The Neutrality of the invasion reproduction number for the Two-Slot Model

A Mathematica Notebook for Appendix D in "A story of viral co-infection, co-transmission and co-feeding in ticks: how to compute an invasion reproduction number" by Belluccini, Lin, Williams, Lou, Vatansever, Lopez-Garcia, Lythe, Leitner, Romero-Severson, Molina-Paris.

1. Model Setting

1.1 Variables

- Susceptible tick: m_0
- Strain-1 singly-infected tick: m_1
- Strain-2 singly-infected tick: m_2
- Strain 1 & 2 co-infected tick: m_C, 2 units of viral load
- Strain-1 doubly-infected tick: M_1, 2 units of viral load
- Strain-2 doubly-infected tick: M_2, 2 units of viral load

1.2 Parameters

- single transmission of strain 1: $m_0 + m_1 \to m_1 + m_1$ at rate α_1
- single transmission of strain 2: $m_0 + m_2 \to m_2 + m_2$ at rate α_2
- probability that co-infected host only transmits one unit viral load, either strain 1 or strain 2: $1 - \epsilon_C$
- probability that strain-1 doubly-infected host only transmits one unit viral load: $1 - \epsilon_1$
- probability that strain-2 doubly-infected host only transmits one unit viral load: $1 - \epsilon_2$
- rate of one unit viral load of strain-1 transmitted by a co-infected host: δ_1
- rate of one unit viral load of strain-2 transmitted by a co-infected host: δ_2
- rate of one unit viral load of strain-1 transmitted by a strain-1 doubly-infected host: κ_1
- rate of one unit viral load of strain-2 transmitted by a strain-2 doubly-infected host: κ_2
- natural birth rate: Φ

- death rate of susceptible and singly-infected: ν_0, ν_1, ν_2
- death rate of co-infected and doubly-infected: ν_C, υ_1, υ_2

1.3 Transmission events and force-of-infections

- Single transmission + Single infection
  - $m_0 + m_1 \to m_1 + m_1 : \alpha_1$
  - $m_0 + m_2 \to m_2 + m_2 : \alpha_2$
  - $m_1 + m_1 \to M_1 + m_1 : \alpha_1$
  - $m_1 + m_2 \to m_C + m_2 : \alpha_2$
  - $m_2 + m_1 \to m_C + m_1 : \alpha_1$
  - $m_2 + m_2 \to M_2 + m_2 : \alpha_2$
  - $m_0 + M_1 \to m_1 + M_1 : (1 - \epsilon_1)\, 2 \frac{\kappa_1}{\kappa_1+\kappa_1} (\kappa_1 + \kappa_1) = (1 - \epsilon_1)\, 2\, \kappa_1$
  - $m_0 + M_2 \to m_2 + M_2 : (1 - \epsilon_2)\, 2 \frac{\kappa_2}{\kappa_2+\kappa_2} (\kappa_2 + \kappa_2) = (1 - \epsilon_2)\, 2\, \kappa_2$
  - $m_0 + m_C \to m_1 + m_C : (1 - \epsilon_C) \frac{\delta_1}{\delta_1+\delta_2} (\delta_1 + \delta_2) = (1 - \epsilon_C)\, \delta_1$
  - $m_0 + m_C \to m_2 + m_C : (1 - \epsilon_C) \frac{\delta_2}{\delta_1+\delta_2} (\delta_1 + \delta_2) = (1 - \epsilon_C)\, \delta_2$
  - $m_1 + M_1 \to M_1 + M_1 : (1 - \epsilon_1)\, 2 \frac{\kappa_1}{\kappa_1+\kappa_1} (\kappa_1 + \kappa_1) = (1 - \epsilon_1)\, 2\, \kappa_1$
  - $m_1 + M_2 \to m_C + M_2 : (1 - \epsilon_2)\, 2 \frac{\kappa_2}{\kappa_2+\kappa_2} (\kappa_2 + \kappa_2) = (1 - \epsilon_2)\, 2\, \kappa_2$
  - $m_1 + m_C \to M_1 + m_C : (1 - \epsilon_C) \frac{\delta_1}{\delta_1+\delta_2} (\delta_1 + \delta_2) = (1 - \epsilon_C)\, \delta_1$
  - $m_1 + m_C \to m_C + m_C : (1 - \epsilon_C) \frac{\delta_2}{\delta_1+\delta_2} (\delta_1 + \delta_2) = (1 - \epsilon_C)\, \delta_2$
  - $m_2 + M_1 \to m_C + M_1 : (1 - \epsilon_1)\, 2 \frac{\kappa_1}{\kappa_1+\kappa_1} (\kappa_1 + \kappa_1) = (1 - \epsilon_1)\, 2\, \kappa_1$
  - $m_2 + M_2 \to M_2 + M_2 : (1 - \epsilon_2)\, 2 \frac{\kappa_2}{\kappa_2+\kappa_2} (\kappa_2 + \kappa_2) = (1 - \epsilon_2)\, 2\, \kappa_2$
  - $m_2 + m_C \to m_C + m_C : (1 - \epsilon_C) \frac{\delta_1}{\delta_1+\delta_2} (\delta_1 + \delta_2) = (1 - \epsilon_C)\, \delta_1$
  - $m_2 + m_C \to M_2 + m_C : (1 - \epsilon_C) \frac{\delta_2}{\delta_1+\delta_2} (\delta_1 + \delta_2) = (1 - \epsilon_C)\, \delta_2$
- Co-transmission + Single infection
  - $m_1 + m_C \to M_1 + m_C : \epsilon_C \frac{\delta_1}{\delta_1+\delta_2} (\delta_1 + \delta_2) = \epsilon_C\, \delta_1$
  - $m_1 + m_C \to m_C + m_C : \epsilon_C \frac{\delta_2}{\delta_1+\delta_2} (\delta_1 + \delta_2) = \epsilon_C\, \delta_2$
  - $m_1 + M_1 \to M_1 + M_1 : \epsilon_1\, 2 \frac{\kappa_1}{\kappa_1+\kappa_1} (\kappa_1 + \kappa_1) = \epsilon_1\, 2\, \kappa_1$
  - $m_1 + M_2 \to m_C + M_2 : \epsilon_2\, 2 \frac{\kappa_2}{\kappa_2+\kappa_2} (\kappa_2 + \kappa_2) = \epsilon_2\, 2\, \kappa_2$
  - $m_2 + m_C \to m_C + m_C : \epsilon_C \frac{\delta_1}{\delta_1+\delta_2} (\delta_1 + \delta_2) = \epsilon_C\, \delta_1$
  - $m_2 + m_C \to M_2 + m_C : \epsilon_C \frac{\delta_2}{\delta_1+\delta_2} (\delta_1 + \delta_2) = \epsilon_C\, \delta_2$

- $m_2 + M_1 \to m_C + M_1 : \epsilon_1\, 2\, \frac{\kappa_1}{\kappa_1+\kappa_1} (\kappa_1 + \kappa_1) = \epsilon_1\, 2\, \kappa_1$
- $m_2 + M_2 \to M_2 + M_2 : \epsilon_2\, 2\, \frac{\kappa_2}{\kappa_2+\kappa_2} (\kappa_2 + \kappa_2) = \epsilon_2\, 2\, \kappa_2$

- Co-transmission + co-infection
  - $m_0 + m_C \to m_C + m_C : \epsilon_C\, 2\, \frac{\delta_1}{\delta_1+\delta_2} \frac{\delta_2}{\delta_1+\delta_2} (\delta_1 + \delta_2) = \epsilon_C \frac{2\,\delta_1\,\delta_2}{\delta_1+\delta_2}$
  - $m_0 + m_C \to M_1 + m_C : \epsilon_C \frac{\delta_1}{\delta_1+\delta_2} \frac{\delta_1}{\delta_1+\delta_2} (\delta_1 + \delta_2) = \epsilon_C \frac{\delta_1^2}{\delta_1+\delta_2}$
  - $m_0 + m_C \to M_2 + m_C : \epsilon_C \frac{\delta_2}{\delta_1+\delta_2} \frac{\delta_2}{\delta_1+\delta_2} (\delta_1 + \delta_2) = \epsilon_C \frac{\delta_2^2}{\delta_1+\delta_2}$
  - $m_0 + M_1 \to M_1 + M_1 : \epsilon_1\, 2\, \kappa_1$
  - $m_0 + M_2 \to M_2 + M_2 : \epsilon_2\, 2\, \kappa_2$

$\lambda_1 = \alpha_1\, m_1 + (1 - \epsilon_C)\, \delta_1\, m_C + 2\, (1 - \epsilon_1)\, \kappa_1\, M_1$;

$\lambda_2 = \alpha_2\, m_2 + (1 - \epsilon_C)\, \delta_2\, m_C + 2\, (1 - \epsilon_2)\, \kappa_2\, M_2$;

$\Lambda_1 = 2\, \epsilon_1\, \kappa_1\, M_1$; $\Lambda_2 = 2\, \epsilon_2\, \kappa_2\, M_2$;

$\lambda_{C1} = \epsilon_C\, \delta_1\, m_C$; $\lambda_{C2} = \epsilon_C\, \delta_2\, m_C$;

$\Lambda_C = \frac{2\, \epsilon_C\, \delta_1\, \delta_2\, m_C}{\delta_1 + \delta_2}$;

```
In[1]:= λ1[m0_, m1_, m2_, mC_, M1_, M2_] := α₁ m1 + δ₁ (1 - ϵC) mC + 2 κ₁ (1 - ϵ₁) M1
λ2[m0_, m1_, m2_, mC_, M1_, M2_] := α₂ m2 + δ₂ (1 - ϵC) mC + 2 κ₂ (1 - ϵ₂) M2
λC1[m0_, m1_, m2_, mC_, M1_, M2_] := ϵC δ₁ mC
λC2[m0_, m1_, m2_, mC_, M1_, M2_] := ϵC δ₂ mC
ΛC[m0_, m1_, m2_, mC_, M1_, M2_] := (2 ϵC δ₁ δ₂ mC)/(δ₁ + δ₂)
Λ1[m0_, m1_, m2_, mC_, M1_, M2_] := 2 ϵ₁ κ₁ M1
Λ2[m0_, m1_, m2_, mC_, M1_, M2_] := 2 ϵ₂ κ₂ M2
```

