Diffusion of Proteins on Cell Membranes
1D Finite Element Method

Aaron Kaw

Chapter 1

Diffusion

1.1 Conservation of Mass

$$\frac{\partial u}{\partial t} = -\nabla \cdot \vec{J}$$

1.2 Fick's First Law of Diffusion

$$J(\vec{x}, t) = -D(\vec{x}, t)\nabla u(\vec{x}, t)$$

1.3 Diffusion Equation

$$\frac{\partial u(\vec{x}, t)}{\partial t} = \nabla \cdot [D(\vec{x}, t)\ \nabla u(\vec{x}, t)]$$

In spherical coordinates with azimuthal symmetry on the surface of a sphere,

$$\rho^2 \sin(\varphi) \frac{\partial u}{\partial t} = \frac{\partial}{\partial \varphi}\left(D(\phi) \sin(\phi) \frac{\partial u}{\partial \phi} \right)$$

R_v	Pre-Fusion Vesicle Radius
R_c	Pre-Fusion Cell Radius

D_v	Vesicle Diffusivity
D_c	Cell Diffusivity

1.4 Total Concentration

$$\langle \bullet \rangle = 2\pi\rho^2 \int_0^{\pi} \bullet \sin(\varphi)\ \mathrm{d}\varphi$$

Chapter 2

Full Fusion

2.1 Fusion Parameters

$$
\begin{aligned}
D(\varphi) &= D_v H(\varphi_j - \varphi) + D_c H(\varphi - \varphi_j) \\
{R'}^2 &= R_v^2 + R_c^2 \\
\varphi_j &= \operatorname{acos}\left(\frac{R_c^2 - R_v^2}{{R'}^2}\right) \\
R'_s &= \frac{2R_v R_c}{R'}
\end{aligned}
$$

2.2 Initial-and-Boundary Value Problem

$$
\Omega = (0, \pi)
$$

$$
\begin{aligned}
{R'}^2 \sin(\varphi) \frac{\partial u(\varphi, t)}{\partial t} &= \frac{\partial}{\partial \varphi}\left(D(\varphi) \sin(\varphi) \frac{\partial u(\varphi, t)}{\partial \varphi}\right) & \varphi \in \Omega \qquad t \in \mathbb{R}_0^+ \\
u(\varphi, t) &= H(\varphi_j - \varphi) & \varphi \in \Omega \qquad t \in \mathbb{R}_0^+
\end{aligned}
$$

2.3 Weak Form

$$
\begin{aligned}
{R'}^2 \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial t} &= \frac{\partial}{\partial \varphi}\left(D(\varphi) \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} \right) \\
{R'}^2 \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial t} w(\varphi) &= \frac{\partial}{\partial \varphi}\left(D(\varphi) \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} \right) w(\varphi) \\
{R'}^2 \int_\Omega \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial t} w(\varphi) \mathrm{d}\varphi &= \int_\Omega \frac{\partial}{\partial \varphi}\left(D(\varphi) \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} \right) w(\varphi) \mathrm{d}\varphi \\
\frac{1}{2\pi} \left\langle \frac{\partial u(\varphi,t)}{\partial t} w(\varphi) \right\rangle &= \left[D(\varphi) \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} w(\varphi) \right]_\Omega - \int_\Omega D(\varphi) \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} \frac{\partial w(\varphi)}{\partial \varphi} \mathrm{d}\varphi \\
\frac{1}{2\pi} \left\langle \frac{\partial u(\varphi,t)}{\partial t} w(\varphi) \right\rangle &= - \int_\Omega D(\varphi) \sin(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} \frac{\partial w(\varphi)}{\partial \varphi} \mathrm{d}\varphi \\
\frac{1}{2\pi} \left\langle \frac{\partial u(\varphi,t)}{\partial t} w(\varphi) \right\rangle &= - \frac{1}{2\pi {R'}^2} \left\langle D(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} \frac{\partial w(\varphi)}{\partial \varphi} \right\rangle
\end{aligned}
$$

yielding the weak form

$$
0 = \left\langle \frac{\partial u(\varphi,t)}{\partial t} w(\varphi) \right\rangle + \frac{1}{{R'}^2} \left\langle D(\varphi) \frac{\partial u(\varphi,t)}{\partial \varphi} \frac{\partial w(\varphi)}{\partial \varphi} \right\rangle
$$

with total concentration

$$
\langle \bullet \rangle = 2\pi {R'}^2 \int_\Omega \sin(\varphi) \bullet \mathrm{d}\varphi
$$

