Understanding the Comp2FlowMMExchangeReaction Model

This is a two compartment (plasma and parenchymal cell (pc)) exchange model with flow in the plasma compartment. Both spaces are instantaneously well mixed. C and B reversibly convert to each other in the pc compartment.

Note that the units for PsmaxC and PsmaxB, mM*ml/(g*min) do not match the units for flow, Fp, ml/(g*min). The units on the conversion rates, Gc2b and Gb2c, min^(-1), also do not match the units for flow or exchange.

The governing ordinary differential equations are

$$dC_p/dt = \frac{F_p}{V_p}\cdot(C_{in} - C_p) + \frac{PS_{maxC}}{V_p}\cdot\frac{C_{pc}}{K_{mC}+C_{pc}+C_c} - \frac{PS_{maxC}}{V_p}\cdot\frac{C_p}{K_{mC}+C_p+C_{pc}} \quad ,$$

$$dB_p/dt = \frac{F_p}{V_p}\cdot(\quad - B_p) + \frac{PS_{maxB}}{V_p}\cdot\frac{B_{pc}}{K_{mB}+B_{pc}+B_p} - \frac{PS_{maxB}}{V_p}\cdot\frac{B_p}{K_{mB}+B_p+B_{pc}} \quad ,$$

$$dC_{pc}/dt = -G_{c2b}\cdot C_{pc} + G_{b2c}\cdot B_{pc} - \frac{PS_{maxC}}{V_{pc}}\cdot\frac{C_{pc}}{K_{mC}+C_{pc}+C_p} + \frac{PS_{maxC}}{V_{pc}}\cdot\frac{C_p}{K_{mC}+C_p+C_{pc}} \quad ,$$

and

$$dB_{pc}/dt = +G_{c2b}\cdot C_{pc} - G_{b2c}\cdot B_{pc} - \frac{PS_{maxB}}{V_{pc}}\cdot\frac{B_{pc}}{K_{mB}+B_{pc}+B_p} + \frac{PS_{maxB}}{V_{pc}}\cdot\frac{B_p}{K_{mB}+B_p+B_{pc}} \quad .$$

The initial conditions are given as

$$C_p(0)=C_p0,\ C_{pc}(0)=C_{pc}0,\ B_p(0)=B_p0,\ and\ B_{pc}(0)=B_{pc}0.$$

The exchange rates between compartments for C and B can also be expressed as

$$PS_c = \frac{(PS_{maxC}\cdot K_{mC})}{(K_{mC}+C_p)\cdot(K_{mC}+C_{pc})}\ and\ PS_b = \frac{(PS_{maxB}\cdot K_{mB})}{(K_{mB}+B_p)\cdot(K_{mB}+B_{pc})}$$

Which shows their dependency on the concentrations on both sides of the membrane for a given species.

Figures and Explanations

Comments:

Note that the exchange flux terms for dCp/dt

```
  +(PSmaxC/Vp)*(Cpc/(KmC+Cpc+Cp) -(PSmaxC/Vp)*Cp/
(KmC+Cp+Cpc)
```

can be combined and written as

```
    (PSmaxC/Vp)*(Cpc-Cp) /(KmC+Cpc+Cp) .
```

We can write the flux as

```
             PSmaxC
         ----------------------- * (Cpc-Cp)
          Vp*(KmC+Cp+Cpc)
```

Compare this to the non-MM formulation,

```
              (PS/Vp)  * (Cpc-Cp).
```

