Relation of the detectability in strains to the endemicity of an infectious disease: A mathematical model

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Introduction

Numerous studies have provided the evidence of the superinfection/coinfection with multiple strains in various infectious diseases, such as malaria, HBV, HCV, SARS-CoV-2, dengue, particularly common in HIV. Although the characterization of multiple genotypes strains could contribute to identifying the disease infection, it may encounter a difficulty in the detection of novel or mutant strains. On the other hand, the superinfection of a detectable strain could enhance the possibility for infectives to be diagnosed and quarantined, which in turn helps to suppress the disease spread. In this work, we consider the epidemic dynamics of an infectious disease with n strains, focusing on the detectability depending on the strain.

Assumptions

- More dominant strain is more detectable.
- The quarantine efficiency is determined by the most dominant strain, that is, by the most detectable strain in the infective.
- The recovered individual gets the immunity lasting in the epidemic season under consideration.
- The demographic change is negligible in the considered epidemic season.

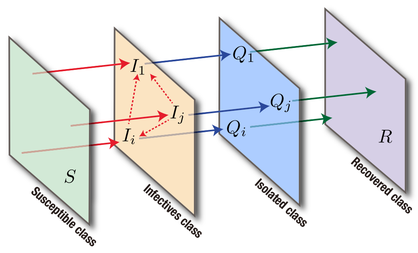

Figure 1. The state transition in the epidemic dynamics of our model. S, I_i, Q_i, and R are population densities of susceptibles, infectives who hold strain i as the strain of the highest dominance, corresponding isolated and recovered individuals respectively, where $1 < i < j$.

Modeling

$$
\begin{aligned}
\frac{dS}{dt} &= \mu N - \sum_{i=1}^{n} \beta_i I_i S - \mu S;\\
\frac{dI_1}{dt} &= \beta_1 I_1 S + \sum_{j=2}^{n} \varepsilon_{1j}\beta_1 I_1 I_j - \sigma_1 I_1 - \rho_1 I_1 - \mu I_1;\\
\frac{dI_i}{dt} &= \beta_i I_i S + \sum_{j=i+1}^{n} \varepsilon_{ij}\beta_i I_i I_j - \sum_{j=1}^{i-1} \varepsilon_{ji}\beta_j I_j I_i - \sigma_i I_i - \rho_i I_i - \mu I_i \quad (1 < i < n);\\
\frac{dI_n}{dt} &= \beta_n I_n S - \sum_{j=1}^{n-1} \varepsilon_{jn}\beta_j I_j I_n - \sigma_n I_n - \rho_n I_n - \mu I_n;\\
\frac{dQ_i}{dt} &= \sigma_i I_i - \alpha_i Q_i - \mu Q_i;\\
\frac{dR}{dt} &= \sum_{i=1}^{n} \rho_i I_i + \sum_{i=1}^{n} \alpha_i Q_i - \mu R,
\end{aligned}
$$

with $N = S + \sum_{i=1}^{n} I_i + \sum_{i=1}^{n} Q_i + R$.

$\beta_i I_i$: the infection force of strain i for the susceptible;
$\varepsilon_{ij}\beta_i I_i$: the infection force of strain i for the infective with strain j of the lower dominance ($0 \le \varepsilon_{ij} \le 1$);
σ_i: the quarantine rate for the infective who holds strain i as the most dominant strain, where $\sigma_i > \sigma_j$ for $i < j$;
ρ_i: the recovery rate for the infective with strain i out of the isolation;
α_i: the recovery rate for the infective with strain i under the isolation;
μ: the natural death rate.

The basic reproduction number（基本再生産数）:

$$\mathscr{R}_0 = \max\{\mathscr{R}_{01}, \mathscr{R}_{02}, \ldots, \mathscr{R}_{0n}\}, \quad \mathscr{R}_{0i} := \frac{\beta_i N}{\sigma_i + \rho_i + \mu}.$$

