Dynamics of HIV infection

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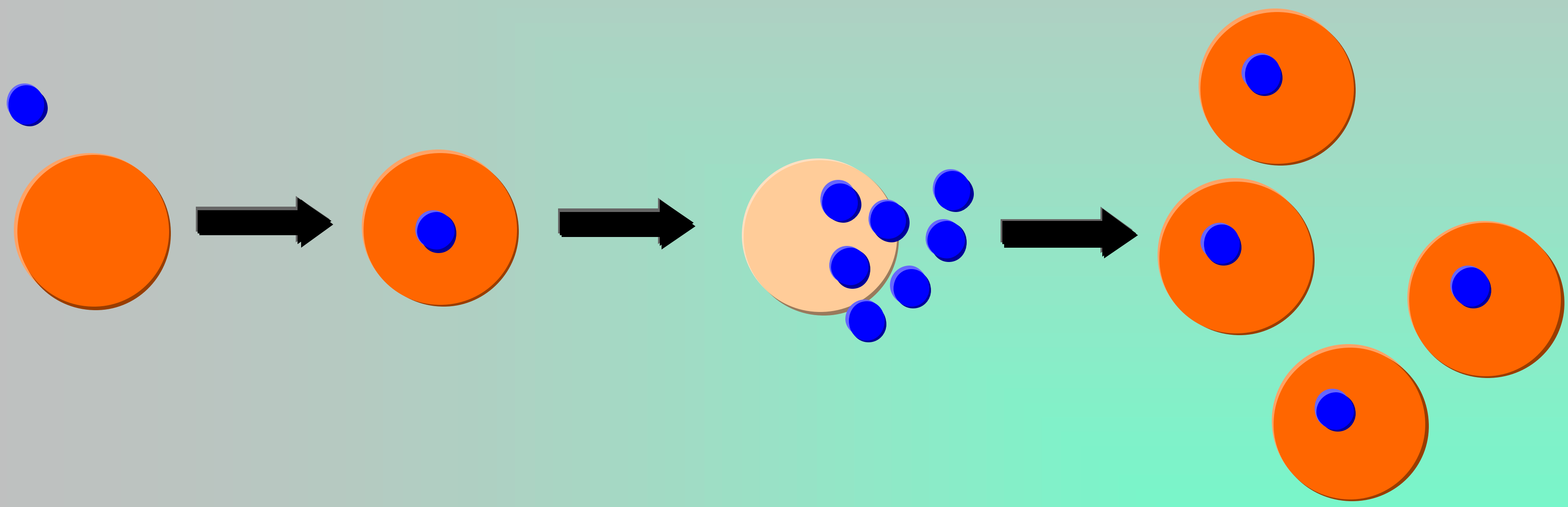
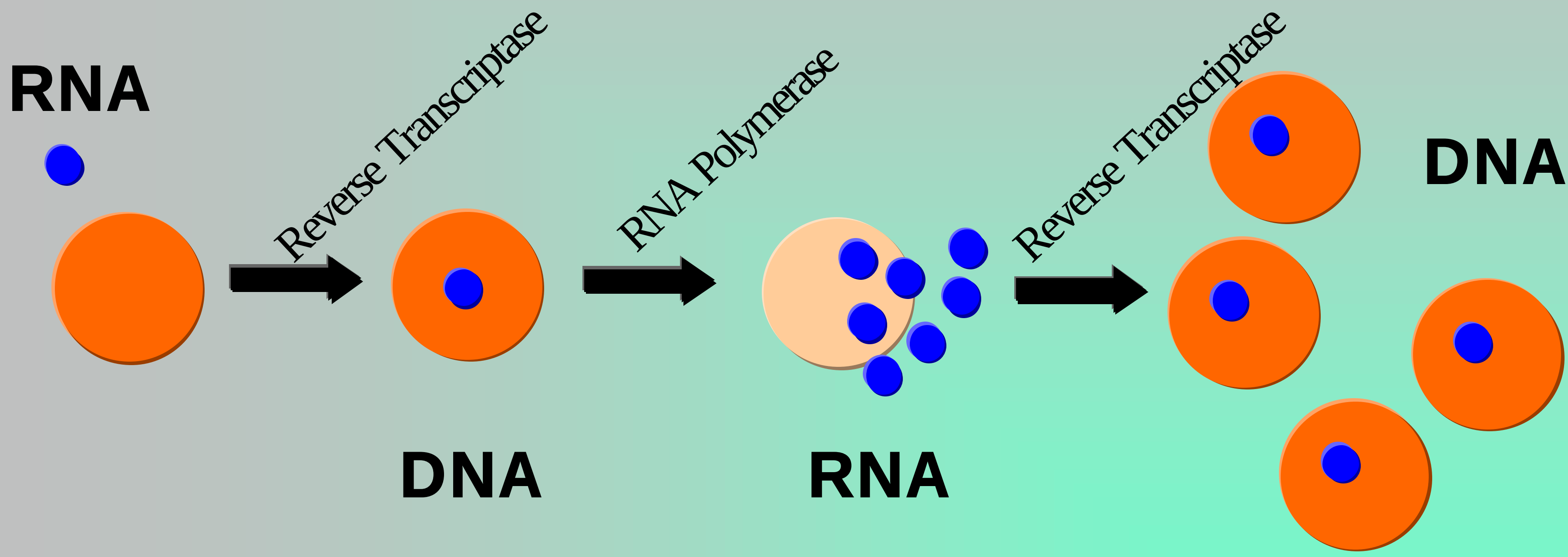
The basic idea of a virus:



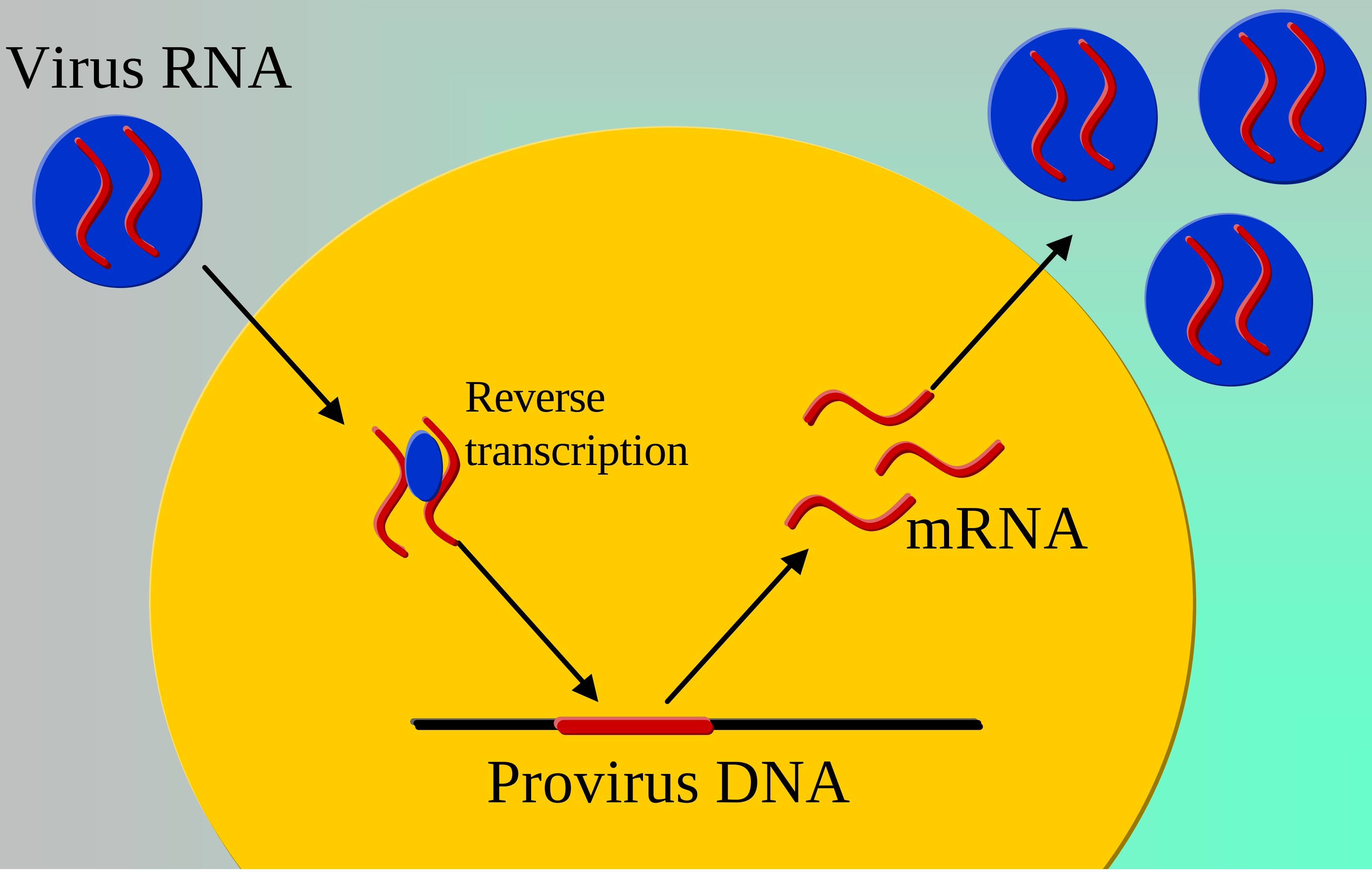
'Replicate me!'

