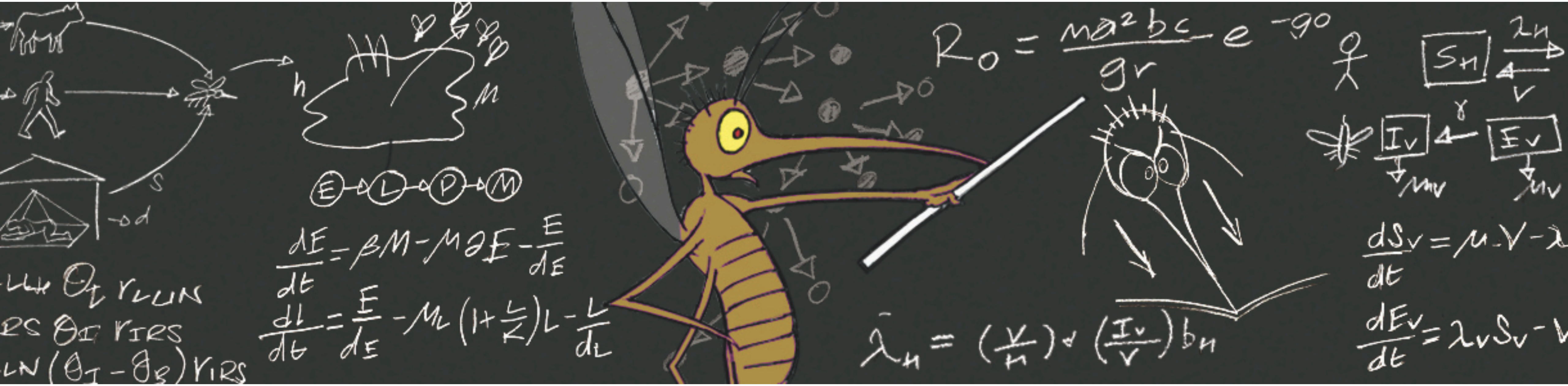
The mathematics of malaria control



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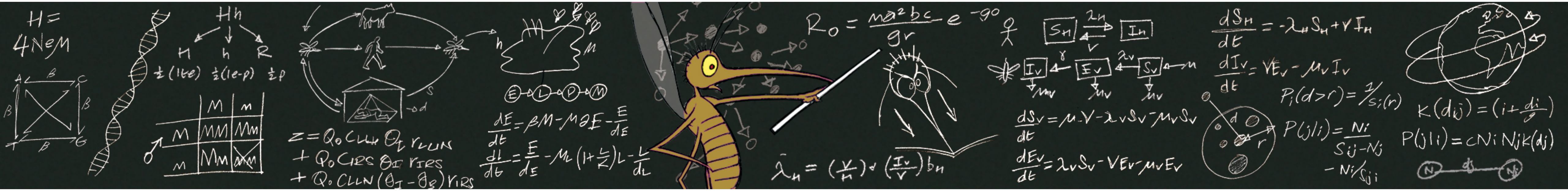
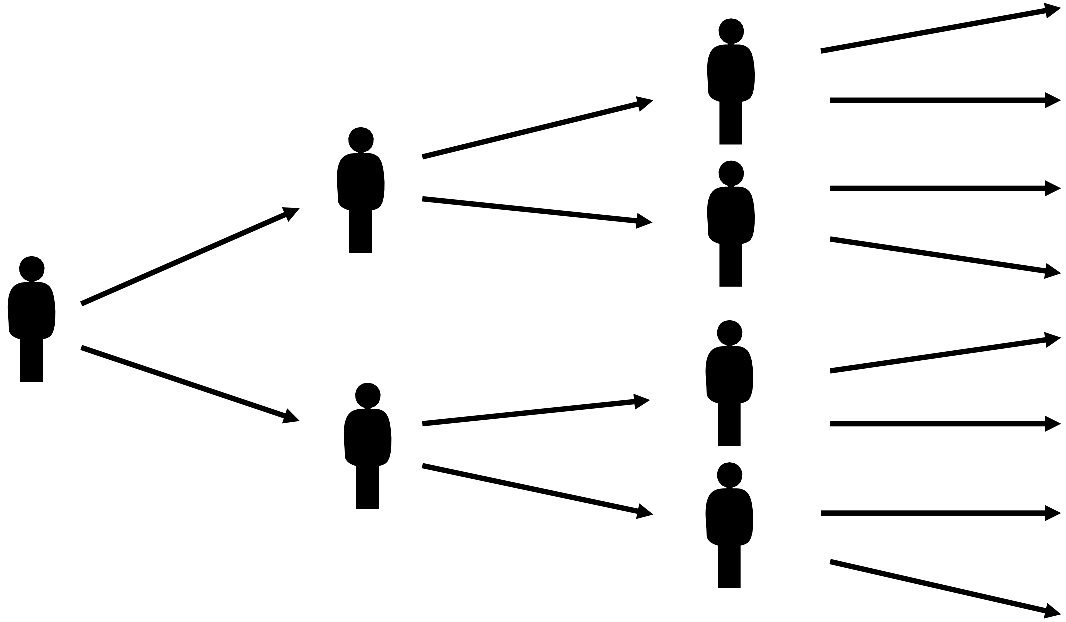
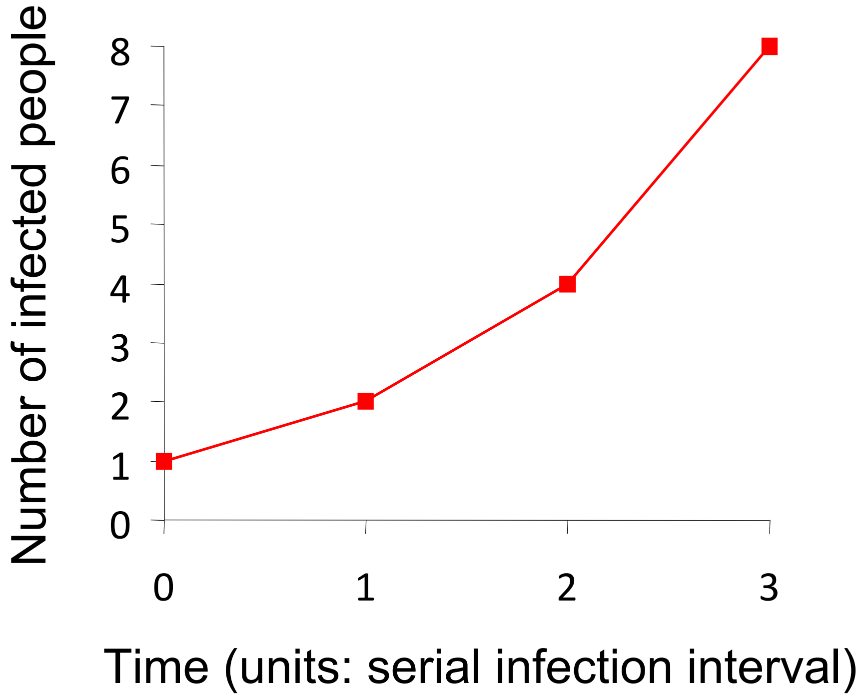
Lecture outline



1. The basic reproductive number of malaria
2. Compartmental models of malaria
3. Modeling human malaria transmission
4. Modeling mosquito ecology

The basic reproductive number, R_0

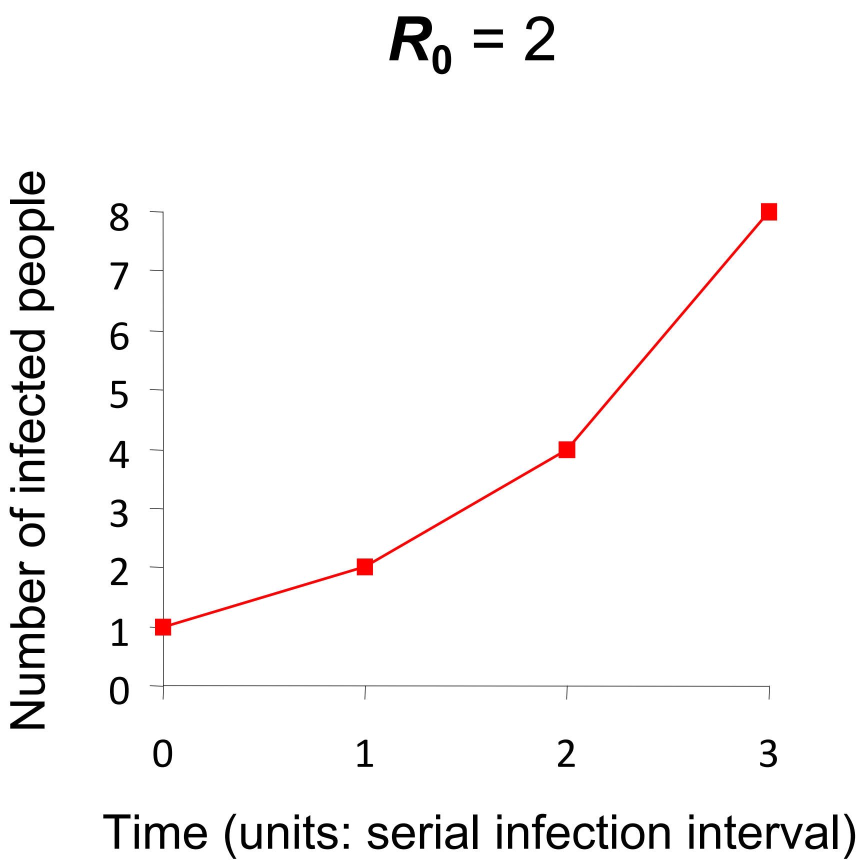


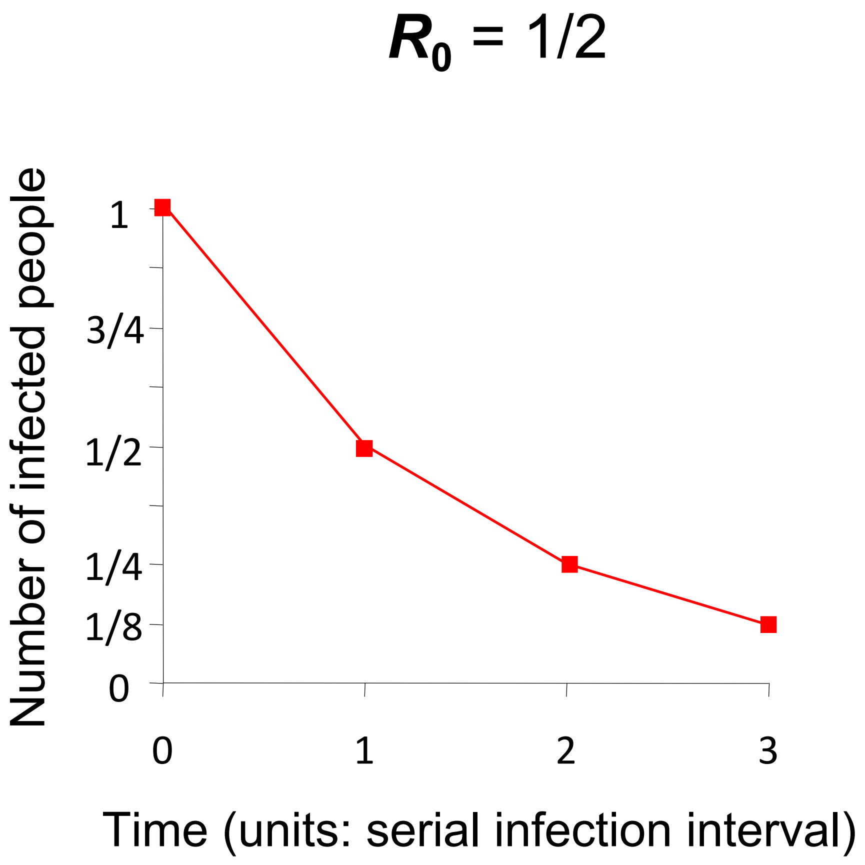


$\boldsymbol{R_0}$ = The average number of people infected by a typical infectious person over their infectious period, in an otherwise entirely susceptible population

