Supplementary Material:
"The potential for viral evolution during the COVID-19 pandemic"

Troy Day, Sylvain Gandon, Sébastien Lion, & Sarah P. Otto
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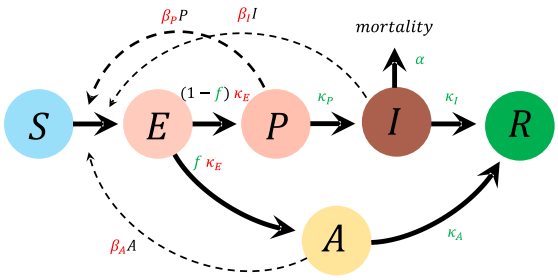
- **Analysis of model with genetic variation (wildtype and mutant subtypes)**

  Based on Figure 2:



We develop ordinary differential equations for both the wildtype (w) and the mutant (m):

```
dSdt = -((βI * Iw + βA * Aw + βP * Pw) + (βIm * Im + βAm * Am + βP * Pm)) * S;
dEwdt = (βI * Iw + βA * Aw + βP * Pw) * S - κE * Ew;
dPwdt = (1 - f) * κE * Ew - κP * Pw;
dIwdt = κP * Pw - α Iw - κI Iw;
dAwdt = f * κE * Ew - κA * Aw;

dEmdt = (βIm * Im + βAm * Am + βPm * Pm) * S - κEm * Em;
dPmdt = (1 - fm) * κEm * Em - κPm * Pm;
dImdt = κPm * Pm - αm Im - κIm Im;
dAmdt = fm * κEm * Em - κAm * Am;
```

We assume that the disease is fairly rare and study its growth by analysing the properties of the local stability matrix:

```
start = {Ew → 0, Aw → 0, Pw → 0, Iw → 0, Em → 0, Am → 0, Pm → 0, Im → 0};

stabmat =
  {{D[dSdt, S], D[dSdt, Ew], D[dSdt, Pw], D[dSdt, Iw], D[dSdt, Aw], D[dSdt, Em], D[dSdt, Pm], D[dSdt, Im], D[dSdt, Am]},
    {D[dEwdt, S], D[dEwdt, Ew], D[dEwdt, Pw], D[dEwdt, Iw], D[dEwdt, Aw],
     D[dEwdt, Em], D[dEwdt, Pm], D[dEwdt, Im], D[dEwdt, Am]},
    {D[dPwdt, S], D[dPwdt, Ew], D[dPwdt, Pw], D[dPwdt, Iw], D[dPwdt, Aw], D[dPwdt, Em],
     D[dPwdt, Pm], D[dPwdt, Im], D[dPwdt, Am]},
    {D[dIwdt, S], D[dIwdt, Ew], D[dIwdt, Pw], D[dIwdt, Iw], D[dIwdt, Aw], D[dIwdt, Em],
     D[dIwdt, Pm], D[dIwdt, Im], D[dIwdt, Am]}, {D[dAwdt, S], D[dAwdt, Ew], D[dAwdt, Pw],
     D[dAwdt, Iw], D[dAwdt, Aw], D[dAwdt, Em], D[dAwdt, Pm], D[dAwdt, Im], D[dAwdt, Am]},
    {D[dEmdt, S], D[dEmdt, Ew], D[dEmdt, Pw], D[dEmdt, Iw], D[dEmdt, Aw], D[dEmdt, Em],
     D[dEmdt, Pm], D[dEmdt, Im], D[dEmdt, Am]},
    {D[dPmdt, S], D[dPmdt, Ew], D[dPmdt, Pw], D[dPmdt, Iw], D[dPmdt, Aw], D[dPmdt, Em],
     D[dPmdt, Pm], D[dPmdt, Im], D[dPmdt, Am]},
    {D[dImdt, S], D[dImdt, Ew], D[dImdt, Pw], D[dImdt, Iw], D[dImdt, Aw], D[dImdt, Em],
     D[dImdt, Pm], D[dImdt, Im], D[dImdt, Am]},
    {D[dAmdt, S], D[dAmdt, Ew], D[dAmdt, Pw], D[dAmdt, Iw], D[dAmdt, Aw], D[dAmdt, Em],
     D[dAmdt, Pm], D[dAmdt, Im], D[dAmdt, Am]}} /. start;
```

In the special case where the exposed class is highly transitory and most infections occur during the pre-symptomatic phase, we have the simpler equations:

dPwdt=(1-f)*βP*Pw-κP*Pw
dPmdt = (1-fm)*βPm*Pm-κPm*Pm;

The change in allele frequency, $p = \frac{Pm}{Pm+Pw}$, is thus given by $\frac{dp}{dt} = \frac{d\left(\frac{Pm}{Pm+Pw}\right)}{dt}$, which is:

```
D[Pm[t]/(Pw[t] + Pm[t]), t] /. Pm'[t] -> (1 - fm) * βPm * S Pm - κPm * Pm /. Pw'[t] -> (1 - f) * βP * S * Pw - κP * Pw /. Pm[t] -> Pm /.
      Pw[t] -> Pw /. fm → f + Δf /. βPm → βP + Δβ /. κPm -> κP + Δκ /. {Pm → p (Pm + Pw), Pw → (1 - p) (Pm + Pw)} // Factor
(-1 + p) p (S βP Δf - S Δβ + f S Δβ + S Δf Δβ + Δκ)
```

Assuming that $\Delta f\,\Delta\beta$ is small, relative to the other terms (weak selection), gives equations (1) and (2).

Returning to the generic model:

```
stabmat // MatrixForm
```

$$\begin{pmatrix} 0 & 0 & -S\,\beta P & -S\,\beta I & -S\,\beta A & 0 & -S\,\beta P & -S\,\beta Im & -S\,\beta Am \\ 0 & -\kappa E & S\,\beta P & S\,\beta I & S\,\beta A & 0 & 0 & 0 & 0 \\ 0 & (1-f)\,\kappa E & -\kappa P & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \kappa P & -\alpha-\kappa I & 0 & 0 & 0 & 0 & 0 \\ 0 & f\,\kappa E & 0 & 0 & -\kappa A & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\kappa Em & S\,\beta Pm & S\,\beta Im & S\,\beta Am \\ 0 & 0 & 0 & 0 & 0 & (1-fm)\,\kappa Em & -\kappa Pm & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \kappa Pm & -\alpha m-\kappa Im & 0 \\ 0 & 0 & 0 & 0 & 0 & fm\,\kappa Em & 0 & 0 & -\kappa Am \end{pmatrix}$$

The eigenvalues, λ, are determined by the roots of the following characteristic polynomial:

```
charpoly = Det[λ IdentityMatrix[9] - stabmat] // Factor
```

$$\begin{aligned}&\lambda\,\big(-S\,\alpha\,\beta P\,\kappa A\,\kappa E+f\,S\,\alpha\,\beta P\,\kappa A\,\kappa E-S\,\beta P\,\kappa A\,\kappa E\,\kappa I+f\,S\,\beta P\,\kappa A\,\kappa E\,\kappa I-f\,S\,\alpha\,\beta A\,\kappa E\,\kappa P+\alpha\,\kappa A\,\kappa E\,\kappa P-S\,\beta I\,\kappa A\,\kappa E\,\kappa P+\\&\quad f\,S\,\beta I\,\kappa A\,\kappa E\,\kappa P-f\,S\,\beta A\,\kappa E\,\kappa I\,\kappa P+\kappa A\,\kappa E\,\kappa I\,\kappa P-f\,S\,\alpha\,\beta A\,\kappa E\,\lambda-S\,\alpha\,\beta P\,\kappa E\,\lambda+f\,S\,\alpha\,\beta P\,\kappa E\,\lambda+\alpha\,\kappa A\,\kappa E\,\lambda-S\,\beta P\,\kappa A\,\kappa E\,\lambda+\\&\quad f\,S\,\beta P\,\kappa A\,\kappa E\,\lambda-f\,S\,\beta A\,\kappa E\,\kappa I\,\lambda-S\,\beta P\,\kappa E\,\kappa I\,\lambda+f\,S\,\beta P\,\kappa E\,\kappa I\,\lambda+\kappa A\,\kappa E\,\kappa I\,\lambda+\alpha\,\kappa A\,\kappa P\,\lambda+\alpha\,\kappa E\,\kappa P\,\lambda-f\,S\,\beta A\,\kappa E\,\kappa P\,\lambda-\\&\quad S\,\beta I\,\kappa E\,\kappa P\,\lambda+f\,S\,\beta I\,\kappa E\,\kappa P\,\lambda+\kappa A\,\kappa E\,\kappa P\,\lambda+\kappa A\,\kappa I\,\kappa P\,\lambda+\kappa E\,\kappa I\,\kappa P\,\lambda+\alpha\,\kappa A\,\lambda^2+\alpha\,\kappa E\,\lambda^2-f\,S\,\beta A\,\kappa E\,\lambda^2-S\,\beta P\,\kappa E\,\lambda^2+\\&\quad f\,S\,\beta P\,\kappa E\,\lambda^2+\kappa A\,\kappa E\,\lambda^2+\kappa A\,\kappa I\,\lambda^2+\kappa E\,\kappa I\,\lambda^2+\alpha\,\kappa P\,\lambda^2+\kappa A\,\kappa P\,\lambda^2+\kappa E\,\kappa P\,\lambda^2+\kappa I\,\kappa P\,\lambda^2+\alpha\,\lambda^3+\kappa A\,\lambda^3+\kappa E\,\lambda^3+\kappa I\,\lambda^3+\kappa P\,\lambda^3+\lambda^4\big)\\&\big(-S\,\alpha m\,\beta Pm\,\kappa Am\,\kappa Em+fm\,S\,\alpha m\,\beta Pm\,\kappa Am\,\kappa Em-S\,\beta Pm\,\kappa Am\,\kappa Em\,\kappa Im+fm\,S\,\beta Pm\,\kappa Am\,\kappa Em\,\kappa Im-fm\,S\,\alpha m\,\beta Am\,\kappa Em\,\kappa Pm+\alpha m\,\kappa Am\,\kappa Em\,\kappa Pm-\\&\quad S\,\beta Im\,\kappa Am\,\kappa Em\,\kappa Pm+fm\,S\,\beta Im\,\kappa Am\,\kappa Em\,\kappa Pm-fm\,S\,\beta Am\,\kappa Em\,\kappa Im\,\kappa Pm+\kappa Am\,\kappa Em\,\kappa Im\,\kappa Pm-fm\,S\,\alpha m\,\beta Am\,\kappa Em\,\lambda-S\,\alpha m\,\beta Pm\,\kappa Em\,\lambda+\\&\quad fm\,S\,\alpha m\,\beta Pm\,\kappa Em\,\lambda+\alpha m\,\kappa Am\,\kappa Em\,\lambda-S\,\beta Pm\,\kappa Am\,\kappa Em\,\lambda+fm\,S\,\beta Pm\,\kappa Am\,\kappa Em\,\lambda-fm\,S\,\beta Am\,\kappa Em\,\kappa Im\,\lambda-S\,\beta Pm\,\kappa Em\,\kappa Im\,\lambda+fm\,S\,\beta Pm\,\kappa Em\,\kappa Im\,\lambda+\\&\quad\kappa Am\,\kappa Em\,\kappa Im\,\lambda+\alpha m\,\kappa Am\,\kappa Pm\,\lambda+\alpha m\,\kappa Em\,\kappa Pm\,\lambda-fm\,S\,\beta Am\,\kappa Em\,\kappa Pm\,\lambda-S\,\beta Im\,\kappa Em\,\kappa Pm\,\lambda+fm\,S\,\beta Im\,\kappa Em\,\kappa Pm\,\lambda+\kappa Am\,\kappa Em\,\kappa Pm\,\lambda^2+\\&\quad\kappa Am\,\kappa Im\,\kappa Pm\,\lambda+\kappa Em\,\kappa Im\,\kappa Pm\,\lambda+\alpha m\,\kappa Am\,\lambda^2+\alpha m\,\kappa Em\,\lambda^2-fm\,S\,\beta Am\,\kappa Em\,\lambda^2-S\,\beta Pm\,\kappa Em\,\lambda^2+fm\,S\,\beta Pm\,\kappa Em\,\lambda^2+\kappa Am\,\kappa Em\,\lambda^2+\\&\quad\kappa Am\,\kappa Im\,\lambda^2+\kappa Em\,\kappa Im\,\lambda^2+\alpha m\,\kappa Pm\,\lambda^2+\kappa Am\,\kappa Pm\,\lambda^2+\kappa Em\,\kappa Pm\,\lambda^2+\kappa Im\,\kappa Pm\,\lambda^2+\alpha m\,\lambda^3+\kappa Am\,\lambda^3+\kappa Em\,\lambda^3+\kappa Im\,\lambda^3+\kappa Pm\,\lambda^3+\lambda^4\big)\end{aligned}$$

This separates into a characteristic polynomial describing the growth of the resident:

```
poly = Collect[ charpoly[[2]], λ, Factor]
```

$$\begin{aligned}&\kappa E\,(-S\,\alpha\,\beta P\,\kappa A+f\,S\,\alpha\,\beta P\,\kappa A-S\,\beta P\,\kappa A\,\kappa I+f\,S\,\beta P\,\kappa A\,\kappa I-f\,S\,\alpha\,\beta A\,\kappa P+\alpha\,\kappa A\,\kappa P-S\,\beta I\,\kappa A\,\kappa P+f\,S\,\beta I\,\kappa A\,\kappa P-f\,S\,\beta A\,\kappa I\,\kappa P+\kappa A\,\kappa I\,\kappa P)+\\&\quad(-f\,S\,\alpha\,\beta A\,\kappa E-S\,\alpha\,\beta P\,\kappa E+f\,S\,\alpha\,\beta P\,\kappa E+\alpha\,\kappa A\,\kappa E-S\,\beta P\,\kappa A\,\kappa E+f\,S\,\beta P\,\kappa A\,\kappa E-f\,S\,\beta A\,\kappa E\,\kappa I-S\,\beta P\,\kappa E\,\kappa I+\\&\qquad f\,S\,\beta P\,\kappa E\,\kappa I+\kappa A\,\kappa E\,\kappa I+\alpha\,\kappa A\,\kappa P+\alpha\,\kappa E\,\kappa P-f\,S\,\beta A\,\kappa E\,\kappa P-S\,\beta I\,\kappa E\,\kappa P+f\,S\,\beta I\,\kappa E\,\kappa P+\kappa A\,\kappa E\,\kappa P+\kappa A\,\kappa I\,\kappa P+\kappa E\,\kappa I\,\kappa P)\,\lambda+\\&\quad(\alpha\,\kappa A+\alpha\,\kappa E-f\,S\,\beta A\,\kappa E-S\,\beta P\,\kappa E+f\,S\,\beta P\,\kappa E+\kappa A\,\kappa E+\kappa A\,\kappa I+\kappa E\,\kappa I+\alpha\,\kappa P+\kappa A\,\kappa P+\kappa E\,\kappa P+\kappa I\,\kappa P)\,\lambda^2+(\alpha+\kappa A+\kappa E+\kappa I+\kappa P)\,\lambda^3+\lambda^4\end{aligned}$$

```
poly /. βI → 0 /. βA → 0 // Factor
```

$$(\kappa A+\lambda)\,(\alpha+\kappa I+\lambda)\,\left(-S\,\beta P\,\kappa E+f\,S\,\beta P\,\kappa E+\kappa E\,\kappa P+\kappa E\,\lambda+\kappa P\,\lambda+\lambda^2\right)$$

