Controlling malaria with indoor residual spraying in spatially heterogeneous environments

Robert Smith?

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Outline

- Epidemiology of malaria

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- Indoor Residual Spraying

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- Research questions

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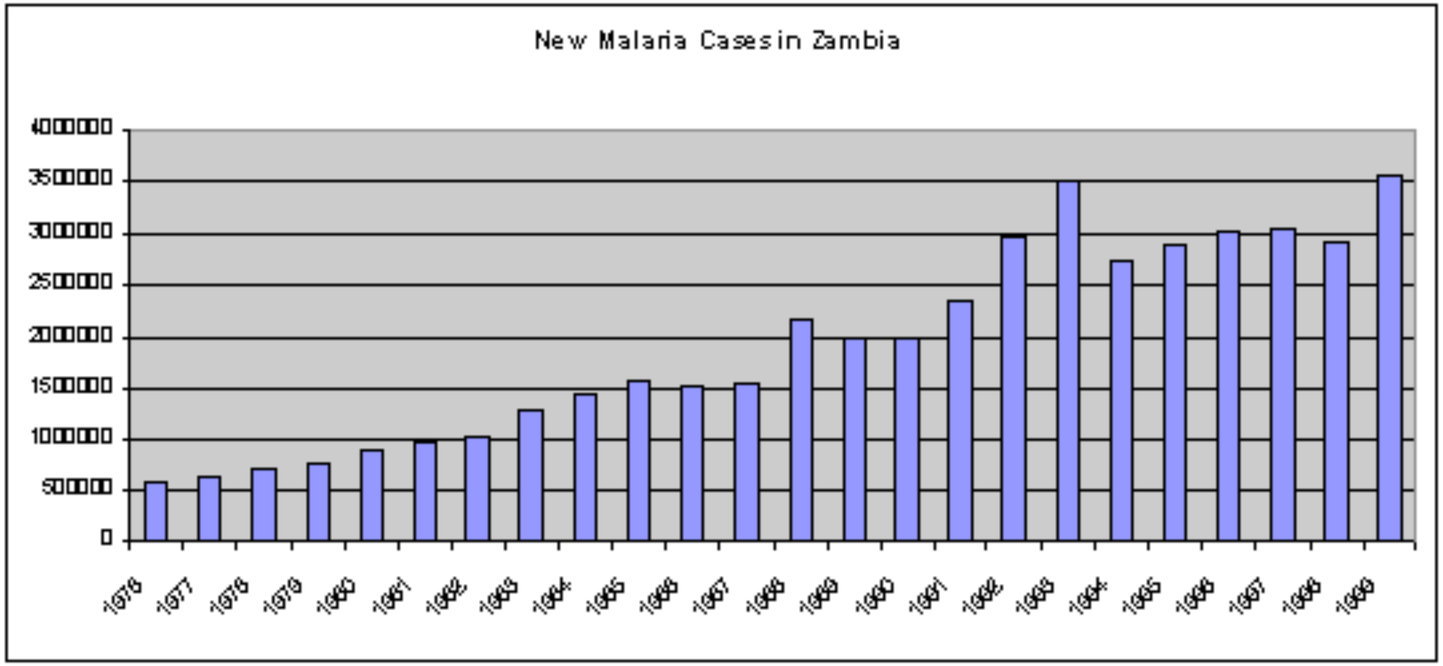
- Spraying in an interior disc
- Fixed vs nonfixed spraying
- The effects of wind.

Malaria

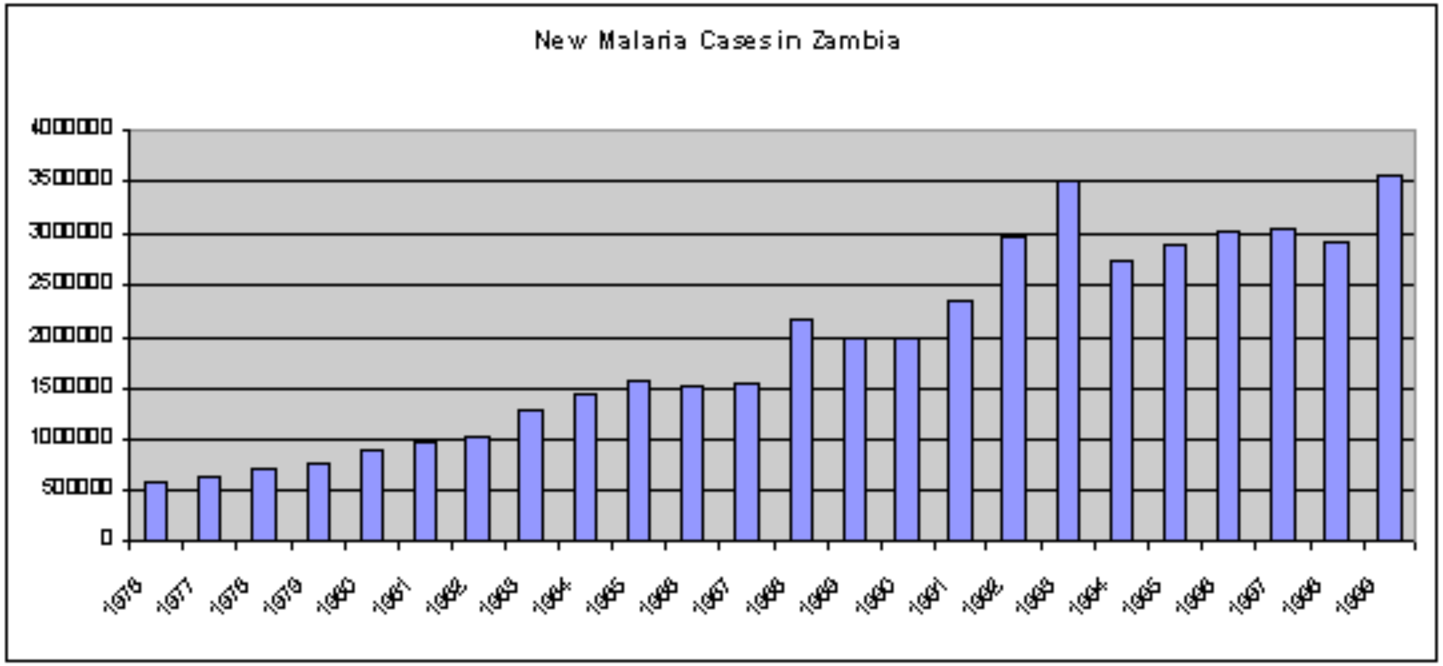
- One of the most important human diseases throughout the tropical and sub-tropical regions of the world



Source: NMCC Central Board of Health, 2000

Malaria

- One of the most important human diseases throughout the tropical and sub-tropical regions of the world
- More than 300 million acute illnesses each year



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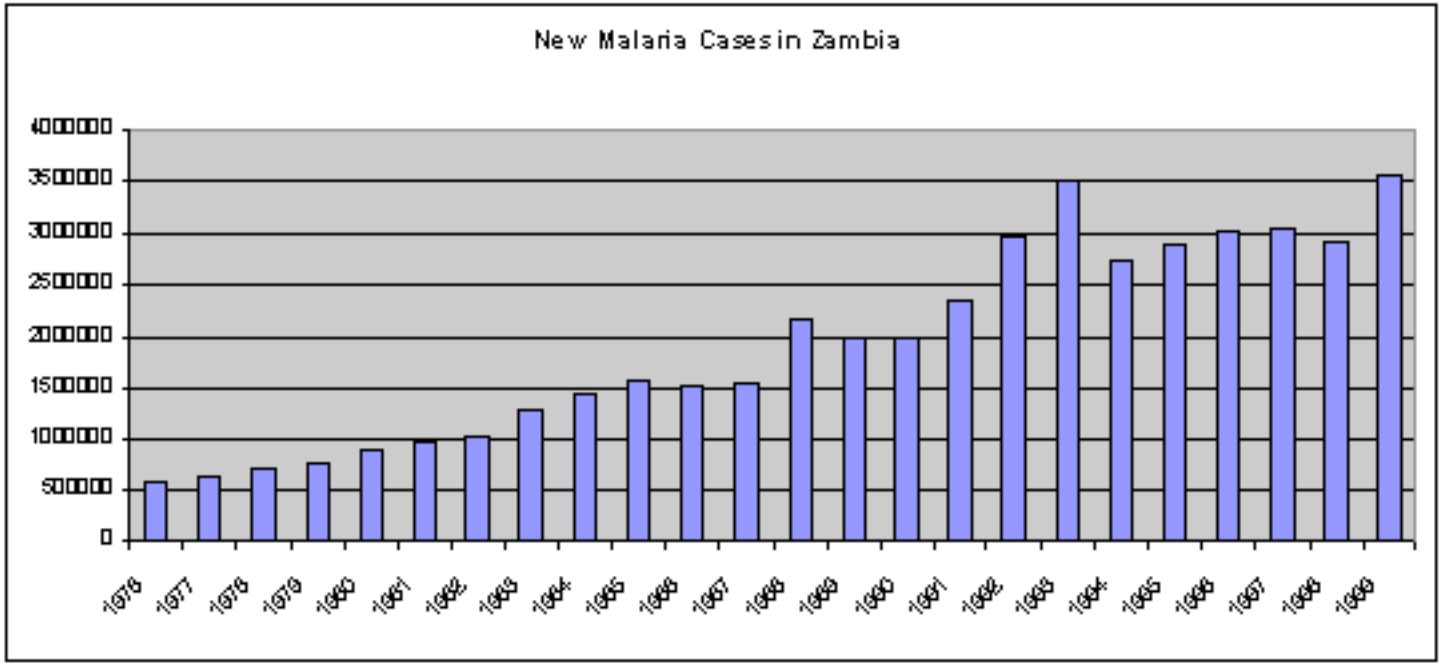
- 1,000,000 deaths annually.



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Symptoms

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- Death.

Endemic areas

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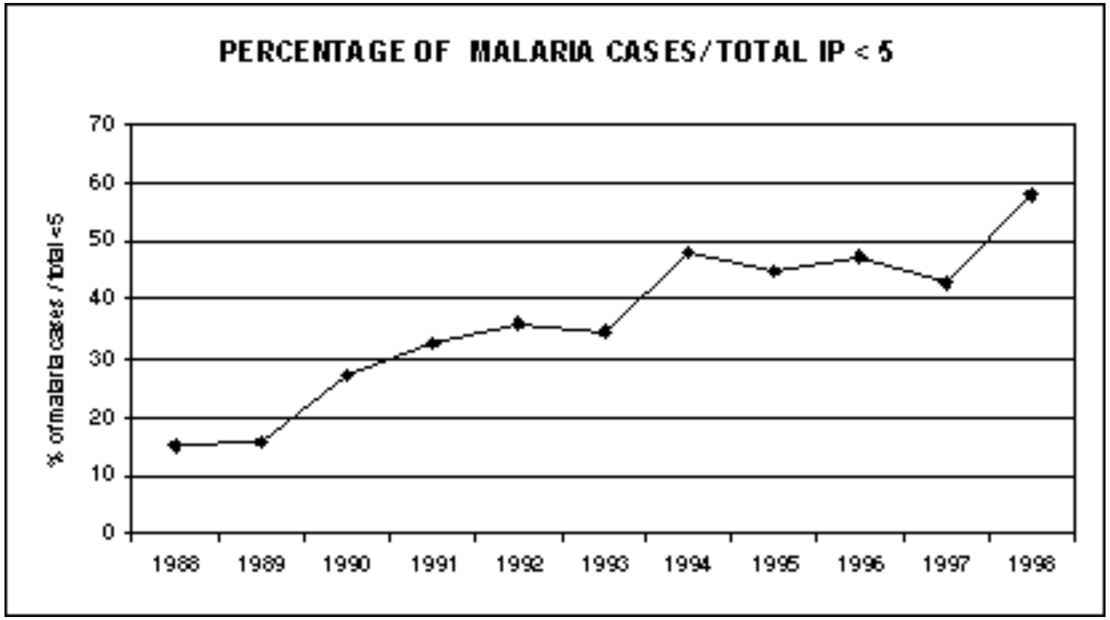

Admissions to St. Kitzo-Matany hospital, Uganda

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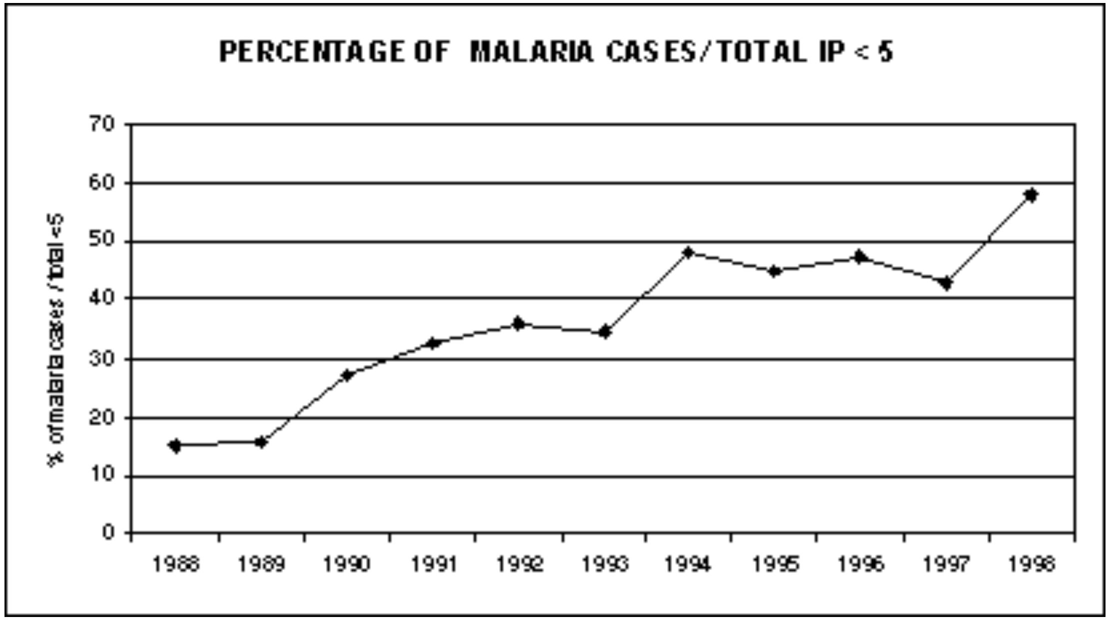

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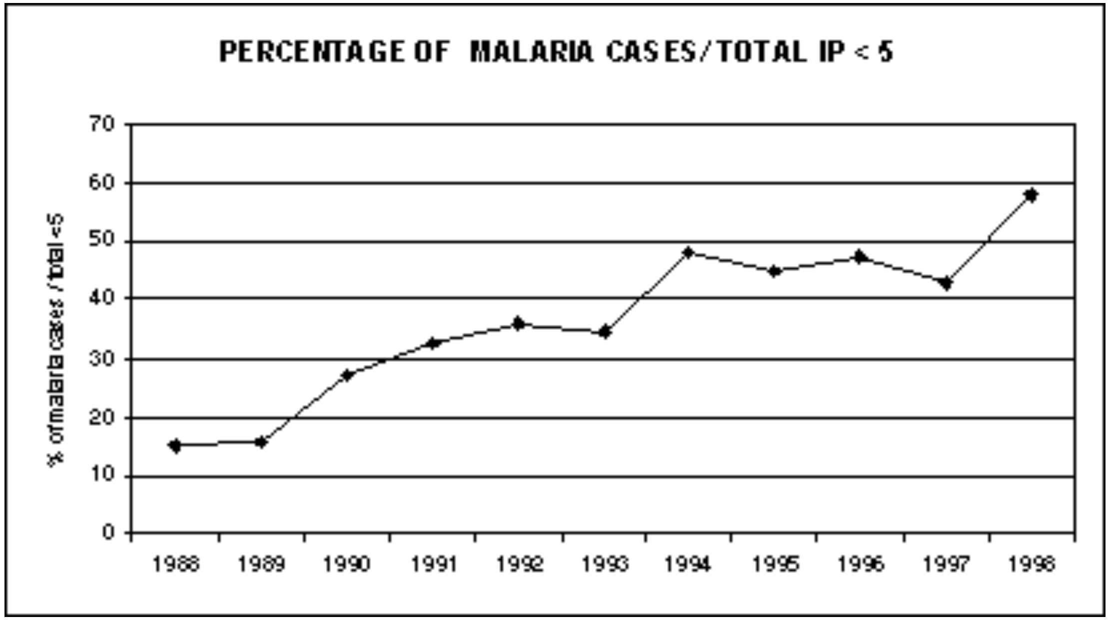
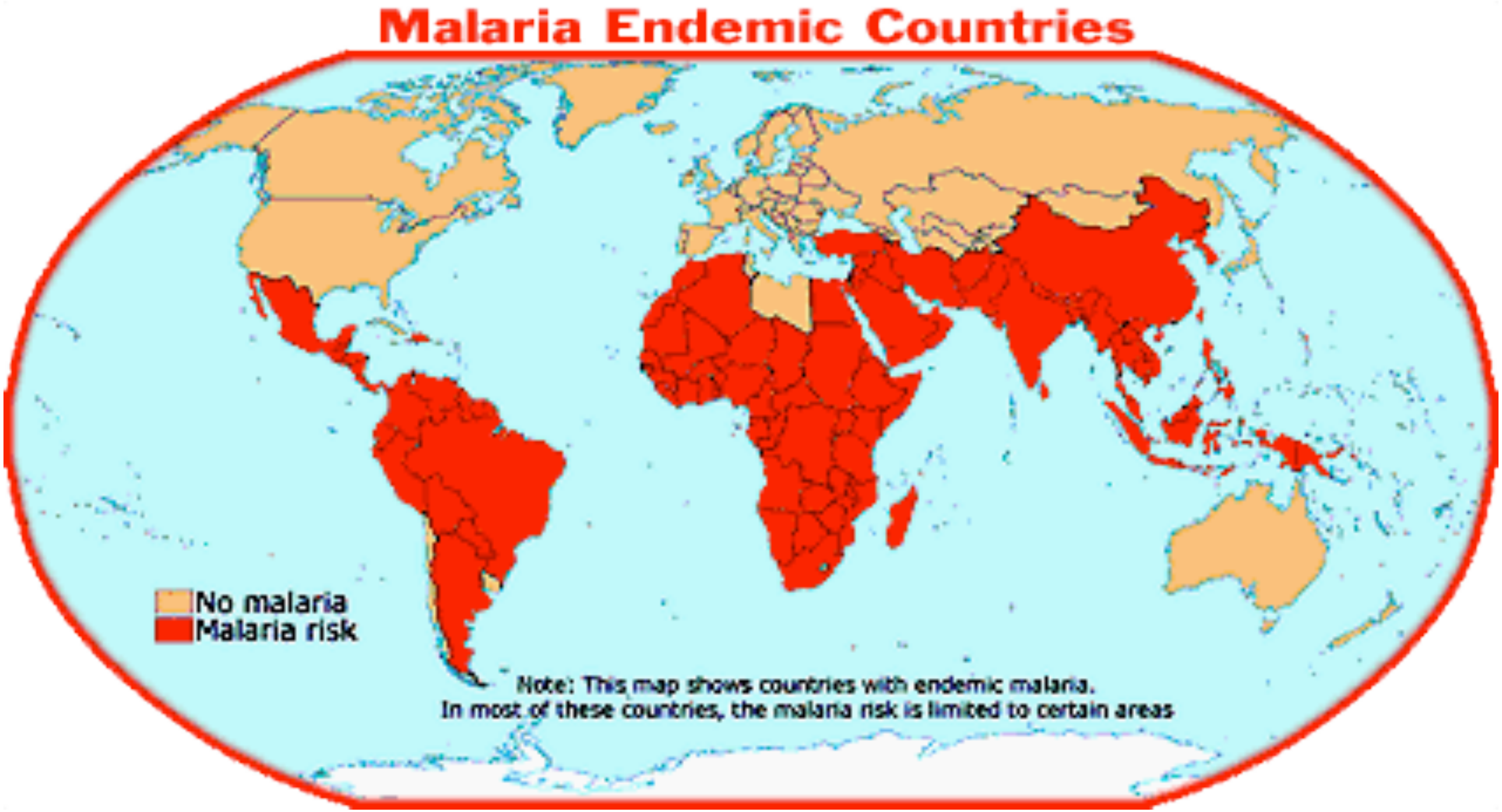
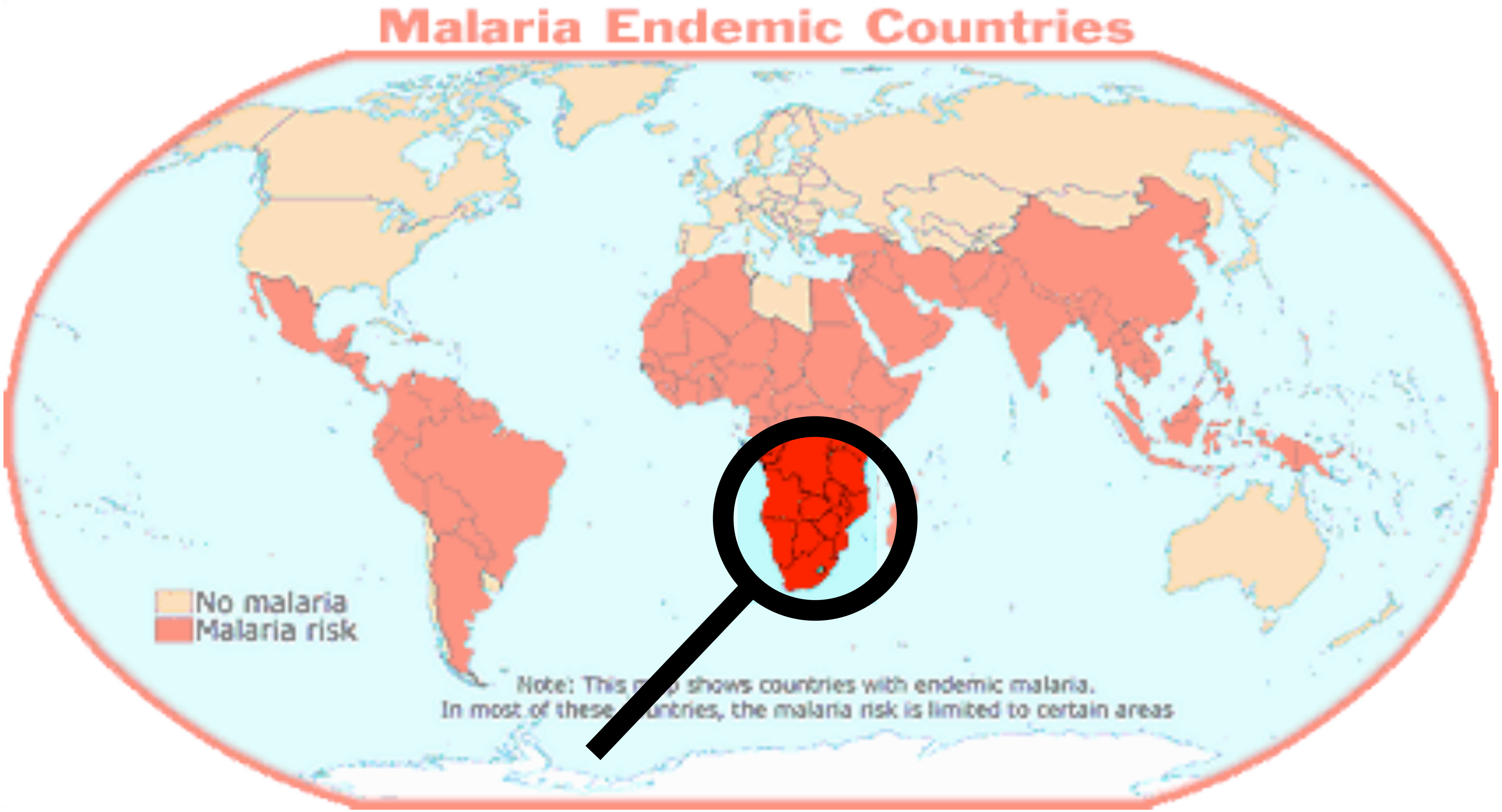


Admissions to St. Kitzo-Matany hospital, Uganda

- Impact of malaria has been estimated to cost Africa $US12 billion every year.


