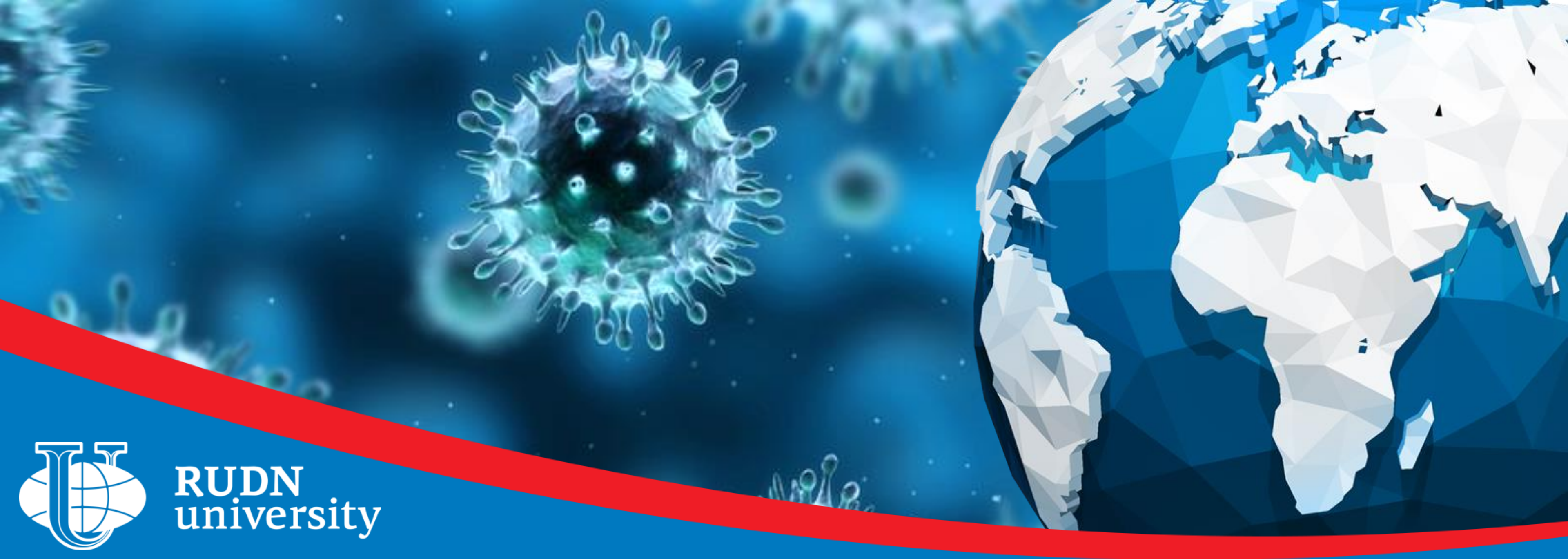

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Реакционно-диффузионная модель сосуществования вирусов

02.11.2020

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Problem statement

Reaction diffusion equation of the evolution of virus density depending on the genotype x (One virus).

$$\boxed{\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + au(1 - bI(u)) - uf(u) - \sigma(x)u}$$

$u(x,t)$ - virus density distribution
x - virus genotype
t - time

Diffusion term - Chain mutations

Genotype x_i:

$$x_{i-1} \rightarrow x_i, x_i \rightarrow x_{i-1};$$

$$x_{i+1} \rightarrow x_i, x_i \rightarrow x_{i+1}$$

$$u_i = u(x_i)$$

- Assuming that the sequence of mutations are reversible, we can write the equation for the density u_i of virus with genotype x_i :

$$\frac{du_i}{dt} = \mu\left(u_{i-1} - u_i\right) + \mu\left(u_{i+1} - u_i\right) \Leftrightarrow \boxed{D\frac{\partial^2 u}{\partial x^2}}$$

μ - frequency of mutations

Virus reproduction

$$\boxed{u(1 - bI(u))}$$

Let $I(u) = u(x,t)$ conventional logistic term.

$$I(u) = \int_{-\infty}^{\infty} \phi(y-x)u(x,t)dx$$ non-local contamination of host cells.