And a characteristic polynomial describing the growth of the mutant:

```
polym = Collect[ charpoly[[3]], λ, Factor] /. λ → λm
```

$$\begin{aligned}&\kappa Em\,(-S\,\alpha m\,\beta Pm\,\kappa Am+fm\,S\,\alpha m\,\beta Pm\,\kappa Am-S\,\beta Pm\,\kappa Am\,\kappa Im+fm\,S\,\beta Pm\,\kappa Am\,\kappa Im-\\&\qquad fm\,S\,\alpha m\,\beta Am\,\kappa Pm+\alpha m\,\kappa Am\,\kappa Pm-S\,\beta Im\,\kappa Am\,\kappa Pm+fm\,S\,\beta Im\,\kappa Am\,\kappa Pm-fm\,S\,\beta Am\,\kappa Im\,\kappa Pm+\kappa Am\,\kappa Im\,\kappa Pm)+\\&\quad(-fm\,S\,\alpha m\,\beta Am\,\kappa Em-S\,\alpha m\,\beta Pm\,\kappa Em+fm\,S\,\alpha m\,\beta Pm\,\kappa Em+\alpha m\,\kappa Am\,\kappa Em-S\,\beta Pm\,\kappa Am\,\kappa Em+fm\,S\,\beta Pm\,\kappa Am\,\kappa Em-\\&\qquad fm\,S\,\beta Am\,\kappa Em\,\kappa Im-S\,\beta Pm\,\kappa Em\,\kappa Im+fm\,S\,\beta Pm\,\kappa Em\,\kappa Im+\kappa Am\,\kappa Em\,\kappa Im+\alpha m\,\kappa Am\,\kappa Pm+\alpha m\,\kappa Em\,\kappa Pm-\\&\qquad fm\,S\,\beta Am\,\kappa Em\,\kappa Pm-S\,\beta Im\,\kappa Em\,\kappa Pm+fm\,S\,\beta Im\,\kappa Em\,\kappa Pm+\kappa Am\,\kappa Em\,\kappa Pm+\kappa Am\,\kappa Im\,\kappa Pm+\kappa Em\,\kappa Im\,\kappa Pm)\,\lambda m+\\&\quad(\alpha m\,\kappa Am+\alpha m\,\kappa Em-fm\,S\,\beta Am\,\kappa Em-S\,\beta Pm\,\kappa Em+fm\,S\,\beta Pm\,\kappa Em+\kappa Am\,\kappa Em+\kappa Am\,\kappa Im+\kappa Em\,\kappa Im+\alpha m\,\kappa Pm+\kappa Am\,\kappa Pm+\kappa Em\,\kappa Pm+\kappa Im\,\kappa Pm)\,\lambda m^2+\\&\quad(\alpha m+\kappa Am+\kappa Em+\kappa Im+\kappa Pm)\,\lambda m^3+\lambda m^4\end{aligned}$$

As expected, when most individuals are susceptible, mutations spread independently and the one with the largest eigenvalue will spread fastest. To determine the difference in the leading eigenvalue, we assume that the mutational effects are small (all of the "m" terms above are near the wildtype rate, with the difference of order ϵ). We can then calculate $\Delta\lambda m=\lambda m-\lambda$, by taking the Taylor series and solving the characteristic polynomial for $\Delta\lambda m$.

```
smallmutant = {αm → α + ϵ * Δα, fm → f + ϵ * Δf, κIm → κI + ϵ * ΔκI, κEm → κE + ϵ * ΔκE,
    κAm → κA + ϵ * ΔκA, κPm → κP + ϵ * ΔκP, βAm → βA + ϵ * ΔβA, βPm → βP + ϵ * ΔβP, βIm → βI + ϵ * ΔβI};
smallterms = {Δα, Δf, ΔκI, ΔκE, ΔκA, ΔκP, ΔβA, ΔβP, ΔβI};
```

As expected, polym is zero to O(1) (reduces to poly for the wildtype, which is zero by definition of the eigenvalues):

```
Factor[Normal[Series[polym /. λm → λ + ϵ * Δλm /. smallmutant, {ϵ, 0, 0}]]]
```

$$\begin{aligned}&-S\,\alpha\,\beta P\,\kappa A\,\kappa E+f\,S\,\alpha\,\beta P\,\kappa A\,\kappa E-S\,\beta P\,\kappa A\,\kappa E\,\kappa I+f\,S\,\beta P\,\kappa A\,\kappa E\,\kappa I-f\,S\,\alpha\,\beta A\,\kappa E\,\kappa P+\alpha\,\kappa A\,\kappa E\,\kappa P-S\,\beta I\,\kappa A\,\kappa E\,\kappa P+\\&\quad f\,S\,\beta I\,\kappa A\,\kappa E\,\kappa P-f\,S\,\beta A\,\kappa E\,\kappa I\,\kappa P+\kappa A\,\kappa E\,\kappa I\,\kappa P-f\,S\,\alpha\,\beta A\,\kappa E\,\lambda-S\,\alpha\,\beta P\,\kappa E\,\lambda+f\,S\,\alpha\,\beta P\,\kappa E\,\lambda+\alpha\,\kappa A\,\kappa E\,\lambda-S\,\beta P\,\kappa A\,\kappa E\,\lambda+\\&\quad f\,S\,\beta P\,\kappa A\,\kappa E\,\lambda-f\,S\,\beta A\,\kappa E\,\kappa I\,\lambda-S\,\beta P\,\kappa E\,\kappa I\,\lambda+f\,S\,\beta P\,\kappa E\,\kappa I\,\lambda+\kappa A\,\kappa E\,\kappa I\,\lambda+\alpha\,\kappa A\,\kappa P\,\lambda+\alpha\,\kappa E\,\kappa P\,\lambda-f\,S\,\beta A\,\kappa E\,\kappa P\,\lambda-\\&\quad S\,\beta I\,\kappa E\,\kappa P\,\lambda+f\,S\,\beta I\,\kappa E\,\kappa P\,\lambda+\kappa A\,\kappa E\,\kappa P\,\lambda+\kappa A\,\kappa I\,\kappa P\,\lambda+\kappa E\,\kappa I\,\kappa P\,\lambda+\alpha\,\kappa A\,\lambda^2+\alpha\,\kappa E\,\lambda^2-f\,S\,\beta A\,\kappa E\,\lambda^2-S\,\beta P\,\kappa E\,\lambda^2+\\&\quad f\,S\,\beta P\,\kappa E\,\lambda^2+\kappa A\,\kappa E\,\lambda^2+\kappa A\,\kappa I\,\lambda^2+\kappa E\,\kappa I\,\lambda^2+\alpha\,\kappa P\,\lambda^2+\kappa A\,\kappa P\,\lambda^2+\kappa E\,\kappa P\,\lambda^2+\kappa I\,\kappa P\,\lambda^2+\alpha\,\lambda^3+\kappa A\,\lambda^3+\kappa E\,\lambda^3+\kappa I\,\lambda^3+\kappa P\,\lambda^3+\lambda^4\end{aligned}$$

```
Factor[% - poly]
```

$$0$$

To order ϵ, we can find effect of the mutation on the rate of growth, $\Delta\lambda m$:

```
Factor[SeriesCoefficient[Series[polym /. λm → λ + ϵ * Δλm /. smallmutant, {ϵ, 0, 1}], 1]];
Factor[Flatten[Solve[% == 0, Δλm]]]
```

$$\{\Delta\lambda m \to -\left(S\,\alpha\,\beta P\,\Delta\kappa E\,\kappa A - f\,S\,\alpha\,\beta P\,\Delta\kappa E\,\kappa A + S\,\alpha\,\beta P\,\Delta\kappa A\,\kappa E - f\,S\,\alpha\,\beta P\,\Delta\kappa A\,\kappa E + f\,S\,\alpha\,\beta A\,\Delta\kappa P\,\kappa E - S\,\alpha\,\beta P\,\Delta f\,\kappa A\,\kappa E + S\,\beta P\,\Delta\alpha\,\kappa A\,\kappa E - f\,S\,\beta P\,\Delta\alpha\,\kappa A\,\kappa E + S\,\alpha\,\Delta\beta P\,\kappa A\,\kappa E - f\,S\,\alpha\,\Delta\beta P\,\kappa A\,\kappa E + S\,\beta P\,\Delta\kappa I\,\kappa A\,\kappa E - f\,S\,\beta P\,\Delta\kappa I\,\kappa A\,\kappa E - \alpha\,\Delta\kappa P\,\kappa A\,\kappa E + S\,\beta I\,\Delta\kappa P\,\kappa A\,\kappa E - f\,S\,\beta I\,\Delta\kappa P\,\kappa A\,\kappa E + S\,\beta P\,\Delta\kappa E\,\kappa A\,\kappa I - f\,S\,\beta P\,\Delta\kappa E\,\kappa A\,\kappa I + S\,\beta P\,\Delta\kappa A\,\kappa E\,\kappa I - f\,S\,\beta P\,\Delta\kappa A\,\kappa E\,\kappa I + f\,S\,\beta A\,\Delta\kappa P\,\kappa E\,\kappa I - 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f\,S\,\beta P\,\Delta\kappa A\,\kappa E\,\lambda + S\,\beta P\,\Delta\kappa I\,\kappa E\,\lambda + f\,S\,\beta P\,\Delta\kappa I\,\kappa E\,\lambda - \alpha\,\Delta\kappa P\,\kappa E\,\lambda + f\,S\,\beta A\,\Delta\kappa P\,\kappa E\,\lambda + S\,\beta I\,\Delta\kappa P\,\kappa E\,\lambda - f\,S\,\beta I\,\Delta\kappa P\,\kappa E\,\lambda - S\,\beta P\,\Delta f\,\kappa A\,\kappa E\,\lambda - \Delta\alpha\,\kappa A\,\kappa E\,\lambda + S\,\Delta\beta P\,\kappa A\,\kappa E\,\lambda - f\,S\,\Delta\beta P\,\kappa A\,\kappa E\,\lambda - \Delta\kappa I\,\kappa A\,\kappa E\,\lambda - \Delta\kappa P\,\kappa A\,\kappa E\,\lambda + f\,S\,\beta A\,\Delta\kappa E\,\kappa I\,\lambda + S\,\beta P\,\Delta\kappa E\,\kappa I\,\lambda - f\,S\,\beta P\,\Delta\kappa E\,\kappa I\,\lambda - \Delta\kappa E\,\kappa A\,\kappa I\,\lambda - \Delta\kappa P\,\kappa A\,\kappa I\,\lambda + S\,\beta A\,\Delta f\,\kappa E\,\kappa I\,\lambda - S\,\beta P\,\Delta f\,\kappa E\,\kappa I\,\lambda + f\,S\,\Delta\beta A\,\kappa E\,\kappa I\,\lambda + S\,\Delta\beta P\,\kappa E\,\kappa I\,\lambda - 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f\,S\,\alpha\,\beta P\,\kappa E - \alpha\,\kappa A\,\kappa E + S\,\beta P\,\kappa A\,\kappa E - f\,S\,\beta P\,\kappa A\,\kappa E + f\,S\,\beta A\,\kappa E\,\kappa I + S\,\beta P\,\kappa E\,\kappa I - f\,S\,\beta P\,\kappa E\,\kappa I - \kappa A\,\kappa E\,\kappa I - \alpha\,\kappa A\,\kappa P - \alpha\,\kappa E\,\kappa P + f\,S\,\beta A\,\kappa E\,\kappa P + S\,\beta I\,\kappa E\,\kappa P - f\,S\,\beta I\,\kappa E\,\kappa P - \kappa A\,\kappa E\,\kappa P - \kappa A\,\kappa I\,\kappa P - \kappa E\,\kappa I\,\kappa P - 2\,\alpha\,\kappa A\,\lambda - 2\,\alpha\,\kappa E\,\lambda + 2\,f\,S\,\beta A\,\kappa E\,\lambda + 2\,S\,\beta P\,\kappa E\,\lambda - 2\,f\,S\,\beta P\,\kappa E\,\lambda - 2\,\kappa A\,\kappa E\,\lambda - 2\,\kappa A\,\kappa I\,\lambda - 2\,\kappa E\,\kappa I\,\lambda - 2\,\alpha\,\kappa P\,\lambda - 2\,\kappa A\,\kappa P\,\lambda - 2\,\kappa E\,\kappa P\,\lambda - 2\,\kappa I\,\kappa P\,\lambda - 3\,\alpha\,\lambda^2 - 3\,\kappa A\,\lambda^2 - 3\,\kappa E\,\lambda^2 - 3\,\kappa I\,\lambda^2 - 3\,\kappa P\,\lambda^2 - 4\,\lambda^3\right)\}$$

The denominator is shared and equals the slope of the characteristic polynomial at the leading eigenvalue (positive given the form of the cubic):

```
denom = D[poly, λ] // Factor
```

$$-f\,S\,\alpha\,\beta A\,\kappa E - S\,\alpha\,\beta P\,\kappa E + f\,S\,\alpha\,\beta P\,\kappa E + \alpha\,\kappa A\,\kappa E - S\,\beta P\,\kappa A\,\kappa E + f\,S\,\beta P\,\kappa A\,\kappa E - f\,S\,\beta A\,\kappa E\,\kappa I - S\,\beta P\,\kappa E\,\kappa I + f\,S\,\beta P\,\kappa E\,\kappa I + \kappa A\,\kappa E\,\kappa I + \alpha\,\kappa A\,\kappa P + \alpha\,\kappa E\,\kappa P - f\,S\,\beta A\,\kappa E\,\kappa P - S\,\beta I\,\kappa E\,\kappa P + f\,S\,\beta I\,\kappa E\,\kappa P + \kappa A\,\kappa E\,\kappa P + \kappa A\,\kappa I\,\kappa P + \kappa E\,\kappa I\,\kappa P + 2\,\alpha\,\kappa A\,\lambda + 2\,\alpha\,\kappa E\,\lambda - 2\,f\,S\,\beta A\,\kappa E\,\lambda - 2\,S\,\beta P\,\kappa E\,\lambda + 2\,f\,S\,\beta P\,\kappa E\,\lambda + 2\,\kappa A\,\kappa E\,\lambda + 2\,\kappa A\,\kappa I\,\lambda + 2\,\kappa E\,\kappa I\,\lambda + 2\,\alpha\,\kappa P\,\lambda + 2\,\kappa A\,\kappa P\,\lambda + 2\,\kappa E\,\kappa P\,\lambda + 2\,\kappa I\,\kappa P\,\lambda + 3\,\alpha\,\lambda^2 + 3\,\kappa A\,\lambda^2 + 3\,\kappa E\,\lambda^2 + 3\,\kappa I\,\lambda^2 + 3\,\kappa P\,\lambda^2 + 4\,\lambda^3$$

```
selection = Collect[denom Δλm / slope /. %%, smallterms, Factor]
```