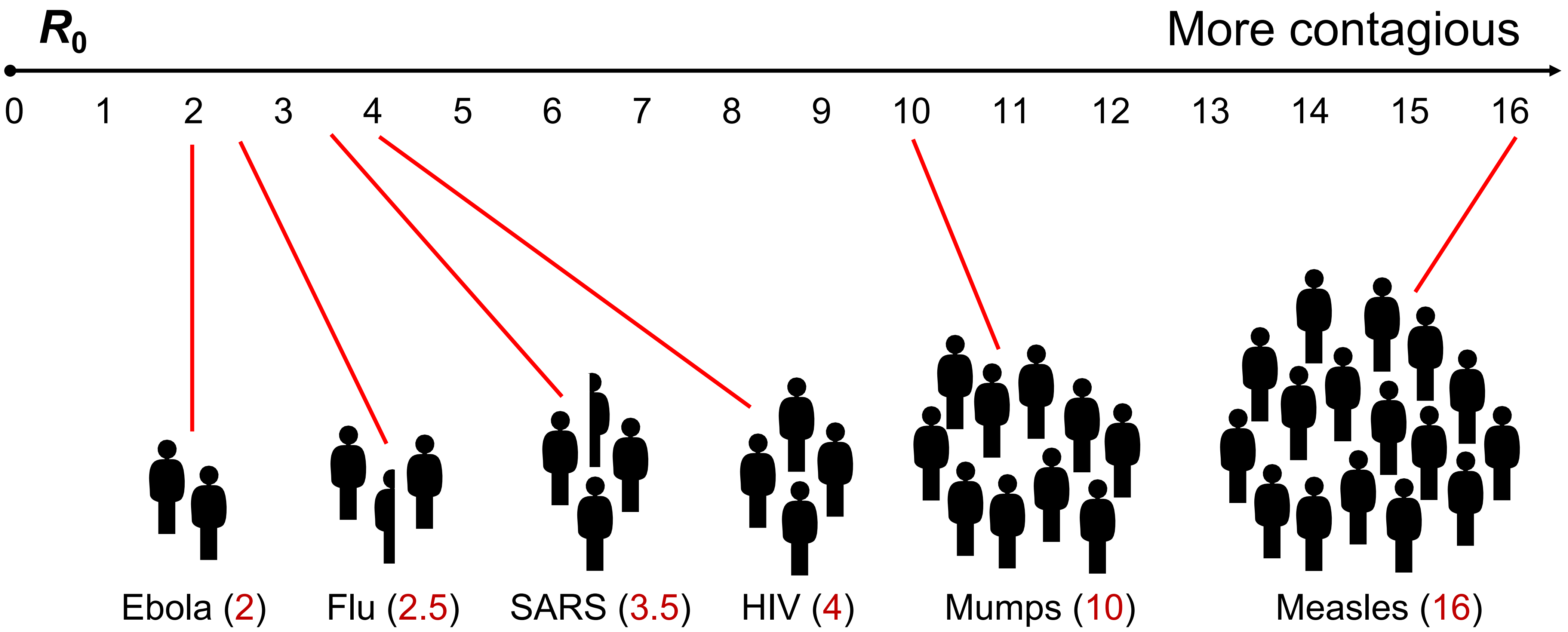
For an epidemic to take off, we require that $\boldsymbol{R_0>1}$

Aim for control is to get $R_0 < 1$

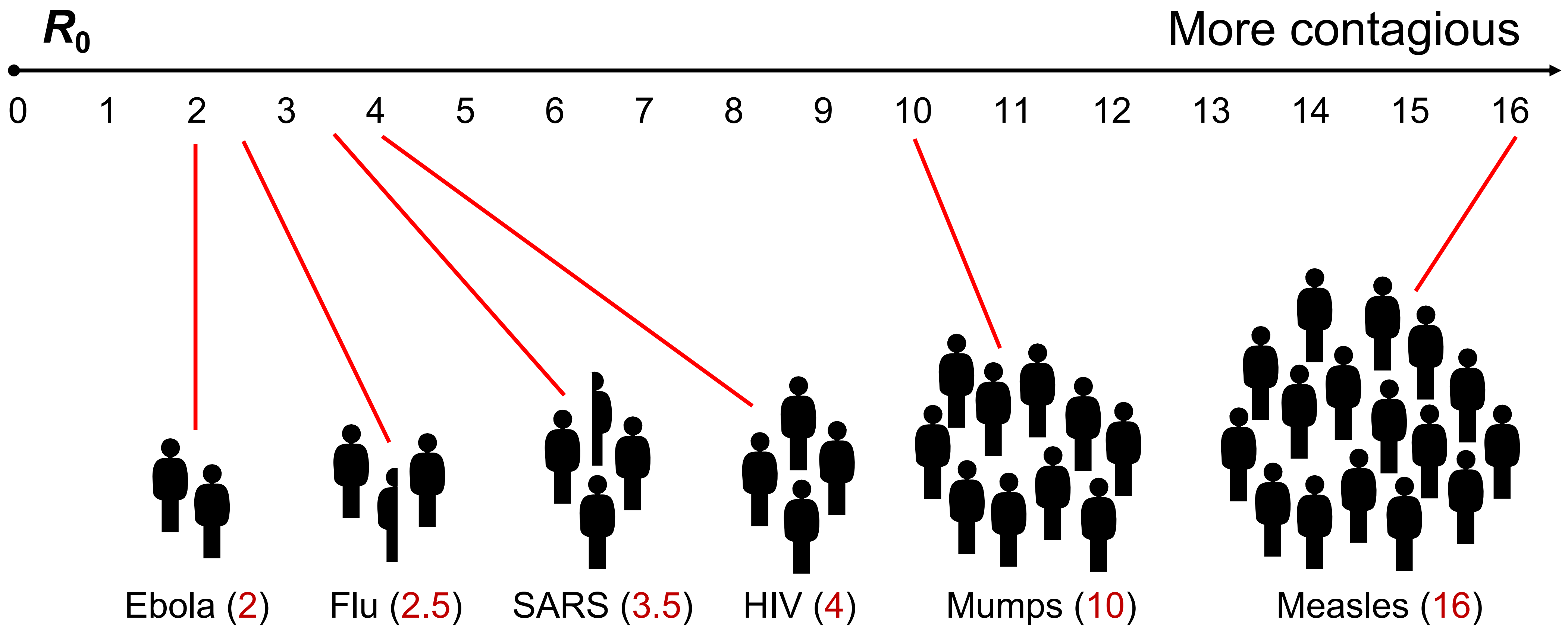




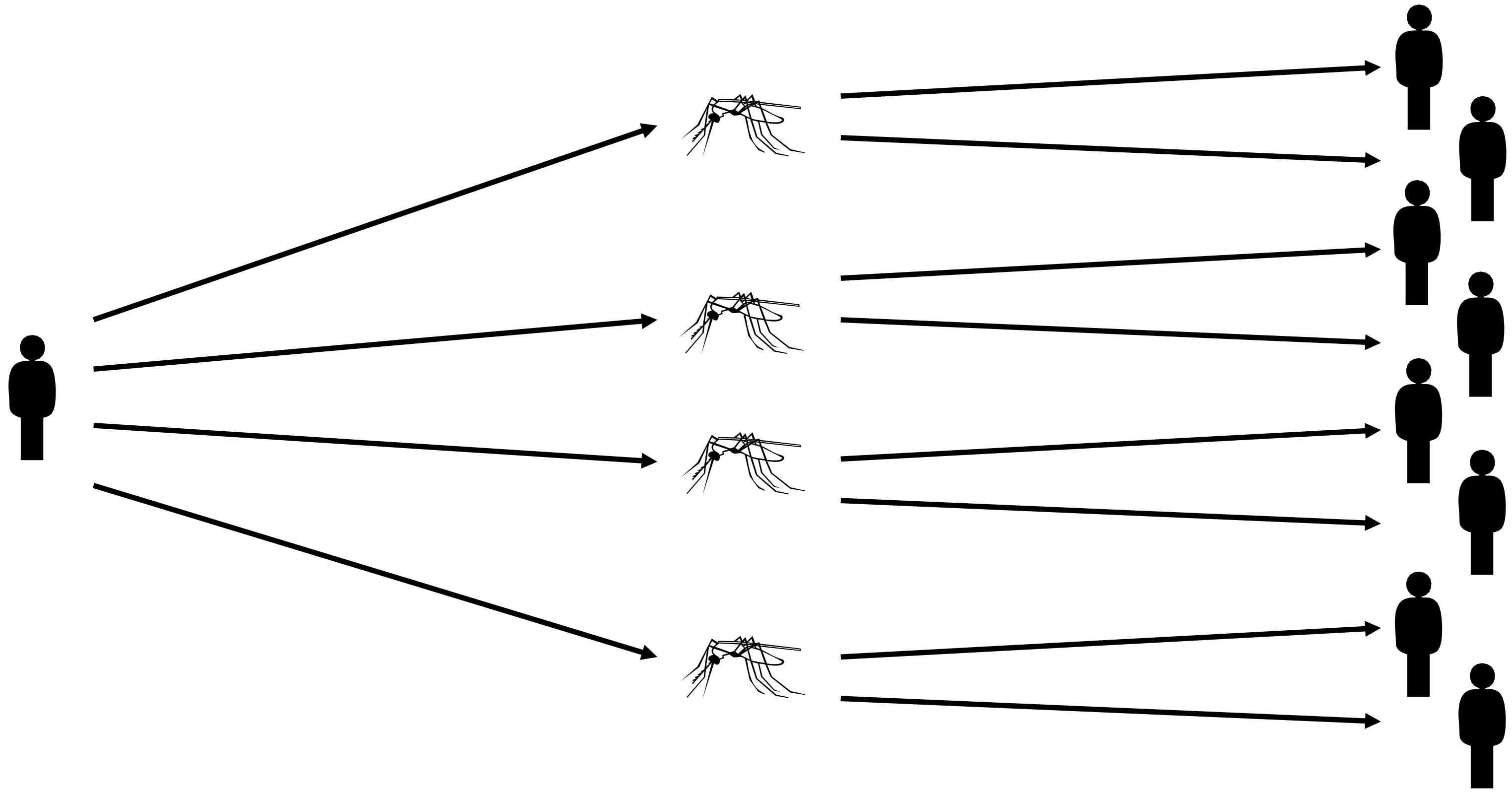
R_0 for other diseases



What do you think the R_0 for malaria is?



