5-12-2006

3-dimentional visualization of cancer metastasis on the liver

Thomas Nowacki

ROCHESTER INSTITUTE OF TECHNOLOGY

A Thesis Submitted to the Faculty of
The College of Imaging Arts and Sciences
In Candidacy for the Degree of
MASTER OF FINE ARTS

3-Dimensional Visualization of Cancer Metastasis on the Liver

By

Thomas Mark Nowacki

5/12/2006

Approvals

Chief Advisor Dr. Richard Doolittle

Date: 5/22/06

Associate Advisor Glen Hintz

Date: 05/22/06

Associate Advisor James Perkins

Date: 6/5/06

Department Chairperson Don Arday

Date: 6/6/06

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I. Introduction

Metastasis is the migration of cancer cells from one site in the body to other places in the body. Cancer cells have a unique ability to break away from surrounding cells and to bypass the extracellular matrix that separates them from other cell types. The cancer cells are then free to travel to other places in the body, through either lymphatic vessels or blood vessels. Cancerous cells, usually from the colon, have penetrated the wall lining the and entered the tissue of the portal venous system. All blood from the portal venous system flows through the liver for filtration and then to the heart. The liver is the second most commonly involved organ in metastatic cancer, second only to the lymph nodes. Certain conditions make the liver so susceptible, including the liver's dual blood supply, the hepatic artery and portal vein, and certain humoral factors present that promote cell growth. These cancer cells traveling the portal venous system to the liver have a propensity for embedding themselves in the space of Disse, a small area between the endothelium and hepatocytes of the liver. Generally, kupffer cells block most tumor cells, but spaces in the endothelium allow cancer cells a refuge from the kupffer cells and provide an anchor due to the collagen fibers present in the space of Disse. Most liver metastases are multiple, involving both lobes. This is metastasis on the liver.

The primary purpose of this thesis is to demonstrate how 3-Dimensional artwork and animation can illustrate a disease and the complex process such as cancer metastasis, on a gross, as well as cellular level. Previously, a project was completed depicting a gross visual and cellular landscape of the pancreas. Continuing

with this prior project on the pancreas, I will primarily use Maya 7.0 to model another organ, the liver, focusing on the histological pathways and events occurring during metastasis. Taking the project a step further, I will incorporate the 3-D models in an interactive website developed using Macromedia Suite and illustrations made using Adobe Suite. The primary intent for this thesis and the supplementary website is to develop such animations or websites for a pharmaceutical company to use as educational supplement or for marketing purposes.

While I am continuing with a previous project, my goals and methods remain my own. My primary goal is to display the inner lining of a liver sinusoid and its various cellular structures. Displaying such a cellular landscape is not without its own difficulties though. Commonly, most histological sections are viewed in cross-section under a microscope. While these sections are a viable method of educating those already familiar with histology, others lacking a science education or background might find it difficult to understand what they are viewing, especially for those not trained in visualizing such material. Other methods, such as electron microscopy is more beneficial but most often the cellular structures are not of those in a live animal or even human for that matter.

My goal entails showcasing a journey through a liver sinusoid using the Maya software. Later I will take the footage from Maya and incorporate it in a website made using Flash, Fireworks, and Dreamweaver. The website (www.rit.edu/~tmn0646/thesis) also contains other supplemental lessons that explain metastasis in the liver through illustrations made in Photoshop and Illustrator. In essence, this thesis encompasses almost every aspect of my education during my Master of Fine Arts in Medical Illustration at Rochester Institute of Technology.

II. Visualizing the Sinusoid

The most important component of this thesis is the 3-D model of the liver sinusoid and visualizing the migration of a cancer cell to the space of Disse in the liver. It was very important to accurately display the sinusoid utilizing contemporary thoughts as to how a living, human sinusoid would appear. To determine how the sinusoid should look I compiled images of actual liver cells in histological cross-section and electron microscopy in addition to images from text sources. Typically cross-section images are taken with a light microscope and cells are stained to create contrast. As stated earlier, this is the most familiar form of viewing liver cells and most other cells for that matter. The cross-section is a valuable tool, but much is left to interpretation and assumption. It is almost never one layer of cells, but multiple layers stacked like pancakes. As a result, sometimes cell boundaries can be blurred. Even with these limitations, a trained eye can still discern what the general shape and size of many of the cells are and their relative position. On the other hand, images created by a scanning electron microscope are of much greater magnification and even reveal surface details in addition to general size and shape.

