Implantable Human Lenses with Adjustable Focal Distance as a Solution for Cataract Treatment

by

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THESIS
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To Francesca,

always near

despite distances.
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FM
PREFACE

This project, as the final stage of my master’s studies, has really provided me the experience and abilities that I was hoping to acquire in the field of semiconductor and micro-fabrication techniques. The opportunity to work with Prof. Metlushko allowed my research to explore and use state-of-the-art equipment and processes. The considerable interdisciplinary nature of the project and the guidance provided by Dr. Gaynes and Dr. Khanna gave me a totally new perspective on research methods and expanded my vision beyond a purely engineering perspective.
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Different types of haptics design in current IOLs
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<tr>
<td>AccIOL</td>
<td>Accommodative Intraocular Lens</td>
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<td>ACL</td>
<td>Anterior Chamber Lens</td>
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<td>AFM</td>
<td>Atomic Force Microscopy</td>
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<tr>
<td>CCC</td>
<td>Continuous Circular Capsulorhexis</td>
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<td>ChG</td>
<td>Chalcogenide Glass</td>
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<td>CMTF</td>
<td>Critical Modulation Transfer Function</td>
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<td>CNT</td>
<td>Carbon Nano-Tube</td>
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<td>CVD</td>
<td>Chemical Vapor Deposition</td>
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<td>D</td>
<td>Diopters</td>
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<td>DMD</td>
<td>Digital Micro-mirror Device</td>
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<td>DPL</td>
<td>Dip Pen Lithography</td>
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<tr>
<td>DUV</td>
<td>Deep Ultra-Violet</td>
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<tr>
<td>EA</td>
<td>Ethyl Acrylate</td>
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<tr>
<td>EBL</td>
<td>Electron Beam Lithography</td>
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<tr>
<td>ECCE</td>
<td>Extra-Capsular Cataract Extraction</td>
</tr>
<tr>
<td>EHT</td>
<td>Extra-High Tension</td>
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<tr>
<td>EMA</td>
<td>Ethyl Methacrylate</td>
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xi
<table>
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<th>Abbreviation</th>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>FE</td>
<td>Field Emission</td>
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<td>GSL</td>
<td>Gray Scale Lithography</td>
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<td>GTM</td>
<td>Gray Tone Mask</td>
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<td>HEBS</td>
<td>High-Energy-Beam-Sensitive</td>
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<tr>
<td>HEMA</td>
<td>2-Hydroxyhexyl Methacrylate</td>
</tr>
<tr>
<td>HEXMA</td>
<td>6-Hydroxyhexyl Methacrylate</td>
</tr>
<tr>
<td>HSQ</td>
<td>Hydrogen Silsequioxane</td>
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<tr>
<td>ICCE</td>
<td>Intra-Capsular Cataract Extraction</td>
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<tr>
<td>IOL</td>
<td>Intraocular Lens</td>
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<tr>
<td>LDW</td>
<td>Laser Direct-Write</td>
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<tr>
<td>MAP</td>
<td>Multi-photon Absorption Polymerization</td>
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<tr>
<td>MBE</td>
<td>Molecular Beam Epitaxy</td>
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<tr>
<td>MEMS</td>
<td>Micro-Electro-Mechanical Systems</td>
</tr>
<tr>
<td>MMA</td>
<td>Methyl Methacrylate</td>
</tr>
<tr>
<td>MOEMS</td>
<td>Micro-Opto-Electro-Mechanical Systems</td>
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<tr>
<td>MRAM</td>
<td>Magneto-Resistive Random Access Memory</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>NCF</td>
<td>Nanotechnology Core Facility</td>
</tr>
<tr>
<td>NEMS</td>
<td>Nano-Electro-Mechanical Systems</td>
</tr>
<tr>
<td>NIL</td>
<td>Nano-Imprint Lithography</td>
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<tr>
<td>OPC</td>
<td>Optical Proximity Correction</td>
</tr>
<tr>
<td>PCL</td>
<td>Posterior Chamber Lens</td>
</tr>
<tr>
<td>PCO</td>
<td>Posterior Capsule Opacification</td>
</tr>
<tr>
<td>PDMDPS</td>
<td>Polydimethylsiloxane</td>
</tr>
<tr>
<td>PDMS</td>
<td>Polydimethylsiloxane</td>
</tr>
<tr>
<td>PEA</td>
<td>2-Phenethyl Acrylate</td>
</tr>
<tr>
<td>PEMA</td>
<td>2-Phenethyl Methacrylate</td>
</tr>
<tr>
<td>PMMA</td>
<td>Poly(methyl methacrylate)</td>
</tr>
<tr>
<td>PE</td>
<td>Phacoemulsification</td>
</tr>
<tr>
<td>PL</td>
<td>Photolithography</td>
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<tr>
<td>PR</td>
<td>Photo resist</td>
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<td>RCS</td>
<td>Refractive Cataract Surgery</td>
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<td>RIE</td>
<td>Reactive Ion Etching</td>
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<td>SAD</td>
<td>Self-Amplified Depolymerization</td>
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<td>SEM</td>
<td>Scanning Electron Microscopy</td>
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<tr>
<td>Acronym</td>
<td>Description</td>
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<tr>
<td>SPL</td>
<td>Scanning Probe Lithography</td>
</tr>
<tr>
<td>SPM</td>
<td>Scanning Probe Microscopy</td>
</tr>
<tr>
<td>TEM</td>
<td>Tunneling Electron Microscopes</td>
</tr>
<tr>
<td>TFE</td>
<td>Thermal Field Emission</td>
</tr>
<tr>
<td>TFEMA</td>
<td>2-Trifluoroethyl Methacrylate</td>
</tr>
<tr>
<td>UIC</td>
<td>University of Illinois at Chicago</td>
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<tr>
<td>XUV</td>
<td>Extreme UV</td>
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SUMMARY

This work started from the impressive data regarding the spread of cataract, an eye condition which is the leading cause of blindness worldwide. The only truly effective treatment of cataract is surgery to replace the lens with an artificial implant, which is known as an intraocular lens (IOL). The ultimate IOL should optimize vision and accommodation entirely like the original unaged lens of the eye.

We conceived a novel design, based on the Fresnel lens principle, of a spiral mold composed of nano channels. The fabrication process will take advantage of 3D electron beam lithography, a leading equipment in the production of MEMS and semiconductor structures, available at UIC. Using the technique of soft lithography, the IOL will be created from this mold. The main goal is to design a new type of IOL that will be reliable, versatile, cost and time effective.
1.1 Motivation of study

Eye diseases are a common cause of grave morbidity affecting people worldwide. Recent estimations conducted by the World Health Organization [1] report that approximately 285 million people are visually impaired in the world: 39 million are blind while 246 million suffer from low vision. Almost 19 million of these people are children below age 15. An estimated 3.1% of deaths are related to eye diseases such as cataract, glaucoma, trachoma, and onchocerciasis.

Although it would be possible to avoid or cure 80% of all visual impairments, 90% of people in the world who suffer from those conditions live in developing countries, where treatments are not readily affordable.

Cataract, which is clouding of the crystalline lens of the eye, is the leading cause of blindness worldwide. It has been, and still is, the focus of many global health initiatives. VISION 2020: The Right to Sight is a joint initiative of the WHO and the International Agency for the Prevention of Blindness whose goal is to eliminate preventable blindness by the year 2020. Cataracts affect approximately 18 million people, with the higher rates in low-income countries, particularly in Africa, South America and the Caribbean nations.

Even in the western world cataracts remain the leading cause of vision loss. In the US the rate of blindness due to cataracts is especially high in the Hispanic and African-American
populations at 27%. Treatments of cataract comprise 60% of all Medicare costs related to vision. Moreover, the constant aging of the population makes this problem even more relevant. According to some projections, cataract will increase 50% and rise to 30.1 million by 2020.

In children, cataract is one of the most important causes of visual impairment and is responsible for 20% of pediatric blindness. Many causes can lead to cataracts present at birth, such as prenatal infections (rubella, cytomegalovirus), maternal diabetes and hereditary disorders. Referred to as congenital cataracts, they can severely impair vision. Timely surgical intervention is extremely important in order to achieve good vision and sensory functioning. In children, if cataracts are not removed within the first year of life, vision will never be fully regained. Furthermore, even though cataracts can be easily removed by surgery, it is imperative that the child receive glasses to correct loss of focus by removal of the lens; otherwise, the child will develop permanent visual impairment.

It’s difficult to have a complete and accurate scenario of the total amount of blindness in society, but in any case the rates are staggering and cannot be ignored. Nowadays, the only truly effective treatment of cataract is surgery to replace the lens with an artificial implant, known as an intraocular lens (IOL).
1.2 The human eye

1.2.1 Overview

A good understanding of the anatomy of the human eye is necessary for a good foundation before going on any further in our dissertation. No research or design in the field of IOLs can be meaningful without knowledge of the anatomical and physiological properties of the human visual system.

The eye is a complex transducer able to convert an optical image into an electrical signal. This conversion process follows these steps: the eye receives light from the external environment, regulates its intensity through a diaphragm, focuses it through an adjustable group of lenses and converts it into a set of electrical signals to be transmitted to the brain.

With the help of figure 1, let’s break down light’s path inside the eye, following the aforementioned steps. The first element of the eye to encounter external light is the cornea. Its transparency, enhanced by the absence of blood vessels, is of prime importance for good vision. The cornea is also rich in nerve endings, which make it very sensitive to external stimuli such as temperature, touch and chemicals. From the optical point of view, the cornea contributes to approximately two-thirds of the eye’s total refracting power [2], but its curvature (and thus its focus) is fixed.

After the cornea, the light crosses the anterior chamber of the eye, a cavity enclosed by the cornea and the iris, filled with aqueous humor. The latter is a transparent fluid with the main purpose to provide indispensable nutrients to avascular ocular tissues, such as the cornea and the crystalline lens. Light then passes through the pupil, a hole in the center of the iris which
regulates the amount of light that enters the eye and decreases the aberrations. The iris is able to expand and contract, behaving as an aperture stop and thus regulating the flux of light into the eye.

Once past the iris, light enters the posterior chamber and hits the crystalline lens, a transparent, biconvex structure. The lens accounts for the remaining one-third of the eye’s total optical power [2] and, unlike the cornea, its shape can be changed, thus modifying the focal...
power of the eye. This adjustment is known as accommodation, and will be further discussed in the next section of the chapter.

Finally the light enters the posterior segment of the eye, a larger chamber filled with a transparent, gelatinous mass called vitreous humor. The inner surface of this cavity is covered by the retina, a light-sensitive layer of tissue which acts like the film in a camera. The retinal tissue contains a layer of cells called photoreceptors, which are directly receptive to light. The two main types of photoreceptors are the rods, which are responsible for black and white vision, and the cones, who provide the perception of different colors. These cells convert light stimulus into neural signals, which are further processed and encoded, and finally sent to the brain via the optic nerve.

1.2.2 Accommodation

We previously said that the crystalline lens allows the accommodation mechanism. This process is indispensable in order to maintain a clear focus of an external object at various distances.

The most accredited theory of accommodation is the one proposed in 1855 by German physician and physicist Hermann von Helmholtz [3]. According to von Helmholtz’s assumption, accommodation is the consequence of a ciliary muscle contraction. This muscle is able to contract and relax, and its movement is transmitted to the lens by a ring of fibrous strands called zonule of Zinn.

When a person looks at a far object, the ciliary sphincter muscle relaxes, hence tightening the zonule’s fibers which pull on the lens, flattening it. On the other hand, when focusing on a
Figure 2: Accommodation mechanism.

near object, the contraction of the ciliary muscle causes the zonule’s fibers to slacken and the lens springs back into a thicker, more convex form. These two behaviors are depicted in figure 2.

A new theory of accommodation has been proposed by Daniel Goldberg [4] and it is based on a new understanding of the anatomy of the zonular apparatus. In this model the vitreous zonules are distinguished into three different components: anterior, intermediate, and posterior zonule. The reciprocal action of these zonules allows the lens to accommodate.

Accommodation, together with convergence of the eyes and constriction of the pupil (called miosis), allows to have stereopsis, the perception of depth and distance.

In its ideal working conditions, the eye is always able to focus images exactly on the retina, and perfectly focused vision is achieved. This situation is called emmetropia. However the presence of imperfections in the lens and in the cornea can lead to refractive errors, and consequently to common vision defects such as myopia, hyperopia, and astigmatism (see figure 3).

Myopia, commonly known as nearsightedness, is the condition where the light from distant objects is focused in front of the retina, instead of being focused on it. As a consequence,
the person affected by myopia sees distant objects out of focus. The opposite situation is hyperopia, or farsightedness, where the light from near objects is focused behind the retina, causing difficulty focusing on near objects. Astigmatism is caused by irregular or asymmetric curvature of the cornea or lens, leading to refractive errors that cause an inability to reproduce a sharp image on the retina, correctly focused.

Another important condition is presbyopia. Unlike the previous ones, it is not related to a refractive defect, but to a progressive loss of efficiency of the accommodative apparatus, particularly due to progressive loss of lens elasticity. Presbyopia is associated with the natural course of aging, since its first signs are usually first noticed between the ages of 40 and 50.

1.2.3 **Lens structure and formation**

As previously stated in the summary of this thesis, our final goal is to design a novel accommodative IOL. Since the intent of an IOL is to restore, or at least support, the accommodative functionalities of the crystalline lens, let’s focus our attention on this last element of the eye. Without claiming to do a complete physiological description of the lens, which in not of concern
in this dissertation, we will concentrate on its cellular structure and embryology, in order to better understand the origin of the lens optical properties.

The images in figure 4 follow the development of the lens in a human [5]. Around the fourth week of gestation, the optic vesicle and the surface ectoderm are originated from the embryo’s prosencephalon (figure 4.A). The contact between the ectoderm and the optic vesicle produces a thickening in the ectoderm which evolves in the lens placode (figure 4.B). Subsequently, both the lens placode and the optic vesicle begin to invaginate, forming the lens pit which is the primitive lens, and the optical cup which will later host the retina (figure 4.C). Between the fifth and the sixth week of gestation, the continuing movement of the lens placode causes the separation of the latter from the surface ectoderm and the formation of the lens vesicle, a closed capsule bounded by epithelial cells whose thickness varies along the perimeter: thinner in the anterior part and thicker towards the optic cup (figure 4.D). The cells in the posterior part of the lens vesicle begin to elongate toward the anterior layer by approximately the seventh week of gestation, completely filling the cavity inside the lens and becoming the primary lens fibers (figure 4.E). Finally a thin capsule, called the basal lamina, develops around the lens.

