# On a four-dimensional oncolytic Virotherapy model (*E*=1)

This Mathematica Notebook is a supplementary material to the paper "On a three-dimensional and two four-dimensional

oncolytic viro-therapy models". It contains some of the calculations and illustrations appearing in the paper.

## 4) Section 3.5(in paper): 4-Dim. Viro-therapy model when $\epsilon=1$

4-1)Definition of the model and fixed points when  $\epsilon$ =1

```
In[@]:= SetDirectory[NotebookDirectory[]];
      AppendTo[$Path, Directory];
      Clear["Global`*"];
      Clear["K"];
       (*Some aliases*)
      Format[\betay] = Subscript[\beta, y];
       Format[\betav] = Subscript[\beta, v];
       Format[\beta z] = Subscript[\beta, z];
      Unprotect[Power];
      Power[0, 0] = 1;
      Protect[Power];
      par = \{b, \beta, \lambda, \delta, \beta y, \beta v, \beta z, c, \gamma, K, \epsilon\};
       cp = Join[Thread[Drop[par, {1}] > 0], {b > 1}];
       cKga1 = \{K \rightarrow 1, \gamma \rightarrow 1\};
       cep1 = \{\epsilon \rightarrow 1\};
      R0 = b \beta K / (\beta K + \delta) (* Reproduction number*);
       (*cnb={b→50};
       cE1ri=Join[\{\beta y\rightarrow 1/48, K\rightarrow 2139.258, \beta\rightarrow .0002, \lambda\rightarrow .2062,
           \gamma \rightarrow 1/18, \delta \rightarrow .025, \beta v \rightarrow 2*10^{(-8)}, c \rightarrow 10^{(-3)}, \beta z \rightarrow .027, cep1];*)
      cF1 = \left\{\beta \rightarrow \frac{87}{2}, \lambda \rightarrow 1, \gamma \rightarrow \frac{1}{128}, \delta \rightarrow 1/2, \beta y \rightarrow 1, \beta v \rightarrow 1, K \rightarrow 1, \beta z \rightarrow 1, c \rightarrow 1, \epsilon \rightarrow 1\right\};
       (***** Four dim Deterministic epidemic model with Logistic growth ****)
      x1 = \lambda x (1 - (x + y) / K) - \beta x v;
      y1 = \beta \times V - \beta y y z - \gamma y;
      v1 = -\beta x v - \beta v v z + b \gamma y - \delta v;
      z1 = z (\beta z y - c z^{\epsilon});
      dyn = \{x1, y1, v1, z1\};
      dyn3 = \{x1, y1, v1\} /.z \rightarrow 0; (*3dim case used for E* *)
      Print[" (y') =", dyn // FullSimplify // MatrixForm]
      Print["b0=", b0 = b /. Apart[Solve[R0 == 1, b] [1]] // FullSimplify]]
       (***Fixed point when z\rightarrow 0**)
      eq = Thread[dyn3 == {0, 0, 0}];
       sol = Solve[eq, {x, y, v}] // FullSimplify;
       Es = \{x, y, v\} /. sol[3]; (*Endemic point with z=0*);
      Print[" Endemic point with z=0 is E*=", Es // FullSimplify]
```

$$\begin{aligned} \mathbf{x}' & \\ (\mathbf{y}') & = \begin{pmatrix} -\mathbf{v} \times \beta + \mathbf{x} \left( \mathbf{1} - \frac{\mathbf{x} + \mathbf{y}}{K} \right) \lambda \\ \mathbf{v} \times \beta - \mathbf{y} \left( \mathbf{z} \beta_{\mathbf{y}} + \gamma \right) \\ \mathbf{b} \mathbf{y} \gamma - \mathbf{v} \left( \mathbf{x} \beta + \mathbf{z} \beta_{\mathbf{v}} + \delta \right) \\ \mathbf{z} \left( -\mathbf{c} \mathbf{z}^{\epsilon} + \mathbf{y} \beta_{\mathbf{z}} \right) \end{aligned}$$

$$\mathbf{b} \mathbf{0} = \mathbf{1} + \frac{\delta}{K \beta}$$

Endemic point with z=0 is E $\star$ =

$$\left\{\frac{\delta}{\left(-\mathbf{1}+\mathbf{b}\right)\beta}, \frac{\left(\left(-\mathbf{1}+\mathbf{b}\right) \mathsf{K}\beta - \delta\right)\delta\lambda}{\left(-\mathbf{1}+\mathbf{b}\right)\beta\left(\left(-\mathbf{1}+\mathbf{b}\right) \mathsf{K}\beta\gamma + \delta\lambda\right)}, \frac{\gamma\left(\left(-\mathbf{1}+\mathbf{b}\right) \mathsf{K}\beta - \delta\right)\lambda}{\beta\left(\left(-\mathbf{1}+\mathbf{b}\right) \mathsf{K}\beta\gamma + \delta\lambda\right)}\right\}$$

