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STEADY-STATE ANALYSIS OF A TWO-DIMENSIONAL MODEL FOR PERCUTANEOUS DRUG TRANSPORT

1.1 SEPARATION OF VARIABLES IN 2-D CARTESIAN COORDINATES

The Laplace's equation in two-dimensional Cartesian coordinates takes the form

$$\frac{\partial^2 c(x,y)}{\partial x^2} + \frac{\partial^2 c(x,y)}{\partial y^2} = 0 \tag{1.1}$$

which is solved to give

$$c(x,y) = F_1(y - xi) + F_2(y + xi) \tag{1.2}$$

where F_1 and F_2 are arbitrary functions of $y - xi$ and $y + xi$, respectively, and $i^2 = -1$. This solution can be obtained in Maple using the command *pdsolve*. However, Eq. (1.2) is rarely used, in practice. Instead, the method of **separation of variables** is adopted. The goal of this technique is to reduce the original problem into a system of ordinary differential equations in one variable (Rice & Do, 1995).

A solution of Eq. (1.1) is $c(x,y) = f(x) + g(y)$. These two functions satisfy the equations

$$\frac{d^2 f(x)}{dx^2} = -c_1 \tag{1.3}$$

Closed-form Solutions for Drug Transport through Controlled-Release Devices in Two and Three Dimensions, First Edition. Laurent Simon and Juan Ospina.

and

$$\frac{d^2g(y)}{dy^2} = c_1 \tag{1.4}$$

where c_1 represents an arbitrary constant. After solving Eqs. (1.3) and (1.4) for $f(x)$ and $g(y)$, we obtain

$$c(x,y) = -\frac{1}{2}c_1x^2 + C_1x + C_2 + \frac{1}{2}c_1y^2 + C_3y \tag{1.5}$$

The solution (1.5) is expressed as an **additive separation of variables** (Cherniavsky, 2010). Another method for solving Eq. (1.1) is the use of a **multiplicative separation of variables** such that $c(x,y) = f(x)g(y)$. In this case, $f(x)$ and $g(y)$ satisfy the following ordinary differential equations:

$$\frac{d^2f(x)}{dx^2} = c_2f(x) \tag{1.6}$$

and

$$\frac{d^2g(y)}{dy^2} = -c_2g(y) \tag{1.7}$$

After solving Eqs. (1.6) and (1.7), the solution is

$$c(x,y) = (D_1e^{x\sqrt{c_2}} + D_2e^{-x\sqrt{c_2}})(D_3\sin(y\sqrt{c_2}) + D_4\cos(y\sqrt{c_2})) \tag{1.8}$$

Given that c_2 is an arbitrary constant, it is possible to apply the **principle of superposition** (Farlow, 1993) to get

$$c(x,y) = \int [(D_1(\eta)e^{x\sqrt{\eta}} + D_2(\eta)e^{-x\sqrt{\eta}})(D_3(\eta)\sin(y\sqrt{\eta}) + D_4(\eta)\cos(y\sqrt{\eta}))]d\eta \tag{1.9}$$

The discrete form of Eq. (1.9) is

$$c(x,y) = \sum_{\eta}[(D_{1\eta}e^{x\sqrt{\eta}} + D_{2\eta}e^{-x\sqrt{\eta}})(D_{3\eta}\sin(y\sqrt{\eta}) + D_{4\eta}\cos(y\sqrt{\eta}))] \tag{1.10}$$

The types of boundary conditions determine the choice of Eq. (1.9) or (1.10). In cases where Eqs. (1.5) and (1.9) are both solutions, their sum is also a solution:

$$\begin{aligned} c(x,y) = &-\frac{1}{2}c_1x^2 + C_1x + C_2 + \frac{1}{2}c_1y^2 + C_3y \\ &+ \int [(D_1(\eta)e^{x\sqrt{\eta}} + D_2(\eta)e^{-x\sqrt{\eta}})(D_3(\eta)\sin(y\sqrt{\eta}) + D_4(\eta)\cos(y\sqrt{\eta}))]d\eta \end{aligned} \tag{1.11}$$

or

$$\begin{aligned} c(x,y) = &-\frac{1}{2}c_1x^2 + C_1x + C_2 + \frac{1}{2}c_1y^2 + C_3y \\ &+ \sum_{\eta}[(D_{1\eta}e^{x\sqrt{\eta}} + D_{2\eta}e^{-x\sqrt{\eta}})(D_{3\eta}\sin(y\sqrt{\eta}) + D_{4\eta}\cos(y\sqrt{\eta}))] \end{aligned} \tag{1.12}$$

after using the discretized form of Eq. (1.9).

