I. WORKFLOW

The goal of these exercises is to gain a better understanding about the use and applicability of boundary integral equations (BIEs) to solve partial differential equations (PDEs) and how to deploy them in our diffusive oxygen transport model that features intricate branching geometries. Here we aim to solve problems of increasing complexity to investigate the effect of changing the parameter, geometry, and solution Ansätze in detail and build a fundamental understanding.

The system: A two-dimensional diffusion-reaction problem where oxygen diffuses through a hollow, permeable one-dimensional channel and into the two-dimensional surrounding tissue domain following its chemical gradient. The channel can be thought of as oxygen source and the tissue as oxygen sink with a concentration-dependent oxygen uptake rate. We want to solve for the oxygen concentration field 1) inside the branching network of permeable channels and 2) across the surrounding tissue plane. The channel has radius $R(s)$ and length L. The coordinate along the channel is described by s and the radial coordinate in the direction perpendicular to the channel by r. In the channel, oxygen diffuses with diffusivity D_1 and is additionally free to diffuse across the channel boundary with permeability κ into the tissue. In the tissue, oxygen diffuses with diffusivity D_2 and is consumed by the tissue at a rate ν proportional to the amount of oxygen present. Governing equations:

$$(\nabla^2 - \phi^2)u = 0 \qquad \text{in } \Omega \tag{1}$$

$$\begin{aligned} u^+(s) &= U(s) + l u_n^+(s) \qquad \text{on } \Gamma \\ u^-(s) &= U(s) - l u_n^-(s) \qquad \text{on } \Gamma \end{aligned} \tag{2}$$

with $\phi^2 = \frac{\nu}{D_2}$ and $l = \frac{D_2}{\kappa}$.

The oxygen flux through the channel is defined by $j_s = U'(s)$ and the flux in the direction of the outside pointing normal from the channel by $j_n = u_n^+ - u_n^-$. The flux conservation law lets us derive a third relationship between these terms considering further the gradient-building source function $S(s)$ (of units $\frac{conc.}{length*time}$) that allows for the conservation of fluxes in the "pseudo steady-state" we aim to describe:

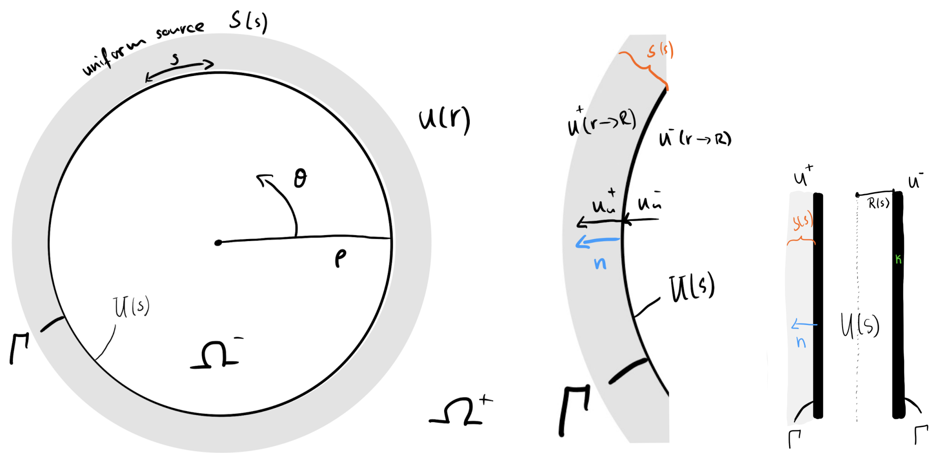
$$\begin{aligned} -D_1 R(s)(j_s' + S(s)) &= -D_2 j_n \\ U''(s) + S(s) &= \frac{\alpha}{R(s)}(u_n^+(s) - u_n^-(s)) \end{aligned} \tag{3}$$

where $\alpha = D_2/D_1$.

CONTENTS

II. LAPLACE PROBLEM

A. Analytical solution to circle with uniform source



Consider a one-dimensional circular perfusing channel with arc length s embedded in a two-dimensional tissue domain Ω. The channel forms the interface boundary Γ which splits the domain into Ω^+ and Ω^+. In the following problem, the channel has a constant oxygen concentration $U(s)$ which is supplied by a constant and uniform source of oxygen $S(s)$ (over time) on Γ. Oxygen can diffuse into the tissue domain Ω. To start with the simplest problem possible, the tissue domain is considered passive, meaning it does not take up oxygen, so $\phi^2 = 0$ and thus reduces our problem to the interior Laplace problem:

$$\nabla^2 u(r,\theta) = 0 \qquad \text{in } \Omega \tag{4}$$

$$S(s) = const. = 1 \qquad \text{on } \Gamma \tag{5}$$

$$U(s) = const. = U \qquad \text{inside the 1D channel} \tag{6}$$

In a two-dimensional tissue space ($n = 2$) the following radial solution (for $r = |x|$) for the Laplacian leverages it's symmetric nature and reduces our PDE problem giving us two regimes for $r > \rho$ and $r < \rho$ in which we can find a solution:

$$u(r) = \begin{cases} u^+ : c\ln(\frac{1}{r}) + c_1 & \text{for } r > \rho \\ u^- : d & \text{for } r < \rho \end{cases} \tag{7}$$

where for $x \in \mathbb{R}^n, |x| \neq 0$ is a solution of Laplace's equation in $\mathbb{R}^n - \{0\}$. We can compute the derivatives $u'(r)$ and $u''(r)$ for both regimes:

$$u'(r) = \begin{cases} u_n^+ : -c/r & \text{for } r > \rho \\ u_n^- : 0 & \text{for } r < \rho \end{cases} \tag{8}$$

We can solve for c, c_1, d, and U by computing the sum and difference of boundary condition 2 on Γ and the flux conservation boundary condition 3:

$$\begin{aligned} 2U(\theta) &= u^+ + u^- - l(u_n^+ - u_n^-) && \text{for } BC^+ + BC^- \\ 0 &= u^+ - u^- - l(u_n^+ + u_n^-) && \text{for } BC^+ - BC^- \\ -D_1 RU'' + 1 &= -D_2(u_n^+ - u_n^-) && \text{for } BC\ 2 \end{aligned} \tag{9}$$

Substituting these formulae into our equations we can derive:

$$
\begin{aligned}
2U &= c\ln(\frac{1}{r}) + c_1 + d + lc/r && \text{for } BC^+ + BC^- \\
0 &= c\ln(\frac{1}{r}) + c_1 - d + lc/r && \text{for } BC^+ - BC^- \\
1 &= D_2 c/r && \text{for } BC\ 2
\end{aligned}
\tag{10}
$$