(\*\*\*\*Fixed points of 4-dim model using P(y)\*\*\*) In[ • ]:= fy=(c  $\gamma(b-1)-y \beta y \beta z$ ); gy=( $\beta v \beta z y+c \delta$ ); hy=( $\gamma +y \beta z \beta y/c$ ); xey=hy gy/( $\beta$  fy); vey=y fy/gy; zey=  $\beta$ z y /c; ys=y/.sol[3](\* y of E\* jacD=Grad[dyn,{x,y,v,z}]; Py= $\lambda(1-y/K)-\beta$  y fy/gy- $\lambda$  hy gy/( $\beta$  K fy); yb=c  $\gamma$  (b-1)/( $\beta$ y  $\beta$ z); Qy= $\lambda$  fy gy(1- y /K)- $\lambda$  hy gy^2/( $\beta$  K)-y  $\beta$  fy^2; Qycol=Collect[Together[Qy],y]; Qycoef=CoefficientList[Qycol,y]; Print["f(y) = ", fy, ", g(y) = ", gy, ", h(y) = ", hy]Print["p(y) =", Py//FullSimplify] Print["The polynomial Q(y) is of order ", Length[Qycoef]-1] Print["Coefficients of Q(y) are ", Qycoef//FullSimplify] Dis=Collect[Discriminant[Qy,y],b]; Discoef=CoefficientList[Dis,b];Length[Discoef]; Disn=Dis//.cF1//N; bL=50;  $Plot[\{0,Disn\},\{b,0,2\ bL\},AxesLabel\rightarrow \{"b","Dis"\},PlotRange\rightarrow \{\{0,bL\},\{-10,12\}\}]$ Print["Roots of Dis[b] = 0 are: ",solbE=Solve[Disn==0,b]]

$$f\left(y\right)=-y\;\beta_{y}\;\beta_{z}\;+\;\left(-1+b\right)\;c\;\gamma\;\text{ ,g}\left(y\right)=y\;\beta_{v}\;\beta_{z}\;+\;c\;\delta\;\text{ , }\;h\left(y\right)=\frac{y\;\beta_{y}\;\beta_{z}}{c}\;+\;\gamma$$

$$p\left(y\right) = \frac{y\;\beta\;\left(y\;\beta_{y}\;\beta_{z}\;-\;\left(-1+b\right)\;c\;\gamma\right)}{y\;\beta_{v}\;\beta_{z}\;+\;c\;\delta}\;+\;\lambda\;-\;\frac{y\;\lambda}{K}\;-\;\frac{\left(\frac{y\;\beta_{y}\;\beta_{z}}{c}\;+\;\gamma\right)\;\left(y\;\beta_{v}\;\beta_{z}\;+\;c\;\delta\right)\;\;\lambda}{K\;\beta\;\left(-y\;\beta_{y}\;\beta_{z}\;+\;\left(-1+b\right)\;c\;\gamma\right)}$$

The polynomial Q(y) is of order 3

Coefficients of Q(y) are 
$$\left\{ \frac{c^2 \, \gamma \, (\, (-1+b) \, \, K \, \beta - \delta) \, \, \delta \, \lambda}{K \, \beta} \right.$$

$$-\frac{c\,\left(\beta_{z}\,\left(\delta\,\left(2\,\beta_{v}\,\gamma+\beta_{y}\,\delta\right)+K\,\beta\,\left(\beta_{v}\,\gamma-b\,\beta_{v}\,\gamma+\beta_{y}\,\delta\right)\right)\,\lambda+\,\left(-1+b\right)\,c\,\beta\,\gamma\,\left(\,\left(-1+b\right)\,K\,\beta\,\gamma+\delta\,\lambda\right)\right)}{K\,\beta}\,,$$

$$\frac{\beta_{z}\,\left(-\beta_{v}\,\beta_{z}\,\left(\mathsf{K}\,\beta\,\beta_{y}+\beta_{v}\,\gamma+2\,\beta_{y}\,\delta\right)\,\lambda+c\,\beta\,\left(2\times\left(-1+b\right)\,\mathsf{K}\,\beta\,\beta_{y}\,\gamma+\beta_{v}\,\left(\gamma-b\,\gamma\right)\,\lambda+\beta_{y}\,\delta\,\lambda\right)\right)}{\mathsf{K}\,\beta}$$

$$-\frac{\beta_{\mathbf{y}}\;\beta_{\mathbf{z}}^{2}\;\left(\beta_{\mathbf{v}}^{2}\;\beta_{\mathbf{z}}\;\lambda+c\;\beta\;\left(\mathbf{K}\;\beta\;\beta_{\mathbf{y}}-\beta_{\mathbf{v}}\;\lambda\right)\right)}{c\;\mathbf{K}\;\beta}\;\right\}$$

```
Dis
        10
        5
 Out[ • ]=
                                                                   ___ b
                     10
                                20
                                            30
                                                        40
       -10
       Roots of Dis[b] = 0 are:
        \{\{b\rightarrow -126.518\}\text{, }\{b\rightarrow -63.\}\text{, }\{b\rightarrow -63.\}\text{, }\{b\rightarrow -24.5518\}\text{, }\{b\rightarrow 29.361\}\text{, }\{b\rightarrow 45.9232\}\}
        QR=Solve[Qy==0,y,Cubics→False]//ToRadicals(*casus irreducibilis*);
In[ • ]:=
        ym= y/.QR[2];
        yp= y/.QR[[1]];yi= y/.QR[[3]];
        Em1={xey,ym,vey,zey}//.y→ym;
        Ep1={xey,yp,vey,zey}//.y→yp;
        Eim1={xey,yi,vey,zey}//.y→yi;
        Es1=Join[{x,y,v}/.sol[3],{0}];
        {Chop[yp],Chop[ym]}//.cF1//N;
        jacE1K=jacD/.cep1/.x\rightarrow K/.y\rightarrow 0/.v\rightarrow 0/.z\rightarrow 0;
        Print["J(EK) =", jacE1K//MatrixForm]
        (*Jacobians of the fixed points**)
        jEs1=jacD/.cep1/.sol[3]/.z→0;
        jEm1=jacD/.cep1/.x→xey/.v→vey/.z→zey/.y→ym;
        jEim1=jacD/.cep1/.x→xey/.v→vey/.z→zey/.y→yi;
        jEp1=jacD/.cep1/.x→xey/.v→vey/.z→zey/.y→yp;
        Print["Eig.val of J(EK) are:", Eigenvalues[jacE1K]//FullSimplify]
        jacE1=jacD/.cep1/.x→xey/.v→vey/.z→zey/.y→y//FullSimplify;
        jacE1 //MatrixForm;
        Det[jacE1]//FullSimplify;
        Print[" Trace of either Ei, E+ or E- is : ", Tr[jacE1]//FullSimplify]
        Print["J(E_*) is"]
        jEs1//FullSimplify//MatrixForm
```

