

Multiscale Mathematical Modelling of Viral Infection

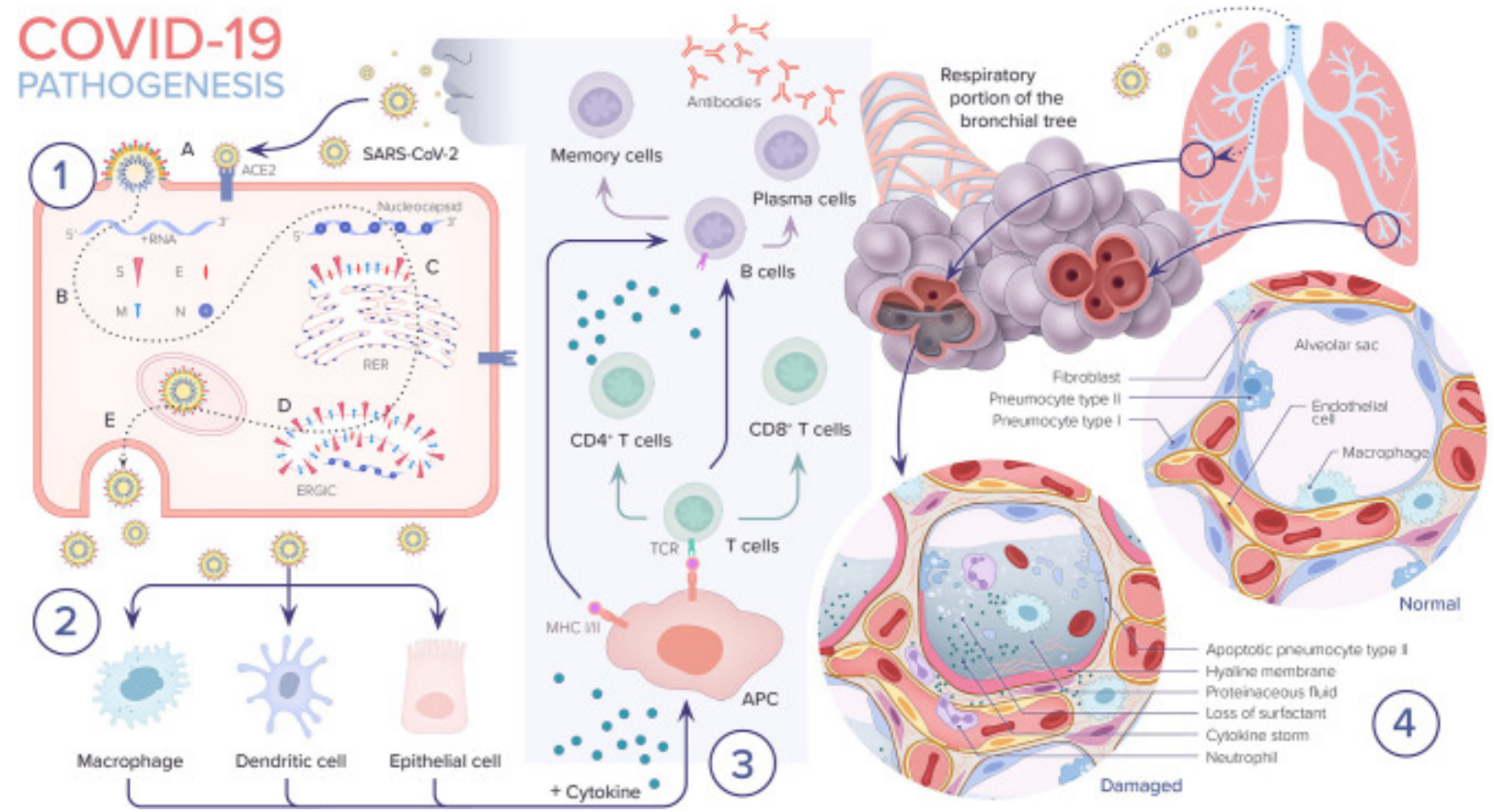
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COVID-19 pathogenesis.

- 1. SARS-CoV-2 enters the epithelial cell
- 2. SARS-CoV-2 infection induces inflammatory factors
- 3. Antigen presentation of SARS-CoV-2 stimulates humoral and cellular immunity resulting
- 4. In severe COVID-19 cases, the virus reaches the lower respiratory tract and infects type II pneumocytes leading



How Covid-19 affects the body

Eyes

Conjunctivitis, inflammation of the membrane that lines the front of the eye and inner eyelid, is common in the sickest patients

Lungs

Virus causes the air sacs in the lungs to become inflamed and damaging to the walls - this results in coughs, fevers and laboured breathing. It can lead to a potentially fatal condition known as acute respiratory distress syndrome (ARDS)

Kidneys

Kidney damage is common in severe cases and makes death more likely

Intestines

Virus can infect lower gastrointestinal tract, which can cause about 20% of patients to suffer from diarrhoea

Brain

Some patients have suffered strokes, seizures, confusion and brain inflammation

Nose

Some patients lose sense of smell. Scientists believe virus moves along nose's nerve endings and damage cells

Windpipe

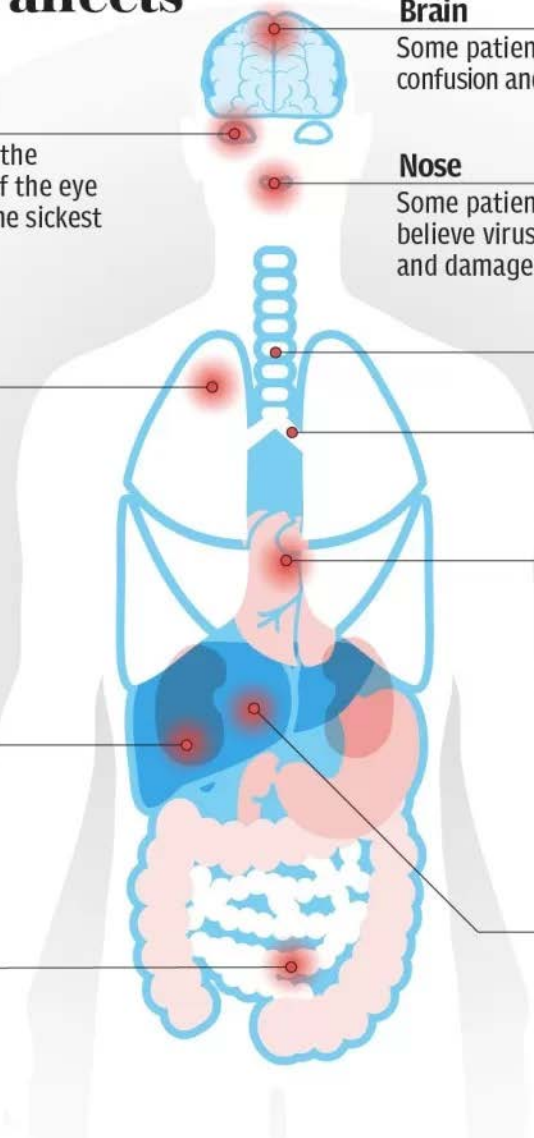
Bronchii

Heart and blood vessels

Scientists believe infection may promote blood clots, heart attacks and cardiac inflammation as the virus binds to ACE2 receptors and enters cells lining blood vessels

