A background image showing several cells in a fluorescence microscopy format. The cells are stained with different fluorescent dyes, appearing in red, green, and blue colors against a dark background. The text is overlaid on this image.

# **OMERO.searcher: extensible, cross-platform content-based image search**

Ivan E. Cao-Berg

Murphy Lab

Ray & Stephanie Lane Center for Computational Biology

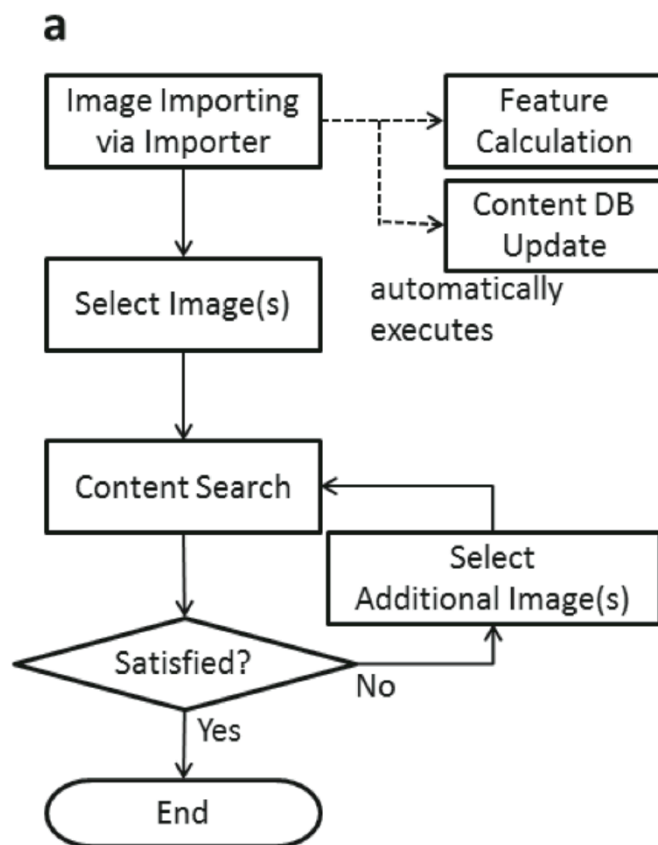
School of Computer Science

Carnegie Mellon University

# Content-based Image Search

- Also called Query-by-image-content (QBIC)
- Find images whose content, as reflected by image features, is similar to one or more query images
- Can use positive and/or negative examples
- Can be iterative (relevance feedback)

# OMERO.searcher Workflow





# OMERO.searcher: content-based image search for microscope images

Baek Hwan Cho, Ivan Cao-Berg, Jennifer Ann Bakal & Robert F Murphy

[Affiliations](#) | [Corresponding author](#)

*Nature Methods* **9**, 633–634 (2012) | doi:10.1038/nmeth.2086

Published online 28 June 2012

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To the Editor:

Fluorescence microscopy is growing dramatically both in terms of technical capabilities and the volume of images generated. Online repositories have been created to provide public access to images and opportunities for joint research for many scientists<sup>1</sup>. This has reintroduced challenges faced when sequence and structure databases were being established: developing fast and

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## Selected feature

### Fluorescent proteins and sensors: A practical discussion

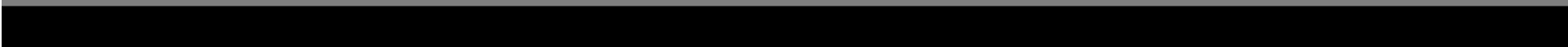


#### Fluorescent proteins and sensors webinar

Robert Campbell, David Piston and Thomas Knopfel  
Fluorescent proteins are invaluable tools for  
fluorescent microscopy in the life sciences but  
researchers still have practical questions about

