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INVERSE FINITE ELEMENT ANALYSIS OF COMPRESSED MOUSE LENSES FOR MECHANICAL INSIGHTS INTO PRESBYOPIA

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ABSTRACT

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Presbyopia is the gradual loss of accommodation ability with age. This is generally thought to be due to age-related lens stiffening. Compression testing has been used to evaluate lens stiffness; however, stiffness is an extrinsic metric as it is affected by size, shape, and mechanical heterogeneity. To overcome this difficulty, an inverse finite element analysis of a compression test was used to determine the elastic modulus (an intrinsic measurement of stiffness) of the lens. Lenses from 17-week-old mice from six different induced genetic backgrounds were evaluated using compression testing and compared to wild type lenses. The dimensional values of the lens were assigned from photographs of the lens collected during the experiment. Inverse finite element analysis was used to estimate and determine the elastic moduli of the nucleus, cortex, and capsule by comparing the experimental force-displacement data with the model-predicted force-displacement relationship up to 10% axial compression. Results show a similar trend in both the experimental and computer-simulated force-displacement data with estimated Young's modulus values of 85kPa, 107kPa, and 104kPa for the nucleus, cortex, and capsule respectively. Additional mechanical tests were used to confirm independently the elastic moduli of the lens capsule and nucleus.

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CHAPTER ONE: INTRODUCTION

In 2012, the total cost for optical corrections in the United States was over $30 billion. Since presbyopia is the most common ocular condition that affects everyone by age 40, the cost of treatment continues to increase as the population ages: 28% more citizens will be over 55 by 2020. The crystalline lens within our eyes is analogous to a camera lens in that it can dynamically alter its optical power to achieve a clear image at various distances. However, it achieves this using a very different mechanism. The lens is made out of three distinct components: capsule, cortex, and nucleus which elastically deform to focus light rays onto the retina. Near vision requires a more spherical lens and results from contraction of the ciliary muscles and zonular fibers. With age, the range of accommodation decreases as the lens becomes more rigid and focuses the light rays behind the retina leading to blurry vision. This is primarily due to protein aggregation and crosslinking within the lens that eventually hardens the entire structure.

Researchers have already developed numerous mouse models in which lens-specific proteins have been knocked out or mutated. [1] Connexins (Cx), or gap junctions, are major proteins of the lens involved with growth, development, and transparency. Aquaporin(s) are a group of integral membrane proteins that behave like ion channels. Specific to the lens, Aquaporin0 (AQP0) is expressed by the Major intrinsic protein (MIP) gene and functions to channel water and additionally play a role in cellular adhesion[2]. Variations in gene mutation that either remove or replace specific lens proteins have been extensively studied. In a recent study, lenses from mice having six different genotypes were mechanically characterized using a compression test. These include models with modified expression of Cx46, Cx50, and MIP, with wildtype lenses (i.e. those with no genetic modification) served as a control (Figure 1).

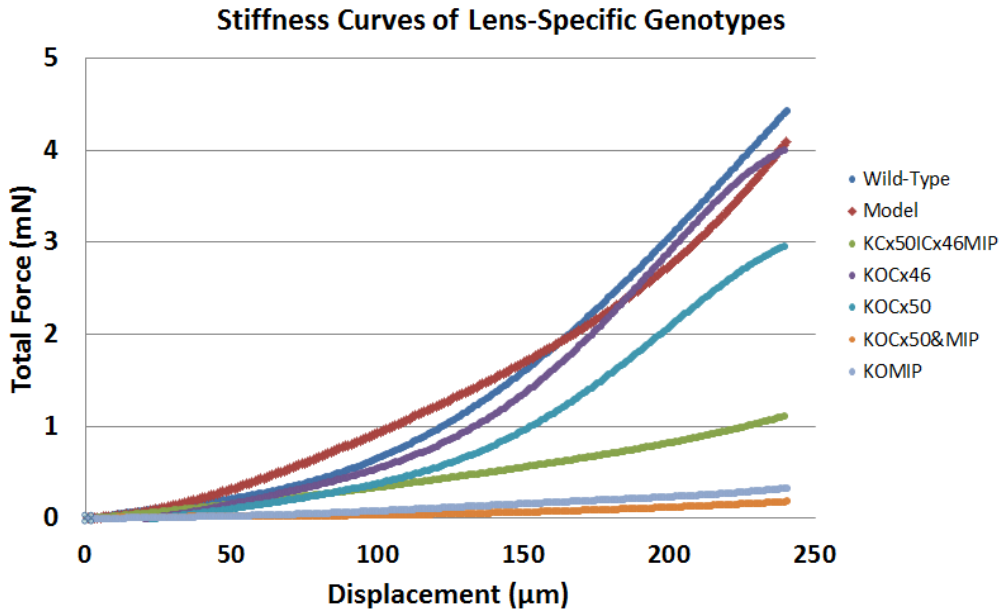


Figure 1: Average stiffness curves of different genotypes. Gene mutations of mouse lenses show obvious differences in force-displacement trends. Each data set may be described by a different set of elastic modulus values, though no such results have been published at this time.

Compression tests on seven lens-specific genotypes using parallel plates were performed to generate characteristic force-displacement curves at strains similar to those seen during physiological accommodation. A downward displacement applied to the axial pole of dissected mouse lenses provide force and displacement data. All lenses will have observable stiffness values that correlate to elastic moduli analogous to an elastic spring in classical mechanics equations.

1.1 THEORY

Applying the Theory of Elasticity lead to the use of mechanical models such as one developed by Hertz (source) where a spherical object of homogeneity is compressed by two parallel plates meeting three criteria. First, the radius of contact is smaller than the undeformed radius. Second, the decreased axial length is within the linear elastic limits, and lastly, the

absence of adhesion and frictional forces. With an applied force, *F*, the spherical elastic modulus, *E*, and Poisson's ratio, *v*, the sample deforms, u, accordingly to:

$$F = \frac{\sqrt{2}}{3}(E/1 - v^2)\, R_o^{1/2} u^{3/2}$$

The Hertz model was then extended to large strains by Tatara [3-5], but it was further simplified and applied to lens compression by Ravi et al. [6]. Here, the external force is a function of the term *dr*, representing the change in equatorial radius, and the Young's modulus *E* and initial radius R_0 as

$$F = 5.9238 E R_0 (dr).$$

These models assume that the lens is a mechanically homogeneous, incompressible sphere. However, with the nature of the mouse lens which must be tested with its capsule intact, the models are invalid as they vary in size, have a marked mechanical inhomogeneity, and have an ellipsoid shape. With these differences, the compression test will reveal extrinsic measurements of stiffness and cannot compare to other lenses. Much like how the weight of an object is influenced by its position within a gravitational field, the geometry of the lens will affect the calculations of stress and force.

1.2 PREVIOUS METHODS

Fisher [7] determined the Young's modulus of human lenses by observing the axial and equatorial displacements caused by rapid rotation on its polar axis. The measurements obtained were used to determine elastic modulus values for the lens nucleus and cortex assuming a non-homogeneous linearly elastic model. Lens spinning test are not applicable to mouse lenses due to their small size.

A recent study by Baradia [8] attempts to measure the stiffness of mouse lenses by two methods. In the first, incremental compressive forces were generated by the placement of microscope cover-slips on the mouse lens. Images were then taken to record the change in diameter. The second involved an automated actuator system used to create incremental compressive forces applied to mice lenses by a plate. Similar images are taken to record the displacements of the radii. Both methods reveal extrinsic properties of the lens-capsule composite with no indications of how the nucleus or cortex regions play a role in the lens' stiffness.

