Finding bifurcations in mathematical epidemiology via reaction network methods

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ABSTRACT (original article):
CITATION (original article):

Constants definition and numerical conditions

Defining constants directly to speed up computation of numerical model.

In[1]:=
```
ClearAll["Global`*"]
SetDirectory[NotebookDirectory[]];
SetOptions[$FrontEndSession, NotebookAutoSave → True];
NotebookSave[];

Format[γr] := Subscript[γ, r];
Format[γs] := Subscript[γ, s]; Format[γi] := Subscript[γ, i];
Format[μr] := Subscript[μ, r];
Format[μs] := Subscript[μ, s];
Format[μi] := Subscript[μ, i];
```

$$\text{sd} = \frac{\lambda\ (\gamma r + \mu r)}{\gamma s\ \mu r + \gamma r\ \mu s + \mu r\ \mu s};\ \text{R0} = \frac{\text{sd}\ \beta}{a + \gamma i + \mu i};\ \text{rd} = \Lambda / \mu - \text{sd};$$

$$\text{b0} = \frac{(a + \gamma i + \mu i)\ (\gamma s\ \mu r + \gamma r\ \mu s + \mu r\ \mu s)}{\lambda\ (\gamma r + \mu r)};$$

```
cncut = {λ → 1 + 11 ξ / 10, a → (ξ - 3) ^2, b → ξ - 4, γr → 1, μr → 1, μs → 1 / 10, μi → 2,
    β → 1, γi → 1, γs → 1} (*Numerical condition with ξ kept unknown*);

csi = {s → ξ, i → 1} (*numerical endemic point*);

(*critical value of ξH when Hopf bifurcation arise*)
```

$$\text{xiH} = \frac{1}{620} * \left(4351 - \sqrt{584161}\right);$$

We define the symbolic model using a stoichiometric matrix S and a vector of rates Vg, then we specialize the model in the case of non linear treatment function and linear incidence function:

In[11]:=
```
var= { s, i, r};
S={{1,-1,0,1,-1,-1,0,0},
   {0,1,-1,0,0,0,-1,0},
   {0,0,1,-1,1,0,0,-1}};(*The stochiometric matrix*)
Vg={λ, f[s,i],h[i], γr r, γs s,s μs,i μi ,r  μr};
RHS=S . Vg;
par = Complement[Variables[RHS], var];

Print["The symbolic  RHS ",RHS//MatrixForm , " has ", par//Length , " par given by ",par]

(*The case of quadratic f(s,i) and Michaelis Menten h(i)*)
cex={f[s,i]→β s i, h[i]→γi i+ a i/(1+b i)};
RHSx= RHS//.cex; parx=Complement[Variables[RHSx], var]; cpx=Thread[parx>0];
RHSxn=RHSx//.cncut;

Print["When f is quadratic  and h is Michaelis Menten, the  RHS becomes ", RHSx//MatrixForm ,
" and it has ", parx//Length, " pars",parx ]

Print["check total= ",Total[RHSx]//FullSimplify]
```

The symbolic RHS $\begin{pmatrix} r\gamma_r - s\gamma_s + \lambda - s\mu_s - f[s,i] \\ -i\mu_i + f[s,i] - h[i] \\ -r\gamma_r + s\gamma_s - r\mu_r + h[i] \end{pmatrix}$

has 8 par given by $\{\gamma_r, \gamma_s, \lambda, \mu_i, \mu_r, \mu_s, f[s,i], h[i]\}$

When f is quadratic and h is Michaelis Menten, the RHS becomes

$\begin{pmatrix} -i s \beta + r\gamma_r - s\gamma_s + \lambda - s\mu_s \\ -\frac{a i}{1+b i} + i s \beta - i\gamma_i - i\mu_i \\ \frac{a i}{1+b i} + i\gamma_i - r\gamma_r + s\gamma_s - r\mu_r \end{pmatrix}$ and it has 10 pars $\{a, b, \beta, \gamma_i, \gamma_r, \gamma_s, \lambda, \mu_i, \mu_r, \mu_s\}$

check total= $\lambda - i\mu_i - r\mu_r - s\mu_s$

Time and phase plots suggest the existence of periodic solutions at different values of ξ

Illustration of the time and phase plot when ξ=6 (when the eigenvalues of the Jacobian at the unstable endemic point are (–2.33284, 0.116421 ± 1.23678 Im)) , show the existence of a stable limit cycle:

