On Conditions of Asymptotic Stability in SIR-Models of Mathematical Epidemiology

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ABSTRACT

SLIAR-model of epidemic of acute respiratory disease has been considered. There have been obtained the conditions of local stability of stationary state corresponding to the absence of disease. Consideration has been also given to the model of coexistence of two virus strains for which there are presented stability conditions for three stationary states. Stability conditions are expressed in terms of virus reproduction rates.

Key words: acute respiratory disease, coexistence of two virus strains, virus reproduction rate, stationary state.

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Introduction

Influenza and acute respiratory diseases remain one of the most urgent medical and social problems due to their high sickness rate, risk of complication development, acute attacks of chronic disease and as result — lethality [1, 2]. Hence, of urgency is the development of adequate models of epidemic spread. The challenge of model construction is connected with a large number of factors which affect the development of epidemic process. Construction of new models is related to selection of one or other leading factors.

The works [3–5] have presented the review of SIR-models which are traditionally applied in mathematical epidemiology and whose construction has been studied in numerous works. At the same time less consideration has been given to the matter concerning stability of SIR-models, which, as a rule, refer to the class of nonlinear ones.

Hence, the goal of this work is the construction of design conditions of asymptotic stability in SIRmodels of epidemic of acute respiratory disease.

Investigation of SLIAR-model

Let *N* be the size of the considered human population. It is assumed constant, i.e., over the time of epidemic being considered (as a rule, it takes a couple of months) a mortality due to disease does not affect the size of population, and the influence of natural mortality μ is covered by the birth rate, i.e.,

$$0 = N' = \mu N - \mu N$$

We analyze the following compartments which correspond to such subpopulations: S — susceptible, L — latent, I — infected, A — asymptotic, R recovered persons. Hence, we have the diagram of transition states (Figure 1).

On its basis we consider the model

$$S' = \mu N - S\beta(I + \delta A) - \mu S,$$

$$L' = S\beta(I + \delta A) - (\mu + \kappa) L,$$

$$I' = \rho \kappa L - (\mu + \alpha) I,$$

$$A' = (1 - p) \kappa L - (\mu + \eta) A,$$

$$R' = \alpha l + \eta A - \mu R.$$

(1)

The equation for R in the system (1) can be eliminated since for any t

$$S(t) + L(t) + I(t) + A(t) + R(t) = N = \text{const.}$$

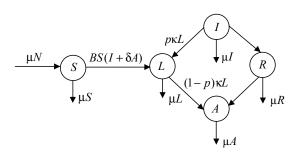


Figure 1

Hence, as the basis model we consider the model

$$S' = \mu(N - S) - S\beta(I + \delta A),$$

$$L' = S\beta(I + \delta A) - (\mu + \kappa)L,$$

$$I' = \rho\kappa L - (\mu + \alpha)I,$$

$$A' = (1 - \rho)\kappa L - (\mu + \eta)A.$$
(2)

Note, that in terms of biology the significant domain $\Omega = \{(S, L, I, A) \in R^4_+ | S + L + I + A \le N\}$ is positively invariant for the system (2) since the vector field on the boundary of Ω does not go outside Ω .

To analyze the equilibrium points of the system (2) we introduce the parameter, i.e., — the reproduction rate

$$\Re_0 = \beta \left[\frac{p}{\alpha} + \frac{\delta(1-p)}{\eta} \right].$$
(3)

Its biological content consists in the fact that a latent person upon hitting a population of S_0 susceptible persons will become infected with probability p (in this case it will cause $\beta S_0/\alpha$ infections over the infection period of duration $1/\alpha$) or will become asymptotic with probability 1-p (in this case it will cause $\delta_\beta S_0/\eta$ infections over the asymptotic period of duration η).

We will find the equilibrium states of system (2) which belong to the boundary of domain Ω :

$$\begin{aligned} & \mu(N-S) - S\beta(I+\delta A) = 0, \\ & S\beta(I+\delta A) - (\mu+k)L = 0, \\ & pkL - (\mu+\alpha)I = 0, \\ & (1-p)kL - (\mu+\eta)A = 0, \\ & S+L+I+A = 0. \end{aligned}$$

This implies $E_0 = (N, 0, 0, 0)$ — the stationary state which corresponds to the absence of disease.

