Ex Vivo Maintenance of Heart Viability: Comparison of Two Methods

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Executive Summary:

Currently established methods of tissue preservation for heart transplantation involve placing the harvested donor heart in a cold, nutrient-rich cardioplegic solution. Clinically, methods like these have only been shown to preserve heart tissue for a matter of hours. A new solution for tissue preservation developed by Transmedics Inc involves placing the heart in a chamber that mimics the physiological conditions of the human chest cavity. This solution maintains the heart in a beating state and pumps blood and nutrients through the myocardial circulation. This preservation technique has been clinically shown to improve the length of time that a heart can be preserved ex-vivo and when properly implemented, could theoretically preserve a donor heart indefinitely.

A computer simulation using Finite-Element analysis was performed with the intention of comparing how well these two methods work to perfuse heart tissue with oxygen over a long period of time. As expected, it was shown that the Transmedics cart could keep the concentration of oxygen in the heart tissue at optimal levels indefinitely while the immersion technique could only keep the concentrations of oxygen in the tissue above healthy levels for around 5.5 hours. Investigations into the effect of temperature on each preservation technique found that the Transmedics preservation is most effective at 37 degrees Celsius, body temperature; while the immersion technique is most effective at 4 degrees Celsius. Though the Transmedics device was shown to be far superior in many areas, other considerations, like the cost and the ease of implementation of each technique have lead us to conclude that there are still certain situations in which tissue preservation by cooling is the best option for heart transplantation.

Introduction:

In heart transplantation, one of the most important factors for success of the process is the transport of the heart itself. Hearts have a high rate of failure during transport due to very basic transport systems that do not realistically mimic the physiologic conditions in the body. Our goal is to model two systems of heart transport that keep the heart alive in different ways. From these models we can draw conclusions as to which method is most effective. The first method uses a more primitive design involving submerging the heart in a nutrient bath while the second involves introducing an artificial coronary blood supply where the oxygen and nutrients are delivered in a more physiologically correct manner. If our model proves one method to be more effective, it could ultimately allow for a greater success rate of heart transplantation.

We are concerned with heart viability *ex vivo* when being transported for transplant. Standard procedure currently involves cooling the heart in a nutrient-rich fluid while it is outside of the body. However, during this process the heart still slowly decays. It has been shown that keeping the heart at body temperature and providing it with the necessary nutrients can mimic *in vivo* conditions and keep the heart in a healthier state. This requires pumping fluid through the coronary arteries to the cells of the heart. We wish to study the efficacy of these two methods of heart preservation.

We anticipate that the immersion solution will not be better the new procedure, but it would be more economical. For this reason, even if this method of nutrient delivery should prove insufficient on the scale of the human heart, it may still suffice on other smaller scales for laboratory experimentation. It is also possible that the immersion solution can be optimized to keep the heart alive for a longer amount of time by investigating the effect that temperature has on tissue preservation.

For each of these heart preservation methods different models are required. When pumping fluid through the heart the oxygen will diffuse through capillary walls - we will model this as an axisymmetric cylinder of tissue surrounding a capillary. When suspending the heart in a nutrient-rich fluid - we will model the heart as a rectangular 2-D slab with constant concentration boundary conditions along the edges. For this study, we will limit ourselves to investigating the diffusion of oxygen in the tissue.

Objectives:

By looking at the concentration profiles of oxygen in the tissue over time we can discern the efficacy of each method in the following ways:

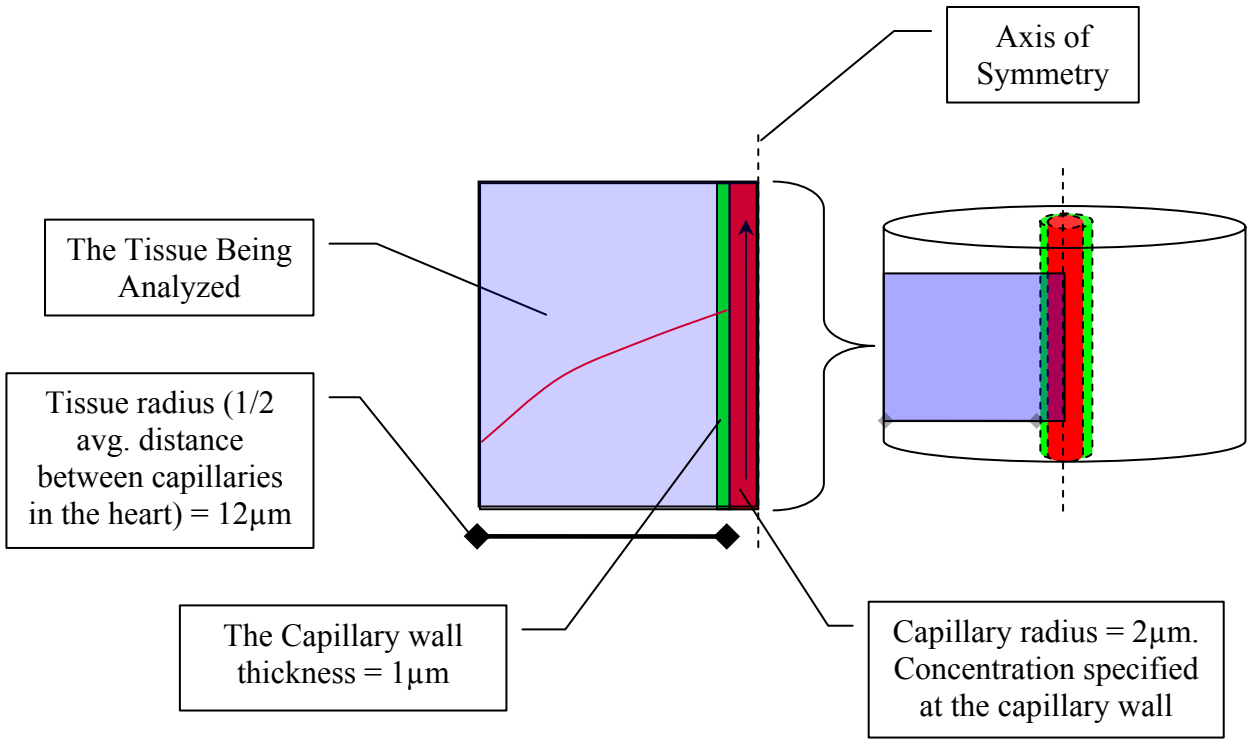
- Determine how long each method can keep oxygen levels above the minimum for cardiac tissue survival at all points in the tissue.

- If the concentration never drops to the minimum we wish to see how long it takes for the average concentration of the tissue to reach optimal conditions for each method.

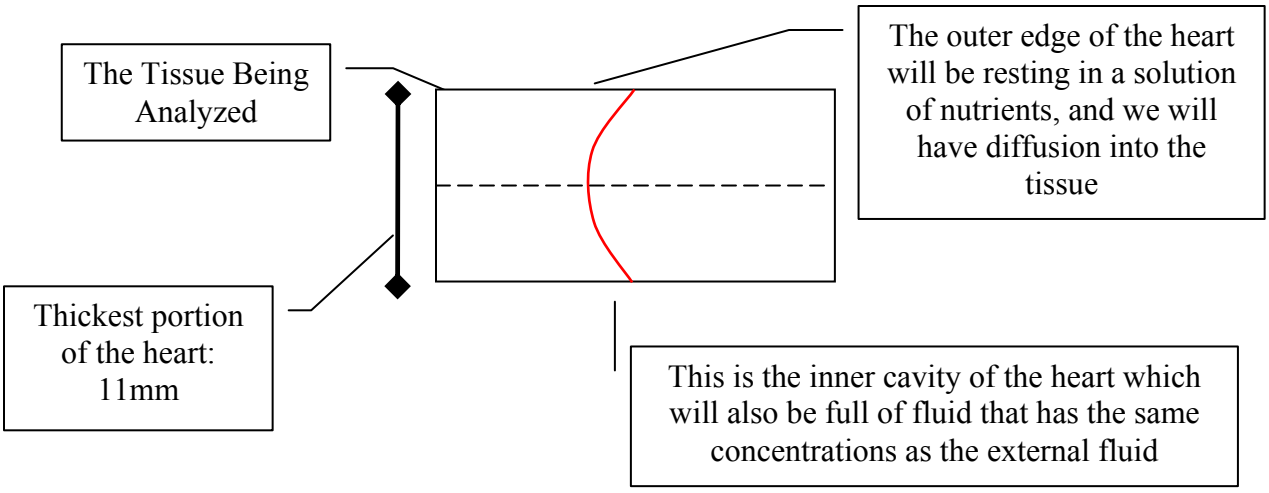
Sensitivity analysis for the effect of lowering the temperature of the tissue will be performed to investigate the feasibility of each method at a reduced temperature. As an alternative, non-computational means of comparison, we will also consider the economics and feasibility of implementing each method.