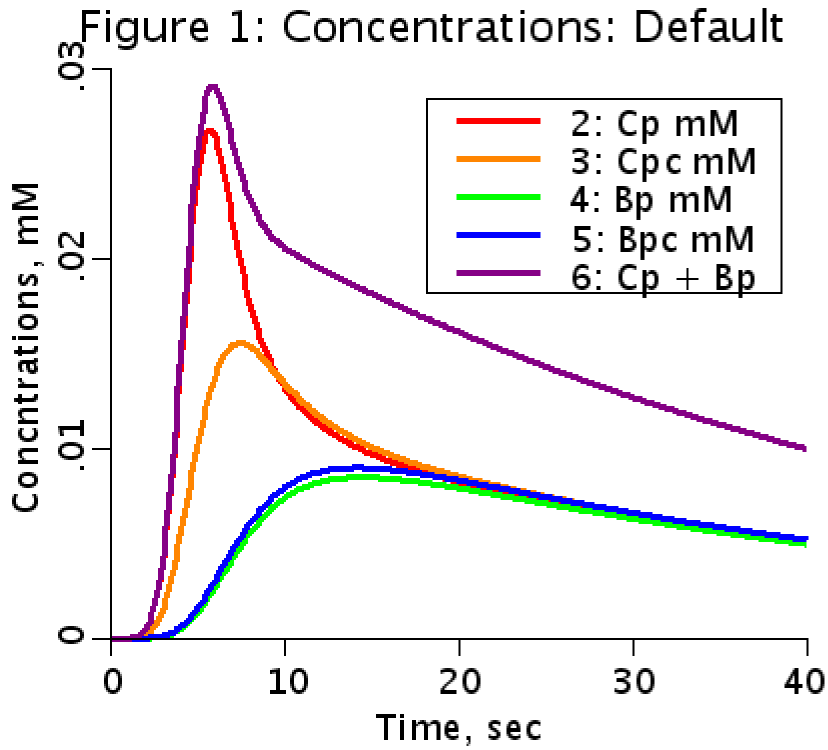
The concentration on both sides of the membrane for the same species are dependent on each other because of the terms in the denominator which are a function of both Cp and Cpc.

For KmC>>Cp, KmC>>Cpc, the MM formulation reduces to

```
           ( (PSmaxC/KmC)/Vp )*(Cpc-Cp),
```

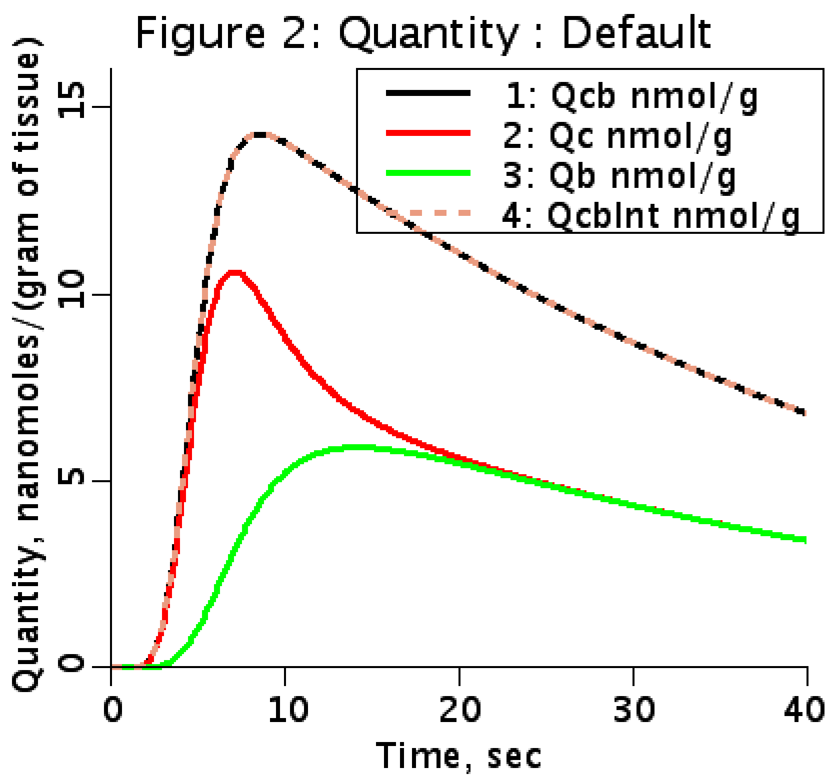
which is equivalent to the non-MM formulation.

Figure 1: Concentrations: Default parameter set



The concentrations of the two species in two compartments are plotted as functions of time. The total outflow, Cp+Bp, is also plotted.