Liver

Up to 50% of hospitalised patients have indication of struggling liver function. The immune system in overdrive or drugs given to fight the virus may be causing damage



Circulating virus in the organism

$$\frac{\partial U}{\partial t} = -aUV,$$

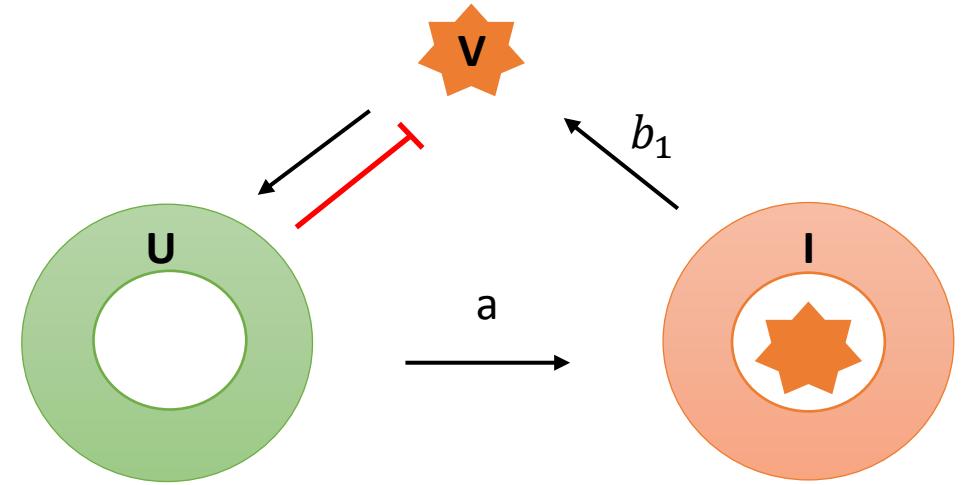
$$\frac{\partial I}{\partial t} = aUV - \beta I,$$

$$\frac{\partial V}{\partial t} = D \frac{\partial^2 V}{\partial x^2} + b_1 I_\tau - \sigma_1 V$$

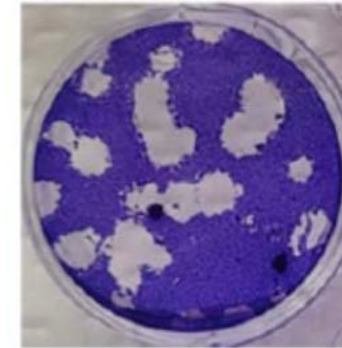
(1) **U** Concentration of uninfected cells

(2) **I** Concentration of infected cells

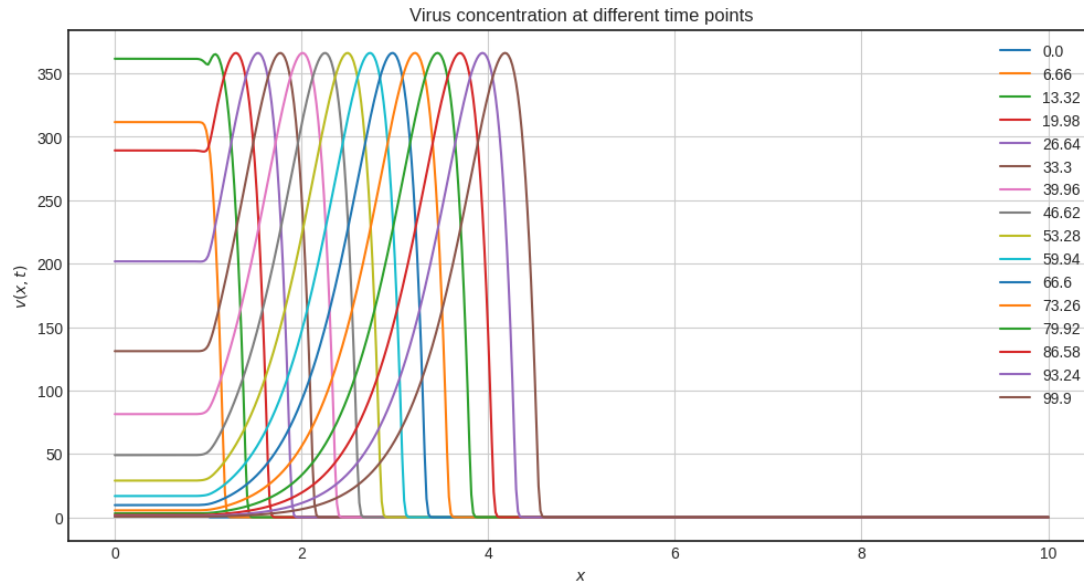
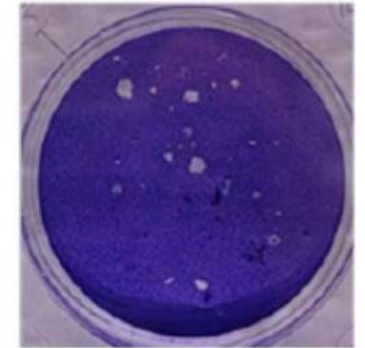
(3) **V** Concentration of virus in tissue



