Team 15: The Effects of 3D Scaffold Dimensions on Chondrocyte Glucose and Oxygen Diffusion

Kevin Chang, Jefferson DeKloe, Botao Peng, Laura Taylor, Connie Yu

***Abstract*—Degradation of cartilage, an inevitable result of everyday movement, is commonly treated with autografts of chondrocytes. Due to the limitations of autografts, there is now a shift towards implantation of artificially produced cartilage. The goal of this study was to examine the effects of dimensions for a scaffold composed of wireframe cubes on chondrocyte viability, mainly by modeling limitations of glucose and oxygen diffusion. Based on anatomical knee cartilage dimensions, scaffolds of the same thickness (3.2 mm) but varying cube side lengths (50um, 100um, and 200um) were modeled in COMSOL. The volume within the pores was assumed to be filled with chondrocytes and given a set oxygen and glucose diffusivity based on previously done research. By surrounding the model in media of constant, initial oxygen and glucose concentrations, it was possible to simulate transport of oxygen and glucose through the scaffold. Similar trends for glucose and oxygen concentrations were reflected in all models of the different scaffold dimensions, suggesting that different pore dimensions had no significant effect on glucose and oxygen diffusion through the scaffold. Glucose concentration remained above the 0.5 mM threshold required for cell viability throughout the entire scaffold [1], with the lowest concentration at approximately 2 mM. However, oxygen levels in the model fell below zero past 0.8 mm from the face of the scaffold exposed to media, suggesting that the models equation for oxygen consumption fails at low oxygen concentrations and a scaffold of the thickness required for knee cartilage implants would likely fail to provide adequate oxygen transport for pore sizes from 50-200um.**

I. Introduction

LOCATED at most joints throughout the body, hyaline cartilage provides the basis for low-friction articular surfaces used in everyday movements, as opposed to the elastic cartilage in the ears and nose. The complex extracellular matrix (ECM) composed primarily of collagen, water, fibronectin, and elastin allows for bones to smoothly glide over one another while remaining resistant to wear. However, cartilage can degrade over time with the onset of osteoarthritis (OA). OA limits movement and compounds bone damage, and in the most extreme cases, cartilage may even be worn away to reveal the ends of bones at the joint. Due to its avascularity and low mitotic activity, cartilage has poor regenerative ability. Thus, OA is generally treated with autografts transplants in which surgeons transfer cartilage from a native site to an area of cartilage deficiency. While this method is largely successful, it is not always an option: possible limitations include degree of deformation at injured region and an excessive amount of cartilage required for transplantation[2].

Tissue engineering therapies provide a method to artificially produce, maintain, and repair damaged cartilage without the restrictions of autografts. Chondrocytes, the cells that produce the ECM for cartilage structural and biochemical support, can be grown in a 3D scaffold immersed in a bioreactor that provides nutrients for growth. Cartilage provides a unique challenge for tissue engineering because it does not vascularize; thus, diffusion of nutrients is the mechanism of transport necessary for the survival and proliferation of these cells. Difficulty in developing cartilage scaffolds is often attributed to the diffusion limits of nutrients such as glucose and oxygen [3]. Therefore, research regarding the geometries of the scaffold to determine the limits of diffusion required for chondrocyte survival is necessary. Through the use of COMSOL modeling for steady state transport of a dilute species, the model examined the effect of pore size on the diffusion rates of glucose and oxygen through a scaffold composed of wireframe cubes, with the goal of producing a scaffold that would be appropriate for the needs of a knee cartilage transplant.

II. Methods

A. Modeling

IT has been shown that pore size and porosity (ratio of scaffold to empty space) are two of the key defining characteristics for a scaffolds geometry[4], [5], [6], [7], [8]. This model specifically varied pore size, while keeping porosity constant for all models so as to observe only the effects of altered geometry. Three models of scaffolds, with pore side lengths of 50um, 100um, and 200um, were generated using the modeling software COMSOL version 5.2.

The scaffold model was made from a repeating square grid pattern such that there would be a repeating pattern of connected channels of cells going through the entire scaffold [4], [5], [6], [9], [10]. Because the study focused on testing the survival of chondrocytes after full tissue development in the scaffold, it was assumed that all channels of the scaffold would be full of cells wherein the consumption rates of the nutrients would be maximized. The grid pattern was chosen to model a scaffold that could potentially be 3D printed. Each modular unit of the scaffold was modeled as a cube with three channels cut out - one channel between each of the opposing faces of the cube. These channels represent the volume available for chondrocyte cells. Figure 1 shows a stack of three modular units of these channels.