Non-dimensionalization

$$\tau := \mu t,\ u := \frac{S}{N},\ v_i := \frac{I_i}{N},\ q_i := \frac{Q_i}{N},\ w := \frac{R}{N},\ \gamma_i := \frac{\sigma_i}{\mu},\ a_i := \frac{\alpha_i}{\mu},\ \eta_i := \frac{\rho_i}{\mu}.$$

$$
\begin{aligned}
\frac{du}{d\tau} &= 1 - \sum_{i=1}^{n}(1+\gamma_i+\eta_i)\mathscr{R}_{0i}v_i u - u;\\
\frac{dv_1}{d\tau} &= (1+\gamma_1+\eta_1)\mathscr{R}_{01}v_1 u + \sum_{j=2}^{n}\varepsilon_{1j}(1+\gamma_1+\eta_1)\mathscr{R}_{01}v_1 v_j - (1+\gamma_1+\eta_1)v_1;\\
\frac{dv_i}{d\tau} &= (1+\gamma_i+\eta_i)\mathscr{R}_{0i}v_i u + \sum_{j=i+1}^{n}\varepsilon_{ij}(1+\gamma_i+\eta_i)\mathscr{R}_{0i}v_i v_j\\
&\quad - \sum_{j=1}^{i-1}\varepsilon_{ji}(1+\gamma_j+\eta_j)\mathscr{R}_{0j}v_j v_i - (1+\gamma_i+\eta_i)v_i \quad (1 < i < n);\\
\frac{dv_n}{d\tau} &= (1+\gamma_n+\eta_n)\mathscr{R}_{0n}v_n u - \sum_{j=1}^{n-1}\varepsilon_{jn}(1+\gamma_j+\eta_j)\mathscr{R}_{0j}v_j v_n - (1+\gamma_n+\eta_n)v_n;\\
\frac{dq_i}{d\tau} &= \gamma_i v_i - a_i q_i - q_i;\\
\frac{dw}{d\tau} &= \sum_{i=1}^{n}\eta_i v_i + \sum_{i=1}^{n} a_i q_i - w,
\end{aligned}
$$

with $u + \sum_{i=1}^{n} v_i + \sum_{i=1}^{n} q_i + w = 1$.

Model without superinfection ($\varepsilon_{ij} = 0$)

Theorem 1

For the model without superinfection ($\varepsilon_{ij} = 0$),

(i) if and only if $\mathscr{R}_0 \le 1$, the disease-free equilibrium $E_0 = (1, 0, \ldots, 0)$ is globally asymptotically stable;

(ii) we have the unique locally asymptotically stable endemic equilibrium with a single strain i such that $\mathscr{R}_{0i} > 1$ and $\mathscr{R}_{0i} > \mathscr{R}_{0j}$ for any $j \ne i$, given by

$$u^* = \frac{1}{\mathscr{R}_{0i}};\ v_i^* = \frac{1}{1+\gamma_i+\eta_i}\left(1 - \frac{1}{\mathscr{R}_{0i}}\right);\ v_j^* = 0;\ q_i^* = \frac{\gamma_i v_i^*}{a_i+1},\ q_j^* = 0.$$

Two strain model ($n = 2$)

$$
\begin{aligned}
\frac{du}{d\tau} &= 1 - (1+\gamma_1+\eta_1)\mathscr{R}_{01}v_1 u - (1+\gamma_2+\eta_2)\mathscr{R}_{02}v_2 u - u;\\
\frac{dv_1}{d\tau} &= (1+\gamma_1+\eta_1)\mathscr{R}_{01}v_1 u + \varepsilon_{12}(1+\gamma_1+\eta_1)\mathscr{R}_{01}v_1 v_2 - (1+\gamma_1+\eta_1)v_1;\\
\frac{dv_2}{d\tau} &= (1+\gamma_2+\eta_2)\mathscr{R}_{02}v_2 u - \varepsilon_{12}(1+\gamma_1+\eta_1)\mathscr{R}_{01}v_1 v_2 - (1+\gamma_2+\eta_2)v_2;\\
\frac{dq_1}{d\tau} &= \gamma_1 v_1 - a_1 q_1 - q_1;\\
\frac{dq_2}{d\tau} &= \gamma_2 v_2 - a_2 q_2 - q_2;\\
\frac{dw}{d\tau} &= \eta_1 v_1 + \eta_2 v_2 + a_1 q_1 + a_2 q_2 - w,
\end{aligned}
$$

with $u + v_1 + v_2 + q_1 + q_2 + w = 1$.

