За ролята на преносителя в епидемиологичното моделиране

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Outline

Aedes

- In tropical areas, *Aedes* mosquitos cause more than 100 million symptomatic cases/year of viral diseases, such as dengue, yellow fever, chikungunya and Zika, and thousands of deaths.

- With increasing trade and travel, several *Aedes* species have been introduced into Europe and are now spreading rapidly becoming a widespread significant public health risk which needs to be effectively addressed, as testified by recent cases of autochthonous chikungunya and dengue transmission in Croatia, France, Italy, Portugal and Spain.

Dengue fever
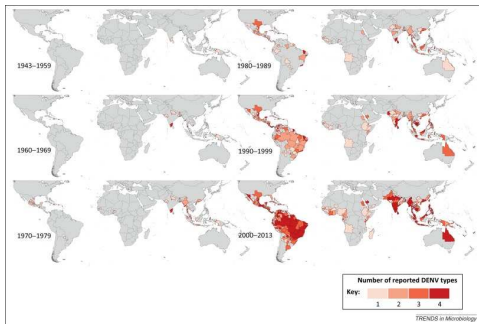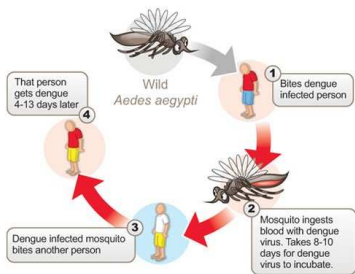
Dengue fever modelling

- **vector-host** two-strain Dengue model (10 dim)
  Feng and Velasco-Hernández, Competitive exclusion in a vector-host model for the dengue fever, *J Math Biol* (1997)

- **large** multi-strain Dengue model (10 dim)
  Aguiar, Ballesteros, Kooi and Stollenwerk, The role of seasonality and import in a minimalistic multi-strain dengue model capturing differences between primary and secondary infections: complex dynamics and its implications for data analysis, *J Theor Biol* (2011)

- **small** single-strain Dengue model (2-3 dim)
  Rocha, Aguiar, Souza and Stollenwerk, Time-scale separation and centre manifold analysis describing vector-borne disease dynamics, *Int J Computer Math* (2013)

Dengue fever modelling

Rashkov, Venturino, Aguiar, Stollenwerk, and Kooi. On the role of vector modelling in a minimalistic epidemic model, *в рецензия.*
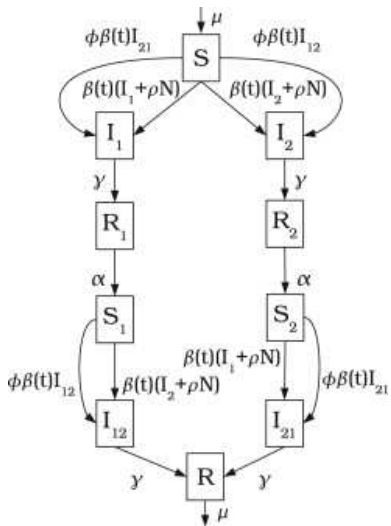
host   vector
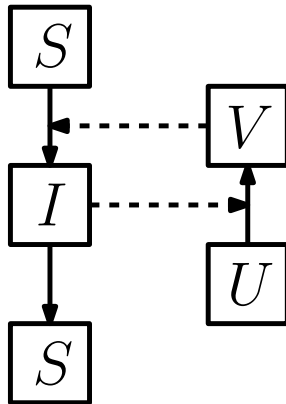
State variables

Var.	Description
Host	
N	Host population density
S	Susceptible Host population density
I	Infected Host population density
R	Recovered Host population density
Vector	
M	Vector population density
U	Susceptible Vector population density
V	Infected Vector population density

SISUV-model Host–Vector model

host   vector

Four dimensional system
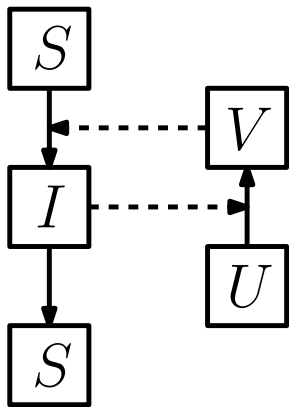
$$\frac{dS}{dt} = -\frac{\beta}{M}SV + \mu I$$

$$\frac{dI}{dt} = \frac{\beta}{M}SV - \mu I$$

$$\frac{dU}{dt} = -\frac{\vartheta}{N}UI + \nu V$$

$$\frac{dV}{dt} = \frac{\vartheta}{N}UI - \nu V$$

SISUV-model Host–Vector model

Constant host and vector population densities
$N = S(t) + I(t)$ and $M = U(t) + V(t)$
Two dimensional equivalent system

$$\frac{dI}{dt} = \frac{\beta}{M}(N - I)V - \mu I$$

$$\frac{dV}{dt} = \frac{\vartheta}{N}(M - V)I - \nu V$$

Analysis of the SISUV-model

- trivial, disease-free equilibrium $I^0 = 0$, $V^0 = 0$ and $S^0 = N$, $U^0 = M$
- interior, endemic equilibrium given by:

$$I^* = N\frac{\beta\vartheta - \mu\nu}{(\mu + \beta)\vartheta}$$

$$V^* = M\frac{\beta\vartheta - \mu\nu}{\beta(\nu + \vartheta)}$$

also $S^* = N - I^*$ and $U^* = M - V^*$

Evaluated at this equilibrium the trace and the determinant read:

$$\mathrm{Tr}\ \mathbf{J} = -(\varepsilon\mu + \nu)$$

$$\det \mathbf{J} = \varepsilon(\mu\nu - \beta\vartheta)$$

For the reference values we have $\beta = 2\mu$ and $\vartheta = 2\nu$
Then the determinant is negative:

$$\det \mathbf{J} = \varepsilon(\mu\nu - 4\mu\nu) = -3\varepsilon\mu\nu < 0$$

Hence, the Routh-Hurwitz criterion shows instability of the trivial equilibrium

At the interior point (I^*, V^*) we have

$$\mathrm{Tr}\ \mathbf{J} = \epsilon \left(\frac{\nu\mu - \beta\vartheta}{\nu + \vartheta} - \mu \right) + \frac{\nu\mu - \beta\vartheta}{\mu + \beta} - \nu \ , \ \ \det \mathbf{J} = -\epsilon(\mu\nu - \beta\vartheta)$$

The determinant has just the opposite value of the trivial equilibrium. It changes sign when $\mu\nu = \beta\vartheta$. At this point both equilibria coincide and the trace $\mathrm{Tr}\ \mathbf{J} < 0$ is again negative.

For the reference values of the parameter β above this point we have $\det \mathbf{J} > 0$ and the interior equilibrium is asymptotically stable.

Phase-space plot SISUV-model
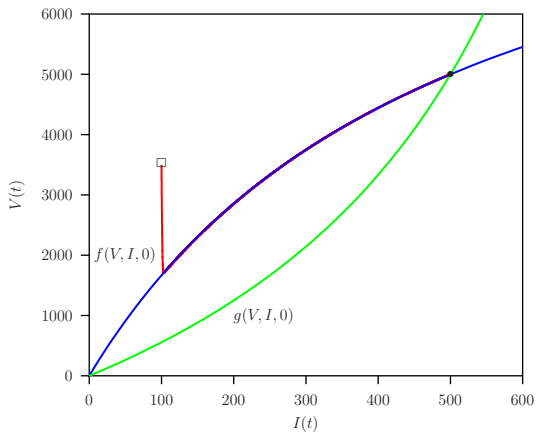
The solid line is the trajectory starting at the point □. Two curves represent the two nullclines $f(V, I, 0) = 0$ and $g(V, I, 0) = 0$

SISUV-model Singular perturbation problem

Singular perturbation theory deals with systems whose solutions evolve on different time scales whose ratio is characterised by a small parameter $0 < \varepsilon \ll 1$.

It uses invariant manifolds in phase space in order to understand the global structure of the phase space or to construct orbits with desired properties.

$$\frac{dI}{dt} = \varepsilon g(V, I, \varepsilon) = \varepsilon \left(\frac{\beta}{M}(N - I)V - \mu I \right)$$

$$\frac{dV}{dt} = f(V, I, \varepsilon) = \frac{\vartheta}{N}(M - V)I - \nu V$$

SISUV-model – fast system

With $\varepsilon = 0$ we have the fast system

$$\frac{dI}{dt} = 0$$

$$\frac{dV}{dt} = f(V, I(0), 0) = \frac{\vartheta}{N}(M - V)I(0) - \nu V$$

The infected population $I(t)$ remains constant, so that the trajectory is the vertical line in the phase-space (I, V) plot

SISUV-model – slow system

With a change of time-scale $\tau = \varepsilon t$ the resulting system with $\varepsilon \ll 1$ is called the *slow or reduced system*:

$$\varepsilon \frac{dI}{d\tau} = \varepsilon g(V, I, \varepsilon) = \varepsilon \left(\frac{\beta}{M}(N - I)V - \mu I \right)$$

$$\varepsilon \frac{dV}{d\tau} = f(V, I, \varepsilon) = \frac{\vartheta}{N}(M - V)I - \nu V$$

After substitution of $\varepsilon = 0$ we get:

$$0 = f(V, I, 0) \quad \Leftrightarrow \quad V = \frac{IM}{I + \frac{N\nu}{\vartheta}}$$

$$\frac{dI}{d\tau} = g(V, I, 0) = \frac{\beta}{M}(N - I)V - \mu I$$

This is a differential algebraic equation that describes the evolution of the slow variable $I(\tau)$ constrained to the set $f(V, I, 0) = 0$.

Time-scale separation

These heuristic results suggest the following approach for dealing with the two different time scales:

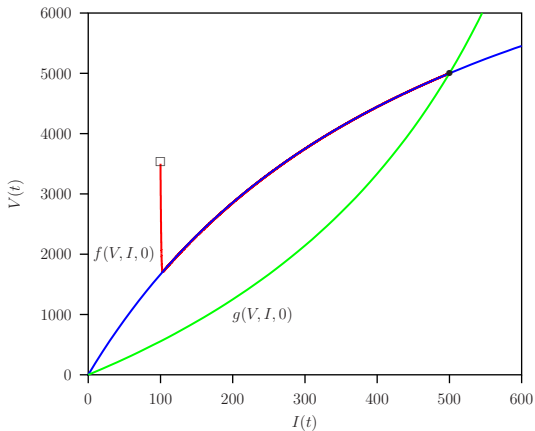1. set $\varepsilon = 0$, which gives the set of fast equilibria of the fast system yielding the algebraic equation.