$$-\frac{(-1+f)\,S\,\Delta\beta I\,\kappa E\,\kappa P\,(\kappa A+\lambda)}{\text{slope}} - \frac{(-1+f)\,S\,\Delta\beta P\,\kappa E\,(\kappa A+\lambda)\,(\alpha+\kappa I+\lambda)}{\text{slope}} + \frac{f\,S\,\Delta\beta A\,\kappa E\,(\alpha+\kappa I+\lambda)\,(\kappa P+\lambda)}{\text{slope}} - \frac{1}{\text{slope}}$$
$$S\,\Delta f\,\kappa E\,\left(\alpha\,\beta P\,\kappa A + \beta P\,\kappa A\,\kappa I - \alpha\,\beta A\,\kappa P + \beta I\,\kappa A\,\kappa P - \beta A\,\kappa I\,\kappa P - \alpha\,\beta A\,\lambda + \alpha\,\beta P\,\lambda + \beta P\,\kappa A\,\lambda - \beta A\,\kappa I\,\lambda + \beta P\,\kappa I\,\lambda - \beta A\,\kappa P\,\lambda + \beta I\,\kappa P\,\lambda - \beta A\,\lambda^2 + \beta P\,\lambda^2\right) +$$
$$\frac{1}{\text{slope}}\Delta\kappa P\,\left(f\,S\,\alpha\,\beta A\,\kappa E - \alpha\,\kappa A\,\kappa E + S\,\beta I\,\kappa A\,\kappa E - f\,S\,\beta I\,\kappa A\,\kappa E + f\,S\,\beta A\,\kappa E\,\kappa I - \kappa A\,\kappa E\,\kappa I - \alpha\,\kappa A\,\lambda - \alpha\,\kappa E\,\lambda + f\,S\,\beta A\,\kappa E\,\lambda + S\,\beta I\,\kappa E\,\lambda - f\,S\,\beta I\,\kappa E\,\lambda - \kappa A\,\kappa E\,\lambda - \kappa A\,\kappa I\,\lambda - \kappa E\,\kappa I\,\lambda - \alpha\,\lambda^2 - \kappa A\,\lambda^2 - \kappa E\,\lambda^2 - \kappa I\,\lambda^2 - \lambda^3\right) +$$
$$\frac{1}{\text{slope}}\Delta\alpha\,\left(S\,\beta P\,\kappa A\,\kappa E - f\,S\,\beta P\,\kappa A\,\kappa E + f\,S\,\beta A\,\kappa E\,\kappa P - \kappa A\,\kappa E\,\kappa P + f\,S\,\beta A\,\kappa E\,\lambda + S\,\beta P\,\kappa E\,\lambda - f\,S\,\beta P\,\kappa E\,\lambda - \kappa A\,\kappa E\,\lambda - \kappa A\,\kappa P\,\lambda - \kappa E\,\kappa P\,\lambda - \kappa A\,\lambda^2 - \kappa E\,\lambda^2 - \kappa P\,\lambda^2 - \lambda^3\right) + \frac{1}{\text{slope}}\Delta\kappa I\,\left(S\,\beta P\,\kappa A\,\kappa E - f\,S\,\beta P\,\kappa A\,\kappa E + f\,S\,\beta A\,\kappa E\,\kappa P - \kappa A\,\kappa E\,\kappa P + f\,S\,\beta A\,\kappa E\,\lambda + S\,\beta P\,\kappa E\,\lambda - f\,S\,\beta P\,\kappa E\,\lambda - \kappa A\,\kappa E\,\lambda - \kappa A\,\kappa P\,\lambda - \kappa E\,\kappa P\,\lambda - \kappa A\,\lambda^2 - \kappa E\,\lambda^2 - \kappa P\,\lambda^2 - \lambda^3\right) +$$
$$\frac{1}{\text{slope}}\Delta\kappa E\,\left(S\,\alpha\,\beta P\,\kappa A - f\,S\,\alpha\,\beta P\,\kappa A + S\,\beta P\,\kappa A\,\kappa I - f\,S\,\beta P\,\kappa A\,\kappa I + f\,S\,\alpha\,\beta A\,\kappa P - \alpha\,\kappa A\,\kappa P + S\,\beta I\,\kappa A\,\kappa P - f\,S\,\beta I\,\kappa A\,\kappa P + f\,S\,\beta A\,\kappa I\,\kappa P - \kappa A\,\kappa I\,\kappa P + f\,S\,\alpha\,\beta A\,\lambda + S\,\alpha\,\beta P\,\lambda - f\,S\,\alpha\,\beta P\,\lambda - \alpha\,\kappa A\,\lambda + S\,\beta P\,\kappa A\,\lambda - f\,S\,\beta P\,\kappa A\,\lambda + f\,S\,\beta A\,\kappa I\,\lambda + S\,\beta P\,\kappa I\,\lambda - f\,S\,\beta P\,\kappa I\,\lambda - \kappa A\,\kappa I\,\lambda + \alpha\,\kappa P\,\lambda + f\,S\,\beta A\,\kappa P\,\lambda + S\,\beta I\,\kappa P\,\lambda - f\,S\,\beta I\,\kappa P\,\lambda - \kappa A\,\kappa P\,\lambda - \kappa I\,\kappa P\,\lambda - \alpha\,\lambda^2 + f\,S\,\beta A\,\lambda^2 + S\,\beta P\,\lambda^2 - f\,S\,\beta P\,\lambda^2 - \kappa A\,\lambda^2 - \kappa I\,\lambda^2 - \kappa P\,\lambda^2 - \lambda^3\right) -$$
$$\frac{1}{\text{slope}}\Delta\kappa A\,\left(-S\,\alpha\,\beta P\,\kappa E + f\,S\,\alpha\,\beta P\,\kappa E - S\,\beta P\,\kappa E\,\kappa I + f\,S\,\beta P\,\kappa E\,\kappa I + \alpha\,\kappa E\,\kappa P - S\,\beta I\,\kappa E\,\kappa P + f\,S\,\beta I\,\kappa E\,\kappa P + \kappa E\,\kappa I\,\kappa P + \alpha\,\kappa E\,\lambda - S\,\beta P\,\kappa E\,\lambda + f\,S\,\beta P\,\kappa E\,\lambda + \kappa E\,\kappa I\,\lambda + \alpha\,\kappa P\,\lambda + \kappa E\,\kappa P\,\lambda + \kappa I\,\kappa P\,\lambda + \alpha\,\lambda^2 + \kappa E\,\lambda^2 + \kappa I\,\lambda^2 + \kappa P\,\lambda^2 + \lambda^3\right)$$

We can also understand selection on mutants by using the method in Box 10.2 of Otto and Day, calculating selection as $\frac{d\lambda}{dz} = \frac{v^T \frac{dM}{dz} u}{v^T u}$, where z represents some underlying trait that the mutation affects (e.g., replication rate) and v^T and u are the left and right eigenvectors of **M**, the matrix describing movement between the infected classes for the resident:

```
submat = stabmat[[2 ;; 5, 2 ;; 5]];
% // MatrixForm
```

$$\begin{pmatrix} -\kappa E & S\,\beta P & S\,\beta I & S\,\beta A \\ (1-f)\,\kappa E & -\kappa P & 0 & 0 \\ 0 & \kappa P & -\alpha-\kappa I & 0 \\ f\,\kappa E & 0 & 0 & -\kappa A \end{pmatrix}$$

and for the mutant:

```
submatm = stabmat[[6 ;; 9, 6 ;; 9]];
% // MatrixForm
```

$$\begin{pmatrix} -\kappa Em & S\,\beta Pm & S\,\beta Im & S\,\beta Am \\ (1-fm)\,\kappa Em & -\kappa Pm & 0 & 0 \\ 0 & \kappa Pm & -\alpha m-\kappa Im & 0 \\ fm\,\kappa Em & 0 & 0 & -\kappa Am \end{pmatrix}$$

Calculating the relative reproductive values (the left eigenvector):

```
left = {vE, vP, vI, vA};

left.submat - λ left
```

$$\{f\,vA\,\kappa E - vE\,\kappa E + (1-f)\,vP\,\kappa E - vE\,\lambda,\ S\,vE\,\beta P + vI\,\kappa P - vP\,\kappa P - vP\,\lambda,\ S\,vE\,\beta I + vI\,(-\alpha-\kappa I) - vI\,\lambda,\ S\,vE\,\beta A - vA\,\kappa A - vA\,\lambda\}$$

```
leftvector = left /. Flatten[Solve[(%[[2 ;; 4]]) == 0, Table[left[[i]], {i, 2, 4}]]] // Simplify
```

$$\left\{vE,\ \frac{S\,vE\,(\alpha\,\beta P + \beta I\,\kappa P + \beta P\,(\kappa I+\lambda))}{(\alpha+\kappa I+\lambda)\,(\kappa P+\lambda)},\ \frac{S\,vE\,\beta I}{\alpha+\kappa I+\lambda},\ \frac{S\,vE\,\beta A}{\kappa A+\lambda}\right\}$$

In addition, the fact that the characteristic polynomial is zero guarantees that the first term in v M − v λ is also zero:

```
((left.submat - λ left)[[1]] /. Table[left[[i]] → leftvector[[i]], {i, 1, 4}] // Factor) /. Factor[poly] → 0
```

0

Calculating the proportion in each class (the right eigenvector):

```
right = {uE, uP, uI, uA};

submat.right - λ right
```

$$\{S\,uA\,\beta A + S\,uI\,\beta I + S\,uP\,\beta P - uE\,\kappa E - uE\,\lambda,\ (1-f)\,uE\,\kappa E - uP\,\kappa P - uP\,\lambda,\ uI\,(-\alpha-\kappa I) + uP\,\kappa P - uI\,\lambda,\ -uA\,\kappa A + f\,uE\,\kappa E - uA\,\lambda\}$$

```
rightvector = right /. Flatten[Solve[(%[[2 ;; 4]]) == 0, Table[right[[i]], {i, 2, 4}]]] // Simplify
```

$$\left\{uE,\ -\frac{(-1+f)\,uE\,\kappa E}{\kappa P+\lambda},\ -\frac{(-1+f)\,uE\,\kappa E\,\kappa P}{(\alpha+\kappa I+\lambda)\,(\kappa P+\lambda)},\ \frac{f\,uE\,\kappa E}{\kappa A+\lambda}\right\}$$

In addition, the fact that the characteristic polynomial is zero guarantees that the first term in v M − v λ is also zero:

```
((submat.right - λ right)[[1]] /. Table[right[[i]] → rightvector[[i]], {i, 1, 4}] // Factor) /. Factor[poly] → 0
```

0

Note that the elements of both left and right eigenvectors are positive in a growing population (λ>0). Although the length of these eigenvectors is arbitrary, we constrain them so that $v^T u$ in the denominator of $\frac{d\lambda}{dz} = \frac{v^T \frac{dM}{dz} u}{v^T u}$ is one by rescaling the right eigenvector (choosing this one keeps the left eigenvector easier to read):

$$\text{rightvector} = \frac{\text{rightvector}}{\text{leftvector.rightvector}};$$

$\frac{dM}{dz}$ represents the mutational effect on the transition matrix for a viral genotype:

```
mutmat = Factor[Normal[Series[submatm - submat /. smallmutant, {ϵ, 0, 1}]] /. ϵ → 1];
MatrixForm[%]
```

$$\begin{pmatrix} -\Delta\kappa E & S\,\Delta\beta P & S\,\Delta\beta I & S\,\Delta\beta A \\ \Delta\kappa E - f\,\Delta\kappa E - \Delta f\,\kappa E & -\Delta\kappa P & 0 & 0 \\ 0 & \Delta\kappa P & -\Delta\alpha - \Delta\kappa I & 0 \\ f\,\Delta\kappa E + \Delta f\,\kappa E & 0 & 0 & -\Delta\kappa A \end{pmatrix}$$

This gives us an equivalent way to write the selection coefficient on the mutation, using the fact that the characteristic polynomial is zero:

```
Factor[leftvector.mutmat.rightvector - (selection /. slope -> denom)] /. Factor[poly] → 0
```

0

Selection is thus proportional to:

```
Collect[Table[left[[i]], {i, 1, 4}].mutmat.Table[right[[i]], {i, 1, 4}], smallterms, Factor]
```

$$-uI\,vI\,\Delta\alpha + S\,uA\,vE\,\Delta\beta A + S\,uI\,vE\,\Delta\beta I + S\,uP\,vE\,\Delta\beta P - uA\,vA\,\Delta\kappa A + uE\,(f\,vA - vE + vP - f\,vP)\,\Delta\kappa E - uI\,vI\,\Delta\kappa I + uP\,(vI - vP)\,\Delta\kappa P + uE\,(vA - vP)\,\Delta f\,\kappa E$$

S vE (uA $\Delta\beta$A+ uI $\Delta\beta$I + uP $\Delta\beta$P)−uI vI $\Delta\alpha$+uE ((1−f)vP+f vA−vE) $\Delta\kappa$E+uE (vA−vP) Δf κE−uI vI $\Delta\kappa$I−uP (vP−vI) $\Delta\kappa$P−uA vA $\Delta\kappa$A

This way of calculating selection makes it clearer what selection acts upon when a disease is spreading (λ>0):

* Always favors increased transmission [$\Delta\beta$A, $\Delta\beta$P, $\Delta\beta$I]
* Always favors lower virulence [$\Delta\alpha$] and slower recovery [$\Delta\kappa$I]
* Always favors faster progression from E -> A/P [$\Delta\kappa$E] because (1−f)vP+f vA>vE [see Note 1]
* Favors slower progression from P -> I [$\Delta\kappa$P] if vP > vI [always true if βI ≤ βP (1+1/(Dλ) − see Note 2]
* Favors more asymptomatics individuals [Δf] only if vA>vP [true only with high enough βA − see Note 3]
* Never favors faster progression from A -> R [$\Delta\kappa$Am]

[Note 1] In a spreading disease, (1−f)vP+f vA is always greater than vE because the next stage individuals (P&A) pass on the disease earlier than exposed individuals, contributing earlier to growth.

```
Factor[(1 - f) leftvector[[2]] + (f) leftvector[[4]] - leftvector[[1]] /. Solve[poly == 0, βP]]
```

$$\left\{\frac{vE\,\lambda}{\kappa E}\right\}$$

[Note 2] vP is greater than vI as long as $\beta I \leq \beta P\ (1+(\alpha+\gamma)/(\lambda))$ because infected individuals have less time to pass on the disease than pre-asymptomatics.

```
Factor[leftvector[[3]] - leftvector[[2]]]
```

$$\frac{S\,vE\ (-\alpha\,\beta P-\beta P\,\kappa I+\beta I\,\lambda-\beta P\,\lambda)}{(\alpha+\kappa I+\lambda)\ (\kappa P+\lambda)}$$

```
Solve[% == 0, βI] // Simplify
```

$$\left\{\left\{\beta I\to\frac{\beta P\ (\alpha+\kappa I+\lambda)}{\lambda}\right\}\right\}$$

[Note 3] vP is greater than vA as long as presymptomatics are expected to give rise to enough more cases than asymptomatics that $\frac{\beta P}{\kappa P+\lambda} \geq \frac{\beta A}{\kappa A+\lambda}$ (symptomatic infectious individuals make this condition even easier to satisfy).

```
Collect[leftvector[[4]] - leftvector[[2]], {βP, βI, βA}, Factor]
```

$$\frac{S\,vE\,\beta A}{\kappa A+\lambda}-\frac{S\,vE\,\beta P}{\kappa P+\lambda}-\frac{S\,vE\,\beta I\,\kappa P}{(\alpha+\kappa I+\lambda)\ (\kappa P+\lambda)}$$

- Figure 3 - Numerical analyses
- Code

Common settings

```
Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;
```

```
parvec = {β, βm, α, αm, κyP, κyPm, f, fm, κyE, κyI, κyA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] := finalfreq[vec] = Block[
    {β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], κyP = vec[[5]], κyPm = vec[[6]], f = vec[[7]], fm = vec[[8]],
     κyE = vec[[9]], κyI = vec[[10]], κyA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

    (*REMAINING PARAMETERS*)
    βyA = β / 10; βyP = β; βyI = β / 3;
    κyAm = κyA; κyIm = κyI;
    βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

    (* E: Exposed (non-infectious) cases *)
    (* A: asymptomatic cases *)
    (* P: pre-symptomatic cases *)
    (* S: symptomatic cases *)
    (* f: proportion of fsymptomatic hosts *)
    (* c: amount of distancing applied *)

    (*INOCULATION*)
    start = 10^-5;

    t =.;
    c =.;

    c[t_] :=
     Evaluate[If[t < t1min, 0, If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]]];
    h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
    hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

    sys = {S'[t] == -(h[t] + hm[t]) S[t],
      yE'[t] == h[t] S[t] - κyE yE[t],
      yA'[t] == f κyE yE[t] - κyA yA[t],
      yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
      yI'[t] == κyP yP[t] - (κyI + α) yI[t],
      yR'[t] == κyA yA[t] + κyI yI[t],
      yD'[t] == α yI[t]};  (*yD serves as a counter of the cumulative number of deaths*)

    sysm = {
      yEm'[t] == hm[t] S[t] - κyE yEm[t],
```

```
    yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
    yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
    yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
    yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
    yDm'[t] == αm yIm[t]};  (*yDm serves as a counter of the cumulative number of deaths*)

  (*FIRST BOUT OF CONTROL*)
  t1min = 75;
  t1max = 150;
  (*SECOND BOUT OF CONTROL*)
  t2min = 225;
  t2max = 300;
  (*THIRD BOUT OF CONTROL*)
  t3min = 375;
  t3max = 450;

  init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
  initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

  var = {S, yE, yA, yP, yI, yR, yD};
  varm = {yEm, yAm, yPm, yIm, yRm, yDm};

  NSolution[vec] =
   NDSolve[
    Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

  (*R0*)
  Print["R0 of the wild type = ", βyA f / κyA + (1 - f) (βyP (α + κyI) + βyI κyP) / ((α + κyI) κyP)];

  (*Rm*)
  Print["R0 of the mutant type = ", βyAm f / κyAm + (1 - f) (βyPm (αm + κyIm) + βyIm κyPm) / ((αm + κyIm) κyPm)];

  (*CASE MORTALITY*)
  Print["Case mortality = ", (1 - f) α / (κyI + α)];

  Print["Case mortality (mutant) = ", (1 - fm) αm / (κyI + αm)];

  (*CUMULATIVE MORTALITY*)
  Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
  Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];

 ]
```

