Pattern analysis of mouse liver: Morphological effects of gender, aging and diet

(doing Science with OME)

open microscopy environment

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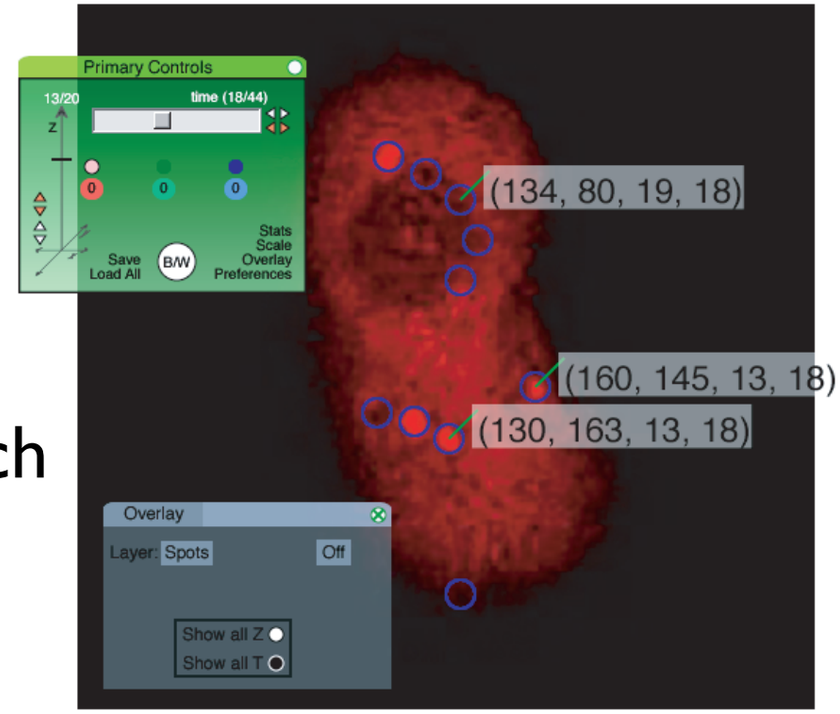
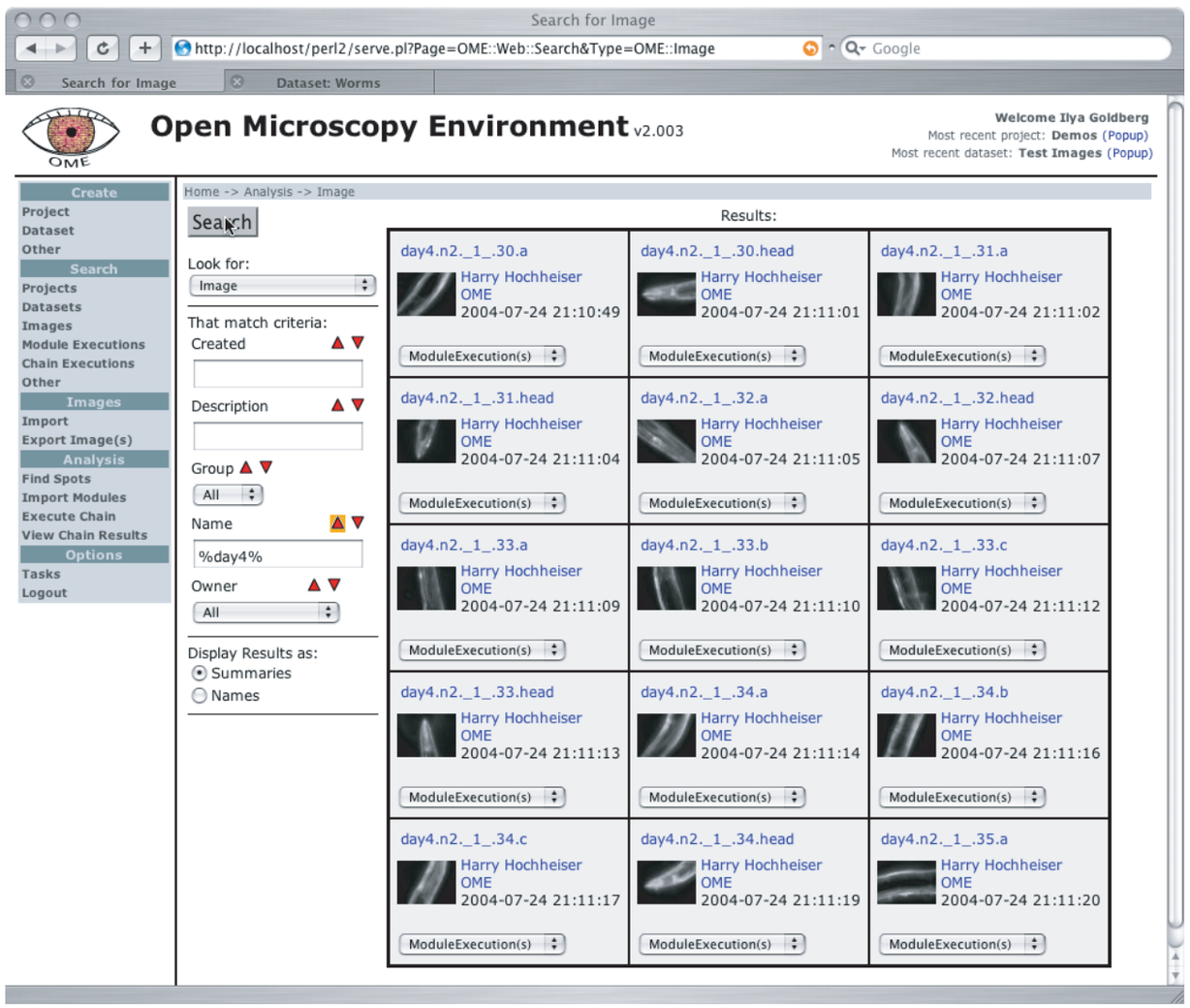
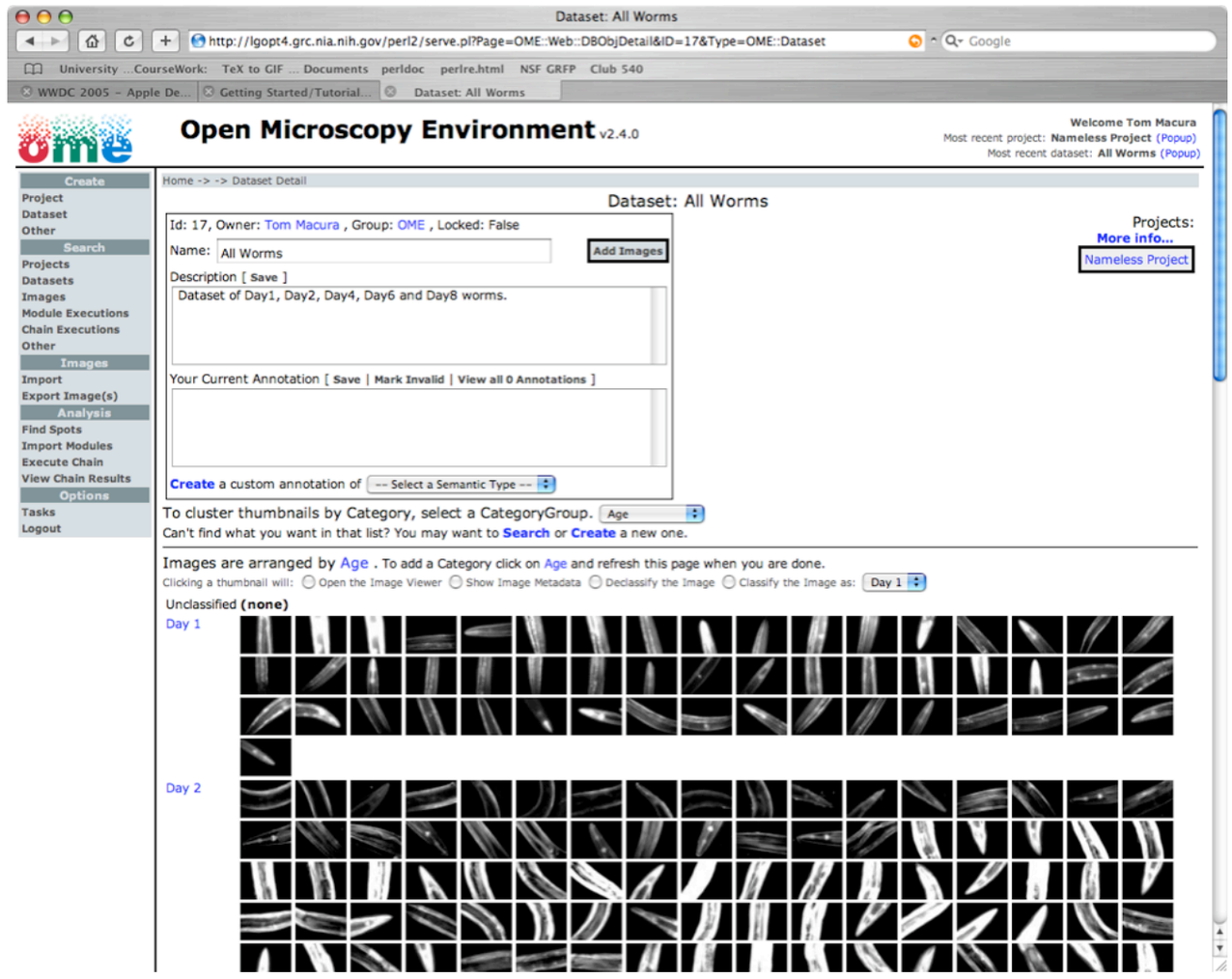
Made in USA