Malaria Endemic Countries
No malaria
Malaria risk
Note: This map shows countries with endemic malaria.
In most of these countries, the malaria risk is limited to certain areas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- chemoprophylaxis
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- vector control
  - insecticides, larvacides, etc
  - aim is to reduce vector population density and survival.

Indoor Residual Spraying

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- Indoor Residual Spraying (IRS) involves spraying houses or dwellings on the inside and under eaves on the outside
- Kills mosquitos after they've fed
- Duration of effective action is 2-6 months.

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- IRS has been responsible for suppression of at least one vector of malaria transmission, *An. funestus*
- Indoor residual spraying is a powerful method of malaria control, but is limited to the physical location of structures.

Limitations of a spraying program

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  - urban/rural population densities

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- IRS cannot be used in areas devoid of structures
  - eg forests, swamps
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  - eg landspace
  - urban/rural population densities
  - distribution of structures.

Crucial questions

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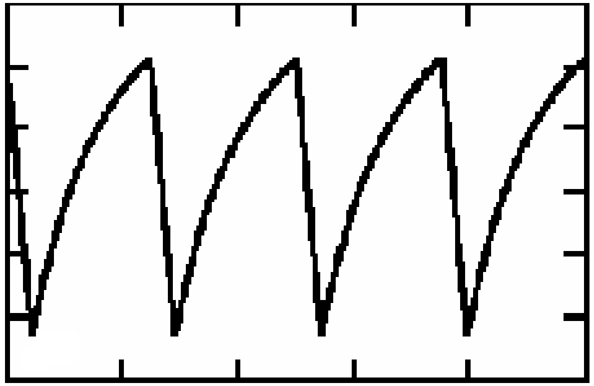
How do the results depend on the regularity of spraying?

Can we alter our control strategies to account for asymmetric phenomena such as wind?

Impulsive differential equations

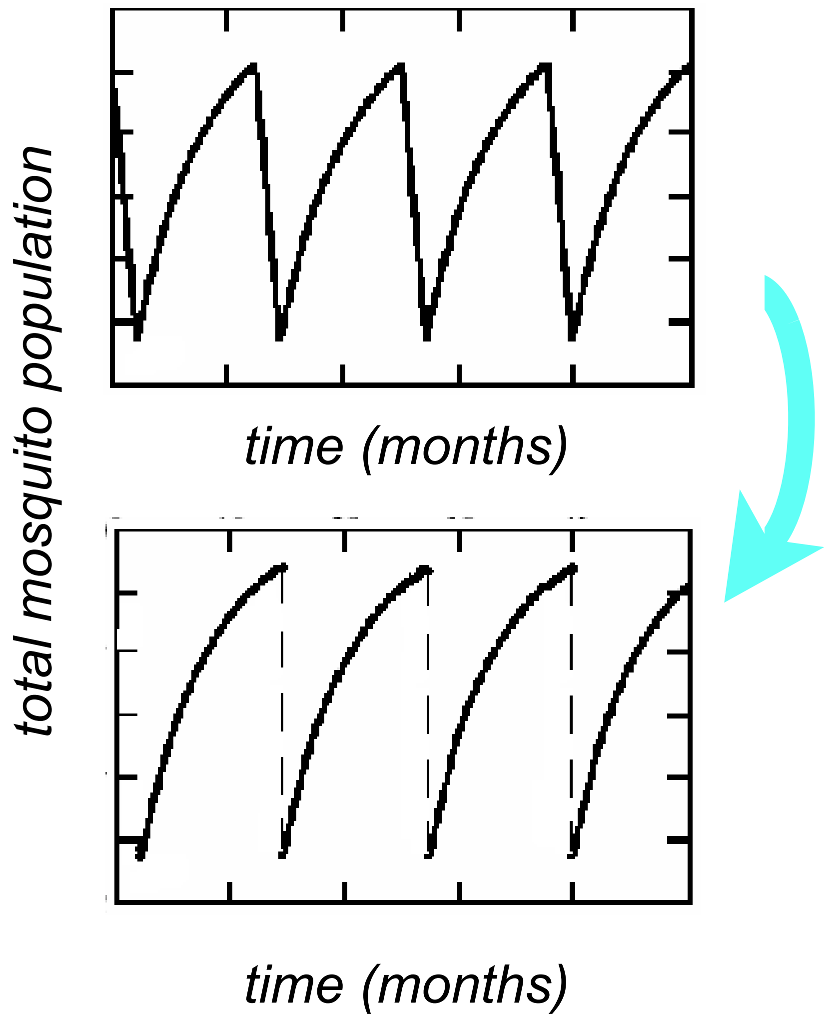
- Assume spraying is instantaneous



time (months)

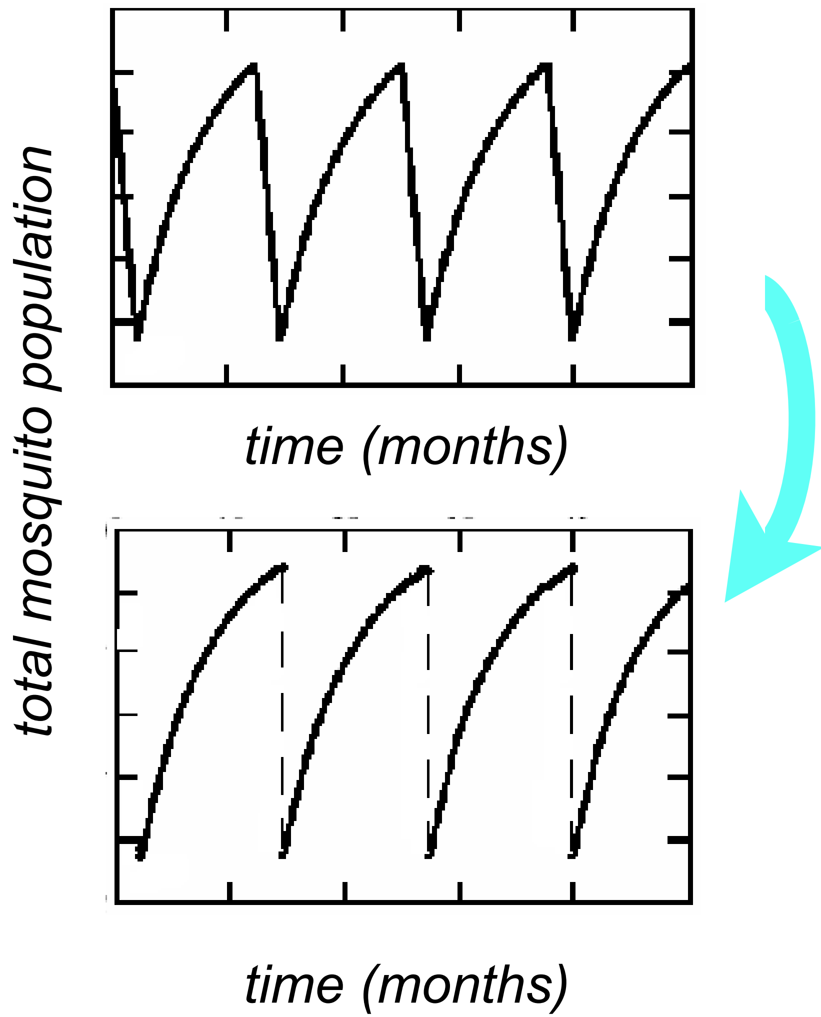
Impulsive differential equations

- Assume spraying is instantaneous
- That is, the delay in mosquito reduction is assumed to be negligible



Impulsive differential equations

- Assume spraying is instantaneous
- That is, the delay in mosquito reduction is assumed to be negligible
- This results in a system of *impulsive differential equations*.



Impulsive effect

- According to impulsive theory, we can describe the nature of the impulse at time r_k via the difference equation

$$y(r_k^+) - y(r_k^-) = f(r_k, y(r_k^-))$$

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Difference equation

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$$y(r_k^+) - y(r_k^-) = f(r_k, y(r_k^-))$$

Difference equation

Depends on the time of impulse and the state immediately beforehand.

Impulsive DEs

- Solutions are continuous for $t \neq r_k$

r_k=impulse time

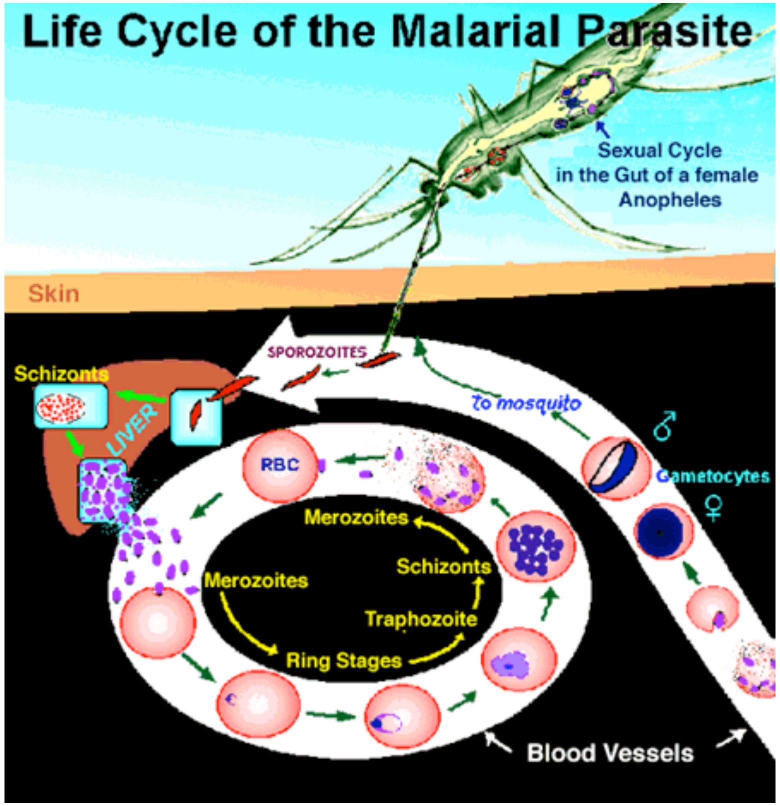
Impulsive DEs

- Solutions are continuous for $t \neq r_k$
- Solutions undergo an instantaneous change in state when $t = r_k$.

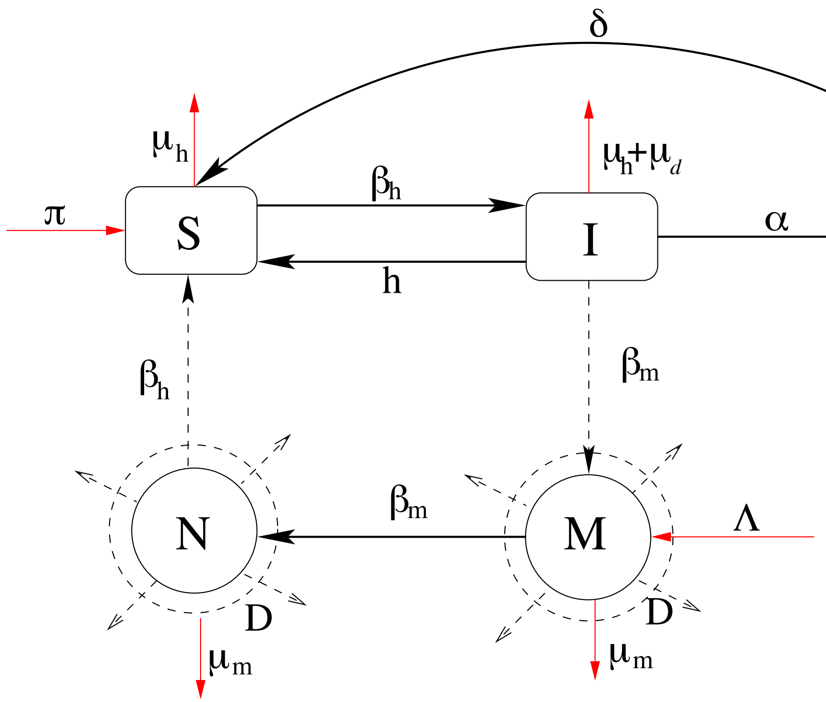
r_k=impulse time

Putting it together

- The model thus consists of a system of ODEs (humans), together with PDEs and difference equations (mosquitos).



The model



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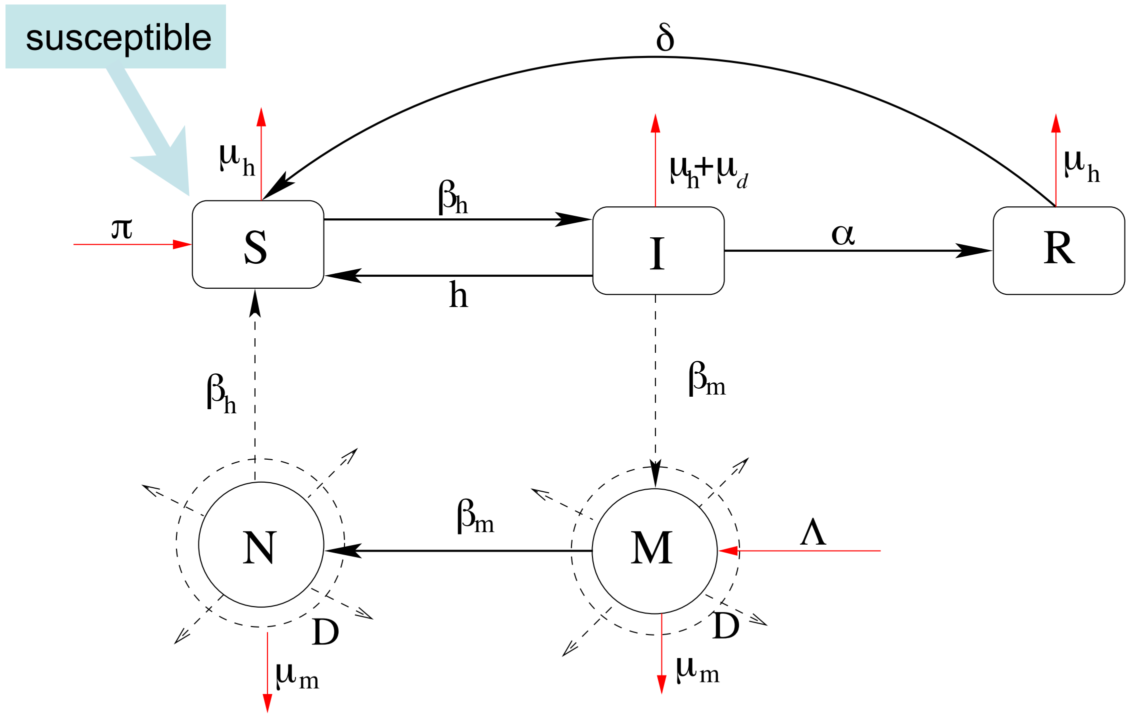
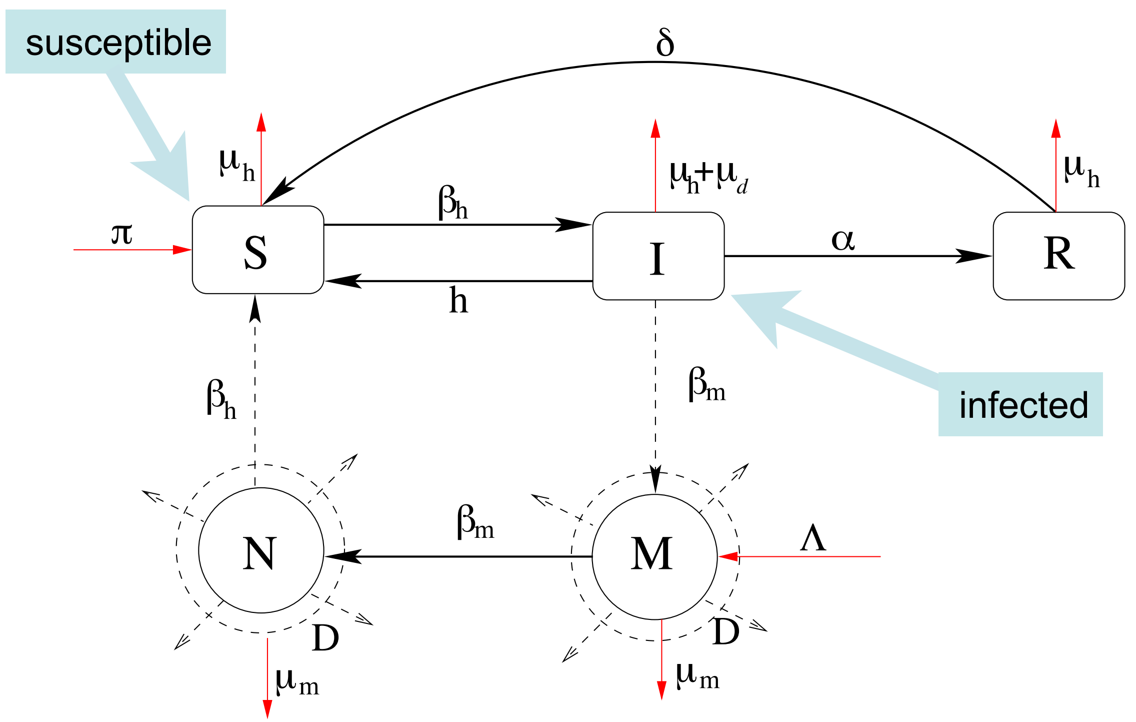
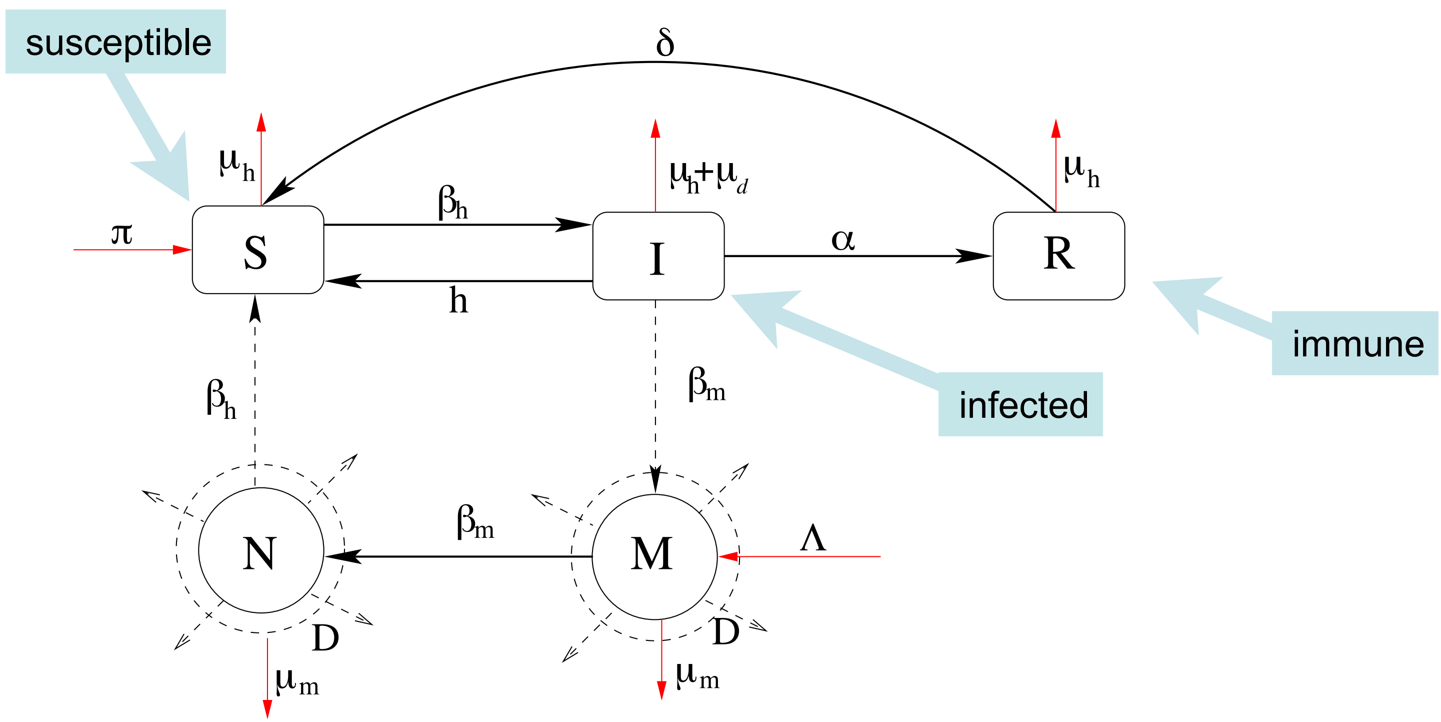


susceptible
δ
μ_h
$\mu_h+\mu_d$
μ_h
β_h
π
S
I
α
R
h
β_h
β_m
β_m
N
M
Λ
D
D
μ_m
μ_m