1.2 MODEL FOR DRUG TRANSPORT ACROSS THE SKIN

The steady-state drug transport across the skin is described by Laplace's equation (1.1). The drug is contained in a patch of length h_c (Fig. 1.1). During treatment, the drug concentration in the reservoir remains unchanged (Simon & Ospina, 2013). Two segments perpendicular to the skin surface, h_u and h_d, are chosen in this application. There is no exchange of material with the environment except at the skin/capillary boundary. A first-order elimination kinetics is observed at the interface. After using the dimensionless variables and constants,

$$x = \frac{x_1}{l_s}, y = \frac{x_2}{l_s}, c = \frac{C}{C_b}, w = \frac{l_s K_{cl}}{D}, L_d = \frac{h_d}{l_s}$$
$$L_c = \frac{h_c}{l_s}, L_u = \frac{h_c + h_u}{l_s} \tag{1.13}$$

the boundary conditions are

$$\alpha(y)c(0,y) + \beta(y)\left.\frac{\partial c\,(x,y)}{\partial x}\right|_{x=0} = \delta(y) \tag{1.14}$$

$$\left.\frac{\partial c\,(x,y)}{\partial y}\right|_{y=-L_d} = 0, 0 \le x \le 1 \tag{1.15}$$

$$\left.\frac{\partial c\,(x,y)}{\partial y}\right|_{y=L_u} = 0, 0 \le x \le 1 \tag{1.16}$$

$$\left.\frac{\partial c\,(x,y)}{\partial x}\right|_{x=1} + wc(1,y,\tau) = 0, -L_d \le y \le L_u \tag{1.17}$$

where

$$\alpha(y) = \delta(y) = \text{ Heaviside}(y) - \text{Heaviside}(y - L_c) \tag{1.18}$$

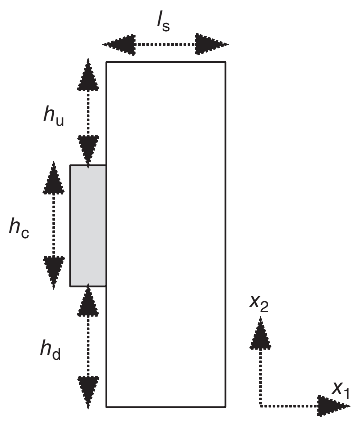

Figure 1.1 Diagram of the drug absorption model.

and "Heaviside$(y-a)$" is the step function defined as

$$\text{Heaviside}(y-a) = \begin{cases} 1 & a \le y \\ 0 & \text{otherwise} \end{cases} \tag{1.19}$$

The coefficients D and K_{cl} are the drug diffusivity and clearance at the skin/capillary boundary; C_b and C are the concentrations in the reservoir and in the skin, respectively. Also,

$$\beta(y) = \alpha(y) - 1 \tag{1.20}$$

Note that Eq. (1.14) is equivalent to the following three conditions:

$$\frac{\partial c(0,y)}{\partial x} = 0, -L_d \le y < 0 \tag{1.21}$$

$$c(0,y) = 1, 0 \le y \le L_c \tag{1.22}$$

and

$$\frac{\partial c(0,y)}{\partial x} = 0, L_c < y \le L_u \tag{1.23}$$

1.3 ANALYTICAL SOLUTION OF THE DIFFUSION MODEL IN 2-D CARTESIAN SYSTEMS

We look for a solution to Eq. (1.1) of the form $c(x,y) = f(x)g(y)$ (i.e., multiplicative separation of variables). Eq (1.8) is used in this case. Condition (1.15) leads to

$$D_4 = -\frac{D_3 \cos(L_d\sqrt{c_2})}{\sin(L_d\sqrt{c_2})} \tag{1.24}$$

Replacing Eq. (1.24) in Eq. (1.8) and applying condition (1.16) yield

$$\sin((L_u + L_d)\sqrt{c_2}) = 0 \tag{1.25}$$

leading to

$$c_2 = \frac{n^2\pi^2}{(L_u + L_d)^2} \tag{1.26}$$

Equation (1.8) becomes

$$c(x,y) = -\frac{\cos\left(\frac{n\pi(y+L_d)}{L_u+L_d}\right)\left(D_1 e^{\frac{n\pi x}{L_u+L_d}} + D_2 e^{-\frac{n\pi x}{L_u+L_d}}\right)}{\sin\left(\frac{n\pi L_d}{L_u+L_d}\right)} \tag{1.27}$$