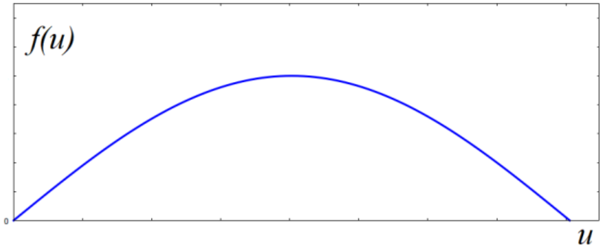
$$\boxed{I(u) = \int_{-\infty}^{\infty} u(x,t)dx}$$ total quantity virus.

Virus elimination

Immune response

$$\boxed{uf(u)}$$

- Stimulated by antigens (increasing branch of $f(u)$)
- Can be suppressed in the case of high virus concentration (decreasing branch of $f(u)$)



Death of virus

$$\boxed{\sigma(x)u}$$

- Virus natural death.
- Describes reaction to some antiviral treatment.
- Depends of virus genotype.

Proposed model

Reaction-diffusion model of viruses' competition

$$\begin{cases} \dfrac{\partial u}{\partial t} = D_1 \dfrac{\partial^2 u}{\partial x^2} + \alpha_1 u(1 - \beta_1 I(u) - \gamma_1 I(v)) - \sigma_1(x)u, \\ \\ \dfrac{\partial v}{\partial t} = D_2 \dfrac{\partial^2 v}{\partial y^2} + \alpha_2 v(1 - \beta_2 I(u) - \gamma_2 I(v)) - \sigma_2(y)v. \end{cases}$$

$u(x,t),\ v(y,t)$ - virus density distribution

x, y - virus genotypes

t - time

Existence of stationary solutions

$$\begin{cases} D_1 u'' + \alpha_1 u(1 - \beta_1 I(u) - \gamma_1 I(v)) - \sigma_1(x) u = 0, \\ D_2 v'' + \alpha_2 v(1 - \beta_2 I(u) - \gamma_2 I(v)) - \sigma_2(y) v = 0 \end{cases}$$