Once enough images of what a sinusoid should look were compiled and compared, I began creating sketches of possible approaches to modeling and animating the images in Maya.

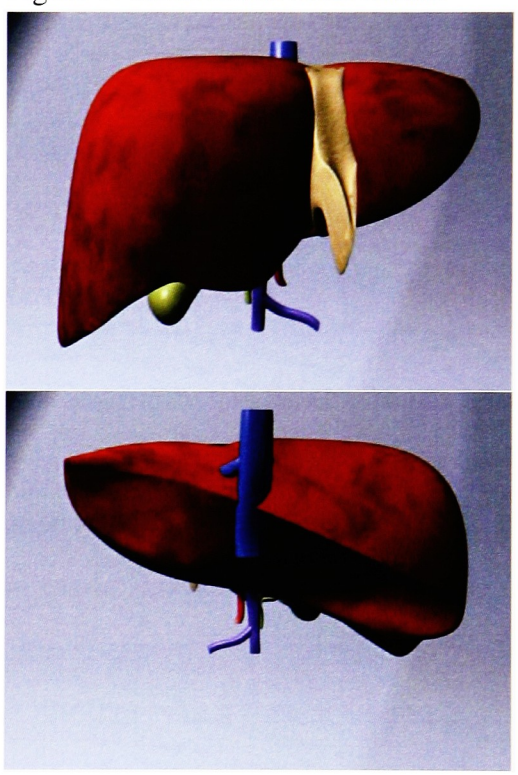
III. Modeling the Components

Maya 7.0 gives the user three basic methods of modeling including polygons, NURBs, and subdivisions. In my experience, I have come to rely on subdivisions more than any other of the methods due to the fact that they combine aspects from both polygons and NURBs and can be readily converted to either. Although, beginning my models, I use whatever method seems the most direct. As a result, many of my models initially created used one method but eventually became subdivisions as will be explained later.

A. The Gross Liver

This was the simplest component to model given that it was on a gross level and many reference photos were readily available. The liver was completely modeled using subdivisions (Figure 1.) I decided to include the gallbladder and falciform ligament with the liver in addition to notable vessels in order to give a realistic feel of the organ and provide anatomical reference. The surface texture and color was created using a fractal map.

Figure 1: Subdivision Liver Model



B. The Liver Lobules

The lobule was one of the more difficult models to sculpt not because of its shape, but how to portray it in a realistic manner. Initially, one of my main concerns dealt with the fact that this would not be an accurate portrayal of the liver lobule. In reality, the view most commonly seen view of a liver lobule is in the cross-section, which is not how the liver is actually viewed. Also, the other portions the thesis depict a realistic or interpreted realistic view of the liver. After much consideration I finally rationalized that this model would benefit the viewer by paying homage to the liver cross-section many are so familiar with and help lead into the sinusoid view.

I created many multiple models using an actual liver cross-section as reference, then used the bevel tool and outputted them as subdivisions. Typically liver cross-sections are taken from another animal other than human, usually a monkey. This is mainly due to the fact that human liver lobules have borders that are impossible to differentiate. Monkey livers, on the other hand, have readily identifiable borders much more suited to classroom. The liver specimen the lobules were shaped after was from a monkey's but I increased their widths so they would overlap one another and the borders would disappear. Since I was using subdivisions, I was able to create a unique bump map (Figure 2a) in Photoshop giving the lobules some texture and creating the illusion of sinusoids on the surface. Taking some artistic license, I decided to give each lobule its own color map (Figure 2b), also made in Photoshop, making each lobule somewhat distinguishable from one another. As a final touch, a portal triad, including a bile duct, portal vein, and hepatic artery were added to the side of one lobule that would later be shown in the animation.

After some consideration, the decision was made to use this component as a simple segue to the

more important sinusoid, which also became the most complicated portion of the modeling process.

Figure 2: Examples of a Bump map (a) and color map (b)for the lobules.