The length of a side of each cube before removing the channels were 80 um, 160 um, and 320 um. To vary the pore size between models, three dimensions of the empty spaces in the cells - 50 um x 50 um x 80 um, 100 um x 100 um x

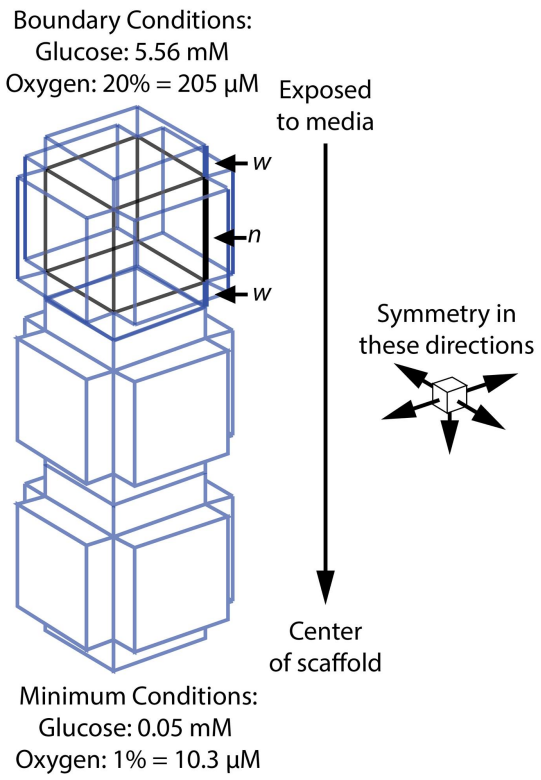

Fig. 1. An example of three units of a scaffold column. In the actual model, units are repeated until 1.6 mm is reached. Also shown are the boundary and minimum conditions we modeled with, the lengths *n* and *w*, and the symmetry conditions set in COMSOL.

160 um, and 200 um x 200 um x 320 um respectively. Using equation (1),

$$Porosity = \frac{n^3 + 6(n^2 * w)}{(2w + n)^3} \tag{1}$$

this gives a porosity of 68% for all three models (see Figure 1). From the literature, 68% is within the range of typical porosities [11], [12], [13]. By examining the strength of a common 3D printed material, PLA, and examining what kind of stresses this structure would need to withstand in the knee, it is also shown that this porosity would withstand the mechanical stresses typical of a cartilage knee implant. Assuming compressive strength of 57.8MPa and medial tibia stresses of 12.1MPa allowed for an area fraction of 0.21 PLA. Calculations in equations (2) and (3) show how the Area fraction was determined. This area fraction of 0.21 translates to a maximum porosity of about 79% [14], [15]. This is consistent with the proposed model.

$$\sigma_{failure} * A_{PLA} = \sigma_{implant} * A_{implant} \tag{2}$$

$$\frac{A_{PLA}}{A_{implant}} = \frac{\sigma_{implant}}{\sigma_{failure}} = \frac{12.1MPa}{57.8MPa} \approx 20.9MPa \tag{3}$$

B. Assumptions and Boundary Conditions

As a worst case scenario, the column of scaffold examined in COMSOL was chosen as the column that would have the lowest exposure to oxygen and glucose from the media - the column at the center of the scaffold. Since this is a model for the knee cartilage, the scaffold would be much longer than its height. Based on this, it was assumed that the amount of oxygen or glucose that would diffuse to the center column of the scaffold from either side of the scaffold would be much smaller than the amount that would diffuse from the media on the top and bottom of the scaffold. Edge effects of diffusion from the media on the sides of the scaffold were neglected. Each face of the column that would connect to a different column in the full scaffold had a symmetry condition applied in COMSOL, meaning that this model assumes an infinitely wide scaffold.

Because there is media above and below the column of cells, the top and bottom halves of the column should behave the same through symmetry. From this simplification, only the top half of the scaffold was modeled and symmetry was applied to the bottom of the column of cells. In the worse scenario, it assumed that nutrients would diffuse through the cells only and that there would be no diffusion through the scaffold material; thus, diffusivity of glucose and oxygen through the scaffold material was set to zero so that only the diffusivity of the nutrients through chondrocytes mattered.