   This is the *critical manifold*, namely the set of equilibria on the hyperbola $f(V, I, 0) = 0$.

2. With a good hypothesis the hyperbola $f(V, I, 0) = 0$ is equivalent to $I = q(V)$ and we can substitute $V = q^{-1}(I)$.

   This is the blue line in the following phase-space plot.

Phase-space plot SISUV-model

The solid line is the trajectory starting at the point □. Two curves represent the two nullclines $f(V, I, 0) = 0$ and $g(V, I, 0) = 0$

Result is the one dimensional reduced system with $\varepsilon = 0$:

$$\frac{dI}{d\tau} = g(q^{-1}(I), I, 0) = \frac{\beta}{M}(N - I)q^{-1}(I) - \mu I$$

Hence we started with a four dimensional system and it is reduced to a one dimensional system in two steps:

- Constant total number of individuals in the populations host and vector (reduction by two)
- Time scale argument (reduction by one)

Invariance equation

In order to get a better approximation for $0 < \varepsilon \ll 1$ we need an invariance equation

Using the chain rule for $I = q(V)$

$$\frac{dI}{d\tau} = g(V, q(V)) = \frac{dq}{dV}\frac{dV}{d\tau}$$

we get formally the Invariance equation :

$$\frac{dV}{d\tau} = \frac{\frac{\beta}{M}(N - q(V))V - \mu q(V)}{dq/dV} \quad , \quad \frac{dq}{dV} = \frac{\nu N M}{\vartheta (M - V)^2}$$

Geometric singular perturbation technique

For the case $0 < \varepsilon \ll 1$, we follow the geometric singular perturbation techniques.

For $\varepsilon = 0$ the f-nullcline

$$\left\{(V, I) | f(V, I, 0) = 0, V \geq 0, I \geq 0\right\}$$

consists of the critical manifold

$$\mathcal{M} = \left\{(V, I) | I = \frac{\nu V N}{\vartheta(M - V)}, \ 0 \leq V \leq M, 0 \leq I \leq N\right\}$$

$\mathcal{M}$ forms a set of equilibria of the fast system

Fenichel's theorem

Theorem

Suppose $\mathcal{M}$ is compact and normally hyperbolic, that is, the eigenvalues λ of the Jacobian $\frac{\partial f}{\partial V}(V, I)|_{\mathcal{M}}$ are uniformly bounded away from the imaginary axis.

Then the critical manifold persists as a locally invariant slow manifold $\mathcal{M}_\varepsilon$ of the full problem that is $\mathcal{O}(\varepsilon)$ close to $\mathcal{M}$ for sufficiently small $\varepsilon > 0$.

The restriction of the flow to $\mathcal{M}_\varepsilon$ is a small perturbation of the flow of the limiting problem.[a]

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[a] G. Hek, Geometric singular perturbation theory in biological practice, *J Math Biol*, **60** (2010), 347–386.

We assume: critical manifold $\mathcal{M}$ is normally hyperbolic
If not, then canards can occur.

Application of Fenichel's theorem

Fenichel's theorem states that there exists ε_0 such that for $0 < \varepsilon < \varepsilon_0$, there are locally invariant manifolds $\mathcal{M}_\varepsilon$. Using its invariance, the perturbed manifold $\mathcal{M}_\varepsilon$ can be approximated by asymptotic expansion in ε. It can (at least locally) be described as a graph

$$\big\{(V, I) | I = q(V, \varepsilon), V \geq 0, I \geq 0\big\}$$

due to normal hyperbolicity and inverse function theorem.
This manifold is invariant when the following equality holds

$$\frac{dI}{d\tau} = \frac{dI}{dV}\frac{dV}{d\tau} = \frac{\partial q(V, \varepsilon)}{\partial V}\frac{dV}{d\tau}$$

which yields with $I = q(V, \varepsilon)$ the invariance equation for the SISUV model:

$$\frac{\partial q(V, \varepsilon)}{\partial V}\left(\frac{\vartheta}{N}(M - V)q(V, \varepsilon) - \nu V\right) = \varepsilon\left(\frac{\beta}{M}(N - q(V, \varepsilon))V - \mu q(V, \varepsilon)\right)$$

Asymptotic expansion for the SISUV model

The following asymptotic expansion in $0 < \varepsilon \ll 1$ is introduced:

$$I(V) = q(V, \varepsilon) = q_0(V) + \varepsilon q_1(V) + \varepsilon^2 q_2(V) + \dots$$

hence

$$\frac{\partial q}{\partial V} = \frac{dq_0}{dV} + \varepsilon \frac{dq_1}{dV} + \varepsilon^2 \frac{dq_2}{dV} + \dots$$

Substitution into the invariance equation gives

$$
(\frac{dq_0}{dV} + \varepsilon \frac{dq_1}{dV} + \varepsilon^2 \frac{dq_2}{dV} + \ldots)
$$
$$
\left(\frac{\vartheta}{N}(M - V)(q_0(V) + \varepsilon q_1(V) + \varepsilon^2 q_2(V) + \ldots) - \nu V \right)
$$
$$
= \varepsilon \left(\frac{\beta}{M}(N - (q_0(V) + \varepsilon q_1(V) + \varepsilon^2 q_2(V) + \ldots))V \right.
$$
$$
\left. -\mu(q_0(V) + \varepsilon q_1(V) + \varepsilon^2 q_2(V) + \ldots) \right)
$$