The model


susceptible
δ
μ_h
$\mu_h+\mu_d$
μ_h
β_h
π
S
I
α
R
h
β_h
β_m
infected
β_m
N
M
Λ
D
D
μ_m
μ_m

The model


susceptible
δ
μ_h
$\mu_h+\mu_d$
μ_h
β_h
π
S
I
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immune
β_m
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M
Λ
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D
μ_m
μ_m

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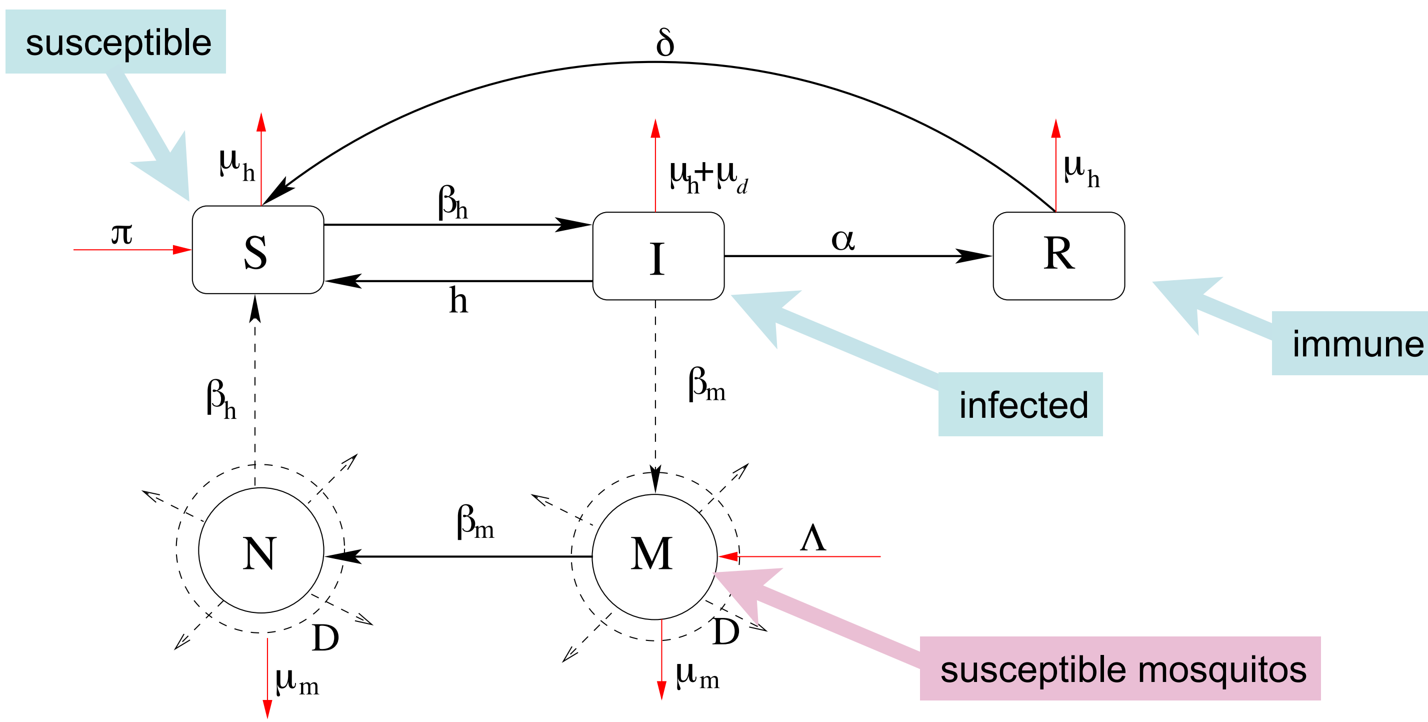
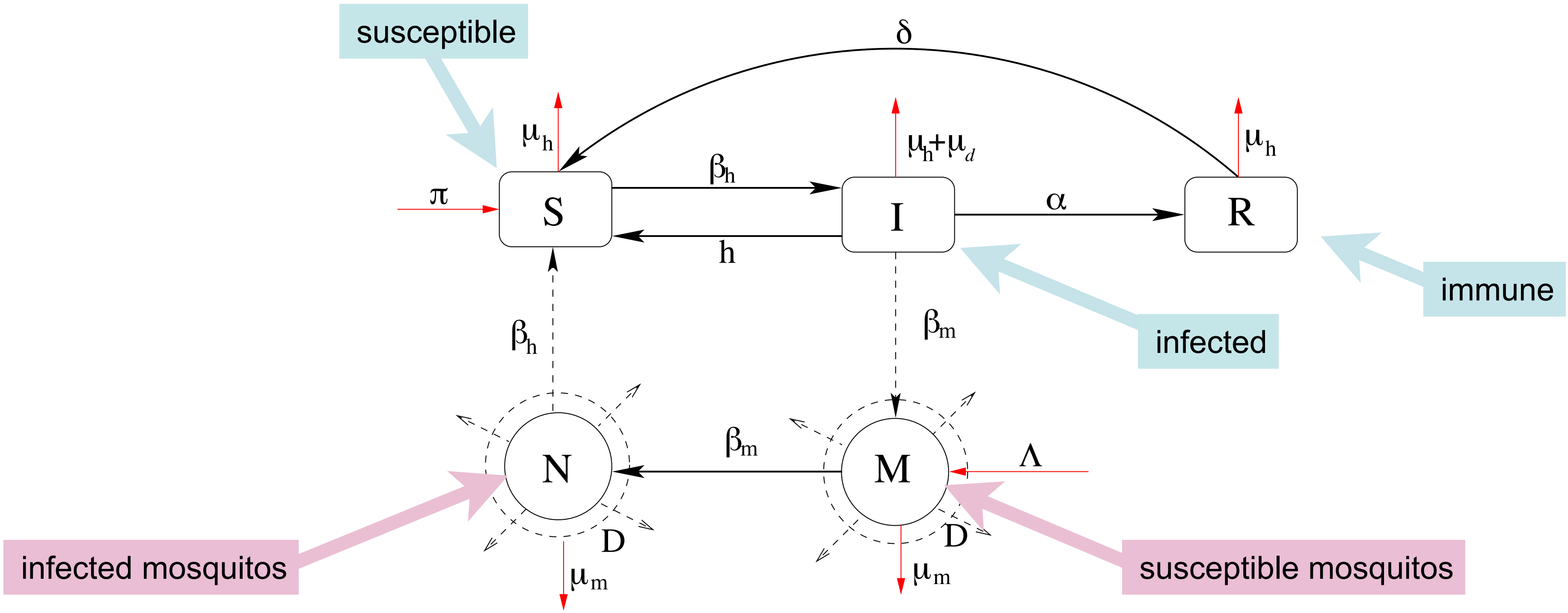


susceptible
δ
μ_h
$\mu_h+\mu_d$
μ_h
β_h
π
S
I
α
R
h
infected
immune
β_h
β_m
β_m
N
M
Λ
D
D
μ_m
μ_m
susceptible mosquitos

The model



susceptible
δ
μ_h
μ_h+μ_d
μ_h
β_h
π
S
I
α
R
h
immune
β_h
β_m
infected
β_m
N
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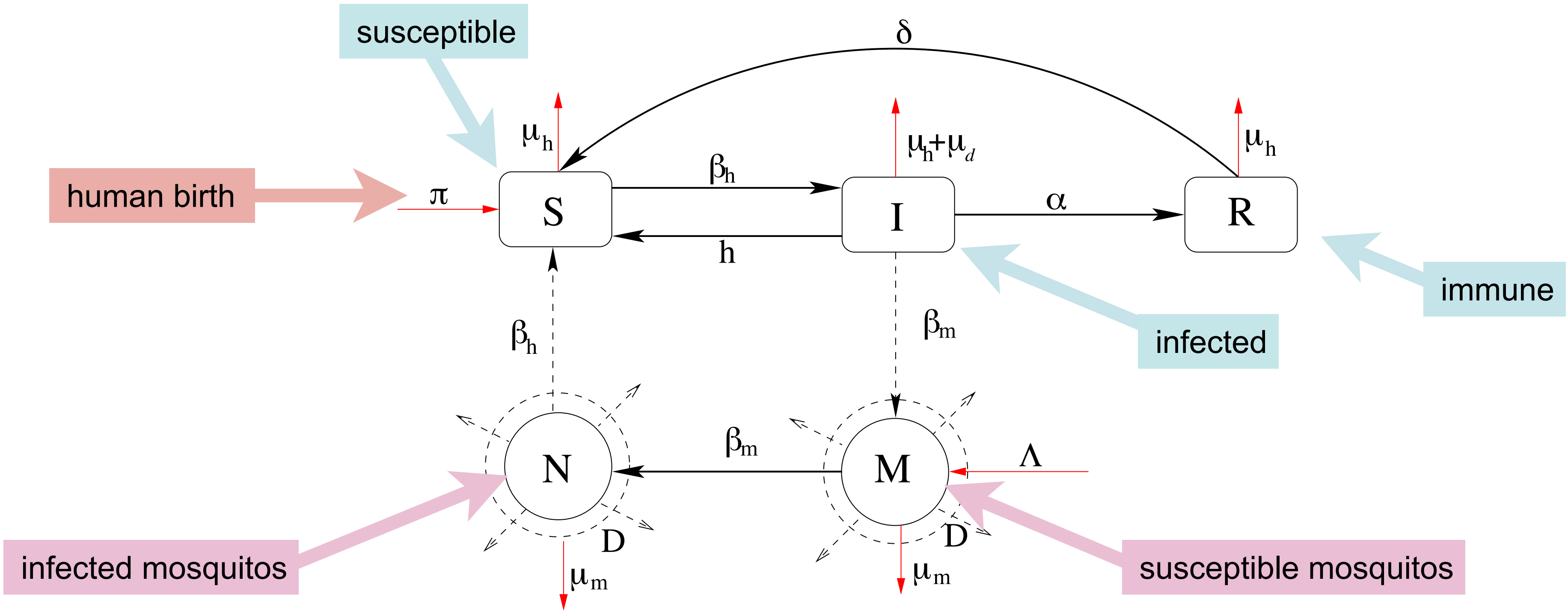
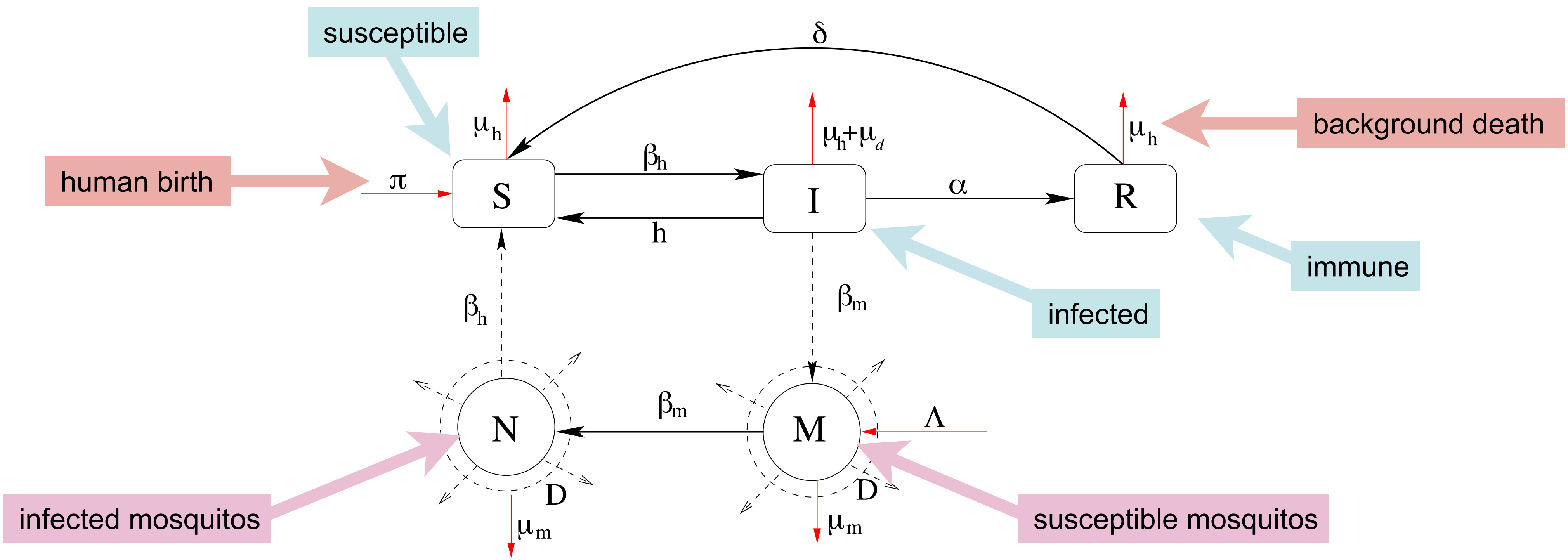
Λ
D
D
μ_m
μ_m
infected mosquitos
susceptible mosquitos

The model

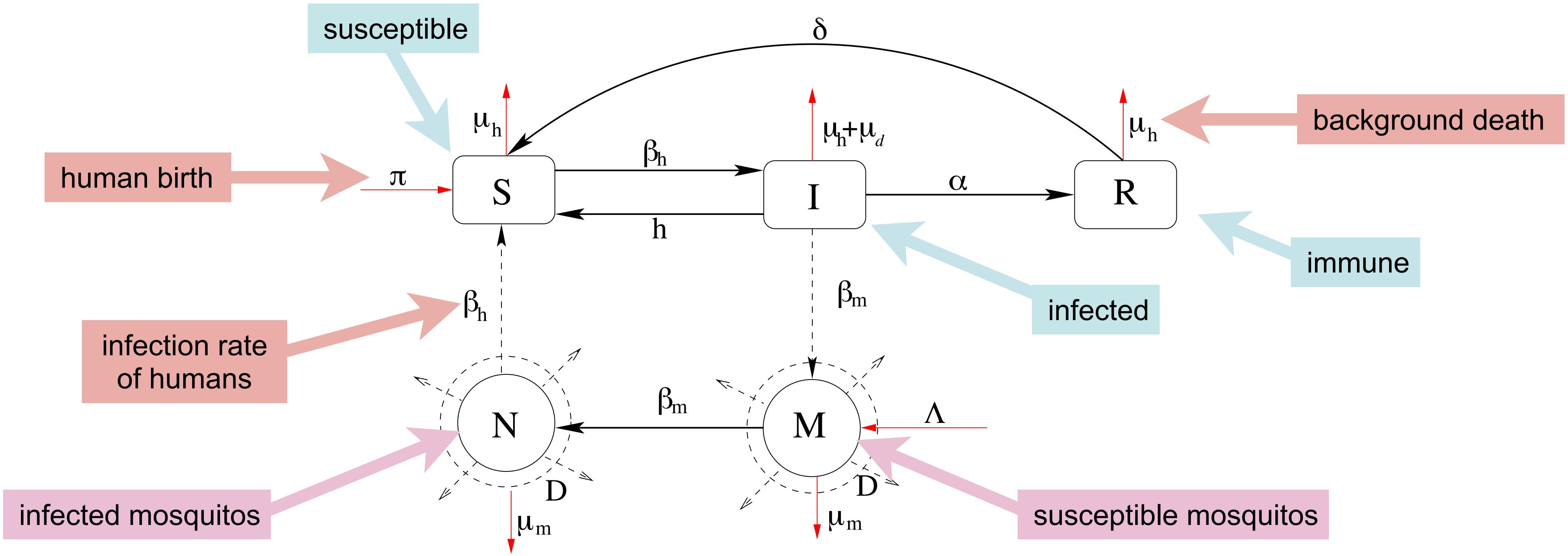

susceptible
δ
μ_h
$\mu_h+\mu_d$
μ_h
human birth
π
β_h
S
I
α
R
h
immune
β_m
infected
β_h
β_m
N
M
Λ
D
D
infected mosquitos
μ_m
μ_m
susceptible mosquitos

The model



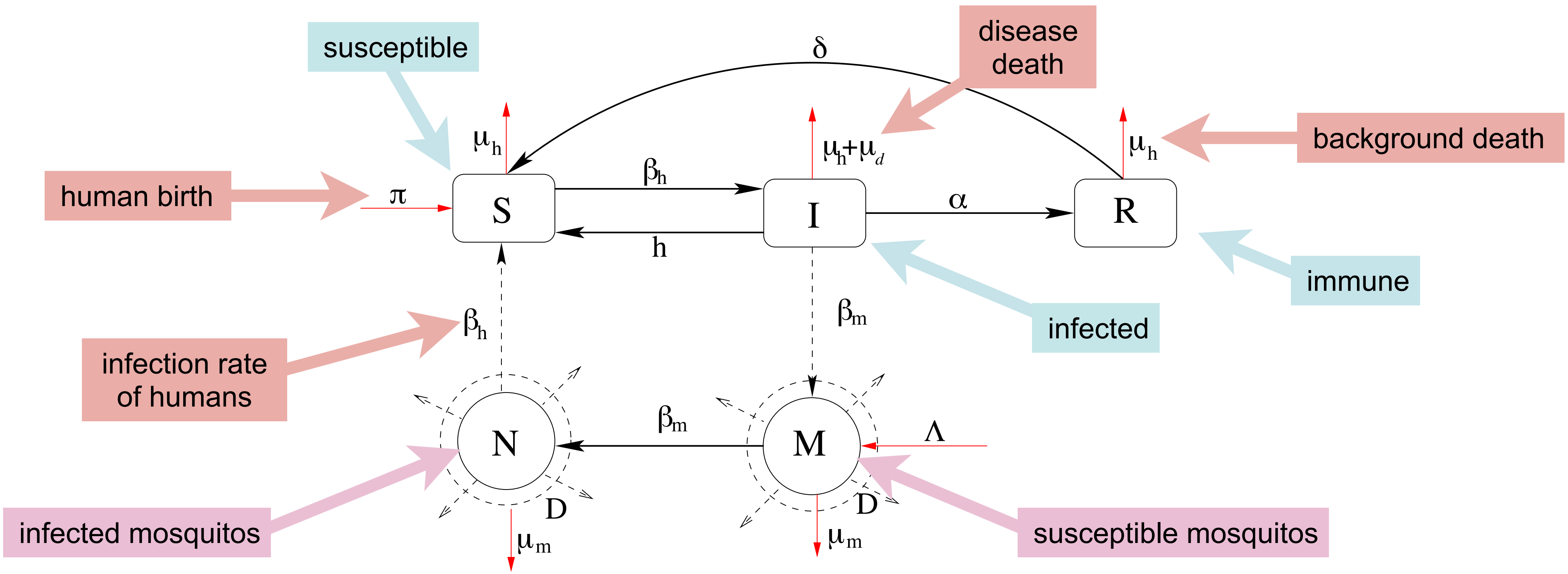
susceptible
δ
background death
μh
μh+μd
μh
βh
human birth
π
S
I
α
R
h
immune
βm
infected
βh
βm
N
M
Λ
D
D
μm
μm
infected mosquitos
susceptible mosquitos