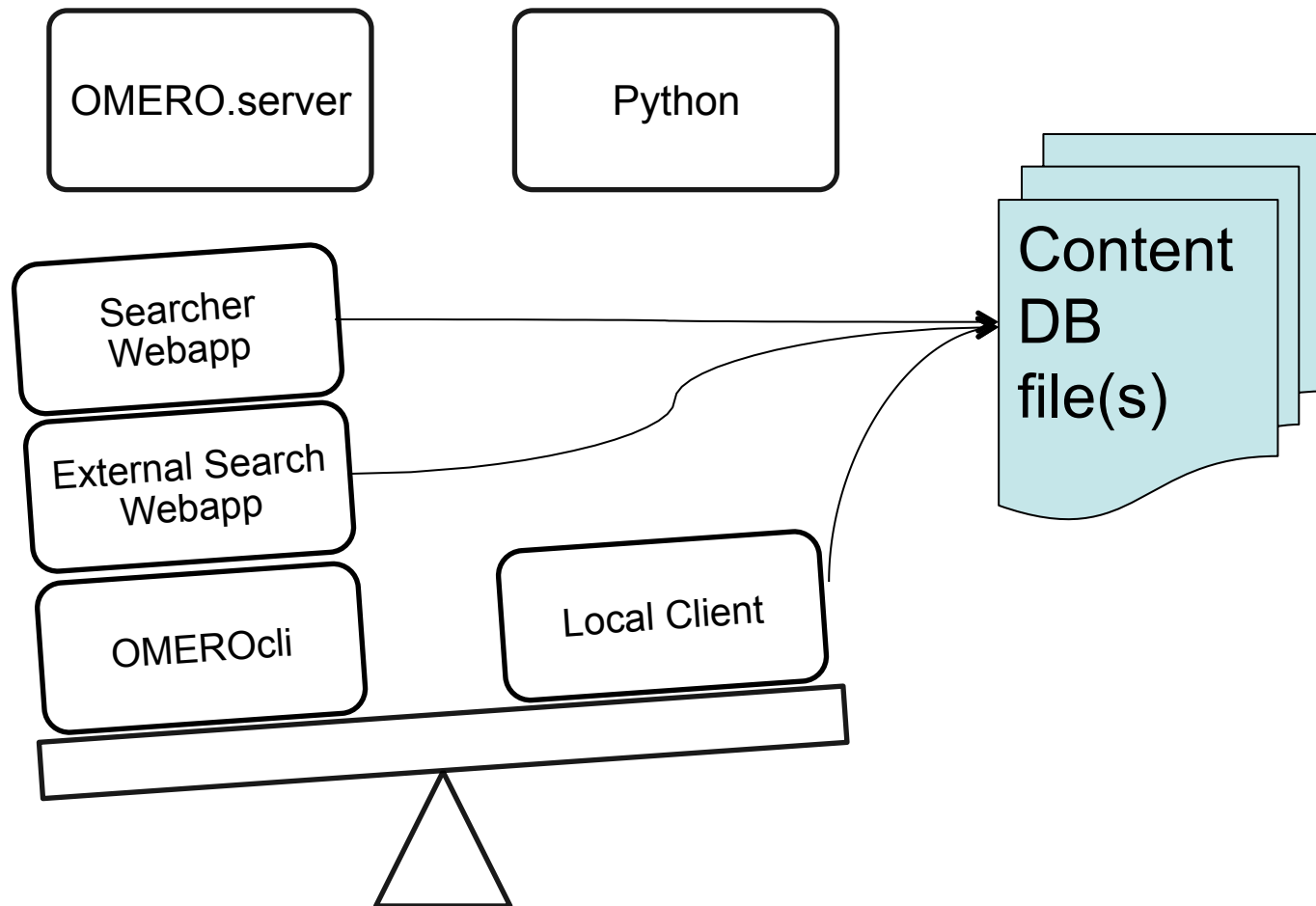


# OMERO.searcher ContentDB

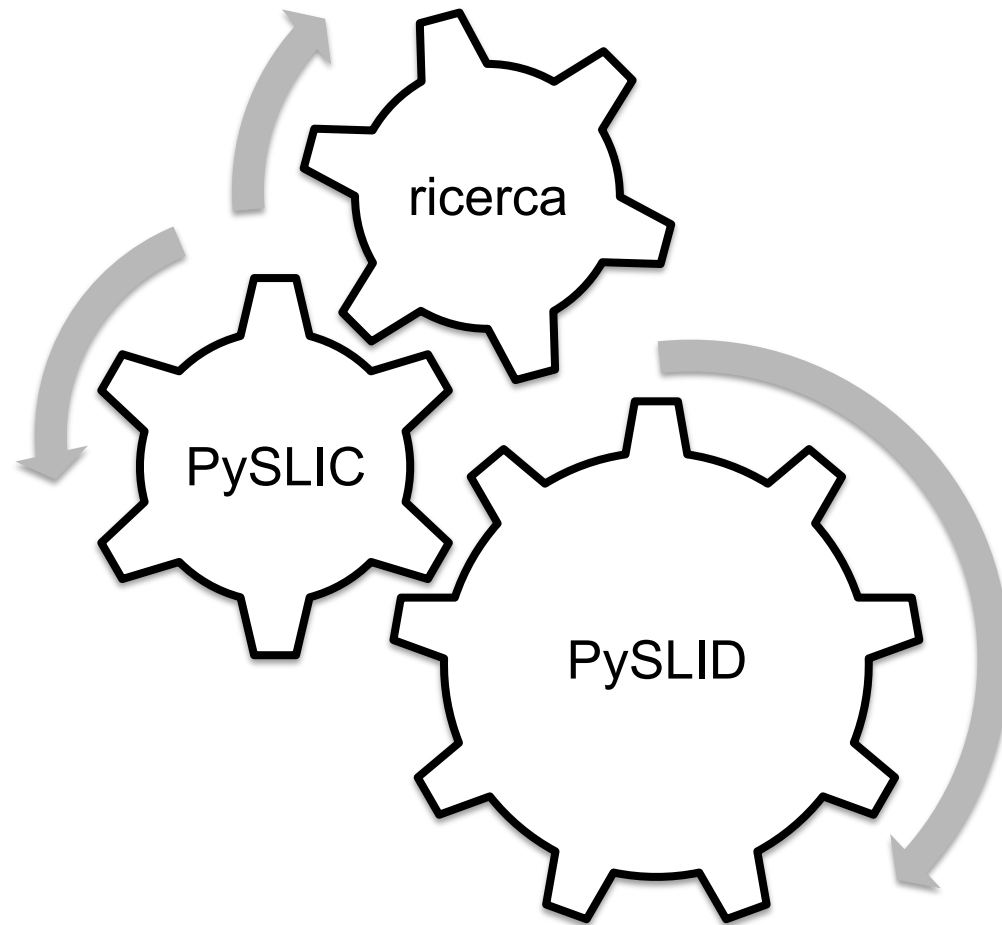
- **ContentDB** key to content searching
  - Contains features describing each image in a database and links to the image and its annotations
  - Supports any feature set if Python code is provided for calculating it
  - Portable
- 



# Components

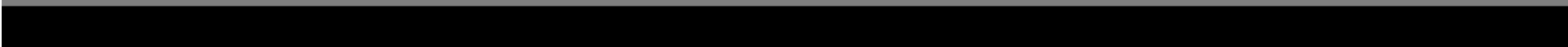


# OMERO.searcher Python libraries





# Python Libraries Updates

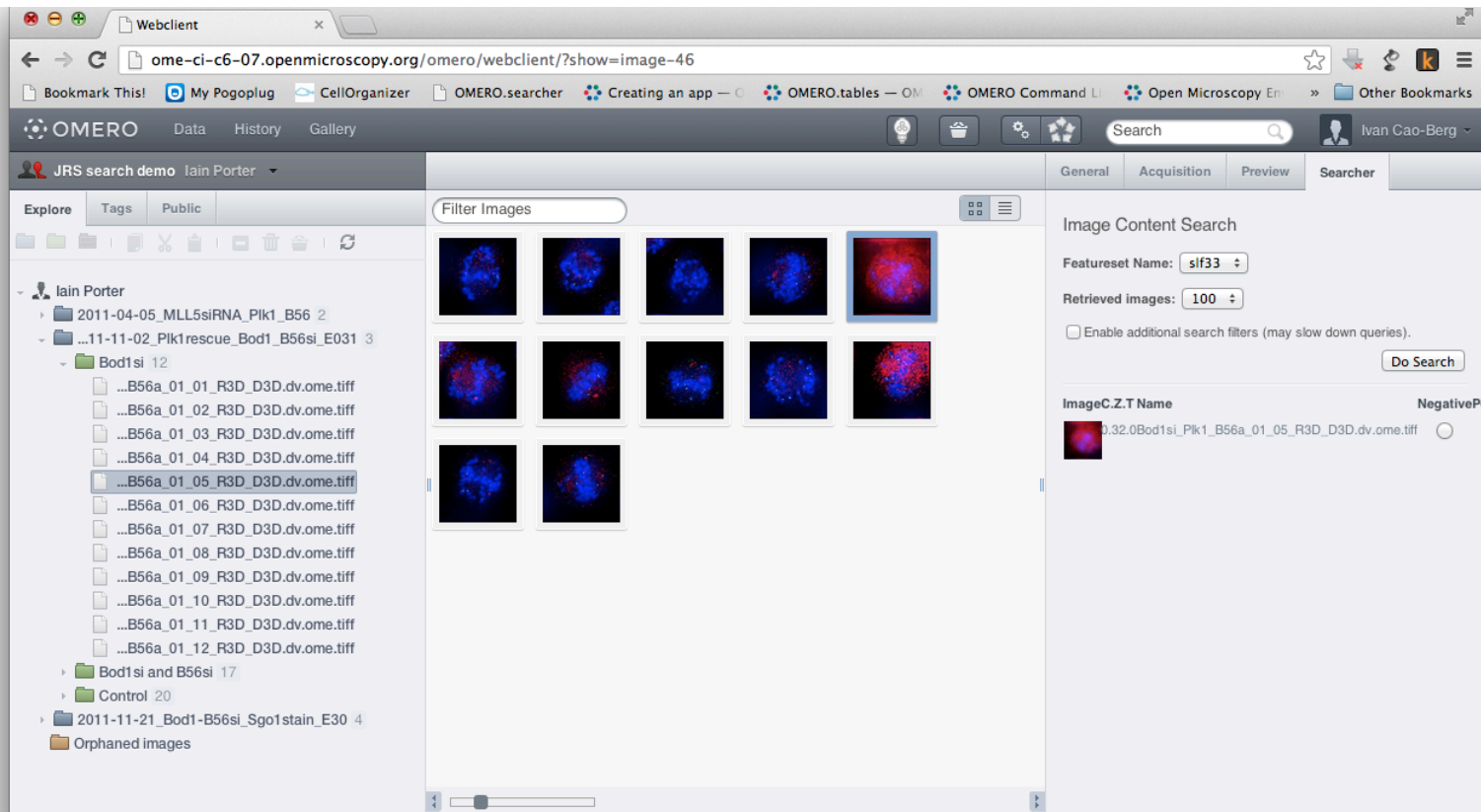
- `ricerca`: (1) updated definition of content databases to support changes implemented in Local Client
  - `PySLID`: (1) deprecated older methods, (2) optimized existing methods and (3) improved handling of edge cases
  - `PySLIC`: (1) minimal bug fixes
- 