Delta



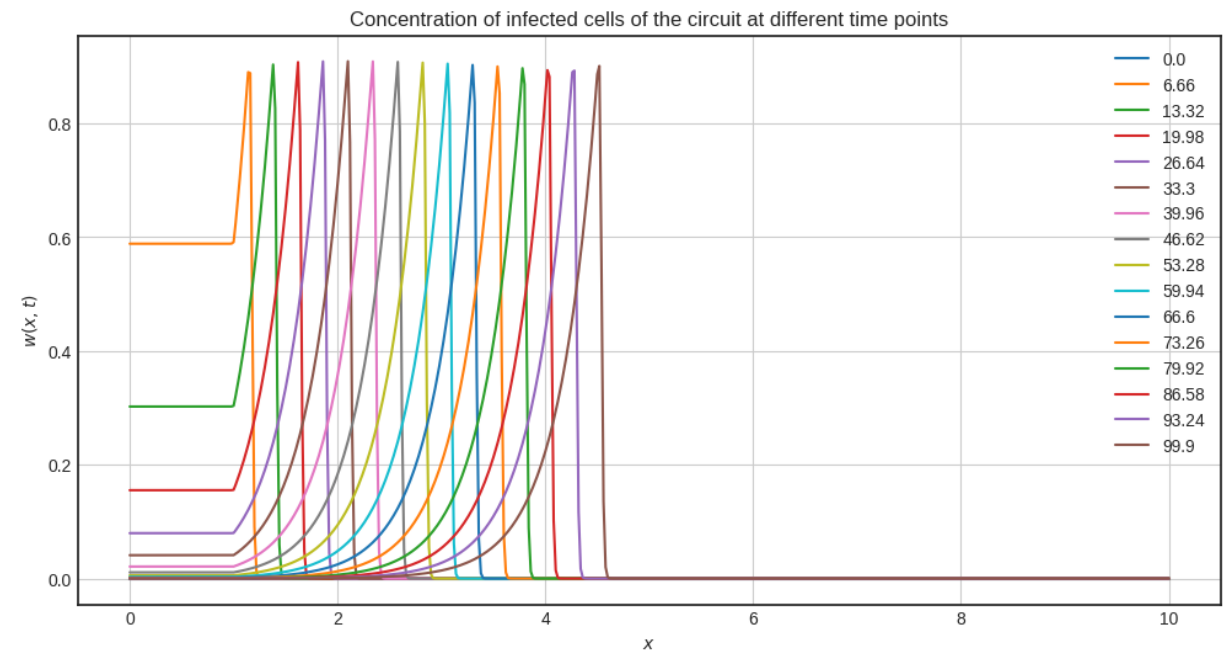
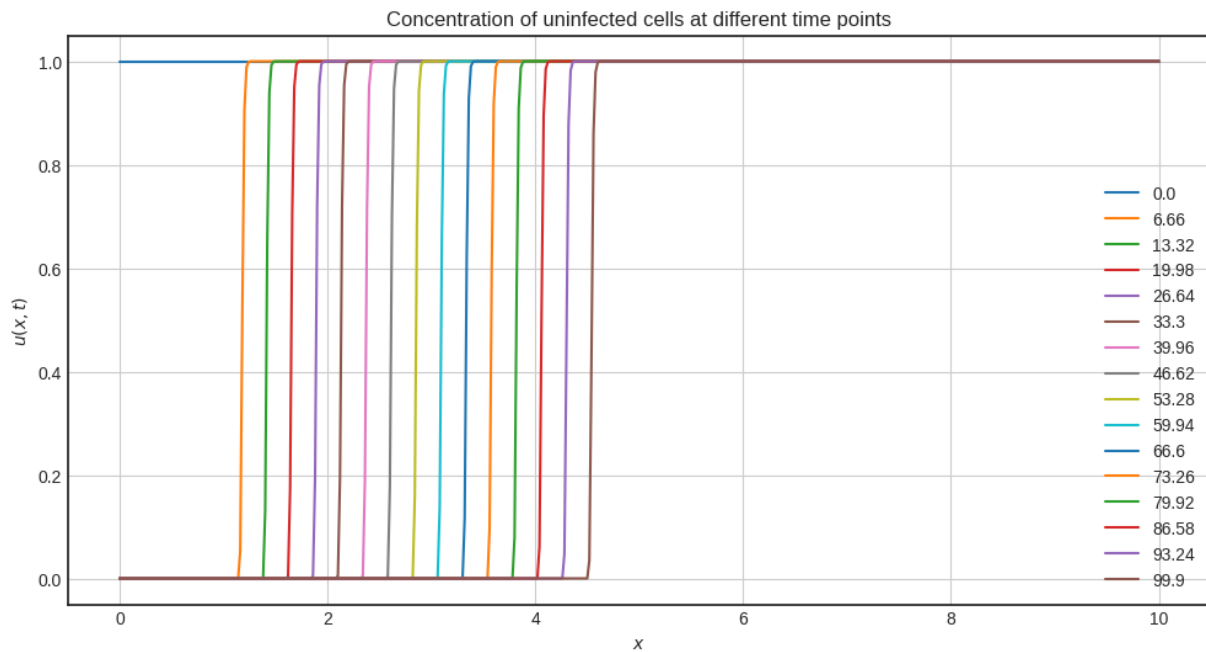
Omicron



$$V_x \approx bcu_0 / (\beta\sigma)$$

$$c = \min_{\mu > \mu_0} F(\mu) \equiv \frac{\sqrt{D}\mu}{\sqrt{\mu + \sigma - abu_0 e^{-\mu\tau} / (\mu + \beta)}}$$

Concentration of Uninfected and Infected



Circulating virus in the organism

$$\frac{\partial U}{\partial t} = -aUV,$$

(1) **U** Concentration of uninfected cells

$$\frac{\partial I}{\partial t} = aUV - \beta(T)I,$$

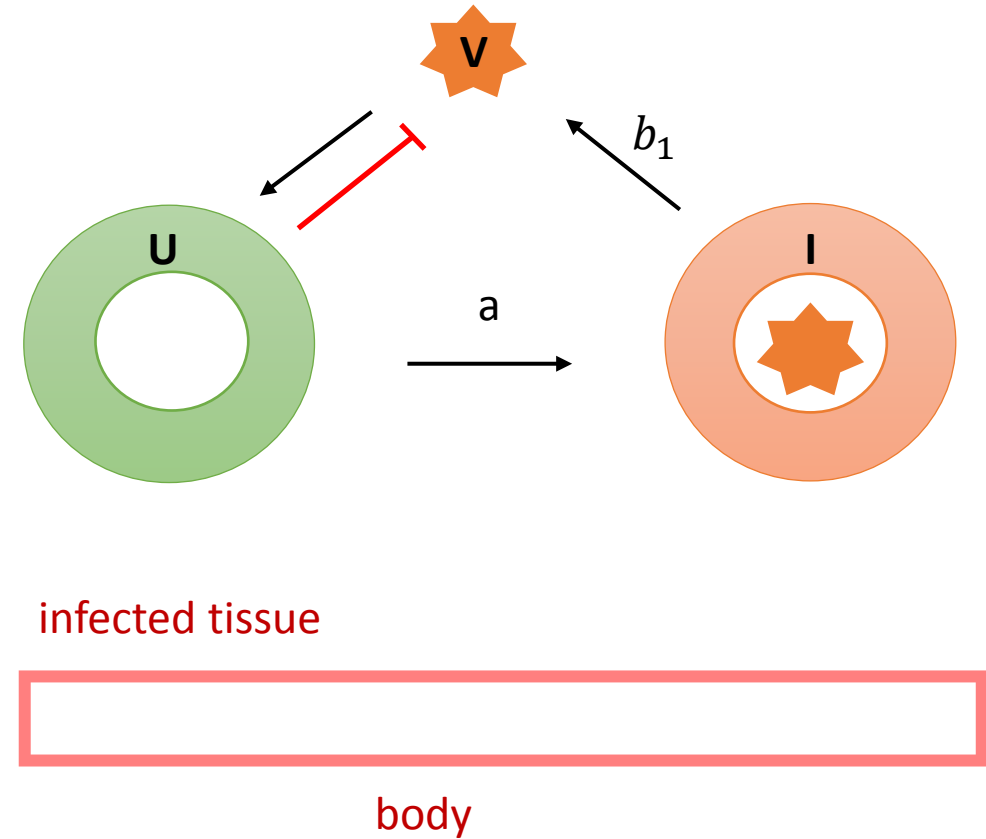
(2) **I** Concentration of infected cells

$$\frac{\partial V}{\partial t} = D \frac{\partial^2 V}{\partial x^2} + b_1 I_\tau - (k_2 + \sigma_1)V,$$

