

# Development of a Medical Animation on Acetaminophen Metabolization and Hepatotoxicity

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# Overview

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  - Roles
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    - Pre-production
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    - Production
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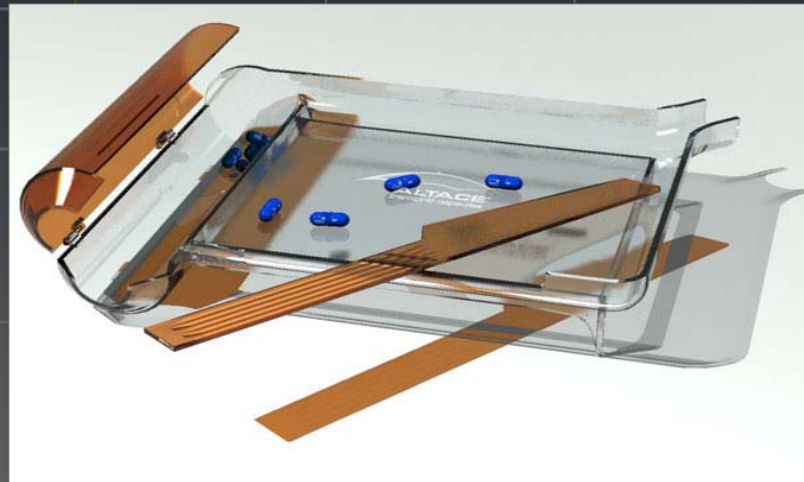
# Project Inspiration

Why this topic?

# Project Inspiration

## Pharmacy

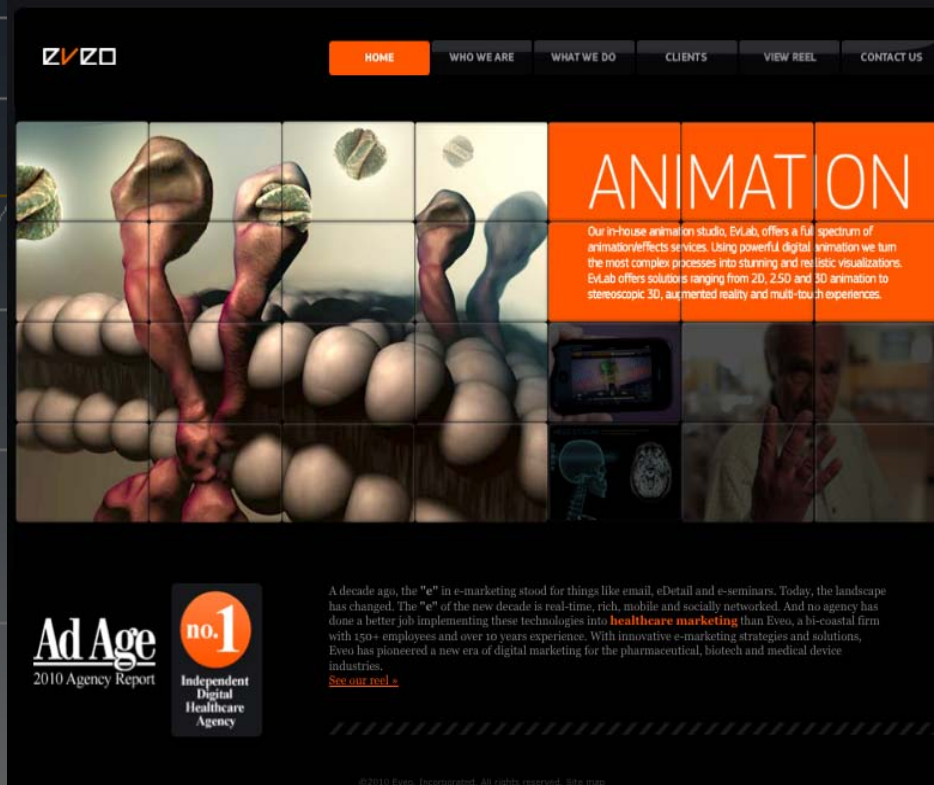
- Pharmacy technician role
  - Fill and deliver prescriptions to patients
- Pharmacist role
  - Patient education
  - Knowledge of APAP danger



# Project Inspiration

## Medical Media Agency

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



<http://www.eveo.com/>

# Project Inspiration

## Warnings on acetaminophen in the news

- 2009 FDA recommendations

The screenshot shows the MSNBC website's 'Health' section. The main headline is 'FDA recommends acetaminophen warnings' with a sub-headline 'New report calls for dose limits to help reduce risk of liver damage'. The article is attributed to the Associated Press and dated 5/27/2009. The text of the article is partially visible, mentioning a report from the Food and Drug Administration regarding stronger warnings and dose limits for acetaminophen. To the right of the article is a Groupon advertisement for food delivery services in San Jose, Los Angeles, and San Diego.

msnbc.com Home U.S. World Politics Business Sports Entertainment **Health** Tech & science Travel Local Weather

### FDA recommends acetaminophen warnings

New report calls for dose limits to help reduce risk of liver damage

advertisement | ad info

San Jose:	Los Angeles:	San Diego:
\$20 for \$40 Worth of ...	\$10 for ...	\$49 for \$125 Worth of ...
\$20	\$10	\$49
<a href="#">Shop</a>	<a href="#">Shop</a>	<a href="#">Shop</a>

GROUPON

Ap Associated Press  
updated 5/27/2009 6:01:55 PM ET

Share | Print | Font: A + -

NEW YORK — A Food and Drug Administration report released Wednesday recommends stronger warnings and dose limits on drugs containing the painkiller acetaminophen, citing an increased risk of liver injury.

The recommendation covers both prescription doses and over-the-counter medication, of which Johnson & Johnson's Tylenol is the most well-known. Acetaminophen is also widely available as a generic over-the-

<http://www.msnbc.msn.com/id/30969044/>

# 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?

# Information Research



## Tylenol® Drug label

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

Drug Facts	
Active ingredient (in each caplet)	Purpose
Acetaminophen 500 mg .....	Pain reliever/ fever reducer
<b>Uses</b> Temporarily relieves minor aches and pains due to:	
<ul style="list-style-type: none"><li>■ headache</li><li>■ backache</li><li>■ the common cold</li><li>■ premenstrual and menstrual cramps</li></ul>	<ul style="list-style-type: none"><li>■ muscular aches</li><li>■ minor pain of arthritis</li><li>■ toothache</li><li>■ reduces fever</li></ul>
<b>Warnings</b>	
<b>Alcohol warning:</b> 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.	
<b>Do not use</b>	
<ul style="list-style-type: none"><li>■ with any other products containing acetaminophen</li></ul>	
<b>Stop use and ask a doctor if:</b>	
<ul style="list-style-type: none"><li>■ new symptoms occur</li><li>■ redness or swelling is present</li><li>■ pain gets worse or lasts for more than 10 days</li><li>■ fever gets worse or lasts for more than 3 days</li></ul>	
These could be signs of a serious condition.	
<b>If pregnant or breast-feeding,</b> ask a health professional before use.	
<b>Keep out of reach of children.</b>	
<b>Overdose warning:</b> Taking more than the recommended dose (overdose) may cause liver damage. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs of symptoms.	

<http://www.tylenol.com/page.jhtml?id=tylenol/painex/subhowto.inc>



# Information Research

## Tylenol® Professional Product Information (PPI)

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

### TYLENOL® (acetaminophen)

#### 1. AMERICAN HOSPITAL FORMULARY SERVICE (AHFS)\* CLASSIFICATION NUMBER

28:08.92

#### 2. GENERIC NAME

USAN: acetaminophen

INN: paracetamol

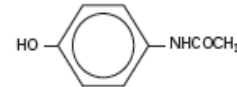
CAS#: 103-90-2

#### 3. SOURCE OF SUPPLY (Trade Name and Manufacturer)

TYLENOL® (acetaminophen) —  
McNeil Consumer Healthcare

#### 4. PHYSICAL PROPERTIES OF THE CHEMICAL ENTITY<sup>1</sup>

##### a. Structural Formula



##### b. Molecular Formula

C<sub>9</sub>H<sub>9</sub>NO<sub>2</sub>

##### c. Molecular Weight

151.16

##### d. Macroscopic Appearance

Acetaminophen is a white, crystalline powder.

##### e. Solubility

water	1:70
boiling water	1:20
alcohol	1:10
chloroform	1:50
glycerin	1:40
ether	slightly soluble

#### 5. CHEMICAL PROPERTIES

##### a. Structural Similarities/Differences of the Drug to Other Available Compounds or Groups of Compounds

Acetaminophen is a synthetic, nonopioid, centrally acting analgesic derived from *p*-aminophenol. The full chemical name is *N*-acetyl-*p*-aminophenol.

##### b. pKa

The pKa of acetaminophen is 9.51 at 25°C.

##### c. Stability of the Drug to Temperature, Light, and Moisture

Acetaminophen is stable to temperature, light, and moisture.

##### d. pH Range Over Which Drug is Stable in Solution

Acetaminophen is stable at a pH between 4 and 7 at 25°C.

##### e. pH of Commercially Available Liquid Products

Acetaminophen oral solution (ie, elixir, adult liquid) has a pH of 3.8 to 6.1 and the oral suspension (ie, infants' drops, children's suspension) has a pH of 5.4 to 6.9.

# Information Research

## Protein Data Bank

- Information
- 3D .pdb files



The screenshot displays the PDB website interface for the entry 1EOH. The page is organized into several sections:

- Header:** Includes the PDB logo, the text "An Information Portal to Biological Macromolecular Structures", and a timestamp "As of Tuesday Jul 20, 2010 at 5 PM PDT there are 66633 Structures".
- Navigation Bar:** Contains links for "HELP | PRINT", a search bar, and "Advanced Search".
- Left Sidebar:** Features a "Home" section with links to News & Publications, Usage/Reference Policies, Deposition Policies, Website FAQ, Deposition FAQ, Contact Us, About Us, Careers, External Links, and New Website Features. Below this is a "Deposition" section with links to All Deposition Services, Electron Microscopy, X-ray | NMR, Validation Server, and BioRxiv. A "Search" section includes Advanced Search, Latest Releases, Latest Publications, Sequence Search, Chemical Components, Unreleased Entries, Browse Database, and Histograms. An "Explorer" section shows the "Last Structure: 1EOH" and a "Query (345 hits)" section with links to Query Results, Query Details, Query History, and Save Query to MyPDB. A "Tools" section includes File Downloads, FTP Services, File Formats, Services: RESTful | SOAP, Widgets, and Compare Structures. An "Education" section includes Understanding PDB Data, Molecule of the Month, and Educational Resources.
- Main Content Area:**
  - Summary:** Displays the entry name "GLUTATHIONE TRANSFERASE P1-1", the ID "1EOH", and the DOI "10.2210/pdb1eoh/pdb".
  - Primary Citation:** Lists the authors (Rosjohn, J., McKinsty, W.J., Oakley, A.J., Parker, M.W., Stenberg, G., Mannervik, B., Dragani, B., Cocco, R., Acuto, A.), the journal (J. Mol. Biol. 302: 295-302), the PubMed ID (10970734), and the DOI (10.1006/j.mol.2000.4054).
  - Molecular Description:** Provides the classification (Transferase), structure weight (185621.59), molecule (GLUTATHIONE S-TRANSFERASE), polymer (1), type (polypeptide(L)), chains (A, B, C, D, E, F, G, H), EC (2.5.1.18), and mutation (D152A).
  - Source:** Lists the polymer (1), scientific name (Homo sapiens), common name (Human), expression system (Escherichia coli), and system (Cell).
  - Related PDB Entries:** Shows the ID (1EOH), details (S149A MUTANT OF GST), and sequence (wild type GST).
  - Derived Data:** Lists the SCOP Classification v1.75 (16 Domains), CATH Classification v3.3.0 (16 Domains), PFAM Classification (16 Domains), and GO Terms (7 Terms).
  - Deposition Summary:** Lists the authors (Rosjohn, J., McKinsty, W.J., Oakley, A.J., Parker, M.W., Stenberg, G., Mannervik, B., Dragani, B., Cocco, R., Acuto, A.), the deposition date (2000-03-22), the release date (2000-10-18), and the last modified date (2009-02-24).
  - Experimental Details:** Lists the method (X-RAY DIFFRACTION), experimental data (EDS), resolution (2.50 Å), R-value (0.231 (work)), R-free (0.286), space group (P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub>), and unit cell parameters (a = 82.97 Å, b = 84.02 Å, c = 236.97 Å, α = 90.00°, β = 90.00°, γ = 90.00°).

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

# Information Research

## PubChem

- Information
- 3D .sdf files

NCBI PubChem Compound

PubChem Compound - GO

PubMed | Entrez | Structure | PubChem | Help

PubChem > Compound Summary

### Acetaminophen - Compound Summary (CID 1983)

Analgesic antipyretic derivative of acetanilide. It has weak anti-inflammatory properties and is used as a common analgesic, but may cause liver, blood cell, and kidney damage.

#### Table of Contents

- BioMedication Annotation
  - Medication Information
  - Pharmacological Action
  - Pharmacological Classification
  - Chemical Classification
  - Safety and Toxicology
  - Literature Links
  - Literature Mining
- BioAssay Results
- Protein Structures
- Synonyms
- Properties
- Descriptors
- Compound Information
- Substance Information
  - Category
- Exports

#### BioMedication Annotation: (Total:1)

#### Acetaminophen

##### Medication Information

- Up and up temporary minor arthritis pain relief (ACETAMINOPHEN) [Target Corporation]
  - Indication & Usage
  - Warnings
  - Dosage & Administration

#### Structure & Quick Link Bar

2D 3D

PC3D Viewer Download

Compound ID	1983
Molecular Weight	151.16256 [g/mol]
Molecular Formula	C <sub>8</sub> H <sub>9</sub> NO <sub>2</sub>
XLogP3	0.5
H-Bond Donor	2
H-Bond Acceptor	2

#### Links

- Protein Structure (5)
- PubMed (212)
- Gene (64286)
- Taxonomy (10)
- Omim (28)
- NLM Toxicology Link

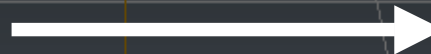
<http://www.ncbi.nlm.nih.gov/>

# 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
- Compositor
- QA



One  
Researcher?