- Force-of-Infection summary:
  - $m_0 \to m_1 : \lambda_1$
  - $m_0 \to m_2 : \lambda_2$
  - $m_0 \to m_C : \Lambda_C$
  - $m_0 \to M_1 : \Lambda_1 + \frac{\delta_1}{\delta_1+\delta_2} \lambda_{C1}$
  - $m_0 \to M_2 : \Lambda_2 + \frac{\delta_2}{\delta_1+\delta_2} \lambda_{C2}$
  - $m_1 \to m_C : \lambda_2 + \Lambda_2 + \lambda_{C2}$
  - $m_1 \to M_1 : \lambda_1 + \Lambda_1 + \lambda_{C1}$
  - $m_2 \to m_C : \lambda_1 + \Lambda_1 + \lambda_{C1}$
  - $m_2 \to M_2 : \lambda_2 + \Lambda_2 + \lambda_{C2}$

1.4 Differential equations

$$\frac{dm_0}{dt} = \Phi - \nu_0\, m_0 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\, m_0$$

$$\frac{dm_1}{dt} = -\nu_1\, m_1 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\, m_1 + \lambda_1\, m_0$$

$$\frac{dm_2}{dt} = -\nu_2\, m_2 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\, m_2 + \lambda_2\, m_0$$

$$\frac{dm_C}{dt} = -\nu_C\, m_C + (\lambda_2 + \lambda_{C2} + \Lambda_2)\, m_1 + (\lambda_1 + \lambda_{C1} + \Lambda_1)\, m_2 + \Lambda_C\, m_0$$

$$\frac{dM_1}{dt} = -\upsilon_1\, M_1 + (\lambda_1 + \lambda_{C1} + \Lambda_1)\, m_1 + \left(\frac{\delta_1}{\delta_1 + \delta_2}\, \lambda_{C1} + \Lambda_1\right) m_0$$

$$\frac{dM_2}{dt} = -\upsilon_2\, M_2 + (\lambda_2 + \lambda_{C2} + \Lambda_2)\, m_2 + \left(\frac{\delta_2}{\delta_1 + \delta_2}\, \lambda_{C2} + \Lambda_2\right) m_0$$

In[8]:=
```
dm0dt[m0_, m1_, m2_, mC_, M1_, M2_] :=
  Φ - ν0 * m0 - (λ1[m0, m1, m2, mC, M1, M2] + λ2[m0, m1, m2, mC, M1, M2] +
      λC1[m0, m1, m2, mC, M1, M2] + λC2[m0, m1, m2, mC, M1, M2] +
      Λ1[m0, m1, m2, mC, M1, M2] + Λ2[m0, m1, m2, mC, M1, M2]) m0;
dm1dt[m0_, m1_, m2_, mC_, M1_, M2_] := -ν1 * m1 -
   (λ1[m0, m1, m2, mC, M1, M2] + λ2[m0, m1, m2, mC, M1, M2] + λC1[m0, m1, m2, mC, M1, M2] +
      λC2[m0, m1, m2, mC, M1, M2] + Λ1[m0, m1, m2, mC, M1, M2] +
      Λ2[m0, m1, m2, mC, M1, M2]) m1 + λ1[m0, m1, m2, mC, M1, M2] * m0;
dm2dt[m0_, m1_, m2_, mC_, M1_, M2_] := -ν2 * m2 -
   (λ1[m0, m1, m2, mC, M1, M2] + λ2[m0, m1, m2, mC, M1, M2] + λC1[m0, m1, m2, mC, M1, M2] +
      λC2[m0, m1, m2, mC, M1, M2] + Λ1[m0, m1, m2, mC, M1, M2] +
      Λ2[m0, m1, m2, mC, M1, M2]) m2 + λ2[m0, m1, m2, mC, M1, M2] * m0;
dmCdt[m0_, m1_, m2_, mC_, M1_, M2_] := -νC * mC +
  (λ2[m0, m1, m2, mC, M1, M2] + λC2[m0, m1, m2, mC, M1, M2] + Λ2[m0, m1, m2, mC, M1, M2])
   m1 + (λ1[m0, m1, m2, mC, M1, M2] + λC1[m0, m1, m2, mC, M1, M2] +
     Λ1[m0, m1, m2, mC, M1, M2]) m2 + ΛC[m0, m1, m2, mC, M1, M2] * m0
dM1dt[m0_, m1_, m2_, mC_, M1_, M2_] := -υ1 * M1 +
   (λ1[m0, m1, m2, mC, M1, M2] + λC1[m0, m1, m2, mC, M1, M2] + Λ1[m0, m1, m2, mC, M1, M2])
    m1 + (Λ1[m0, m1, m2, mC, M1, M2] + δ1/(δ1 + δ2) * λC1[m0, m1, m2, mC, M1, M2]) m0;
dM2dt[m0_, m1_, m2_, mC_, M1_, M2_] := -υ2 * M2 +
   (λ2[m0, m1, m2, mC, M1, M2] + λC2[m0, m1, m2, mC, M1, M2] + Λ2[m0, m1, m2, mC, M1, M2])
    m2 + (Λ2[m0, m1, m2, mC, M1, M2] + δ2/(δ1 + δ2) * λC2[m0, m1, m2, mC, M1, M2]) m0;
```

2. Basic reproduction number of the resident strain V_1

The Virus-Free Equilibrium (VFE) is $E_0 = \left(\frac{\Phi}{\nu_0},\ 0, 0, 0, 0, 0\right)$. We first consider the sub-system for resident strain V_1.

$$\frac{dm_0}{dt} = \Phi - \nu_0\, m_0 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\, m_0$$
$$\frac{dm_1}{dt} = -\nu_1\, m_1 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\, m_1 + \lambda_1\, m_0$$
$$\frac{dM_1}{dt} = -\upsilon_1\, M_1 + (\lambda_1 + \lambda_{C1} + \Lambda_1)\, m_1 + \left(\frac{\delta_1}{\delta_1 + \delta_2}\, \lambda_{C1} + \Lambda_1\right) m_0$$

We then have the Jacobian matrix J and the F, V matrices:

In[14]:=
```
J = FullSimplify[
    D[{dm1dt[m0, m1, m2, mC, M1, M2],
      dM1dt[m0, m1, m2, mC, M1, M2]},
     {{m1, M1}}]] /. {m0 → Φ/ν0, m1 → 0, m2 → 0, mC → 0, M1 → 0, M2 → 0} // MatrixForm
```

Out[14]//MatrixForm=
$$\begin{pmatrix} \frac{\Phi\,\alpha_1}{\nu_0} - \nu_1 & -\frac{2\,\Phi\,(-1+\epsilon_1)\,\kappa_1}{\nu_0} \\ 0 & \frac{2\,\Phi\,\epsilon_1\,\kappa_1}{\nu_0} - \upsilon_1 \end{pmatrix}$$

In[15]:=
```
F = {{Φ α1/ν0, 2 Φ κ1 (1 - ϵ1)/ν0}, {0, 2 Φ ϵ1 κ1/ν0}};
T = {{ν1, 0}, {0, υ1}};
```

We then can compute the eigenvalues of $F[V]^{-1}$ to get the basic reproduction number.

In[17]:=
```
Eigenvalues[F.Inverse[T]] // FullSimplify
```

Out[17]=
$$\left\{\frac{2\,\Phi\,\epsilon_1\,\kappa_1}{\nu_0\,\upsilon_1}, \frac{\Phi\,\alpha_1}{\nu_0\,\nu_1}\right\}$$

We define the following notations for the components of the basic reproduction number, and the basic reproduction number of V_1 is $R_1^{'} = \max\left\{\frac{\Phi\,\alpha_1}{\nu_0\,\nu_1}, \frac{2\,\Phi\,\epsilon_1\,\kappa_1}{\nu_0\,\upsilon_1}\right\}$.

In[18]:=
```
r1 = Φ α1/(ν0 ν1); r11 = 2 Φ ϵ1 κ1/(ν0 υ1);
```

Without loss of generality, we assume $\nu_0 = \nu_1 = \nu_2 = \nu_C = \upsilon_1 = \upsilon_2 = \nu$, such that we can have the V_1 basic reproduction number as:

In[19]:=
```
R1[Φ_, ν_, α_, ϵ_, κ_] := Max[Φ α/ν^2, 2 Φ ϵ κ/ν^2];
```

3. Invasive reproduction number of strain-2

3.1 Endemic Equilibrium of the resident strain $E_1^{'}$

We first compute the strain-1 equilibrium E_1 for the sub-system at $m_2 = 0$, $m_C = 0$, and $M_2 = 0$, and with the assumption $v_0 = v_1 = v_2 = \sigma_C = \sigma_1 = \sigma_2 = v$:

$$\frac{dm_0}{dt} = \Phi - \nu\, m_0 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\, m_0 = 0$$

$$\frac{dm_1}{dt} = -\nu\, m_1 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\, m_1 + \lambda_1\, m_0 = 0$$

$$\frac{dM_1}{dt} = -\nu\, M_1 + (\lambda_1 + \lambda_{C1} + \Lambda_1)\, m_1 + \left(\frac{\delta_1}{\delta_1 + \delta_2}\, \lambda_{C1} + \Lambda_1\right) m_0 = 0$$

In[20]:=

$$E1 = \{\text{FullSimplify}[\text{dm0dt}[m_0, m_1, m_2, m_C, M_1, M_2] == 0], \text{FullSimplify}[\text{dm1dt}[m_0, m_1, m_2, m_C, M_1, M_2] == 0], \text{FullSimplify}[\text{dM1dt}[m_0, m_1, m_2, m_C, M_1, M_2] == 0]\} \mathbin{/.} \{m_2 \to 0, m_C \to 0, M_2 \to 0\} \mathbin{/.} \{\nu_0 \to \nu, \nu_1 \to \nu, \upsilon_1 \to \nu\}$$

Out[20]=

$$\{\Phi == m_0\, (\nu + m_1\, \alpha_1 + 2\, M_1\, \kappa_1),\; m_0\, (m_1\, \alpha_1 - 2\, M_1\, (-1 + \epsilon_1)\, \kappa_1) == m_1\, (\nu + m_1\, \alpha_1 + 2\, M_1\, \kappa_1),\; m_1^2\, \alpha_1 + 2\, m_1\, M_1\, \kappa_1 + 2\, m_0\, M_1\, \epsilon_1\, \kappa_1 == \nu\, M_1\}$$

We formulate M_1 as a function of m_0 and m_1, from the first equation:

In[21]:=

$$\text{Solve}[\Phi == m_0\, (\nu + m_1\, \alpha_1 + 2\, M_1\, \kappa_1), M_1] \mathbin{//} \text{FullSimplify}$$

Out[21]=

$$\left\{\left\{M_1 \to \frac{\Phi - m_0\, (\nu + m_1\, \alpha_1)}{2\, m_0\, \kappa_1}\right\}\right\}$$

We formulate M_1 as a function of m_0 and m_1, from the second equation:

In[22]:=

$$\text{Solve}[m_0\, (m_1\, \alpha_1 - 2\, M_1\, (-1 + \epsilon_1)\, \kappa_1) == m_1\, (\nu + m_1\, \alpha_1 + 2\, M_1\, \kappa_1), M_1] \mathbin{//} \text{FullSimplify}$$

Out[22]=

$$\left\{\left\{M_1 \to -\frac{m_1\, (\nu + (-m_0 + m_1)\, \alpha_1)}{2\, (m_1 + m_0\, (-1 + \epsilon_1))\, \kappa_1}\right\}\right\}$$

By setting the two above expressions equal, we get the expression of m_1 as a function of m_0:

In[23]:=

$$\text{Solve}\left[\frac{\Phi - m_0\, (\nu + m_1\, \alpha_1)}{2\, m_0\, \kappa_1} == -\frac{m_1\, (\nu + (-m_0 + m_1)\, \alpha_1)}{2\, (m_1 + m_0\, (-1 + \epsilon_1))\, \kappa_1}, m_1\right] \mathbin{//} \text{FullSimplify}$$

Out[23]=

$$\left\{\left\{m_1 \to \frac{m_0\, (\Phi - \nu\, m_0)\, (-1 + \epsilon_1)}{-\Phi + m_0^2\, \alpha_1\, \epsilon_1}\right\}\right\}$$

By inserting the expression of m_1 into either expression of M_1, we then get the expression of M_1 as a function of m_0 only:

In[24]:=

$$\left(\frac{\Phi - m_0\, (\nu + m_1\, \alpha_1)}{2\, m_0\, \kappa_1}\right) \mathbin{/.} \left\{m_1 \to \frac{m_0\, (\Phi - \nu\, m_0)\, (-1 + \epsilon_1)}{-\Phi + m_0^2\, \alpha_1\, \epsilon_1}\right\} \mathbin{//} \text{FullSimplify}$$

Out[24]=

$$-\frac{(\Phi - \nu\, m_0)\, \left(\Phi - m_0^2\, \alpha_1\right)}{2\, m_0\, \left(-\Phi + m_0^2\, \alpha_1\, \epsilon_1\right)\, \kappa_1}$$

In[25]:= $\left(-\frac{m_1\ (\nu + (-m_0 + m_1)\ \alpha_1)}{2\ (m_1 + m_0\ (-1 + \epsilon_1))\ \kappa_1}\right)$ /. $\left\{m_1 \to \frac{m_0\ (\Phi - \nu\ m_0)\ (-1 + \epsilon_1)}{-\Phi + m_0^2\ \alpha_1\ \epsilon_1}\right\}$ // FullSimplify

Out[25]=

$$-\frac{(\Phi - \nu\ m_0)\ \left(\Phi - m_0^2\ \alpha_1\right)}{2\ m_0\ \left(-\Phi + m_0^2\ \alpha_1\ \epsilon_1\right)\ \kappa_1}$$

In the third equation, replacing m_1 and M_1 by their expressions as a function of m_0 only, we then get an equation regarding m_0 only:

In[26]:= $(2\ m_0\ M_1\ \epsilon_1\ \kappa_1 + m_1\ (m_1\ \alpha_1 + 2\ M_1\ \kappa_1) == \nu\ M_1)$ /.

$\left\{m_1 \to \frac{m_0\ (\Phi - \nu\ m_0)\ (-1 + \epsilon_1)}{-\Phi + m_0^2\ \alpha_1\ \epsilon_1},\ M_1 \to -\frac{(\Phi - \nu\ m_0)\ \left(\Phi - m_0^2\ \alpha_1\right)}{2\ m_0\ \left(-\Phi + m_0^2\ \alpha_1\ \epsilon_1\right)\ \kappa_1}\right\}$ // FullSimplify

Out[26]=

$$\frac{(\Phi - \nu\ m_0)\ \left(-\nu\ \Phi + \nu\ m_0^2\ \alpha_1 + 2\ m_0\ (\Phi - m_0\ (\nu + (-\nu + m_0\ \alpha_1)\ \epsilon_1))\ \kappa_1\right)}{m_0\ \left(-\Phi + m_0^2\ \alpha_1\ \epsilon_1\right)\ \kappa_1} == 0$$

Since $m_0 = \frac{\Phi}{\nu}$ is the DFE and we only want the EE, we need to solve the second term (i.e., a cubic term) in the numerator:

In[27]:= Series$\left[\left(-\nu\ \Phi + \nu\ m_0^2\ \alpha_1 + 2\ m_0\ (\Phi - m_0\ (\nu + (-\nu + m_0\ \alpha_1)\ \epsilon_1))\ \kappa_1\right),\ \{m_0,\ 0,\ 3\}\right]$

Out[27]=

$$-\nu\ \Phi + 2\ \Phi\ \kappa_1\ m_0 + (\nu\ \alpha_1 + 2\ (-\nu + \nu\ \epsilon_1)\ \kappa_1)\ m_0^2 - 2\ (\alpha_1\ \epsilon_1\ \kappa_1)\ m_0^3 + O[m_0]^4$$

3.2 Existence of real roots of the Cubic Equation $Q(m_0) = 0$

We now explore how many roots the cubic equation has. We first define:

$$Q\ (m_0)\ = A_3\ m_0^3 + A_2\ m_0^2 + A_1\ m_0 + A_0\ = 0$$

Recall the basic reproduction number $R_1^{'} = \max\{r_1, r_{11}\}$ where $r_1 = \frac{\Phi \alpha_1}{\nu^2}$ and $r_{11} = \frac{2 \Phi \epsilon_1 \kappa_1}{\nu^2}$. We can further notate:

$A_3\ = -2\ \alpha_1\ \epsilon_1\ \kappa_1 < 0;$

$A_2\ = \nu\ (\alpha_1 - 2\ \kappa_1 + 2\ \epsilon_1\ \kappa_1)\ =$

$$\nu\ \left(\frac{\nu^2}{\Phi}\ \left(\frac{\Phi\ \alpha}{\nu^2} + \frac{2\ \Phi\ \epsilon_1\ \kappa_1}{\nu^2}\right) - 2\ \kappa_1\right) < \nu\ \left(2\ \frac{\nu^2}{\Phi}\ R_1^{'} - 2\ \kappa_1\right) = 2\ \nu\ \left(\frac{\nu^2}{\Phi}\ R_1^{'} - \kappa_1\right),\ \text{depends on } R_1^{'};$$

$A_1\ = 2\ \Phi\ \kappa_1 > 0;$

$A_0\ = -\Phi\ \nu < 0;$

We have the following observations about the cubic function $Q(m_0)$:

- $A_3 < 0$: The cubic function first decreases, then increases, and eventually decreases, from negative m_0 to positive m_0.
- $Q(0) = A_0 < 0$ and $A_3 < 0$: There always exists a negative real root.
- $Q^{'}(m_0) = 3 A_3\ m_0^2 + 2 A_2\ m_0 + A_1$, then $Q^{'}(0) = A_1 > 0$: At $m_0 = 0$, $Q(m_0)$ is increasing.

Substitute $m_0 = t - \frac{A_2}{3 A_3}$ and get the equation $t^3 + p\,t + q = 0$. Then, we discuss the number of real roots of the cubic function $t^3 + p\,t + q$, so that we derive the roots of $Q(m_0)$.
Note that we use an analytical method to find the number of real roots in Appendix D.2. Here we validate our analysis numerically.

In[28]:=
$$\text{Series}\left[\left\{A_3\, m_0^3 + A_2\, m_0^2 + A_1\, m_0 + A_0 == 0\right\} \;/.\; \left\{m_0 \to t - \frac{A_2}{3\, A_3}\right\},\ \{t, 0, 3\}\right]$$

Out[28]=
$$\left\{\left(A_0 + \frac{2\, A_2^3}{27\, A_3^2} - \frac{A_1\, A_2}{3\, A_3}\right) + \left(A_1 - \frac{A_2^2}{3\, A_3}\right) t + A_3\, t^3 + O[t]^4 == 0\right\}$$

- Define the discriminant $\Delta = 4\,p^3 + 27\,q^2$, where $p = \frac{A_1}{A_3} - \frac{A_2^2}{3 A_3^2}$, $q = \frac{A_0}{A_3} + \frac{2 A_2^3}{27 A_3^3} - \frac{A_1 A_2}{3 A_3^2}$ (https://en.wikipedia.org/wiki/Cubic_equation#Discriminant_and_nature_of_the_roots)
- when $\Delta < 0$, there are three real roots; when $\Delta > 0$, there are two complex roots and one real root

In[29]:=
$$A_3 = -2\, \alpha_1\, \epsilon_1\, \kappa_1;\ A_2 = \nu\, (\alpha_1 - 2\, \kappa_1 + 2\, \epsilon_1\, \kappa_1);\ A_1 = 2\, \Phi\, \kappa_1;\ A_0 = -\Phi\, \nu;$$
$$p = \frac{A_1}{A_3} - \frac{A_2^2}{3\, A_3^2};$$
$$q = \frac{A_0}{A_3} + \frac{2\, A_2^3}{27\, A_3^3} - \frac{A_1\, A_2}{3\, A_3^2};$$

Here, we plot the values of Δ given the proposed ranges of parameters in Table 1 of the main text to determine the sign of Δ:

In[31]:=
$$\text{FullSimplify}\left[\left(4\, p^3 + 27\, q^2\right) \;/.\; \{\alpha_1 \to \alpha,\ \epsilon_1 \to \epsilon,\ \kappa_1 \to \kappa\}\right]$$

Out[31]=
$$\frac{1}{432\, \alpha^6\, \epsilon^6\, \kappa^6}\left(-\left((\alpha + 2\, (-1+\epsilon)\, \kappa)^2\, \nu^2 + 12\, \alpha\, \epsilon\, \kappa^2\, \Phi\right)^3 + \left((\alpha + 2\, (-1+\epsilon)\, \kappa)^3\, \nu^3 + 18\, \alpha\, \epsilon\, \kappa^2\, (\alpha - 3\, \alpha\, \epsilon + 2\, (-1+\epsilon)\, \kappa)\, \nu\, \Phi\right)^2\right)$$