Geometry and Design Schematics:

Diffusion in the capillaries will be assumed to be axisymmentric:



Diffusion by immersion will be modeled as a 2-D slab with its thickness equal to the thickest part of the heart wall (the part of the heart where it will be hardest to keep the nutrients at acceptable levels):

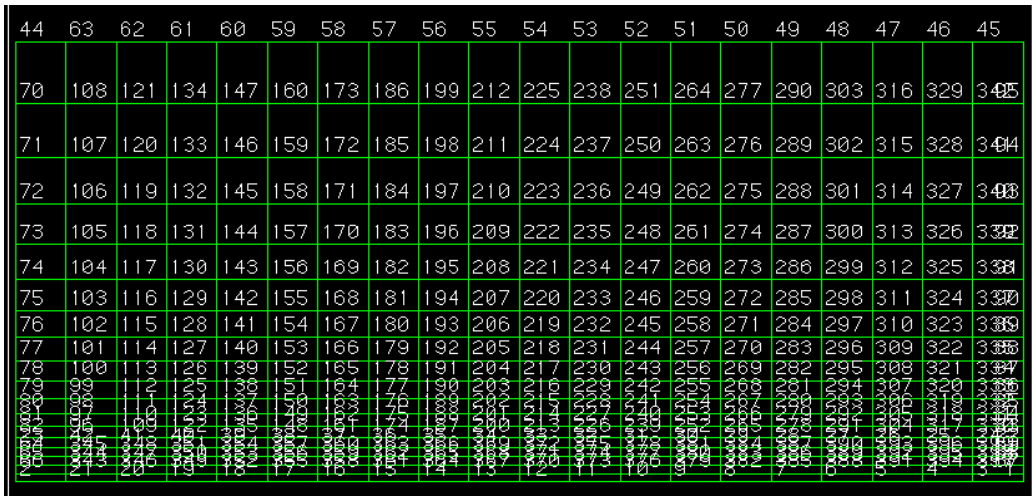


Note: These two methods of heart preservation will be called the 'Immersion' and 'Capillary/Perfusion' methods in the following sections of the paper.

Capillary Mesh:

As figure 1 below shows, we created a mesh that was tighter as it got closer to the capillary wall. This was done because the changes in concentration are greater near the capillary and a finer mesh was needed to accurately visualize these changes in concentration. During testing we varied the density of the mesh to ensure that it was not affecting our final results. We found indeed the solution due to the mesh had converged.

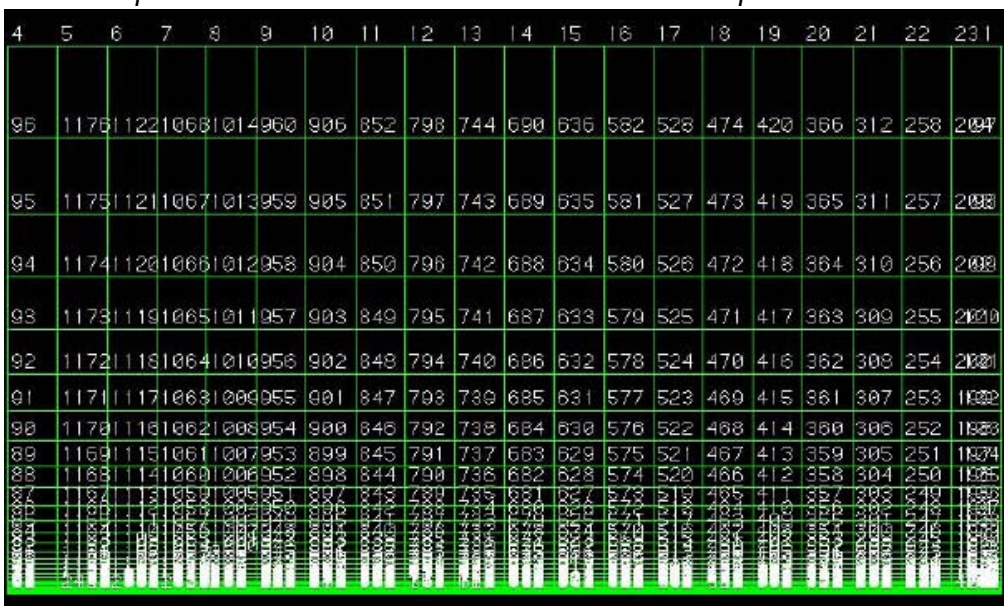
Figure 1: Visual of the mesh with node numbers for the capillary. The bottom of the screen is the edge of the capillary wall while the top of the screen is the middle of the tissue between two capillaries.



Immersion mesh:

Again, as figure 2 below shows, we used a tighter mesh at the edge of the heart where the tissue interacted with the nutrient bath. The nutrients at the wall undergo a larger gradient, and in turn the finer mesh is needed to obtain accurate results at this location. As shown later, we varied the testing to show that our solution converged for this mesh density, validating figure 2 as the mesh used for our solutions.

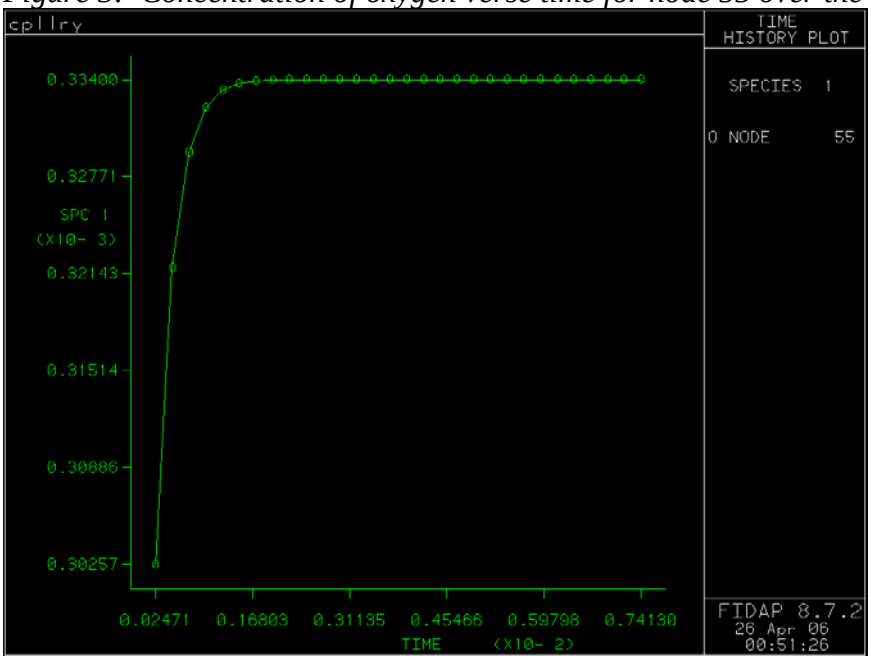
Figure 2: Visual of the immersion mesh with node numbers. The bottom of the screen is the edge of the heart in contact with the nutrient bath while the top of the screen is the middle of the tissue between the inner and outer walls of the heart.



Capillary Solutions:

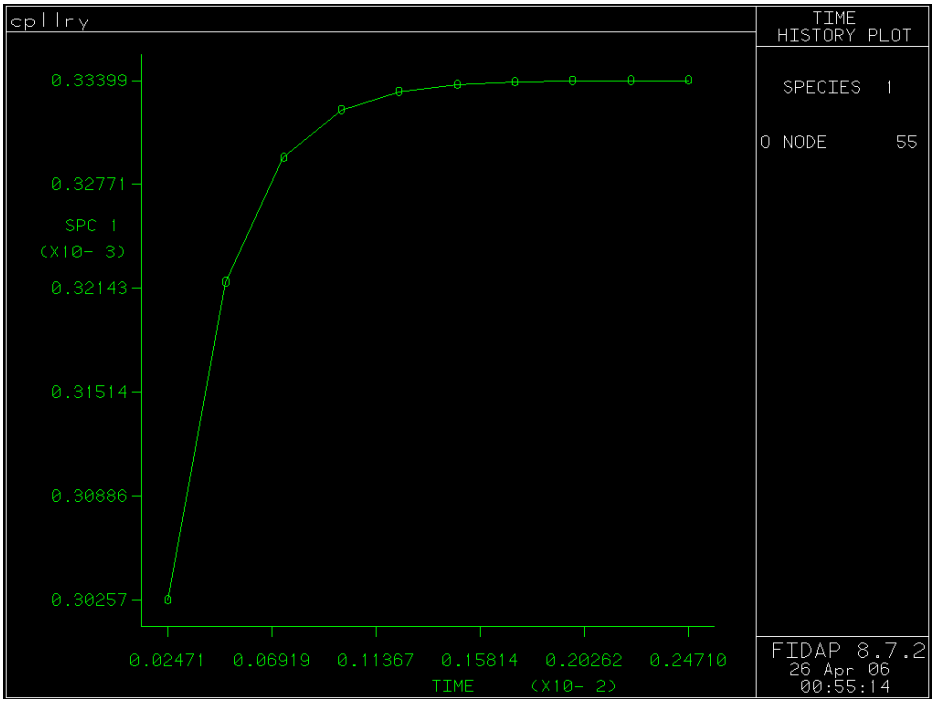
In heart transplantation, we are interested in preserving all of the tissue. In turn we need to look at the tissue that gets the least nutrients, the section of the mesh that is furthest away from the capillary. This area is essentially the 'weakest link.' If we know the furthest tissue has adequate nutrients, then we know the rest of the tissue also has enough nutrients. We chose to analyze node 55 for this purpose, which you can see on the top of figure 1. Figure 3 below shows concentration of oxygen against time at this node.

Figure 3: Concentration of oxygen verse time for node 55 over the course of 3 seconds.