The model



susceptible
δ
background death
human birth
π
S
I
R
α
h
infected
immune
infection rate of humans
N
M
Λ
D
D
infected mosquitos
susceptible mosquitos

The model



susceptible
disease death
background death
human birth
infection rate of humans
infected
immune
infected mosquitos
susceptible mosquitos
S
I
R
N
M
δ
μ_h
$\mu_h+\mu_d$
μ_h
π
β_h
h
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β_h
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Λ
D
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μ_m
μ_m

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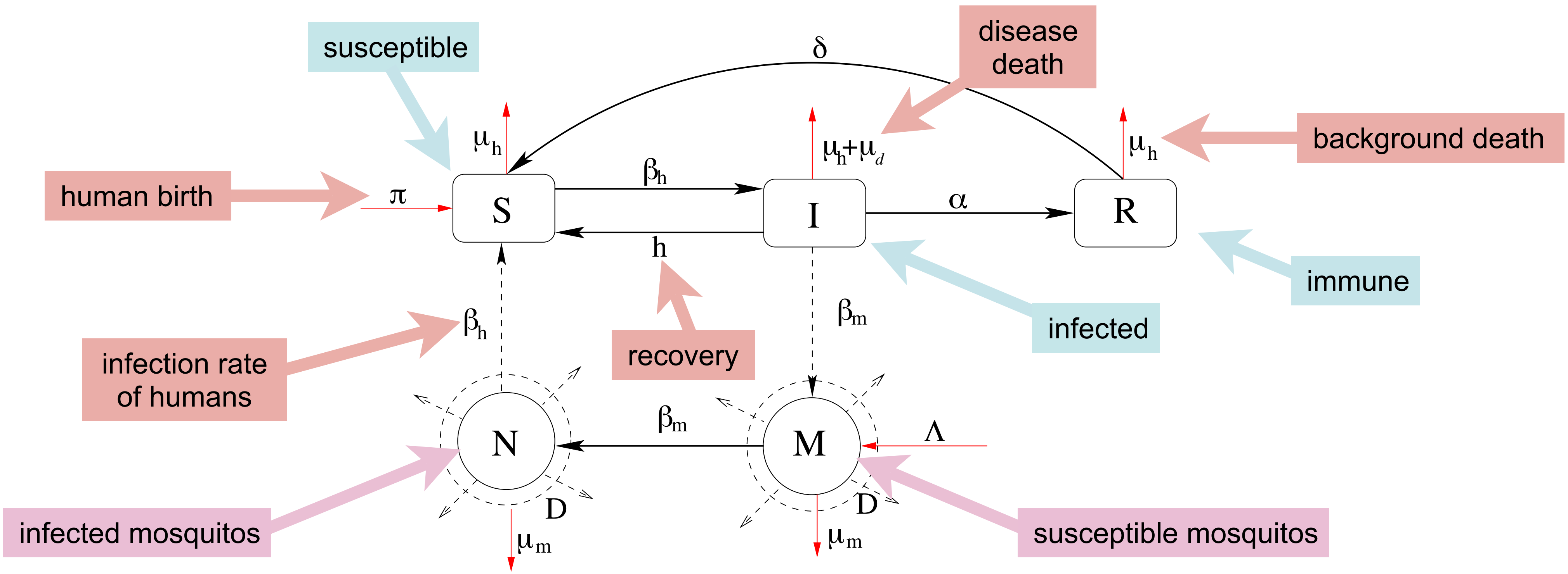
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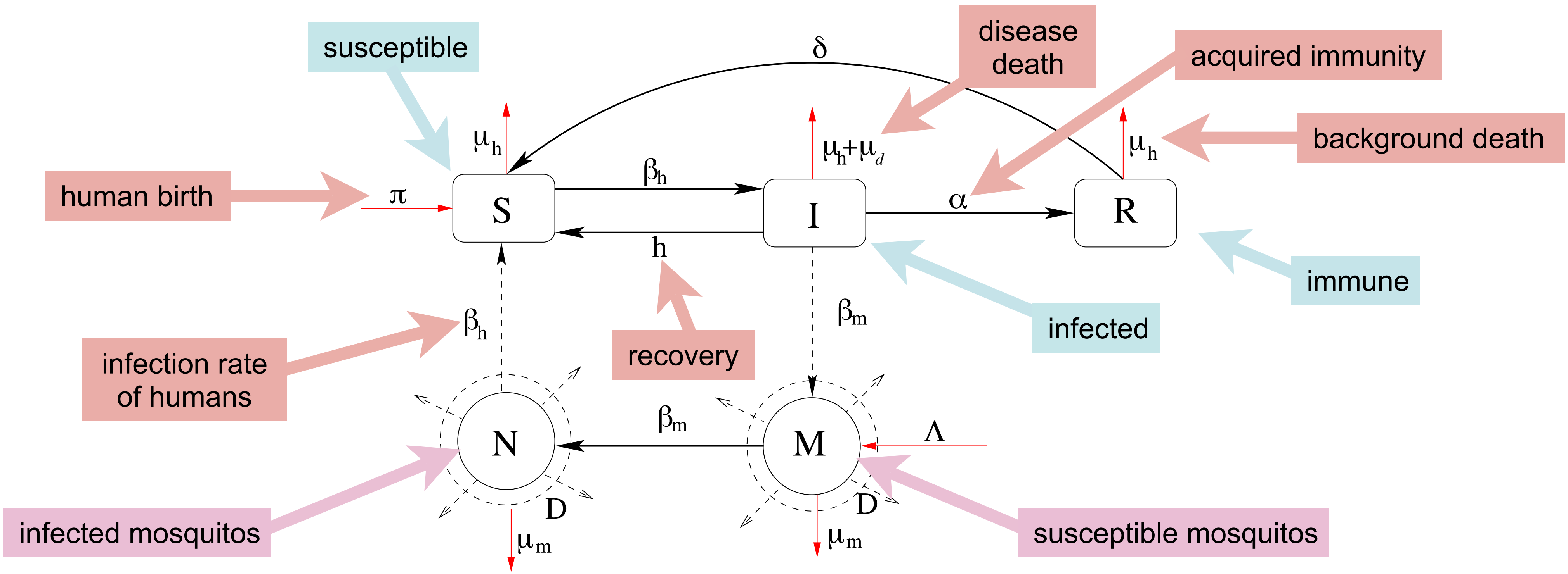
immune
infected
recovery
β_h
β_m
infection rate of humans
β_m
N
M
Λ
D
D
μ_m
μ_m
infected mosquitos
susceptible mosquitos

The model



susceptible
disease death
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infection rate of humans
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infected
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infected mosquitos
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δ
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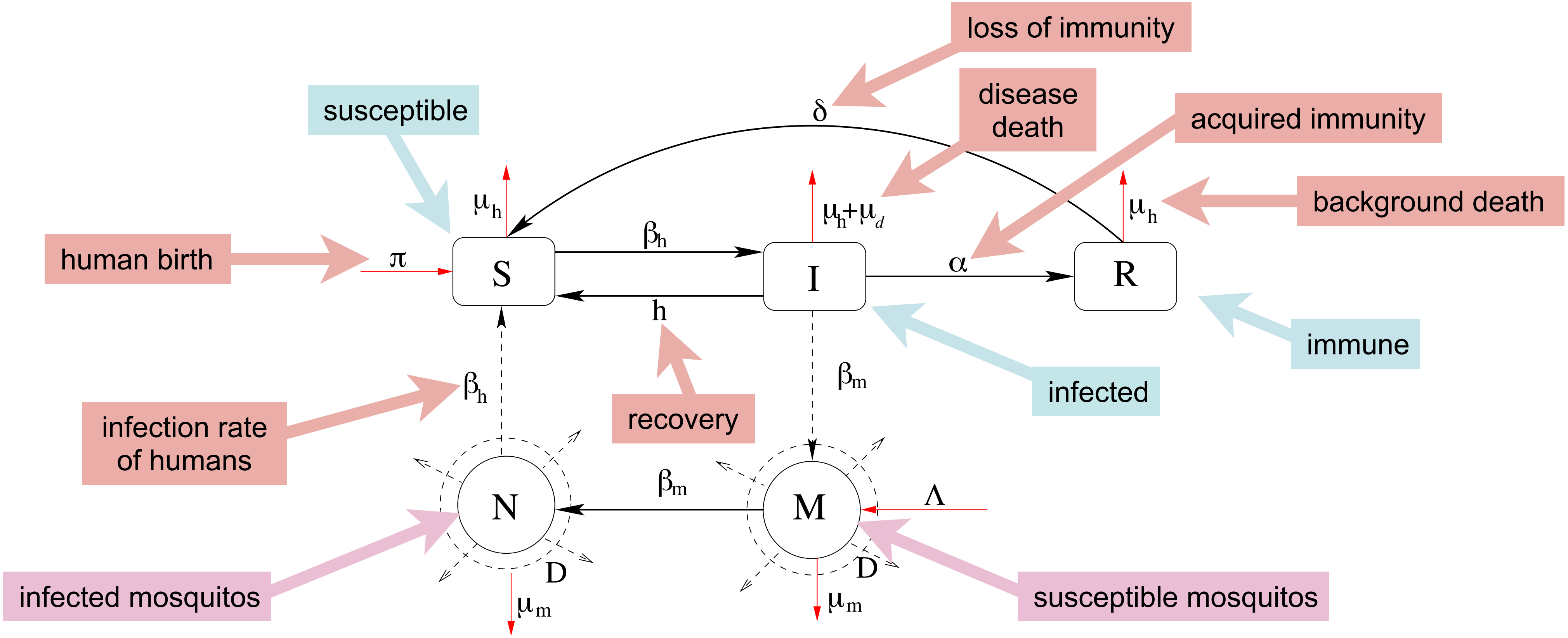

loss of immunity
δ
disease
death
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μh
μh+μd
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human birth
π
βh
S
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βm
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M
Λ
D
D
infected mosquitos
μm
μm
susceptible mosquitos

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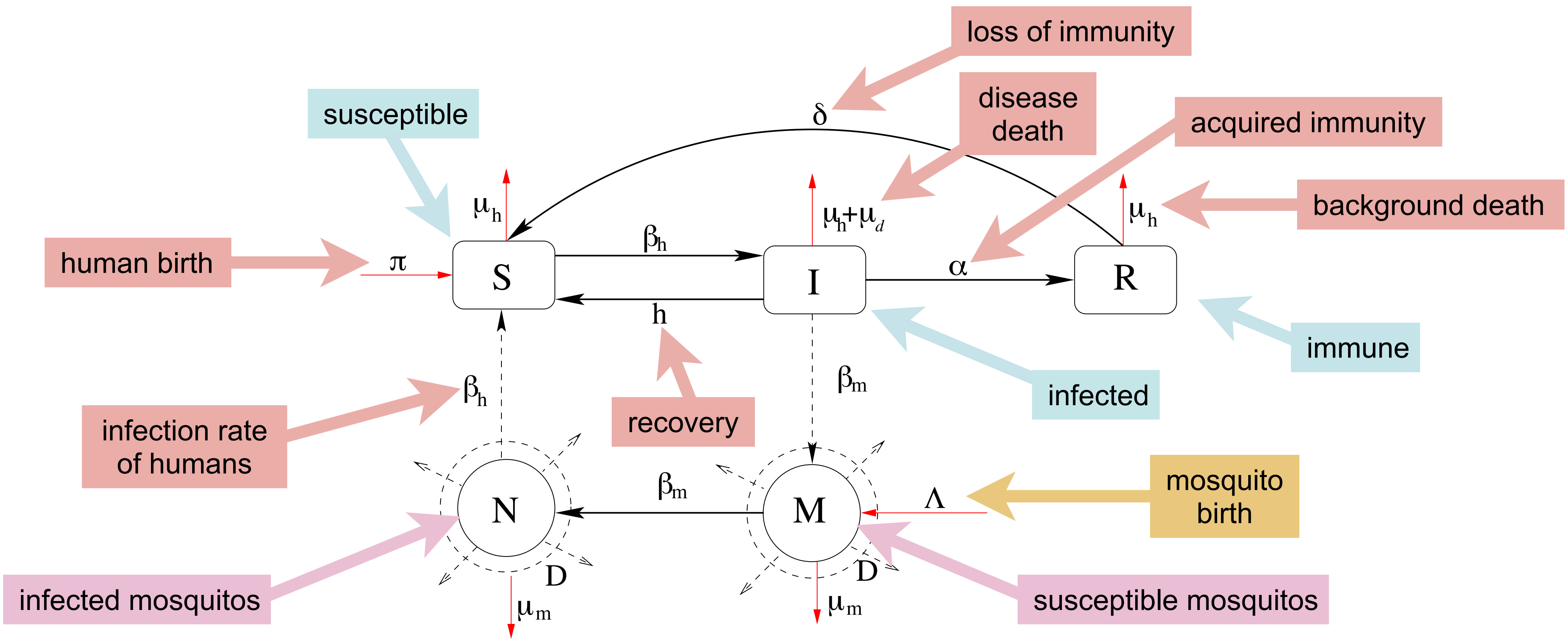
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birth
βm
Λ
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M
D
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infected mosquitos
μm
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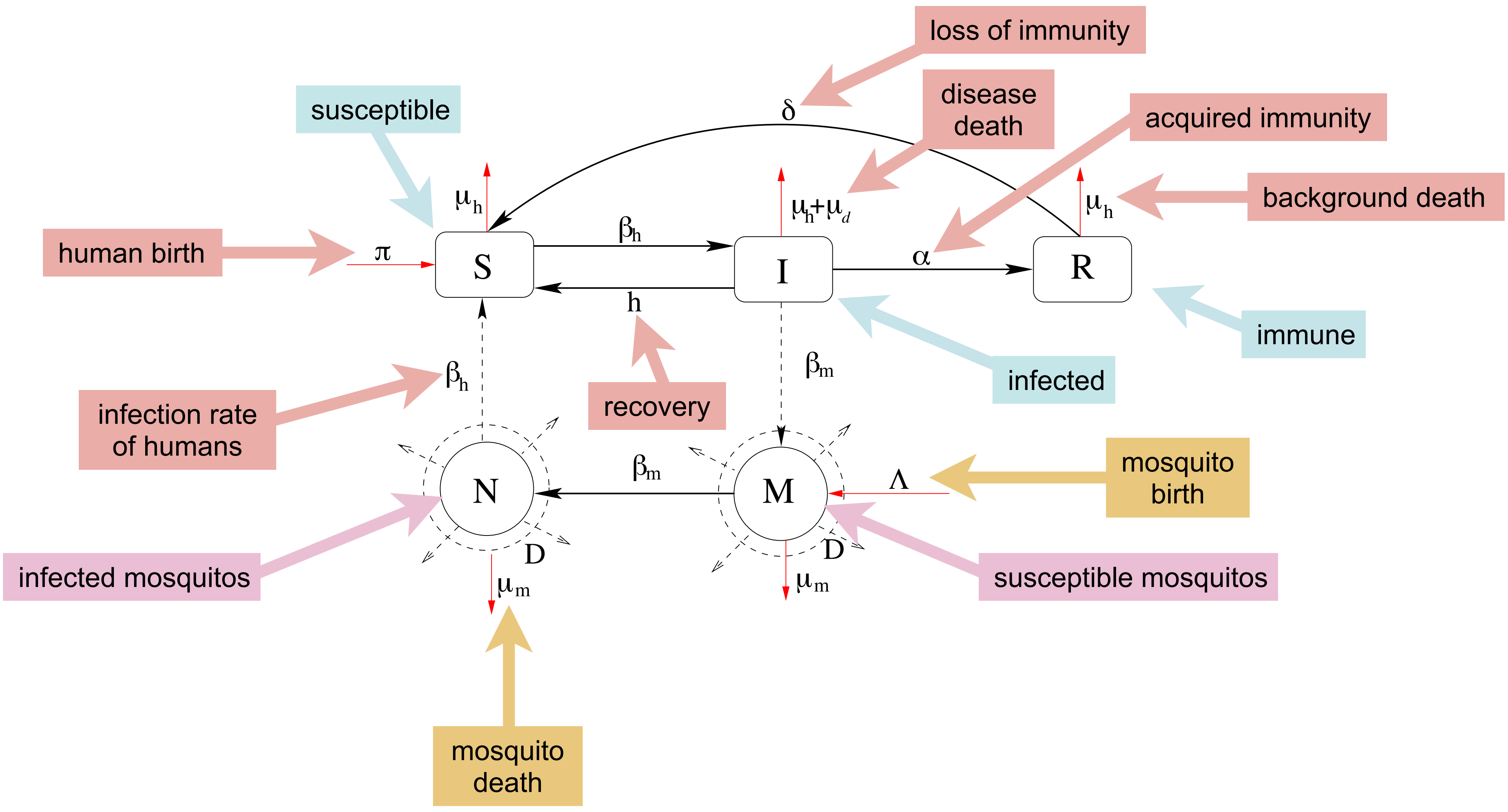
The model



loss of immunity
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μh
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βm
N
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Λ
mosquito birth
D
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infected mosquitos
μm
μm
susceptible mosquitos
mosquito death

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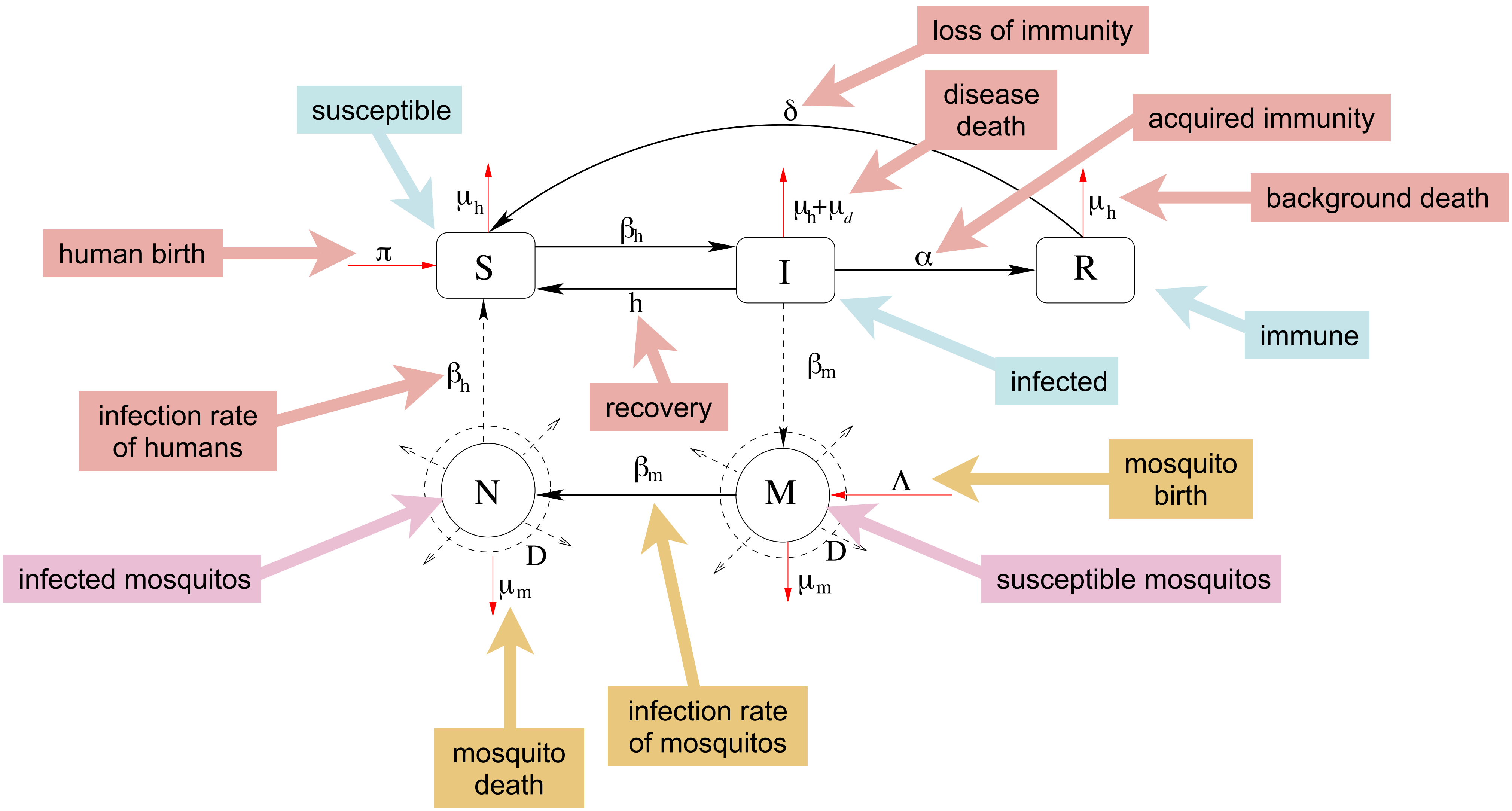
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mosquito birth
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μm
μm
infection rate of mosquitos
mosquito death