We introduce the notation $\Re_1 = \beta \left(\frac{\mu(\delta p - \delta - p)}{\alpha \eta} \right).$

Theorem 1. At $\Re_0 < \Re_1 E_0$ is locally asymptotically stable in Ω .

Proof. Jacobian of the system (2) has the form

$$DF(E) = \begin{bmatrix} -\mu - \beta(I + \delta A) & 0 & -S_{\beta} & -S_{\beta}\delta \\ \beta(I + \delta A) & -(\mu + \kappa) & S_{\beta} & S_{\beta}\delta \\ 0 & \rho\kappa & -(\mu + \alpha) & 0 \\ 0 & (1 - \rho)\kappa & 0 & -(\mu + \eta) \end{bmatrix},$$

i.e.,
$$DF(E_0) = \begin{bmatrix} -\mu & 0 & -N_{\beta} & -N_{\beta}\delta \\ 0 & -(\mu + \kappa) & N_{\beta} & N_{\beta}\delta \\ 0 & -(\mu + \kappa) & N_{\beta} & N_{\beta}\delta \\ 0 & \rho\kappa & -(\mu + \alpha) & 0 \\ 0 & (1 - \rho)\kappa & 0 & -(\mu + \eta) \end{bmatrix}.$$

The eigenvalues of $DF(E_0)$ represent $-\mu$ and the roots of polynomial

$$A(z) = z^3 + a_1 z^2 + a_2 z + a_3$$

where

$$\begin{split} a_1 &= \kappa + \eta + \alpha + 3\mu, \\ a_2 &= \alpha \eta - \rho \kappa N \beta + 2\mu \alpha + \kappa N \beta \delta \rho + \kappa \eta + \kappa \alpha + 3\mu^2 + 2\mu \eta + 2\kappa \mu - \kappa N \beta \delta, \\ a_3 &= \kappa \alpha \eta + \kappa N \beta \delta \mu \rho - \kappa N \beta \delta \mu - \rho \kappa N \beta \mu + \mu^2 \eta - \rho \kappa N \beta \eta - \kappa N \beta \delta \alpha + \kappa \mu^2 + \\ &+ \kappa N \beta \delta \rho \alpha + \mu^2 \alpha + \mu^3 + \kappa \alpha \mu + \mu \alpha \eta + \kappa \mu \eta. \end{split}$$

According to Routh–Hurwitz criterion in order that the real parts of roots of the polynomial be positive it is necessary and sufficient that the condition

$$a_1 > 0, \ a_3 > 0, \ a_1 a_2 - a_3 > 0$$

be fulfilled.

We have

$$a_{2} = \alpha \eta - \kappa N \beta (\rho - \delta \rho + \delta) + 2\mu \alpha + \kappa \eta + \kappa \alpha + 3\mu^{2} + 2\mu \eta + 2\kappa \mu =$$

= $\alpha \eta + \kappa N \frac{\alpha \eta}{\mu} \left[\beta \left(\frac{\mu (\delta \rho - \delta - \rho)}{\alpha \eta} \right) \right] + 2\mu \alpha + \kappa \eta + \kappa \alpha + 3\mu^{2} + 2\mu \eta + 2\kappa \mu =$
= $\alpha \eta + \kappa N \frac{\alpha \eta}{\mu} \Re_{1} + 2\mu \alpha + \kappa \eta + \kappa \alpha + 3\mu^{2} + 2\mu \eta + 2\kappa \mu.$

Since

$$\Re_0 = \beta \left[\frac{P}{\alpha} + \frac{\delta(1-\rho)}{\eta} \right] = \beta \frac{\rho \eta + \delta \alpha (1-\rho)}{\alpha \eta} = \frac{\beta \rho \eta + \beta \delta \alpha - \beta \delta \alpha \rho}{\alpha \eta},$$

we obtain

$$a_{3} = \kappa\alpha\eta + \kappa N(\beta\mu\delta\rho - \beta\mu\delta - \beta\mu\rho) + \mu^{2}\eta - \kappa N(\beta\rho\eta + \beta\delta\alpha - \beta\delta\alpha\rho) + \kappa\mu^{2} + \mu^{2}\alpha + \mu^{3} + \kappa\alpha\mu + \mu\alpha\eta + \kappa\mu\eta =$$