An indentation method was performed on human lenses by Weeber [9] to measure the intrinsic properties. Samples were stored at -70°C immediately after enucleation. The samples were later sectioned in half to introduce the indentation probe to the center of the lens. This method requires sectioning of non-fixed tissue that is not possible with a mouse lens once again due to its small size.

Burd [10] introduced a finite element inverse analysis continuing from Fisher's lens spinning test. Finite element analysis is a computerized method to model and approximate solutions of objects reacting to various forces so long as boundary values are specified. This method allows for the inclusion of the lens capsule but only if specific details are known about the capsule. In addition, Burd applied a numerical optimization procedure to acquire the stiffness parameters that best fit the finite element model with the experimental data.

Reilly and Ravi [11] performed microindentation testing on sectioned porcine lenses to directly quantify the elastic modulus distribution. However, even with a microindenter, the mouse lens is far too small to analyze in this manner.

1.3 PROPOSED METHOD

Computerized reconstruction of the experimental setup accounts for the geometric differences among lenses including layer thickness and axial/equatorial radii. Post-processing tools allow for the calculations of multiple mechanical properties that include internal stress, reaction forces, strain energy, and optimized elastic moduli. Identifying the elasticity of these mouse lenses will provide insights into how specific proteins contribute to developing presbyopia.

CHAPTER TWO: THESIS STATEMENT

In this project, the intrinsic mechanical properties of lenses from adult mouse of the same age but differing genotypes was objectively determined. Inverse finite element analysis was used to simulate the experimental set up and available post-processing tools allowed for data extraction. A model was constructed using COMSOL Multiphysics and Matlab software. Previous studies have measured the extrinsic stiffness from compression test and thus do not allow a rigorous comparison between lenses of different ages or genotypes. Iterative optimization of the Young's Moduli of all three layers was carried out by best fitting the force-displacement data to the experimental force-displacement data.

CHAPTER THREE: MODELING AND POST-PROCESSING

All computational modeling was carried out by COMSOL Multiphysics. Replication of the experimental set is broken down into several stages, followed by optimization using COMSOL with MATLAB.

3.1 Geometry and Physics

To demonstrate this novel method, computational modeling focused on a single wildtype lens (17 week old) that was provided by the University of Texas Health Science Center at San Antonio. An axial symmetric coordinate system allowed for a semi-ellipsoid and rectangles to represent the mouse lens and parallel plates respectively. This is based on the assumption of the lens being an axisymmetric body of revolution. Axisymmetric dimensional values were assigned from photographs of the lens collected during the experiment (Figure 2). A lateral view revealed both the axial and equatorial radii. Structural mechanics equations were solved by COMSOL Multiphysics to simulate the compression of the lens. A prescribed displacement node was assigned to the top plate while a fixed constraint was applied to the lower plate. Mimicking the experiment, a 10% downward displacement of the upper plate along the axial pole makes contact with the lens (ellipsoid). Lastly, the material properties for each object (lens and cylindrical plates) were assigned appropriately. Because the elastic moduli for the three layers are variables, an initial guess was programmed to complete the modeling process. Remaining parameters are assigned accordingly (Table 1).

Table 1: Parameters used in computational model

Parameter Name	Value	Description
h_capsule	0.0114 [mm]	Capsule thinkness (Danysh et al., 2008)
u0	240 [um]	Applied displacement
E_capsule	$1x10^6$ [Pa]	Capsule Modulus
E_cortex	120000 [Pa]	Cortex Modulus
E_nucleus	120000 [Pa]	Nucleus Modulus
nu_capsule	0.49	Capsule Poisson's Ratio
nu_cortex	0.49	Cortex Poisson's Ratio
nu_nucleus	0.49	Nucleus Poisson's Ratio
r_plate	12.42 [mm]	Lower Plate radius
t_plate	1.23 [mm]	Lower Plate Thickness
ax_radius	1.039375[mm]	axial radius of lens
eq_radius	1.20125[mm]	equitorial radius of lens
h_nucleus	eq_radius/2	radius of nucleus
h_cortex	eq_radius-h_nucleus-h_capsule	Thickness of cortex
ABS_radius	4.715[mm]	ABS plate radius
ABS_thickness	5.22[mm]	ABS plate thickness
E_ABS	3e9[Pa]	ABS Elastic Modulus
nu_ABS	0.35	ABS Poisson's Ratio
rho_ABS	1050	ABS Density

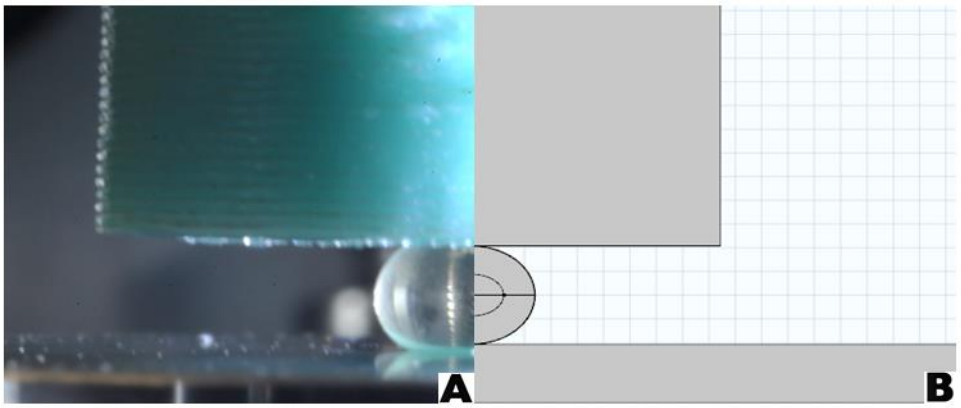


Figure 2: Computer Modeling (A) Dimensional values and material properties were assigned accordingly from experimental setup. (B) Using an axisymmetric layout, the mechanical model was constructed as a multi-layered ellipsoid that represents the lens capsule, cortex and nucleus. Compression plates were formed at opposite ends of the axial pole: one plate remained fixed while the other allowed axial displacement.

3.2 Discretization

With an axisymmetric analysis of the mechanical model, a two-dimensional mesh of the cross section of the lens simplifies a three dimensional study and significantly reduces computational time. A mapping mesh was applied to the plate and lens capsule only due to the uniform thickness as seen in (Figure 3). The remaining geometry was built using triangular elements.