(3) **V** Concentration of virus in tissue

$$\frac{dW}{dt} = k_3 J(V) - \sigma_2 W,$$

(4) **W** Concentration of virus in body



$$J(V) = \int_{-\infty}^{\infty} V(x, t) dx$$

Circulating virus in the organism

$$\frac{\partial U}{\partial t} = -aUV,$$

(1) **U** Concentration of uninfected cells

$$\frac{\partial I}{\partial t} = aUV - \beta(T)I,$$

(2) **I** Concentration of infected cells

$$\frac{\partial V}{\partial t} = D \frac{\partial^2 V}{\partial x^2} + \frac{b_1}{1 + k_1 Z} I_\tau - (k_2 + \sigma_1)V,$$

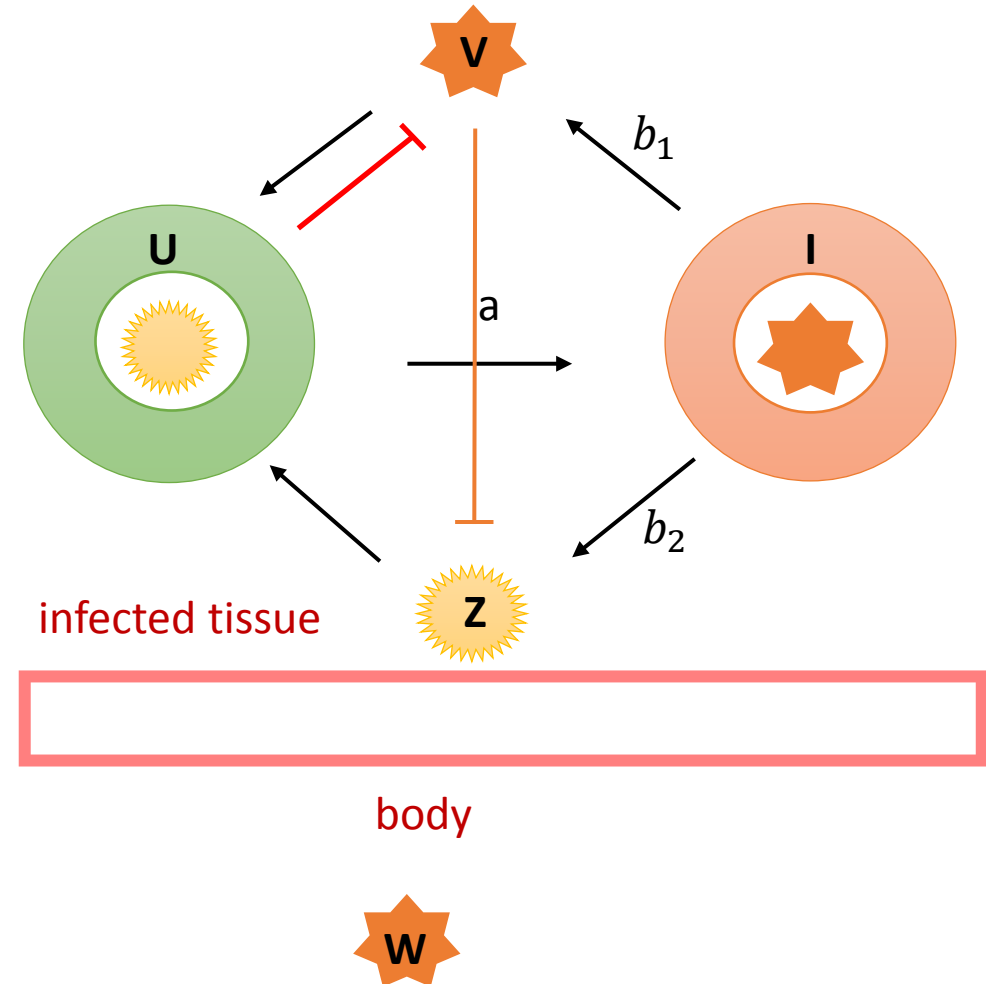
(3) **V** Concentration of virus in tissue

$$\frac{dW}{dt} = k_3 J(V) - \sigma_2(A)W,$$

(4) **W** Concentration of virus in body

$$\frac{dZ}{dt} = b_2 J(I) e^{-k_4 J(V)} - \sigma_3 Z$$

(5) **Z** Concentration of interferon



$$J(I) = \int_{-\infty}^{\infty} I(x, t) dx, \quad J(V) = \int_{-\infty}^{\infty} V(x, t) dx$$

Circulating virus in the organism

$$\frac{\partial U}{\partial t} = -aUV,$$

$$\frac{\partial I}{\partial t} = aUV - \beta(T)I,$$

$$\frac{\partial V}{\partial t} = D \frac{\partial^2 V}{\partial x^2} + \frac{b_1}{1 + k_1 Z} I_\tau - (k_2 + \sigma_1(A))V,$$