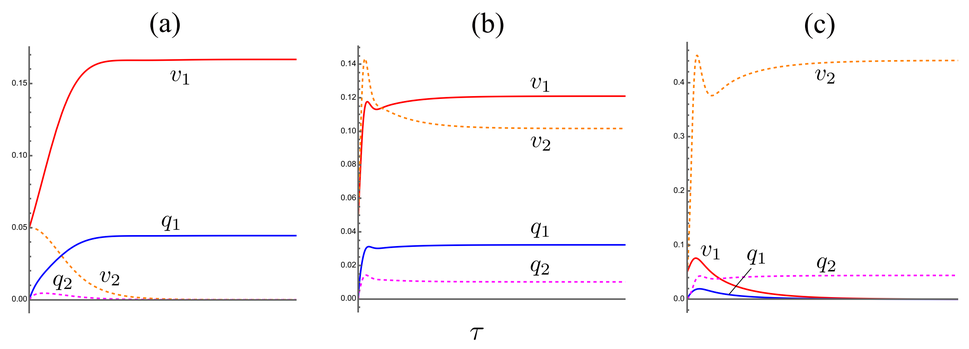

Figure 2. Temporal variations for the two strain model. Numerically drawn with (a) $\mathscr{R}_{02} = 1.2$; (b) $\mathscr{R}_{02} = 2.0$; (c) $\mathscr{R}_{02} = 4.0$, and $\mathscr{R}_{01} = 1.5$; $1+\gamma_1+\eta_1 = 2.0$; $1+\gamma_2+\eta_2 = 1.7$; $\varepsilon_{12} = 0.8$; $a_1 = 2.0$; $a_2 = 3.0$; $(u(0), v_1(0), v_2(0), q_1(0), q_2(0), w(0)) = (0.9, 0.05, 0.05, 0, 0, 0)$.

Theorem 2

For the two strain model, the disease-free equilibrium $E_0 = (1, 0, 0, 0, 0, 0)$ is globally asymptotically stable if and only if $\mathscr{R}_{01} \le 1$ and $\mathscr{R}_{02} \le 1$.

Theorem 3

For the two strain model,

(i) when $\mathscr{R}_{01} > 1$, the endemic equilibrium $E_1 = (u^*, v_1^*, 0, q_1^*, 0, w^*)$ is locally asymptotically stable if

$$\frac{1}{\mathscr{R}_{02}} > \frac{(1/\mathscr{R}_{01})^2}{1/\mathscr{R}_{01} + (1 - 1/\mathscr{R}_{01})\varepsilon_{12}/(1+\gamma_2+\eta_2)};$$

(ii) when $\mathscr{R}_{02} > 1$, the endemic equilibrium $E_2 = (u^*, 0, v_2^*, 0, q_2^*, w^*)$ is locally asymptotically stable if

$$\frac{1}{\mathscr{R}_{02}} < \frac{1/\mathscr{R}_{01} - \varepsilon_{12}/(1+\gamma_2+\eta_2)}{1 - \varepsilon_{12}/(1+\gamma_2+\eta_2)};$$

(iii) if

$$\frac{1/\mathscr{R}_{01} - \varepsilon_{12}/(1+\gamma_2+\eta_2)}{1 - \varepsilon_{12}/(1+\gamma_2+\eta_2)} < \frac{1}{\mathscr{R}_{02}} < \frac{(1/\mathscr{R}_{01})^2}{1/\mathscr{R}_{01} + (1 - 1/\mathscr{R}_{01})\varepsilon_{12}/(1+\gamma_2+\eta_2)},$$

the endemic equilibrium $E_{1,2} = (u^*, v_1^*, v_2^*, q_1^*, q_2^*, w^*)$ with

$$u^* = \frac{1}{\frac{\mathscr{R}_{02}(1+\gamma_2+\eta_2)}{\varepsilon_{12}}\left(\frac{1}{\mathscr{R}_{01}} - \frac{1}{\mathscr{R}_{02}}\right) + 1};\ v_1^* = \frac{1}{\varepsilon_{12}}\frac{1+\gamma_2+\eta_2\mathscr{R}_{02}}{1+\gamma_1+\eta_1\mathscr{R}_{01}}\left(u^* - \frac{1}{\mathscr{R}_{02}}\right);\ v_2^* = \frac{1}{\varepsilon_{12}}\left(\frac{1}{\mathscr{R}_{01}} - u^*\right);\ q_1^* = \frac{\gamma_1 v_1^*}{a_1+1};\ q_2^* = \frac{\gamma_2 v_2^*}{a_2+1},$$

and $w^* = 1 - u^* - v_1^* - v_2^* - q_1^* - q_2^*$, is locally asymptotically stable, while E_1 and E_2 are unstable.

