TB model

2025-06-05

```r
# Multi-strain TB system with drug resistance

# Initial Setup
E1_initial <- 1 # Latent DS
I1_initial <- 7 # Infectious DS

E2_initial <- 1 # Latent H-resistant
I2_initial <- 2 # Infectious H-resistant

E3_initial <- 1 # Latent R-resistant
I3_initial <- 5 # Infectious R-resistant

E4_initial <- 1 # Latent MDR
I4_initial <- 9 # Infectious MDR

D_initial <- 0 # Initial deaths

N_initial <- 100      # total US population

S_initial <- N_initial - (
  E1_initial + I1_initial +
  E2_initial + I2_initial +
  E3_initial + I3_initial +
  E4_initial + I4_initial +
  D_initial
)



# Time periods
years <- 50
dt <- .01
time <- seq(0, years, by = dt)
n <- length(time)


# Assumption of parameters
a2 <- 0.1     # Proportion of initial latent TB cases that are H-resistant
a3 <- 0.1     # Proportion of initial latent TB cases that are R-resistant
a4 <- 0.1     # Proportion of initial latent TB cases that are MDR

alpha <- 0.00425   # Immigration rate into the US (fixed)

b <- .5     # Proportion of initial active TB cases that are drug-susceptible
```

```r
gamma <- .5  # Proportion of H-resistance acquisition cases

l <- 0.1      # Proportion of immigrants that have LTBI

lambda <- .5  # Effective contact rate

mu <- 0.05    # TB-specific mortality rate
mu0 <- 0.013  # Background (non-TB) mortality rate (fixed)

p <- 0.2      # Proportion of exogenous infections that are acute

phi1 <- 0.2  # Rate of end of treatment for DS TB
phi2 <- 0.2   # Rate of end of treatment for H-resistant TB
phi3 <- 0.1  # Rate of end of treatment for R-resistant TB
phi4 <- 0.1   # Rate of end of treatment for MDR TB

q <- 0.1      # Proportion of active TB cases that are infectious

r2 <- 0.1     # Proportion of immigrant H-resistant LTBI cases
r3 <- 0.1     # Proportion of immigrant R-resistant LTBI cases
r4 <- 0.1     # Proportion of immigrant MDR LTBI cases

rho <- 0.0179 # US birth rate (fixed)

t1 <- 0.05    # Time in treatment for DS
t2 <- 0.05    # Time in treatment for H-resistant
t3 <- 0.05    # Time in treatment for R-resistant
t4 <- 0.05    # Time in treatment for MDR

vL <- 0.005   # Progression rate from latent to active TB

y1 <- 0.05    # Failed treatment leading to H/R resistance from DS
y2 <- 0.05    # Failed treatment leading to MDR from H- or R-resistant TB


z1 <- 0.6    # Success rate of DS TB treatment
z2 <- 0.6     # Success rate of H-resistant TB treatment
z3 <- 0.6     # Success rate of R-resistant TB treatment
z4 <- 0.4    # Success rate of MDR TB treatment

# Variable Setup
S <- numeric(length(time))
E1 <- numeric(length(time))
I1 <- numeric(length(time))
E2 <- numeric(length(time))
I2 <- numeric(length(time))
E3 <- numeric(length(time))
I3 <- numeric(length(time))
E4 <- numeric(length(time))
I4 <- numeric(length(time))
D <- numeric(length(time))
N_vec <- numeric(length(time))
```

```r
# Initial values
S[1]  <- S_initial
E1[1] <- E1_initial
I1[1] <- I1_initial
E2[1] <- E2_initial
I2[1] <- I2_initial
E3[1] <- E3_initial
I3[1] <- I3_initial
E4[1] <- E4_initial
I4[1] <- I4_initial
D[1]  <- D_initial
N_vec[1] <- N_initial

# Simulation
for (t in 1:(length(time) - 1)) {
  dS <- (rho * N_vec[t]
    - q * t1 * lambda * S[t] * I1[t] / N_vec[t]
    - q * t2 * lambda * S[t] * I2[t] / N_vec[t]
    - q * t3 * lambda * S[t] * I3[t] / N_vec[t]
    - q * t4 * lambda * S[t] * I4[t] / N_vec[t]
    + z1 * phi1 * I1[t] + z2 * phi2 * I2[t] + z3 * phi3 * I3[t] + z4 * phi4 * I4[t]
    + (1 - l) * alpha * N_vec[t]
    - mu0 * S[t])

  dE1 <- ((1 - p) * q * t1 * lambda * S[t] * I1[t] / N_vec[t]
      - vL * E1[t]
      + (1 - y1) * (1 - z1) * phi1 * I1[t]
      + l * alpha * (1 - r2 - r3 - r4) * N_vec[t]
      - mu0 * E1[t])

    dI1 <- (q * t1 * lambda * S[t] * I1[t] / N_vec[t]
        + vL * E1[t]
        - phi1 * I1[t]
        - mu0 * I1[t]
        - mu * I1[t])

  dE2 <- ((1 - p) * q * t2 * lambda * S[t] * I2[t] / N_vec[t]
     - vL * E2[t]
     + (1 - y2) * (1 - z2) * phi2 * I2[t]
     + gamma * (1 - z1) * y1 * phi1 * I1[t]
     + l * alpha * r2 * N_vec[t]
     - mu0 * E2[t])

    dI2 <- (q * t2 * lambda * S[t] * I2[t] / N_vec[t]
        + vL * E2[t]
        - phi2 * I2[t]
        - mu0 * I2[t]
        - mu * I2[t])

    dE3 <- ((1 - p) * q * t3 * lambda * S[t] * I3[t] / N_vec[t]
        - vL * E3[t]
        + (1 - y2) * (1 - z3) * phi3 * I3[t]
        + (1 - gamma) * (1 - z1) * y1 * phi1 * I1[t]
```

