Modeling and design of stents to optimize the effect of the dose

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Abstract

Stents are used in interventional cardiology to keep a diseased vessel open. New stents are coated with a medicinal agent to prevent early reclosure due to the proliferation of smooth muscle cells. It is the dose of the agent which effectively acts on the cells in the wall of the vessel. This paper gives mathematical models of the dose for a periodic stent and an asymptotic stent. It studies the effect of the number of struts and the ratio between the area of the coated struts and the targeted area of the vessel. Theoretical and numerical results are presented along with some open design problems for non-periodic stents.
1 Introduction

The use of stents in interventional cardiology is fairly recent$^5$. An electrical engineer, Dominik M. Wiktor (Bellcore, Morristown) underwent open heart surgery to correct an aortic dissection in 1984. Following the procedure, he wondered why such a vascular repair couldn’t be done with less surgical trauma, and began to read about angioplasty. He came up with a variety of stent designs and signed a consulting agreement with Medtronic in 1988.

The “Wiktor Stent,” an intravascular stent (U.S. patent No. 4,886,062) provides an important solution to coronary artery reconstruction and recanalization. The stent keeps a diseased vessel open and prevents reclosure. Made of tantalum, a noncorrosive and malleable metal which is easily seen by the cardiologist during fluoroscopy, the stent is extremely easy to handle, deliver and deploy, which is of the utmost importance in emergency and routine situations.

In the case of the Wiktor Stent, the delivering catheter is inflated to expand and deploy the stent to maintain the opening. The balloon is then deflated and the catheter removed. Within a month, the stent becomes incorporated into the artery wall. Today, Medtronics O Wiktor stent has a 20 percent market share in Europe.

Figure 1: Wiktor Stent as drawn in U.S. patent No. 4,886,062

More than forty percent of patients treated for atherosclerosis present restenosis within six months of the operation. Indeed, implanting a stent generally leads to complications, thrombosis and proliferation of smooth-muscle cells being the root causes of restenosis. A great deal of research has been conducted on medicinal agents designed to have an anti-thrombotic effect or to limit the proliferation of smooth-muscle cells. This type of medication can be delivered in two ways: systematically or locally. The primary disadvantage of systemic delivery is generally its greater toxicity in the body, since, to be effective, a much higher dose of the medication is a priori required than for local delivery. For this reason, the local solution is the preferred choice. For instance a typical system consists of a stent coated with a thin layer of polymer which has been impregnated with a molecule that has an effect on the proliferation of smooth-muscle cells $^{1, 9}$.

There are many aspects to the design of a stent. Mechanically the stent has to be strong enough to exert a sufficiently strong pressure on the wall of the vessel to keep it open and to restore a normal flow of blood. Once the purely mechanical parameters are set, there are a number of parameters left to control the delivery of the molecule to the wall. It is generally accepted that it is the effect of the concentration of the product over time that effectively cures the damaged wall of the vessel (cf. $^2, 9$). This naturally leads to the notion of dose in each point of the artery. Mathematically the dose is defined as the integral of the concentration over all times ranging from 0 to $\infty$.

In this paper we study the effect of the density of the struts and the pattern of the stent on the distribution of the dose. We use a very crude model of the lumen and the wall of the vessel: two concentric cylinders long enough not to affect the design in the target area where the stent will be deployed. For simplicity, the stent is made up of a finite number of rings of radius $R$ with no thickness and uniform width. In its undeployed state we assume that all the struts are side by side without spacing between them. When the stent is deployed to fill the target area, space is created between the struts. We call $\rho$ the ratio between the surface occupied by the struts to the surface of the target area. It is a number between 0 and 1. When the struts are periodically spaced $1 - \rho$ is a measure of the percentage of the area of the interface lumen/wall in the target area which is open to chemical/biological exchanges.

The necessity of such exchanges through the stent has apparently not received much attention in the literature.

In our analysis we assume that the mass per unit area of the product impregnated in the thin layer on the stent is constant. We study the distribution of the dose in the artery with respect to the number of struts and the ratio $\rho$ while keeping the surface of the target area constant. For a fixed $\rho$, as the number of struts increases, their width and the space between two struts decrease. So we are naturally led to introduce the notion of an asymptotic stent. We obtain the equations for the dose of the asymptotic stent and study the distribution of the dose in the artery. When the product is applied on the inner and outer surfaces of the stent, the asymptotic model predicts that the two sides contribute to increase the total dose in the wall.

§ 2 presents the time-space diffusion-transport equations for the concentration of the product using appropriate conditions on the flow at both ends of the artery. § 3 gives the equations for the dose and the variational model.

$^5$New Jersey Hall of Fame: Inventor of the year 1996 (http://www.njinvent.njit.edu/).
Since the thickness of the layer of polymer is small compared to the other geometric parameters, we let the thickness of the layer go to zero in the variational model and obtain a new variational model for the dose which is a reasonable approximation in § 4. The construction of the asymptotic stent\(^6\) and the corresponding variational equation for the dose are given in § 5. The asymptotic model is related to the Neumann sieve studied in [12], [5], and [7] where the plane surface is replaced by the interface lumen/wall in the lateral boundary of a cylinder. However in our limiting process the surface of the holes does not go to zero and we don’t get a jump in the dose across the interface lumen/wall in the target area. § 6 presents some numerical simulations for a stent with 1, 6, 12, 24, 48, 96, 192, 384 struts, and the symtotic case for \(\rho\) equal to 0.1, 0.2, 0.5 and 0.9. A table of the integral of the dose in the wall of the artery is presented as a function of the ratio \(\rho\) and the number of struts \(N\). Complete results and details on the numerical implementation will be available in a more specialized paper. This paper concentrates on the theory. § 7 discusses some design issues and open problems for stents which do not necessarily have a periodic pattern.

2 Equations for the concentration of product

Consider a section of cylindric artery of length \(H\) where the stent will be deployed. For simplicity assume that the artery is made up of two homogeneous regions: the lumen and the wall. More realistic mutilayer models of the wall can be considered [10], but this will be sufficient for our purposes. Before the insertion of the stent, the lumen is assumed to be the open cylinder

\[
C_R = \{(x_1, x_2, z) : x_1^2 + x_2^2 < R^2, \quad 0 < z < H\}
\]  

of radius \(R\) and length \(H\). The wall is the open domain

\[
C_{R+E} \setminus C_R
\]  

between the closed cylinder \(\overline{C_R}\) and the open cylinder

\[
C_{R+E} = \{(x_1, x_2, z) : x_1^2 + x_2^2 < (R+E)^2, \quad 0 < z < H\}
\]  

of radius \(R+E\) and length \(H\), where \(E\) is the radial thickness of the wall.

A stent of zero thickness will be deployed in the target area

\[
\tilde{\Sigma} = \{(x_1, x_2, z) : x_1^2 + x_2^2 = R^2, \quad \frac{H - L_s}{2} \leq z \leq \frac{H + L_s}{2}\}
\]  

of the interface between the lumen and the wall. The length of the target region is \(L_s < H\). The actual stent will be characterized by a closed subset \(\tilde{\Sigma}_s\) of the surface \(\tilde{\Sigma}\) (cf. for instance one of the periodic patterns in Figure 2).

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{stent_patterns.png}
\caption{Typical patterns of stents.}
\end{figure}

By construction the region \(\tilde{\Sigma}\) is centered in \(H/2\) at equal distance

\[
z_0 = (H - L_s)/2 > 0
\]  

from the boundaries of \(C_{R+E}\) in \(z = 0\) and \(z = H\) which are artificial boundaries introduced for the analysis of the problem. The length \(H\) of the section of the artery is assumed to be sufficiently longer than \(L_s\) so that the effect of

\(^6\)When the number of struts goes to infinity and the width of each strut goes to zero while the surface of the target area, the ratio \(\rho\), and the mass per unit area of product are kept fixed.
introducing an artificial boundary in \( z = 0 \) and \( z = H \) is negligible. It also means that the region \( \tilde{\Sigma} \) does not touch the boundaries of the cylinder \( C_{R+E} \) in \( z = 0 \) and \( z = H \).

The zero-thickness stent is coated with a polymer. Coating can exist on both sides of the stent. The regions occupied by the polymer are denoted

\[
\tilde{\Omega}_s^+ \coloneqq \left\{ (x_1, x_2, z) : \left( \frac{R (x_1, x_2)}{\sqrt{x_1^2 + x_2^2}}, z \right) \in \tilde{\Sigma}_s \text{ and } R < \sqrt{x_1^2 + x_2^2} < R + e^+ \right\},
\]

\[
\tilde{\Omega}_s^- \coloneqq \left\{ (x_1, x_2, z) : \left( \frac{R (x_1, x_2)}{\sqrt{x_1^2 + x_2^2}}, z \right) \in \tilde{\Sigma}_s \text{ and } R - e^- < \sqrt{x_1^2 + x_2^2} < R \right\},
\]

\[
\tilde{\Omega}_s \coloneqq \tilde{\Omega}_s^+ \cup \tilde{\Omega}_s^-.
\]

where \( e^+ \) and \( e^- \) are the respective thicknesses of the coating on the upper and lower surfaces of \( \tilde{\Sigma}_s \). Once the stent is deployed, the open regions \( \tilde{\Omega}_l \) and \( \tilde{\Omega}_w \) occupied by the lumen and the wall are

\[
\tilde{\Omega}_l \coloneqq C_R \backslash \tilde{\Sigma}_s
\]

\[
\tilde{\Omega}_w \coloneqq C_{R+E} \backslash \tilde{\Sigma}_s \cup C_R.
\]

Mathematically \( \tilde{\Omega}_l, \tilde{\Omega}_w \) and \( \tilde{\Omega}_s^+ \) are open domains in \( \mathbb{R}^3 \).

