Scenarios in deliberate release of infective agents:

Vaccination policies and spread in space

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Mathematical Epidemiology
= Mathematics of Infectious Diseases
can provide:

- conditions for transmission of disease
- estimating the size of epidemics
- designing prevention policies

Probability of deliberate release
and design of release cannot be modeled !

Present situation:

- recent public attention does not reflect the presence of immediate threat
- possible future threats
- with low probability
- but large damages
- affecting individual lives
- and economic and social structure

Problems of implementation:

Ethic dilemma of public health: balance individual goals with economic restrictions

Vaccination as an example:
individual and public goals may diverge because of vaccination risk !

Variable public attention: Example HIV !

Release of infectious agents is an **ethical** and a **political** problem !!

Several **scenarios** with distinctive features

- agent communicable from host to host

- only from the environment to the host

- agent released locally from one or several sources

- is released locally and spreads by wind

- agent is spread out over a wide area

Combination of these features: few basic scenarios some of which are more likely than others.

Example:
local emission of non-communicable agent
mathematics restricted to risk analysis
and estimates for prevention policies
theory of rare events (Gumbel)
health insurance versus industrial insurance

Our Scenario:
communicable agent released
at one or few locations in space

We do not consider the probability for deliberate release to occur, instead we study

conditions for spread

policies which reduce the impact

Aspects:

- rate of transmission from infecteds to susceptibles
- rate of removal of infecteds
- contacts between individuals at different space positions
- vaccination policies

Basic models with vaccination

susceptibles S, infecteds I, recovereds R

$$\begin{aligned}\dot{S} &= -\beta SI - \psi S \\ \dot{I} &= \beta SI - \alpha I \\ \dot{R} &= \alpha I + \psi S\end{aligned}$$

β infection rate, α recovery rate,
ψ vaccination rate

"reproduction number"

$$R(\psi) = \beta/\alpha$$

independent of ψ

disease dies out for lack of susceptibles

How many cases?

We must study the **transient** evolution !

Endemic situation only if new susceptibles supplied by loss of immunity
or by demographic renewal

$$\begin{aligned}\dot{S} &= \mu - \beta S I - \mu S - \psi S \\ \dot{I} &= \beta S I - \alpha I - \mu I \\ \dot{R} &= \alpha I - \mu R + \psi S\end{aligned}$$

Reproduction number

$$R(\psi) = \frac{\mu\beta}{(\alpha+\mu)(\mu+\psi)} = R_0 - \frac{\psi}{(\mu+\psi)} R_0$$

Prevalence

$$\bar{I}(\psi) = \frac{\mu\beta - (\alpha+\mu)(\mu+\psi)}{\beta(\alpha+\mu)}$$

critical vaccination rate

$$\psi_0 = \mu(\frac{\beta}{\alpha + \mu} - 1) = \mu(R_0 - 1)$$

which drives $\bar{I}(\psi)$ to zero and $R(\psi)$ to below 1 simultaneously

In general **two different problems:**

I) Vaccinate to reduce reproduction number
linear theory at uninfected equilibrium

II) Vaccinate to reduce prevalence
nonlinear theory at infected equilibrium

Klaus Dietz, Martin Eichner, Johannes Müller
Maximal reduction at given costs
Achieve goal at minimal costs
H. + Müller 1993, Müller 2000/2001

in simple cases bifurcation is **forward**
in multigroup models (vaccination, education, control) there may be **backward** bifurcations

Levin, Liu, Iwasa, Hethcote, Castillo-Chavez+H., van den Driessche +H.

backward bifurcation implies:

- critical levels for crucial parameters **cannot** be obtained by linearizing at uninfected state
- reproduction number **loses** significance
- there may be **hysteresis** effects

Hysteresis: Let a situation deteriorate by not enforcing vaccination policies, and later return to the original strict policy, then prevalence will not respond, but only, when a much more rigorous program is installed

Message: Low impact control or weak education policies are worse than doing nothing

Spread in space

population structured by space

contact distribution versus diffusion
D. Kendall 1965
J.V. Noble 1974, A. Källén 1984

contact model

$$\begin{aligned} S_t &= -\beta\, S\, k * I \\ I_t &= \beta\, S\, k * I - \alpha I \end{aligned}$$

$k \geq 0$ is a convolution kernel, $k * 1 = 1$

diffusion model

$$\begin{aligned} S_t &= -\beta S I \\ I_t &= \beta S I - \alpha I + D(k * I - I) \end{aligned}$$

limiting cases of a general model with **sedentary** and **migrating** infecteds

$$\begin{aligned} S_t &= -S(\beta_1 U + \beta_2 V) \\ V_t &= \delta(k * V - V) - \alpha V + \gamma_1 U - \gamma_2 V \\ U_t &= S(\beta_1 U + \beta_2 V) - \alpha U - \gamma_1 U + \gamma_2 V \end{aligned}$$