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         + l * alpha * r3 * N_vec[t]
         - mu0 * E3[t])

    dI3 <- (q * t3 * lambda * S[t] * I3[t] / N_vec[t]
        + vL * E3[t]
        - phi3 * I3[t]
        - mu0 * I3[t]
        - mu * I3[t])

  dE4 <- ((1 - p) * q * t4 * lambda * S[t] * I4[t] / N_vec[t]
      - vL * E4[t]
      + (1 - z2) * y2 * phi2 * I2[t]
      + (1 - z3) * y2 * phi3 * I3[t]
      + l * alpha * r4 * N_vec[t]
      - mu0 * E4[t])

    dI4 <- (q * t4 * lambda * S[t] * I4[t] / N_vec[t]
        + vL * E4[t]
        - phi4 * I4[t]
        - mu0 * I4[t]
        - mu * I4[t])

  dD <- (mu * (I1[t] + I2[t] + I3[t] + I4[t]))

  dN <- (rho * N_vec[t]
     + alpha * N_vec[t]
     - mu * (I1[t] + I2[t] + I3[t] + I4[t])
     - mu0 * N_vec[t])



    # Update the value for next day
  S[t + 1]  <- S[t]  + dS  * dt
  E1[t + 1] <- E1[t] + dE1 * dt
  I1[t + 1] <- I1[t] + dI1 * dt
  E2[t + 1] <- E2[t] + dE2 * dt
  I2[t + 1] <- I2[t] + dI2 * dt
  E3[t + 1] <- E3[t] + dE3 * dt
  I3[t + 1] <- I3[t] + dI3 * dt
  E4[t + 1] <- E4[t] + dE4 * dt
  I4[t + 1] <- I4[t] + dI4 * dt
  D[t + 1]  <- D[t]  + dD  * dt
  N_vec[t + 1] <- N_vec[t] + dN * dt

}
head(data.frame(
  time = time,
  S = S,
  E1 = E1,
  I1 = I1,
  E2 = E2,
  I2 = I2,
  E3 = E3,
```