Figure 3: The lumen \( \tilde{\Omega}_l \), the stent \( \tilde{\Omega}_s \) and the wall \( \tilde{\Omega}_w \) in \( \mathbb{R}^3 \) and the associated 2-dimensional generating surfaces \( \Omega_l \) for the lumen, \( \Omega_s \) for the stent, and \( \Omega_w \) for the wall

![Diagram showing the lumen, stent, and wall domains](image)

It is the design of the set \( \tilde{\Sigma}_s \) which is the ultimate objective of the analysis. There are several aspects to this design. For instance, the stent has to be mechanically strong enough to keep the lumen open. In this paper we neglect this aspect and concentrate on the delivery of the product to the wall. For simplicity we start with a periodic
stent (in the \(z\)-direction) with cylindric symmetry. Further assume that it is only coated on its upper surface, that is \(e^z = 0\), \(\Omega^w_s = \emptyset\), and \(\Omega_s = \Omega^w_s\) (cf. Figure 3). In addition, the stent is assumed to be a set of \(N\) equally spaced rings of width \(\lambda\) and zero thickness with coating of thickness \(e^z\), that is, the region between the radius \(R\) and the radius \(R + e\). The centerlines of the rings are located at coordinates

\[
\{ z_i : 1 \leq i \leq N \} , \quad z_0 < z_1 < z_2 < \ldots < z_N < z_0 + L_s ,
\]

along the \(z\)-axis as shown in the second Figure 3 with \(z_i + \lambda < z_{i+1}\). Thus all the rings are contained in the target region \(\tilde{\Sigma}\). The domains \(\tilde{\Omega}_l\), \(\tilde{\Omega}_w\), and \(\tilde{\Omega}_s\) are generated by rotation of the two-dimensional open domains \(\Omega_l, \Omega_w, \Omega_s\) and the interfaces \(\Sigma\) and \(\Sigma_s\) (cf. Figure 3) around the axis \(\Gamma_0\). In the sequel the tilded object will always denote the three-dimensional object generated by rotation around the axis \(\Gamma_0\).

The boundary \(\Gamma_l = \partial \tilde{\Omega}_l\) of the lumen \(\tilde{\Omega}_l\) is made up of four parts:

- \(\tilde{\Sigma}_s\), the interface between \(\tilde{\Omega}_l\) and the region \(\tilde{\Omega}_s\) occupied by the polymer;
- \(\tilde{\Gamma}_{lw}\), the interface between \(\tilde{\Omega}_l\) and the region \(\tilde{\Omega}_w\) occupied by the wall;
- \(\tilde{\Gamma}_{li}\), the part of the boundary of \(\tilde{\Omega}_l\) where the blood comes in;
- \(\tilde{\Gamma}_{lo}\), the part of the boundary of \(\tilde{\Omega}_l\) where the blood comes out.

The corresponding parts of the generating surface are \(\Sigma_s, \Gamma_{lw}, \Gamma_{li}, \Gamma_{lo}\), and the centerline or axis \(\Gamma_0\) of the cylinders (cf. Figure 4).

The boundary \(\Gamma_w = \partial \tilde{\Omega}_w\) of the wall \(\tilde{\Omega}_w\) is made up of five parts:

- \(\tilde{\Gamma}_{lw}\), the interface between \(\tilde{\Omega}_w\) and the region \(\tilde{\Omega}_l\) occupied by the lumen;
- \(\tilde{\Gamma}_{ws}\), the interface between \(\tilde{\Omega}_w\) and the region \(\tilde{\Omega}_s\) occupied by the polymer;
- \(\tilde{\Gamma}_{wi}\), the part of the boundary of \(\tilde{\Omega}_w\) where \(z = 0\);
- \(\tilde{\Gamma}_{wo}\), the part of the boundary of \(\tilde{\Omega}_w\) where \(z = H\);
- \(\tilde{\Gamma}_{R+E}\), the outer lateral boundary of the cylinder of radius \(R + E\).

The corresponding parts of the generating surface are \(\Gamma_{lw}, \Gamma_{ws}, \Gamma_{wi}, \Gamma_{wo}\), and the upper boundary \(\Gamma_{R+E}\) at \(r = R + E\) (cf. Figure 4).

The fluid (here the blood) in the lumen is assumed to be incompressible

\[
\text{div } u = 0 \text{ in } \tilde{\Omega}_l ,
\]

where \(u\) is the \textit{velocity of the fluid}. Further assume that

\[
(2.10) \quad u \cdot n_l \leq 0 \text{ on } \tilde{\Gamma}_{li} \text{ and } u \cdot n_l \geq 0 \text{ on } \tilde{\Gamma}_{lo} \quad u \cdot n_l = 0 \text{ or } u = 0 \text{ on } \Sigma_s \cup \tilde{\Gamma}_{lw} .
\]

Condition (2.10) means that the blood is coming in through the cross-section \(\tilde{\Gamma}_{li}\) and coming out through the cross-section \(\tilde{\Gamma}_{lo}\). The velocity \(u\) and the pressure \(p\) will also verify the Navier-Stokes equation with the condition \(u = 0\) on \(\Sigma_s \cup \tilde{\Gamma}_{lw}\). Yet the diffusion-transport equations will still make sense under the weaker condition \(u \cdot n_l = 0\) on \(\Sigma_s \cup \tilde{\Gamma}_{lw}\). This would correspond to a different model of the blood circulation. For instance experimental data show that the white corpuscles are rolling near the surface of the wall and that the red corpuscles in the center of the lumen are \textit{slipping} on them.
Assume that the concentration \( c(x, t) \) of product is given by the diffusion-transport equation (lumen) and diffusion equations (wall and the polymer):

\[
\begin{align*}
\frac{\partial c}{\partial t} &= \text{div}(D_w \nabla c) \text{ in } \tilde{\Omega}_w, \\
\frac{\partial c}{\partial t} &= \text{div}(D_s \nabla c) \text{ in } \tilde{\Omega}_s, \\
\frac{\partial c}{\partial t} + u \cdot \nabla c &= \text{div}(D_l \nabla c) \text{ in } \tilde{\Omega}_l, \\
\end{align*}
\]

where \( D_w, D_s, \) and \( D_l \), are the respective diffusion constants in the wall, the polymer, and the lumen. The \textit{inner product} of two vectors \( u = (u_1, u_2, u_3) \) and \( v = (v_1, v_2, v_3) \) in \( \mathbb{R}^3 \) is denoted

\[
\langle u \cdot v \rangle \overset{\text{def}}{=} \sum_{i=1}^{3} u_i v_i.
\]

In view of the incompressibility condition (2.9), equation (2.14) can be rewritten

\[
\frac{\partial c}{\partial t} = \text{div}(D_l \nabla c - cu) \text{ in } \tilde{\Omega}_l,
\]

since \( \text{div} u = 0 \) implies \( \text{div}(cu) = \nabla c \cdot u + c \text{div} u = \nabla c \cdot u \).

The boundary conditions on \( c \) are

\[
\begin{align*}
\text{wall} & \quad \left\{ \begin{array}{l}
\frac{\partial c}{\partial n_w} = 0 \text{ on } \tilde{\Gamma}_{wi} \cup \tilde{\Gamma}_{wo} \cup \tilde{\Gamma}_{R+E} \\
\frac{\partial c}{\partial n_l} - u \cdot n_l c = 0 \text{ or } c = 0 \text{ on } \tilde{\Gamma}_{li} \\
\frac{\partial c}{\partial n_l} = 0 \text{ on } \tilde{\Gamma}_{lo},
\end{array} \right.
\end{align*}
\]

(2.16)

\[
\text{lumen}
\]

where \( n_w, n_l \) and \( n_s \) are the respective unit outward normals to \( \tilde{\Omega}_w, \tilde{\Omega}_l, \) and \( \tilde{\Omega}_s \). The first boundary conditions involving \( u \) at the entry \( \tilde{\Gamma}_{li} \) of the lumen is a \textit{transparent condition} similar to the ones used in [2]. It allows for some backward diffusion at the interface \( \tilde{\Gamma}_{li} \). In that case the first condition (2.10) has to be strengthened to

\[
\exists \beta > 0 \text{ such that } -u \cdot n_l \geq \begin{cases} 
0 & \text{on } \tilde{\Gamma}_{li} \setminus \tilde{\gamma}_{li} \\
\beta & \text{on } \tilde{\gamma}_{li} \subset \tilde{\Gamma}_{li} \text{ and } u \cdot n_l \geq 0 \text{ on } \tilde{\Gamma}_{lo}, 
\end{cases}
\]

(2.17)

where \( \tilde{\gamma}_{li} \) is some fixed subarea of the cross-section \( \tilde{\Gamma}_{li} \) around its center. The second case with \( c = 0 \) on \( \tilde{\Gamma}_{li} \) corresponds to the assumption that \( \tilde{\Gamma}_{li} \) is chosen sufficiently far from the region of the stent \( \tilde{\Sigma}_s \) that the concentration \( c \) on \( \tilde{\Gamma}_{li} \) can be taken as zero.

The conditions on \( c \) at the interfaces are

\[
\begin{align*}
\text{wall/polymer} & \quad D_w \frac{\partial c}{\partial n_w} + D_s \frac{\partial c}{\partial n_s} = 0 \text{ on } \tilde{\Gamma}_{ws} \\
\text{wall/lumen} & \quad D_w \frac{\partial c}{\partial n_w} + D_l \frac{\partial c}{\partial n_l} = 0 \text{ on } \tilde{\Gamma}_{lw} \\
\text{polymer/lumen} & \quad \frac{\partial c^+}{\partial n_s} = 0 \text{ and } \frac{\partial c^-}{\partial n_l} = 0 \text{ on } \tilde{\Sigma}_s.
\end{align*}
\]

(2.18)

Recall that the lumen is isolated from the polymer and that there is an upper trace \( c^+ \) and a lower trace \( c^- \) of the concentration on the two sides of the interface \( \tilde{\Sigma}_s \). \( \tilde{\Sigma}_s \) is made up of the \( N \) ring-shaped cracks in the three-dimensional domain and different boundary conditions are specified on each side.