- Adaptation for one researcher

# Animation Production Steps

- Pre-production
- Design
- Production
- Post-production

# Pre-Production

- Content development
- Science reference deck
- Script
  - Outline
  - Voice over (VO)
  - Animation notes
- Storyboards
- Animated storyboards

# Science Reference Deck

Character Name (molecular level)	PDB/ PubChem	Also known as/ Type	Size/Weight	Pronunciation	Notes
Acetaminophen	CID_1983	APAP, paracetamol, Tylenol <sup>®</sup>	151.17 g/mol	<a href="#">acetamin-o phen</a> ă-sē-tă-'mī-nă-fən, -ă-să-tă-	
Acetaminophen cysteine	CID_83997	APAP metabolite	254.31 g/mol	<a href="#">cys teine</a> 'sis-tă-,ēn	
Acetaminophen glucuronide	CID_83944	APAP metabolite	327.29 g/mol	<a href="#">gluc-uro-nide</a> glū-'kyur-ă-,nīd	
Acetaminophen sulfate	CID_83939	APAP metabolite	231.23 g/mol	<a href="#">sul-fate</a> 'səl-,fāt	
Acetaminophen glutathione	CID_83998	APAP metabolite	327.29 g/mol	<a href="#">glu ta thi one</a> glūt-ă-'thī-,ōn	
Acetaminophen mercapturate	CID_539698	APAP metabolite	312.34 g/mol	mer-cap-'TŪR-ate	
NAC	CID_12035	N-acetylcysteine, overdose antidote	163.19 g/mol	<a href="#">ace tyl-cys to ine</a> ă-sēt-'l-'sis-tă-,ēn	
Cytochrome P450	2J0D	Enzyme, CYP2E1, CYP1A2, CYP3A4	Length [Å] a = 67.25 b = 210.71 c = 161.25	<a href="#">cy to chrome</a> 'sit-ă-,krōm	
Glutathione	CID_124886	GSH, tripeptide, cofactor	307.32 g/mol	<a href="#">glu ta thi one</a> glūt-ă-'thī-,ōn	
Glutathione transferase	1EOH	Enzyme, protein, polypeptide	Length [Å] a = 82.97 b = 84.02 c = 236.97	<a href="#">glu ta thi one</a> glūt-ă-'thī-,ōn	
NAPQI	CID_39763	N-acetyl-p-benzoquinoneimine, APAP bioactive metabolite	149.15 g/mol		
COX	1PRH, 4COX	Enzyme, Cyclooxygenase	Length [Å] a = 179.80 b = 133.60 c = 118.40		Not used in the animation
Character Name (cellular/systems level)					
Liver	N/A	Organ			
Hepatocyte	N/A	Cell		<a href="#">he pa to cyte</a> hi-'pat-ă-,sīt	
Smooth endoplasmic reticulum (ER)	N/A	Organelle		<a href="#">en do plas mic</a> en-dă-'plaz-mik <a href="#">retic u lum</a> ri-'tik-yă-ləm	
Golgi apparatus	N/A	Organelle			



# Script Outline

Script outline  
UICJAK Acetaminophen Metabolism  
3-29-10

1. Acetaminophen (APAP)
  - a. Basic details
    - i. Drug type
    - ii. Dosage amounts
  - b. Absorption
    - i. Dissociation of tablet in upper GI (reveal of molecular structure)
    - ii. Entry into bloodstream (by capillary)
  - c. Function
    - i. Analgesic
    - ii. Antipyretic
    - iii. Inhibition of COX enzyme
2. APAP Metabolism
  - a. Site of metabolism
    - i. Gross system level - Liver
    - ii. Cellular level - Liver cells (Hepatocytes)
    - iii. Molecular level - Hepatocyte interior (Smooth ER)
  - b. Pathways of metabolism - APAP metabolites in urine {{127 Tylenol 1999; }}
    - i. Conjugation with glucuronide to glucuronide 46.8 – 62.2%
    - ii. Conjugation with sulfate to sulfate 25.4 – 35.9%
    - iii. Oxidation to NAPQI "Oxidation via the cytochrome, P450-dependent, mixed-function oxidative enzyme pathway to NAPQI"
3. APAP hepatotoxicity
  - a. NAPQI Deactivation {{127 Tylenol 1999; }}
    - i. To mercapturate 2.7 – 5.0%
    - ii. To cysteine conjugate 2.1 – 3.0%
    - iii. Free acetaminophen in urine 3.4 – 8.7%
  - b. Overwhelming of pathways
    - i. Too much APAP (overdose)
    - ii. Not enough GSH to deactivate NAPQI
  - c. Damage...
    - i. to intracellular structures
    - ii. to hepatocyte
    - iii. to liver
  - d. Prevention
    - i. Antidote
    - ii. Prevention of overdose

- Bullet point list
- Names of characters
- Story order








# Script and Storyboards

Storyboards

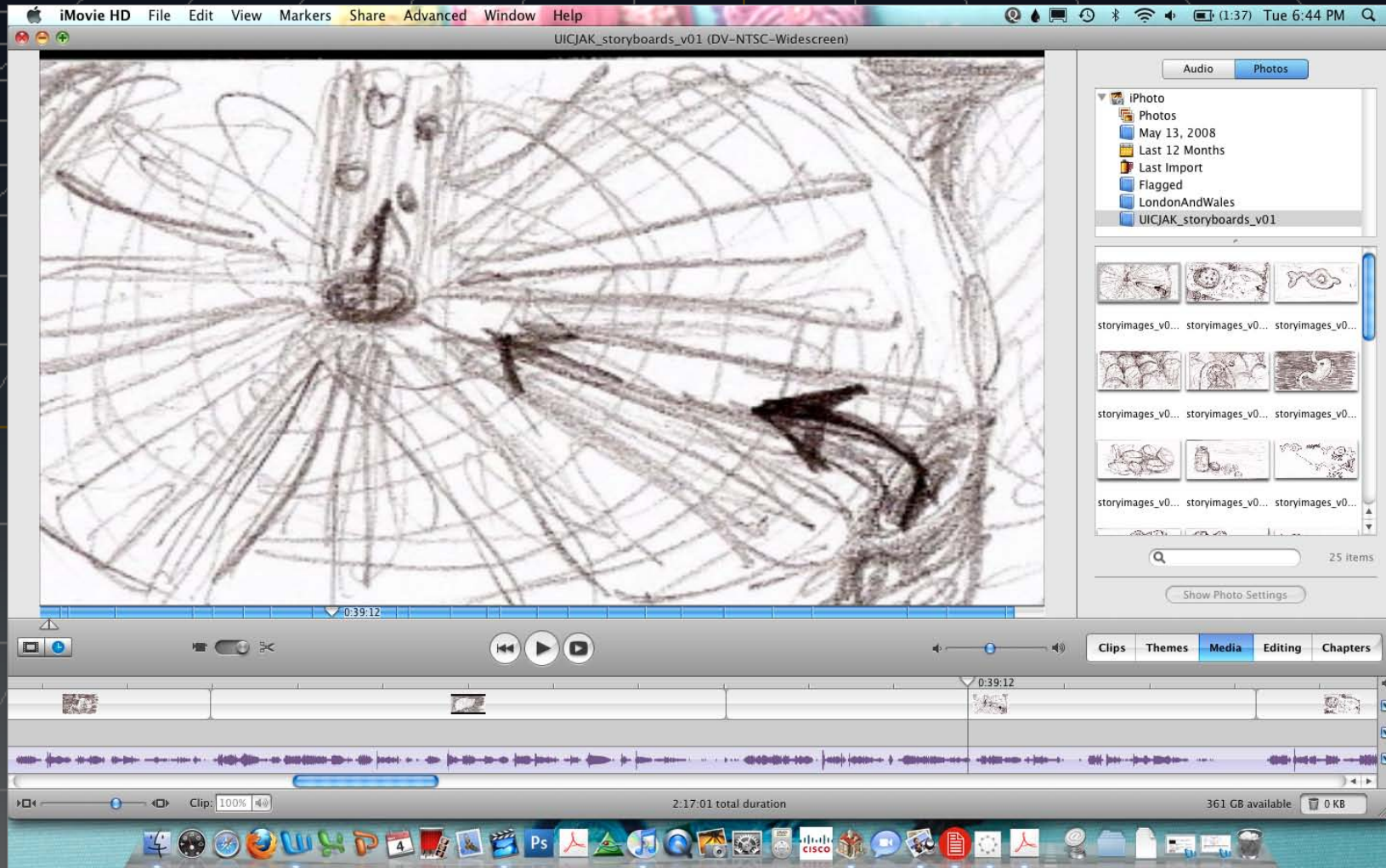
VO

Characters

Notes

	APAP enters the bloodstream and is carried to sites of action.		Picture-in-picture cross fades to show APAP passing through the surface of the villi into a blood vessel and swept away.
	The liver metabolizes APAP and produces metabolites required for function.	Liver	Stomach fades off and liver fades on.
	Many metabolic pathways occur in the liver to rid excess APAP and other substances from the body.	Liver Lobule	Cut to interior of liver. Healthy hepatocytes are arranged in a symmetrical pattern. Blood cells are flowing along arrow path.
	APAP is metabolized in the hepatocyte's smooth endoplasmic reticulum.	Hepatocyte	Cut to single hepatocyte that nearly fills the screen. Simple cellular contents are shown including; nucleus, endoplasmic reticulum, golgi, mitochondria etc.
	The majority of APAP...	APAP	Cut to a simple intracellular space environment, the same color of the smooth endoplasmic reticulum. The APAP molecule structure is shown. More molecules will be seen in the background throughout all molecular shots.

