Opening Comments: Blood Tissue Exchange (BTEX) Models

The BTEX models represent tissue cylinders of increasing complexity – regions separated by barriers or clefts across which transport occurs as linear processes. The simplest model in this sequence of models is btex10_pde which represents flow through a plasma region with axial diffusion and consumption of the metabolite. The most complex model in this sequence is btex50_pde which incorporates btex10_pde and includes transport into an endothelial cell region, an interstitial fluid region, a parenchymal cell region, and a mitochondrial region. Consumption and axial diffusion processes can occur in all of these regions. These models are segmented in one dimension because of the aspect ratio of a capillary

Links to Descriptions of the Individual Models

BTEX10 (just the plasma region)

BTEX20 (plasma and interstitial fluid regions)

BTEX30 (plasma, interstitial fluid, and parenchymal cell regions)

BTEX40 (plasma, endothelial cell, interstitial fluid, and parenchymal cell regions)

BTEX50 (plasma, endothelial cell, interstitial fluid, and parenchymal cell regions with mitochondria)

Equation for Region with Flow

The derivation of the governing equations proceeds as follows:

Consider a flow carrying a concentration of a metabolite through a tube. In a small region of the tube, we write the equation for mass conservation in one dimension as:

$$\frac{d(V \cdot C)}{dt} = \frac{\partial(V \cdot C)}{\partial t} + U \cdot \frac{\partial(V \cdot C)}{\partial x} = Sources - Sinks + V \cdot Diffusion,$$

where V is the volume, C is the concentration, and U is the velocity.

$\frac{d(V \cdot C)}{dt} = \frac{\partial(V \cdot C)}{\partial t} + U \cdot \frac{\partial(V \cdot C)}{\partial x}$ means that the total derivative (also called the material derivative) is equal to the local rate of change plus the advection of a gradient. See any standard text of fluid dynamics for a fuller explanation.

The advection of the gradient term is moved to the left hand side of the equation. Assuming the volume, V, is a constant, we rewrite the equation as

$$\frac{V \cdot \partial C}{\partial t} = -U \cdot V \cdot \frac{\partial C}{\partial x} + Sources - Sinks + V \cdot Diffusion.$$

Let the velocity multiplying the volume be given as

$$U \cdot V = \left(\frac{Flow}{Area}\right)(Area \cdot L) = Flow \cdot L.$$

Dividing both sides by the volume yields

$$\frac{\partial C}{\partial t} = \frac{-Flow \cdot L}{V} \cdot \frac{\partial C}{\partial x} + \frac{(Sources - Sinks + V \cdot Diffusion)}{V}.$$

where L is the length of the capillary (~ 0.1 cm).

The advection of the gradient term is similar to the inflow and outflow terms of a compartmental model.

$$\frac{dC}{dt} = \frac{Flow}{V} \cdot (Cin - Cout) = \frac{-Flow \cdot L}{V} \cdot \frac{(Cout - Cin)}{L} \simeq \frac{-Flow \cdot L}{V} \cdot \frac{(C(L) - C(0))}{L} \simeq \frac{-Flow \cdot L}{V} \cdot \frac{\partial C}{\partial x}$$

Source/Sink Terms

A typical Source/Sink term involves the passive transport of material from one region to another across a membrane. For example, let region *1* and region *2* have volumes *V1* and *V2* and concentrations *C1* and *C2* respectively. Let the exchange rate be given by a permeability-surface area product called *PS*. The transport equations are written as

$$\frac{\partial C1}{\partial t} = \frac{PS \cdot (C2 - C1)}{V1}.$$

$$\frac{\partial C2}{\partial t} = \frac{PS \cdot (C1 - C2)}{V2}.$$

Every barrier or gap will contribute Source/Sink terms such as these to the mass balance equations.

Consumption/Clearance of Metabolite

Other Sink terms are the consumption of a metabolite. The consumption rate is represented by the letter G. The mass balance equation is - $\frac{\partial C}{\partial t} = \frac{-G \cdot C}{V}$.

Axial Diffusion

The diffusion term, *Diffusion* for a region is given by a diffusion coefficient multiplying the second spatial derivative, i.e.,

$$\frac{\partial C_{region}}{\partial t} = D_{region} \cdot \frac{\partial^2 C_{region}}{\partial x^2}$$

Other Source/Sink Terms

Additional source and sink terms are contributed by processes with enzymes, transporters, binding sites, metabolic processes, conversion, sequestration, synthesis, etc.

Putting it all together

The typical regions for these type of transport problems are plasma (*p*), endothelial cells (*ec*), the interstitial fluid region (*isf*), parenchymal cells (*pc*), and mitochondria (*mito*).