At this point the lens is formed (figure 4.F): the anterior lens cuboidal cells form the epithelium, which covers all the anterior part and just a small portion of the posterior one, right after the equator, while no epithelium is present on the backside if the lens. Moving toward the lens equator, we encounter a region with a high mitotic activity (germinative zone), where the cells divide and give rise to new ones. Most of these new cells undergo a process of differentiation and elongation, in order to form secondary lens fibers, while a few of them remain
Figure 4: Normal development of the human crystalline lens. Abbreviations used in the above image: LP, lens pit; LPL, lens placode; LV, lens vesicle; NR, neuroretina; OC, optic cup; OS, optic stalk; OV, optic vesicle; PF, primary fibers; PNR, presumptive neuroretina; SE, surface ectoderm.
as undifferentiated epithelial cells [6]. The germinative zone, which is the only region of the adult lens where the cells remain capable of mitosis, continues to produce secondary lens fibers throughout life. New and younger layers overlay the older ones, displacing them toward the center of the lens. Since these layers are never removed, the lens center becomes denser, and it is called lens nucleus. The more superficial layers of younger cells are called lens cortex. The elongated cells displaced toward the nucleus undergo a process of denucleation, where they lose the nucleus and other intracellular organelles to form mature fibers. This process, alongside with the lack of blood vessels and nerves in the lens, guarantees for the transparency of the tissue. Denucleation also helps cell preservation, keeping oxidative damage at a manageable level for decades. The ends where the fibers meet on the anterior and posterior side of the lens form the so called Y-shaped sutures. The arrangement of fibers into concentric shells, resembling to the structure of an onion, characterize the anatomy of the lens and is responsible for the asymmetrical spheroidal shape.

Modern microscopy techniques, such as atomic force microscopy (AFM) and scanning electron microscopy (SEM), allow for detailed imaging and more accurate measuring of the structures under study. The layered and onion-like arrangement of the lens fibers can be seen in figure 5, which displays the sections of two human crystalline lenses, while figure 6 shows a close up of the lens fibers in a chicken lens. It is easy to notice how packed these hexagonal cells are, since almost no extracellular space is visible between them. Moreover the process of denuclearization is revealed by the homogeneous cytoplasm inside the cells.
Figure 5: SEM images of human lenses.

Figure 6: SEM image of the lens fibers in a chicken eye.
In summary, we can say that the basic lens structure is composed of three main parts: the lens fibers, arranged in concentric layers around the central nucleus, the epithelium which covers the anterior part of the lens, and the capsule that encloses the whole system. The capsule has also the task to distribute on the lens the forces from the ciliary body and the zonules, making accommodation possible [7].

A regular adult human lens has a thickness (measure of the distance between the anterior and the posterior poles) of about 3.5 to 4.0 mm, and its equatorial diameter typically ranges between 9.0 and 10.0 mm [7]. However, it is important to remember that the lens grows throughout life, being more round during childhood and flattening out in old age. This modification of the shape is partially cause of the loss of accommodation in older people. Another reason for this chronic impairment is due to loss of elasticity: since the lens fibers keep compressing toward the nucleus, all the structure increase in rigidity, thus reducing the lens accommodative efficiency. This change in density of the lens is called nuclear sclerosis.
1.3 Cataract and eye surgery

1.3.1 Cataract

The main purpose of the ocular lens is to transmit the incident light from the external environment and to focus it precisely on the retina. Transparency is an important feature of the lens which depends not only on the highly regular organization of the lens fibers, but also on the extensive concentration of proteins present in the lens cytoplasm. This extremely high concentration of proteins results in a significant increase of the index of refraction, compared with the one of the surrounding fluids, and it gives rise to the lens refracting capabilities [8].

The term cataract refers to the process of clouding of the crystalline lens (figure 7). When it occurs, the lens transparency is lost, and visual acuity is compromised. Cataracts can originate from a wide range of events. The majority of clinical types of cataracts known today are related to biological aging. According to some estimations, more than 75% of people older than 75 years have lens opacities [9]. Other common causes of cataract formation include trauma, long-term exposure to radiation (in particular ultraviolet light), certain drugs, metabolic disorders such as diabetes, skin diseases or genetic predisposition.

Age-related cataracts are mostly due to the combination of pigment deposition within the lens and deterioration of the normal architecture of the lens fibers. The deformation of these cells caused by nuclear sclerosis increases light scattering, contributing to the formation of cataract.
The age-related accumulation of pigments inside the lens can cause a change in color, called brunescence. Although some amount of brunescence can reduce glare, in advanced stages it causes a serious reduction in sensitivity and high-contrast acuity [7].

1.3.2 Cataract surgery

When the visual function of a patient is compromised because of cataract, the most effective treatment available today is surgical extraction and replacement of the human lens with an intraocular lens implant. Cataract surgery is nowadays one of the most cost-effective surgical interventions [10], and it has proven to be highly successful and generally safe [11].

Before achieving today’s reliability, different cataract surgery techniques were explored. The earliest documented form of cataract surgery is couching, which dislocate the lens into the
vitreous cavity by means of a sharp pointed tool. The technique of couching dates back to the Assyrian Code of King Hammurabi around 1700 BC, which includes a schedule of payments for the surgeon, in case of restored sight, along with the penalty of the removal of the surgeon’s fingers in case of patient death or eye loss. Couching remained popular in Greek and Roman times, as noted by the Latin encyclopedist Celsus in 29 AD in *De Medicinae*, and it remained the only widely practiced treatment for cataracts until the 19th century. Although nowadays couching plays no role in the ophthalmic surgical practice, it is still popular in some developing countries, especially in Sub-Saharan Africa [12], where it is difficult to access modern surgery or where traditional treatments are still preferred by the local population.

From the beginning of the 20th century, intra-capsular cataract extraction (ICCE) was the standard. This procedure consists of removing both the lens and the capsule in one single piece. The lens can be replaced by an IOL placed in the anterior chamber, between the cornea and the iris. This method leaves the eye with no barrier separating the anterior and the posterior chambers, thus causing disturbance and stress to the iris, vitreous, retina, and choroid. Moreover, the large incision required to remove the whole crystalline lens can easily lead to complications in the recovery of the patient.

Opposed to the ICCE procedure is the extra-capsular cataract extraction (ECCE). It involves the removal of the nucleus and the cortex of the lens, while the posterior part of the lens elastic capsule is left in place, in order to allow the implantation of an IOL. Since the lens still was almost entirely removed, this method still requires a large incision (10-12 mm).
The Madurai intraocular lens implant study demonstrated for the first time the superiority of extracapsular cataract surgery (ECCE) with posterior chamber intraocular lens implantation over ICCE [13]. Both were able to achieve similar results regarding visual acuity, but ECCE had fewer complications and resulted in a better uncorrected vision.

Several major events, such as introduction of ophthalmic sutures and improving of anesthesia techniques, raised the quality of cataract surgery to a new level, but the two main breakthroughs were the implantation of the first IOL by British surgeon Harold Ridley in 1949, and the introduction of phacoemulsification (PE) by Charles Kelman in 1967.

Phacoemulsification of the nucleus is the most common technique being used in developed countries. It uses an ultrasonic probe equipped with a titanium or steel tip which is able to emulsify the nucleus of the lens. With the help of another fine instrument, the nucleus is chopped into small pieces. This fragmentation eases the emulsification process. Since the lens is not removed in a single piece but is firstly chopped, the incision needed for this type of surgery is smaller (less than 3 mm) compared to the previous techniques. Once all the pieces of the lens are aspirated, a folded IOL can be implanted in the capsule.

As said before, cataract surgery has become quite routine. Before undergoing a cataract surgery, all needed measurements must be performed on patient’s eyes to select an appropriate IOL. These measurements include a detailed evaluation of the corneal curvature and axial length of the eye. These measurements are necessary to calculate the power of the IOL to be implanted.
The actual surgery then begins by putting the patient under sedation and local anesthesia. By means of a lid speculum, the eyelids are kept open. A small incision is then made into the cornea and anesthetic and viscoelastic gel are injected into the eye in order to anesthetize and stabilize the pressure and the internal structure. A circular incision is cut in the anterior capsule and its central part is removed (figure 8.A). With the help of the ultrasonic probe inserted into the eye through a small incision, the cataract lens is sculpted or chopped into pieces which are one-by-one brought into the anterior chamber, emulsified and then removed (figure 8.B). Once the nucleus and cortex are totally removed, a folded IOL is inserted in the empty capsular bag (figure 8.C). Finally the IOL spreads and centers itself in the eye by mean of the haptics (figure 8.D).

Some complications can occur as a consequence of cataract surgery. Posterior capsule opacification (PCO), also known as aftercataract, is an opacification of the natural lens capsule following surgery. PCO can occur several months or years after cataract surgery and it can cause vision loss. There is a simple procedure called neodymium:yttrium-aluminum-garnet (Nd:YAG) laser capsulotomy that can correct the issue. This is an outpatient procedure in which a laser is used to cut a hole in the posterior portion of the lens capsule. Without the opaque capsule disrupting light, vision is then restored.
Figure 8: Main steps of cataract surgery.

(a) First step.  
(b) Second step.  
(c) Third step.  
(d) Fourth step.
1.4 **Objective**

In this first part of our thesis, we discussed the anatomy of the human eye and the aging of the human lens into a cataract. Evolution of the treatment of cataract was also discussed. This was necessary to introduce the main target of our investigation.

Our research focuses on a new design of IOL. The goal of the ultimate IOL is to fully restore vision and accommodative properties, like the original crystalline lens.

The ideas we propose and develop in this paper find their foundations in the work of Nithya Jayapratha and Evan Zaker at the Nanotechnology Core Facility at the University of Illinois at Chicago. In their innovative approach they used micro-fabrication techniques for the creation of an accommodative IOL. However, none of them was able to produce a prototype ready for animal testing.

Our objective is to expand and improve their design, creating a full scale working prototype to be implanted and tested in rabbit models, and create a new type of flexible, cost-effective, fully accommodative IOL.

With the essential contributions of Bruce Gaynes, OD, PharmD and Anuradha Khanna, MD from the Ophthalmology Department at Loyola University, we were able to approach the subject not only from an engineering point of view, but also from the medical one. This strategy, paired with the state of the art nano-fabrication technology available at the NCF, puts our work on the edge of current biomedical engineering research.
CHAPTER 2

INTRAOCULAR LENSES

As stated in the previous chapter, modern surgery with replacement of the crystalline lens with an artificial IOL is the most effective and successful treatment for cataract. IOL implant plays an important role in the successful treatment of visual impairment from cataract.

In this chapter we are presenting an overview of the currently available IOLs and of their future developments, but before doing this we need to understand the fundamental optical principles on which these lenses are based. This will also allow us to become familiar with some of the main terms and quantities used in optics.

2.1 Basic optics

The broad subject of basic optics can be divided into two main branches: geometrical (or ray) optics, where the main phenomenon is refraction, and physical (or wave) optics, dominated by diffraction. The border between this two fields depends on the physical dimensions of the objects we are working with when compared to the considered light wavelength. Since we are considering human vision, we deal with visible light, which is usually defined has having a wavelength in the range of 400 nm to 700 nm [14]. Moreover, since the human lens has dimensions which are several orders of magnitude bigger than visible light wavelength, we can focus our interest in the geometrical optics field.
In geometrical optics, the analysis of how light interacts with plane and curved surfaces can be carried out using light rays, which are imaginaries lines directed along the path that the light follows. The useful geometric construct of light rays allows to easily illustrate propagation, reflection, and refraction.

2.1.1 Refraction

Refraction is a surface phenomenon, and it acts as a change in direction of a wave due to a change in its transmission medium. It is the very reason why lenses function as they do. To understand how refraction works, let us use figure 9 as an example.

The incident ray propagating in the first medium hits the interface between the two different materials at an angle $\theta_i$ and, while part of it is reflected with an angle $\theta_R = \theta_i$, another portion is transmitted through the second medium at an angle $\theta_r$ which is generally different from $\theta_i$. This difference between the angle of incidence and the angle of refraction is due, as
previously stated, to the change of material in which the light is propagating. It is therefore necessary to identify a quantity to describe the transmission properties of a given medium.

This quantity is the refractive index, and it is a measure of the speed at which light travels through a material. In vacuum, light travels at a constant speed \( c = 299792458 \, \text{m/s} \), but at different speeds through various materials. The ratio of the speed of light travelling through a particular material \( v \) and the constant speed of light through vacuum \( c \) is the refractive index \( n \).

\[
n = \frac{c}{v}
\]

Sometimes called the mean refractive index, it is measured in the middle of the visible spectrum (yellow-green). Specifically, the index can be measured at 587.56 nm wavelength for the helium \( d \) line \( (n_d) \) or 546.07 nm for the mercury \( e \) line \( (n_e) \).

The refractive index of materials is not constant for all wavelengths of light. Constringence (Abbe number) relates the mean refractive index of the blue and red ends of the visible spectrum. Constringence can be calculated as

\[
V_d = \frac{n_d - 1}{n_F - n_C}
\]

where \( n_C \) and \( n_F \) represent the F- and C- spectral lines (486.1 nm and 656.3 nm) respectively.

The effect of constringence is most observable in the spreading of different colors of light by a prism. If this occurred in IOL, the color fringing would be very disabling. Therefore, constringence must be kept to a minimum in the materials used to fabricate IOLs. Luckily, constringence tends to decrease as the refractive index increases. Polymethyl metacrylate (PMMA), a pop-
ular material in IOL fabrication, has a measured value of 58 for constringence, which is the same as the high-index crown glass used in the early production of glasses. The reciprocal of constringence is dispersive power, which is more commonly used for measurement.