Gathering zero order terms of ε and assuming $V > 0$ results in the following formula, accurate of order $\mathcal{O}(\varepsilon)$:

$$
q_0(V) = \frac{\nu N V}{\vartheta(M - V)} \tag{1}
$$

Gathering the first order terms of ε and assuming $V > 0$ results in the following formula, accurate of order $\mathcal{O}(\varepsilon^2)$:
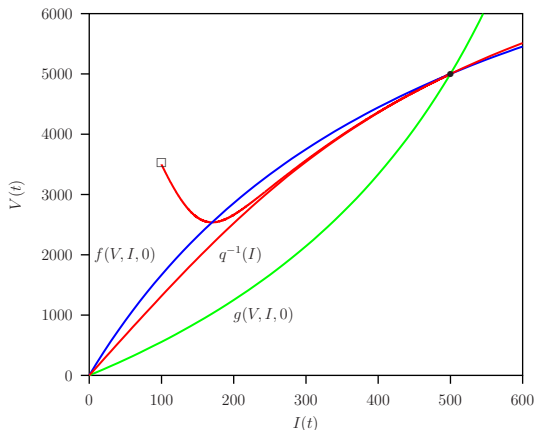
$$q_1(V) = \left(\frac{\beta}{\nu M}(M - V - \frac{\nu}{\vartheta}V) - \frac{\mu}{\vartheta} \right) \frac{NV}{M} . \qquad (2)$$

Substitution of expression for $q_0(V)$ and $q_1(V)$ in

$$I(V, \varepsilon) = q(V, \varepsilon) = q_0(V) + \varepsilon q_1(V)$$

gives the first order approximation

Phase-space plot SISUV-model

One line is the trajectory starting at the point □. The other is the curve $V(I) = q^{-1}(I)$ Two curves represent the two nullclines $f(V, I, 0) = 0$ and $g(V, I, 0) = 0$

In order to get the slow dynamics along this curve we can solve the ODE for the reduced one-dimensional system

$$\frac{dI}{dt} = \beta(N - I)q^{-1}(I) - \mu I$$

where $V = q^{-1}(I)$. Alternatively the same asymptotic expansion procedure as for $V = q^{-1}(I, \varepsilon)$
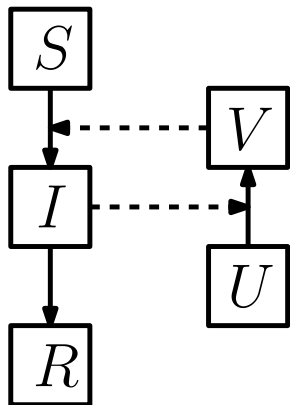
The results are not shown here
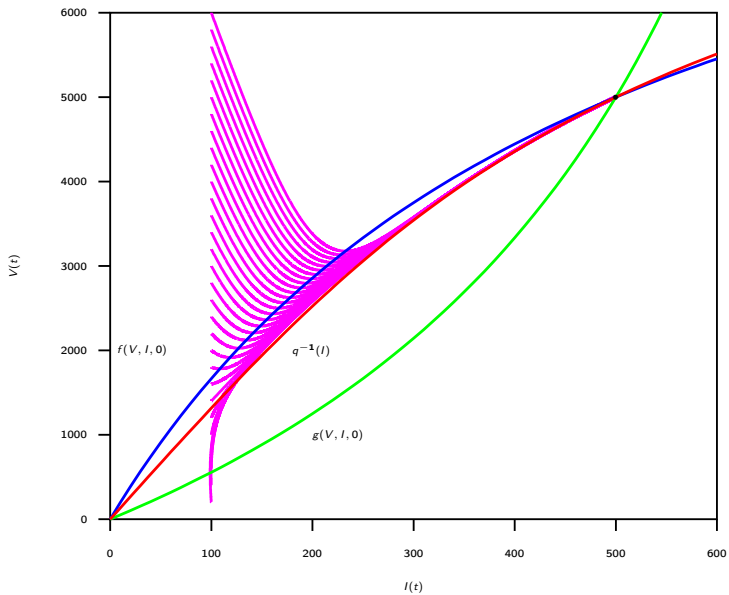
SIRUV-model Host–Vector model

$$\frac{dS}{dt} = -\frac{\beta}{M}SV + \mu(N - S)$$

$$\frac{dI}{dt} = \frac{\beta}{M}SV - (\gamma + \mu)I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

$$\frac{dU}{dt} = -\frac{\vartheta}{N}UI + \nu(M - U)$$

$$\frac{dV}{dt} = \frac{\vartheta}{N}UI - \nu V$$

Constant host and vector population densities

$$N = S(t) + I(t) + R(t), \quad M = U(t) + V(t), \quad \forall t \geq 0$$

Three dimensional system

$$\frac{dS}{dt} = \varepsilon g_1(S, I, V) = \varepsilon \left(-\frac{\beta}{M} SV + \mu(N - S) \right) ,$$

$$\frac{dI}{dt} = \varepsilon g_2(S, I, V) = \varepsilon \left(\frac{\beta}{M} SV - (\gamma + \mu)I \right) ,$$