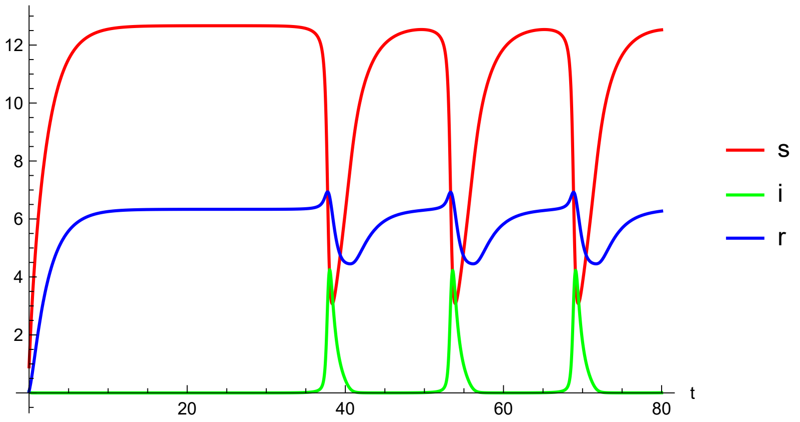
In[422]:=

```
Xt=Map[#[t]&,var ];
ct=Thread[var→Xt];
RHSt=RHSxn/.ct;
ss=RHSt[[1]] ;
ii=RHSt[[2]];
rr=RHSt[[3]];
X0={0.9,0.05,0.05};
ode={s'[t]==ss,i'[t]==ii,r'[t]==rr,s[0]==X0[[1]],i[0]==X0[[2]],r[0]==X0[[3]]};
T=800;
odeN=ode/.ξ→6;
sol=NDSolve[odeN,var,{t,0,T}]

plT=Plot[Evaluate@{  s[t]/.sol,i[t]/.sol,r[t]/.sol},{t,0,T/10},PlotRange→Full,
PlotStyle→{Red,Green,Blue},AxesLabel→{"t",""},PlotLegends→{"s","i","r"}]
Export["plT6.pdf",plT]
```

Out[432]=

```
{{s → InterpolatingFunction[ Domain: {{0., 800.}} Output: scalar ],
  i → InterpolatingFunction[ Domain: {{0., 800.}} Output: scalar ],
  r → InterpolatingFunction[ Domain: {{0., 800.}} Output: scalar ]}}
```

Out[433]=



Out[434]= plT6.pdf

We will now produce a phase plot when ξ=6 showing convergence to a limit cycle around the endemic point , starting outside the cycle, then inside the cycle, and gathering the parametric plots inside a phase portrait.