The basic idea of a retrovirus:

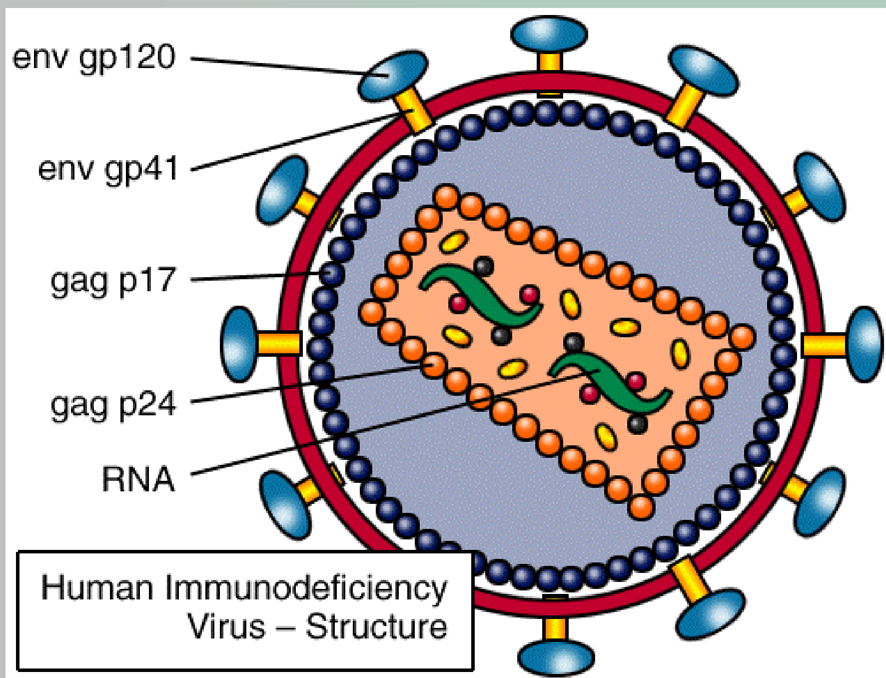


'Reverse transcribe me!
Integrate me!
RNA polymerase me!'

The basic idea of a retrovirus:



HIV is a retrovirus



RNA — Virion

↑↓

DNA — Cell

Viral DNA integrates into the host cell genome.

Images of HIV

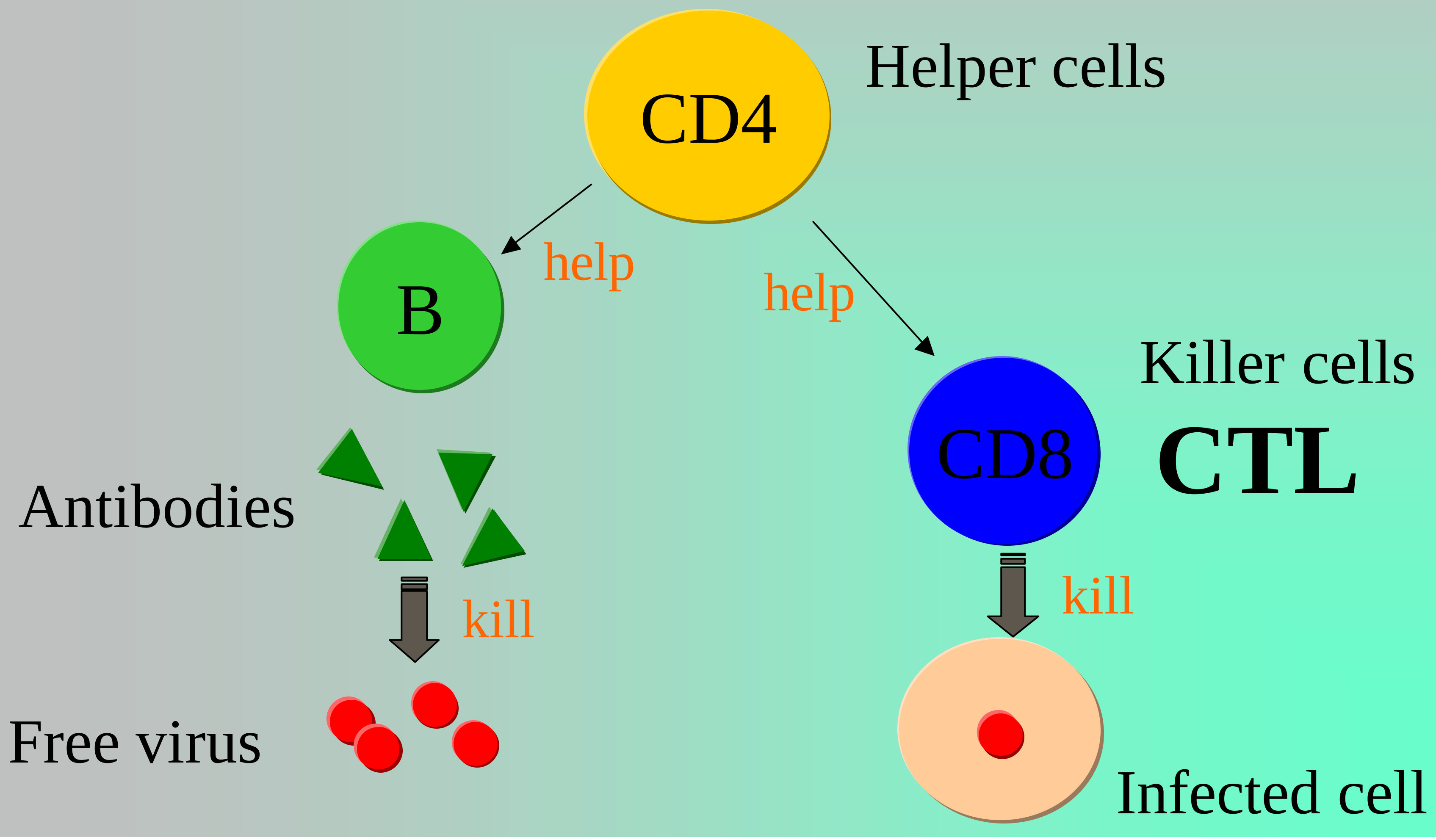
Human immunodeficiency virus (HIV)

- HIV was discovered in 1984.
- Now there are 35 million infected, 15 million dead.
- There is anti-viral therapy with problematic side effects.
- There is no vaccine.