Considering $r = \rho = 1$ and choosing an arbitrary constant for $c_1 = 0$ we have:

$$u^+(1) = 0 \qquad u^-(1) = d \qquad u_n^+(1) = -c \qquad u_n^-(1) = 0 \tag{11}$$

which gives us:

$$
\begin{aligned}
2U &= d + lc && \text{for } BC^+ + BC^- \\
0 &= lc - d && \text{for } BC^+ - BC^- \\
1 &= D_2 c && \text{for } BC\ 3
\end{aligned}
\tag{12}
$$

For $l = \frac{D_2}{\kappa}$ we get the solution:

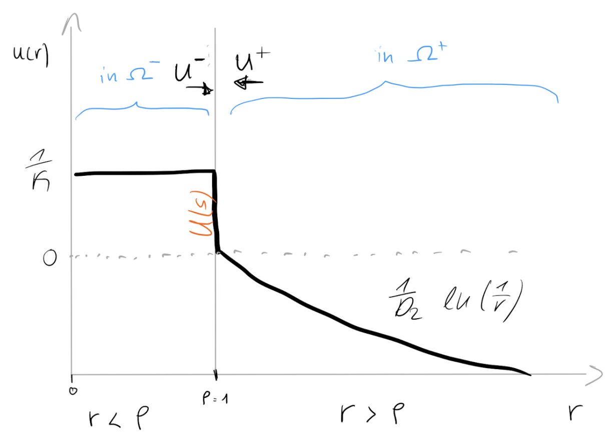
$$c = \frac{1}{D_2} \qquad d = \frac{1}{\kappa} \qquad U = \frac{1}{\kappa} \tag{13}$$

After substituting the solutions of our constants into the initial equations we yield the following expressions

$$u(r) = \begin{cases} u^+ : \frac{1}{D_2}\ln(\frac{1}{r}) + c_1 & \text{for } r > \rho \\ u^- : \frac{1}{\kappa} & \text{for } r < \rho \end{cases} \tag{14}$$

$$U(s) = \frac{1}{\kappa} \tag{15}$$

that describe the behavior of our system as illustrated in the figure below. We see that $u^-(r) = U(s)$ which satisfies our Laplace problem. The jump on the boundary Γ from $U(s)$ to $u^+(r)$ at $r = \rho = 1$ is $\frac{1}{\kappa}$ and decreases logarithmically from $u^+(r)$ into the tissue domain Ω^+.



III. MODIFIED BESSEL PROBLEM

Guiding equations:

$$(\nabla^2 - \phi^2)u(\theta, r) = 0 \qquad \text{in } \Omega \tag{16}$$

$$S(s) = S(\theta) \qquad \text{on } \Gamma \tag{17}$$

For problem stated above, we can consider additional different states:

- 1. $\phi > 0$, $S(s) = const.$,
  implying that the tissue uptake rate is now positive creating a concentration gradient in both regimes of Ω,
- 2. $\phi = 0$, $S(s) = S(\theta)$,
  implying that the oxygen source is non-uniform inside the channel creating non-uniform fluxes along Γ into the tissue,
- 3. $\phi > 0$, $S(s) = S(\theta)$,
  implying that the oxygen source is non uniform on Γ and the tissue uptake rate is positive in Ω.

For (1.) and (3.) in which the tissue is regarded as an active domain with a (linear) oxygen uptake rate ν, so $\phi^2 \neq 0$, the problem is no longer satisfying Laplace equation. Through separation of variables we can decompose the PDE into two ODEs that we solve separately for to yield the modified Bessel equation, for which known solutions exists, called the modified Bessel functions of the first I_z and second K_z kind.

$$u(r, \theta) = P(r)\Theta(\theta) \tag{18}$$

$$\begin{aligned} \nabla^2(P(r)\Theta(\theta)) &= \phi^2 P(r)\Theta(\theta) \\ \frac{r^2}{P(r)}\frac{d}{dr}\left(r\frac{dP(r)}{dr}\right) - \phi^2 r^2 &= -\frac{1}{\Theta(\theta)}\frac{d^2\Theta(\theta)}{d\theta^2} = m^2 \end{aligned} \tag{19}$$

For $\Theta(\theta)$ we derive the equation

$$\frac{d^2\Theta(\theta)}{d\theta^2} = -m^2\Theta(\theta) \tag{20}$$

that has the simple solution:

$$\Theta(\theta) = Ae^{im\theta}. \tag{21}$$

For $P(r)$ we derive the equation:

$$\frac{\tilde{r}^2}{\tilde{P}(\tilde{r})}\frac{d}{d\tilde{r}}\left(\tilde{r}\frac{d\tilde{P}(\tilde{r})}{d\tilde{r}}\right) - (\tilde{r}^2 + m^2) = 0 \tag{22}$$

where $\tilde{r} = \phi r$ and $P(r) = P(\phi/\tilde{r}) =: \tilde{P}(\tilde{r})$ which is known as the modified Bessel equation. The solution to this equation is a linear combination of the modified Bessel functions I_m and K_m

$$\begin{aligned} \tilde{P}(\tilde{r}) &= d_0 I_m(\tilde{r}) + c_0 K_m(\tilde{r}) \\ P(\phi r) &= d_0 I_m(\phi r) + c_0 K_m(\phi r) \end{aligned} \tag{23}$$

Substituting these solution back into $u(r, \theta)$ we yield

$$u(r, \theta) = e^{im\theta}(d_0 I_m(\phi r) + c_0 K_m(\phi r)) \tag{24}$$

with the three unknown constants m, c_0, and d_0.
For intuition:

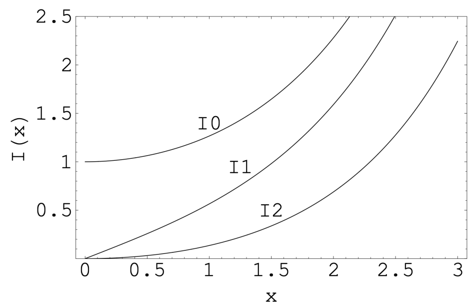


Figure 4.3: Plot of the Modified Bessel Functions of the First Kind, Integer Order

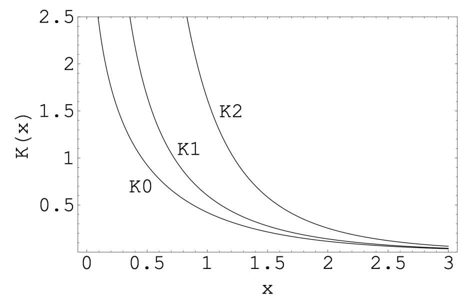


Figure 4.4: Plot of the Modified Bessel Functions of the Second Kind, Integer Order