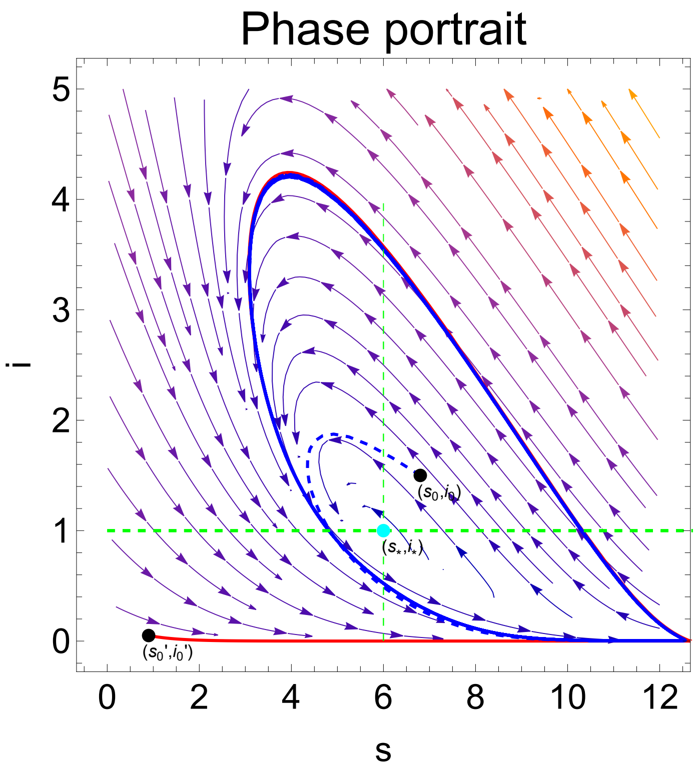
In[435]:=

```
pp=ParametricPlot[{  s[t],i[t]}/.sol,{t,0,50}, AxesLabel→{"s","i"},PlotStyle→{Red},Epilog→
{{PointSize[Large],Point[{X0⟦1⟧,X0⟦2⟧}]},Text["(s0,i0)",Offset[{10,8},{X0⟦1⟧,X0⟦2⟧}]]},AxesO
Show[pp,PlotRange→All];

sp=StreamPlot[Drop[RHSxn/.r→ξ-1//.ξ→6,-1],{s,0,12},{i,0,5},
   ColorFunction→"Pastel",Frame→True,FrameLabel→{"s","i"}, PlotLabel→Style["Phase portrait",L
   PlotRange→All];

  Print["The unstable endemic point has the following coordinates "]
   fp={ξ,1}//.ξ→6//N
   Show[sp,pp,Epilog→
{{PointSize[Large],Point[{X0⟦1⟧,X0⟦2⟧}]},Text["(s0,i0)",Offset[{10,8},{X0⟦1⟧,X0⟦2⟧}]],
{PointSize[Large],Point[{fp⟦1⟧,fp⟦2⟧}]},
Text["(s*,i*)",Offset[{10,8},{fp⟦1⟧,fp⟦2⟧}]]},PlotRange→All];



(*Now by strating from inside the cycle*)
X02={6.8,1.5,1.5}(*Different initial values*);
ode={s'[t]==ss,i'[t]==ii,r'[t]==rr,s[0]==X02⟦1⟧,i[0]==X02⟦2⟧,r[0]==X02⟦3⟧};
T=300;
odeN=ode/.ξ→6;
sol=NDSolve[odeN,var,{t,0,T}];

cyB=ParametricPlot[{  s[t],i[t]}/.sol,{t,0,250}, AxesLabel→{"s","i"},
PlotRange→Full,PlotStyle→{Dashed,Blue}];

pyn=Plot[(1),{t,0,T},PlotStyle→{Dashed,Green}];
cyc=Show[{cyB,pyn, Graphics[{Green,Dashed,
Line[{{fp⟦1⟧,0},{fp⟦1⟧,4}}]}] },
Epilog→{{Text["(s*,i*)",Offset[{10,10},{(fp⟦1⟧),(fp⟦2⟧)}]],
{PointSize[Large],Style[Point[{(fp⟦1⟧),(fp⟦2⟧)}],Black]}},
{PointSize[Large],Point[{X02⟦1⟧,X02⟦2⟧}]},Text["(s0,i0)",Offset[{-10,8},{X02⟦1⟧,X02⟦2⟧}]]}];

fin=Show[{sp,pp,pyn,cyc,Graphics[{Green,Dashed,
Line[{{fp⟦1⟧,0},{fp⟦1⟧,3}}]}]},
Epilog→{Text["(s0,i0)",Offset[{10,-8},{X02⟦1⟧,X02⟦2⟧}]],
{PointSize[Large],Point[{X0⟦1⟧,X0⟦2⟧}]},{Text["(s*,i*)",Offset[{10,-8},{(fp⟦1⟧),(fp⟦2⟧)}]],
{PointSize[Large],Style[Point[{(fp⟦1⟧),(fp⟦2⟧)}],Cyan]}},
{PointSize[Large],Point[{X02⟦1⟧,X02⟦2⟧}]},
Text["(s0',i0')",Offset[{10,-8},{X0⟦1⟧,X0⟦2⟧}]]}]
Export["PPV6.pdf",fin]
```

The unstable endemic point has the following coordinates

Out[439]= {6., 1.}

Out[449]=



Out[450]= PPV6.pdf

IIlustration of the time plot when ξ=ξH (the eigenvalues of the Jacobian at the endemic point are (–2.31501, ±1.29094 Im)) suggest the existence of a unique limit cycle :

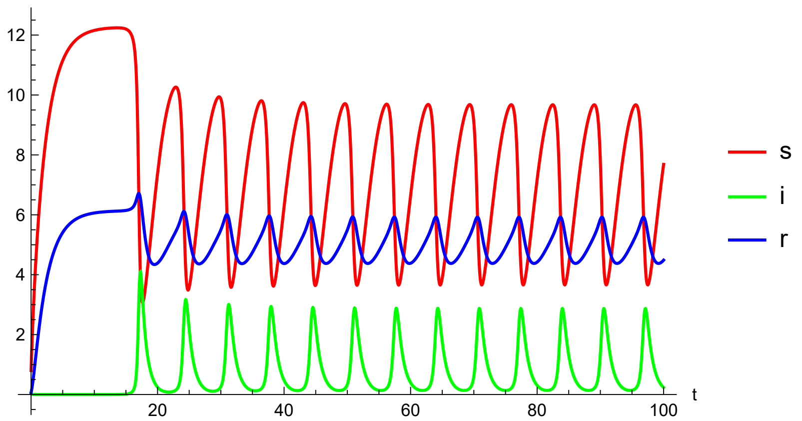
In[ ]:=

```
X0={0.8,0.05,0.05} (*Initial conditions*);
ode={s'[t]==ss,i'[t]==ii,r'[t]==rr,s[0]==X0[[1]],i[0]==X0[[2]],r[0]==X0[[3]]};
T=300;
odeN=ode/.ξ→xiH;
sol=NDSolve[odeN,var,{t,0,T}]

plT=Plot[Evaluate@{ s[t]/.sol,i[t]/.sol,r[t]/.sol},{t,0,T/3},PlotRange→Full,
PlotStyle→{Red,Green,Blue},AxesLabel→{"t",""},PlotLegends→{"s","i","r"}]

Export["plTH.pdf",plT]
```

