

Development of a Medical Animation on
Acetaminophen Metabolization and
Hepatotoxicity

Julia A. Klein
M.S. Biomedical Visualization
University of Illinois at Chicago
August 2nd, 2010

1

Overview

- Project Inspiration
- Research Questions
- Information Research
- Animation Workflow
 - Roles
 - Production Steps
 - Pre-production
 - Design
 - Production
 - Post-production
 - Project Management
- Conclusions

2

Project Inspiration


Why this topic?

3

Project Inspiration

Pharmacy

- Pharmacy technician role
 - Fill and deliver prescriptions to patients
- Pharmacist role
 - Patient education
 - Knowledge of APAP danger



4

Project Inspiration

Medical Media Agency

- Visual Science Specialist Role
 - MOA and MOD 3D animations




5

Project Inspiration

Warnings on acetaminophen in the news

- 2009 FDA recommendations




6

Research Questions

- How can the APAP metabolic pathway and its potential for hepatotoxicity be visually explained to an audience of healthcare providers?
- Could a short medical animation be created that represents the APAP metabolic process?
- Can the production roles and steps from a professional medical animation workflow be consolidated and done by one researcher rather than a team of people?

7

Information Research



Drug Facts

Active ingredient (in each tablet):
Acetaminophen 500 mg

Purpose:
Pain relief
Fever reducer

Uses: Temporarily relieves minor aches and pains due to:
 • headache • muscle aches
 • toothache • minor pain of arthritis
 • the common cold • sore throat
 • premenstrual and menstrual cramps • reduce fever

Warnings:
Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.
Do not use:
 • with any other products containing acetaminophen
Stop use and ask a doctor if:
 • new symptoms occur • redness or swelling is present
 • pain gets worse or lasts for more than 10 days
 • fever gets worse or lasts for more than 3 days
 These could be signs of a serious condition.
If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children.
Overdose warning: Taking more than the recommended dose (overdosing) may cause liver damage. Signs of overdose and medical help or control for adults as well as for children even if you do not notice any signs of overdose. • Call your doctor. • Get medical attention if critical.

http://www.tylenol.com/page.jhtml?id=tylenol/painrel/whbtoxts.tsc

Tylenol® Drug label


- Active ingredient
- Purpose & Uses
- Warnings
- Overdose warning

8

Information Research

Tylenol® Professional Product Information (PPI)

- Drug facts
- MOA
- MOD of overdose
- Overdose treatments




9

Information Research

Protein Data Bank

- Information
- 3D .pdb files



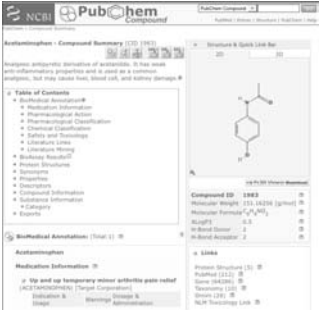
<http://www.pdb.org/>

10

Information Research

PubChem

- Information
- 3D .sdf files



<http://www.ncbi.nlm.nih.gov/>

11

Animation Workflow

- Based on a professional medical animation workflow
- Roles
 - Science content consultant
 - Medical writer
 - VO talent
 - Producer
 - Art director
 - Storyboard artist
 - 2D artist
 - Modeler
 - Animator
 - Composer
 - QA
- Adaptation for one researcher

One Researcher?

12

Design

- Mood Boards
- Concept Art
- 3D Models
 - Model Book
 - Modeling
- Textures and Lighting

19

Mood Board - Metabolic Pathways

APAP Metabolic Pathways

These are some of the various metabolic pathways that will be shown in the animation. The animation will present them much more dynamically as opposed to these static illustrations.

20

Mood Board - APAP

APAP Tablets

The model of the APAP bottle will resemble a bottle of an over the counter product. The medicine tablets will have a chalky white surface.

21

Mood Board - GI Tract Villi

GI Tract Villi

Villus Capillary
Molecular Models Tutorial

The scene with the stomach will feature an overlay of a villus capillary showing the site of absorption. A tutorial will be referenced from <http://www.molecularmodels.com/learning/index.html>

22

Mood Board - Liver

Liver

PHOTORESEARCHERS

The model of the liver will be featured in a illustrative style. The stomach (not shown) will also match this style of representation.