Chapter 3

Kiss-and-Run Fusion

R_j Post-Fusion Junction Radius

3.1 Fusion Parameters

$$R'_v = \frac{2R_v^2}{\sqrt{4R_v^2 - R_j^2}}$$
$$R'_c = \frac{2R_c^2}{\sqrt{4R_c^2 - R_j^2}}$$
$$\phi_v = \pi - \operatorname{asin}\left(\frac{R_j}{R'_v}\right)$$
$$\psi_c = \pi - \operatorname{asin}\left(\frac{R_j}{R'_c}\right)$$

3.2 Initial-and-Boundary Value Problem

$$\Omega_v = (0, \phi_v)$$
$$\Omega_c = (\pi - \psi_c, \pi)$$

$$R'^{\,2}_v \sin(\phi) \frac{\partial v(\phi,t)}{\partial t} = D_v \frac{\partial}{\partial \phi}\left(\sin(\phi)\frac{\partial v(\phi,t)}{\partial \phi}\right) \qquad \phi \in \Omega_v \qquad t \in \mathbb{R}_0^+$$
$$R'^{\,2}_c \sin(\psi) \frac{\partial c(\psi,t)}{\partial t} = D_c \frac{\partial}{\partial \psi}\left(\sin(\psi)\frac{\partial c(\psi,t)}{\partial \psi}\right) \qquad \psi \in \Omega_c \qquad t \in \mathbb{R}_0^+$$

At the junction,

$$
\begin{aligned}
v(\phi,t) &= c(\psi,t) & \phi &= \sup\Omega_v & \psi &= \inf\Omega_c & t &\in \mathbb{R}_0^+ \\
\frac{D_v}{R'_v}\frac{\partial v(\phi,t)}{\partial\phi} &= \frac{D_c}{R'_c}\frac{\partial c(\psi,t)}{\partial\psi} & \phi &= \sup\Omega_v & \psi &= \inf\Omega_c & t &\in \mathbb{R}_0^+
\end{aligned}
$$

Initially,

$$
\begin{aligned}
&v(\phi,t) = 1 && \phi \in \Omega_v && && t \in \mathbb{R}_0^+ \\
&c(\psi,t) = 0 && && \psi \in \Omega_c && t \in \mathbb{R}_0^+ \\
&v(\phi,t) = c(\psi,t) = 0.5 && \phi \in \Omega_v && \psi \in \Omega_c && t \in \mathbb{R}_0^+
\end{aligned}
$$

3.3 Weak Form

On the vesicle,

$$
\begin{aligned}
{R'_v}^2 \sin(\phi)\frac{\partial v(\phi,t)}{\partial t} &= D_v \frac{\partial}{\partial\phi}\left(\sin(\phi)\frac{\partial v(\phi,t)}{\partial\phi}\right) \\
{R'_v}^2 \sin(\phi)\frac{\partial v(\phi,t)}{\partial t} f(\phi) &= D_v \frac{\partial}{\partial\phi}\left(\sin(\phi)\frac{\partial v(\phi,t)}{\partial\phi}\right) f(\phi) \\
{R'_v}^2 \int_{\Omega_v} \sin(\phi)\frac{\partial v(\phi,t)}{\partial t} f(\phi)\ \mathrm{d}\phi &= D_v \int_{\Omega_v} \frac{\partial}{\partial\phi}\left(\sin(\phi)\frac{\partial v(\phi,t)}{\partial\phi}\right) f(\phi)\ \mathrm{d}\phi \\
{R'_v}^2 \int_{\Omega_v} \sin(\phi)\frac{\partial v(\phi,t)}{\partial t} f(\phi)\ \mathrm{d}\phi &= D_v \int_{\Omega_v} \frac{\partial}{\partial\phi}\left(\sin(\phi)\frac{\partial v(\phi,t)}{\partial\phi}\right) f(\phi)\ \mathrm{d}\phi \\
\frac{1}{2\pi}\left\langle \frac{\partial v(\phi,t)}{\partial t} f(\phi) \right\rangle_v &= D_v\left(\left[\sin(\phi)\frac{\partial v(\phi,t)}{\partial\phi} f(\phi)\right]_{\Omega_v} - \int_{\Omega_v} \sin(\phi)\frac{\partial v(\phi,t)}{\partial\phi}\frac{\partial f(\phi)}{\partial\phi}\ \mathrm{d}\phi\right) \\
\frac{1}{2\pi}\left\langle \frac{\partial v(\phi,t)}{\partial t} f(\phi) \right\rangle_v &= D_v\left(\left[\sin(\phi_v)\frac{\partial v(\phi_v,t)}{\partial\phi} f(\phi_v) - 0\right] - \frac{1}{2\pi {R'_v}^2}\left\langle \frac{\partial v(\phi,t)}{\partial\phi}\frac{\partial f(\phi)}{\partial\phi}\right\rangle\right) \\
\frac{1}{2\pi}\left\langle \frac{\partial v(\phi,t)}{\partial t} f(\phi) \right\rangle_v &= D_v\left(\sin(\phi_v)\frac{\partial v(\phi_v,t)}{\partial\phi} f(\phi_v) - \frac{1}{2\pi {R'_v}^2}\left\langle \frac{\partial v(\phi,t)}{\partial\phi}\frac{\partial f(\phi)}{\partial\phi}\right\rangle\right)
\end{aligned}
$$