We said before that, when refraction occurs, we generally have $\theta_r \neq \theta_i$. Now that we introduced the concept of refractive index, it is possible to quantify this difference, using the formula known as Snell’s Law:

$$\frac{\sin \theta_1}{\sin \theta_2} = \frac{n_2}{n_1}$$

Refractive index is then an indication of how much the angle changes when travelling between two materials. The higher the refractive index, the more a lens bends light, and the thinner a lens can be. The change in angle along a non-planar surface, such as a sphere, results in a converging or diverging effect that causes magnification. Fundamentally, a lens is simply an object that converges or focuses light to a certain point, i.e., the retina.

Refraction is apparent in the way objects appear to be bent underwater. The interface is made up of water with a $n$ of 1.333 and air with a $n$ close to 1, and light rays bend when they exit (and enter) the water. Refraction is also the reason that objects look distorted when we see under water. The cornea and aqueous humor have a refractive index of 1.376 and 1.336, respectively, and are very close to that of water. The lens, however, has a higher index of refraction: 1.41 [15]. Therefore, when we see under water, most of the light is bent only by the lens and not the cornea or aqueous humor.
2.1.2 Lenses

The terms power and focal distance are used to describe the focusing ability of a lens system. Focal length of a lens is the distance $f$ from a lens that collimated rays converge, as shown in figure 10. Focal length can be measured using any unit of length, yet is usually given in meters for theoretical calculations and millimeters for camera lenses used in photography.

The thin lens formula shows how focal length relates to the focusing of an image (see figure 11), specifically, the distance to an object, $S_o$, and the distance to the image in focus, $S_i$:

$$\frac{1}{f} = \frac{1}{S_i} + \frac{1}{S_o}$$
At a very large distance for example, looking at an object across a field $S_o$ approaches infinity. The equation then results in the image being in focus at the focal distance of the lens system:

$$\frac{1}{f} = \frac{1}{S_i} + \frac{1}{\infty} \rightarrow \frac{1}{f} = \frac{1}{S_i} \rightarrow S_i = f$$

Because images must be in focus on the retina and the size of the eye is fixed, the focal distance of the eye must change in order to accommodate for objects at different distances.

Power is also a measure of focus and is equal to the reciprocal of focal distance. The unit for power is diopter (D), which is equal to an inverse meter ($m^{-1}$). Using power $P$, and vergence,
$V_O$ and $V_I$ of the object and image, respectively, simplifies the lens equation by removing the reciprocal terms and making them directly additive.

$$V_O + V_I = P$$

Using the measurement of power is especially useful in dual lens systems as it allows the lens powers to add directly.

For a thin lens the focal distance can be calculated as

$$\frac{1}{f} = \frac{n_2 - n_1}{n_1} \left( \frac{1}{R_1} - \frac{1}{R_2} \right)$$

where $n_2$ is the refractive index of the lens material; $n_1$ is the refractive index of medium surrounding the lens, such as air or water; $R_1$ is the radius of curvature of the front of the lens; and $R_2$ is radius of curvature for the back of the lens.

However, in practice, the thick lens equation is a better approximation for realistic lenses. The thick lens equation takes into account the thickness between the front and back surfaces of the lens. The thick lens equation is also known as the lens maker equation and is represented as follows:

$$\frac{1}{f} = (n - 1) \left[ \frac{1}{R_1} - \frac{1}{R_2} + \frac{(n - 1)d}{nR_1R_2} \right]$$
Because it is assumed that an external lens, such as in eyeglasses, is surrounded by air (i.e., $n_1 = 1.000$), $n$ represents the refractive index of the lens material. The thickness of the lens is represented by $d$.

In general, increased radius of curvature $R$ will physically increase the thickness of the lens $d$. This is why higher refractive index materials will allow for higher power lenses without increasing the thickness of the lenses. Another way to avoid a thicker lens and get the desired power is to exploit the concept of Fresnel lenses, which is introduced in the next section.

2.1.3 Fresnel lens

A Fresnel lens is an optical element which can be used as an alternative to classic lenses with continuous optical surfaces. It was invented and developed specifically for lighthouses in 1827 by French physicist Augustin-Jean Fresnel. Its use was later extended to many other fields.

The working principle of a Fresnel lens is relatively simple: since the refractive power of a lens is a property of the optical interfaces, it is possible to remove a great portion of material which does not affect the curvature of the external surface (see figure 12). This allows for a much thinner lens compared to a conventional one with the same optical power.

Though it may have the same focal distance, the Fresnel lens does not have as good of image quality as compared to the traditional thick lens. This is due to the discontinuities between the zones, which cause scattering at those points.

Despite their decreased image quality, Fresnel lenses are good enough for use in inexpensive portable book-reading aids. Other applications include collimating light sources for lighthouses, automobile lights, projectors, etc. Image quality can be improved by increasing the number of
Fresnel zones. In theory, an infinite number of zones would have equivalent image quality as the thick lens structure.

2.2 History of intraocular lenses

The first IOL implantation was performed on November 29, 1949 in London by Sir Harold Ridley. In his documentation, he only noted extra-capsular ext. for extracting the cataract, not implanting the IOL [16]. For 2 years he observed the patient before reporting his case to the Oxford Ophthalmological Congress in July 1951. The work was published in Trans Ophthalmol Soc UK 1951, 71; 617-621, and it is widely accepted as the first IOL implantation performed [17].
Ridley’s IOL itself was a circular biconvex disc much like the shape of the natural lens with extensions from the optic component, known as haptics, to fix and stabilize it in the eye. It was made of the transparent thermoplastic PMMA, also known as acrylic glass, which was the same basic material used to manufacture cockpit canopies in airplanes of the time period. A large part of the success was due to the impeccable manufacture of the IOL by Rayner & Keeler, Ltd, UK, which is a prominent optical company in the United Kingdom. Some of these original IOLs were in eyes of patients for over 40 years [16].

Despite being greatly innovative, there were some disadvantages with the early IOLs: anterior chamber collapse, glaucoma, uvetis and iris atrophy. The first generation lenses were much heavier due to the PMMA material and had poor fixation to the lens capsule allowed dislocation into the vitreous cavity. In addition, the natural healing process caused clouding over of the lens capsule membrane that held the IOL a condition known as capsular fibrosis.

In the 1950s, the second generation lens was developed: the anterior chamber lens (ACL), which is shown in figure 13. As can be deduced from the name, the IOL was placed in the anterior chamber instead of the posterior chamber, where the first generation IOLs were implanted. The ACL procedure was easier, because the implantation was in front of the iris. Multiple haptics allowed for angle fixation and prevented dislocation and loss into the vitreous cavity. Even so, there were complications: the rigid haptic structure damaged the adjoining tissue; rotation of undersized IOLs or excessive vaulting caused contact to the cornea, or corneal endothelial, and led to opacification of the cornea, or endothelial corneal dystrophy; oversized IOLs caused chronic pain and inflammation; and in the early 1950s, impurity and initial poor quality finish
of the PMMA led to uvetis, glaucoma, and hypema, known as UGH Syndrome [11]. UGH Syndrome was still a problem into the 1970s due to deformation of lens haptics.

In the late 1950s, the third generation lens was developed: the iris-supported IOL, shown in figure 14. These IOLs were still implanted in the anterior chamber but were affixed to the iris with sutures, metal clips, and haptics through the pupil. The advantage of iris-supported IOLs was that they avoided contact with the cornea and the chamber angle by being fixed to the iris. However, the procedure was complicated by the difficulty placing the lens; and there were still problems with dislocation. Other disadvantages included dehydration of the cornea,
or corneal decompensation, and adhesion between the iris and the vitreous causing papillary block. Some of the complications with ACL were further addressed with the fourth generation IOLs: the flexibility of haptics was increased; the polish was improved to decrease irritation; and there were multiple haptic diameters available to improve sizing.

IOLs are currently of the fifth generation design. They are either 1-piece or 3-piece in structure and are considered posterior chamber lenses (PCLs) (shown in figure 15), because they are placed where the natural lens was originally located. The optical component is made of PMMA, acrylic, silicone, or other innovative viscoelastic materials. In the 3-piece design, the two haptics are either flexible PMMA or polypropylene.
The introduction of continuous circular capsulorhexis (CCC) allows for several fixation options. Small compressible haptics are compatible with either the capsular bag or the sulcus, with or without iris sutures. Normally, the PCL is fixed in the capsular bag, which is the best location, but this requires an intact posterior capsule. It can also be fixed to the sulcus in the case of a large 1-piece PMMA, 3-piece silicone foldable or 3-piece acrylic foldable IOL. Of course, if there is no capsular support, ACLs can still be implanted or you can use iris-fixed IOL that use a McCannel suture instead of an iris claw. However, the PCL has the least amount of tissue damage. The PCL vaults towards the posterior and as such, avoids contact with the iris and prevents pupil capture.
2.3 Different available types of intraocular lenses

We discuss now the main types of intraocular lenses used today in standard cataract surgery. The reasons that lead to the choice of the IOL can vary from clinical considerations to economical motivations.

2.3.1 Mono-focal

All of the early IOLs were of the mono-focal type; lenses had only a single focal distance and either provided excellent distance or close-up vision. In 1962, Dr. Warren Reese and Dr. Turgut Hamdi suggested a bifocal IOL, the first of multi-focal type IOLs. The idea was to have an IOL that had sections with different focal distances, specifically 2 in the case of the bifocal lens, that provide focus at far, near and possibly even intermediate distances. These were intended to overcome the lack of accommodation experienced by IOL (pseudophakic) patients. However, it was not until 1980 that Mr. John Pearce, protégé of Ridley’s in England, made the early prototype bifocal IOL [16]. The quality of vision was not satisfactory for widespread use. Although there have since been improvements in the design of multi-focal IOLs, even today they have side effects, such as decreased contrast sensitivity, glare disability and halos [18].

2.3.2 Toric

Even the best fabricated IOLs have some level of positive spherical aberration. This increases the total ocular spherical aberration and degrades visual quality. Astigmatism can be a disabling refractive error. Astigmatism can be natural or caused by surgical trauma. Even though astigmatism post-cataract surgery is minimized through new surgical techniques, at least 15 to 20% of cataract patients have 1.5 diopters of astigmatism [19]. Toric IOLs, such as Acri.Comfort
(a) Monofocal IOL.  
(b) Multifocal IOL.

Figure 16: Difference between monofocal and multifocal IOLs.
35

646 TLC IOL (Acri.Tec/Carl Zeiss Meditec), have been reported to be an effective method of reducing astigmatism [20] and are a good solution for patients who desire independence from glasses [21].

2.3.3  Multi-focal

Several companies are now manufacturing multi-focal IOLs. There are 3 types of multi-focal IOLs: multi-zone refractive, diffractive and hybrid refractive-diffractive [18]. Refractive IOLs are based on Fresnel lens and have different powers in zones that are usually in concentric rings that form 2 primary focal points [16] [18]. One example of the refractive IOL is the bifocal Lentis Mplus (Oculentis GmbH). It is a single piece with 2 sectors: the main yielding 2.50 D and a lower one for near vision of 3.00 D. Another example is the Array (Advanced Medical Optics; Santa Ana, CA), and it has five concentric zones that are staggered between distant and near vision. A small study showed that excellent results were achieved [22]. An example of an IOL of the diffractive type is the CreeOn 811 E (AMO, Groningen, the Netherlands) that has wavefront-adjusted optics to improve the quality of vision. Current multi-focal IOLs are of the hybrid type a combination of refractive-diffractive.

2.3.4  Accommodative IOL

The ultimate goal of an IOL is not to give partial vision and be a mediocre improvement compared to a cataract eye but rather to restore vision and accommodation back to the level of a healthy, natural lens.

An accommodative IOL (AccIOL) must be optimized to act much like the natural lens, including the full range of accommodation. For comparison, a healthy, youthful human eye
has approximately 12 D of accommodative power, of which the amplitude needed for reading purposes is 3 to 4 D [23]. It is also necessary that AccIOLs have stable accommodation and the same focusing ability for the same amount of muscle force from the ciliary muscles.

Even with mono-focal IOLs, there might be some apparent accommodation (i.e., pseudo-accommodation) due to the positional movement of the IOL [24]. Multi-focal IOLs may also appear accommodative, but in reality, they only have a fixed set of focal distances defined by physical structures in the IOL. True accommodation requires continuous variance of focal distances. This could be done through axial shifts that move the lens forward and backward (focus-shift) or by changing of the curvature of the IOL with the contraction and relaxation of the ciliary muscles, much like the actual lens does.

As of 2006, AccIOLs, such as the Model AT-45 crystalens (Eyeonics, Aliso Viejo, CA) and the 1 CU (HumanOptics, Mannheim, Germany), showed potential but had limited and inconsistent accommodation. The 1 CU, for instance, has shown a shift of 0.75–2.00 D [25], but more recently less than 0.5 D [24]. Both of these AccIOLs were designed using the passive focus-shift approach, that means when the ciliary muscles contracted, they moved forward, and when they relaxed, their natural tension restored them. Some focus-shift IOLs contain two optics separated with springs to increase the power during the shift. These dual-element IOLs have been able to reach an accommodation range up to 2.2 D [26]. Active focus-shift IOLs use a driving force, such as repulsing mini-magnets. Currently marketed AccIOL are passive focus-shift IOL only.
2.4 Future developments

There is progress with AccIOLs on the market and in clinical trials that are more and more accommodative, but they have not yet matched that of the natural human lens. There have been several active focus-shift IOLs patented. One includes an annular Fresnel lens constructed of a material, such as PMMA, that changes the index of refraction based on radiant or electrical energy applied [27]. The design involves introducing electrical power via the glasses of the patient. Two other designs are very similar and involve electro-optic crystals that change depending on the applied voltage field [28] [29]. Another two involve micro-motors that variably adjust a lens system [30] [31]. Despite these solutions being straight-forward conceptually, they are rather complex when put into practice. Motors and related components have to be powered and microprocessors must be able determine the adjustment needed and control the motors. Due to these challenges and lack of technology at the time, the designs have never been physically realized.