In[32]:=
$$\text{Delta}[\Phi\_,\ \nu\_,\ \alpha\_,\ \epsilon\_,\ \kappa\_] := \frac{1}{432\, \alpha^6\, \epsilon^6\, \kappa^6}\left(-\left((\alpha + 2\, (-1+\epsilon)\, \kappa)^2\, \nu^2 + 12\, \alpha\, \epsilon\, \kappa^2\, \Phi\right)^3 + \left((\alpha + 2\, (-1+\epsilon)\, \kappa)^3\, \nu^3 + 18\, \alpha\, \epsilon\, \kappa^2\, (\alpha - 3\, \alpha\, \epsilon + 2\, (-1+\epsilon)\, \kappa)\, \nu\, \Phi\right)^2\right);$$

In[33]:=
```
Manipulate[ListPlot[Table[{ϵ, Boole[R1[Φ, 10^-2, α, ϵ, κ] > 1] * Delta[Φ, 10^-2, α, ϵ, κ]},
    {ϵ, 0, 1, .001}], PlotRange → All, AxesLabel → {ϵ1, Δ}],
  {{Φ, 1}, .5, 3.5}, {{α, 7 * 10^-5}, 10^-6, 10^-4}, {{κ, 7 * 10^-5}, 10^-6, 10^-4}]
```

Out[33]=

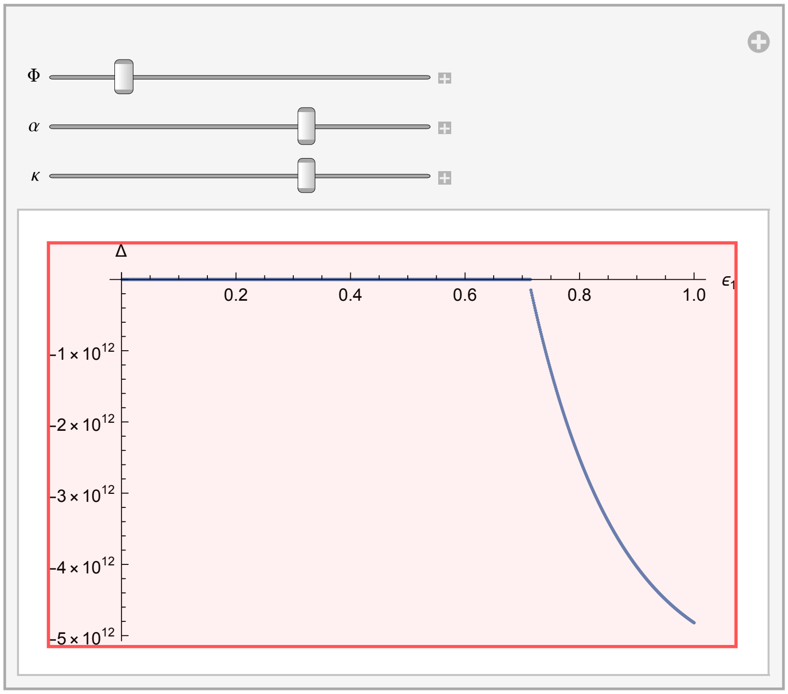

Figure 1: Values of the discriminant Δ versus the co-transmission probability of M_1, ϵ_1, from 0 to 1, with the given parameter ranges and $R_l^{'} > 1$.

When $R_1^{'} > 1$, we get $\Delta < 0$ within the given ranges, thus we can ensure three real roots for $t^3 + p\,t + q = 0$ as well as $Q(m_0) = 0$. We get the same conclusion in Appendix D.2.

3.3 Computation of positive $m_0^{'}$, $m_1^{'}$, and $M_1^{'}$

3.3.1 A general form for the cubic roots

Since $\Delta < 0$, then we can guarantee three real roots. Let's get to the general forms of these roots (https://en.wikipedia.org/wiki/Cubic_equation#General_cubic_formula):

- recall $Q(m_0) = A_3\,m_0^3 + A_2\,m_0^2 + A_1\,m_0 + A_0 = 0$, we define $\Delta_0 = A_2^2 - 3\,A_3\,A_1$, $\Delta_1 = 2\,A_2^3 - 9\,A_3\,A_2\,A_1 + 27\,A_3^2\,A_0$

In[34]:=
```
Delta0 = A2^2 - 3 A3 A1; Delta1 = 2 A2^3 - 9 A3 A2 A1 + 27 A3^2 A0;
```

- then we define $C_1 = \left(\frac{\Delta_1 + \left(\Delta_1^2 - 4\,\Delta_0^3\right)^{1/2}}{2}\right)^{1/3}$

In[35]:=
```
C1 = ((Delta1 + (Delta1^2 - 4 * Delta0^3)^(1/2)) / 2)^(1/3);
```

Then, we can express the roots as $m_0^{(k)} = -\frac{1}{3A_3}\left(A_2 + \xi^k C_1 + \frac{\Delta_0}{\xi^k C_1}\right)$ for $k = 0, 1, 2$, where $\xi = \frac{-1+(-3)^{1/2}}{2}$. Now we are going to determine for which value of k we have the correct expression of $m_0^{'}$ which is positive and induces positive $m_1^{'}$ and $M_1^{'}$ as well, by studying the three cases $k = 0, 1, 2$.

3.3.2 Determining the correct expression of $m_0^{'}$ by studying the three cases $k = 0, 1, 2$

- (1) When $k = 0$, we have the expression of $m_0^{'}$ as follows. Using this expression, we study the positivity of the three variables $m_0^{'}$, $m_1^{'}$ and $M_1^{'}$ numerically:

In[36]:=
$$-\frac{1}{3\,A_3}\left(A_2 + \mathrm{C1} + \frac{\mathrm{Delta0}}{\mathrm{C1}}\right)\ /.\ \{\alpha_1 \to \alpha,\ \epsilon_1 \to \epsilon,\ \kappa_1 \to \kappa\}\ //\ \mathrm{FullSimplify}$$

Out[36]=
$$\frac{1}{6\,\alpha\,\epsilon\,\kappa}\Bigg((\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu + \left((\alpha + 2\,(-1+\epsilon)\,\kappa)^2\,\nu^2 + 12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)\Big/\Bigg((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 - 54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi + \frac{1}{2}\sqrt{\left(-4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^2\,\nu^2 + 12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3 + 4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha - 3\,\alpha\,\epsilon + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Bigg)^{1/3} + \Bigg((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 - 54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi + \frac{1}{2}\sqrt{\left(-4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^2\,\nu^2 + 12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3 + 4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha - 3\,\alpha\,\epsilon + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Bigg)^{1/3}\Bigg)$$

In[37]:=
$$\mathrm{root0}[\Phi\_,\ \nu\_,\ \alpha\_,\ \epsilon\_,\ \kappa\_] := \frac{1}{6\,\alpha\,\epsilon\,\kappa}\Bigg((\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu + \left((\alpha + 2\,(-1+\epsilon)\,\kappa)^2\,\nu^2 + 12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)\Big/\Bigg((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 - 54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi + \frac{1}{2}\sqrt{\left(-4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^2\,\nu^2 + 12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3 + 4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha - 3\,\alpha\,\epsilon + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Bigg)^{1/3} + \Bigg((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 - 54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi + \frac{1}{2}\sqrt{\left(-4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^2\,\nu^2 + 12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3 + 4\left((\alpha + 2\,(-1+\epsilon)\,\kappa)^3\,\nu^3 + 18\,\alpha\,\epsilon\,\kappa^2\,(\alpha - 3\,\alpha\,\epsilon + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Bigg)^{1/3}\Bigg);$$

In[38]:=
```
Manipulate[
 ListPlot[Table[{ϵ, N[Boole[R1[Φ, 10^-2, α, ϵ, κ] > 1] * root0[Φ, 10^-2, α, ϵ, κ], 500]},
   {ϵ, 0, 1, .001}], PlotRange → All, AxesLabel → {ϵ1, "m0(0)"}],
 {{Φ, 1}, .5, 3.5}, {{α, 7 * 10^-5}, 10^-6, 10^-4}, {{κ, 7 * 10^-5}, 10^-6, 10^-4}]
```

Out[38]=

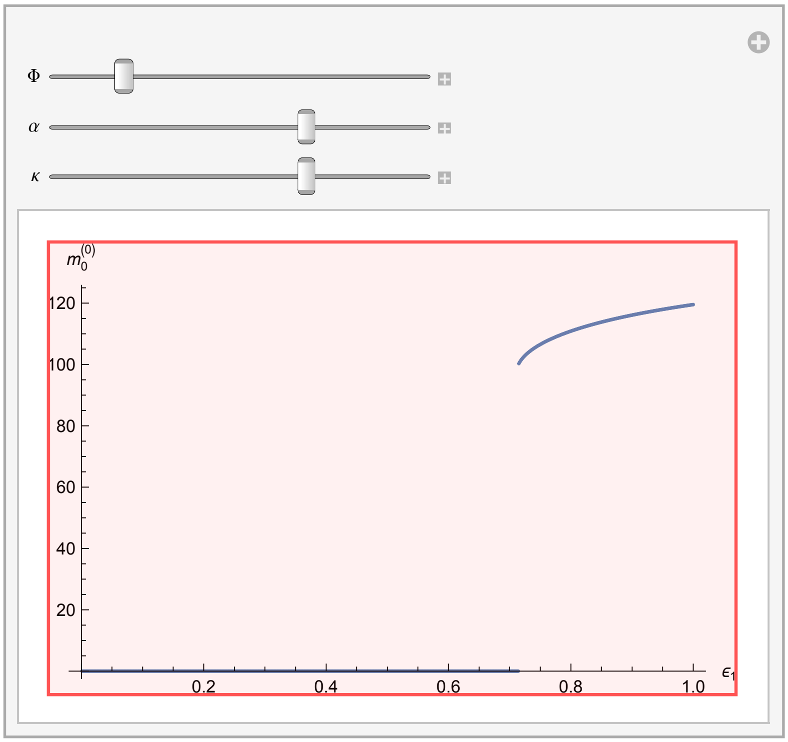

Figure 2: The values of $m_0^{(0)}$ versus the co-transmission probability of M_1, ϵ_1, from 0 to 1, with the given parameter ranges and $R_l^{'} > 1$.