# Animated Storyboards - iMovie



# Design

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

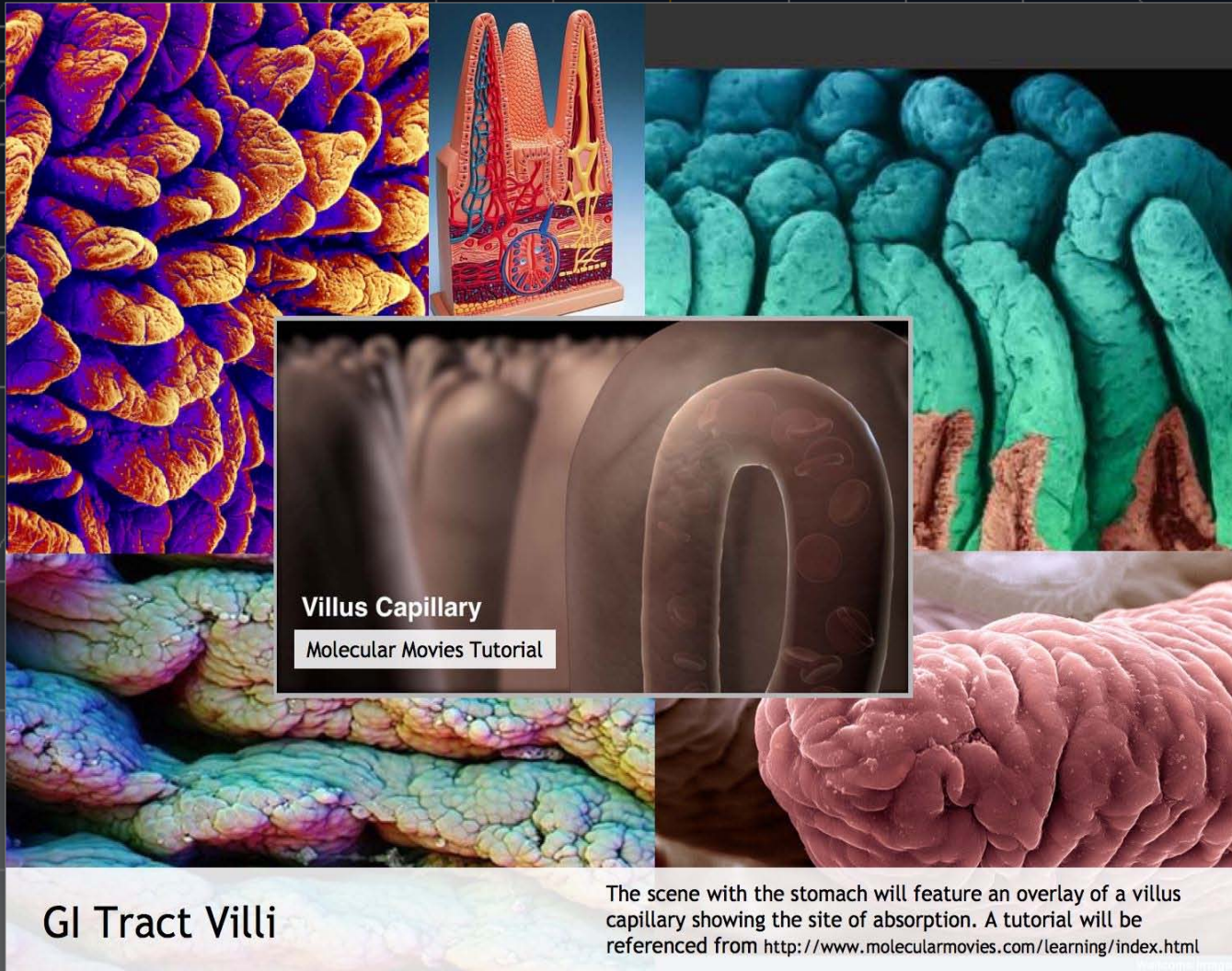
## 20



# Mood Board - APAP

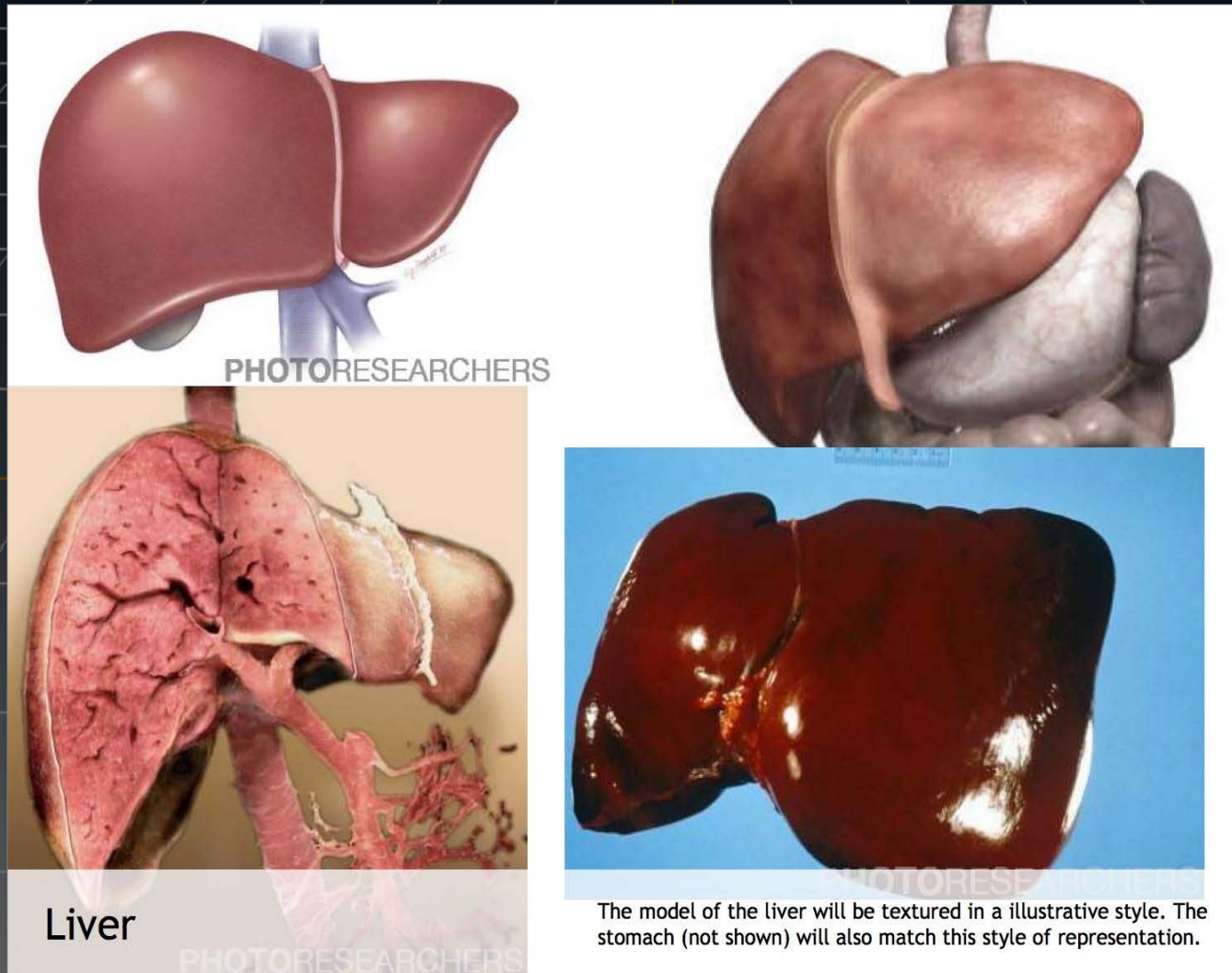


# Mood Board - GI Tract Villi

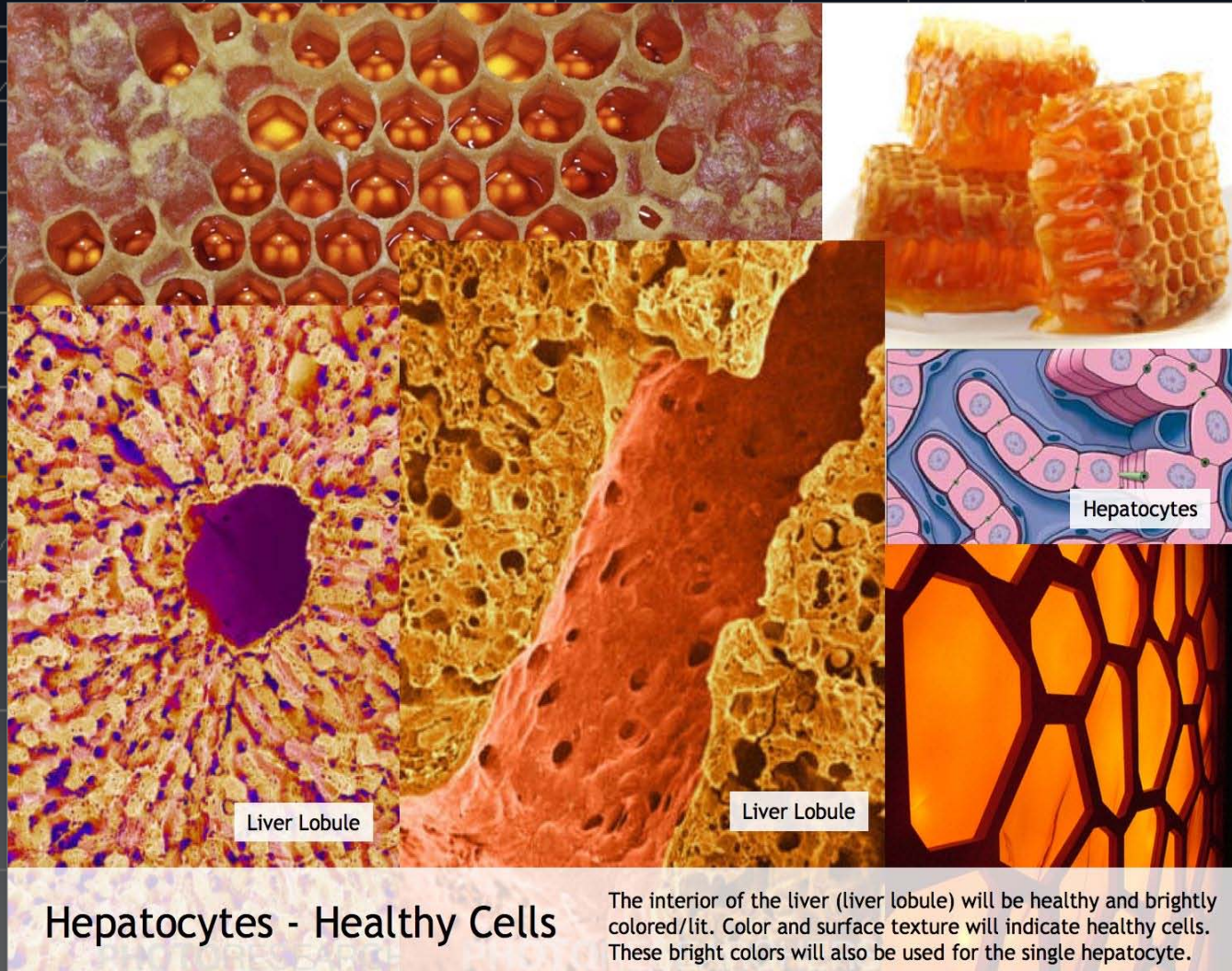




# Mood Board - Liver



# Mood Board - Healthy Hepatocytes



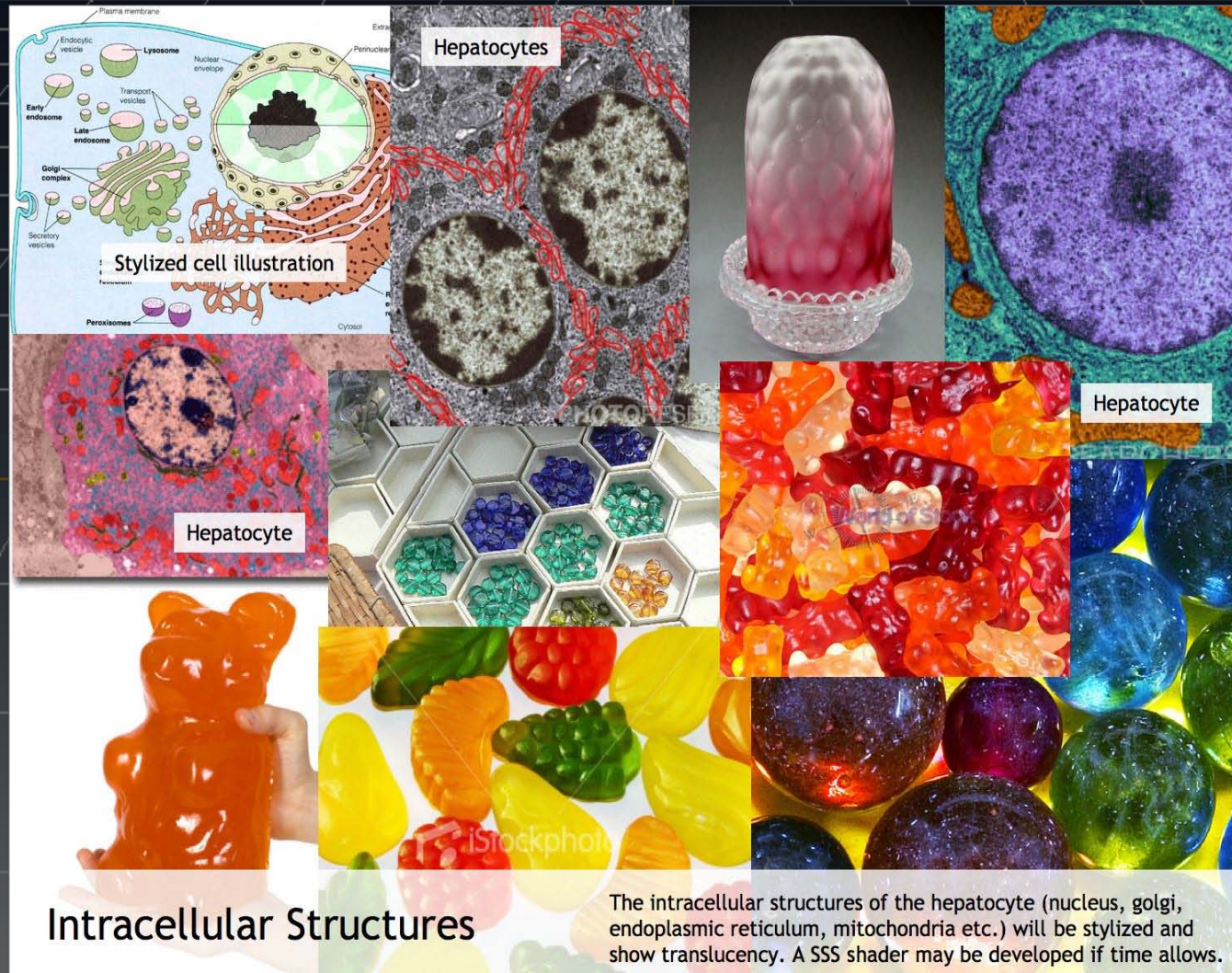


# Mood Board - Damaged Hepatocytes





# Mood Board - Intracellular Structures





# Mood Board - Metabolites



APAP/Metabolite Molecules

The small molecules will have a chalky surface that resembles the initial APAP tablet. The various metabolites will have distinct colors to indicate different types.