One promising design is a fluidic AccIOL that was inspired by the natural human lens. The design involves a support ring surrounded by two chambers that are filled with an optical fluid. The membrane and support ring are constructed of polydimethylsiloxane (PDMS) because of the desired optical/mechanical properties and its biocompatibility. Because of the thickened capsular bag, the optical fluid must have a higher refractive index than the natural crystalline lens in order to achieve the desired amount of accommodation. A total tuning range as large as 200 D was demonstrated. In addition, this AccIOL design was able to achieve 12 D of
accommodation in the same amount of movement (0.286 mm) that a focus-shift IOL achieved 2.5 D.

Introduced in 2003 [32], light-adjustable lenses (LAL) developed by Calhoun Vision offer the ability to fine tune the IOL after implantation. The material, which constructs the IOL, is embedded with a photosensitive macromer that polymerizes when exposed to certain forms of light. This allows for precise changes to the lens thickness and shape in order to correct hyperopia, myopia and astigmatism without invasive adjustment. These IOLs are not available in the United States and have been under US Food and Drug Administration (FDA) review since 2009, but they are starting to be available in the European Union (EU). Several studies have found that LALs are safe and some results have shown that the technology gives better than 20/20 vision. Technologies similar to LALs will most likely be used in future AccIOLs in order to precisely tune the vision and make necessary adjustments throughout a patient’s life.

There are even methods that attempt to repair the lens in place, instead of fully replacing it. In lens refilling, the capsular bag is evacuated and then injected with elastic polymer solutions, such as silicone, silicone oil or poloxamer hydrogel. The pressure of the fluid restores some of the shape of the lens and, due to the flexibility of the injected solutions, the lens is able to change curvatures responding to varying zonular tension. Lens refilling has been tested in pig [33] and primate [23] [34] models.

Studies involving lens filling have been able to achieve a maximum of 6.7 D accommodation; however, there are still limitations with this approach. Even though the refilled lens does accommodate, the amount of accommodation decreases over time and is not stable between
1.0 to 4.5 D [34]. It is also important that there be adequate response to zonular relaxation. In the relaxed state (emmetropia), the focus should be at 20 feet. In order for this technology to be applied in human cases, the level of accommodation also needs to be higher. Lower levels of accommodation are mostly due to the lower refractive index of the injected material. Another challenge is improving the image quality during accommodation. In one study there was increased spherical aberration [33].

Besides basic problems with accommodation, lens filling has several other unremedied problems. Because silicone has a lower specific gravity than water, it is extremely difficult to use in the filling application. Silicone has a long setting time, up to 12 hours, so there is an increased risk of leakage during and immediately following the surgery [35]. One study showed that it was feasible, yet difficult, to use a silicone plug to seal the capsular opening and prevent leakage [34]. In addition, injected silicone also is associated with severe PCO. In all of the related studies referenced here, the lenses were useless after 3 months [33] [34] [35] [36]. PCO is caused by leftover lens epithelial cells (LECs) from surgery. The usual treatment for this condition Nd:YAG laser capsulotomy can change the accommodation of the silicone filled lens. There has been mild effectiveness in reducing the development of PCO by treatment with actinomycin D and cycloheximid [36].

Lens filling may carry the potential to fully restore accommodation, but many improvements have yet to be made. The ideal material has several attributes. First of all, it must be non-toxic because it is being implanted inside the body (in vivo) for long periods of time. Next, it must be transparent and have good optical properties. Third, it must be easily injectable into
the lens capsular bag without leaking. It must form a solid yet elastic physical gel inside the capsular bag. Preferably, this would be done rapidly and on demand from an external source. Once the material is hardened, it must have modulus and relaxation times that are constant, so that it will have a stable reaction during accommodation. The material (and procedure) must also prevent PCO; otherwise, the lens filling procedure will be useless. Lastly, it must be inexpensive and sustain functionality. With all of these problems left to answer, IOLs, although not perfect, are still preferred and already offer stable accommodative ability.

2.5 Materials

Material plays a crucial role in quality and performance of IOL design. First of all, the material must be bio-compatible. Second, the material must be of certain quality with the desirable refractive properties. Lastly, the material must also be flexible. Each of these requirements is discussed in further detail below.

Biocompatibility is the ability of a material to maintain mechanical, chemical and structural integrity in order to exhibit safe and effective performance within the body of a living creature. The surface characteristics are especially important: smoothness/roughness, wet-ability, charge, polarity, etc. A material’s biocompatibility and performance are also dependent on the specific application for which they are used. For example, a material appropriate for orthopedic surgery could be disastrous in cardiovascular application because of a tendency to create blood clots (thrombogenic properties).

Biocompatibility is difficult to measure, and is determined by comparing laboratory tests with standardized experimental conditions. Adsorption of proteins and other bio-molecules is
a major factor in biocompatibility. These can trigger inflammatory responses such as blood clotting, foreign body reactions and fibrous encapsulation. The more biocompatible a material, the less response the host should exhibit and the more favorable the material for applications such as IOLs.

PMMA has a long and proven history of biocompatibility. Ridley noticed the compatibility of the material with the eyes when working with injured pilots whose canopies had shattered [37]. The shards of PMMA were not rejected from their eyes. PMMA is also easy to manipulate and was used in the first IOL. Modern-day PMMA demonstrates even greater biocompatibility because of its higher quality. It can be manufactured in a variety of different molecular weights, and the optical quality of the IOL can be highly variable when mixed with different materials. Each manufacturer has a special formulation for different PMMA compounds. Of all of the materials used for IOLs, PMMA remains the most popular among ophthalmic surgeons [38].

The need for flexibility was the main reason other materials were considered. Solid PMMA IOLs require that the incision size be as large as the minimum IOL dimension, which is generally 5.5 mm. IOLs composed of flexible polymers, such as hydrophobic acrylics, hydrophilic hydrogels, silicone elastomers and porcine collagen [39], are able to fold and be implanted through much smaller incisions. In addition, zonules and the capsular bag become brittle following the RCS procedure, so there is less muscle force to control the IOL [26]. AccIOLs must be flexible enough to move under these forces.

Pure PMMA, made of polymerized methyl methacrylate (MMA), is rigid. Foldable IOLs use a variety of materials, such as 2-phenethyl acrylate (PEA), 2-phenethyl methacrylate (PEMA),
**TABLE I: COMMON IOL MATERIALS.**

<table>
<thead>
<tr>
<th>Lens</th>
<th>Material</th>
<th>Refractive index</th>
<th>Water content</th>
<th>Flexibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMMA</td>
<td>MMA</td>
<td>1.49</td>
<td>&lt;1%</td>
<td>Rigid</td>
</tr>
<tr>
<td>Alcon Acrylsoft</td>
<td>PEA/PEMA</td>
<td>1.55</td>
<td>1%</td>
<td>Foldable</td>
</tr>
<tr>
<td>Allergan Clariflex</td>
<td>EA/EMA/TFEMA</td>
<td>1.47</td>
<td>1%</td>
<td>Foldable</td>
</tr>
<tr>
<td>ORC Memory Lens</td>
<td>HEMA/MMA</td>
<td>1.47</td>
<td>20%</td>
<td>Foldable</td>
</tr>
<tr>
<td>Storz Hydروview</td>
<td>HEXMA/HEMA</td>
<td>1.47</td>
<td>18%</td>
<td>Foldable</td>
</tr>
<tr>
<td>Chiron C10UB</td>
<td>HEMA</td>
<td>1.44</td>
<td>38%</td>
<td>Foldable</td>
</tr>
<tr>
<td>Iolab Soflex</td>
<td>PDMS</td>
<td>1.41</td>
<td>1%</td>
<td>Foldable</td>
</tr>
<tr>
<td>Allergan SI-30NB</td>
<td>PDMDPS</td>
<td>1.43/1.46</td>
<td>1%</td>
<td>Foldable</td>
</tr>
</tbody>
</table>

ethyl acrylate (EA), ethyl methacrylate (EMA), 2,2,2-trifluoroethyl methacrylate (TFEMA), 6-hydroxyhexyl methacrylate (HEXMA), 2-hydroxyethyl methacrylate (HEMA), poly (dimethylsiloxane) (PDMS) and poly(dimethyldiphenylsiloxane) (PDMDMS). Some common IOLs are described in Table I.

Of special note is PDMS. It is a chemically inert, non-flammable and biocompatible material that is widely used as a biomedical implant material [40]. It has favorable optical properties, such as transparency above 230 nm and very low auto-fluorescence [41], and has been used for a long time in ophthalmology for IOL. PDMS is also extremely flexible due to its very low Young’s modulus. As such, it has become the preferred soft substrate due to its ease of processing [42].

One major complication that arises with IOLs is opacification. It is caused by calcium phosphate hydroxide granular deposits under the surface of the IOL. Opacification has been linked to local agents, such as viscoelastic devices and the antibiotic mitomycin C; systemic
conditions, such as diabetes mellitus, hypertension, ischemic heart disease and uveitis; and even the migration of silicone from the packaging of an IOL. Opacification also happens primarily to IOL made of hydrophilic material [43]. Exchanging opaque IOLs is challenging and can undo the advantages of the otherwise low-impact RCS procedure.

PMMA can be designed with an affinity to water (hydrophilic) or not (hydrophobic), with varying degrees in between. IOLs made from hydrophobic PMMA have more glistening, which effects visual quality, but hydrophilic PMMA has poor PCO performance. Hydration of PMMA to make it hydrophilic may cause opalescence or change the refractive index of the material. In the hydrophilic IOL, visual acuity decreased 9%, most likely due to the increased opalescence caused by greater water content. Overall, results show that hydrophobic PMMA has better optical quality than hydrophilic PMMA [17]. Silicone has been shown to be statistically superior to PMMA and equal to AcrySof for reducing PCO [44].

Other material considerations include the index of refraction and its reaction to Nd:YAG. Finer details (higher spatial frequencies) were more viewable with PMMA IOLs as opposed to silicone IOLs. This can be attributed to the higher index of refraction of PMMA compared to silicone as well as the lower convexity that can be achieved by PMMA [38]. However, during Nd:YAG, PMMA with lower polymerization tend to crack and scar more easily than higher polymerization [17].

2.6 Traditional fabrication and cost of IOLs

IOLs are fabricated much like regular optical lenses and newer ones are even more so like contact lenses. The first step is to reduce the raw material to a manageable size, referred to as
a puck or blank. These can either be cut from the bulk material in the case of harder materials or, in the case of softer materials, extruded from the bulk material. The polymer pucks or blanks are available from distributors with consistent and precise dimensions. Companies like Benz Research and Development provide high quality raw materials, such as 2-HEMA, at 99.9% purity for the IOL industry. This purity eliminates the possibility of opacification caused by the appearance of calcium phosphate particles.

The polymer blanks are then milled to the proper curvature. Unlike regular lenses, which are cut down in the lapping process by a crown tool with an industrial diamond [45], IOLs are precisely milled and turned by fully automated machinery. Lathes, like the one pictured in figure 17, might be used for spherical, aspheric, toric, multi-focal and other irregular cornea fits [46]. Haptics are then drilled for 1-piece IOLs. Otherwise, they can be milled and attached later in 3-piece IOLs. Alternatively, IOLs can also be molded to the right curvature. Some IOLs are even molded on one side and milled on the other.

Next the polishing and hydration steps are performed. Hydration makes the material soft and flexible. Much like contact lens that are milled while a hard material, they become flexible after soaking in a balanced pH saline solution for several hours. Most hydrophilic IOLs are tumble polished after hydration. Other solid IOLs may be polished with a fine abrasive. Depending on the manufacture, once the lenses are fully machined and polished, the surface can be coated with chemicals for protection, to increase visual quality or to enhance biocompatibility. Finally, the lens is inspected, labeled and packaged. Current IOLs cost between $1500 and $3000 [47].
Figure 17: DAC International MLC Mill/Lathe Combination System.
CHAPTER 3

MICRO- AND NANO-FABRICATION

In our design we will use modern state-of-the-art fabrication techniques. Let us give insight into these procedures.

3.1 Introduction

Micro-fabrication techniques emerged as the result of the increasing complexity and decreasing size of integrated circuits in very large scale integration (VLSI) technology. Although they are normally used in the manufacture of electronics, micro-fabrication processes and techniques have been adapted to mechanical systems since the 1970s [48]. In general, these devices are grouped into the category of micro-electro-mechanical systems (MEMS). Not only does micro-fabrication allow mechanical devices to be fabricated on the same chip as the electricity circuitry to which they are connected, but some devices, such as in micro-fluidics, might not have an electrical connection at all and rely on the mechanics of the device alone. Micro-fabrication has spurred several sub fields in different industries, such as BioMEMS.

There are two approaches to micro-fabrication: bottom-up and top-down. In the bottom-up approach, which is used less widely, the process starts with a blank substrate and the structures are grown or assembled from original seeds. A substrate might start at the atomic or molecular level with a seed crystal or single polymer. This is referred to as self-assembly, which is found in the natural world. The bottom-up approach allows for smaller geometries than what is
currently available using the top-down approach, but it is limited by the growth rates and therefore, working devices are difficult to mass produce. Currently, many labs are researching the creation of nanodots, nanowires, nanotube transistors, and monolayers using bottom-up approaches. Specific techniques that are commonly used in this approach are molecular beam epitaxy (MBE) and molecular self-assembly.

The top-down approach represents the inverse idea and involves transforming bulk material into smaller devices. The first step is to create the bulk material that is going to be modified. Silicon wafers are common substrates and are cut from a large ingot grown from a single silicon crystal. Thin films are then deposited on the wafer through processes such as electron beam evaporation or chemical vapor deposition. The thin films are then shaped by either etching or lift off. Photolithography (PL) is the process by which patterns are created on the thin films. In PL a layer of photo resist (PR), which is a light-sensitive chemical, is spread on the wafer and/or thin film layer. The PR is then exposed to light and treated in a developer solution in order to reveal the pattern.