$$I(u) = \int_{-\infty}^{\infty} u(x)dx,$$

$$I(v) = \int_{-\infty}^{\infty} v(y)dy.$$

$$u(\pm\infty) = 0, u(x) > 0$$

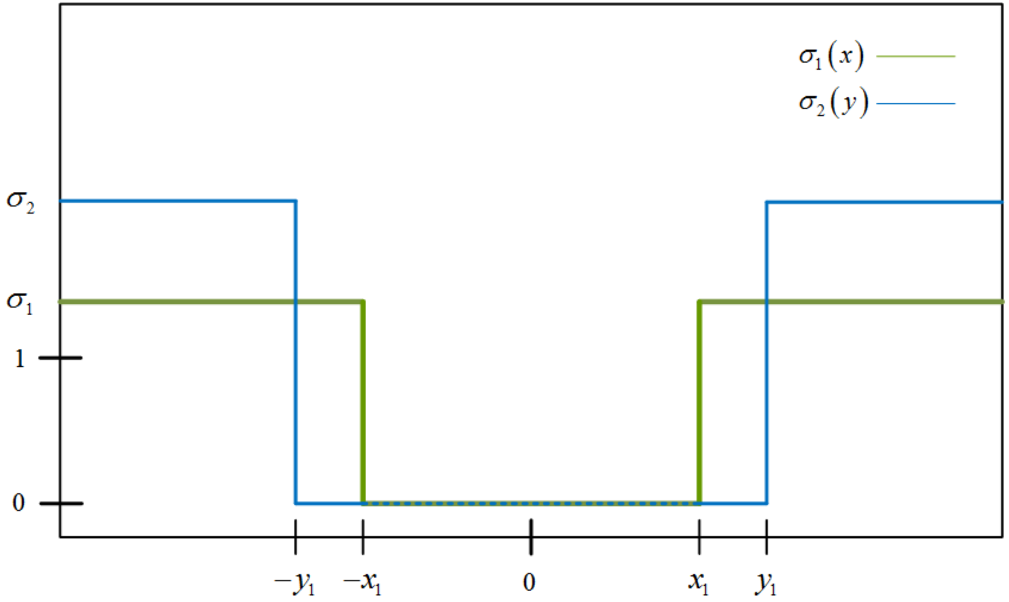
$$v(\pm\infty) = 0, v(y) > 0$$

$$\sigma_1(x), \sigma_2(y)$$

Functions $\sigma_1(x)$ and $\sigma_2(y)$

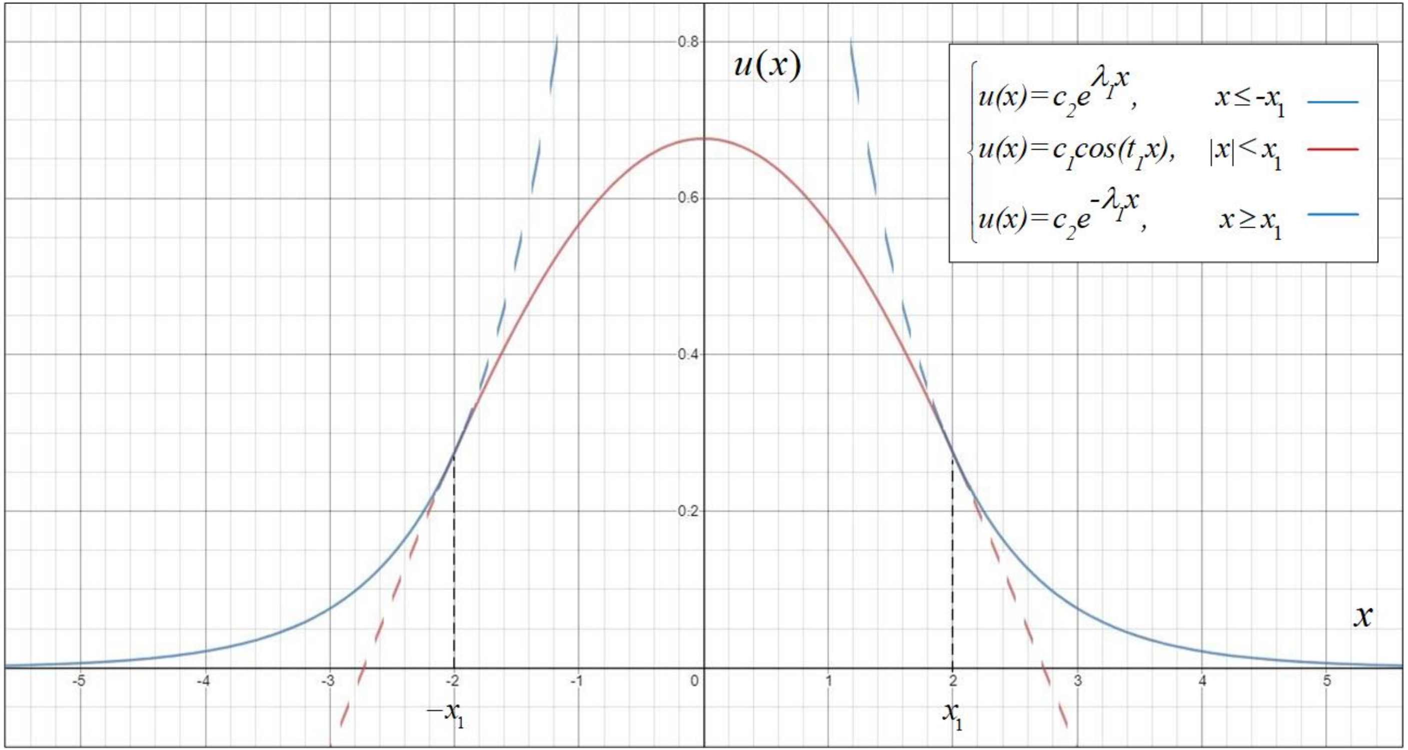
$$\sigma_1(x) = \begin{cases} \sigma_1, & \text{when} \quad |x| \geq x_1 \\ 0, & \text{when} \quad |x| < x_1 \end{cases}$$