Basic reproductive number, R_0, for malaria

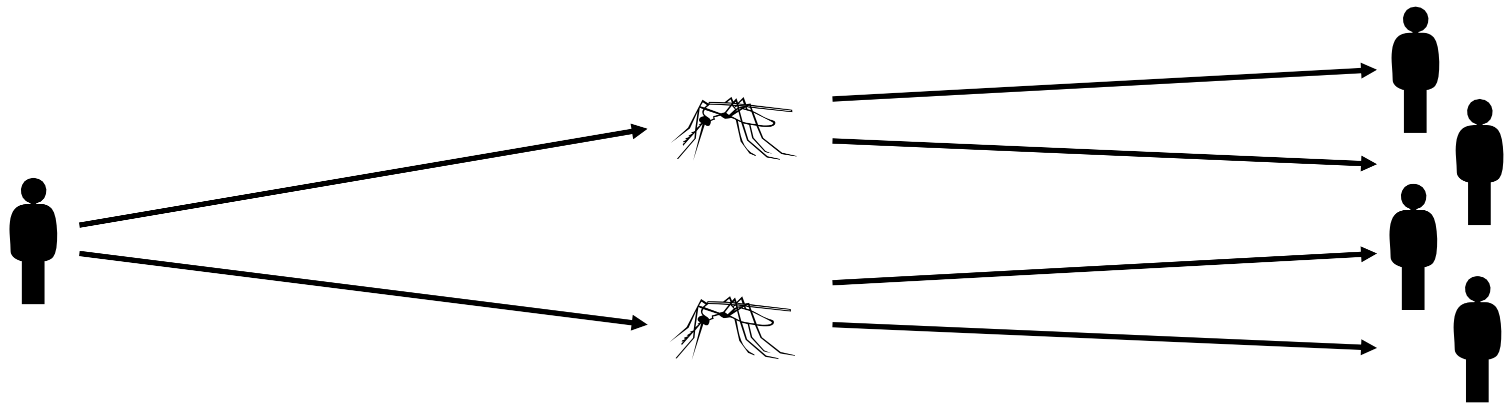


$\boldsymbol{R_0}$ = $\boldsymbol{R_{0,H \to V}}$ x $\boldsymbol{R_{0,V \to H}}$

Average number of mosquitoes infected by a typical infectious person

Average number of people infected by a typical infectious mosquito

Basic reproductive number, R_0, for malaria



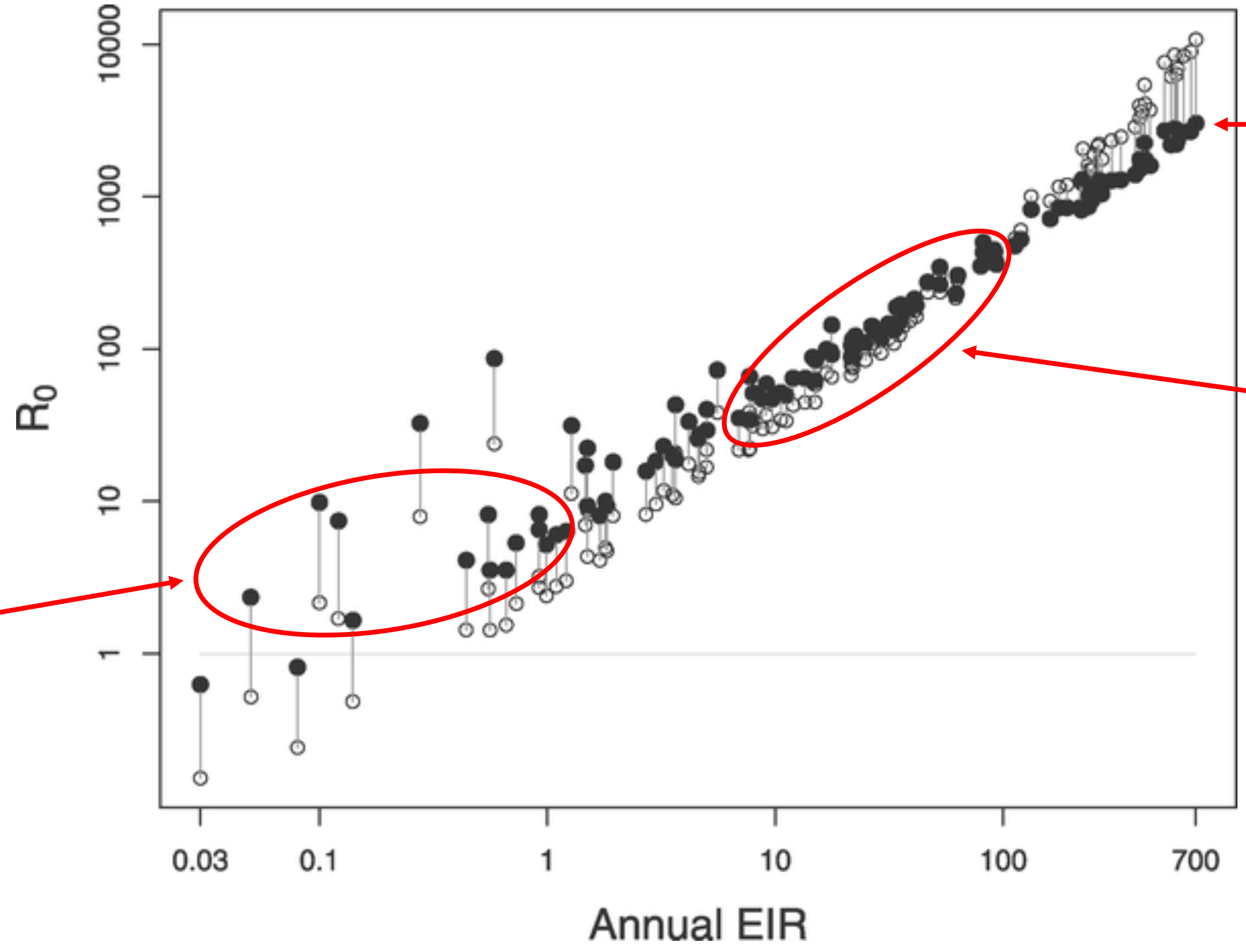
$\boldsymbol{R_0}$ = $\boldsymbol{R_{0,H \rightarrow V}}$ x $\boldsymbol{R_{0,V \rightarrow H}}$

Average number of mosquitoes infected by a typical infectious person x Average number of people infected by a typical infectious mosquito

$$= a \times \left(\frac{V}{H}\right) \times b_V \times \left(\frac{1}{r}\right) \quad \text{x} \quad a \times b_H \times \left(\frac{1}{\mu_V}\right) \times e^{-\mu_V \tau}$$

- a: Rate at which a mosquito bites humans
- $\frac{V}{H}$: Number of mosquitoes per human
- b_V: Probability mosquito becomes infected
- $\frac{1}{r}$: Duration of human infection
- a: Rate at which a mosquito bites humans
- b_H: Probability human becomes infected
- $\frac{1}{\mu_V}$: Mosquito lifetime
- $e^{-\mu_V \tau}$: Fraction of mosquitoes that survive malaria incubation

Basic reproductive number, R_0, for malaria



Places with R_0 < 10 have promise for elimination

R_0 for malaria can be as high as 3,000

For highly-endemic areas in sub-Saharan Africa, R_0 tends to be ~100 (50-200)

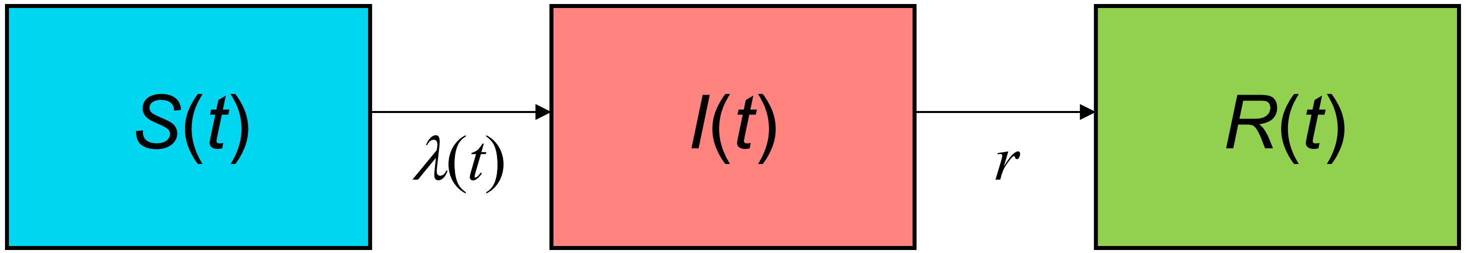
- Smith DL, McKenzie FE, Snow RW, Hay SI (2007) PLoS Biology 5: e42

Compartmental models: The SIR model

S(*t*) = Number susceptible people at time *t*

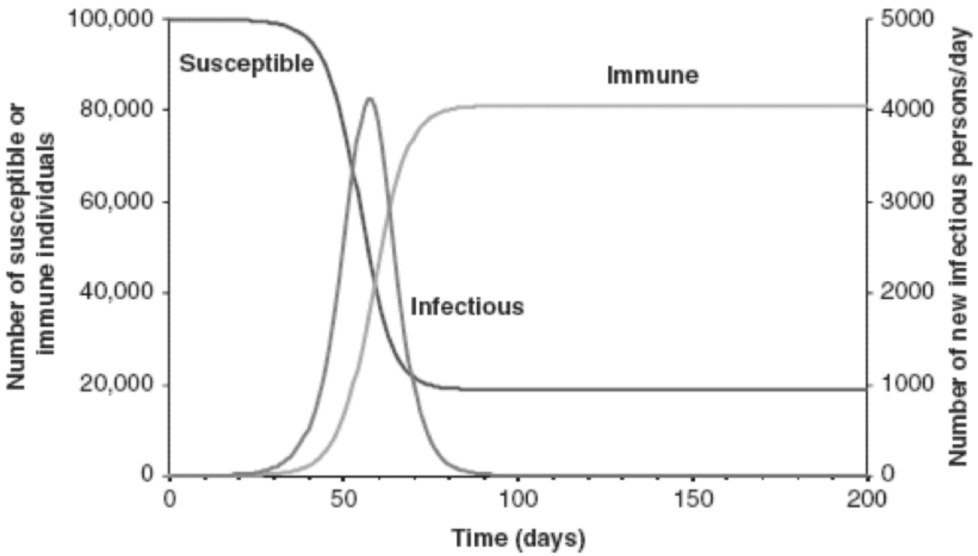
I(*t*) = Number infectious people at time *t*

R(*t*) = Number recovered people at time *t*



$\lambda(t)$ = Rate of infection per person per unit time

r = Recovery rate



Compartmental models: The SIR model

B. *Constant Rates.*

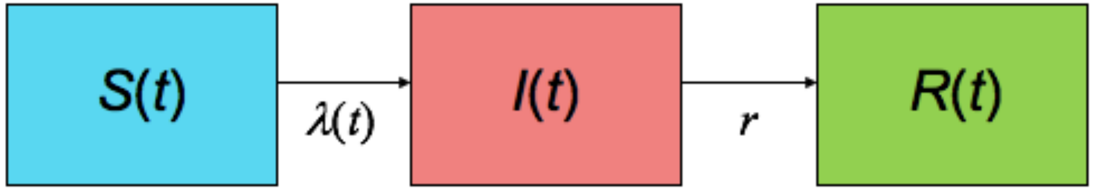
(10) Much insight can be obtained as to the process by which epidemics in limited populations run their peculiar courses, and end in final extinction,

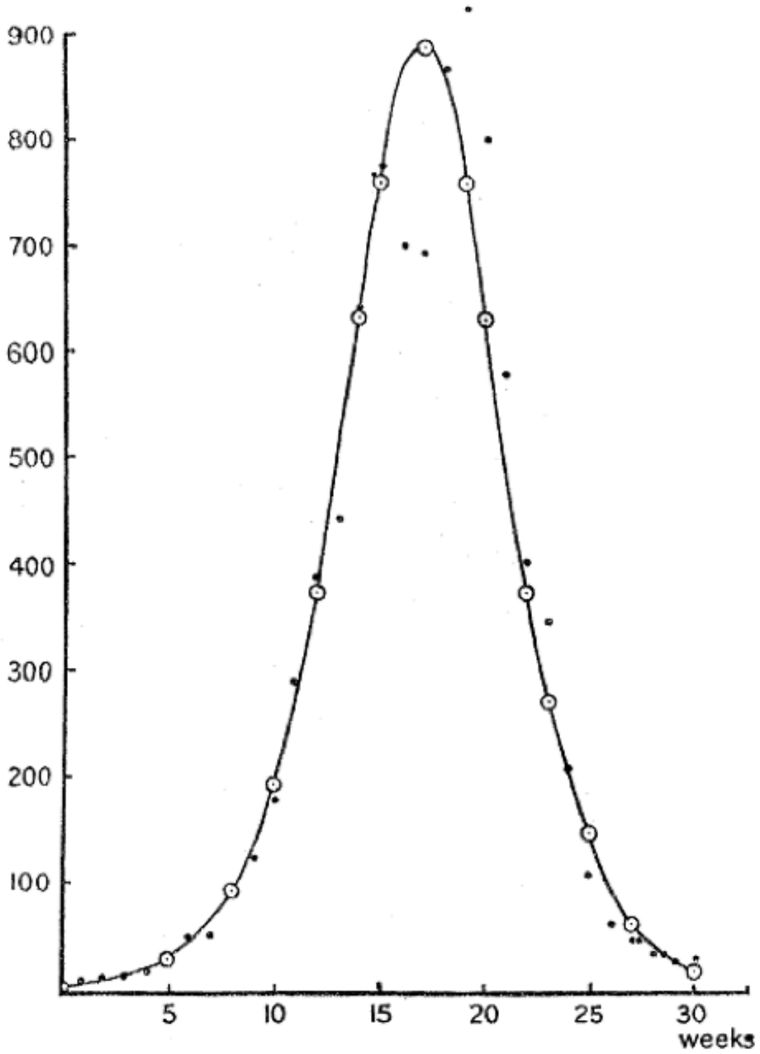
from the consideration of the special case in which ϕ and ψ are constants κ and l respectively.