To model a fully packed scaffold of chondrocytes and their consumption behavior, values for consumption rates, initial values, and diffusivities were found from peer-reviewed literature:

TABLE I
METABOLIC PARAMETERS

Parameter	Value
Rate of Glucose Consumption[1]	$-2.165 * 10^{-4} \frac{mol}{m^3}$
$D_{glucose}$[4]	$1 * 10^{-10} cm^2/s$
D_{oxygen}[19]	$3 * 10^{-5} cm^2/s$
Initial Glucose Concentration[1]	5.56 mM
Initial Oxygen Concentration[19]	20% $Oxygen\ Tension = 205\mu$M
Minimum Oxygen Concentration[18]	1% $Oxygen\ Tension = 10.3\mu$M
Minimum Glucose Concentration[20]	$0.05mM$

Oxygen tensions are converted from tension percents to concentration at a rate of $10.268\mu M/$ %oxygen[19]. The initial oxygen tension of 20% gave a 0.205 mM initial concentration. The consumption rate for glucose was assumed to be constant at steady state [1]. The consumption rate for oxygen posed a unique challenge in that it depends on the concentration of glucose present. Referencing a paper that studied oxygen consumption of chondrocytes, a best-fit line was applied to that paper's data of oxygen consumption versus glucose concentration, resulting in the line in equation (4) where X

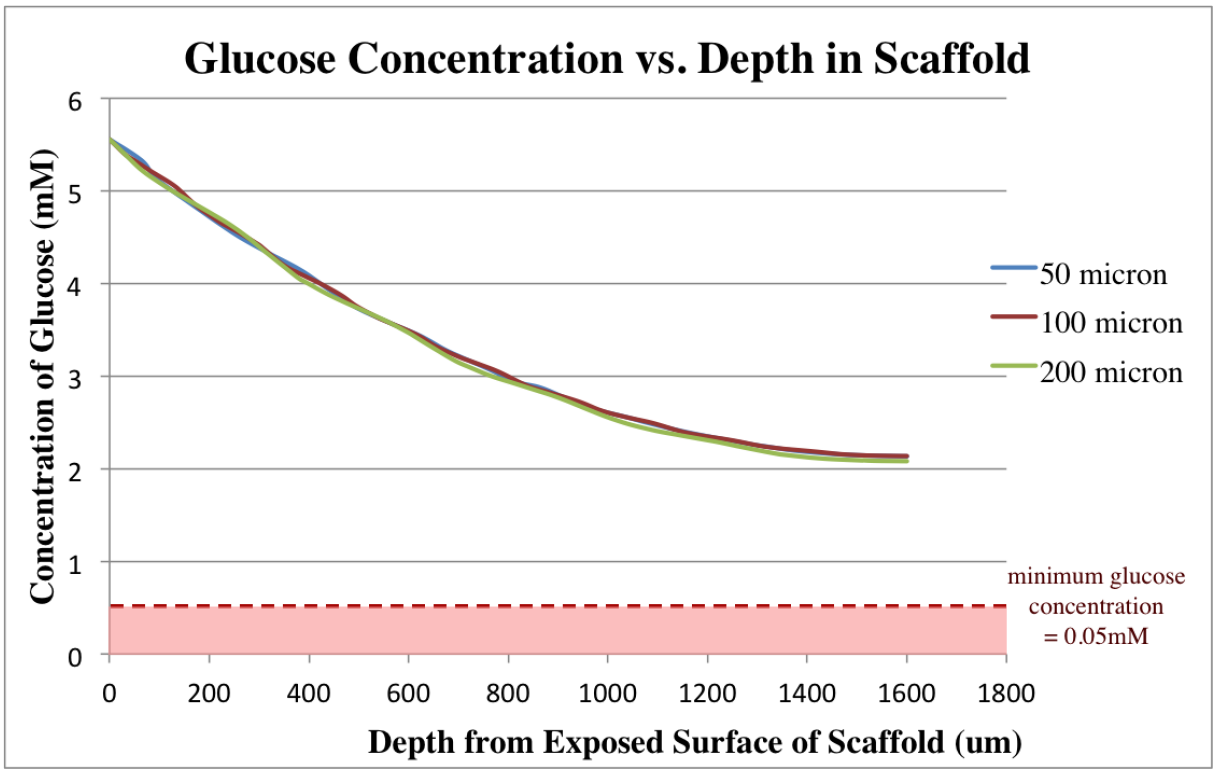

Fig. 2. The concentration gradient of glucose, as modeled by COMSOL. The red shaded region represents the concentrations at which the chondrocytes will not survive.