Given that there is a solution for every value of $n = 0, 1, 2, \cdots$, we write

$$c_n(x,y) = -\frac{\cos\left(\frac{n\pi(y+L_d)}{L_u+L_d}\right)\left(A_n e^{\frac{n\pi x}{L_u+L_d}} + B_n e^{-\frac{n\pi x}{L_u+L_d}}\right)}{\sin\left(\frac{n\pi L_d}{L_u+L_d}\right)} \tag{1.28}$$

Applying the principle of superposition for linear equations, we have

$$c(x,y)=\sum_{n=0}^{\infty}\left[-\frac{\cos\left(\frac{n\pi(y+L_d)}{L_u+L_d}\right)\left(A_n e^{\frac{n\pi x}{L_u+L_d}}+B_n e^{-\frac{n\pi x}{L_u+L_d}}\right)}{\sin\left(\frac{n\pi L_d}{L_u+L_d}\right)}\right] \tag{1.29}$$

The use of condition (1.17) in Eq. (1.29) results in

$$B_n=\frac{A_n e^{\left(\frac{2n\pi}{L_u+L_d}\right)}(n\pi+wL_u+wL_d)}{n\pi-wL_u-wL_d} \tag{1.30}$$

Therefore, the concentration is

$$\begin{aligned} c(x,y)=&-\frac{2A_0(wx-1-w)}{L_d w}\\ &+\sum_{n=1}^{\infty}\left[-\frac{\cos\left(\frac{n\pi(y+L_d)}{L_u+L_d}\right)\left(e^{\frac{n\pi x}{L_u+L_d}}+\frac{e^{\left(\frac{2n\pi}{L_u+L_d}\right)}(n\pi+wL_u+wL_d)}{n\pi-wL_u-wL_d}e^{-\frac{n\pi x}{L_u+L_d}}\right)A_n}{\sin\left(\frac{n\pi L_d}{L_u+L_d}\right)}\right] \end{aligned} \tag{1.31}$$

Finally, after applying Eq. (1.14) to Eq. (1.31), we have

$$\begin{aligned} &\alpha(y)\left[\frac{2A_0\,(1+w)}{L_d w}+\sum_{n=1}^{\infty}\left[-\frac{\cos\left(\frac{n\pi(y+L_d)}{L_u+L_d}\right)\left(1+\frac{e^{\left(\frac{2n\pi}{L_u+L_d}\right)}(n\pi+wL_u+wL_d)}{n\pi-wL_u-wL_d}\right)A_n}{\sin\left(\frac{n\pi L_d}{L_u+L_d}\right)}\right]\right]\\ &-\beta(y)\left[\frac{2A_0}{L_d}+\sum_{n=1}^{\infty}\left[\frac{n\pi}{L_u+L_d}\frac{\cos\left(\frac{n\pi(y+L_d)}{L_u+L_d}\right)}{\sin\left(\frac{n\pi L_d}{L_u+L_d}\right)}\times\left(e^{\frac{n\pi x}{L_u+L_d}}-\frac{e^{\left(\frac{2n\pi}{L_u+L_d}\right)}(n\pi+wL_u+wL_d)}{n\pi-wL_u-wL_d}e^{-\frac{n\pi x}{L_u+L_d}}\right)A_n\right]\right]=\delta(y) \end{aligned} \tag{1.32}$$

The solution to the problem, defined by Eqs. (1.1), (1.14)–(1.17), is given by Eqs. (1.31) and (1.32). Using Eq. (1.32), it is possible to develop successive approximations. For example, a zero-order solution can be obtained by setting $A_n = 0$ with $n = 1, 2, \ldots, \infty$. In this case, Eq. (1.31) reduces to

$$c(x,y)=-\frac{2A_0(wx-1-w)}{L_d w} \tag{1.33}$$

The coefficient A_0 is calculated from Eq. (1.32) resulting in the following “zero-order” approximation of the concentration (Fig. 1.2):

