ME 405 Fall 2006 Professor John M. Cimbala Lecture 07 09/20/2006

Today, we will:

- Continue our discussion of dose and dose response in **Section 2.7**
- Review first-order ordinary differential equations (ODEs) and their application to body burden
- Do some example problems
- Finish our discussion of Chapter 2 – Chapter 3 begins on Friday (start reading it)

Dose & Dose Response (continued)

Definitions: ① Exposure = D = Dose = total mass of a chemical to which the body is exposed or subjected

D_{min} = Dose Rate (per minute)

"minute" - not minimum

E.g. for a gas of species j, $D_{min} = (QC_j)_{min}$

units typ. mg/min

D_t = total dose

$$\boxed{D_t = \int_0^t QC_j \, dt}$$

for some time period t (typ. 8 hrs for OSHA)

② Absorption Define M_{bb} = body burden

≡ mass of the contaminant actually in the body at a given time

[typically absorbed into the body - resides in liver, bloodstream, etc]

③ Response R_p [various units - see text]

R_p depends on dose & absorption = how the body reacts to the chemical

Dose-response data and the problem with extrapolation:

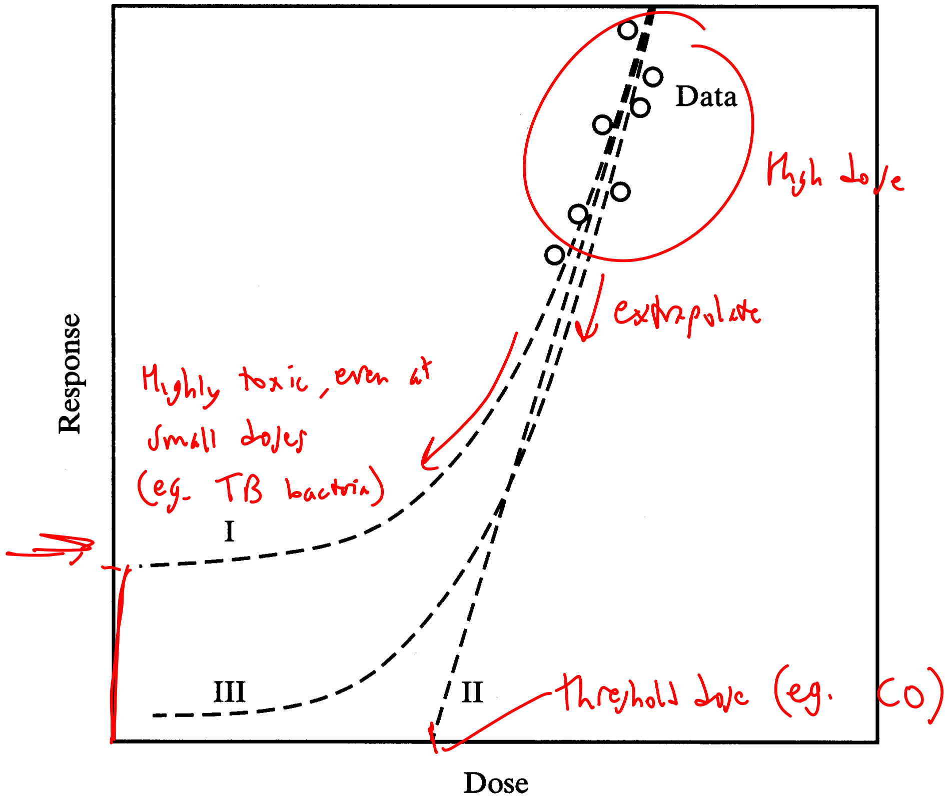


Figure 2.40 Methods to extrapolate dose-response data for three classes of toxins (from Heinsohn & Kabel, 1999).

The Ehrlich Index – typically used for medicines.