The PR can be either negative or positive. In positive PR, exposure to light breaks the bonds in the chemical and allows it to be removed in the developer. Negative PR performs in the opposite manner: exposure polymerizes the chemical, making it insolvent in the developer. The developer dissolves and removes the PR in the desired areas and a pattern is formed. The PR can protect portions of the metal from etching, or the PR can be dissolved to lift off the metal in certain sections.
There are two main parameters used to characterize photoresist: contrast and Critical Modulation Transfer Function (CMTF). Modulation transfer function is simply a measure of dark versus light intensity produced by an exposure system. CMTF is used to define the same quantity for the resist and is roughly the minimum optical transfer function needed to resolve a pattern in the resist. Contrast is an experimentally determined parameter for each resist, and its value is extracted from plots obtained by using different exposure doses, developing the resist and measuring the thickness that remains (figure 18). For positive resist, less exposure leaves more resist. For negative resist the opposite is true: higher exposure levels leave more resist. Contrast is the slope of the transition region in such contrast curves.
Mathematically, contrast is defined as

\[
\gamma = \frac{1}{\log_{10} \frac{Q_f}{Q_0}}
\]

where \(Q_0\) is the exposure dose that starts the transition and \(Q_f\) is where it stops.

Photolithography is the main limitation in micro-fabrication. There are several different forms of photolithography as each one progressively decrease the wavelength of light used because the highest resolution that can be achieved with photolithography is \(\lambda/4\), in which \(\lambda\) is the wavelength of the light used. UV light is the source for the vast majority of photolithography, but it has considerable drawbacks when narrowing down the length scale because it is not possible to reduce the size of the features below the diffraction limit of the UV light. Deep ultra-violet (DUV) decreases the wavelength further. Extreme UV can get a resolution of around 11 to 14 nm [49].

There are many improvements, such as phase shift masks, optical proximity correction (OPC) and high refractive index imaging. Phase shift masks use destructive interference to minimize diffraction effects. Parts of the masks that interfere with each other have a material added that would give a 90-degree phase shift to the incoming light. Then when the light meets, they will cancel and produce an area without light that was not supposed to have light before [50]. Diffraction causes the lines to be softer as they reach the surface, so edges become rounded. OPC estimates the error caused by diffraction and corrects for it by modifying the pattern structure. Diffraction effects are lessened in immersion lithography by performing
lithography in a high refractive index material \((n \sim 1.7)\). Both Intel and IBM implement immersion lithography in order to reach smaller resolution. Intel has already pushed the technology to producing 22 nm dimensions. All of these corrections and adaptations make the photolithography system more complex and therefore more expensive.

The LIGA (Lithography, Electroplating, and Molding) process is another approach to fabricate advanced 3D structures. In this process, synchrotron generated radiation (X-ray) is used to pattern the photo resist. The process is capable of creating high aspect ratio structures (30 nm x 5 \(\mu\)m), but access to synchrotron radiation prohibits the usage of the method.

Multi-photon Absorption Polymerization (MAP) is another advanced technique which used to create sophisticated 3D structures. The process utilizes a non-linear optical effect created using an ultra fast Titanium Sapphire laser. In this process, the resist is exposed to the laser and, by changing the focusing point inside the polymer; polymerization can be done according to the desired pattern. After developing the resist, un-polymerized areas can be washed away. Laser excitation can generate features with transverse dimension as small as 80\(nm^2\). Among these, few are highly appropriate for high resolution.

Even without the limits of resolution, photolithography is not the best candidate for advanced 3D micro-fabrication. Direct write methods allow you to create structures without the use of masks, which can decrease cost and increase the complexity (layers) in the structures. They also allow for exposure of non-planar substrates [49]. In Scanning Probe Lithography (SPL), scanning probe microscopes (SPMs) have been used to draw lines and construct nano-scale features. SPL methods include Dip Pen Lithography (DPL) and Nano-imprint Lithog-
raphy (NIL). DPL, which is able to pattern in the sub-100-nm scale, involves depositing an ink chemical depending on the application to the substrate via the probe. NIL mechanically imprints patterns and demonstrated a 25 nm resolution by displacing atoms from the substrate surface.

Heated tips have shown sufficient energy to break chemical bonds of a material and decompose it into volatile monomer units, but this process was slow. Most recently, heated scanning probes have been used to write in resist. Using self-amplified de-polymerization (SAD) polymers, structures were written at less than 2 $\mu$s per pixel and resulted in a total write time of 143 s for an image comprising $5 \cdot 10^5$ pixels. The tip was heated to 700$^\circ$C and could create 40 nm lateral and 1 nm vertical resolution. In another study using a similar technique, resolution down to 15 nm and a writing rate of $5 \cdot 10^4 \mu m^2/hour$ was achieved.

These SPL methods can be massively parallelized. Around the world, there are attempts to develop integrations of hundreds and even thousands of tips. Future densities could increase to the millions. Each tip can be either active (lowered and drawing) or passive (raised and inactive). As the head scans the substrate, basic algorithms control the tips mode in order to write the pattern. There have been several improvements to the writing speeds of these devices [51]. Although a writing time on the order of hundreds of seconds is attractive, electron beam lithography has the best advantage in resolution.

### 3.2 Electron Beam Lithography

Another state of the art fabrication technology capable of producing high resolution patterns is electron beam lithography (EBL). In EBL an electron beam is used to directly write on the
surface of a sample, so it is a direct write method and does not involve masks. In the regular EBL patterning process, an electron beam is scanned across the surface exposing the resist to enough energy to break the polymer chains throughout the entire thickness of the resist down to the substrate. Even though photolithography has been pushed by enhancements such as liquid immersion, phase-shift masks and optical proximity correction, the next-generation lithography technique of EBL offers better resolution. Early on, it was common to convert electron microscopes to EBL using accessories, but dedicated systems have produced resolutions of less than 10 nm.

An EBL system is rather complex. Figure 19 diagrams an EBL system based on the one used in this project. Each component will be developed in the following sub sections.

### 3.2.1 Electron Theory

Electrons can either act as a wave or as a particle. This wave-particle duality is routinely encountered in SEM and EBL. In both the photoelectric effect and scattering (explained more later), electrons behave like particles, but electrons are still affected by diffraction, which is a wave phenomenon. In general, electrons have lower wavelength than UV, deep UV and even extreme UV (XUV) light. The wavelength of an electron is calculated by the de Broglie equation:

$$\lambda = \frac{h}{p}$$

where $h = 6.626 \cdot 10^{-34} kg \cdot m^2/s$ is Planck’s constant, and $p$ is the momentum of the electron. The momentum of an electron can be related to electron volts (eV), which is the amount of
Figure 19: Schematic of an EBL system.
energy that an electron gains in the presence of an electric field of 1 V. For example, electrons in an SEM could be accelerated by 10 kV:

\[
p = \frac{E \cdot e}{c} = \frac{10000V \cdot 1.602 \cdot 10^{-19}C}{2.9979 \cdot 10^8 m/s} = 5.344 \cdot 10^{-24} kg \cdot m/s \rightarrow \lambda = 0.124 nm
\]

With such a low wavelength, much lower than even XUV (124 nm), the theoretical resolution is much better.

### 3.2.2 Vacuum Systems

One of the reasons EBL is more expensive than other lithography methods is that it requires the use of vacuum systems. A practical electron gun must operate in a vacuum. An electron is a small particle with a mass of \(9.109 \cdot 10^{-31} kg\) and can be throw off course very easily if the electron were to encounter, for example, an oxygen molecule of mass of \(5.3 \cdot 10^{-26} kg\). There are also plenty of electron clouds of each air molecule that would deflect electrons. At atmospheric pressure (760 Torr), there are about \(2.4811 \cdot 10^{25}\) molecules in one cubic meter. In a typical vacuum of a chamber for EBL with a pressure of \(1 \cdot 10^{-5}\) Torr, there are \(3.260 \cdot 10^{17}\) molecules. This is a difference of 8 orders of magnitude, and makes a significant difference. It is easier to see and more fitting to put it in terms of mean free path (\(l\)):

\[
l = \frac{RT}{\sqrt{2\pi d^2 N_A P}}
\]

where \(R\) is the universal gas constant, \(T\) is the temperature, \(d\) is the diameter of the gas molecule, \(N_A\) is Avogadro’s number, and \(P\) is the pressure. Estimation is done assuming a
pure nitrogen ($N_2$) environment, yet normal air contains 78%. This estimation also assumes
the electron to be the same size as every other gas molecule. At atmosphere, the mean path
is only around 0.1 nm. At the high vacuum level ($10^{-5}$), it is estimated around 7 m [52].
This difference is substantial, and allows for the vast majority of electrons to make it through
the electron gun unobstructed. Vacuum in the electron gun itself may be under $10^{-7}$ further
increasing the benefits.

Vacuum plays another role. Due to the high potentials used in the electron gun, there needs
to be an insulating medium (vacuum) to prevent arcing. The electrical breakdown of air is
about 3 kV/mm. In high vacuum, it can be raised 10 times to 30 kV/mm [53]. This is more
important in higher power (potential) equipment.

With vacuum chambers and systems, comes bake-out. This is a maintenance step where
the chamber is put under vacuum and heated. The walls of the chamber heat to help vaporize
materials and release gases that remain in the system. For this bake-out procedure to work,
all equipment inside the chamber needs to be compatible with the temperatures used in the
process.

For the levels and range required, multiple stage vacuum systems are necessary. Multiple
stages are used because of the different efficiencies of specific vacuum pumps. This is often the
case with other fabrication equipment that require vacuum chambers such as e-beam deposition,
reactive ion etching (RIE) and chemical vapor deposition (CVD) tools. For example, roughing
pumps, which are usually piston type, are used to pump down to $10^{-3}$ Torr, and pumps such
as turbo-molecular ones are used to pump down to higher vacuum: $10^{-5} – 10^{-7}$ Torr.
3.2.3 Electron Sources

The electron gun in an EBL or SEM system needs to have a source of electrons. Electron emission involves giving enough energy to an electron so that it can overcome the binding potential (work function) and escape from the surface of a material. An example of an energy band diagram for a generic material is represented in figure 20.

The area below $E_V$ is the valence band, where most of the electrons are in a material. The conduction band at energy $E_C$ is the place electrons conduct in a material. The Fermi energy level $E_F$ is the level at which 50% of the electrons will be found. The vacuum level, or free energy state, is that above $E_0$. At this energy level, the electron is no longer bound by the material. The work function is the energy needed to reach that level. Electron sources must
provide a simple and consistent source of these electrons. These can be either thermionic or field emission sources.

Thermionic emission involves introducing enough energy to electrons through heat. Electrons have an energy related to temperature by the Boltzmann constant ($k = 8.617398 \cdot 10^{-5} \text{eV/K}$):

$$E = kT$$

Temperature $T$ is expressed in Kelvin degrees. For example, at 2700 K, electrons will have energies of about 0.23 eV.

Early on, a thermionic source would simply be a thin (0.1 mm) wire of tungsten (W). Tungsten can operate at very high temperatures without melting or evaporating. Current is run through the wire and it heats up much like a filament in a light bulb. Running this process in a vacuum helps in multiple ways. It allows the element to heat up with less energy because there are fewer molecules to allow for heat dissipation, and less air molecules prevent the filament from oxidizing. This is also why a light bulb is a vacuum. Thermionic sources are quite simple in construction and are used on various equipment such as electron beam evaporation systems.

The amount of electrons emitted from a thermionic source (emission flux) can be expressed by the Richardson-Dushman equation:

$$J = \frac{\Phi}{AT^2e^{\frac{-\Phi}{kT}}}$$
where $A$ is a constant typical of the used material and $J$ is the current density emitted. For tungsten, $A$ equals $60 A/cm^2 K^2$ and the work function ($\Phi$) is 4.5 eV. From this equation, theory shows that electron current will increase exponentially with temperature. For tungsten, this relationship is true from 2500 K to when it melts at 3100 K. Current is increased until the emission of electrons saturates. Higher temperatures do provide more electrons, but they also sacrifice filament lifetime. At 3 to 4 A, tungsten runs at 2500 to 2700 K [54].

The size of emission is important because it has an effect on the overall beam size. Finer focused emission needs less area for condensing lenses, maintains a higher current density, and ultimately requires less demagnification by the column. Narrower light will also result in less energy spread, which is comparable to monochromatic light. Because of this size requirement, the shape of the source is important. Newer thermionic sources use a crystal of lanthanum hexaboride ($\text{LaB}_6$). The tip shape then directs emission to a narrow column. The material, also known as only lanthanum boride ($\text{LaB}$), is a ceramic material that has a very low work function that allows it to have some of the highest electron emissivity known.

A Wehnelt cup helps collect electrons that are emitted from the electron source. The cup encompasses the source. It is kept at a negative potential around -300 V in order to confine electrons. A small hole at the bottom of the cup allows for the electrons to be pulled toward the anode part of the electron gun.

Field emission (FE) sources involve using an electric field that is sufficiently strong to tunnel electrons through the barrier. The sources are usually tungsten tips sharpened to a needle point. Tungsten can also be shaped to very sharp points possibly the tip of a single atom. The sharp
point allows for a higher field to be active increasing electron emission and allows for tighter control of the emission location. The cathode of the source, comparative to the Wehnelt cup, is referred to as the suppressor. The anode is simply the extractor.

Cold (field) emission sources only use the voltage as an extraction force. These sources are used primarily in electron microscopes rather than EBL because of their instability including long term drift. Newer equipment uses Mueller-emitter-based sources that are a combination of both types and known as thermal field emission (TFE). These operate at high temperature and employ an extraction voltage. Heated sources are more stable because they drive off gases that might interfere with a cold source and can be stable for months at a time. Often TFE sources are tungsten tips coated with zirconium dioxide, which lowers the work function of the material.

An overview on the main parameters of some of the discussed electron sources is given in Table II (71).
There are other electron sources being researched, such as carbon nano-tubes (CNTs). These sources offer the possibility of thermionic and photoemission. For thermionic emission, single- and multi-walled CNTs intercalated with potassium, a temperature-independent work function below 600 K with a minimum of 2.0 eV has been observed. Also, Nd:YAG laser can be used to illuminate the same CNTs causing an increase in electron energy distribution [55]. High brightness has been found in multi-walled CNTs [56], and they may prove to be a future replacement for electron sources.