# Searcher *Server* version update

- Searcher *Server* does queries using images from within an OMERO database for images in the same OMERO database
- Originally a patch to OMERO.web
- Now implemented as a Webapp

# Searcher Webapp



# Searcher Webapp

The screenshot displays the OMERO Searcher Webapp interface. The browser address bar shows the URL: `ome-ci-c6-07.openmicroscopy.org/omero/omero_searcher/searchpage/`. The OMERO logo and navigation links (Data, History, Gallery) are visible in the top left. A search bar and user profile (Ivan Cao-Berg) are in the top right. The main content area features a search results table with columns: Image, Rank, C.Z.T, Name, Negative, and Positive. The table lists 10 search results, each with a thumbnail image. On the left, there is a sidebar with search filters, including 'Feature-set: sif33', 'Retrieved images: 10', and a 'Do Search' button. On the right, there are tabs for 'General', 'Acquisition', and 'Preview', with 'General' currently selected.

Image	Rank	C.Z.T	Name	Negative	Positive
	1	0.32.0	Bod1si_Plk1_B56a_01_05_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	2	3.16.0	__Volumes__Imf__mposch__2-SDS-2_fixed_305_decon__SDS-RNAi3-24_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	3	0.32.0	CTR_Plk1_B56a_01_02_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	4	0.20.0	CSFV__VRAQ_05.r3d_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	5	0.32.0	Bod1si_Sgo1_Plk1_01_08_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	6	0.32.0	CTRandB56si_Sgo1_Plk1_01_06_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	7	0.32.0	CTRsi_Sgo1_Plk1_01_08_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	8	0.20.0	CSFV__VRAQ_04.r3d_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	9	0.32.0	Bod1si_aand_B56si_Plk1_B56a_01_16_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>
	10	0.32.0	CTR_Plk1_B56a_01_10_R3D_D3D.dv.ome.tiff	<input type="radio"/>	<input type="radio"/>

10 results returned in 7.467401 seconds

# OMERO.searcher *External Search*

- *External Search* can use a user-supplied image(s) (e.g., from local computer) as a query to find images within an OMERO database
- Originally implemented as a separate Django
- Plan to make it a Webapp also
- Tentative release at end of summer

# OMERO.searcher *CLI*

- PySLID and ricerca were designed so that users can write their own OMERO.scripts.

# OMERO.searcher *Local Client*

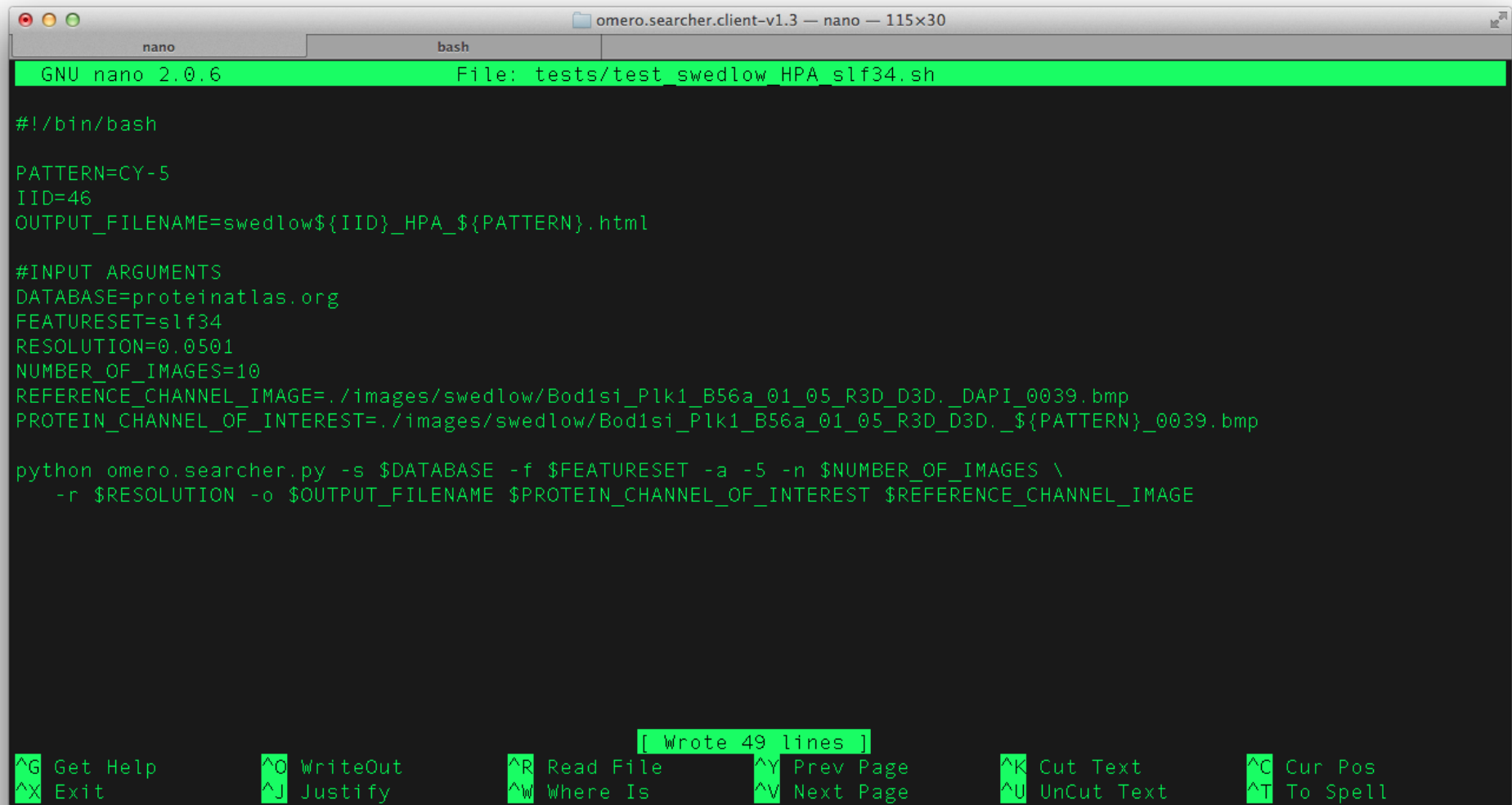
- *Local Client* runs as a standalone program on your local computer, using your files as queries
- Can search any database for which you have access to a contentDB (both OMERO and non-OMERO)
- Automatically checks for updates to contentDBs and downloads