On the cell,

$$
\begin{aligned}
{R'_c}^2 \sin(\psi)\frac{\partial c(\psi,t)}{\partial t} &= D_c \frac{\partial}{\partial\psi}\left(\sin(\psi)\frac{\partial c(\psi,t)}{\partial\psi}\right) \\
\frac{1}{2\pi}\left\langle \frac{\partial c(\psi,t)}{\partial t} g(\psi) \right\rangle_c &= D_c\left(\left[\sin(\psi)\frac{\partial c(\psi,t)}{\partial\psi} g(\psi)\right]_{\Omega_v} - \int_{\Omega_v} \sin(\psi)\frac{\partial c(\psi,t)}{\partial\psi}\frac{\partial g(\psi)}{\partial\psi}\ \mathrm{d}\psi\right) \\
\frac{1}{2\pi}\left\langle \frac{\partial c(\psi,t)}{\partial t} g(\psi) \right\rangle_c &= D_c\left(\left[0 - \sin(\pi-\psi_v)\frac{\partial c(\pi-\psi_v,t)}{\partial\psi} g(\pi-\psi_v)\right] - \frac{1}{2\pi {R'_c}^2}\left\langle \frac{\partial c(\psi,t)}{\partial\psi}\frac{\partial g(\psi)}{\partial\psi}\right\rangle\right) \\
\frac{1}{2\pi}\left\langle \frac{\partial c(\psi,t)}{\partial t} g(\psi) \right\rangle_c &= -D_c\left(\sin(\pi-\psi_v)\frac{\partial c(\pi-\psi_v,t)}{\partial\psi} g(\pi-\psi_v) + \frac{1}{2\pi {R'_c}^2}\left\langle \frac{\partial c(\psi,t)}{\partial\psi}\frac{\partial g(\psi)}{\partial\psi}\right\rangle\right)
\end{aligned}
$$

Adding the two expressions,

$$
\begin{aligned}
&\left\langle \frac{\partial v(\phi,t)}{\partial t} f(\phi) \right\rangle_v + \left\langle \frac{\partial c(\psi,t)}{\partial t} g(\psi) \right\rangle_c \\
&\quad = D_v \sin(\phi_v) \frac{\partial v(\phi_v,t)}{\partial \phi} f(\phi_v) - D_c \sin(\pi - \psi_v) \frac{\partial c(\pi - \psi_v,t)}{\partial \psi} g(\pi - \psi_v) \\
&\qquad - \left(\frac{D_v}{{R_v'}^2} \left\langle \frac{\partial v(\phi,t)}{\partial \phi} \frac{\partial f(\phi)}{\partial \phi} \right\rangle + \frac{D_c}{{R_c'}^2} \left\langle \frac{\partial c(\psi,t)}{\partial \psi} \frac{\partial g(\psi)}{\partial \psi} \right\rangle \right)
\end{aligned}
$$

