COMPARTMENTAL MODELING

1. MASS BALANCE

Compartmental Modeling is built on the simple concept of mass balance equations.

Let V be the volume of a compartment. Let C be the concentration of a substance in the compartment.

The total amount of the substance, Q, in the compartment is given by

Q=V*C.

The change in the amount of substance is given by

$$\frac{\partial}{\partial t} Q = \frac{\partial}{\partial t} (V C).$$

The change in the amount of substance equals the Sources minus the sinks for the substance.

$$\frac{\partial}{\partial t} (V C) = Sources - Sinks.$$

We now make two additional assumptions: (1) The material in the compartment is instantaneously well mixed (this is always assumed to be true); and (2) the volume is constant (true only when given as true--it is possible to have volumes which are time dependent, e.g. left ventricle).

With these two assumptions, we can write
$V\left(\frac{\partial}{\partial t} C\right) = Sources - Sinks$. We sometimes write $\frac{\partial}{\partial t} C$ as $\frac{\partial}{\partial t} C(t)$.

2. UNITS

QUESTION: What are typical units for V, C, Q, $\frac{\partial}{\partial t} C$, t ?

V=ml, ml/g. C=M, mM, uM. Q=mole, mmol, umol. $\frac{\partial}{\partial t} C$=M/s, mM/s,uM/s. The units for time are s (also sec). Additional units and prefixes can be found in JSim documentation.

3. SOURCES & SINKS

Typical sources are inflow of material into the compartment (instantaneously well mixed), flux of material from another compartment, synthesis of material from another substance, and release of a substance from a binding protein.

Typical sinks are outflow of material from the compartment, flux of material out of the compartment, conversion of material into another substance, and substance becoming bound.

Example: A one compartment model with flow assumed to be constant:
$V\left(\frac{\mathrm{d}}{\mathrm{d}t}C(t)\right) = F\,Cin(t) - F\,Cout(t)$. Since the compartment is instantaneously well mixed, this equation can be written as
$\frac{\partial}{\partial t}C = \frac{F\,(Cin - C)}{V}$. (We have dropped "(t)", replaced Cout with C, and divided both sides by V.)

This is an ordinary differential equation (ODE) and requires an initial condition (I.C. or IC) for solution. We will
choose C(0)=C0, which means at time equals zero, the concentration is C0 (some value). We will choose Cin(t), the inflowing concentration of material to be zero. The solution is given as

$$C(t) = C0\,\mathrm{e}^{-\frac{Ft}{V}}$$

Substituting $\tau = \frac{V}{F}$, we have

$C(t) = C0\,\mathrm{e}^{-\frac{t}{\tau}}$ where tau has the units of time, so that the exponential operates on a dimesnionless quantity.

4. AREA, TRANSIT TIME ($\overline{t}$), VARIANCE (SD^2), and RELATIVE DISPERSION (RD)

The area of an outflow curve is calculated as
$Area = \int_0^\infty C(t)\,\mathrm{d}t$. For $C(t) = C0\,\mathrm{e}^{-\frac{t}{\tau}}$, $Area = \tau\,C0$.
The transit time of an outflow curve is calculated as
$\overline{t} = \frac{\int_0^\infty C(t)\,t\,\mathrm{d}t}{Area}$. For $C(t) = C0\,\mathrm{e}^{-\frac{t}{\tau}}$, $\overline{t} = \tau$.
The variance of an out flow curve is calculated as
$SD^2 = \frac{\int_0^\infty C(t)\,(t-\tau)^2\,\mathrm{d}t}{Area}$. For $C(t) = C0\,\mathrm{e}^{-\frac{t}{\tau}}$, $SD^2 = \tau^2$.
The relative dispersion of an outflow curve is calculated as
$RD = \frac{\sqrt{SD^2}}{\overline{t}}$.For $C(t) = C0\,\mathrm{e}^{-\frac{t}{\tau}}$, $RD=1$.

5. VARIANCE AND TRANSIT TIME (CONTINUED)

$\overline{t_{input}} + \overline{t_{systen}} = \overline{t_{output}}$. The transit time of an input curve plus the transit time of the "system" equals the transit time of the output curve.

If there is no consumption or synthesis in an arrangement of compartment models, the transit time is also given as

$\overline{t} = \frac{\sum_{i=1}^{n} V_i}{F}$, where V_i are the volumes of connected compartments.

$SD^2_{input} + SD^2_{system} = SD^2_{output}$. Variances also add.
These two equations are true as long as everything that enters the "system" as input exits the system as output. From the input and output curves (inflow and outflow concentrations), the transit time and the relative dispersion of the system can be determined.

#1. The transit time and relative dispersion for a compartmental systems are independent of the shape of the input and output functions as long as everything that enters the system also exits the system.

6. CONSEQUENCES:
What is the RD of N-stirred tanks in series, each with volume V/N?

Each tank has transit time $\overline{t_{SingleTank}} = \frac{\tau}{N}$. The total transit time of the system is $\overline{t_{system}} = \tau$. The variance of each stirred tank is

$SD^2_{SingleTank} = \left(\frac{\tau}{N}\right)^2$. The total variance is $SD^2_{system} = \frac{\tau^2}{N}$. The relative dispersion of the system is

$RD = \sqrt{\frac{1}{N}}$. The relative dispersion in arteries of the human leg has been determined to be 0.18 (1) which would require 31 stirred tanks in series.

References:

1. Bassingthwaighte, J.B. Plasma indicator dispersion in arteries of the human leg. Circ. Res. 19: 332 -346, 1966.

CODING COMPARTMENTAL MODELS IN JSIM

1. Single Compartment with flow:

```
import nsrunit; // load the jsim units file
unit conversion on; // unit check equations
math comp1flow { // use the
realDomain t s; t.min=0; t.max=30; t.delta=0.1; //realDomain are the independent
variables
real C(t) uM, C0=1 uM, Cout(t) uM;
extern real Cin(t) uM;
real F=1 ml*g^(-1)*min^(-1);
real V=0.05 ml/g;
when(t=t.min) {C=C0;}
C:t=(F/V)*(Cin-Cout);
real Qint(t) mole/g, Q(t) mole/g;
when(t=t.min) {Qint=V*C0;}
Qint:t=F*(Cin-Cout);
Q=V*C;
Cout=C;
}
```

2. Two Compartments with flow:

```
import nsrunit; // load the jsim units file
unit conversion on; // unit check equations
math comp1flow { // use the
realDomain t s; t.min=0; t.max=30; t.delta=0.1; //realDomain are the independent
variables
real C1(t) uM, C2(t) uM, Cout(t) uM;
extern real Cin(t) uM;
real F=1 ml*g^(-1)*min^(-1);
real PS12 = 1 ml*g^(-1)*min^(-1), PS21=PS12;
real V1=0.05 ml/g, V2=0.10 ml/g;
when(t=t.min) {C1=0; C2=0;}
C1:t=(F/V1)*(Cin-Cout)-(PS12/V1)*C1+(PS21/V1)*C2;
C2:t=(PS12/V2)*C1-(PS21/V2)*C2;

Cout=C;
}
```