In this case the equations are

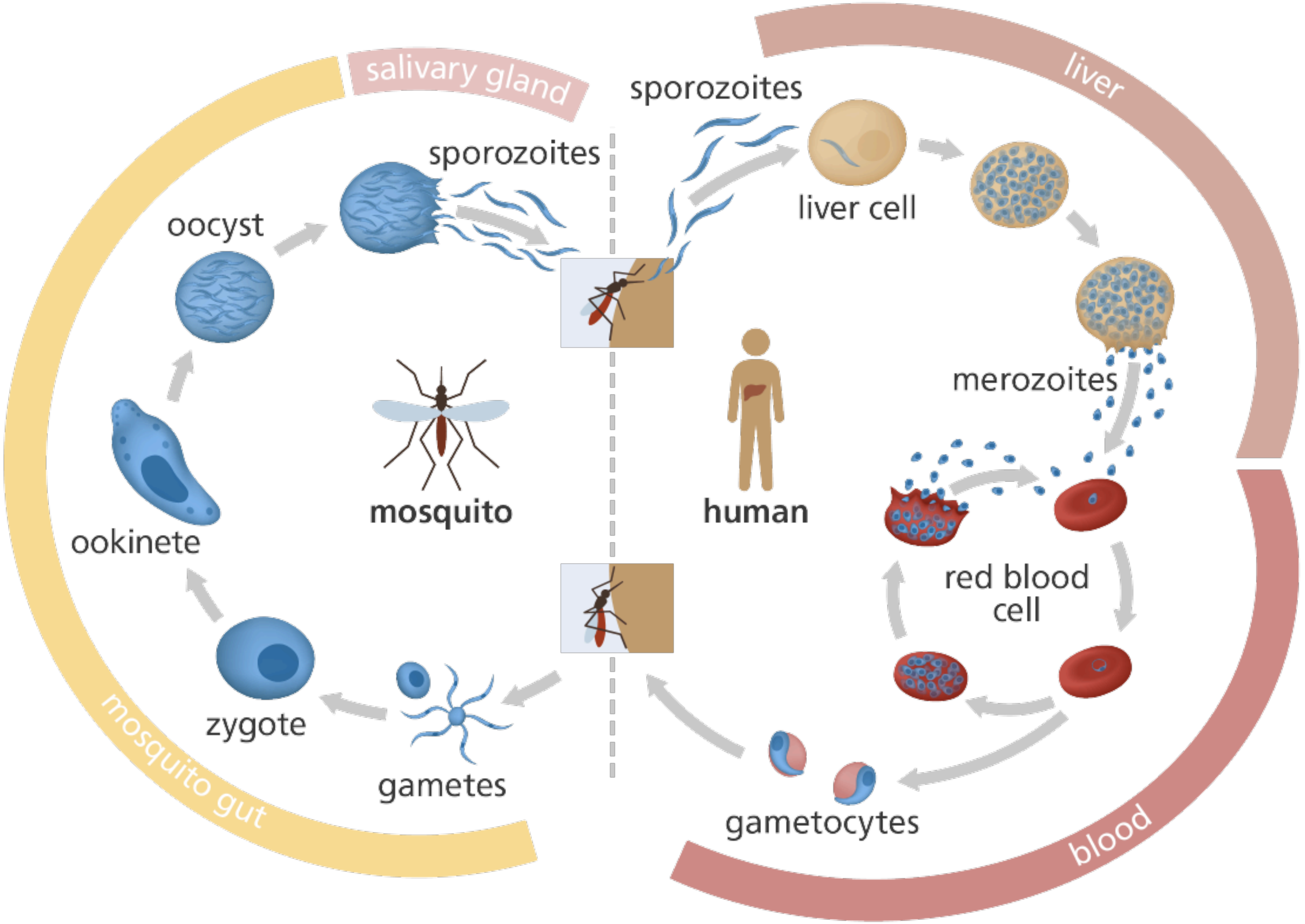
$$\left.\begin{aligned} \frac{dx}{dt} &= -\kappa xy \\ \frac{dy}{dt} &= \kappa xy - ly \\ \frac{dz}{dt} &= ly \end{aligned}\right\} \qquad (29)$$

and as before $x + y + z = \mathrm{N}$.



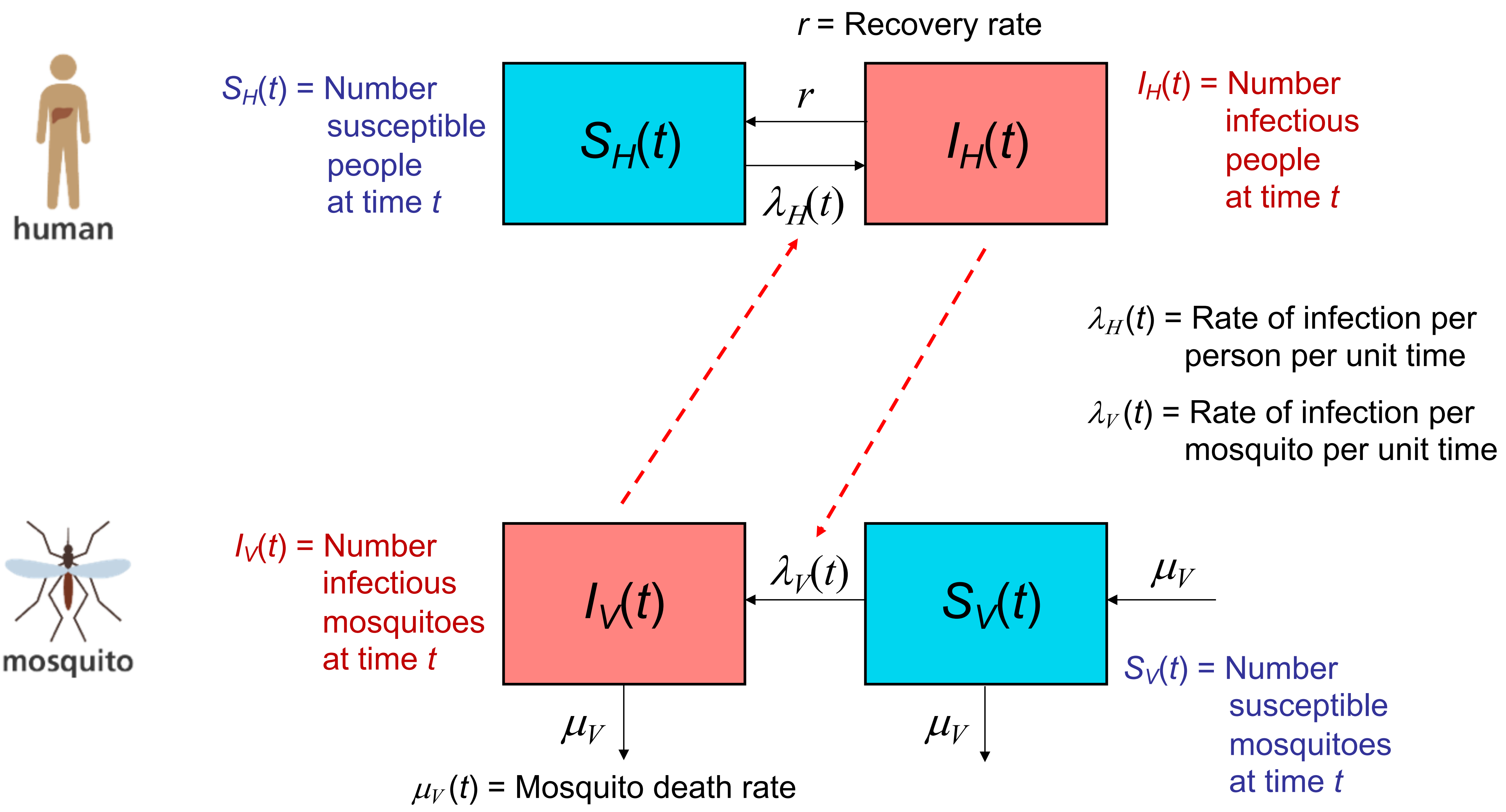


- Kermack WO, McKendrick AG (1927) Proc Roy Soc London A 115: 700-721



salivary gland
liver
sporozoites
sporozoites
oocyst
liver cell
mosquito
human
merozoites
ookinete
red blood cell
zygote
gametes
gametocytes
mosquito gut
blood

Compartmental models: Malaria



Compartmental models: Malaria

An Application of the Theory of Probabilities to the Study of a priori *Pathometry.*—Part I.

By Lieut.-Colonel Sir RONALD ROSS, K.C.B., F.R.S., R.A.M.C.T.F.

(Received July 14, 1915.)

CONTENTS.

I.

Prefatory.—It is somewhat surprising that so little mathematical work should have been done on the subject of epidemics, and, indeed, on the

20th August 1897

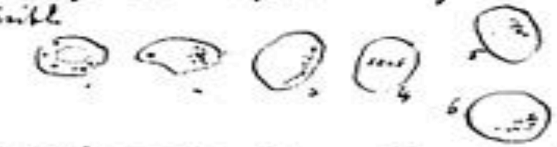
(36). Imago of 16th (4th day) dead. Brown with white wings &c.
As usual some cells with yellowish fat granules [illegible]
In [illegible] no [illegible]

(37) Imago of 16 (4th day) dead. Small, crumpled, black
[illegible]

(38). Imago of 16th (4th day) living. Brown with white wings &c
The stomach just under its outer surface contains some large cells with pigment (?) & numerous granules

The pigment sometimes oscillates, is quite black like that of human malaria; & is not found outside these cells. In 8 it is arranged in a circle. The granules do not change position & the cells do not change shape. The outline of the cell is generally clear, but in the smaller ones sometimes delicate. About 12 – 16μ in diameter.
This specimen irrigated with 40% formalin & sealed with Hollis's glue.