OME for Image Management

OME is a centralized image management solution enabling scientists to store, view, annotate, and search their and their collaborators' microscopy images.



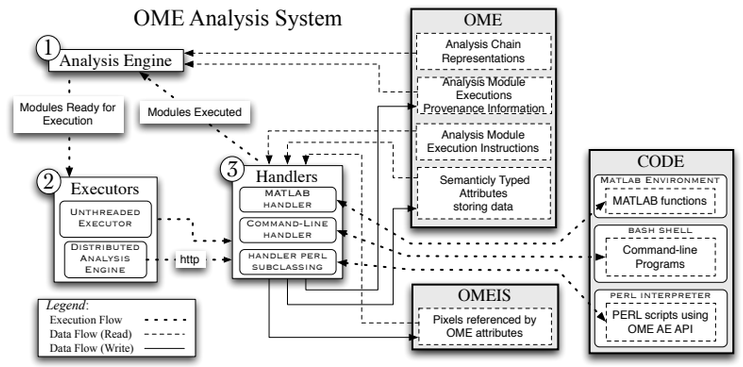




OME for Quantitative Analysis

- Modeling Workflows in OME:
  - Semantic Types are OME's extensible ontology for data-modeling.
  - Analysis Modules are an language-independent, modular, re-usable computational algorithm representation.
  - Groups of analysis modules can be combined, by linking their inputs/ outputs, into OME Analysis Chain workflows.

- Executing Workflows in the OME Analysis System
  - The Analysis System provides managed algorithm execution (discussed later)



Complicated Schematic of the OME Analysis System

OME + WND-CHARM

OME = Informatics Platform for Visual Assays

WND-CHARM = Pattern Analysis to Score Visual Assays

OME + WND-CHARM = End to End Solution for High Throughput Imaging

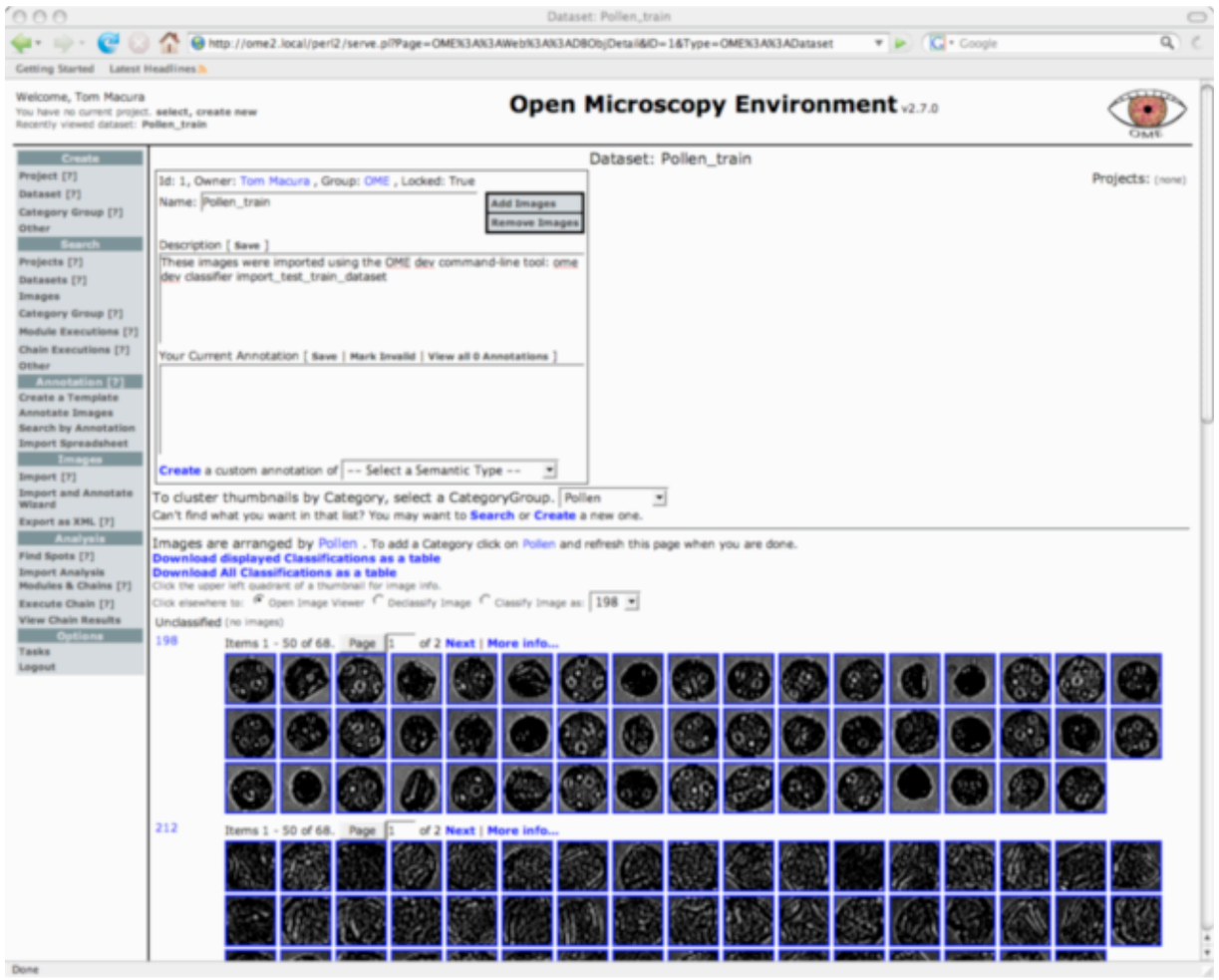
Integration of OME with WND-CHARM was finished in March.