# OMERO.searcher *Local Client*

- Runs from Python command line
- GUI version coming
- Tentative release at end of summer



# OMERO.searcher *Local Client*



The screenshot shows a terminal window titled "omero.searcher.client-v1.3 — nano — 115x30". The nano text editor is open, editing a file named "tests/test\_swedlow\_HPA\_slf34.sh". The script content is as follows:

```
GNU nano 2.0.6      File: tests/test_swedlow_HPA_slf34.sh

#!/bin/bash

PATTERN=CY-5
IID=46
OUTPUT_FILENAME=swedlow${IID}_HPA_${PATTERN}.html

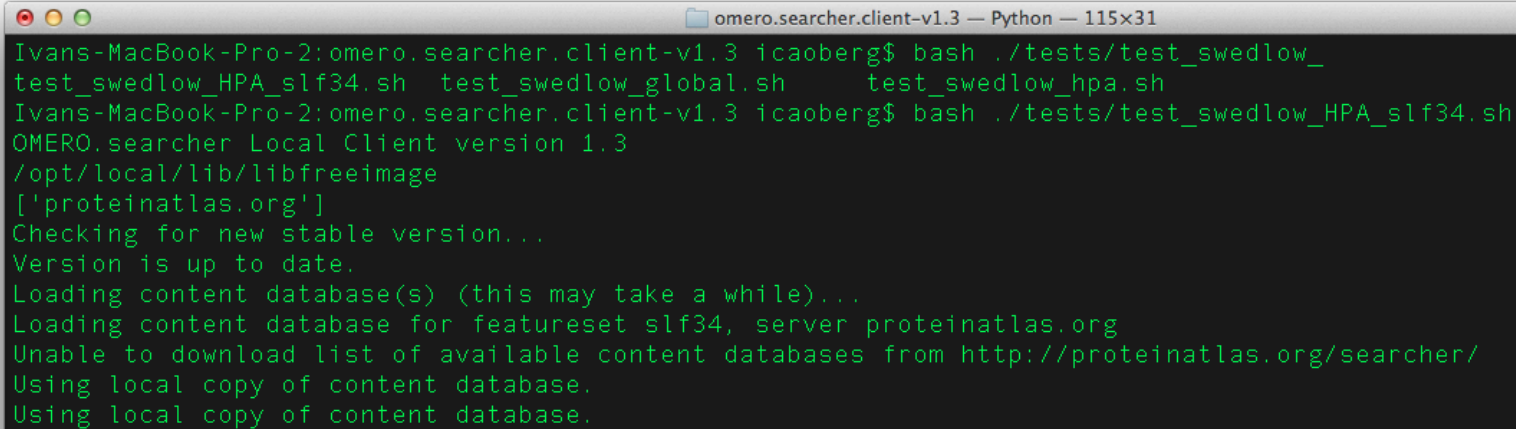
#INPUT ARGUMENTS
DATABASE=proteinatlas.org
FEATURESET=slf34
RESOLUTION=0.0501
NUMBER_OF_IMAGES=10
REFERENCE_CHANNEL_IMAGE=./images/swedlow/Bod1si_Plk1_B56a_01_05_R3D_D3D._DAPI_0039.bmp
PROTEIN_CHANNEL_OF_INTEREST=./images/swedlow/Bod1si_Plk1_B56a_01_05_R3D_D3D._${PATTERN}_0039.bmp

python omero.searcher.py -s $DATABASE -f $FEATURESET -a -5 -n $NUMBER_OF_IMAGES \
    -r $RESOLUTION -o $OUTPUT_FILENAME $PROTEIN_CHANNEL_OF_INTEREST $REFERENCE_CHANNEL_IMAGE
```

At the bottom of the terminal, a status bar indicates "[ Wrote 49 lines ]" and provides a list of nano editor shortcuts:

<b>^G</b> Get Help	<b>^O</b> WriteOut	<b>^R</b> Read File	<b>^Y</b> Prev Page	<b>^K</b> Cut Text	<b>^C</b> Cur Pos
<b>^X</b> Exit	<b>^J</b> Justify	<b>^W</b> Where Is	<b>^V</b> Next Page	<b>^U</b> UnCut Text	<b>^T</b> To Spell

# OMERO.searcher *Local Client*



A terminal window titled "omero.searcher.client-v1.3 — Python — 115x31" is shown. The terminal output is as follows:

```
Ivans-MacBook-Pro-2:omero.searcher.client-v1.3 icaoberg$ bash ./tests/test_swedlow_
test_swedlow_HPA_slf34.sh test_swedlow_global.sh test_swedlow_hpa.sh
Ivans-MacBook-Pro-2:omero.searcher.client-v1.3 icaoberg$ bash ./tests/test_swedlow_HPA_slf34.sh
OMERO.searcher Local Client version 1.3
/opt/local/lib/libfreeimage
['proteinatlas.org']
Checking for new stable version...
Version is up to date.
Loading content database(s) (this may take a while)...
Loading content database for featureset slf34, server proteinatlas.org
Unable to download list of available content databases from http://proteinatlas.org/searcher/
Using local copy of content database.
Using local copy of content database.
```

# Local Client

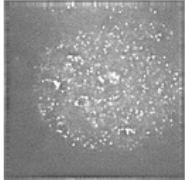
file:///Users/icaoberg/Desktop/omero.searcher.client-v1.3/swedlow46\_HPA\_FITC.html

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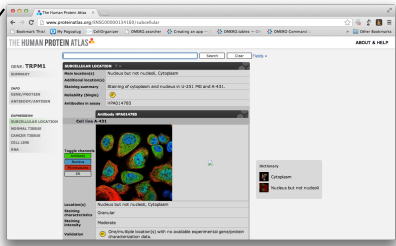
## OMERO.searcher results

/images/swedlow/Bod1si\_Plk1\_B56a\_01\_05\_R3D\_D3D\_FITC\_0039.bmp  
/images/swedlow/Bod1si\_Plk1\_B56a\_01\_05\_R3D\_D3D\_DAPI\_0039.bmp











**Query Image(s)**



**Content Database** ['proteinatlas.org-slf34-v2.pkl']  
**Original Scale** 0.0501  
**Comparison Scale/s** [0.08, 0.16, 0.32, 0.64, 1.28]  
**Feature Set** slf34  
**Number to Retrieve** 10



**Results**

0.08		0.16		0.32		0.64		1.28	
Thumbnail	Image Data	Thumbnail	Image Data	Thumbnail	Image Data	Thumbnail	Image Data	Thumbnail	Image Data
	<a href="#">Info</a>		<a href="#">Info</a>		<a href="#">Info</a>		<a href="#">Info</a>		<a href="#">Info</a>
	<a href="#">Info</a>		<a href="#">Info</a>		<a href="#">Info</a>		<a href="#">Info</a>		<a href="#">Info</a>

# Local Client

www.proteinatlas.org/ENSG00000134160/subcellular

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THE HUMAN PROTEIN ATLAS ABOUT & HELP

GENE: **TRPM1**

SUMMARY

INFO

GENE/PROTEIN

ANTIBODY/ANTIGEN

EXPRESSION

SUBCELLULAR LOCATION

NORMAL TISSUE

CANCER TISSUE

CELL LINE

RNA

**SUBCELLULAR LOCATION** ? »

Main location(s) Nucleus but not nucleoli, Cytoplasm

Additional location(s)

Staining summary Staining of cytoplasm and nucleus in U-251 MG and A-431.