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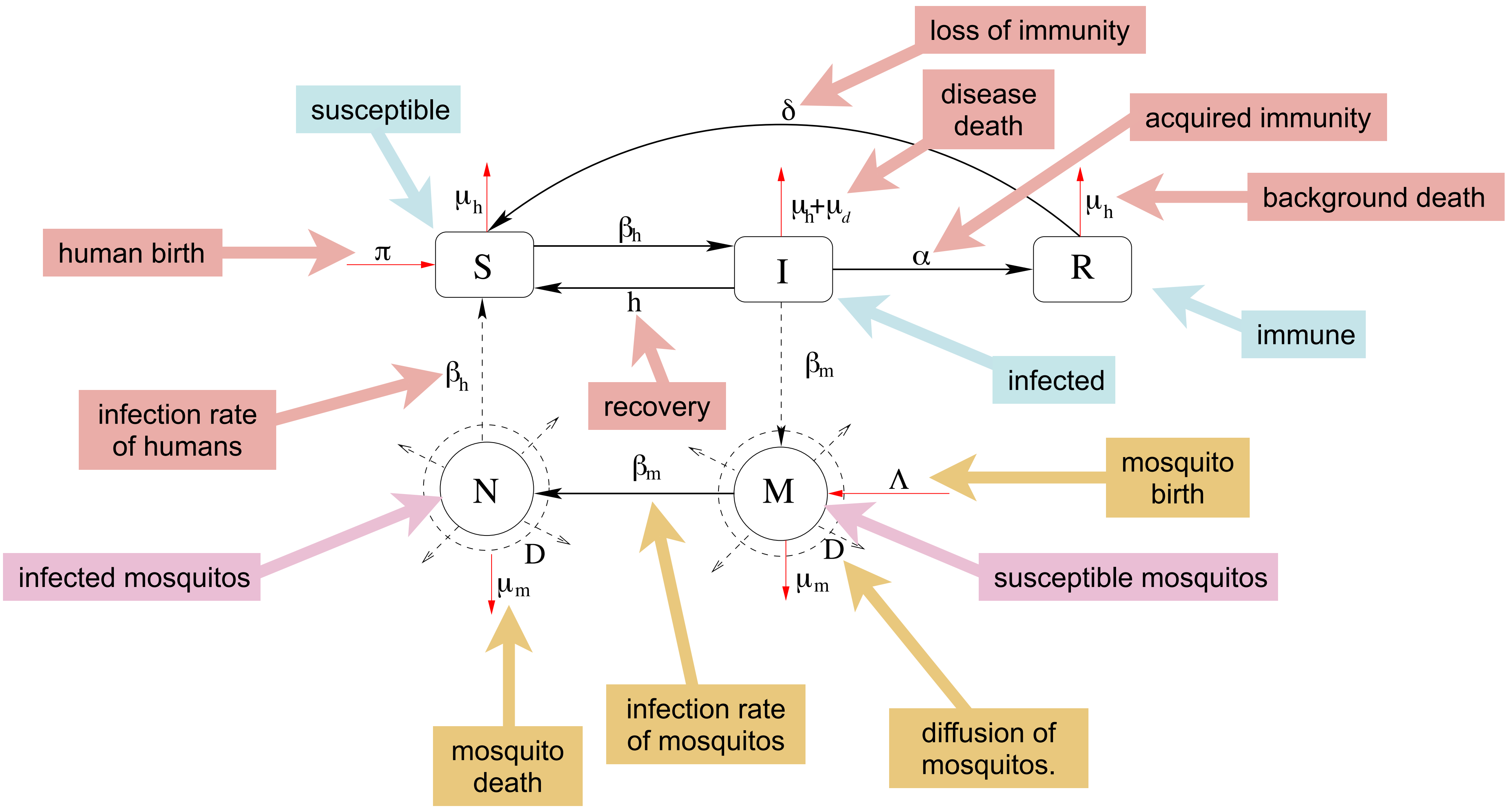

loss of immunity
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disease death
acquired immunity
susceptible
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μh
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π
S
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h
immune
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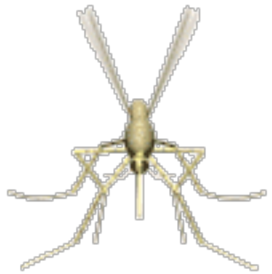
βm
infected
infection rate of humans
recovery
βm
mosquito birth
Λ
N
M
infected mosquitos
D
D
susceptible mosquitos
μm
μm
infection rate of mosquitos
diffusion of mosquitos.
mosquito death

The differential equations

- At non-spraying times, the PDEs are



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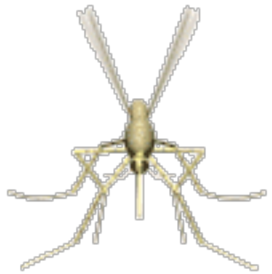

$$S_t = \pi - \beta_h SN + hI + \delta R - \mu_h S$$
$$I_t = \beta_h SN - hI - \alpha I - (\mu_h + \gamma) I$$
$$R_t = \alpha I - \delta R - \mu_h R$$
$$M_t = \Lambda - \mu_m M - \beta_m MI + D\Delta M \qquad t \neq t_k$$
$$N_t = -\mu_m N + \beta_m MI + D\Delta N \qquad t \neq t_k$$

S=Susceptible humans
I=Infected humans
R=Recovered humans
M=Susceptible mosq.
N=Infected mosq.
π,Λ=*birth rates D=diffusion*
μ_m,μ_H=*death rates*
β_H,β_M=*transmissibility*
μ_d=*malaria death rate*
h=recovery rate α=*immunity rate* δ=*loss of immunity*

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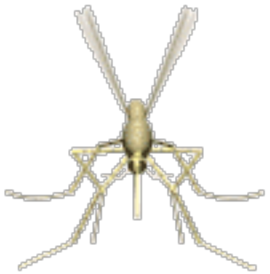

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- Boundary conditions:

S=Susceptible humans
I=Infected humans
R=Recovered humans
M=Susceptible mosq.
N=Infected mosq.
π,Λ=birth rates D=diffusion
μ_m,μ_H=death rates
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The differential equations

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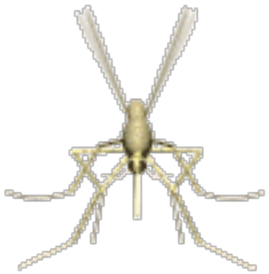

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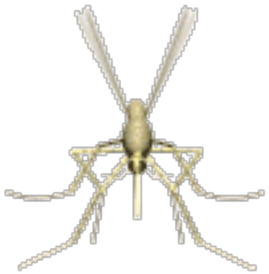

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$$c_{n,k}=\frac{-2}{\rho_0 z'_n J_2^2(z'_n)}\exp((\mu_m+\left|\frac{z'_n}{\rho_0}\right|^2 D)t_k)\int_0^{\rho_0}\rho\Psi_\rho(t_k^+,\rho)J_1(\frac{z'_n}{\rho_0}\rho)d\rho$$

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where J_0, J_1 and J_2 are Bessel functions, satisfying

$$J_0(x)=1-\frac{x^2}{2^2}+\frac{x^4}{2^2 4^2}-...$$

$$J_1(x)=-J_0'(x)$$

$$J_2(x)=J_0-2J_1'(x).$$

Endpoints t_m satisfy a recursion relation

$$\Psi(t_{k+1}^-,\rho) = \frac{\Lambda}{\mu_m}[1 - \exp(-\mu_m(t_{k+1} - t_k))]$$
$$+ [(1-r)\Psi(t_k^-,0) - \sum_{n=1}^{\infty} b_{n,k}] \exp(-\mu_m(t_{k+1} - t_k))$$
$$+ \sum_{n=1}^{\infty} b_{n,k} \exp((-\mu_m - \left|\frac{z_n'}{\rho_0}\right|^2 D)(t_{k+1} - t_k)),$$

$$b_{n,k} = \frac{-2}{\rho_0 z_n' J_2^2(z_n')} \int_0^{\rho_0} \rho \Psi_\rho(t_k^+,\rho) J_1(\frac{z_n'}{\rho_0}\rho) d\rho$$
$$= \frac{-2}{\rho_0 z_n' J_2^2(z_n')}(1-r) \int_0^{\rho_0} \rho \Psi_\rho(t_k^-,\rho) J_1(\frac{z_n'}{\rho_0}\rho) d\rho.$$

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- (1-r)^{m-1}\exp(-\mu_m m\tau)\Bigg] + (1-r)^m\Psi_0(0)\exp(-\mu_m m\tau) \\
- (1-r)^{m-1}\exp(-\mu_m m\tau)\sum_{n=0}^{\infty} b_{n,0} \\
+ (1-r)^{m-1}\exp(-\mu_m m\tau)\sum_{n=1}^{\infty} b_{n,0}\exp(-\left|\frac{z_n'}{\rho_0}\right|^2 Dm\tau)J_0(\frac{z_n'}{\rho_0}\rho).
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$$\tilde{\tau} = -\frac{1}{\mu_m}\ln\left[\frac{\Lambda-\mu_m\tilde{\Psi}}{\Lambda+\mu_m\tilde{\Psi}(r-1))}\right].$$

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- Hence we can bound the maximum number of mosquitos per cycle by a desired threshold.

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- Note that, to find such a time, we need to know the previous two spraying times.

Fixed spraying in an interior disc

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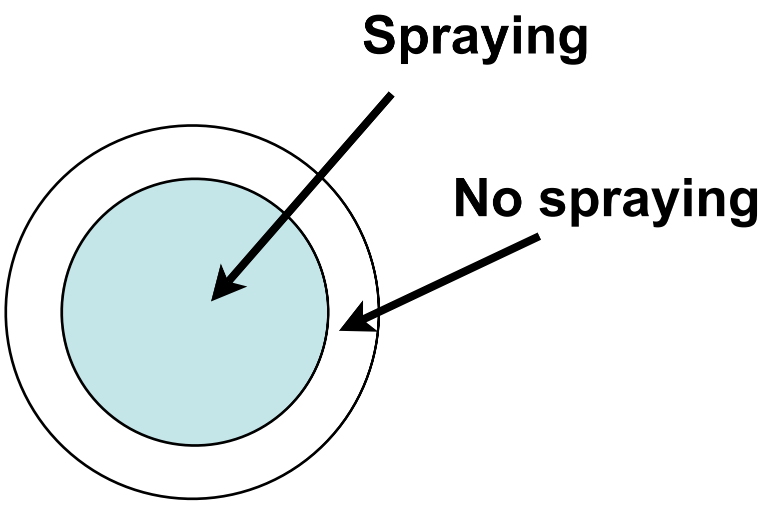

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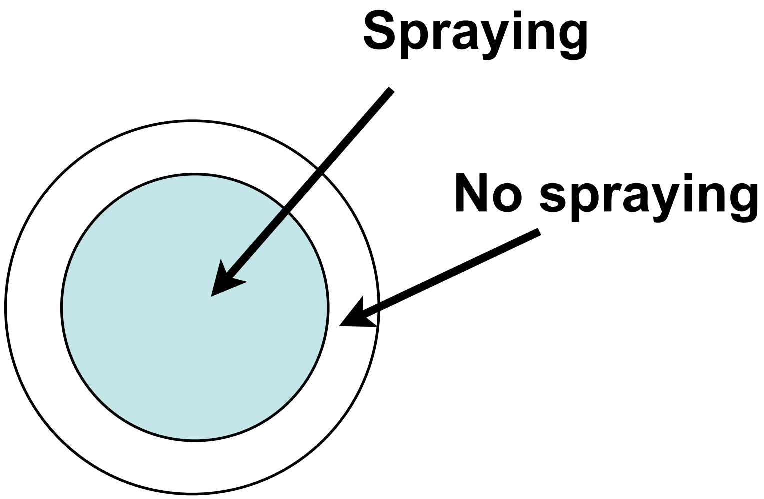

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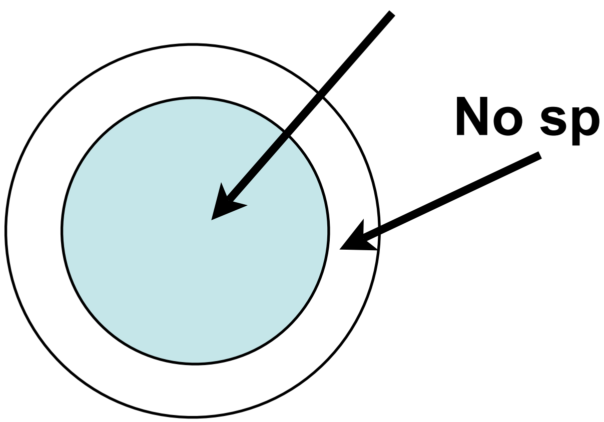

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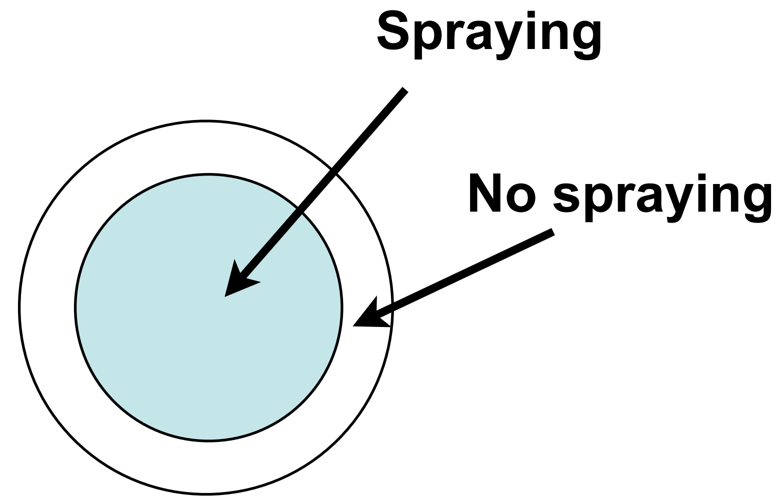

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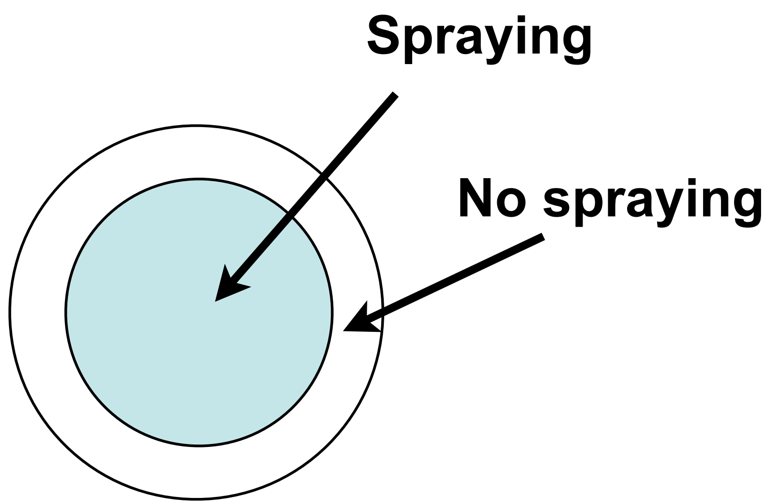

$$\Psi(t_{k+1}^-,\rho) \to \frac{\Lambda}{\mu_m}\left[1-\frac{r\exp(-\mu_m\tau)}{1-(1-r)\exp(-\mu_m\tau)}\right]\chi_{[0,\rho_{00}]}(\rho) + \frac{\Lambda}{\mu_m}\chi_{[\rho_{00},\rho_0]}(\rho).$$

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- These differ from the previous threshold in the term $\breve{\Psi}$.

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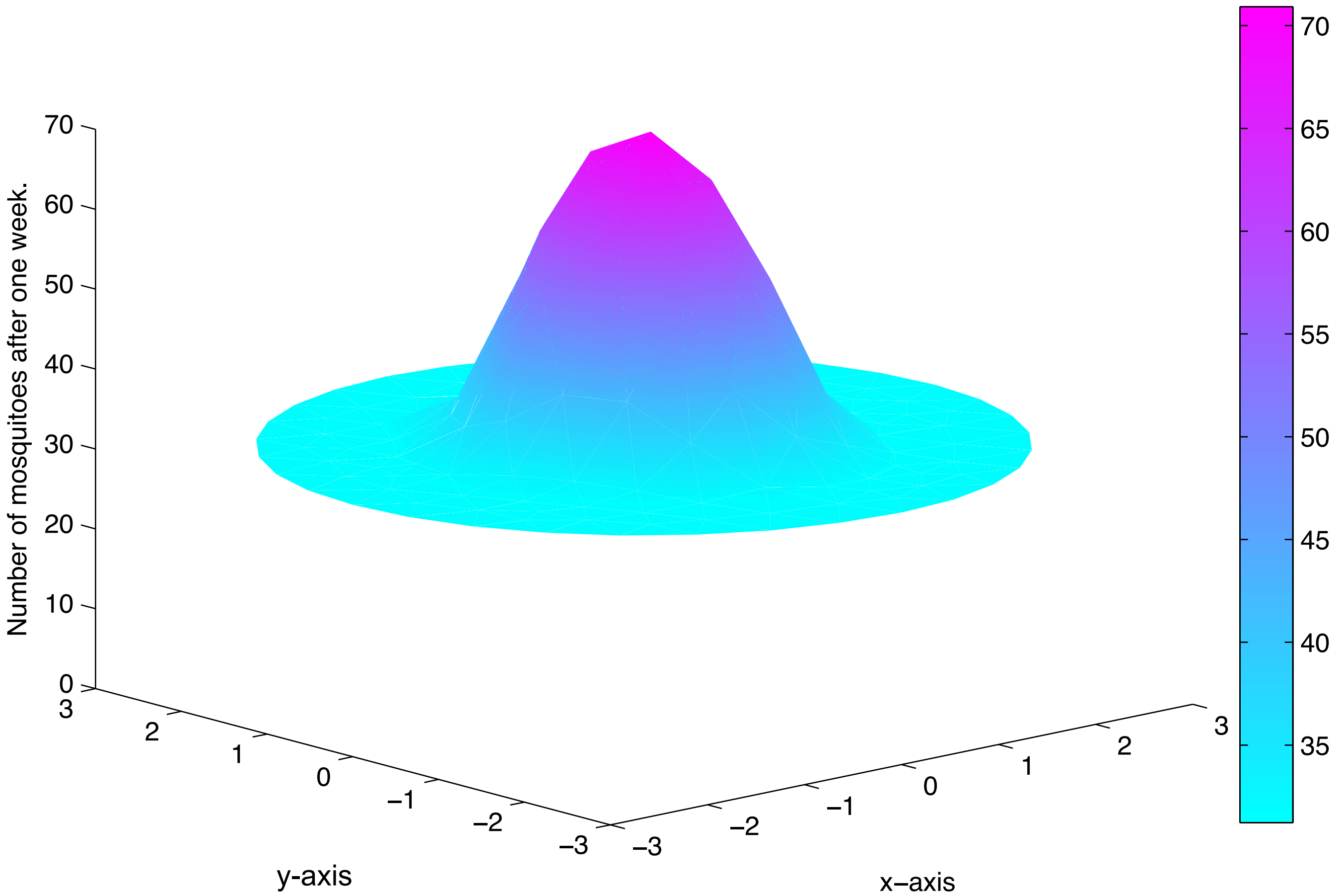
- Thus, spatial considerations force us to spray more frequently if regular spraying occurs only inside an interior disc.