bbs=b/.Solve[yb==(y/.sol[3]),b][1](\*long expression\*);

$$J\left(\mathsf{EK}\right) = \begin{pmatrix} -\lambda & -\lambda & -\mathsf{K}\,\beta & \emptyset \\ \emptyset & -\gamma & \mathsf{K}\,\beta & \emptyset \\ \emptyset & b\,\gamma & -\mathsf{K}\,\beta - \delta & \emptyset \\ \emptyset & 0 & \emptyset & \emptyset \end{pmatrix}$$

$$\mathsf{Eig.val} \ \, \mathsf{of} \ \, \mathsf{J}\left(\mathsf{EK}\right) \ \, \mathsf{are} \colon \left\{\emptyset, \, \frac{1}{2}\, \left(-\mathsf{K}\,\beta - \gamma - \delta - \sqrt{-4\,\gamma\,\left(\mathsf{K}\,\left(\beta - b\,\beta\right) + \delta\right) + \left(\mathsf{K}\,\beta + \gamma + \delta\right)^{\,2}}\,\right), \, -\lambda\right\}$$

$$\frac{1}{2}\, \left(-\mathsf{K}\,\beta - \gamma - \delta + \sqrt{-4\,\gamma\,\left(\mathsf{K}\,\left(\beta - b\,\beta\right) + \delta\right) + \left(\mathsf{K}\,\beta + \gamma + \delta\right)^{\,2}}\,\right), \, -\lambda\right\}$$

$$\mathsf{Trace} \ \, \mathsf{of} \ \, \mathsf{either} \ \, \mathsf{Ei}, \, \, \mathsf{E} + \ \, \mathsf{or} \, \, \mathsf{E} - \ \, \mathsf{is} \, : \, -\mathsf{y}\,\beta_{\mathsf{z}} - \frac{\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\gamma}{\mathsf{c}} + \frac{\mathsf{y}^{2}\,\beta\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}}}{\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\delta} - \frac{\left(-1 + \mathsf{b}\right)\,\mathsf{c}\,\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\delta}{\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\delta} + \frac{\mathsf{b}\,\gamma\,\left(\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\delta\right)}{\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\delta} + \frac{\mathsf{b}\,\gamma\,\left(\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\delta\right)}{\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} - \left(-1 + \mathsf{b}\right)\,\mathsf{c}\,\gamma} + \lambda - \frac{\mathsf{y}\,\lambda}{\mathsf{K}} - \frac{2\,\left(\frac{\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}}}{\mathsf{c}} + \gamma\right)\,\left(\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + \mathsf{c}\,\delta\right)\,\lambda}{\mathsf{K}\,\beta\,(-\mathsf{y}\,\beta_{\mathsf{y}}\,\beta_{\mathsf{z}} + (-1 + \mathsf{b})\,\mathsf{c}\,\gamma\right)}$$

$$\mathsf{J}\left(\mathsf{E}_{-}\star\right) \ \, \mathsf{is}$$

$$\mathsf{atrixForm=} \left( \begin{array}{c} \frac{\delta\,\lambda}{\mathsf{K}\,\beta - \mathsf{b}\,\mathsf{K}\,\beta} & \frac{\delta\,\lambda}{\mathsf{K}\,\beta - \mathsf{b}\,\mathsf{K}\,\beta} & -\frac{\delta}{-1 + \mathsf{b}} & \emptyset \\ \mathsf{y}\,\varsigma\,\left(\mathsf{K}\,\left(\beta - \mathsf{b}\,\beta\right) + \delta\right)\,\lambda \end{array} \right)$$

Out[ •]//MatrixForm=

$$\begin{pmatrix} \frac{\delta \lambda}{\mathsf{K} \, \beta - \mathsf{b} \, \mathsf{K} \, \beta} & \frac{\delta \lambda}{\mathsf{K} \, \beta - \mathsf{b} \, \mathsf{K} \, \beta} & -\frac{\delta}{-1 + \mathsf{b}} & \mathbf{0} \\ \frac{\gamma \, (\, (\, -1 + \mathsf{b}) \, \, \mathsf{K} \, \beta - \delta) \, \, \lambda}{(\, -1 + \mathsf{b}) \, \, \mathsf{K} \, \beta \gamma + \delta \, \lambda} & -\gamma & \frac{\delta}{-1 + \mathsf{b}} & \frac{\beta_y \, \delta \, \, (\mathsf{K} \, \, (\beta - \mathsf{b} \, \beta) + \delta) \, \, \lambda}{(\, -1 + \mathsf{b}) \, \, \mathsf{K} \, \beta \gamma + \delta \, \lambda} \\ \frac{\gamma \, \, (\mathsf{K} \, \, (\beta - \mathsf{b} \, \beta) + \delta) \, \, \lambda}{(\, -1 + \mathsf{b}) \, \, \mathsf{K} \, \beta \gamma + \delta \, \lambda} & \mathsf{b} \, \gamma & \frac{\mathsf{b} \, \delta}{1 - \mathsf{b}} & \frac{\beta_v \, \gamma \, \, (\mathsf{K} \, \, (\beta - \mathsf{b} \, \beta) + \delta) \, \, \lambda}{\beta \, \, \, \, \, \, (\, -1 + \mathsf{b}) \, \, \mathsf{K} \, \beta \gamma + \delta \, \lambda)} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \frac{\beta_z \, \, (\, (\, -1 + \mathsf{b}) \, \, \mathsf{K} \, \beta \gamma + \delta \, \lambda)}{(\, -1 + \mathsf{b}) \, \, \, \mathsf{K} \, \beta \gamma + \delta \, \lambda)} \\ \end{pmatrix}$$