$$\sigma_2(y) = \begin{cases} \sigma_2, & \text{when} \quad |y| \geq y_1 \\ 0, & \text{when} \quad |y| < y_1 \end{cases}$$

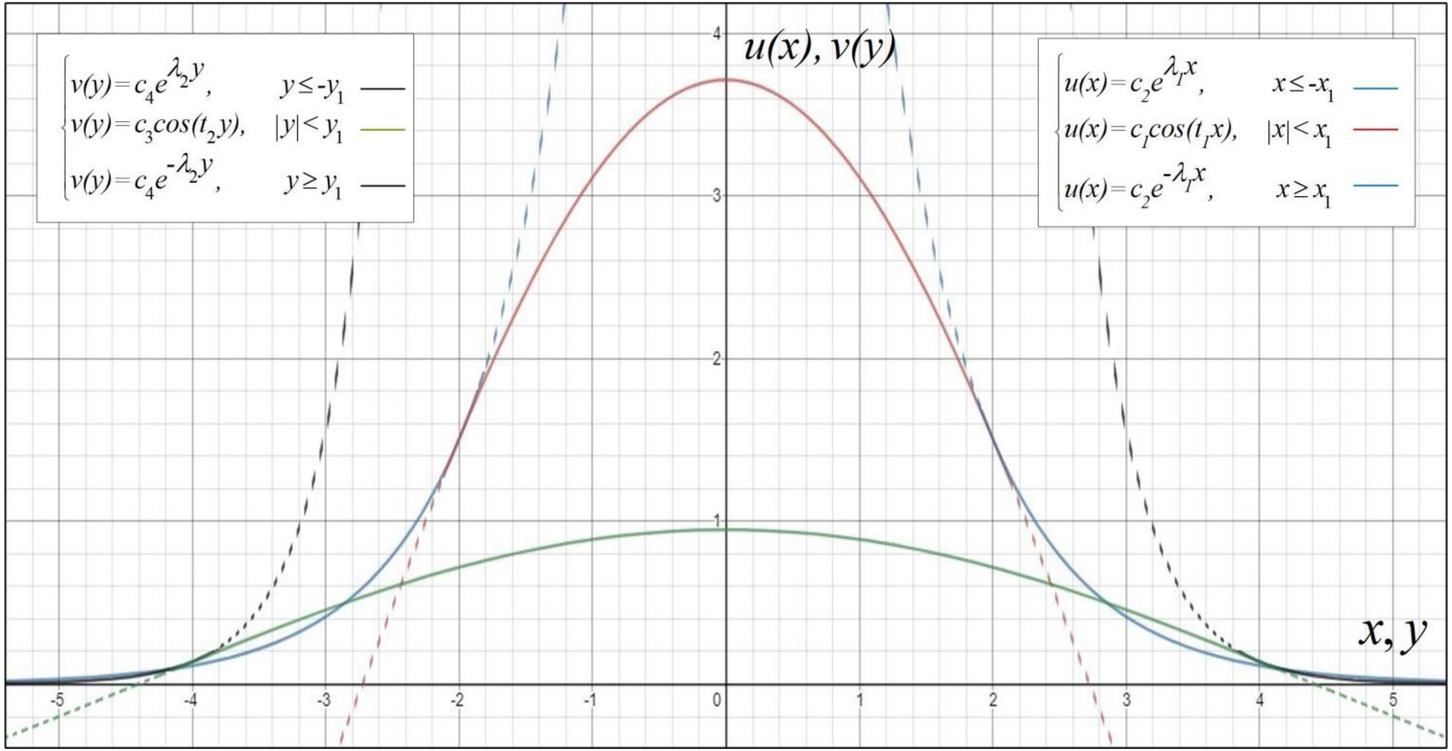


$$\sigma_{1,2} > 1.$$

Example of analytical solution



Example of analytical solution



Conditions to coexistence of viruses

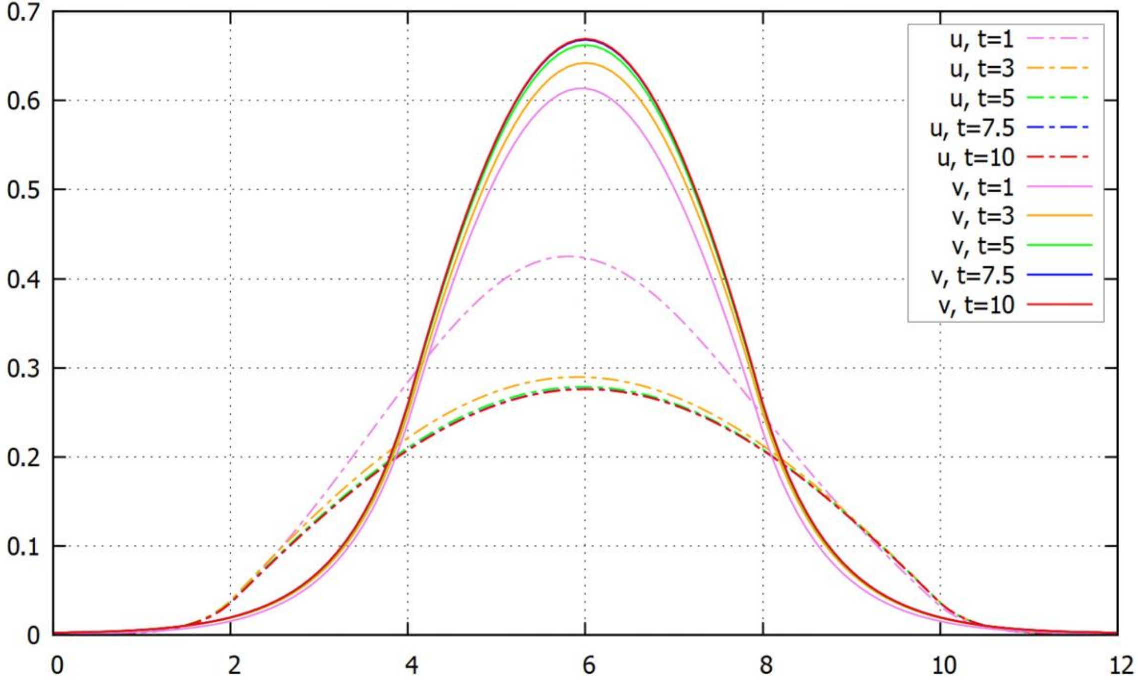
- The existence of both positive components $u(x)$ and $v(y)$ is possible only if the interval of non-mortality of functions $\sigma_1(x)$, $\sigma_2(y)$ is greater than the critical value

$$\xi_i^* = \frac{1}{\sqrt{\alpha_i}} \arccos\left(\sqrt{\frac{\alpha_i}{\sigma_i}}\right) \qquad i = 1, 2$$

- The existence of positive solutions depends of the relation between the values of the coefficients $\alpha_{1,2}, \beta_{1,2}, \gamma_{1,2}$. If $\alpha_1 > \alpha_2$, then both components of the solutions are positive for