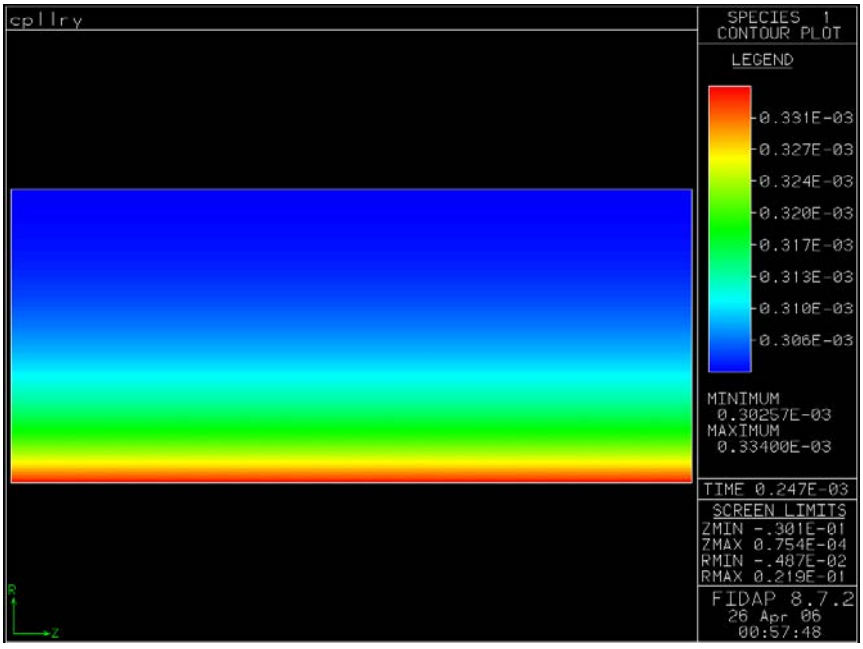
As you can see in figure 3, the concentration rapidly increases, and is at its maximum concentration very shortly. Within one second, the concentration of oxygen has reached steady state levels and would theoretically remain there indefinitely. This graph basically shows that the capillaries are extremely effective in the diffusion of oxygen to surrounding tissue. In order to more closely see what happens initially, look at figure 4 on the next page to 'zoom' into the first second of blood flow.

Figure 4: *Concentration of oxygen verse time for node 55 over the course of 1 second.*



As figure 4 shows, the concentration takes about half a second to reach maximum levels, which is extremely fast. Pumping blood through the capillaries effectively eliminates the oxygen deficiency problem. We also created a contour plot for the entire mesh at about 1 second after the start of blood flow, which shows how node 55 is the last to receive the needed oxygen. This is seen in figure 5 below.

Figure 5: Contour plot of the concentration of oxygen in the capillary wall and cardiac tissue

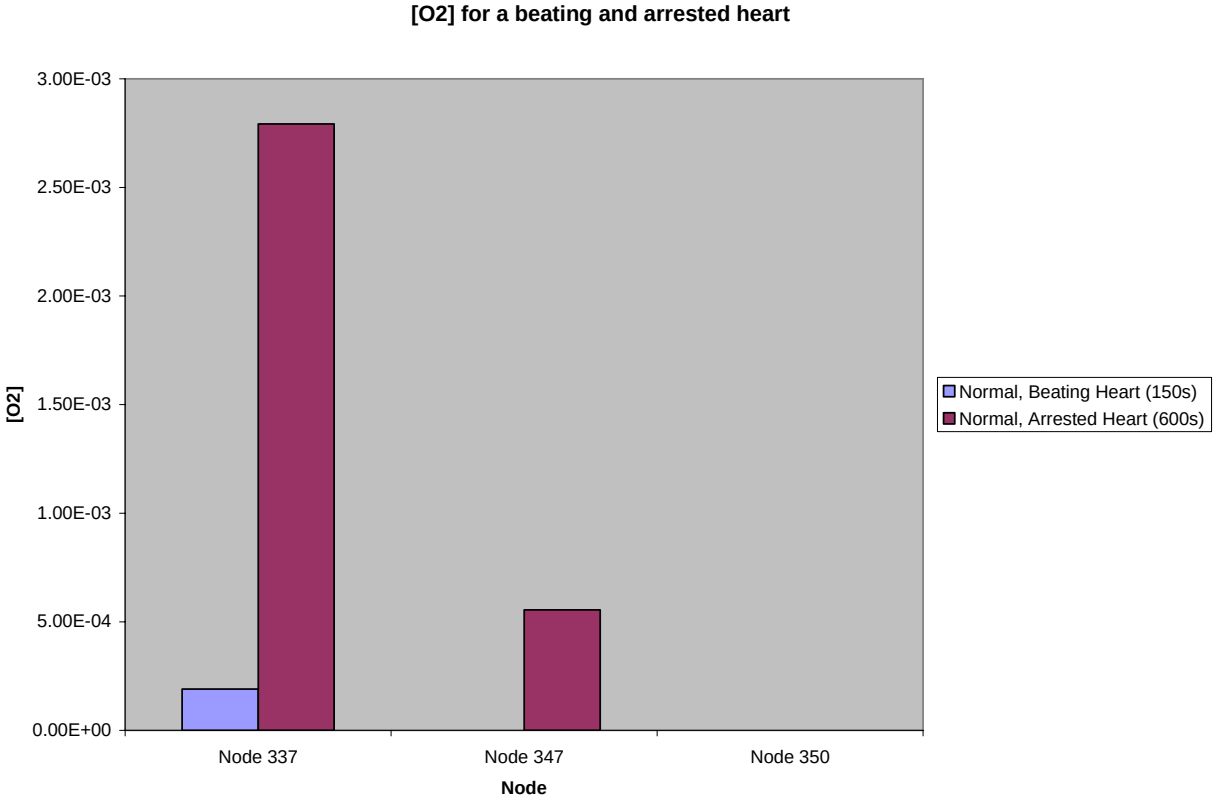


Immersion Solutions:

We initially considered the case where the heart is in a solution at body temperature. First metabolic rates for normal beating hearts were used. For this case, apart from areas very close to the edge, the entire heart was below our minimum specified concentration of oxygen within 2.5 minutes.

It was found that by using a cardioplegic solution to arrest the heart, the oxygen consumption can be reduced by up to 75% even at body temperature. Using a new metabolic rate, we reran the experiment for four times as long and found an improvement in the amount of oxygen delivered. However there was still no oxygen diffusion reaching the middle of the heart.

Figure 6: Comparison of oxygen concentrations at various points in the heart. The red bars show the concentration for a normal, arrested heart after 600 seconds, while the blue bars show the concentration for a normal, beating heart after 150 seconds.



Note: Node 337 is approximately 0.5 cm from the heart wall, 347 is 1 cm and 350 is 2 cm.

Since this was insufficient to protect the heart from damage, we investigated the effects of lowering the temperature reducing the metabolism of oxygen in the tissue. This is included in the sensitivity analysis section.

Sensitivity Analysis

We investigated the effect that varying several critical variables used in the software had on our solution. These include a temperature, initial conditions and the boundary conditions. Temperature has an effect on the diffusivity of oxygen in the tissue and also on the consumption rate of oxygen in the tissue. For our purposes, in both the immersion and capillary preservation techniques, temperature and other variables should be optimized in order to maximize the concentration of oxygen in the tissue. The following gives our range of reasonable variations in parameters:

Oxygen Concentration in the Blood:

The saturation of hemoglobin is related to the partial pressure of oxygen. Air at sea level is normally 21% oxygen, giving a partial pressure of 100mm Hg, and in turn a concentration of 233ml oxygen per liter of blood. With pure oxygen, and 100% saturation, the concentration only rises slightly to 239ml oxygen per liter of blood. At high altitudes blood has a low partial pressure of 40mm Hg, and in turn a 42% saturation, correlating to 96ml oxygen per liter of blood.

Due to the above data, we feel an accurate range to test the oxygen concentration is a normal value of 233 ml O2/L blood, a minimum of 96 ml O2/L blood, and a maximum of 239 ml O2/L blood. Converting these values to kg O2/L blood we have a normal value of $3.34*10^{-4}$ kg O2/L blood, a minimum of $1.37*10^{-4}$ kg O2/L blood, and a maximum of $3.42*10^{-4}$ kg O2/L blood

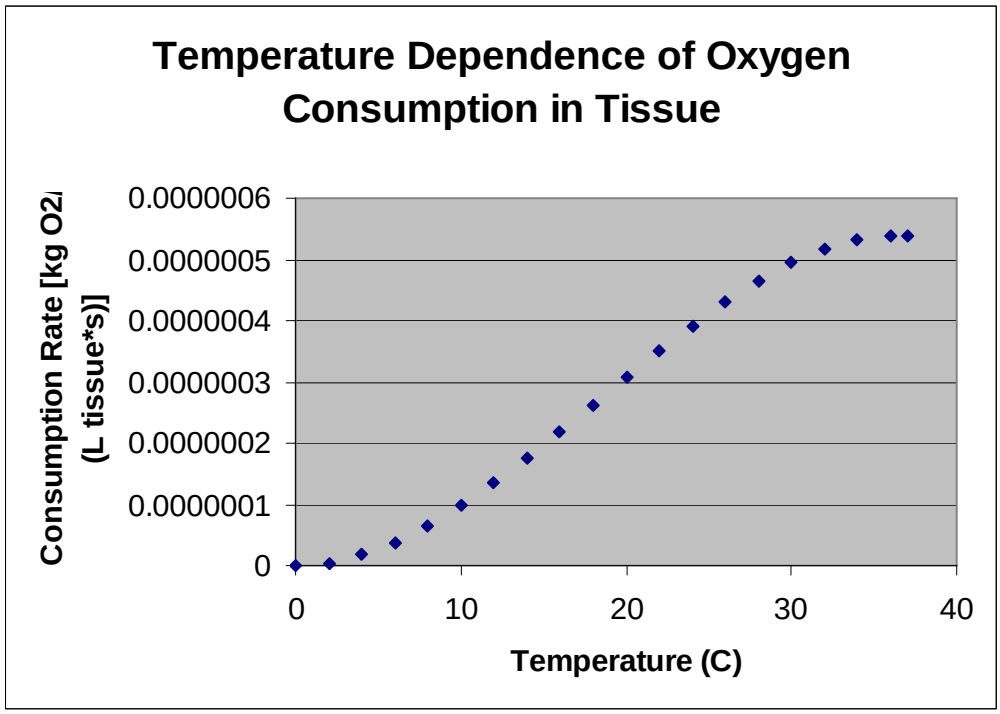
Initial Concentration of Oxygen in Tissue:

The normal concentration of oxygen in healthy heart tissue is $2.6*10^{-4}$ kg O2/L tissue. If the concentration drops below $3.7*10^{-5}$ kg O2/L tissue there is tissue death, resulting in an unviable heart for transplant. In our computations we are assuming a fast and efficient harvesting of the heart, and in turn having an initial concentration at the optimal level. For the sensitivity analysis we are comparing the results to a heart where the concentration has dropped down to the minimum concentration of $3.7*10^{-5}$ kg O2/L tissue and the intermediate value of $1.5*10^{-4}$ kg O2/L tissue.

Diffusion and Consumption of Oxygen in Tissue Due to Temperature:

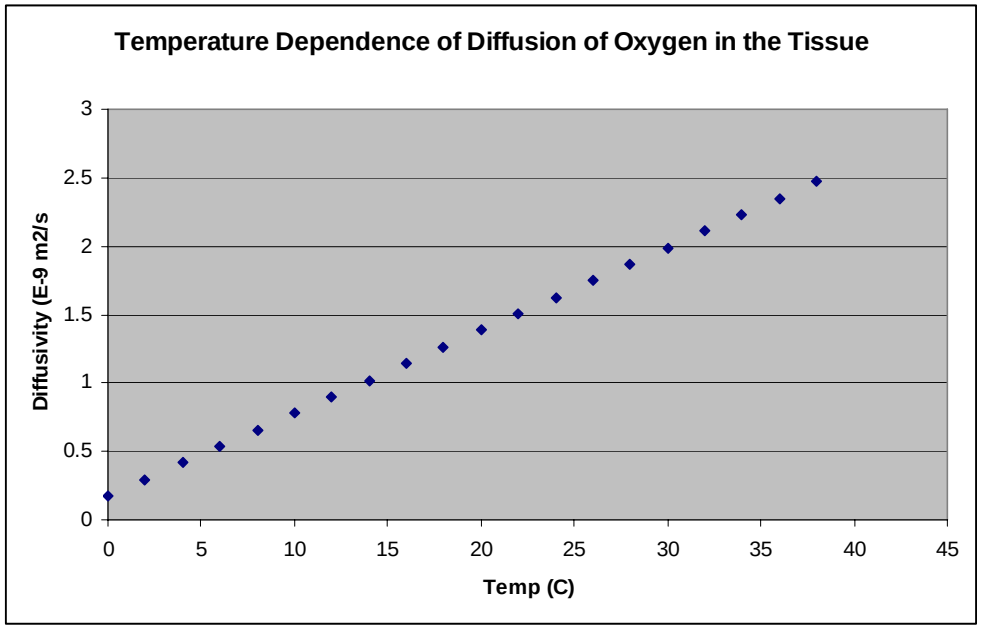
Myocardial oxygen consumption was found to be directly related to systemic temperature during cardiac arrest, with the formula Y=-0.3 x X +1.10 x X(2)-0.02 x X(3) (Y, myocardial oxygen consumption; X, rectal temperature; R(2)=0.533; P<0.0001) fitting the data collected clinically. Using this relationship, we were able to determine the effect of temperature on metabolic rate for our model. This is graphically represented below for a reasonable range of temperatures for cardiac preservation.

Figure 7: Plot showing how the consumption rate of oxygen depends on temperature



Other information was found relating the effect of temperature on the diffusivity of oxygen in mammalian muscle. A temperature coefficient of 4.60%/degrees C was found relating diffusivity of oxygen in the tissue to temperature, for a reasonable range of temperatures (between 11 and 37 degrees C). Using this relationship and known diffusivities at 11 and 37 degrees, values for diffusivity across the temperature range were linearly interpolated as shown below.

Figure 8: Plot showing how the diffusion of oxygen depends on temperature



Based upon the information on the previous page, the effect of the temperature of the tissue was investigated across a reasonable range, between 4 and 37 degrees Celsius. Tissue death occurs at -20 Celsius, so the values that we looked at are within a practical range.

In addition, two diffusivity values were found in the literature for 37 degrees C. The effect of varying the diffusivity at this temperature was investigated. A diffusivity of 2.4×10^{-9} m^2/s was used by the authors who found the temperature dependence of the diffusivity of oxygen in tissue so for our temperature sensitivity analysis, the other diffusivities were calculated from this value.

Mesh Convergence:

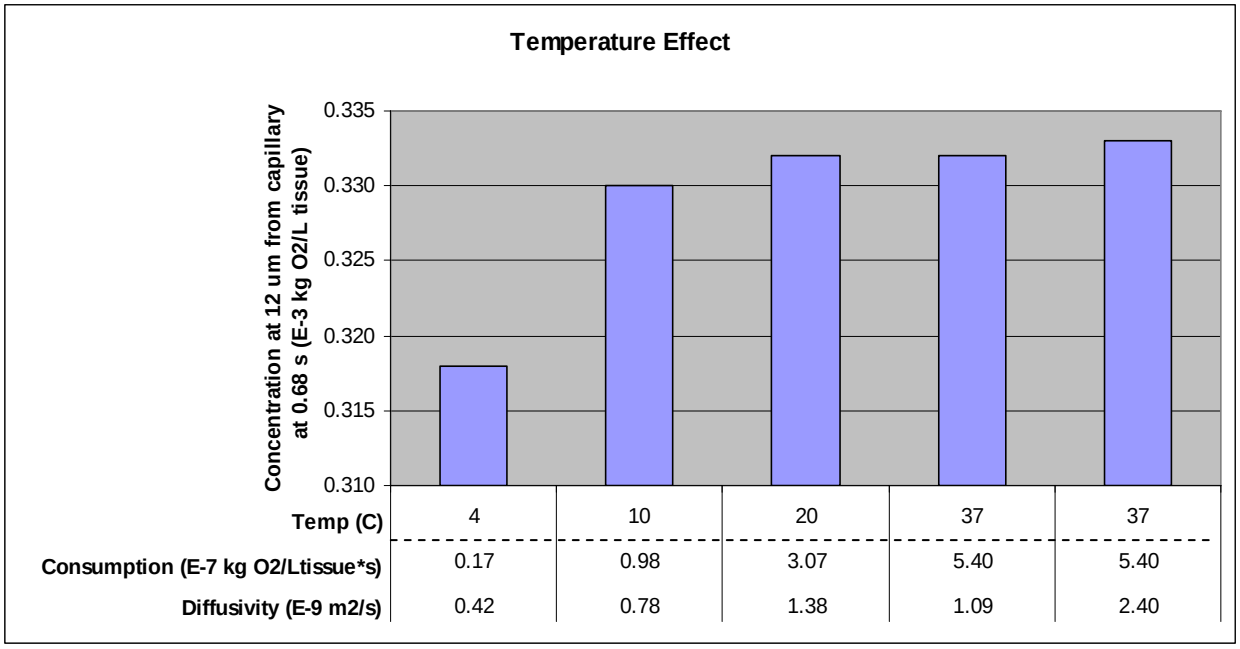
In order to minimize discretization error, we performed a thorough check to see whether the resolution of our mesh was sufficient. We generated plots showing how the solution was affected by the number of nodes in the mesh to check that it had converged. We confirmed that our solution was independent of the mesh resolution. This convergence can be seen in Appendix B.

Capillary Sensitivity Analysis:

In the design of a preservation technique or device - temperature is an easily controlled variable that can effect the concentration of oxygen in living tissue. The effect of temperature on the solution to the capillary preservation method was investigated, incorporating changes in diffusivity and consumption rate. The results for a range of reasonable temperatures are presented below. Generally speaking, a temperature should be chosen which results in the greatest concentration of oxygen in the tissue. Using this basis, it appears that the tissue is most fully perfused with oxygen at 37 degrees celcius, body temperature.

At this scale, it appears that the diffusivity of the tissue dominates over the metabolic consumption of oxygen. That is, though the metabolic consumption is less at lower temperatures, the diffusivity is also diminished. Since the concentration of oxygen in the tissue is the least at lowest temperatures, we can conclude that at this scale the effect of temperature on diffusion is more important in this case than its effect on metabolism.