$$= \kappa\alpha\eta + \kappa N\beta\mu(\delta\rho - \delta - \rho) + \mu^{2}\eta - \kappa N\beta(\rho\eta + \delta\alpha - \delta\alpha\rho) + \kappa\mu^{2} + \mu^{2}\alpha + \mu^{3} + \kappa\alpha\mu + \mu\alpha\eta + \kappa\mu\eta = \kappa\alpha\eta + \kappa N\alpha\eta\beta\left(\frac{\mu(\delta\rho - \delta - \rho)}{\alpha\eta}\right) + \mu^{2}\eta - \kappa N\alpha\eta\beta\left(\frac{\rho}{\alpha} + \frac{\delta(1-\rho)}{\eta}\right) + \kappa\mu^{2} + \mu^{2}\alpha\mu^{3} + \kappa\alpha\mu + \mu\alpha\eta + \kappa\mu\eta =$$

$$= \kappa N\alpha\eta\left[\beta\left(\frac{\mu(\delta\rho - \delta - \rho)}{\alpha\eta}\right) - \Re_{0}\right] + \kappa\alpha\eta + \mu^{2}\eta + \kappa\mu^{2} + \mu^{2}\alpha =$$

$$= \mu^{3} + \kappa\alpha\mu + \mu\alpha\eta + \kappa\mu\eta = \kappa N\alpha\eta[\Re_{1} - \Re_{0}] + \kappa\alpha\eta + \mu^{2}\eta + \kappa\mu^{2}$$

If $\Re_0 < \Re_1$, then the coefficients of A(z) are positive. We can also verify that $a_1a_2 > a_3$. According to Routh–Hurwitz criterion the roots of A(z) have negative real parts if $\Re_0 < \Re_1$. The theorem has been proved.

The model of existence of two influenza strains

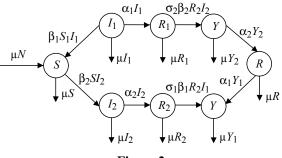
The model is assigned for describing a spread of various virus strains (for example, pandemic and seasonal influenza). In the model there are made the assumptions:

1) compartments of latent persons are not considered;

2) influenza spread is assumed to be necessarily accompanied by the symptoms, i.e., the absence of compartments of the asymptotically infected;

3) a general size of population N is considered constant.

Hence we consider the diagram of transition states (Figure 2).





Here we have compartments that correspond to such subpopulations: S — susceptible, I_1 — infected by the first virus strain, I_2 — infected by the second virus strain, R_1 recovered after the first virus strain, R_2 recovered after the second virus strain, Y_1 reinfected, (but now by the first strain), Y_2 reinfected (but now by the second virus strain), R — recovered after being twice infected.

On its basis we have the system

$$S' = \mu(N - S) - (\beta_1 I_1 + \beta_2 I_2) S,$$

$$I' = \beta_i S I_i - (\mu + \alpha_i) I_i, \quad i = 1, 2,$$

$$R'_i = \alpha_i I_i - (\mu + \sigma_j \beta_j I_j) R_i; \quad i, j = 1, 2, \quad i \neq j,$$

$$Y'_i = \sigma_i \beta_i R_j I_i - (\mu + \alpha_i) Y_i; \quad i, j = 1, 2, \quad i \neq j,$$

$$R' = \alpha_1 Y_1 + \alpha_2 Y_2 - \mu R.$$
(4)

Since for any $t S + I_1 + I_2 + R_1 + R_2 + Y_1 + Y_2 + R = N$, then in the last equation of (4) R can be eliminated and then we will have the following epidemiological system:

$$S' = \mu(N - S) - (\beta_1 I_1 + \beta_2 I_2) S,$$

$$I'_i = \beta_i S I_i - (\mu + \alpha_i) I_i,$$

$$R'_i = \alpha_i I_i - (\mu + \sigma_j \beta_j I_j) R_i,$$

$$Y'_i = \theta_i \beta_i R_i I_i - (\mu + \alpha_i) Y_i.$$
(5)

Here $i, j = 1, 2, i \neq j$.

The biologically significant domain for (5) represents

$$\Omega = \{ (S, I_1, I_2, R_1, R_2, Y_1, Y_2) \in R_+^7 \mid S + I_1 + I_2 + R_1 + R_2 + Y_1 + Y_2 \le N \}$$

Note, that Ω is positively invariant for the system (5) since the vector field on the boundary of Ω does not go outside of Ω .