This root with $k = 0$ is positive, then we check the positivity of the other two variables $m_1^{'}$ and $M_1^{'}$:

In[39]:=
```
m1t[Φ_, ν_, α_, ϵ_, κ_] :=
  (Φ - ν * root0[Φ, ν, α, ϵ, κ]) ((1 - ϵ) * root0[Φ, ν, α, ϵ, κ]) / (Φ - α ϵ * root0[Φ, ν, α, ϵ, κ] * root0[Φ, ν, α, ϵ, κ]);
M1t[Φ_, ν_, α_, ϵ_, κ_] := (Φ - ν * root0[Φ, ν, α, ϵ, κ])
  (Φ - α * root0[Φ, ν, α, ϵ, κ] * root0[Φ, ν, α, ϵ, κ]) / (2 * root0[Φ, ν, α, ϵ, κ] * (Φ - α ϵ * root0[Φ, ν, α, ϵ, κ] * root0[Φ, ν, α, ϵ, κ]) κ);
```

In[41]:=
```
Manipulate[ListPlot[Table[{ϵ, N[M1t[Φ, 10^-2, α, ϵ, κ], 500]}, {ϵ, 0, 1, .001}],
  PlotRange → All, AxesLabel → {ϵ1, "M1(0)"}], {{Φ, 1}, .5, 3.5},
 {{α, 7 * 10^-5}, 10^-6, 10^-4}, {{κ, 7 * 10^-5}, 10^-6, 10^-4}]
```

Out[41]=

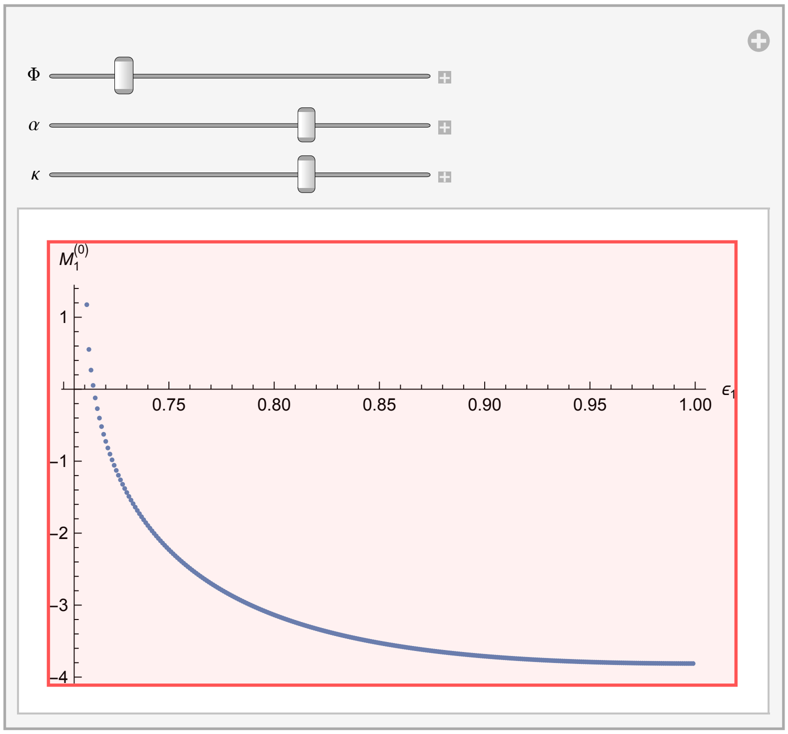

Figure 3: The values of $M_1^{(0)}$ derived from $m_0^{(0)}$, *versus the co-transmission probability of* M_1, ϵ_1, *from 0 to 1, with the given parameter ranges.*

Therefore, we see that $M_1^{'} < 0$ for some combinations of the parameters when $k = 0$. Thus, we exclude the root corresponding to $k = 0$.

- (2) When $k = 1$, $\xi = \frac{-1+(-3)^{1/2}}{2}$

In[42]:= $\xi = \frac{-1 + (-3)^{1/2}}{2};$

In[43]:=

$$-\frac{1}{3\,A_3}\left(A_2+\xi * C1+\frac{\text{Delta0}}{\xi * C1}\right)\text{ /. }\{\alpha_1\to\alpha,\ \epsilon_1\to\epsilon,\ \kappa_1\to\kappa\}\text{ // FullSimplify}$$

Out[43]=

$$\frac{1}{6\,\alpha\,\epsilon\,\kappa}\Bigg((\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu+\Big((-1)^{1/3}\left(-(\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2-12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)\Big)\Big/\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\left(-4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3+4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Big)^{1/3}+\frac{1}{2}\,i\,\left(i+\sqrt{3}\right)\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\left(-4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3+4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Big)^{1/3}\Bigg)$$

In[44]:= **root1[Φ_, ν_, α_, ϵ_, κ_] :=**

$$\frac{1}{6\,\alpha\,\epsilon\,\kappa}\Bigg((\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu+\Big((-1)^{1/3}\left(-(\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2-12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)\Big)\Big/\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\left(-4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3+4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Big)^{1/3}+\frac{1}{2}\,i\,\left(i+\sqrt{3}\right)\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\left(-4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\right)^3+4\left((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\right)^2\right)}\Big)^{1/3}\Bigg);$$

In[45]:=
```
Manipulate[
 ListPlot[Table[{ϵ, N[Boole[R1[Φ, 10^-2, α, ϵ, κ] > 1] * root1[Φ, 10^-2, α, ϵ, κ], 500]},
   {ϵ, 0, 1, .001}], PlotRange → All, AxesLabel → {ϵ1, "m0^(1)"}],
 {{Φ, 1}, .5, 3.5}, {{α, 7 * 10^-5}, 10^-6, 10^-4}, {{κ, 7 * 10^-5}, 10^-6, 10^-4}]
```

Out[45]=

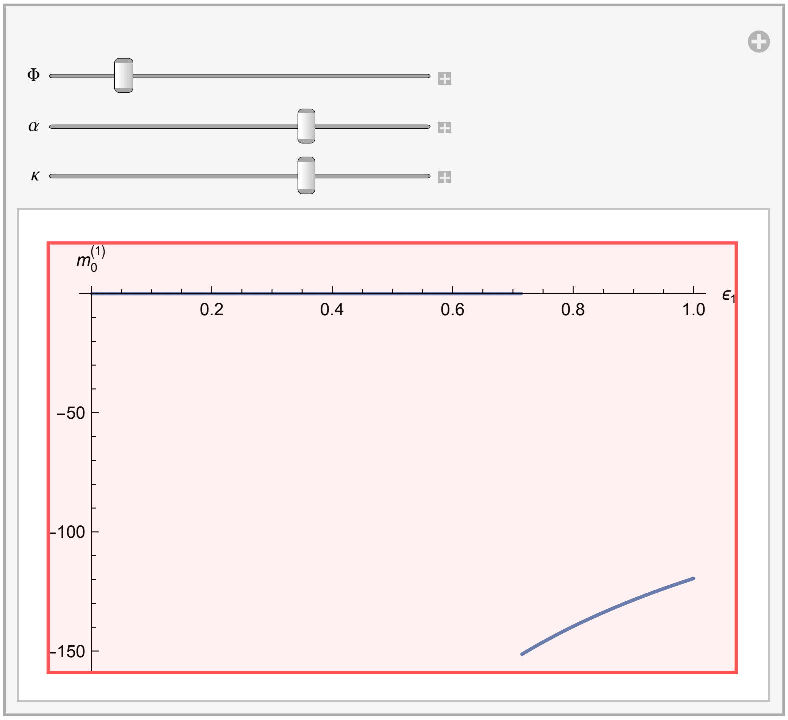

Figure 4: The values of $m_0^{(1)}$ versus the co-transmission probability of M_1, ϵ_1, from 0 to 1, with the given parameter ranges and $R_l^{'} > 1$.

We see that $m_0^{'} < 0$ when $k = 1$, therefore we exclude the root corresponding to $k = 1$ without studying the positivity of the other two variables $m_1^{'}$ and $M_1^{'}$.

- (3) When $k = 2$, $\xi = \frac{-1+(-3)^{1/2}}{2}$

In[46]:= $-\frac{1}{3\,A_3}\left(A_2+\xi^2*C1+\frac{\text{Delta0}}{\xi^2*C1}\right)$ /. $\{\alpha_1\to\alpha,\ \epsilon_1\to\epsilon,\ \kappa_1\to\kappa\}$ // FullSimplify

Out[46]=

$$\frac{1}{6\,\alpha\,\epsilon\,\kappa}\Bigg((\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu+\Big((-1)^{2/3}\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\big)\Big)\Big/\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\Big(-4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\big)^3+4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\big)^2\Big)}\Big)^{1/3}-\frac{1}{2}\,i\,\big(-i+\sqrt{3}\big)\,\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\Big(-4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\big)^3+4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\big)^2\Big)}\Big)^{1/3}\Bigg)$$

In[47]:= root2[Φ_, ν_, α_, ϵ_, κ_] :=

$$\frac{1}{6\,\alpha\,\epsilon\,\kappa}\Bigg((\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu+\Big((-1)^{2/3}\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\big)\Big)\Big/\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\Big(-4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\big)^3+4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\big)^2\Big)}\Big)^{1/3}-\frac{1}{2}\,i\,\big(-i+\sqrt{3}\big)\,\Big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3-54\,\alpha^2\,\epsilon^2\,\kappa^2\,\nu\,\Phi+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi+\frac{1}{2}\sqrt{\Big(-4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^2\,\nu^2+12\,\alpha\,\epsilon\,\kappa^2\,\Phi\big)^3+4\,\big((\alpha+2\,(-1+\epsilon)\,\kappa)^3\,\nu^3+18\,\alpha\,\epsilon\,\kappa^2\,(\alpha-3\,\alpha\,\epsilon+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi\big)^2\Big)}\Big)^{1/3}\Bigg);$$

In[48]:=
```
Manipulate[
 ListPlot[Table[{ϵ, N[Boole[R1[Φ, 10^-2, α, ϵ, κ] > 1] * root2[Φ, 10^-2, α, ϵ, κ], 500]},
   {ϵ, 0, 1, .001}], PlotRange → All , AxesLabel → {ϵ1, "m0^(2)"}],
 {{Φ, 1}, .5, 3.5}, {{α, 7 * 10^-5}, 10^-6, 10^-4}, {{κ, 7 * 10^-5}, 10^-6, 10^-4}]
```