# Mood Board - Protein Structure



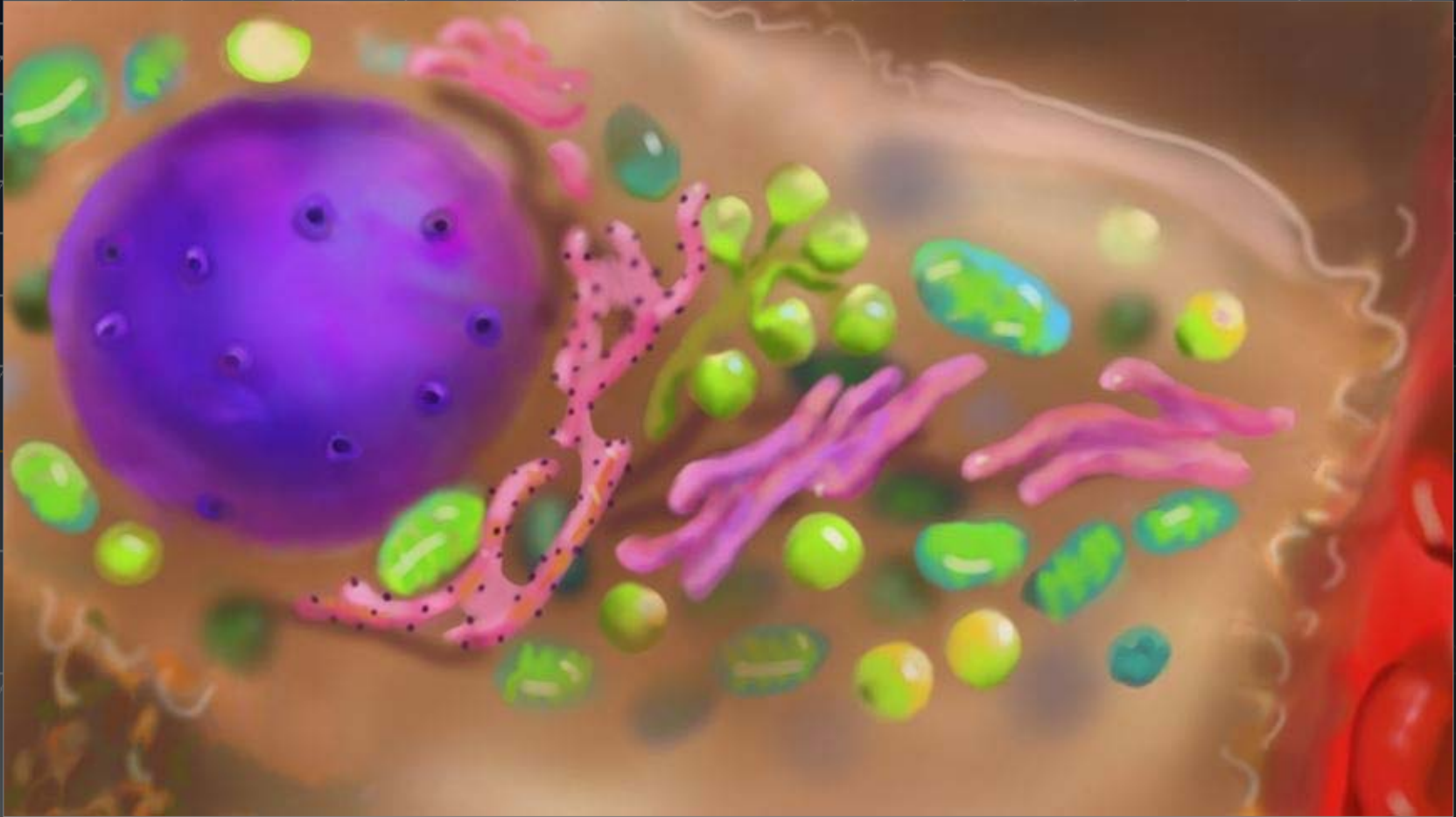


# Concept Art



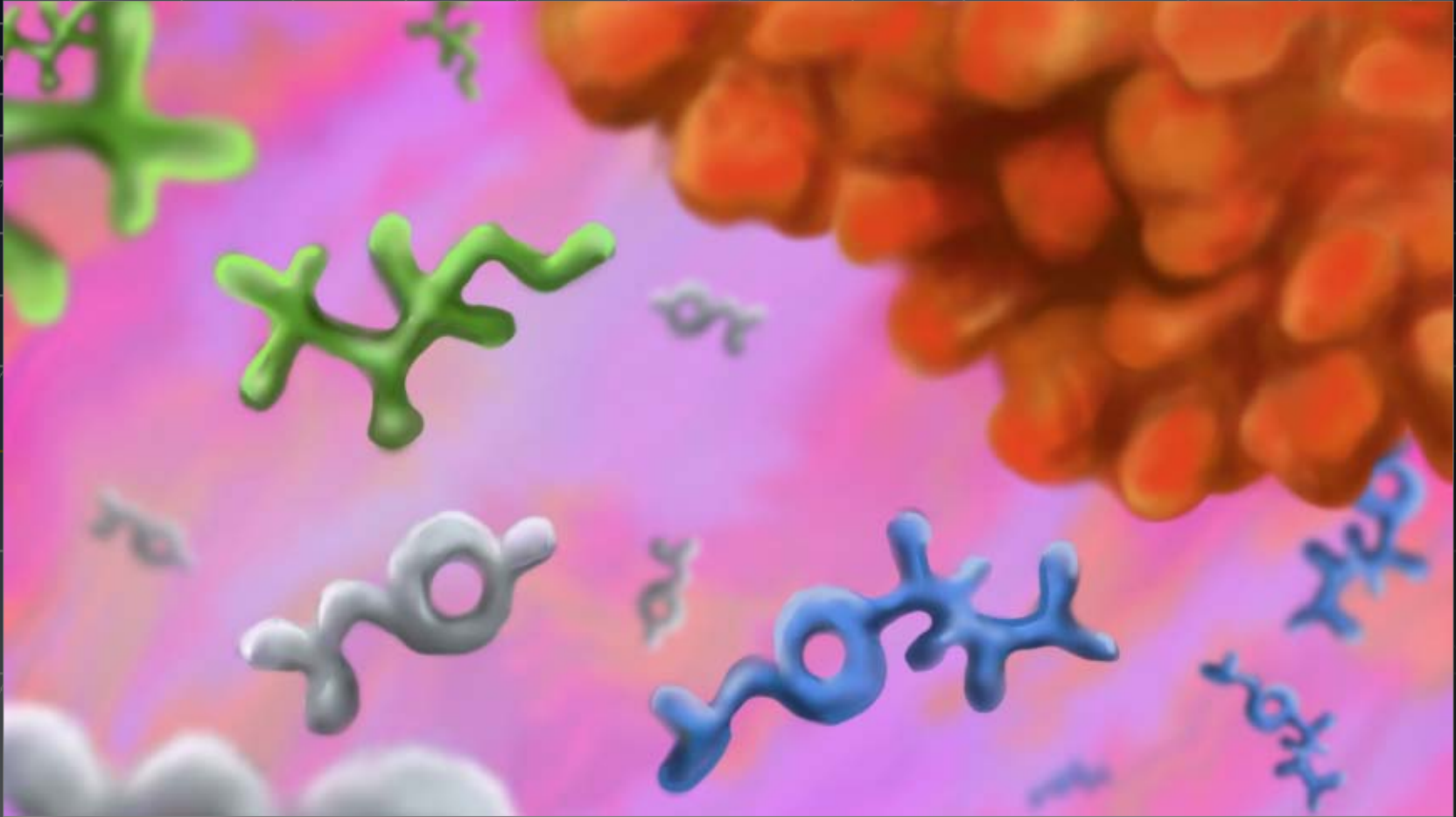
Liver Lobule

# Concept Art



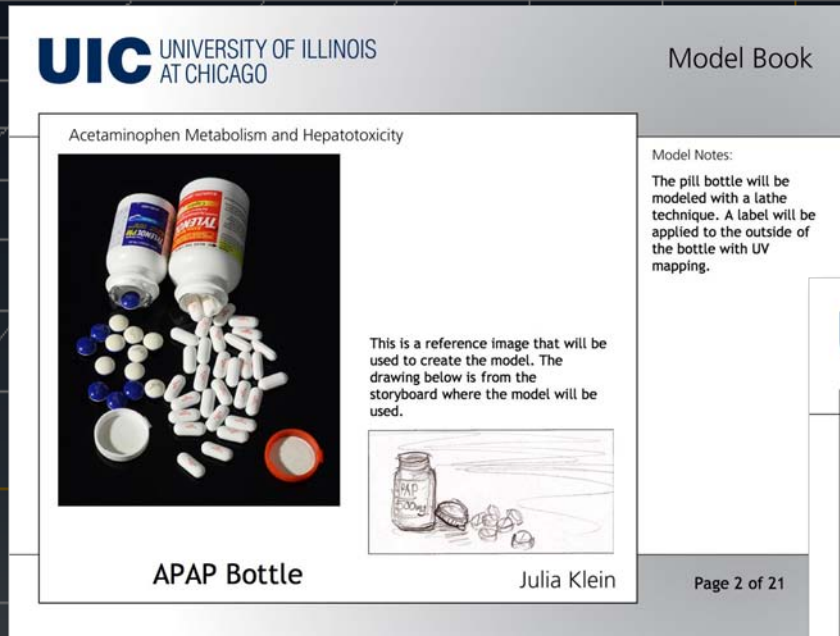
Hepatocyte

# Concept Art



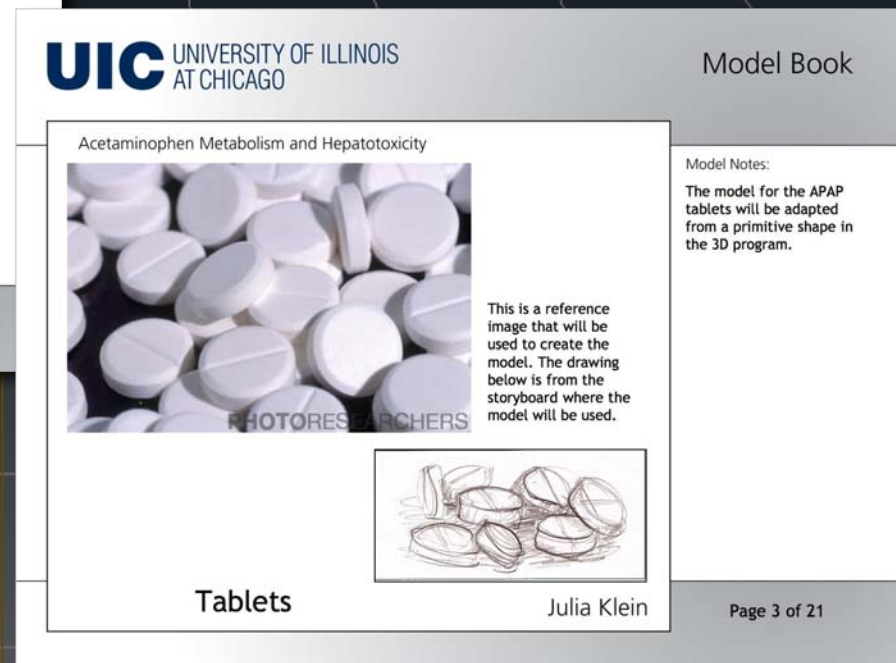
Intracellular Structures

# Model Book



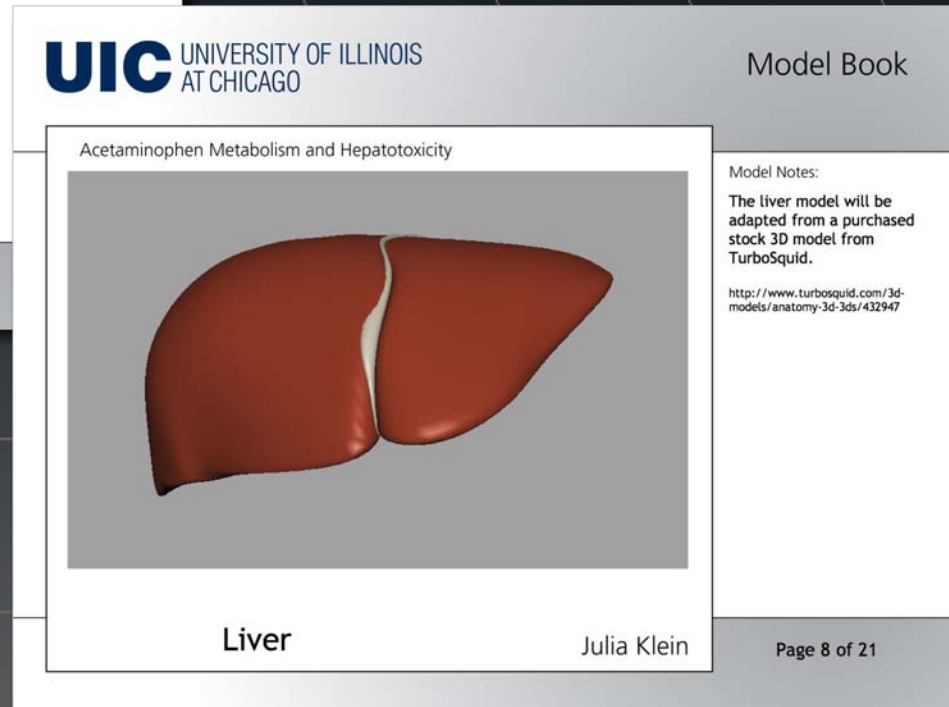
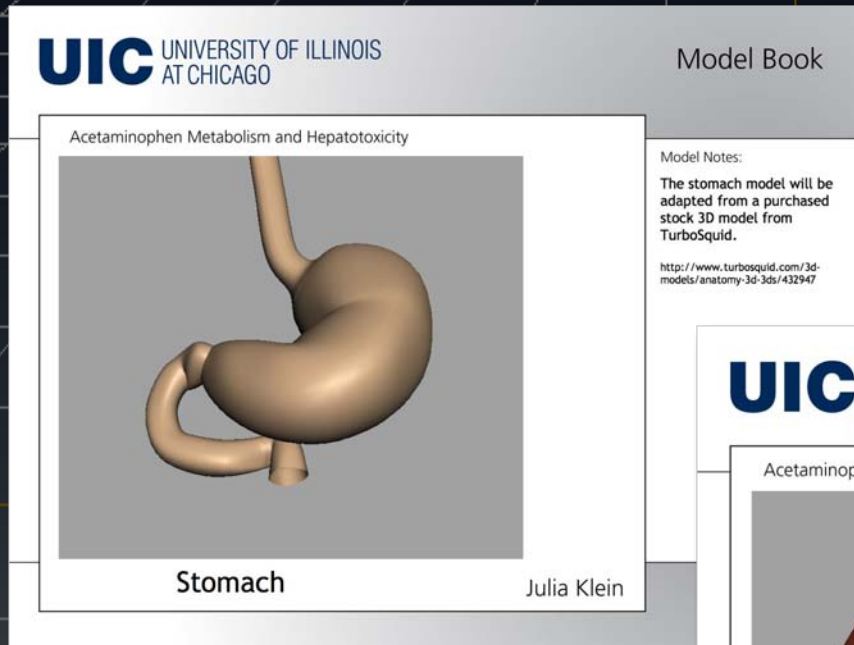
## Acetaminophen models

- APAP bottle
- APAP tablets





# Model Book



## Purchased models

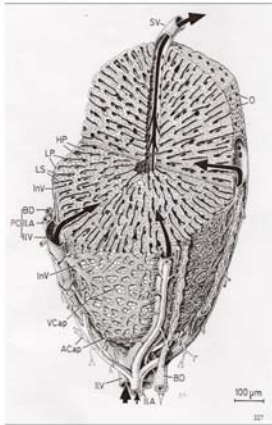
- Stomach
- Liver

# Model Book

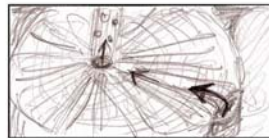
**UIC** UNIVERSITY OF ILLINOIS  
AT CHICAGO

Model Book

Acetaminophen Metabolism and Hepatotoxicity



This is a reference image that will be used to create the model. The drawing below is from the storyboard where the model will be used.



Liver Lobule

Julia Klein

Model Notes:

The liver lobule model will be created as a base shape in Maya and then sculpted in Zbrush or Mudbox.

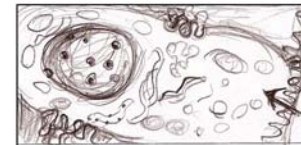
**UIC** UNIVERSITY OF ILLINOIS  
AT CHICAGO

Model Book

Acetaminophen Metabolism and Hepatotoxicity



This is a reference image that will be used to create the model. The drawing below is from the storyboard where the model will be used.



Hepatocyte

Julia Klein

Model Notes:

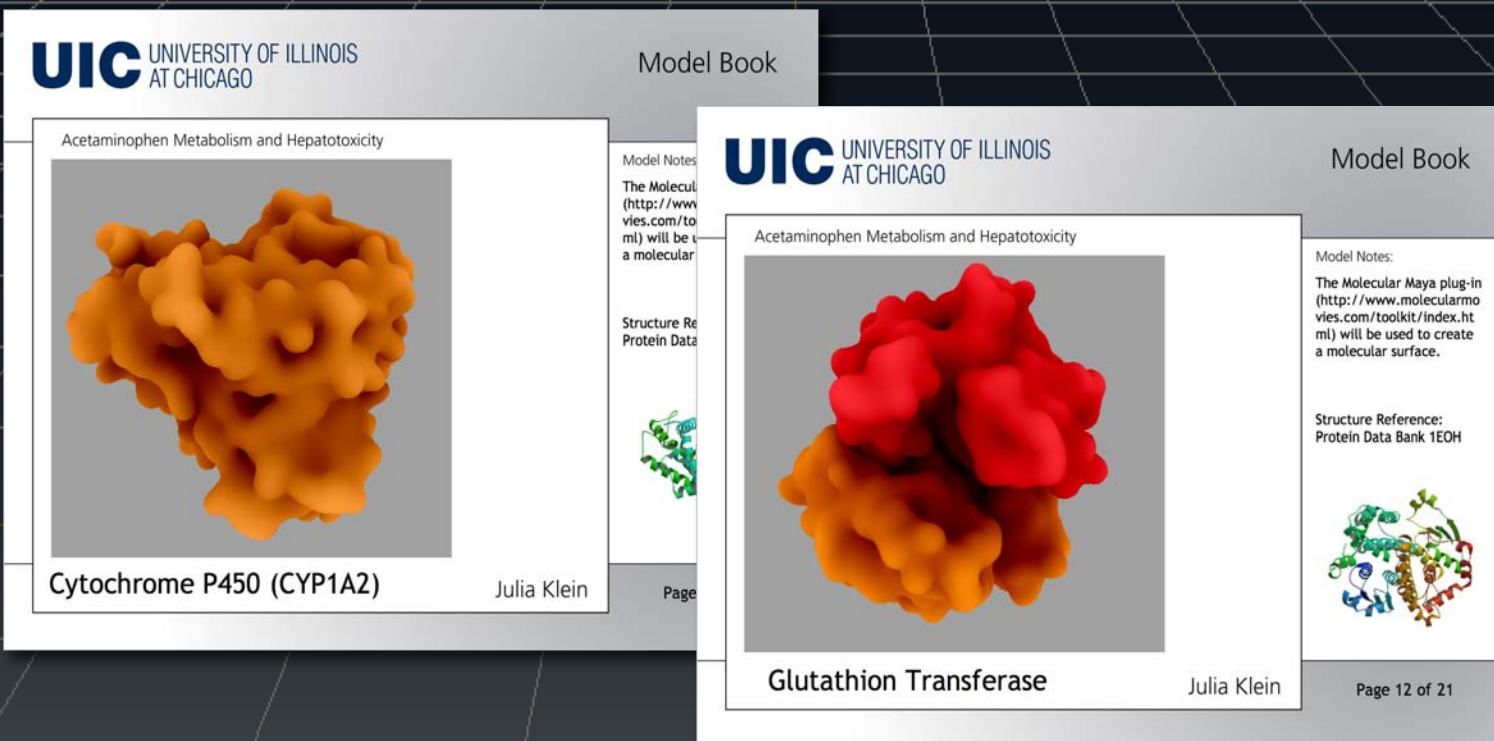
The hepatocyte model will be a composite of multiple smaller intracellular shapes. The individual models of those shapes will use simple geometry to represent a stylized interior of a cell.