23

Mood Board - Healthy Hepatocytes

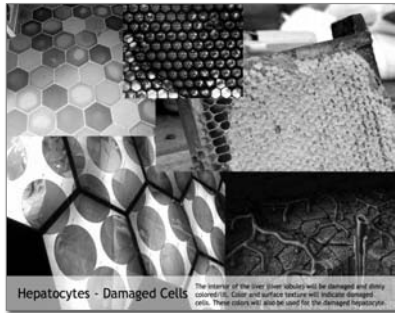
Hepatocytes - Healthy Cells

Liver Lobule
Hepatocytes

The interior of the liver (liver lobules) will be healthy and brightly colored (in). Color and surface texture will indicate healthy cells. These bright colors will also be used for the single hepatocytes.

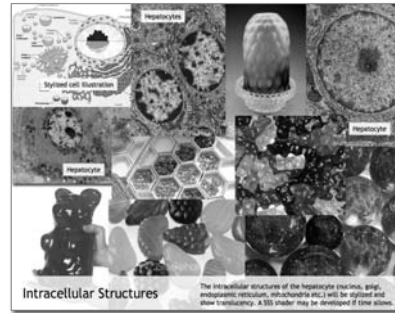
24

Mood Board - Damaged Hepatocytes



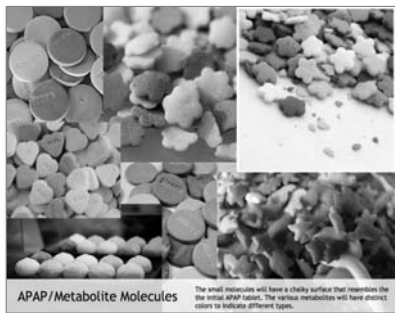
25

Mood Board - Intracellular Structures



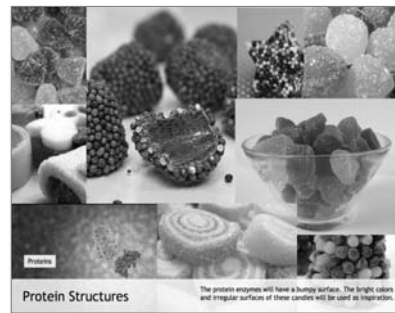
26

Mood Board - Metabolites



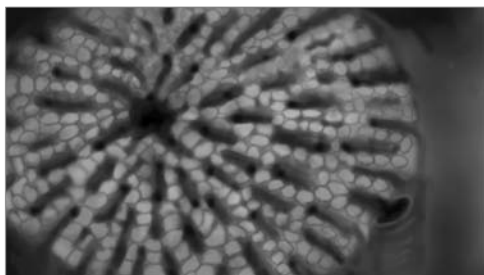
27

Mood Board - Protein Structure



28

Concept Art



Liver Lobule

29

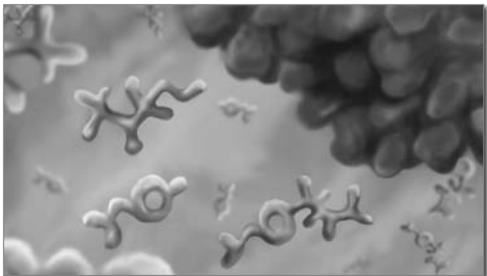
Concept Art



Hepatocyte

30

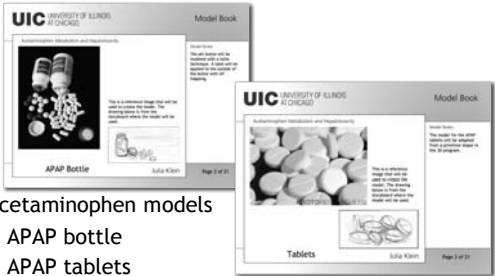
Concept Art



Intracellular Structures

31

Model Book

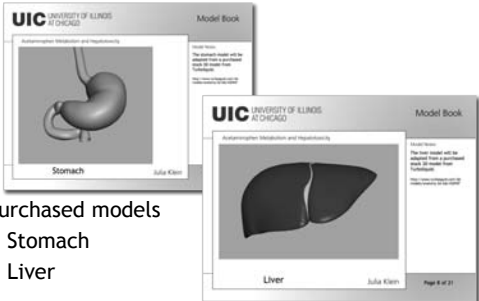


Acetaminophen models

- APAP bottle
- APAP tablets

32

Model Book

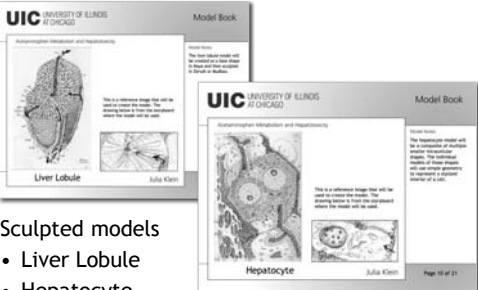


Purchased models

- Stomach
- Liver

33

Model Book

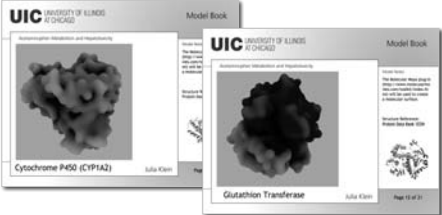


Sculpted models

- Liver Lobule
- Hepatocyte

34

Model Book



Protein Data Bank models

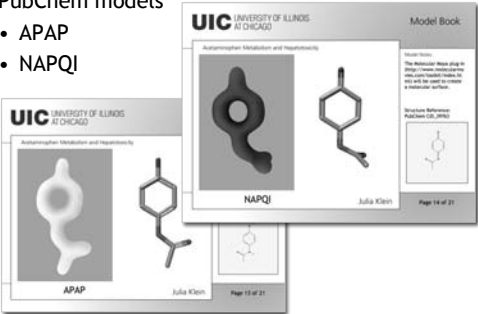
- Cytochrome P450
- Glutathione Transferase

35

Model Book

PubChem models