$$\frac{dV}{dt} = f(S, I, V) = \frac{\vartheta}{N}(M - V)I - \nu V .$$

There is a trivial equilibrium $S^0 = N, I^0 = 0, V^0 = 0$

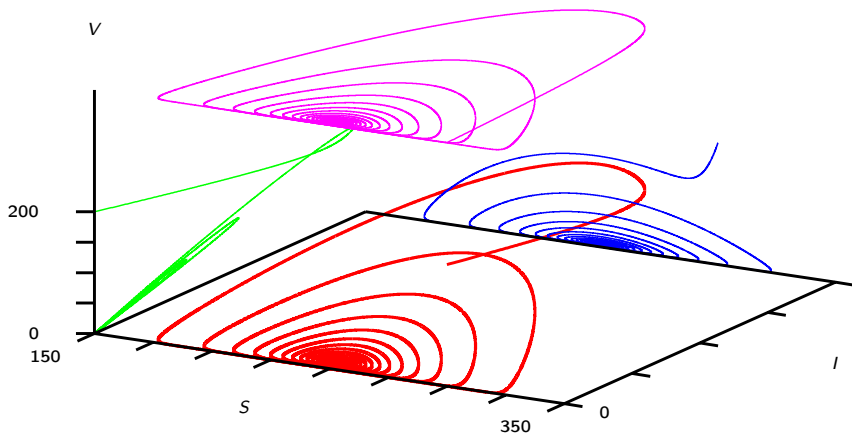And an interior equilibrium (whenever $\nu(\mu + \gamma) < \vartheta\beta$) given by:

$$S^* = N\frac{\nu(\gamma + \mu) + \mu\vartheta}{\vartheta(\beta + \mu)}$$

$$I^* = \mu N\frac{\beta\vartheta - \nu(\gamma + \mu)}{\vartheta(\beta + \mu)(\gamma + \mu)}$$

$$V^* = \mu M\frac{\beta\vartheta - \nu(\gamma + \mu)}{\beta(\nu(\gamma + \mu) + \mu\vartheta)} \ ,$$

and furthermore $R^* = N - (S^* + I^*)$ and $U^* = M - V^*$

Theorem

When the interior equilibrium exists, it is locally asymptotically stable and a spiral as long as μ is sufficiently small.

Figure: Phase-space result for the SIRUV-model.

Heuristic analysis of the SIRUV model

It is convenient to analyse the behaviour of the fast variable V in the VI-system with the slow variable $\bar{S}$ as a parameter

$$\frac{dI}{dt} = \frac{\beta}{M}\bar{S}V - (\mu + \gamma)I$$

$$\frac{dV}{dt} = \frac{\vartheta}{N}(M - V)I - \nu V$$
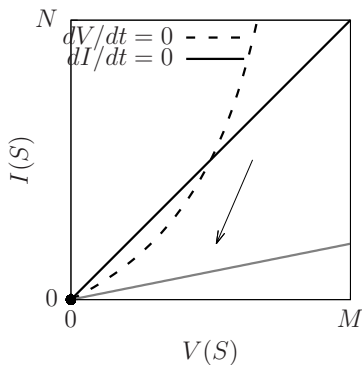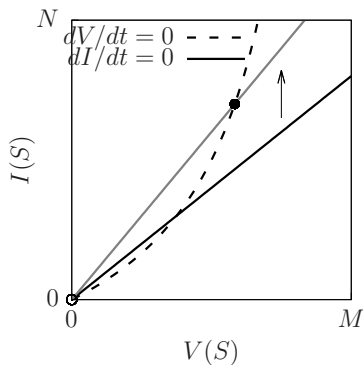
The interior equilibrium dependent on $\bar{S}$ given by

$$I^*(\bar{S}) = \frac{\beta\bar{S}}{(\mu + \gamma)}\left(1 - \frac{\nu(\mu + \gamma)N}{\vartheta\beta\bar{S}}\right) \ , \ V^*(\bar{S}) = M\left(1 - \frac{\nu(\mu + \gamma)N}{\vartheta\beta\bar{S}}\right)$$

Theorem

For $\bar{S} \leq S_c$, trivial equilibrium $(0,0)$ is single local and global asymptotically stable equilibrium.
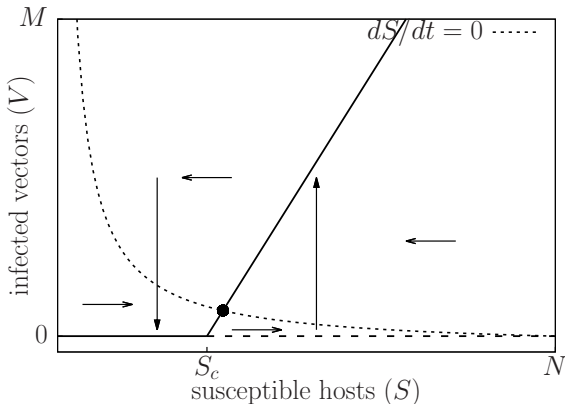
For $\bar{S} \geq S_c$: interior equilibrium $V^*(\bar{S}), I^*(\bar{S})$ is locally and globally asymptotically stable.