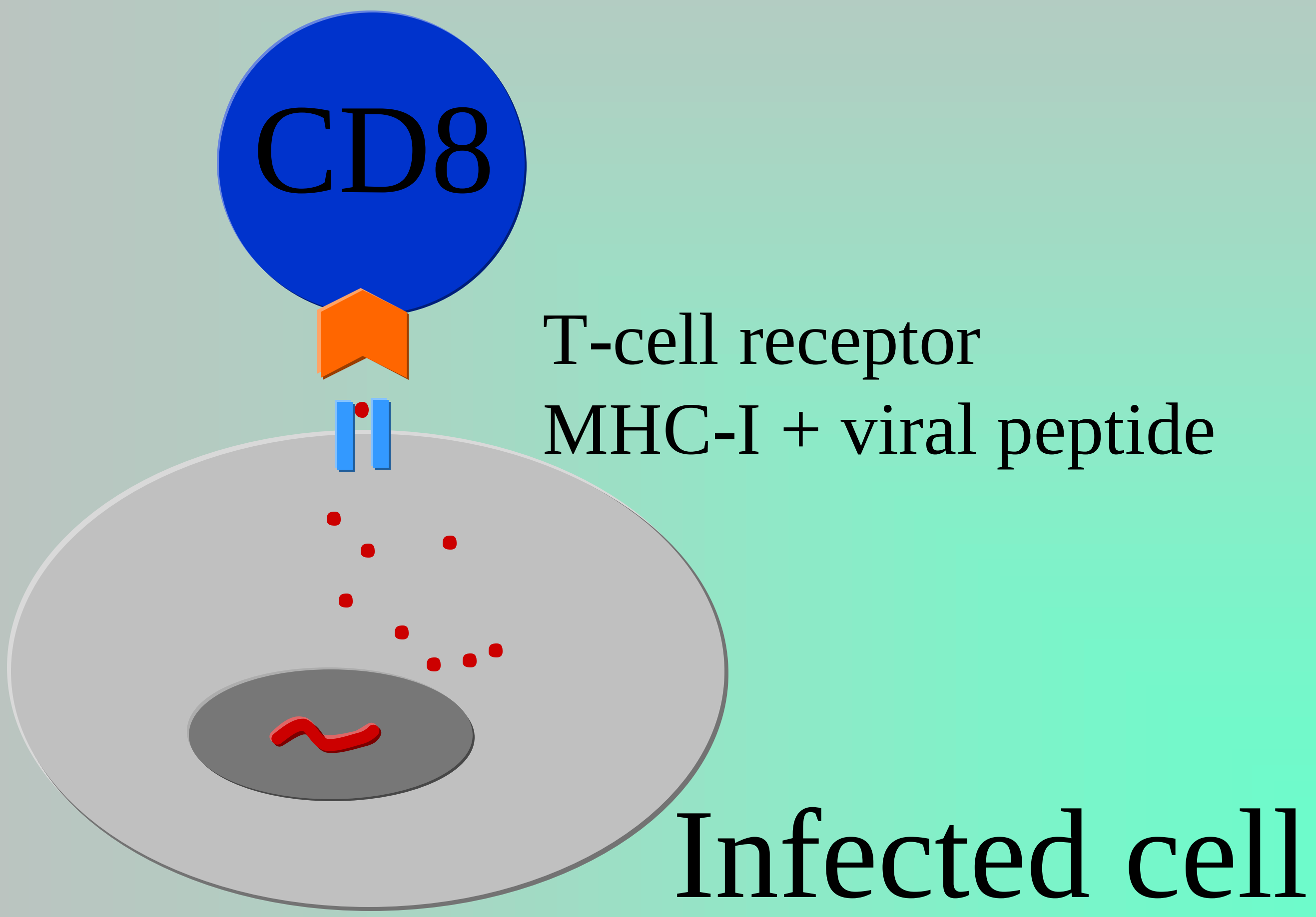
Retroviruses

- Oncoviruses (HTLV)
- Lentiviruses (HIV, SIV, FIV, EIAV, ...)
- Spumaviruses

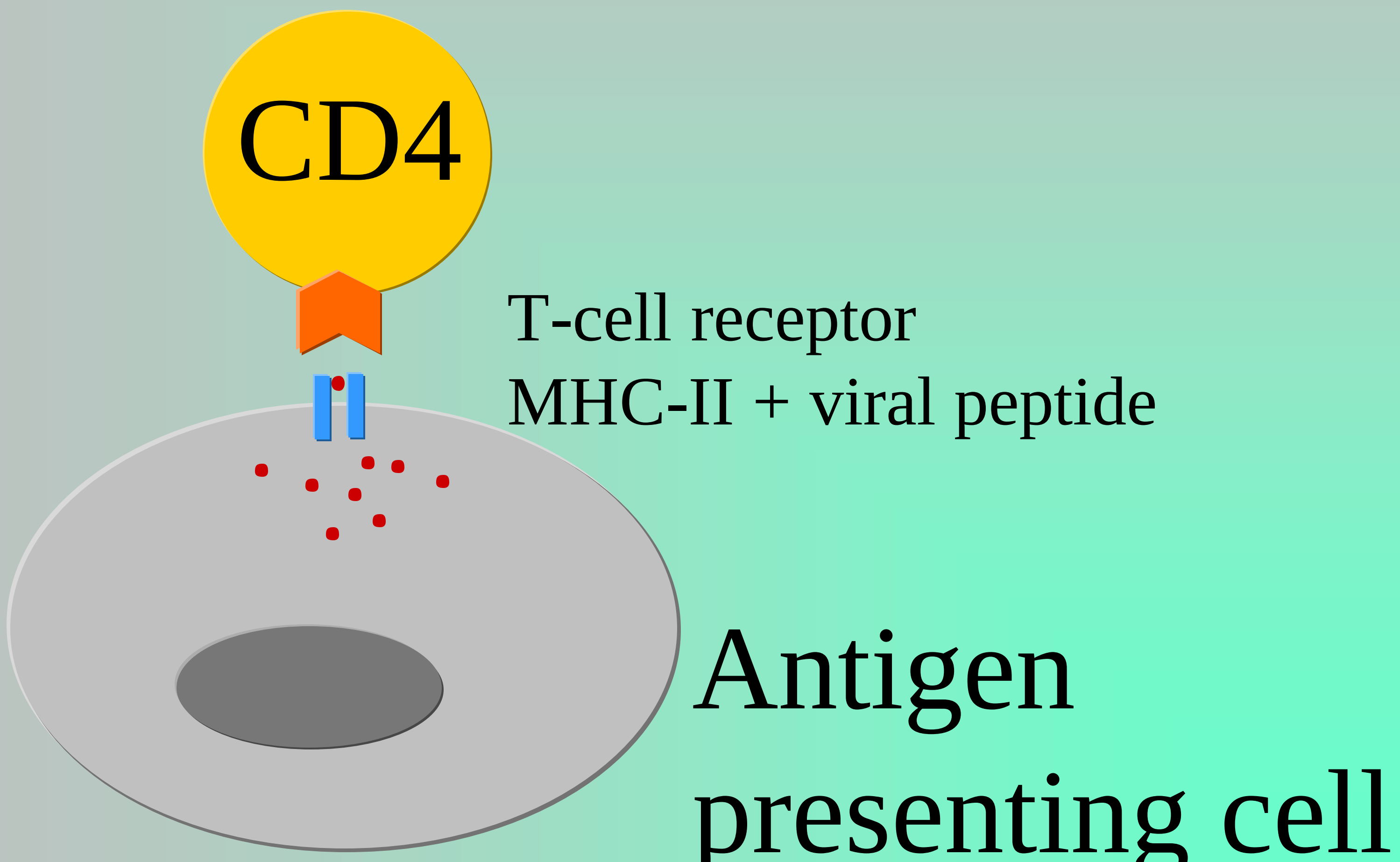
Viruses are opposed by immune responses



