = \frac{1}{x\sigma\sqrt{2\pi}} \exp\left[\frac{-(\log x - \mu)^2}{2\sigma^2}\right]$$

- LogNormal4(m,cv) with median, m, and coefficient of variation, cv, both on the natural scale

$$P(x;\boldsymbol{m},\boldsymbol{cv}) = \frac{1}{x\sqrt{\log(cv^2+1)}\sqrt{2\pi}} \exp\left[\frac{-[\log(x/m)]^2}{2\log(cv^2+1)}\right]$$

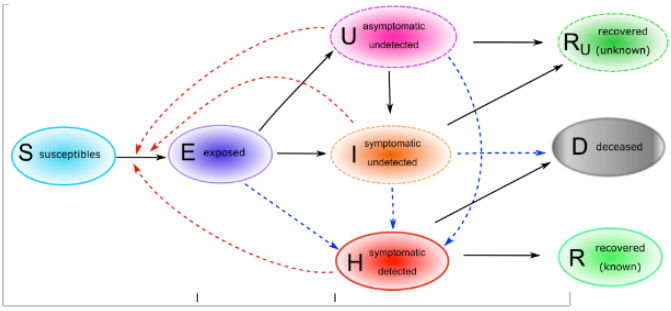




SEIR Model

Barbarossa MV, Fuhrmann J, Meinke JH, Krieg S, Varma HV, Castelletti N, et al. (2020)
Modeling the spread of COVID-19 in Germany: Early assessment and possible scenarios.
PLoS ONE 15(9): e0238559.
18 April 2020
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0238559

Fuhrmann, J., Barbarossa, M.V.
The significance of case detection ratios for predictions on the outcome of an epidemic - a message from mathematical modelers.
Arch Public Health **78,** 63 (2020).
4 May 2020
https://doi.org/10.1186/s13690-020-00445-8
https://archpublichealth.biomedcentral.com/articles/10.1186/s13690-020-00445-8



symptomatic not yet detected infectives

S ---lambda---> E --- (1 - eta$_0$) rho$_o$ gamma$_E$ ----> I --- (1 - eta$_1$) gamma$_I$ ----------> T symptomatic undetected

I I v

I eta$_1$ gamma$_I$ R

I v ^

+---- eta$_o$ rho$_o$ gamma$_E$ --------> H --- (1 - delta$_H$) gamma$_H$ ---------+ detected

I ^

I eta$^1_1$ gamma$_U$

I I

+---- (1 - rho$_o$) gamma$_E$ --------> U --- (1 - eta$^1_1$) gamma$_U$ ----------> R$_U$ asymptomatic undetected

asymptomatic undetected infectives

dS / dt = - lambda S	(susceptibles)
dE/ dt = lambda S - gamma$_E$ E	(exposeds, i.e. without symptoms)
dU/ dt = (1 - rho$_o$) gamma$_E$ E - gamma$_U$ U	(asymptomatic infectives)
dI/ dt = (1 - eta$_o$) rho$_o$ gamma$_E$ E - gamma$_I$ I	(symptomatic infectives)
dH / dt = eta$_o$ rho$_o$ gamma$_E$ E + eta$^1_1$ gamma$_U$ U + eta$_1$ gamma$_I$ I - gamma$_H$ H	(diagnosed infectives (cases))
dR / dt = (1 - eta$_1$) gamma$_I$ I + (1 - delta$_H$) gamma$_H$ H	(recovered from detected infectives)
dR$_U$ / dt = (1 - eta$^1_1$) gamma$_U$ U + (1 - eta$_1$) gamma$_I$ I	(recovered from asymptomatics)
dD / dt = delta$_H$ gamma$_H$ H	(deceaseds)

notation

- S = number of susceptibles
- E = number of individuals, who
  - became exposed & infected but
  - are neither symptomatic nor infective
- U = number of asymptomatic undetected infectives
- I = number of symptomatic not yet detected infectives
- H = number of reported cases (tested infectives)
- N = 83 10^6
- $\lambda = (\beta_I I + \beta_U U + \beta_H H)/(N - D)$
  - fitted β_U mean (5 ...95 percentile) = 1.59 (1.36...1.89), (mean ln2/β_U = 0.44 d)
  - $\beta_I = 0.8\ \beta_U$ (mean ln2/β_I = 0.85 d)
  - $\beta_H = 0.1\ \beta_U$ (mean ln2/β_H = 7 d)
- 1 / gamma$_E$ = mean incubation period ----------> 5.5 d (literature)
- 1 / gamma$_I$ = 1 / gamma$_H$ mean duration of symptomatic infection ----------> 7 d (literature)
- 1 / gamma$_U$ = mean duration of asymptomatic infection ----------> 7 d (literature)
- delta$_H$ = case mortality of undetected infectives ----------> 0.057 (literature)
- rho$_o$ = probability of developing symptoms (after 5.5 days) ----------> 0.67 (literature)
- eta$_o$ = probability of disease being detected during latency in symptomatics ----------> fitted
  (1 - eta$_o$) mean (5 ...95 percentile) = 0.23 (0.58 ... 0.92)
- eta$_1$ = probability of disease being detected while symptomatic ----------> fitted
- eta$^1_1$ = probability of disease being detected while asymptomatic ----------> assumed
- R ----------> mean (5 ...95 percentile) = 6.99 (5.84...8.35)
- $$\mathcal{R}_0 = \frac{(1-\eta_0)\rho_0\beta_I}{\gamma_I} + \frac{\beta_H}{\gamma_H}(\eta_0\rho_0 + (1-\eta_0)\rho_0\eta_1 + (1-\rho_0)\hat{\eta}_1) + \frac{\beta_U(1-\rho_0)}{\gamma_U}.$$

Susceptible individuals can be infected via contacts with

- asymptomatic (transmission rate β_U),
- symptomatic undetected (β_I) and
- reported cases (β_H).

We assume that

- asymptomatic infectives do not restrict their contacts to others, and therefore have higher transmission rates than symptomatic infected individuals.
- detected (reported) cases to reduce their contacts even further.

Due to limitations in the identifiability of the parameters with the available data,

- we fix the ratios β_I / β_H and β_I / β_U and estimate the latter.

NCBI SARS-CoV-2 Resources

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Joachim Gruber