### 4-2) Trace, Det and third criterion of Routh Hurwitz applied to E\*:

Det and Trace of of E\* and Analysis of the stability of E\* in 4 dim when  $\epsilon$ =1:

```
Print["Tr[J[E*]]="]
In[ • ]:=
                  trEs1=Tr[jacD//.Join[sol[3],cep1,{z→0}]]//FullSimplify
                  Print["Det[J[E*]]="]
                  detEs1=Det[jacD//.Join[sol[3]],cep1,{z→0}]]//FullSimplify
                  pc=Collect[Det[\psi IdentityMatrix[4] - (jEs1/.cep1)],\psi];
                  coT=CoefficientList[pc,\psi]//FullSimplify;
                  Length[coT]
                  a1=coT[[4]]//FullSimplify ;a2=coT[[3]]//FullSimplify;a3=coT[[2]]//FullSimplify ; a4=coT[[1]]//FullSimplify
                  Print["a<sub>1</sub>=",a1, ", a<sub>2</sub>=",a2, ", a<sub>3</sub>=",a3, ",a<sub>4</sub>=", a4]
                  H4=a1*a2*a3-a3^2+a1^2 a4;
                  Print["H2(b0)=",H4/.b→b0//FullSimplify]
                  Print["Denominator of H2 is ",Denominator[Together[H4]]//FullSimplify]
                  φb4=Collect[Numerator[Together[H4]],b];
                  cofi=CoefficientList[φb4,b];
                  Length[cofi]
                  (*Print["value of \phi(b) at crit b is "]
                  \phib4/.b\rightarrowb0//FullSimplify; (*so long expression*)*)
              Tr[J[E*]]=
                   \text{K } \delta \text{ } (2 \times (-1 + b) \text{ } \beta \text{ } \gamma + b \text{ } \beta \text{ } \delta + \beta_{z} \text{ } \delta) \text{ } \lambda + \delta^{2} \text{ } \lambda^{2} + (-1 + b) \text{ } \text{K}^{2} \text{ } \beta \text{ } (\beta \text{ } \gamma \text{ } (\text{ } (-1 + b) \text{ } \gamma + b \text{ } \delta) \text{ } - \beta_{z} \text{ } \delta \text{ } \lambda) 
                                                                                   (-1+b) K \beta ((-1+b) K \beta \gamma + \delta \lambda)
              Det[J[E*]]=
 \textit{Outf*J=} - \frac{\beta_z \gamma \delta^2 (K (\beta - b \beta) + \delta)^2 \lambda^2}{(-1 + b)^2 K \beta^2 ((-1 + b) K \beta \gamma + \delta \lambda)}
 Out[•]= 5
              a_{1} = \frac{K \delta (2 \times (-1 + b) \beta \gamma + b \beta \delta + \beta_{z} \delta) \lambda + \delta^{2} \lambda^{2} + (-1 + b) K^{2} \beta (\beta \gamma ((-1 + b) \gamma + b \delta) - \beta_{z} \delta \lambda)}{(-1 + b) \beta \gamma + b \beta \delta + \beta_{z} \delta \lambda)}
                                                                               (-1 + b) K \beta ((-1 + b) K \beta \gamma + \delta \lambda)
                 , a_2 = \left( \left( \delta \lambda \left( - \left( \left( -1 + b \right) \right) K^2 \beta^2 \left( \left( -1 + b \right) \left( \beta + \beta_z \right) \gamma + b \beta_z \delta \right) \right) + \left( b \beta + \beta_z \right) \delta^2 \lambda + b \beta_z \delta \right) \right)
                                 \mathsf{K}\,\beta\;(\beta_{\mathsf{z}}\,\delta\;(\;(-\mathsf{1}+\mathsf{b})\;\gamma+\mathsf{b}\;\delta+\lambda-\mathsf{b}\;\lambda)\;+\;(-\mathsf{1}+\mathsf{b})\;\beta\;\gamma\;(\;(-\mathsf{1}+\mathsf{b})\;\gamma+\delta-\lambda+\mathsf{b}\;(\delta+\lambda)\;)\;)\;)\;)
                       ((-1+b)^{2} K \beta^{2} ((-1+b) K \beta \gamma + \delta \lambda))), a_{3}=
                  \left(\;\left(\;\left(\;\left(-\mathbf{1}+\mathbf{b}\right)\;\mathsf{K}\;\beta-\delta\right)\;\delta\;\lambda\;\left(\delta^{2}\;\left(\;\left(-\mathbf{1}+\mathbf{b}\right)^{\;2}\;\beta\;\gamma-\mathbf{b}\;\beta_{z}\;\delta\right)\;\lambda^{2}+\;\left(-\mathbf{1}+\mathbf{b}\right)^{\;2}\;\mathsf{K}^{2}\;\beta^{2}\;\gamma\;\left(\;\left(-\mathbf{1}+\mathbf{b}\right)^{\;2}\;\beta\;\gamma^{2}+\beta_{z}\;\delta\;\lambda\right)\;+\right)\right)
                                  (-1 + b) K \beta \gamma \delta \lambda (2 (-1 + b)^{2} \beta \gamma - \beta_{z} ((-1 + b) \gamma + \delta - \lambda + b (\delta + \lambda)))))
                       \left(\;\left(-\mathbf{1}+\mathbf{b}\right)^{\;3}\;\mathsf{K}\;\beta^{2}\;\left(\;\left(-\mathbf{1}+\mathbf{b}\right)\;\mathsf{K}\;\beta\;\gamma+\delta\;\lambda\right)^{\;2}\right)\left)\quad\text{, }\mathsf{a}_{4}=-\frac{\;\beta_{z}\;\gamma\;\delta^{2}\;\left(\mathsf{K}\;\left(\beta-\mathsf{b}\;\beta\right)\;+\delta\right)^{\;2}\;\lambda^{2}}{\left(-\mathbf{1}+\mathsf{b}\right)^{\;2}\;\mathsf{K}\;\beta^{2}\;\left(\;\left(-\mathbf{1}+\mathsf{b}\right)\;\mathsf{K}\;\beta\;\gamma+\delta\;\lambda\right)^{\;2}}\right)
              H2(b0) = 0
              Denominator of H2 is (-1+b)^6 K^3 \beta^5 ((-1+b) K \beta \gamma + \delta \lambda)^4
  Out[ • ]= 11
```