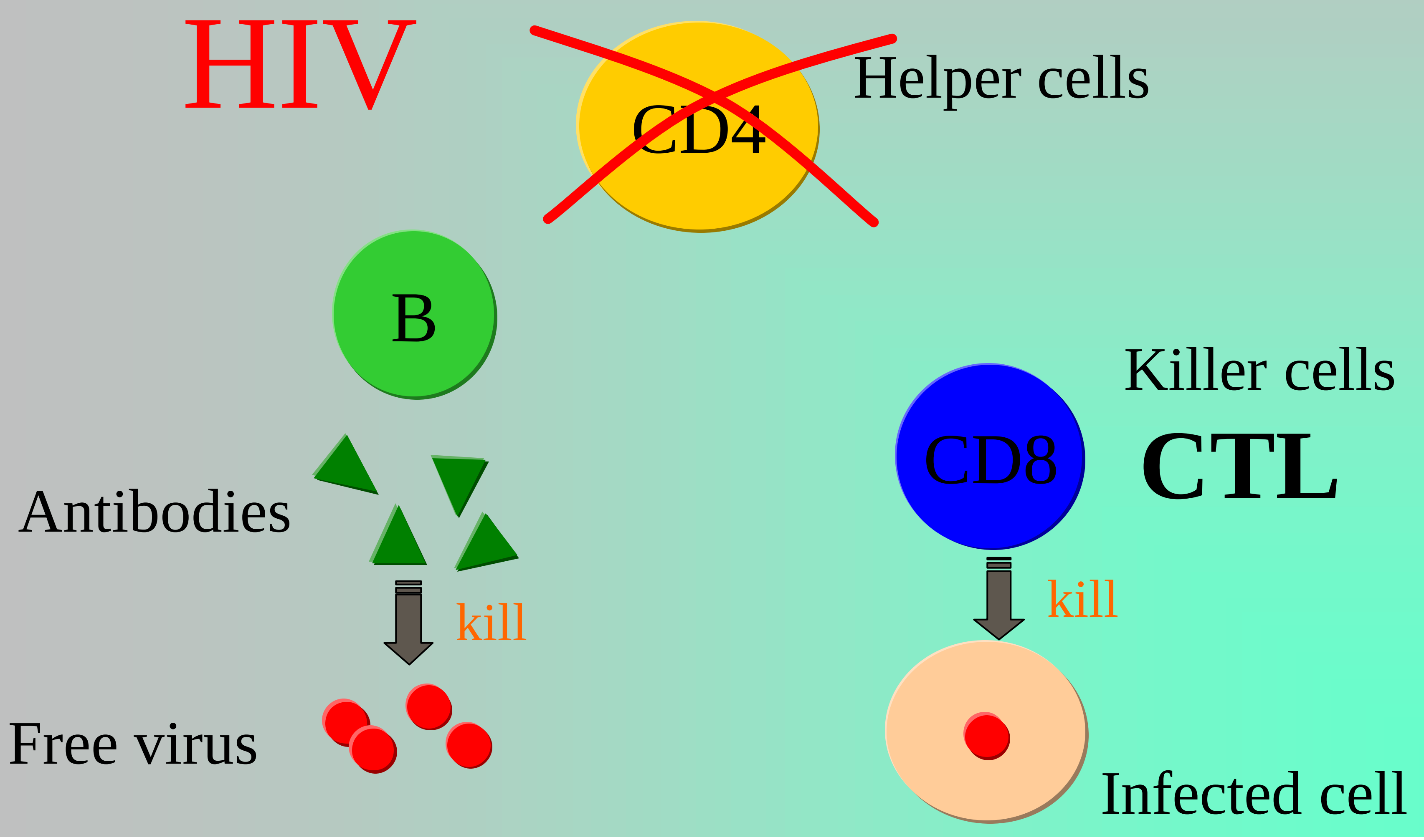
CD8 cell recognition



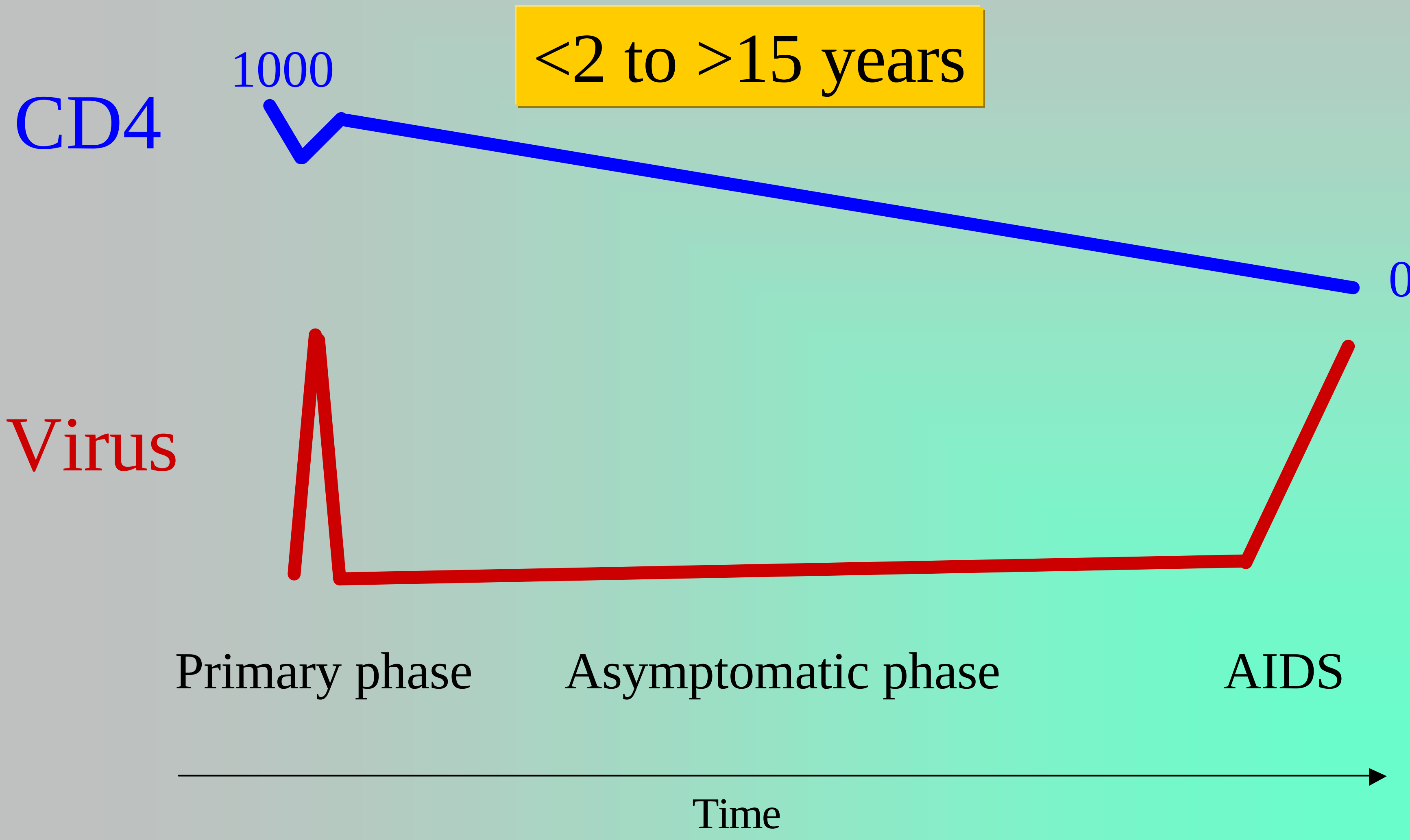
CD4 cell recognition



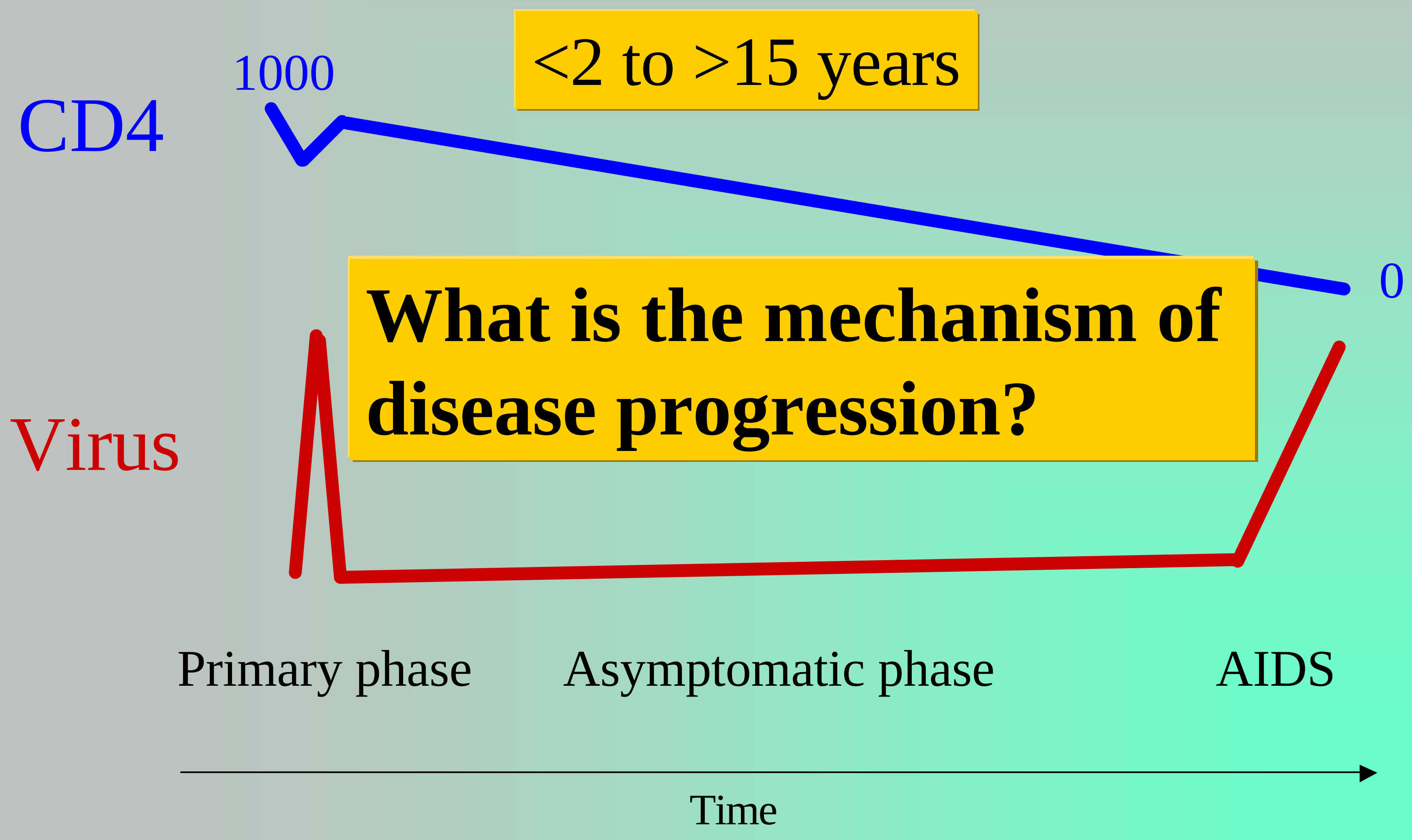
HIV kills CD4 cells



HIV-1: clinical profile



HIV-1: clinical profile



