
Bacterial regrowth modeling and simulation package

This package simulates changes in bacterial regrowth rate as a function of time after antibiotic dose administration. It also calculates area under regrowth rate- time curve (AURTC) over time interval from bacterial inoculation till the end of antibiotic action, the equivalent unexposed bacterial inoculum regrowth rate (RGR_i) and the expected percent survival, to plot dose-response curve.

This package was written by Ahmed A. El-Sherbeni, University of Alberta, Canada. Any suggestions please e-mail me at elsherbe@ualberta.ca.

INSTALLATION

After downloading RGM package, unzip, then put the RGM.m file in Mathematica folder, usually at:

C:\Program Files\Wolfram Research\Mathematica\5.0\AddOns\Applications

Number varied according to Mathematica version

USING RGM PACKAGE

1. Open Mathematica and type:

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<<RGM.m
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Press Enter+Shift

This will load RGM package.

2. Enter antibiotic parameters:

Note: Parameters are to be entered as absolute values, i.e. without algebraic sign.

a. Pharmacokinetics parameters:

If you intend to use one-compartment open model with first-order elimination, no absorption, type:

PK1[k, Vd, f] Press Enter+Shift

Where k is the elimination rate constant in hr^{-1} , Vd is the volume of distribution in liter or liter/kg, and f is the fraction of unbound antibiotic concentration.

If you intend to use one-compartment open model with first-order absorption and elimination, type:

PK2[k, ka, aVd, f] Press Enter+Shift

Where k is the elimination rate constant in hr^{-1} , ka is the absorption rate constant in hr^{-1} , aVd is the apparent volume of distribution in liter or liter/kg, and f is the fraction of unbound antibiotic concentration.

b. Pharmacodynamics parameters

Type:

PD[DRmin, DRmax, EC50, h, RGRmax] Press Enter+Shift

Where DRmax and DRmin are the maximum and the minimum deterioration rate, respectively, EC50 is the antibiotic concentration at which the effect is at half of its maximum (DRmax - DRmin); and h denotes the Hill slope, see figure 1. RGRmax is the maximum value of regrowth rate can be reached in cfu/hr. DRmin and DRmax are in hr^{-1} and EC50 is in mg/kg.

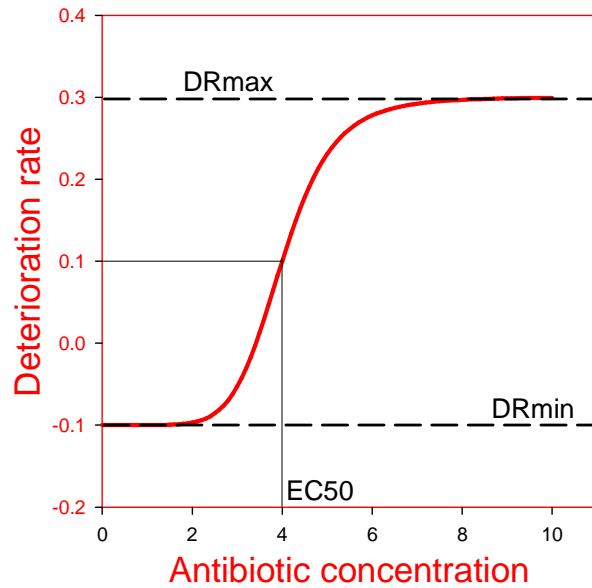


Figure 1. DRmin, DRmax and EC50 in a concentration-effect curve.

c. Model parameters

Type:

Model[RGR_i, MinDose, MaxDose, N]

Where RGR_i is the initial regrowth rate of bacterial inoculum to be simulated in cfu/hr, N is the number of doses within MinDose and MaxDose which are the minimum and the maximum antibiotic dose, respectively, in mg or mg/kg.

d. Pharmacological parameters

Type:

PG[RGR50, Hill]

Where RGR50 is the initial regrowth rate of unexposed inoculum at which percent survival is 50%, in cfu/hr; and Hill denotes the Hill slope.

3. Predicting dose-response curve

To calculate AURTC, RGR_i , duration of action and percent survival, type:

PKPD

The calculated AURTC is in cfu, RGR_i is in cfu/hr and duration of action is in hr.

To plot dose-percent survival curve, type:

DRcurve

4. Simulating regrowth rate dynamics

To simulate changes in bacterial regrowth rate by time after an antibiotic dose, xx, type:

TimeCurve[xx]

Two graphs will shown, the first represents changes in free concentration by time, the second represents changes in regrowth rate by time till the end of antibiotic dose action.

5. Additional commands

a. To add another curve to the predicted dose-percent survival curve, type:

experimental={{dose1, percent survival1} , { dose2, percent survival2} ,}

b. To begin new round of calculations and simulations, type:

NewRound

or close Mathematica and reopen.

c. Time elapsed between bacterial inoculum and the beginning of treatment is 2 hr by default. To change it type:

waiting=xx

Where xx is the number of hours elapsed.