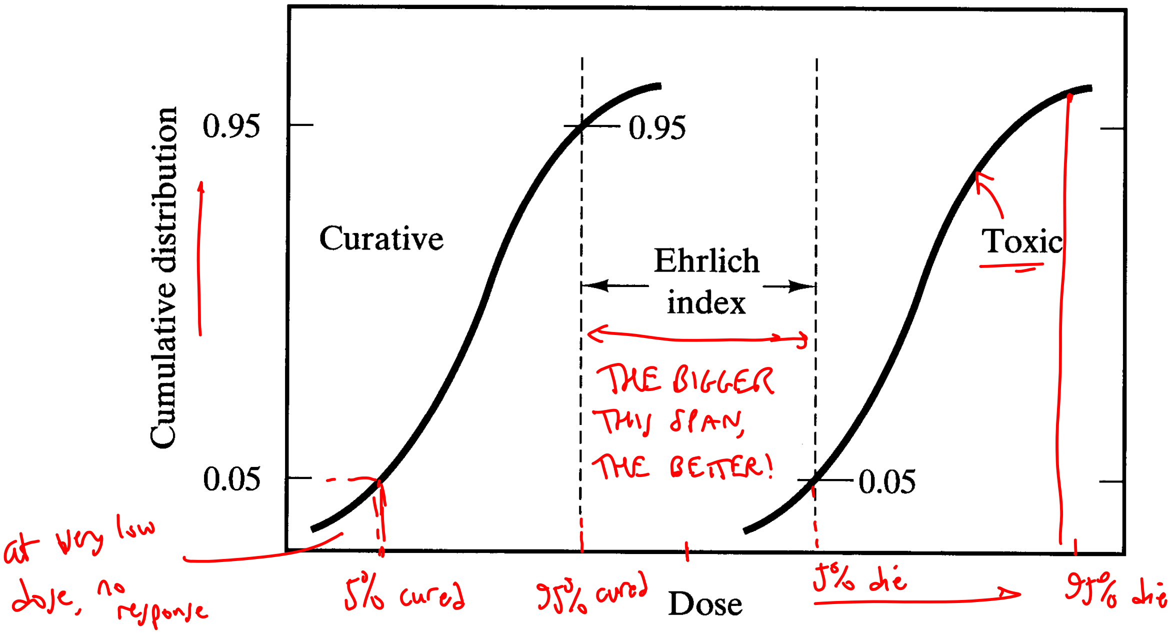


Figure 2.39 The Ehrlich index, defined by the curative and toxic dose-response curves.

Body burden, m_{bb} behaves as a first-order ODE

Eq (2-49):

$$\boxed{\frac{dm_{bb}}{dt} = FQC_{inspired} - k_r m_{bb}}$$

$C = C_j$ (drop j subscript)

variable	description	dimensions	units
m_{bb}	body burden	mass	mg
t	time	time	min & hr
k_r	rate constant - How fast the contaminant is absorbed/removed from the body	$\frac{1}{time}$	$\frac{1}{min}$ or $\frac{1}{hr}$
F	bioavailability ratio = ratio of mass of contaminant absorbed by the body to the mass of contaminant in the inspired air e.g. If breathe in 10 μg of a contaminant & the body absorbs 4 μg of the ", $F = 0.40$ (40%)	—	—
Q	volume flow rate of inspired air	$\frac{Vol}{time}$	$\frac{m^3}{min}$ $\frac{m^3}{hr}$ or $\frac{L}{min}$
$C_{inspired}$	mass conc. of the contam. in the inspired air	$\frac{mass}{Vol}$	$\frac{mg}{m^3}$

SOLUTION OF FIRST-ORDER ODES:

See Sec. 1.5.8 in text

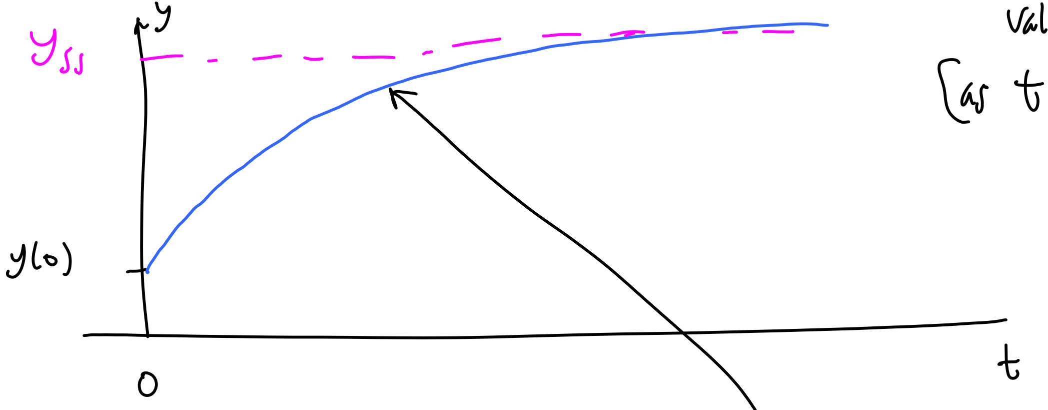
For $y = y(t)$

- Standard form for a 1st-order ODE is $\boxed{\frac{dy}{dt} = B - Ay}$
- Also need to know the initial condition, $\underline{y(0) = y \text{ @ } t=0}$
- A & B may be constants (can obtain an analytical soln)

or A & B are fnc's of time (will do a numerical solution)

Consider a sudden change @ $t=0$:

y_{ss} = steady-state value of y [as $t \to \infty$]