Case 1: Fast switching between the sedentary and the migrating state

Scaling

$$\gamma_1 = \rho_1/\epsilon, \quad \gamma_2 = \rho_2/\epsilon$$

reaction diffusion system for susceptibles and total number of infecteds

$$\begin{aligned} S_t &= -\beta_m S I \\ I_t &= \beta_m S I - \alpha I + D_m (k * I - I) \end{aligned}$$

with **effective** transmission rate

$$\beta_m = \frac{\beta_1 \rho_2 + \beta_2 \rho_1}{\rho_1 + \rho_2} = \frac{\beta_1 \gamma_2 + \beta_2 \gamma_1}{\gamma_1 + \gamma_2}$$

and **effective** diffusion rate

$$D_m = \frac{\rho_1}{\rho_1 + \rho_2} \delta = \frac{\gamma_1}{\gamma_1 + \gamma_2} \delta$$

Case 2: Rapid excursions of highly infectious individuals

Scaling

$$\beta_2 = \bar{\beta}_2/\epsilon, \quad \gamma_2 = \bar{\gamma}_2/\epsilon, \quad \delta = \bar{\delta}/\epsilon$$

Migrating infecteds move very fast but each time just for a short period. They make rapid excursions and they are highly infective.
At any given moment there are only few migrating infectives.

$$\begin{aligned} S_t &= -S((\beta_1 + \frac{\bar{\beta}_2\gamma_1}{\bar{\gamma}_2 + \bar{\delta}})I + \frac{\bar{\beta}_2\gamma_1\bar{\delta}}{(\bar{\gamma}_2 + \bar{\delta})\bar{\gamma}_2}\hat{k} * I) \\ I_t &= S((\beta_1 + \frac{\bar{\beta}_2\gamma_1}{\bar{\gamma}_2 + \bar{\delta}})I + \frac{\bar{\beta}_2\gamma_1\bar{\delta}}{(\bar{\gamma}_2 + \bar{\delta})\bar{\gamma}_2}\hat{k} * I) - \alpha I \\ &\quad + \frac{\gamma_1\bar{\delta}}{\bar{\gamma}_2 + \bar{\delta}}(\hat{k} * I - I). \end{aligned}$$

Further scaling

$$\bar{\beta}_2 = \hat{\beta}_2/\varepsilon, \quad \gamma_1 = \varepsilon\hat{\gamma}_1$$

contact system

$$\begin{aligned} S_t &= -S(\beta_c I + D_c \tilde{k} * I) \\ I_t &= S(\beta_c I + D_c \tilde{k} * I) - \alpha I \end{aligned}$$

with effective rates

$$\beta_c = \beta_1 + \frac{\hat{\beta}_2\hat{\gamma}_1}{\bar{\gamma}_2 + \bar{\delta}} = \beta_1 + \frac{\beta_2\gamma_1}{\gamma_2 + \delta}$$

$$D_c = \frac{\hat{\beta}_2\hat{\gamma}_1\bar{\delta}}{(\bar{\gamma}_2 + \bar{\delta})\bar{\gamma}_2} = \frac{\beta_2\delta}{(\gamma_2 + \delta)\gamma_2}$$

Speed of epidemic waves

For a spatial epidemic the **basic reproduction number** is only one characteristic feature. It determines whether an outbreak can or will occur.

The **speed of the epidemic wave** seems more important.

Compare reaction diffusion system and contact system using the diffusion approximation of the kernel

$$k * I = I + \sigma^2 I_{xx}$$

where

$$\sigma^2 = \frac{1}{2} \int_{-\infty}^{\infty} y^2 k(y) dy$$

Minimal wave speed:

Reaction diffusion system:

$$c_m = 2\sigma\sqrt{\frac{\delta\gamma_1}{\gamma_1+\gamma_2}\left(\frac{\beta_1\gamma_2+\beta_2\gamma_1}{\gamma_1+\gamma_2}-\alpha\right)}$$

speed largely determined by **migration rate**

contact system:

$$c_c = 2\sigma\sqrt{\frac{\delta\beta_2\gamma_1}{(\gamma_2+\delta)\gamma_2}\left(\frac{\beta_1\gamma_2+\beta_2\gamma_1}{\gamma_2}-\alpha\right)}$$

speed strongly influenced by **transmission rate**