■ Figure 3a: Evolution of transmission β, no control measures

```
pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
   α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
   κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

   f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
   κyE → 0.25, (* 1/TIME IN EXPOSED CLASS *)
   κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
   κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

   (*Strength of control measures*)
   c1 -> 0, c2 -> 0, c3 → 0
  };
```

The doublng time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```
Sort[Solve[
   (κE (-S α βP κA + f S α βP κA - S βP κA κI + f S βP κA κI - f S α βA κP + α κA κP - S βI κA κP + f S βI κA κP - f S βA κI κP + κA κI κP) + (-f S α
                     βA κE - S α βP κE + f S α βP κE + α κA κE - S βP κA κE + f S βP κA κE - f S βA κE κI - S βP κE κI + f S βP κE κI + κA κE κI +
                   α κA κP + α κE κP - f S βA κE κP - S βI κE κP + f S βI κE κP + κA κE κP + κA κI κP + κE κI κP) λ + (α κA + α κE - f S βA κE -
                   S βP κE + f S βP κE + κA κE + κA κI + κE κI + α κP + κA κP + κE κP + κI κP) λ^2 + (α + κA + κE + κI + κP) λ^3 + λ^4 /. S → 1 /.
            βA -> β / 10 /. βP -> β /. βI -> β / 3 /. κA -> κyA /. κE -> κyE /. κP -> κyP /. κI -> κyI /. pars) == 0, λ]]
Solve[
 (Exp[
     λ
       t] ==
    2) /.
  Last[
   %],
 t]
```

```
{{λ → -1.145}, {λ → -0.431496}, {λ → -0.115364}, {λ → 0.126863}}
```

Solve::ifun : Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information. >>

```
{{t → 5.46374}}
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.73916

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

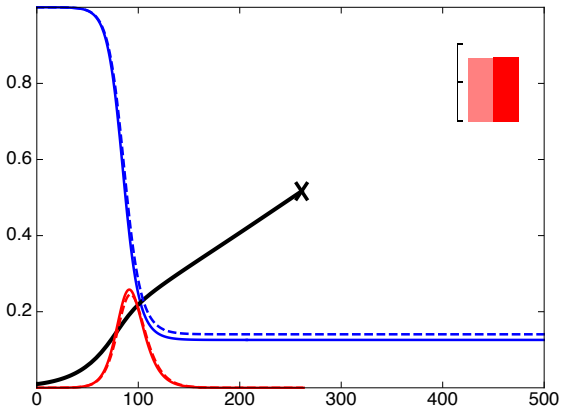
Cumulative mortality (total) = 0.0167685

Cumulative mortality (mutant) = 0.

265

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[ (yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{ (yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) } /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.73916

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0170565

Cumulative mortality (mutant) = 0.00329928

261

{0.516598}
```



- **Figure 3b: Evolution of asymptomatic fraction f, no control measures**

```
pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.28263

R0 of the mutant type = 2.28263

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0167685

Cumulative mortality (mutant) = 0.

265
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.28263

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0168822

Cumulative mortality (mutant) = 0.000797917

264

{0.039494}
```

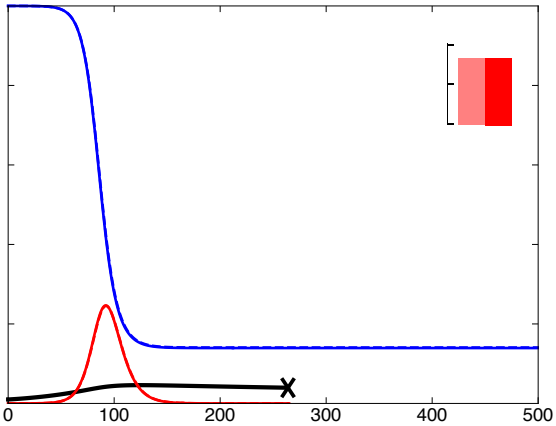


Figure 3c: Evolution of pre-symptomatic phase κ, no control measures

```
pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.28263

R0 of the mutant type = 2.68263

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0167685

Cumulative mortality (mutant) = 0.

265
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.68263

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0169484

Cumulative mortality (mutant) = 0.00228206

262

{0.359268}

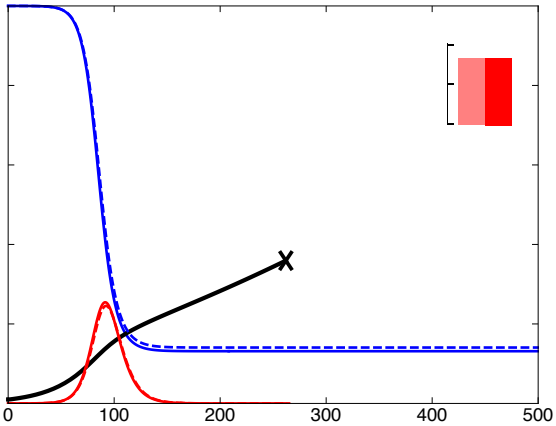


Figure 3d: Evolution of virulence α, no control measures

```
pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.0, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.28263

R0 of the mutant type = 2.31515

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0167685

Cumulative mortality (mutant) = 0.

265
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.31515

Case mortality = 0.0195122

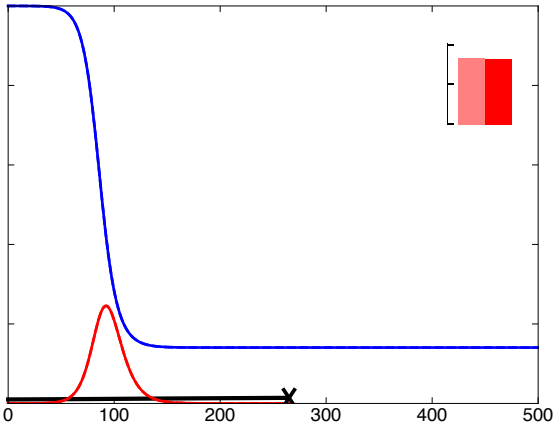
Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0165804

Cumulative mortality (mutant) = 0.

265

{0.0140646}

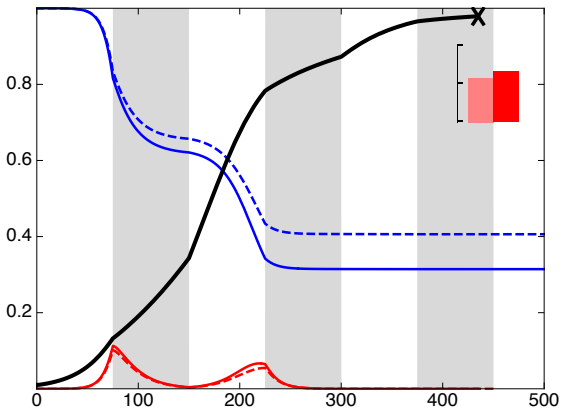


■ Figure 3e: Evolution of transmission β, control measures

```
pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.28263

R0 of the mutant type = 2.73916

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0115874

Cumulative mortality (mutant) = 0.

449
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.73916

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0133774

Cumulative mortality (mutant) = 0.00545342

435

{0.979012}
```



■ Figure 3f: Evolution of asymptomatic fraction f, control measures

```
pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.28263

R0 of the mutant type = 2.28263

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0115874

Cumulative mortality (mutant) = 0.

449
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.28263

Case mortality = 0.0195122

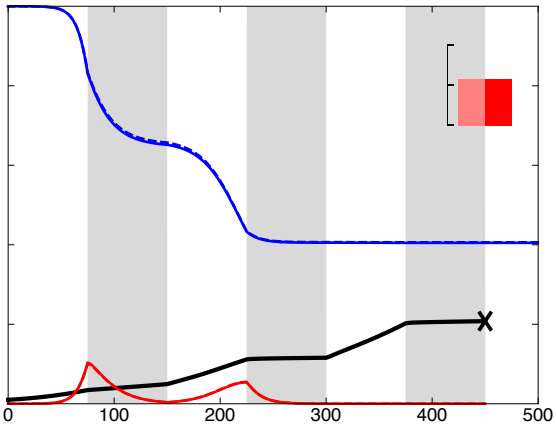
Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0117056

Cumulative mortality (mutant) = 0.000832288

450

{0.207847}

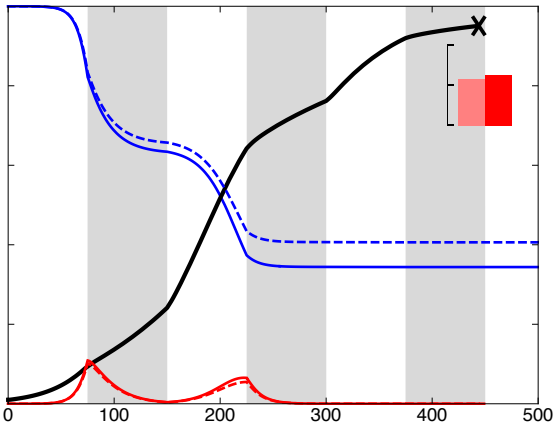


▪ Figure 3g: Evolution of pre-symptomatic phase κ, control measures

```
pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.28263

R0 of the mutant type = 2.68263

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0115874

Cumulative mortality (mutant) = 0.

449
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
    PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
    {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
     Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
        ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
     Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
     Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
     Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
      {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.68263

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0128022

Cumulative mortality (mutant) = 0.00397109

444

{0.950803}
```



■ Figure 3h: Evolution of virulence α, control measures

```
pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.00, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.28263

R0 of the mutant type = 2.31515

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0115874

Cumulative mortality (mutant) = 0.

449
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.31515

Case mortality = 0.0195122

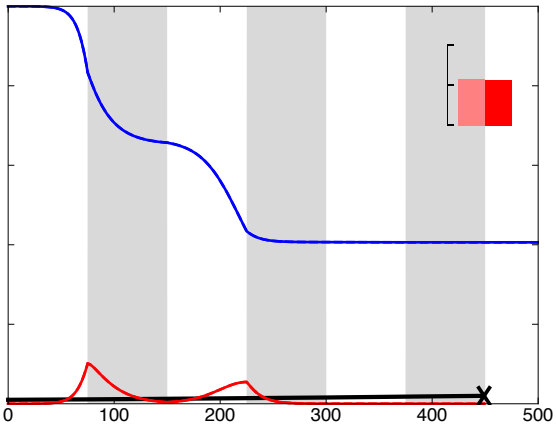
Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0114448

Cumulative mortality (mutant) = 0.

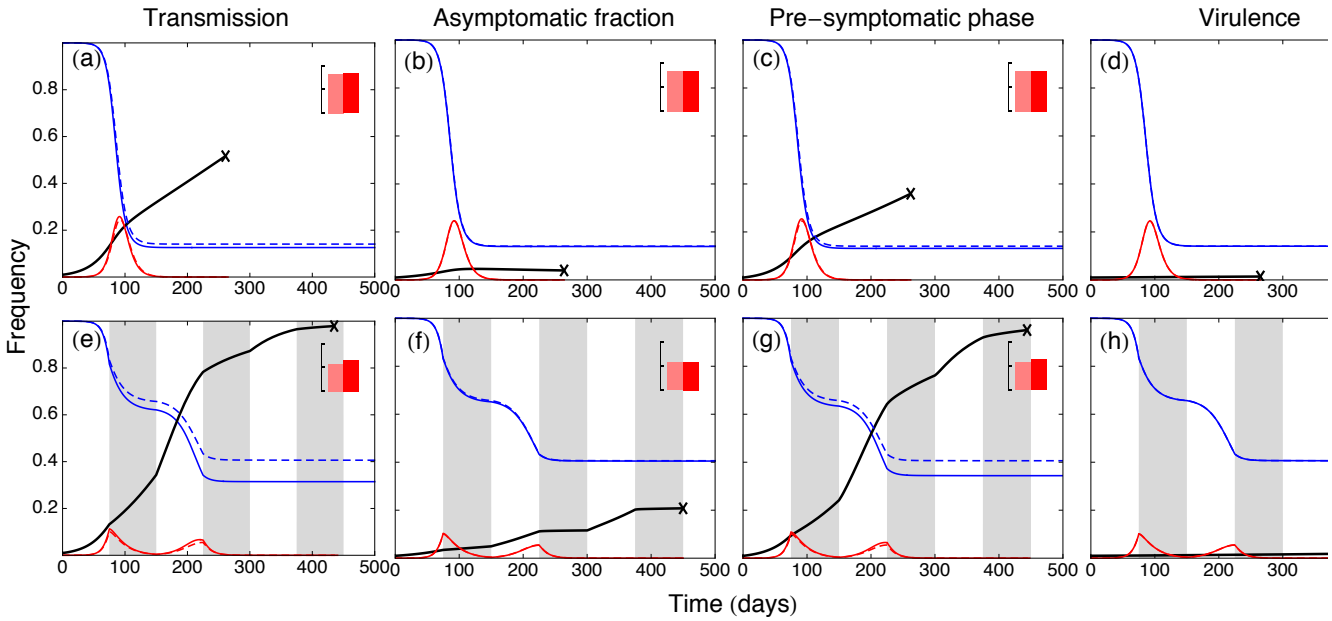
449

{0.0199521}



Altogether

```
Show[
 GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
  FrameLabel → label, Spacings → {-10, 10}],
 Graphics[Text[Style["(a)", 16, FontFamily -> "Helvetica"], {50, -33}]],
 Graphics[Text[Style["(b)", 16, FontFamily -> "Helvetica"], {384, -33}]],
 Graphics[Text[Style["(c)", 16, FontFamily -> "Helvetica"], {734, -33}]],
 Graphics[Text[Style["(d)", 16, FontFamily -> "Helvetica"], {1084, -33}]],
 Graphics[Text[Style["(e)", 16, FontFamily -> "Helvetica"], {50, -315}]],
 Graphics[Text[Style["(f)", 16, FontFamily -> "Helvetica"], {384, -315}]],
 Graphics[Text[Style["(g)", 16, FontFamily -> "Helvetica"], {734, -315}]],
 Graphics[Text[Style["(h)", 16, FontFamily -> "Helvetica"], {1084, -315}]],
 Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
 Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], { 520, 10}]],
 Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
 Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
 Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
 Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```




```
Export["Fig3.pdf", %];
```

Figure 4 - Numerical analyses

Code

Common settings

```
Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;
```

```
parvec = {β, βm, α, αm, κyP, κyPm, f, fm, κyE, κyI, κyA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] := finalfreq[vec] = Block[
    {β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], κyP = vec[[5]], κyPm = vec[[6]], f = vec[[7]], fm = vec[[8]],
     κyE = vec[[9]], κyI = vec[[10]], κyA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

    (*REMAINING PARAMETERS*)
    βyA = β / 10; βyP = β; βyI = β / 3;
    κyAm = κyA; κyIm = κyI;
    βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

    (* E: Exposed (non-infectious) cases *)
    (* A: asymptomatic cases *)
    (* P: pre-symptomatic cases *)
    (* S: symptomatic cases *)
```

```
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start = 10^-5;

t =.;
c =.;

c[t_] :=
 Evaluate[If[t < t1min, 0, If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]]];
h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

sys = {S'[t] == -(h[t] + hm[t]) S[t],
  yE'[t] == h[t] S[t] - κyE yE[t],
  yA'[t] == f κyE yE[t] - κyA yA[t],
  yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
  yI'[t] == κyP yP[t] - (κyI + α) yI[t],
  yR'[t] == κyA yA[t] + κyI yI[t],
  yD'[t] == α yI[t]};  (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
  yEm'[t] == hm[t] S[t] - κyE yEm[t],
  yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
  yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
  yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
  yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
  yDm'[t] == αm yIm[t]};  (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
 NDSolve[
  Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

(*R0*)
Print["R0 of the wild type = ", βyA f / κyA + ((1 - f) (βyP (α + κyI) + βyI κyP)) / ((α + κyI) κyP)];

(*Rm*)
Print["R0 of the mutant type = ", βyAm f / κyAm + ((1 - f) (βyPm (αm + κyIm) + βyIm κyPm)) / ((αm + κyIm) κyPm)];

(*CASE MORTALITY*)
Print["Case mortality = ", (1 - f) α / (κyI + α)];
Print["Case mortality (mutant) = ", (1 - fm) αm / (κyI + αm)];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];

]
```