Dependence of nullclines on $\bar{S}$

Left panel: $\bar{S}$ increasing, system converges to the interior equilibrium
Right panel: when $\bar{S}$ drops beyond threshold $S_c = \frac{\nu(\mu+\gamma)}{\vartheta\beta}N$, system
approaches the origin

Fast and slow flow in the SV-plane

The locus of *fast* equilibria V^* is shown as solid line.
long arrows: Direction fast V-flow
short arrows: direction slow S-flow
The interior equilibrium (S^*, V^*) is shown as a filled circle

Singular perturbation of SIRUV-model

The slow manifold is in this case two-dimensional. Using the time-scale argument we get for $\varepsilon = 0$ the two-dimensional f-nullspace, the set

$$\big\{ V(S, I) \big| \ g_1(S, V, I) = 0, \ g_2(S, V, I) = 0 \big\}$$

In case of the SIRUV-model, using the QSSA approach with $\varepsilon = 0$, the two-dimensional slow manifold is

$$\mathcal{M} = \Big\{ 0 \leq S \leq N, \ I = \frac{\nu N V}{\vartheta(M - V)}, 0 \leq I \leq N \big| 0 \leq V \leq M \Big\},$$
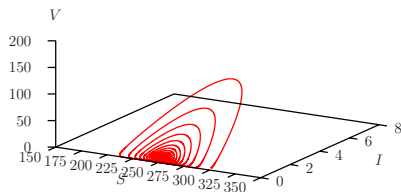
The system with hyperbolic expression

$$V = \frac{MI}{\nu N / \vartheta + I}$$

is the reduced system

$V(S, I)$ with hyperbolic expression is saturation with respect to I is the same as that for $V(I)$ in the SISUV-model

SIRUV-model
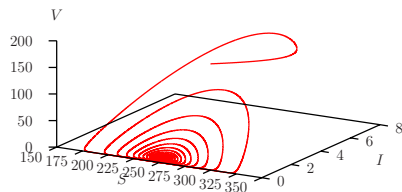
Left panel: Phase-space result for the SIRUV-model
Right panel: Phase-space result for the reduced system where $V(S, I)$ is described by the zero order asymptotic expansion or QSSA approach

We assume: critical manifold $\mathcal{M}$ is normally hyperbolic
Fenichel's theorem states that there exists ε_0 such that for $0 < \varepsilon < \varepsilon_0$, there are locally invariant manifolds $\mathcal{M}_\varepsilon$. Using its invariance, the perturbed manifold $\mathcal{M}_\varepsilon$ can be approximated by asymptotic expansion in ε. It can be described as a graph

$$\left\{ (V, S, I) | V = p(S, I, \varepsilon), V \geq 0, I \geq 0 \right\}$$

This manifold is invariant when the following equality holds

$$\frac{dV}{d\tau} = \frac{\partial V}{\partial S} \frac{dS}{d\tau} + \frac{\partial V}{\partial I} \frac{dI}{d\tau}$$

which yields with $V = p(S, I, \varepsilon)$ the invariance equation for the SISUV model:

$$\frac{dp(S, I)}{d\tau} = \frac{\partial p(S, I)}{\partial S} \frac{dS}{d\tau} + \frac{\partial p(S, I)}{\partial I} \frac{dI}{d\tau}$$

Asymptotic expansion for the SIRUV model

The following asymptotic expansion in $0 < \varepsilon \ll 1$ is now introduced:

$$V(S, I) = p(S, I, \varepsilon) = p_0(S, I) + \varepsilon p_1(S, I) + \varepsilon^2 p_2(S, I) + \ldots$$

hence

$$\frac{dp(S, I, \varepsilon)}{d\tau} = \frac{\partial p_0}{\partial S}\frac{dS}{d\tau} + \frac{\partial p_0}{\partial I}\frac{dI}{d\tau} + \varepsilon\left(\frac{\partial p_1}{\partial S}\frac{dS}{d\tau} + \frac{\partial p_1}{\partial I}\frac{dI}{d\tau}\right) + \ldots$$

Substituting into the invariance equation leads to

$$\frac{\vartheta}{N}(M - p_0(S,I) - \varepsilon p_1(S,I) - \ldots)I - \nu(p_0(S,I) + \varepsilon p_1(S,I) + \ldots) =$$

$$\varepsilon \frac{\partial p_0}{\partial S}\left((-\frac{\beta}{M}S(p_0(S,I) + \varepsilon p_1(S,I) + \ldots) + \mu(N-S)\right) +$$

$$\varepsilon \frac{\partial p_0}{\partial I}\left(\frac{\beta}{M}S(p_0(S,I) + \varepsilon p_1(S,I) + \ldots) - (\gamma + \mu)I\right) +$$

$$\varepsilon^2\left(\frac{\partial p_1}{\partial S}(-\frac{\beta}{M}SV + \mu(N-S)) + \frac{\partial p_1}{\partial I}(\frac{\beta}{M}SV - (\gamma + \mu)I)\right) + \ldots .$$

Gathering the zero order terms of ε and assuming $V > 0$ gives the following result with $\mathcal{O}(1)$ accuracy:

$$p_0(S, I) = \frac{MI}{I + \nu \frac{N}{\vartheta}} \ , \tag{3}$$

and this is the same expression we found for the SISUV-model and for the QSSA result

Gathering the first orders of ε results in the formula with accuracy $\mathcal{O}(2)$:

$$p_1(S, I) = -\frac{M\nu\vartheta N^2}{(\vartheta I + \nu N)^3}\left(\frac{\beta\vartheta SI}{\vartheta I + \nu N} - (\gamma + \mu)I\right). \tag{4}$$