Reliability (Single) IF

Antibodies in assay HPA014785

**Antibody HPA014785**

Cell line A-431

Toggle channels

Antibody

Nucleus

Microtubules

ER

Location(s) Nucleus but not nucleoli, Cytoplasm

Staining characteristics Granular

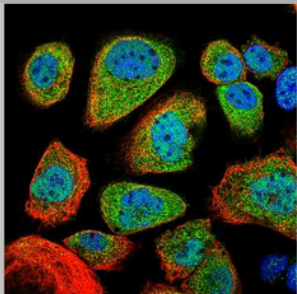
Staining intensity Moderate

Validation IF One/multiple location(s) with no available experimental gene/protein characterization data.

Dictionary

Cytoplasm

Nucleus but not nucleoli



## ***Local Client***

- Allow search across images of different resolutions
- Allow search of more than one contentDB at a time

# Local Client

- Currently available contentDBs
  - Human Protein Atlas
  - PSLID RandTag
  - The Cell Library
  - more coming...

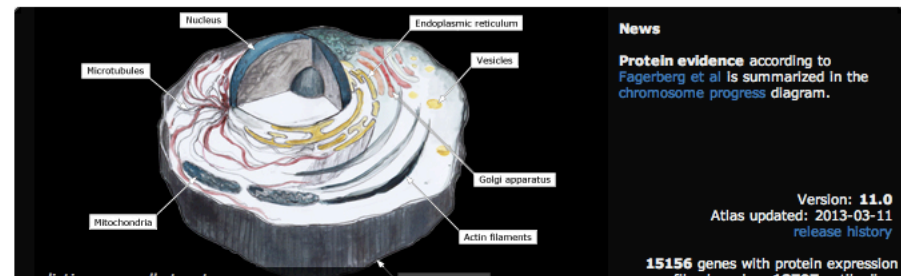
## THE HUMAN PROTEIN ATLAS

ABOUT & HELP

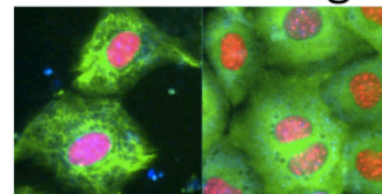
SEARCH ? »

Search Clear Fields »

e.g. CD44, ELF3, KLK3, or use Fields to search specific fields such as [protein\\_class:Transcription factors](#) or [chromosome:X](#)



### PSLID-RandTag2



The RandTag database contains information on a large collection of NIH 3T3 clones expressing eGFP

THE CELL<sup>TM</sup>  
an image library



Search  
[Advanced](#)

Submit

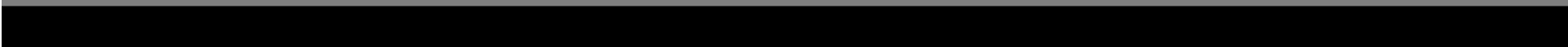
Cell Process

Cell Component

Cell Type



# Future Directions

- Support for
    - Search across multiple servers from within the Webapps
    - BioFormats for reading images using *Local Client*
    - Trigger feature calculation using bridge
- 



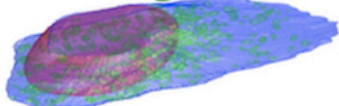
A fluorescence microscopy image showing several cells against a black background. The cells are stained with three different fluorescent dyes: red, green, and blue. The red staining appears to be localized in certain organelles or structures within the cells. The green staining is more widespread, often outlining the cell periphery or filling specific regions. The blue staining is typically concentrated in the nuclei, indicating the presence of DNA. The overall effect is a multi-colored visualization of cellular components.

# CellOrganizer

# Image-Derived Generative Models

- Goal is to model the reality underlying microscope images
- Build models that capture
  - distributions of all cellular components
  - how these change from cell type to cell type
  - how specific aspects of these models are changed by perturbagens

# CellOrganizer



Images ↔ Models

RAY AND STEPHANIE LANE  
Center for Computational Biology



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May 17, 2013: **Version 1.9.0 released!**

**New:** Now allows synthesis of cell and nuclear shape instances for HeLa cells using a diffeomorphic model.

The **CellOrganizer** project provides tools for

- learning generative models of cell organization directly from images
- storing and retrieving those models in XML files
- synthesizing cell images (or other representations) from one or more models

Model learning captures variation among cells in a collection of images. Images used for model learning and instances synthesized from models can be two- or three-dimensional static images or movies.

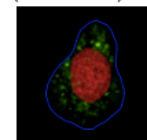
**CellOrganizer** can learn models of

- cell shape
- nuclear shape
- chromatin texture
- vesicular organelle size, shape and position
- microtubule distribution.

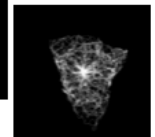
These models can be *conditional* upon each other. For example, for a given synthesized cell instance, organelle position is dependent upon the cell and nuclear shape of that instance.

Cell types for which generative models for at least some organelles have been built include human HeLa cells, mouse NIH 3T3 cells, and Arabidopsis protoplasts. Planned projects include mouse T lymphocytes and rat PC12 cells.

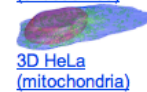
Synthesized Cell Images  
(click to view)



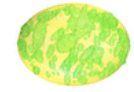
[2D HeLa  
\(endosomes\)](#)



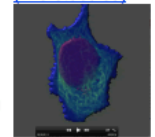
[3D HeLa  
\(microtubules\)](#)



[3D HeLa  
\(mitochondria\)](#)



[3D protoplast  
\(chloroplasts\)](#)



[3D HeLa movie](#)

Support for **CellOrganizer** has been provided by grants GM075205 and GM090033 from the [National Institute of General Medical Sciences](#), grants MCB1121919 and MCB1121793 from the [U.S. National Science Foundation](#), by a [Forschungspreis from the Alexander von Humboldt Foundation](#), and by the [School of Life Sciences of the Freiburg Institute for Advanced Studies](#).