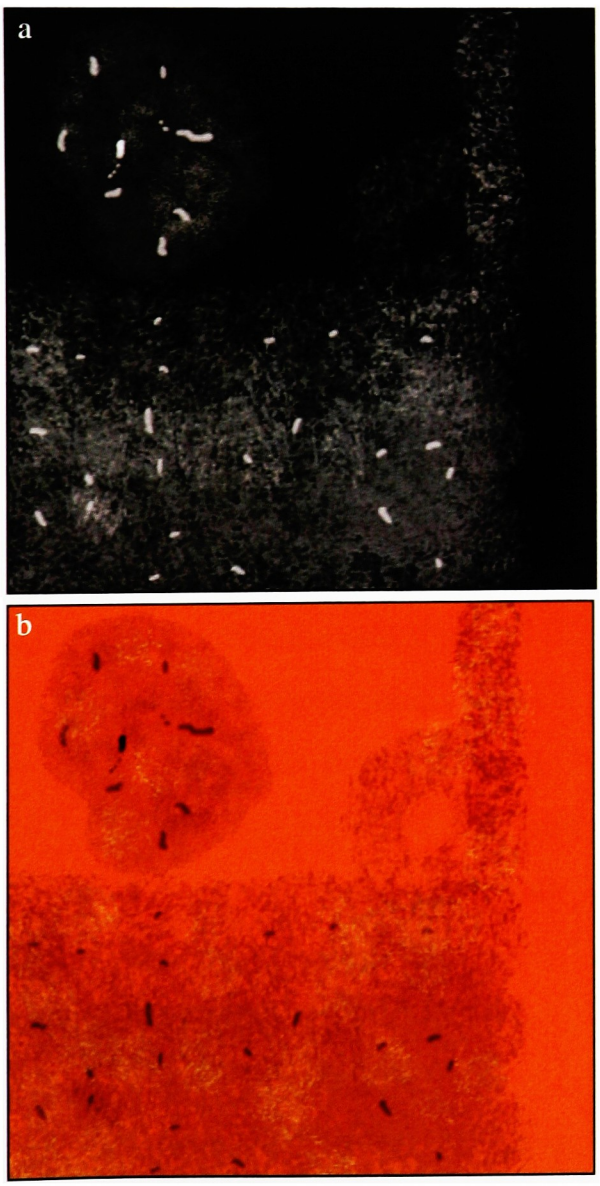
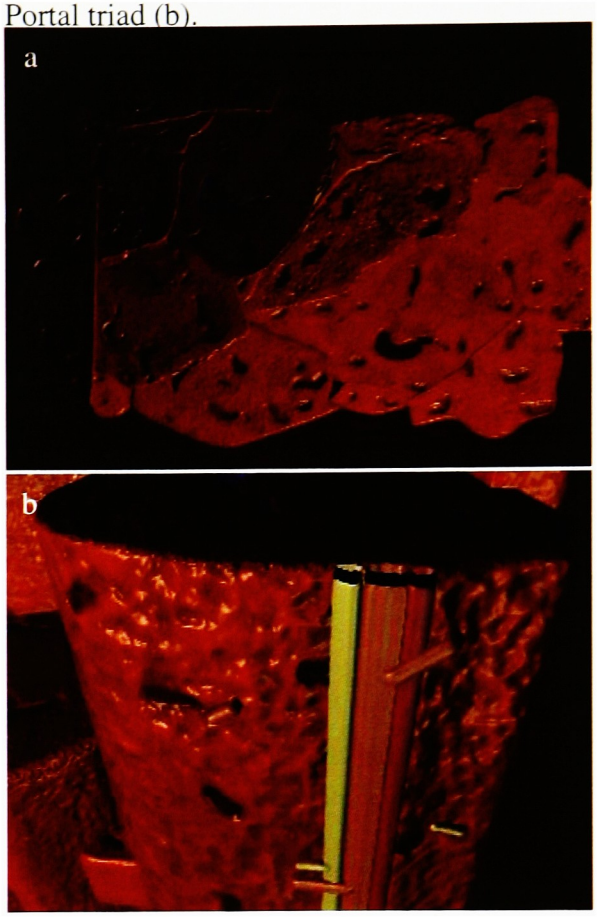


Figure 3: Lobule rendered; Top view (a), Portal triad (b).



C. Modeling the Sinusoid

The sinusoid was easily the most problematic component to model due in part to its many individual components, namely the hepatocytes, endothelial cells, the kupffer cell, and the various parts of the sinusoid itself.