The initial condition is

\[
\begin{align*}
c(0, x) = \begin{cases} 
c_0(x), & \text{in } \tilde{\Omega}_s \\
0, & \text{in } \tilde{\Omega}_w \cup \tilde{\Omega}_l,
\end{cases}
\end{align*}
\]

(2.19)

for some positive function \( c_0(x) \geq 0 \) representing the initial concentration of the product at time 0 in the polymer.
3 Mathematical models for the dose

The dose is the cumulative concentration over time in a given position $x$ over all times ranging from 0 to infinity, that is

$$q(x) \overset{\text{def}}{=} \int_0^\infty c(t, x) \, dt. \quad (3.1)$$

3.1 Equations for the dose

Since all our equations are linear, the equations, boundary conditions and interface conditions for $q$ are readily obtained from the ones for $c$. The equations for the dose $q(x)$ are

$$\text{div}(D_w \nabla q) = 0 \text{ in } \tilde{\Omega}_w \quad (3.2)$$

$$\text{div}(D_s \nabla q) = -c_0 \text{ in } \tilde{\Omega}_s \quad (3.3)$$

$$\text{div}(D_l \nabla q - qu) = 0 \text{ in } \tilde{\Omega}_l. \quad (3.4)$$

The boundary conditions are

$$\begin{align*}
\text{wall} & \quad \frac{\partial q}{\partial n_w} = 0 \text{ on } \tilde{\Gamma}_{wI} \cup \tilde{\Gamma}_{we} \cup \tilde{\Gamma}_{R+E} \\
\text{lumen} & \quad \frac{\partial q}{\partial n_l} = 0 \text{ on } \tilde{\Gamma}_{lo}.
\end{align*} \quad (3.5)$$

Again the choice of the first transparent condition on $\tilde{\Gamma}_{li}$ requires the stronger condition (2.17) on $u$. The conditions at the interfaces are

$$\begin{align*}
\text{wall/polymer} & \quad D_w \frac{\partial q}{\partial n_w} + D_s \frac{\partial q}{\partial n_s} = 0 \text{ on } \tilde{\Gamma}_{ws} \\
\text{wall/lumen} & \quad D_w \frac{\partial q}{\partial n_w} + D_l \frac{\partial q}{\partial n_l} = 0 \text{ on } \tilde{\Gamma}_{lw} \\
\text{polymer/lumen} & \quad \frac{\partial q^+}{\partial n_s} = 0 \text{ and } \frac{\partial q^-}{\partial n_l} = 0 \text{ on } \tilde{\Sigma}_s. \quad (3.6)
\end{align*}$$

3.2 Variational equation for the dose

In this section we construct a variational formulation of the equations of the dose over the domain

$$\tilde{\Omega} \overset{\text{def}}{=} \left\{ (x_1, x_2, z) : |x_1|^2 + |x_2|^2 < (R + E)^2, 0 < z < H \right\} \setminus \tilde{\Sigma}_s, \quad (3.7)$$

that is, $C_{R+E} \setminus \tilde{\Sigma}_s$. It is a bounded connected open domain with 2-dimensional cracks along the polymer/lumen interfaces $\tilde{\Sigma}_s$. This is not a Lipschitzian domain.

The associated space of solution is

$$V(\tilde{\Omega}) \overset{\text{def}}{=} \begin{cases} H^1(\tilde{\Omega}) & \text{with condition (2.17) on } u \\ \left\{ v \in H^1(\tilde{\Omega}) : v|_{\tilde{\Gamma}_{li}} = 0 \right\} & \text{with condition (2.10) on } u. \end{cases} \quad (3.8)$$

First multiply the equations for $q$ by a test function $v \in V(\tilde{\Omega})$, integrate by parts using Green’s theorem, and sum up everything to get cancellations using the boundary and interface conditions:

$$0 = -\int_{\tilde{\Omega}_w} \text{div}(D_w \nabla q) \, v \, dx = \int_{\tilde{\Omega}_w} D_w \nabla q \cdot \nabla v \, dx - \int_{\partial \tilde{\Omega}_w} D_w \frac{\partial q}{\partial n_w} \, v \, d\Gamma \quad (3.9)$$
Figure 5: Schematic representation of the lumen, the polymer and the wall.

\[
\begin{align*}
\int_{\Omega_s} c_0 v \, dx &= - \int_{\Omega_s} \text{div}(D_s \nabla q) v \, dx = \int_{\Omega_s} D_s \nabla q \cdot \nabla v \, dx - \int_{\partial \Omega_s} D_s \frac{\partial q}{\partial n_s} v \, d\Gamma \\
0 &= - \int_{\Omega_l} \text{div}(D_l \nabla q - qu) v \, dx \\
&= \int_{\Omega_l} (D_l \nabla q - qu) \cdot \nabla v \, dx - \int_{\partial \Omega_l} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma.
\end{align*}
\]

Now turn to the computation of the boundary terms. For the wall

\[
\int_{\partial \Omega_w} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma = \int_{\Gamma_{ws}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma + \int_{\Gamma_{lw}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma + \int_{\Gamma_{wa}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma \\
+ \int_{\Gamma_{lw}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma + \int_{\Gamma_{wa}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma + \int_{\Gamma_{wa}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma \\
= \int_{\Gamma_{ws}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma + \int_{\Gamma_{lw}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma;
\]

for the polymer

\[
\int_{\partial \Omega_s} D_s \frac{\partial q}{\partial n_s} v \, d\Gamma = \int_{\Gamma_{ws}} D_s \frac{\partial q}{\partial n_s} v \, d\Gamma + \int_{\Gamma_{lz}} D_s \frac{\partial q}{\partial n_s} v \, d\Gamma;
\]

for the lumen

\[
\begin{align*}
\int_{\partial \Omega_l} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma &= \int_{\Gamma_{lw}} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma + \int_{\Gamma_{lo}} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma \\
+ \int_{\Gamma_{lw}} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma + \int_{\Gamma_{io}} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma \\
= \int_{\Gamma_{lw}} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma + \int_{\Gamma_{io}} \left( D_l \frac{\partial q}{\partial n_l} - u \cdot n_l q \right) v \, d\Gamma.
\end{align*}
\]
Sum up the previous identities and use the conditions at the interfaces

\[
\iint_{\Omega_w} D_w \nabla q \cdot \nabla v \, dx + \iint_{\Omega_s} D_s \nabla q \cdot \nabla v \, dx + \iint_{\Omega_l} (D_l \nabla q - qu) \cdot \nabla v \, dx = \iint_{\Omega_s} c_0 v \, dx + \iint_{\Gamma_{ws}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma + \iint_{\Gamma_{iw}} D_w \frac{\partial q}{\partial n_w} v \, d\Gamma \\
+ \iint_{\Gamma_{ws}} D_s \frac{\partial q}{\partial n_s} v \, d\Gamma + \iint_{\Gamma_{is}} D_s \frac{\partial q}{\partial n_s} v \, d\Gamma \\
+ \iint_{\Gamma_{lw}} D_l \frac{\partial q}{\partial n_l} v \, d\Gamma + \iint_{\Gamma_{il}} D_l \frac{\partial q}{\partial n_l} v \, d\Gamma - \iint_{\Gamma_{lo}} u \cdot n_l q v \, d\Gamma \\
= \iint_{\Omega_s} c_0 v \, dx - \iint_{\Gamma_{lo}} u \cdot n_l q v \, d\Gamma.
\]

Introduce the following bilinear form

\[
a(q, v) \overset{\text{def}}{=} \int_{\Omega_w} D_w \nabla q \cdot \nabla v \, dx + \int_{\Omega_s} D_s \nabla q \cdot \nabla v \, dx + \int_{\Omega_l} (D_l \nabla q - qu) \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q v \, d\Gamma.
\]

Then \( q \in V(\hat{\Omega}) \) must verify the variational equation

\[
(3.12) \quad \forall v \in V(\hat{\Omega}), \quad a(q, v) = \iint_{\hat{\Omega}_s} c_0 v \, dx.
\]

The bilinear form can be rewritten as

\[
a(q, v) = \int_{\hat{\Omega}} D \nabla q \cdot \nabla v \, dx - \int_{\hat{\Omega}_l} q u \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q v \, d\Gamma,
\]

by introducing the space-dependent diffusion defined almost everywhere on \( \hat{\Omega} \)

\[
D(x) \overset{\text{def}}{=} \begin{cases} 
D_w & \text{if } x \in \hat{\Omega}_w \\
D_s & \text{if } x \in \hat{\Omega}_s \\
D_l & \text{if } x \in \hat{\Omega}_l.
\end{cases}
\]

The bilinear form \( a \) is not symmetrical, but it is coercive on \( V(\hat{\Omega}) \) under the two boundary conditions (2.10) and (2.11) on the velocity field \( u \) and \( q = 0 \) on \( \hat{\Gamma}_l \) and under the two boundary conditions (2.17) and (2.11) on the velocity field \( u \) for the transparent condition on \( q \). Indeed let \( \alpha > 0 \) be the minimum of \( D_w, D_s, \) and \( D_l \). Therefore using the fact that \( \text{div} \ u = 0 \)

\[
a(q, q) = \int_{\hat{\Omega}} D \nabla q \cdot \nabla q \, dx - \int_{\hat{\Omega}_l} q u \cdot \nabla q \, dx + \int_{\Gamma_{lo}} u \cdot n_l |q|^2 \, d\Gamma \\
\geq \alpha \int_{\hat{\Omega}} |\nabla q|^2 \, dx - \int_{\hat{\Omega}_l} q u \cdot \nabla q \, dx + \int_{\Gamma_{lo}} u \cdot n_l |q|^2 \, d\Gamma \\
= \alpha \int_{\hat{\Omega}} |\nabla q|^2 \, dx - \int_{\hat{\Omega}_l} \frac{1}{2} u \cdot \nabla |q|^2 \, dx + \int_{\Gamma_{lo}} u \cdot n_l |q|^2 \, d\Gamma \\
= \alpha \int_{\hat{\Omega}} |\nabla q|^2 \, dx - \frac{1}{2} \int_{\hat{\Omega}_l} \text{div}(u |q|^2) \, dx + \frac{1}{2} \int_{\hat{\Omega}_l} |q|^2 \, dx \\
+ \int_{\Gamma_{lo}} u \cdot n_l |q|^2 \, d\Gamma \\
= \alpha \int_{\hat{\Omega}} |\nabla q|^2 \, dx - \frac{1}{2} \int_{\Gamma_{lw}} u \cdot n_l |q|^2 \, d\Gamma + \int_{\Gamma_{il}} u \cdot n_l |q|^2 \, d\Gamma.
\]

Since \( u \cdot n_l = 0 \) on \( \hat{\Sigma}_s \cup \hat{\Gamma}_{lw} \) and

\[
u \cdot n_l \leq 0 \text{ on } \hat{\Gamma}_l \text{ and } u \cdot n_l \geq 0 \text{ on } \hat{\Gamma}_{lo}
\]

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where \( z \) the new domain occupied by the polymer as struts and \( \lambda \) made up of \( N \).

In this section we construct new equations for the dose as the thickness of the polymer goes to zero while keeping the thickness of the polymer.

4 Equations for the dose as the thickness of the polymer goes to zero

Start from the zero-thickness stent

4.1 Parametrization of the thickness

Start from the zero-thickness stent

made up of \( N \) identical equally spaced flat rings with \( L > 0 \) the distance between the center of two consecutive struts, \( \lambda, 0 < \lambda < L \), the width of the rings, and \( \epsilon > 0 \) the thickness of the polymer.