Spraying in a disc (one week)



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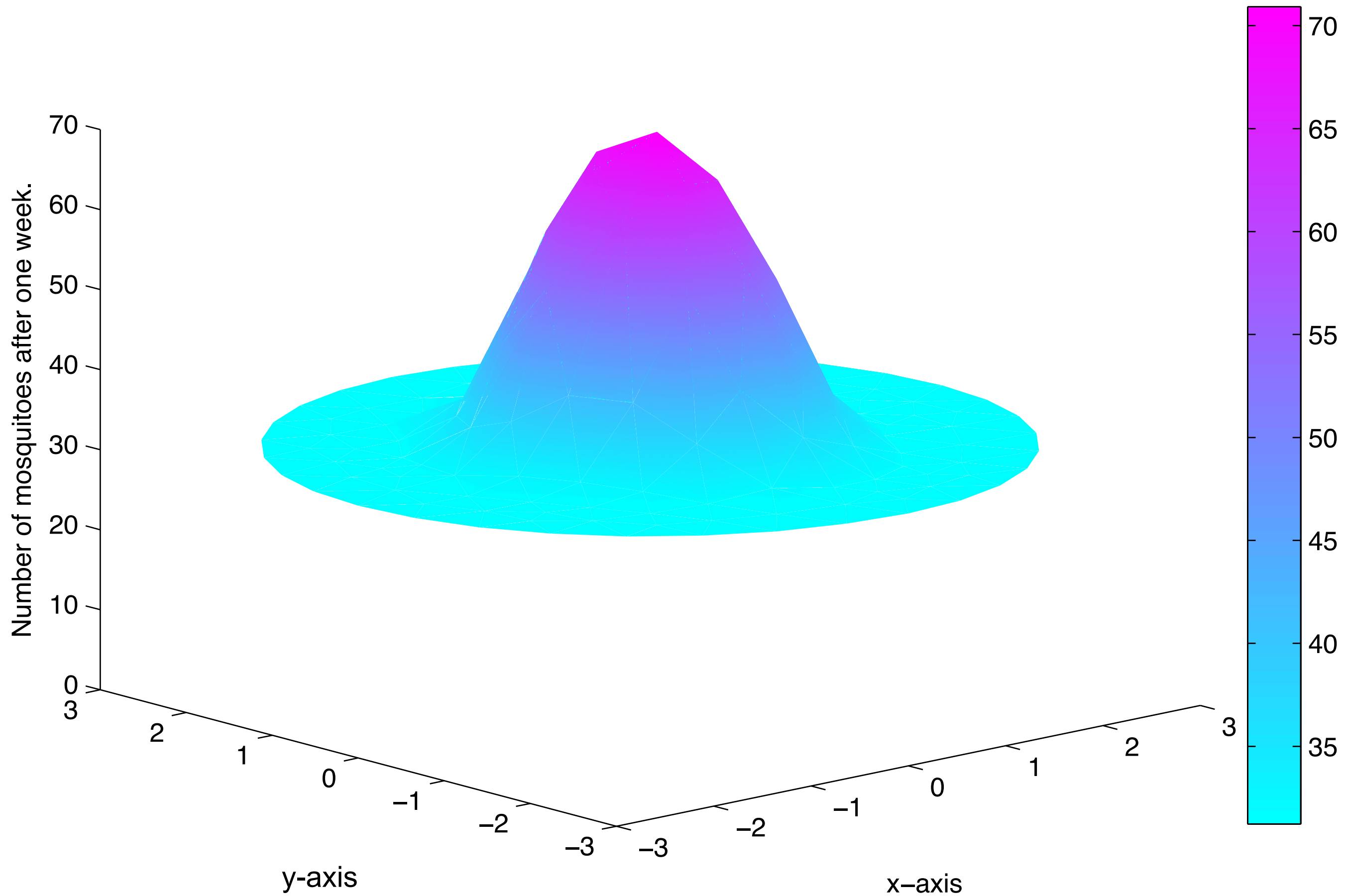

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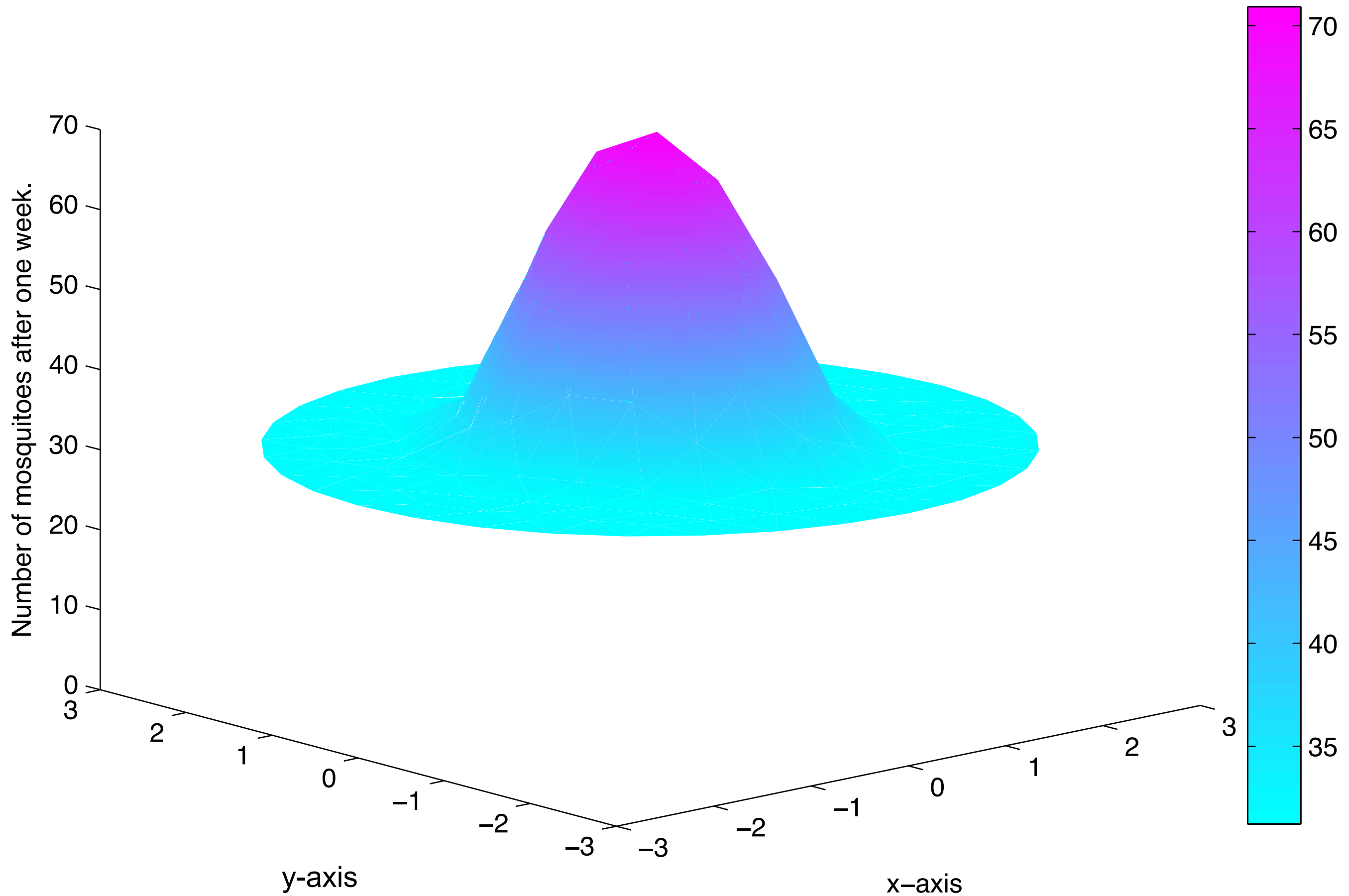
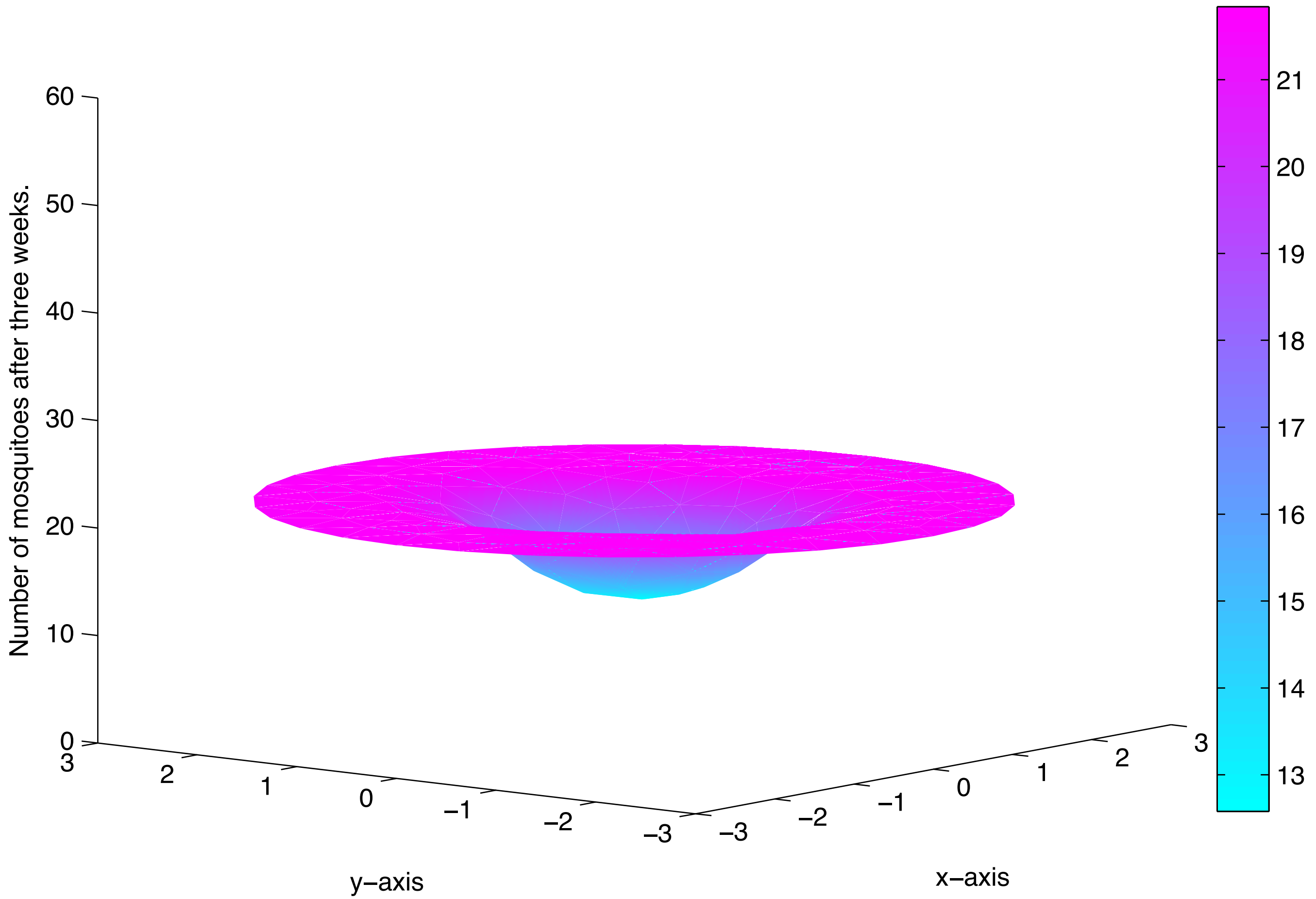
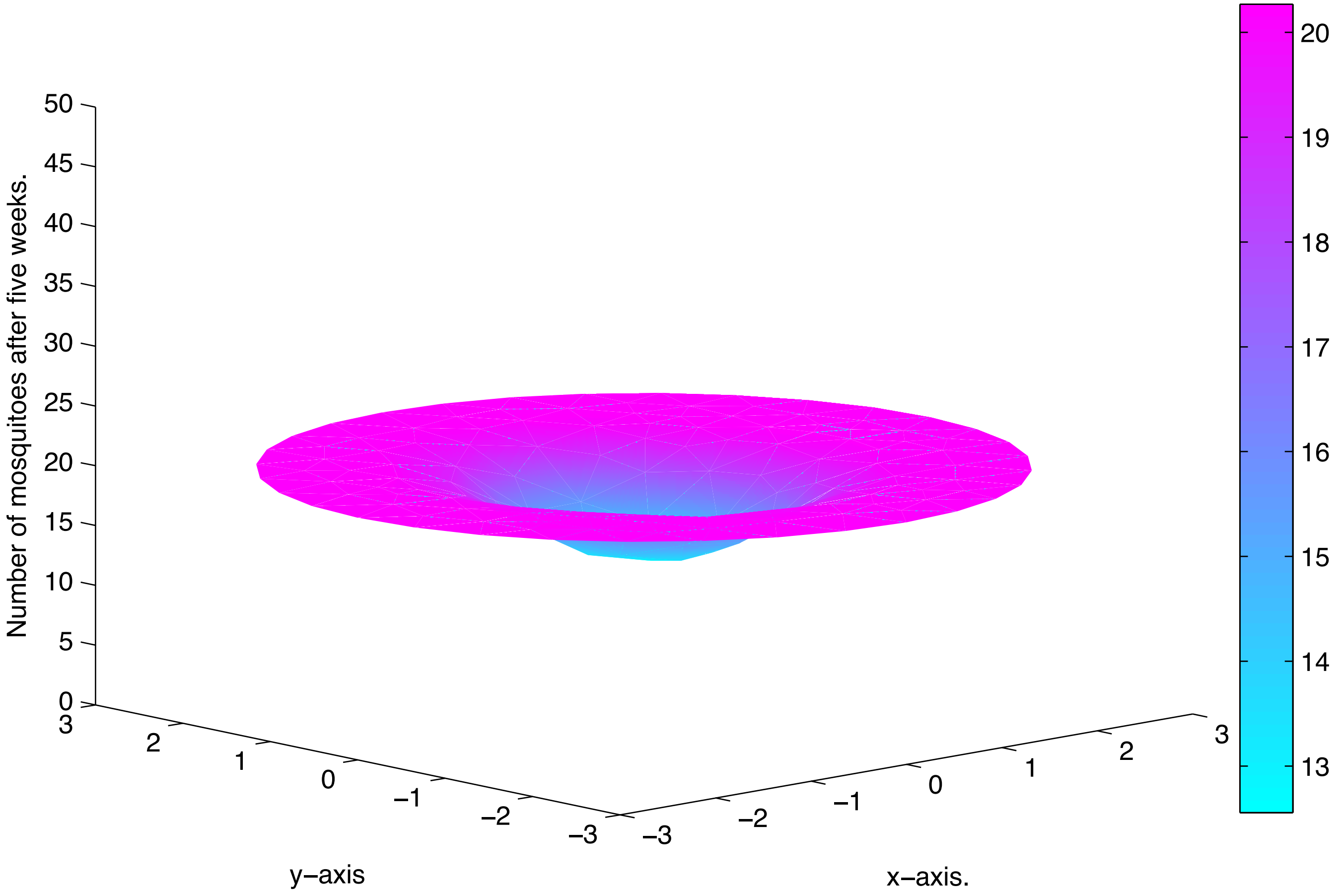


- Initially there are more mosquitos in the centre
- Diffusion is now included.

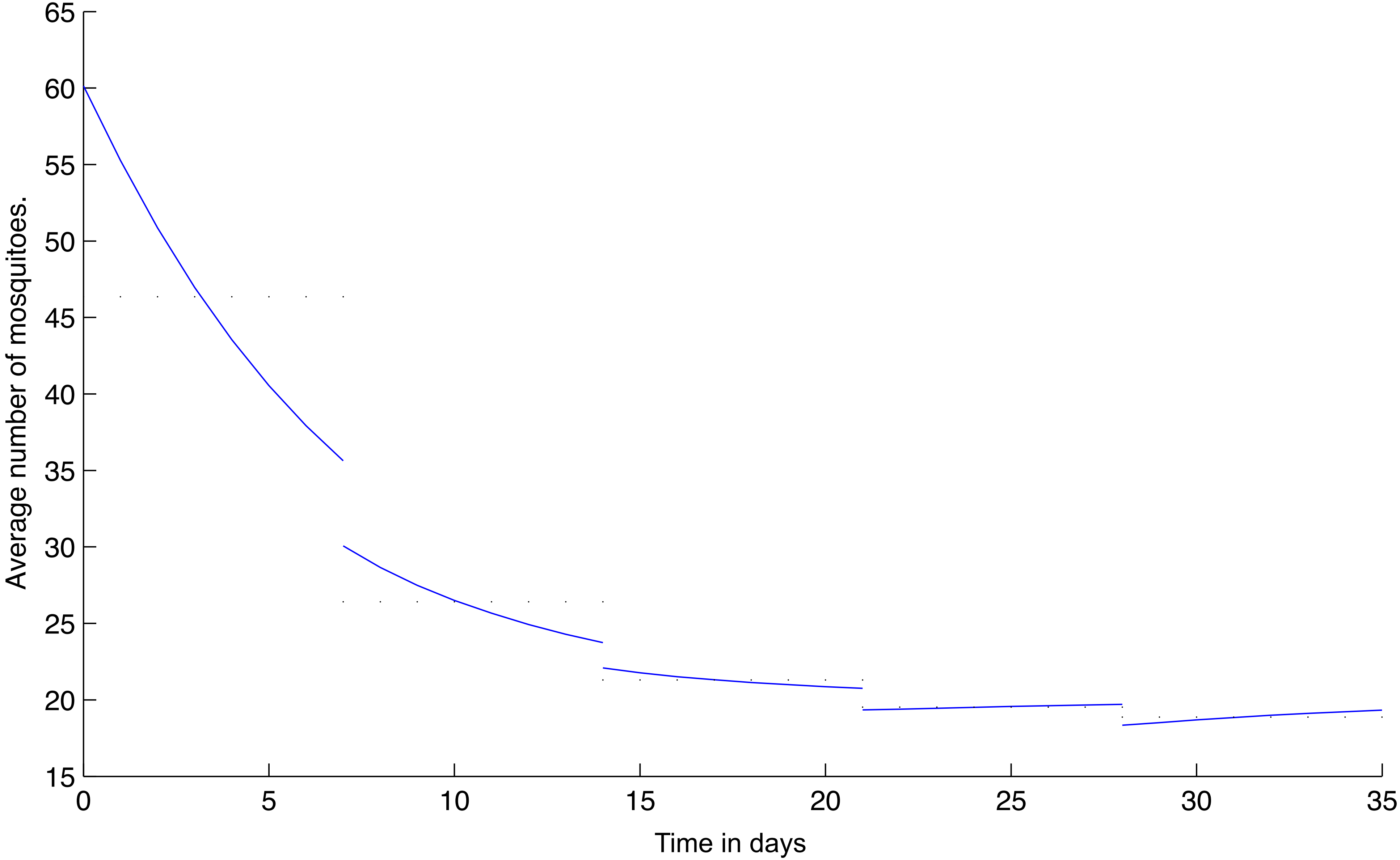
Spraying in a disc (three weeks)



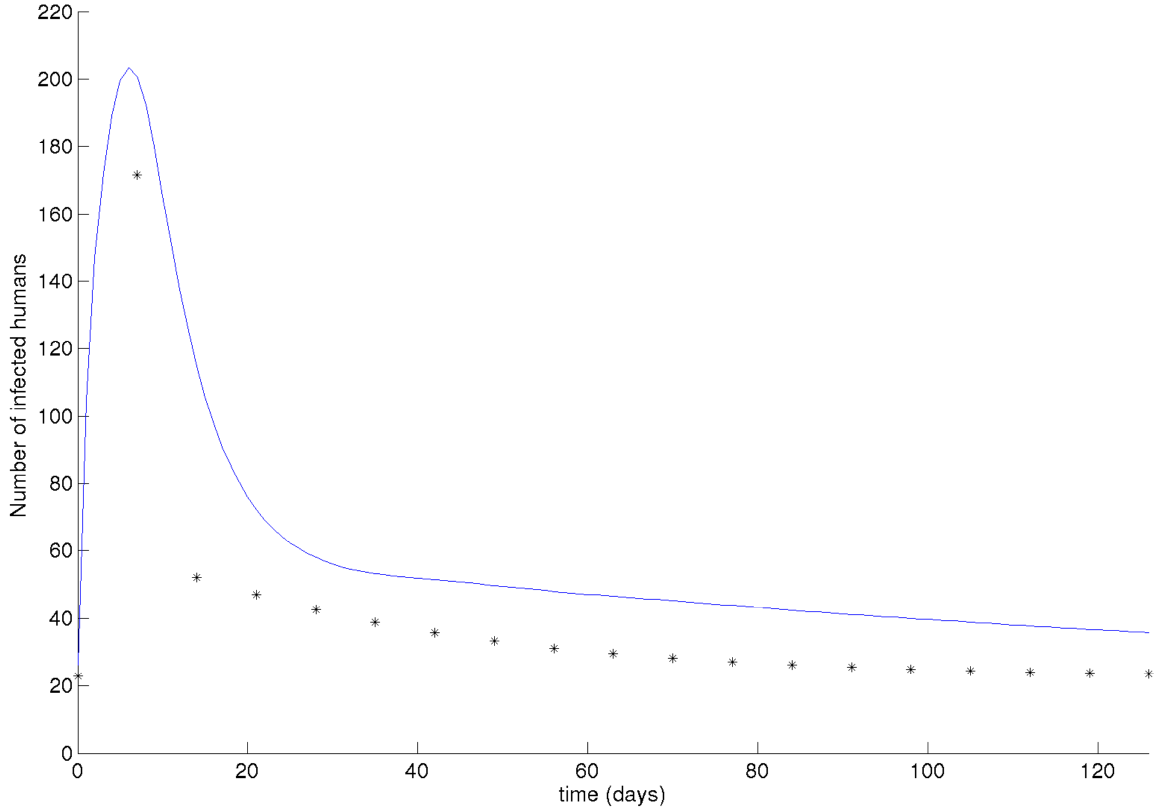
Spraying in a disc (five weeks)



Spraying in a disc (average)