21st August
Yesterday's sealed specimen. Pigmented bodies still present, but not so well visible



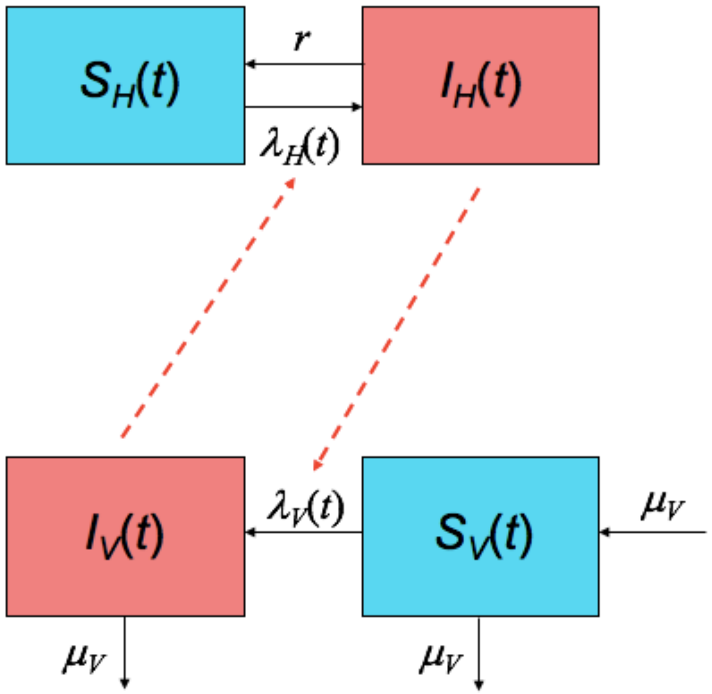
All at rest, not moving

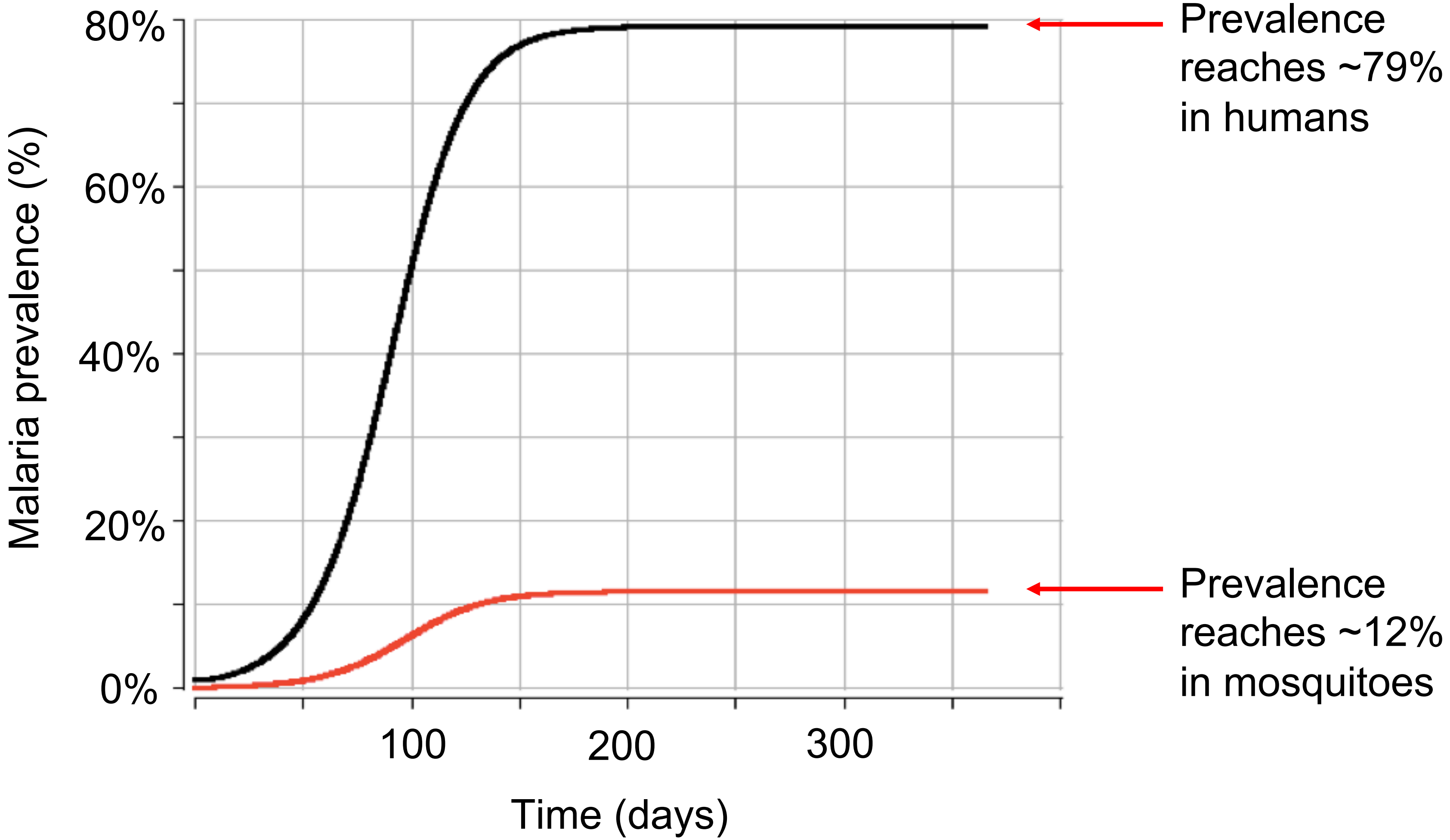
No 5 shows signs of a nucleus & Nos 5 & 6 are distinctly more fleshy & bright than yesterday.

(39) Imago of 16th (5th day) alive. Large, brown, white wings &c.
The same cells in stomach under superficial layer – only in this larger & better defined

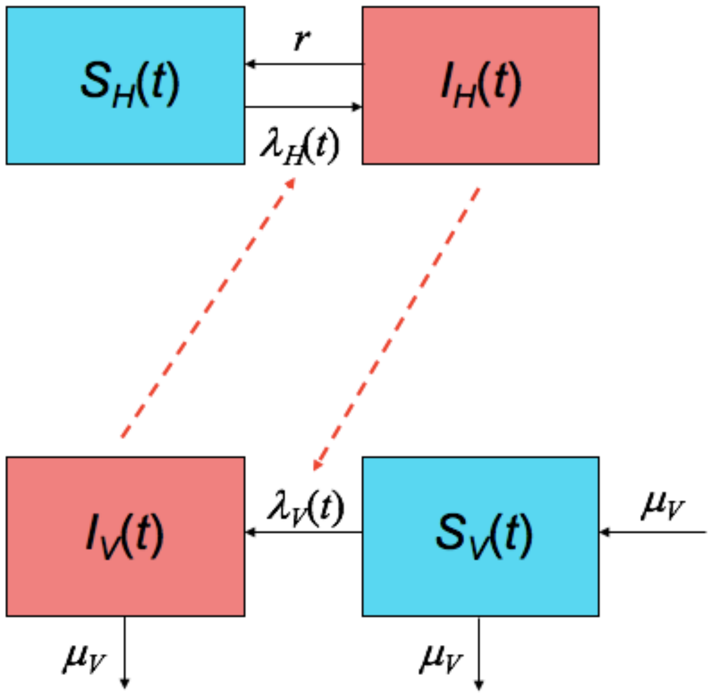
Pigment oscillating in some. Largest about 20μ in diam. Outline much thicker. 21 of them in stomach, chiefly toward upper end.

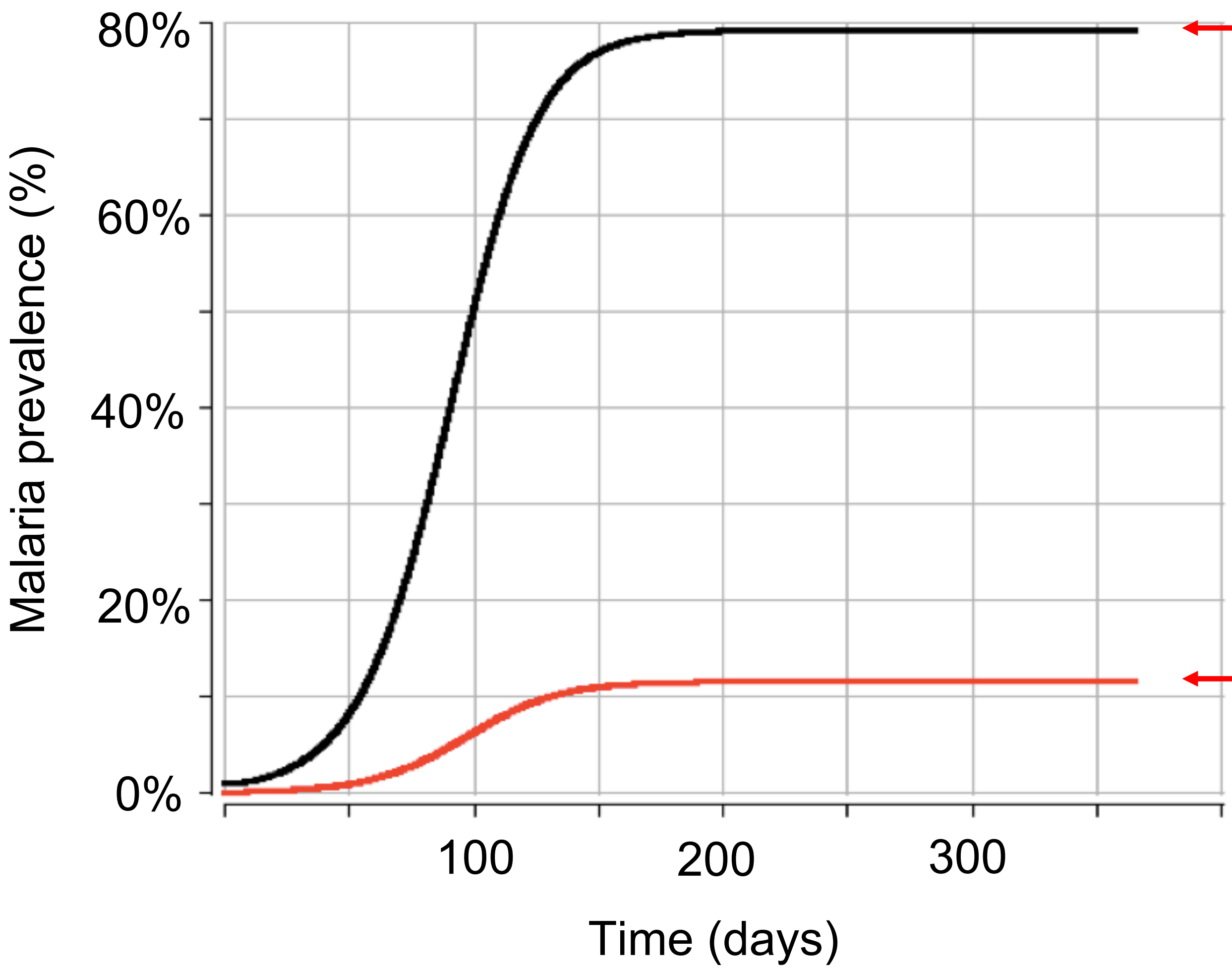
Predictions from first malaria model





What % of mosquitoes are infectious for malaria?