### 3.2.4 Acceleration Potential

Once you have electrons emanating from the source, they need to be accelerated down the column towards the substrate. This is done by extra-high tension (EHT) through the electron gun: the source is the cathode, and at the end is the aperture, which is the anode. This EHT can range from 0 to 100 kV in EBL and even 200 kV in tunneling electron microscopes (TEM). Higher energy electrons allow for examination of thicker sample, but they might also cause damage to the sample. Not only does higher energy pierce deep into the resist and substrate, the beam diameter also decreases. The EHT should not only be high voltage, but it must also be stable. Any change in the acceleration potential would change the energy with which the electron hits the substrate.

### 3.2.5 Beam Blanker

In lithography, the pattern being written is not always made up of continuous lines. In order to do this, the beam will need to be stopped and started. Both the electron source and the acceleration voltage cannot be cycled off quickly. Instead, it is easier to turn the beam off
and on by deflecting it from the substrate. This can be accomplished by a simple electrostatic
deflector, which is a pair of plates. A blanking amplifier with fast response time is connected
to the plates. When the plates are energized, the beam is deflected off its perpendicular path
down the column. If the blanker is not positioned close to a focal point of the beam, streaks can
occur on the sample when the beam is deflected off axis. Higher energy systems might require
elaborate blanking systems with multiple plates and delay lines in order to prevent motion of
the beam during the blanking process.

3.2.6 Lenses

The Wehnelt cup and the acceleration potential confine the beam a small amount and
provide a coarse amount of focusing. However, the stream of electron emission is still quite
divergent and requires further focusing by lenses. The goal of the lenses is to condense the
electron emission into a relatively parallel (collimated) beam. In principle, lenses in electron
columns behave the same as lenses in optical systems. To understand lenses in an electron
column, electron trajectories can be considered like light rays, and the ideas of converging and
focal points are the same.

Though electron lenses might be similar to optical lenses, the quality of the focusing in terms
of aberrations is not nearly as good as with optical lenses. Spherical and chromatic aberrations
are two types that are critical to EBL. Spherical aberrations are caused by a difference in
power between the inner and outer areas of the lens. Chromatic aberrations occur because
electrons of different energies (wavelengths/color) are focused to different points. There is no
current mechanism to correct for chromatic aberrations, so narrow dispersions of the electron
beam from the source are needed. Both of these aberrations can be minimized by confining the electrons to the center of the lenses, but this will greatly reduce beam current by limiting electrons.

Lenses in electron columns can either use electrostatic or magnetic forces. Electrostatic lenses are not used for fine focusing because of more serious aberrations than magnetic ones. When they are used, they are often found at the beginning of the gun region because they can be combined with the extractor anode. A simple electrostatic lens is diagramed in figure 21.

In the Einzel lens, there are 3 apertures in series. The outer two have no potential (grounded), and the inner one has a voltage that can be varied. The focusing comes from drawing electrons back to the center of the column with positive potential. Lens power is controlled by changing the voltage.
A magnetic field can be used to bend electrons inward and converge them to a focal point. This force is represented by the law of magnetic (Lorentz) force:

\[ \vec{F} = q(\vec{v} \times \vec{B}) \]

where \( q \) is the charge of an electron, \( \vec{v} \) is the velocity vector of the electron and \( B \) is the magnetic field from the lens. The power of a magnetic lens can be created by using electromagnets. Electromagnets are coils of wire, usually copper, encased in a high permeability material, such as iron, to concentrate the magnetic field. An opening in the casing focuses the field toward the center of the column (figure 22).
Multiple lenses may be used to further increase the focus of the beam. The job of first condenser lens is to collect the electrons from the source. The second lens’ job is to converge the beam at the specimen. The sharper the focus the fewer electrons are intercepted by the apertures and the higher the beam current.

3.2.7 **Stigmators**

Because the construction and operation of the lenses are not perfect, there will be errors in the circular beam shape. Astigmatism is an elliptical distortion of the beam caused by differences around the circumference of the lenses. Stigmators are special lenses that are used to compensate for these imperfections by adjusting x and y directions independently. Like lenses, stigmators can be either electrostatic or magnetic. They may have 4 or more poles (8 is typical) arranged around the optical axis. There may be even two stigmators to make the beam its optimum shape.

3.2.8 **Apertures**

The main job of the aperture is to filter out electrons that were not tightly focused into the beam. This makes sure that the electrons are normally incident to the sample. It also intercepts the beam when it is deflected (turned off). The aperture is also used to shape the beam. Earlier beams were gaussian in shape, but to create continuous patterns, it is useful to force the beam into a shape such as a square. Creating an area of known exposure dose makes patterning more continuous. They can then be treated as pixels and exposed individually to create patterns. Overall, different sized apertures vary the beam current.
3.2.9 Scanning

Once the beam is formed, it needs to be scanned across the surface of the sample in order to render an image in an SEM or write an image in an EBL. This is done by deflecting the beam to different parts of the sample. One scanner (deflector) tilts the beam towards another part of the sample. Alone, this would introduce an angle between the beam and the sample. Translating is done with 2 deflectors: one to tilt it to a new position, and the second to correct it back to being perpendicular to the sample. Deflecting the beam causes aberrations and enlarges the beam diameter. The maximum extent of the deflectors creates the area known as the write-field.

Like lenses, beam deflectors can be either electrostatic plates or magnetic coils. Again, electromagnetic coils provide fewer distortions than the electrostatic ones; however electrostatic deflection can perform at much higher speeds. Electromagnetic coils cannot respond to the higher frequencies of charging and discharging. A compromise with both electrostatic and magnetic is used in some systems: magnetic is used for long-range deflection and electrostatic is used for short-range and high-speed. Deflection systems are frequently placed inside the final lens, so ferrite is used to cover the final lens to minimize field interactions from the scanners.

3.2.10 Stitching

Beam translation only allows for a certain write-field size that is determined by the ability of deflection and the acceptance of aberrations and distortion. In order to write patterns larger than the write-field, the sample and therefore the stage must be moved. When this process is used to continue a pattern, it is called stitching. Stage movement is done through two different
methods. Coarse movement is done by servomechanisms (servos) while fine movement is done by piezoelectric motors (piezo-motors).

Servos are electric motors that involve error-feedback via encoders to allow for precise position control. Due to the mechanical nature of the servos, alone they are not accurate enough for moving the stage.

Piezo-motors rely on the change in shape of materials when voltage is applied. The deformation of these piezoelectric materials is known very precisely and allows for very fine movements. Confirmation of the movement is done on both axis (X and Y) by an interferometer. An interferometer involves using a laser to measure the distance traveled in both directions. Laser interferometers are highly accurate and allow for stitching errors to be in the range of single nanometers.

3.2.11 Substrates

There may be some limitation on what substrates are compatible with EBL. Electrons, being charged particles, tend to charge substrates negatively unless they can quickly gain a path to ground. If they are not dissipated quickly enough or become trapped, the substrate becomes charged. When a substrate is charged, it will deflect further electrons due to the repelling of similar charge. This is known as charging effect and will disrupt further exposure of the substrate. The charging effect creates the same limitation in SEM imaging that requires non-conductive samples to be coated with metal.

Especially in high-energy electron beam lithography, it is important to have paths assisting the electrons to ground. On silicon wafers virtually all electrons stop at the wafer where they
can follow a path to ground; however, masks, which are made of materials such as quartz (insulators), often have embedded electrons that will take much longer to move to ground. For low energy exposures, negative charge can be controlled by adding a conductive layer to insulating surfaces. For high energy exposures ($\gtrsim 10$ keV), electrons can pass through the resist and conductive compensation layers and end up in the substrate.

### 3.2.12 Resists

SU-8 is a chemically amplified epoxy based negative UV-resist originally developed by IBM. It has shown continued use in lithography from UV in photolithography to X-ray lithography before being used in electron beam lithography. Due to its capability for high-aspect ratio structures thanks to a low absorption coefficient at wavelengths above 360 nm, it has been widely used in MEMS fabrication.

As mentioned before, SU-8 is chemically amplified. Exposure created an acid that initiates cross-linking. The post-exposure bake is very critical and provides the thermal energy needed to complete the polymerization of SU-8 monomers. Overall, SU-8 seems to be the most popular resists [57]. SU-8 is developed in a PGMEA (propylene Glycol Methyl Ether Acetate) bath [58]. It is also durable and resistant to most chemicals and solvents, which can be beneficial in processing.

PMMA is plastic that can act as a negative photoresist for EBL. Although it requires a larger exposure dose ($50-500\mu C/cm^2$) than SU-8 ($3\mu C/cm^2$) [59], PMMA has a higher resolution [60]. It is a transparent resist that lends itself to being used for optical devices. It is also easy to apply and develop. PMMA avoids charging during EBL and exposes well. PMMA has demonstrated
a 20 nm resolution while another popular resist, ZEP-520, has only demonstrated 60 nm [61]. If PMMA is used on insulating substrates, a thin coating of metal, such as aluminum, chrome or copper may be used to help dissipate the charge accumulation [62].

Chalcogenide glass (ChG) can be used by multiple sources: UV, x-ray, and e-beam. It is claimed that ChG offers many benefits over polymer resists, especially for optical device fabrication because it is transparent in the visible and IR regions of light. This would prove important to the device in this paper. For EBL, ChG exhibits near linear height dependence with electron irradiation dose. This makes it clearer to create images from an actual structure: no correction is needed. Additional simplicity comes with the elimination of pre- and post-bake procedures that are required by polymer-based PR.

There are also several other benefits that ChG exhibits that aren’t directly beneficial to this project. ChG has a much greater hardness resulting in greater etch selectivity than organic photoresists. This hardness also extended to acids, where it shows an etching ratio of around 10 via RIE, which is a five-fold increase from traditional PR. ChG allows for increased flexibility in that it acts as both a positive and negative PR depending on the alkaline developer used. Negative etch can also be performed in plasma containing CF$_4$, Ar, and O$_2$. The smallest features demonstrated in As$_{35}$S$_{65}$ ChG resist are lines of $\sim$ 17 nm width and $\sim$ 80 nm height with $\sim$ 7 nm spacing. Exposed 365 nm, 8.4 mW/cm$^2$, Karl SUSS MA-6 mask aligner. Etched in non-aqueous amine-based solvent. Some complications do balance out the ease that comes with ChG. As$_2$S$_3$ ChG needs to be deposited via high-vacuum thermal evaporation-deposition
instead of spinning. Also, during exposure, 20 Pa of nitrogen gas (N\textsubscript{2}) was needed to avoid charging of the substrate.

Hydrogen silsequioxane (HSQ) has been show to be an excellent tone resist in high resolution high aspect ratio EBL. It was demonstrated in multiple-step 100 keV EBL that lateral dimensions down to 30 nm in thickness up to 1 m was possible. In these experiments, silicon nitride (Si\textsubscript{3}N\textsubscript{4}) was used because of the optical characteristics for x-ray lenses to reduce photon beam absorption. Also, it allowed for the high energy EBL by sparing proximity correction. There is negligible backscattering in the thin nitride membrane. 600 K PMMA was used on top. The spot size was estimated at 10 nm with a current of 40 nA and resulted in a dose of 1000 µC/cm\textsuperscript{2}. Development was done in 7:3 IPA:H\textsubscript{2}O. Samples were supercritically dried. A second layer, this time of HSQ, was applied at 1000 rpm for 60 s, 1µm thick layer.

### 3.2.13 Resolution

The diameter of the beam is changed throughout its path through the column. First, there is the size of the virtual source

\[
d_v = \frac{1}{\pi} \sqrt{\frac{i}{\beta}}
\]

where \(i\) is the beam current and \(\beta\) is the brightness of the beam [63]. The virtual source is then multiplied by the magnification of the column (\(M\)) resulting in the diameter of the beam leaving the gun:

\[
d_g = d_v M = \frac{2}{\alpha} \frac{1}{\pi} \sqrt{\frac{i}{\beta}}
\]
The convergence angle is represented by $\alpha$. Apertures are used to limit convergence angles. Second, because the lenses of the system are not perfect, the diameter caused by spherical aberration needs to be taken into account. It can be calculated as

$$d_s = \frac{1}{2} C_s \alpha^3$$

where $C_s$ is the spherical aberration coefficient. Third, there are also chromatic aberrations from the column lenses. Different energies of electrons result in different wavelengths (colors). At present, electromagnetic lenses cannot be made to adjust for this. The diameter due to these aberrations can be calculated

$$d_c = C_c \alpha \frac{DV}{V_b}$$

where $C_c$ is the chromatic coefficient, $DV$ is the energy spread of the electrons and $V_b$ is the beam voltage. Last, as mentioned before with electrons acting like waves, electrons are affected by diffraction. Diameter due to the diffraction due to the apertures is calculated

$$d_d = 0.6 \frac{\lambda}{\alpha}$$

where $\lambda$ is the wavelength of the electrons:

$$\lambda = \frac{1.22}{\sqrt{V_b}}$$
The total beam diameter is shown to be a combination of effects:

\[ d_t = \sqrt{d_g^2 + d_s^2 + d_d^2} \]

The beam diameter of standard EBL systems ranges in the single nm levels. State-of-the-art SEM can produce beams of 10 to 100 Angstroms in width. Although beam diameter is critical in resolution, there are other effects such as the proximity effect that limits it.
3.2.14 Scattering and Proximity Effect

The path of the electrons is not perfect. Though they are largely unaffected by interactions while traversing down the column, when electrons hit the solid resist layer, the story is different. Electrons start experiencing a larger frequency of scattering events due to the interactions with the dense molecules in the resist. Scattering is a particle interaction and can be either forward or back scattering (figure 24).

Forward scattering is a small angle interaction in which the majority of the electron trajectory maintains its continued forward (deeper into the resist) movement. These small angle scattering events are due to the inelastic collisions or deflection by electrons in the resist. Over-
all, forward scattering results in a widening of the effective beam diameter in the resist. The increase in diameter is given by

\[ d_i = 0.9 \left( \frac{R_t}{V_b} \right)^{1.5} \]

where \( R_t \) is the resist thickness and \( V_b \) is the beam voltage in kilovolts. From the equation, it can be seen that using higher acceleration voltage and thinner resist will result in less beam diameter increase.