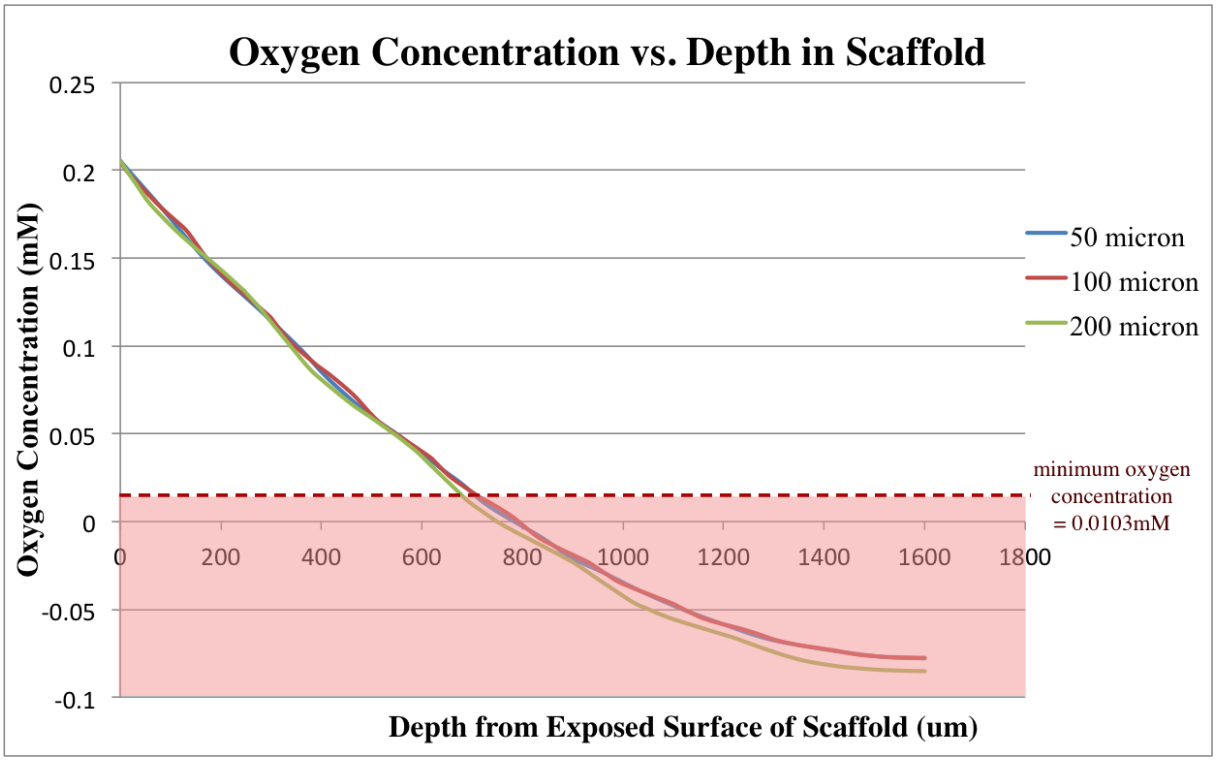

Fig. 3. The concentration gradient of oxygen, as modeled by COMSOL. The red shaded region represents the concentrations at which the chondrocytes will not survive.

is the glucose concentration and Y is the estimated oxygen consumption rate in $\frac{mol}{m^3 s}$[21].

$$Y = 3.827x10^{-6} * X^{-0.492} \quad (4)$$

III. Results and Discussion

FROM the COMSOL model, it was found that changing the pore size does not significantly affect the concentration profiles for either glucose or oxygen between the models.

Figure 2 shows the changes in glucose concentration as the distance from the media increases up to the center of the scaffold. The glucose concentration drops from 5.56 mM to approximately 2.1 mM for models of all pore sizes. Normally, chondrocytes require a minimum glucose concentration of 0.5 mM for survival [1]. The glucose concentrations in the scaffold models remained above 2 mM throughout the entire scaffold regardless of pore dimensions, leading us to believe that diffusion of glucose through the wireframe scaffold model is relatively independent of pore size for the range of pore sizes examined here. It is evident that a scaffold, with the pore dimensions as tested, allows for sufficient glucose diffusion when the glucose concentration in the media is held constant at 5.56 mM.

In Figure 3, there is no significant difference in the oxygen profiles between the different pore sizes examined. When using an initial concentration of 20% oxygen (0.205 mM), the results display that the oxygen levels in the very center of the scaffold drop below 0. This suggests that the equation modeling oxygen is not applicable at extremely low oxygen concentrations. Regardless, it is cause for concern, since if oxygen is unable to diffuse into the center of the scaffold, the cells in the center will die from oxygen deprivation. There is evidence that when grown at 20% oxygen, chondrocytes lose expression of certain key phenotypic markers; passaging at 5% oxygen was able to restore phenotype [17], suggesting that hypoxic conditions are favorable. Because cartilage is avascular, typical physiological oxygen levels are estimated at 1-7% oxygen [18]. Therefore, increasing the oxygen concentration too much would result in the loss of chondrocyte phenotypic markers and potentially make the scaffold useless. If the implant aims to achieve physiological levels in the center of the scaffold, the cells at the edges of the scaffold will not be in ideal oxygen conditions. Maintaining an ideal range of oxygen concentration over the entire height of the scaffold, where it is neither high enough to significantly affect cell phenotype nor low enough to starve the cells of oxygen is a goal that will have to be researched further.