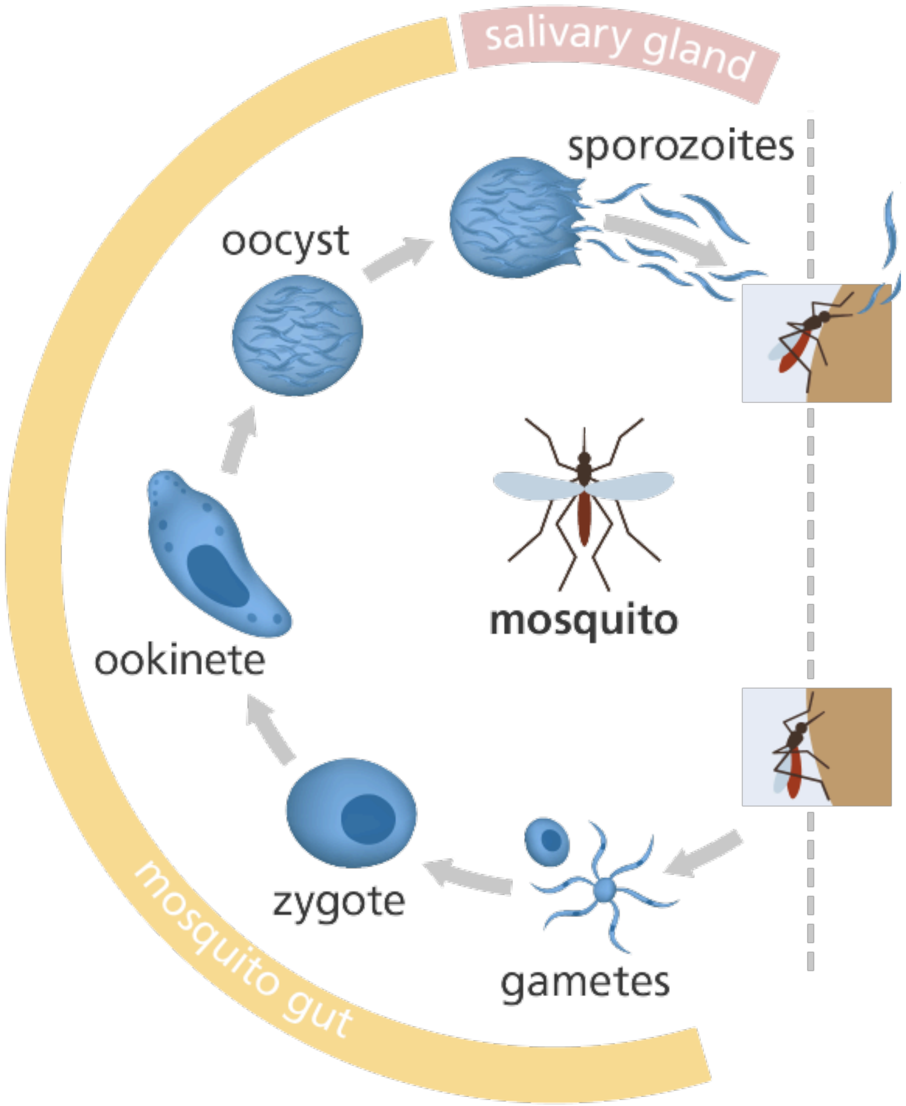


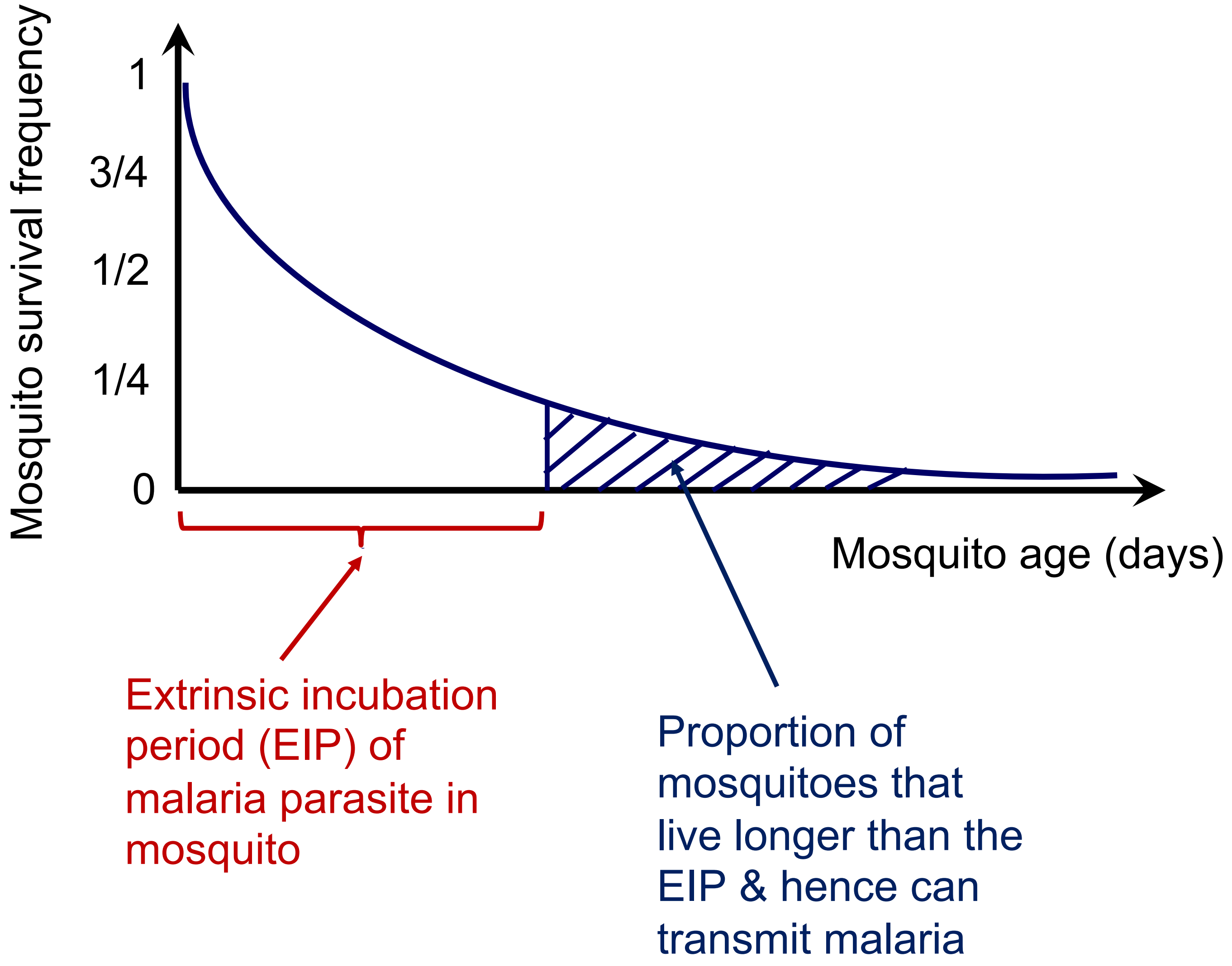


Prevalence reaches ~79% in humans

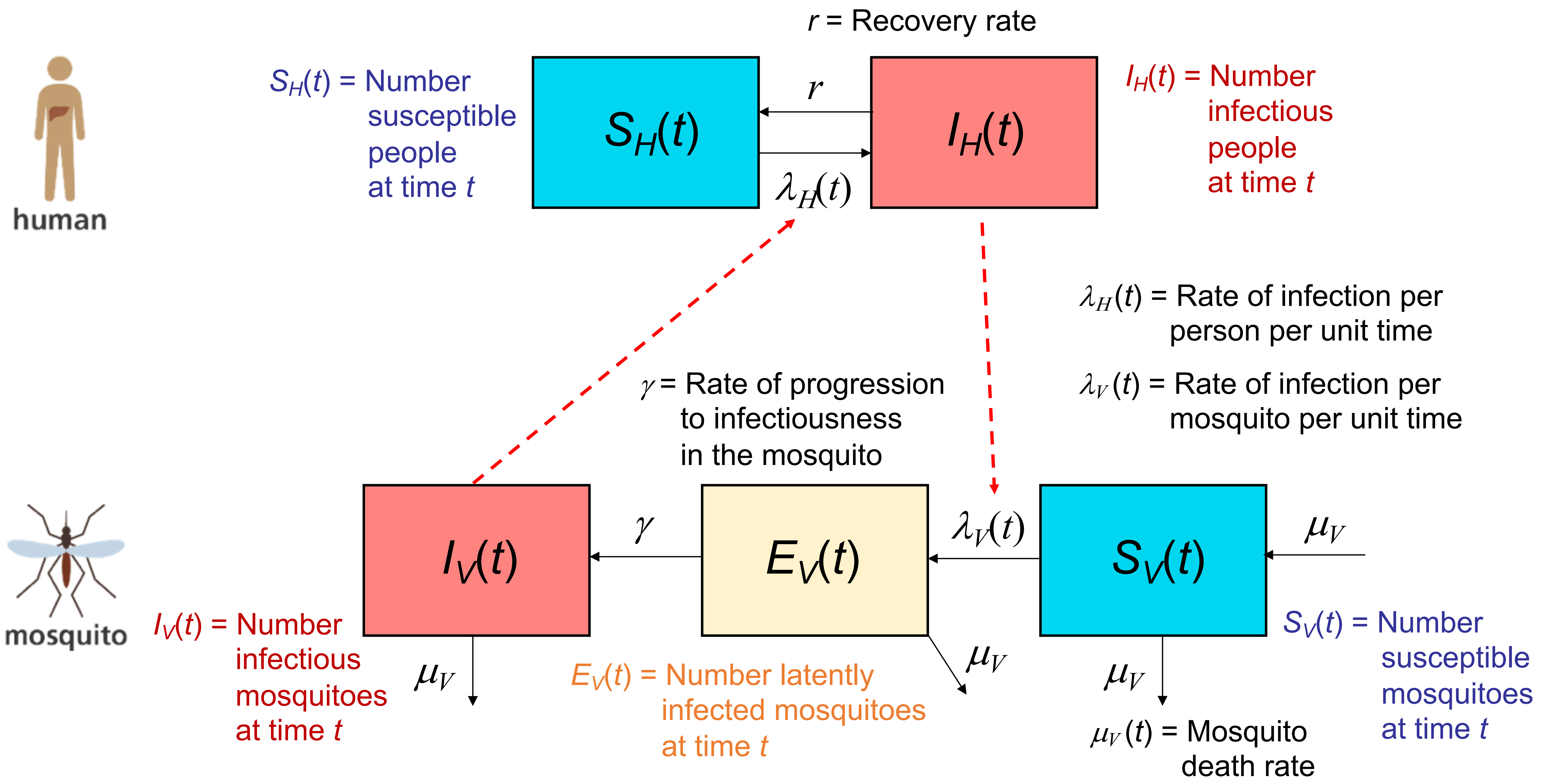
Prevalence reaches ~12% in mosquitoes

Importance of the extrinsic incubation period (EIP)