We will determine the equilibrium states of the system (5) that belong to the boundary of Ω from the system of algebraic equations

$$\mu(N-S) - (\beta_{1}I_{1} + \beta_{2}I_{2}) S = 0,$$

$$\beta_{i}SI_{i} - (\mu + \alpha_{i}) I_{i} = 0,$$

$$\alpha_{i}I_{i} - (\mu + \sigma_{j}\beta_{j}I_{j}) R_{i} = 0,$$

$$\theta_{i}\beta_{i}R_{j}I_{i} - (\mu + \alpha_{i}) Y_{i} = 0,$$

$$i, j = 1, 2, i \neq j.$$

We have three equilibrium states

$$E_0 = (N, 0, 0, 0, 0, 0, 0),$$

$$E_1 = (S_1^*, I_1^*, 0, R_1^*, 0, 0, 0),$$

$$E_2 = (S_2^*, I_2^*, 0, R_2^*, 0, 0).$$

Here

$$S_1^* = \frac{\mu + \alpha_1}{\beta_1}, \ I_1^* = \frac{\mu(N\beta_1 - \mu - \alpha_1)}{\beta_1(\mu + \alpha_1)}, \ R_1^* = \frac{\alpha_1(N\beta_1 - \mu - \alpha_1)}{\beta_1(\mu + \alpha_1)},$$
$$S_2^* = \frac{\mu + \alpha_2}{\beta_2}, \ I_2^* = \frac{\mu(N\beta_2 - \mu - \alpha_2)}{\beta_2(\mu + \alpha_2)}, \ R_2^* = \frac{\alpha_2(N\beta_2 - \mu - \alpha_2)}{\beta_2(\mu + \alpha_2)}.$$

Having denoted the basic reproduction rates

$$\Re_1 = \frac{\beta_1 N}{\mu + \alpha_1}, \ \Re_2 = \frac{\beta_2 N}{\mu + \alpha_2},$$

we have

$$S_1^* = \frac{N}{R_1}, \ I_1^* = \frac{\mu}{\beta_1}(\mathfrak{R}_1 - 1), \ R_1^* = \frac{\alpha_1}{\beta_1}(\mathfrak{R}_1 - 1),$$
$$S_2^* = \frac{N}{R_2}, \ I_2^* = \frac{\mu}{\beta_2}(\mathfrak{R}_2 - 1), \ R_2^* = \frac{\alpha_2}{\beta_2}(\mathfrak{R}_2 - 1).$$

The equilibrium states in terms of epidemiology can be treated as follows: E_0 — the absence of disease; E_1 the presence of strain 1 alone; E_2 — the state of the presence of strain 2 alone.

Stability of equilibrium states in the model of coexistence of two influenza strains

Denote $\Re_0 = \max{\{\Re_1, \Re_2\}}$. If $\Re_0 \le 1$, then E_0 is the unique equilibrium state in Ω . If $\Re_0 > 1$, then either E_1 or E_2 or both of them belong to Ω .

We will investigate the stability conditions of equilibrium state which corresponds to the absence of disease.

Theorem 2. If $\mathfrak{R}_0 < 1$, then E_0 is locally asymptotically stable in Ω . If $\mathfrak{R}_0 > 1$, then E_0 is the saddle point.

Proof. Jacobian of the system (5) has the form

$$DF(E) = \begin{bmatrix} \mu - \beta_1 I_1 - \beta_2 I_2 & -\beta_1 S & -\beta_2 S & 0 & 0 & 0 & 0 \\ \beta_1 I_1 & -\beta_1 S - \mu - \alpha_1 & 0 & 0 & 0 & 0 & 0 \\ \beta_1 I_1 & 0 & \beta_2 S - \mu - \alpha_2 & 0 & 0 & 0 & 0 \\ 0 & \alpha_1 & -\sigma_2 \beta_2 R_1 & -\mu - \sigma_2 \beta_2 I_2 & 0 & 0 & 0 \\ 0 & -\sigma_1 \beta_1 R_1 & \alpha_2 & 0 & -\mu - \sigma_1 \beta_1 I_1 & 0 & 0 \\ 0 & 0 & \sigma_2 \beta_2 R_1 & \sigma_2 \beta_2 I_1 & 0 & 0 & -\mu - \alpha_2 \end{bmatrix},$$