A. Circle with uniform source, and oxygen consumption

$$(\nabla^2 - \phi^2)u(\theta, r) = 0 \qquad \text{in } \Omega \tag{25}$$

$$S(s) = const. = 1 \qquad \text{on } \Gamma \tag{26}$$

$$U(s) = const. = U \qquad \text{inside the 1D channel} \tag{27}$$

$$\begin{aligned} u^+ &= U + lu_n^+ \qquad \text{on } \Gamma \\ u^- &= U - lu_n^- \qquad \text{on } \Gamma \end{aligned} \tag{28}$$

For a uniform O_2 source $S(\theta) = 1$ and a uniform O_2 take up rate ν in a circular geometry we loose the angular dependence in our problem, which reduces the dependence of $u(r, \theta)$ to $u(r)$ and reduces the order of the modified Bessel function to $m = 0$:

$$u(r) = d_0 I_0(\phi r) + d_0 K_0(\phi r) \tag{29}$$

The modified Bessel function of the second kind K_m diverges at $r = 0$ with the singularity being of logarithmic type, which is why we the solution to $u(r)$ is defined for K_m in the regime $r > \rho$ and I_m in the regime $r < \rho$:

$$u(r) = \begin{cases} u^+ : c_0 K_0(\phi r) & \text{for } r > \rho \\ u^- : d_0 I_0(\phi r) & \text{for } r < \rho \end{cases} \tag{30}$$

We can compute the derivative $u'(r)$ for both regimes:

$$u'(r) = \begin{cases} u_n^+ : -c_0 K_0'(\phi r) = -c_0 \phi K_1(\phi r)) & \text{for } r > \rho \\ u_n^- : d_0 I_0'(\phi r) = d_0 \phi I_1(\phi r)) & \text{for } r < \rho \end{cases} \tag{31}$$

To determine our unknown coefficients c_0, d_0, and U we apply our boundary conditions, computing the sum and difference of equations 28 on Γ and the flux conservation boundary condition 3 as given in 9 for $r = \rho = 1$:

$$\begin{aligned} 2U &= c_0 K_0(\phi) + d_0 I_0(\phi) - l(-c_0 \phi K_1(\phi)) - d_0 \phi I_1(\phi))) \qquad \text{for } BC^+ + BC^- \\ 0 &= c_0 K_0(\phi) - d_0 I_0(\phi) - l(-c_0 \phi K_1(\phi)) + d_0 \phi I_1(\phi))) \qquad \text{for } BC^+ - BC^- \\ -D_1 R U'' + 1 &= -D_2(-c_0 \phi K_1(\phi)) - d_0 \phi I_1(\phi))) \qquad \text{for } BC\ 3 \end{aligned} \tag{32}$$

For our unknown coefficients c_0, d_0, and U we can derive the following expressions

$$c_0 = \frac{1}{D_2\phi}\frac{I_0(\phi)+l\phi I_1(\phi)}{I_0(\phi)K_1(\phi)+K_0(\phi)I_1(\phi)+2l\phi K_1(\phi)I_1(\phi)} \tag{33}$$

$$d_0 = \frac{1}{D_2\phi}\frac{K_0(\phi)+l\phi K_1(\phi)}{I_0(\phi)K_1(\phi)+K_0(\phi)I_1(\phi)+2l\phi K_1(\phi)I_1(\phi)} \tag{34}$$

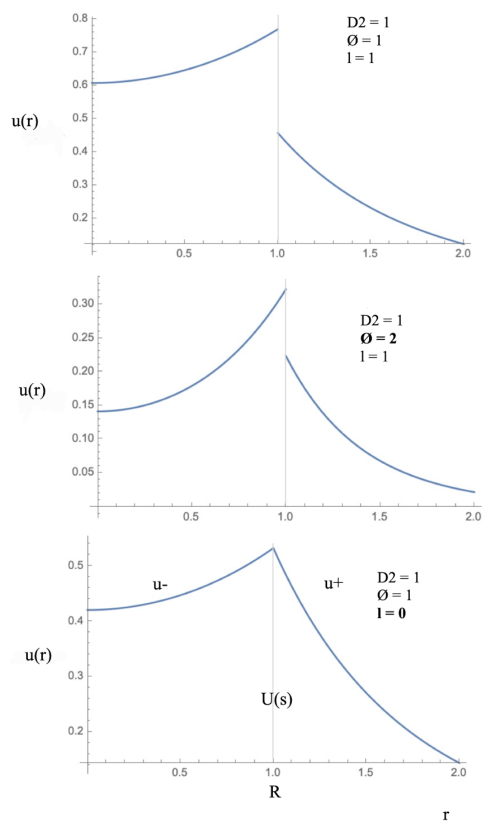
$$U = \frac{1}{D_2\phi}\frac{(I_0(\phi)+l\phi I_1(\phi))(K_0(\phi)+l\phi K_1(\phi))}{I_0(\phi)K_1(\phi)+K_0(\phi)I_1(\phi)+2l\phi K_1(\phi)I_1(\phi)} \tag{35}$$

with $\upsilon = I_0(\phi)K_1(\phi)+K_0(\phi)I_1(\phi)+2l\phi K_1(\phi)I_1(\phi)$.
For the concentration fiel in the tissue $u(r)$ and in the one-dimensional channel $U(s)$ we can now define:

$$u(r) = \begin{cases} u^+ : \frac{1}{D_2\phi}\frac{I_0(\phi)+l\phi I_1(\phi)}{I_0(\phi)K_1(\phi)+K_0(\phi)I_1(\phi)+2l\phi K_1(\phi)I_1(\phi)}K_0(\phi r) & \text{for } r > \rho \\ u^- : \frac{1}{D_2\phi}\frac{K_0(\phi)+l\phi K_1(\phi)}{I_0(\phi)K_1(\phi)+K_0(\phi)I_1(\phi)+2l\phi K_1(\phi)I_1(\phi)}I_0(\phi r) & \text{for } r < \rho \end{cases} \tag{36}$$

$$U(s) = \frac{1}{D_2\phi}\frac{(I_0(\phi)+l\phi I_1(\phi))(K_0(\phi)+l\phi K_1(\phi))}{I_0(\phi)K_1(\phi)+K_0(\phi)I_1(\phi)+2l\phi K_1(\phi)I_1(\phi)} \tag{37}$$

(Modified) Bessel function can be (approximately) evaluated for a given order m and at a given value for r which can provide us with a better intuition and approximate solution to the system of equations stated above. Setting and varying parameter values of D_2, ϕ and l we can investigate the system behavior as demonstrated in the following:



B. Small ϕ asymptotics of the $\phi > 0$ case

From the Digital Library of Mathematical Functions, looking up the limiting forms for small ϕ for different orders of the Bessel functions yields: $I_0(\phi) \sim 1$, $I_1(\phi) \sim \phi/2$, $K_0(\phi) \sim -\ln\phi$, $K_1(\phi) \sim 1/\phi$.