Figure 9: Effect of temperature on final results for the capillary solution

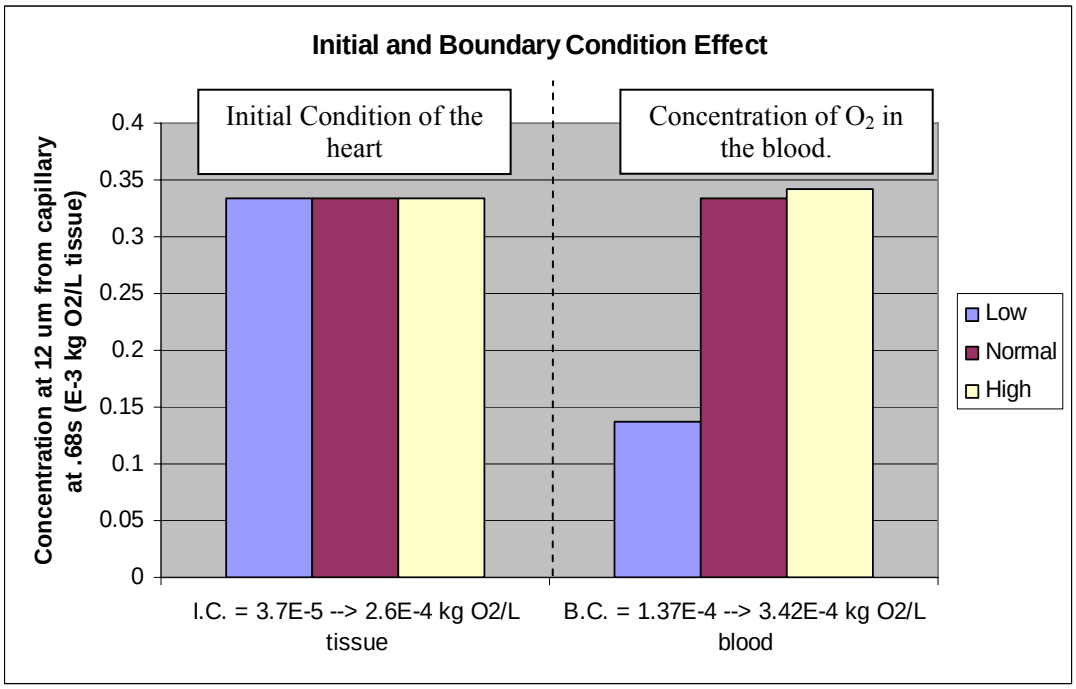


Temp (C)	4	10	20	37	37
Consumption (E-7 kg O2/Ltissue*s)	0.17	0.98	3.07	5.40	5.40
Diffusivity (E-9 m2/s)	0.42	0.78	1.38	1.09	2.40

Other parameters that can be realistically controlled in the design of a cardiac preservation technique or device are the concentration of oxygen in the blood and the concentration of oxygen in the heart before it is preserved (after harvesting). The effect of varying these conditions was investigated for a reasonable range of values.

It appears that the initial condition of the heart has relatively little effect on the efficacy of preservation for the capillary method - assuming that none of the tissue has died. As expected, it also appears that the best concentration of oxygen in the blood for preservation is the fully saturated case, but it does not appear to be significantly better than the natural physiological condition.

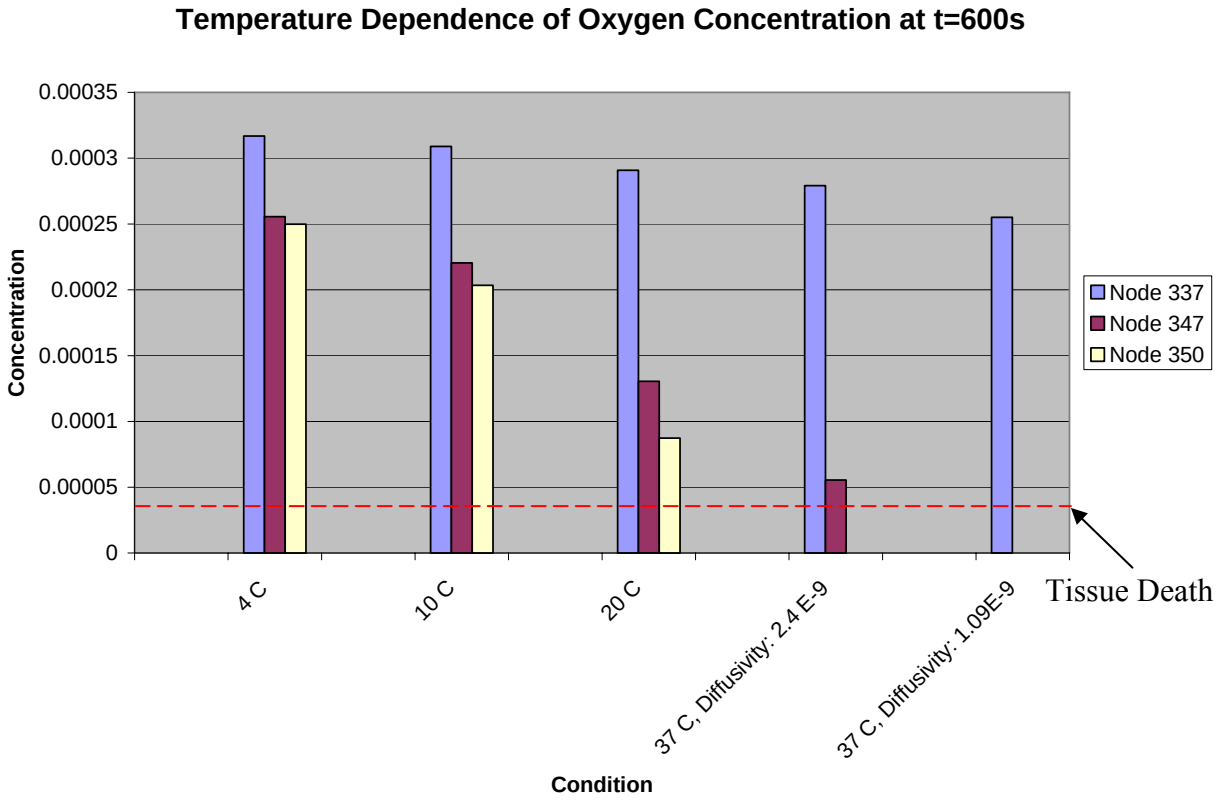
Figure 10: Effect of realistic variation in initial conditions and boundary conditions on final results for the capillary solution



Immersion Sensitivity Analysis:

Realistically speaking, the immersion preservation technique would not practically be implemented at body temperature because of the relatively high levels of oxygen consumption at this temperature. Donor hearts are typically immersed in a cardioplegic solution at or near zero degrees Celcius - at this temperature diffusivity of the tissue is reduced, but the metabolism of oxygen is also signifcantly reduced. When implementing the immersion preservation technique, temperature can be easily controlled. Sensitivity analysis was performed to optimize the concentration of oxygen in the cardiac tissue for a realistic range of temperatures and their respective diffusivities and metabolic rates.

Figure 11: Effect of temperature on final results for the immersion method



The figure above shows that for the immersion preservation technique, lower temperatures more effectively keep the cardiac oxygen concentration levels above the level of tissue death than higher temperatures; this is consistent with our expectations. We can conclude that for this situation, at the larger scale - reducing the metabolic oxygen consumption is more important than keeping the diffusivity of oxygen at a high level. For the most part, the diffusion of oxygen from the edges of the heart wall never reaches the center of the heart in a practical amount of time. When this simulation was run for longer periods of time at four degrees Celcius, it was found that the immersion solution could keep the heart tissue viable for approximately 5.5 hours.