then substituting the membrane angle sizes

$$
\begin{aligned}
&\frac{1}{2\pi} \left(\left\langle \frac{\partial v(\phi,t)}{\partial t} f(\phi) \right\rangle_v + \left\langle \frac{\partial c(\psi,t)}{\partial t} g(\psi) \right\rangle_c \right) \\
&\quad = D_v \frac{R_j}{R_v'} \frac{\partial v(\phi_v,t)}{\partial \phi} f(\phi_v) - D_c \frac{R_j}{R_c'} \frac{\partial c(\pi - \psi_v,t)}{\partial \psi} g(\pi - \psi_v) \\
&\qquad - \frac{1}{2\pi} \left(\frac{D_v}{{R_v'}^2} \left\langle \frac{\partial v(\phi,t)}{\partial \phi} \frac{\partial f(\phi)}{\partial \phi} \right\rangle + \frac{D_c}{{R_c'}^2} \left\langle \frac{\partial c(\psi,t)}{\partial \psi} \frac{\partial g(\psi)}{\partial \psi} \right\rangle \right)
\end{aligned}
$$

Select $f(\phi)$ and $g(\psi)$ such that

$$f(\phi_v) = g(\pi - \psi_c).$$

so

$$
\begin{aligned}
0 &= \left\langle \frac{\partial v(\phi,t)}{\partial t} f(\phi) \right\rangle_v + \left\langle \frac{\partial c(\psi,t)}{\partial t} g(\psi) \right\rangle_c \\
&\quad + \frac{D_v}{{R_v'}^2} \left\langle \frac{\partial v(\phi,t)}{\partial \phi} \frac{\partial f(\phi)}{\partial \phi} \right\rangle + \frac{D_c}{{R_c'}^2} \left\langle \frac{\partial c(\psi,t)}{\partial \psi} \frac{\partial g(\psi)}{\partial \psi} \right\rangle
\end{aligned}
$$

Define arc-length transformation such that

$$
\begin{aligned}
s_j &= R_v' \phi_v \\
s_P &= s_j + R_c' \psi_c \\
s &= \begin{cases} R_v' \phi & \phi \in \Omega_v \\ s_j + R_c'(\psi + \psi_c - \pi) & \psi \in \Omega_c \end{cases}
\end{aligned}
$$

so inverse transformations are

$$
\begin{aligned}
\Gamma_v &= (0, s_j) \\
\Gamma_c &= (s_j, s_P) \\
\Gamma &= \mathrm{conv}(\Gamma_v \cup \Gamma_c) \\
\phi(s) &= \frac{s}{R_v'} \\
\psi(s) &= \frac{s - s_j}{R_c'} + \pi - \psi_c \\
\omega(s) &= \begin{cases} \phi(s) & s \in \Gamma_v \\ \psi(s) & s \in \Gamma_c \end{cases}
\end{aligned}
$$

and define $u(s,t)$ such that

$$u(s,t) = \begin{cases} v(\phi(s),t) & s \in \Gamma_v \\ c(\psi(s),t) & s \in \Gamma_c \end{cases}$$

so derivatives become

$$\begin{aligned}
\mathrm{d}\phi &= \frac{1}{R'_v}\,\mathrm{d}s \\
\mathrm{d}\psi &= \frac{1}{R'_c}\,\mathrm{d}s \\
\frac{\partial v(\phi,t)}{\partial \phi} &= R'_v \frac{\partial u(s,t)}{\partial s} \\
\frac{\partial c(\psi,t)}{\partial \psi} &= R'_c \frac{\partial u(s,t)}{\partial s}
\end{aligned}$$

and define

$$w(s) = \begin{cases} f(\phi(s),t) & s \in \Gamma_v \\ g(\psi(s),t) & s \in \Gamma_c \end{cases}$$