Backscattering is a large angle scattering event, which results in the electron returning back through the resist. The returning electrons cause additional exposure around the incident beam. This is called the proximity effect. The additional exposure results in errors in the surrounding profile. The amount of electrons that are backscattered is mostly independent of beam energy; however the spread is increased by it. The substrate material has the greatest effect on the amount of backscattering. Low atomic number materials give less backscatter. For example, typical ratios of backscatter in silicon is 0.17 and 0.50 for tungsten and gold. Electron acceleration voltage is a key parameter to control forward and back scattering. Increasing the acceleration voltage intensifies the back scattering while simultaneously inhibiting the forward scattering and vice versa. Monte Carlo simulations show the combination of both forward and backscattering.

### 3.2.15 Environment

Overall, EBL systems are very precise equipment and are very sensitive. The systems should be installed in clean environments to minimize contamination of the samples, chamber, optics and vacuum systems. They should be in a temperature and physically stable environment.
Temperature and humidity should be well controlled, preferably to a tenth of a degree. Any fluctuation can adjust the physical size and thickness of many pieces of the equipment. Vibration isolation is usually recommended. The environment should also be electrically and magnetically quiet. Noise from transformers, power panels, etc and stray magnetic fields can have an unwanted effect on the entire system and ultimately the electron path. Commonly, great care is needed on the analog and digital grounds to minimize high frequency noise from entering the system.

3.3 Gray-scale Lithography

Normal (binary) lithography involves, in theory, either complete exposure of the resist down to the substrate or no exposure at all. This creates a binary profile composed of substrate level and the resist level, as shown in figure 25.

To achieve this, there is a need to have a sharp difference between light and dark areas. This is where diffraction comes into being a problem. Diffraction spreads the light out, so by the time it hits the resist, there may be, instead of dark and light areas, less dark and less light areas. If the difference is too great, you will have incomplete exposure. To help compensate this, resists with higher contrasts are used. Ideally, the contrast curve of a resist used in binary lithography would be a step functionfigure 26; there would be an immediate cut off between the energy needed for complete development and the amount needed for no development (infinite contrast).

Exposure dose is

\[ E = I_0 t \]
Figure 25: Binary lithography exposure via mask and resulting resist profile.

Figure 26: Idealized photoresist contrast curve.
where $I_0$ is the electromagnetic flux (mW/cm$^2$) present at the surface of the resist and $t$ is the time (sec). The amount of energy absorbed at a depth $z$ in the resist is

$$W(z) = \alpha I(z) t$$

where $\alpha$ is the absorption coefficient (cm$^{-1}$) and the electromagnetic intensity

$$I(z) = (1 - R) I_0 e^{-\alpha z}$$

where $R$ is the reflectivity of the resist. Together the equations give

$$W(z) = \alpha (1 - R) I_0 t e^{-\alpha z}$$

which is graphically represented in figure 27.

Resist at $z$ will clear where $W(z) > W_0$, so the maximum depth that will clear is $d$. Using $d$ in $W$ will then give us the ability to get the direct relation between energy input and the cleared depth:

$$W(d) = W_0 = \alpha (1 - R) I_0 t e^{-\alpha z}$$

$$d = -\frac{1}{\alpha} \ln \left( \frac{W_0}{\alpha (1 - R) I_0 t} \right) = \frac{1}{\alpha} \left[ \ln \left( \frac{\alpha (1 - R)}{W_0} \right) + \ln(I_0 t) (1 - R) I_0 t \right]$$

$$d = A + B \log E$$

$$A = \frac{1}{\alpha} \ln \left( \frac{\alpha (1 - R)}{W_0} \right)$$
The dose depth relationship can then be represented by the equation

\[ z = A \left( e^{ \frac{D}{B} } - 1 \right) \]

where \( D \) is the dosing. It can now be seen that varying the dose will clear different amounts (depths) of resist (figure 28).

In reality, doses between \( Q_0 \) and \( Q_f \) will result in partial development and make up the gray region of the resist. Gray-scale lithography uses this region to an advantage. Many 3D structures and topographies can be fabricated in a single exposure step. Accurate 3D
structures are useful in creating integrated micro optics, such as Fresnel lenses [60], micro-opto-electro-mechanical systems (MOEMS), and blazed gratings diffractive elements, micro-fluidics such as “lab-on-a-chip” and micromechanical structures, such as MEMS, micro-turbines and compressors [49]. For conventional photolithography to produce a stair-stepped shape like the one above or any 3D structure, it would require multiple applications of resist and multiple masks.
Because gray-scale lithography involves varying degrees of exposure, CMTF is less meaningful, and the performance of resists is primarily characterized by contrast. The gray-scale contrast can be defined as

$$\gamma = 2.3 \left( 1 + \frac{A}{z} \right) \left( 1 + \frac{z}{B} \right)$$

and evaluated at the depth $z$. It is very important to understand this intermediate dosing region along the slope of the contrast curve. In fact, it is beneficial to have a large gray region. A shallower slope gives more increments of dosing and allows increased control over levels of exposure. Unlike in binary photolithography, where resolution is smallest feature size you can properly image, in gray-scale, it represents the control over exposure levels. In this case, higher resolution means it is easier to write varying heights (different levels of gray). PMMA is preferred because it has a very low contrast [64], so it exhibits very high resolution, which is beneficial to fabricating 3D structures.

There are several forms of lithography and irradiation that have been adapted to perform GSL. The first is an adaptation of photolithography methods involving gray-tone masks (GTMs). A binary approximation of GTMs known as half-tone, were used first. These masks involved using a varying density of dots or other amounts of coverage to partially shade sections of the mask figure 29. This technique can be seen on early dot-matrix printers. In fact, these have even been fabricated by ink jet printers [65]. The limitation of this technique is based on the resolution of the image. The dots used for shading must be much smaller than the minimum feature size. Otherwise, the dots themselves will be imaged instead of simply
regulating the amount of transmitted light. This was usually accomplished by using the masks in 5:1 projection photolithography [66].

True gray-tone (continuous tone) masks have been fabricated using high-energy-beam-sensitive (HEBS) glass. Commercially available from Canyon Materials, Inc, the glass has silver alkali-halide complex crystals diffused, about 3 µm, into the surface [?]. HEBS does not require etching [67]. When exposed to different amounts of energy (UV or e-beam), the crystals become metallic silver and optical opaqueness changes [68]. The fabrication of continuous tone masks requires a GSL method itself. Color has also been used to vary the intensity of light in a mask by using the ink-jet method talked about above [65]. The benefit of using a mask, again, is that a large area can be written in a single shot. Although parallel processing might be faster, direct write options are much more flexible.

Continuous profile writing can be done with a shaped light beam [66]. A homogeneous light illuminates an aperture that changes the shape of the light beam. The light dose distribution is related to the shape of the beam. The light beam’s shape can be modulated by a LCD device. Similar, laser direct-write (LDW) or laser-beam writing can be used. In LDW, an acousto-optic
modulator regulates the intensity of the laser beam. In the first example, UV light is used and in the second a helium-cadmium (HeCd) laser was used.

Parallel direct-write or mask-less systems are a great mix between photolithography and direct write lithography methods. It is not only possible to do binary writing with digital micro-mirror devices (DMDs) but to also perform gray-scale exposure. The SF-100 Maskless Lithography system from Intelligent Micropatterning LLC contains a UV lamp, shutter timer and smart filter that controls the DMDs from a PC. Each DMD images one pixel, and the “software mask” orients these appropriately in order to produce a pattern. By varying the time (duty cycle) each mirror exposes a pixel, a differing dose level is obtained. An field exposure of 16 by 11 mm has been done with 256 levels of dosing.

3.3.1 3D Electron Beam Lithography

Another direct-write method capable of utilizing the gray-scale lithography method is EBL. Gray-scale EBL or 3D-EBL utilizes dose modulation to create a whole other state-of-the-art fabrication technique that is capable of producing sophisticated high aspect ratio 3D structures. In this more advanced technique, a dose matrix is used. With a dose matrix, different areas of the resist are exposed to varying levels of energy resulting in the break of polymer chains throughout part of the resist. Development then leads to varying depths depending on the dosing of the regions leading to 3D structures.

Dose, as described before, is the amount of energy per area:

\[ D = \frac{I \times T}{A} \]
where \( I \) is the beam current, \( T \) is the exposure time, and \( A \) is the area. The key is to have control over the incident energy. The area is pretty much fixed by the focus of the electron gun, and beam current is difficult to change without changing the area. These parameters also cannot be changed very quickly. The most obvious parameter to change dose is time. If the area and beam current are maintained relatively steadily, time can be varied and therefore dose will also be varied. The area of exposure, which is usually thought of as a pixel, is the step size squared. The time that the area is exposed is referred to as the dwell time. The current of the beam is measured, and then dose for each pixel can be calculated. This is known as shot modulation. 3D-EBL offers freedom to pattern with a combination of widths and depths. Unlike RIE, which is limited by the lag effect, the shrinking effect that is present in EBL can be compensated.

Some of the resist suitable for EBL can be utilized in 3D lithography. SU-8 does have a small contrast, so it can be used for 3D-EBL \[58\], but it may be difficult to deal with. SU-8 is a negative resist, so the hardening is happening from the top down. In gray-scale exposure, hardening is done incompletely, so the base might not be fully hardened, and the pattern can lift off of the surface. Transparent substrates can be used in order to expose the resist at the bottom, but this would change the standard flow considerably \[?\]. ChG has also shown to make grayscale patterns but only to 600 nm resolution \[69\]. PMMA offers lower contrast than SU-8 and higher resolution than ChG.

Although the speed of EBL is a drawback, 3D-EBL has the added benefit of single pass patterning. Not only does the direct write method of EBL not require a mask, but 3D-EBL does
not require the multiple masks that would be needed to realize these 3D structures normally. Due to the ability to vary levels, a single scan exposes the 3D pattern in entirety. There is no need for multiple steps in which alignment could be off. Furthermore, with thermal reflow post-treatment, these stair-stepped patterns can be averaged (smoothed) creating continuous patterns [70]. The EBL system is a flexible and an ideal solution for a wide range of applications in engineering, bio, medical and micro-fluidics which requires a resolution under 50nm. 3D-EBL is good for machining MEMS devices, such as optical elements (coupling for optical fibers, tilted mirrors, compound micro-prisms) [71], and especially necessary for high-frequency gratings, photonic band-gap crystals, magneto-resistive random access memory (MRAM) and other nano-electro-mechanical systems (NEMS) [72]. 3D-EBL has also been demonstrated on functionalized SU-8 resist to fabricated single-model solid state dye laser devices. The resolution is a major attractor to EBL, but due to the speed limitation, 3D-EBL is primarily used for mask making and nano-imprint lithography utilizing the soft lithography process explained in the next section.

### 3.3.2 Soft Lithography

Soft lithography is an extension of molding techniques into the world of micro- and even nano-fabrication technologies. The technique is not used to produce an original pattern itself but merely replicate a micro or nano pattern already created through another process. The materials are poured onto molds that were already fabricated with a pattern. They are then peeled away and result with an imprint of the pattern. The resolution has been maintained down to less than 20 nm [73].
The term soft refers to the use of elastomeric materials in the process. The use of these materials allows for the conformal contact of the surface even at the sub micrometer level. Flexible materials are also easier to remove from the molds because they resist breaking when peeled from the template. Many of the elastomeric materials resist adherence to the template material. Soft materials can also be imprinted through thermoplastic or photo methods, such as in NIL.

In general, the soft lithography process also allows patterning of materials that are not photosensitive or cannot be patterned directly through other lithography processes. This expands the application of micro-fabrication from electronics to the fields of bioengineering and other medical technology, such as cardiac stents. Different materials, which are biocompatible, can be micro patterned. Drug-embedded polymers have been used, and even directly shaping drugs to improve delivery is being studied.

The molding process in soft lithography can also be used to increase the mass production ability and lower the cost. Expensive lithography equipment only needs to be used for making the molds and not for each pattern after that. Soft lithography can also be performed in normal laboratory settings; therefore opening the door to application in more locations. The imprint process has been adapted to other forms of mass production much like that of a printing press.
CHAPTER 4

DESIGN PROCESS

The ultimate goal of this project is to create an IOL that has adjustable power, which is precisely tunable by design and producible in fabrication and accurately repeatable during normal functioning. Instead of coming up with original and artificial designs to obtain the goal, the plan is to mimic the concepts shown in natural design. This procedure is known as bio-mimicry and is an ever more popular idea being utilized in biology, medical and several other engineering fields. A lot has been learned and improved by looking closer at how nature creates structures and runs processes.

The general idea of bio-mimicry is that nature has already tested out the possibilities, sometimes over the course of millions of years, and, for the most part, found a better and possibly the best way to do something. Even though advances in technology and engineering have created ideas and devices that have no comparison to something in nature, there are plenty of cases where the man-made option is less fitting then its natural counterpart. However, it is not about which one is better, man-made or natural, but that we should first understand nature and build from that solid foundation. The method of bio-mimicry especially makes sense when designing an artificial direct replacement for a natural object, such as the lens in the body.
4.1 **Starting point**

Following the bio-mimicry method explained above, we start by looking at the shape of the human lens (figure 30).

From this initial shape we create a simple model using MATLAB (the full script can be found in appendix A). The dimensions of this first model and their change due to accommodation are derived from recent studies which used magnetic resonance imaging (MRI) to accurately analyze changes in the crystalline lens and ciliary body with accommodation and aging [74].

Our model was a simple biconvex lens. We had to adjust the size of this lens because of the difference in the index of refraction between PMMA (\(n = 1.49\)) and the human lens.
\( n = 1.406 \). To accomplish this task we used the lensmaker equation already introduced in the second chapter:

\[
P = (n - 1) \left( \frac{1}{R_1} - \frac{1}{R_2} + \frac{(n - 1)t}{n \cdot R_1 \cdot R_2} \right)
\]

Being \( n \) the refractive index of the used material, we were able to find the values of \( R_1 \) and \( R_2 \) providing the same optical power \( P \) of the human lens.