Taking only up to the first order terms into account, the reduced model is described by the reduced two-dimensional system with $V(S, I)$ given by the following asymptotic expansion up to the first order:

$$V(S, I) = p(S, I, \varepsilon) = p_0(S, I) + \varepsilon p_1(S, I),$$

Figure: Plots of the coefficients of first two terms in the asymptotic expansion for $V = p(S, I, \varepsilon)$ with $\varepsilon = 1/365$
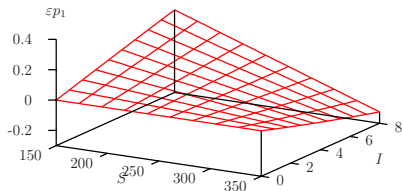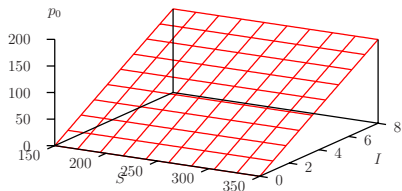
The size of the first-order term in the right panel shows that the contribution of the p_1 term is marginal

The usage of such a power series approximation is, however, counterproductive if we don't know its radius of convergence

Numerical experiments show that

- either spurious equilibria can occur when the trajectory starts not sufficiently close to the equilibrium
- or the trajectory escapes to infinity

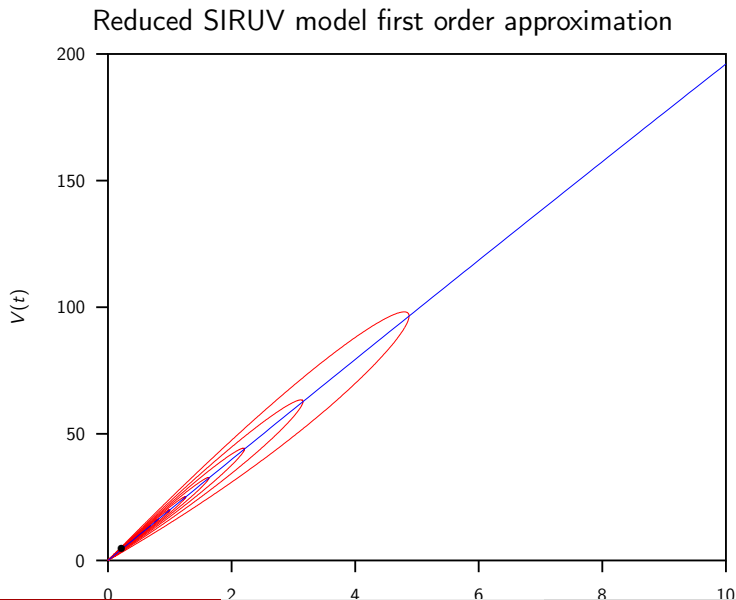Refer also to the examples in Hek (2010)[1]

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[1] G. Hek, Geometric singular perturbation theory in biological practice, *J Math Biol*, **60** (2010), 347–386.

SIRUV model

Trajectory in (I, V) space
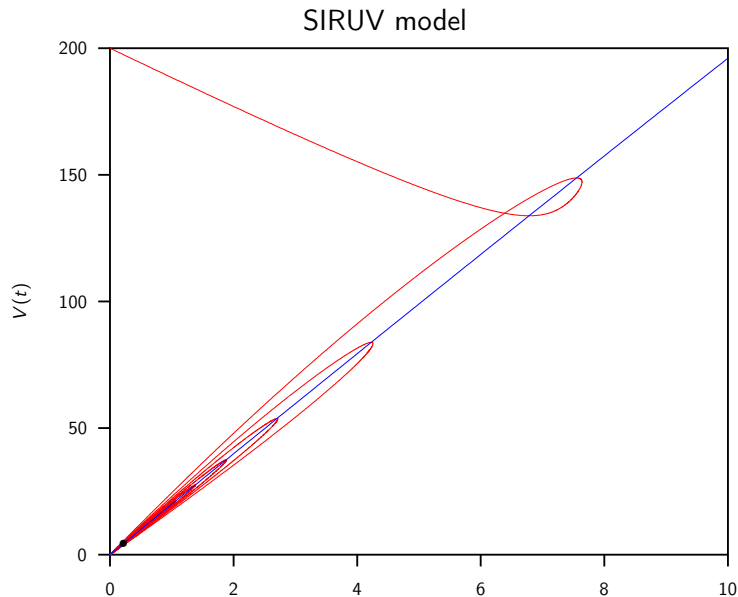
Reduced SIRUV model first order approximation

Host-only model

It is interesting to compare the SIRUV-model with the simplest host-only model where the vector dynamics is taken into account implicitly

There, contact rates between the susceptible and infected host individuals are described by the law of mass action

To this end we use the linearized version of the hyperbolic expression $I = \frac{\nu NV}{\vartheta(M-V)}$ at its origin, namely $V = \frac{MI}{\nu N/\vartheta + I}$
This gives for the hidden infected vector population density V:

$$\frac{V_{\mathrm{QSSA}}}{M} = \frac{\vartheta}{\nu} \frac{I}{N}$$

Host-only model

The host-only model with infection rate

$$B = \frac{\vartheta}{\nu}\beta$$

$$\frac{dS}{dt} = -\frac{B}{N}SI + \mu(N - S) \,, \; \frac{dI}{dt} = \frac{B}{N}SI - (\gamma + \mu)I \,, \; \frac{dR}{dt} = \gamma I - \mu R$$

This version can be considered as a simplified version of the model formulated when the density of the infected vector population is proportional to the infected host population