Substituting these into u^+ and u_- yields:

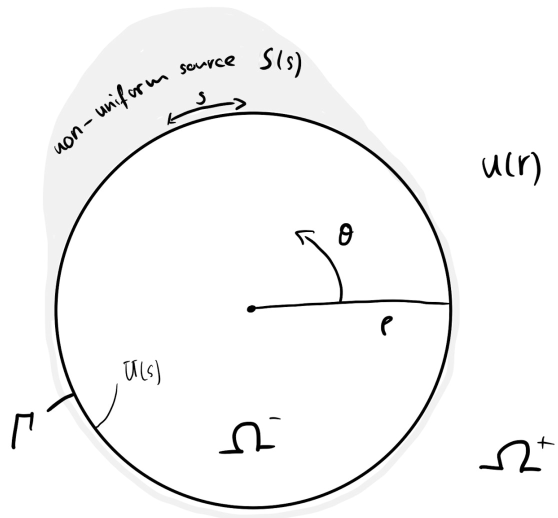
$$
\begin{aligned}
u^+ &= \frac{1}{D_2\phi}\frac{1 + l\phi^2/2}{1/\phi - \phi/2\ln\phi + l\phi}(-\ln(\phi r)) = \frac{1}{D_2}\frac{1 + l\phi^2/2}{1 - \frac{1}{2}\phi\ln\phi + l\phi^2}(\ln\frac{1}{r} - \ln\phi) \\
u^- &= \frac{1}{D_2\phi}\frac{l - \ln\phi}{1/\phi - \phi/2\ln\phi + l\phi} = \frac{1}{D_2}\frac{l - \ln\phi}{1 - \frac{1}{2}\phi\ln\phi + l\phi^2}
\end{aligned}
\tag{38}
$$

And taking ϕ to zero:

$$
\begin{aligned}
u^+ &\sim \frac{1}{D_2}\ln\frac{1}{r} - \frac{1}{D_2}\ln\phi \\
u^- &\sim \frac{l}{D_2} = \frac{1}{\kappa}
\end{aligned}
\tag{39}
$$

Note that u^- agrees completely with the $\phi = 0$ case, while u^+ agrees to first order and has a second-order $\ln\phi$ correction.

C. Circle with non-uniform source, and oxygen consumption



To test our system understand how the jump function across the boundary Γ behaves for a non-uniform function. We are thus concerned with in a θ-dependent problem:

$$(\nabla^2 - \phi^2)u(\theta, r) = 0 \qquad \text{in } \Omega \tag{40}$$

$$S(s) = S(\theta) \qquad \text{inside the 1D channel} \tag{41}$$

In this example, we define $S(\theta)$ by a simple periodic "bump" function on the circle - for now undefined. We need to solve for $u(\theta, r) = e^{im\theta}(d_0 I_m(\phi r) + c_0 K_m(\phi r))$ derived in section III. We define:

$$u(\theta, r) = \begin{cases} u^+ : \sum_m c_m e^{im\theta} K_m(\phi r) & \text{for } r > \rho \\ u^- : \sum_m d_m e^{im\theta} I_m(\phi r) & \text{for } r < \rho \end{cases} \tag{42}$$

and for the corresponding derivatives in the cases where $m \neq 0$:

$$u'(\theta, r) = \begin{cases} u_n^+ := \sum_m -c_m e^{im\theta}(\frac{m}{r} K_m(\phi r) + \phi K_{m+1}(\phi r)) & \text{for } r > \rho \\ u_n^- := \sum_m d_m e^{im\theta}(\frac{m}{r} I_m(\phi r) + \phi I_{m+1}(\phi r)) & \text{for } r < \rho \end{cases} \tag{43}$$

considering $r = \rho = 1$ we simplify to:

$$u'(\theta, 1) = \begin{cases} u_n^+ := \sum_m -c_m e^{im\theta}(m K_m(\phi) + \phi K_{m+1}(\phi)) & \text{for } r > \rho \\ u_n^- := \sum_m d_m e^{im\theta}(m I_m(\phi) + \phi I_{m+1}(\phi)) & \text{for } r < \rho \end{cases} \tag{44}$$

$$\begin{aligned} U(s) = U(\theta) &= \sum_m U_m e^{im\theta} \\ U''(\theta) &= \sum_m -m^2 U_m e^{im\theta} \end{aligned} \tag{45}$$

$$
\begin{aligned}
2U(\theta) &= u^+ + u^- - l(u_n^+ - u_n^-) \qquad &&\text{for } BC^+ + BC^- \\
0 &= u^+ - u^- - l(u_n^+ + u_n^-) \qquad &&\text{for } BC^+ - BC^- \\
U'' + S(s) &= \frac{\alpha}{R(s)}(u_n^+ - u_n^-) \qquad &&\text{for } BC\ 2
\end{aligned}
\tag{46}
$$

Substituting our new terms into this system of equations (illustrated above):

$$
\begin{aligned}
2\sum_m U_m e^{im\theta} = \sum_m e^{im\theta}\Big(&c_m K_m(\phi) + d_m I_m(\phi) \\
&+ lc_m(mK_m(\phi) + \phi K_{m+1}(\phi)) + ld_m(mI_m(\phi) + \phi I_{m+1}(\phi))\Big) \qquad \text{for } BC^+ + BC^-
\end{aligned}
\tag{47}
$$

$$
\begin{aligned}
0 = \sum_m e^{im\theta}\Big(&c_m K_m(\phi) - d_m I_m(\phi r) \\
&+ lc_m(mK_m(\phi) + \phi K_{m+1}(\phi)) - ld_m(mI_m(\phi) + \phi I_{m+1}(\phi))\Big) \qquad \text{for } BC^+ - BC^-
\end{aligned}
\tag{48}
$$

$$
\begin{aligned}
&\sum_m -m^2 U_m e^{im\theta} + S(\theta) = \\
&\quad -\frac{\alpha}{R(s)}\sum_m e^{im\theta}\Big(c_m(mK_m(\phi) + \phi K_{m+1}(\phi)) + d_m(mI_m(\phi) + \phi I_{m+1}(\phi))\Big) \qquad \text{for } BC\ 2
\end{aligned}
\tag{49}
$$