Alexander von Humboldt  
Stiftung/Foundation

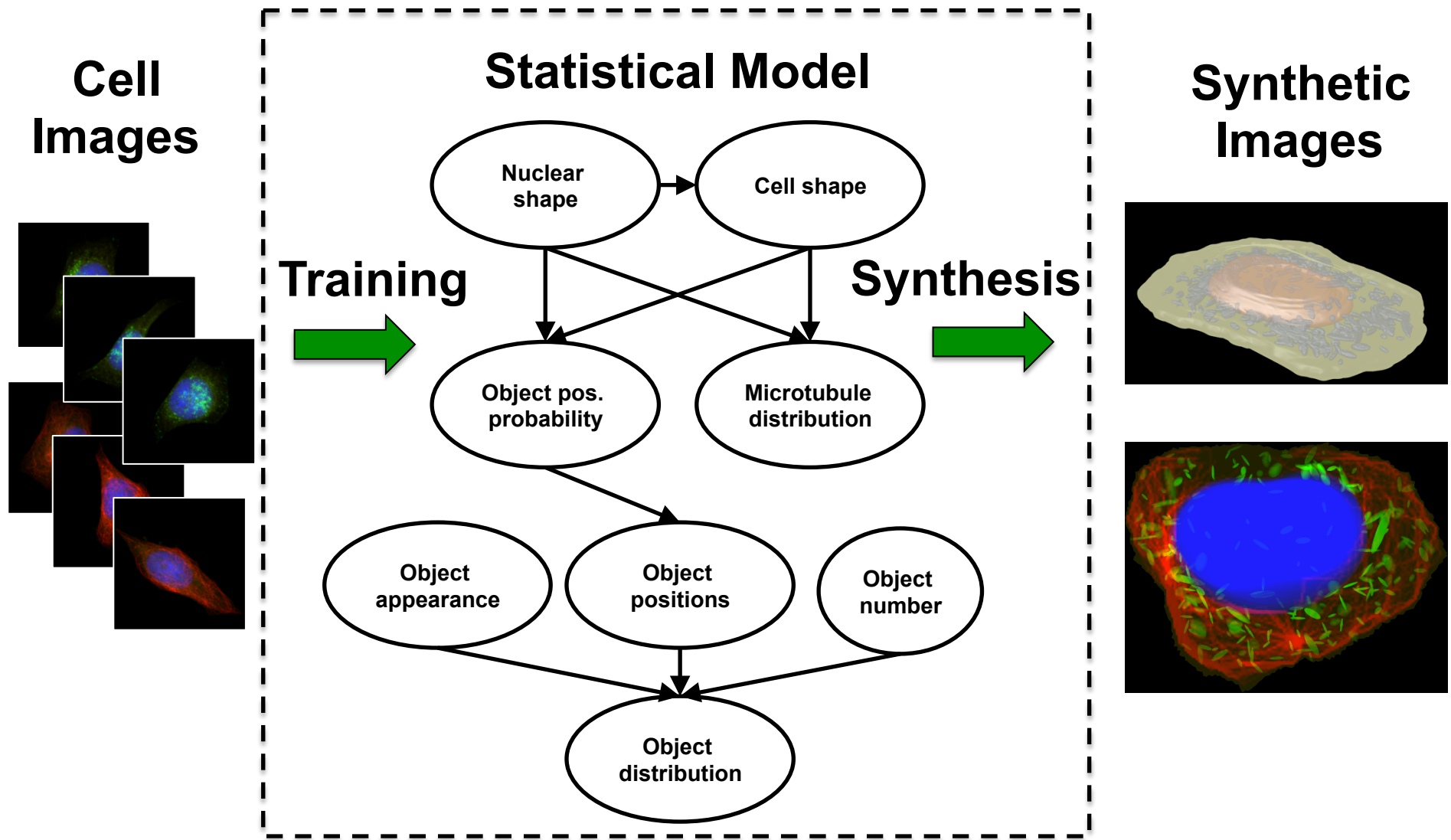


ALBERT-LUDWIGS-  
UNIVERSITÄT FREIBURG



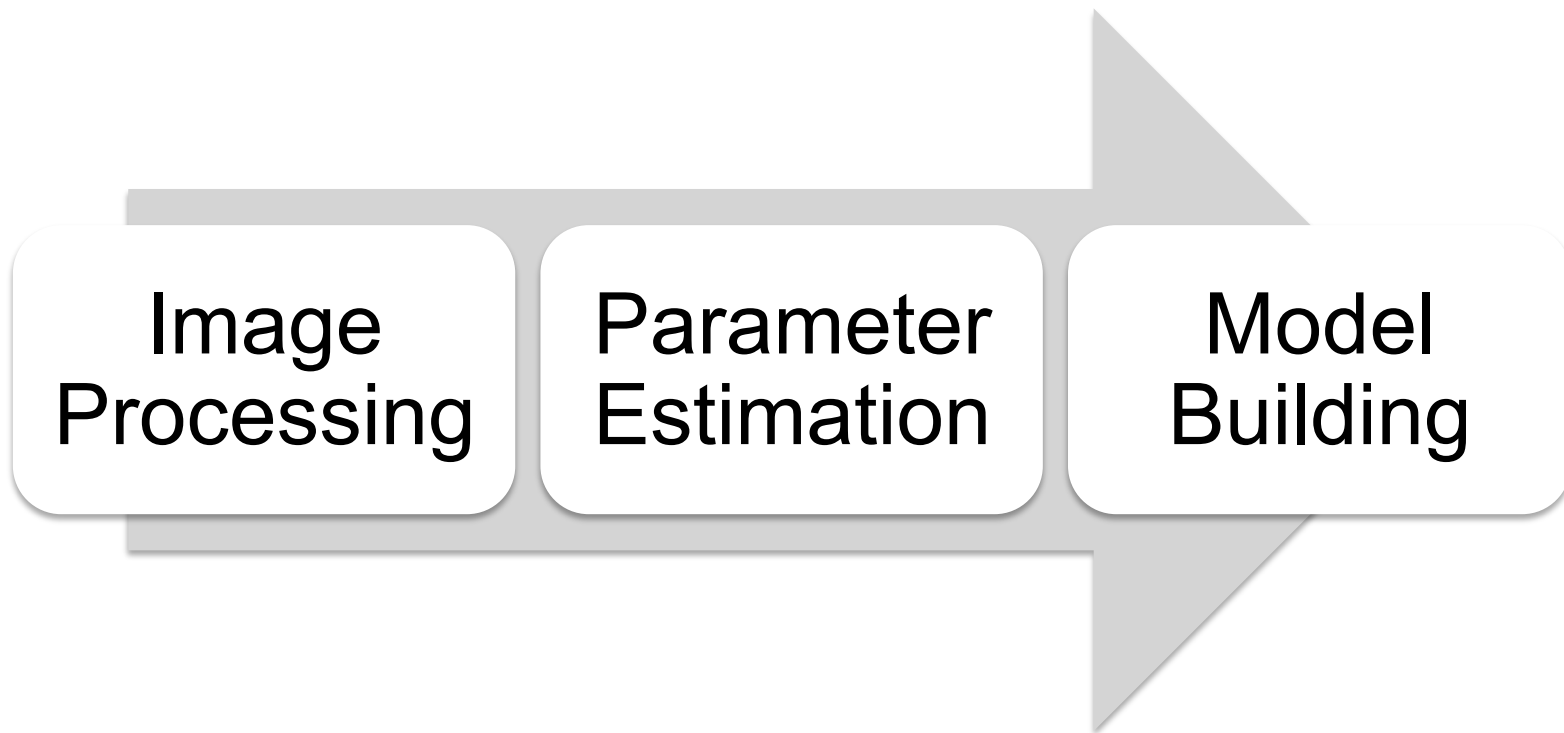
