# Time-varying epidemic transmission in heterogeneous networks

Sara Sottile\*
University of Trento

June 10, 2021 PhD Seminar at University of Groningen

\*Joint work with Prof. Xinzhi Liu - University of Waterloo

► Epidemic models:

- ► Epidemic models:
  - ightharpoonup assumptions and formulation

- ► Epidemic models:
  - assumptions and formulation
  - ► Basic Reproduction Number

- ► Epidemic models:
  - assumptions and formulation
  - ► Basic Reproduction Number
  - ► classic results

- ► Epidemic models:
  - ▶ assumptions and formulation
  - ► Basic Reproduction Number
  - ► classic results

► Beyond classic models:

- ► Epidemic models:
  - assumptions and formulation
  - ► Basic Reproduction Number
  - ► classic results

- ▶ Beyond classic models:
  - ► heterogeneous networks

- ► Epidemic models:
  - assumptions and formulation
  - ► Basic Reproduction Number
  - ► classic results

- ▶ Beyond classic models:
  - ► heterogeneous networks
  - ▶ switched transmission rate

- ► Epidemic models:
  - assumptions and formulation
  - ► Basic Reproduction Number
  - ► classic results

- ▶ Beyond classic models:
  - ► heterogeneous networks
  - ▶ switched transmission rate
  - stability results

- ► Epidemic models:
  - assumptions and formulation
  - ► Basic Reproduction Number
  - ► classic results

- ▶ Beyond classic models:
  - ► heterogeneous networks
  - ▶ switched transmission rate
  - ▶ stability results
  - ► case study: the SVEIR model

ightharpoonup Constant population N: model can be normalized.

- ightharpoonup Constant population N: model can be normalized.
- ► Multi-compartment model: Susceptible S, Infectious I, Recovered R, Exposed E, Vaccinated V, etc.

- ightharpoonup Constant population N: model can be normalized.
- ► Multi-compartment model: Susceptible S, Infectious I, Recovered R, Exposed E, Vaccinated V, etc.
- ► Mass mixing: all the individuals have a uniform contact pattern.

- ► Constant population N: model can be normalized.
- ► Multi-compartment model: Susceptible S, Infectious I, Recovered R, Exposed E, Vaccinated V, etc.
- ► Mass mixing: all the individuals have a uniform contact pattern.
- ▶ Parameters are constant in time: no seasonality in transmission rate, recovery rate, birth/death rate.

- ightharpoonup Constant population N: model can be normalized.
- ► Multi-compartment model: Susceptible S, Infectious I, Recovered R, Exposed E, Vaccinated V, etc.
- ► Mass mixing: all the individuals have a uniform contact pattern.
- ▶ Parameters are constant in time: no seasonality in transmission rate, recovery rate, birth/death rate.
- ▶ Negligible incubation period: no delay term in equations.

 ${\bf System\ of\ ODEs}\hbox{: movements between compartments}.$ 

System of ODEs: movements between compartments.

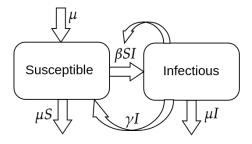
Force of the infection = contact rate 
$$\times$$
 risk of infection  $\times$  proportion of infectious = transmission rate  $\times$  proportion of infectious =  $\beta \times \frac{I}{N}$ .

## SIS Model

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{dt}} S(t) = \mu - \beta SI - \mu S + \gamma I, \\ \frac{\mathrm{d}}{\mathrm{dt}} I(t) = \beta SI - (\gamma + \mu)I. \end{cases}$$

## SIS Model

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{dt}} S(t) = \mu - \beta SI - \mu S + \gamma I, \\ \frac{\mathrm{d}}{\mathrm{dt}} I(t) = \beta SI - (\gamma + \mu)I. \end{cases}$$

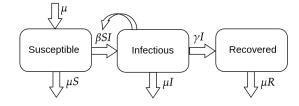


## SIR Model

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{dt}} S(t) = \mu - \beta SI - \mu S, \\ \frac{\mathrm{d}}{\mathrm{dt}} I(t) = \beta SI - (\gamma + \mu)I, \\ \frac{\mathrm{d}}{\mathrm{dt}} R(t) = \gamma I - \mu R. \end{cases}$$

### SIR Model

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{dt}} S(t) = \mu - \beta SI - \mu S, \\ \frac{\mathrm{d}}{\mathrm{dt}} I(t) = \beta SI - (\gamma + \mu)I, \\ \frac{\mathrm{d}}{\mathrm{dt}} R(t) = \gamma I - \mu R. \end{cases}$$



### Definition

The **Basic Reproduction Number** (BRN), denoted by  $\mathcal{R}_0$ , is defined as the average number of secondary cases an average primary case produces in a totally susceptible population.