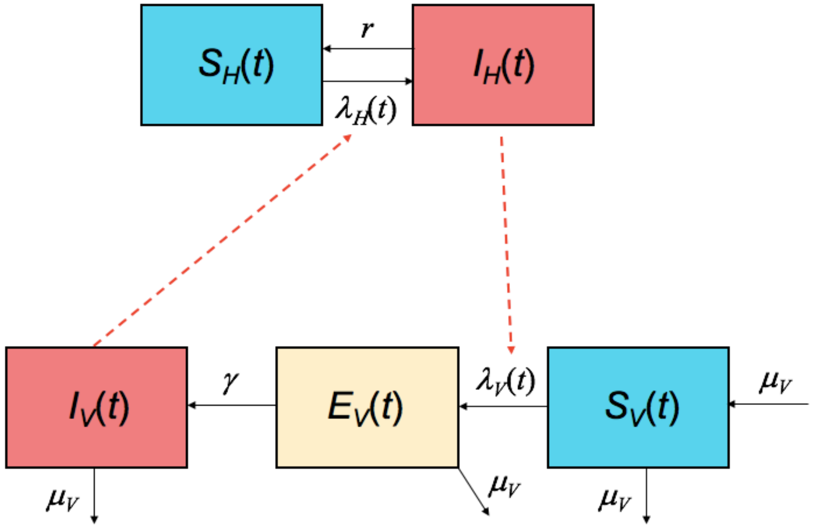


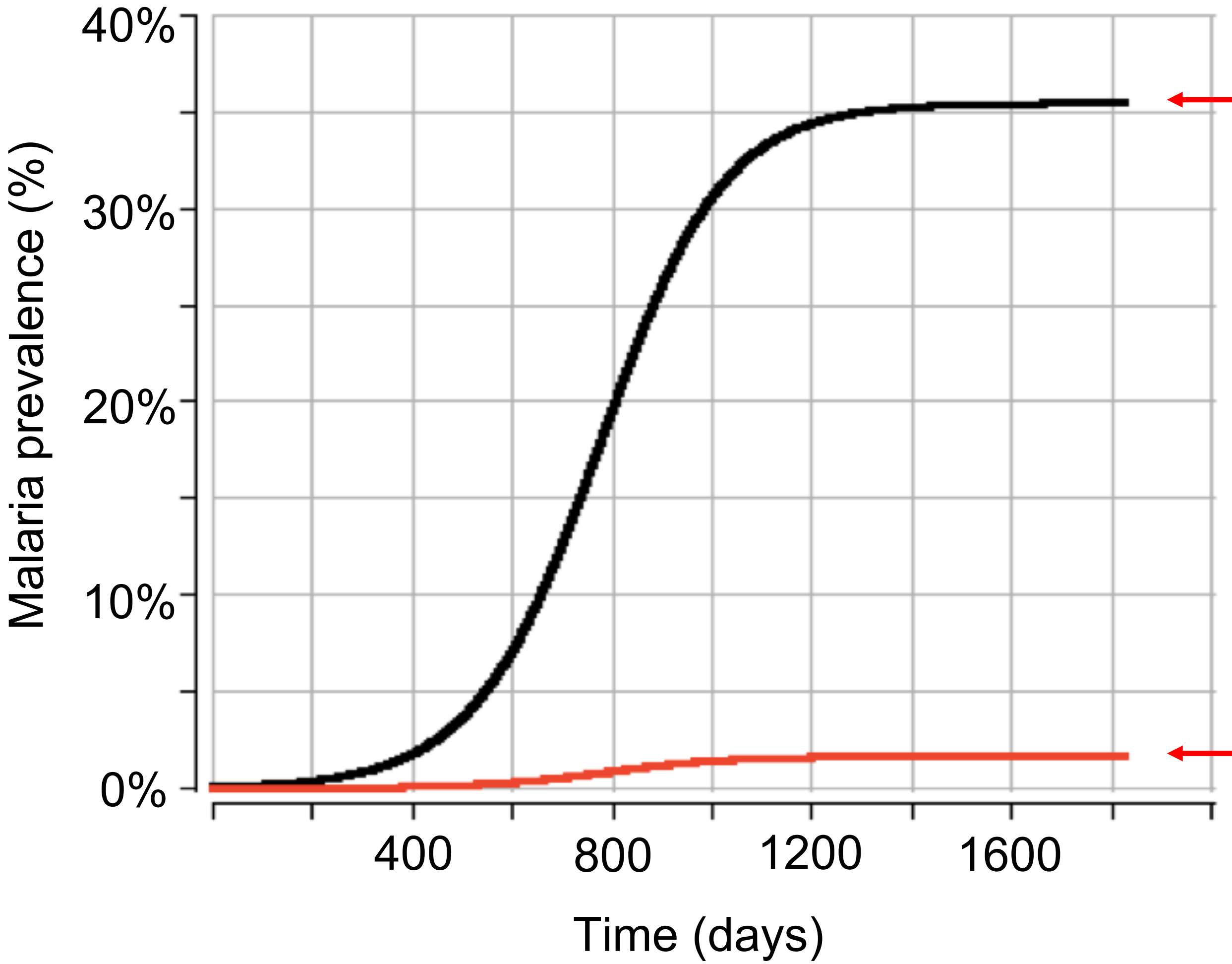


Compartmental models: Malaria



Predictions from second malaria model

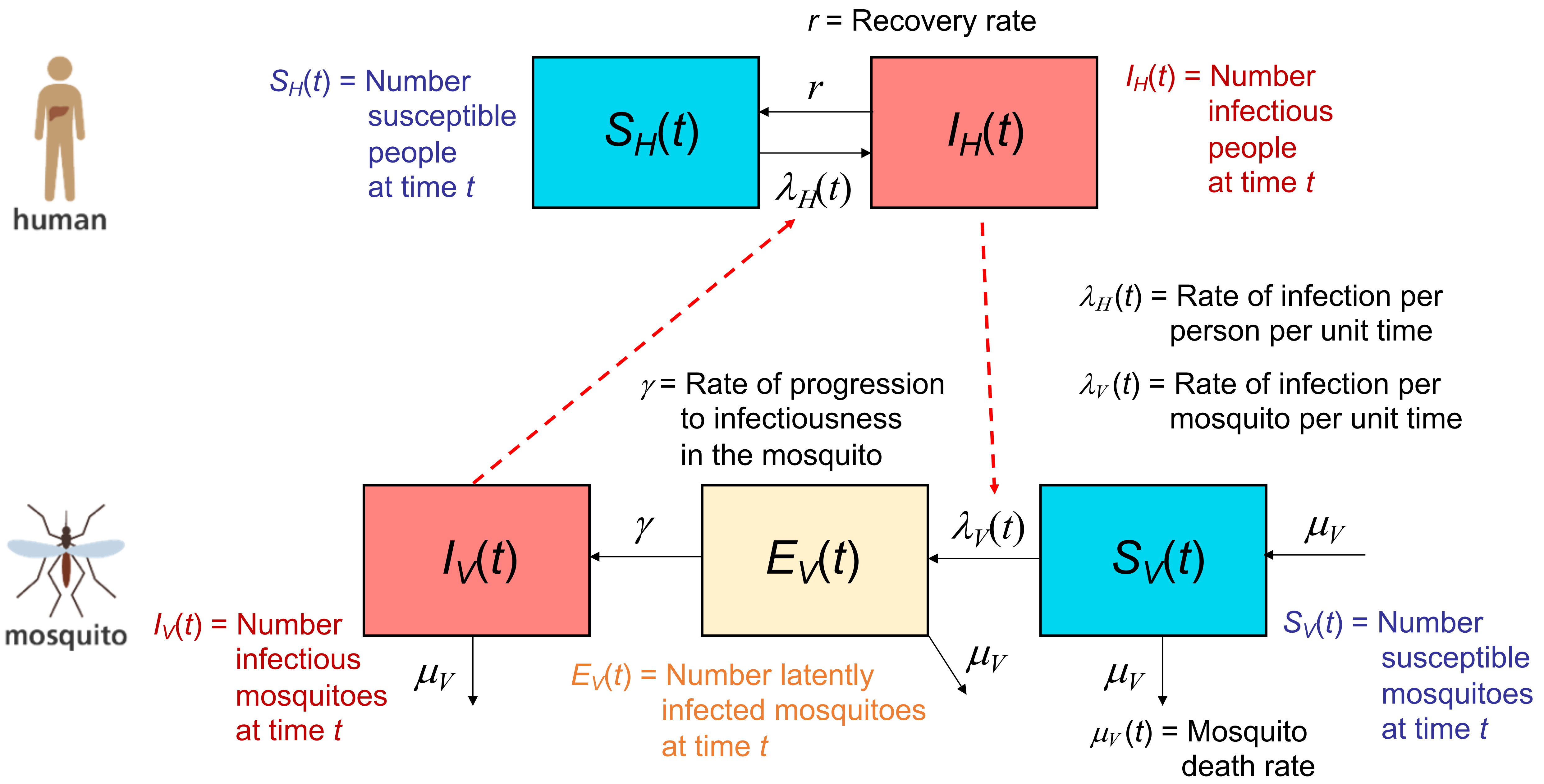




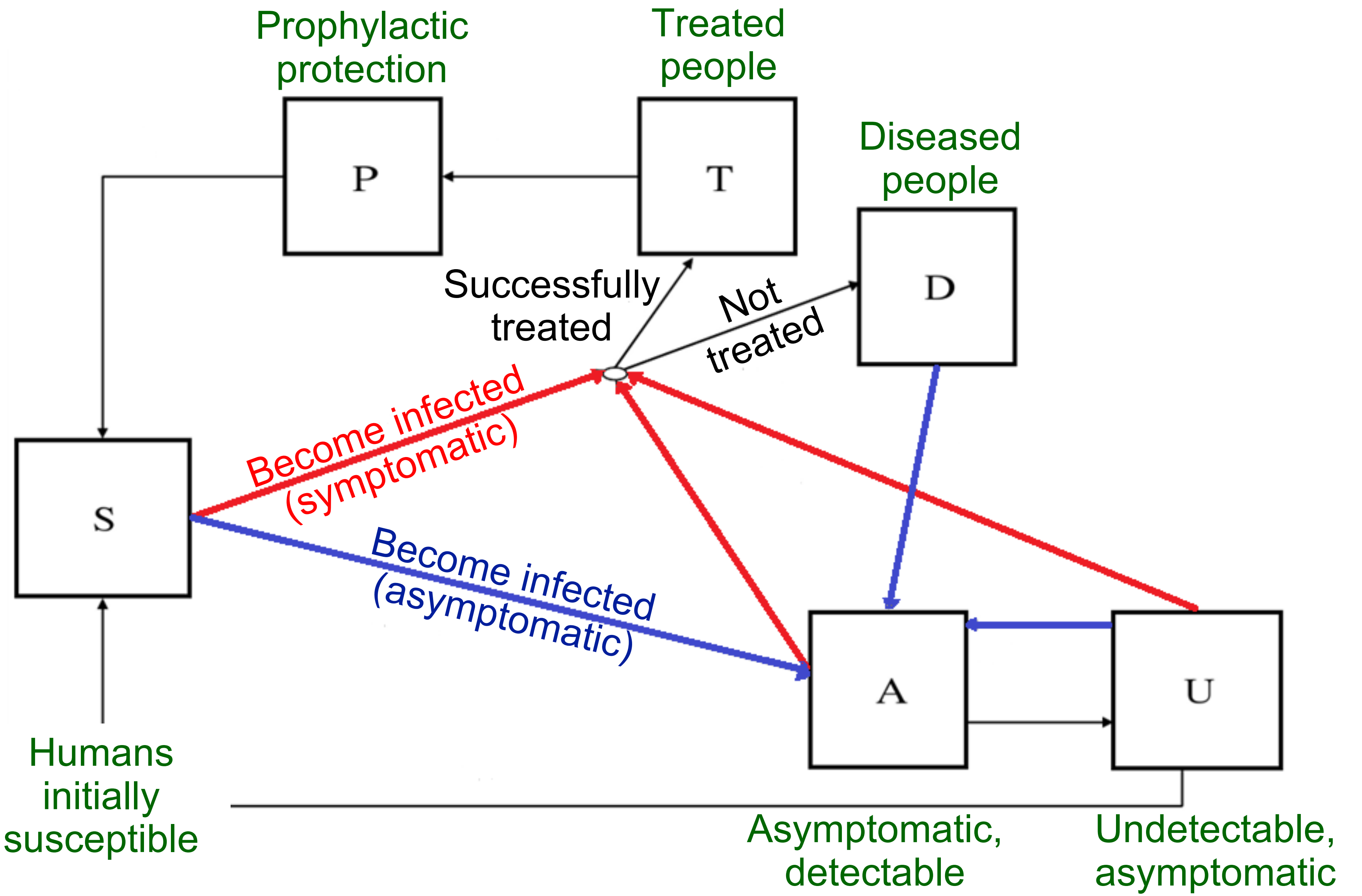
Prevalence reaches ~36% in humans

Prevalence reaches 1-2% in mosquitoes

What else would you include in a malaria model?