FRIAS  
FREIBURG INSTITUTE  
FOR ADVANCED STUDIES  
LIFE SCIENCES - LIFE NET

# CellOrganizer

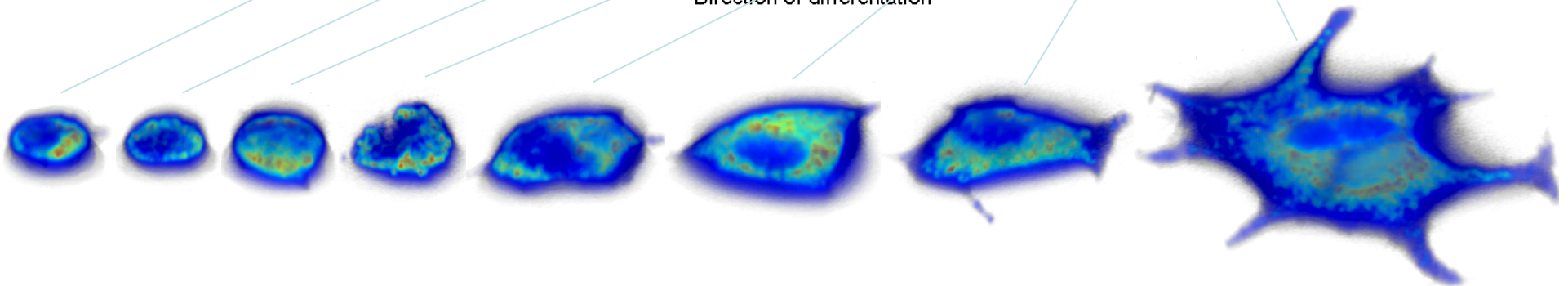
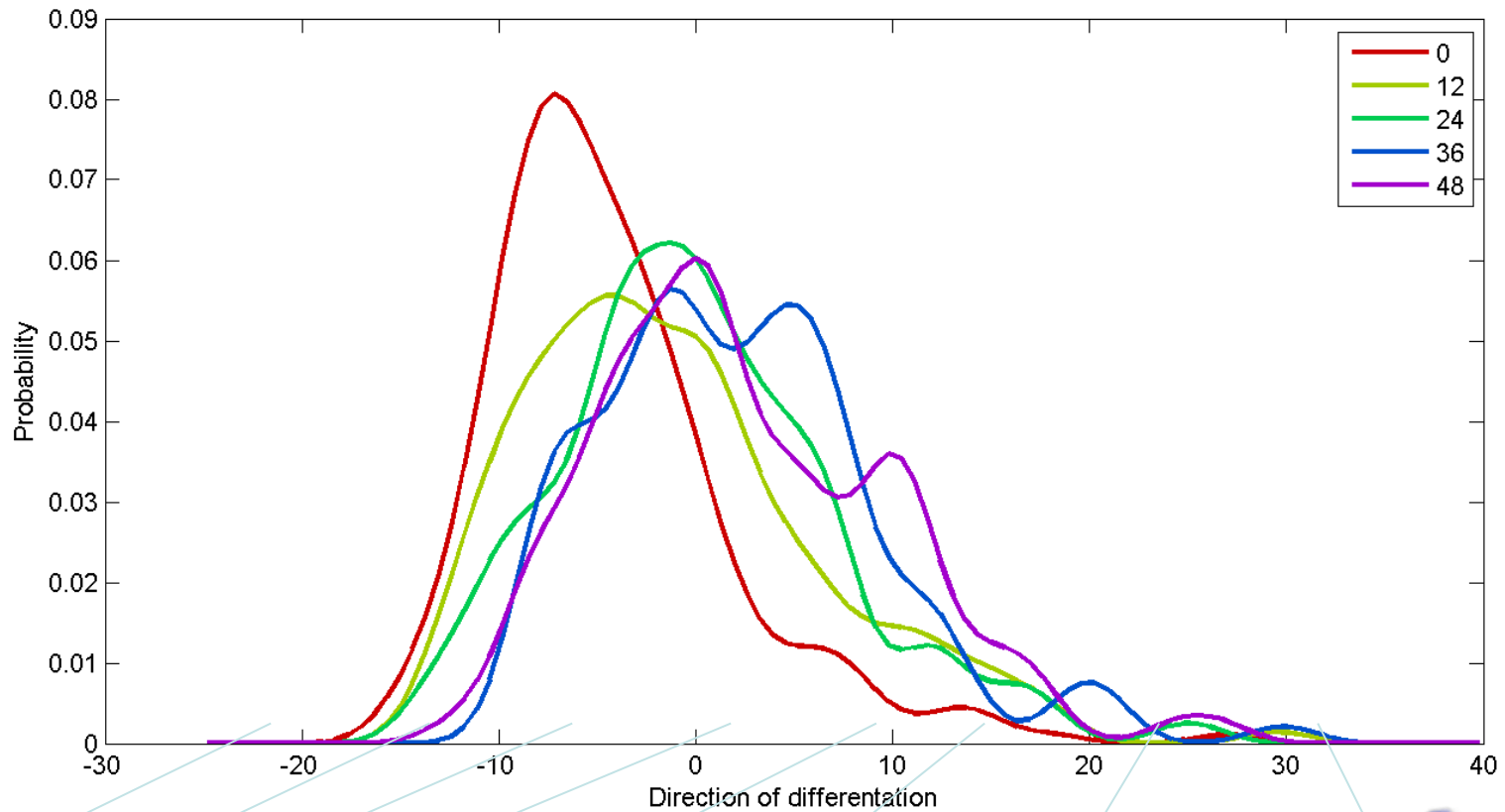