### Definition

The **Basic Reproduction Number** (BRN), denoted by  $\mathcal{R}_0$ , is defined as the average number of secondary cases an average primary case produces in a totally susceptible population.

Disease	BRN
Measles	12 - 18
Pertussis	12 - 17
Rubella	6 - 7
Influenza	1.5 - 1.8

In the epidemic models with demography the system admits always a **disease-free equilibrium**, that is the equilibrium point in which  $I^* = 0$ . Moreover, under certain conditions, it admits also an **endemic equilibrium**, that is the equilibrium in which the epidemic is persistent.

In the epidemic models with demography the system admits always a **disease-free equilibrium**, that is the equilibrium point in which  $I^* = 0$ . Moreover, under certain conditions, it admits also an **endemic equilibrium**, that is the equilibrium in which the epidemic is persistent.

It can be shown that the following result holds.

#### Theorem

- The disease-free equilibrium is globally asymptotically stable (g.a.s.) if  $\mathcal{R}_0 < 1$ .
- ▶ If  $\mathcal{R}_0 \geq 1$ , then the endemic equilibrium exists and it is g.a.s.

Goals

Goal: reduce the value of the BRN below the unity.

Goals 9

Goal: reduce the value of the BRN below the unity.

 ${\bf Tools:}\ \ quarantine,\ travel\ restrictions,\ vaccination.$ 

Nodes in the network represent individuals and edges the interactions among them. The **degree** of a node is defined as the number of edges (neighbourhood) of an individual.

Nodes in the network represent individuals and edges the interactions among them. The **degree** of a node is defined as the number of edges (neighbourhood) of an individual.

Degree-based mean-field (DBMF): grouping nodes with respect to their state and degree.

Nodes in the network represent individuals and edges the interactions among them. The **degree** of a node is defined as the number of edges (neighbourhood) of an individual.

Degree-based mean-field (DBMF): grouping nodes with respect to their state and degree.

We denote with K the set of all assumed degrees in the network and with  $X_k(t)$  the proportion of nodes of degree k at time  $t \geq 0$  in the compartment X.

Force of the infection = degree-dependent infection rate 
$$\times \text{ proportion of infectious}$$
 
$$= \lambda(k) \times \Theta(t),$$

Force of the infection = degree-dependent infection rate 
$$\times \text{ proportion of infectious}$$
 
$$= \lambda(k) \times \Theta(t),$$

where

$$\Theta(t) = \frac{1}{\langle k \rangle} \sum_{k \in K} \varphi(k) p(k) I_k(t); \qquad (uncorrelated network)$$

Force of the infection = degree-dependent infection rate  $\times \text{ proportion of infectious}$   $= \lambda(k) \times \Theta(t),$ 

where

- $\Theta(t) = \frac{1}{\langle k \rangle} \sum_{k \in K} \varphi(k) p(k) I_k(t); \qquad (uncorrelated network)$
- $\triangleright \varphi(k)$  is the *infectivity*, that is the average number of links from which a node with degree k can transmit the disease.

Seasonality of the disease  $\Longrightarrow$  switched transmission rate.

Seasonality of the disease  $\Longrightarrow$  switched transmission rate.

Consider a switching rule

$$\sigma: [0, +\infty) \longrightarrow P := \{1, \dots, m\}.$$

and a set of switching times  $\{t_l\}$ .

Seasonality of the disease  $\Longrightarrow$  switched transmission rate.

Consider a switching rule

$$\sigma: [0, +\infty) \longrightarrow P := \{1, \dots, m\}.$$

and a set of switching times  $\{t_l\}$ .