IV. Conclusions

THIS model demonstrated that alterations in the 3D scaffold's pore size, from 50um to 100 um to 200 um for each cube's side length, do not have a significant impact on the concentration gradient of nutrients in the media diffusing through the scaffold. While the glucose profile indicates that glucose will not be fully consumed, the oxygen profile falling into negative values suggests the model does not represent a viable method for growing chondrocytes. This model assumes a zeroth-order reaction for glucose consumption while, in reality, glucose consumption relies on a variety of factors, including, but not limited to, the amount of glucose available to the cell, the cell's own metabolic needs, and oxygen concentration. However, since the results demonstrate that there is still ample glucose to be consumed by the time it diffuses into the very center of the model, the slight difference in consumption is unlikely to change the fact, that for the needs defined by the initial assumptions, glucose is not a limiting factor. Future research on this topic might consider improving the accuracy of the glucose reaction model as this may play a part in optimizing the maximum height possible for the scaffold or the minimum glucose needed to be provided in the media. When oxygen levels drop significantly, rate of glucose consumption changes as does production of potentially toxic lactate. To account for such issues, oxygen levels below 1%, which is the lowest level seen physiologically, were considered to be detrimental to the cells and therefore a failure of the scaffold [cite19!]. However, the absence of lactate is a limitation in the model. Additional modeling should be done to account for the production and transport of lactate as well as the interdependence of glucose consumption and oxygen consumption. Moreover, the results demonstrate that, for the thickest cartilage replacements, there is a necessity for investigating alternate methods of oxygen delivery. This could possibly be achieved by developing methods of facilitated diffusion or delivery such that oxygen levels can be more consistent throughout the scaffold. Depending on the material choice for scaffold there may be a non-trivial amount of diffusion of oxygen within the scaffold. Scaffolds have even been designed to slowly release oxygen into the surrounding area [22]. Thus, the model simulates the worst-case scenario where there is only an influx of glucose from the top of the scaffold and none from the sides. Additionally, modeling studied the scenario where an extremely thick cartilage for full knee replacement was needed; simple diffusion is perhaps sufficient for situations where the scaffold does not need to be as thick. Improvements to the model would include better simulations of oxygen consumption at low oxygen levels. Reports from literature point to physiological levels of oxygen tension in cartilage to be between 1% to 7% [18]. Since it is avascular, cartilage may have unique oxygen consumption trends, especially at these lower oxygen concentrations. A more accurate understanding of the oxygen consumption would allow for a better model of the exact limits on scaffold height that is feasible under the starting conditions.

Acknowledgments

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Appendix I

Meeting Minutes

Meeting Notes 5/2
Feedback on Poster

- Things look good but
    - Don't need all 3D concentration profiles
    - Put all 1D plots of concentration on one plot per solute

By Next Time

- Tao: to work on abstract and intro
- Jefferson: to work on methods of glucose model and conclusions drawn from glucose model
- Laura: To work on Methods for all models and glucose conditions
- Kevin: Methods for making and Conclusions drawn from oxygen model
- Connie: Rework graphs from COMSOL into Excel

Meeting Notes 4/25
For the negative oxygen values can discuss that the equation used to model oxygen does not work as well when you get to low glucose concentrations

Should check the starting values for oxygen again - want to start at the maximum amount of oxygen that could be dissolved in the media (can approximate that with the amount of oxygen that would be dissolved in water)

Laura, re-run the model with changed oxygen values?
He was roughtly calculating the start value for oxygen and he got a lower value than what we used but I can't remember the exact math that we used to get to 0.2

If he got even a lower starting concentration for oxygen, then wouldn't the final oxygen concentration be even lower?

Yep he said that - and for the poster we can just put what we have but he was saying that we should check our initial value and if its too high for how much oxygen you could actually get to dissolve in the media then we should rerun it with the actual value and put that in our paper - and that would basically come out saying that we would probably have less cells that are getting adequate oxygen

So, change the equation but keep the conclusion?
We just want it to reflect realistic values but it shouldnt affect the conclusions we're drawing
I'm not completely sure if we need to redo it though - we just need to double check how we got to that number and make sure that amount could be dissolved in water - I just don't know our conversion method well enough to say if we put too high of a value or not

I'll ask Kevin when he comes today

Meeting Notes 4/22
Members Present: All
Agenda

- Create scaffold dimensions
- Put in place metabolic parameters
- Run model
- Get images

Notes:

- The sizes decided on were .5*100um, 1*100um and 2*100um
- The width added was .5*30um, 1*30um and 2*30um
- Kevin designed reaction rate using best fit
- Length was 3.2mm because it will fit and even number of blocks