$$\frac{dW}{dt} = k_3 J(V) - \sigma_2(A)W,$$

$$\frac{dZ}{dt} = b_2 J(I) e^{-k_4 J(V)} - \sigma_3 Z,$$

$$\frac{dT}{dt} = b_3 W - \sigma_4 T J(I),$$

$$\frac{dA}{dt} = b_4 W - \sigma_5 WA.$$

(1) U Concentration of uninfected cells

(2) I Concentration of infected cells

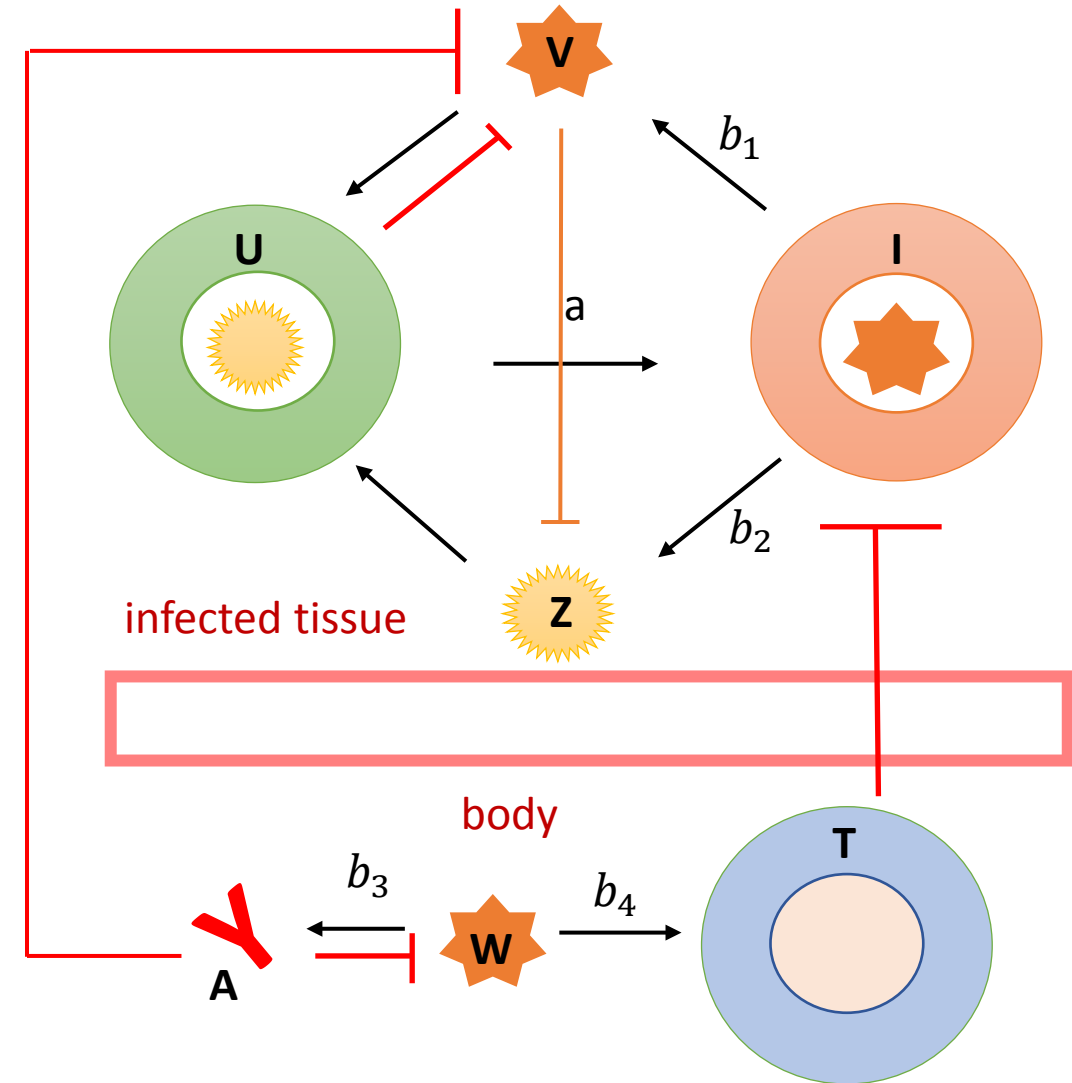
(3) V Concentration of virus in tissue

(4) W Concentration of virus in body

(5) Z Concentration of interferon

(6) T Concentration of cytotoxic T-lymphocytes

(7) A Concentration of antibodies



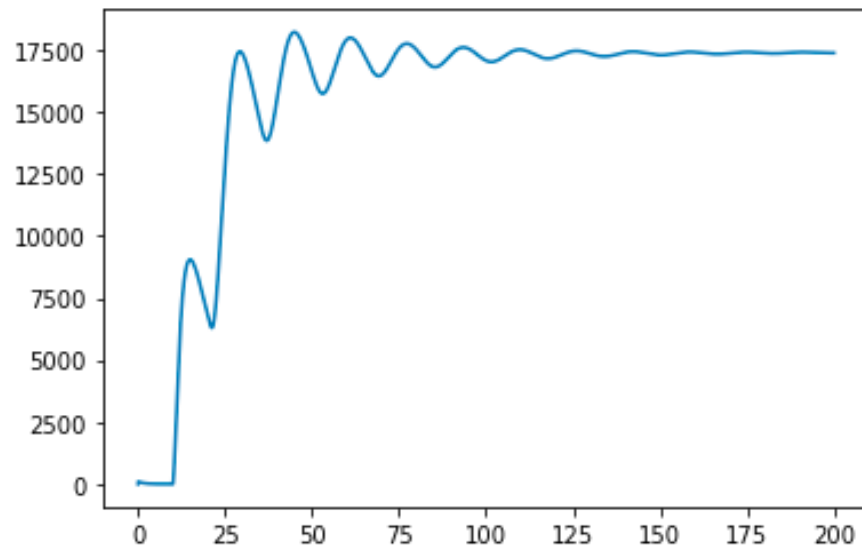
$$J(I) = \int_{-\infty}^{\infty} I(x, t) dx, \quad J(V) = \int_{-\infty}^{\infty} V(x, t) dx$$

Analytical solution

$$J(v) = \frac{cu_0}{\beta(\theta)(k_2 + \sigma_1(y))} b(J) = \frac{cu_0}{\beta(\theta)(k_2 + \sigma_1(y))} (b_1 - \alpha(y)J(v)e^{-k_4J(v)})$$