---

# Model Training



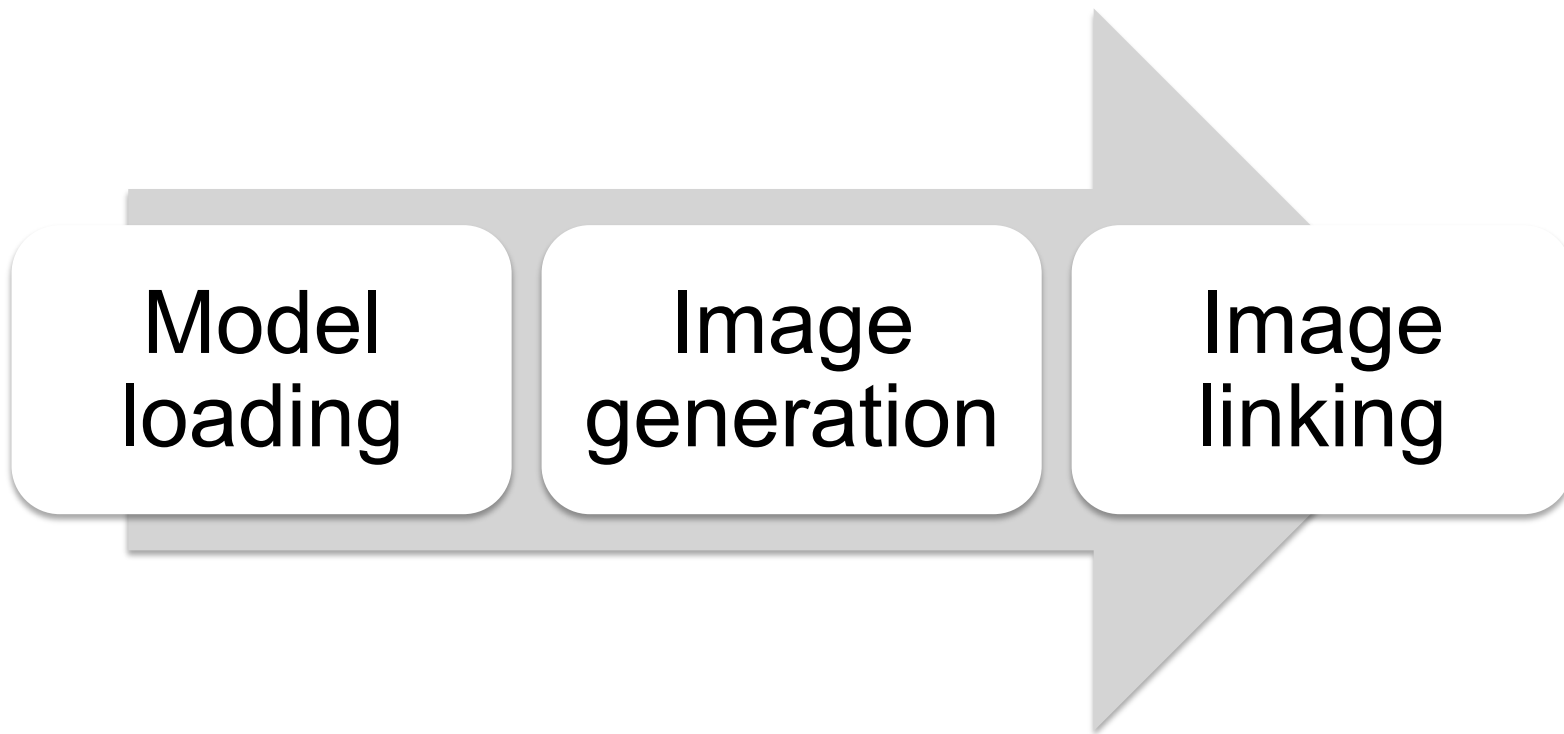
# PC12 cells undergoing differentiation



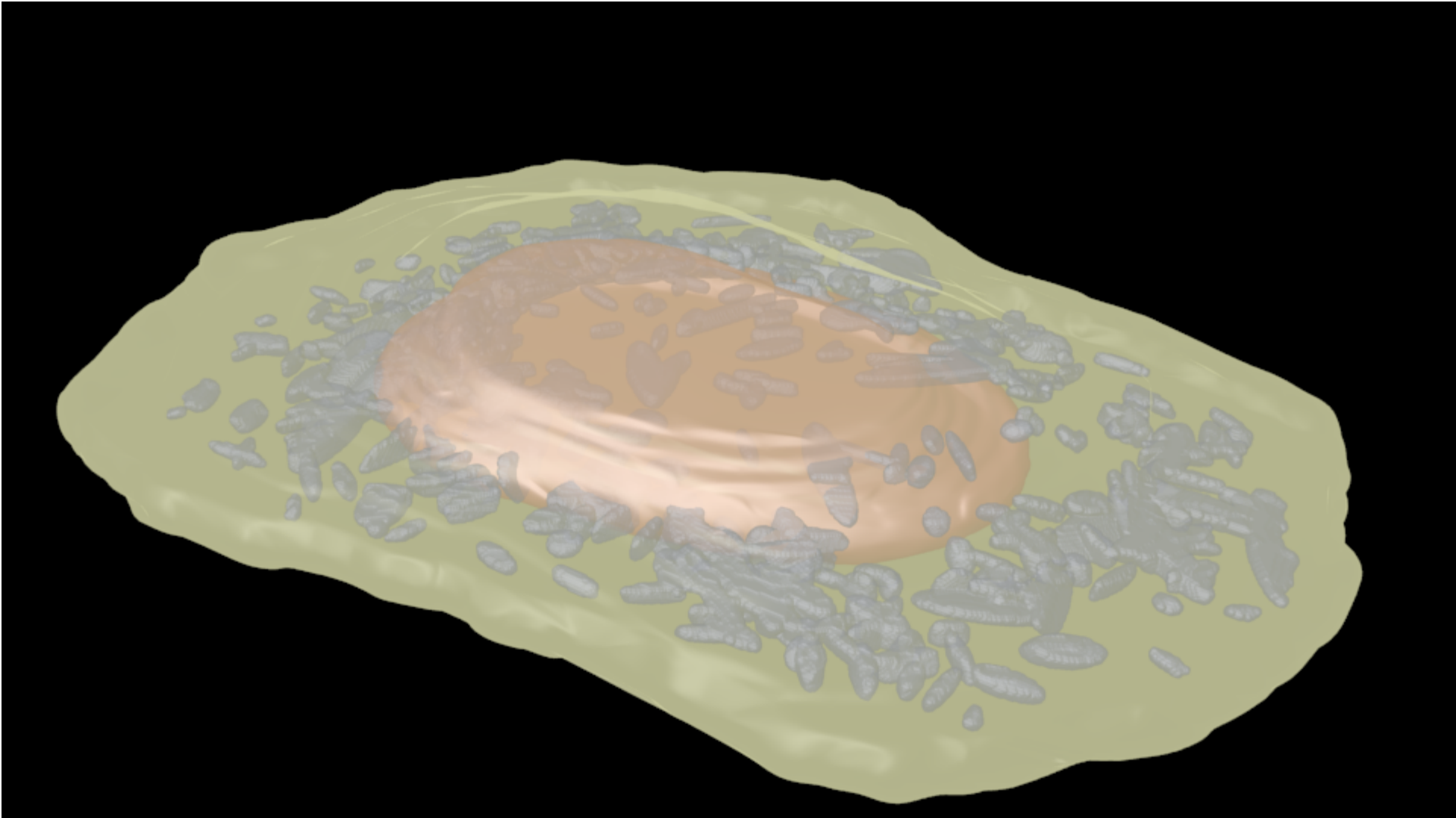


---

# Image Synthesis

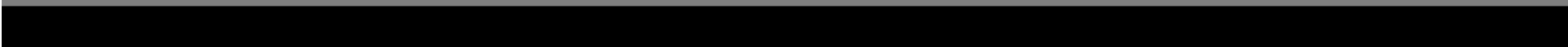








# CellOrganizer

- v2.0 (expected release at the end of the summer)
  - Open source (Matlab and C) [and python!]
  - *Contributions/collaborations welcome!*
- 



# Future Directions

- Interface with OMERO for
    - Preprocessing images
    - Feature calculation
    - Storing models
    - Storing generated images
  - Interfaces to cell simulation engines
    - Store and export models on demand
- 