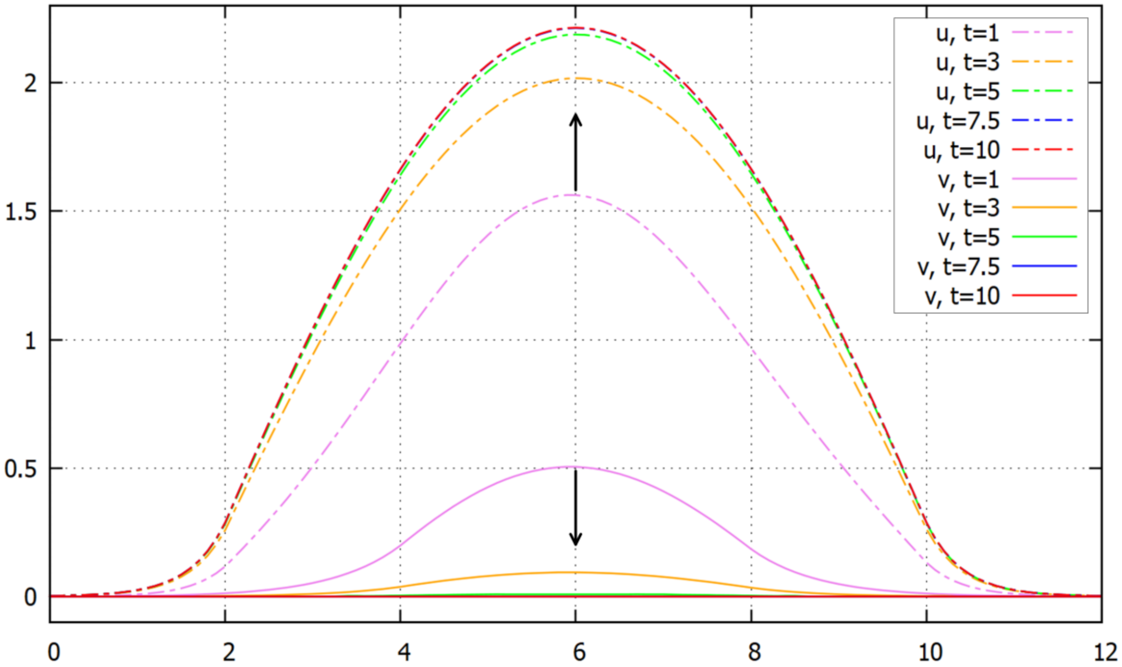
$$\beta_1 \geq \beta_2 \left(\frac{\alpha - k_1^2}{\alpha - k_2^2}\right) \quad \text{and} \quad \gamma_1 > \frac{\beta_1}{\beta_2}\gamma_2.$$

Numerical simulations of virus coexistence



$L = 12, D_1 = D_2 = \alpha_1 = \alpha_2 = 1, \beta_1 = 0.2, \gamma_1 = 0.1, \beta_2 = 0.1, \gamma_2 = 0.4$

Numerical simulations of virus coexistence



$L = 12, D_1 = D_2 = \alpha_1 = \alpha_2 = 1\ \beta_1 = 0.1, \gamma_1 = 0.1, \beta_2 = 0.1, \gamma_2 = \mathbf{0.07}$

Equal coefficients

$$\boxed{\alpha_1 = \alpha_2, \beta_1 = \beta_2, \gamma_1 = \gamma_2}$$

- We determinate that $u(x)$ is positive and $v(y)$ is negative. We have not found the values of parameters for which both components of the solution are positives.

- The existence of the only positive component is defined by the length of the interval of no mortality. Here x_1 must be greater than

$$\xi_1 = \frac{1}{\sqrt{\alpha}} \arctan\left(\sqrt{\frac{\sigma_1}{\alpha} - 1}\right)$$

Generalization of the virus mortality functions

- $\sigma_1(x), \sigma_2(y)$ are a bounded non-negative sufficiently smooth functions.