Rearranging the second equation $BC^+ - BC^-$ (equation 48) and considering $e^{im\theta} \neq 0$, we derive the following term for all $m \neq 0$:

$$
\begin{aligned}
0 = c_m(K_m(\phi) + lmK_m(\phi) + l\phi K_{m+1}(\phi)) - d_m(I_m(\phi) + lmI_m(\phi) + l\phi I_{m+1}(\phi)) \\
c_m = d_m \frac{I_m(\phi) + lmI_m(\phi) + l\phi I_{m+1}(\phi)}{K_m(\phi) + lmK_m(\phi) + l\phi K_{m+1}(\phi)} \\
c_m = d_m \frac{b_m}{a_m}
\end{aligned}
\tag{50}
$$

with:

$$
\begin{aligned}
a_m &= K_m(\phi) + lmK_m(\phi) + l\phi K_{m+1}(\phi) \\
b_m &= I_m(\phi) + lmI_m(\phi) + l\phi I_{m+1}(\phi).
\end{aligned}
\tag{51}
$$

Using the term for c_m, from the first equation $BC^+ + BC^-$ (equation 47) we can derive an expression for the coefficient U_m for all $m \neq 0$:

$$
\begin{aligned}
0 = c_m(K_m(\phi) + lmK_m(\phi) + l\phi K_{m+1}(\phi)) + d_m(I_m(\phi) + lmI_m(\phi) + l\phi I_{m+1}(\phi))) - 2U_m \\
2U_m = c_m a_m + d_m b_m \\
2U_m = d_m \frac{b_m}{a_m} a_m + d_m b_m \\
U_m = d_m b_m
\end{aligned}
\tag{52}
$$

Last, we use the obtained expressions for c_m and U_m in the third boundary condition (equation 49) to derive an expression for $S(\theta)$ in terms of d_m:

$$
\begin{aligned}
S(\theta) &= \sum_m e^{im\theta}\Big(-\frac{\alpha}{R(s)}c_m(mK_m(\phi)+\phi K_{m+1}(\phi)) - \frac{\alpha}{R(s)}d_m(mI_m(\phi)+\phi I_{m+1}(\phi)) + m^2U_m\Big) \\
S(\theta) &= \sum_m e^{im\theta}d_m\Big(-\frac{\alpha}{R(s)}\frac{b_m}{a_m}(mK_m(\phi)+\phi K_{m+1}(\phi)) - \frac{\alpha}{R(s)}(mI_m(\phi)+\phi I_{m+1}(\phi)) + m^2b_m\Big) \\
S(\theta) &= \sum_m e^{im\theta}d_m\Big(\frac{-\frac{\alpha}{R(s)}(b_m(mK_m(\phi)+\phi K_{m+1}(\phi)) + a_m(mI_m(\phi)+\phi I_{m+1}(\phi))) + m^2b_ma_m}{a_m}\Big)
\end{aligned}
\tag{53}
$$

$$S(\theta) = \sum_m e^{im\theta}d_m\frac{X_m}{a_m} \tag{54}$$

Where:

$$X_m = -\frac{\alpha}{R(s)}(b_m(mK_m(\phi)+\phi K_{m+1}(\phi)) + a_m(mI_m(\phi)+\phi I_{m+1}(\phi))) + m^2b_ma_m \tag{55}$$

We derived an expression for $S(\theta)$ that is a defined as the sum of different terms involving the modified Bessel functions ($I_m(\phi), I_{m+1}, I_K(\phi)$, and K_{m+1}) and some of our parameters α, ϕ, l, and $R(s)$. For a continuous function $S(\theta)$ it is possible expand $S(\theta)$ as the sum of the elementary functions, which allows us to solve for the yet unknown coefficients d_m. To do so, we leverage the property of the function $e^{-in\theta}$ that is orthogonal to $e^{im\theta}$ so that:

$$\int_0^{2\pi} S(\theta)e^{-in\theta}d\theta = \begin{cases} 0 & m \neq n \\ 2\pi & m = n \end{cases} \tag{56}$$

each side of the equation derived for $S(\theta)$ is multiplied by $e^{-in\theta}$ and integrated from $[0, 2\pi]$; doing this, we get:

$$\int_0^{2\pi} S(\theta)e^{-in\theta}d\theta = d_m\frac{X_m}{a_m}\int_0^{2\pi} e^{im\theta}e^{-in\theta}d\theta = 2\pi d_m\frac{X_m}{a_m} \tag{57}$$

All other terms drop out due to the orthogonality property. We define:

$$s_n = \frac{1}{2\pi}\int_0^{2\pi} S(\theta)e^{-in\theta}d\theta \tag{58}$$

and can finally derive the following terms giving us all coefficents in terms of the integral form s_n of $S(\theta)$:

$$d_m = s_n\frac{a_m}{X_m}, \qquad c_m = s_n\frac{b_m}{X_m}, \qquad U_m = s_n\frac{a_mb_m}{X_m} \tag{59}$$

$$d_m = s_n\frac{K_m(\phi) + lmK_m(\phi) + l\phi K_{m+1}(\phi)}{-\frac{\alpha}{R(s)}(b_m(mK_m(\phi)+\phi K_{m+1}(\phi)) + a_m(mI_m(\phi)+\phi I_{m+1}(\phi))) + m^2b_ma_m} \tag{60}$$

$$c_m = s_n\frac{I_m(\phi) + lmI_m(\phi) + l\phi I_{m+1}(\phi)}{-\frac{\alpha}{R(s)}(b_m(mK_m(\phi)+\phi K_{m+1}(\phi)) + a_m(mI_m(\phi)+\phi I_{m+1}(\phi))) + m^2b_ma_m} \tag{61}$$

$$U_m = s_n\frac{(K_m(\phi) + lmK_m(\phi) + l\phi K_{m+1}(\phi))(I_m(\phi) + lmI_m(\phi) + l\phi I_{m+1}(\phi))}{-\frac{\alpha}{R(s)}(b_m(mK_m(\phi)+\phi K_{m+1}(\phi)) + a_m(mI_m(\phi)+\phi I_{m+1}(\phi))) + m^2b_ma_m} \tag{62}$$