Numerical values  $\epsilon$ =1:

```
cn=Join[cF1]; cnb=\{b\rightarrow 40\};
In[ • ]:=
          cb=NSolve[(\phi b4//.cn) == 0, b, WorkingPrecision \rightarrow 10]
          bM=Max[Table[Re[b/.cb[i]]],{i,Length[cb]}]];
          Print["bH=",bH=N[bM,30]]
          Print["b0=",b0/.cn//N]
          Print["E*",Es1//.cn/.cnb//N]
          Print["E+=",Em1//.cn/.cnb//N]
          Print["Eim=",Eim1//.cn/.cnb//N]
          Print["roots of Dis[b]=0:", bcE1=NSolve[(Dis//.cn)==0,b]]
          bc1=Chop[Evaluate[b/.bcE1[5]]];
          bc2=Chop[Evaluate[b/.bcE1[6]]];
          Print["b1*=", bc1]
          Print[" b2*=", bc2]
 Out[•]= \{\{b \to -258.7317419\}, \{b \to -0.01615999598\},
          \{b \rightarrow 0.060848063 - 10.686990738 \ \dot{\mathbb{1}} \}, \{b \rightarrow 0.060848063 + 10.686990738 \ \dot{\mathbb{1}} \},
          \{b \rightarrow 0.8448282668 - 0.9299250641 \pm \}, \{b \rightarrow 0.8448282668 + 0.9299250641 \pm \},
          \{b \to 0.8878046288\}, \{b \to 1.011494253\}, \{b \to 1.022996712\}, \{b \to 1.152364263\}\}
        bH=1.152364263
        b0=1.01149
        E * \{0.000294724, 0.0363426, 0.0221463, 0.\}
        E += \left\{0.00262408 + 5.51068 \times 10^{-19} \text{ i, } 0.0462057 + 8.67362 \times 10^{-18} \text{ i,} \right.
           0.021866 + 3.02367 \times 10<sup>-18</sup> \dot{\text{i}}, 0.0462057 + 8.67362 \times 10<sup>-18</sup> \dot{\text{i}} \right\}
        \text{Eim} = \left\{ 0.114678 - 9.26732 \times 10^{-17} \text{ i, } 0.263221 - 2.77556 \times 10^{-17} \text{ i, } \right.
           0.0143012 + 8.58446 \times 10^{-18} i, 0.263221 - 2.77556 \times 10^{-17} i
        roots of Dis[b]=0:
          \{\{b \rightarrow -126.518\}, \{b \rightarrow -63.\}, \{b \rightarrow -63.\}, \{b \rightarrow -24.5518\}, \{b \rightarrow 29.361\}, \{b \rightarrow 45.9232\}\}
        b1 * = 29.361
          b2 * = 45.9232
```

#### 4-3) Bifurcation diagrams:

Numerical solution of the stability (Bifurcation diagram) wrt y:

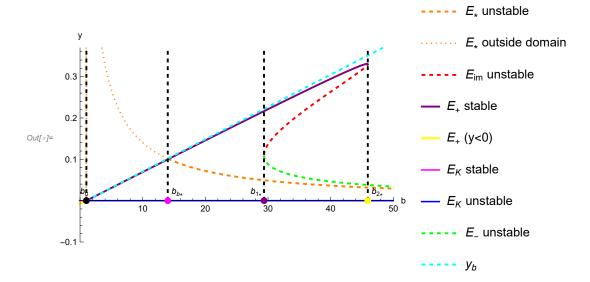
```
ln[∗]= (*Checks on the stability of the fixed points**)
     Print["Eigenvalues of E* when b=20 and when b=40, respectively "]
     Eigenvalues[jEs1] //. cF1 /. b \rightarrow 20 // N
     Eigenvalues[jEs1] //. cF1 /. b \rightarrow 40 // N
     Print["Eigenvalues of E+ when b=40"]
     Chop[Eigenvalues[jEp1 //. cF1 /. b \rightarrow 20 // N]]
     Print["Eigenvalues of Eim when b=40"]
     Chop[Eigenvalues[jEim1 //. cF1 /. b \rightarrow 40 // N]]
     Print["Eigenvalues of E- between b1* and b2* "]
     Chop[Eigenvalues[jEm1 //. cF1 /. b \rightarrow 35 // N]]
     Print["Eigenvalues of E- between 0 and b1*"]
     Chop[Eigenvalues[jEm1 //. cF1 /. b \rightarrow 20 // N]]
     Eigenvalues of E∗ when b=20 and when b=40, respectively
Out_{e} = \{0.0718263, -0.586224, 0.0257451 - 0.0774375 i, 0.0257451 + 0.0774375 i\}
Out[*]= \{0.0363426, -0.555066, 0.017069 - 0.082122 i, 0.017069 + 0.082122 i\}
     Eigenvalues of E+ when b=40
Out = \{-36.8126, -0.800277, -0.073135 + 0.126319 \pm, -0.073135 - 0.126319 \pm \}
     Eigenvalues of Eim when b=40
Out_{e} = \{-24.7847, -0.377551, -0.150826 + 0.260466 i, -0.150826 - 0.260466 i\}
     Eigenvalues of E- between b1* and b2*
Out_{e} = \{-4.10357, 0.346228, -0.0664887 + 0.180685 \, i, -0.0664887 - 0.180685 \, i\}
     Eigenvalues of E- between 0 and b1\star
Out[\bullet]= { -0.840551 + 1.00512 i, 0.242338 <math>-0.343832 i,
      0.0933864 + 0.157103 i, -0.0937105 + 0.0144354 i}
```

```
cut=cF1;bL=50;max=0.37;
In[ • ]:=
                  b0n=b0//.cn;
                  b1=Chop[bbs//.cF1//N];
                  Print["b0=",b0n//N, " ,b_{b*}=", b1, ", b1*=", bc1, " , b2*=", bc2]
                  lin1=Line[{{ bc1,0},{ bc1,max}}];
                  li1=Graphics[{Thick,Black,Dashed,lin1}];
                  lin2=Line[{{ bc2,0},{ bc2,max}}];
                  li2=Graphics[{Thick,Black,Dashed,lin2}];
                  lin3=Line[{{ b0n,0},{ b0n,max}}];
                  li3=Graphics[{Thick,Black,Dashed,lin3}];
                  lin4=Line[{{ b1,0},{ b1,max}}];
                  li4=Graphics[{Thick,Black,Dashed,lin4}];
                  pyb=Plot[{yb}//.cut,{b,0,bL},PlotStyle→{Dashed,Thick,Cyan},
                  PlotRange \rightarrow { {0,200}, {0,max}}, PlotLegends \rightarrow { "y_b "}];
                   (*pym1n=Plot[{ym}//.cut,{b,0,bL},PlotStyle→{Green,Thick},PlotRange→All,PlotPoints→200,
                  PlotLegends→{"E_ unstable"}];*)
                  pym=Plot[\{ym\}//.cut,\{b,0,bL\},PlotStyle\rightarrow \{Green,Dashed,Thick\},PlotRange\rightarrow All,PlotPoints\rightarrow 180,BlotRange\rightarrow All,PlotPoints\rightarrow 180,BlotRange\rightarrow All,PlotPoints\rightarrow 180,BlotRange\rightarrow All,PlotPoints\rightarrow 180,BlotRange\rightarrow All,PlotRange\rightarrow 180,BlotRange\rightarrow 180
                  PlotLegends→{"E_ unstable"}];
                  pyK1=Plot[0,\{b,0,b0n\},PlotStyle\rightarrow\{Magenta\},PlotRange\rightarrow All,PlotLegends\rightarrow\{"E_K stable"\}];
                  pyK2=Plot[0,\{b,b0n,bL\},PlotStyle\rightarrow\{Blue\},PlotRange\rightarrowAll,PlotLegends\rightarrow\{"E_K unstable"\}];
                  pyi=Plot[{yi}//.cut,{b,0, bL},PlotStyle→{Red,Dashed,Thick},PlotRange→All,
                  PlotLegends→{"E<sub>im</sub> unstable"}];
                  pyp=Plot[\{yp\}//.cut,\{b,b0n,bL\},PlotStyle \rightarrow \{Purple, Thick\},PlotRange \rightarrow All,
                  PlotLegends→{"E, stable"}];
                  pypn=Plot[{yp}//.cut,{b,0,b0n},PlotStyle→{Yellow, Thick},PlotRange→All,
                  PlotLegends \rightarrow {"E, (y<0)"}];
                  N[{yp}/.cut/.b\rightarrow 40,20] (*check*)
                  Print["Q(yp) at b0 is "]
                  Qy/.y→yp/.b→b0//FullSimplify
                  Show[pyp,pyb,li3,li1,li2,li4];
                  pys1=Plot[\{ys\}//.cut,\{b,0,b1\},PlotStyle\rightarrow\{0range,\ Dotted\},
                  PlotRange→{{0,200},{0,max}},
                  PlotLegends→{"E<sub>*</sub> outside domain"}];
                  pys2=Plot[{ys}//.cut,{b,b1,bL},PlotStyle→{Orange,Thick,Dashed},
                  PlotRange→{{0,200},{0,max}},
                  PlotLegends→{"E<sub>*</sub> unstable"}];
                  Print["y*'(b0)=",D[ys,b]/.b→b0n//.cut//N//FullSimplify]
                  Chop[ys/.b→b0n//.cut//N](*Check*);
                  bifep1=Show[{pys2,pys1,pyi,pyp,pypn,pyK1,pyK2,pym,pyb,li3,li1,li2,li4},
                  Epilog→{Text["b<sub>0</sub>",Offset[{-2,10},{ b0n//.cut,0}]],{PointSize[Large],
                  Style[Point[{ b0n//.cut,0}],Black]},
                  Text["b<sub>1*</sub>",Offset[{-8,10},{ bc1,0}]],{PointSize[Large],
                  Style[Point[{ bc1,0}],Purple]},
                  Text["b2*",Offset[{10,10},{ bc2,0}]],{PointSize[Large],
                  Style[Point[{ bc2,0}], Yellow]}, Text["b<sub>b*</sub>", Offset[{10,10}, { b1,0}]], {PointSize[Large],
                  Style[Point[{ b1,0}],Magenta]},AxesLabel \rightarrow {"b","y"},PlotRange \rightarrow {{-0.2,bL},{-0.1,max}}]
                  Export["EriB.pdf",bifep1]
```

```
b0=1.01149 ,b_{b*}=14.0011, b1*=29.361 , b2*=45.9232
Out[\circ]= \{0.29448140956728204616 + <math>0.\times10^{-21} i\}
```

$$Q\left(yp\right) \text{ at b0 is}$$
 Out[\*]= 0

y \* (b0) = 86.3256



Out[ ]= EriB.pdf

(x,b)-Bifurcation diagram:

Determination of the endemic points with respect to x when  $\epsilon$ =1:

$$ln[\circ]:= Solve[((y1) /. vex /. y \rightarrow yex) == 0, z]$$

$$Out[\circ] = \left\{ \left\{ z \rightarrow \frac{-c \, \gamma - \frac{c \, x \, \lambda}{\kappa} - \beta_z \, \sqrt{\frac{4 \, c \, \beta_y \, \left( x \, \lambda - \frac{x^2 \, \lambda}{\kappa} \right)}{\beta_z} + \left( -\frac{c \, \gamma}{\beta_z} - \frac{c \, x \, \lambda}{\kappa \, \beta_z} \right)^2} \right\}$$

$$\left\{ z \rightarrow \frac{-c \, \gamma - \frac{c \, x \, \lambda}{\kappa} + \beta_z \, \sqrt{\frac{4 \, c \, \beta_y \, \left( x \, \lambda - \frac{x^2 \, \lambda}{\kappa} \right)}{\beta_z} + \left( -\frac{c \, \gamma}{\beta_z} - \frac{c \, x \, \lambda}{\kappa \, \beta_z} \right)^2} \right\}$$

$$\left\{ z \rightarrow \frac{-c \, \gamma - \frac{c \, x \, \lambda}{\kappa} + \beta_z \, \sqrt{\frac{4 \, c \, \beta_y \, \left( x \, \lambda - \frac{x^2 \, \lambda}{\kappa} \right)}{\beta_z} + \left( -\frac{c \, \gamma}{\beta_z} - \frac{c \, x \, \lambda}{\kappa \, \beta_z} \right)^2} \right\}$$

```
yex=c z/\beta z; (*Frome Solve[(z1/z/.cep1)==0,y]*)
In[ • ]:=
       Print["ye(x)=",yex]
        Print["ve(x)="]
        vex=Solve[(x1/x)==0,v][[1]]
       Print["ze(x)="]
        zex=Solve[((y1)/.vex/.y\rightarrow yex)=0,z][1]]//FullSimplify
        (v1/.vex/.y→yex/.zex );
        xex=Solve[((v1/.vex/.y→yex/.zex )/.cF1) ==0,x,Cubics→False];
        (*or // ComplexExpand[\#, TargetFunctions \rightarrow {Re, Im}] &*)
        (*so long time when it's not numeric**)
        Print["Number of endemic x"]
        Length[xex]
        Print["Numerical check"]
        xex/.b→40//N
```

$$ye(x) = \frac{c z}{\beta_z}$$

$$ve(x) = \frac{c (K - x - y) \lambda}{k \beta}$$

$$ze(x) = \frac{c (K - x - y) \lambda}{k \beta}$$

$$ze(x) = \frac{c (K - x - x) \lambda}{k \beta}$$

$$ze(x) = \frac{c (K - x) \lambda}{k \beta}$$

$$xe(x) = \frac{c (K - x) \lambda}{k \beta}$$

Print["Eigenvalues of E+ between b1\* and b2\*"] Chop[Eigenvalues[jEpx //. cF1 /. b  $\rightarrow$  42 // N]] Print["Eigenvalues of E- between b1\* and b2\* "] Chop[Eigenvalues[jEmx //. cF1 /. b  $\rightarrow$  40 // N]] Print["Eigenvalues of Eim between b0 and b1\*"] Chop[Eigenvalues[jEimx //. cF1 /. b  $\rightarrow$  20 // N]] Print["Eigenvalues of Eim between b1\* and b2\*"] Chop[Eigenvalues[jEimx //. cF1 /. b  $\rightarrow$  40 // N]]

Print["Eigenvalues of Eim after b2\*"]

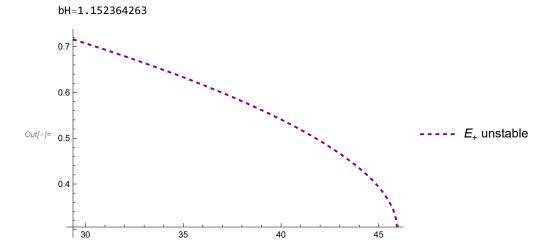
Chop[Eigenvalues[jEimx //. cF1 /. b  $\rightarrow$  80 // N]]