Public Announcement to OME developers' lists was made on April 2nd.

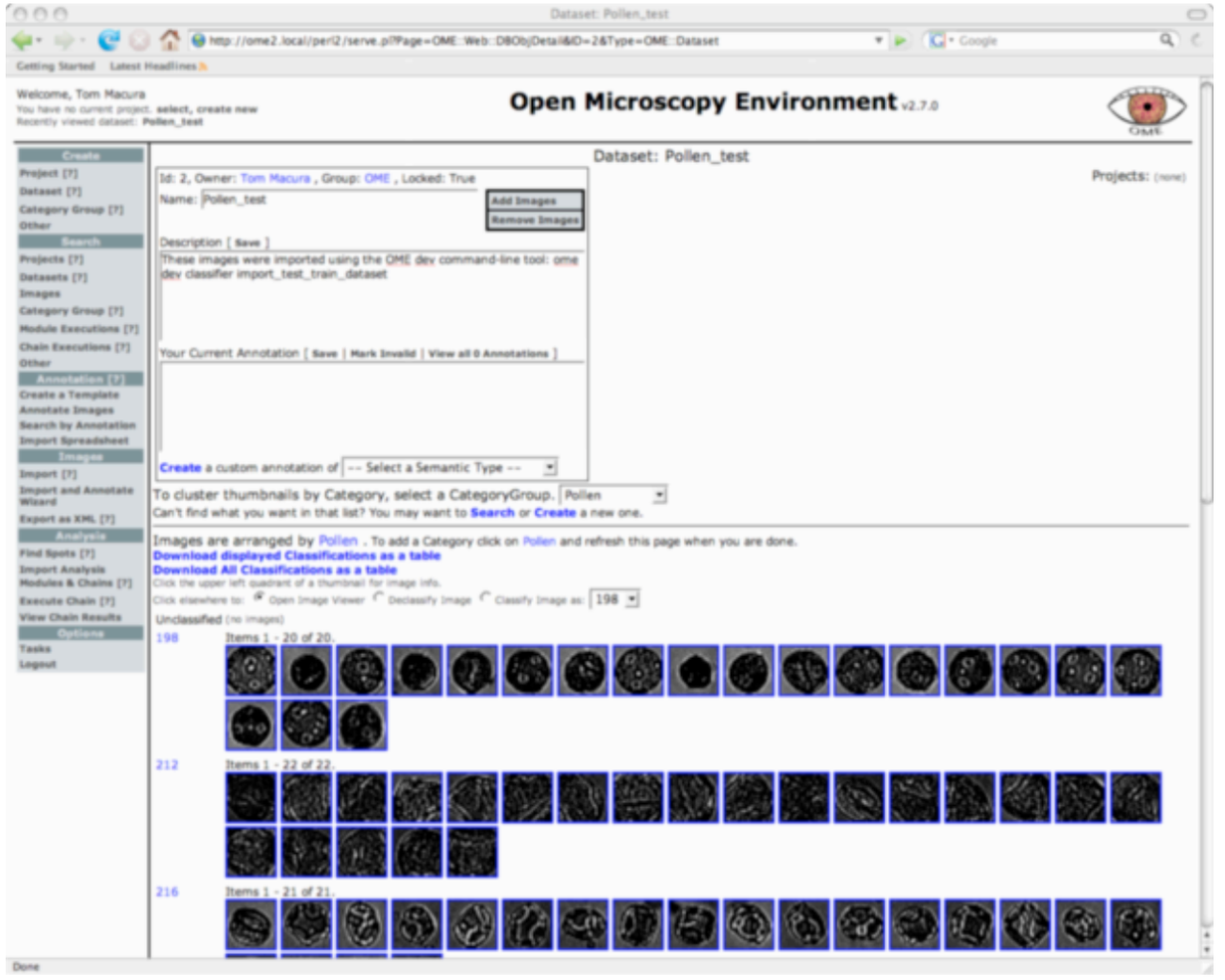
The "Full" OME+WND-CHARM release will use Lior's C/C++ implementation, eliminating the dependence on MATLAB.