If  $\sigma(t) = i_l \in P$  for all  $t \in [t_{l-1}, t_l)$ , then  $\lambda(t) = \lambda_{i_l}$ .

Seasonality of the disease  $\Longrightarrow$  switched transmission rate.

Consider a switching rule

$$\sigma: [0, +\infty) \longrightarrow P := \{1, \dots, m\}.$$

and a set of switching times  $\{t_l\}$ .

If  $\sigma(t) = i_l \in P$  for all  $t \in [t_{l-1}, t_l)$ , then  $\lambda(t) = \lambda_{i_l}$ .

▶ Different BRNs for each subsystem.

Seasonality of the disease  $\Longrightarrow$  switched transmission rate.

Consider a switching rule

$$\sigma: [0, +\infty) \longrightarrow P := \{1, \dots, m\}.$$

and a set of switching times  $\{t_l\}$ .

If  $\sigma(t) = i_l \in P$  for all  $t \in [t_{l-1}, t_l)$ , then  $\lambda(t) = \lambda_{i_l}$ .

- ▶ Different BRNs for each subsystem.
- ► Time-weighted average BRN

$$\langle \mathcal{R}_{\sigma} \rangle = \sup_{t \geq h} \frac{1}{t} \sum_{i \in P} \mathcal{R}_{0,i} T_i(t), \text{ for some } h > 0.$$

where  $\{T_i(t)\}\$  are the total activation times.

### Theorem (SIS, SIR, SIRS, SEIR)

If  $\mathcal{R}_{0,i} \leq 1$  for all  $i \in P$ , then the disease-free equilibrium is asymptotically stable in the biologically relevant domain.

#### Theorem (SIS, SIR, SIRS, SEIR)

If  $\mathcal{R}_{0,i} \leq 1$  for all  $i \in P$ , then the disease-free equilibrium is asymptotically stable in the biologically relevant domain.

## Theorem (SIS, SIR, SIRS)

If  $\langle \mathcal{R}_{\sigma} \rangle \leq 1$ , then the disease-free equilibrium is exponentially stable in the biologically relevant domain.

### Theorem (SIS, SIR, SIRS, SEIR)

If  $\mathcal{R}_{0,i} \leq 1$  for all  $i \in P$ , then the disease-free equilibrium is asymptotically stable in the biologically relevant domain.

# Theorem (SIS, SIR, SIRS)

If  $\langle \mathcal{R}_{\sigma} \rangle \leq 1$ , then the disease-free equilibrium is exponentially stable in the biologically relevant domain.

**SEIR Model:** it is not possible to prove a result for  $\langle \mathcal{R}_{\sigma} \rangle$ .

► Not constant population: the model is subject to a constraint.

- ▶ Not constant population: the model is subject to a constraint.
- ► Control with imperfect vaccination: vaccines administrated to newborns, immigrants and susceptible.

- ▶ Not constant population: the model is subject to a constraint.
- ► Control with imperfect vaccination: vaccines administrated to newborns, immigrants and susceptible.
- ▶ Peak every third years:

$$\lambda_i(t) = \begin{cases} \lambda_1 & \text{every third years,} \\ \lambda_2 & \text{otherwise,} \end{cases}$$

with  $\lambda_1 \gg \lambda_2$ .

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{dt}} S_k(t) = (1-p)\rho + (1-\chi)\alpha V_k - (\nu+\rho)S_k + \psi I_k S_k - \lambda_i k S_k \Theta, \\ \frac{\mathrm{d}}{\mathrm{dt}} V_k(t) = p\rho + \nu S_k - ((1-\chi)\alpha + \omega \chi + \rho)V_k + \psi I_k V_k, \\ \frac{\mathrm{d}}{\mathrm{dt}} E_k(t) = \lambda_i k S_k \Theta - \psi E_k I_k - (\sigma+\rho)E_k, \\ \frac{\mathrm{d}}{\mathrm{dt}} I_k(t) = \sigma E_k - (\gamma+\rho+\psi)I_k + \psi I_k^2, \end{cases}$$

where  $k \in K$  and i = 1, 2.