By next time

- Assemble paper

4/17

Members present: All

Agenda:

- Discuss deliverables from last meeting
- Discuss initial comsol model requirements

Meeting Notes:

- Diffusivity through cells
    -
- Deliverables from last time:
- Cell density (Jefferson):
    -
- Geometries(Laura/Tao): Most use an easily modeled lattice structure
    - Pore size and porosity most important
- Metabolism data (Kevin):
    - Glucose:
        - "Glucose diffusion coefficient in the cell phase D= 1.0 * 10^-6 cm2/s Galban and Locke (1999a)"
        - Maximum consumption rate of glucose: R= 3:0 * 10^-2 1/s Galban and Locke (1999a)
        - Analysis of collagen and glucose modulated cell growth within tissue engineered scaffolds Glucose consumption: 3.9×10^{-5} kg/(m^3s)
        - Initial conc 5.56 mM same papers as ^
            - http://www.sciencedirect.com/science/article/pii/S2215017X14000587
        - ^^: C.A. Chung Analysis of Cell Growth: http://onlinelibrary.wiley.com/doi/10.1002/bit.20944/epdf
    - Oxygen requirements depend on glucose concentration
        - Oxygen tension of 20% loses phenotypic markers of chondrocytes
        - Oxygen tension of 5% is ideal for maintaining markers
        - ^^: http://www.ncbi.nlm.nih.gov/pubmed/15095292
        - http://www.ncbi.nlm.nih.gov/pubmed/16155906
        - Lines of best fit from above data
            - y=1.996E-15 x^(-4.186E-1)
                - Y is O2 consumption in mol/(hr*cell)
                    - Converstion:
                        - -3.827E-6(.001c)^-.492
                    -
                - X is [Gluc] in mM

    - Line of best fit only for data from 5.3 down because it describes our system better
- Need team name:
    - Membrainacs
    - No Flux Zone

Radius of Chondrocyte cells: ~ 5 um
Diameter: ~ 10 um

COMSOL ideas:

- Vary the ratio between scaffold and cell volume
- Is it necessary to have diffusion in the scaffold, and if so, what diffusion is necessary
- Model a single section in the center with nutrients only diffusing from the media on top of the scaffold, using symmetry to only model the top half
- Assume its much wider than thick

Things we need to begin modelling:

- Thickness of scaffold lattice
- Total height of implant - can use the total height of cartilage in the knee
- Diffusivity of the scaffold material-probably zero
- glucose and oxygen or lactate

Next Week Plan:

- Meet with tdj for Monday OH
- Begin modelling on Wed
- Put together poster weekend

TDJ:

If structural polymer, probably no diffusion
Hydrogels? Would have diffusion in this case

- Find diffusivity in hydrogel?
- Assume no diffusion through structural material as worst case scenario
- Problem simplifies to diffusion + reaction
    - Computationally determine due to complex geometry
- Find how much structure we need by volume
    - What is smallest size of pore (to fill with ECM fast) such that the cells dont die from lack of diffusion?
    - Steady state is fine
    - Maybe compare different patterns or compare different pore sizes
    - Find limitation of 3D printing resolution for pore size?

PIck one implant

- Look at cartilage in the knee, assume worst case has to be X thick
- If you had to do total replacement of knee cartilage, etc
- Conservative case assumes no diffusion from sides

Suggests do with glucose, oxygen, maybe discuss lactate in discussion/conclusion

- "This is what we didn't do, here is what we could do later"

R=-2.165e-4
Dij=1e-10
c0=5.56
http://www.sciencedirect.com/science/article/pii/S2215017X14000587

Iniital conc of oxygen: 205uM
Same source^: 10.268uM/%oxygen

Oxygen percentage and phenotype (5% ideal)

4/4/16 9:30PM
Attendance: Connie, Kevin, Laura, Jefferson
Agenda:

1) Brainstorm and Decide on an idea:

- Laura suggested a device measuring blood clotting
  - http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4729824/
- Jefferson Suggested modeling the movement of nematocysts (Jellyfish) in water
- **Connie suggested modeling diffusion in engineered cell scaffolds**
  - Model geometric specifications
  - Model geometry
  - http://onlinelibrary.wiley.com/doi/10.1002/jbm.b.33054/full
- Kevin look at drug delivery in the blood brain barrier
  - What parameters do we need for therapeutic BBB drug delivery
- Kevin other idea: google diabetic contact lens

2) Possible Problems

- Scaffolds:
  - What geometries do we model
  - We may not need to look at all layers but simply on

3)Input from TDJ

- Questions:
  - Can we ignore the flow on top
  - Suggestions how to model
  - How to simplify the geometry