- APAP
- NAPQI



36

Model Book

PubChem APAP Metabolites

- Cysteine
- Glucuronide
- Sulfate
- Glutathione
- Mercapturate

37

3D Modeling

Molecular Maya (mMaya)
<http://www.molecularmovies.com/toolkit/index.html>

38

3D Modeling

Mudbox® sculpting

- Liver lobule

39

3D Modeling

Mudbox® sculpting

- Hepatocyte

40

3D Modeling

- Golgi apparatus

41

Texture and Lighting

42

Production

- Shot List
- 3D Animatic
- Rough Cut

43

Shot List

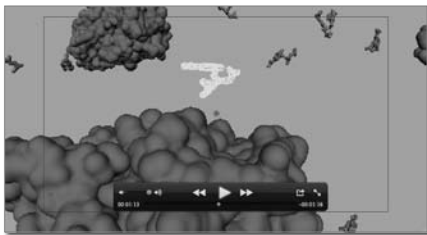
- Shot numbers
- Storyboards
- VO Script
- Labels
- Characters
- Shot lengths

Shot Number	Storyboard	VO Script	Labels	Characters	Shot Lengths
10	[Storyboard thumbnail]	[VO Script thumbnail]	[Labels thumbnail]	[Characters thumbnail]	[Shot Lengths thumbnail]
11	[Storyboard thumbnail]	[VO Script thumbnail]	[Labels thumbnail]	[Characters thumbnail]	[Shot Lengths thumbnail]
12	[Storyboard thumbnail]	[VO Script thumbnail]	[Labels thumbnail]	[Characters thumbnail]	[Shot Lengths thumbnail]
13	[Storyboard thumbnail]	[VO Script thumbnail]	[Labels thumbnail]	[Characters thumbnail]	[Shot Lengths thumbnail]
14	[Storyboard thumbnail]	[VO Script thumbnail]	[Labels thumbnail]	[Characters thumbnail]	[Shot Lengths thumbnail]
15	[Storyboard thumbnail]	[VO Script thumbnail]	[Labels thumbnail]	[Characters thumbnail]	[Shot Lengths thumbnail]