1. Hepatocyte

I began with the intention of modeling each cell with as much detail as possible. As such, the hepatocyte would require a roughly quadratic shape with a fold along various sides where neighboring other hepatocytes meet, thus, denoting the bile canaliculi. My initial thought was that subdivisions wouldn't have the finesse to depict the detail I thought was necessary. Creating the outline of a hepatocyte with the canaliculi and then lofting it as a NURB created the desired shape but also some undesirable overlapping at the ends due to the odd shape. Realizing that perhaps subdivisions were once again the safest choice, I restarted the hepatocyte. At this point it was realized that perhaps the level of detail intended was not absolutely necessary. Using subdivisions, any shaped hepatocyte could be created with no overlapping unless, of course, it was intended. After all, hepatocytes come in many different forms mainly determined by what they are bordered by, contrary to most illustrations of hepatocytes where they appear as cube-like cells in lines and rows. The bile canaliculi were also made with less detail, simply as folds on the sides the cells.

After modeling the cell, I was faced with dilemma of the microvilli-like surface that faces the underside of the endothelial cells. Initially creating a bump map in Photoshop to simulate the texture, I realized after rendering that perhaps a more dramatic approach would be necessary. Utilizing a displacement map seemed like the best choice, also created in Photoshop. While a bump map is basically an illusionary texture, a displacement map actually changes the surface it is applied to, able to make much more pronounced textures. Reviewing liver cross-sections, it can be rationalized that the microvilli-like structures contribute to a loose lock-and-key-like relationship between the underside of

the endothelium and the hepatocytes, thus creating the space of Disse. When it came time to model the organelles of the hepatocyte, I decided to only include the nucleus in order to save the costly expense of render time and memory. Lastly, the hepatocyte was made transparent to display the nucleus inside.

Figure 5: Hepatocyte version 1

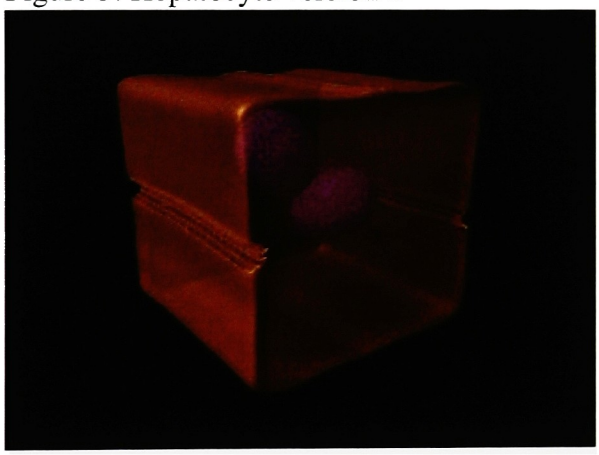
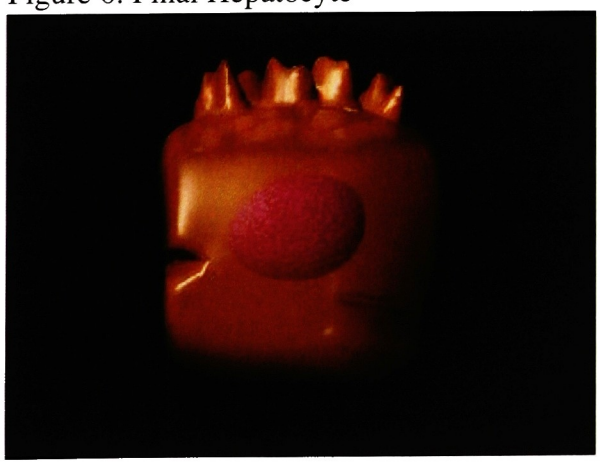


Figure 6: Final Hepatocyte



2. Endothelial cell

These cells were relatively simple to create. Starting with a simple NURB sphere and scaling it to a flat, pancake shape. Later some of the edges were rotated to give it a more organic feel. The only complicated aspect of creating the endothelial cell was what type of texture to give it. The endothelial cells of the liver sinusoid often have a fenestrated appearance with occasional gaps. Since the surface only required an appearance of fenestration, a bump map (Figure 7) was used. The underside of the endothelial cell that is adjacent to the hepatocyte was created by using the sculpt tool (Figure 8b.)