■ Figure 4a: Evolution with positive pleiotropy between transmission β and virulence α, no control measures

```
pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.01, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
Print["Case mortality = ", α/(κyI + α) /. pars];

Print["Case mortality (mutant) = ", αm/(κyI + αm) /. pars];
```

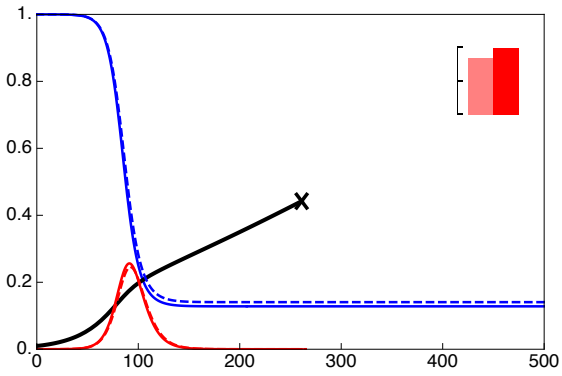
```
Case mortality = 0.0243902

Case mortality (mutant) = 0.047619
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.70199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0167685

Cumulative mortality (mutant) = 0.

265
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0, 0.2, 0.4, 0.6, 0.8, 1}], None}, {{0, 100, 200, 300, 400, 500}, None}}, FrameLabel → {None, None}]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.70199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0198733

Cumulative mortality (mutant) = 0.00586488

261

{0.442172}
```



▪ Figure 4b: Evolution with negative pleiotropy between transmission β and virulence α, no control measures

```
pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.000, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
Print["Case mortality = ", α/(κyI + α) /. pars];

Print["Case mortality (mutant) = ", αm/(κyI + αm) /. pars];
```

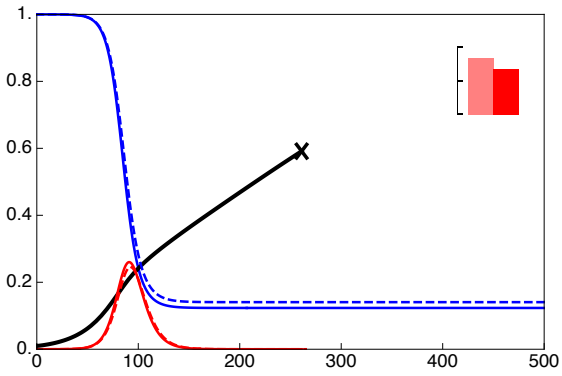
```
Case mortality = 0.0243902

Case mortality (mutant) = 0.
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.77818

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0167685

Cumulative mortality (mutant) = 0.

265
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0, 0.2, 0.4, 0.6, 0.8, 1}], None}, {{0, 100, 200, 300, 400, 500}, None}}, FrameLabel → {None, None}]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.77818

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0134869

Cumulative mortality (mutant) = 0.

261

{0.591416}
```



▪ Figure 4c: Evolution with positive pleiotropy between transmission β and virulence α, control measures

```
pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.01, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
Print["Case mortality = ", α/(κyI + α) /. pars];

Print["Case mortality (mutant) = ", αm/(κyI + αm) /. pars];
```

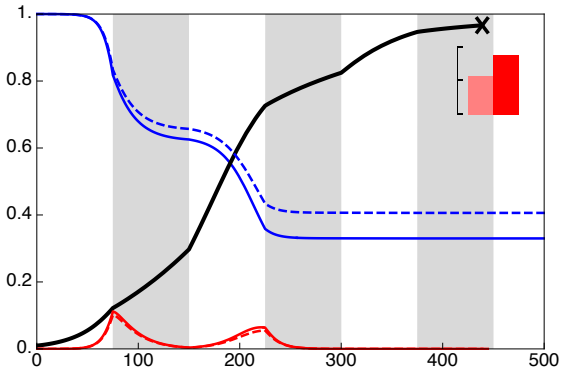
```
Case mortality = 0.0243902

Case mortality (mutant) = 0.047619
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.70199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0115874

Cumulative mortality (mutant) = 0.

449
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0, 0.2, 0.4, 0.6, 0.8, 1}], None}, {{0, 100, 200, 300, 400, 500}, None}}, FrameLabel → {None, None}]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.70199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0176922

Cumulative mortality (mutant) = 0.0094659

439

{0.966437}
```



If we increase the pleiotropic effect on the length of the pre-symptomatic phase, however, the mutant allele no longer rises in frequency if κyPm>

```
tab = Table[
   Flatten[{κ, finalfreq[parvec /. κyPm → κ /. pars /. mut → 0.01]; Evaluate[(yEm[tfig] + yAm[tfig] + yPm[tfig] + yIm[tfig]) /
        (yE[tfig] + yA[tfig] + yP[tfig] + yI[tfig] + yEm[tfig] + yAm[tfig] + yPm[tfig] + yIm[tfig]) /.
       Flatten[NSolution[parvec /. κyPm → κ /. pars /. mut → 0.01]]]}], {κ, 1, 2, 0.05}];
```

```
ReplaceAll::reps : {NSolution[{1, 1.2, 0.005, 0.01, 1, 1., 0.2, 0.2, 0.25, 0.2, 0.11, 0.6, 0.6, 0.6, 0.01]}}
      is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing. ≫
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.70199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0176922

Cumulative mortality (mutant) = 0.0094659

ReplaceAll::reps : {NSolution[{1, 1.2, 0.005, 0.01, 1, 1.05, 0.2, 0.2, 0.25, 0.2, 0.11, 0.6, 0.6, 0.6, 0.01}]}
      is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing. ≫

R0 of the wild type = 2.28263

R0 of the mutant type = 2.65628

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.016212

Cumulative mortality (mutant) = 0.00731841

ReplaceAll::reps : {NSolution[{1, 1.2, 0.005, 0.01, 1, 1.1, 0.2, 0.2, 0.25, 0.2, 0.11, 0.6, 0.6, 0.6, 0.01}]}
      is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing. ≫

General::stop : Further output of ReplaceAll::reps will be suppressed during this calculation. ≫

R0 of the wild type = 2.28263

R0 of the mutant type = 2.61472

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0149464

Cumulative mortality (mutant) = 0.00546339

R0 of the wild type = 2.28263

R0 of the mutant type = 2.57677

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0139649

Cumulative mortality (mutant) = 0.0039964

R0 of the wild type = 2.28263

R0 of the mutant type = 2.54199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0132536

Cumulative mortality (mutant) = 0.002905

R0 of the wild type = 2.28263

R0 of the mutant type = 2.50999

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0127587

Cumulative mortality (mutant) = 0.00212146

R0 of the wild type = 2.28263

R0 of the mutant type = 2.48045

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0124211

Cumulative mortality (mutant) = 0.0015676

R0 of the wild type = 2.28263

R0 of the mutant type = 2.4531

Case mortality = 0.0195122
```

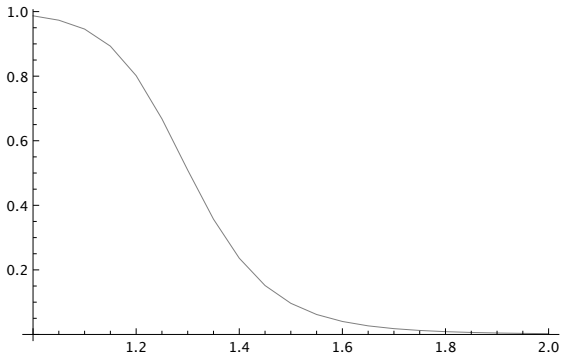
```
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0121919
Cumulative mortality (mutant) = 0.00117673
R0 of the wild type = 2.28263
R0 of the mutant type = 2.42771
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0120355
Cumulative mortality (mutant) = 0.000898881
R0 of the wild type = 2.28263
R0 of the mutant type = 2.40406
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0119277
Cumulative mortality (mutant) = 0.000698954
R0 of the wild type = 2.28263
R0 of the mutant type = 2.38199
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0118524
Cumulative mortality (mutant) = 0.000552961
R0 of the wild type = 2.28263
R0 of the mutant type = 2.36135
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0117991
Cumulative mortality (mutant) = 0.000444664
R0 of the wild type = 2.28263
R0 of the mutant type = 2.34199
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0117607
Cumulative mortality (mutant) = 0.000363051
R0 of the wild type = 2.28263
R0 of the mutant type = 2.32381
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0117327
Cumulative mortality (mutant) = 0.000300597
R0 of the wild type = 2.28263
R0 of the mutant type = 2.3067
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0117119
Cumulative mortality (mutant) = 0.0002521
R0 of the wild type = 2.28263
R0 of the mutant type = 2.29056
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
```

```
Cumulative mortality (total) = 0.0116962

Cumulative mortality (mutant) = 0.000213919

R0 of the wild type = 2.28263

R0 of the mutant type = 2.27532

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0116843

Cumulative mortality (mutant) = 0.00018347

R0 of the wild type = 2.28263

R0 of the mutant type = 2.26091

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0116752

Cumulative mortality (mutant) = 0.000158896

R0 of the wild type = 2.28263

R0 of the mutant type = 2.24725

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.011668

Cumulative mortality (mutant) = 0.000138841

R0 of the wild type = 2.28263

R0 of the mutant type = 2.2343

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0116623

Cumulative mortality (mutant) = 0.000122305

R0 of the wild type = 2.28263

R0 of the mutant type = 2.22199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0116578

Cumulative mortality (mutant) = 0.000108541
```

tab

```
{{1., 0.986936}, {1.05, 0.973369}, {1.1, 0.945886}, {1.15, 0.892974}, {1.2, 0.801584},
 {1.25, 0.667858}, {1.3, 0.509017}, {1.35, 0.357082}, {1.4, 0.236172}, {1.45, 0.151524}, {1.5, 0.0964691},
 {1.55, 0.0618317}, {1.6, 0.0402133}, {1.65, 0.0266361}, {1.7, 0.0179921}, {1.75, 0.012394},
 {1.8, 0.00870141}, {1.85, 0.00622027}, {1.9, 0.00452286}, {1.95, 0.00334145}, {2., 0.00250564}}
```

plot1 = ListPlot[tab, Joined → True, PlotStyle → Gray]



▪ Figure 4d: Evolution with negative pleiotropy between transmission β and virulence α, control measures

```
pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.000, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
Print["Case mortality = ", α/(κyI + α) /. pars];

Print["Case mortality (mutant) = ", αm/(κyI + αm) /. pars];
```

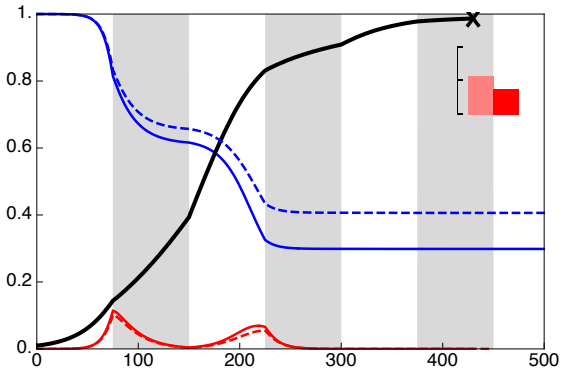
```
Case mortality = 0.0243902

Case mortality (mutant) = 0.
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.77818

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0115874

Cumulative mortality (mutant) = 0.

449
```

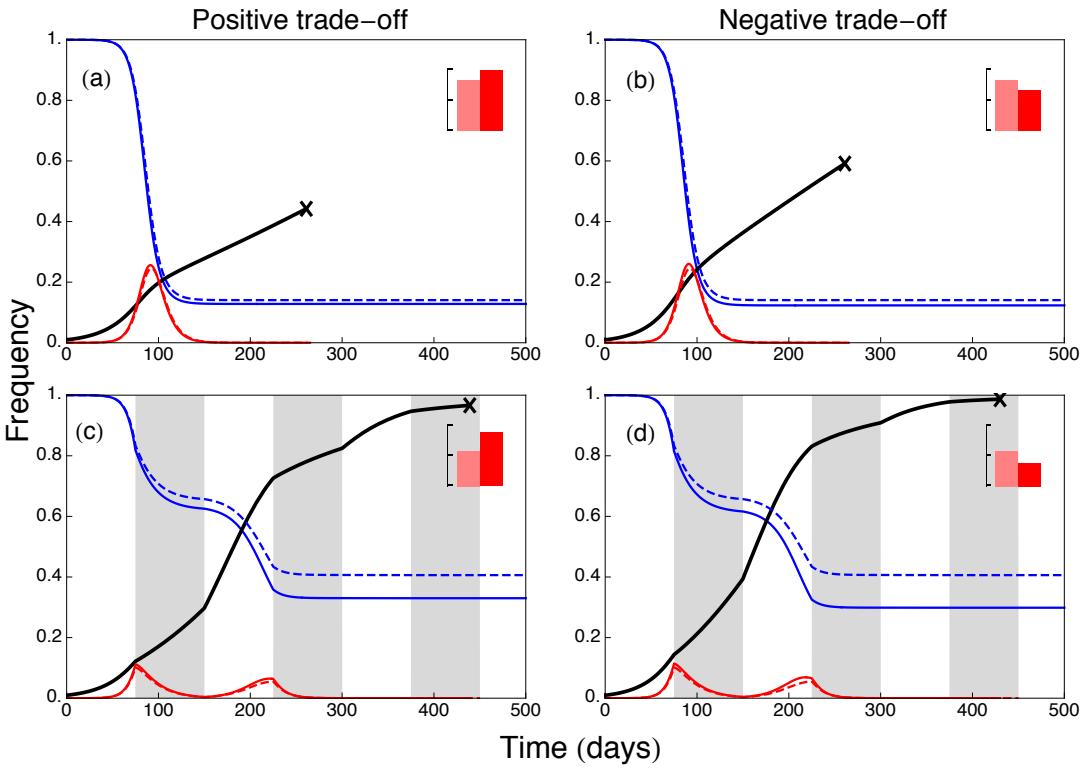
```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0, 0.2, 0.4, 0.6, 0.8, 1}], None}, {{0, 100, 200, 300, 400, 500}, None}}, FrameLabel → {None, None}]
```

```
R0 of the wild type = 2.28263

R0 of the mutant type = 2.77818

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.00762998

Cumulative mortality (mutant) = 0.

430

{0.986768}
```



Altogether

```
Show[
 GraphicsGrid[{{FigTOP1, FigTOP2}, {FigBOT1, FigBOT2}}, FrameLabel → label],
 Graphics[Text[Style["(a)", 16, FontFamily -> "Helvetica"], {55, -43}]],
 Graphics[Text[Style["(b)", 16, FontFamily -> "Helvetica"], {443, -43}]],
 Graphics[Text[Style["(c)", 16, FontFamily -> "Helvetica"], {50, -295}]],
 Graphics[Text[Style["(d)", 16, FontFamily -> "Helvetica"], {443, -295}]],
 Graphics[Text[Style["Positive trade-off", 18, FontFamily -> "Helvetica"], {200, 0}]],
 Graphics[Text[Style["Negative trade-off", 18, FontFamily -> "Helvetica"], { 580, 0}]],
 Graphics[Text[Style["Time (days)", 20, FontFamily -> "Helvetica"], {400, -520}]],
 Graphics[Rotate[Text[Style["Frequency", 20, FontFamily -> "Helvetica"], {0, -250}], Pi / 2]]
]
```




```
Export["Fig4.pdf", %];
```

Figure 3alt - Main change is a longer presymptomatic phase (κyP=0.4)

β adjusted to keep R0 and doubling time of the disease within range observed.