Figure 12: Effect of initial condition on final results for the immersion method

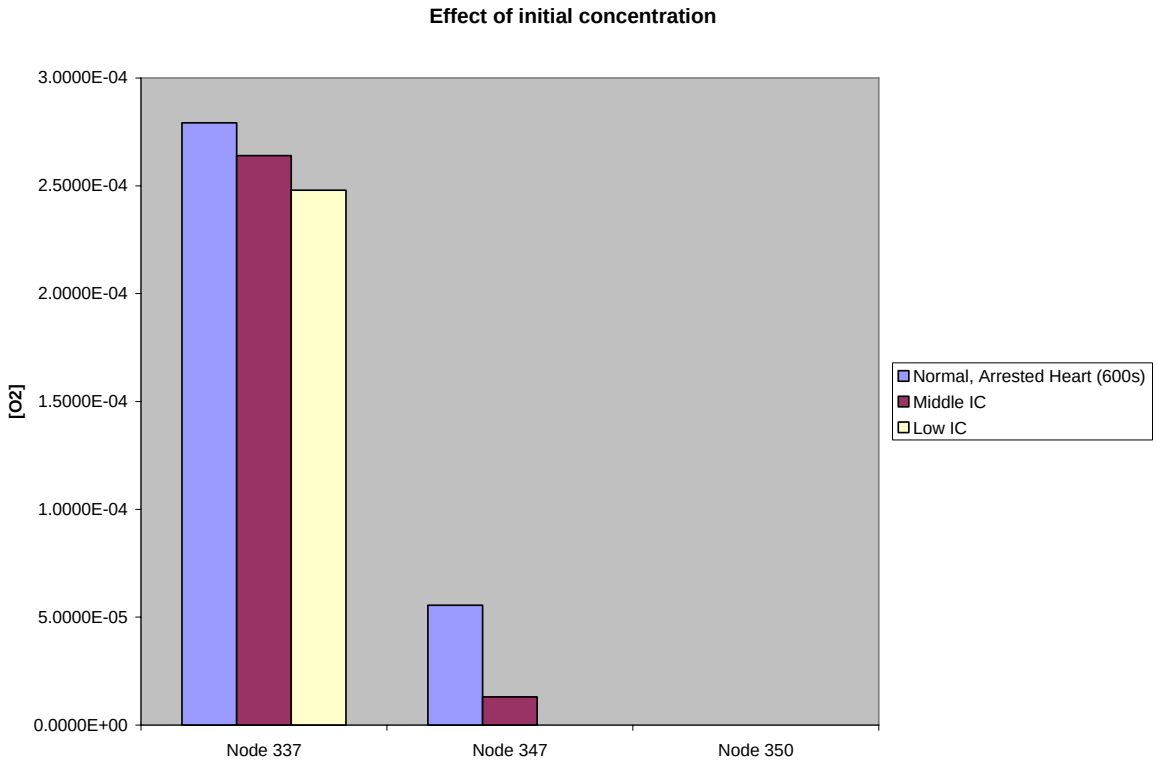
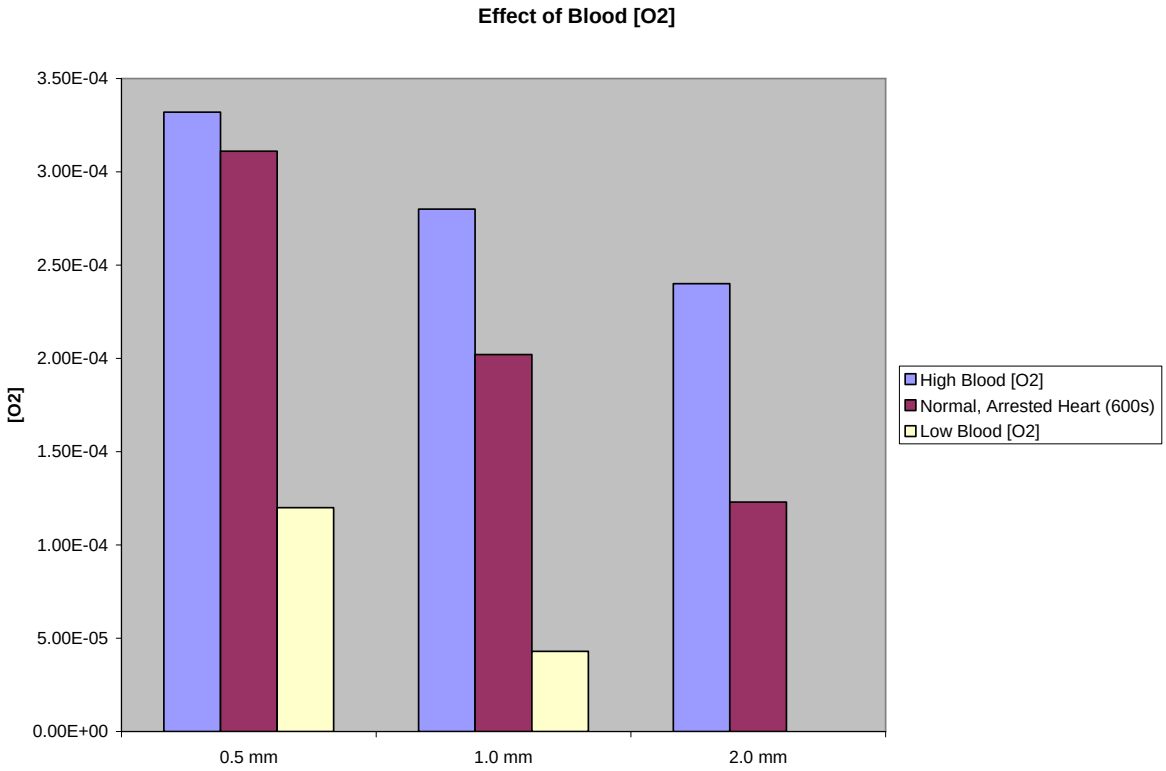


Figure 13: Effect of boundary condition on final results for the immersion method



As illustrated in the figures above, the effect of varying the initial concentration and the boundary condition was investigated. For our solution we initially assumed perfect harvesting of the donor heart, in which the concentrations of oxygen in the tissue are at optimal levels when the tissue is placed in the preservation device. If however, the initial concentration of oxygen had been allowed to drop slightly before placing in the solution, the effects are seen in the graph of initial concentrations. Initial concentration is key in the immersion solution because the diffusion is so limited so efficient harvesting and placing in cardioplegic solution on ice would be crucial.

In the case where the solution surrounding the hard were to have higher or lower concentration of oxygen, there is also a noticeable effect, higher than expected farther away from the heart wall. Therefore it would also be very important to keep the oxygen concentration in the solution as high as possible to maximize the health of the tissue.

Conclusion and Other Considerations:

Our computational model showed that the Transmedics cart, in which the heart is maintained at body temperature and blood is pumped through the capillaries, is extremely effective at perfusing the cardiac tissue with oxygen. From the start of preservation, it took less than a second for the concentration of oxygen in the tissue to match the concentration of blood pumped through the capillaries.

The other technique, in which the heart is placed in a cold cardioplegic solution showed a slow decay of oxygen as it was metabolized by the tissue. This metabolic consumption can be reduced by lowering the temperature of the solution to 4 degrees Celcius without many problems, since oxygen never really diffuses fully into the heart wall. Under these conditions our model showed heart viability for around 5.5 hours.

Extensive research went into this project in order to come up with accurate values for the various parameters used. However, the literature available was not always consistent and is not necessarily accurate. Much of our data did not come directly from studies dealing with heart tissue preservation, many of our parameters instead came from studies on cardiac bypass surgery, where the heart is temporarily cut-off from blood circulation. To ensure that our conclusions are valid, we conducted the sensitivity analysis which showed that our results are minimally effected even if the parameters are slightly off. We also assumed that there was a constant concentration at the capillary wall for the perfusion method. Since red blood cells are only slightly smaller than the capillaries in myocardial circulation, the momentum equation would be not apply. However, a constant concentration is not completely accurate. There is not a continuous line of red blood cells going through capillaries; instead there are spaces between them. The concentration of oxygen at the capillary wall is likely to vary with the rate of red blood cells traveling through the capillary at a given time. This is something that needs to be taken into consideration when finalizing a device such as the Transmedics cart, yet we feel it does not contribute significantly to error in our solution

A large part of our project was analyzing the effect of temperature on the ability to preserve the heart when considering oxygen consumption. While the cooling of the heart does make the immersion method more successful by reducing metabolic consumption of oxygen, it would also be important to look into any harmful effects the cold temperature could have. It is likely that holding the temperature of the tissue at body temperature is far less damaging since this situation more realistically mimics the physiologic condition of the chest cavity (as in the Transmedics cart). Additionally, we only looked at the diffusion of oxygen in cardiac tissue. There are many more nutrients involved in the maintenance of the heart which are important to survival that should be investigated. These could also be affected by cooling and/or warming the heart tissue.

It is important to note that the Transmedics device is not yet available for commercial use and that when it is, it is sure to be expensive. In most cases, the perfusion method discussed may be the best option, but perhaps not economically. Building a device like it is obviously no simple matter. Some things that must be taken into consider for production are: creating a long lasting, efficient and reliable battery supply; configuring electric impulse nodes for activating the

pumping action of the heart; finding a pump capable of pushing blood through the filter system; using an oxygen tank for higher diffusion rates; using biomechanical piping that can be attached to veins / arteries without causing damage or loss of blood flow; and creating a fast acting filter capable of removing waste from cellular respiration and other build up. All these things are vital to the production of heart pump, and each one adds another set of variables necessary to understand and control. For example, hooking up piping to the coronary artery in the heart may require special training for paramedics – introducing further added costs. Further, when such a device does become commercially available, the costs will be quite high until production is undertaken on a larger scale.

No product is worth selling that doesn't make a company money, and although it was difficult to estimate the costs associated with many of the necessary parts of such a machine, we decided to look at the next best option as way of gauging what the cost might be. Hearts are obviously a valuable commodity. Currently heart transplants cost anywhere between $75,000 and $125,000. If the perfusion device were able to allow for the survival of even a single heart, as we predict it will be able to, then it will be of considerable economic benefit to the hospital that operates it. Furthermore, such a device could potentially be used for other organ transplants like kidneys. Roughly speaking, this machine will probably cost between $50,000 and $150,000 to make (depending upon production levels), and will likely be sold for between $100,000 and $250,000. There is obviously quite a bit of uncertainty associated with such an estimate. External factors like how well such a machine performs in the field, its functionality in other areas of medicine/research, and demands from hospitals could largely impact the cost of production.

The demand of hearts for transplant is extremely high compared to the supply, and in turn money isn't as much of a consideration as usual. Because of this, the Transmedics device will most likely become prevalent among major hospitals that more frequently take out hearts for transplantation. It is likely that the large need for hearts will offset the high cost of the necessary equipment. Cooling of the entire heart is the current method of heart preservation, and while it is inferior to the perfusion method employed by the Transmedics device, it is far easier to implement only requiring cold cardioplegic solution. Transmedics preservation requires the use of a complicated device, hooking up the myocardial circulation of the heart, and constant monitoring of the tissue condition based on what fluids are being pumped through. It is not likely that the Transmedics device will be used outside of large hospitals and special heart transportation services. The common ambulance, doctor's office, etc, will most likely not have the capacity to use the Transmedics device in the near future.