SIRUV-model
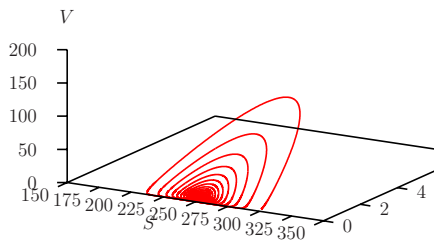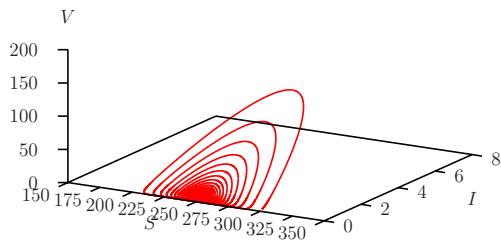
Left panel: Phase-space result for the reduced system where $V(S, I)$ is described by the zero order asymptotic expansion (hyperbolic)
Right panel: Phase-space result for the host-only model (linear, mass action)

Hyperbolic expression resembles Holling type II functional response, well known in predator-prey models and Michaelis-Menten in bio-chemistry with application of singular perturbation theory

In ecology the quantity $N\nu/\vartheta$ is half-saturation constant, in bio-chemistry the Michaelis constant

In ecology mechanistic derivation is obtained when besides searching time also handling time of the predator to digest a prey individual is introduced

In the epidemiological literature it has also been considered to describe the infection mechanism.[2]

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[2]V. Capasso and G. Serio, A Generalization of the Kermack-McKendrick Deterministic Epidemic Model, *Math Biosci*, **42**, (1978), 43–61.

Motivated by Holling's derivation it is tempting to follow a similar approach in to obtain the hyperbolic expression in epidemics. In Diekmann and Heesterbeek (2000) it is argued why this is impossible.[3]

In fact, in the ecological predator-prey setting the two populations are treated independently, whereas in epidemiology there is one population in which individuals can reside in two states, namely susceptible and infective.

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[3]O. Diekmann and J.A.P. Heesterbeek, *Mathematical epidemiology of infectious diseases*, Wiley series in mathematical and computational biology, Wiley, Chichester, 2000, p.155 and p.277-280.

Role of seasonality

Seasonality is introduced in the non-seasonal, autonomous SIRUV-system by assuming that the density of the vector population changes in a perfect sinusoidal way, this assumption being motivated by dengue fever epidemiology observed data

Seasonality was introduced as a sinusoidal fluctuation of density of the vector population $M(t)$

Expression for the density of vector population $M(t)$, now time-dependent, reads

$$M(t) = M_0 \left(1 + \rho \cos(2\pi t)\right).$$

M_0 is reference value and amplitude is $\rho = 0.9$

Consistent with taking in the expression for host infection rate when infection rate is linearised hyperbolic QSSA expression for infected vector population density V

$$\frac{\beta}{M_0} S V_{\text{QSSA}} = \frac{\beta}{M_0} \frac{\vartheta M}{\nu N} SI = \frac{\beta \vartheta (1 + \rho \cos(2\pi t))}{\nu N} SI = \frac{B}{N} SI$$

where

$$B_0 = \frac{\vartheta}{\nu} \beta \quad B(t) = B_0(1 + \rho \cos(2\pi t))$$

Numerical bifurcation analysis for reference parameter set gives role of vector on the epidemics by calculation of the threshold value

One-parameter diagram for the parameter β
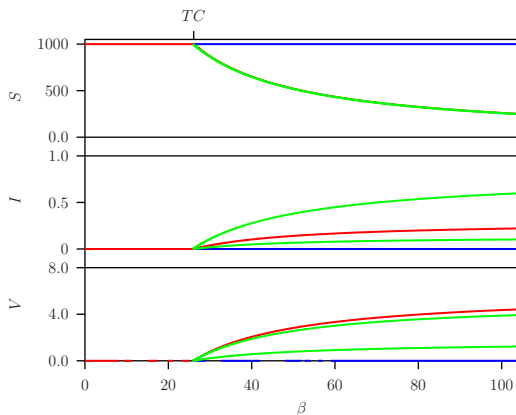
curve: non-seasonal equilibria
curve: seasonal maximum and minimum

Conclusions

- We used a singular perturbation technique in opposition to Rocha et al. where a centre manifold technique was used
- For both the non-seasonal and the seasonal case the computed value of the bifurcation parameter β for TC was almost the same and indistinguishable in the one-parameter diagram
- Seasonal susceptible Host population density S amplitude is very small while the forced vector amplitude is large
- Both bifurcation curves non-seasonal and seasonal SIRUV model in the two parameter diagram are barely distinguishable

Perspectives

- Implementation of vector model in large 2-strain dengue model
- Implementation of saturated contact model in large 2-strain dengue model
- Sensitivity analysis giving role of vector dynamics
- Sensitivity analysis giving role of vector dynamics combined with seasonal forcing
- Introduction of control measures in the model (repellents, vaccines), optimal control problem

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Parameters

Par.	Description	SIRUV	SISUV
Host			
N	Host population density	1000	1000
β	Infection rate	730/7	0.2
μ	Susceptible birth rate	1/65	0.1
γ	Recovery rate	365/7	n/a
Vector			
M	Vector population density	10000	10000
ϑ	Infection rate	73	73
ν	Susceptible birth rate	36.5	36.5
ρ	Magnitude sinusoidal fluctuation vector	0.9	n/a