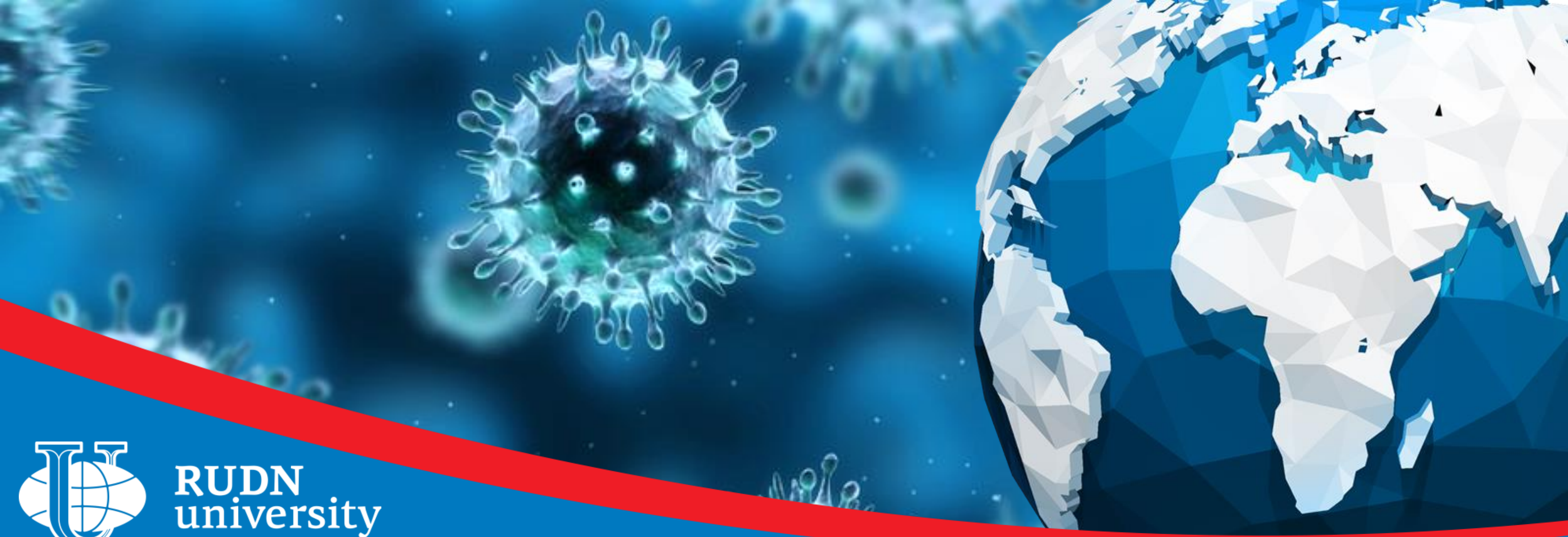
Theorem. *Suppose that $\sigma_1(x), \sigma_2(y)$ are sufficiently smooth bounded functions such that*

$$\sigma_1(x) = \begin{cases} \sigma_1 > \alpha_1, & |x| \geq x_1 \\ 0, & |x| \leq x_0 \end{cases}, \qquad \sigma_2(y) = \begin{cases} \sigma_2 > \alpha_2, & |y| \geq y_1 \\ 0, & |y| \leq y_0 \end{cases},$$

where $x_1 > x_0 > \frac{\pi}{2}$ and $y_1 > y_0 > \frac{\pi}{2}$. Then system of equations has positive solutions decaying at infinity.

Results and their biological interpretation

- The admissible interval where virus multiplication rate is larger than its mortality rate should be sufficiently long, and the mutation rate should be small enough.
- For equals coefficients, the competition between two viruses results in the disappearance of one of them and persistence of another one.
- For different coefficients, the coexistence of virus is subject to the correlation coefficient’s α, β and γ.



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Thank you!

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Mathematical Modelling in Biomedicine