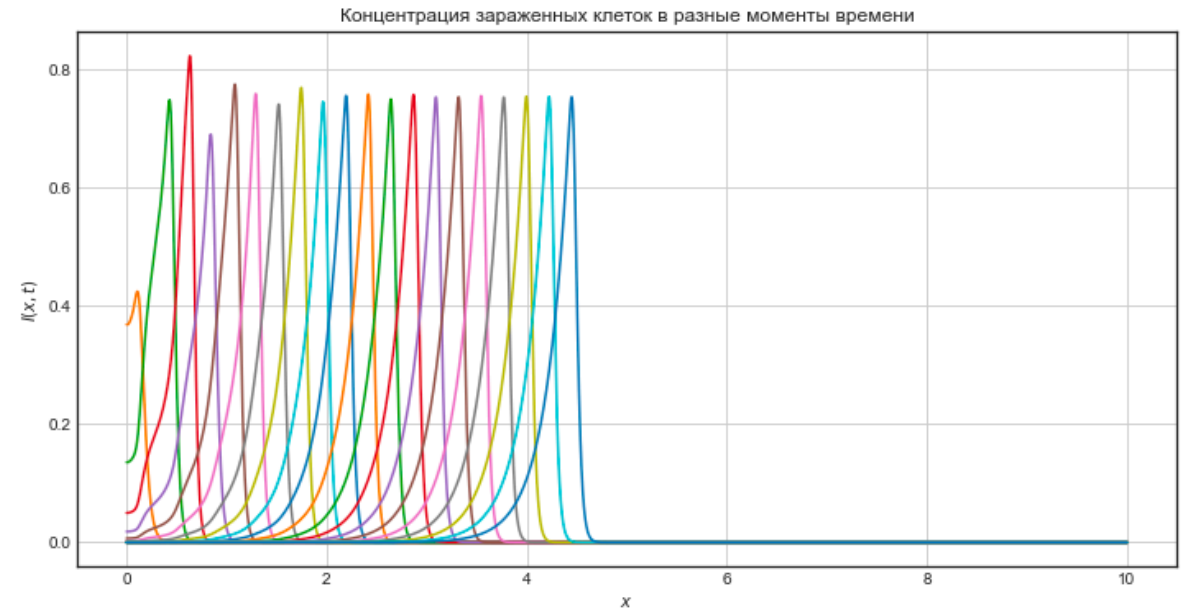
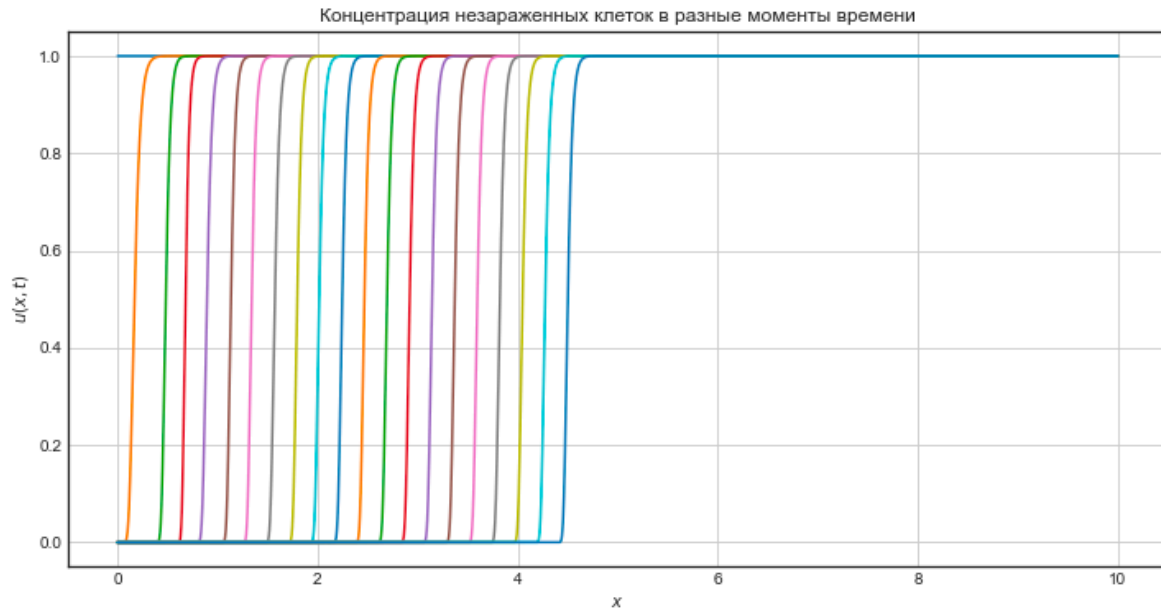
$$w = \frac{cu_0\sigma}{\beta(\theta)(k_2 + \sigma_1(y))} (b_1 - \alpha(y)J(v)e^{-k_4J(v)}), \quad \sigma = \frac{k_3\sigma_{51}}{\sigma_{20}\sigma_{51} + \sigma_{21}b_4}$$

$$c^2 = \frac{D\mu^2(\mu + \beta(\theta))}{(\mu + \sigma_1(y) + k_2)(\mu + \beta(\theta)) - au_0b(J)e^{-\mu\tau}}$$



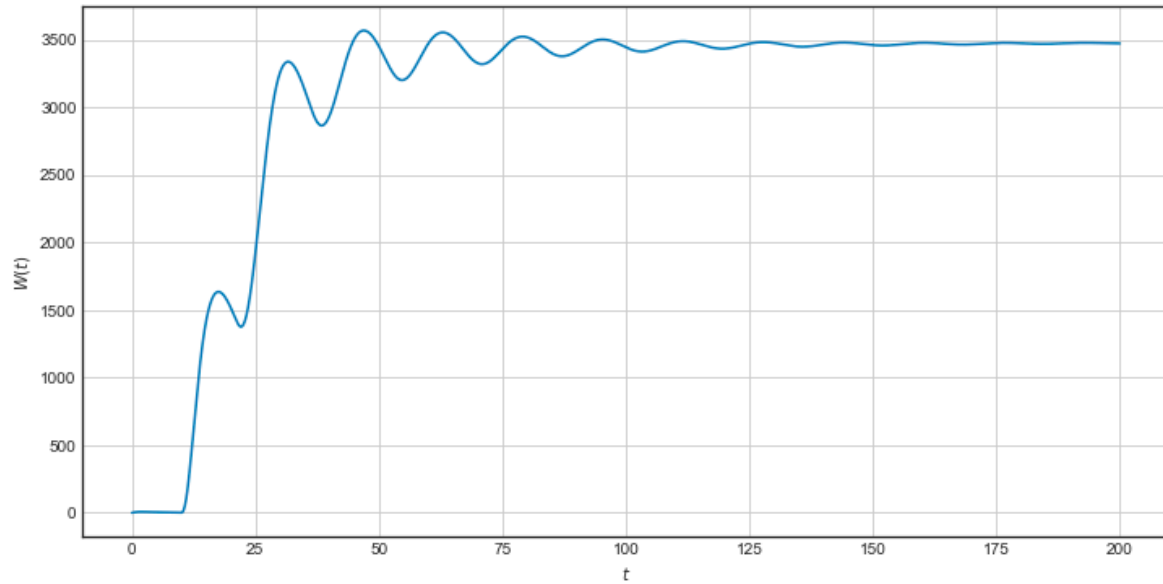
parameter	numerical	analitical
J(v)	17334.7119	17450.6305
w	34673.7332	34901.2610
wave speed	0.0225	0.0228