HIV-1: disease progression

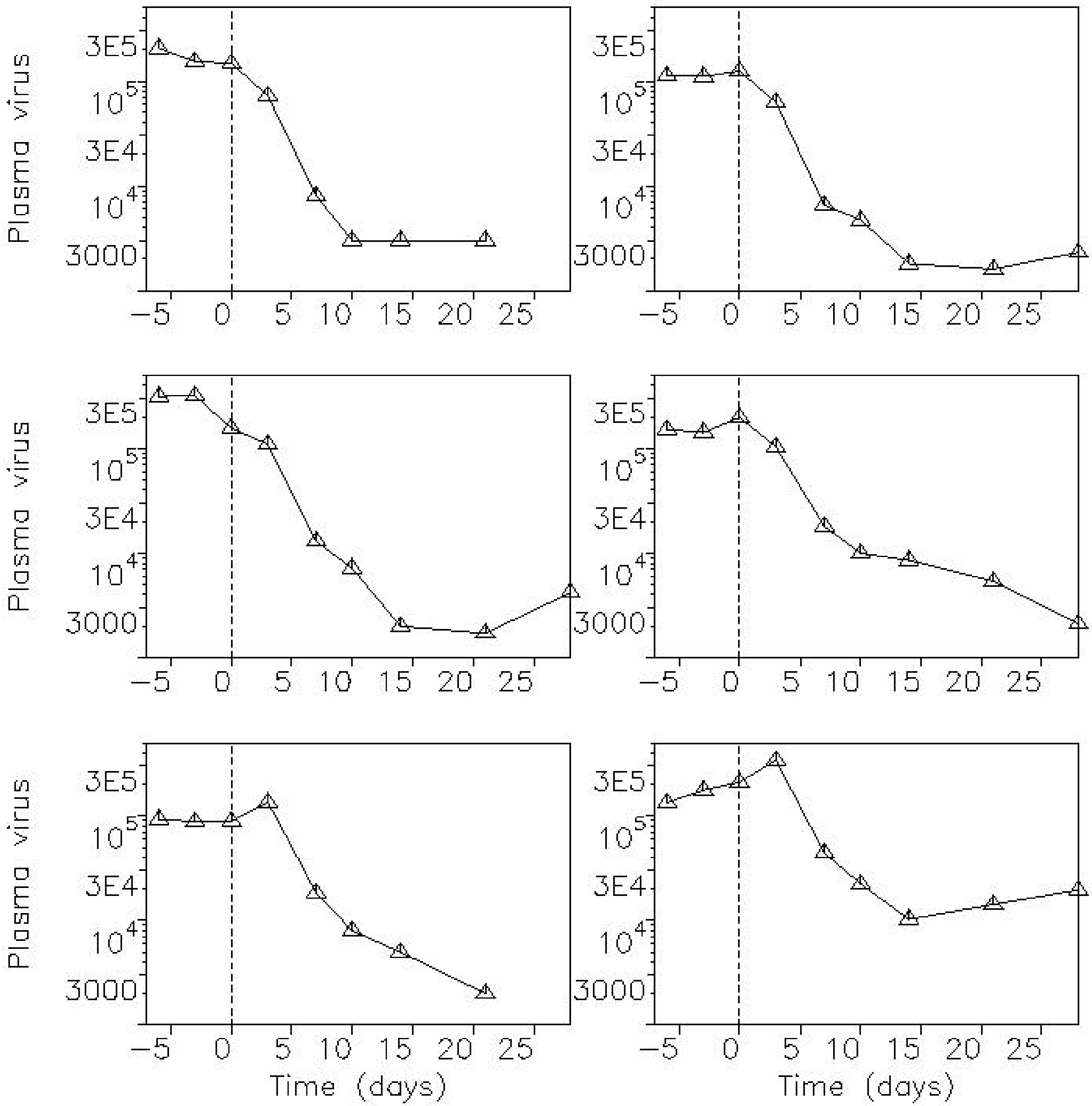
Fast progressors: high virus load

What makes the difference?
Can treatment help?

Slow progressors: low virus load

How fast does HIV-1 reproduce in vivo ?