During research involving smaller animal hearts, currently, hearts are often just left out to sit while the experiment takes place. We did not specifically investigate a scaling effect, but we did notice that for the small-scale case (the capillary solution), diffusion of oxygen in the tissue tended to be more important than the metabolic consumption of oxygen; while in the large scale case (the immersion solution), the opposite was true. Thus, the cooling technique may be more effective for smaller geometries where diffusion can reach all of the tissue. Our results show that at the very least, cooling a smaller heart could improve the survival of the heart during experimentation. A cheaper device, similar to the Transmedics unit, could also be designed for use specifically in animal research. Such a device could expand the research capabilities of scientists at a reasonable cost, and instability of the tissue would be less of a concern.

Appendix A:

Governing Equations:

Equation for capillary diffusion using cylindrical coordinates:

$$\frac{\partial c}{\partial t} = D\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial c}{\partial r}\right)+\frac{\partial^2 c}{\partial z^2}\right)+R$$

Equation for diffusion in blood bath:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}+R$$

Note: for both of these scenarios there is no bulk flow, so that term was eliminated for the equations

Non-Dimensionalization:

As mentioned earlier, the radius of a section of capillary tissue is around 12 micrometers - this scale was far too small for computer implementation so we used a non-dimensionalized form of the Diffusion equation for the capillary solution:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}+R \quad \rightarrow \quad \frac{\partial c}{\partial\left(\frac{tD}{L_o^2}\right)} = 1*\frac{\partial^2 c}{\partial\left(\frac{x}{L_o}\right)^2}+\frac{R}{\left(\frac{D}{L_o^2}\right)}$$

The characteristic length, L_o was arbitrarily chosen to be 10^{-3} m and the characteristic Diffusivity constant was chosen to be 2.4E-9 m^2/s, the diffusivity of oxygen in the tissue at 37 degrees C.

Boundary Conditions and Essential Information:

For capillary diffusion:

- Concentration of oxygen at capillary wall (concentration of solution) = 0.334 g O_2/L blood
- Initial concentration of oxygen in the tissue = 0.26 g O_2/L tissue
- Rate of metabolic consumption of oxygen in the tissue = 129.6 μg O_2/ g tissue/ min
- Rate of diffusion of oxygen through the capillary wall = $2.4*10^{-5}$ cm^2/s
- Rate of diffusion of oxygen through the cardiac tissue = $2.4 * 10^{-5}$ cm^2/s
- Flux on all sides except capillary wall = 0
- Flux at center of the capillary = 0 (because axi-symmetric)

For nutrient bath:

- Concentration of oxygen at heart wall (concentration of solution) = 0.334 g O_2/L
- Initial concentration of oxygen in the tissue = 0.26 g O_2/L tissue
- Rate of metabolic consumption of oxygen in the tissue (beating heart) = 129.6 μg O_2/ g tissue/ min
- Rate of metabolic consumption of oxygen in the tissue (arrested heart) = 32.4 μg O_2/ g tissue/ min
- Rate of diffusion of oxygen through the cardiac tissue = 2.4 * 10^{-5} cm^2/s
- Flux at the center of the heart = 0

General Information:

- Minimum concentration of oxygen for tissue survival = 0.037 g O_2/L tissue
- Optimal (normal) concentration of oxygen in tissue = 0.26 g O_2/L tissue

Nondimensionalized Variables for Capillary Solution:

Variable	Def'n	Value (Dimensional)	Value (Non-Dim)
Diffusivity capillary wall (37°)	D_1/D	2.4E-9 m^2/s	1.0
Diffusivity cardiac tissue (37°)	D_2/D	2.4E-9 m^2/s	1.0
Metabolic consumption of oxygen (37°)	$R/(D/L_o)^2$	5.40E-07 kg O2/ (L tissue*s)	9.375E4
Duration of the simulation	$(t_d*D)/L_o^2$	3s	7.413E-3
Time step	$(t_t*D)/L_o^2$	0.1s	2.471E-4
Capillary Tissue Radius	L/L_o	12E-6 m	0.012

Calculations:

Metabolic consumption = 129.6 μg O_2/ g tissue/ min * 1 min/60 s * 1 kg/ 10^9 μg * 1000 g / L = 2.16E-06 kg O2/L tissue

For paraplegic situation: 2.16E-06 kg O2/ L tissue * 25% = 5.4E-07

Appendix B:

Capillary .FIINP File:

```
/
/  INPUT FILE CREATED ON 03 May 06 AT  18:57:31
/
/
/ ***  FICONV Conversion Commands ***
/ ***  Remove / to uncomment as needed
/
/  FICONV(NEUTRAL,NORESULTS,INPUT)
/  INPUT(FILE= "cpllry.FDNEUT")
/  END
/  *** of FICONV Conversion Commands
/
TITLE

/
/ ***  FIPREP  Commands ***
/
FIPREP
 PROB (AXI-, ISOT, NOMO, TRAN, LINE, FIXE, NEWT, INCO, SPEC = 1.0)
 PRES (MIXE = 0.100000000000E-08, DISC)
 EXEC (NEWJ)
 SOLU (S.S. = 50, VELC = 0.100000000000E-02, RESC = 0.100000000000E-01,
       SCHA = 0.000000000000E+00, ACCF = 0.000000000000E+00)
 TIME (BACK, FIXE, TSTA = 0.000000000000E+00, TEND = 0.741300000000E-02,
       DT = 0.247100000000E-03, NSTE = 100)
 OPTI (SIDE)
 DATA (CONT)
 PRIN (NONE)
 POST (RESU)
 SCAL (VALU = 1.0)
 ENTI (NAME = "Capillary Wall", SOLI, PROP = "mat1", SPEC = 1.0,
       MDIF = "C1_Capillary Wall", MREA = "C1_Capillary Wall")
 ENTI (NAME = "Tissue", SOLI, PROP = "mat2", SPEC = 1.0, MDIF = "C1_Tissue",
       MREA = "C1_Tissue")
 ENTI (NAME = "Wall Bottom", PLOT)
 ENTI (NAME = "Tissue Bottom", PLOT)
 ENTI (NAME = "Tissue End", PLOT)
 ENTI (NAME = "Tissue Top", PLOT)
 ENTI (NAME = "Wall Top", PLOT)
 ENTI (NAME = "Wall Edge", PLOT)
 ENTI (NAME = "Capillary Edge", PLOT)
 DIFF (SET = "C1_Capillary Wall", CONS = 1.0)
 DIFF (SET = "C1_Tissue", CONS = 1.0)
 REAC (SET = "C1_Capillary Wall", TERM = 1, KINE)
  -0.5900000000E-03,  0.3100000000E+03,  0.0000000000E+00,  0.1000000000E+01,
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00
 REAC (SET = "C1_Tissue", TERM = 1, KINE)
  -0.5900000000E-03,  0.3100000000E+03,  0.0000000000E+00,  0.1000000000E+01,
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,
```

```
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00,
   0.0000000000E+00,  0.0000000000E+00,  0.0000000000E+00
 BCNO (SPEC = 1.0, CONS = 0.334000000000E-03, ENTI = "Capillary Edge")
 BCFL (SPEC = 1.0, CONS = 0.000000000000E+00, ENTI = "Wall Bottom")
 BCFL (SPEC = 1.0, CONS = 0.000000000000E+00, ENTI = "Tissue Bottom")
 BCFL (SPEC = 1.0, CONS = 0.000000000000E+00, ENTI = "Wall Top")
 ICNO (SPEC = 1.0, CONS = 0.260000000000E-03, ALL)
 EXTR (ON, AFTE = 5, EVER = 5, ORDE = 3, NOKE, NOFR)
END
/  *** of FIPREP Commands
CREATE(FIPREP,DELE)
CREATE(FISOLV)
PARAMETER(LIST)
```

Problem Statement Keywords:
PROB (AXI-, ISOT, NOMO, TRAN, LINE, FIXE, NEWT, INCO, SPEC = 1.0)

Descriptor	Value	Explanation
Geometry Type	AXISYMMETRIC	System is symmetric about an axis
Temperature Dependence	ISOTHERMAL	Constant temperature system
Flow Type	NO MOMENTUM	No bulk flow
Simulation Type	TRANSIENT	Solution is time dependent
Convective Term	LINEAR	No convective term
Surface Type	FIXED	Surface is fixed
Fluid Type	NEWTONIAN	Fluid can be considered Newtonian
Flow Regime	INCOMPRESSIBLE	Fluids are incompressible
Species Dependence	SPECIES=1	Species present

Solution Statement Keywords:
SOLU (S.S. = 50, VELC = 0.100000000000E-02, RESC = 0.100000000000E-01,
SCHA = 0.000000000000E+00, ACCF = 0.000000000000E+00)

Descriptor	Value	Explanation
Solution Method	Successive Substitution = 50	Maximum number of iterations
Velocity Convergence	.1e-02	Velocity convergence tolerance
Residual Convergence	.1e-1	Residual vector convergence tolerance
Solution Change	0	Default percentage change in solution magnitude
Relaxation Factor	ACCF = 0	For acceleration of convergence

Time Integration Keywords:
TIME (BACK, FIXE, TSTA = 0.000000000000E+00, TEND = 0.741300000000E-02,
DT = 0.247100000000E-03, NSTE = 100)

Descriptor	Value	Explanation
Time Integration	BACKWARD	FIDAP uses implicit method (t + Δt)
Time Step Algorithm	FIXED	Time step is constant
Start Time	0	Our problem starts at t = 0s
End Time	0.007413	Our problem ends at t = 3s
Time Step	0.0002471	Time increment is 0.1s
Number of Time Steps	100	There are 100 fixed time steps