$$c(x,y)=-\frac{L_c(wx-1-w)}{L_c+wL_u+wL_d} \tag{1.34}$$

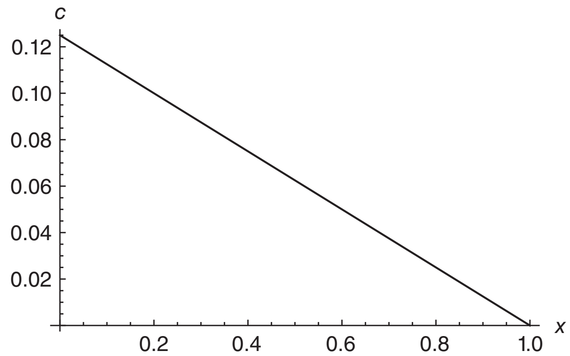

Figure 1.2 Normalized drug concentration in the skin: $L_c = 0.5$, $L_d = 2.5$, $L_u = 3.0$, and $w = 54825$.

1.4 SUMMARY

The method of separation of variables was applied to solve Laplace's equation in two dimensions. In this technique, the partial differential equation is reduced to ordinary differential equations in one variable. The principle of linear superposition was implemented to add the solutions of the subproblems and generate the solution of the initial PDE model. This procedure helps derive the spatial distribution of drug across the skin.

1.5 APPENDIX: MAPLE, MATHEMATICA, AND MAXIMA CODE LISTINGS

1.5.1 Maple Code: steadytwo.mws

```
> restart:with(VectorCalculus):with(PDETools);
[CanonicalCoordinates, ChangeSymmetry, CharacteristicQ,
   CharacteristicQInvariants, ConservedCurrentTest, ConservedCurrents,
   ConsistencyTest, D_Dx, DeterminingPDE, Eta_k, Euler, FromJet,
   FunctionFieldSolutions, InfinitesimalGenerator, Infinitesimals,
   IntegratingFactorTest, IntegratingFactors, InvariantEquation,
   InvariantSolutions, InvariantTransformation, Invariants, Laplace,
   Library, PDEplot, PolynomialSolutions, ReducedForm,
   SimilaritySolutions, SimilarityTransformation, Solve,
   SymmetryCommutator, SymmetryGauge, SymmetrySolutions, SymmetryTest,
   SymmetryTransformation, TWSolutions, ToJet, build, casesplit,
   charstrip, dchange, dcoeffs, declare, diff_table, difforder,
   dplolyform, dsubs,mapde, separability, splitstrip, splitsys,
   undeclare]

> eq:=Laplacian(c(x,y),cartesian[x,y])=0;
```

$$eq := \frac{\partial^2}{\partial x^2}\, c(x,\ y) + \frac{\partial^2}{\partial y^2}\, c(x,\ y) = 0$$

```
> eq1:=alpha(y)*c(0,y)+beta(y)*Eval(diff(c(x,y),x),x=0)=delta(y):
> eq2:=Eval(diff(c(x,y),y),y=-L[d])=0:
```

```
> eq3:=Eval(diff(c(x,y),y),y=L[u])=0:
> eq4:=Eval(diff(c(x,y),x),x=1)+w*c(1,y)=0:
> eq5:=pdsolve(eq,HINT=f(x)*g(y)):
> eq6:=factor(build(eq5)):
> eq7:=eval(diff(rhs(eq6),y),y=-L[d])=0:
>
> eq8:=isolate(eq7,_C4):
> eq9:=factor(subs(eq8,eq6)):
> eq10:=subs(_C3=1,eq9):
> eq11:=factor(combine((eq10),sin)):
> eq12:=eval(diff(rhs(eq11),y),y=L[u])=0:
> eq13:=sin(_c[1]^(1/2)*(L[u]+L[d]))=0:
>
> eq14:=_c[1]^(1/2)*(L[u]+L[d])=n*Pi:
> eq15:=isolate(eq14,_c[1]):
> eq16:=simplify(subs(eq15,eq11),power,symbolic):
> eq17:=subs(_C1=A[n],_C2=B[n],c=c[n],eq16):
> eq18:=c(x,y)=Sum(rhs(eq17),n=0..infinity);
```