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## Sculpted models

- Liver Lobule
- Hepatocyte

# Model Book



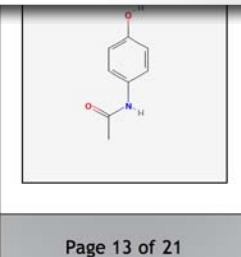
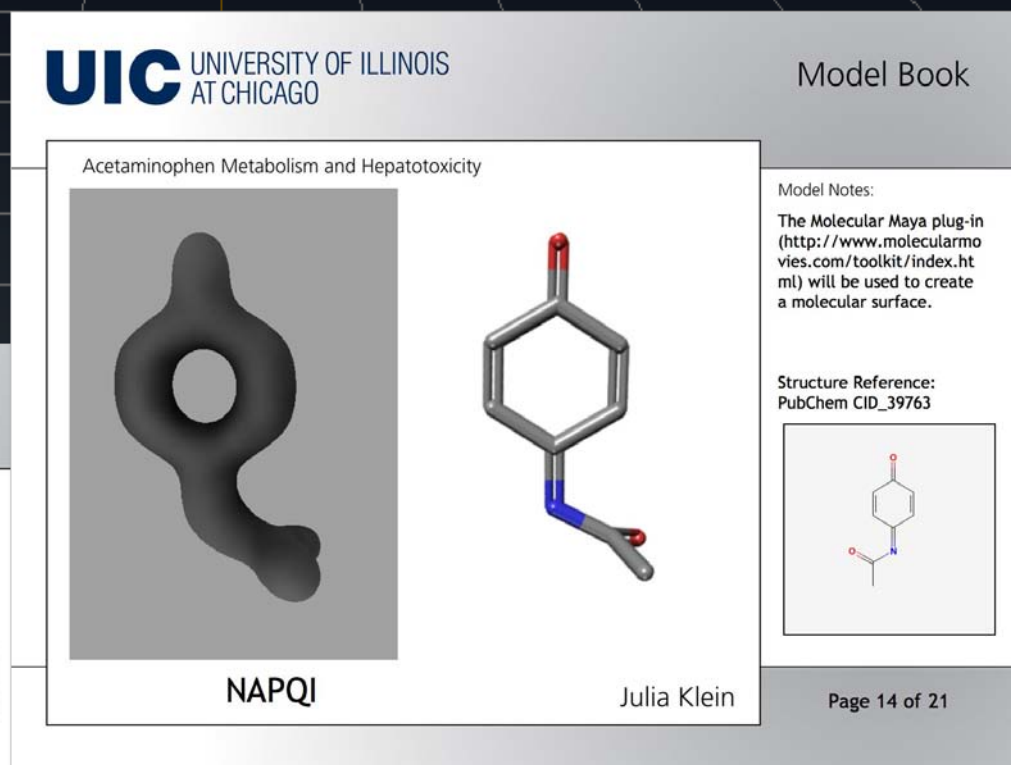
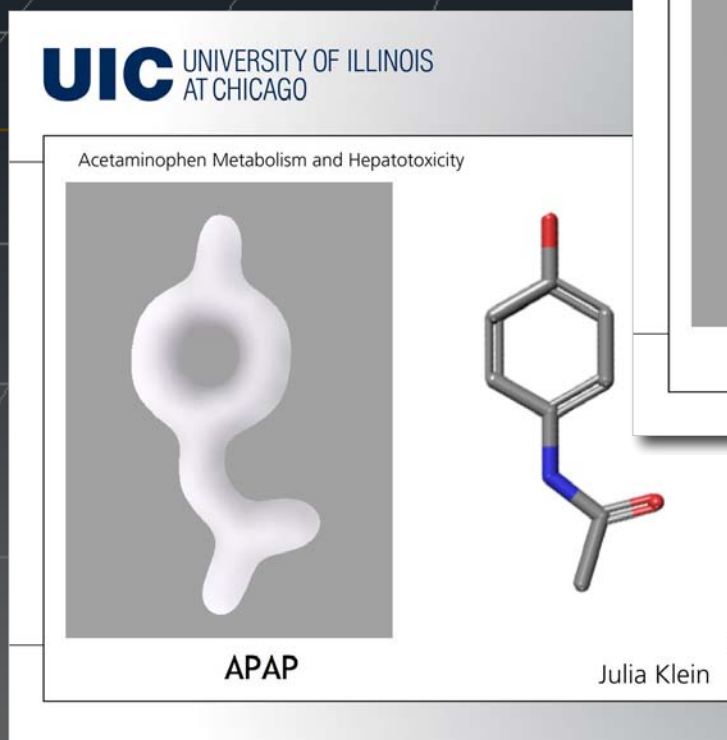
## Protein Data Bank models

- Cytochrome P450
- Glutathione Transferase

# Model Book

## PubChem models

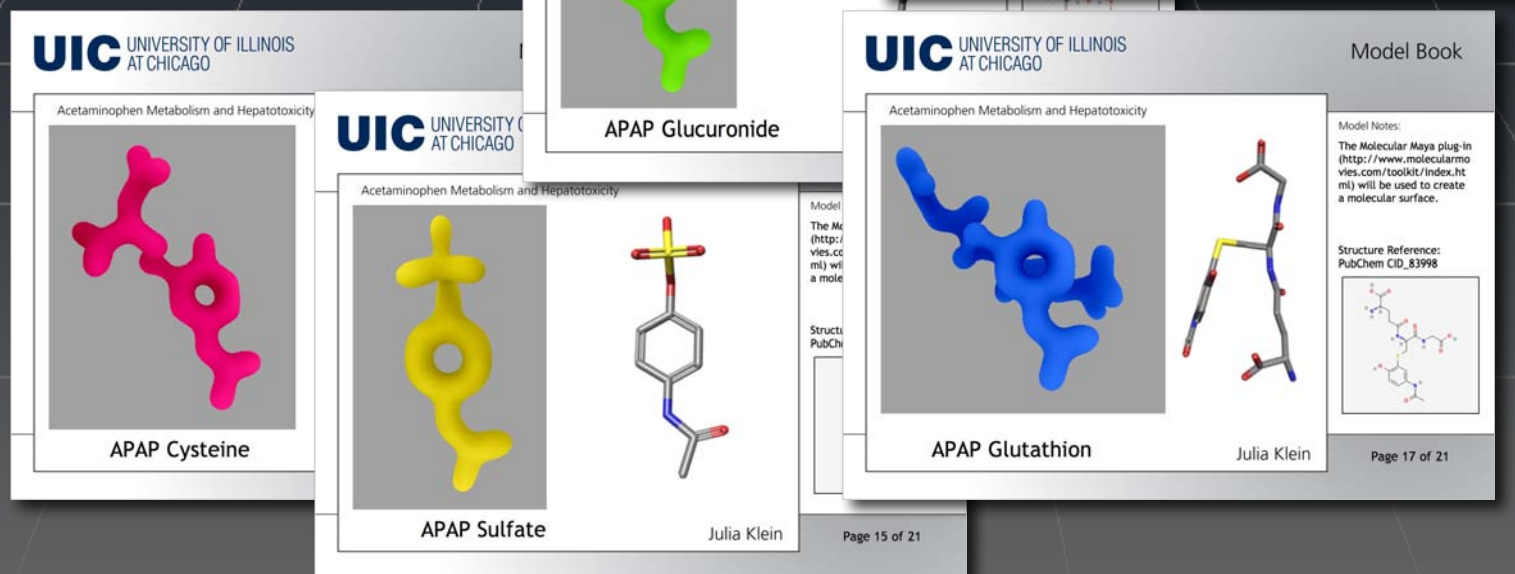
- APAP
- NAPQI



# Model Book

## PubChem APAP Metabolites

- Cysteine
- Glucuronide
- Sulfate
- Glutathione
- Mercapturate

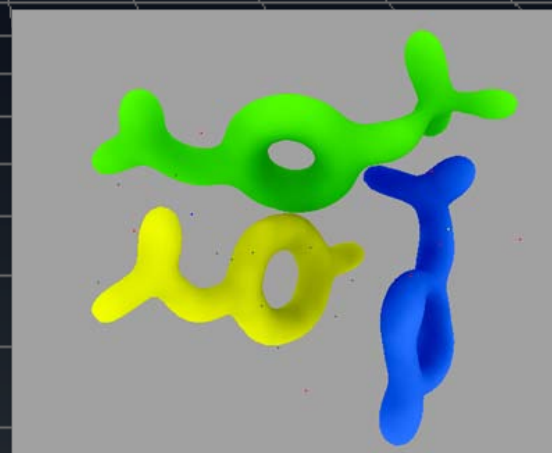
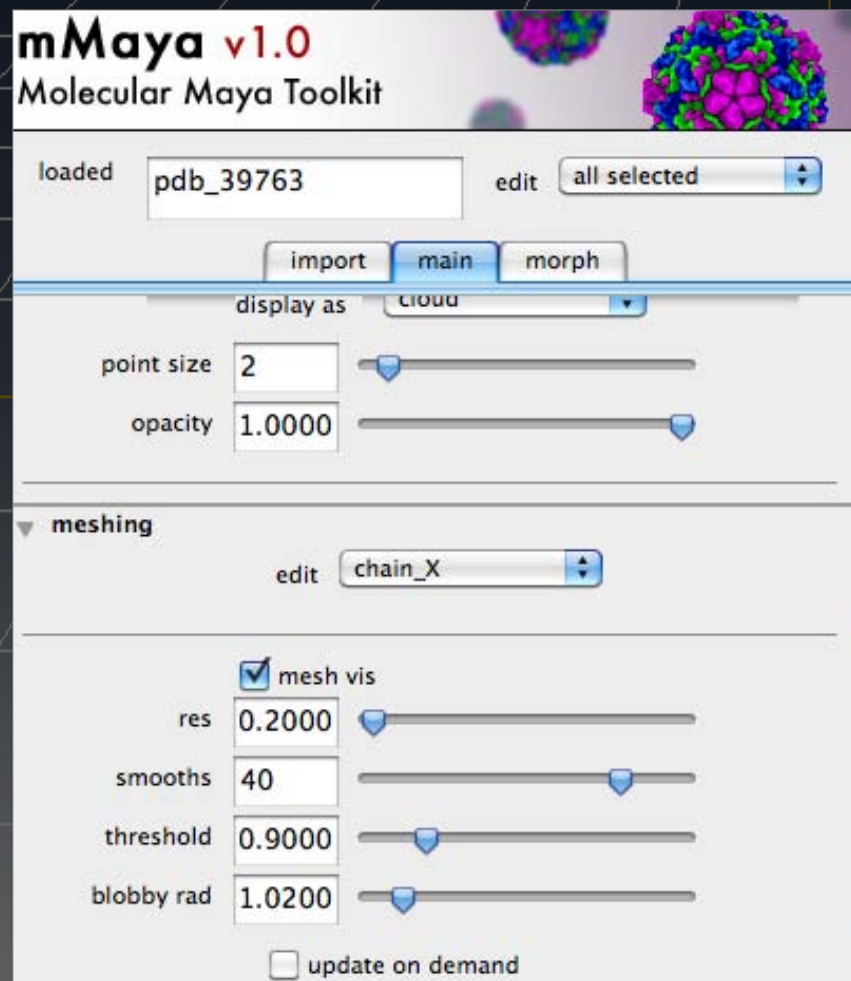