Out[ ]=

```
{{s → InterpolatingFunction[ Domain: {{0., 300.}} Output: scalar ],
  i → InterpolatingFunction[ Domain: {{0., 300.}} Output: scalar ],
  r → InterpolatingFunction[ Domain: {{0., 300.}} Output: scalar ]}}
```

Out[ ]=

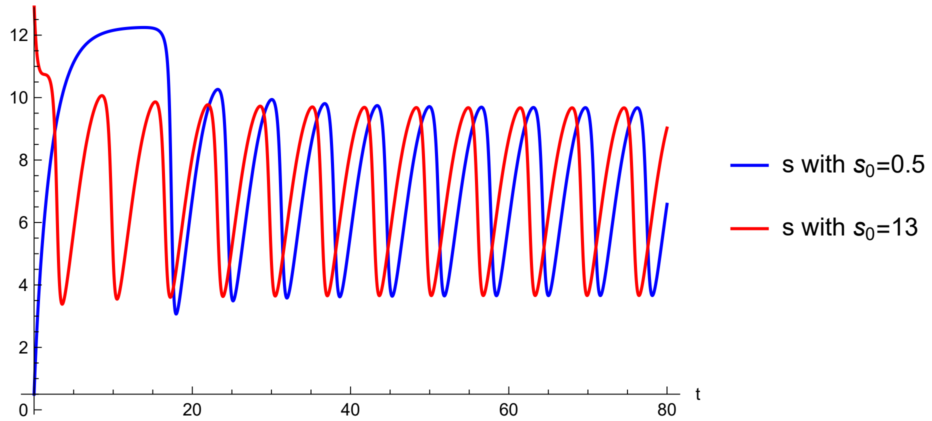


Out[ ]= `plTH.pdf`

In the following, we chose different starting points, and we illustrate the time plots of s from different initial points. This suggest the existence of a unique limit cycle:

In[ ]:=
```
 X0={0.5,0.05,0.05} (*Initial conditions*);
ode={s'[t]==ss,i'[t]==ii,r'[t]==rr,s[0]==X0[[1]],i[0]==X0[[2]],r[0]==X0[[3]]};
T=300;
odeN=ode/.ξ→xiH;
sol=NDSolve[odeN,var,{t,0,T}];

plT1=Plot[Evaluate@{  s[t]/.sol},{t,0,80},PlotRange→Full,
PlotStyle→{Blue},AxesLabel→{"t",""},PlotLegends→{"s with s0=0.5"}];

X0={13,0.02,0.01} (*Different Initial conditions*);
ode={s'[t]==ss,i'[t]==ii,r'[t]==rr,s[0]==X0[[1]],i[0]==X0[[2]],r[0]==X0[[3]]};
T=300;
odeN=ode/.ξ→xiH;
sol=NDSolve[odeN,var,{t,0,T}];

plT2=Plot[Evaluate@{  s[t]/.sol},{t,0,80},PlotRange→Full,
PlotStyle→{Red},AxesLabel→{"t",""},PlotLegends→{"s with s0=13"}];


tot=Show[plT1,plT2]

Export["plTHs.pdf",tot]
```

Out[ ]=



Out[ ]= plTHs.pdf

Analysis of the saddle node bifurcation dis=0:

In this cell we give an alternative solution to the zero eigenvalue bifurcation point, using our package Epid