$$\mathrm{eq18} := c(x,y) = \sum_{n=0}^{\infty}\left[-\frac{\cos\left(\frac{n\pi\,(y+L_d)}{L_u+L_d}\right)\left(A_n e^{\frac{n\pi x}{L_u+L_d}} + B_n e^{-\frac{n\pi x}{L_u+L_d}}\right)}{\sin\left(\frac{\pi n L_d}{L_u+L_d}\right)}\right]$$

```
>
> eq22:=subs(c=c[n],eq4):
>
> eq23:=subs(x=1,eq17):
> eq24:=factor(eval(subs(Eval=eval,subs(eq23,subs(eq17,eq22))))):
> eq25:=simplify(simplify(factor(isolate(eq24,B[n])),power,symbolic),
exp):
> eq26:=collect(subs(eq25,eq17),A[n]):
> eq26A:=subs(n=0,simplify(series(rhs(eq26),n=0,4))):
> eq27:=c(x,y)=eq26A+Sum(rhs(eq26),n=1..infinity):
>
> eq19:=eq1:
>
> eq19A:=eval(subs(x=0,eq27)):
> eq20:=factor(eval(subs(Eval=eval,subs(eq19A,subs(eq27,eq19))))):
>
============= Zero-order approximation======================
> eq28:=factor(eval(subs(Sum=sum,subs(A[n]=0,eq20)))):
> eq29:=simplify(subs(y=z,Int(lhs(eq28),y=-L[d]..L[u])=Int(rhs(eq28),
y=-L[d]..L[u]))):
> eq30:=isolate(eq29,A[0]):
> eq31:=eval(subs(Sum=sum,subs(A[n]=0,eq27))):
> eq32:=subs(eq30,eq31):
> ñas:=alpha(y)=Heaviside(y)-Heaviside(y-L[c]):
```

```
> ñasA:=beta(y)=alpha(y)-1:
> ñasB:=delta(y)=alpha(y):
> eq32A:=subs(y=z,ñas):
> eq32B:=subs(y=z,ñasA):
> eq32C:=subs(y=z,ñasB):
> eq32D:=eval(subs(Int=int,subs(eq32A,subs(eq32C,eq32B,eq32))))
assuming L[c]>0 and L[d]>0 and L[u]>0 and L[u]>L[c];
```

$$eq32D := c(x, y) = -\frac{L_c(wx-w-1)}{wL_d+wL_u+L_c}$$

```
>
```

1.5.2 wxMaxima Code: steadytwo.wxm

```
(%i1) eq: diff(C(x,y),x,2)+diff(C(x,y),y,2)=0;
```

$$(\%o1)\ \frac{d^2}{d\ y^2}C(x,\ y)+\frac{d^2}{d\ x^2}C(x,\ y)=0$$

```
(%i2) eq1: C(x,y)=f(x)*g(y)$
(%i3) eq2: (subst(eq1,eq))$
(%i4) eq3: eq2,simp, diff$
(%i5) eq4: eq3/rhs(eq1)$
(%i6) eq5: eq4, expand$
(%i7) eq6: f(x)=f$
(%i8) eq7: subst(eq6,lhs(eq5))= -alpha $
(%i9) eq8: eq7, simp, diff $
(%i10) eq9: g(y) =g $
(%i11) eq10: subst(eq9,lhs(eq5))=alpha $
(%i12) eq11: eq10, simp, diff $
(%i13) eq12: desolve(diff(g(y),y,2)=-alpha*g(y),g(y)) $
Is α positive, negative or zero? positive;
(%i14) eq13: desolve(diff(f(x),x,2)=alpha*f(x),f(x))$
Is α positive, negative or zero? positive;
(%i15) eq14: subst([g(0)=A,(at('diff(g(y),y,1),y=0))=B*sqrt(alpha)],
eq12)$
(%i16) eq14A: subst([f(0)=C,(at('diff(f(x),x,1),x=0))=D*sqrt(alpha)],
eq13)$
(%i17) eq15: C(x,y)=rhs(eq14A)*rhs(eq14)$
(%i18) eq16: subst(y=-L[d],diff(rhs(eq15),y))=0 $
(%i19) eq17: solve(eq16, A) $
(%i20) eq18: subst(eq17,eq15) $
(%i21) eq19: eq18, factor $
(%i22) eq20: subst(B=sin(sqrt(alpha)*L[d]),eq19)$
(%i23) eq21: sin(sqrt(alpha)*L[d])*sin(sqrt(alpha)*y)-cos(sqrt(alpha)*
L[d])*cos(sqrt(alpha)*y)=-cos(sqrt(alpha)*(y+L[d]))$
(%i24) eq22: subst(eq21,eq20)$
(%i25) eq23: subst(y=L[u],diff(rhs(eq22),y))=0$
(%i26) eq24: sin(sqrt(alpha)*(L[u]+L[d]))=0 $
(%i27) eq25: sqrt(alpha)*(L[u]+L[d])= n*%pi $
(%i28) eq26: solve(eq25,alpha) $
Is n(LuLd)  positive, negative or zero? positive;
```

```
(%i29) eq26A: factor(eq26) $
(%i30) eq27: subst(eq26A,eq22) $
(%i31) assume_pos: n $
(%i32) eq28: eq27, simp $
(%i33) eq29: C = A[n] $
(%i34) eq30: D = B[n] $
(%i35) eq31: C[n](x,y)=subst(eq30,subst(eq29,rhs(eq28))) $
(%i36) eq32: C(x,y)=sum (rhs(eq31), n, 0, inf);
```