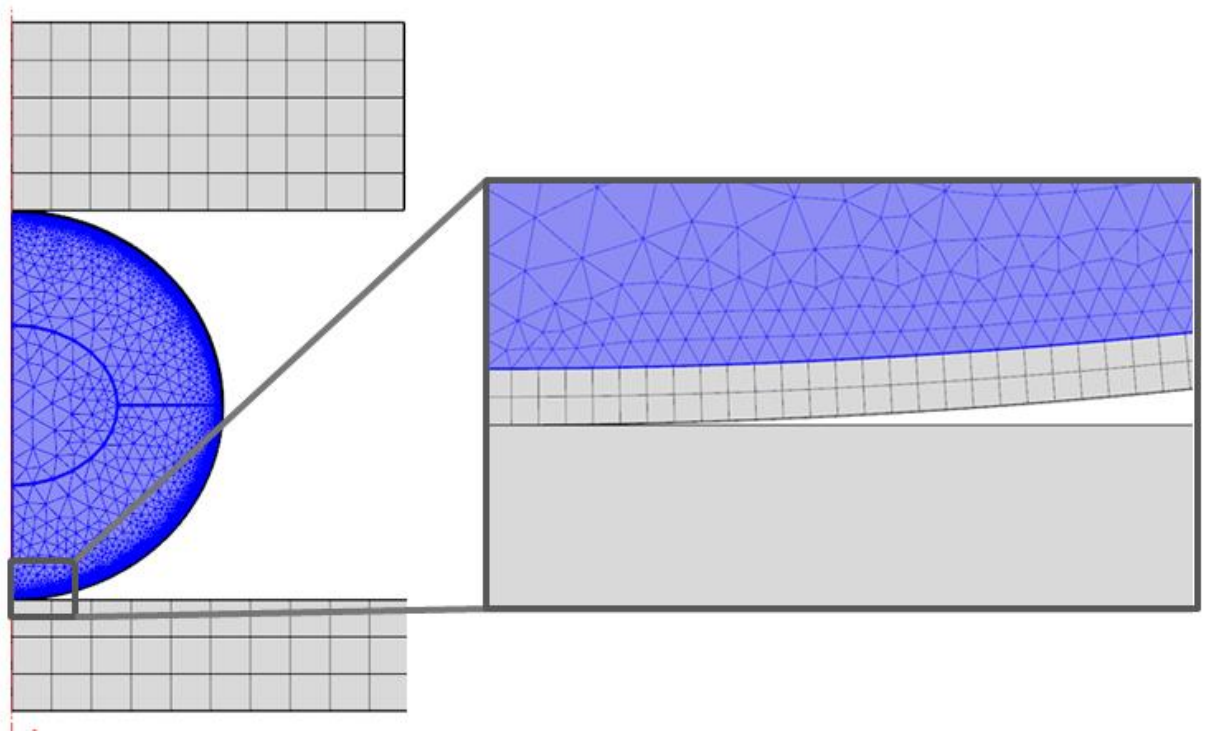


Figure 3: Meshing The lens capsule mapped mesh was comprised of 1300 total elements. Both plates have a coarse mesh since they are relatively rigid with respect to the lens. The lens cortex and nucleus were meshed using a free triangular mesh with maximum density near the capsule and minimum density within the core.

The entire geometry of the lens totaled roughly 9200 triangular elements under the "Finer" mesh option. To ensure accuracy for each simulation, a "Normal" mesh with 8800 elements and an "Extremely Fine" mesh with 19700 elements (3600 elements within the lens)

were also solved. The three values of stress that represent the elastic properties of regions of the lens were used as a metric for assessing mesh independency. An acceptable convergence was determined when the difference in stress was less than 0.1% when different mesh densities were used to solve the problem. The calculations of percent difference are as follows. An experimental data set was selected, a simulation then followed with a normal density mesh (8836 triangular elements). The resulting stress values were then used as next initial stress values for the next simulation. This method continued for the "Finer" mesh (9258 triangular elements) as was as the "Extremely Fine" mesh (19732 triangular elements). The method in determining the appropriate mesh density is shown in the appendix.

A finer mesh density demonstrated convergence of the force-displacement curve as it did not differ beyond 0.1% between the "Finer" and "Extremely Fine" meshes. Once the convergence study was completed, the remaining simulations were performed using the "Finer" mesh setting since this was deemed to be the minimum mesh density needed in order to accurately solve the model.

3.3 Force Calculation

A parametric sweep function allows for multiple calculations when varying a parameter, in this study, displacement (0-190μm) was solved in intervals of 10μm. To compute force-displacement data, the stress tensor acting on the vertical axis on the surface of the lens in the direction of compression was integrated over the equatorial plane of the lens (surface area) to generate the total force *F* applied with each corresponding displacement as follows:

$$F = \int \sigma_{zz} dA,$$

where σ_{zz} is the true normal stress in the direction of compression and *dA* is the differential surface area at the equator in the same direction. Two contact pair surfaces were assigned to separate and prevent penetration of the ellipsoid and cylinder. A fine mesh containing approximately 4,300 triangular elements was assigned to the entirety of the model.

3.4 Regression Analysis:

The elastic moduli of the lens capsule, cortex, and nucleus were estimated by minimizing the squared errors between the model-predictive curve and experimental data using MATLAB's *fminsearch* function. This function treated the initial guessed moduli as variables and implements an iterative optimization loop to run and correct the COMSOL model until the force-displacement curves optimally match the experimental data. For preliminary data, this was performed for one lens from a 17-week-old wild type mouse from a c57bl/6 genetic background.

CHAPTER FOUR: RESULTS

A control to verify the calculation of the total force was a simple beam (cylindrical) compression of both noncontact and contact with plates. Integration of the stress tensor of the cross-sectional area revealed forces within a one percent error. Once verified, simulation of the compressed wildtype lens follows. In this section, these results are presented.

4.1 Validation Study

Using the same formula as shown:

$$F = \int \sigma_{zz} dA$$

the simple beam compression model of contact vs noncontact are shown below (Table 3). The total force required to achieve a specified displacement are within 0.3% of values determined analytically. This indicates the use of contact displacement does not significantly differ in the calculation of force as with the compression test.

Table 2: Control The calculation of total force on control using COMSOL Multiphysics. As the results are similar validates the use of contact plates for the simulation of lens compression.

CONTROL BEAM COMPRESSION		
Method	CONTACT WITH PLATES	NO PLATES
Total Force (N)	0.47923	0.48069

4.2 Genotype and Model Comparison

After accounting for the geometry of the lens, four different gene-specific lens types are shown with a best fit match (Figure 4) as well of the average elastic values comparing to the Hertz results (Figure 5).

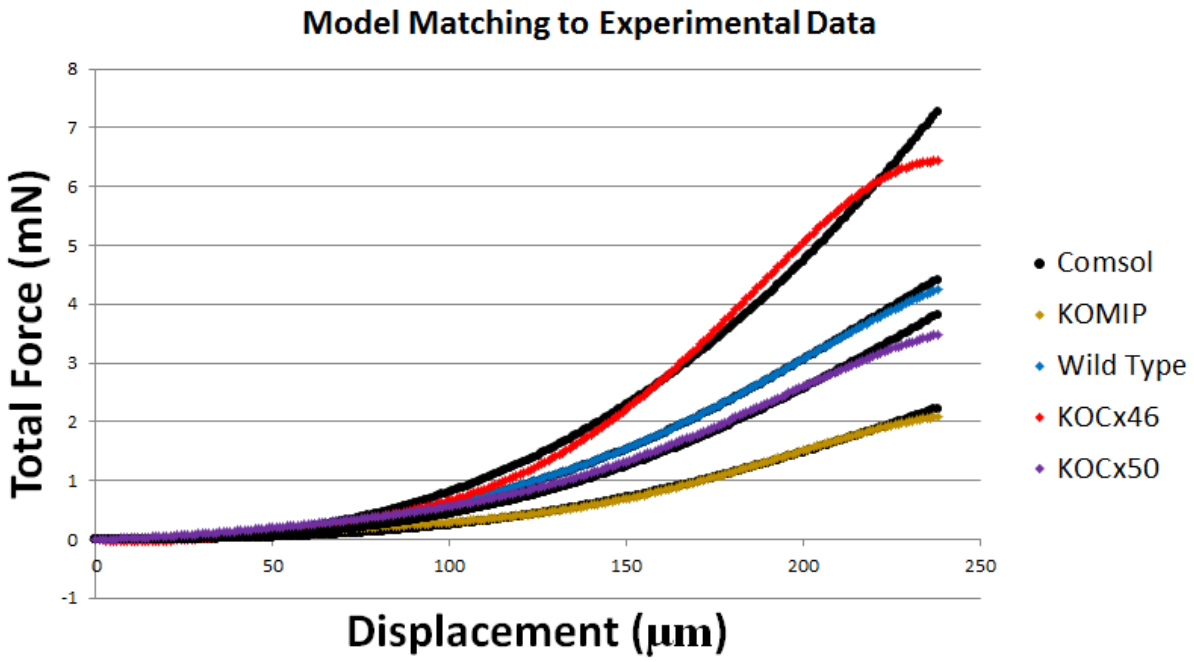


Figure 4: Force-Displacement Trend of Model and Samples. Optimization of all three elastic moduli of three layers of the mouse lens resulted in unique values for the lens nucleus, cortex, and capsule respectively. Data from each genotype were fitted well by the model.