Out[48]=

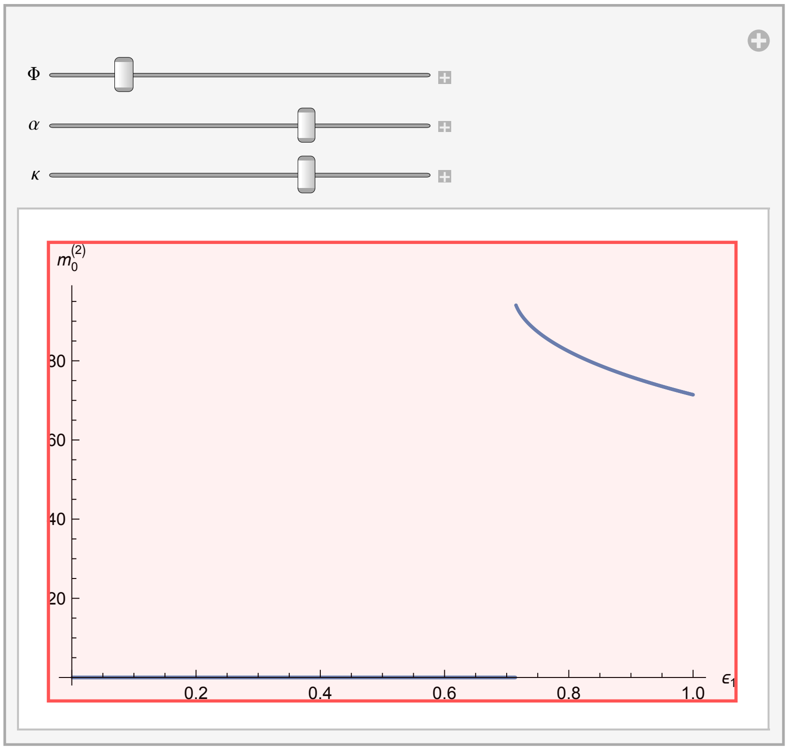

Figure 5: The values of $m_0^{(2)}$ versus the co-transmission probability of M_1, ϵ_1, from 0 to 1, with the given parameter ranges and $R_l^{'} > 1$.

Now we check the signs of $m_1^{'}$ and $M_1^{'}$:

In[49]:=
```
m1[Φ_, ν_, α_, ϵ_, κ_] :=
  (Φ - ν * root2[Φ, ν, α, ϵ, κ]) ((1 - ϵ) * root2[Φ, ν, α, ϵ, κ]) /
    (Φ - α ϵ * root2[Φ, ν, α, ϵ, κ] * root2[Φ, ν, α, ϵ, κ]);
M1[Φ_, ν_, α_, ϵ_, κ_] := (Φ - ν * root2[Φ, ν, α, ϵ, κ])
   (Φ - α * root2[Φ, ν, α, ϵ, κ] * root2[Φ, ν, α, ϵ, κ]) /
   (2 * root2[Φ, ν, α, ϵ, κ] * (Φ - α ϵ * root2[Φ, ν, α, ϵ, κ] * root2[Φ, ν, α, ϵ, κ]) κ);
```

In[51]:=
```
Manipulate[ListPlot[Table[{ϵ, N[M1[Φ, 10^-2, α, ϵ, κ], 500]}, {ϵ, 0, 1, .001}],
  PlotRange → All, AxesLabel → {ϵ1, "M1(2)"}], {{Φ, 1}, .5, 3.5},
 {{α, 7 * 10^-5}, 10^-6, 10^-4}, {{κ, 7 * 10^-5}, 10^-6, 10^-4}]
```

Out[51]=

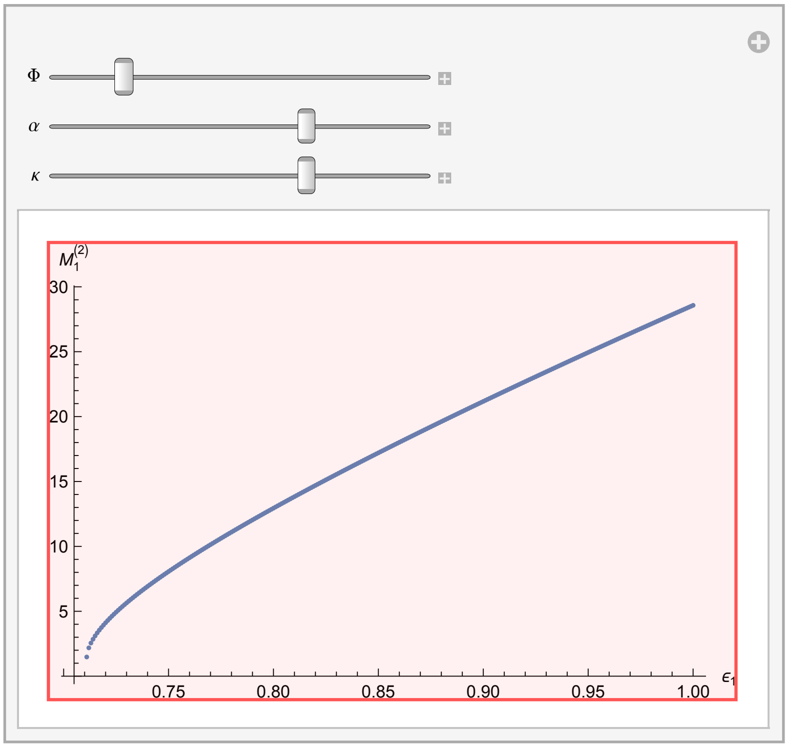

Figure 6: The values of $M_1^{(2)}$ derived from $m_0^{(2)}$, *versus the co-transmission probability of* M_1, ϵ_1, *from 0 to 1, with the given parameter ranges.*

In[52]:=
```
Manipulate[ListPlot[Table[{ϵ, N[m1[Φ, 10^-2, α, ϵ, κ], 500]}, {ϵ, 0, 1, .001}],
  PlotRange → All, AxesLabel → {ϵ1, "m1^(2)"}], {{Φ, 1}, .5, 3.5},
 {{α, 7 * 10^-5}, 10^-6, 10^-4}, {{κ, 7 * 10^-5}, 10^-6, 10^-4}]
```

Out[52]=

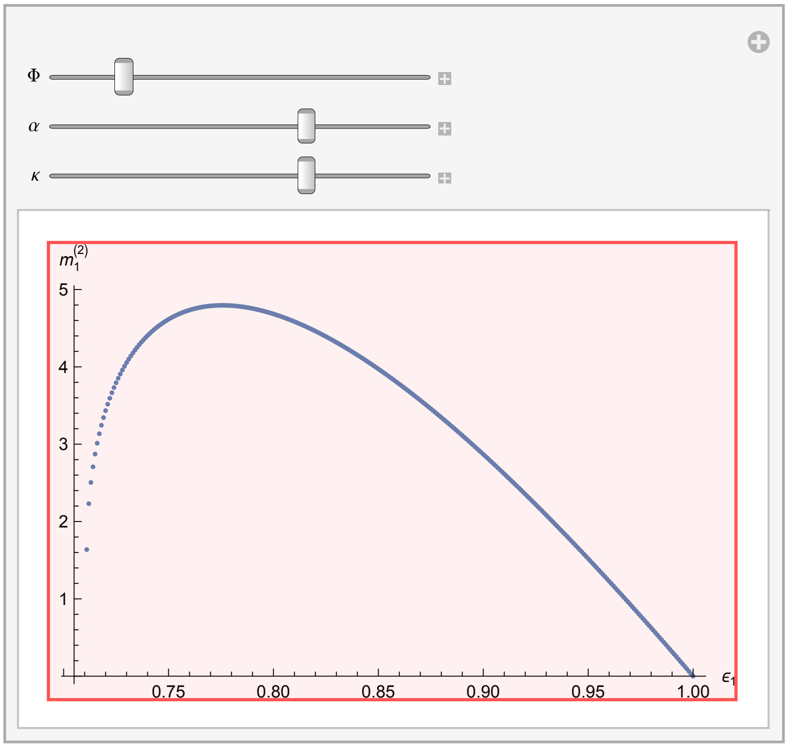

Figure 7: The values of $m_1^{(2)}$ derived from $m_0^{(2)}$, *versus the co-transmission probability of* M_1, ϵ_1, *from 0 to 1, with the given parameter ranges.*

Since all the variables $m_0^{'}$, $m_1^{'}$ and $M_1^{'}$ are positive only in the case $k = 2$, we conclude that we have the expression of $m_0^{'}$ when $k = 2$.

In[53]:=
```
m0[Φ_, ν_, α_, ϵ_, κ_] := root2[Φ, ν, α, ϵ, κ];
```

$m_0^{'}$, $m_1^{'}$, $M_1^{'} > 0$ when $R_1^{'} > 1$ and $k = 2$. Here's our root that satisfies all the conditions.