OME+WND-CHARM (screenshots)

Training Pollen images with known categories



Pollen images predictions made with WND-CHARM



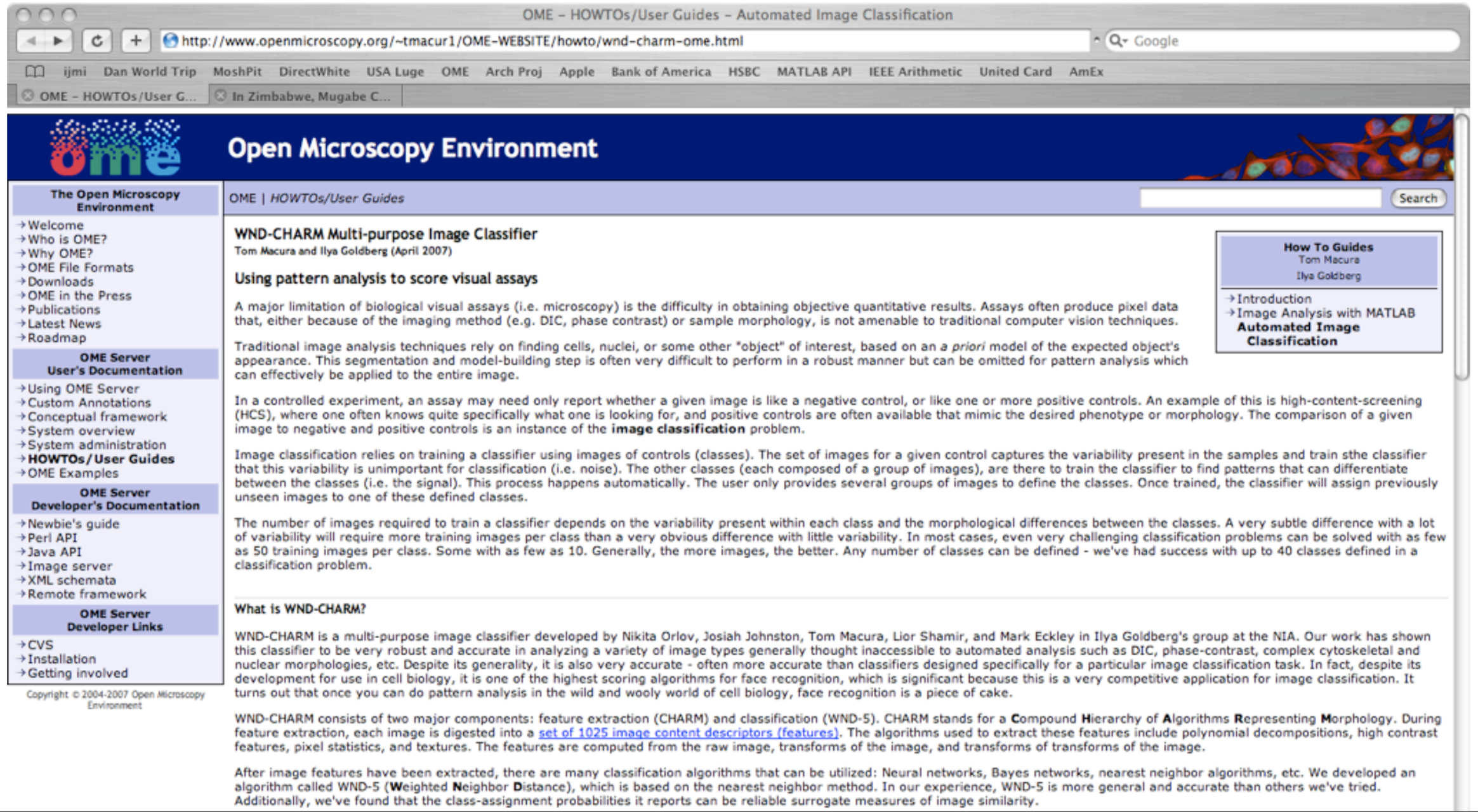
Several Command-Line Scripts Later

OME+WND-CHARM (How-To)

Step-by-step instructions for using OME+WND-CHARM are available on-line:

http://www.openmicroscopy.org/~tmacur1/OME-WEBSITE/howto/wnd-charm-ome.html

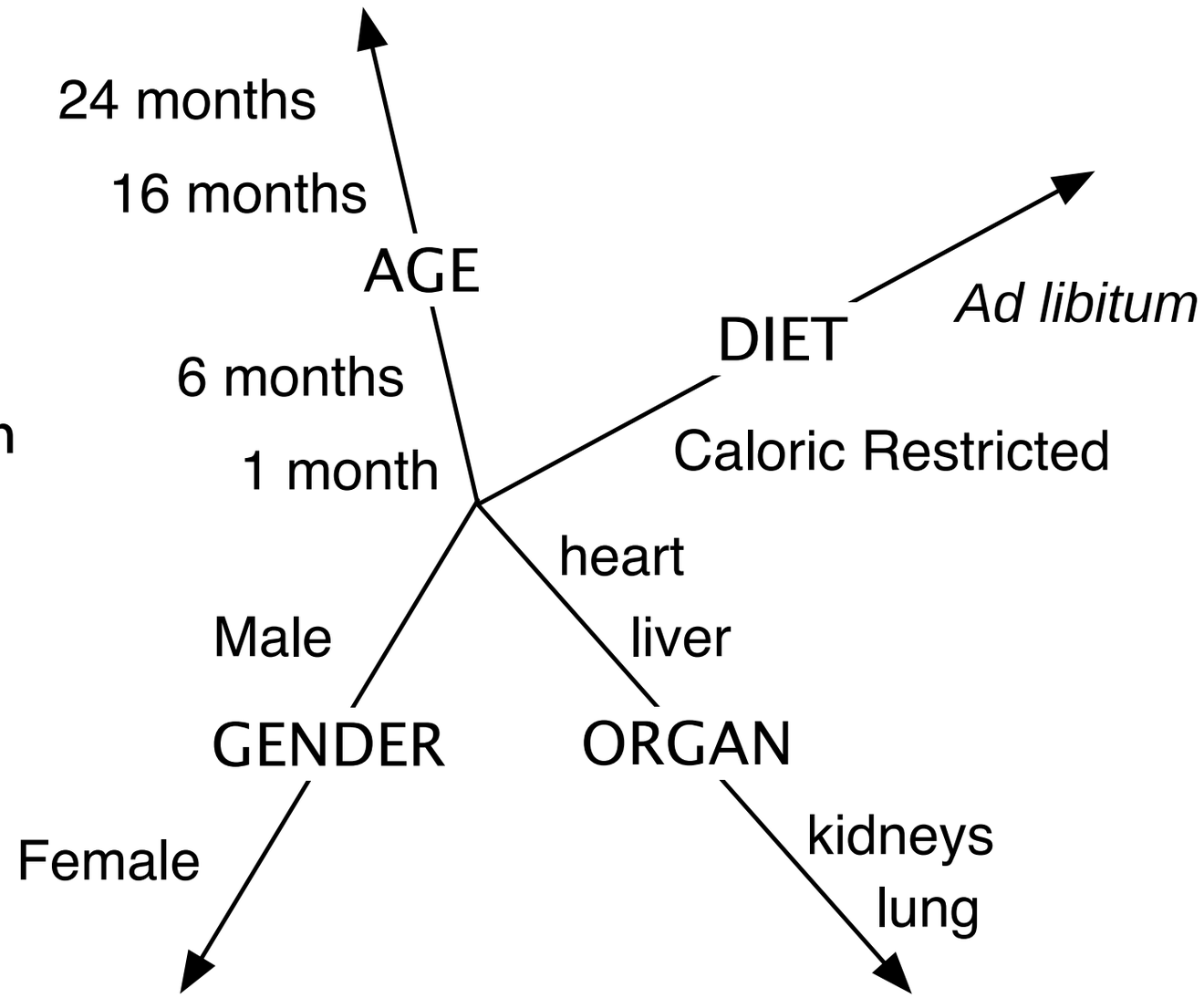
By following the How-To's instructions, Lior has reproduced my results.



AGEMAP

- AGEMAP (*Atlas of Gene Expression in Mouse Aging Project*)
  - initiated to investigate molecular bio-markers of aging and diet
  - 3 mice per data-point (gender, age, diet). 48 mice in total
  - individual organs were harvested, sectioned, stained and put on slides
  - we are using the tissue sections to search for structural biomarkers of aging and diet

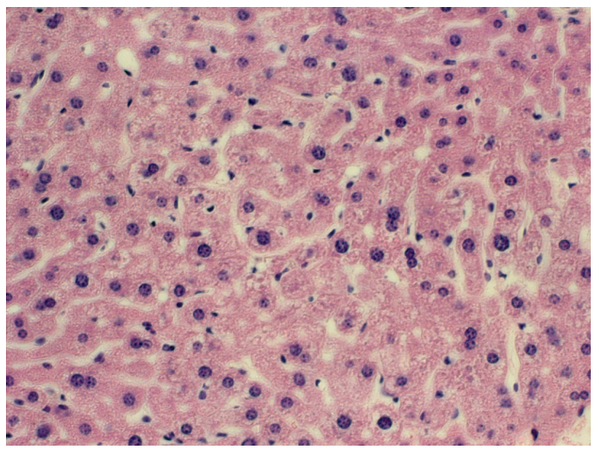
- our initial investigations focus on livers because it is a uniform tissue that is expected to display age effects
- but our future plans are to analyze all organs.



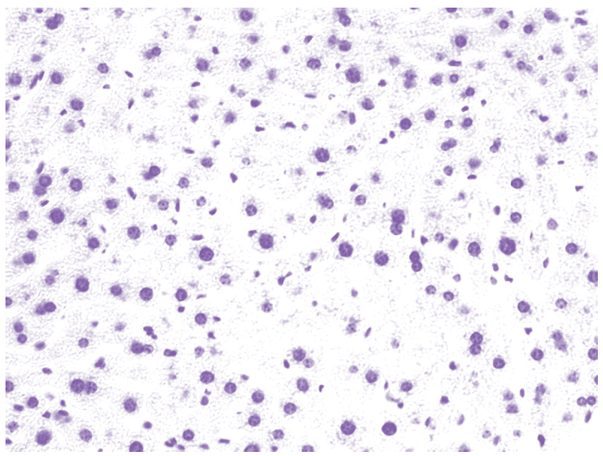
Collecting AGEMAP Images

- 29 mouse livers, sectioned and stained with H&E
- ~50 RGB images of each liver acquired at 40x. Each image is 1388x1040 pixels with 12bits of quantization.