4.1 Parametrization of the thickness

Start from the zero-thickness stent

(4.1) 

made up of \( N \) identical equally spaced flat rings with \( L > 0 \) the distance between the centerlines of two consecutive struts and \( \lambda, 0 < \lambda < L \), the width of the rings. Let \( \epsilon, 0 < \epsilon \leq \epsilon \), be the variable thickness of the polymer and define the new domain occupied by the polymer as

where \( z_i \) is the position of the \( i \)-th strut along the \( z \)-axis. This induces a new domain for the wall

\[
\tilde{\Omega}_w \coloneqq \left\{ (x_1, x_2, z) : \begin{array}{l}
R^2 < |x_1|^2 + |x_2|^2 < (R + \epsilon)^2 \\
0 < z < H \\
0 < z < H \quad \text{and} \quad |z - z_i| \leq \lambda/2
\end{array} \right\}.
\]

But the last term on the right-hand side is an equivalent norm on \( H^1(\tilde{\Omega}) \) and \( a \) is coercive on it. Therefore, by the Lax-Milgram Theorem (cf. [8]), there exists a unique \( v \in V(\tilde{\Omega}) \) solution of the variational equation (3.12).

4 Equations for the dose as the thickness of the polymer goes to zero

In this section we construct new equations for the dose as the thickness of the polymer goes to zero while keeping the total mass of product constant in the polymer. It is obtained from the stent made up of \( N \) identical equally spaced flat rings with \( L > 0 \) the distance between the center of two consecutive struts, \( \lambda, 0 < \lambda < L \), the width of the rings, and \( \epsilon > 0 \) the thickness of the polymer.
For \( \varepsilon = 0 \), \( \tilde{\Omega}_s^0 = \emptyset \) and
\[
\tilde{\Omega}_w^0 = \left\{ (x_1, x_2, z) : \frac{R^2}{2} < |x_1|^2 + |x_2|^2 < (R + E)^2 \right\} = C_{R+E} \setminus C_R.
\]

Since, up to a set of zero measure, \( \tilde{\Omega}_w^\varepsilon \cup \tilde{\Omega}_s^\varepsilon = \tilde{\Omega}_w^0 \) and \( \tilde{\Omega} = \tilde{\Omega}_w^\varepsilon \cup \tilde{\Omega}_s^\varepsilon \cup \tilde{\Omega}_l = \tilde{\Omega}_w^0 \cup \tilde{\Omega}_l \), it will be convenient to define the new space-dependent diffusion \( D^\varepsilon \) almost everywhere on \( \tilde{\Omega} \) as
\[
D^\varepsilon(x) \overset{\text{def}}{=} \begin{cases} 
\quad D_w & \text{if } x \in \tilde{\Omega}_w^\varepsilon \\
\quad D_s & \text{if } x \in \tilde{\Omega}_s^\varepsilon \\
\quad D_l & \text{if } x \in \tilde{\Omega}_l
\end{cases}
\]
and the new bilinear form
\[
\alpha^\varepsilon(q, v) \overset{\text{def}}{=} \int_{\tilde{\Omega}} D^\varepsilon \nabla q \cdot \nabla v \, dx - \int_{\tilde{\Omega}_l} q u \cdot \nabla v \, dx + \int_{\tilde{\Gamma}_l} u \cdot n_l q v \, d\Gamma
\]
which turns out to be coercive with the same constant (independent of \( \varepsilon \)) as for the bilinear form \( \alpha(q, v) \) on \( V(\tilde{\Omega}) \). Here to make the connection with the notation of the previous sections the bilinear form \( \alpha(q, v) \) is now equal to \( \alpha^\varepsilon(q, v) \). Note that the parameter \( \varepsilon \) only occurs in the definition of the diffusion coefficient \( D^\varepsilon \) and not in the domains over which the integrals are defined.

The initial linear right-hand side
\[
\ell(v) \overset{\text{def}}{=} \int_{\tilde{\Omega}_s} c_0 v \, dx
\]
(for the thickness \( e \)) has to be adjusted in order to deliver the same mass of product for a thickness \( \varepsilon \). Assume that the initial concentration \( c_0 \) is constant in \( \tilde{\Omega}_s \), that is, the total mass of product in the polymer is
\[
m \overset{\text{def}}{=} c_0 \int_{\tilde{\Omega}_s} dx = c_0 \sum_{i=1}^N \int_{z_i - \lambda/2}^{z_i + \lambda/2} dz \int_R^{R+\varepsilon} 2\pi r \, dr
\]
\[
= c_0 N \lambda \pi \left[ (R + e)^2 - R^2 \right] = c_0 N \lambda \pi e (2R + e).
\]
Define the new concentration \( c_0^\varepsilon \) such that the total mass remains \( m \) over the new domain \( \tilde{\Omega}_s^\varepsilon \), that is,
\[
m = \int_{\tilde{\Omega}_s^\varepsilon} c_0^\varepsilon \, dx = \sum_{i=1}^N \int_{z_i - \lambda/2}^{z_i + \lambda/2} dz \int_R^{R+\varepsilon} c_0^\varepsilon 2\pi r \, dr
\]
\[
= c_0^\varepsilon N \lambda \pi \left[ (R + e)^2 - R^2 \right] = c_0^\varepsilon N \lambda \pi e (2R + e).
\]
In the domain \( \tilde{\Omega}_s^\varepsilon \) occupied by the polymer, choose the new concentration
\[
c_0^\varepsilon \overset{\text{def}}{=} \frac{1}{\varepsilon} \frac{1}{\lambda (2R + e) \pi N} m
\]
and the corresponding linear right-hand side
\[
\ell^\varepsilon(v) \overset{\text{def}}{=} \int_{\tilde{\Omega}_s^\varepsilon} c_0^\varepsilon v \, dx.
\]

The new variational problems indexed by \( \varepsilon \), \( 0 < \varepsilon \leq e \), are
\[
\exists q^\varepsilon \in V(\tilde{\Omega}), \forall v \in V(\tilde{\Omega}), \quad \alpha^\varepsilon(q^\varepsilon, v) = \ell^\varepsilon(v),
\]
where \( \tilde{\Omega} \) is the open cylinder \( C_{R+E} \) minus the stent \( \tilde{\Sigma}_s \) as defined in (3.7).
4.2 Limiting process

The next step is to determine the limit \( q^0 \) of the dose \( q^\varepsilon \) as \( \varepsilon \) goes to zero and to show that it is a solution of a new variational equation.

**Theorem 4.1.** As \( \varepsilon > 0 \) goes to zero, the solution \( q_\varepsilon \in V(\tilde{\Omega}) \) of (4.4) weakly converges to the solution \( q^0 \in V(\tilde{\Omega}) \) of the variational equation

\[
\forall v \in V(\tilde{\Omega}), \quad a^0(q^0, v) = \ell^0(v),
\]

where

\[
\ell^0(v) \overset{\text{def}}{=} \int_{\Sigma_s} c_s v^+ \, dx, \quad c_s \overset{\text{def}}{=} \frac{1}{\lambda 2 R \pi N},
\]

\[
a^0(q^0, v) \overset{\text{def}}{=} \int_{\Omega} \nabla q^0 \cdot D^0 \nabla v \, dx - \int_{\Omega_l} q^0 u \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q^0 v \, d\Gamma.
\]

are the respective continuous linear and bilinear forms on \( V(\tilde{\Omega}) \), \( c_s \) is the surface density of the product in \( \text{kg/m}^2 \), \( v^+ \) is the trace of \( v \) on the upper side of \( \Sigma_s \), and \( D^0 \) is the diffusion defined almost everywhere in \( \Omega \).

\[
D^0(x) \overset{\text{def}}{=} \begin{cases} 
D_w & \text{if } x \in \tilde{\Omega}_w^0 \\
D_l & \text{if } x \in \tilde{\Omega}_l.
\end{cases}
\]

**Proof.** (i) (Convergence of \( \ell^\varepsilon \) to \( \ell^0 \)). We first prove that the linear form \( \ell^\varepsilon \) is uniformly bounded with respect to \( \varepsilon \). Consider the volume integral which is rewritten in cylindric coordinates

\[
\int_{\tilde{\Omega}^\varepsilon} v \, dx = \sum_{i=1}^N \int_{z_i-\lambda/2}^{z_i+\lambda/2} dz \int_{R}^{R+\varepsilon} \int_0^{2\pi} dr \int_0^{2\pi} d\theta v(r, \theta, z).
\]

Then, using the identity

\[
v(r, \theta, z) = v(R, \theta, z) + \int_{R}^{r} \frac{\partial v}{\partial \rho}(\rho, \theta, z) \, d\rho,
\]

we get

\[
\int_{\tilde{\Omega}^\varepsilon} v \, dx = \sum_{i=1}^N \int_{z_i-\lambda/2}^{z_i+\lambda/2} dz \int_{R}^{R+\varepsilon} \int_0^{2\pi} dr \int_0^{2\pi} d\theta v(R^+, \theta, z)
\]

\[
+ \sum_{i=1}^N \int_{z_i-\lambda/2}^{z_i+\lambda/2} dz \int_{R}^{R+\varepsilon} \int_0^{2\pi} dr \int_0^{2\pi} d\theta \int_{R}^{r} \frac{\partial v}{\partial \rho}(\rho, \theta, z) \, d\rho
\]

\[
= \frac{(R+\varepsilon)^2 - R^2}{2} \sum_{i=1}^N \int_{z_i-\lambda/2}^{z_i+\lambda/2} dz \int_0^{2\pi} d\theta v(R^+, \theta, z)
\]

\[
+ \sum_{i=1}^N \int_{z_i-\lambda/2}^{z_i+\lambda/2} dz \int_{R}^{R+\varepsilon} \int_{\rho}^{R+\varepsilon} dr \int_0^{2\pi} d\theta \frac{\partial v}{\partial \rho}(\rho, \theta, z)
\]
But

\[
\int_{\tilde{\Omega}} v \, dx = \sum_{i=1}^{N} \int_{z_{i-\lambda'/2}}^{z_{i+\lambda'/2}} \int_{0}^{2\pi} \, d\theta \, \varepsilon \frac{2R + \varepsilon}{2} v(R^+, \theta, z) \, dz
\]