Figure 7: Bump map of Endothelium

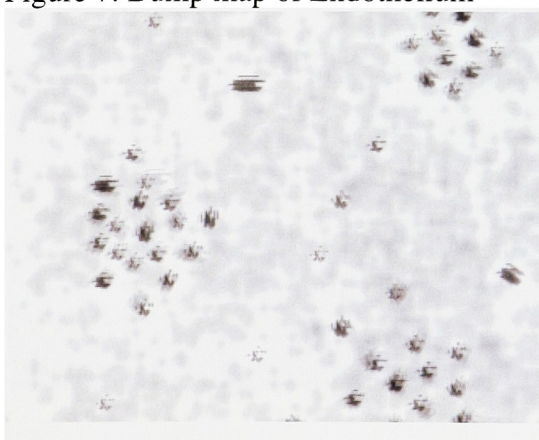
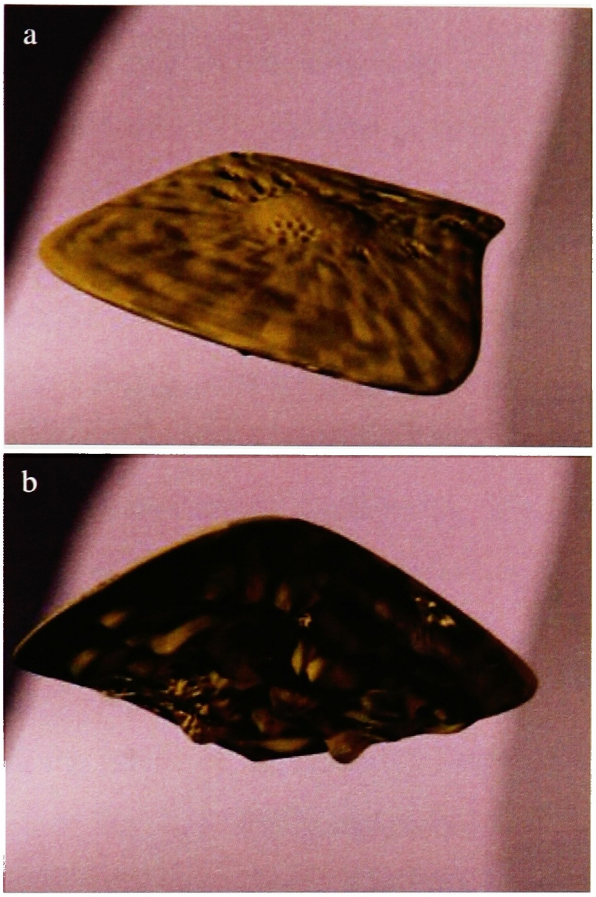


Figure 8: Dorsal (a) and ventral (b) view of endothelium.



3. Kupffer Cell

The largest cell in the sinusoid, the kupffer cell was also relatively simple to model. I once again started with a subdivision and sculpted various areas to make filopodia extensions that would stretch across the sinusoid. The texture was created by duplicating the kupffer cell and slightly decreasing the scale, then placing the scaled down version inside the original. Later, a bump map (Figure 9) was created and applied to the outside layer, giving the cell a more ruffled appearance. The original cell was then given a color and transparency so as to still see the inside, scaled-down version, thereby creating a ruffled appearance.

Figure 9: Bump map of kupffer cell.

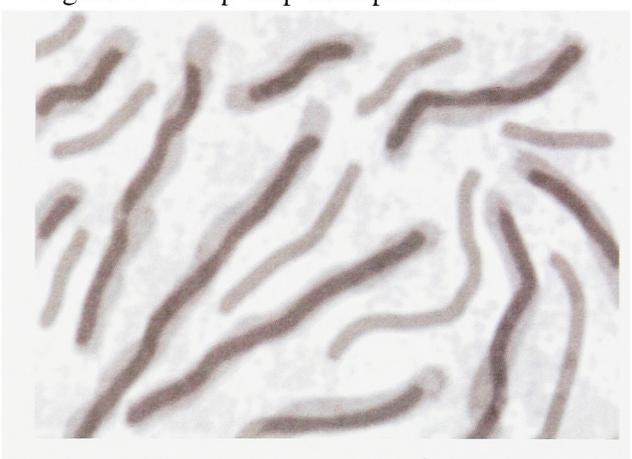
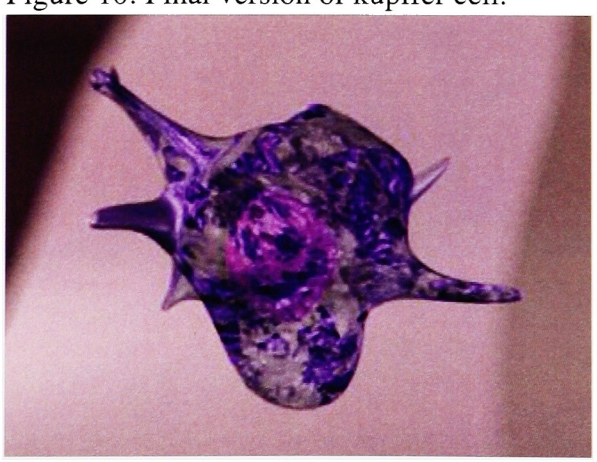