Code

Common settings

```
Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;
```

```
parvec = {β, βm, α, αm, κyP, κyPm, f, fm, κyE, κyI, κyA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] := finalfreq[vec] = Block[
    {β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], κyP = vec[[5]], κyPm = vec[[6]], f = vec[[7]], fm = vec[[8]],
     κyE = vec[[9]], κyI = vec[[10]], κyA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

    (*REMAINING PARAMETERS*)
    βyA = β / 10; βyP = β; βyI = β / 3;
    κyAm = κyA; κyIm = κyI;
    βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

    (* E: Exposed (non-infectious) cases *)
    (* A: asymptomatic cases *)
```

```
(* P: pre-symptomatic cases *)
(* S: symptomatic cases *)
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start = 10^-5;

t =.;
c =.;

c[t_] :=
 Evaluate[If[t < t1min, 0, If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]]];
h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

sys = {S'[t] == -(h[t] + hm[t]) S[t],
  yE'[t] == h[t] S[t] - κyE yE[t],
  yA'[t] == f κyE yE[t] - κyA yA[t],
  yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
  yI'[t] == κyP yP[t] - (κyI + α) yI[t],
  yR'[t] == κyA yA[t] + κyI yI[t],
  yD'[t] == α yI[t]};  (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
  yEm'[t] == hm[t] S[t] - κyE yEm[t],
  yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
  yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
  yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
  yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
  yDm'[t] == αm yIm[t]};  (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
 NDSolve[
  Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

(*R0*)
Print["R0 of the wild type = ", βyA f/κyA + ((1 - f) (βyP (α + κyI) + βyI κyP))/((α + κyI) κyP)];

(*Rm*)
Print["R0 of the mutant type = ", βyAm f/κyAm + ((1 - f) (βyPm (αm + κyIm) + βyIm κyPm))/((αm + κyIm) κyPm)];

(*CASE MORTALITY*)
Print["Case mortality = ", (1 - f) α/(κyI + α)];

Print["Case mortality (mutant) = ", (1 - fm) αm/(κyI + αm)];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];

]
```

- **Figure 3a: Evolution of transmission β, no control measures**

```
pars = {β → 0.7, βm → 0.7 × 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE → 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
```

The doublng time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```
Sort[Solve[
   (κE (-S α βP κA + f S α βP κA - S βP κA κI + f S βP κA κI - f S α βA κP + α κA κP - S βI κA κP + f S βI κA κP - f S βA κI κP + κA κI κP) + (-f S α
                      βA κE - S α βP κE + f S α βP κE + α κA κE - S βP κA κE + f S βP κA κE - f S βA κE κI - S βP κE κI + f S βP κE κI + κA κE κI +
                    α κA κP + α κE κP - f S βA κE κP - S βI κE κP + f S βI κE κP + κA κE κP + κA κI κP + κE κI κP) λ + (α κA + α κE - f S βA κE -
                    S βP κE + f S βP κE + κA κE + κA κI + κE κI + α κP + κA κP + κE κP + κI κP) λ^2 + (α + κA + κE + κI + κP) λ^3 + λ^4 /. S → 1 /.
              βA -> β / 10 /. βP -> β /. βI -> β / 3 /. κA -> κyA /. κE -> κyE /. κP -> κyP /. κI -> κyI /. pars) == 0, λ]]
Solve[
 (Exp[
     λ
      t] ==
    2) /.
  Last[
   %],
 t]
```

```
{{λ → -0.649407}, {λ → -0.334169}, {λ → -0.113297}, {λ → 0.131873}}
```

Solve::ifun : Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information. >>

```
{{t → 5.25617}}
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 2.92541

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0172518

Cumulative mortality (mutant) = 0.

254
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 2.92541

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.017457

Cumulative mortality (mutant) = 0.00278104

251

{0.413578}
```

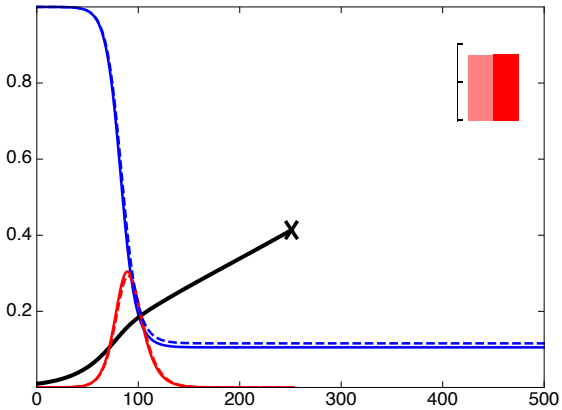


Figure 3b: Evolution of asymptomatic fraction f, no control measures

```
pars = {β → 0.7, βm → 0.7 , (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.43784

R0 of the mutant type = 2.43784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0172518

Cumulative mortality (mutant) = 0.

254
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 2.43784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0173758

Cumulative mortality (mutant) = 0.0008657

253

{0.0491962}
```

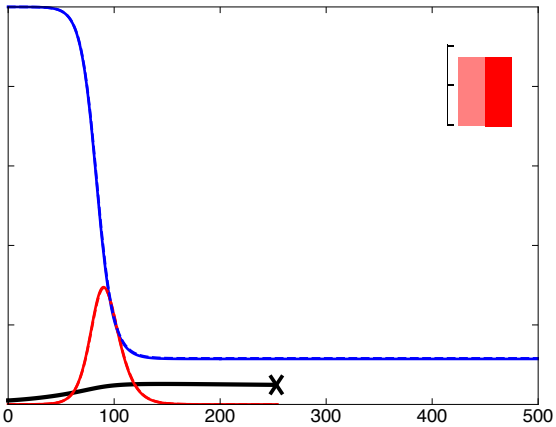


Figure 3c: Evolution of pre-symptomatic phase κ, no control measures

```
pars = {β → 0.7, βm → 0.7, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 4, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784

R0 of the mutant type = 3.27784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0172518

Cumulative mortality (mutant) = 0.

254
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 3.27784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0176696

Cumulative mortality (mutant) = 0.00353411

256

{0.807354}
```

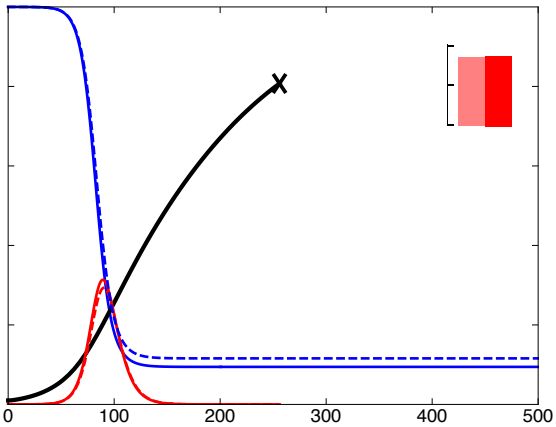


Figure 3d: Evolution of virulence α, no control measures

```
pars = {β → 0.7, βm → 0.7, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm → 0, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.43784

R0 of the mutant type = 2.46061

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0172518

Cumulative mortality (mutant) = 0.

254
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 2.46061

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0170685

Cumulative mortality (mutant) = 0.

254

{0.0124554}
```

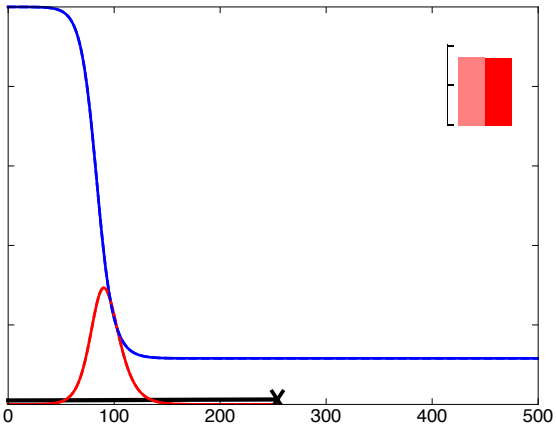


Figure 3e: Evolution of transmission β, control measures

```
pars = {β → 0.7, βm → 0.7 × 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784

R0 of the mutant type = 2.92541

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0113614

Cumulative mortality (mutant) = 0.

500
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 2.92541

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0125869

Cumulative mortality (mutant) = 0.00364809

500

{0.994766}
```

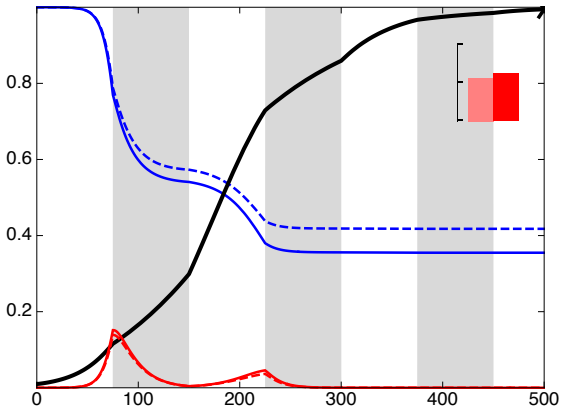
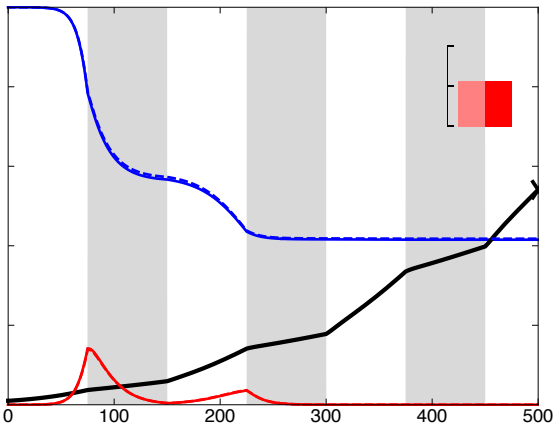


Figure 3f: Evolution of asymptomatic fraction f, control measures

```
pars = {β → 0.7, βm → 0.7, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784

R0 of the mutant type = 2.43784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0113614

Cumulative mortality (mutant) = 0.

500
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 2.43784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.011499

Cumulative mortality (mutant) = 0.000804302

500

{0.540783}
```

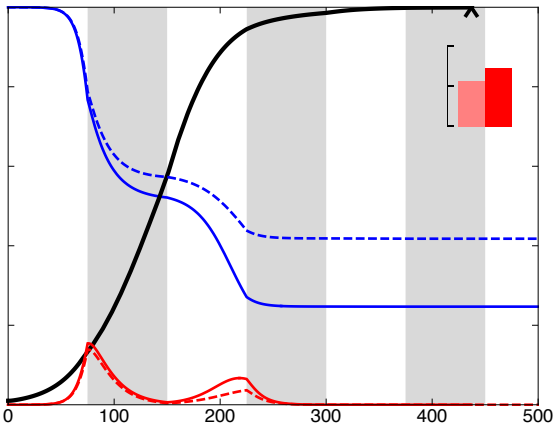


▪ Figure 3g: Evolution of pre-symptomatic phase κ, control measures

```
pars = {β → 0.7, βm → 0.7, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 4, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784

R0 of the mutant type = 3.27784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0113614

Cumulative mortality (mutant) = 0.

500
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 3.27784

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0146959

Cumulative mortality (mutant) = 0.00651372

437

{0.99953}
```

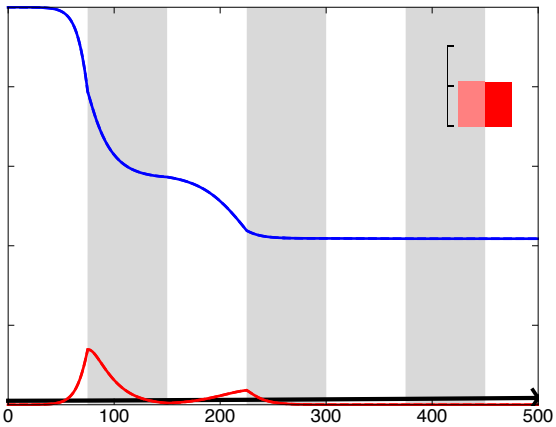


■ Figure 3h: Evolution of virulence α, control measures

```
pars = {β → 0.7, βm → 0.7, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm → 0, (*VIRULENCE OF THE MUTANT*)
    κyP → 1 / 2.5, κyPm → 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.43784

R0 of the mutant type = 2.46061

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0113614

Cumulative mortality (mutant) = 0.

500
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.43784

R0 of the mutant type = 2.46061

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0112358

Cumulative mortality (mutant) = 0.

500

{0.0171055}
```



Altogether

```
Show[
 GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
  FrameLabel → label, Spacings → {-10, 10}],
 Graphics[Text[Style["(a)", 16, FontFamily -> "Helvetica"], {50, -33}]],
 Graphics[Text[Style["(b)", 16, FontFamily -> "Helvetica"], {384, -33}]],
 Graphics[Text[Style["(c)", 16, FontFamily -> "Helvetica"], {734, -33}]],
 Graphics[Text[Style["(d)", 16, FontFamily -> "Helvetica"], {1084, -33}]],
 Graphics[Text[Style["(e)", 16, FontFamily -> "Helvetica"], {50, -315}]],
 Graphics[Text[Style["(f)", 16, FontFamily -> "Helvetica"], {384, -315}]],
 Graphics[Text[Style["(g)", 16, FontFamily -> "Helvetica"], {734, -315}]],
 Graphics[Text[Style["(h)", 16, FontFamily -> "Helvetica"], {1084, -315}]],
 Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
 Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
 Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
 Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
 Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
 Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```

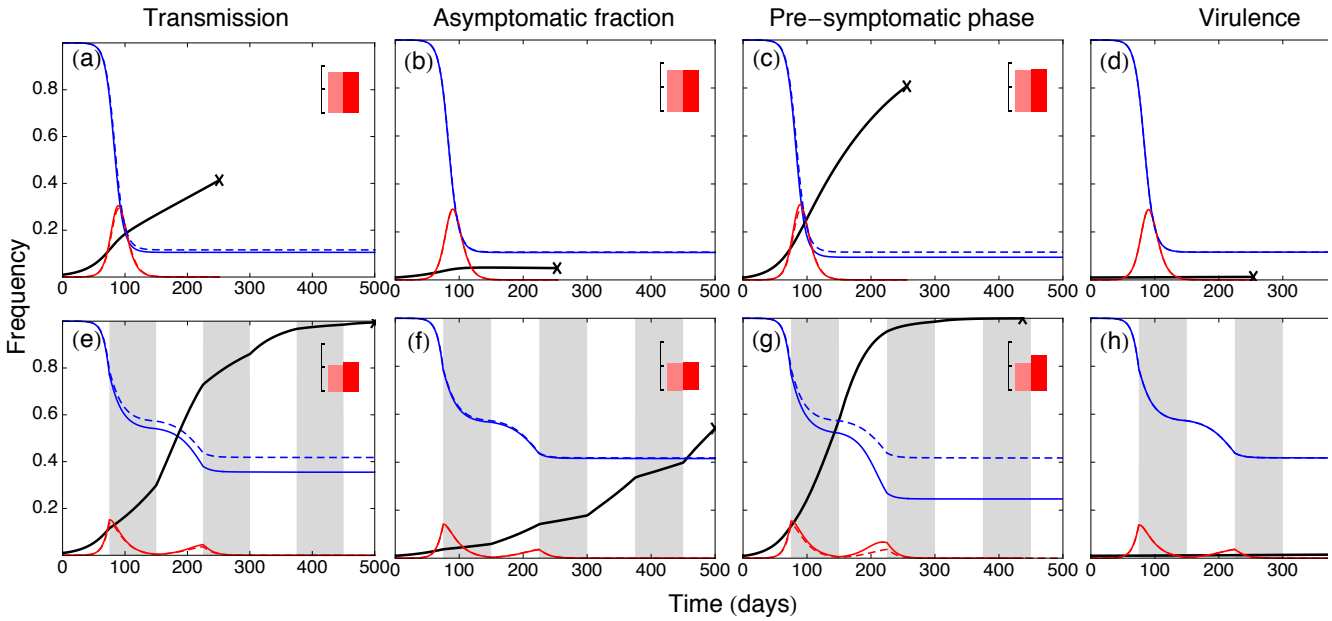


Figure 3alt - Main change is more asymptomatics (f=0.4)

β adjusted to keep R0 and doubling time of the disease within range observed.