(%o36) $C(x,\ y) = -\sum_{n=0}^{\infty}\left(B_n \sinh\left(\frac{\pi\ n\ x}{L_u+L_d}\right)+A_n\ \cosh\left(\frac{\pi\ n\ x}{L_u+L_d}\right)\right)\ \cos\left(\frac{\pi\ n\ \left(y+L_d\right)}{L_u+L_d}\right)$

```
(%i37) eq33: subst(x=1,diff(rhs(eq31),x))+w*subst(x=1,rhs(eq31))=0 $
(%i38) eq34: factor(solve(eq33,B[n])) $
(%i39) eq35: factor(subst(eq34,eq31)) $
(%i40) eq36: taylor(rhs(eq35),n,0,1), factor $
(%i41) eq37: C(x,y)=sum(rhs(eq35),n,1,inf)+eq36 $
(%i42) eq38: alpha(y)*subst(x=0,rhs(eq37))+b(y)*subst(x=0,diff(rhs
(eq37),x))=delta(y) $
Zero order approximation:
(%i43) eq39: subst(A[n]=0,eq38) $
(%i44) eq40: subst(y=z,eq39) $
(%i45) eq41: factor(integrate(lhs(eq40),z,-L[d],L[u]))=integrate(rhs
(eq40),z,-L[d],L[u]) $
(%i46) eq42: solve(eq41,A[0]) $
(%i47) eq43: subst(A[n]=0,eq37) $
(%i48) eq44: subst(eq42,eq43);
```

(%o48) $C(x,\ y) = \frac{(wx-w-1)\int_{-L_d}^{L_u}\delta(z)dz}{\int_{-L_d}^{L_u} w\ b(z)-w\ \alpha(z)-\alpha(z)dz}$

1.5.3 Mathematica Code: steadytwo.nb

```
eq = ∂x,x C[x, y] + ∂y,y C[x, y]
C^(0,2)[x, y] + C^(2,0)[x, y]
eq2 = eq/.C → Function[{x, y}, X[x]Y[y]];
eq3 = Expand[eq2/(X[x] ∗ Y[y])] == 0;
eq4 = X''[x]/X[x] == α;
eq4A = Y''[y]/Y[y] == −α;
eq5 = DSolve[eq4, X, x];
eq5A = (DSolve[eq4A, Y, y]/.C[1] − > A[1])/.C[2] → B[1];
eq6 = (e^(x√α) C[1] + e^(−x√α) C[2]) ∗ (A[1]Cos[y√α] + B[1]Sin[y√α]);
eq7 = ((∂y eq6)/.y → -Ld) == 0;
eq8 = Solve [eq7, A[1]];
eq9 = eq6/.A[1] → -B[1]Cot[√α Ld];
eq10 = eq9/.B[1] → 1;
eq11 = Simplify[eq10];
eq12 = ((∂y eq11)/.y → Lu) == 0;
```