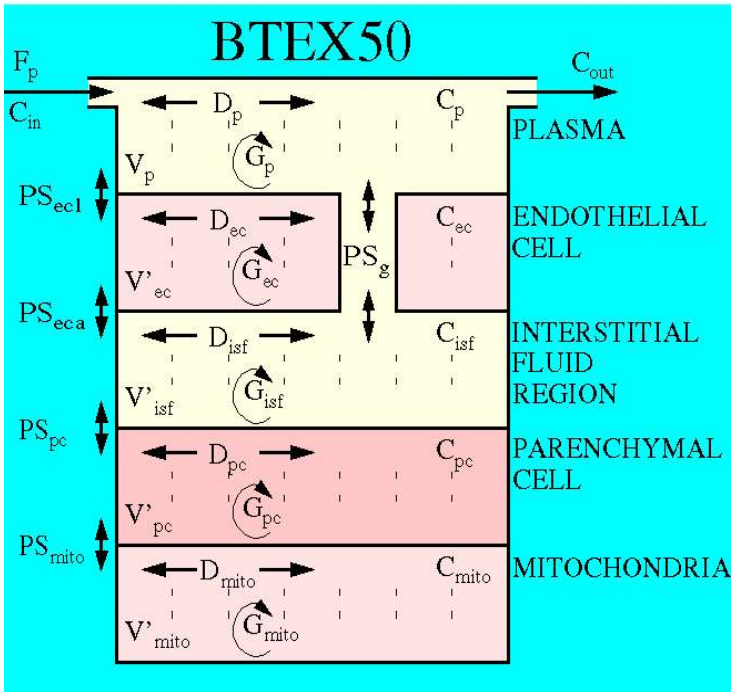
The exchange rates between the regions are given as *PSg* for the gap between the plasma and the interstitial fluid region; *PSecl* for the barrier between the endothelial cell and the plasma on the lumenal side (facing the lumen or capillary) of the endothelial cell; *PSeca* for the barrier between the endothelial cell and the interstitial fluid region on the ablumenal side (facing away from the lumen or capillary) of the endothelial cell; *PSpc* for the barrier between the interstitial fluid region and the parenchymal cell; and *PSmito* for the barrier between the parenchymal cell and the mitochondria.

Consumption rates in these regions are given as *Gp, Gec, Gisf, Gpc,* and *Gmito.*

Diffusion rates are given as *Dp, Dec, Disf, Dpc*, and *Dmito.*

The plasma volume is given as *Vp.* All the other volumes are considered to be volumes of distribution, that is they may be larger than the physical volumes associated with the regions to account for the affinity of a metabolite in a particular region, such as oxygen in the red blood cell. The volumes of distribution are given as *V'isf, V'ec, V'pc,* and *V'mito*, but usually spelled as *Visfp, Vecp, Vpcp,* and *Vmitop,* where the *p* stands for the prime.

BTEX50 Partial Differential Equations in JSim's Mathematical Modeling Language



Cp:t = -Fp*L/Vp*Cp:x -Gp/Vp*Cp+ Dp*Cp:x:x + PSg/Vp*(Cisf-Cp) + PSecl/Vp*(Cec-Cp);

Cisf:t = -Gisf/Visfp*Cisf + Disf*Cisf:x:x + PSg/Visfp*(Cp-Cisf) + PSeca/Visfp*(Cec-Cisf)+ PSpc/Visfp*(Cpc-Cisf);

Cec:t = -Gec/Vecp*Cec +Dec*Cec:x:x +PSecl/Vecp*(Cp-Cec) +PSeca/Vecp*(Cisf-Cec);

Cpc:t = -Gpc/Vpcp*Cpc +Dpc*Cpc:x:x + PSpc/Vpcp*(Cisf-Cpc) + PSmito/Vpcp*(Cmito-Cpc);

Cmito:t = -Gmito/Vmitop*Cmito +Dmito*Cmito:x:x + PSmito/Vmitop*(Cpc-Cmito);

Initial and Boundary Conditions

If the inflow is from the left to the right and the direction is taken as positive, the Left Hand Boundary Condition is given as

when (x=x.min) (-F*L/V)*(Cp-Cin) + Dp*Cp:x=0; for the Flowing region. This is known as the **Total Flux boundary condition**.)

The Right Boundary Condition for the flowing region is given as **when (x=x.max) Dp*Cp:x=0;**

This is known as a **Neumann boundary condition**.

The Initial condition is given as

when(t=t.min) Cp=C0;

It can also be given as **when(t=t.min) Cp=C0(x);** where C0 is a constant, and C0(x) is a function of x.

The other boundary conditions are all Neumann conditions, e.g.

when(x=x.min) {Disf*Cisf:x=0; Dec*Cec:x=0; Dpc*Cpc:x=0; Dmito*Cmito:x=0;}

when(x=x.max) {Disf*Cisf:x=0; Dec*Cec:x=0; Dpc*Cpc:x=0; Dmito*Cmito:x=0;}

and the rest of the initial conditions are given as

when(t=t.min) {Cisf=Cifs0; Cec=Cec0; Cpd=Cpc0; Cmito=Cmito0;}

The other BTEX models use a reduced set of equations by omitting different regions.

BTEX10 is just the plasma region. BTEX20 is plasma and isf regions. BTEX30 is plasma, interstitial fluid, and parenchymal cell regions. BTEX40 is plasma, endothelial cell, interstitial fluid, and parenchymal cell regions.