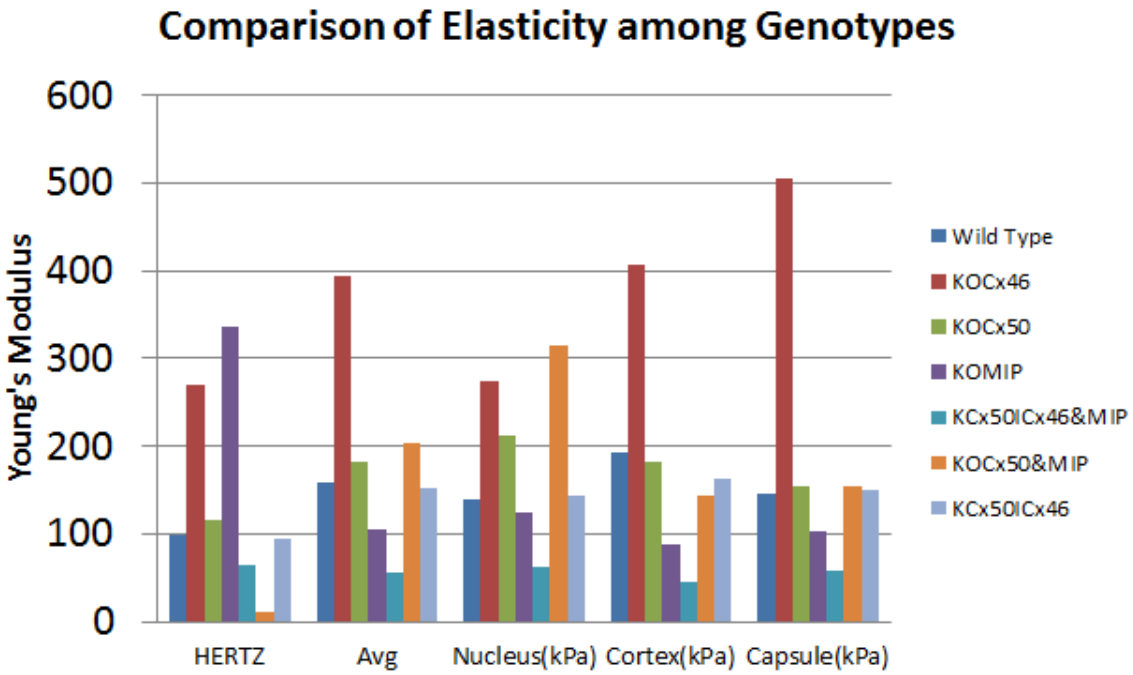


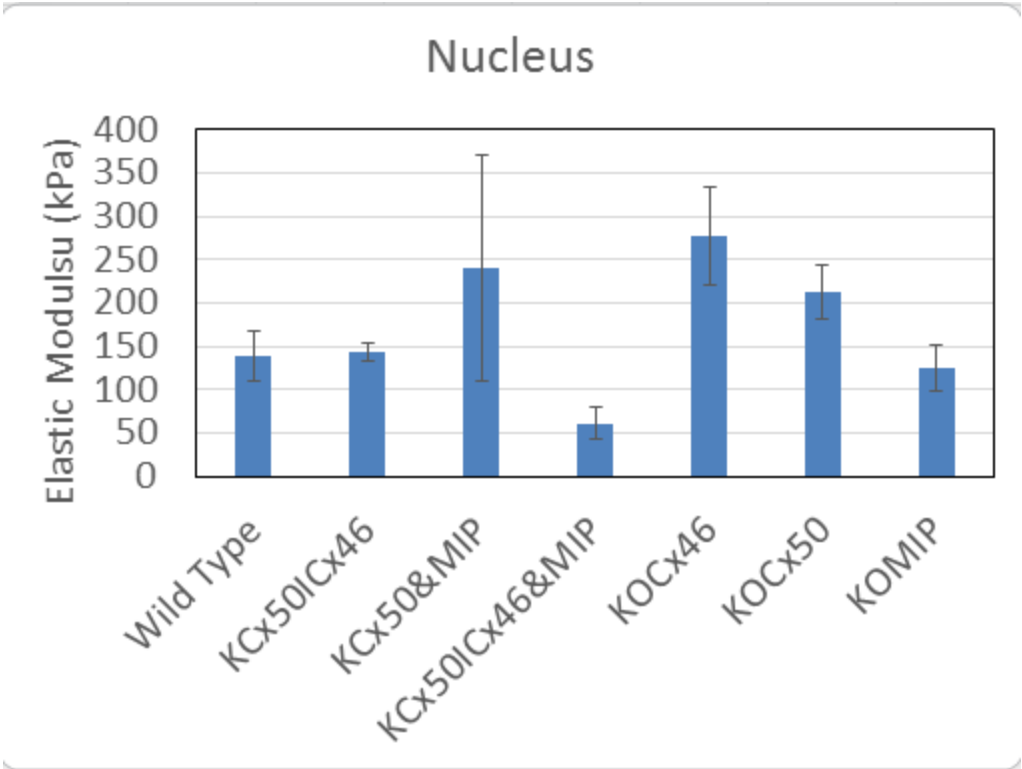
Figure 5: Comparison of Elasticity: The results of the hertz model are shown along with the average values of the three regions. Slight agreements are seen with specific genotype.

Table 3: Simulation Results: The following table reveals the elastic moduli in units of kilopascals of the lens' nucleus (N), cortex (CR), and capsule (CS). The range of the values falls in the hundred kilopascal range which were within an order of magnitude of the values obtained using the Hertz model. The table below only reveals lenses which were successfully characterized during experiments and excludes lenses damaged during dissection or otherwise excluded for reasons unrelated to this modeling exercise.