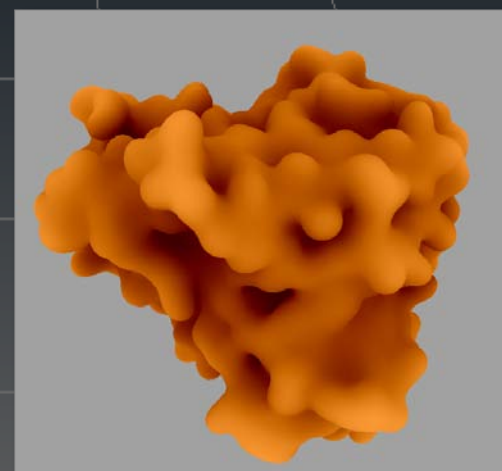
# 3D Modeling

## Molecular Maya (mMaya)

<http://www.molecularmovies.com/toolkit/index.html>



PubChem models



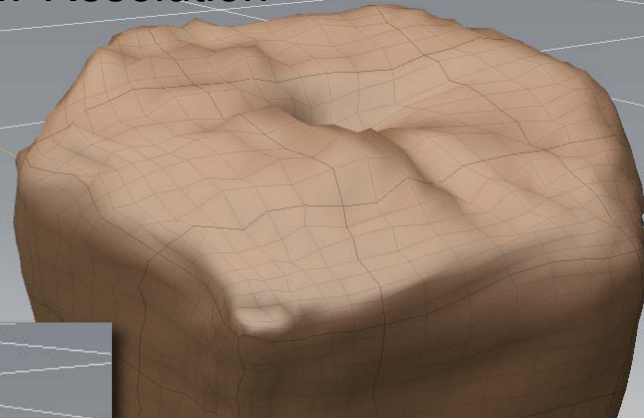
PDB model

# 3D Modeling

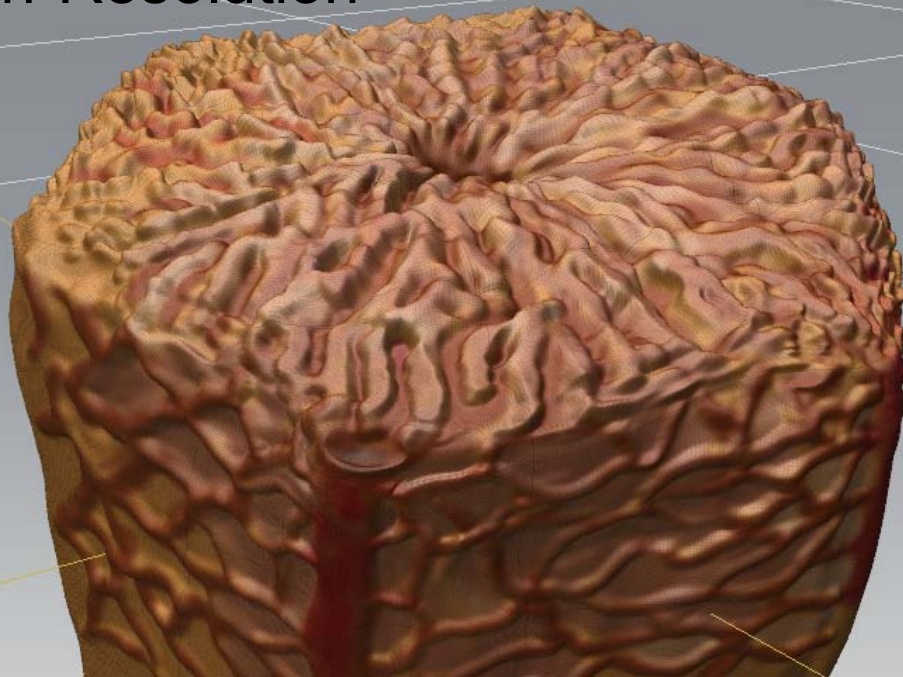
## Mudbox® sculpting

- Liver lobule

Low-Resolution



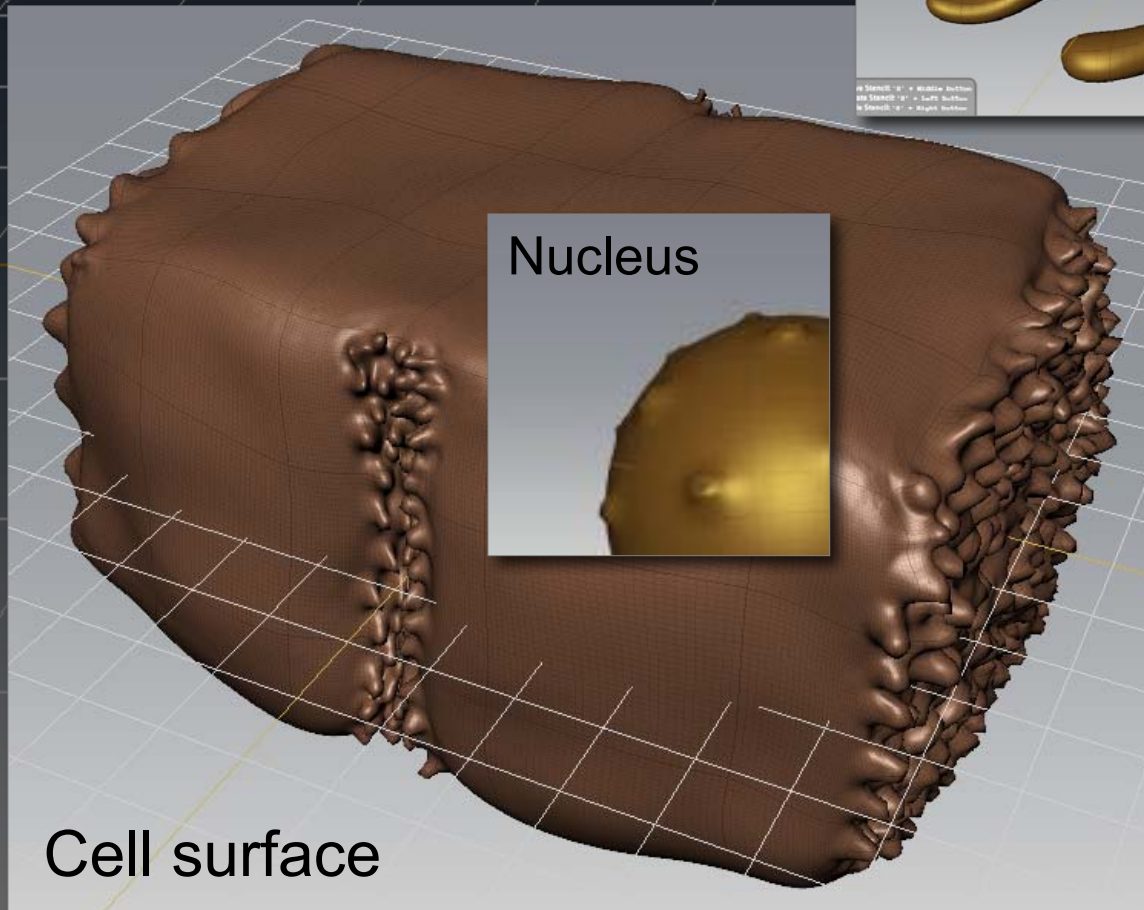
High-Resolution



# 3D Modeling

## Mudbox® sculpting

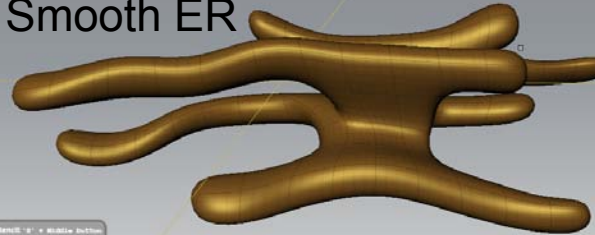
- Hepatocyte



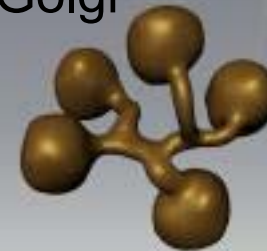
Nucleus



Smooth ER



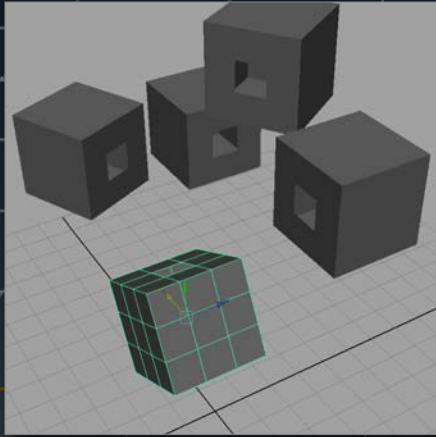
Golgi



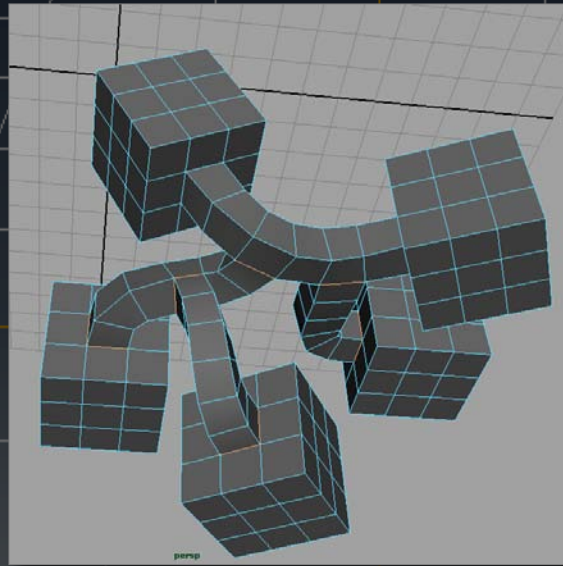


# 3D Modeling

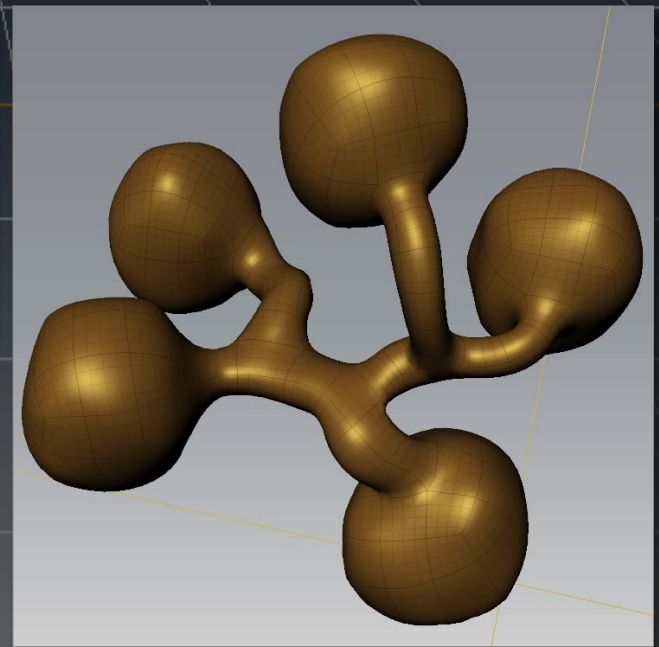
- Golgi apparatus



Primitive shapes



Connection

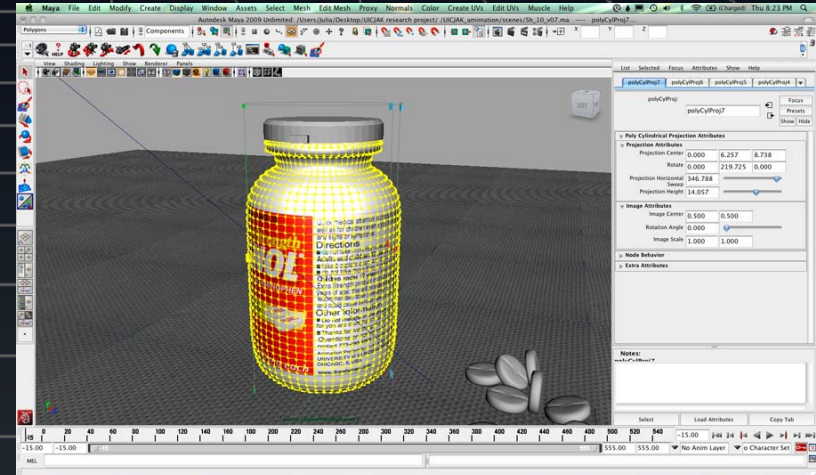


Smoothing

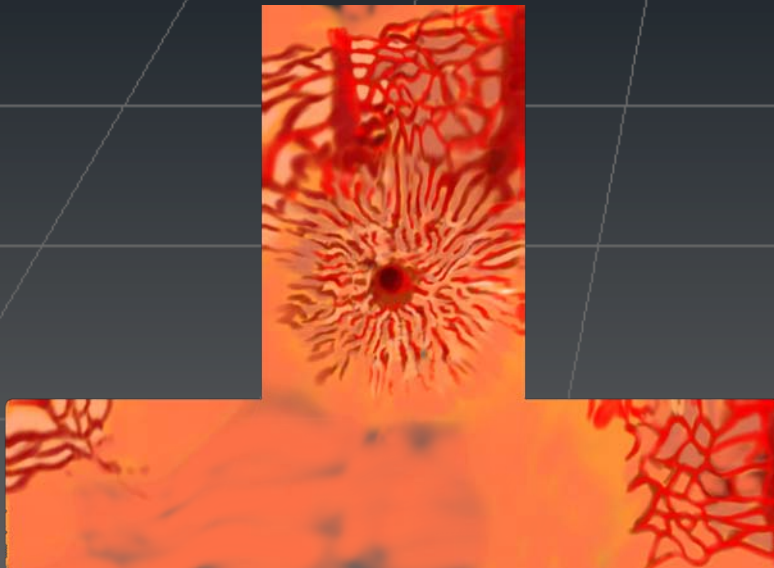
# Texture and Lighting



Bottle label



UV Placement



Unwrapping



Final map paintings

# Production




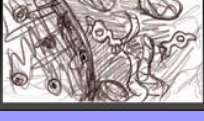
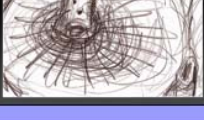
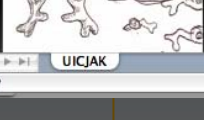
- Shot List
- 3D Animatic
- Rough Cut

# Shot List

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

Script Version: UICJAK\_Script\_v13.doc 864x486 30fps

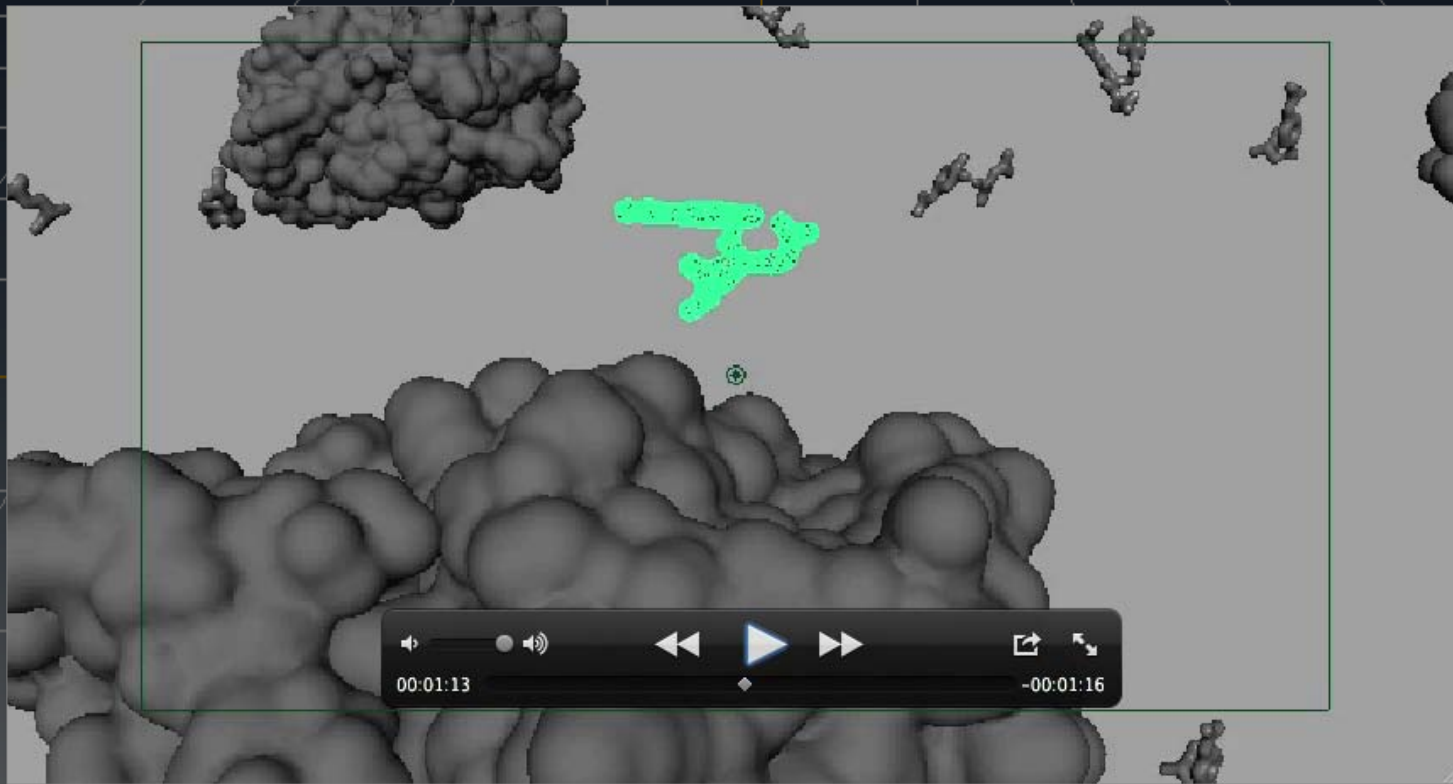
UICJAK\_shotlist\_v03.xls

Status	SHOT	BOARD	SCRIPT	Shot Description	ANIMATION NOTES Camera	Models / Env.	Frame
	50		The situation changes if an excessive amount of APAP enters the system. An overdose of 7-10 grams of APAP in one day...	Camera Animation: Slight Pan Character Animation: Rotation in the Y.	MS	APAP	276
	55		...quickly exhausts the GSH available for NAPQI deactivation.	Camera Animation: N/A Character Animation: Rotation	MS	GSH	122
	60		NAPQI is toxic to cellular proteins and nucleic acids.	Camera Animation: N/A Character Animation: Rotation	Extreme CU	NAPQI	151
	65		Damage to intracellular structures causes irreversible harm to the hepatocyte.	Camera Animation: Hold Character Animation: Slight rotation	CU	Hepatocyte	154
	70		Spreading hepatocyte destruction can lead to hepatic failure and patient death.	Camera Animation: Slight pan and rotation Character Animation: N/A	MS	Liver Lobule	180
	75		There are ways to avoid such consequences. N-acetylcysteine, called NAC is the antidote for APAP.	Camera Animation: Slight pan Character Animation:	MS	NAC, GSH, APAP, NAPQI	429