Comments from 4/5 meeting with TDJ:
Need to narrow down to one type of scaffold that does a certain thing
Or could test different scaffold shapes on a single cell type
Need a specific problem - ex implantable x type of tissue, liver on a chip
Literature search to see what variable you want to test
One or maybe two variables that you change
Give nanomaterial mesh a diffusivity
Modeling worst case scenario - take vertical slice of the center
We can pick our flow rate

Direction for research:
Researching cartilage
3D printed scaffolds - focus on geometry, flow and diffusivity
Isolate a particular media and what is the most important element in the media
Look for what type of cells papers are using-chondrocytes

Agenda for meeting this weekend 4/10/16:

Create protocol/outline for COMSOL:
Before next meeting:
Research

- Geometries of scaffolds
- Necessary cell nutrients
- Amount of nutrients in the bath
- Speed of flow?

Basic outline of how to model in comsol
Useful paper:http://www.hh.um.es/pdf/Vol_17/17_4/Mobasheri-17-1239-1267-2002.pdf

Timeline:
Tuesday 4/26 at noon - poster pdf due
Project poster presentations: Monday 5/2 10AM-noon
Project paper (in PDF format) due by Friday 5/6 at 3PM

Week of 4/4: Get feedback on our ideas Scaffold+ Research
Week of 4/11: Model design in COMSOL and compile results
Week of 4/18: Put together poster
Week of 4/25: Turn in poster pdf by 26th, compile paper rough draft
Week of 5/2: Poster presentation on monday, edit and revise paper based on feedback from poster

Appendix II

Project Member Goals

Kevin Chang:

Goal Statement:

> I would like to get more experience with working in teams. I am pursuing a career in medicine, and I see this career as one that relies heavily on cooperation and teamwork. However, in my classes thus far at Berkeley, I feel that this aspect has not been focused on. In addition, I would like to hone my problem solving skills in a topic that is related to, or models, a real life problem. The idea of tackling a problem that has no set answer and no set way to approach will be beneficial to my intellectual development.

Group Endorsements:

Jefferson DeKloe: Kevin was proactive and involved in all meetings. He was very helpful and ambitious by tackling the oxygen model.

Botao Peng: Kevin was extremely helpful with researching the boundary conditions and the oxygen modeling for the system. Furthermore, he did a great job formating the poster and creating the wireframe models in both the poster and the paper.

Laura Taylor: Kevin was excellent in researching oxygen consumption and coming up with and debugging a way factor in oxygen consumption into the model. He also created a figure for the model from scratch and was very helpful with the paper.

Connie Yu: Kevin did did a great job researching how to factor oxygen consumption into the modeling. His work in illustrator to format the poster and create the model figure was similarly invaluable.

Jefferson DeKloe:

Goal Statement:

The project will be a test of both modeling technical skills as well as analytical analysis . This entails creating a model based on a multitude of assumptions. Regardless of the results of the model, it will be important to ensure that the limitations are stated and assessed. The toughest thing will be to ensure that all assumptions and limitations are noted and addressed at some point. This project will require a great deal of coordination and organization to ensure that it is carried out efficiently and in a timely manner. I hope to improve my communication and bookkeeping skills.

Group Endorsements:

Kevin Chang: Jefferson did a good job of keeping the group writings coordinated, first by writing up the minutes and by putting together the final paper. He also put in a lot of work finding the boundary conditions of our system and modeling it.

Botao Peng: Jefferson was very organized with meeting minutes and formatting the final paper. He was also very helpful with finding the initial conditions and modeling the oxygen portion of the project.

Laura Taylor: Jefferson was very helpful in designing the model and identifying boundary and initial conditions from the literature as well as debugging in COMSOL.

Connie Yu: Jefferson had helpful input on the modeling parameters and final COMSOL modeling geometry. He also handled coordination of meeting minutes very well.

Botao Peng:

Goal Statement:

I have often been the quiet one in many group projects; I tend not to speak up and communicate my ideas openly. Therefore, I hope to open up myself more this project. I want to learn how to interact with the other members in my group more fluently, and not spend time in the background not contributing my ideas. I plan on becoming more like the role of a brainstormer. I generally have many ideas and I believe that they will contribute to the project. Therefore, I want to convey those ideas to the rest of the group. As a result, I hope to understand how to interact more smoothly with my partners and how to communicate my ideas more effectively through this final project. Through these goals, I hope to become a better team member that I hope will help me work better in groups in the future.

Group Endorsements:

Kevin Chang: Tao definitely cooperated well in the group. He brought up good points in our discussions and was a valuable member of the team. He wasn't shy about inputting improvements to our writing or figures and helped to improve our work overall.