Number of infected humans



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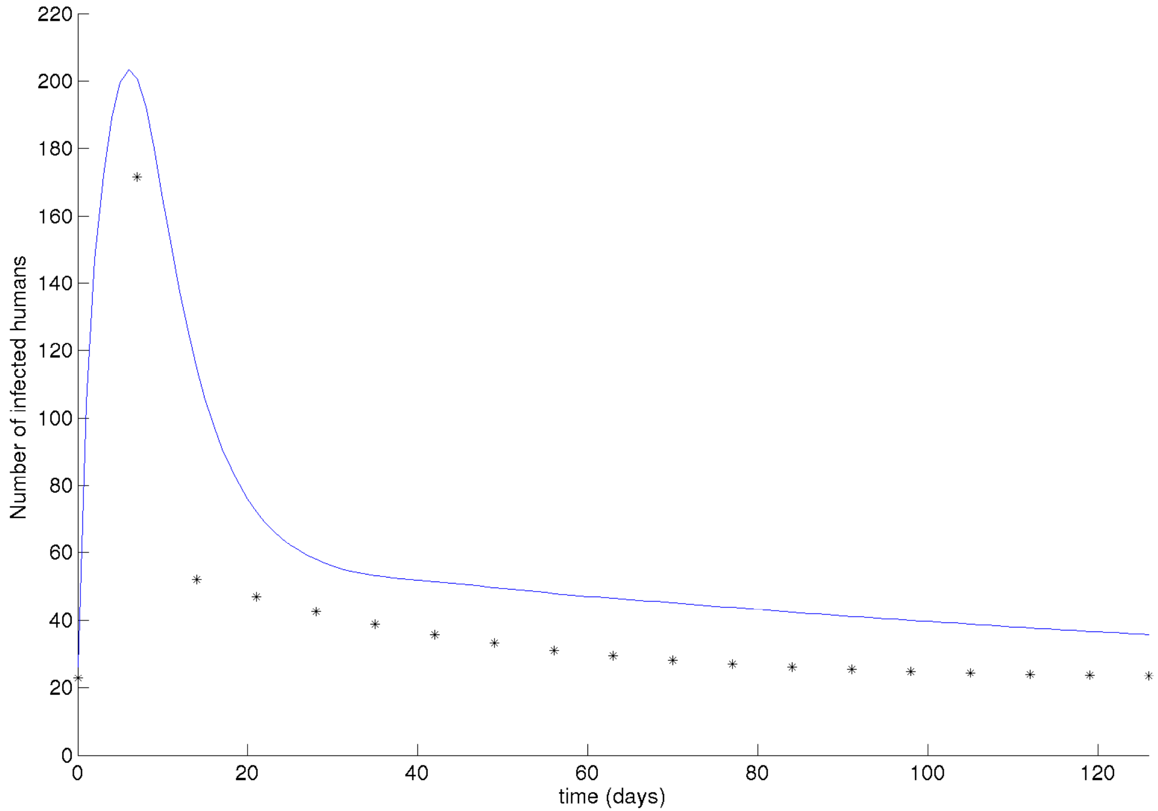

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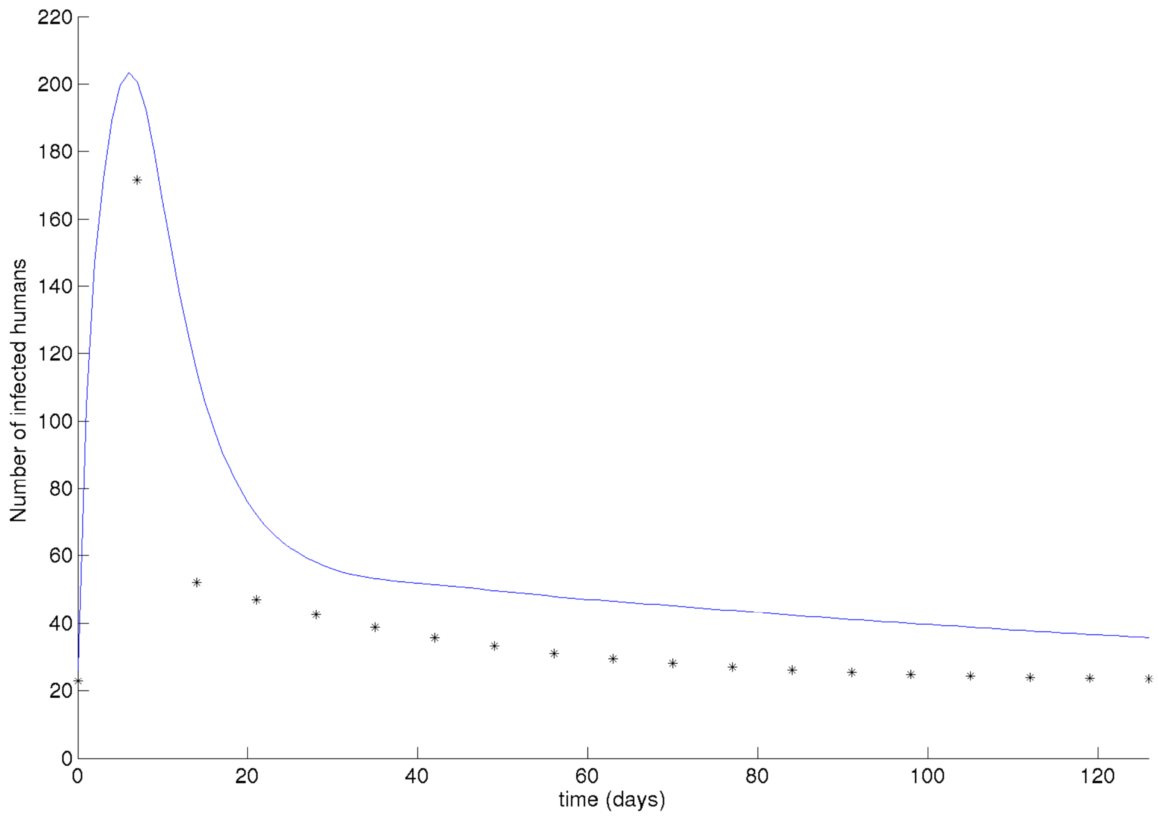

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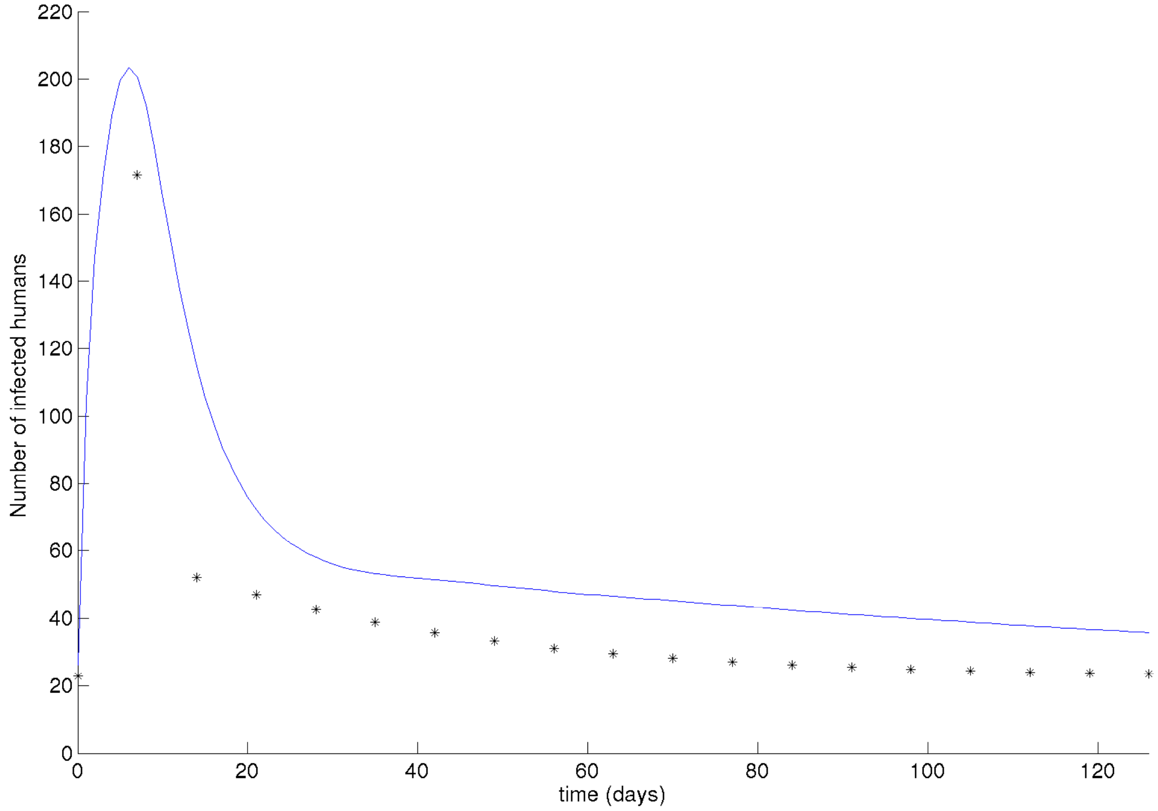

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- (the stars represent the number of infected humans immediately before spraying is applied).

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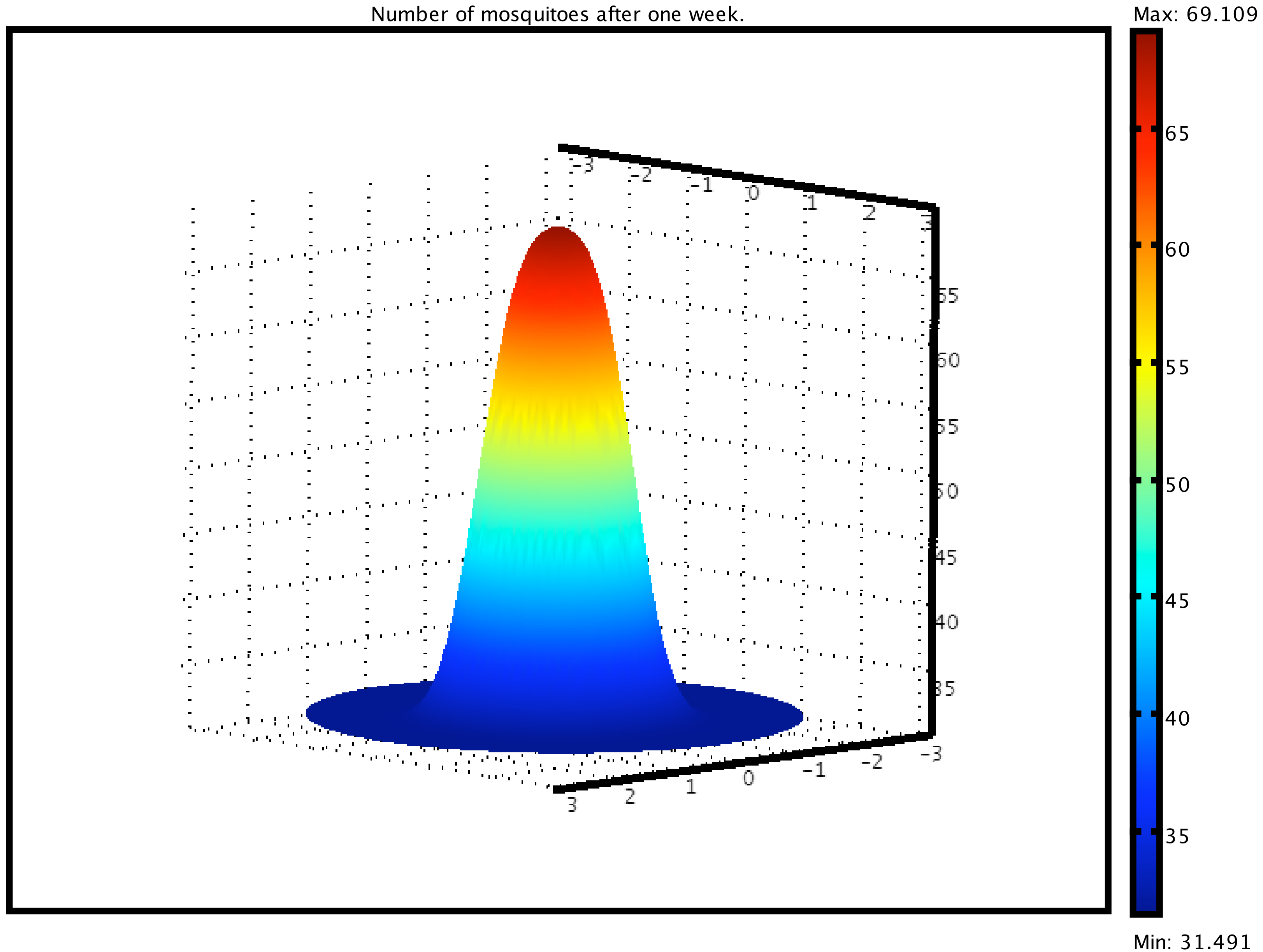
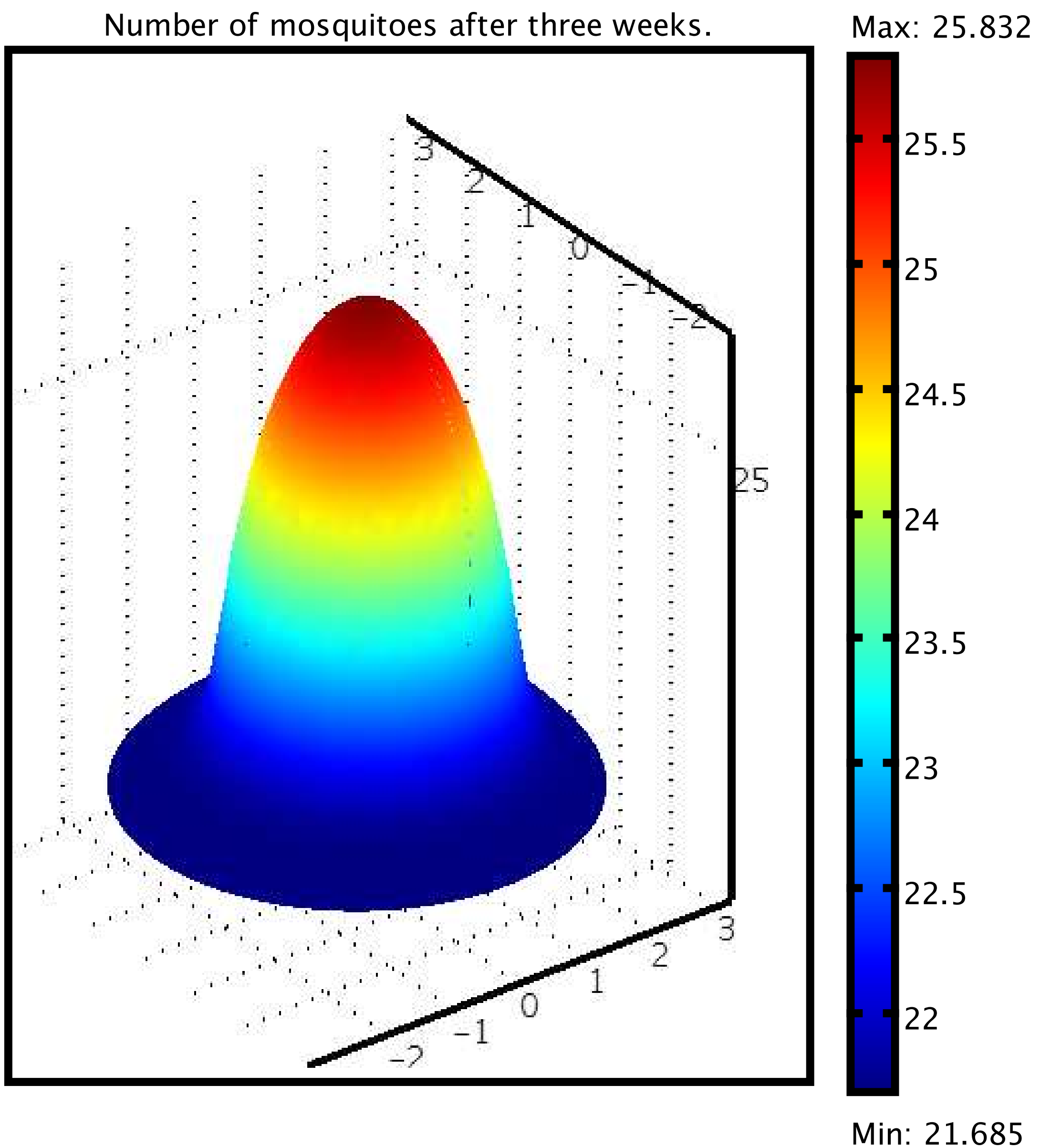
where $a_{n,m}$ and $b_{n,m}$ are determined using trigonometric identities.

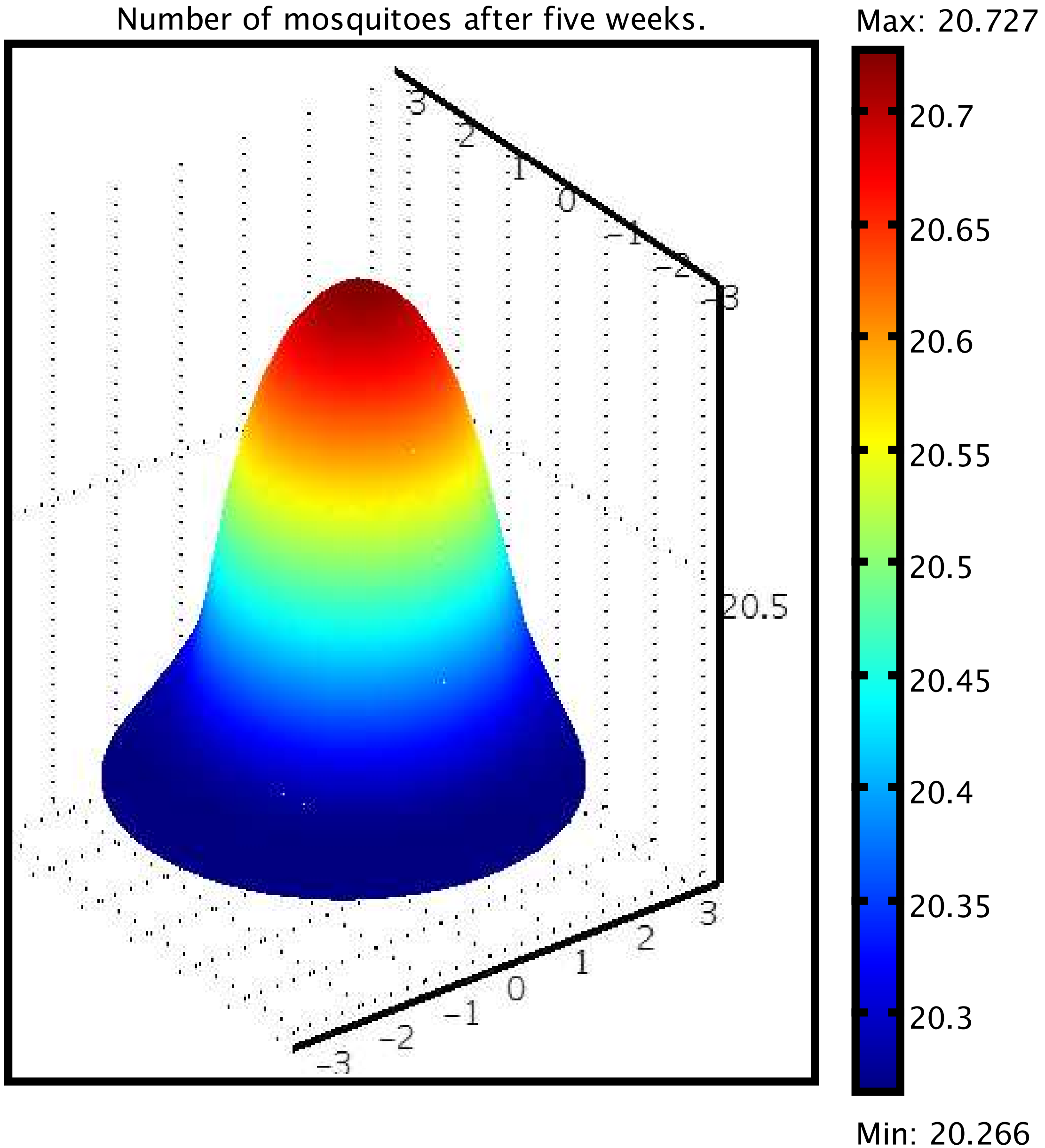
Wind impact, no spraying (1 week)



Wind impact, no spraying (3 weeks)



Wind impact, no spraying (5 weeks)