so our weak form becomes

$$\begin{aligned}
0 &= \left\langle \frac{\partial v(\phi,t)}{\partial t} f(\phi) \right\rangle_v + \left\langle \frac{\partial c(\psi,t)}{\partial t} g(\psi) \right\rangle_c \\
&\quad + \frac{D_v}{{R'_v}^2} \left\langle \frac{\partial v(\phi,t)}{\partial \phi} \frac{\partial f(\phi)}{\partial \phi} \right\rangle + \frac{D_c}{{R'_c}^2} \left\langle \frac{\partial c(\psi,t)}{\partial \psi} \frac{\partial g(\psi)}{\partial \psi} \right\rangle \\
0 &= {R'_v}^2 \int_{\Omega_v} \sin(\phi) \frac{\partial v(\phi,t)}{\partial t} f(\phi)\mathrm{d}\phi + {R'_c}^2 \int_{\Omega_c} \sin(\psi) \frac{\partial c(\psi,t)}{\partial t} g(\psi)\mathrm{d}\psi \\
&\quad + D_v \int_{\Omega_v} \sin(\phi) \frac{\partial v(\phi,t)}{\partial \phi} \frac{\partial f(\phi)}{\partial \phi}\mathrm{d}\phi + D_c \int_{\Omega_c} \sin(\psi) \frac{\partial c(\psi,t)}{\partial \psi} \frac{\partial g(\psi)}{\partial \psi}\mathrm{d}\psi \\
0 &= R'_v \int_{\Gamma_v} \sin\left(\phi(s)\right) \frac{\partial u(s,t)}{\partial t} w(s)\,\mathrm{d}s + R'_c \int_{\Gamma_c} \sin\left(\psi(s)\right) \frac{\partial u(s,t)}{\partial t} w(s)\,\mathrm{d}s \\
&\quad + D_v \int_{\Gamma_v} \sin\left(\phi(s)\right) \frac{\partial u(s,t)}{\partial s} \frac{\partial w(s)}{\partial s}\,\mathrm{d}s + D_c \int_{\Gamma_c} \sin\left(\psi(s)\right) \frac{\partial u(s,t)}{\partial s} \frac{\partial w(s)}{\partial s}\,\mathrm{d}s \\
0 &= \int_{\Gamma} \sin\left(\omega(s)\right) R'(s) \frac{\partial u(s,t)}{\partial t} w(s) + \int_{\Gamma} \sin\left(\omega(s)\right) D(s) \frac{\partial u(s,t)}{\partial s} \frac{\partial w(s)}{\partial s}\,\mathrm{d}s
\end{aligned}$$

yielding our weak form in arc-length

$$0 = \left\langle \frac{\partial u(s,t)}{\partial t} w(s) \right\rangle + \left\langle \frac{D(s)}{R'(s)} \frac{\partial u(s,t)}{\partial s} \frac{\partial w(s)}{\partial s} \right\rangle$$

with

$$R'(s) = \begin{cases} R'_v & s \in \Gamma_v \\ R'_c & s \in \Gamma_c \end{cases}$$
$$\langle \bullet \rangle = 2\pi \int R'(s) \sin\left(\omega(s)\right) \bullet \,\mathrm{d}s$$

Chapter 4

Finite Element Method

The finite element method expressed generically for the fusion modes of full and kiss-and-run takes a weak formulation

$$0 = \left\langle \frac{\partial u(s,t)}{\partial t} w(s) \right\rangle + \left\langle \frac{D(s)}{R(s)} \frac{\partial u(s,t)}{\partial s} \frac{\partial w(s)}{\partial s} \right\rangle$$

with

$$\langle \bullet \rangle = 2\pi \int_{\Gamma} R(s) \sin\left(\omega(s)\right) \bullet \, \mathrm{d}s$$

for Γ, s, $D(s)$, $R(s)$, and $\omega(s)$ defined by the fusion mode model.

4.1 Spatial Discretisation

Select positive integers p_j and P such that

$$p_j < P$$

Define

$$\mathbb{P} = \{0, 1, 2, ..., P\}$$

Select values s_p for $p \in \mathbb{P}$ such that

$$0 = s_0 < s_1 < \cdots s_{p_j - 1} < s_{p_j} = s_j < s_{p_j + 1} < \cdots < s_{P-1} < s_P$$

Define their spacing,

$$h_p = s_p - s_{p-1} \qquad\qquad s \in \mathbb{P}^+$$

Define hat functions such that

$$\Lambda_p(s) = \begin{cases} 1 & s = s_p \\ \dfrac{s - s_{p-1}}{h_p} & s \in (s_{p-1}, s_p) \\ \dfrac{s_{p+1} - s}{h_{p+1}} & s \in (s_p, s_{p+1}) \\ 0 & \text{otherwise} \end{cases}$$

Transform the weak form into a system of equations by selecting

$$w(s) = \Lambda_p(s) \qquad p \in \mathbb{P}$$

so

$$0 = \left\langle \frac{\partial u(s,t)}{\partial t} \Lambda_p(s) \right\rangle + \left\langle \frac{D(s)}{R(s)} \frac{\partial u(s,t)}{\partial s} \frac{\partial \Lambda_p(s)}{\partial s} \right\rangle \qquad p \in \mathbb{P}$$

Project the solution $u(s,t)$ onto the space of piecewise-linear functions defined on the discrete grid s_p, and define this projection as

$$u_h(s,t) = \sum_{q=0}^{P} U_q(t) \Lambda_q(s)$$

and impose this by substitution so

$$0 = \frac{\partial U_q(t)}{\partial t} \langle \Lambda_q(s) \Lambda_p(s) \rangle + U_q(t) \left\langle \frac{D(s)}{R(s)} \frac{\partial \Lambda_q(s)}{\partial s} \frac{\partial \Lambda_p(s)}{\partial s} \right\rangle$$

in Einstein notation.