```r
  I3 = I3,
  E4 = E4,
  I4 = I4,
  D = D,
  N = N_vec
))
```

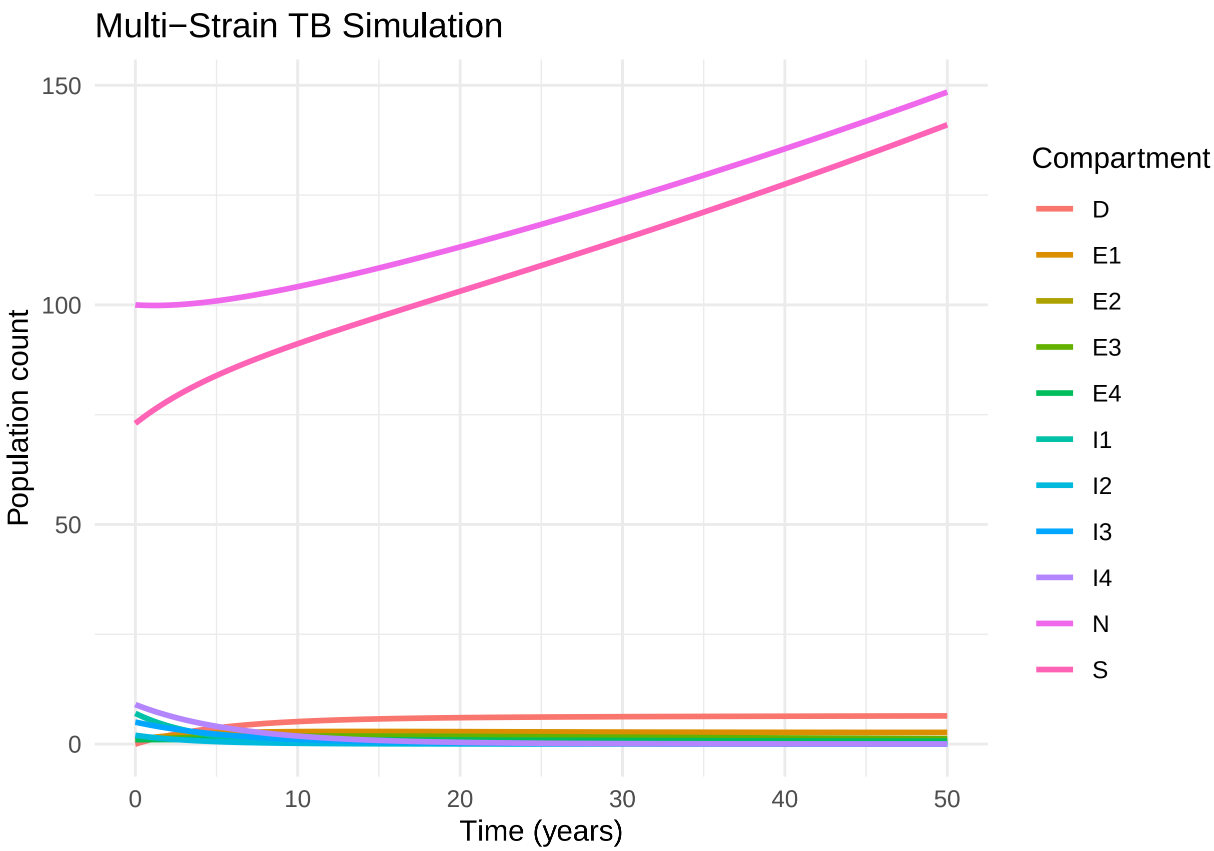
```
##   time        S       E1       I1       E2       I2       E3       I3       E4
## 1 0.00 73.00000 1.000000 7.000000 1.000000 2.000000 1.000000 5.000000 1.000000
## 2 0.01 73.02922 1.005540 6.981768 1.001552 1.994827 1.001975 4.991991 1.000174
## 3 0.02 73.05839 1.011064 6.963583 1.003099 1.989667 1.003947 4.983996 1.000347
## 4 0.03 73.08752 1.016574 6.945447 1.004641 1.984520 1.005915 4.976013 1.000520
## 5 0.04 73.11661 1.022068 6.927358 1.006179 1.979387 1.007879 4.968043 1.000692
## 6 0.05 73.14565 1.027548 6.909317 1.007712 1.974268 1.009839 4.960086 1.000864
##         I4          D         N
## 1 9.000000 0.00000000 100.00000
## 2 8.985544 0.01150000  99.99765
## 3 8.971112 0.02297706  99.99532
## 4 8.956703 0.03443124  99.99302
## 5 8.942317 0.04586259  99.99074
## 6 8.927955 0.05727114  99.98848
```