Concentration of Uninfected and Infected

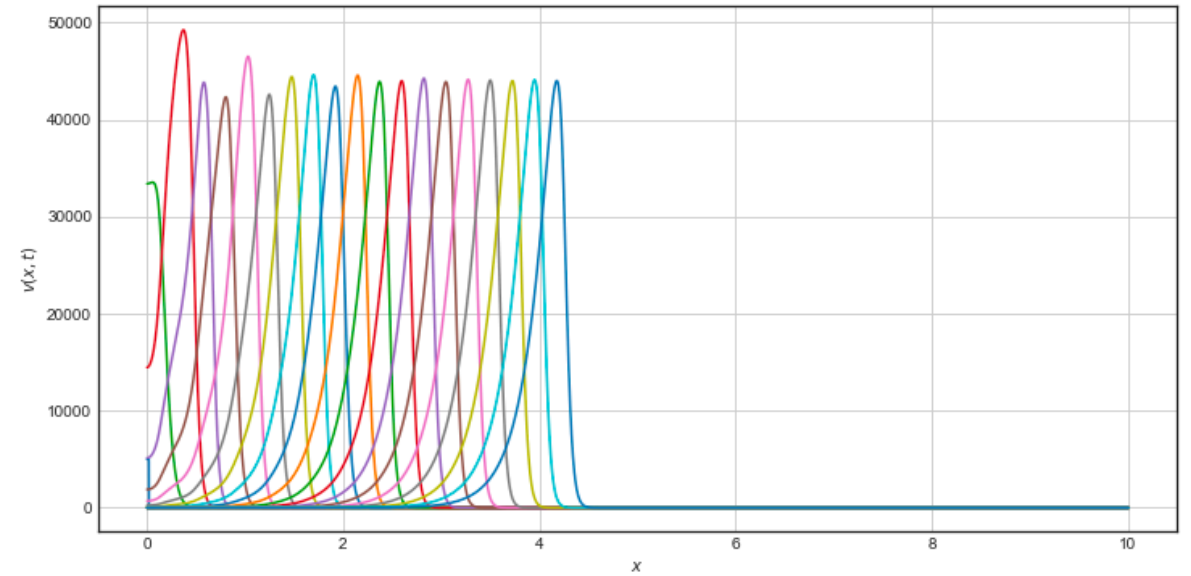


Concentration of Virus

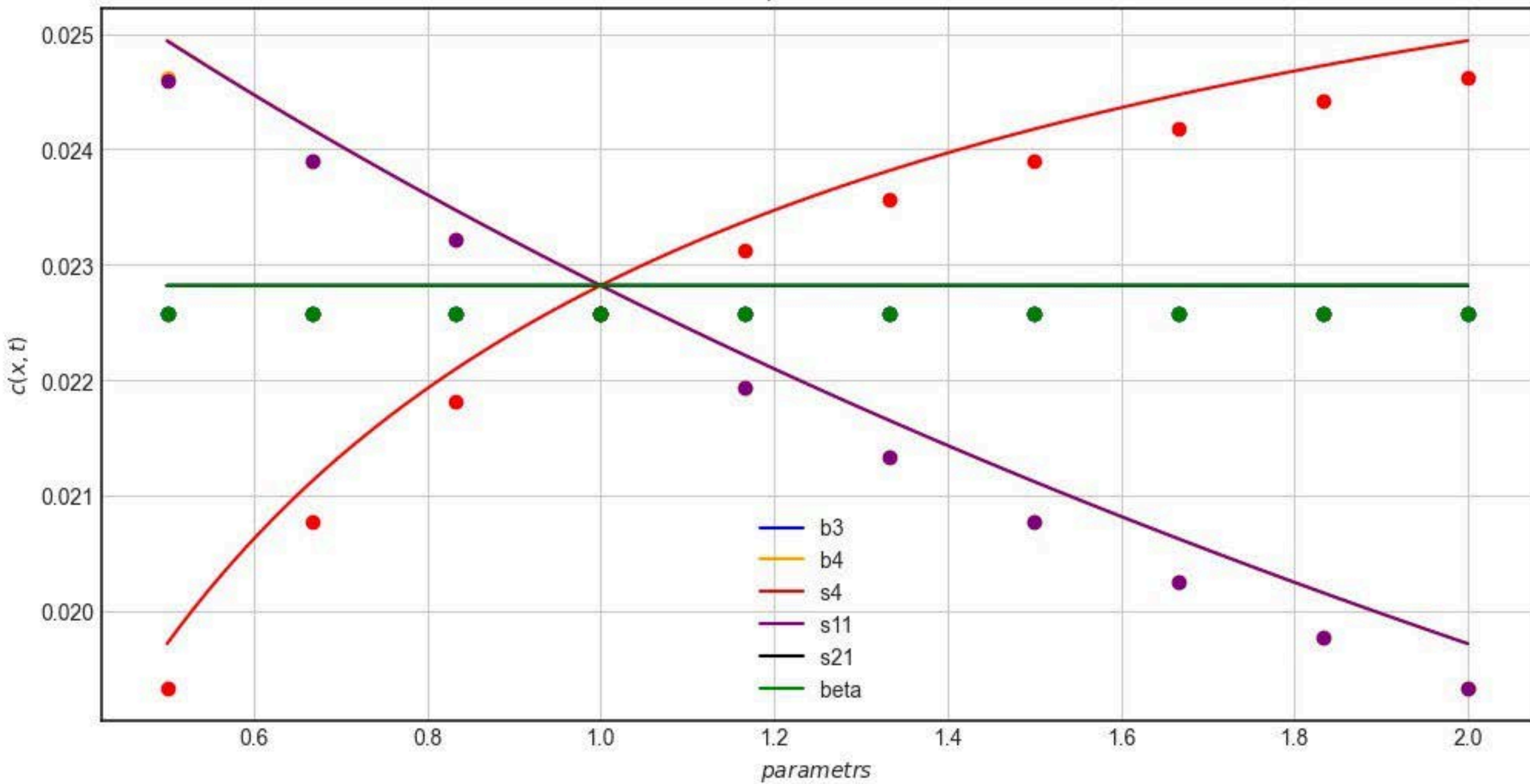
Концентрация вируса в кровотоке



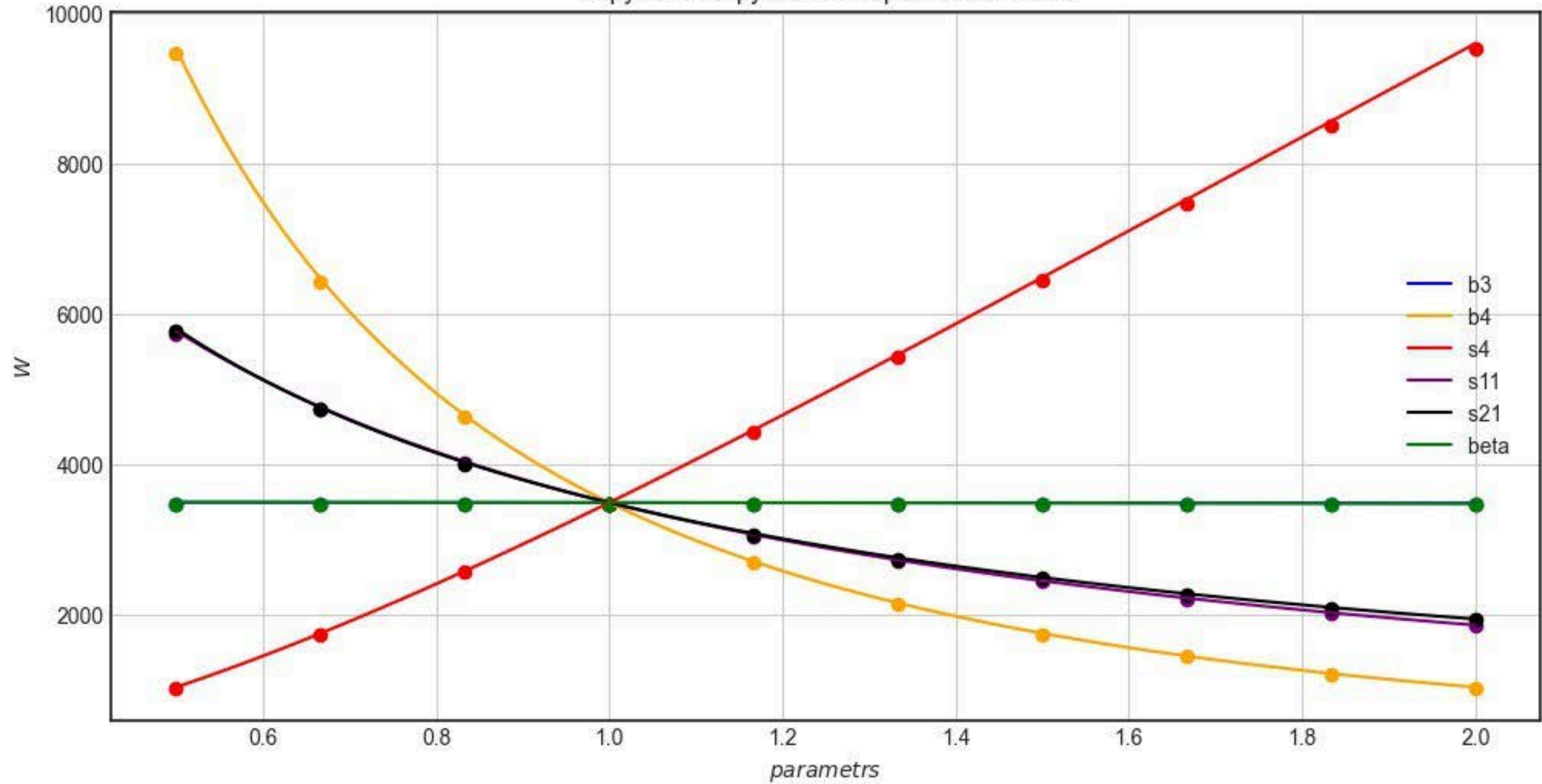
Концентрация вируса в разные моменты времени



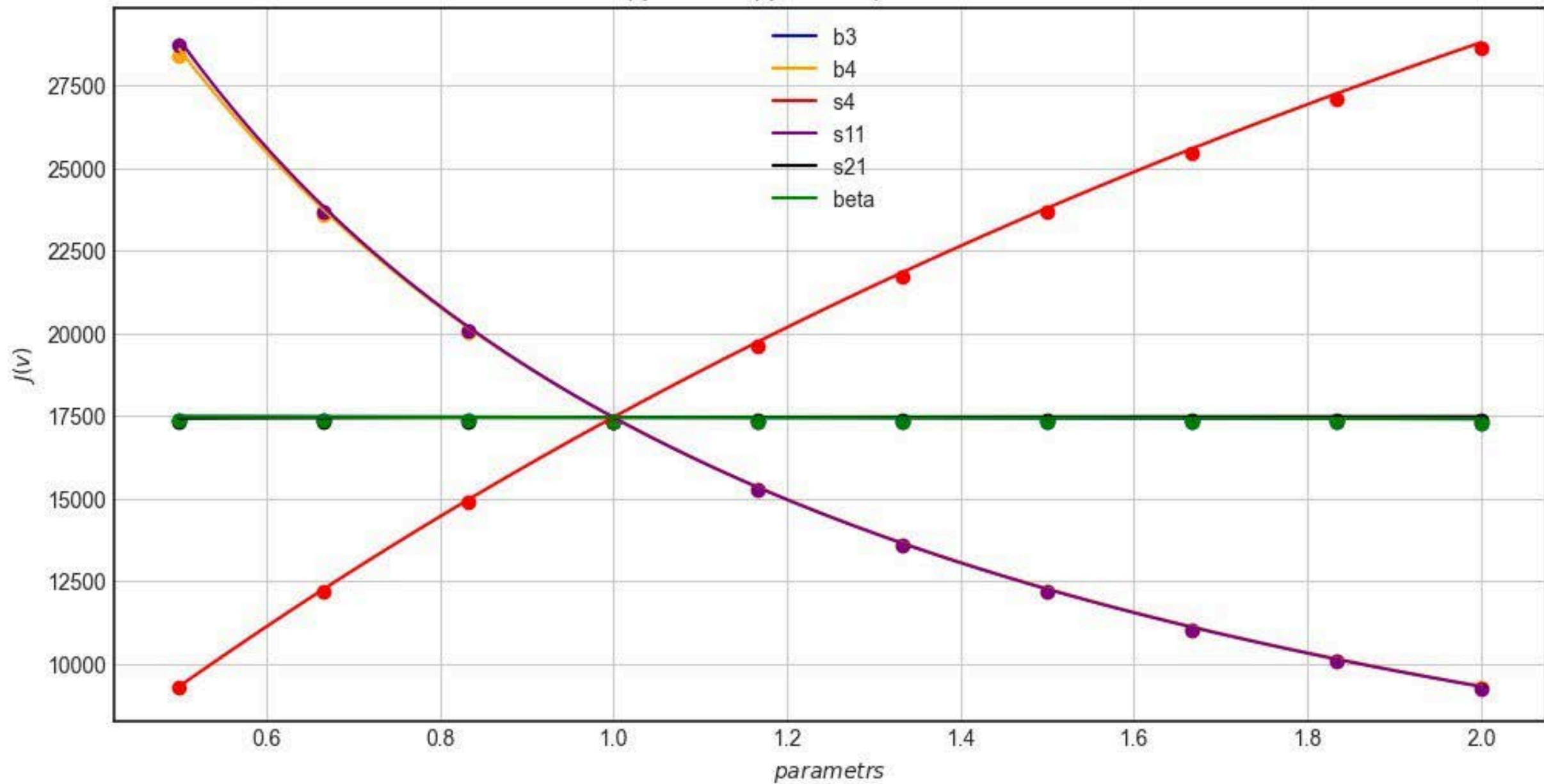
Скорость волны



Вирусная нагрузка вне зараженной ткани



Вирусная нагрузка в зараженной ткани



Conclusion

- Numerical and analytical calculations of the model taking into account circulating virus were performed.
- The dependence of the wave velocity and viral load on the parameters of the initial and adaptive immune response was obtained.
- The influence of the intensity of the initial and adaptive immune response on the rate of virus spread and total viral load was evaluated.

Thank you for your attention