For the concentration fiel in the tissue $u(r,\theta)$ and in the one-dimensional channel $U(s)$ we thus get:

$$u(\theta,r)=\begin{cases}u^+:\sum_m s_n\frac{b_m}{X_m}e^{im\theta}K_m(\phi r) & \text{for } r>\rho\\ u^-:\sum_m s_n\frac{a_m}{X_m}e^{im\theta}I_m(\phi r) & \text{for } r<\rho\end{cases} \tag{63}$$

$$U(\theta)=\sum_m s_n\frac{a_m b_m}{X_m}e^{im\theta} \tag{64}$$

D. Proof of correctness for case $m=0$

For the special case, where $m=0$, meaning that our problem looses the angular dependence and hence $S(\theta)=1$ we can derive the following expressions,

$$s_0=1 \qquad a_m=K_0(\phi)+l\phi K_1(\phi) \qquad b_m=I_0(\phi)+l\phi I_1(\phi) \tag{65}$$

giving us,

$$\begin{aligned}d_0&=\frac{K_0(\phi)+l\phi K_1(\phi)}{I_0(\phi)K_1(\phi)+I_1(\phi)K_0(\phi)+2l\phi I_1(\phi)K_1(\phi)}\\ c_0&=\frac{I_0(\phi)+l\phi I_1(\phi)}{I_0(\phi)K_1(\phi)+I_1(\phi)K_0(\phi)+2l\phi I_1(\phi)K_1(\phi)}\\ U_0&=\frac{R(s)}{\alpha\phi}\frac{(I_0(\phi)+l\phi I_1(\phi))(K_0(\phi)+l\phi K_1(\phi))}{I_0(\phi)K_1(\phi)+I_1(\phi)K_0(\phi)+2l\phi I_1(\phi)K_1(\phi)}\end{aligned} \tag{66}$$

which are the (almost - U_m pre-term involving $R(s)$ and α diverges) exact solutions (33, 34, and 35) obtained in section (III A) and thus validate our here derived formulae.

E. Adding a non-constant source function or Investigation of the associated Fourier modes

Given a function $S(\theta)$, we determine the Fourier coefficients s_m such that $S(\theta)=\sum_m s_m e^{im\theta}$ by:

$$s_n=\frac{1}{2\pi}\int_0^{2\pi}S(\theta)e^{-in\theta}d\theta \tag{67}$$

Taking the periodic top-hat function:

$$S(\theta)=\begin{cases}A & 0<\theta<2\pi D\\ 0 & 2\pi D<\theta<2\pi\end{cases} \tag{68}$$

where A is the height of the top hat and $0<D<1$, we get:

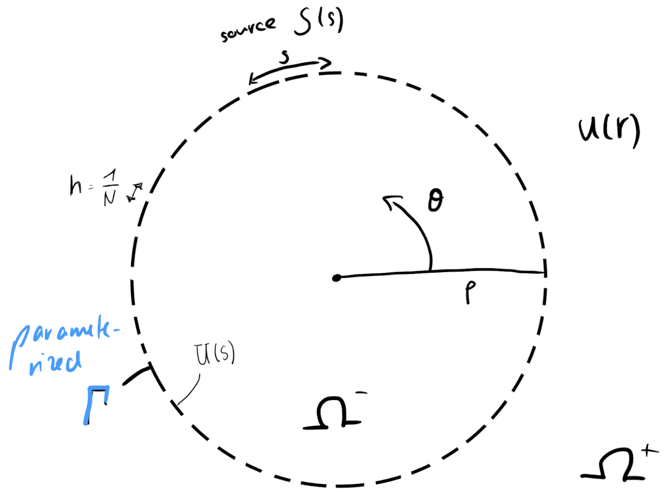
$$\begin{aligned}s_0&=AD\\ s_n&=\frac{Ai}{2\pi n}(e^{-2\pi iDn}-1) \qquad m\neq 0\end{aligned} \tag{69}$$

Our oxygen concentration field equations can thus be formulated as follows for cases $m\neq 0$: For the concentration fiel in the tissue $u(r,\theta)$ and in the one-dimensional channel $U(s)$ we thus get:

$$u(\theta,r)=\begin{cases}u^+:\sum_m \frac{Ai}{2\pi n}(e^{-2\pi iDn}-1)\frac{b_m}{X_m}e^{im\theta}K_m(\phi r) & \text{for } r>\rho\\ u^-:\sum_m \frac{Ai}{2\pi n}(e^{-2\pi iDn}-1)\frac{a_m}{X_m}e^{im\theta}I_m(\phi r) & \text{for } r<\rho\end{cases} \tag{70}$$

$$U(\theta)=\sum_m\frac{Ai}{2\pi n}(e^{-2\pi iDn}-1)\frac{a_m b_m}{X_m}e^{im\theta} \tag{71}$$

IV. BIES ON CIRCLE



To solve this problem using BIEs, we make use of potential theory, we parameterize our boundary curve and then use quadrature to approximate the integral equation on the boundary. The application of potential theory allows us to calculate the density potential from a source point ξ on the boundary Γ to a target point x in Ω using the principal of superposition. For a linear operator $(\nabla^2 - \phi^2)$ a fundamental solution $\Phi(x,\xi) \coloneqq \Phi(x,\xi)$ exists that if applied to the operator gives us the Dirac Delta function:

$$\begin{aligned}(\nabla^2 - \phi^2)u &= 0 \\ (\nabla^2 - \phi^2)\Phi(x,\xi) &= \delta(x-\xi)\end{aligned} \tag{72}$$

The fundamental solution to the modified Helmholtz equation is defined by

$$\Phi(x,\xi) = \frac{1}{2\pi} K_0(\phi|x-\xi|) \tag{73}$$

with the corresponding outward-pointing normal derivative:

$$\frac{\partial\Phi(x,\xi)}{\partial n_\xi} = -\frac{n_\xi \phi}{2\pi} K_1(\phi|x-\xi|)\frac{x-\xi}{|x-\xi|} \tag{74}$$

In the following we make the ansatz of representing $u(x)$ for $x \in \Omega/\Gamma$ by a linear combination of a single layer potential (SLP) $\mathcal{S}$ with density σ and a double layer potential (DLP) $\mathcal{D}$ with density τ given by:

$$\begin{aligned}\text{SLP:} \qquad (\mathcal{S}\sigma)(x) &= \int_\Gamma \Phi(x,\xi)\sigma(\xi)ds_\xi \\ \text{DLP:} \qquad (\mathcal{D}\tau)(x) &= \int_\Gamma \frac{\partial\Phi(x,\xi)}{\partial n_\xi}\tau(\xi)ds_\xi\end{aligned} \tag{75}$$