For i = 1, 2

For i = 1, 2

$$\mathcal{R}_{0,i} = \frac{\lambda_i \sigma \rho [(1-\chi)\alpha + (\omega \chi + \rho)(1-p)]}{(\sigma + \rho)(\gamma + \rho + \psi)[(\nu + \rho)(\omega \chi + \rho) + (1-\chi)\alpha \rho]} \frac{\langle k^2 \rangle}{\langle k \rangle}.$$

For i = 1, 2

$$\mathcal{R}_{0,i} = \frac{\lambda_i \sigma \rho [(1-\chi)\alpha + (\omega \chi + \rho)(1-p)]}{(\sigma + \rho)(\gamma + \rho + \psi)[(\nu + \rho)(\omega \chi + \rho) + (1-\chi)\alpha \rho]} \frac{\langle k^2 \rangle}{\langle k \rangle}.$$

Since the switching rule is periodic

$$\langle \mathcal{R}_0 \rangle = \frac{1}{\Omega} \sum_{i \in P} \mathcal{R}_{0,i} \tau_i.$$

In our model we find  $\Omega = 3$ ,  $\tau_1 = 1$  and  $\tau_2 = 2$ , then

$$\langle \mathcal{R}_0^{\text{SVEIR}} \rangle = \frac{1}{3} \left( \mathcal{R}_{0,1} + 2 \cdot \mathcal{R}_{0,2} \right).$$

► Scale free-network.

- ► Scale free-network.
  - $\blacktriangleright\,$  Preferential Attachment Algorithm (PAA).

- ► Scale free-network.
  - ▶ Preferential Attachment Algorithm (PAA).
  - ▶ Power-degree distribution  $p(k) = \frac{2m^2}{k^3}$ .

- ► Scale free-network.
  - ► Preferential Attachment Algorithm (PAA).
  - ▶ Power-degree distribution  $p(k) = \frac{2m^2}{k^3}$ .
- ▶ Network with 100 nodes,  $\langle k \rangle = 4.4823$  and  $\langle k^2 \rangle = 17.0203$ .  $k \in \{2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 21, 22, 32\}$ .

17

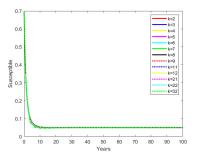
- ► Scale free-network.
  - ► Preferential Attachment Algorithm (PAA).
  - ▶ Power-degree distribution  $p(k) = \frac{2m^2}{k^3}$ .
- ▶ Network with 100 nodes,  $\langle k \rangle = 4.4823$  and  $\langle k^2 \rangle = 17.0203$ .  $k \in \{2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 21, 22, 32\}$ .

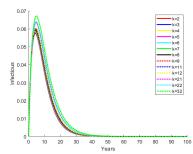


Both  $\mathcal{R}_{0,1}, \mathcal{R}_{0,2} \leq 1$  and  $\langle \mathcal{R}_{\sigma}^{\text{SVEIR}} \rangle < 1$ .

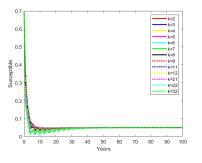
The disease-free equilibrium point  $E_0$  is reached.

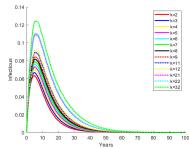
Both  $\mathcal{R}_{0,1}, \mathcal{R}_{0,2} \leq 1$  and  $\langle \mathcal{R}_{\sigma}^{\mathrm{SVEIR}} \rangle < 1$ . The disease-free equilibrium point  $E_0$  is reached.





 $\mathcal{R}_{0,1} > 1$  and  $\mathcal{R}_{0,2} \leq 1$ , but  $\langle \mathcal{R}_{\sigma}^{\mathrm{SVEIR}} \rangle < 1$ . The disease-free equilibrium point  $E_0$  is reached.  $\mathcal{R}_{0,1} > 1$  and  $\mathcal{R}_{0,2} \leq 1$ , but  $\langle \mathcal{R}_{\sigma}^{\mathrm{SVEIR}} \rangle < 1$ . The disease-free equilibrium point  $E_0$  is reached.





Both  $\mathcal{R}_{0,1}, \mathcal{R}_{0,2} \geq 1$  and  $\langle \mathcal{R}_{\sigma}^{\text{SVEIR}} \rangle > 1$ .