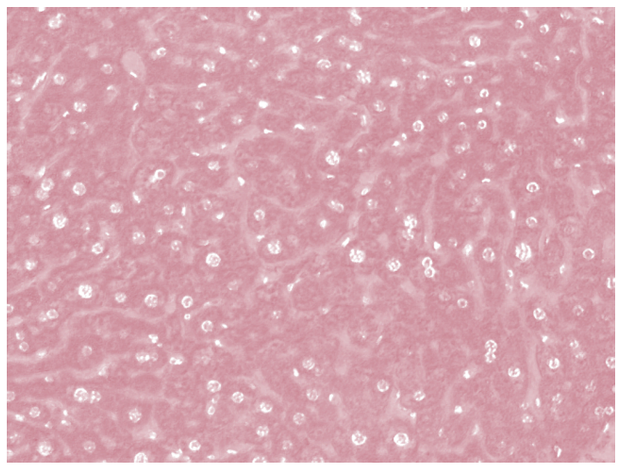
- "Colour Deconvolution" was used to convert camera's Red, Green, Blue channels into "Hematoxylin" and "Eosin" channels.



Original RGB Image



Computed Hematoxylin Channel



Computed Eosin Channel

- Images were divided into 4x4 tiles and CHARM signatures were computed separately on tiles' H and E components.

Quantitative Analysis of AGEMAP requires BIG!! Machinery

- Organizational Challenges:
  - 29 Mice => 1500 RGB Images => 3000 H&E Images => 50,000 tiles => 50 million "Features"
  - All 50 million features need to be mapped to meta-data (Mouse ID, Image ID, Age, Diet, Gender) that is essential to data analysis

- Computational Challenges:
  - 8GB of raw pixels => 125 GB of 'computed pixels' (e.g. Fourier/ Wavelet/Chebysev transforms)
  - Each tile takes approximately 22 seconds to calculate signatures => 275 hours in total (using 6 processors!).

- OME's "managed analysis", and a network of computers, are essential to dealing with current challenges that will grow 5x as we proceed to analyze other organs. --- *50 days of 24-7 computation and 600 GB of disk space.*

After all the data processing, we have preliminary results

WND-CHARM detects structural differences between Male and Female livers

- Classifiers were trained on age/diet matched Male and Female mice (2560 tiles).
- Remaining tiles were used for testing.
- The training/testing splits were done per image (so all tiles for a particular image were either used for testing or training).

1 Months AL: **93%**

	Female	Male
Female	276	44
Male	9	311

16 Months AL: **95%**

	Female	Male
Female	1269	43
Male	31	289

6 Months AL: **95%**

	Female	Male
Female	466	14
Male	33	447

24 Months AL: **86%**

	Female	Male
Female	430	82
Male	52	412

WND-CHARM detects structural changes in mouse livers that are due to aging

- Classifiers were trained on ad-libitum mouse by age classes.
- Male and Female mice were analyzed separately (5120 training tiles).

Female AL: **70%**

	1 Month	6 Months	16 Months	24 Months
1 Months	**270**	34	16	0
6 Months	69	**855**	131	65
16 Months	114	149	**1022**	27
24 Months	126	303	150	**573**

Male AL: **70%**

	1 Month	6 Months	16 Months	24 Months
1 Months	**276**	28	10	6
6 Months	67	**931**	80	42
16 Months	4	40	**273**	3
24 Months	37	95	149	**823**

- When we performed randomized Negative Controls we obtained expected results.

WND-CHARM detects structural differences between CR and AL livers

- We only have complete CR data points for 6 and 16 Month Female mice (1293 training tiles).