In[∘]:=

```
<<Epid.wl;
mod={RHSx,var,parx};
pol=(RUR[mod,2]〚2〛/i//Simplify)〚1〛;
dis=Discriminant[pol,i];
cof=CoefficientList[dis,β]//FullSimplify;
Print["discriminant of RUR pol is a polyn of degree ",cof//Length-1," in β, with disc",dib=Dis
" which is always positive"]
so=Solve[dis==0,β]//FullSimplify;
Print["There are two critical β"]
Timing[ze=Solve[Append[cpx,dis==0],β]//FullSimplify]
Print["which may both be positive",so//.Append[Drop[cncut,{8}],ξ→xiH]//N]
jacx=Grad[RHSx,var]//.{s→ξ,i→1,r→ξ-1};jacx//MatrixForm
tra2=Tr[jacx];
cncutt=Drop[cncut,{-3}];
eq=Flatten[Append[cpx,dis==0&&tra2==0]];
BTP=Solve[eq//.cncutt,{β,ξ}]//Flatten;
Print["On the cut, there is a unique BTP  with dis= tr=0: ",BTP," = ",BTP//N ]
```

discriminant of RUR pol is a polyn of degree $(-1+\text{Length})\left[\left\{b^2(\gamma_i+\mu_i)^2(\gamma_s\mu_r+(\gamma_r+\mu_r)\mu_s)^2,\right.\right.$ $-2b(\gamma_r\mu_i(2a+\gamma_i+\mu_i)+(\gamma_i+\mu_i)(a+\gamma_i+\mu_i)\mu_r+b\lambda(\gamma_i+\mu_i)(\gamma_r+\mu_r))(\gamma_s\mu_r+(\gamma_r+\mu_r)\mu_s),$ $\left.\left.b^2\lambda^2(\gamma_r+\mu_r)^2+2b\lambda(\gamma_r+\mu_r)(\gamma_r\mu_i+(-a+\gamma_i+\mu_i)\mu_r)+(\gamma_r\mu_i+(a+\gamma_i+\mu_i)\mu_r)^2\right\}\right]$ in β, with disc$16ab^2(\gamma_r\mu_i+(\gamma_i+\mu_i)\mu_r)(\gamma_r\mu_i(a+\gamma_i+\mu_i)+b\lambda(\gamma_i+\mu_i)(\gamma_r+\mu_r))$ $(\gamma_s\mu_r+(\gamma_r+\mu_r)\mu_s)^2$ which is always positive

There are two critical β

Out[∘]= $\{0.125, \{\{\beta\to$ $(b(\gamma_s\mu_r+(\gamma_r+\mu_r)\mu_s)(\gamma_r\mu_i(2a+\gamma_i+\mu_i)+(\gamma_i+\mu_i)(a+\gamma_i+\mu_i)\mu_r+b\lambda(\gamma_i+\mu_i$
$2\sqrt{a(\gamma_r\mu_i+(\gamma_i+\mu_i)\mu_r)(\gamma_r\mu_i(a+\gamma_i+\mu_i)+b\lambda(\gamma_i+\mu_i)(\gamma_r+\mu_r))}$ Sign
$(\gamma_r+\mu_r)^2+2b\lambda(\gamma_r+\mu_r)(\gamma_r\mu_i+(-a+\gamma_i+\mu_i)\mu_r)+(\gamma_r\mu_i+(a+\gamma_i+$
$(b^2\lambda^2(\gamma_r+\mu_r)^2+2b\lambda(\gamma_r+\mu_r)(\gamma_r\mu_i+(-a+\gamma_i+\mu_i)\mu_r)+(\gamma_r\mu_i+(a+\gamma_i+\mu_i)$
if $a>0$ && $b>0$ && $\gamma_i>0$ &&
$\gamma_r>0$ &&
$\gamma_s>0$ &&
$\lambda>0$ && $\mu_i>0$ &&
$\mu_r>0$ && $\mu_s>0$

which may both be positive$\{\{\beta\to 0.0706311\},\{\beta\to 0.82476\}\}$

Out[∘]//MatrixForm=

$$\begin{pmatrix} -\beta-\gamma_s-\mu_s & -\beta\xi & \gamma_r \\ \beta & \frac{ab}{(1+b)^2}-\frac{a}{1+b}-\gamma_i-\mu_i+\beta\xi & 0 \\ \gamma_s & -\frac{ab}{(1+b)^2}+\frac{a}{1+b}+\gamma_i & -\gamma_r-\mu_r \end{pmatrix}$$

On the cut, there is a unique BTP with dis= tr=0:

$$\left\{\beta\to\boxed{0.993\ldots},\ \xi\to\frac{324385}{30457}-\frac{4244910\,\boxed{0.993\ldots}}{2162447}-\frac{1654400\,\boxed{0.993\ldots}^2}{2162447}+\frac{447000\,\boxed{0.993\ldots}^3}{2162447}\right\}$$

$= \{\beta\to 0.993166,\ \xi\to 8.14886\}$

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