Define

$$\begin{aligned} \vec{U}(t) &= [U_0(t) \; U_1(t) \; \cdots \; U_P(t)]^{\mathrm{T}} \\ [M]_{pq} &= \langle \Lambda_q(s) \Lambda_p(s) \rangle \\ [S]_{pq} &= \left\langle \frac{D(s)}{R(s)} \frac{\partial \Lambda_q(s)}{\partial s} \frac{\partial \Lambda_p(s)}{\partial s} \right\rangle \end{aligned}$$

so we have our system

$$0 = M \frac{\mathrm{d}\vec{U}(t)}{\mathrm{d}t} + S\vec{U}(t)$$

4.2 Temporal Discretisation

Due to stiffness, we select a backward Euler dynamic timestepping scheme. Define

$$\begin{aligned} 0 = t_0 &< t_1 < \cdots \\ \vec{U}^n &= \vec{U}(t_n) \qquad n \in \mathbb{Z}_0^+ \end{aligned}$$

so

$$
\begin{aligned}
0 &= M\frac{\vec{U}^n - \vec{U}^{n-1}}{\Delta t_n} + S\vec{U}^n \\
0 &= M\left(\vec{U}^n - \vec{U}^{n-1}\right) + \Delta t_n S\vec{U}^n \\
0 &= (M + \Delta t_n S)\vec{U}^n - M\vec{U}^{n-1}
\end{aligned}
$$

yielding the matrix equation

$$
(M + \Delta t_n S)\vec{U}^n = M\vec{U}^{n-1}
$$

Due to accuracy needing small h_p, Simpson's Rule with two subintervals is used to evaluate the integral for the mass matrix to avoid machine rounding errors via division by small h_p values.

$$
\int_a^b f(x)\,\mathrm{d}x \approx \frac{b-a}{6}\left[f(a) + 4f\left(\frac{a+b}{2}\right) + f(b)\right]
$$

Additionally, note the diagonalism, i.e.

$$
\begin{aligned}
[M]_{pq} &= [M]_{qp} \\
[S]_{pq} &= [S]_{qp}
\end{aligned}
$$

thus, WLOG we calculate

$$
\begin{aligned}
&[M]_{pp}, [S]_{pp} && p \in \mathbb{P} && \text{(diagonal)} \\
&[M]_{p-1,p}, [S]_{p-1,p} && p \in \mathbb{P}^+ && \text{(off-diagonal)}
\end{aligned}
$$

For clarity, define

$$
\begin{aligned}
\mathbb{P}_- &= \{0, ..., P-1\} \\
\mathbb{P}_+ &= \{1, ..., P\} \\
R'(s) &= R(s)\sin\left(\omega(s)\right) \\
D'(s) &= D(s)\sin\left(\omega(s)\right)
\end{aligned}
$$

4.3 Mass Matrix

$$
\begin{aligned}
[M]_{pp} &= \left\langle \Lambda_p^2(s) \right\rangle \\
&= 2\pi \int_\Gamma R'(s)\Lambda_p^2(s)\,\mathrm{d}s \\
&= 2\pi\left(I_{\mathbb{P}_+}(p)\int_{s_{p-1}}^{s_p} R'(s)\frac{s - s_{p-1}}{h_p}\,\mathrm{d}s + I_{\mathbb{P}_-}(p)\int_{s_p}^{s_{p+1}} R'(s)\frac{s_{p+1} - s}{h_{p+1}}\,\mathrm{d}s\right)
\end{aligned}
$$