We created both the unaccommodated and the accommodated version, in order to evaluate the change in shape of the lens. Both versions can be seen in figure 31.

The dimensions used for this first model are reported here:

Unaccomodated lens

- Lens diameter: 9 mm
- Upper radius of curvature: 10 mm
- Lower radius of curvature: 6 mm

Accomodated lens:

- Lens diameter: 8.5 mm
- Upper radius of curvature: 7.5 mm
- Lower radius of curvature: 5.5 mm

This dimensions are indicative of the average size of the human lens, which in reality can vary from one person to another. However our MATLAB code is easily customizable to fit the patient needs.
Figure 31: First human lens approximation model.
This layout is very similar to the real human lens; nonetheless it has a relevant drawback: its size makes it impossible to fold during the surgery, thus requiring a very large incision in order to be able to insert it into the eye.

The terrific benefits of a smaller incision during cataract surgery have already been outlined in the first chapter. It was therefore necessary to find a thinner design, so that folding of the lens is made possible.

### 4.2 Fresnel lens design

The problem of the excessive thickness was resolved using Fresnel lenses. Both sides of the biconvex lens were converted into Fresnel lenses. Although being much thinner than the original lens, the Fresnel one brings some aberrations due to the discontinuity in the profile. In order to avoid these aberrations caused by diffraction, the height of the grooves was chosen to be 250 nm, so smaller than the wavelength of visible light. Such low values are possible thanks to the Electron Beam Lithography fabrication technique.

Our model was then adapted to these developments. The result can be seen in figure 32. This figure shows both the anterior and the posterior lens, either in the unaccommodated and in the accommodated case. Notice that just the central part of the Fresnel lens is shown, due to the large difference in the scale of the axis.

Being both of these lenses just 250 nm thick, an extra layer of PMMA (or PDMS) can be inserted between the two parts, so to make the handling possible. However, even after the introduction of this intermediate layer, our lens would still have a thickness of the order of
magnitude of hundreds of microns, allowing for easy folding (or even rolling) of the lens during surgery, and thus minimizing the size of the incision.

A 3D AutoCAD rendering of one of the Fresnel lenses was also produced and is reported in figure 33.

An early prototype of Fresnel lens fabrication was already been produced at NCF [75], and the result is visible in figure 34.

4.3 Flexibility

We proposed the Fresnel lens design as a solution to reduce thickness. Then we approached the accommodation problem. How can we make our lens flexible in order to mimic the behavior
Figure 33: 3D AutoCAD rendering of the Fresnel lens.

Figure 34: AFM image of Fresnel lens prototype.
of the human lens? The solution is to remove some material from the lens so to make it compressible.

There’s not a unique pattern for the removal of the material. Every design that doesn’t impair the optical properties of the lens can be accepted. A first example could be the introduction of nano-bubbles inside the lens. A second approach implies the use of micro/nano-channels. Again, multiple geometries of these channels are available. One example is shown in figure 35.

The option we decided to adopt was the spiral channel, for reasons that are better explained in the next section.
4.3.1 **Spiral channels**

The spiral is a shape that is present throughout nature: spiral formations in shells, such as those of mollusks. Vortices and vortex trains are spiral in shape for curves of a wave peak, the draining of a sink, the funnel of a tornado and hurricanes. The spiral is a progression of material organized through symmetry in transformations of growth and rotation in the natural world. They are also evident on a much larger scale: magnetic forces emanating from the sun in the Parker spiral and even spiral galaxies.

One benefit to a spiral is that it allows for compaction of a relatively long continuous path, for example: the groove on a vinyl record, the data on a CD or hard drive or the bulb of a compact fluorescent. Another benefit is that they maintain physical strength while increasing surface area, such as in the logarithmic spirals in nautilus shells. Spirals have benefits in other ways. The cochlea, an inner organ of the ear, not only saves space but also improves hearing by enhancing vibration and directing different frequencies to different places in the cochlea in order to distinguish them. The concept of the spiral has also been applied in the electrical engineering world: spiral inductors, ferroelectrics of spiral magnetic and broadband antennas for terahertz radiation, which have been fabricated by EBL.

The general definition of a spiral is the path of a point in a plane moving around a central point while continuously receding from or approaching it. Geometrically, the shape of the spiral can be represented in many different ways. The logarithmic spiral represents what is shown more in nature, while the archimedean spiral is the human simplification. A logarithmic spiral
has a distance from its center that is logarithmically increasing. The Archimedean spiral has a linear increase in distance from its center, so each arm is a set distance apart.

Mathematically, it is easy to see the increasing radial distance of the spiral. Because a spiral is a non-unique curve, it is best described using polar coordinates or a set of parametric equations. A logarithmic spiral is described by

\[ r = ae^{b\theta} \]

while an Archimedean spiral is described by

\[ r = a + b\theta \]

where \( a \) and \( b \) are arbitrary coefficients that change size and ratio of growth. The Archimedean spiral is also represented by a set of parametric equations

\[
\begin{align*}
x &= at \sin bt \\
y &= at \cos bt
\end{align*}
\]

with the parameter \( t \).

Although the logarithmic spiral might be more common in nature, the Archimedean spiral’s regular distribution closely resembles that of the regular structure of the eye and is the choice for this project. The equal spacing between each arm of the spiral should provide uniform movement and deformation when the lens is stretched and compressed.
The lens is not just a 2D spiral; overall the spiral shape will be domed (convex) to match the curvature of our Fresnel lens.

The principle of using this spiral cuts as a solution to achieve accommodation is represented in figure 36. A fine adjustment of the accommodation mechanism can be obtained by varying the width and the spacing of the spiral.

Once the spiral design had been chosen, we integrated it into our MATLAB code. Looking at the top plot in figure 37 we see that the spiral channels have been created into our Fresnel lens. If we simulate the compression of the lens (bottom plot), we see that it is possible to reach and even surpass the accommodated profile of the lens. This proves the correctness of our assumptions, and completes the design process of the lens.

The introduction of the channels causes some discontinuities on the surface of the lens when it is totally compressed. These discontinuities are clearly visible in the second graph of
We already know that they are not going to cause visible scattering since their size is in the order of tens of nanometers, but to prove their negligibility we measured, by mean of an atomic force microscopy, the surface roughness of a standard IOL currently on the market, in particular a Bausch&Lomb SofPort A0.

It is easy to notice from figure 38 that the average roughness of the measured IOL is in the order of hundreds of nanometers and even micrometers. This reinforces the choices made with our design, demonstrating the power of EBL fabrication.
Figure 38: AFM measuring of the surface roughness of a standard IOL.
CHAPTER 5

CONCLUSIONS

In our research the complete design of the lens has been developed. The next step is the fabrication of a working prototype in order to test the optical properties of the product. Once all the requirements are satisfied, the mold can be fabricated through EBL and the lenses can be manufactured via soft lithography.

Thanks to Dr. Gaynes and Dr. Kannah of Loyola University, animal trials will be conducted on rabbits. This is a mandatory phase which must be completed before any human testing.

5.1 Further improvements

During the design phase, care has been taken with respect to the compatibility of our lens with existing surgical equipment for cataract surgery, in particular IOL injectors (figure 39).

Further precautions concerning this subject will simplify the use and commercialization of our lenses.

Another important advancement in the design of the lens should be made regarding the haptics (figure 40). In our design they have not only the role to hold the lens in place once deposited in the capsule, but they are also responsible for the transmission of the force from the ciliary body to the lens, thus driving accommodation.

An optimal design must be chosen to maximize force transfer.
Figure 39: Single use IOL injector.
Figure 40: Different types of haptics design in current IOLs.
APPENDIX

MATLAB CODE FOR THE LENS DESIGN

% All units in um

format long e;

clear all; clc; close all;

% CONSTANTS

N = 1e6;  % Evaluation points (10^-6 for external teeth)

substr_thick = 250e-3;  % Thickness of the substrate

inter_layer = 500;  % Thickness of the spiral part

radius_up_unacc = 10e3;

radius_low_unacc = 6e3;

lens_diameter_unacc = 9e3;

radius_up_acc = 7.5e3;

radius_low_acc = 5.5e3;

lens_diameter_acc = 8.5e3;
% UNACCOMODATED LENS

% Upper lens (most external one) - Unaccommodated
[x_up_unacc, y_up_unacc, thickness_up_unacc] = ...

    upper_lens(radius_up_unacc, lens_diameter_unacc, N);

% Lower lens (most internal one) - Unaccommodated
[x_low_unacc, y_low_unacc, thickness_low_unacc] = ...

    lower_lens(radius_low_unacc, lens_diameter_unacc, N);

% Plot of the actual lenses - Unaccommodated
subplot(2,2,1);
plot(x_up_unacc, y_up_unacc);
hold on;
title('Unaccommodated lens');
plot(x_low_unacc, y_low_unacc, 'r');
xlabel('Lens diameter ($\mu$m)');
ylabel('Lens thickness ($\mu$m)');
xlim([-5e3, 5e3]);

% Correcting offset for exact thickness of the central lens
y_up_unacc = ...
    y_up_unacc + substr_thick - rem(thickness_up_unacc, substr_thick);

y_low_unacc = ...
    y_low_unacc - substr_thick + rem(thickness_low_unacc, substr_thick);

% Plot of Fresnel lenses - Unaccomodated
y_up_Fresnel_unacc = ...
    mod(y_up_unacc, substr_thick) + inter_layer/2;
y_low_Fresnel_unacc = ...
    mod(y_low_unacc, substr_thick) - substr_thick - inter_layer/2;

subplot(2,2,2);
plot(x_up_unacc, y_up_Fresnel_unacc);
hold on; xlim([-5e3, 5e3]);
title('Unaccomodated Fresnel lens');
plot(x_low_unacc, y_low_Fresnel_unacc, 'r');
xlabel('Lens diameter (\mum)');
ylabel('Lens thickness (\mum)');

% ACCOMODATED LENS
% Upper lens (most external one) - Accomodated

[x_up_acc, y_up_acc, thickness_up_acc] = ...
upper_lens(radius_up_acc, lens_diameter_acc, N);

% Lower lens (most internal one) - Accomodated

[x_low_acc, y_low_acc, thickness_low_acc] = ...
lower_lens(radius_low_acc, lens_diameter_acc, N);

% Plot of the actual lenses - Accomodated

subplot(2,2,3);
plot(x_up_acc, y_up_acc);
hold on;
title('Accomodated lens');
plot(x_low_acc, y_low_acc, 'r');
xlabel('Lens diameter (\mum)');
ylabel('Lens thickness (\mum)');
xlim([-5e3, 5e3]);

% Correcting offset for exact thickness of the central lens

y_up_acc = ...

y_up_acc + substr_thick - rem(thickness_up_acc, substr_thick);

y_low_acc = ...
\[ y_{\text{low acc}} - \text{substr thick} + \text{rem}\left(\text{thickness}_{\text{low acc}}, \text{substr thick}\right); \]

\% Plot of Fresnel lenses - Accomodated

\[ y_{\text{up Fresnel acc}} = \ldots \]
\[ \text{mod}\left(y_{\text{up acc}}, \text{substr thick}\right) + \text{inter layer}/2; \]

\[ y_{\text{low Fresnel acc}} = \ldots \]
\[ \text{mod}\left(y_{\text{low acc}}, \text{substr thick}\right) - \text{substr thick} - \text{inter layer}/2; \]

subplot(2,2,4);
plot(x_{\text{up acc}}, y_{\text{up Fresnel acc}});
hold on;
title('Accomodated Fresnel lens');
plot(x_{\text{low acc}}, y_{\text{low Fresnel acc}}, 'r');
xlabel('Lens diameter ($\mu$m)');
ylabel('Lens thickness ($\mu$m)');

\% EXTRA GRAPHIC PART

j = 1;
k = 1;
for i = 1:N
    if (x_{\text{up unacc}}(i) > -140 && x_{\text{up unacc}}(i) < 130)

APPENDIX (Continued)

\[
x_{\text{unacc\_short}}(j) = x_{\text{up\_unacc}}(i);
\]
\[
y_{\text{up\_Fresnel\_unacc\_short}}(j) = y_{\text{up\_Fresnel\_unacc}}(i);
\]
\[
y_{\text{low\_Fresnel\_unacc\_short}}(j) = y_{\text{low\_Fresnel\_unacc}}(i);
\]
\[
j = j + 1;
\]
end

if (x_{\text{up\_acc}}(i) > -140 && x_{\text{up\_acc}}(i) < 130)

\[
x_{\text{acc\_short}}(k) = x_{\text{up\_acc}}(i);
\]
\[
y_{\text{up\_Fresnel\_acc\_short}}(k) = y_{\text{up\_Fresnel\_acc}}(i);
\]
\[
y_{\text{low\_Fresnel\_acc\_short}}(k) = y_{\text{low\_Fresnel\_acc}}(i);
\]
\[
k = k + 1;
\]
end
end

figure;

subplot(2,1,1);

plot(x_{\text{unacc\_short}}, y_{\text{up\_Fresnel\_unacc\_short}}, 'k', 'lineWidth', 2);
hold on; grid on; grid minor;
plot(x_{\text{acc\_short}}, y_{\text{up\_Fresnel\_acc\_short}}, 'r', 'lineWidth', 2);
legend('Unaccomodated lens', 'Accomodated lens');
xlim([-130, 130]);
ylim([249.9, 250.4]);
This script uses the following two functions

% Design of the upper lens (most external one)

function [x, y, thickness] = upper_lens(radius, lens_diameter, precision)

thickness = radius - sqrt(radius^2 - (lens_diameter/2)^2);
center = [0, thickness-radius];

x = linspace(-lens_diameter/2, lens_diameter/2, precision);
y = sqrt(radius.^2 - (x-center(1)).^2) + center(2);

% Design of the lower lens (most internal one)
function [x, y, thickness] = lower_lens(radius, lens_diameter, precision)

thickness = radius - sqrt(radius^2 - (lens_diameter/2)^2);
center = [0, radius-thickness];

x = linspace(-lens_diameter/2, lens_diameter/2, precision);
y = -sqrt(radius.^2 - (x-center(1)).^2) + center(2);
CITED LITERATURE


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