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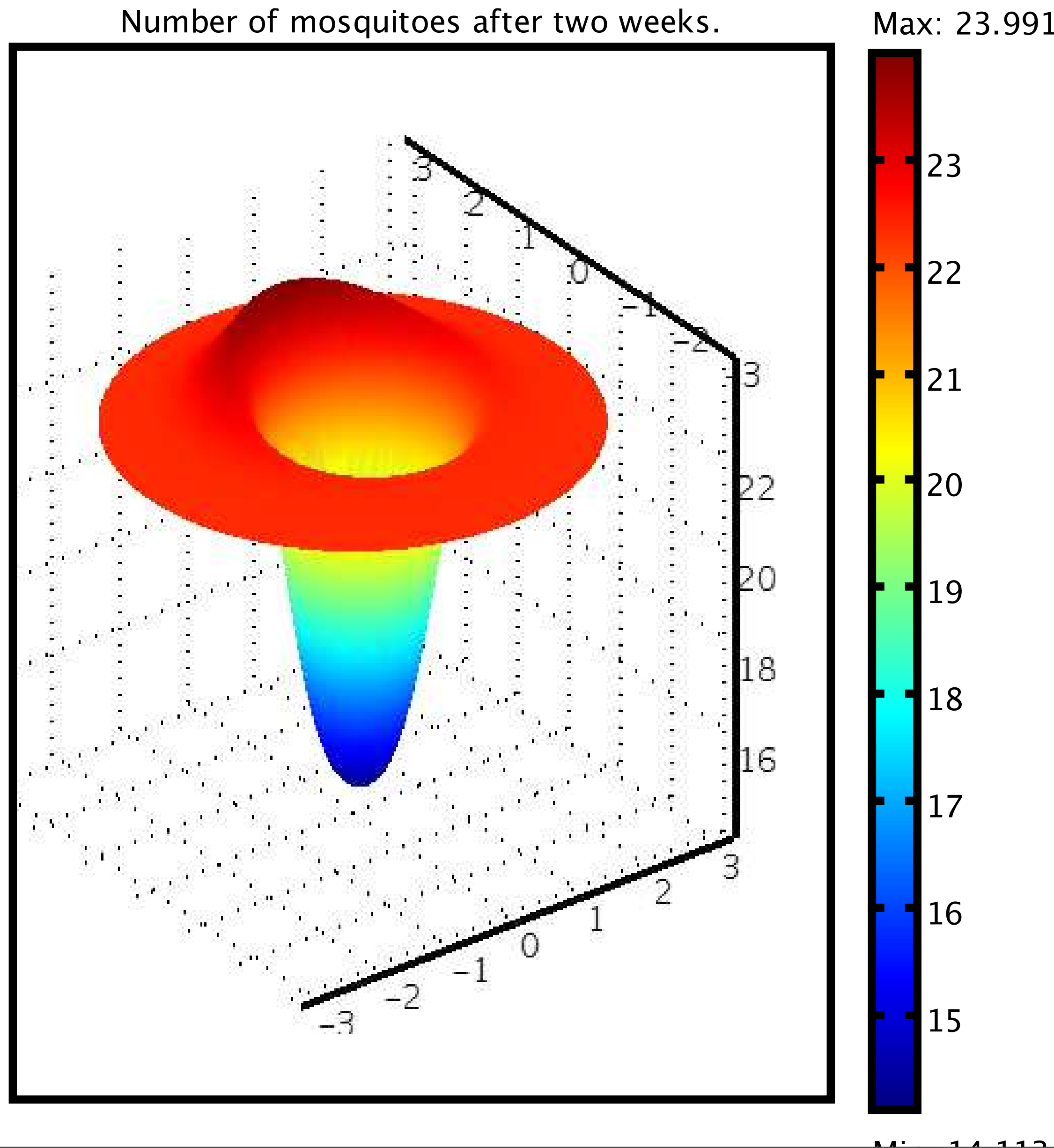
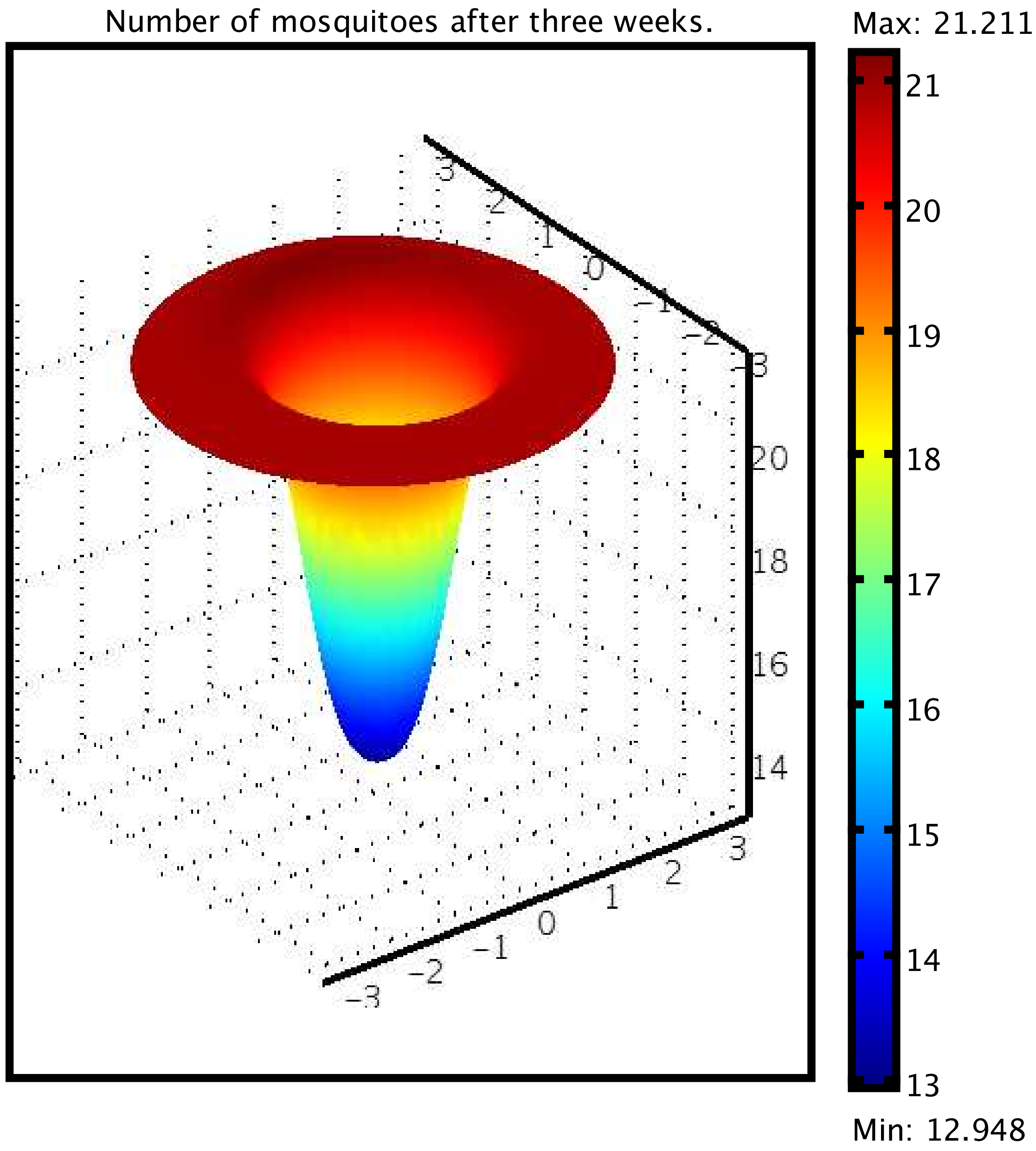
- However, if it is, then the previous results apply.

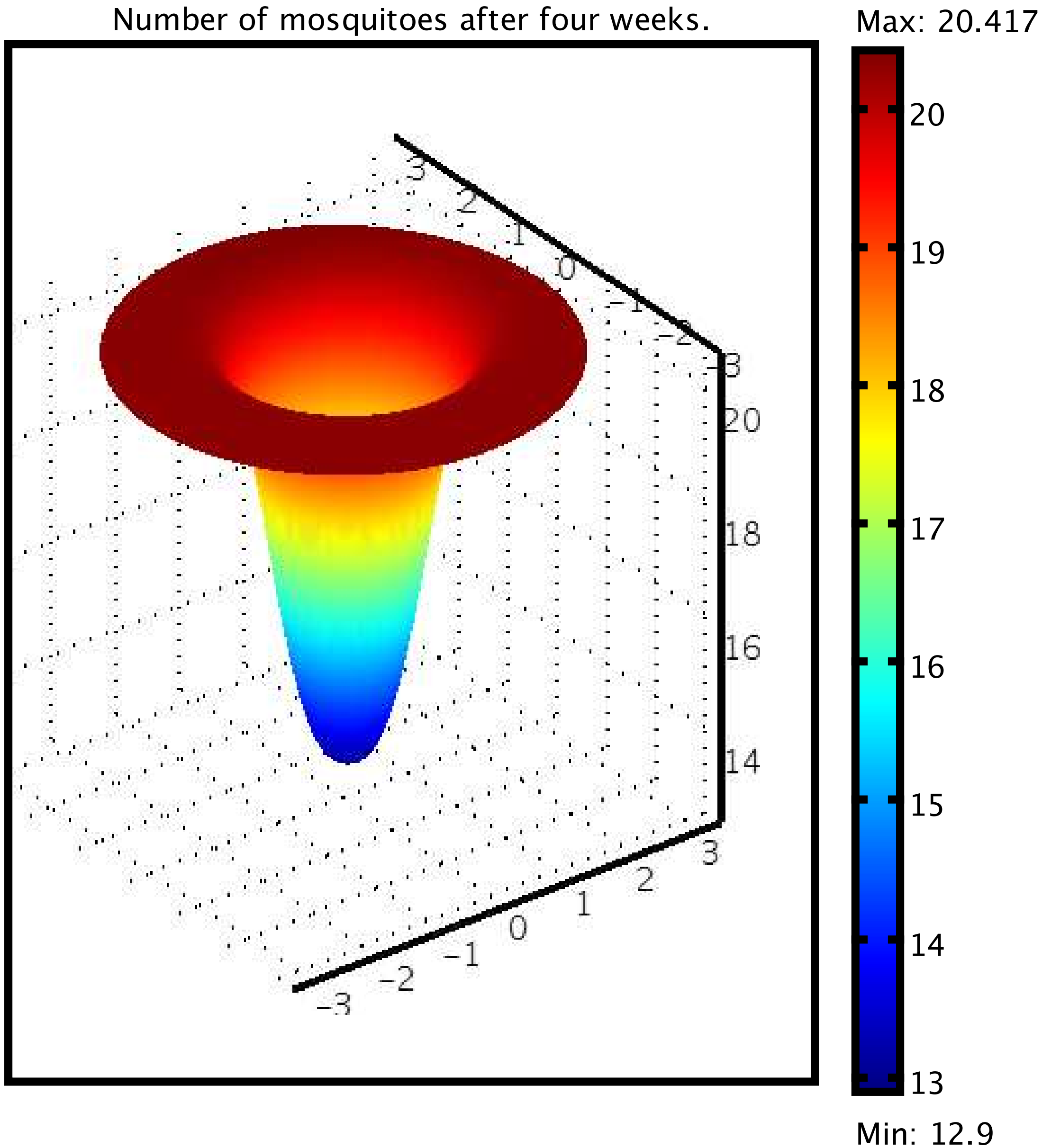
Spraying in a disc, with wind (2 weeks)



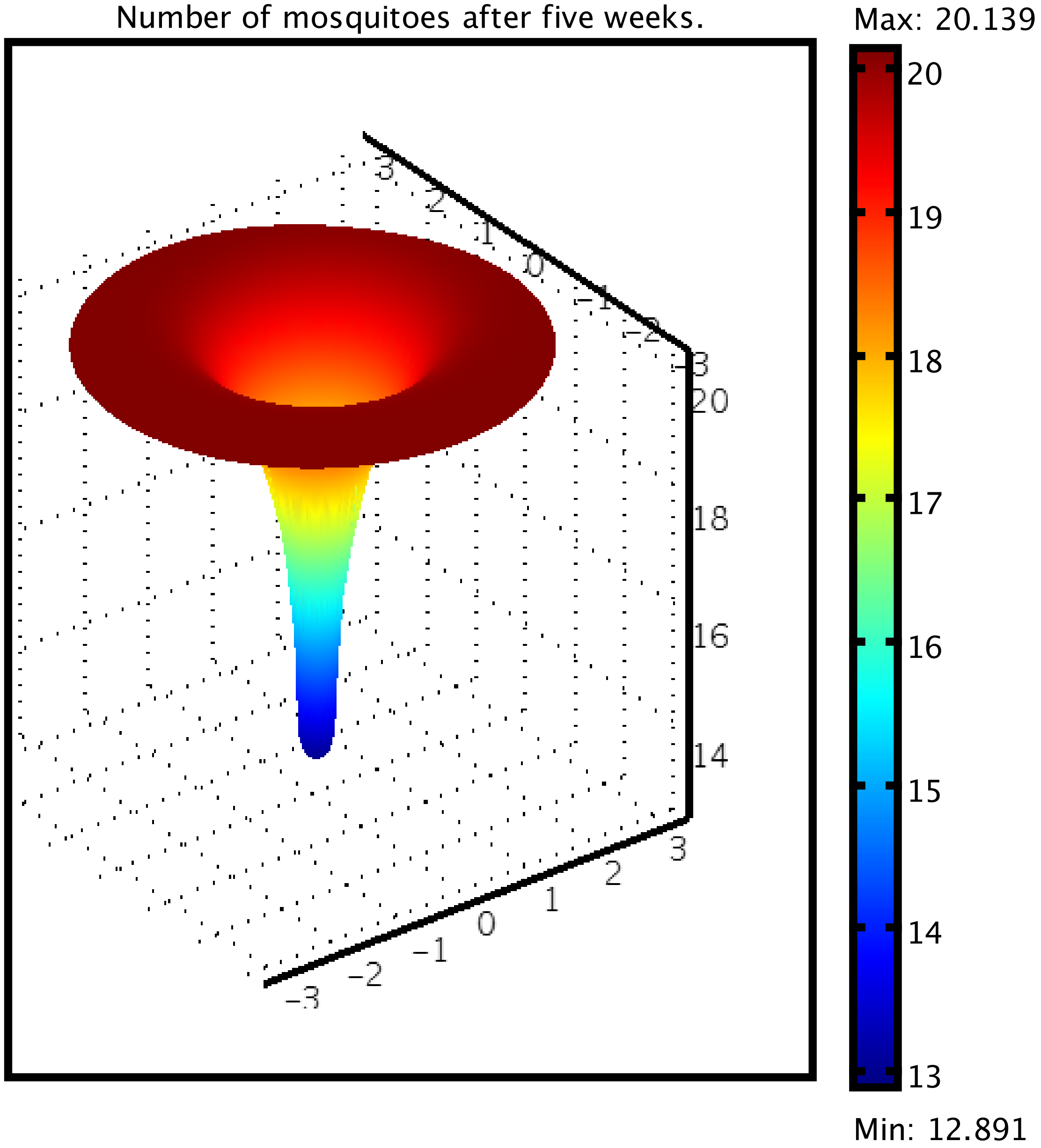
Spraying in a disc, with wind (3 weeks)



Spraying in a disc, with wind (4 weeks)



Spraying in a disc, with wind (5 weeks)



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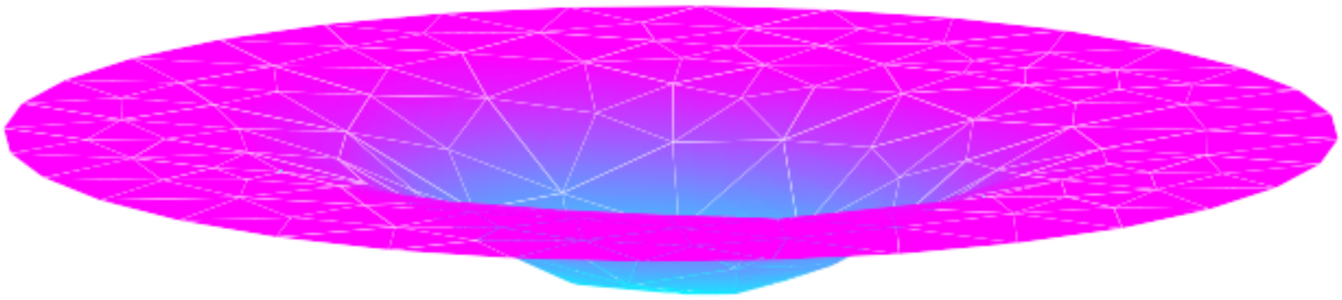
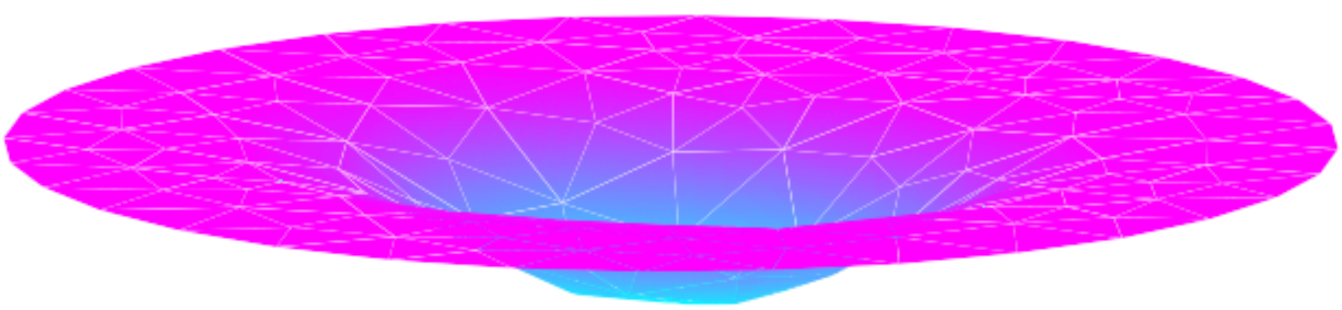


Crucial question #1

What are the effects of spraying in different geographic areas?

- If we have symmetry, then spraying inside a disc can control mosquitos inside that disc
- However, the spraying interval is shorter than spraying for the entire region.



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- We derived formulas for the optimal period when spraying is fixed and occurs either in a disc or in the entire region
- We also derived formulas for the "next best" spraying in the case that spraying is not fixed.

$$t_{m+1} = t_m - \frac{1}{\mu_m} \ln \left[\frac{2 - r - \frac{\tilde{\Psi}\mu_m}{\Lambda}}{1 + r(1-r)\exp(-\mu_m(t_m - t_{m-1}))} \right]$$

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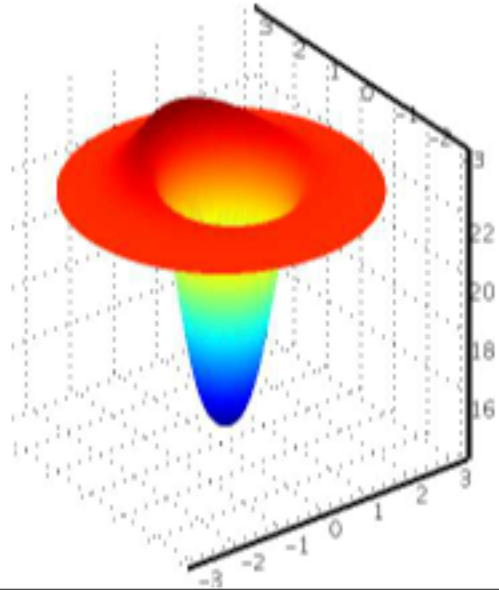
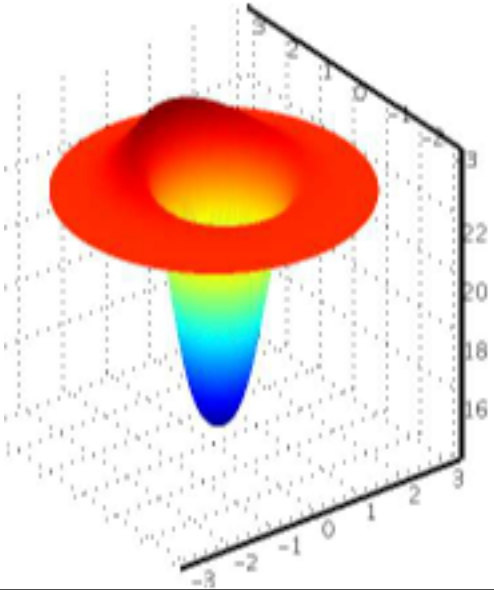


Crucial question #3

Can we alter our control strategies to account for asymmetric phenomena such as wind?

- When advection is included, we could derive solutions for the nonsymmetric case
- If spraying is not affected by wind, then we can spray within a translated disc to control mosquitos in our desired region.



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Results

- We used classical methods to solve nonimpulsive PDEs
- We then applied impulsive conditions and examined the case of constant initial conditions
- Spraying in a heterogeneous landscape has to be applied more frequently, whether fixed or not
- We could also solve the case of advection
- The effects of wind result in a translation in the desired region of spray.

Generalisation

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$$
\begin{aligned}
\frac{\partial \Psi}{\partial t} &= \Lambda - \mu_m \Psi + D\Delta\Psi && \text{in } B(0,\rho_0) && t \neq t_k \\
\frac{\partial \Psi}{\partial \rho}(t,\rho_0) &= 0 && \text{on } \partial B(0,\rho_0) && \\
\Psi^+ &= (1-r)\Psi^- && && t = t_k.
\end{aligned}
$$

Ψ=*total mosq. population*
Λ=*mosq. birth rate*
μ=*mosq. death rate*
r=spraying effectiveness
t_k=*spraying times*

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- We assumed spraying occurs instantly
  - however, impulsive differential equations are a reasonable approximation, even for quite large delays, unless spraying is occurring very frequently
- We also ignored the effect of wind upon the spray itself
  - this may change the outcome if the wind affects mosquitos and spray at different rates.

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- Spatially heterogeneous environments result in an increase in the spraying frequency, but malaria control is still achievable
- However, note that our results do not predict eradication.

References

- M. Al-arydah and R.J. Smith? (2011). Controlling malaria with indoor residual spraying in spatially heterogeneous environments (Mathematical Biosciences and Engineering 8(4), 889-914)
- R.J. Smith? and S.D. Hove-Musekwa (2008). Determining effective spraying periods to control malaria via indoor residual spraying in sub-Saharan Africa (Journal of Applied Mathematics and Decision Sciences Volume 2008, Article ID 745463, 19 pages).