```r
# Plot
tb_df <- data.frame(
  time = time,
  S = S,
  E1 = E1,
  I1 = I1,
  E2 = E2,
  I2 = I2,
  E3 = E3,
  I3 = I3,
  E4 = E4,
  I4 = I4,
  D = D,
  N = N_vec
)

tb_long <- pivot_longer(
  tb_df,
  cols = -time,
  names_to = "Compartment",
  values_to = "Count"
)

# Plot
ggplot(tb_long, aes(x = time, y = Count, color = Compartment)) +
  geom_line(size = 1) +
  labs(
    title = "Multi-Strain TB Simulation",
    x = "Time (years)",
    y = "Population count"
  ) +
  theme_minimal()
```

```
## Warning: Using `size` aesthetic for lines was deprecated in ggplot2 3.4.0.
## i Please use `linewidth` instead.
## This warning is displayed once every 8 hours.
## Call `lifecycle::last_lifecycle_warnings()` to see where this warning was
## generated.
```




```r
# deSolve
library(deSolve)
rm(list=ls())
parms <- c(
  a2 = 0.1,      # Proportion of initial latent TB cases that are H-resistant
  a3 = 0.1,      # Proportion of initial latent TB cases that are R-resistant
  a4 = 0.1,      # Proportion of initial latent TB cases that are MDR

  alpha = 0.00425,    # Immigration rate into the US (fixed)

  b = .5,      # Proportion of initial active TB cases that are drug-susceptible

  gamma = .5,   # Proportion of H-resistance acquisition cases

  l = 0.1,       # Proportion of immigrants that have LTBI

  lambda = .5,   # Effective contact rate

  mu = 0.05,     # TB-specific mortality rate
  mu0 = 0.013,   # Background (non-TB) mortality rate (fixed)
```

```
  p = 0.2,      # Proportion of exogenous infections that are acute

  phi1 = 0.2,  # Rate of end of treatment for DS TB
  phi2 = 0.2,   # Rate of end of treatment for H-resistant TB
  phi3 = 0.1,  # Rate of end of treatment for R-resistant TB
  phi4 = 0.1,   # Rate of end of treatment for MDR TB

  q = 0.1,      # Proportion of active TB cases that are infectious

  r2 = 0.1,     # Proportion of immigrant H-resistant LTBI cases
  r3 = 0.1,     # Proportion of immigrant R-resistant LTBI cases
  r4 = 0.1,     # Proportion of immigrant MDR LTBI cases

  rho = 0.0179, # US birth rate (fixed)

  t1 = 0.05,    # Time in treatment for DS
  t2 = 0.05,    # Time in treatment for H-resistant
  t3 = 0.05,    # Time in treatment for R-resistant
  t4 = 0.05,    # Time in treatment for MDR

  vL = 0.005,   # Progression rate from latent to active TB

  y1 = 0.05,    # Failed treatment leading to H/R resistance from DS
  y2 = 0.05,    # Failed treatment leading to MDR from H- or R-resistant TB


  z1 = 0.6,    # Success rate of DS TB treatment
  z2 = 0.6,     # Success rate of H-resistant TB treatment
  z3 = 0.6,     # Success rate of R-resistant TB treatment
  z4 = 0.4    # Success rate of MDR TB treatment
)

E1_initial <- 1 # Latent DS
I1_initial <- 7 # Infectious DS

E2_initial <- 1 # Latent H-resistant
I2_initial <- 2 # Infectious H-resistant

E3_initial <- 1 # Latent R-resistant
I3_initial <- 5 # Infectious R-resistant

E4_initial <- 1 # Latent MDR
I4_initial <- 9 # Infectious MDR

D_initial <- 0 # Initial deaths

N_initial <- 100      # total US population

S_initial <- N_initial - (
  E1_initial + I1_initial +
  E2_initial + I2_initial +
  E3_initial + I3_initial +
  E4_initial + I4_initial +
```