$$
\begin{aligned}
&\int_{s_{p-1}}^{s_p} R'(s)\frac{s - s_{p-1}}{h_p}\,\mathrm{d}s \\
&\quad = \frac{1}{h_p}\int_{s_{p-1}}^{s_p} R'(s)(s - s_{p-1})\,\mathrm{d}s \\
&\quad \approx \frac{1}{6}\left[R'(s_p)h_p + 4R'(s_{p-1/2})\left(\frac{s_{p-1}+s_p}{2} - s_{p-1}\right)\right] \\
&\quad = \frac{1}{6}\big[R'(s_p)h_p + 2R'(s_{p-1/2})h_p\big]
\end{aligned}
$$

$$
\begin{aligned}
&\int_{s_p}^{s_{p+1}} R'(s)\frac{s_{p+1} - s}{h_{p+1}}\,\mathrm{d}s \\
&\quad = \frac{1}{h_p}\int_{s_p}^{s_{p+1}} R'(s)(s_{p+1} - s)\,\mathrm{d}s \\
&\quad \approx \frac{1}{6}\left[R'(s_p)h_{p+1} + 4R'(s_{p+1/2})\left(s_{p+1} - \frac{s_p+s_{p+1}}{2}\right)\right] \\
&\quad = \frac{1}{6}\big[R'(s_p)h_{p+1} + 2R'(s_{p+1/2}h_{p+1})\big]
\end{aligned}
$$

So

$$
[M]_{pp} \approx \frac{\pi}{3}\big(I_{\mathbb{P}_+}(p)h_p\big[R'(s_p) + 2R'(s_{p-1/2})\big] + I_{\mathbb{P}_-}(p)h_{p+1}\big[R'(s_p) + 2R'(s_{p+1/2})\big]\big)
$$

$$
\begin{aligned}
[M]_{p-1,p} &= \langle \Lambda_{p-1}(s)\Lambda_p(s)\rangle \\
&= 2\pi\int_\Gamma R'(s)\Lambda_{p-1}(s)\Lambda_p(s)\,\mathrm{d}s \\
&= \frac{2\pi}{h_p^2}\int_{s_{p-1}}^{s_p} R'(s)(s_p - s)(s - s_{p-1})\,\mathrm{d}s \\
&\approx \frac{\pi}{3h_p}\left[4R'(s_{p-1/2})\left(s_p - \frac{s_{p-1}+s_p}{2}\right)\left(\frac{s_{p-1}+s_p}{2} - s_{p-1}\right)\right]
\end{aligned}
$$

yielding

$$
[M]_{p-1,p} \approx \frac{\pi h_p}{3}R'(s_{p-1/2})
$$

4.4 Stiffness Matrix

$$
\begin{aligned}
[S]_{pp} &= \left\langle \frac{D(s)}{R(s)} \left(\frac{\partial \Lambda_p(s)}{\partial s} \right)^2 \right\rangle \\
&= 2\pi \int_\Gamma D'(s) \left(\frac{\partial \Lambda_p(s)}{\partial s} \right)^2 \mathrm{d}s \\
&= 2\pi \left(I_{\mathbb{P}_+}(p) \int_{s_{p-1}}^{s_p} D'(s) \frac{1}{h_p^2} \,\mathrm{d}s + I_{\mathbb{P}_-}(p) \int_{s_p}^{s_{p+1}} D'(s) \frac{1}{h_{p+1}^2} \,\mathrm{d}s \right) \\
&= 2\pi \left(\frac{I_{\mathbb{P}_+}(p)}{h_p^2} \int_{s_{p-1}}^{s_p} D'(s) \,\mathrm{d}s + \frac{I_{\mathbb{P}_-}(p)}{h_{p+1}^2} \int_{s_p}^{s_{p+1}} D'(s) \,\mathrm{d}s \right)
\end{aligned}
$$

$$
\begin{aligned}
[S]_{p-1,p} &= \left\langle \frac{D(s)}{R(s)} \frac{\partial \Lambda_{p-1}(s)}{\partial s} \frac{\partial \Lambda_p(s)}{\partial s} \right\rangle \\
&= 2\pi \int_\Gamma D'(s) \frac{\partial \Lambda_{p-1}(s)}{\partial s} \frac{\partial \Lambda_p(s)}{\partial s} \,\mathrm{d}s \\
&= 2\pi \int_{s_{p-1}}^{s_p} D'(s) \frac{-1}{h_p^2} \,\mathrm{d}s \\
&= \frac{-2\pi}{h_p^2} \int_{s_{p-1}}^{s_p} D'(s) \,\mathrm{d}s
\end{aligned}
$$