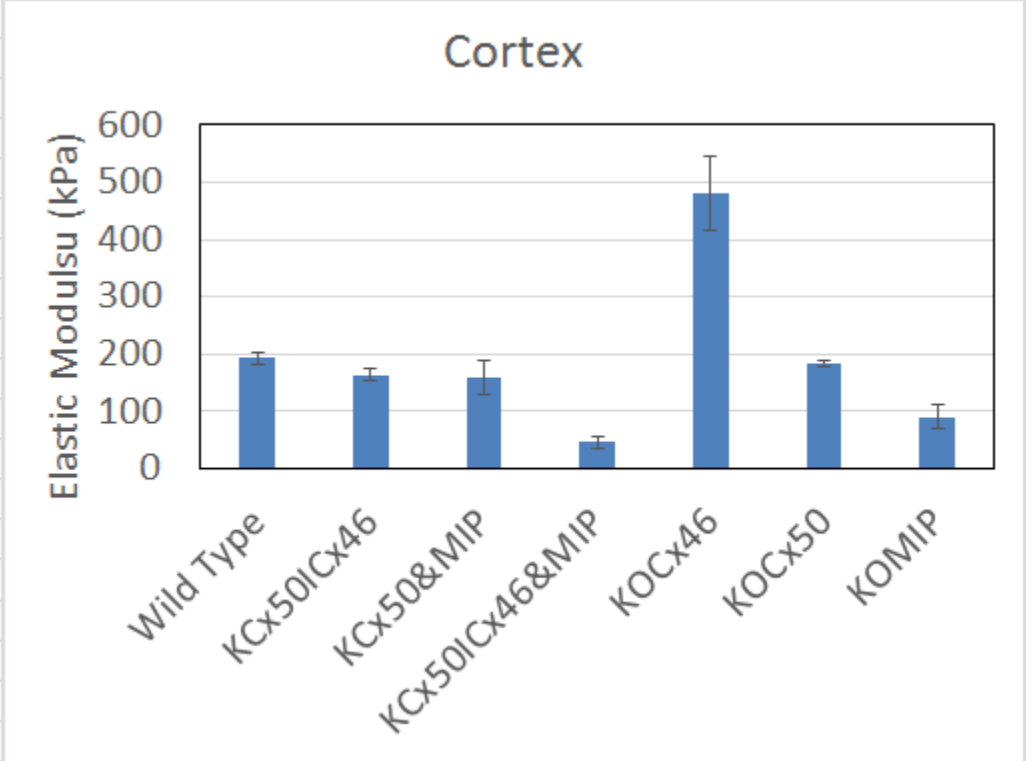
Wild Type	N(kPa)	CR(kPa)	CS (kPa)	KOCx46	N(kPa)	CR(kPa)	CS(kPa)
4	107	147	68	**1**	185	245	354
5	189	191	170	**3**	395	505	458
6	132	196	168	**9**	405	556	636
7	224	220	179	**10**	292	563	457
8	164	188	155	**11**	275	556	475
9	122	155	119	**12**	280	526	420
KCx50ICx46				**KOCx50**			
1	163	135	152	**1**	159	156	177
2	146	170	166	**2**	207	17	203
3	148	169	144	**4**	185	186	134
5	118	178	137	**6**	150	181	126
				7	192	195	132
KCx50&MIP				**8**	197	186	136
12	612	214	203	**9**	393	205	168
13	105	133	152				
14	18	197	201	**KOMIP**			
15	229	85	68	**1**	191	49	34
				2	16	146	155
KCx50ICx46&MIP				**3**	103	8	131
7	116	60	132	**5**	164	168	146
8	118	76	113	**6**	190	145	173
9	9	15	8	**7**	161	100	168
10	70	57	40	**8**	14	14	9
11	17	19	10	**10**	16	7	10
13	39	46	47				

Figures 6 provide a visual comparison of the modulus values for each anatomical region for each genotype.

a)


Nucleus
Elastic Modulsu (kPa)
400
350
300
250
200
150
100
50
0
Wild Type
KCx50ICx46
KCx50&MIP
KCx50ICx46&MIP
KOCx46
KOCx50
KOMIP

b)


Cortex
Elastic Modulsu (kPa)
600
500
400
300
200
100
0
Wild Type
KCx50ICx46
KCx50&MIP
KCx50ICx46&MIP
KOCx46
KOCx50
KOMIP

c)

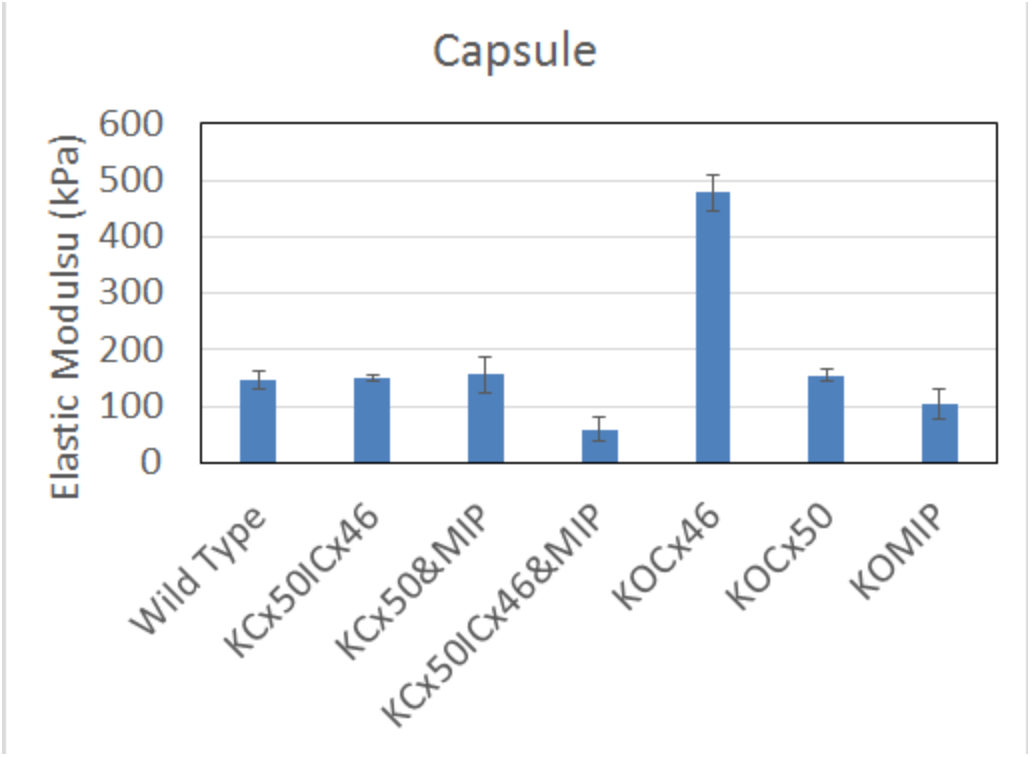
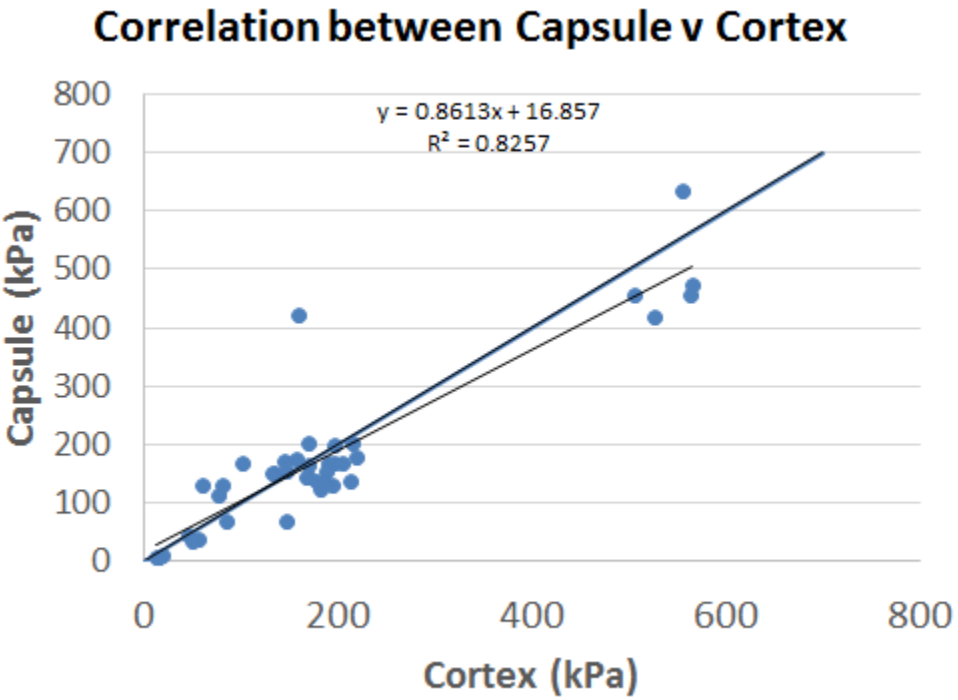


Figure 6: Modulus of Elasticity with each respective region. a) Average values for the Nucleus b) average values for the cortex c) average values for the capsule.