44

3D Animatic

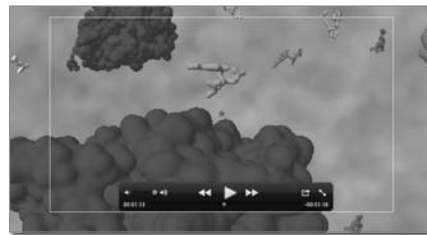
- First pass movie with 3D models



45

Rough Cut

- Unrendered movie with final animation



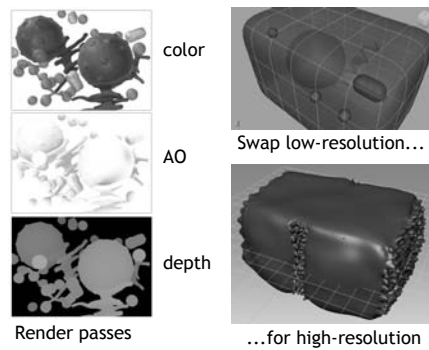
46

Post-Production

- Rendering
- Compositing
- VO and music
- Final animation

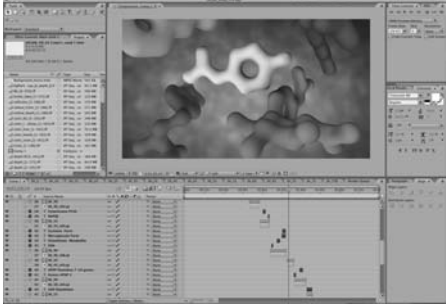
47

Rendering



48

Compositing




Adobe After Effects

49

VO Recording -VO Script

- Pronunciation guide



VO	Pronunciation Guide
...it absorbs rapidly in the upper GI tract.	...it ab-sorbz rap-ee-ly in the up-per GI tract.
APAP enters the bloodstream and is carried to sites of action.	APAP en-ters the blood-stream and is car-ied to sites of ac-tion.
The liver metabolizes APAP and produces metabolites required for function.	The liver me-tabol-izes APAP and pro-ducez me-tabol-ites re-quired for func-tion.
Many metabolic pathways occur in the liver to rid the body of APAP and other substances from the body.	Man-ee me-tabol-ic path-ways oc-cure in the liver to rid the bod-ee of APAP and oth-er sub-stances from the bod-ee.
APAP is metabolized to the hydroquinone smooth muscle relaxant.	APAP is me-tabol-ized to the hy-dro-quin-one smooth mus-cle re-lax-ant.
The majority of APAP is conjugated by enzymes into inert glucuronide and acetaminophen metabolites.	The ma-jor-ity of APAP is con-ju-gat-ed by en-zymes into inert glu-cu-ron-ide and ac-e-ta-min-oph-en me-tabol-ites.
An enzyme, glucosyltransferase , converts the remaining APAP to NAPQ.	An en-zyme, glu-cos-yl-trans-fer-ase , con-verts the re-main-ing APAP to NAPQ.
NAPQ can be combined with GSTA, to create an intermediate glucuronide metabolite.	NAPQ can be com-bined with GSTA, to cre-ate an in-ter-me-diate glu-cu-ron-ide me-tabol-ite.
Further conjugation results in glucuronide and acetaminophen forms.	Further con-ju-ga-tion re-sults in glu-cu-ron-ide and ac-e-ta-min-oph-en forms.

50


VO Recording

- Apple Garage Band
- Podcast recording settings



51

Final Animation



52

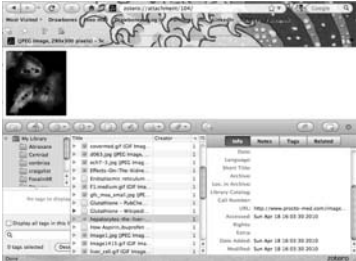
Project Management

How to organize a project!

53

Zotero <http://www.zotero.org/>


- Tracker of online references and images



54

Papers <http://mekentosj.com/papers/>

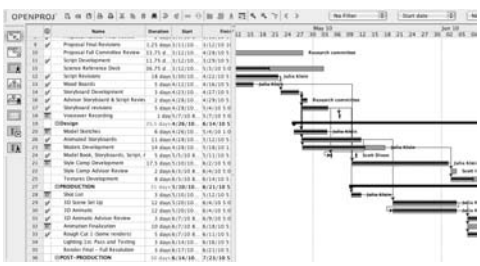
- PDF organizer and search tool



55

OpenProj <http://openproj.org/>

- Timeline manager



56

Project Website <http://www.drawbones.com/UICJAK/>



- Created to organize project files
- Links to YouTube
- Will be updated as new progress is made

57

Conclusions

- An animation was created that visually explains the APAP metabolic pathway and its potential for hepatotoxicity
- Project research provided a level of detail appropriate for an audience of healthcare providers
- Production roles and steps from a professional medical animation workflow were consolidated and successfully performed by one researcher

58

Thanks!

- Eveo medical animation team
 - Baron, Dario, Erich, Fred, Henry, Kevin, Sara, Rick, Bob, Carly, Paul, Nicole, Monica and many others
- Fred Meyer Pharmacy
 - Pharmacists
 - Pharmacy technicians
- Research committee members
 - Scott Dixon
 - John Daugherty
 - Scott Barrows
- Tim Stack
- Carol Babin
- Everyone else who encouraged this project along the way

59

Questions?

julia@drawbones.com

<http://www.drawbones.com/UICJAK/>

60