\[
+ \sum_{i=1}^{N} \int_{z_{i-\lambda'/2}}^{z_{i+\lambda'/2}} \, dx \int_{0}^{2\pi} \, d\theta \int_{R}^{R+\varepsilon} (R + \varepsilon)^2 - \rho^2 \frac{\partial v}{\partial \rho}(\rho, \theta, z) \, d\rho
\]

\[
= \varepsilon \frac{(2R + \varepsilon)}{2R} \int_{\tilde{\Sigma}_s} v^+ \, d\Gamma
\]

\[
+ \sum_{i=1}^{N} \int_{z_{i-\lambda'/2}}^{z_{i+\lambda'/2}} \, dx \int_{R}^{R+\varepsilon} (R + \varepsilon)^2 - \rho^2 \frac{\partial v}{\partial \rho}(\rho, \theta, z) \, d\rho
\]

\[
= \varepsilon \frac{(2R + \varepsilon)}{2R} \int_{\tilde{\Omega}_s} v^+ \, dx
\]

\[
+ \sum_{i=1}^{N} \int_{z_{i-\lambda'/2}}^{z_{i+\lambda'/2}} \, dx \int_{R}^{R+\varepsilon} (R + \varepsilon)^2 - \rho^2 \frac{\partial v}{\partial \rho}(\rho, \theta, z) \, d\rho
\]

\[
\leq \frac{(2R + \varepsilon)}{2R} \int_{\tilde{\Omega}_s} |\nabla v| \, dx \leq \varepsilon \frac{(2R + \varepsilon)}{2R} \quad m(\tilde{\Omega}_s)^{1/2} \left\{ \int_{\tilde{\Omega}_s} |\nabla v|^2 \, dx \right\}^{1/2}.
\]

We finally get the following estimate

\[
\left| \int_{\tilde{\Omega}_s} v \, dx \right| \leq \varepsilon \frac{(2R + \varepsilon)}{2R} \left\{ \int_{\tilde{\Sigma}_s} v^+ \, d\Gamma \right\} + m(\tilde{\Omega}_s)^{1/2} \left\{ \int_{\tilde{\Omega}_s} |\nabla v|^2 \, dx \right\}^{1/2}.
\]

Now, using the above estimate and the definition of $c_0$,

\[
c_0 \varepsilon \frac{(2R + \varepsilon)}{2R} = \frac{m}{\lambda 2\pi R N},
\]

we finally get the following estimate for $\ell^\varepsilon(v)$

\[
|\ell^\varepsilon(v)| = \left| \int_{\tilde{\Omega}_s} c_0^\varepsilon v \, dx \right|
\]

\[
\leq \frac{1}{\lambda 2\pi R N} \left\{ \int_{\tilde{\Sigma}_s} v^+ \, d\Gamma \right\} + m(\tilde{\Omega})^{1/2} \left\{ \int_{\tilde{\Omega}} |\nabla v|^2 \, dx \right\}^{1/2}
\]

\[
\leq c \left[ \int_{\tilde{\Omega}} |\nabla v|^2 \, dx + \int_{\tilde{\Omega}} |v|^2 \, dx \right]^{1/2} = c\|v\|_{H^1(\tilde{\Omega})}
\]

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for some constant $c$ since the upper and lower traces of a function $v$ in $V(\tilde{\Omega})$ on the cylinder of radius $R$ (and hence the upper trace on $\Sigma_s$) are continuous. Therefore the linear forms $\ell^\varepsilon$ are indeed uniformly bounded.

As for the convergence, from the above estimates, it is easy to see that, for each $v$ in $V(\tilde{\Omega})$, $\ell^\varepsilon(v)$ converges to $\ell^0(v)$ since

$$|\ell^\varepsilon(v) - \ell^0(v)| \leq \frac{1}{\lambda 2\pi R N} m(\tilde{\Omega}^\varepsilon) \left[ \int_{\tilde{\Omega}} |\nabla v|^2 \, dx \right]^{1/2}$$

goes to zero because the volume $m(\tilde{\Omega}^\varepsilon)$ goes to zero as $\varepsilon$ goes to zero.

(ii) (Convergence of the $q^\varepsilon$’s). For each $\varepsilon$, $0 < \varepsilon \leq \epsilon$, problem (4.4) has a unique solution. We now go to the limit as $\varepsilon_n$ goes to zero in the variational equation for $q_n$. By uniform coercivity of $\alpha^\varepsilon$ and continuity of $\ell^\varepsilon$

$$\alpha\|q^\varepsilon\|^2_{H^1(\tilde{\Omega})} \leq a^\varepsilon(q^\varepsilon, q^\varepsilon) = \ell^\varepsilon(q^\varepsilon) \leq c \|q^\varepsilon\|_{H^1(\tilde{\Omega})}$$

and $\|q^\varepsilon\|_{H^1(\tilde{\Omega})} \leq c/\alpha$.

Therefore there exists $q^0 \in H^1(\tilde{\Omega})$ and a sequence $q_n = q^n$ such that

$$q_n \rightharpoonup q^0 \text{ in } H^1(\tilde{\Omega})-\text{weak.}$$

For the quadratic form

$$a^\varepsilon(q_n, v) \overset{\text{def}}{=} \int_{\tilde{\Omega}} \nabla q_n \cdot D^\varepsilon n \nabla v \, dx - \int_{\tilde{\Omega}_l} q_n u \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q_n v \, d\Gamma,$$

the last two terms converge to

$$\int_{\tilde{\Omega}_l} q_n u \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q_n v \, d\Gamma \rightarrow \int_{\tilde{\Omega}_l} q^0 u \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q^0 v \, d\Gamma.$$

As for the first term we first show that

$$D^\varepsilon n \nabla v \rightarrow D^0 \nabla v \text{ in } L^2(\tilde{\Omega})-\text{strong,}$$

where $D^0$ is given by (4.8). Indeed

\[
\begin{cases}
D^\varepsilon n \nabla v = 0, & \text{in } \tilde{\Omega}_w^\varepsilon \\
(D_s - D_w) \nabla v, & \text{in } \tilde{\Sigma}_s^\varepsilon \\
0, & \text{in } \tilde{\Omega}_l^\varepsilon
\end{cases}
\]

$$\Rightarrow \|D^\varepsilon n \nabla v\|_{L^2(\tilde{\Omega})} \leq \|D_s - D_w\| \|\nabla v\|_{L^2(\tilde{\Omega})} \rightarrow 0 \text{ as } \varepsilon \rightarrow 0.$$  

But, since $m(\tilde{\Omega}^\varepsilon)$ goes to zero, $D^\varepsilon n \nabla v$ strongly converges to $D^0 \nabla v$ and $q_n$ weakly converges to $q^0$, their inner product converges, and

$$a^\varepsilon(q_n, v) = \int_{\tilde{\Omega}} \nabla q_n \cdot D^\varepsilon n \nabla v \, dx - \int_{\tilde{\Omega}_l} q_n u \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q_n v \, d\Gamma$$

$$\rightarrow a^0(q^0, v) \overset{\text{def}}{=} \int_{\tilde{\Omega}} \nabla q^0 \cdot D^0 \nabla v \, dx - \int_{\tilde{\Omega}_l} q^0 u \cdot \nabla v \, dx + \int_{\Gamma_{lo}} u \cdot n_l q^0 v \, d\Gamma.$$  

Combining this result with the convergence of the linear form $\ell^\varepsilon(v)$ to $\ell^0(v)$ the function $q^0 \in V(\tilde{\Omega})$ is a solution of the variational equation

$$\forall v \in V(\tilde{\Omega}), \quad a^0(q^0, v) = \ell^0(v).$$

The bilinear form $a^0$ is coercive and the linear form $\ell^0$ is continuous for the same constants. Therefore the solution is unique and any weakly converging subsequence of $\{q^\varepsilon\}$ converges to the unique $q^0$ in $V(\tilde{\Omega})$. Hence $q^\varepsilon$ weakly converges to $q^0$ in $V(\tilde{\Omega})$ as $\varepsilon$ goes to zero.  

\[ \square \]
4.3 Equations for $q^0$

From the variational equation (4.5) for $q^0$ we get the following set of equations for the dose $q^0(x, t)$

\[
\text{div}(D_w \nabla q^0) = 0 \text{ in } \tilde{\Omega}_w^0 \tag{4.9}
\]
\[
\text{div}(D_l \nabla q^0 - q^0 u) = 0 \text{ in } \tilde{\Omega}_l. \tag{4.10}
\]

The boundary conditions are

\[
\text{wall} \quad \begin{cases} 
\frac{\partial q^0}{\partial n_w} = 0 & \text{on } \tilde{\Gamma}_{wi} \cup \tilde{\Gamma}_{wo} \cup \tilde{\Gamma}_{R+E} \\
D_w \frac{\partial q^0}{\partial n_w} = c_s & \text{on } \tilde{\Sigma}_s \tag{4.11}
\end{cases}
\]

\[
\text{lumen} \quad \begin{cases} 
D_l \frac{\partial q^0}{\partial n_l} - u \cdot n_l q^0 = 0 \text{ or } q^0 = 0 & \text{on } \tilde{\Gamma}_{li} \\
\frac{\partial q^0}{\partial n_l} = 0 & \text{on } \tilde{\Sigma}_s
\end{cases}
\]

The condition at the interface is

\[
\text{wall/lumen} \quad D_w \frac{\partial q^0}{\partial n_w} + D_l \frac{\partial q^0}{\partial n_l} = 0 \text{ on } \tilde{\Gamma}_{lw}. \tag{4.12}
\]

5 Asymptotic stent

In the design of the stent we are left with several parameters: the surface density of product $c_s = m/(2\pi RN\lambda)$, the total length of the space occupied by the stent $L_s = NL$, the ratio $\rho = N\lambda/NL = \lambda/L$ between the width of a strut $\lambda$ and the distance $L$ between two successive struts, and the total number $N$ of struts.