$$\begin{aligned}
&\texttt{eq13} = \texttt{Sin}[\sqrt{\alpha}(L_d + L_u)] == 0;\\
&\texttt{eq14} = \sqrt{\alpha}(L_d + L_u) == n\pi;\\
&\texttt{eq15} = \texttt{Solve}[\texttt{eq14}, \alpha];\\
&\texttt{eq16} = \texttt{eq11}/.\alpha \to \frac{n^2\pi^2}{(L_d+L_u)^2};\\
&\texttt{eq17} = \texttt{Simplify}[\texttt{Simplify}[\texttt{eq16}, n > 0], L_d + L_u > 0];\\
&\texttt{eq18} = (\texttt{eq17}/.C[1] \to A_n)/.C[2] \to B_n;\\
&\texttt{eq19} = C[x,y] == \texttt{Sum}\left[-e^{-\frac{n\pi x}{L_d+L_u}}\texttt{Cos}\left[\frac{n\pi(y+L_d)}{L_d+L_u}\right]\texttt{Csc}\left[\frac{n\pi L_d}{L_d+L_u}\right]\left(e^{\frac{2n\pi x}{L_d+L_u}}A_n + B_n\right), \{n, 0, \texttt{inf}\}\right];\\
&\texttt{eq20} = ((\partial_x \texttt{eq18})/.x \to 1) + (w(\texttt{eq18}/.x \to 1)) == 0;\\
&\texttt{eq21} = \texttt{Solve}[\texttt{eq20}, B_n];\\
&\texttt{eq22} = \texttt{eq19}/.B_n \to \frac{e^{\frac{2n\pi}{L_d+L_u}}A_n(n\pi + wL_d + wL_u)}{n\pi - wL_d - wL_u};\\
&\texttt{eq23} = \texttt{eq18}/.B_n \to \frac{e^{\frac{2n\pi}{L_d+L_u}}A_n(n\pi + wL_d + wL_u)}{n\pi - wL_d - wL_u};\\
&\texttt{eq24} = \texttt{Simplify}[\texttt{Series}[\texttt{Expand}[\texttt{eq23}A_n], \{n, 0, 0\}]];
\end{aligned}$$

$$\texttt{eq25} = C[x,y] == A_0\texttt{Factor}\left[\frac{2+2w-2wx}{wL_d}\right] + \texttt{Sum}\left[-e^{-\frac{n\pi x}{L_d+L_u}}\texttt{Cos}\left[\frac{n\pi(y+L_d)}{L_d+L_u}\right]\texttt{Csc}\left[\frac{n\pi L_d}{L_d+L_u}\right]\left(e^{\frac{2n\pi x}{L_d+L_u}}A_n + \frac{e^{\frac{2n\pi}{L_d+L_u}}A_n(n\pi+wL_d+wL_u)}{n\pi - wL_d - wL_u}\right), \{n, 0, \texttt{inf}\}\right];$$

$$\texttt{eq26} = A_0\texttt{Factor}\left[\frac{2+2w-2wx}{wL_d}\right] + \texttt{Sum}\left[-e^{-\frac{n\pi x}{L_d+L_u}}\texttt{Cos}\left[\frac{n\pi(y+L_d)}{L_d+L_u}\right]\texttt{Csc}\left[\frac{n\pi L_d}{L_d+L_u}\right]\left(e^{\frac{2n\pi x}{L_d+L_u}}A_n + \frac{e^{\frac{2n\pi}{L_d+L_u}}A_n(n\pi+wL_d+wL_u)}{n\pi - wL_d - wL_u}\right), \{n, 0, \texttt{inf}\}\right];$$

$$\texttt{eq27} = \alpha[y](\texttt{eq26}/.x \to 0) + b[y]((\partial_x \texttt{eq26})/.x \to 0) == d[y];$$

(* Approximation of zero order *)

$$\begin{aligned}
&\texttt{eq28} = \alpha[y]\left(\left(-\frac{2(-1-w+wx)A_0}{wL_d}\right)/.x \to 0\right) + b[y]\left(\left(\partial_x\left(-\frac{2(-1-w+wx)A_0}{wL_d}\right)\right)/.x \to 0\right) == d[y];\\
&\texttt{eq29} = \texttt{eq28}/.y \to z;\\
&\texttt{eq30} = A_0\left(\texttt{Integrate}\left[-\frac{2b[z]}{L_d} - \frac{2(-1-w)\alpha[z]}{wL_d}, \{z, -L_d, L_u\}\right]\right) == \texttt{Integrate}[d[z], \{z, -L_d, L_u\}];\\
&\texttt{eq31} = \texttt{Simplify}[\texttt{Solve}[\texttt{eq30}, A_0]];\\
&\texttt{eq32} = C[x,y] == \left(A_0\texttt{Factor}\left[\frac{2+2w-2wx}{wL_d}\right]\right)/.A_0 \to \frac{\int_{-L_d}^{L_u} d[z]\,dz}{\int_{-L_d}^{L_u}\frac{2(-wb[z]+(1+w)\alpha[z])}{wL_d}\,dz};\\
&\texttt{eq33} = \texttt{Apart}[\texttt{eq32}]\\
&C[x,y] == -\frac{2(-1-w+wx)\int_{-L_d}^{L_u} d[z]\,dz}{w\left(\int_{-L_d}^{L_u}\frac{2(-wb[z]+(1+w)\alpha[z])}{wL_d}\,dz\right)L_d}
\end{aligned}$$