6 Months F: **88%**

	AL	CR
AL	404	76
CR	43	485

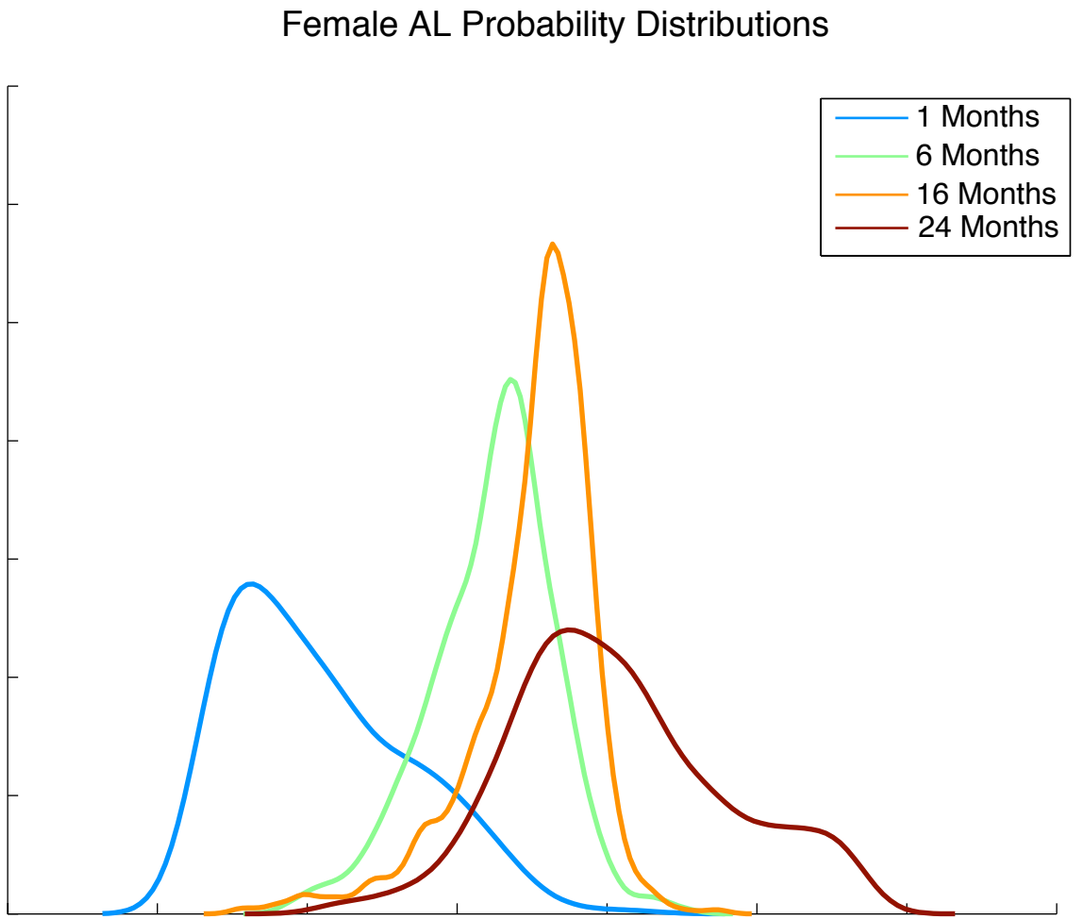
16 Months F: **95%**

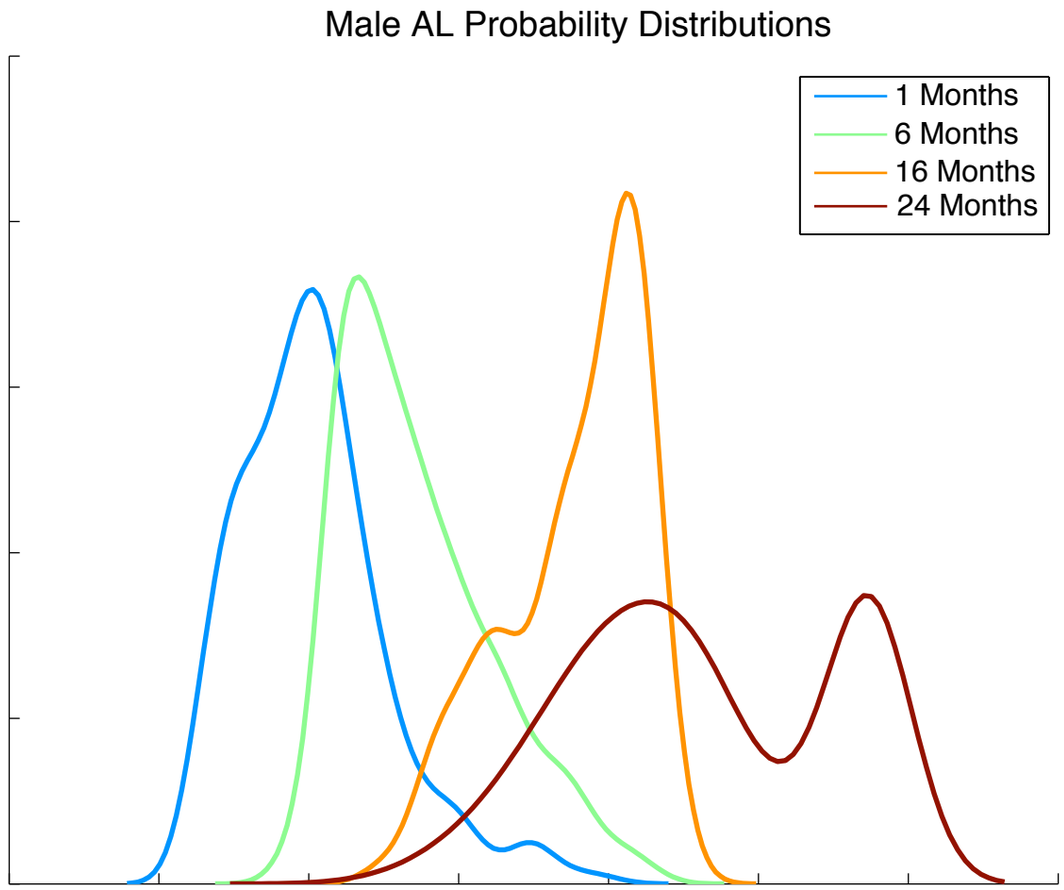
	AL	CR
AL	1219	80
CR	6	317

- When we performed randomized Negative Controls we obtained expected results.

WND-CHARM Similarity Measure

- We've applied Josiah's Image Similarity tools to AGEMAP data
- There appear to be three states of aging





WND-CHARM Similarity Measure

- Female CR livers appear younger than Female AL livers.