Ready Sum=0 SCRL CAPS NUM

# 3D Animatic

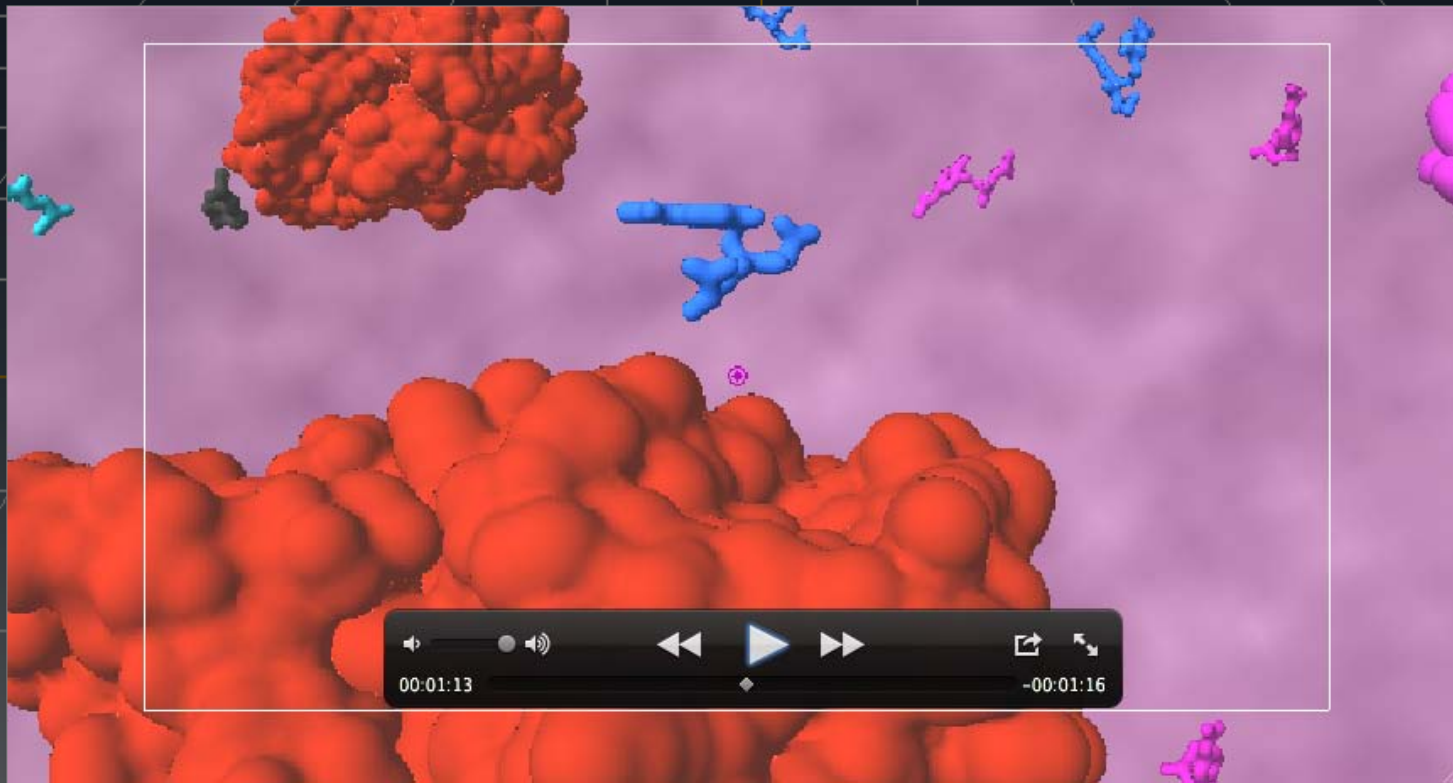
- First pass movie with 3D models





# Rough Cut

- Unrendered movie with final animation

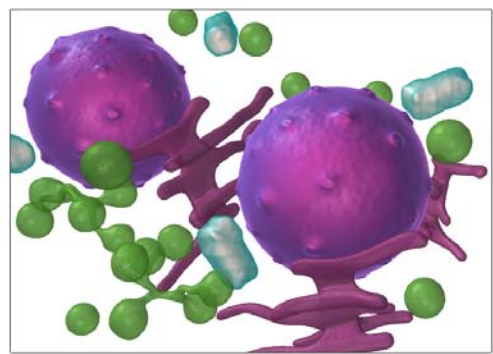


# Post-Production

- Rendering
- Compositing
- VO and music
- Final animation



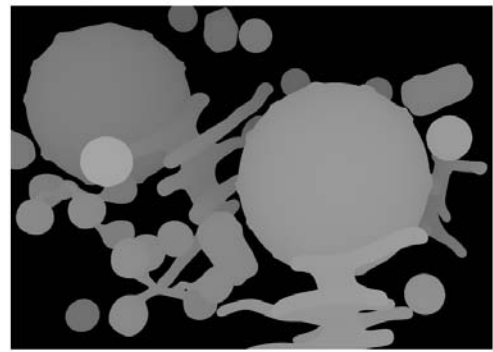
# Rendering



color

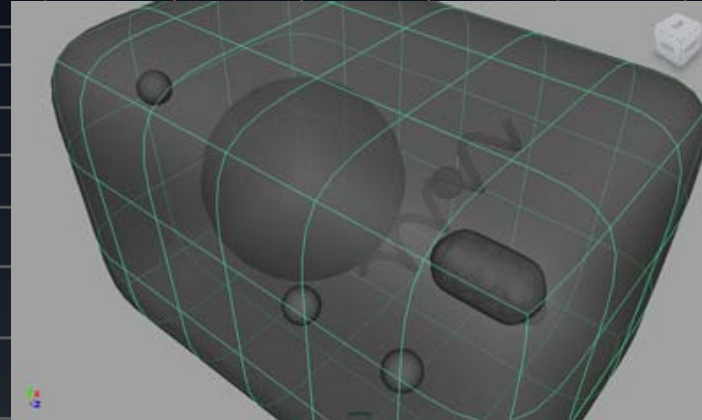


AO

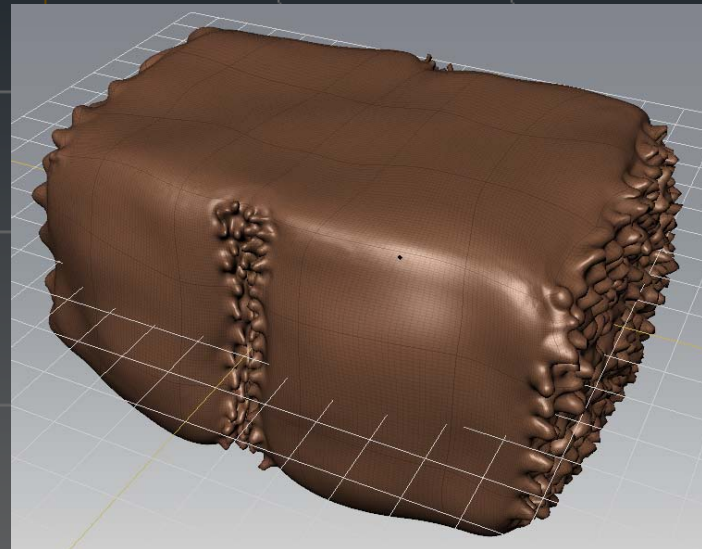


depth

Render passes

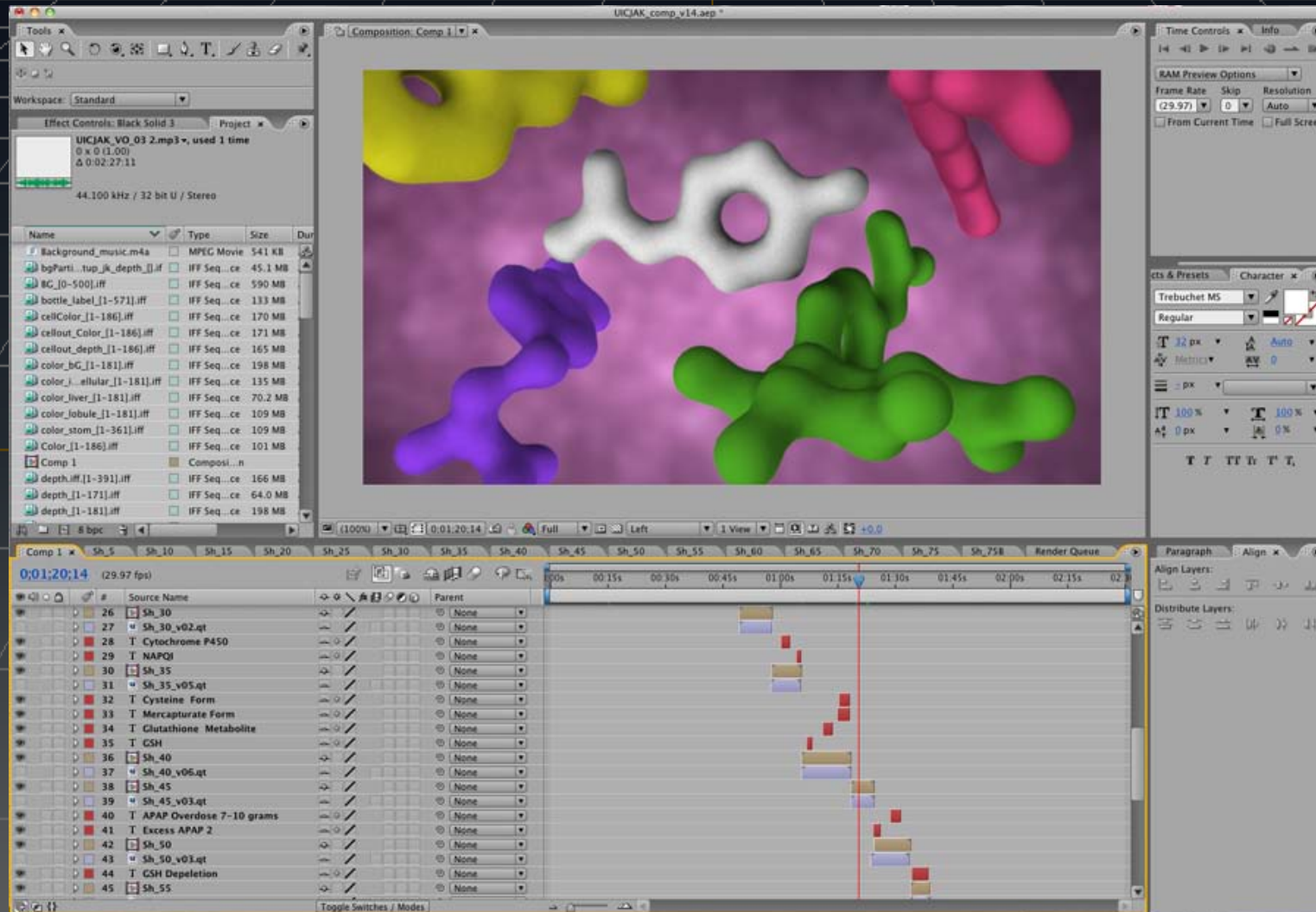


Swap low-resolution...



...for high-resolution

# Compositing



Adobe After Effects

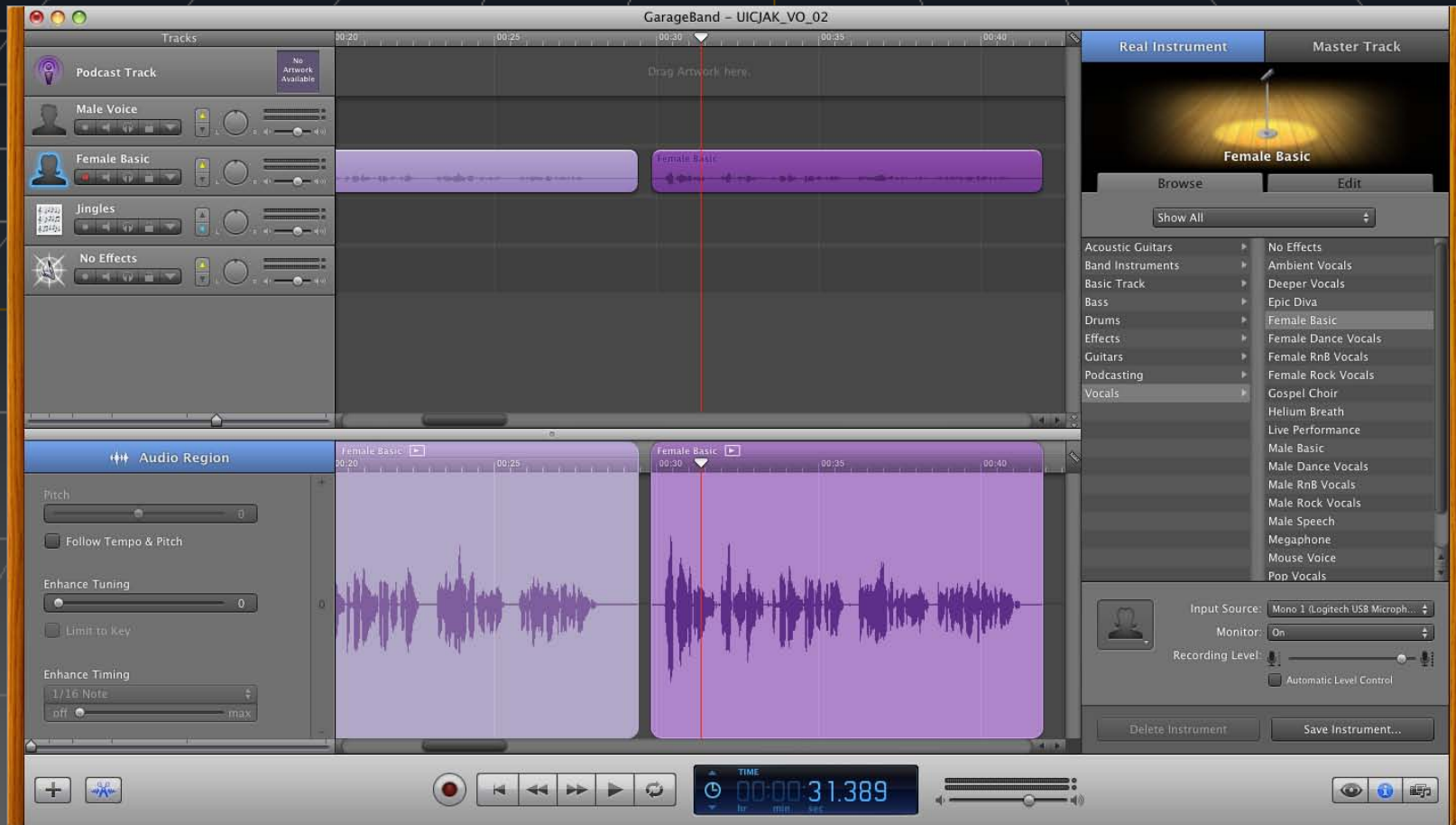
# VO Recording -VO Script

- Pronunciation guide

VO	Pronunciation Guide
<p><b>Acetaminophen</b> or APAP is a widely used medication with <b>analgesic</b> and <b>antipyretic</b> properties.</p> <p>The FDA recommends a maximum dose of 4 grams of APAP per day. Consuming more APAP than recommended can potentially cause severe liver damage.</p> <p>When APAP is taken orally... ...it absorbs rapidly in the upper GI tract.</p> <p>APAP enters the bloodstream and is carried to sites of action.</p> <p>The liver metabolizes APAP and produces metabolites required for function.</p> <p>Many metabolic pathways occur in the liver to rid excess APAP and other substances from the body.</p> <p>APAP is metabolized in the <b>hepatocyte's</b> smooth <b>endoplasmic reticulum</b>.</p> <p>The majority of APAP... ...is conjugated by enzymes into inert <b>sulfate</b> and <b>glucuronide</b> metabolites.</p> <p>An enzyme, <b>cytochrome P450</b>, converts the remaining APAP... ...to NAPQI.</p> <p>NAPQI can be combined with GSH... ...to create an intermediate <b>glutathione</b> metabolite.</p> <p>Further conjugation results in <b>mercapturate</b> and <b>cysteine</b> forms.</p>	<p><u>acet-amin-o-phen</u> ə-,sē-tə-'mi-nə-fən, ,ə-sə-tə-</p> <p><u>an-al-ge-sic</u> \-'jē-zik, -sik\</p> <p><u>an-ti-py-ret-ic</u> \-pī-'ret-ik\</p> <p><u>he-pa-to-cyte</u> hi-'pat-ə-,sīt</p> <p><u>en-do-plas-mic</u> ,en-də-'plaz-mik</p> <p><u>re-tic-u-lum</u> ri-'tik-yə-ləm</p> <p><u>sul-fate</u> 'sol-,fāt</p> <p><u>gluc-uro-nide</u> glū-'kyur-ə-,nīd</p> <p><u>cy-to-chrome</u> 'sīt-ə-,krōm</p> <p>P four fifty</p> <p><u>glu-ta-thi-one</u> ,glūt-ə-'thī-,ōn</p> <p>mer-cap-TUR-ate</p> <p><u>cys-teine</u> 'sis-tə-,ēn</p>