Recall that the stent is specified by the set

\[
\tilde{\Sigma}_s^N \overset{\text{def}}{=} \bigcup_{i=1}^{N} \left\{ (x_1, x_2, z) : \begin{array}{l} x_1^2 + x_2^2 = R^2 \\
 z_i - \lambda/2 \leq z \leq z_i + \lambda/2 \end{array} \right\} \tag{5.1}
\]

\[
z_i = z_0 + \left( i - \frac{1}{2} \right) L, \quad 1 \leq i \leq N, \tag{5.2}
\]

Figure 6: Stent/lumen and stent/wall interfaces as $N$ goes to infinity.
where the superscript emphasizes the dependence on \( N \). Recall that

\[
    z_0 = \frac{H - L_s}{2} > 0.
\]

Therefore the \( N \)-strut stent and the asymptotic stent will be centered in the region \([0, H]\)

\[
    [z_0, z_0 + L_s] = [z_0, z_0 + NL] \subset [0, H] \text{ and } z_0 + \frac{NL}{2} = \frac{H}{2}.
\]

In this section we construct an asymptotic model for the dose \( q_N^0 = q^0 \) as the number of struts goes to infinity while keeping constant the length \( L_s \), the ratio \( \rho \), and the surface density of the product \( c_s \). Again the superscript on \( q_N^0 \) emphasizes the dependence of \( q^0 \) on \( N \). The main technical difference with the asymptotic analysis in the previous section is that the space of solution will also depend on \( N \). In general, even if we can find a uniform bound in a large enough function space independent of \( N \), we will not be able to use test functions in the fixed larger space unless the projection onto the \( N \)-dependent solution spaces is strongly continuous. This asymptotic problem is very similar to the Neumann sieve studied by [12], [5], and [7] where the plane surface is replaced by the lateral boundary of the cylinder of radius \( R \). Fortunately here the total surface of the holes is constant and different from zero in the limiting process and there will be no discontinuity of the trace of the asymptotic solution.

### 5.1 Construction of the asymptotic problem

Recall that for fixed \( N \), the dose \( q_N^0 \) is the solution in the space

\[
    V(\hat{\Omega}^N) \overset{\text{def}}{=} \begin{cases} 
    H^1(\hat{\Omega}^N), & \text{condition (2.17) on } u \\
    \{ v \in H^1(\hat{\Omega}^N) : v|_{\Gamma_1} = 0 \}, & \text{condition (2.10) on } u 
    \end{cases}
\]

\[
    \tilde{\Omega}^N \overset{\text{def}}{=} \{(x_1, x_2, z) : |x_1|^2 + |x_2|^2 < (R + E)^2, 0 < z < H\} \lessdot \tilde{\Sigma}_s^N,
\]

of the variational equation

\[
    \forall v \in V_N, \quad a^0(q_N^0, v) = \ell_N^0(v).
\]

The linear form can now be rewritten in terms of the following characteristic function on \([0, H]\)

\[
    \chi_N(z) \overset{\text{def}}{=} \begin{cases} 
    1, & \text{if } z \in \bigcup_{i=1}^N[z_i - \lambda / 2, z_i + \lambda / 2], \\
    0, & \text{otherwise}
    \end{cases}
\]

\[
    \ell_N^0(v) = \int_{\tilde{\Sigma}_s^N} c_s v^+ \, dx = \sum_{i=1}^N \int_{z_i - \lambda / 2}^{z_i + \lambda / 2} dz \int_0^{2\pi} d\theta c_s v(R^+, \theta, z)
\]

\[
    = c_s \int_0^H dz \chi_N(z) R \int_0^{2\pi} d\theta v(R^+, \theta, z).
\]

or in term of the characteristic function \( \chi_{\tilde{\Sigma}_s^N} \) defined on the target area \( \tilde{\Sigma} \) in the lateral boundary of the cylinder \( C_R \)

\[
    \ell_N^0(v) = \int_{\tilde{\Sigma}} \chi_{\tilde{\Sigma}_s^N} v^+ \, d\tilde{\Sigma}, \quad \chi_{\tilde{\Sigma}_s^N}(x) \overset{\text{def}}{=} \begin{cases} 
    1, & \text{if } x \in \tilde{\Sigma}_s^N, \\
    0, & \text{otherwise}
    \end{cases}
\]

The bilinear form

\[
    a^0(w, v)
\]

\[
    = \int_{\hat{\Omega}_s^0} D_w \nabla w \cdot \nabla v \, dx + \int_{\hat{\Omega}_1} (D_1 \nabla w - w u) \cdot \nabla v \, dx + \int_{\Gamma_1} u \cdot n_l w v \, d\Gamma
\]

is independent of \( N \). Assuming that there exist constants \( L_s, 0 < L_s < H \), and \( \rho, 0 < \rho < 1 \), such that, as \( N \) goes to infinity, \( LN = L_s \) and \( \lambda N = \rho L_s \), it is readily seen that the sequence \( \{\chi_N\} \) is uniformly bounded in \( L^2(0, H) \) and
weakly convergent:
\[
\forall p \geq 1, \quad \int_0^H (\chi_N)^p \, dz = \int_0^H \chi_N \, dz = N\lambda = \rho L_s = \text{constant}
\]
\[
\Rightarrow \chi_N \rightharpoonup \rho \chi_{[z_0, z_0+L_s]} \quad \text{in } L^2(0, H)-\text{weak for } p = 2,
\]
\[
\forall \varphi \in L^2(0, H), \quad \int_0^H \chi_N \varphi \, dz \rightharpoonup \rho \int_{z_0}^{z_0+L_s} \varphi \, dz,
\]
where
\[
\chi_{[z_0, z_0+L_s]}(z) \overset{\text{def}}{=} \begin{cases} 1, & z \in [z_0, z_0 + L_s] \\ 0, & \text{otherwise}. \end{cases}
\]
Equivalently
\[
\chi_{\tilde{\Sigma}^N} \rightharpoonup \rho \chi_{\tilde{\Sigma}} \quad \text{in } L^2(\tilde{\Sigma})-\text{weak},
\]
\[
\forall \varphi \in L^2(\tilde{\Sigma}), \quad \int_{\tilde{\Sigma}} \chi_{\tilde{\Sigma}^N} \varphi \, d\Sigma \rightharpoonup \rho \int_{\tilde{\Sigma}} \varphi \, d\Sigma,
\]
where \(\tilde{\Sigma}\) is the target area as defined in (2.4).
Since \(L_s = NL, \lambda N = \rho L_s\) and \(\rho = \lambda/L\) are constant in the limiting process, we get for all \(v\) in \(L^2(\tilde{\Sigma})\)
\[
\ell_N^0(v) = c_s \int_{\tilde{\Sigma}} \chi_{\tilde{\Sigma}^N} \, d\Sigma = c_s \int_0^H \, dz \, \chi_N(z) \, R \int_0^{2\pi} \, d\theta \, v(R^+, \theta, z)
\]
\[
\rightarrow \ell_\infty^0(v) = c_s \rho \int_{z_0}^{z_0+L_s} \, dz \, R \int_0^{2\pi} \, d\theta \, v(R^+, \theta, z) = c_s \rho \int_{\tilde{\Sigma}} v^+ \, d\Gamma.
\]
This suggests to introduce the new domain \(\tilde{\Omega}^\infty\)
\[
\tilde{\Omega}^\infty \overset{\text{def}}{=} \tilde{\Omega}^0 \backslash \tilde{\Sigma}
\]
in the open cylinder \(C_{R+E}\)
\[
\tilde{\Omega}^0 \overset{\text{def}}{=} C_{R+E} = \{(x_1, x_2, z) : |x_1|^2 + |x_2|^2 < (R+E)^2, 0 < z < H\}
\]
along with the new larger space of solution
\[
V(\tilde{\Omega}^\infty) \overset{\text{def}}{=} \begin{cases} H^1(\tilde{\Omega}^\infty), & \text{condition (2.17) on } u \\ \{ v \in H^1(\tilde{\Omega}^\infty) : v|_{\tilde{\Gamma}_{ti}} = 0 \}, & \text{condition (2.10) on } u \end{cases}
\]
and the smaller space
\[
V(\tilde{\Omega}) \overset{\text{def}}{=} \begin{cases} H^1(\tilde{\Omega}), & \text{condition (2.17) on } u \\ \{ v \in H^1(\tilde{\Omega}) : v|_{\tilde{\Gamma}_{ti}} = 0 \}, & \text{condition (2.10) on } u \end{cases}
\]
Observe that for all \(N \geq 1, V(\tilde{\Omega}) \subset V(\tilde{\Omega}^N) \subset V(\tilde{\Omega}^\infty)\) and recall that the linear term only acts on the upper part of the new crack \(\tilde{\Sigma}\), that is
\[
\ell_\infty^0(v) \overset{\text{def}}{=} \int_{\tilde{\Sigma}} \rho c_s v^+ \, d\Gamma.
\]
It is easy to show that the solutions \(q_N^0\) are uniformly bounded in the norm of \(V(\tilde{\Omega}^\infty)\), that there is a subsequence which weakly converges to some \(q_\infty^0 \in V(\tilde{\Omega}^\infty)\), and that \(q_\infty^0\) is a solution of the variational equation
\[
\forall v \in V(\tilde{\Omega}), \quad a_\infty(q_\infty^0, v) = \ell_\infty^0(v).
\]
However this equation is incomplete since the test function belongs to the smaller space \(H^1(\tilde{\Omega})\) which does not see the crack \(\tilde{\Sigma}\).
Theorem 5.1. Assume that there exist constants \( L_s, 0 < L_s < H \), and \( \rho, 0 < \rho < 1 \), such that, as \( N \to \infty \), \( LN = L_s \) and \( \lambda N = \rho L_s \). The sequence of solutions \( q_N^0 \in V(\Omega^N) \) converges in \( V(\Omega^\infty) \)-weak to \( q_\infty^0 \) which is the solution in \( V(\tilde{\Omega}^0) \) of the variational equation
\[
\exists q_\infty^0 \in V(\tilde{\Omega}^0), \forall v \in V(\tilde{\Omega}^0), \quad d^0(q_\infty^0, v) = \ell_\infty^0(v),
\]
where the continuous bilinear and the linear forms \( d^0 \) and \( \ell_\infty^0 \) are given by the expressions (5.8) and (5.14).