FOR CONSTANT A & B, analytical soln is:

$$\boxed{y_{ss} = \frac{B}{A}}$$

$$\boxed{y(t) = y_{ss} - \left[y_{ss} - y(0)\right] \exp(-At)}$$

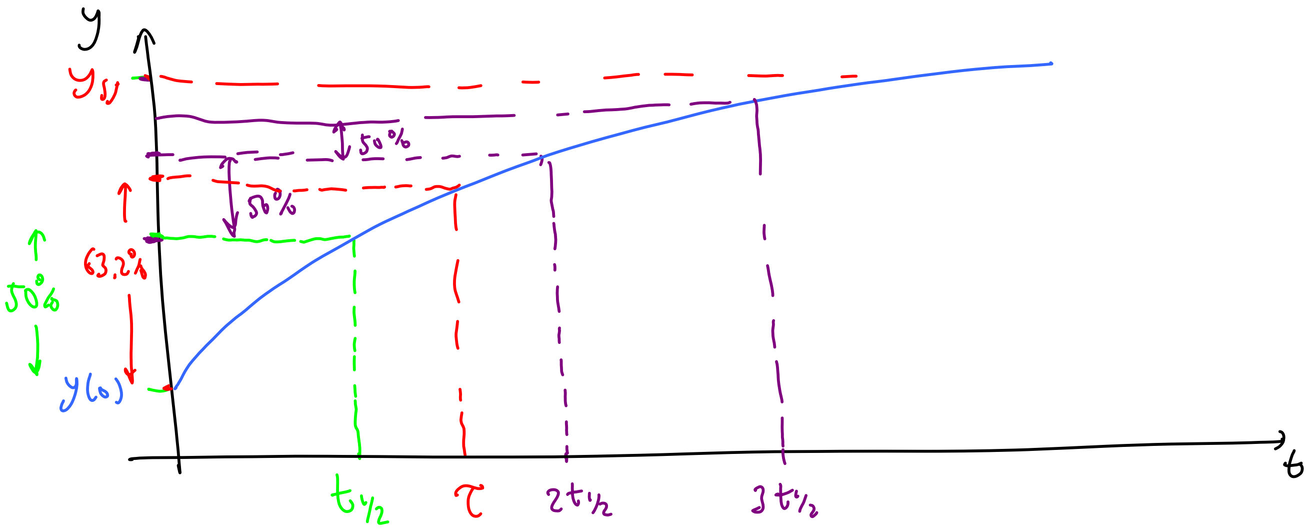
or

$$\boxed{y(t) = y(0) + \left[y_{ss} - y(0)\right]\left[1 - \exp(-At)\right]}$$

Let $\boxed{\underline{\tau = \text{First-order time constant}} \equiv 1/A}$

τ = time required for y to grow (or decay) to ≈ 63.2% of its final change.

$$\left[1 - e^{-1} = 0.632\right]$$



Also define $\underline{t_{1/2} = \text{half life}}$ ≡ time required for y to grow (or decay) to half (50%) of its final change

$$t_{1/2} = \frac{-\ln(1/2)}{A} = -\ln(1/2)\tau$$

$$\boxed{t_{1/2} = 0.693\,\tau}$$

Example

Given: A first-order differential equation and initial condition:

- $\frac{dy}{dt} = \overset{B}{\boxed{10.0}} - \underset{A}{\boxed{3.82}}\, y$
- $y(0) = \underline{7.60}$

(*a*) To do: Calculate the steady-state value of y (as $t \to \infty$).

Solution: In standard form $\frac{dy}{dt} = B - Ay$

$A = 3.82$

$B = 10.0$

$$y_{ss} = \frac{B}{A} = \frac{10.0}{3.82} = 2.618$$

$$\boxed{y_{ss} = 2.62}$$

(*b*) To do: Calculate the half-life $t_{1/2}$ of this system.

Solution:

$$t_{1/2} = \frac{-\ln(1/2)}{A} = 0.1814$$

$$\boxed{t_{1/2} = 0.181}$$

(*c*) To do: Calculate y at $\underline{t = 0.54}$.