Jefferson DeKloe: Toa was key in keeping the group on track. He was sure to ensure that the group was on the right track and staying on it's toes. Without Tao I don't know how many hours we would have spent on mistakes he had caught

Laura Taylor: Tao was very helpful in suggesting improvements to the model and contributed significantly to developing the paper and ensuring that the different sections were clear and cohesive.

Connie Yu: Tao had many helpful suggestions and edits to contribute throughout the modeling and final write up. His contributions in final paper really helped with ensuring that everything was clearly cited and explained.

Laura Taylor:

Goal Statement: One of my main goals is to work on the brainstorming and refining the design of the model. I want to focus a lot on working on the technical design aspects of the project and solidifying my understanding of Comsol in the process. I really want to finish the project having a better understanding of how to go through the process of originally starting to just brainstorm ideas to solidifying a concrete plan. I also would like to focus on methods to evaluate a model design and work on ways to troubleshoot potential problems. Additionally, I want to have a better understanding of the process of putting together a scientific paper. I would like to get more practice effectively identifying relevant and helpful scientific papers for background information. Also if possible depending on how the work gets broken up in the project group I would like to contribute largely to the results and discussion portion of the paper and get a better understanding of how to format that type of section (particularly what to include in the discussion). In terms of working in the group, I want to be more of a leader in coming up with the model design. Overall, I think my main goal is to feel more comfortable taking theoretical knowledge and applying it to a specific situation or question.

Group Endorsements:

Kevin Chang: Laura played a big part in the modeling of our COMSOL model, and helped greatly with the writing of our paper. She also helped with moving from theoretical problem to fully developed question

Jefferson DeKloe: Laura was very keen to keep us on track with our assumptions as well as putting in lots of time toward constructing the models.

Botao Peng: Laura really helped the most with modeling in COMSOL. Without her, we would have struggled much more with simulating oxygen and glucose transport.

Connie Yu: Laura worked diligently to handle a lot of the modeling troubleshooting. She also did a lot of research to make sure our assumptions were well cited by peer reviewed literature.

Connie Yu:

Goal Statement:

> In the bigger picture, I hope to gain experience in applying what I've learned to tackle a real-world problem. We've done a few modeling studies in COMSOL during the lab sections, and I'd like to apply that knowledge to create original models without guidance and learn from the trial-by-error mistakes. The lab handouts have been comprehensive crutches where all values and equations have been provided so I think it'll be a good opportunity to go into a COMSOL project with preliminary research required. Beyond the academics, I hope that the additional aspect of working in a team will help with my collaboration skills, as I sometimes have trouble communicating my ideas effectively.

Group Endorsements:

Kevin Chang: Connie came up with our problem, cleanly applying our modeling knowledge to a real problem. She also came up with some clever methods of troubleshooting and working around limitations of our model.

Jefferson DeKloe: Connie was very good at ensuring that our model stayed grounded in reality and would provide real information. Connie also helped organize and analyze our data from COMSOL.

Laura Taylor: Connie was very helpful in researching and refining our problem and our approach to modeling as well as putting together the result figures from the COMSOL models and editing the paper.

Botao Peng: Connie was very helpful in proofreading the paper; she made it much easier to read while adding in much more information. Furthermore, she helped much with the research and found much of our sources.

Contract for Final Project

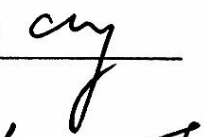
We, the undersigned, have agreed to work together on a final research project. Each of us understands that we are jointly responsible for the final product as a whole, and though we may split the work up amongst ourselves, all of us will be expected to comprehend and be able to explain any part of the final product.

For a 4 unit course with one unit of lab, each student is expected to attend 3 hours of lecture, 3 hours of lab, and perform ~6 hours of work on their own on a weekly basis. Each of us understands that we will personally be responsible to put in approximately 4-6 hours of work per week into the final project. If you are unable to do so due to **unforeseen** and **extraordinary** circumstances, it is *your* responsibility to inform the instructor *as soon as possible* so that alternate arrangements can be made. The instructor reserves the right to assign different grades to various members of the group if the workload is not distributed and carried out evenly.

Each of us promise to adhere to the Berkeley Code of Student Conduct (http://students.berkeley.edu/uga/conduct.asp) and understand that plagiarism of any kind will not be tolerated.

Project group title:
The Effects of 3D Scaffold Dimensions on Chondrocyte Glucose and Oxygen Diffusion

Brief description of project (in its current form):
We are investigating the diffusion of glucose and oxygen into a scaffold filled with chondrocytes for the purpose of growing cartilage for a knee joint replacement.

Name (printed): Kevin Chang Signature: 

Name (printed): Laura Taylor Signature: 

Name (printed): Jefferson DeVos Signature: 

Name (printed): Connie Yu Signature: 

Botao Peng