1994:
protease inhibitors
and
quantitative PCR

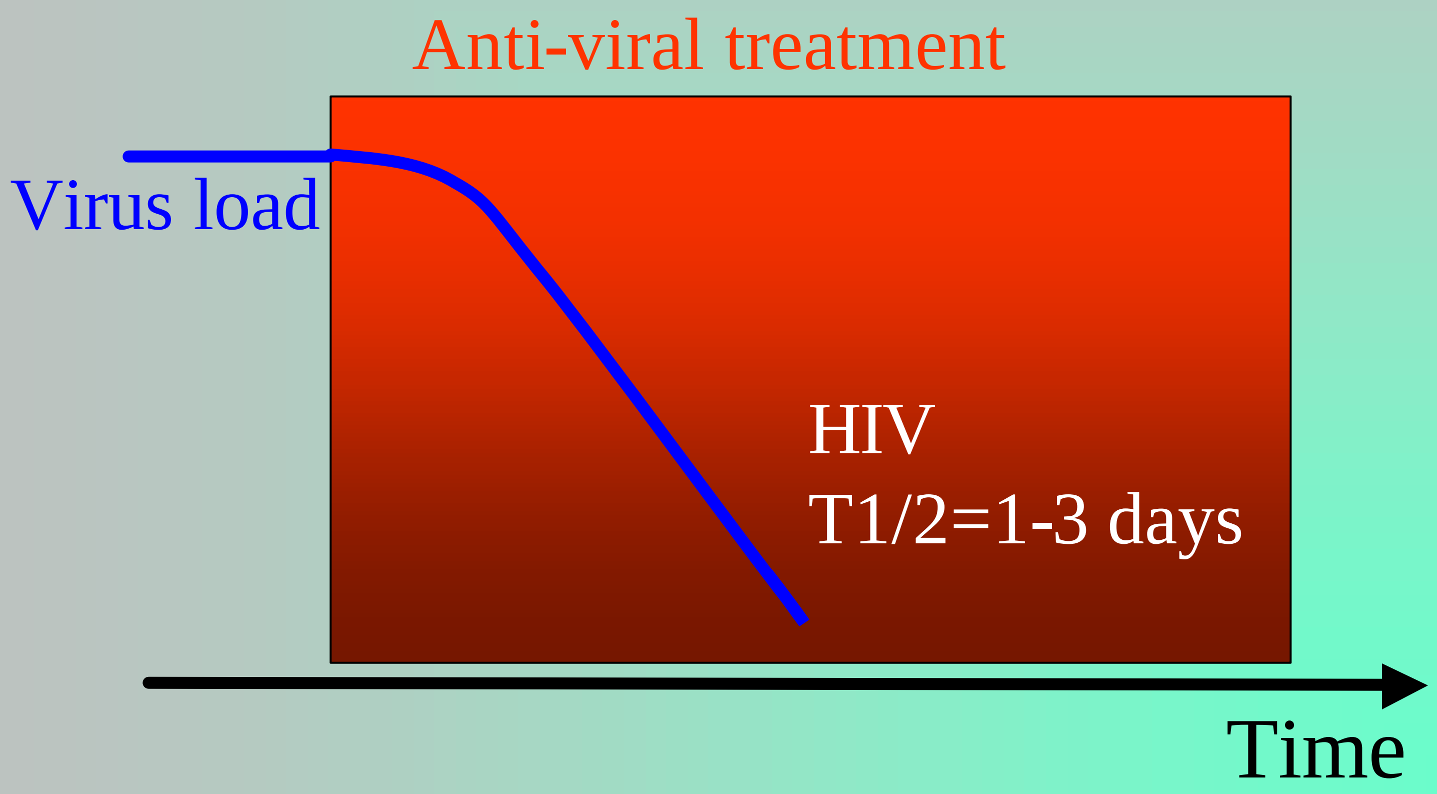


George Shaw

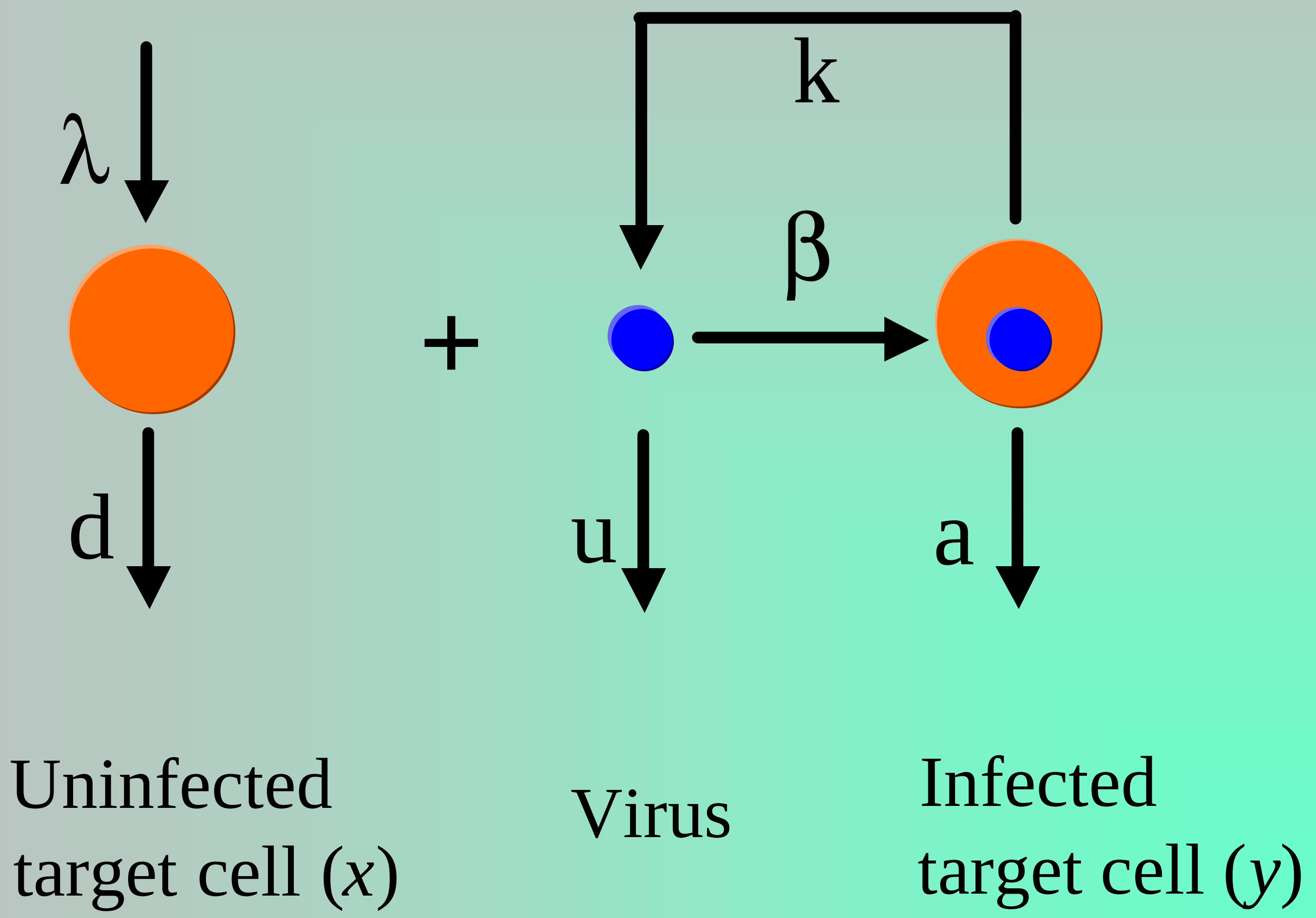
Anti-HIV drugs

- Reverse transcriptase inhibitors
- Protease inhibitors

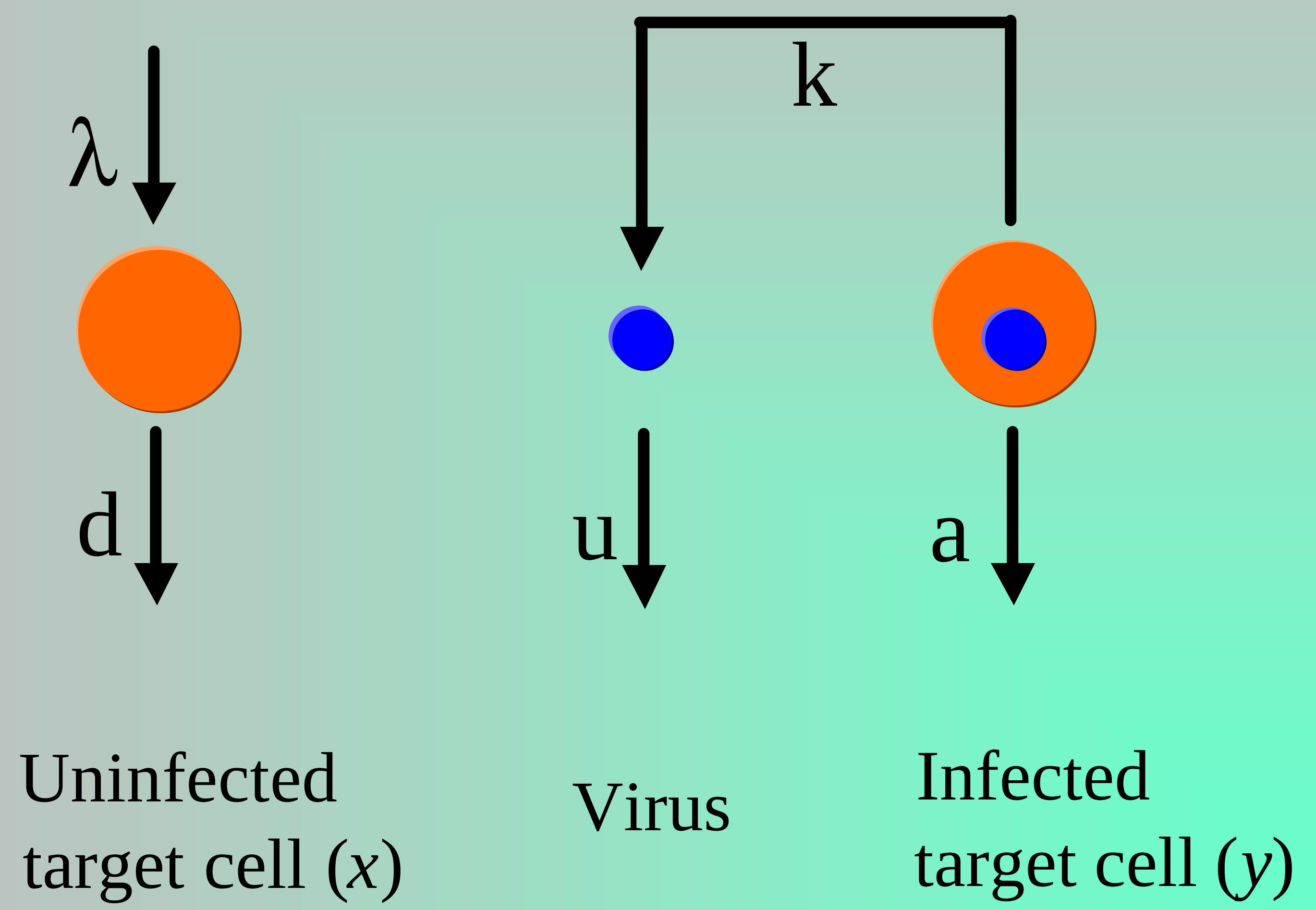
Treatment leads to a rapid decline in virus load