Solution:

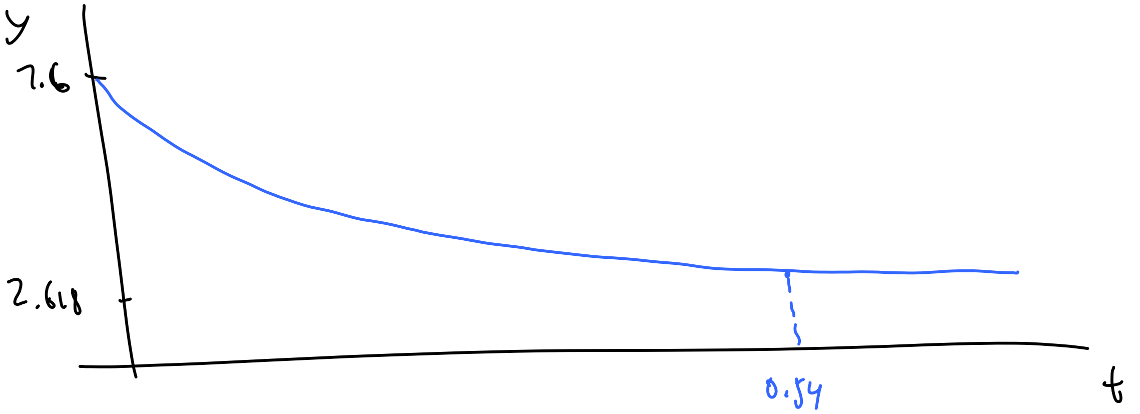
Since A & B are const, we use the analytical soln:

$$y(t) = y(0) + \left[y_{ss} - y(0)\right]\left[1 - \exp(-At)\right]$$

$$= 7.60 + \left[2.618 - 7.60\right]\left[1 - \exp\left((-3.82)(0.54)\right)\right]$$

$$= 3.25$$

$$\boxed{y(t = 0.54) = \underline{\underline{3.25}}}$$



We can also solve this numerically using the Runge-Kutta technique

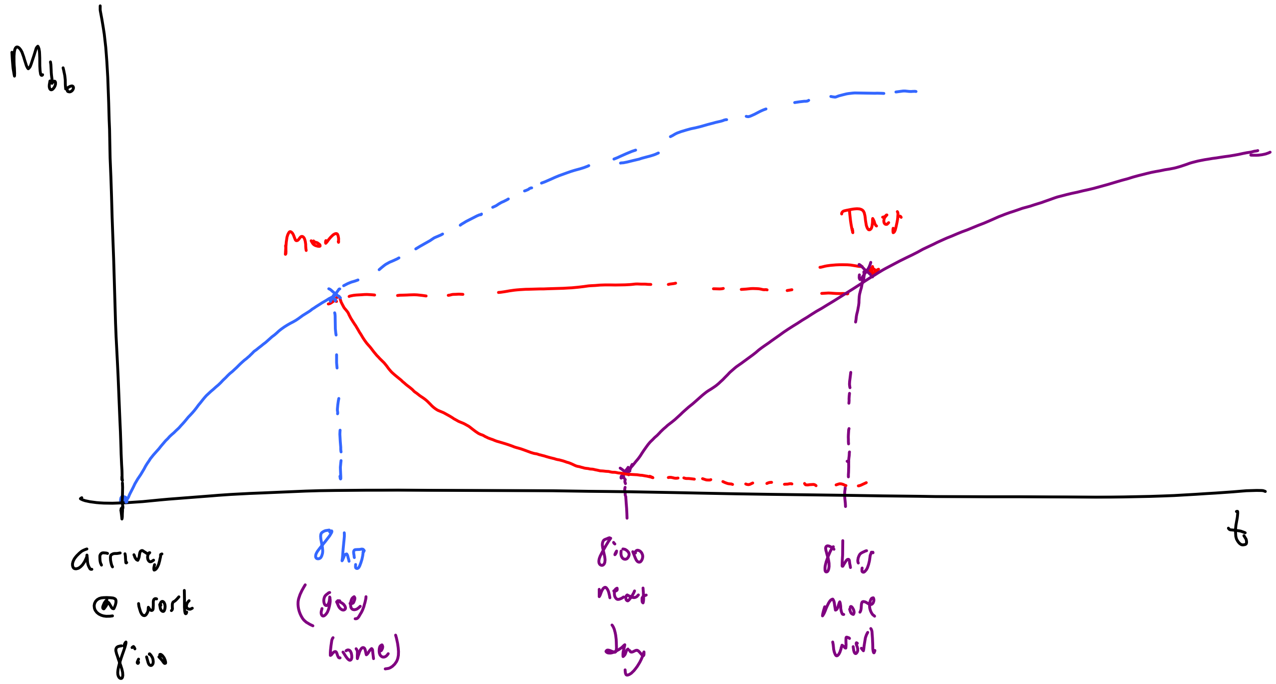
✪ SEE App A-12

Show live demo's of solving a 1st-order ODE in

- Mathcad
- Excel
- EES

We can use these same tools for calculation of the body burden as a fnc. of time since M_{bb} behaves as a first-order ODE

QUALITATIVELY: A worker is exposed to a chemical for 8 hrs each working day (Mon-Fri)



★ So - the worker's body burden on Tuesday at quitting time is greater than his body burden on Monday at quitting time.