The choice of potential to use for the solution ansatz depends on the boundary condition of our problem, where the SLP is applied in representing problems with a jump in the derivative (Neuman problems) while the DLP representation is used in problems with a jump in the value of the function (Drichlet problems). Since we are concerned with a boundary condition that links both types of problems in form of a Robin boundary condition we need to formulate a BIE that involves both the SlP and the DLP ansatz as follows:

$$\begin{aligned}u(x) &= (\mathcal{S}\sigma)(x) + (\mathcal{D}\tau)(x) \\ u(x) &= \int_\Gamma \Phi(x,\xi)\sigma(\xi)ds_\xi + \int_\Gamma \frac{\partial\Phi(x,\xi)}{\partial n_\xi}\tau(\xi)ds_\xi\end{aligned} \tag{76}$$

Importantly, potential theory of the DLP states that for the limit approaching the boundary values $u^{\pm}(x) := \lim_{h\to 0} u(x \pm hn_x)$ differ on the two sides, which is why we define a jump relation that contains an extra density correction term on the point x.

$$u^{\pm}(x) = \begin{cases} u^+ : (\mathcal{S}\sigma)(x) + (\mathcal{D}\tau)(x) + \frac{1}{2}\tau(x) = f(x) \\ u^- : (\mathcal{S}\sigma)(x) + (\mathcal{D}\tau)(x) - \frac{1}{2}\tau(x) = f(x) \end{cases} \qquad \text{for } x \in \Gamma \tag{77}$$

or written out:

$$u^{\pm}(x) = \begin{cases} u^+ : \int_\Gamma \Phi(x,\xi)\sigma(\xi)ds_\xi + \int_\Gamma \frac{\partial\Phi(x,\xi)}{\partial n_\xi}\tau(\xi)ds_\xi + \frac{1}{2}\tau(x) = f(x) \\ u^- : \int_\Gamma \Phi(x,\xi)\sigma(\xi)ds_\xi + \int_\Gamma \frac{\partial\Phi(x,\xi)}{\partial n_\xi}\tau(\xi)ds_\xi - \frac{1}{2}\tau(x) = f(x) \end{cases} \qquad \text{for } x \in \Gamma \tag{78}$$

Because we want to solve for both the interior and the exterior problem in $\Omega^{\pm}$ we need to evaluate both cases $u^+(x)$ and $u^-(x)$. Given:

$$\begin{aligned} 2U &= u^+ + u^- - l(u_n^+ - u_n^-) && \text{for } BC^+ + BC^- \\ 0 &= u^+ - u^- - l(u_n^+ + u_n^-) && \text{for } BC^+ - BC^- \\ R\nabla U + S(s) &= \alpha(u_n^+ - u_n^-) && \text{for } BC\ 2 \end{aligned} \tag{79}$$

and rewriting our BIEs for $u^{\pm}$ like:

$$u^{\pm} = \begin{cases} u^+ : (\frac{1}{2}I + \mathcal{D})\tau + \mathcal{S}\sigma \\ u^- : (-\frac{1}{2}I + \mathcal{D})\tau + \mathcal{S}\sigma \end{cases} \tag{80}$$

we can make use of the definition of the SLP density $l(u_n^+ - u_n^-) = \sigma$ and the DLP density $(u_n^+ + u_n^-) = 2\mathcal{S}'\sigma + 2\mathcal{D}'\tau$ and substitute our new terms $u^{\pm}$ into this system of equations (illustrated above)

$$\begin{aligned} U &= \mathcal{D}\tau + (\mathcal{S} - \frac{1}{2}I)\sigma && \text{for } BC^+ + BC^- \\ 0 &= I\tau - l(2\mathcal{S}'\sigma + 2\mathcal{D}'\tau) && \text{for } BC^+ - BC^- \\ R\nabla U + S(s) &= \frac{\alpha}{l}\sigma && \text{for } BC\ 2 \end{aligned} \tag{81}$$

We now write our problem in the way that we can evaluate numerical solutions:

$$\begin{bmatrix} \mathcal{S} - \frac{l}{2}I & \mathcal{D} & -I \\ -2\mathcal{S}' & \frac{I}{l} - 2\mathcal{D}' & 0 \\ -\frac{\alpha}{l}I & 0 & R\nabla \end{bmatrix} \begin{bmatrix} \sigma \\ \tau \\ U \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ g \end{bmatrix} \tag{82}$$

Letting $\mathcal{S}' = \mathcal{D}$ and $\mathcal{D}' = \mathcal{T}$ we get:

$$\begin{bmatrix} \mathcal{S} - \frac{l}{2}I & \mathcal{D} & -I \\ -2\mathcal{D} & \frac{I}{l} - 2\mathcal{T} & 0 \\ -\frac{\alpha}{l}I & 0 & R\nabla \end{bmatrix} \begin{bmatrix} \sigma \\ \tau \\ U \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ g \end{bmatrix} \tag{83}$$

A. Parameterization of boundary

We now need to parameterize our boundary Γ by applying a function that provides a mapping $Z(s)[0, 2\pi) \to \Gamma$ and allows us to rewrite the integral 76 in terms of s instead of the arc length of the curve as

$$u(x) = \int_0^{2\pi} \Phi(x, Z(s))\sigma(Z(s))|Z'(s)|ds + \int_0^{2\pi} \frac{\partial \Phi(x, Z(s))}{\partial n_{Z(s)}} \tau(Z(s))|Z'(s)|ds. \tag{84}$$

which is simultaneously done for both equations $u^{\pm}(x)$. We are changing parameter x to be defined as a function $Z(t)$ to finally retrieve our direct BIE for all $t \in [0, 2\pi)$:

$$u(t) = \int_0^{2\pi} \Phi(Z(t), Z(s))\sigma(Z(s))|Z'(s)|ds + \int_0^{2\pi} \frac{\partial \Phi(Z(t), Z(s))}{\partial n_{Z(s)}} \tau(Z(s))|Z'(s)|ds. \tag{85}$$

and we define:

$$\begin{aligned} S(t, s) &= \Phi(Z(t), Z(s))|Z'(s)| \\ D(t, s) &= \frac{\partial \Phi(Z(t), Z(s))}{\partial n_{Z(s)}} |Z'(s)| \end{aligned} \tag{86}$$

which gives us the equation for $u^{\pm}(t)$ at the limit where $x \in \Gamma$:

$$u^{\pm}(t) = \begin{cases} u^{+} : \int_0^{2\pi} S(t, s)\sigma(s)ds + \int_0^{2\pi} D(t, s)\tau(s)ds + \frac{1}{2}\tau(t) = f(t) \\ u^{-} : \int_0^{2\pi} S(t, s)\sigma(s)ds + \int_0^{2\pi} D(t, s)\tau(s)ds - \frac{1}{2}\tau(t) = f(t) \end{cases} \quad \text{for } x \in \Gamma \tag{87}$$

where we simplify $u(Z(t)) = u(t)$, $f(Z(t)) = f(t)$, $\sigma(Z(s)) = \sigma(s)$, $\tau(Z(s)) = \tau(s)$, and $\tau(Z(t)) = \tau(t)$