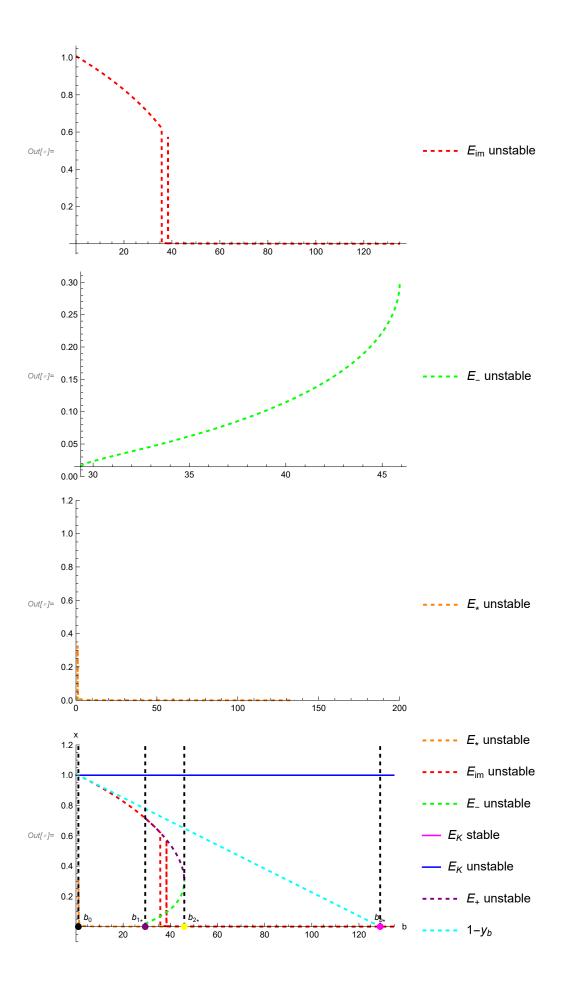
```
Eigenvalues of E*:
      between b0 and b1 \!\star
Out[*]= \{0.0950185, -0.606269, 0.0309604 - 0.074022 i, 0.0309604 + 0.074022 i\}
      between b1* and b2*
Out[*] = {0.0363426, -0.555066, 0.017069 -0.082122 i, 0.017069 + 0.082122 i}
     Eigenvalues of E+ between b1* and b2*
Out[\bullet]= {-22.7478, 0.942561 + 0.7947 i, 0.942561 - 0.7947 i, 0.792692}
     Eigenvalues of E- between b1* and b2*
Out[*]= \{-6.37039, 0.799512, 0.558507 + 0.38198 i, 0.558507 - 0.38198 i\}
     Eigenvalues of Eim between b0 and b1*
Out[\sigma]= {-36.7873, 1.03926 + 0.963099 i, 1.03926 - 0.963099 i, 0.329033}
     Eigenvalues of Eim between b1* and b2*
Out[*]= \{-0.802619, 0.144164 + 0.190903 \,\dot{\mathbb{1}}, 0.144164 - 0.190903 \,\dot{\mathbb{1}}, 0.0596342\}
     Eigenvalues of Eim after b2*
```

 $Out[*] = \{-0.601147, 0.062694 + 0.153094 i, 0.062694 - 0.153094 i, 0.027413\}$ 

```
cut=cF1;bL=135;max=1.2;
In[ • ]:=
                 b0n=b0//.cn;
                 b1=Chop[b/.Solve[(Es1[1]) == (1-yb),b][2]]//.cF1//N]
                 Print["bH=",bH]
                 lin1=Line[{{ bc1,0},{ bc1,max}}];
                 li1=Graphics[{Thick,Black,Dashed,lin1}];
                 lin2=Line[{{ bc2,0},{ bc2,max}}];
                 li2=Graphics[{Thick,Black,Dashed,lin2}];
                 lin3=Line[{{ b0n,0},{ b0n,max}}];
                 li3=Graphics[{Thick,Black,Dashed,lin3}];
                 lin4=Line[{{ b1,0},{ b1,max}}];
                 li4=Graphics[{Thick,Black,Dashed,lin4}];
                 pxm2=Plot[\{x/.xex[3]\}//.cut,\{b,0,bL\},PlotStyle\rightarrow\{Purple,Dashed,Thick\},PlotRange\rightarrow All,PlotPoints,PlotRange,PlotPoints,PlotRange,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,PlotPoints,Plot
                 PlotLegends→{"E, unstable"}]
                 pxK1=Plot[K//.cut, \{b,0,b0n\}, PlotStyle \rightarrow \{Magenta\}, PlotRange \rightarrow All, PlotLegends \rightarrow \{"E_K stable"\}];
                 pxK2=Plot[K//.cut, \{b,b0n,bL\}, PlotStyle \rightarrow \{Blue\}, PlotRange \rightarrow All, PlotLegends \rightarrow \{"E_K unstable"\}];
                 pxi=Plot[{x/.xex[1]}}//.cut,{b,0, bL},PlotStyle→{Red, Dashed,Thick},PlotRange→All,
                 PlotLegends \rightarrow \{"E_{im} unstable"\}]
                 pxp=Plot[{x/.xex[2]}//.cut,{b,0,bL},PlotStyle→{Green,Dashed, Thick},PlotRange→All,
                 PlotLegends→{"E_ unstable"}]
                 pxs2=Plot[{x/.sol[3]}//.cut,{b,0,bL},PlotStyle\rightarrow{Orange,Thick,Dashed},
                 PlotRange \rightarrow \{\{0,200\},\{0,\max\}\},
                 {\tt PlotLegends} {\to} \{{\tt "E}_{\star} \ {\tt unstable"} \} ]
                 pxb=Plot[{1-yb}//.cut,{b,0,bL},PlotStyle→{Dashed,Thick,Cyan},
                 PlotRange \rightarrow { {0,200}, {0,max}}, PlotLegends \rightarrow {"1-y_b"}];
                 bifep1=Show[{pxs2,pxi,pxp,pxK1,pxK2,pxm2,pxb,li3,li1,li2,li4},
                 \label{eq:continuous} \begin{split} & Epilog \rightarrow \{ Text["b_0", Offset[\{10,10\}, \{ b0n//.cut, 0\}]], \{ PointSize[Large], \} \end{split}
                 Style[Point[{ b0n//.cut,0}],Black]},
                Text["b_{1\star}",Offset[\{-8,10\},\{\ bc1,0\}]],\{PointSize[Large],
                 Style[Point[{ bc1,0}],Purple]},
                 Text["b2*",Offset[{10,10},{ bc2,0}]],{PointSize[Large],
                 Style[Point[{ bc2,0}], Yellow]}, Text["b<sub>b*</sub>", Offset[{0,10}, { b1,0}]], {PointSize[Large],
                 Style[Point[{ b1,0}],Magenta]},AxesLabel \rightarrow {"b","x"},PlotRange \rightarrow {{-0.1,bL},{-0.1,max}}]
                 Export["Bif1x.pdf",bifep1]
```

#### Out[-] = 128.989





Out[\*]= Bif1x.pdf