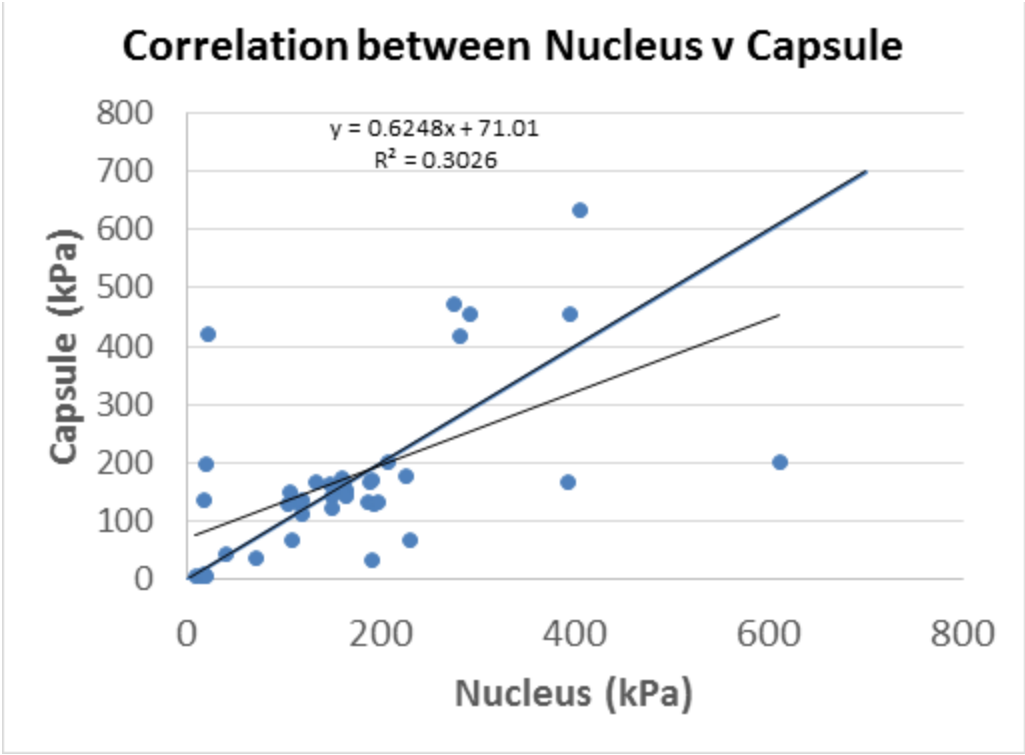
A type 1 ANOVA along with independent t-tests provided in Microsoft Excel 2013 were conducted to determine significant differences between groups. Level of significance (α) was set to 0.05 and was compared with the calculated p-value. Further investigation was conducted between wild type lenses and mutated KOCx46 and KOCx50 since those two induced genotypes showed marked alterations to their elasticity. T-tests were conducted to compare genotypes to the wild type, and p-values less than 0.05 indicate that no significant differences are observed for the nucleus elasticity. As for the cortex, genotypes KOMIP, KOCx46, and KCx50Icx46&MIP show differences. The capsule has significance for KCx50Icx46&MIP, KOCx46 and KOCx50. Observation of the elasticity among regions was noted. Figure 7 reveals a linear trend between

the elastic values of the cortex and capsule regions with results clustering around the line $y=x$, indicating that the cortical elasticity may control the solution. This is not unexpected due to the thinness of the capsule and its primary mode of deformation being bending in the compression test.



a)

b)



c)

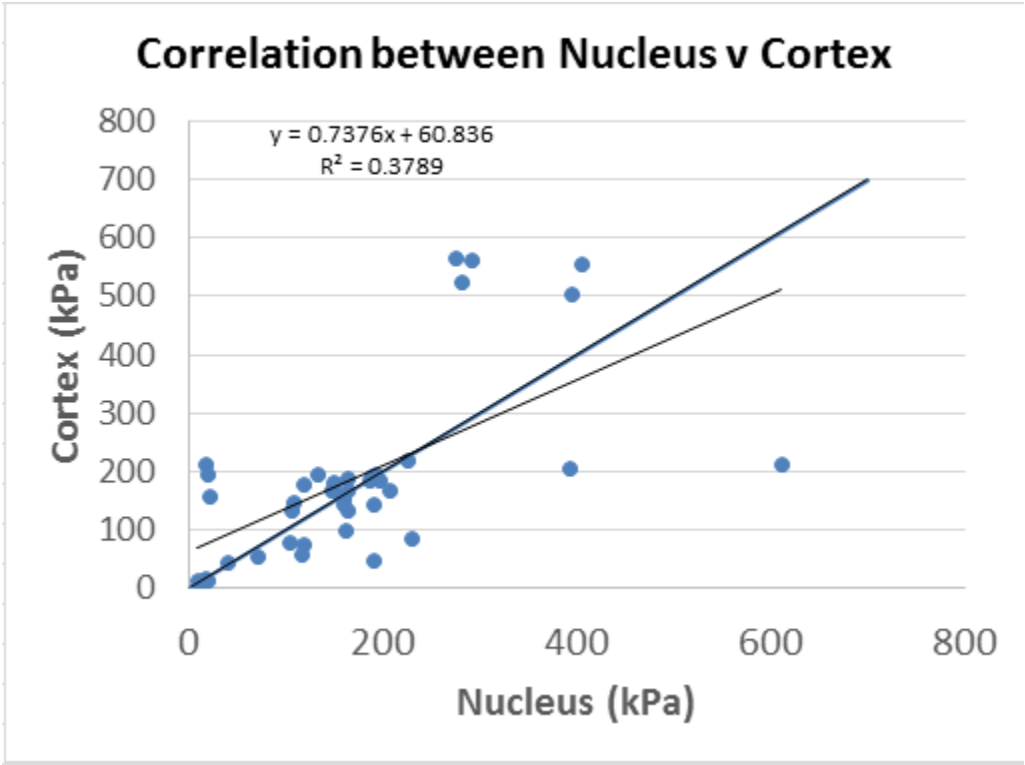


Figure 7: Modulus of Elasticity among regions. a) Elastic modulus values between the cortex and capsule. b) Direct plot of the elasticity between the nucleus and capsule c) direct plot of the elasticity between the nucleus and cortex. Among the three plots, (a) reveals a stronger linear

correlation suggesting that the capsule is a thin membrane with little bending stiffness which likely does not contribute significantly to the force generated during a lens compression test.