Figure 10: Final version of kupffer cell.



4. The Sinusoid

Once all the cells were completed a new file was created where all the cells would be referenced, thereby saving valuable memory and render time. A basic sinusoidal shell was created with subdivisions to serve as guide to where endothelial cells and hepatocytes would conform to. The basic endothelial cell was referenced and then duplicated multiple times. Each duplicate was then scaled to fit the inside of the sinusoidal shell. Once the shell was completely lined with cells, the sides and bottom faces were deleted. This was done to create some emptiness where spaces between endothelial cells would occur and where, eventually, a cancer cell would enter the space of Disse. Once the endothelial cells were aligned, the hepatocyte was referenced into the file, duplicated and arranged outside the endothelial cells. The entire sinusoid did not need to be lined with hepatocytes since only a small portion would be visible in the eventual animation (Figure 11.)

After the sinusoid was finished, a portal vein and central vein needed to be attached at both ends. These were made by creating a series of curves and then lofting them to form a tube. Other tubes made similarly were then intersected with larger tubes creating a network of venous passages. One such network was placed horizontally, the portal vein, and another placed vertically and opposing ends of the sinusoid. A bump map was then once again created in Photoshop to simulate the endothelium of the vessels.

Figure 11: Outside the sinusoid.

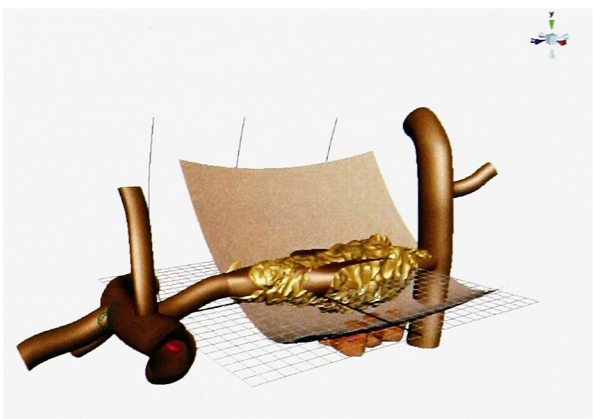


Figure 12: Inside the sinusoid.

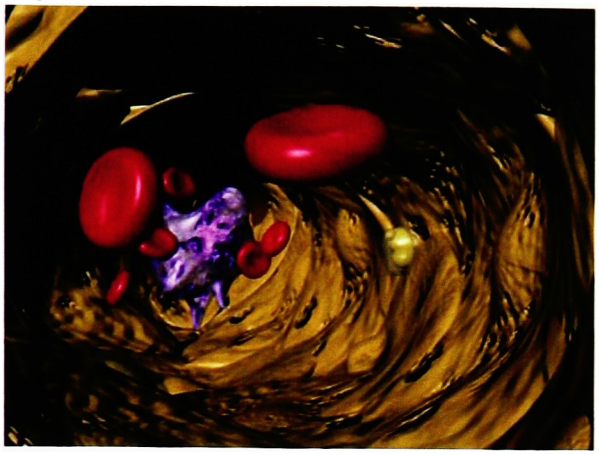
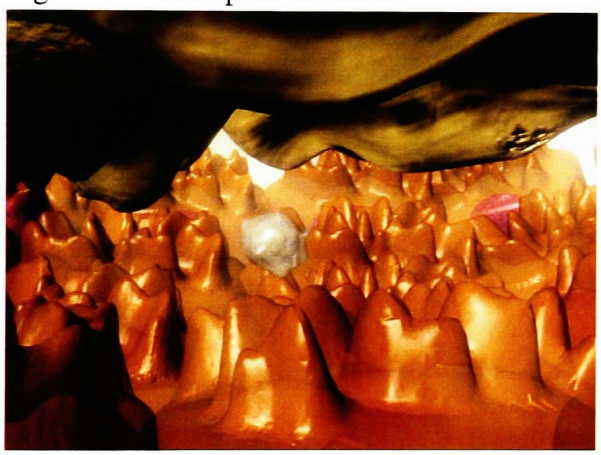


Figure 13: The space of Disse.