$$DF(E_0) = \begin{bmatrix} -\mu & -\beta_1 N & -\beta_2 N & 0 & 0 & 0 & 0 \\ 0 & \beta_1 N_1 - \mu - \alpha_1 & 0 & 0 & 0 & 0 \\ 0 & \beta_2 N - \mu - \alpha_2 & 0 & 0 & 0 & 0 \\ 0 & \alpha_1 & 0 & -\mu & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & 0 - \mu & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu - \alpha_1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\mu - \alpha_2 \end{bmatrix}.$$

$$(6)$$

 $DF(E_0)$ has eigenvalues: $-\mu$ (of multiplicity 3), $-(\mu + \alpha_1)$, $-(\mu + \alpha_2)$, $\beta_1 N - \mu - \alpha_1 = \beta_2 N - \mu - \alpha_2 = (\mu + \alpha_2)(\Re_2 - 1)$.

Hence, E_0 is locally asymptotically stable if $\Re_0 < 1$ and is the saddle point at $\Re_0 > 1$. Theorem has been proved.

We will investigate the stability of equilibrium states E_i , u = 1, 2. At $\Re_1 > 1$ the equilibrium state E_1 is in Ω . Its stability is determined by Jacobian of the system (5) at this point:

$$DF(E_1) = \begin{bmatrix} \mu - \beta_1 I_1^* & -\beta_1 S_1^* & -\beta_2 S_2^* & 0 & 0 & 0 & 0 \\ \beta_1 I_1^* & -\beta_1 S_1^* - \mu - \alpha_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 S_1^* - \mu - \alpha_2 & 0 & 0 & 0 & 0 \\ 0 & \alpha_1 & -\sigma_2 \beta_2 R_1^* & -\mu & 0 & 0 & 0 \\ 0 & -\sigma_1 \beta_1 R_1^* & \alpha_2 & 0 & -\mu - \sigma_1 \beta_1 I_1^* & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma_1 \beta_1 I_1^* & -\mu - \alpha_1 & 0 \\ 0 & 0 & \sigma_2 \beta_2 R_1^* & 0 & 0 & 0 & -\mu - \alpha_2 \end{bmatrix},$$

which has the eigenvalues

$$\lambda_1 = -\mu, \lambda_2 = -(\mu + \lambda_1), \lambda_3 = -(\mu + \lambda_2), \lambda_4 = -\left[\left(\mu + \lambda_2 - \frac{\beta_2}{\beta_1}(\mu + \lambda_1)\right)\right],$$
$$\lambda_5 = -\mu\left[1 - \sigma_1 + \frac{\beta_1 N}{\mu} + \alpha_1\right] = -\mu[\Re_1 + 1 - \sigma_1]$$

and the roots of polynomial

$$A_{1}(z) = z^{2} + \mu \Re_{1} z + \Re_{1} \mu (\mu + \alpha_{1}) - \frac{\mu}{\mu + \alpha_{1}} (\alpha_{1}^{2} + 2\mu \alpha_{1} + \mu_{1}^{2}) =$$

= $z^{2} + \mu \Re_{1} z + \Re_{1} \mu (\mu + \alpha_{1}) - \mu (\mu + \alpha_{1}) = z^{2} + \mu \Re_{1} z + \mu (\mu + \alpha_{1}) [\Re_{1} - 1].$

It is obvious, that $\lambda_4 < 0$ if $\Re_1 > \Re_2$. In its turn $\lambda_5 < 0$ if $\Re_1 > \sigma_1 - 1$.

According to Routh–Hurwitz criterion the roots of polynomial $A_1(z)$ have negative real parts if and only if $\Re_1 > 1$. Thus, on the whole we have the result.

Theorem 3. E_1 is the locally asymptotically stable state of the system (5) if $\Re_1 > \max\{1, \sigma_1 - 1\}$ and the inequality

$$\mathfrak{R}_2 < \mathfrak{R}_1 \tag{7}$$

holds true.

If the inequality (7) does not hold, then E_1 is unstable.