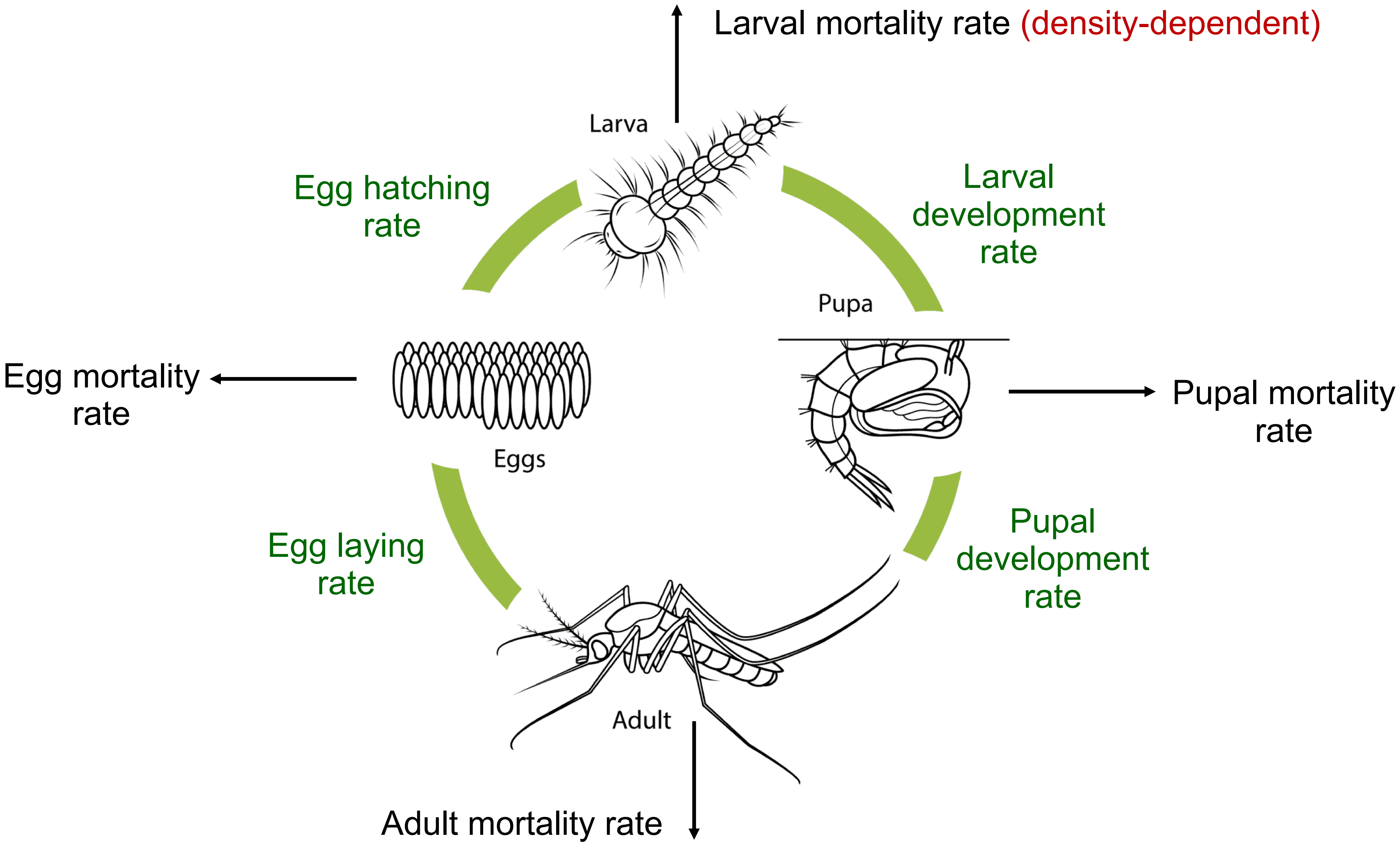


Imperial College human malaria model

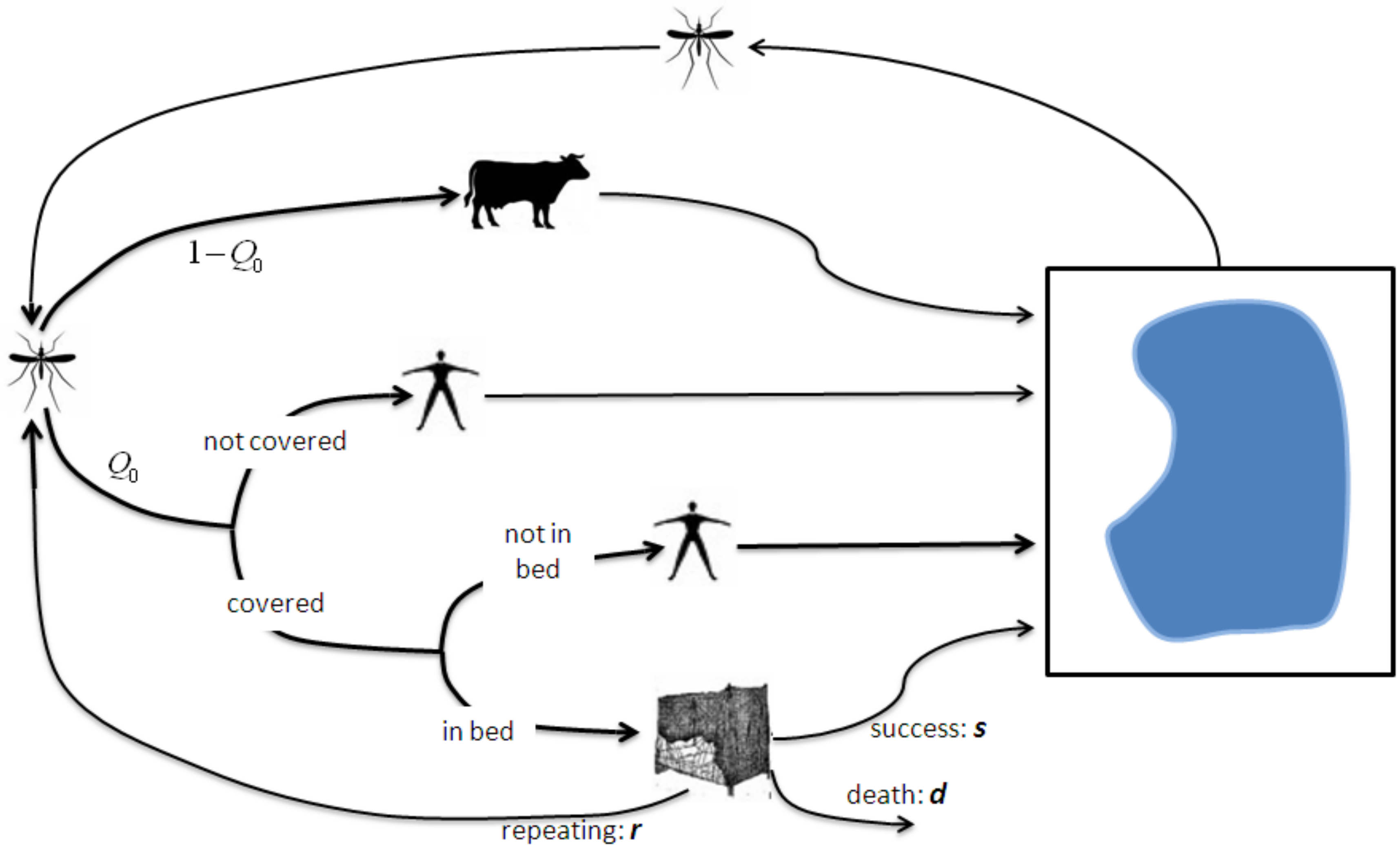


- Griffin JT, Hollingsworth DT, Okell LC, Churcher TS, White M *et al.* (2010) PLoS Medicine 7: e1000324

Mosquito life history model

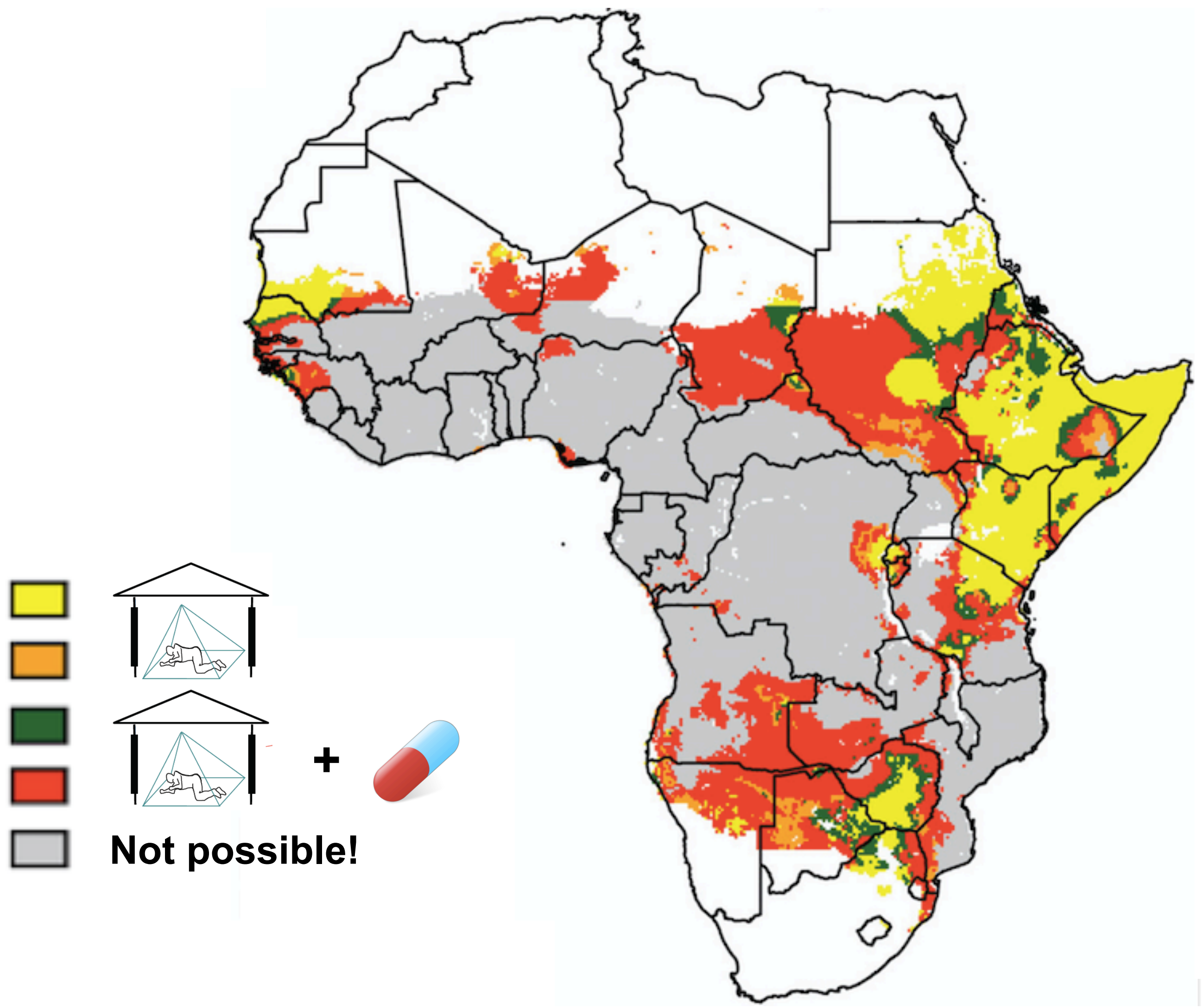


More detailed mosquito control model



- Le Menach A, Takala S, McKenzie FE, Perisse A, Harris A *et al.* (2007) Malaria Journal 6: 10

Optimal interventions to eliminate malaria



- Walker PGT, Griffin JT, Ferguson NM, Ghani AC (2016) Lancet Global Health 4: E474-E484