Virus dynamics



Virus dynamics with treatment



The basic model of virus dynamics

Uninfected cells $\dot{x} = l - dx - b\,xv$

Infected cells $\dot{y} = b\,xv - ay$

Free virus $\dot{v} = ky - uv$

Micro-epidemiology within infected host

Anti-viral treatment

Uninfected cells	$\dot{x} = l - dx - bxv$
Infected cells	$\dot{y} = bxv - ay$
Free virus	$\dot{v} = ky - uv$

Virus decline

Infected cells $\dot{y} = -ay$

Free virus $\dot{v} = ky - uv$

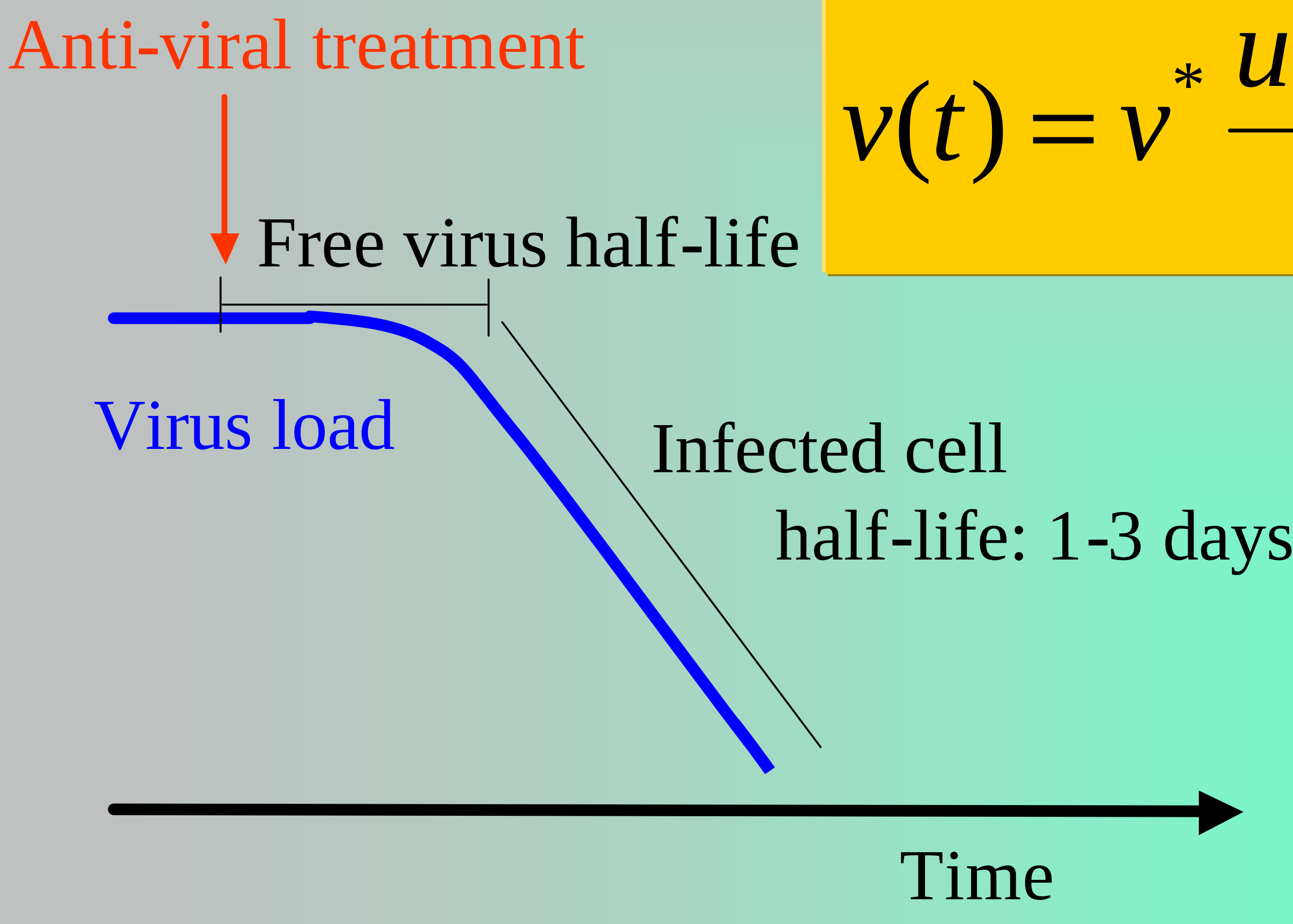
Analytic solution

$$y(t) = y(0)e^{-at}$$

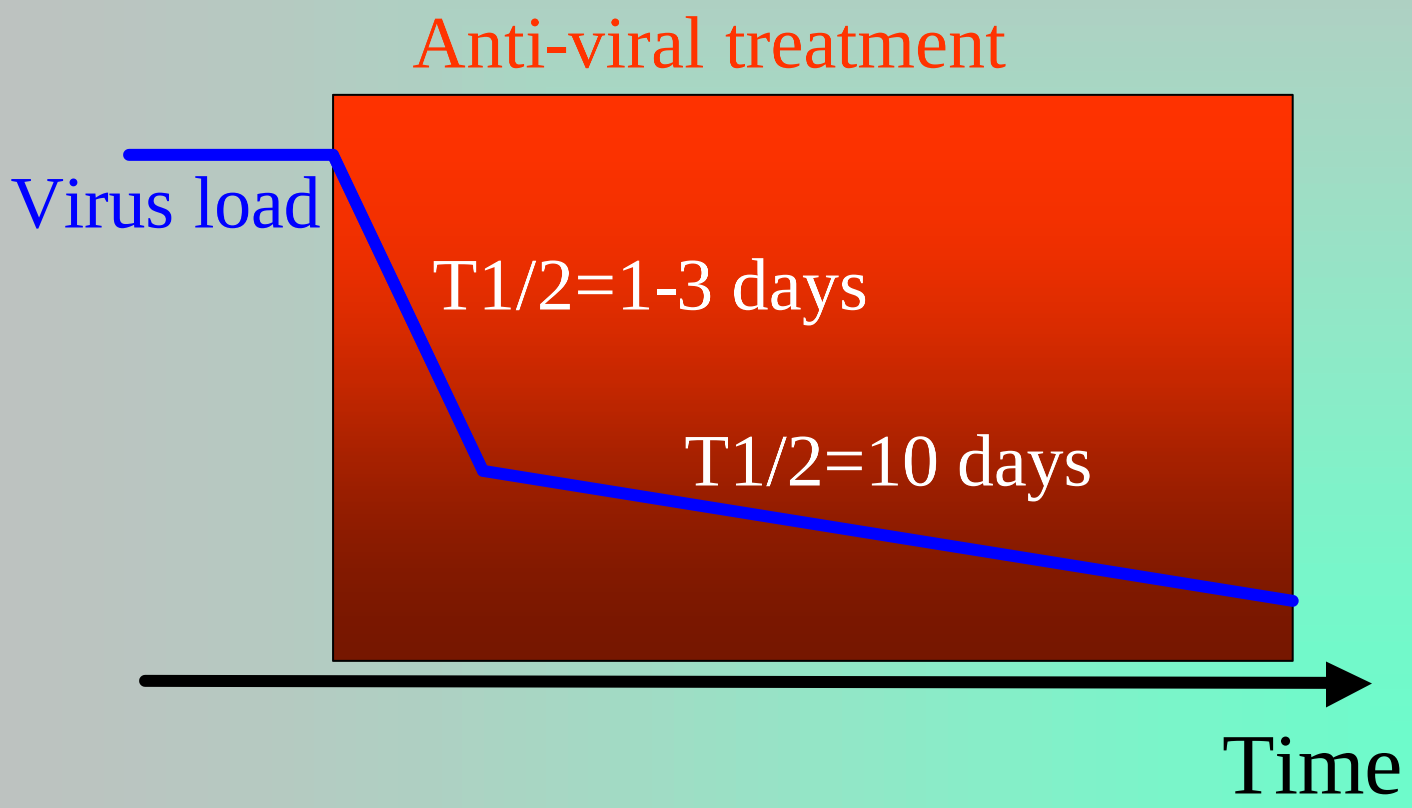
$$v(t) = v(0)\frac{ue^{-at} - ae^{-ut}}{u-a}$$

Virus declines as

$$v(t) = v^* \frac{ue^{-at} - ae^{-ut}}{u - a}$$



Latently infected cells



An extended model of virus dynamics

Uninfected cells	$\dot{x} = l - dx - b\,xv$
Productively infected cells	$\dot{y}_1 = q_1 b\,xv - a_1 y_1 + a\,y_2$
Latently infected cell	$\dot{y}_2 = q_2 b\,xv - a_2 y_2 - a\,y_2$
Cells with defective provirus	$\dot{y}_3 = q_3 b\,xv - a_3 y_3$
Free virus	$\dot{v} = ky_1 - uv$

HIV-1 half-lives

- Productively infected cells : 1-3 days
- Latently infected cells : 10 days
- Defective provirus : 100 days
- Free virus : hours

HIV-1 half-lives

⌘Productively infected cells	:	1-3	days
⌘Latently infected cells	:	10	days
⌘Defective provirus	:	100	days
⌘Free virus	:	hours	

HIV eradication requires 1-3 years of effective therapy.