4.3 Sensitivity Analysis

As the radius of the nucleus cannot be determined by image processing, the dimension for all simulations was assigned as half of the entire equatorial radius. A sensitivity analysis was performed to determine the significance in geometric dimension to the elastic properties of the lens regions. The method follows similar to that of Sigal [12] who analyzed 21 input factors. A data set was selected as well as geometry as baseline values while the thickness of the regions varied by 5%. The capsule and cortex of the lens were the only two regions that were changed in this sensitivity study. The Young's moduli (E) obtained in the base simulation were assigned as the elastic properties when the cortex thickness was increased and decreased by 5 % in two separate simulations. The percent difference was calculated as well as the RMS value to determine if the geometry must be measure accurately when using inverse FEA analysis. The same method was repeated for the lens capsule. The results of the sensitivity immediately reveal the radius of the cortex/nucleus boundary as a significant component. The baseline value compared to the increased value of the cortex shows an 8% difference of the E value of the nucleus.

CHAPTER FIVE: DISCUSSION

It is important to note several assumptions made for this study. The first is the material behavior of the layers. Analogous to the spring in simple mechanics problems where the stiffness *k* is the proportionality constant between the force applied and the displaced deformation, the lens is treated as a linear elastic material. In this study, the *k* constant of the entire lens was substituted with three elastic moduli for the three regions in the lens. The prescribed displacements acted on the model lens generated the force to create compression.

A second assumption was the len's geometry in the model. A multi-layered ellipsoid was chosen to represent the lens. Although the equatorial and axial radii were gathered from image analysis, the thickness of the cortex cannot be determined as the images do not reveal a clear separation between the nucleus and cortex. The next logical step would be to further dissect the capsule; however, attempts to dissect the capsule from the lens led to decreased integrity of the cortex due to the lenses small and fragile size. Therefore, the capsule of the mouse lens remained intact in order to preserve the mechanical properties. The thickness of the capsule was obtained by Danysh [13] , and it was assigned to be 11.4 μm for all simulations. The nucleus was assigned as half the equatorial radius which left the balance of the lens as the cortex. To obtain reliable and accurate elastic modulus values, the dimensions of the dissected lens must be obtained without disrupting its structural integrity.

The next assumption is the reliability of the experimental data; no samples were created or tested in this study. The results obtained in this study are purely data driven. The force-displacement data of the compressed lenses was gathered in another study, and the dissection of the mouse lenses were performed at another research facility. A few data sets revealed a zero-

slope correlation between force and displacement indicating poor contact and were not included in the simulation due to their exclusion by the experimenters.

An important note to discuss is the lack of an existing model to obtain the elastic modulus of a multilayer spherical/ellipsoid. As mentioned earlier, the Hertz model is the only relevant equation in determining the elastic modulus; however the geometrical assumption must be a spherical object of material homogeneity. Comparing to the young's modulus to the previous study which introduced the hertz model, the results of this study proved the Hertz equation inapplicable to the determination of the mechanical properties. As there is no existing model to obtain the elastic properties of the inner regions of the mouse lens, the validation of my proposed method is reliant on discretization and the replication of the experimental set up.

CHAPTER SIX: CONCLUSIONS

The purpose of this study was to explore an alternative method in measuring the mechanical properties of adult mouse lenses. The proposed method introduced an inverse finite element analysis approach which was successfully accomplished under a few assumptions. A model was created to replicate the experimental design, accounting for axial displacement, lens geometry, boundary conditions, and contact method. As no model exists to analytically determine the mechanical (elastic) properties of shell objects, this study relies on experimentally derived data. A statistical comparison between the Hertz model and the averaged values of the three regions calculated by inverse FEA showed no statistical difference; this in part validates the proposed study; however, inverse FEA provides further information about regional variations in the mechanical properties of the mouse lens.

Increasing the number of simulations for each lens-specific genotype while also accurately obtaining dimensions of the three regions could bring significant improvement to this study. Successful simulations with optimization reveal distinct values for the elastic properties for the three regions of the lens. Future work will include simulating mouse lenses of different ages as the lenses in this study were all obtained from 17-week-old mice.

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CHAPTER SEVEN: APPLICATIONS OF RESEARCH

The novelty of this project allows for the determination of elastic modulus of a mouse lens. Previous methods to determine the elastic modulus failed to account for the different mechanical responses of the cortex and nucleus. Obtaining the mechanical properties of these regions would require separation of the capsule; however, with the delicacy of the lens a dissection would disrupt the natural internal structures and thus alter the results. With computer modeling, the radius of each region can be addressed to only perform the compression test. Computerized modeling can be extended to multiple structures that may contain internal structures too delicate to isolate.

As for the calculation of the elastic moduli, previous literature only reveals one value of elastic modulus for the entirety of the mouse lens. This again fails to count for the differences in material regions specifically the cortex and nucleus. The proposed method in this study that gives this study strength compared to previously-published methods for estimating mouse lens properties using compression testing is the ability to objectively estimate the intrinsic, regional properties of the lens.

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APPENDIX

A. Calculation of Mesh Discretization

The following are the values in matlab format:
c = [nucleus, cortex, capsule]

ef = c(1,:) = [85280 107360 104090];
f = c(2,:) = [85220 107410 104030];
n = c(3,:) = [84910 107260 111870];

% difference calculation:

((ef-f)./(ef))*100 = [0.0704 -0.0466 0.0576]

((ef-n)./(ef))*100 = [0.4339 0.0931 -7.4743]

((f-n)./(f))*100 = [0.3638 0.1397 -7.5363]

Since the % difference is below 0.1 comparing ext.fine(ef) to finer(f),
I can conclude that finer mesh is acceptable to use for the remainder
of the simulations.