Proof. By weak convergence of \( \{q_N^0\} \) in \( V(\Omega^\infty) \) the jump
\[
[q_N^0] = (q_N^0+ - q_N^0-) \big|_\Sigma
\]
of \( q_N^0 \) across \( \Sigma \) strongly converges:
\[
[q_N^0] \rightarrow [q_\infty^0] \quad \text{in } L^2(\Sigma)\text{-strong.}
\]
By continuity of the trace of \( q_N^0 \) across the region of the holes \( \Sigma \backslash \Sigma^N_s \)
\[
\forall \varphi \in L^2(\Sigma), \quad \int_{\Sigma \backslash \Sigma^N_s} [q_N^0] \varphi \, d\Gamma = 0.
\]
Since we already have
\[
\chi_N \rightarrow \rho \chi_{[z_0, z_0 + L_s]} \quad \text{in } L^2(0, H)\text{-weak,}
\]
\[
\chi_{z_0} \rightarrow \rho \chi_\Sigma \quad \text{in } L^2(\Sigma)\text{-weak}
\]
Then for all \( \varphi \in L^2(\Sigma) \)
\[
0 = \int_{\Sigma \backslash \Sigma^N_s} [q_N^0] \varphi \, d\Gamma = \int_{\Sigma} \left(1 - \chi_{\Sigma^N} \right) [q_N^0] \varphi \, d\Gamma
\]
\[
\rightarrow \int_{\Sigma} (1 - \rho \chi_\Sigma) [q_\infty^0] \varphi \, d\Gamma = (1 - \rho) \int_{\Sigma} [q_\infty^0] \varphi \, d\Gamma
\]
\[
\Rightarrow \forall \varphi \in L^2(\Sigma), \quad (1 - \rho) \int_{\Sigma} [q_\infty^0] \varphi \, d\Gamma = 0.
\]
Hence for \( 0 \leq \rho < 1 \)
\[
[q_\infty^0] = 0 \quad \text{along } \Sigma \quad \Rightarrow \quad q_\infty^0 \in H^1(\tilde{\Omega}^0) \quad \Rightarrow \quad q_\infty^0 \in V(\tilde{\Omega}^0).
\]
Combining \( q_\infty^0 \in V(\tilde{\Omega}^0) \) with equation (5.15) and the fact that \( a^0 \) is coercive on \( V(\tilde{\Omega}^0) \), we conclude that \( q_\infty^0 \) is the unique solution of the variational equation (5.16).

5.2 Equations for the dose of the asymptotic stent

From the variational equation (5.16) for \( q_\infty^0 \) we get the following set of equations for the dose \( q_\infty^0(x,t) \)
\[
\text{div}(D_w \nabla q_\infty^0) = 0 \quad \text{in } \tilde{\Omega}_w^0
\]
(5.17)
\[
\text{div}(D_l \nabla q_\infty^0 - q_\infty^0 u) = 0 \quad \text{in } \tilde{\Omega}_l.
\]
(5.18)
The boundary conditions are
\[
\begin{aligned}
\text{wall} & \quad \frac{\partial q_\infty^0}{\partial n_w} = 0 \quad \text{on } \tilde{\Gamma}_{w1} \cup \tilde{\Gamma}_{w0} \cup \tilde{\Gamma}_{R+E} \\
\text{lumen} & \quad \begin{cases}
D_l \frac{\partial q_\infty^0}{\partial n_l} - u \cdot n_l q_\infty^0 = 0 & \text{or } q_\infty^0 = 0 \\
\frac{\partial q_\infty^0}{\partial n_l} = 0 & \text{on } \tilde{\Gamma}_{l0}
\end{cases}
\end{aligned}
\]
(5.19)
The condition at the interface is
\[
\begin{aligned}
\text{wall/lumen} & \quad D_w \frac{\partial q_\infty^0}{\partial n_w} + D_l \frac{\partial q_\infty^0}{\partial n_l} = \begin{cases}
0 & \text{on } \tilde{\Gamma}_{lw} \\
\rho c_s & \text{on } \Sigma,
\end{cases}
\end{aligned}
\]
where
\[
\tilde{\Gamma}_{lw} = \left\{(x_1, x_2, z) : x_1^2 + x_2^2 + z^2 = R^2, z \in [0, H[ \backslash [z_0, z_0 + L_s] \right\}.
\]
\footnote{\( L = L_s/N \) and \( \lambda = \rho L_s/N \) both depend on \( N \) and go to zero as \( N \to \infty \).}
6 Numerical experimentation

In this section we present some numerical tests to illustrate the theoretical results and get a feeling for the kind of phenomena involved. The velocity profile $u$ of the flow in the lumen has been obtained by solving the incompressible Navier-Stokes equations (269,000 unknowns). The geometry and the equation of the dose have been scaled in order to work with dimensionless variables. The geometry of the artery, the parameters of the incompressible Navier-Stokes equation, and the characteristics of the diffusion-transport equation are given in Table 1 with the condition $q = 0$ on $\tilde{\Sigma}_l$. As a point of comparison the parameters of the Wiktor Stent were approximatively $L = 0.7$ mm for the distance between the centers of two struts, $\lambda = 0.15$ mm for the width, and 3 to 4 mm for the diameter. The number of struts was $N = 24$ that gives a target area of length $L_s = 16.8$ mm and a ratio $\rho = 0.15/0.7 \approx 0.214$.

We have made the computations for $\rho = 0.1, 0.2, 0.5, 
and 0.9$ and $N$ ranges from 1 to 382. We have chosen to display the dose at the outer radius $R + E$ of the artery for the case $\rho = 0.1$ in order to avoid the large fluctuations at the lumen/wall interface. The graphs of the dose start at $z_0 = 6$ to $z_0 + 18$ which goes slightly beyond the target region of length $L_s = 16.8$ with the variable $z - z_0$ in abscissa. They are displayed for different values of the number of struts $N$. Because of the broad range of numerical values of the dose, three sets of graphs are used. Figure 7 is in the range of $2 \times 10^{-8}$ for $N = 1, 6, 12, 24$. Figure 8 has two sets of graphs: the first one in the range $0.0065$ for $N = 24, 48, 96, 192, 384$, and $N = \infty$, and the second one in the range $0.020$ for $N = 48, 96, 192, 384$, and $N = \infty$.

As an indication of the highly irregular behaviour of the dose in the vicinity of the stent two figures give a $(r, z)$-plot of the dose at the upstream end of the target region occupied by the stent. For $\rho = 0.1$ Figure 9 corresponds to $N = 382$ struts and Figure 10 to the asymptotic stent. Notice the sharp spikes in the area of the struts and the sharp drop between two struts. It is also interesting that, even if the asymptotic theory predicts that the dose is continuous across the wall/lumen interface, a sharp drop is observed in the dose across the target area $\tilde{\Sigma}$ of the wall/lumen interface due to the high level of convection in the lumen. To get sharp and stable results, a very large number of variables was used in the numerical computations. Complete numerical tests and the description of the numerical method used will be reported in a subsequent paper.

Finally Table 2 gives the integral of the dose as a function of the number of struts $N$ and the ratio $\rho$. The results will be discussed in the next section.

7 Some optimal design problems

In this section we slightly generalize the equation of the dose for a stent of zero thickness. The target area

$$\tilde{\Sigma} \overset{\text{def}}{=} \left\{ (x_1, x_2, z) : \begin{array} {c} x_1^2 + x_2^2 = R^2 \\ z_0 \leq z \leq z_0 + L_s \end{array} \right\}$$

Table 1: Parameters.

<table>
<thead>
<tr>
<th>notation</th>
<th>description</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R + E$</td>
<td>radius of the artery</td>
<td>0.63333</td>
</tr>
<tr>
<td>$H$</td>
<td>length of the artery</td>
<td>28.8</td>
</tr>
<tr>
<td>$R$</td>
<td>radius of the lumen</td>
<td>0.5</td>
</tr>
<tr>
<td>$L_s$</td>
<td>length of the target area</td>
<td>16.8</td>
</tr>
<tr>
<td>$z_0$</td>
<td>length of the inlet section</td>
<td>6.0</td>
</tr>
<tr>
<td>$z_0$</td>
<td>length of the outlet section</td>
<td>6.0</td>
</tr>
<tr>
<td>$\rho$</td>
<td>area of the stent/2$\pi R L_s$</td>
<td>0.1 to 0.9</td>
</tr>
</tbody>
</table>

parameters of the flow

<table>
<thead>
<tr>
<th>notation</th>
<th>description</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1/\text{Re}$</td>
<td>Reynold’s number</td>
<td>0.0070518755</td>
</tr>
<tr>
<td>$1/\text{Pe}$</td>
<td>Peclet’s number</td>
<td>$10^{-8}$</td>
</tr>
</tbody>
</table>

parameters of the diffusion

<table>
<thead>
<tr>
<th>notation</th>
<th>description</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$D_l$</td>
<td>diffusion in the lumen</td>
<td>$10^{-8}$</td>
</tr>
<tr>
<td>$D_w$</td>
<td>diffusion in the wall</td>
<td>$10^{-8}$</td>
</tr>
<tr>
<td>$c_s$</td>
<td>surface density of product</td>
<td>$10^{-8}$</td>
</tr>
</tbody>
</table>
is kept a finite distance away from the boundaries of the cylinder at \( z = 0 \) and \( z = H \). Define the domain

\[
\hat{\Omega} \equiv \left\{ (x_1, x_2, z) : x_1^2 + x_2^2 < (R + E)^2 \right\} \setminus \hat{\Sigma} = C_{R+E} \setminus \hat{\Sigma}
\]

and the space of solutions

\[
V(\hat{\Omega}) \equiv \left\{ H^1(\hat{\Omega}) : v|_{\hat{\Gamma}_i} = 0 \right\}
\]

condition (2.17) on \( u \)

Assume that the stent is specified by a characteristic function \( \chi \) on \( \hat{\Sigma} \)

\[
\chi \in X(\hat{\Sigma}) \equiv \left\{ \chi \in L^2(\hat{\Sigma}) : (1 - \chi)\chi = 0 \text{ a.e. in } \hat{\Sigma} \right\}.
\]

Associate with \( \chi \) the zero-thickness stent

\[
\hat{\Sigma}_s(\chi) \equiv \left\{ x \in \hat{\Sigma} : \chi(x) = 1 \right\},
\]

the domain

\[
\hat{\Omega}(\chi) \equiv \left\{ (x_1, x_2, z) : x_1^2 + x_2^2 < (R + E)^2 \right\} \setminus \hat{\Sigma}_s(\chi),
\]

and the space of solutions

\[
V(\chi) = V(\hat{\Omega}(\chi)) \equiv \left\{ v \in V(\hat{\Omega}) : (1 - \chi)v = 0 \text{ on } \hat{\Sigma} \right\}.
\]

Note that the interface, the domain and the space of solutions all depend on \( \chi \). The dose \( q = q(\chi) \) is the solution of the variational equation

\[
\exists q \in V(\chi), \forall v \in V(\chi), \quad a^0(q, v) = \ell^0(\chi; v),
\]

where

\[
a^0(w, v) \quad \text{def} \quad \int_{\hat{\Omega}_p} D_w \nabla w \cdot \nabla v \, dx + \int_{\hat{\Omega}_l} (D_l \nabla w - w u) \cdot \nabla v \, dx + \int_{\hat{\Gamma}_i} u \cdot n_l w v \, d\Gamma
\]

\[
\ell^0(\chi; v) \quad \text{def} \quad \int_{\hat{\Sigma}} c_s \chi v \, d\hat{\Sigma}.
\]

The notation emphasizes the fact that \( \ell^0 \) and \( V \) both depend on \( \chi \).