Code

Common settings

```
Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;
```

```
parvec = {β, βm, α, αm, κyP, κyPm, f, fm, κyE, κyI, κyA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] := finalfreq[vec] = Block[
    {β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], κyP = vec[[5]], κyPm = vec[[6]], f = vec[[7]], fm = vec[[8]],
     κyE = vec[[9]], κyI = vec[[10]], κyA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

    (*REMAINING PARAMETERS*)
    βyA = β / 10; βyP = β; βyI = β / 3;
    κyAm = κyA; κyIm = κyI;
    βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

    (* E: Exposed (non-infectious) cases *)
    (* A: asymptomatic cases *)
    (* P: pre-symptomatic cases *)
    (* S: symptomatic cases *)
```

```
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start = 10^-5;

t =.;
c =.;

c[t_] :=
 Evaluate[If[t < t1min, 0, If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]]];
h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

sys = {S'[t] == -(h[t] + hm[t]) S[t],
  yE'[t] == h[t] S[t] - κyE yE[t],
  yA'[t] == f κyE yE[t] - κyA yA[t],
  yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
  yI'[t] == κyP yP[t] - (κyI + α) yI[t],
  yR'[t] == κyA yA[t] + κyI yI[t],
  yD'[t] == α yI[t]};  (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
  yEm'[t] == hm[t] S[t] - κyE yEm[t],
  yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
  yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
  yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
  yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
  yDm'[t] == αm yIm[t]};  (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
 NDSolve[
  Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

(*R0*)
Print["R0 of the wild type = ", βyA f/κyA + ((1 - f) (βyP (α + κyI) + βyI κyP))/((α + κyI) κyP)];

(*Rm*)
Print["R0 of the mutant type = ", βyAm f/κyAm + ((1 - f) (βyPm (αm + κyIm) + βyIm κyPm))/((αm + κyIm) κyPm)];

(*CASE MORTALITY*)
Print["Case mortality = ", (1 - f) α/(κyI + α)];
Print["Case mortality (mutant) = ", (1 - fm) αm/(κyI + αm)];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];

]
```

- **Figure 3a: Evolution of transmission β, no control measures**

```
pars = {β -> 1.3, βm -> 1.2 × 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE → 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
```

The doublng time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```
Sort[Solve[
   (κE (-S α βP κA + f S α βP κA - S βP κA κI + f S βP κA κI - f S α βA κP + α κA κP - S βI κA κP + f S βI κA κP - f S βA κI κP + κA κI κP) + (-f S α
                      βA κE - S α βP κE + f S α βP κE + α κA κE - S βP κA κE + f S βP κA κE - f S βA κE κI - S βP κE κI + f S βP κE κI + κA κE κI +
                    α κA κP + α κE κP - f S βA κE κP - S βI κE κP + f S βI κE κP + κA κE κP + κA κI κP + κE κI κP) λ + (α κA + α κE - f S βA κE -
                    S βP κE + f S βP κE + κA κE + κA κI + κE κI + α κP + κA κP + κE κP + κI κP) λ^2 + (α + κA + κE + κI + κP) λ^3 + λ^4 /. S → 1 /.
              βA -> β / 10 /. βP -> β /. βI -> β / 3 /. κA -> κyA /. κE -> κyE /. κP -> κyP /. κI -> κyI /. pars) == 0, λ]]
Solve[
 (Exp[
     λ
      t] ==
    2) /.
  Last[
   %],
 t]
```

```
{{λ → -1.14279}, {λ → -0.438351}, {λ → -0.123009}, {λ → 0.139154}}
```

Solve::ifun : Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information. >>

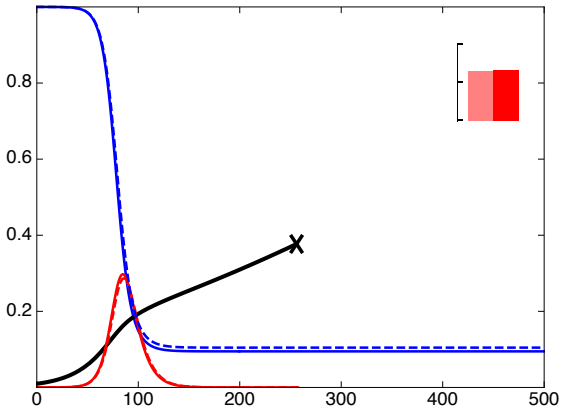
```
{{t → 4.98116}}
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 3.02522

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.013103

Cumulative mortality (mutant) = 0.

260
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 3.02522

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.0132471

Cumulative mortality (mutant) = 0.00214751

256

{0.376943}
```

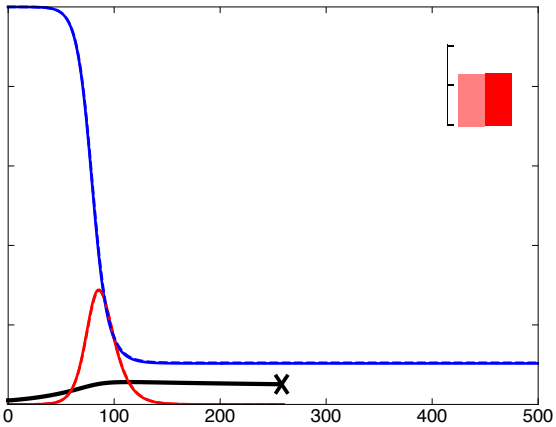


▪ Figure 3b: Evolution of asymptomatic fraction f, no control measures

```
pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.3, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.52102

R0 of the mutant type = 2.52102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0170732

Cumulative mortality (total) = 0.013103

Cumulative mortality (mutant) = 0.

260
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 2.52102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0170732

Cumulative mortality (total) = 0.0132374

Cumulative mortality (mutant) = 0.000791761

258

{0.0507279}
```



▪ Figure 3c: Evolution of pre-symptomatic phase κ, no control measures

```
pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.52102

R0 of the mutant type = 2.91102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.013103

Cumulative mortality (mutant) = 0.

260
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 2.91102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.01317

Cumulative mortality (mutant) = 0.00124589

258

{0.185488}
```

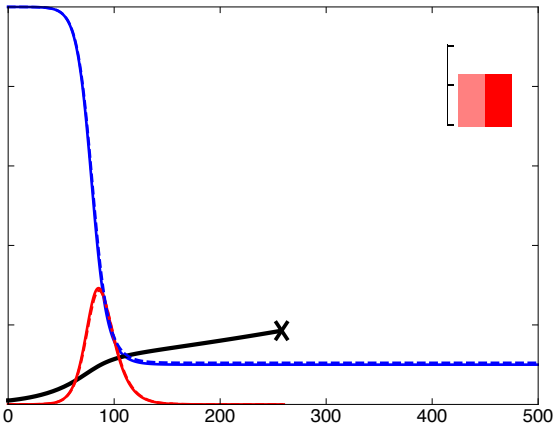


Figure 3d: Evolution of virulence α, no control measures

```
pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.0, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102

R0 of the mutant type = 2.55273

Case mortality = 0.0146341

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.013103

Cumulative mortality (mutant) = 0.

260
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 2.55273

Case mortality = 0.0146341

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0129592

Cumulative mortality (mutant) = 0.

260

{0.0125059}
```

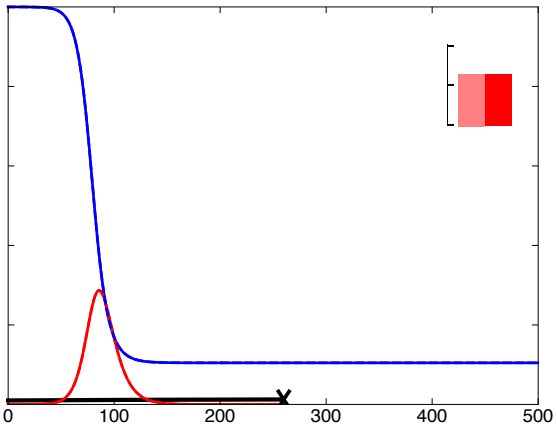
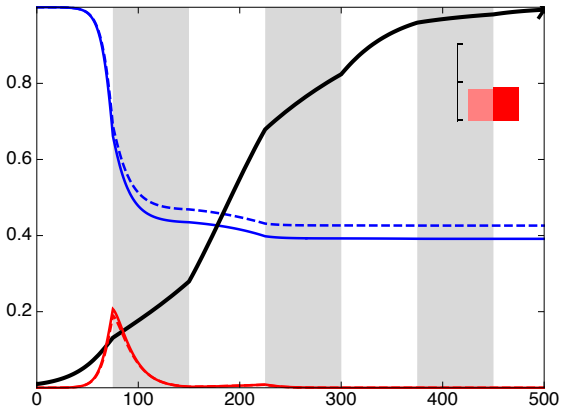


Figure 3e: Evolution of transmission β, control measures

```
pars = {β -> 1.3, βm -> 1.2 × 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102

R0 of the mutant type = 3.02522

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.008397

Cumulative mortality (mutant) = 0.

500
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]  ]],"% (",
       ToString[N[Round[100  (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 3.02522

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.00890626

Cumulative mortality (mutant) = 0.00158136

500

{0.993585}
```

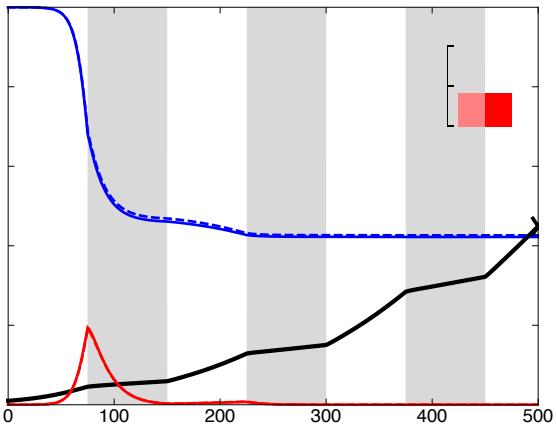


▪ Figure 3f: Evolution of asymptomatic fraction f, control measures

```
pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.3, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102

R0 of the mutant type = 2.52102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0170732

Cumulative mortality (total) = 0.008397

Cumulative mortality (mutant) = 0.

500
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 2.52102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0170732

Cumulative mortality (total) = 0.00853032

Cumulative mortality (mutant) = 0.000512453

500

{0.448727}
```

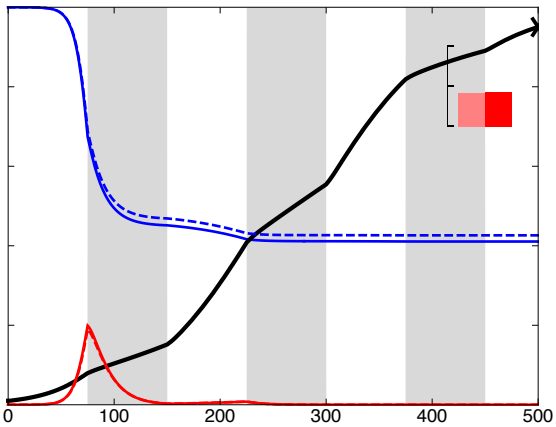


▪ Figure 3g: Evolution of pre-symptomatic phase κ, control measures

```
pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102

R0 of the mutant type = 2.91102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.008397

Cumulative mortality (mutant) = 0.

500
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 2.91102

Case mortality = 0.0146341

Case mortality (mutant) = 0.0146341

Cumulative mortality (total) = 0.00862458

Cumulative mortality (mutant) = 0.000886798

500

{0.950233}
```

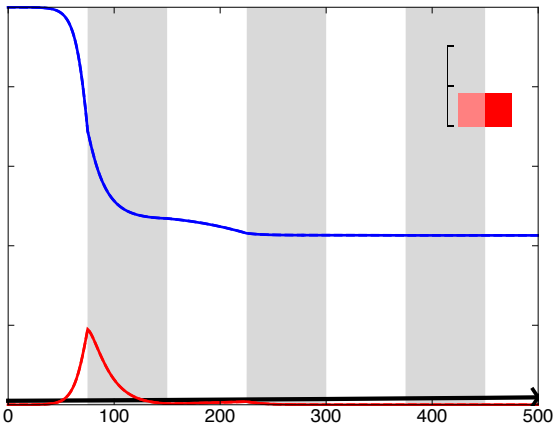


▪ Figure 3h: Evolution of virulence α, control measures

```
pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.00, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.52102

R0 of the mutant type = 2.55273

Case mortality = 0.0146341

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.008397

Cumulative mortality (mutant) = 0.

500
```

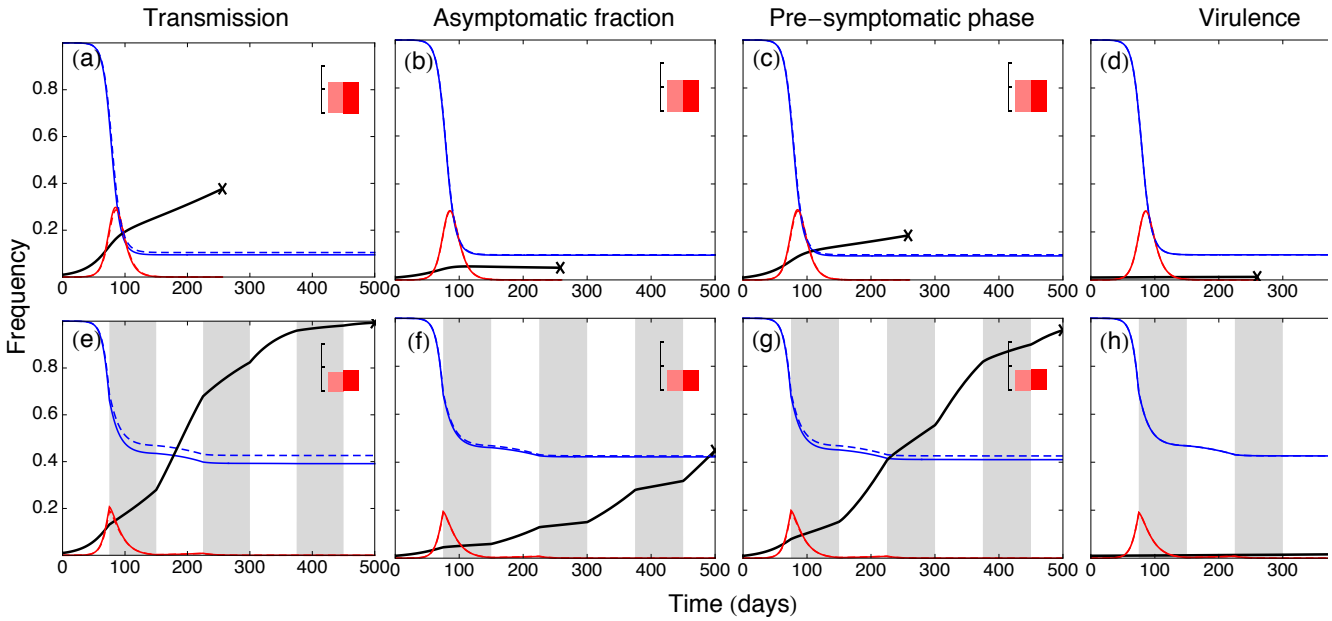
```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.52102

R0 of the mutant type = 2.55273

Case mortality = 0.0146341

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.00830522

Cumulative mortality (mutant) = 0.

500

{0.0186469}
```



Altogether

```
Show[
 GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
  FrameLabel → label, Spacings → {-10, 10}],
 Graphics[Text[Style["(a)", 16, FontFamily -> "Helvetica"], {50, -33}]],
 Graphics[Text[Style["(b)", 16, FontFamily -> "Helvetica"], {384, -33}]],
 Graphics[Text[Style["(c)", 16, FontFamily -> "Helvetica"], {734, -33}]],
 Graphics[Text[Style["(d)", 16, FontFamily -> "Helvetica"], {1084, -33}]],
 Graphics[Text[Style["(e)", 16, FontFamily -> "Helvetica"], {50, -315}]],
 Graphics[Text[Style["(f)", 16, FontFamily -> "Helvetica"], {384, -315}]],
 Graphics[Text[Style["(g)", 16, FontFamily -> "Helvetica"], {734, -315}]],
 Graphics[Text[Style["(h)", 16, FontFamily -> "Helvetica"], {1084, -315}]],
 Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
 Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], { 520, 10}]],
 Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
 Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
 Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
 Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```




```
Export["Fig3.pdf", %];
```

Figure 3alt - Main change is more transmission in infectious stage (βI = βP)

β adjusted to keep R0 and doubling time of the disease within range observed, and mutant effect on κP increased to visualize.