3.3.3 Summary of the resident strain endemic equilibrium

To summarize, we have the strain-1 endemic equilibrium $E_1^{'} = (m_0^{'},\ m_1^{'}, 0, 0, M_1^{'}, 0)$.

$$m_1' = \frac{m_0' \,(\Phi - \nu\, m_0')\,(-1 + \epsilon_1)}{-\Phi + m_0'^{\,2}\,\alpha_1\,\epsilon_1} = (\Phi - \nu\, m_0')\,\frac{m_0'\,(1 - \epsilon_1)}{\Phi - m_0^2\,\alpha_1\,\epsilon_1}$$

$$M_1' = \frac{(\Phi - \nu\, m_0')\left(\Phi - m_0'^{\,2}\,\alpha_1\right)}{2\, m_0'\left(\Phi - m_0'^{\,2}\,\alpha_1\,\epsilon_1\right)\kappa_1} = (\Phi - \nu\, m_0)\,\frac{\Phi - m_0'^{\,2}\,\alpha_1}{2\, m_0'\left(\Phi - m_0'^{\,2}\,\alpha_1\,\epsilon_1\right)\kappa_1}$$

$$m_0' = x_k = -\frac{1}{3\,A_3}\left(A_2 + \xi^2\, C1 + \frac{\Delta_0}{\xi^2\, C1}\right),$$

where $\xi = \frac{-1 + (-3)^{1/2}}{2}$, $C1 = \left(\frac{\Delta_1 + \left(\Delta_1^2 - 4\,\Delta_0^3\right)^{1/2}}{2}\right)^{1/3}$,

$\Delta_0 = A_2^2 - 3\,A_3\,A_1$, $\Delta_1 = 2\,A_2^3 - 9\,A_3\,A_2\,A_1 + 27\,A_3^2\,A_0$,

$A_3 = -2\,\alpha_1\,\epsilon_1\,\kappa_1 < 0$, $A_2 = \nu\,(\alpha_1 - 2\,\kappa_1 + 2\,\epsilon_1\,\kappa_1)$, $A_1 = 2\,\Phi\,\kappa_1 > 0$, $A_0 = -\Phi\,\nu < 0$;

3.4 Invasion reproduction number of V_2

Sine we already have the expression for the V_1 endemic equilibrium $E_1^{'}$, now we can compute the invasion reproduction number $R_I^{'}$ at $E_1^{'}$ for the sub-system of invasive strain V_2:

$$\frac{dm_2}{dt} = -\nu_2\,m_2 - (\lambda_1 + \lambda_2 + \lambda_{C1} + \lambda_{C2} + \Lambda_1 + \Lambda_2)\,m_2 + \lambda_2\,m_0$$

$$\frac{dm_C}{dt} = -\sigma_C\,m_C + (\lambda_2 + \lambda_{C2} + \Lambda_2)\,m_1 + (\lambda_1 + \lambda_{C1} + \Lambda_1)\,m_2 + \Lambda_C\,m_0$$

$$\frac{dM_2}{dt} = -\sigma_2\,M_2 + (\lambda_2 + \lambda_{C2} + \Lambda_2)\,m_2 + \left(\frac{\delta_2}{\delta_1 + \delta_2}\,\lambda_{C2} + \Lambda_2\right)\,m_0$$

We first compute the invasive Jacobian matrix $J^{'}$ and decomposed it into $F^{'}$ and $T^{'}$:

In[55]:=
```
Jprime =
  FullSimplify[D[{dm2dt[m0, m1, m2, mC, M1, M2], dmCdt[m0, m1, m2, mC, M1, M2], dM2dt[
        m0, m1, m2, mC, M1, M2]}, {{m2, mC, M2}}]] /. {m2 → 0, mC → 0, M2 → 0} /.
    {ν0 → ν, ν1 → ν, ν2 → ν, σC → ν, σ1 → ν, σ2 → ν} // FullSimplify // MatrixForm
```

Out[55]//MatrixForm=

$$\begin{pmatrix} -\nu - m_1\,\alpha_1 + m_0\,\alpha_2 - 2\,M_1\,\kappa_1 & -m_0\,\delta_2\,(-1 + \epsilon_C) & -2\,m_0\,(-1 + \epsilon_2)\,\kappa_2 \\ m_1\,(\alpha_1 + \alpha_2) + 2\,M_1\,\kappa_1 & \delta_2\left(m_1 + \frac{2\,m_0\,\delta_1\,\epsilon_C}{\delta_1 + \delta_2}\right) - \nu_C & 2\,m_1\,\kappa_2 \\ 0 & \frac{m_0\,\delta_2^2\,\epsilon_C}{\delta_1 + \delta_2} & 2\,m_0\,\epsilon_2\,\kappa_2 - \upsilon_2 \end{pmatrix}$$

In[56]:=
```
Fprime = {{m0 α2, m0 δ2 (1 - εC), 2 m0 (1 - ε2) κ2},
    {α2 m1, δ2 (m1 + 2 m0 δ1 εC/(δ1 + δ2)), 2 m1 κ2}, {0, m0 δ2^2 εC/(δ1 + δ2), 2 m0 ε2 κ2}};
Tprime = {{ν + m1 α1 + 2 M1 κ1, 0, 0}, {-α1 m1 - 2 M1 κ1, ν, 0}, {0, 0, ν}};
```

In[58]:=
```
Fprime // MatrixForm
```

Out[58]//MatrixForm=

$$\begin{pmatrix} m_0\,\alpha_2 & m_0\,\delta_2\,(1 - \epsilon_C) & 2\,m_0\,(1 - \epsilon_2)\,\kappa_2 \\ m_1\,\alpha_2 & \delta_2\left(m_1 + \frac{2\,m_0\,\delta_1\,\epsilon_C}{\delta_1 + \delta_2}\right) & 2\,m_1\,\kappa_2 \\ 0 & \frac{m_0\,\delta_2^2\,\epsilon_C}{\delta_1 + \delta_2} & 2\,m_0\,\epsilon_2\,\kappa_2 \end{pmatrix}$$

In[59]:=
```
Tprime // MatrixForm
```

Out[59]//MatrixForm=

$$\begin{pmatrix} \nu + m_1\,\alpha_1 + 2\,M_1\,\kappa_1 & 0 & 0 \\ -m_1\,\alpha_1 - 2\,M_1\,\kappa_1 & \nu & 0 \\ 0 & 0 & \nu \end{pmatrix}$$

We then compute the next-generation matrix for the invasive strain V_2 by $F_{\text{inv}}[V_{\text{inv}}]^{-1}$:

In[60]:=
```
NGM = Fprime.Inverse[Tprime] // FullSimplify;
```

In[61]:=
```
NGM // MatrixForm
```

Out[61]//MatrixForm=

$$\begin{pmatrix} \frac{m_0 (\nu \alpha_2 - \delta_2 (-1+\epsilon_C)(m_1 \alpha_1 + 2 M_1 \kappa_1))}{\nu(\nu + m_1 \alpha_1 + 2 M_1 \kappa_1)} & -\frac{m_0 \delta_2 (-1+\epsilon_C)}{\nu} & -\frac{2 m_0 (-1+\epsilon_2) \kappa_2}{\nu} \\ \frac{\nu m_1 \alpha_2 + \delta_2 \left(m_1 + \frac{2 m_0 \delta_1 \epsilon_C}{\delta_1+\delta_2}\right)(m_1 \alpha_1 + 2 M_1 \kappa_1)}{\nu(\nu + m_1 \alpha_1 + 2 M_1 \kappa_1)} & \frac{\delta_2 \left(m_1 + \frac{2 m_0 \delta_1 \epsilon_C}{\delta_1+\delta_2}\right)}{\nu} & \frac{2 m_1 \kappa_2}{\nu} \\ \frac{m_0 \delta_2^2 \epsilon_C (m_1 \alpha_1 + 2 M_1 \kappa_1)}{\nu(\delta_1+\delta_2)(\nu + m_1 \alpha_1 + 2 M_1 \kappa_1)} & \frac{m_0 \delta_2^2 \epsilon_C}{\nu \delta_1 + \nu \delta_2} & \frac{2 m_0 \epsilon_2 \kappa_2}{\nu} \end{pmatrix}$$

We want to prove the neutrality of the invasion reproduction number $R_I^{'}$, that's why we set α_1, $\alpha_2 \to \alpha$, δ_1, δ_2, κ_1, $\kappa_2 \to \kappa$, and ϵ_1, $\epsilon_2 \to \epsilon$ and substituting the expressions of $m_1^{'}$ and $M_1^{'}$:

In[62]:=

$$\text{NGM1} = \text{NGM} \;/.\; \{\alpha_2 \to \alpha, \alpha_1 \to \alpha, \delta_2 \to \kappa, \delta_1 \to \kappa, \kappa_2 \to \kappa, \kappa_1 \to \kappa, \epsilon_1 \to \epsilon, \epsilon_2 \to \epsilon, \epsilon_C \to \epsilon\} \;/.\; \left\{m_1 \to \frac{m_0 (\Phi - \nu m_0)(-1+\epsilon)}{-\Phi + m_0^2 \alpha \epsilon}, M_1 \to -\frac{(\Phi - \nu m_0)\left(\Phi - m_0^2 \alpha\right)}{2 m_0 \left(-\Phi + m_0^2 \alpha \epsilon\right) \kappa}\right\} \text{ // FullSimplify;}$$

In[63]:=
```
NGM1 // MatrixForm
```

Out[63]//MatrixForm=

$$\begin{pmatrix} m_0 \left(\frac{\kappa - \epsilon \kappa}{\nu} + \frac{(\alpha + (-1+\epsilon)\kappa) m_0}{\Phi}\right) & -\frac{(-1+\epsilon)\kappa m_0}{\nu} & -\frac{2(-1+\epsilon)\kappa m_0}{\nu} \\ \frac{m_0 (\Phi - \nu m_0)\left(\kappa \Phi + (-1+\epsilon)(-\alpha+\kappa)\nu m_0 - \alpha \epsilon^2 \kappa m_0^2\right)}{\nu \Phi \left(\Phi - \alpha \epsilon m_0^2\right)} & \frac{\kappa m_0 \left(\epsilon + \frac{(-1+\epsilon)(\Phi - \nu m_0)}{-\Phi + \alpha \epsilon m_0^2}\right)}{\nu} & \frac{2(-1+\epsilon)\kappa m_0 (-\Phi + \nu m_0)}{\nu\left(\Phi - \alpha \epsilon m_0^2\right)} \\ \frac{\epsilon \kappa m_0 (\Phi - \nu m_0)}{2 \nu \Phi} & \frac{\epsilon \kappa m_0}{2 \nu} & \frac{2 \epsilon \kappa m_0}{\nu} \end{pmatrix}$$

By taking the largest eigenvalues of the next-generation matrix, we can have the invasion reproduction number $R_I^{'}$ ***at neutrality***:

In[64]:=
```
Eigenvalues[NGM1] // FullSimplify
```

Out[64]=

$$\left\{\frac{\epsilon \kappa m_0}{\nu}, \frac{1}{2 \nu^2 \Phi \left(\Phi - \alpha \epsilon m_0^2\right)} m_0 \left(2 \kappa \nu \Phi^2 + (\alpha + 2(-1+\epsilon)\kappa)\nu^2 \Phi m_0 - \alpha \epsilon (1+\epsilon)\kappa \nu \Phi m_0^2 - \alpha \epsilon (\alpha + (-1+\epsilon)\kappa)\nu^2 m_0^3 + \sqrt{\left(\nu^2 \left(4 \alpha \epsilon \kappa \nu \Phi m_0 \left(\Phi - \alpha \epsilon m_0^2\right)((-3+\epsilon)\Phi + m_0(\nu - \epsilon \nu + 2 \alpha \epsilon m_0)) + \left(-2 \kappa \Phi^2 + m_0(-((\alpha + 2(-1+\epsilon)\kappa)\nu \Phi) + \alpha \epsilon m_0((1+\epsilon)\kappa \Phi + (\alpha + (-1+\epsilon)\kappa)\nu m_0))\right)^2\right)\right)}\right),\right.$$
$$\left.\frac{1}{2 \nu^2 \Phi \left(\Phi - \alpha \epsilon m_0^2\right)} m_0 \left(2 \kappa \nu \Phi^2 + (\alpha + 2(-1+\epsilon)\kappa)\nu^2 \Phi m_0 - \alpha \epsilon (1+\epsilon)\kappa \nu \Phi m_0^2 - \alpha \epsilon (\alpha + (-1+\epsilon)\kappa)\nu^2 m_0^3 - \sqrt{\left(\nu^2 \left(4 \alpha \epsilon \kappa \nu \Phi m_0 \left(\Phi - \alpha \epsilon m_0^2\right)((-3+\epsilon)\Phi + m_0(\nu - \epsilon \nu + 2 \alpha \epsilon m_0)) + \left(-2 \kappa \Phi^2 + m_0(-((\alpha + 2(-1+\epsilon)\kappa)\nu \Phi) + \alpha \epsilon m_0((1+\epsilon)\kappa \Phi + (\alpha + (-1+\epsilon)\kappa)\nu m_0))\right)^2\right)\right)}\right)\right\}$$

Last, we have the expression of $R_I^{'}$ as a function of $m_0^{'}$:

In[65]:=
$$\text{Rinv} = \frac{1}{2\,\nu^2\,\Phi\,\left(\Phi - \alpha\,\epsilon\,m_0^2\right)}\,m_0\left(2\,\kappa\,\nu\,\Phi^2 + (\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu^2\,\Phi\,m_0 - \alpha\,\epsilon\,(1+\epsilon)\,\kappa\,\nu\,\Phi\,m_0^2 - \alpha\,\epsilon\,(\alpha + (-1+\epsilon)\,\kappa)\,\nu^2\,m_0^3 + \sqrt{\left(\nu^2\left(4\,\alpha\,\epsilon\,\kappa\,\nu\,\Phi\,m_0\left(\Phi - \alpha\,\epsilon\,m_0^2\right)((-3+\epsilon)\,\Phi + m_0\,(\nu - \epsilon\,\nu + 2\,\alpha\,\epsilon\,m_0)) + \left(-2\,\kappa\,\Phi^2 + m_0\,(-((\alpha + 2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi) + \alpha\,\epsilon\,m_0\,((1+\epsilon)\,\kappa\,\Phi + (\alpha + (-1+\epsilon)\,\kappa)\,\nu\,m_0))\right)^2\right)\right)}\right);$$

and prove the neutrality of R_I'.

3.5 Proof of the neutrality of the V_2 invasion reproduction number R_I'

Now we consider two scenarios: (1) $\kappa = \alpha/2$ and (2) $\kappa \neq \alpha/2$:

- (1) we simplify the expression by assuming $\kappa = \alpha/2$:

In[66]:=
$$\text{Rinv} \;/.\; \left\{\kappa \to \frac{\alpha}{2}\right\} \;//\; \text{FullSimplify}$$

Out[66]=
$$\frac{1}{4\,\nu^2\,\Phi\,\left(\Phi - \alpha\,\epsilon\,m_0^2\right)}\,m_0\left(-\alpha^2\,\epsilon\,(1+\epsilon)\,\nu\,m_0^2\,(\Phi + \nu\,m_0) + 2\,\alpha\,\nu\,\Phi\,(\Phi + \epsilon\,\nu\,m_0) + \sqrt{\left(\alpha^2\,\nu^2\left(8\,\epsilon\,\nu\,\Phi\,m_0\left(\Phi - \alpha\,\epsilon\,m_0^2\right)((-3+\epsilon)\,\Phi + m_0\,(\nu - \epsilon\,\nu + 2\,\alpha\,\epsilon\,m_0)) + \left(-2\,\Phi^2 + \epsilon\,m_0\,(-2\,\nu\,\Phi + \alpha\,(1+\epsilon)\,m_0\,(\Phi + \nu\,m_0))\right)^2\right)\right)}\right)$$

In[67]:=
$$\text{Rinv} \;/.\; \left\{\kappa \to \frac{\alpha}{2}\right\} \;/.\; \left\{m_0 \to \frac{\nu}{\alpha}\right\} \;//\; \text{FullSimplify}$$

Out[67]=
$$\frac{-\epsilon\,(1+\epsilon)\,\nu^5 - \alpha\,(-1+\epsilon)\,\epsilon\,\nu^3\,\Phi + 2\,\alpha^2\,\nu\,\Phi^2 + \alpha\sqrt{\frac{\left(\epsilon\,(1+\epsilon)\,\nu^5 + \alpha\,(-5+\epsilon)\,\epsilon\,\nu^3\,\Phi + 2\,\alpha^2\,\nu\,\Phi^2\right)^2}{\alpha^2}}}{4\,\alpha\,\nu\,\Phi\left(-\epsilon\,\nu^2 + \alpha\,\Phi\right)}$$

In[68]:=
$$\left(\frac{-\epsilon\,(1+\epsilon)\,\nu^4 - \alpha\,(-1+\epsilon)\,\epsilon\,\nu^2\,\Phi + 2\,\alpha^2\,\Phi^2 + \epsilon\,(1+\epsilon)\,\nu^4 + \alpha\,(-5+\epsilon)\,\epsilon\,\nu^2\,\Phi + 2\,\alpha^2\,\Phi^2}{4\,\alpha\,\Phi\left(-\epsilon\,\nu^2 + \alpha\,\Phi\right)}\right) \;//\; \text{FullSimplify}$$

Out[68]=
1

- (2) if $\kappa \neq \alpha/2$, we need to prove the neutrality numerically by studying the value of the following function within the proposed ranges of parameters (see Table 1 in the main text):

In[69]:=

$$\mathtt{RI}[\Phi\_,\nu\_,\alpha\_,\epsilon\_,\kappa\_] := \frac{\mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa]}{2\,\nu^2\,\Phi\,(\Phi-\alpha\,\epsilon * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa])}\Big(2\,\kappa\,\nu\,\Phi^2+(\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu^2\,\Phi * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] - \alpha\,\epsilon\,(1+\epsilon)\,\kappa\,\nu\,\Phi * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] - \alpha\,\epsilon\,(\alpha+(-1+\epsilon)\,\kappa)\,\nu^2 * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] + \sqrt{\Big(\nu^2\,\Big(4\,\alpha\,\epsilon\,\kappa\,\nu\,\Phi * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * (\Phi-\alpha\,\epsilon * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa])\,((-3+\epsilon)\,\Phi+\mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * (\nu-\epsilon\,\nu+2\,\alpha\,\epsilon * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa])) + \Big(-2\,\kappa\,\Phi^2+\mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * (-((\alpha+2\,(-1+\epsilon)\,\kappa)\,\nu\,\Phi)+\alpha\,\epsilon * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa] * ((1+\epsilon)\,\kappa\,\Phi+(\alpha+(-1+\epsilon)\,\kappa)\,\nu * \mathtt{m0}[\Phi,\nu,\alpha,\epsilon,\kappa]))\Big)^2\Big)\Big)}\Big);$$

In[70]:=

$$\mathtt{Manipulate}\Big[\mathtt{ListPlot}\Big[\mathtt{Table}\Big[\{\epsilon,\ \mathtt{N}[\mathtt{RI}[\Phi,10^{-2},\alpha,\epsilon,\kappa],500]\},\ \{\epsilon,10^{-6},1,.001\}\Big],\ \mathtt{PlotRange}\to\mathtt{All},\ \mathtt{AxesLabel}\to\{\epsilon,\ \text{"}R_I'\text{"}\}\Big],\ \{\{\Phi,1\},.5,3.5\},\ \{\{\alpha,7*10^{-5}\},10^{-6},10^{-4}\},\ \{\{\kappa,7*10^{-5}\},10^{-6},10^{-4}\}\Big]$$

Out[70]=

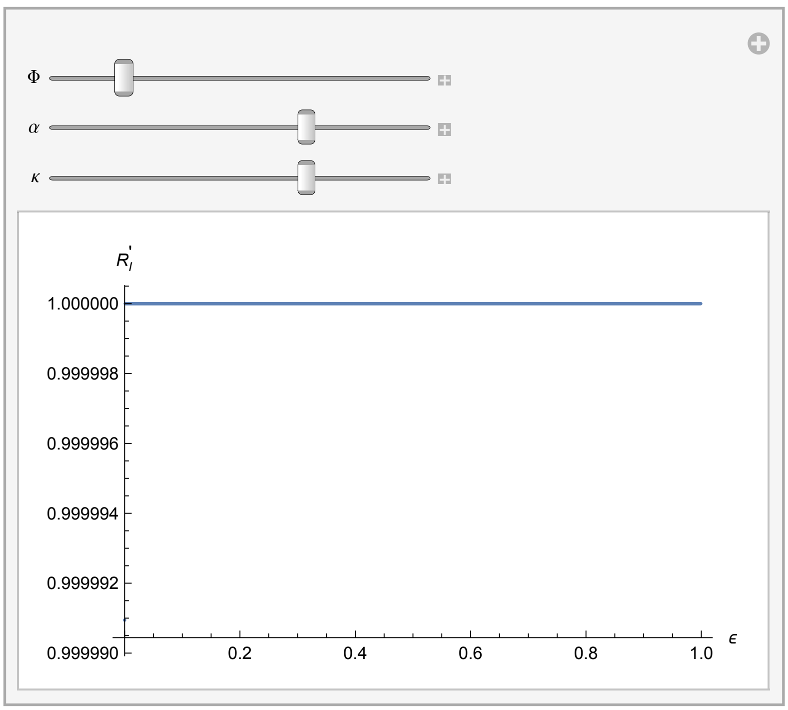

Figure 8: The values of R_I' versus the co-transmission probability ϵ from 0 to 1, with the given parameter ranges, at the limit $\alpha_1,\ \alpha_2 \to \alpha,\ \kappa_1,\ \kappa_2,\ \delta_1,\ \delta_2 \to \kappa,\ \epsilon_1,\ \epsilon_2,\ \epsilon_C \to \epsilon$.

Eventually, we proved the neutrality of R_I' of the two-slot model, without any assumptions (within the given parameter ranges).