HIV-1 half-lives

- Productively infected cells : 1-3 days
- Latently infected cells : 10-100 days
- Defective provirus : 100 days
- Free virus : hours

HIV eradication requires >10 years of effective therapy and is most likely impossible.

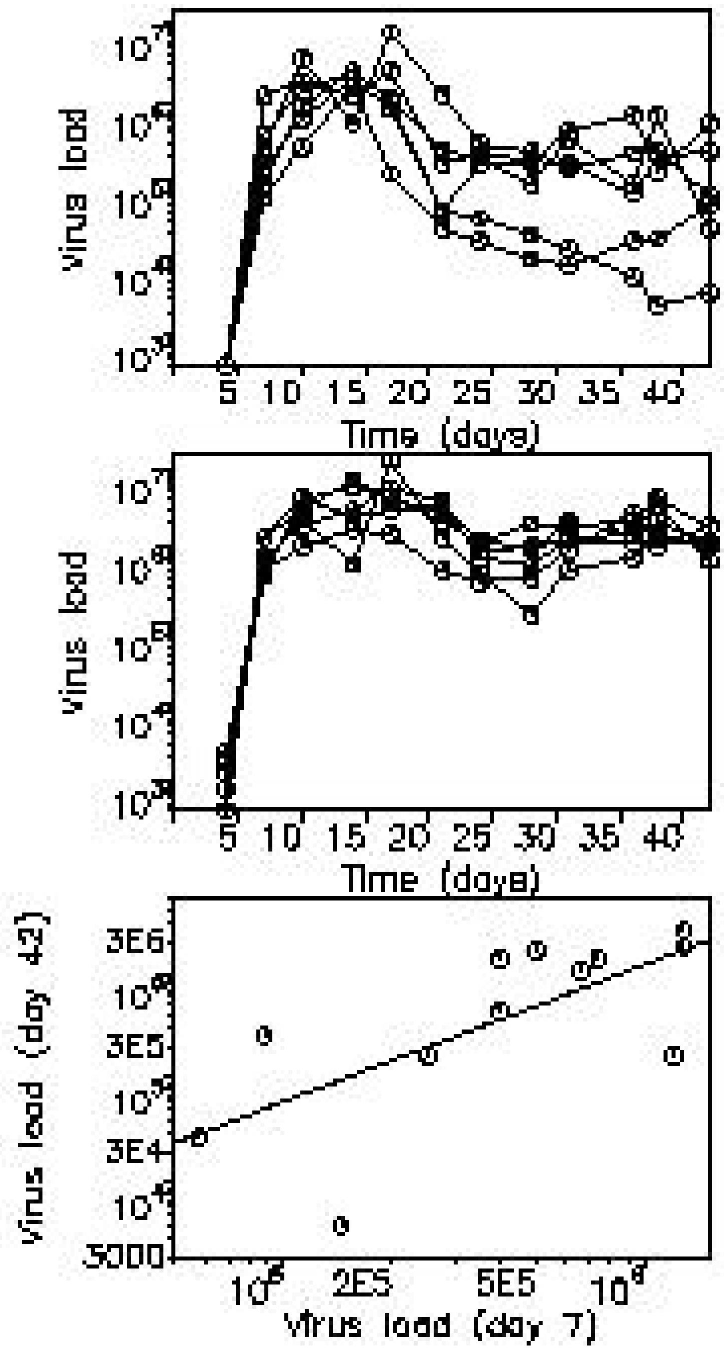
SIV

simian immunodeficiency virus

Study of primary infection shows correlation between virus load in 1st week of infection and virus load at set point after the initial peak.

Virus load at set point is strongly correlated with survival time.

Hence survival time can be predicted from virus growth rate in the first week of infection.



Use basic model to study primary infection

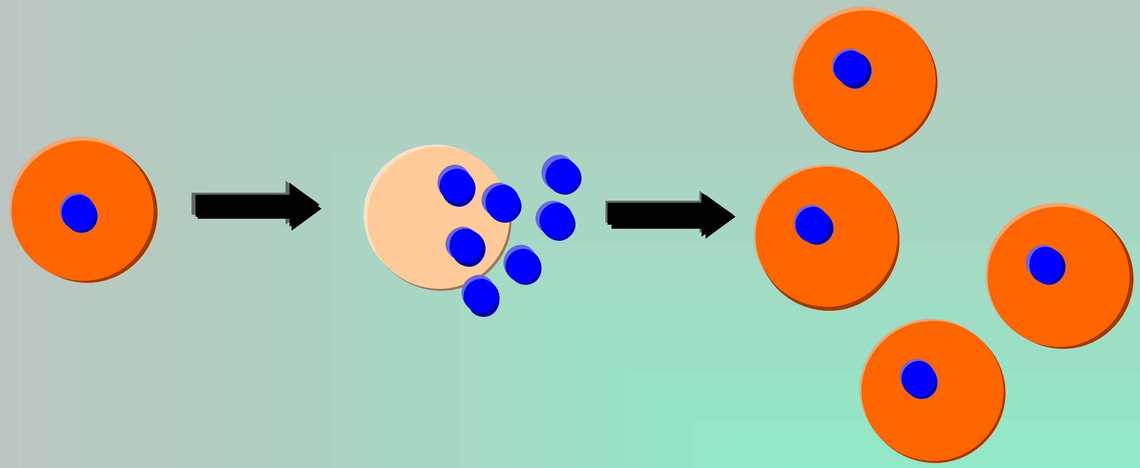
Uninfected cells $\dot{x} = l - dx - b\,xv$

Infected cells $\dot{y} = b\,xv - ay$

Free virus $\dot{v} = ky - uv$

Initial conditions $x(0) = l/d \quad y(0) = 0 \quad v(0) = 0$

Basic reproductive rate (or ratio or number)

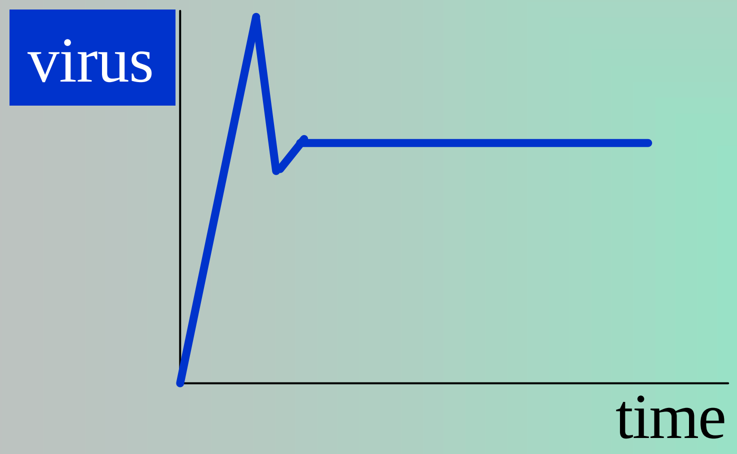


= the number of newly infected cells that arise from one infected cell if most cells are uninfected

$$R_0 = \frac{bk}{au}x(0) = \frac{bkl}{aud}$$

Basic reproductive rate

Infection takes place if $R_0 > 1$



The system goes in damped oscillations to the equilibrium:

$$x^* = \frac{x(0)}{R_0} \ , \quad y^* = (R_0 - 1)\frac{du}{bk} \ , \quad v^* = (R_0 - 1)\frac{d}{b}$$