Code

Common settings

```
Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;
```

```
parvec = {β, βm, α, αm, κyP, κyPm, f, fm, κyE, κyI, κyA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] := finalfreq[vec] = Block[
    {β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], κyP = vec[[5]], κyPm = vec[[6]], f = vec[[7]], fm = vec[[8]],
     κyE = vec[[9]], κyI = vec[[10]], κyA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

    (*REMAINING PARAMETERS*)
    βyA = β / 10; βyP = β; βyI = β;
    κyAm = κyA; κyIm = κyI;
    βyAm = βm / 10; βyPm = βm; βyIm = βm;

    (* E: Exposed (non-infectious) cases *)
    (* A: asymptomatic cases *)
```

```
(* P: pre-symptomatic cases *)
(* S: symptomatic cases *)
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start = 10^-5;

t =.;
c =.;

c[t_] :=
 Evaluate[If[t < t1min, 0, If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]]];
h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

sys = {S'[t] == -(h[t] + hm[t]) S[t],
  yE'[t] == h[t] S[t] - κyE yE[t],
  yA'[t] == f κyE yE[t] - κyA yA[t],
  yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
  yI'[t] == κyP yP[t] - (κyI + α) yI[t],
  yR'[t] == κyA yA[t] + κyI yI[t],
  yD'[t] == α yI[t]};  (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
  yEm'[t] == hm[t] S[t] - κyE yEm[t],
  yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
  yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
  yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
  yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
  yDm'[t] == αm yIm[t]};  (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
 NDSolve[
  Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

(*R0*)
Print["R0 of the wild type = ", βyA f/κyA + ((1 - f) (βyP (α + κyI) + βyI κyP))/((α + κyI) κyP)];

(*Rm*)
Print["R0 of the mutant type = ", βyAm f/κyAm + ((1 - f) (βyPm (αm + κyIm) + βyIm κyPm))/((αm + κyIm) κyPm)];

(*CASE MORTALITY*)
Print["Case mortality = ", (1 - f) α/(κyI + α)];

Print["Case mortality (mutant) = ", (1 - fm) αm/(κyI + αm)];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];

]
```

- **Figure 3a: Evolution of transmission β, no control measures**

```
pars = {β → 0.53, βm -> 1.2 × 0.53, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE → 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
```

The doublng time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```
Sort[Solve[
   (κE (-S α βP κA + f S α βP κA - S βP κA κI + f S βP κA κI - f S α βA κP + α κA κP - S βI κA κP + f S βI κA κP - f S βA κI κP + κA κI κP) + (-f S α
                        βA κE - S α βP κE + f S α βP κE + α κA κE - S βP κA κE + f S βP κA κE - f S βA κE κI - S βP κE κI + f S βP κE κI + κA κE κI +
                      α κA κP + α κE κP - f S βA κE κP - S βI κE κP + f S βI κE κP + κA κE κP + κA κI κP + κE κI κP) λ + (α κA + α κE - f S βA κE -
                      S βP κE + f S βP κE + κA κE + κA κI + κE κI + α κP + κA κP + κE κP + κI κP) λ^2 + (α + κA + κE + κI + κP) λ^3 + λ^4 /. S → 1 /.
              βA -> β / 10 /. βP -> β /. βI -> β / 3 /. κA -> κyA /. κE -> κyE /. κP -> κyP /. κI -> κyI /. pars) == 0, λ]]
Solve[
 (Exp[
     λ
      t] ==
    2) /.
  Last[
   %],
 t]
```

```
{{λ → -1.07935}, {λ → -0.393555}, {λ → -0.116084}, {λ → 0.0239852}}
```

Solve::ifun : Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information. >>

```
{{t → 28.899}}
```

```
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 3.10639

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0176311

Cumulative mortality (mutant) = 0.

249
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 3.10639

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0177853

Cumulative mortality (mutant) = 0.0024515

246

{0.33753}
```

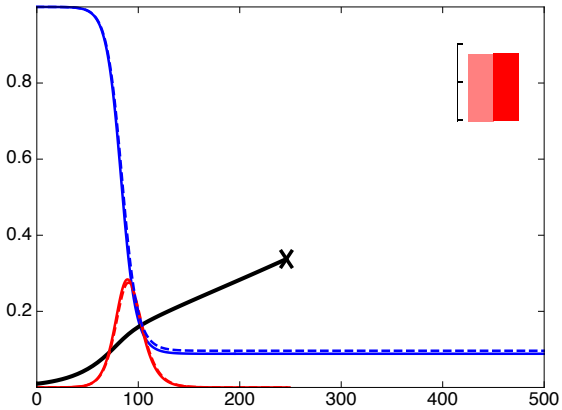


Figure 3b: Evolution of asymptomatic fraction f, no control measures

```
pars = {β → 0.53, βm → 0.53, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.58866

R0 of the mutant type = 2.58866

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0176311

Cumulative mortality (mutant) = 0.

249
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 2.58866

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0177545

Cumulative mortality (mutant) = 0.000875875

248

{0.0498578}
```

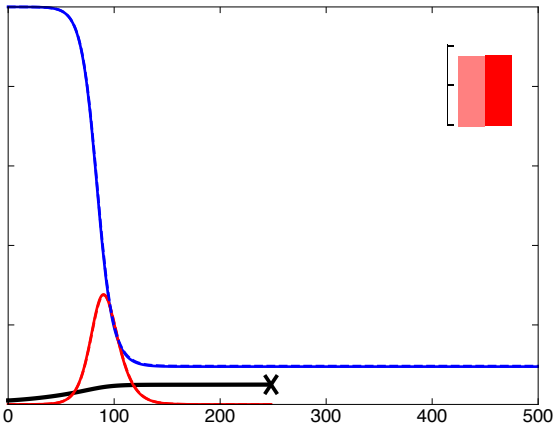


Figure 3c: Evolution of pre-symptomatic phase κ, no control measures

```
pars = {β → 0.53, βm → 0.53, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.58866

R0 of the mutant type = 3.43666

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0176311

Cumulative mortality (mutant) = 0.

249
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 3.43666

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0178757

Cumulative mortality (mutant) = 0.00245761

251

{0.681379}
```

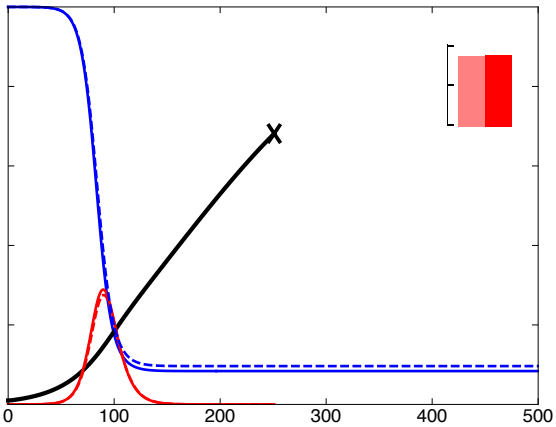


Figure 3d: Evolution of virulence α, no control measures

```
pars = {β → 0.53, βm → 0.53, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.0, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0, c2 -> 0, c3 → 0
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.58866

R0 of the mutant type = 2.64036

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0176311

Cumulative mortality (mutant) = 0.

249
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];


line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];


mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]};*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 2.64036

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.017426

Cumulative mortality (mutant) = 0.

249

{0.0147944}
```

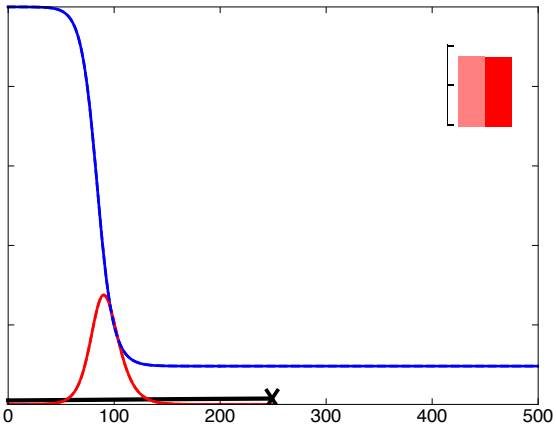


Figure 3e: Evolution of transmission β, control measures

```
pars = {β → 0.53, βm → 0.53 × 1.2, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP → 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.58866

R0 of the mutant type = 3.10639

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0123517

Cumulative mortality (mutant) = 0.

475
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 3.10639

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0133157

Cumulative mortality (mutant) = 0.00344839

500

{0.99107}
```

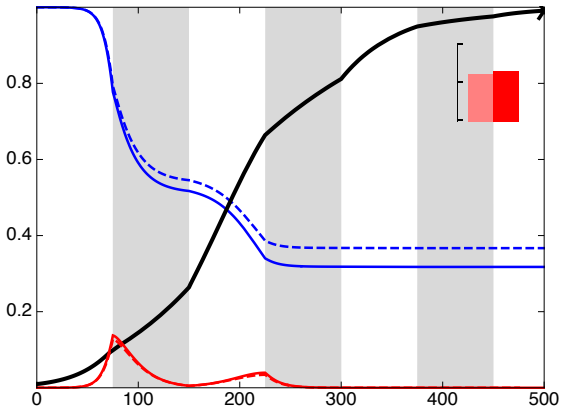
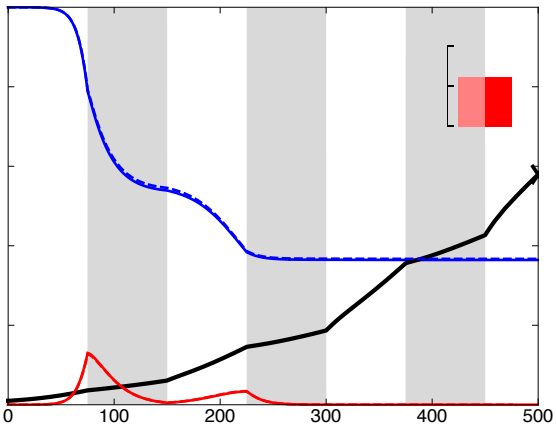


Figure 3f: Evolution of asymptomatic fraction f, control measures

```
pars = {β → 0.53, βm → 0.53, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
   Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
    PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];


R0 of the wild type = 2.58866

R0 of the mutant type = 2.58866

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0123517

Cumulative mortality (mutant) = 0.

475
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 2.58866

Case mortality = 0.0195122

Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0125058

Cumulative mortality (mutant) = 0.000907129

500

{0.579283}
```



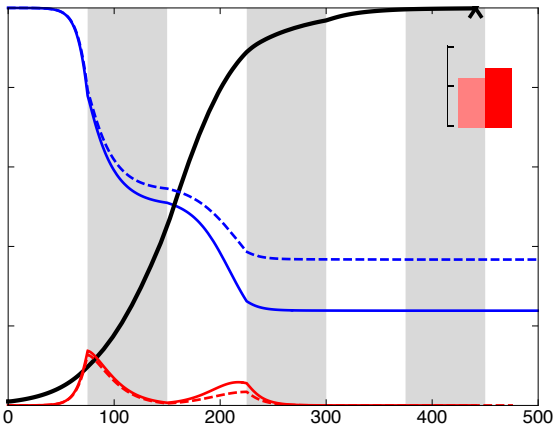
▪ Figure 3g: Evolution of pre-symptomatic phase κ, control measures

```
pars = {β → 0.53, βm → 0.53, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
    κyP -> 1, κyPm → 1 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
   Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
     {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

475

Cumulative mortality (mutant) = 0.

Cumulative mortality (total) = 0.0123517

Case mortality (mutant) = 0.0195122

Case mortality = 0.0195122

R0 of the mutant type = 3.43666

R0 of the wild type = 2.58866

R0 of the wild type = 2.58866

R0 of the mutant type = 2.80066

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0123517

Cumulative mortality (mutant) = 0.

475
```

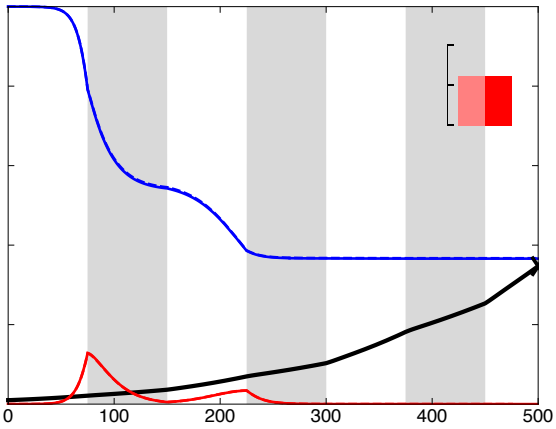
```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1]  ]],"% (",
       ToString[N[Round[100  (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
441
```

```
{0.998914}
```



```
Cumulative mortality (mutant) = 0.00549454

Cumulative mortality (total) = 0.014861

Case mortality (mutant) = 0.0195122

Case mortality = 0.0195122

R0 of the mutant type = 3.43666

R0 of the wild type = 2.58866

R0 of the wild type = 2.58866

R0 of the mutant type = 2.80066

Case mortality = 0.0195122

Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0123701

Cumulative mortality (mutant) = 0.000411584

500

{0.347002}
```



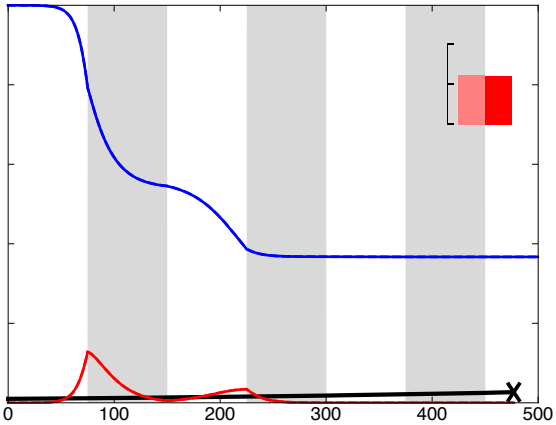
- **Figure 3h: Evolution of virulence α, control measures**

```
pars = {β → 0.53, βm → 0.53, (*TRANSMISSION OF THE MUTANT*)
    α -> 0.005, αm -> 0.00, (*VIRULENCE OF THE MUTANT*)
    ϰyP -> 1, ϰyPm → 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

    f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
    ϰyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
    ϰyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
    ϰyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

    (*Strength of control measures*)
    c1 -> 0.6, c2 -> 0.6, c3 → 0.6
   };
parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]

fnoevol =
  Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t, 0, tNOevolNC},
   PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
    PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 2.64036

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0123517

Cumulative mortality (mutant) = 0.

475
```

```
parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
   {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10^-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC = Evaluate[(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]) /. NSolution[parset]] /. t → tevolNC

FIGfreq =
  Plot[Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
     NSolution[parset]], {t, 0, tevolNC},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
   PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
   PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[
   {Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black,
    Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol,10^-1] ]],"% (",
       ToString[N[Round[100 (mortalityevol),10^-1]]],"%)"],12,FontFamily->"Helvetica"],{(t3min+t3max)/2,0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
    Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black,
    Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9},
     {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks →
   {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
 ]
```

```
R0 of the wild type = 2.58866

R0 of the mutant type = 2.64036

Case mortality = 0.0195122

Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0121948

Cumulative mortality (mutant) = 0.

477

{0.0267739}
```



Altogether

```
Show[
 GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
  FrameLabel → label, Spacings → {-10, 10}],
 Graphics[Text[Style["(a)", 16, FontFamily -> "Helvetica"], {50, -33}]],
 Graphics[Text[Style["(b)", 16, FontFamily -> "Helvetica"], {384, -33}]],
 Graphics[Text[Style["(c)", 16, FontFamily -> "Helvetica"], {734, -33}]],
 Graphics[Text[Style["(d)", 16, FontFamily -> "Helvetica"], {1084, -33}]],
 Graphics[Text[Style["(e)", 16, FontFamily -> "Helvetica"], {50, -315}]],
 Graphics[Text[Style["(f)", 16, FontFamily -> "Helvetica"], {384, -315}]],
 Graphics[Text[Style["(g)", 16, FontFamily -> "Helvetica"], {734, -315}]],
 Graphics[Text[Style["(h)", 16, FontFamily -> "Helvetica"], {1084, -315}]],
 Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
 Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
 Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
 Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
 Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
 Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```