Since the system (5) is symmetric with respect to strains of viruses 1 and 2, then we obtain the analogous result for the equilibrium state E_2

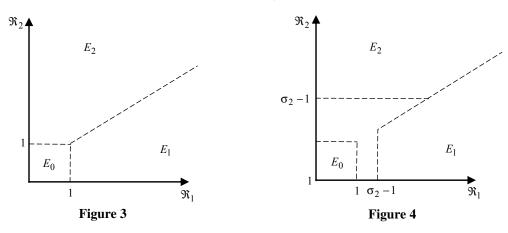
Theorem 4. E_2 is locally asymptotically stable state of system (5) if $\Re_2 > \max\{1, \sigma_2 - 1\}$ and the inequality

$$\mathfrak{R}_1 < \mathfrak{R}_2 \tag{8}$$

holds true.

If the inequality (8) does not hold, then E_2 is unstable.

Since for $\Re_i = \max\{1, \sigma_i - 1\}$ the inequalities (7) and (8) cannot hold true simultaneously, then E_1 and E_2 cannot be locally stable for the same values of the system parameters. Figures 3, 4 depict the domains of existence and stability of equilibrium states E_i .



Example. Consideration is given to the system (5) with the values of parameters

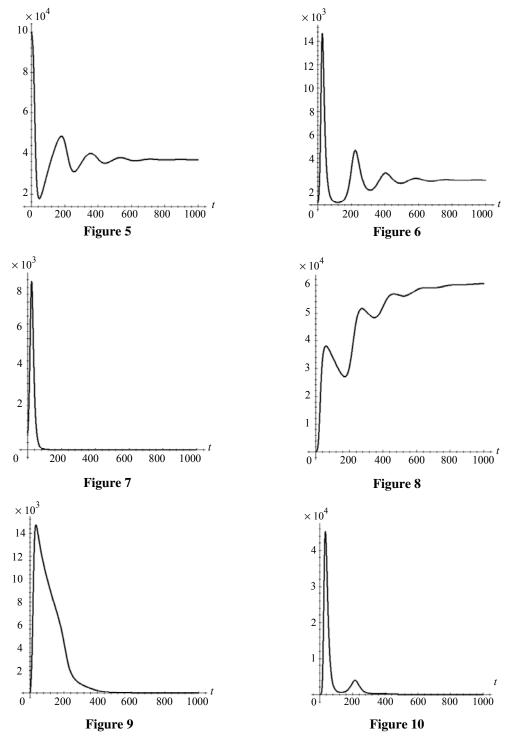
$$N = 10^5$$
, $\mu = 0.005$, $\beta_1 = 0.4 \cdot 10^{-5}$, $\beta_2 = 0.3 \cdot 10^{-5}$,
 $\alpha_1 = 0.1428$, $\alpha_2 = 0.1428$, $\sigma_1 = 1$, $\sigma_2 = 1$.

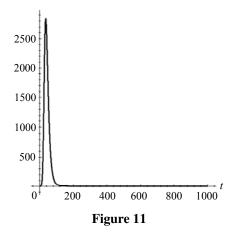
In this case we have

$$\Re_1 = \frac{\beta_1 N}{\mu + \alpha_1} = \frac{4 \cdot 10^{-6} \cdot 10^5}{5 \cdot 10^{-3} + 0.1428} = \frac{0.4}{0.1478} = 2.706,$$

$$\Re_2 = \frac{\beta_2 N}{\mu + \alpha_2} = \frac{3 \cdot 10^{-6} \cdot 10^5}{5 \cdot 10^{-3} + 0.1428} = \frac{0.3}{0.1478} = 2.0298,$$

i.e., $\Re_1 > \Re_2$ and all conditions of Theorem 3 are fulfilled. Results of numerical modeling of the system (5) are depicted in Figure 5–11.





Numerical integration shows the local asymptotic stability of stationary state E_1 .

Conclusion

Hence, the paper in question has studied the matter of stability of SIR-models of epidemic of acute respiratory virus infections (the most common example is an influenza epidemic). While considering SLIAR-model of one strain influenza epidemic there was introduced the concept of epidemic reproduction rate which shows a probable number of infections that might be caused by a person. The analogous concepts were introduced in the models of coexistence of two virus strains. It is worth noting, that the obtained stability conditions have explicit biological sense. The necessary condition $\Re_i > 1$ points at the necessity to retain the same number of infected persons so that a stationary state of the presence of the constant level of the *i*th virus strain would be stable. The condition $\Re_i > \Re_j$ indicates the prevalence of epidemic spread for the *i*th virus strain over the *j*th one that leads to the stationary state of presence of the *i*th strain alone.

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