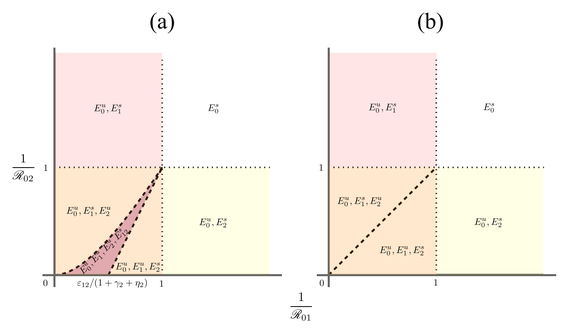

Figure 3. $(1/\mathscr{R}_{01}, 1/\mathscr{R}_{02})$-dependence of the existence and stability of equilibria for the two strain model. Numerically drawn for (a) $\varepsilon_{12}/(1+\gamma_2+\eta_2) = 0.5$; (b) $\varepsilon_{12} = 0$.

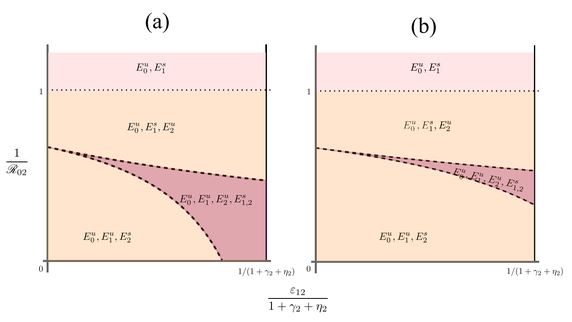

Figure 4. $(\varepsilon_{12}/(1+\gamma_2+\eta_2), 1/\mathscr{R}_{02})$-dependence of the existence and stability of equilibria for the two strain model. Numerically drawn with (a) $1+\gamma_2+\eta_2 = 1.2$; (b) $1+\gamma_2+\eta_2 = 1.8$, and $\mathscr{R}_{01} = 1.5$.

Endemic size

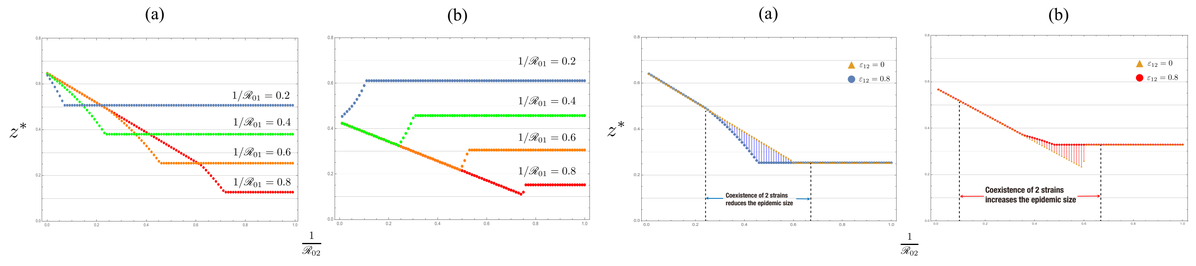

Figure 5. $1/\mathscr{R}_{02}$-dependence of the endemic size $z^* = v_1^* + v_2^* + q_1^* + q_2^*$ for the two strain model. Numerically drawn with (a) $1+\gamma_1+\eta_1 = 2.0$; $1+\gamma_2+\eta_2 = 1.7$; (b) $1+\gamma_1+\eta_1 = 1.4$; $1+\gamma_2+\eta_2 = 3.8$, and $\varepsilon_{12} = 0.8$; $a_1 = 2.0$; $a_2 = 3.0$; $(u(0), v_1(0), v_2(0), q_1(0), q_2(0), w(0)) = (0.9, 0.05, 0.05, 0, 0, 0)$.

Figure 6. $1/\mathscr{R}_{02}$-dependence of the endemic size $z^* = v_1^* + v_2^* + q_1^* + q_2^*$ for the two strain model. Numerically drawn with (a) $1+\gamma_1+\eta_1 = 2.0$; $1+\gamma_2+\eta_2 = 1.7$; (b) $1+\gamma_1+\eta_1 = 1.3$; $1+\gamma_2+\eta_2 = 2.1$, and $\mathscr{R}_{01} = 1.7$; $a_1 = 2.0$; $a_2 = 3.0$; $(u(0), v_1(0), v_2(0), q_1(0), q_2(0), w(0)) = (0.9, 0.05, 0.05, 0, 0, 0)$.

Concluding remarks

- Without superinfection, the disease goes extinct if $\mathscr{R}_0 \le 1$. Otherwise, only the strain i of the highest transmissibility (i.e., the largest $\mathscr{R}_{0i}$) eventually persists in the community, and any other strain goes extinct.
- When there are two strains ($n = 2$) with superinfection, if one of them has a sufficiently high transmissibility, it persists and the other goes extinct in the community.
- If two strains coexist, the coexistence may reduce the endemic size.

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