B. MATLAB scripts used for (a) Solver, (b) CompareData, (c) ComsolModelSolver

(a) Solver

```
%%Andre Cleaver

% Thesis proposal on using inverse finite element analysis to determine
% the intrinsic elastic modulus of the Lens Nucleus, Cortex, and Capsule
% of compressed Mouse Lenses.

%%
% The following script calls for a temporary file name to hold data
% promts user to name a file. This will compare with the experimental
% file upload. MAKE SURE the file name is in the current folder window.

global shortcut;
Filenameprompt = 'Give a name for the exported data from COMSOL\n';
fileExcel = '.csv';
exportedName = input(Filenameprompt,'s');
location = 'C:\Users\utd830\Desktop\AndreThesis2016\';
shortcut = strcat(location,exportedName,fileExcel);
%%
% The following serves to show the progress bar to visually indicate
% convergence; window will pop up showing progress bar and allow
% cancel of "study".
ModelUtil.showProgress(true);
```

```
%%
% Load the COMSOL Model
% Make sure the Comsol File in the current folder window
model = mphload('ThesisModel');

%% Prompting Parameters and directly assigning the prompted values
%  to the Parameters section in COMSOL
axprompt = 'What is the Axial Radius in [mm]?';
ax_radius = input(axprompt,'s');
unitlength = '[mm]';
ax_value = strcat(ax_radius,unitlength);

eqprompt = 'What is the Equitorial Radius in [mm]?';
eq_radius = input(eqprompt,'s');
eq_value = strcat(eq_radius,unitlength);

model.param.set('ax_radius', ax_value, 'axial radius');
model.param.set('eq_radius', eq_value, 'equitorial radius');

%% Refresh the geometry after the parameters are assigned.

% If needed to change the applied displacement term
model.param.set('u0', '190[um]', 'Applied displacement');
model.geom('geom1').run;

%Propmt user for initial Elastic Modulus of Lens Cortex, Nucleus, and
%Capsule

EMprompt = 'Initial Guess of Elastic Modulus of Nucleus in [Pa]?\n';
E_nucleus = input(EMprompt);
E_cortex = input('Cortex?\n');
E_capsule = input('Capsule?\n');

c0 = [E_nucleus E_cortex E_capsule];

%%
% These two lines of script create a reference line for the integration
% feature. The "11" referers to a specific boundary line in the geometry.
% In my project it is part of the parallel plate.
model.result.numerical.create('int1', 'IntLine');
model.result.numerical('int1').selection.set([11]);

%% Optimization Section
%  The following script contains the optimization section. Will
repeatively
%  correct the guess values until minimum error is reached. Optimzation
%  will run only if "Optimize = 1". If Optimize is 0, comsol will solve
%  with initial guess form beninnging of script. File "ThesisCompareData()
%  must also be present in current folder window.

Optimize =1;
if(Optimize)

% tic-toc feature will display the time-elapsed for the optimization
```

```
tic
    problem.objective=@(c) ThesisCompareData(model,Down,Power,c);
    problem.x0=c0;%Initial point for x
    problem.solver='fminsearch';
    problem.options=optimset('Display','iter');

%     plot(Down,f_fit,'k.',Down,Power, 'r-')
    c=fminsearch(problem);
    disp('Finished optimization.');
toc
else %don't optimize - just show results based on initial guess
    c = c0;
end
    c

%%
Optimize =0;
if(Optimize)

% tic-toc feature will display the time-elapsed for the optimization
tic
    problem.objective=@(c) ThesisCompareData(model,Down,Power,c);
    problem.x0=c0;%Initial point for x
    problem.solver='fminsearch';
    problem.options=optimset('Display','iter');

    c=fminsearch(problem);
    disp('Finished optimization.');
toc
else %don't optimize - just show results based on initial guess
    c = c0;
end
    c
%% Evaluate the model with the best-fit parameters
%  The following script will run the optimized values a final time and
then
%  display the experimental and computational results in a plot. It is
%  important that the units must be the same. If not, the graphs may show
a
%  flat-line trend. For this project, micrometers and millinewtons are
used

yfit = SolveCOMSOLModel(model,c,Down);

u=linspace(0,0.000190,length(yfit));
u = u(:);
p=polyfit(u,yfit,5);
f_fit=polyval(p,Down);

plot(Down,f_fit,'k.',Down,Power, 'r-')
xlabel('Displacement (m)'); %  temp from um to m
ylabel('Force (N)') % temp from mN to N
title('Stiffness of Wild Type lens and Model')
```

(b) Compare Data

```
function [SSR,res]=ThesisCompareData(model,Down,Power,parameters)

% This script provided by Dr. Reilly, compares the two data sets using the
% sum of squares method. A polynomial fit must be applied due to the
% differences in the amount of points from both data sets. To quicken the
% COMSOL file, the generated data plots 10 points, compared to the 240+
% points from the experimental data file.
yfit=SolveCOMSOLModel(model,parameters,Down);

u=linspace(0,0.000190,length(yfit));
u = u(:);
[p,S,mu]=polyfit(u,yfit,5);
f_fit=polyval(p,Down,S,mu);


res=Power(:)-f_fit(:);

SSR=sum(res.^2);
```

(c) ComsolModelSolver

```
function yfit=SolveCOMSOLModel(model,c,U)

% The following script is to set up the solver in COMSOL. Create the
table,
% assign appropriate values,

% global variables are created to be seen with other opened matlab files.
global shortcut;
global exportedName;
global fileExcel;

table = 'tbl';
tblNum = 1;
StblNum = num2str(tblNum);
ComTable = strcat(table,StblNum);

c=abs(c);
unitStress = '[Pa]';
c

E_nucleus=c(1);
E_cortex=c(2);
E_capsule=c(3);

%Necessary to convert the numerical format into string in COMSOL with
% included units.
SE_nucleus = num2str(E_nucleus);
SEN = strcat(SE_nucleus,unitStress);
SE_cortex = num2str(E_cortex);
SEC = strcat(SE_cortex,unitStress);
SE_capsule = num2str(E_capsule);
SEP = strcat(SE_capsule,unitStress);
```

```
%script to directly assign the values of elasticity and update the
%parameters list in COMSOL.
model.param.set('E_capsule', SEP, 'Capsule modulus');
model.param.set('E_cortex', SEC, 'Lens modulus');
model.param.set('E_nucleus', SEN, 'Nucleus modulus' );

%% Refresh mesh
%  mesh must be refreshed for every new change in values. The value is in
%  the range of (1-9). It corresponds to the element size options
%  extreamly fine(1) - extreamly coarse(9).

% It is important to know that that COMSOL will likely fail to converge
% if the meshing is too dense. The best soluiton I can up with is to note
% the last value that was chosen during the optimization run and set those
% values as the next initial guess in elastic Modulus.
% model.mesh('mesh1').feature('size').set('hauto', 4);
model.mesh('mesh1').run;

%% Run the study
%  This code runs the simulation, however unsure how the "maxiter" works
in
%  comsol. Decided to set the interations to "123456" to have COMSOL keep
%  guessing for the convergence.
model.sol('sol1').feature('s1').feature('fc1').set('maxiter', '123456');
model.sol('sol1').runAll;

%% Create a table of force vs. Displacement after each model run
%  This code will generate a table of the resuts (Force vs. Displacement)
%  and export the table to be able to compared.
model.result.table.create(ComTable,'Table');
model.result.export.create(ComTable, 'Table');

%% Script to measure the force using intergration and settings

model.result.numerical('int1').set('intorderactive', true);
model.result.numerical('int1').set('method', 'integration');
model.result.numerical('int1').set('unit', 'N');
model.result.numerical('int1').set('table', 'tbl1'); %note the change from
tbl1 to ComTable
model.result.numerical('int1').set('descr', 'Total Force');
model.result.numerical('int1').set('intorder', '10');
model.result.numerical('int1').set('expr', '-solid.sz');
model.result.numerical('int1').set('probetag', 'none');
model.result.numerical('int1').set('descractive', true);
model.result.numerical('int1').set('intsurface', true);
model.result.numerical('int1').set('descr', 'Total Force');
model.result.numerical('int1').setResult;

%% Believed to be the code to connect the exported table to the
integration
%  results.
model.result.numerical('int1').set('table', ComTable);
```

```
%% Export data using temparary variables

temp = shortcut;
tempNam = exportedName;
tempExcel = fileExcel;
model.result.export(ComTable).set('filename',temp);
model.result.export(ComTable).set('header', false);

% Important to know that the table created must also be removed with the
% following command. Otherwise Matlab will state an error was reached
% claiming is simpler words "tab1 was already initialized.
model.result.export(ComTable).run;
model.result.table.remove(ComTable);

%example on reloading/importing
exportedfile = strcat(tempNam,tempExcel);
n = csvread(exportedfile);
COMu = n(:,1);
COMf = n(:,2);

yfit=COMf;
```

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Title of thesis Inverse Finite Element Analysis of Compressed Mouse Lenses For Mechanical Insights into Presbyopia

Term of submission: Spring 2016

Degree to which thesis applies: BS N/A

1st Major Biomedical Engineering

1st Minor

2nd Major

2nd Minor

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