IV. Animation

Once all the basic components were assembled, it was time to create the actual animation. Two main animations were to be fashioned. Each animation in itself would consist of multiple parts showcasing the various components modeled.

The first animation starts by showcasing the gross liver and zooming closer then fades into the lobule view. The camera then flies down and rotates to show the side of one lobule with its portal triad visible. Once again the camera zooms closer, this time to one of the portal veins. The view fades again to show the inside of a portal vein with red blood cells flowing through. Finally, the camera journeys through the portal vein, into the sinusoid, and up through the central vein where the animation ends.

The second animation begins in the portal vein, but this time as the camera begins to travel, a cancer cell comes into view and travels into the sinusoid. There, the cell makes its way to an opening in the endothelium squeezing into the space of Disse where the metastasis takes place.

V. Website

Now that the animations were completed, it was necessary to fashion a website where the animations could be easily accessed. Using Macromedia Flash, a web page was produced following modern web page conventions. The area of the website was 760 x 410, a typical size for an 800 x 600 monitor, taking into consideration the browser tool bar and window control bars. As a method of organization, a single dominant color was used for the "home" page and corresponding colors for each additional section. The home page consisted of an opening animation of metastasis created with images from Photoshop and animated using Flash. This ends with separate navigation buttons, each a different color appearing on the stage. The first three buttons lead to supporting material while the last two lead to the animations from Maya. The animations from Maya were inserted into the Flash document and a control bar was added along the top of each animation for easy playback.

Figure 14: Website homepage.

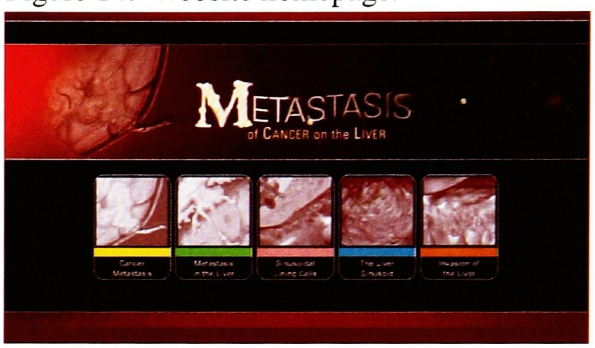
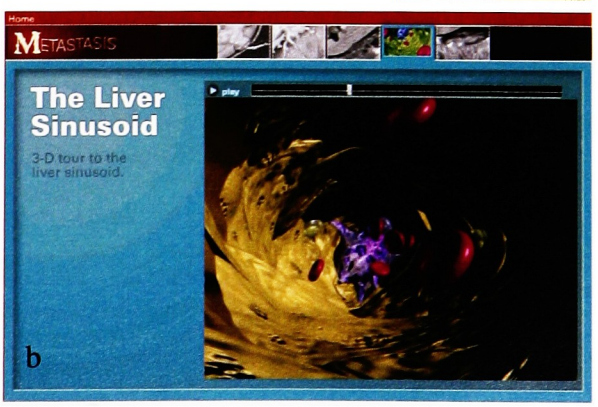


Figure 15: Examples of corresponding sections. (a) page 1,"Cancer Metastasis"; (b) page 4, "The Liver Sinusoid."



VI. Conclusion

In the ever expanding field of medical research, it is imperative that information can be presented to the viewer in a logical, organized, and most importantly, correct manner. From a marketing viewpoint, there is always a need for innovative and inventive methods of sharing the research. One such method is the creation of animations in a 3-dimensional environment that is as life-like as possible. Flat artistic renderings have difficult time actually being lifelike regardless of how well they are delivered for the simple reason that they are only a flat image. Using 3-dimensional, rendered animations can show the viewer a more informative viewpoint by actually putting them in such a surrounding as a liver sinusoid and then witnessing how metastasis occurs.

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