In this case the endemic equilibrium exists in all the subsystems and the epidemic is persistent (with an oscillating beavhiour)

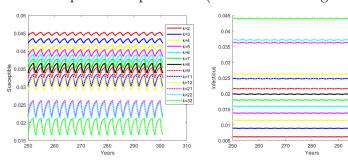
k=3

k=4

k=32

300 310

Both  $\mathcal{R}_{0,1}, \mathcal{R}_{0,2} \geq 1$  and  $\langle \mathcal{R}_{\sigma}^{\text{SVEIR}} \rangle > 1$ . In this case the endemic equilibrium exists in all the subsystems and the epidemic is persistent (with an oscillating beavhiour)

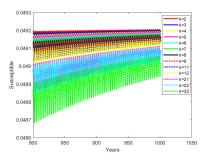


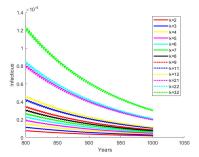
 $\mathcal{R}_{0,1} > 1$  and  $\mathcal{R}_{0,2} \leq 1$ , but  $\langle \mathcal{R}_{\sigma}^{\text{SVEIR}} \rangle > 1$ .

The epidemic is going to the eradication slowly (more than 1000 years). Thus the disease is persistent in the population.

 $\mathcal{R}_{0,1} > 1$  and  $\mathcal{R}_{0,2} \leq 1$ , but  $\langle \mathcal{R}_{\sigma}^{\mathrm{SVEIR}} \rangle > 1$ .

The epidemic is going to the eradication slowly (more than 1000 years). Thus the disease is persistent in the population.





▶ The SEIR model has the same beavhiour, since it is a particular case of the SVEIR. Clearly, without control strategies, we need more years to eradicate the disease when it is possible.

- ▶ The SEIR model has the same beavhiour, since it is a particular case of the SVEIR. Clearly, without control strategies, we need more years to eradicate the disease when it is possible.
- ► The higher the degree, the higher the number of the infectious in that compartment. The opposite happens with susceptible and vaccinated.

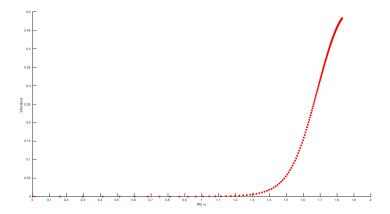
We found some threshold results in order to eradicate the epidemic in model wich take into account both the heterogeneity of the population and the seasonality.

We found some threshold results in order to eradicate the epidemic in model wich take into account both the heterogeneity of the population and the seasonality.

For simpler models (SIR, SIS, SIRS), the threshold's results on the time-weighted average BRN are the same as for the BRN in classic models. For more complicated models, like the SEIR, we found a threshold condition for the eradication of the disease but not for the persistence. For more complicated models, like the SEIR, we found a threshold condition for the eradication of the disease but not for the persistence.

How does  $\langle \mathcal{R}_{\sigma} \rangle$  affect the total number of the infectious in the network? For the SEIR model we studied  $\langle \mathcal{R}_{\sigma} \rangle$  as a function of the parameters of the model and how its expression influences the total number of the infectious in the network. We found that the persitence of the disease occurs when  $\langle \mathcal{R}_{\sigma} \rangle \gtrsim 1.3$ .

For example, if we analyze the expression of  $\langle \mathcal{R}_{\sigma} \rangle$  as a function of the incubation period  $\sigma$ , simulations suggest that the eradication of the disease occurs also for values of  $\langle \mathcal{R}_{\sigma} \rangle > 1$ .



More details about this work can be found in: Sottile, S. and Liu, X. Time-varying epidemic transmission in heterogeneous networks and applications to measles, Journal of Biological Systems, Vol. 28, No. 4 (2020), pp. 1-26.

More details about this work can be found in: Sottile, S. and Liu, X. Time-varying epidemic transmission in heterogeneous networks and applications to measles, Journal of Biological Systems, Vol. 28, No. 4 (2020), pp. 1-26.

#### Further works:

- consider also the infectivity changing according to a switching rule (for example to describe isolations or quarantines);
- ▶ using different switching rules than piecewise functions;
- ▶ applications to temporal networks.

# Thank you for your attention