Table 2: Integral of the dose in the wall as a function of \( \rho \) and \( N \).

<table>
<thead>
<tr>
<th>( N )</th>
<th>( \rho = 0.1 )</th>
<th>( \rho = 0.2 )</th>
<th>( \rho = 0.5 )</th>
<th>( \rho = 0.9 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.44260 ( 10^{-4} )</td>
<td>1.76145 ( 10^{-3} )</td>
<td>2.57996 ( 10^{-3} )</td>
<td>1.47576 ( 10^{-3} )</td>
</tr>
<tr>
<td>6</td>
<td>1.57697 ( 10^{-2} )</td>
<td>7.96223 ( 10^{-2} )</td>
<td>8.84819 ( 10^{-3} )</td>
<td>6.46757 ( 10^{-4} )</td>
</tr>
<tr>
<td>12</td>
<td>7.37995 ( 10^{-3} )</td>
<td>3.14226 ( 10^{-2} )</td>
<td>2.79274 ( 10^{-3} )</td>
<td>1.40548 ( 10^{-3} )</td>
</tr>
<tr>
<td>24</td>
<td>3.82175 ( 10^{-3} )</td>
<td>1.45893 ( 10^{-2} )</td>
<td>1.04696 ( 10^{-3} )</td>
<td>5.27827 ( 10^{-4} )</td>
</tr>
<tr>
<td>48</td>
<td>2.10712 ( 10^{-3} )</td>
<td>7.40946 ( 10^{-3} )</td>
<td>4.83751 ( 10^{-2} )</td>
<td>2.41867 ( 10^{-3} )</td>
</tr>
<tr>
<td>96</td>
<td>1.25858 ( 10^{-3} )</td>
<td>3.80518 ( 10^{-3} )</td>
<td>2.47581 ( 10^{-2} )</td>
<td>1.16833 ( 10^{-2} )</td>
</tr>
<tr>
<td>192</td>
<td>9.4094 ( 10^{-4} )</td>
<td>7.37312 ( 10^{-2} )</td>
<td>3.85586 ( 10^{-3} )</td>
<td>6.94056 ( 10^{-3} )</td>
</tr>
<tr>
<td>384</td>
<td>8.0285 ( 10^{-4} )</td>
<td>7.37995 ( 10^{-2} )</td>
<td>3.85586 ( 10^{-3} )</td>
<td>6.94056 ( 10^{-3} )</td>
</tr>
</tbody>
</table>
There are many ways to define an objective function. For instance choose the total dose of product delivered in the region $S$ of the wall just above the stent

\begin{align}
J(\chi) & \overset{\text{def}}{=} \int_S q(\chi) \, dx \\
S & \overset{\text{def}}{=} \left\{ (x_1, x_2, z) : \begin{array}{l}
R^2 < x_1^2 + x_2^2 < (R + E)^2 \\
z_0 < z < z_0 + L_s
\end{array} \right\}
\end{align}

with the following constraints on the surface of the stent

\[ \int_{\Sigma} \chi \, d\Sigma = \rho 2\pi RL_s = \rho |\Sigma|, \]

that is, the area occupied by the stent is $\rho$ times the area $|\Sigma|$ of $\tilde{\Sigma}$. Finally

\[ \sup_{\chi \in X(\tilde{\Sigma})} \int_{\tilde{\Sigma}} q(\chi) \, dx. \]

Since $X(\tilde{\Sigma})$ is not compact in $L^2(\tilde{\Sigma})$ we can consider the new problem

\[ \sup_{\chi \in \overline{co} X(\tilde{\Sigma})} \int_{\tilde{\Sigma}} q(\chi) \, dx \]

relaxed to the closed convex hull

\[ \overline{co} X(\tilde{\Sigma}) = \left\{ \chi \in L^2(\tilde{\Sigma}) : 0 \leq \chi(x) \leq 1 \right\} \]

of $X(\tilde{\Sigma})$ with the following relaxation of the definition (7.5) of $\tilde{\Sigma}_s(\chi)$

\[ \tilde{\Sigma}_s(\chi) \overset{\text{def}}{=} \left\{ x \in \tilde{\Sigma} : \chi(x) > 0 \right\}. \]

Then the definitions (7.6) and (7.7) of the domain and the solution space readily extend to a function $\chi \in \overline{co} X(\tilde{\Sigma})$ as in [6] (Chapter 3, § 2.5, Theorem 2.9). Unfortunately the projection of an element $v \in V(\tilde{\Omega})$ onto the subspace $V(\chi)$ is not strongly continuous with respect to $\chi$ in the weak $L^2(\tilde{\Sigma})$-topology of the closed convex hull of the characteristic functions on $\tilde{\Sigma}$. The counter-example is provided by the Neumann sieve in [5] where the equivalent of the characteristic functions $\chi_{\tilde{\Sigma}_N}$ strongly converges to 1 on $\tilde{\Sigma}$. If the projection was continuous the \textit{strange term} acting on the jump across the sieve in the limit variational equation would not be there.

If we introduce the following adjoint problem

\[ \exists p \in V(\chi), \forall w \in V(\chi), \quad a^0(w, p) + \int_S w \, dx = 0, \]

then it is easy to check that

\[ l^0(\chi; p(\chi)) + \int_S q(\chi) \, dx = 0 \]

and that the maximization problem is equivalent to the following minimization problem

\[ \inf_{\chi \in X(\tilde{\Sigma})} \int_{\tilde{\Sigma}} c_s \chi p(\chi) \, d\tilde{\Sigma}. \]

The adjoint problem is similar to the initial problem where the direction of the flow is changed. Indeed the variational equation (7.17) yields

\[ \forall w \in V(\chi), \int_{\tilde{\Omega}_p} D_w \nabla w \cdot \nabla p \, dx + \int_{\tilde{\Omega}_t} (D_t \nabla w - w u) \cdot \nabla p \, dx \]

\[ + \int_{\tilde{\Gamma}_w} u \cdot n_t w p \, d\Gamma + \int_S w \, dx = 0. \]
But
\[
\int_{\Omega_i} w u \cdot \nabla p \, dx = \int_{\Omega_i} [\text{div}(w u p) - \text{div}(u w p)] \, dx \\
= \int_{\partial \Omega_i} w p u \cdot n_i \, d\Gamma - \int_{\Omega_i} u \cdot \nabla w p \, dx \\
= \int_{\Gamma_{io}} w p u \cdot n_i \, d\Gamma + \int_{\Omega_i} w p u \cdot n_i \, d\Gamma - \int_{\Omega_i} u \cdot \nabla w p \, dx.
\]
Using the above identity we finally get the variational equation
\[
\forall w \in V(\chi), \quad \int_{\Omega^w_p} D_w \nabla p \cdot \nabla w \, dx + \int_{\Omega_i} (D_t \nabla p - p (-u)) \cdot \nabla w \, dx \\
+ \int_{\Gamma_{li}} (-u) \cdot n_i \, w p \, d\Gamma + \int_{S} w \, dx = 0
\]
(7.21)
which is similar to the variational equation for the dose except that the sign of the velocity \(u\) has been changed and that the roles of the boundary conditions in \(\Gamma_{li}\) and \(\Gamma_{lo}\) have been interchanged. Equivalently in strong form
\[
\begin{align*}
\text{div}(D_w \nabla p) &= \chi_S \text{ in } \Omega_w \\
\text{div}(D_t \nabla p - (-u) p) &= 0 \text{ in } \Omega_i \\
D_t \frac{\partial p}{\partial n_i} - (-u) \cdot n_i p &= 0 \text{ or } p = 0 \text{ on } \Gamma_{io} \\
D_t \frac{\partial p}{\partial n_{li}} &= 0 \text{ on } \Gamma_{li}
\end{align*}
\]
(7.22-7.25)
where the boundary conditions on \(\Gamma_{li}\) and \(\Gamma_{lo}\) have been permuted. The other boundary and interface conditions are
\[
\begin{align*}
D_w \frac{\partial p}{\partial n_w} &= 0 \text{ on } \Gamma_{wi} \cup \Gamma_{wo} \cup \Gamma_{R+E} \\
D_w \frac{\partial p}{\partial n_w} + D_t \frac{\partial p}{\partial n_i} &= 0 \text{ on } \Gamma_{iw} \\
D_t \frac{\partial p^+}{\partial n_{li}} &= 0 \text{ and } D_t \frac{\partial p^-}{\partial n_{li}} \text{ on } \Sigma_s(\chi).
\end{align*}
\]
(7.26-7.28)
Obviously other types of objective functions can be chosen. For instance the integral of the dose on the upper side of the target area \(\Sigma\)
\[
\int_{\Sigma} q(\chi)^+ \, d\Sigma.
\]
(7.29)
If \(c_s\) becomes a design parameter, we could require a minimum dose \(q_{min}\) on the upper side of \(\Sigma\) or a small region \(S'\) above \(\Sigma\)
\[
q(\chi)^+ \geq q_{min} \text{ on } \Sigma \text{ or } q(\chi)^+ \geq q_{min} \text{ on } S',
\]
(7.30)
\[
S' \overset{\text{def}}{=} \left\{ (x_1, x_2, z) : \frac{R^2 + x_2^2}{2} < (R + e')^2, \quad z_0 < z < z_0 + L_s \right\}, \quad 0 < e' < E,
\]
(7.31)
while minimizing \(c_s\).

References


Figure 7: Dose versus the position $z$ along the axis at the exterior radius $R+E = 0.6333$ of the artery as a function of the number of struts $N$ for $\rho = 0.1$
Figure 8: Dose versus the position $z$ along the axis at the exterior radius $R + E = 0.6333$ of the artery as a function of the number of struts $N$ for $\rho = 0.1$
Figure 9: Dose as a function of $(r, z)$ for $N = 382$ at the upstream end of $\tilde{\Sigma}$

Figure 10: Dose as a function of $(r, z)$ for $N = \infty$ at the upstream end of $\tilde{\Sigma}$