Immersion FIINP File:

```
/
/  INPUT FILE CREATED ON 03 May 06 AT  20:32:07
/
/
/ ***  FICONV Conversion Commands ***
/ ***  Remove / to uncomment as needed
/
/  FICONV(NEUTRAL,NORESULTS,INPUT)
/  INPUT(FILE= "heart.FDNEUT")
/  END
/  *** of FICONV Conversion Commands
/
TITLE

/
/ ***  FIPREP  Commands ***
/
FIPREP
 PROB (2-D, ISOT, NOMO, TRAN, LINE, FIXE, NEWT, INCO, SPEC = 1.0)
 PRES (MIXE = 0.100000000000E-08, DISC)
 EXEC (NEWJ)
 SOLU (S.S. = 50, VELC = 0.100000000000E-02, RESC = 0.100000000000E-01,
       SCHA = 0.000000000000E+00, ACCF = 0.000000000000E+00)
 TIME (BACK, FIXE, TSTA = 0.000000000000E+00, TEND = 20000.0, DT = 2.0,
       NSTE = 10000)
 OPTI (SIDE)
 DATA (CONT)
 PRIN (NONE)
 POST (RESU)
 SCAL (VALU = 1.0)
 ENTI (NAME = "TISSUE", SOLI, PROP = "mat1", SPEC = 1.0, MDIF = "C1_TISSUE")
 ENTI (NAME = "RIGHT", PLOT)
 ENTI (NAME = "LEFT", PLOT)
 ENTI (NAME = "CENTER", PLOT)
```

```
 ENTI (NAME = "WALL", PLOT)
 DIFF (SET = "C1_TISSUE", CONS = 0.138380000000E-08)
 BCNO (SPEC = 1.0, CONS = 0.137000000000E-03, ENTI = "WALL")
 BCFL (SPEC = 1.0, CONS = 0.000000000000E+00, ENTI = "RIGHT")
 BCFL (SPEC = 1.0, CONS = 0.000000000000E+00, ENTI = "LEFT")
 BCFL (SPEC = 1.0, CONS = 0.000000000000E+00, ENTI = "CENTER")
 ICNO (SPEC = 1.0, CONS = 0.260000000000E-03, ENTI = "TISSUE")
 EXTR (ON, AFTE = 5, EVER = 5, ORDE = 3, NOKE, NOFR)
END
/  *** of FIPREP Commands
CREATE(FIPREP,DELE)
CREATE(FISOLV)
PARAMETER(LIST)
```

Problem Statement Keywords:
PROB (2-D, ISOT, NOMO, TRAN, LINE, FIXE, NEWT, INCO, SPEC = 1.0)

Descriptor	Value	Explanation
Geometry Type	2-D	Geometry modeled in 2-dimensions
Temperature Dependence	ISOTHERMAL	Constant temperature system
Flow Type	NO MOMENTUM	No bulk flow
Simulation Type	TRANSIENT	Solution is time dependent
Convective Term	LINEAR	No convective term
Surface Type	FIXED	Surface is fixed
Fluid Type	NEWTONIAN	Fluid can be considered Newtonian
Flow Regime	INCOMPRESSIBLE	Fluids are incompressible
Species Dependence	SPECIES=1	Species present

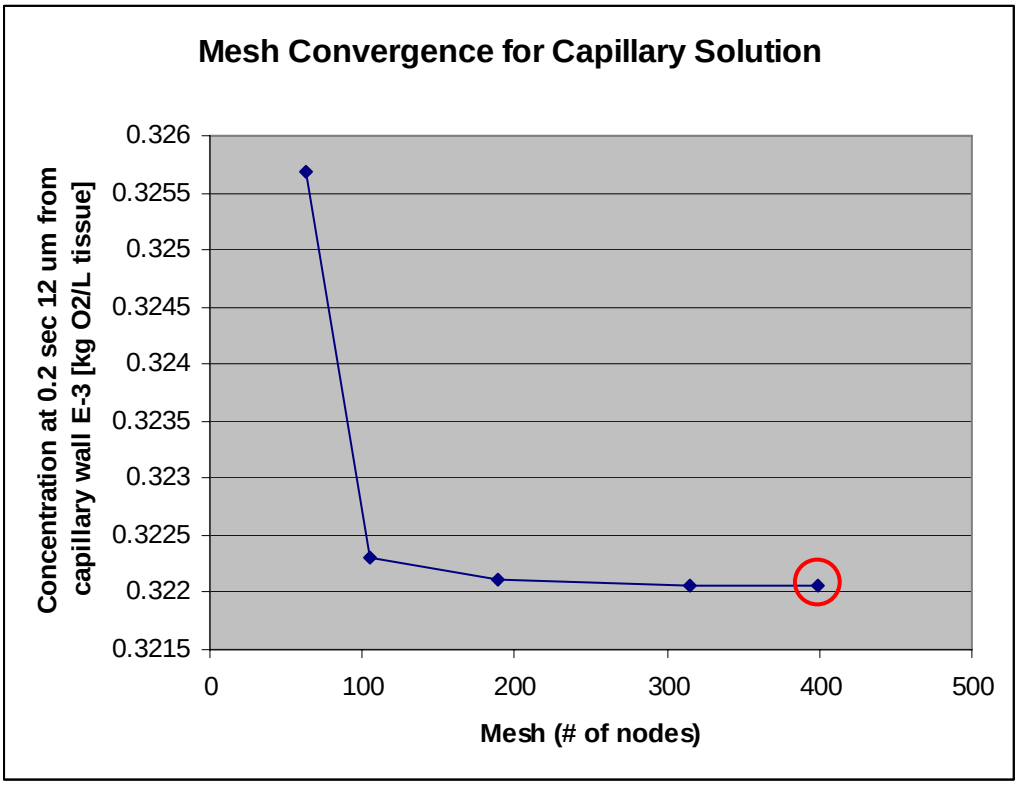
Solution Statement Keywords:
SOLU (S.S. = 50, VELC = 0.100000000000E-02, RESC = 0.100000000000E-01,
SCHA = 0.000000000000E+00, ACCF = 0.000000000000E+00)

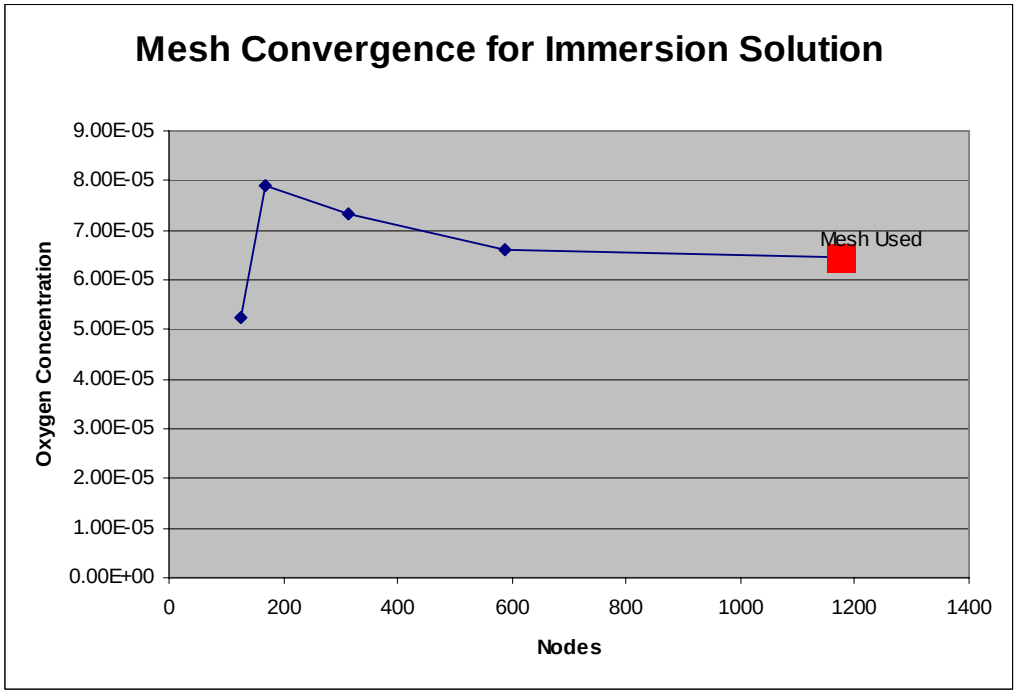
Descriptor	Value	Explanation
Solution Method	Successive Substitution = 50	Maximum number of iterations
Velocity Convergence	.1e-02	Velocity convergence tolerance
Residual Convergence	.1e-1	Residual vector convergence tolerance
Solution Change	0	Default percentage change in solution magnitude
Relaxation Factor	ACCF = 0	For acceleration of convergence

Time Integration Keywords:
TIME (BACK, FIXE, TSTA = 0.000000000000E+00, TEND = 20000.0,
DT = 2.0, NSTE = 10000)

Descriptor	Value	Explanation
Time Integration	BACKWARD	FIDAP uses implicit method ($t + \Delta t$)
Time Step Algorithm	FIXED	Time step is constant
Start Time	0	Our problem starts at t = 0s
End Time	20000	Our problem ends at t = 20000s
Time Step	2.0	Time increment is 2s
Number of Time Steps	10000	There are 10000 fixed time steps

The figures below shows how our solutions for the capillary preservation technique and the immersion preservation technique were affected the resolution of the mesh. Our final solution used a mesh with 399 nodes for the capillary solution as highlighted by the red circle on the graph and 1176 nodes for the immersion solution as shown by the red square. It is clear that at these levels of resolution, our solution is independent of the mesh - further refinement would not have any affect.





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