Figure 2: Quantity : Default parameter set



The amount of substances C and B in nanomoles per gram of tissue, are plotted as functions of time. The amount of both substances is calculated in two different ways:

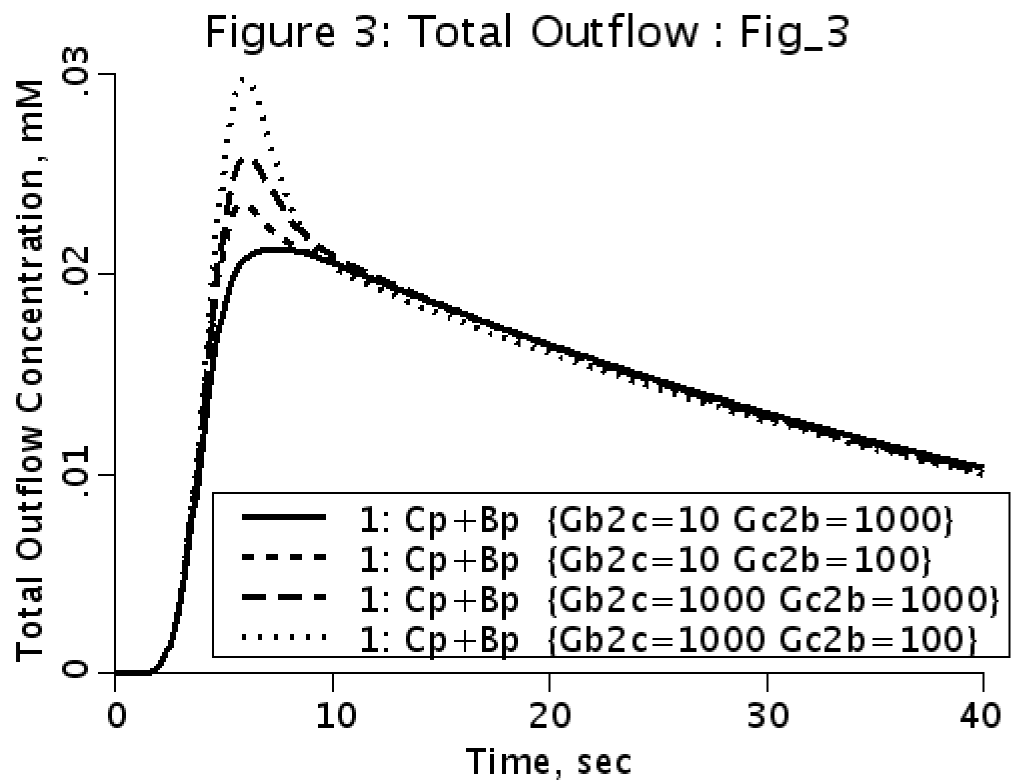
```
  Qcb(t) = Vp*( Cp + Bp ) + Vpc*( Cpc + Bpc )
```

(black line) and also as

```
                / t
  QcbInt(t) =  | Fp*( Cin(t') -Cp(t') - Bp(t') ) dt'
              / t.min
```

(dashed brown line). Because they give the same result, the two lines coincide.

Figure 3: Total Outflow : Fig_3 parameter set



In Comp2FlowExchangeReaction (see Figure 2 from that model), it was determined that the conversion rates, Gc2b and Gb2c, had no effect on the total outflow concentration,when the exchange rates of the two species were equal.
Is that true for this model as well?

The Fig_3 parameter set has been set up so that PSmaxB = PSmaxC and KmC=KmB. Run LOOPS for the four indicated cases.

Change KmC and KmB to 0.2 and run loops again.
Change KmC and KmB to 2.0 and run loops again.

When KmC<<Cp and Cpc and KmB<<Bp and Bpc, the effective permeability-surface area products depend on the concentrations.

When KmC>>Cp and Cpc and KmB>>Bp and Bpc, the concentrations do not affect permeability-surface area products. Why? (See comment (3) above.)