B. Fixing a quadrature rule

Next we want to approximate our solution of the integral equations on the periodic interval $[0, 2\pi)$. Because we our BIEs are expressed as 2π-periodic integrals we can fix a quadrature rule. In the context of differential equations, the term quadrature is used to explain that the solution to the problem is expressed in terms of integral equations. Here we define an additional speed function expressing an N-point quadrature rule that approximates an integral on Γ via a weighted sum of N function evaluations.

$$\int_{\Gamma} f(s)\, ds \approx \sum_{j=1}^{N} w_j f(s_j) \tag{88}$$

segments our boundary Γ into N segments s_j of weight w_j. Many different quadrature methods to approximate integrals exists and the determination of integration points and weights depend on the specific method used and the accuracy required. Since we are concerned with 2π-periodic functions on a circular geometry $[0, 2\pi]$ in this problem, we choose a periodic trapezoidal rule that converges fast given these conditions defining evenly weighted and spaced segments $w_j = \frac{2\pi}{N}$ and $s_j = \frac{2\pi j}{N}$ for $j = 1, ..., N$. Our fixed quadrature rule can now be inserted into the integral yielding for $\sigma(s_j) = \sigma_j$ and $\tau(s_j) = \tau_j$

$$u^{\pm}(t) = \begin{cases} u^{+} : \frac{1}{2}\tau(t) + \sum_{j=1}^{N} S(t, s_j)w_j\sigma_j + D(t, s_j)w_j\tau_j = f(t) \\ u^{-} : -\frac{1}{2}\tau(t) + \sum_{j=1}^{N} S(t, s_j)w_j\sigma_j + D(t, s_j)w_j\tau_j = f(t) \end{cases} \tag{89}$$

We do something that Alex calls "enforce equality at each node" - which basically discretized $x = Z(t) = Z(s_i)$ for $i = 1, ..., N$ so that we can write

$$u^{\pm}(x_i) = \begin{cases} u^+ : \frac{1}{2}\tau_i + \sum_{j=1}^{N} S(s_i, s_j) w_j \sigma_j + D(s_i, s_j) w_j \tau_j = f(x_i) \\ u^- : -\frac{1}{2}\tau_i + \sum_{j=1}^{N} S(s_i, s_j) w_j \sigma_j + D(s_i, s_j) w_j \tau_j = f(x_i) \end{cases} \tag{90}$$

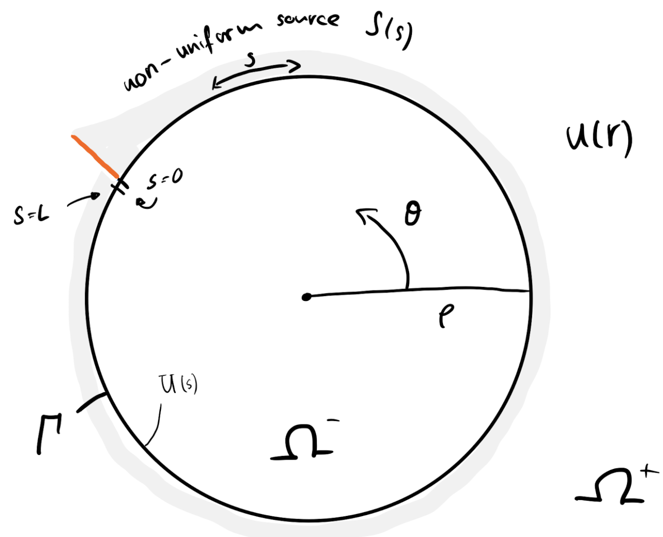
which is a linear system that we will use to solve for our unknown density function σ and τ.

$$u^{\pm}(x_i) = \begin{cases} u^+ : \frac{1}{2}\tau_i + D_{ij}\tau_j + S_{ij}\sigma_j = f(x_i) \\ u^- : -\frac{1}{2}\tau_i + D_{ij}\tau_j + S_{ij}\sigma_j = f(x_i) \end{cases} \tag{91}$$

C. Investigation of the associated Fourier modes and comparison to analytical model

For each "source" find Fourier modes using separation of variables.

D. BIEs on circle with discontinuous source function



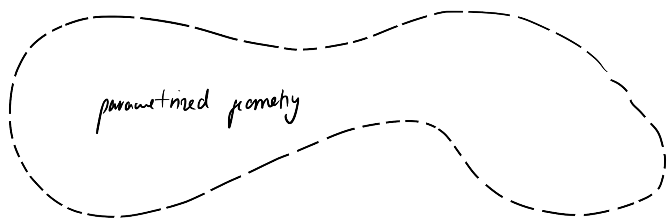
The problem we aim to solve, it is important to understand how we can handle discontinuous functions $U(s)$ on Γ given an initial value

$$U(\theta) = U_0\Big|_{\theta=0} \tag{92}$$

and either a Dirichlet boundary condition or a Neumann boundary condition

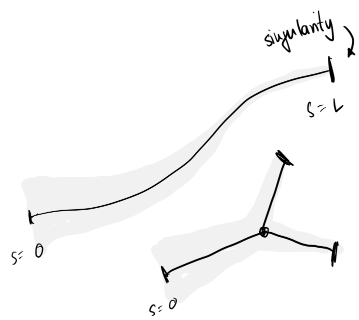
$$U(\theta) = bU_0\Big|_{\theta=2\pi} \qquad \text{or} \qquad \frac{dU(\theta)}{d\theta} = 0\Big|_{\theta=2\pi}. \tag{93}$$

V. BIES ON ARBITRARY CLOSED CURVE GEOMETRY



Before we will be able to solve the problem, we now first have to find a good parametrizing function that describes the arbitrary geometry we are concerned with.

VI. BIES ON ARBITRARY OPEN CURVE OR BRANCH GEOMETRY



Open curves and branched geometries pose a further problem, as the boundary is not closed, we will have to investigate the effect of the singularities faced at the end of the boundary ($s = L$) and the effect of branching/fusing of boundary elements.