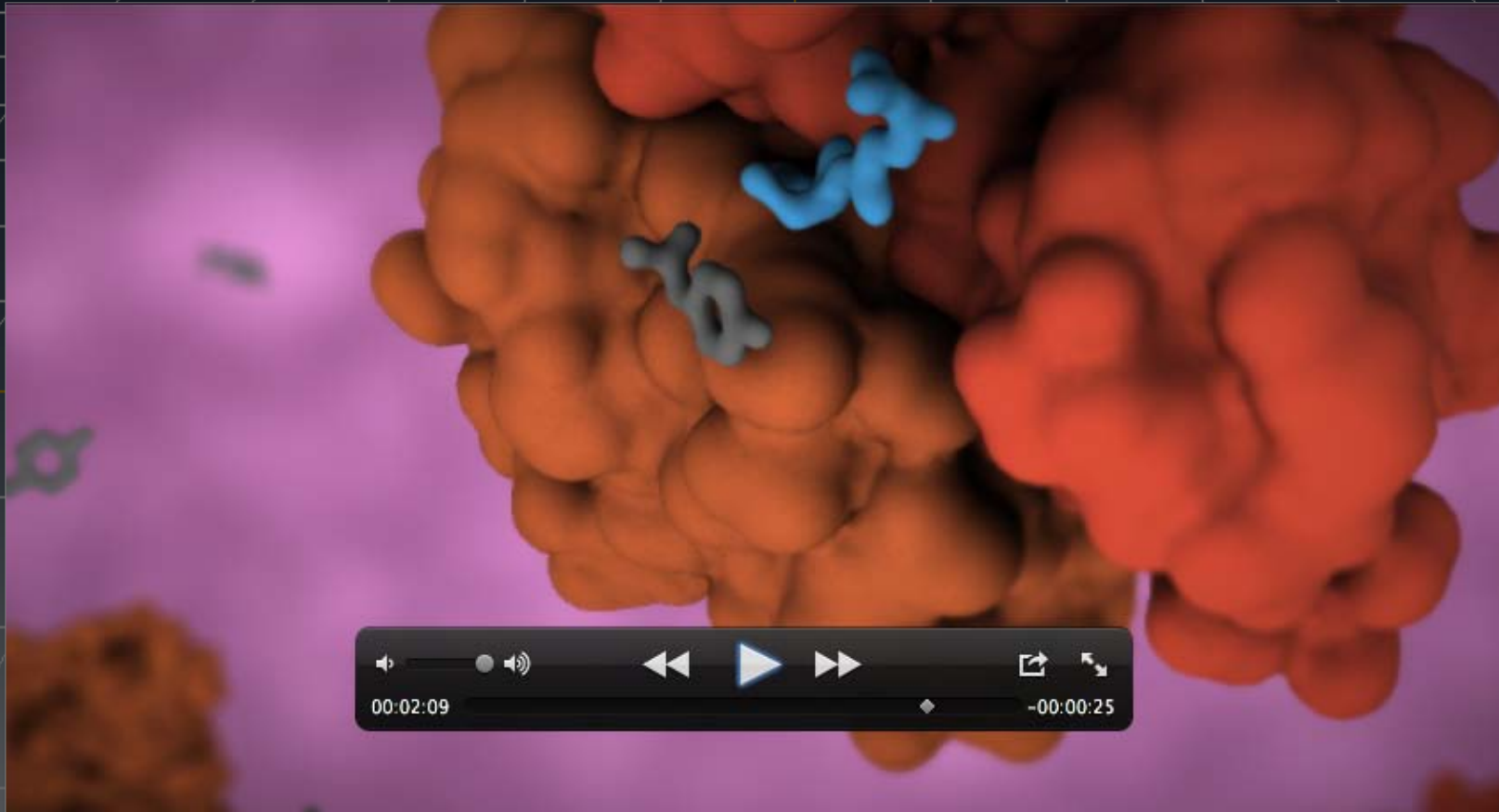
# VO Recording

- Apple Garage Band
- Podcast recording settings





# Final Animation

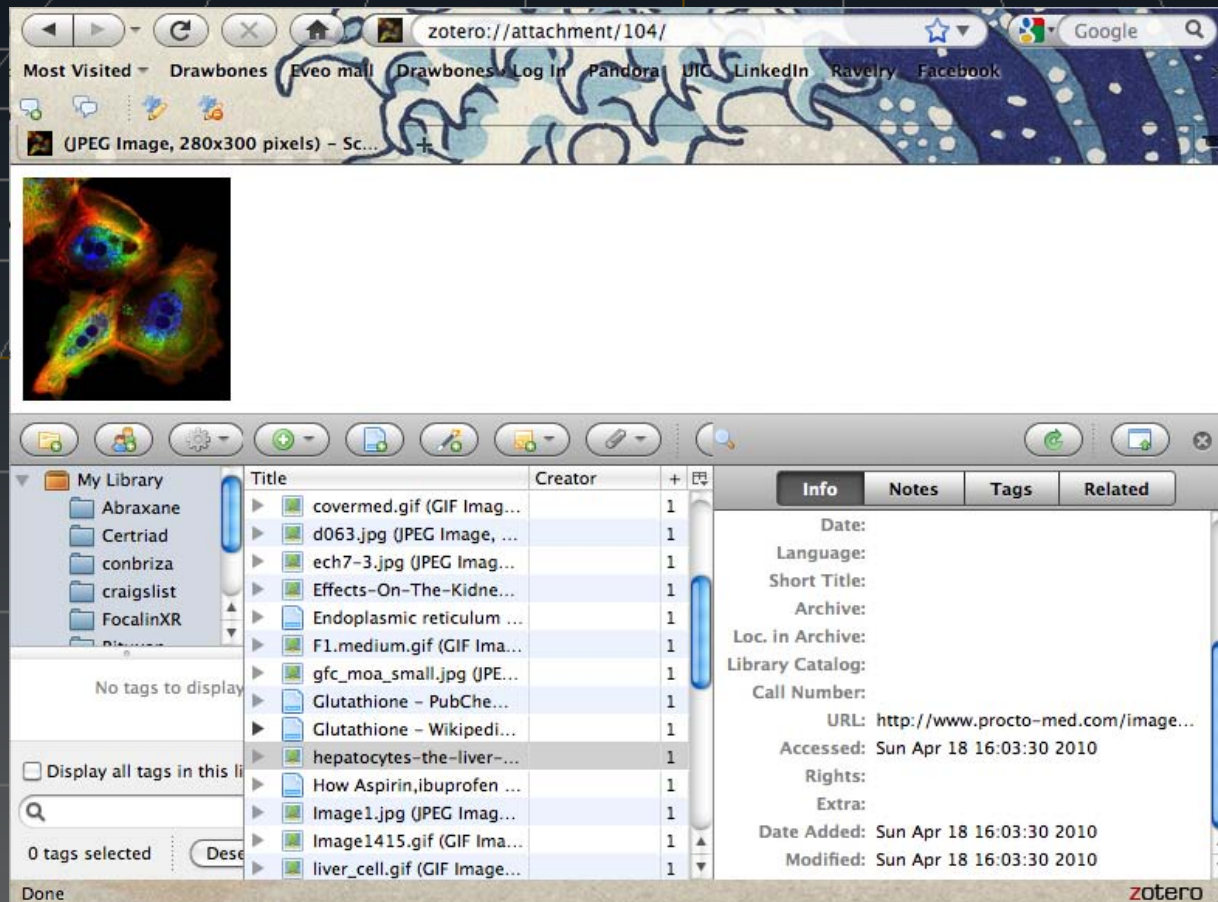


# Project Management

How to organize a project!

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

- Tracker of online references and images



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

- PDF organizer and search tool



The screenshot displays the Papers application window. The left sidebar contains a 'LIBRARY' section with a list of papers, including 'Does therapeutic use of acetaminophen cause acute liver failure?' by Richard C Dart, Elise Bailey. Below the library is a 'DEVICES' section with 'Papers for iPad' and a 'REPOSITORIES' section with various sources like ACM, ADS, arXiv, etc. The main window shows the details of the selected paper, including the title 'ORIGINAL RESEARCH ARTICLE Does Therapeutic Use of Acetaminophen Cause Acute Liver Failure?', authors 'Richard C. Dart, M.D., Ph.D., and Elise Bailey, M.S.P.H.', and a summary of the study objective and design. The bottom of the window shows a toolbar with options like 'Read Fullscreen', 'Open PDF', 'Open URL', 'Email', 'Print', and 'View Mode'. The status bar at the bottom indicates '1 of 131 papers selected'.

**ORIGINAL RESEARCH ARTICLE**

## Does Therapeutic Use of Acetaminophen Cause Acute Liver Failure?

Richard C. Dart, M.D., Ph.D., and Elise Bailey, M.S.P.H.

**Study Objective.** To compare the reported occurrence of liver failure in subjects in prospective trials with that in patients in retrospective reports after repeated use of therapeutic dosages of acetaminophen.

**Design.** Systematic review of the medical literature.

**Data Source.** MEDLINE and EMBASE biomedical and pharmacologic databases.

**Subjects.** Adults who received repeated dosing of acetaminophen 4 g/day or lower for at least 24 hours.

**Does therapeutic use of acetaminophen cause acute liver failure?**

Richard C Dart, Elise Bailey

Rocky Mountain Poison and Drug Center, Denver Health and Hospital Authority, Denver, Colorado 80204, USA. rdart@rmpdc.org

**STUDY OBJECTIVE:** To compare the reported occurrence of liver failure in subjects in prospective trials with that in patients in retrospective reports after repeated use of therapeutic dosages of acetaminophen. **DESIGN:** Systematic review of the medical literature. **DATA SOURCE:** MEDLINE and EMBASE biomedical and pharmacologic databases. **SUBJECTS:** Adults who received repeated dosing of acetaminophen 4 g/day or lower for at least 24 hours. **MEASUREMENTS AND MAIN RESULTS:** Articles written in several languages were abstracted by trained personnel using a structured abstraction form. Data were categorized by methodology (prospective vs retrospective), acetaminophen dosage, and type of liver effect. A total of 791 articles were identified, which included 30,865 subjects in prospective studies and 9337 patients in retrospective reports. The prospective studies reported no cases of fulminant hepatic injury, liver transplantation, or death due to acetaminophen. Of the 30,865 subjects in these studies, 129 (0.4%) were identified who had a serum aminotransferase level that exceeded the upper limit of normal, including 61 subjects in randomized trials in which the proportion of serum aminotransferase level increase was the same as or less than that in the placebo group and 68 subjects in trials without a placebo group. In addition, 4263 (13.8%) received the maximum recommended therapeutic dosage (3.9–4 g/day). In the retrospective reports, 96 patients (1.0%) had a serum alanine aminotransferase level that exceeded the upper limit of normal, one (0.01%) underwent liver transplantation, and six (0.06%) died. Causality relationship of acetaminophen for each retrospective case was assessed with the Naranjo adverse drug reaction probability scale. The mean  $\pm$  SD Naranjo score for all 103 retrospective cases was  $3.2 \pm 1.9$ , indicating a possible relationship between the increased aminotransferase levels and acetaminophen use. Some retrospective reports contained information suggesting that the patient had ingested an overdose, a history of therapeutic use. **CONCLUSION:**

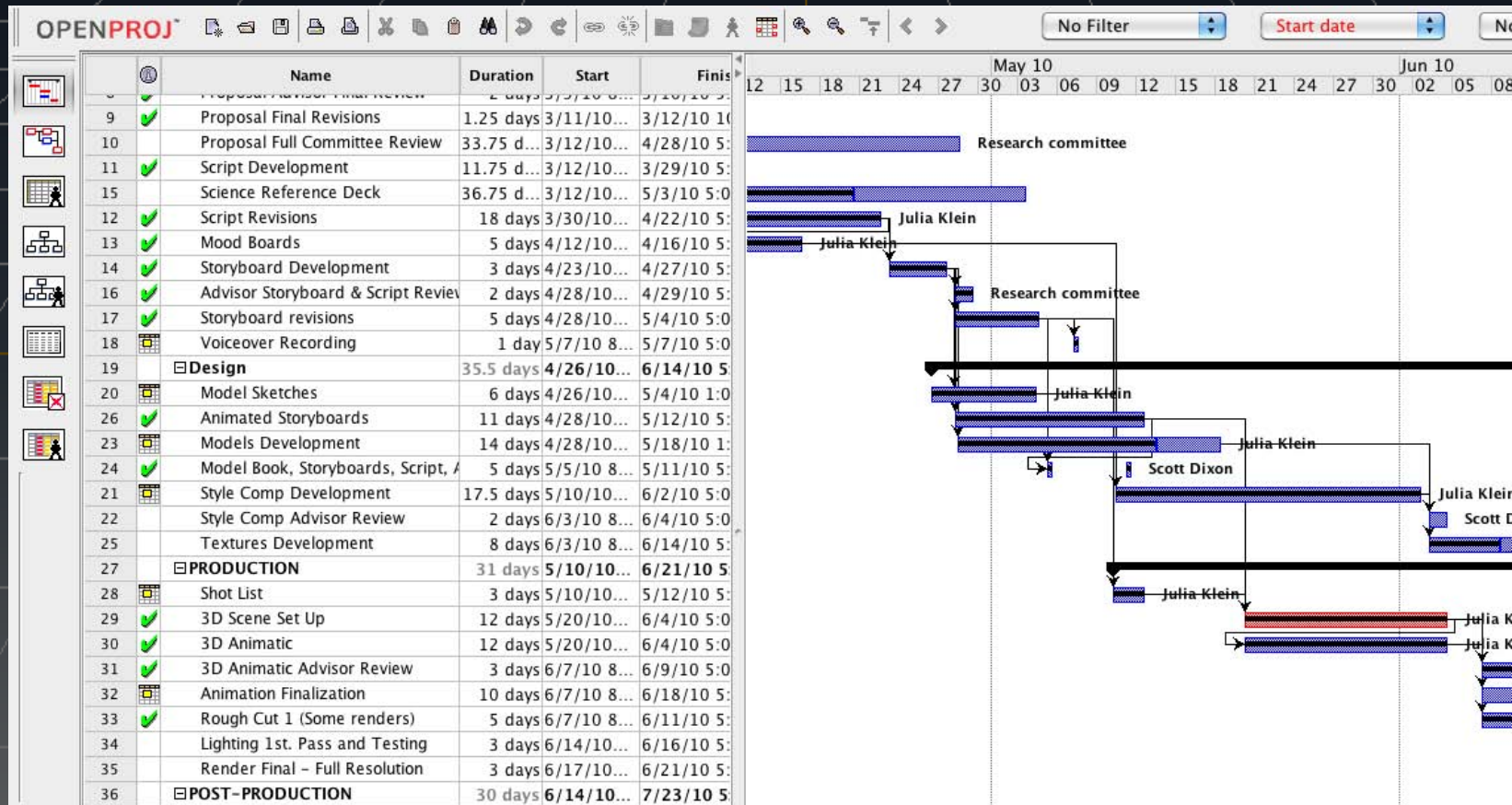
PubMed ID: 17723075

Pharmacotherapy2007Dart.pdf  
105.2 KB



# OpenProj <http://openproj.org/>

- Timeline manager



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

## Project Research on Acetaminophen Metabolization and Hepatotoxicity

Hello everyone,

Please look over these files. I'll provide updates soon. Let me know what you think.

Thanks for looking,

Julia A. Klein

[julia@drawbones.com](mailto:julia@drawbones.com)

### Animation Development Files

[Proposal](#) - word doc file

[Script](#) - PDF file

[Storyboards](#) - PDF file

[Mood Boards](#) - PDF file

[Model Book](#) - PDF file

[Concept Art](#) - PDF file

[Shot List](#) - PDF file

[Project Schedule](#) - PDF file

[Project Paper Draft](#) - PDF file

**Project Presentation Slides** - Coming Soon!

**Project Presentation Handouts** - Coming Soon!

**Final Animation** - Coming Soon!

**Final Rough Cut** - on YouTube



**Rough Cut 1** - on YouTube



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

# 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

# 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





# Questions?

[julia@drawbones.com](mailto:julia@drawbones.com)

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