PROBLEMS

1.1. Show that for a zero-order approximation, the concentration is

$$c(x,y) = \frac{(wx - 1 - w)\int_{-L_d}^{L_u}\delta(z)dz}{\int_{-L_d}^{L_u}(-\alpha(z) - w\alpha(z) + w\beta(z))dz} \tag{1.1}$$

1.2. Consider the case when

$$\begin{aligned}\alpha(y) = \delta(y) &= \text{Heaviside}(y) - \text{Heaviside}(y - L_c)\\ \beta(y) &= \alpha(y) - 1\end{aligned} \tag{1.1}$$

Show that the zero-order approximation of the concentration is

$$c(x, y) = -\frac{L_c(wx - 1 - w)}{L_c + wL_u + wL_d} \tag{1.2}$$

1.3. For

$$\begin{aligned}\alpha(y) = \delta(y) &= \text{Heaviside}(y) - \text{Heaviside}(y - L_c)\\ \beta(y) &= \alpha(y) - 1\end{aligned} \tag{1.1}$$

with $L_c = 1$, $L_d = 2$, and $L_u = 2$, show that the first-order approximation of the concentration is

$$c(x, y) = -\frac{2A_0(wx - 1 - w)}{L_d w} - \frac{\cos\left(\frac{\pi(y+L_d)}{L_u+L_d}\right)\left(e^{\frac{\pi x}{L_u+L_d}} + \frac{e^{\left(\frac{2\pi}{L_u+L_d}\right)}(\pi + wL_u + wL_d)}{\pi - wL_u - wL_d}e^{-\frac{\pi x}{L_u+L_d}}\right)A_1}{\sin\left(\frac{\pi L_d}{L_u+L_d}\right)} \tag{1.2}$$

where

$$\begin{aligned}A_0 &= \frac{w(2872.4w + 1514.5)}{11357.5w^2 + 9319.2w + 1514.5}\\ A_1 &= -\frac{6.3w(75.0w - 58.9)}{11357.5w^2 + 9319.2w + 1514.5}\end{aligned} \tag{1.3}$$

1.4. For

$$\begin{aligned}\alpha(y) = \delta(y) &= \text{Heaviside}(y) - \text{Heaviside}(y - L_c)\\ \beta(y) &= \alpha(y) - 1\end{aligned} \tag{1.1}$$

with $L_c = 2$, $L_d = 3$, and $L_u = 4$, show that the second-order approximation of the concentration is

$$\begin{aligned}c(x, y) = &-\frac{2}{3}\frac{A_0(wx - 1 - w)}{w} - \frac{\cos\left(\frac{\pi(y+3)}{7}\right)\left(e^{\frac{\pi x}{7}} + \frac{e^{\frac{2\pi}{7}}(\pi + 7w)e^{-\frac{\pi x}{7}}}{\pi - 7w}\right)A_1}{\sin\left(\frac{3\pi}{7}\right)}\\ &- \frac{\cos\left(\frac{2\pi(y+3)}{7}\right)\left(e^{\frac{2\pi x}{7}} + \frac{e^{\frac{4\pi}{7}}(2\pi + 7w)e^{-\frac{2\pi x}{7}}}{2\pi - 7w}\right)A_2}{\sin\left(\frac{\pi}{7}\right)}\end{aligned} \tag{1.2}$$

with

$$A_0 = \frac{0.46w(w+0.66)(w+0.22)}{(w+0.94)(w+0.29)(w+0.16)}$$
$$A_1 = -\frac{0.08w(w+0.71)(w-0.45)}{(w+0.94)(w+0.29)(w+0.16)}$$
$$A_2 = -\frac{0.03w(w+0.22)(w-0.90)}{(w+0.94)(w+0.29)(w+0.16)} \tag{1.3}$$

1.5. Consider the case when

$$\alpha(y) = \delta(y) = \text{ Heaviside}(y) - \text{Heaviside}(y - L_c)$$
$$\beta(y) = \alpha(y) - 1 \tag{1.1}$$

Derive an expression for the zero-order approximation of the flux defined by

$$J = -\int_{-L_d}^{L_u} \frac{\partial}{\partial x} c\,(x, y)\bigg|_{x=1} dy \tag{1.2}$$

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