```
  D_initial
)

state_ini <- c(
  S  = S_initial,
  E1 = E1_initial,
  I1 = I1_initial,
  E2 = E2_initial,
  I2 = I2_initial,
  E3 = E3_initial,
  I3 = I3_initial,
  E4 = E4_initial,
  I4 = I4_initial,
  D  = D_initial,
  N  = N_initial
)

tb_model <- function(t, state, parms) {
  with(as.list(c(state, parms)), {

    dS  <- (rho * N -
            q*t1*lambda * S*I1/N -
            q*t2*lambda * S*I2/N -
            q*t3*lambda * S*I3/N -
            q*t4*lambda * S*I4/N +
            z1*phi1*I1 + z2*phi2*I2 + z3*phi3*I3 + z4*phi4*I4 +
            (1 - l)*alpha*N -
            mu0*S)

    dE1 <- ((1 - p)*q*t1*lambda * S*I1/N -
            vL * E1 +
            (1 - y1)*(1 - z1)*phi1 * I1 +
            l*alpha*(1 - r2 - r3 - r4)*N -
            mu0*E1)

    dI1 <- (q*t1*lambda * S*I1/N +
            vL*E1 -
            phi1*I1 -
            mu0*I1 -
            mu*I1)

    dE2 <- ((1 - p)*q*t2*lambda * S*I2/N -
            vL * E2 +
            (1 - y2)*(1 - z2)*phi2 * I2 +
            gamma*(1 - z1)*y1*phi1 * I1 +
            l*alpha*r2*N -
            mu0*E2)

    dI2 <- (q*t2*lambda * S*I2/N +
            vL*E2 -
            phi2*I2 -
            mu0*I2 -
            mu*I2)
```

```r
    dE3 <- ((1 - p)*q*t3*lambda * S*I3/N -
            vL * E3 +
            (1 - y2)*(1 - z3)*phi3 * I3 +
            (1 - gamma)*(1 - z1)*y1*phi1 * I1 +
            l*alpha*r3*N -
            mu0*E3)

    dI3 <- (q*t3*lambda * S*I3/N +
            vL*E3 -
            phi3*I3 -
            mu0*I3 -
            mu*I3)

    dE4 <- ((1 - p)*q*t4*lambda * S*I4/N -
            vL * E4 +
            (1 - z2)*y2*phi2 * I2 +
            (1 - z3)*y2*phi3 * I3 +
            l*alpha*r4*N -
            mu0*E4)

    dI4 <- (q*t4*lambda * S*I4/N +
            vL*E4 -
            phi4*I4 -
            mu0*I4 -
            mu*I4)

    dD  <- (mu * (I1 + I2 + I3 + I4))

    dN  <- (rho*N +
            alpha*N -
            mu*(I1 + I2 + I3 + I4) -
            mu0*N)

    list(c(dS, dE1, dI1, dE2, dI2, dE3, dI3, dE4, dI4, dD, dN))
  })
}

t = seq(0, 50, 0.01)

out <- ode(
  y = state_ini,
  times = t,
  func = tb_model,
  parms = parms
)
head(out)
```

```
##      time        S       E1       I1       E2       I2       E3       I3
## [1,] 0.00 73.00000 1.000000 7.000000 1.000000 2.000000 1.000000 5.000000
## [2,] 0.01 73.02919 1.005532 6.981792 1.001549 1.994833 1.001974 4.991998
## [3,] 0.02 73.05835 1.011049 6.963631 1.003094 1.989680 1.003943 4.984009
## [4,] 0.03 73.08746 1.016551 6.945518 1.004634 1.984541 1.005909 4.976032
## [5,] 0.04 73.11652 1.022039 6.927453 1.006170 1.979414 1.007871 4.968069
```

```
## [6,] 0.05 73.14555 1.027511 6.909435 1.007701 1.974302 1.009830 4.960119
##            E4       I4          D         N
## [1,] 1.000000 9.000000 0.00000000 100.00000
## [2,] 1.000174 8.985556 0.01148854  99.99766
## [3,] 1.000347 8.971135 0.02295420  99.99535
## [4,] 1.000519 8.956738 0.03439702  99.99305
## [5,] 1.000691 8.942364 0.04581705  99.99078
## [6,] 1.000863 8.928013 0.05721434  99.98853
```

```r
# plot
tb_long2 <- as.data.frame(out) %>%
  pivot_longer(-time, names_to="Compartment", values_to="Count")

ggplot(tb_long2, aes(time, Count, color=Compartment)) +
  geom_line() +
  theme_minimal()
```