EPFL

Bioimage Informatics

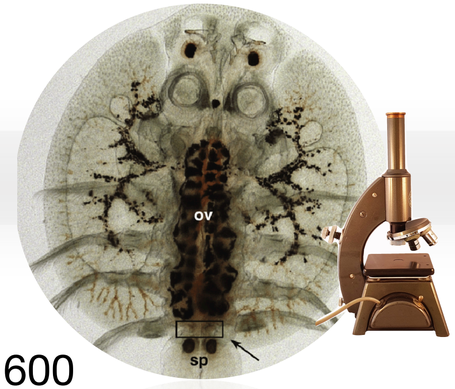
Daniel Sage & Arne Seitz

Course

Introduction to Bioimage Informatics

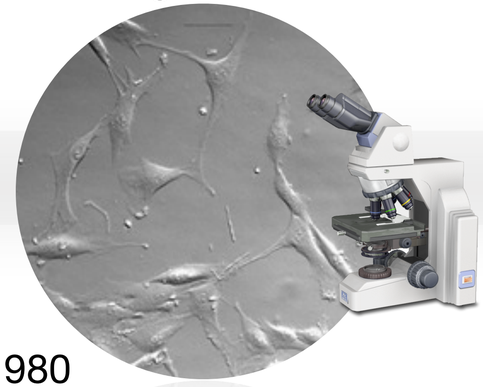
Qualitative to Quantitative Microscopy

Observation



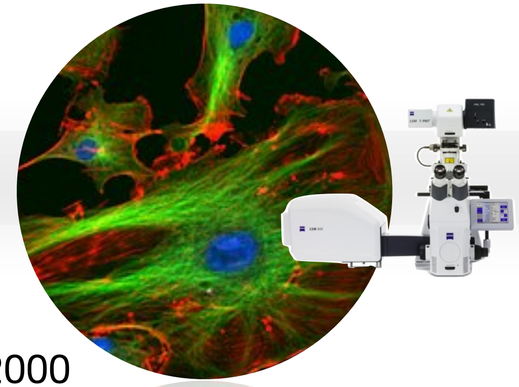
~1600

Digital era



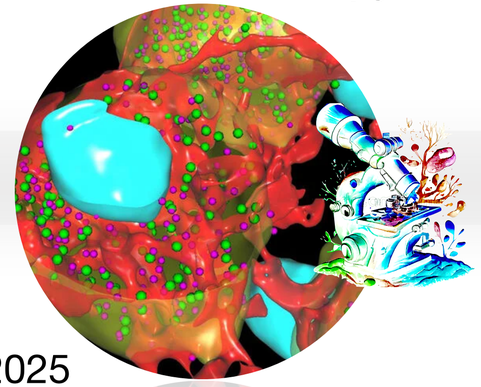
~1980

Modern time



~2000

Smart microscopy

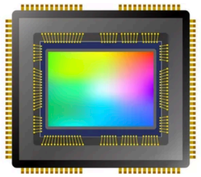


~2025

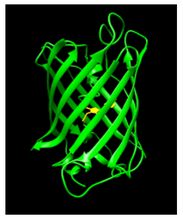
Bioimaging has evolved from its **qualitative** origins, mainly focusing on the visualization of individual biological processes and structures, to a highly **quantitative** discipline, producing **large, multimodal and complex** datasets requiring sophisticated and robust computation and methods for analysis.

Aastha Mather, Building a FAIR ..., 2023

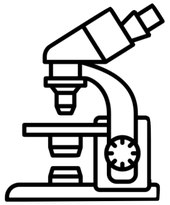
Series of (r)evolutions



Digital
digital camera
storage

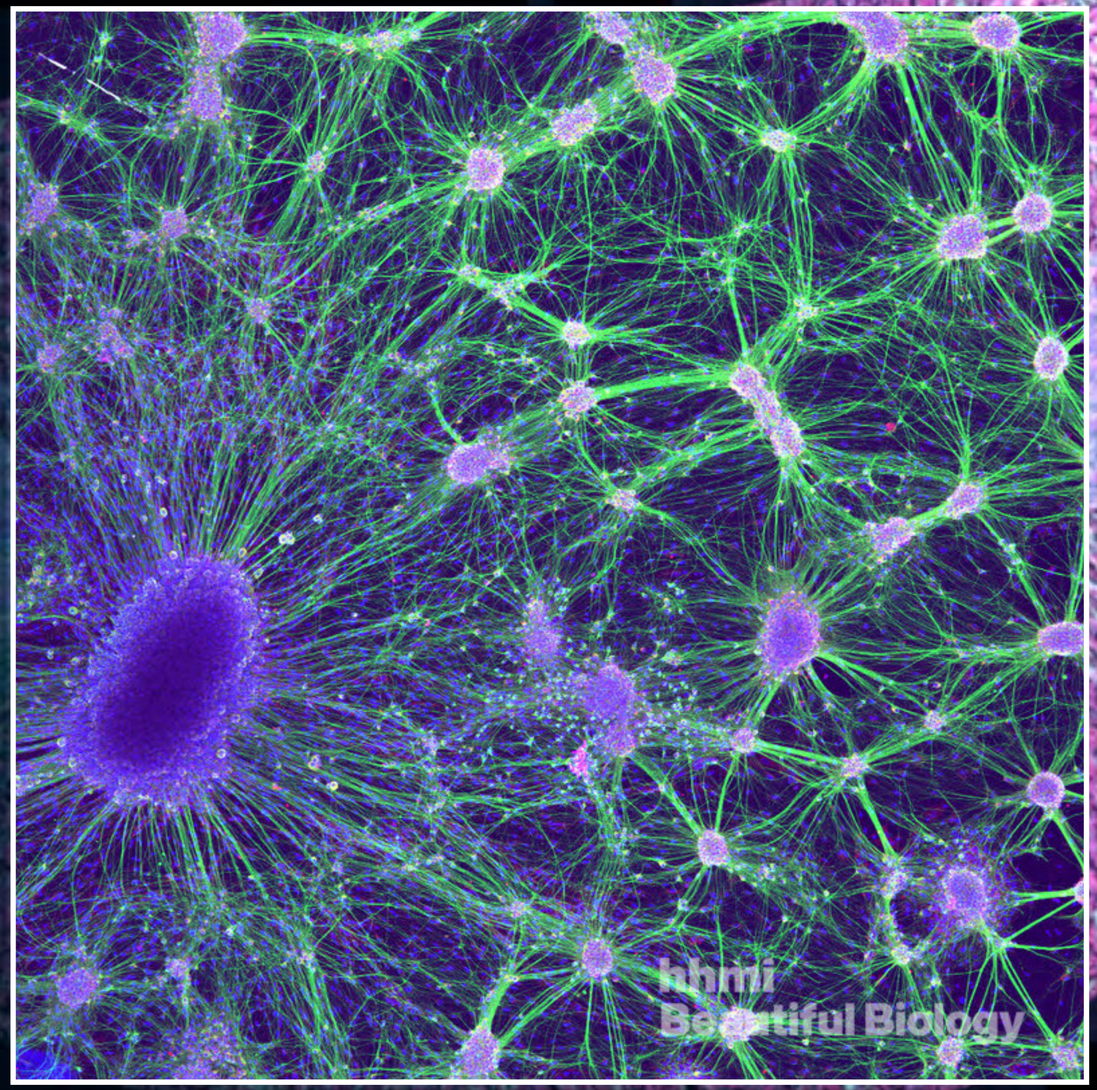


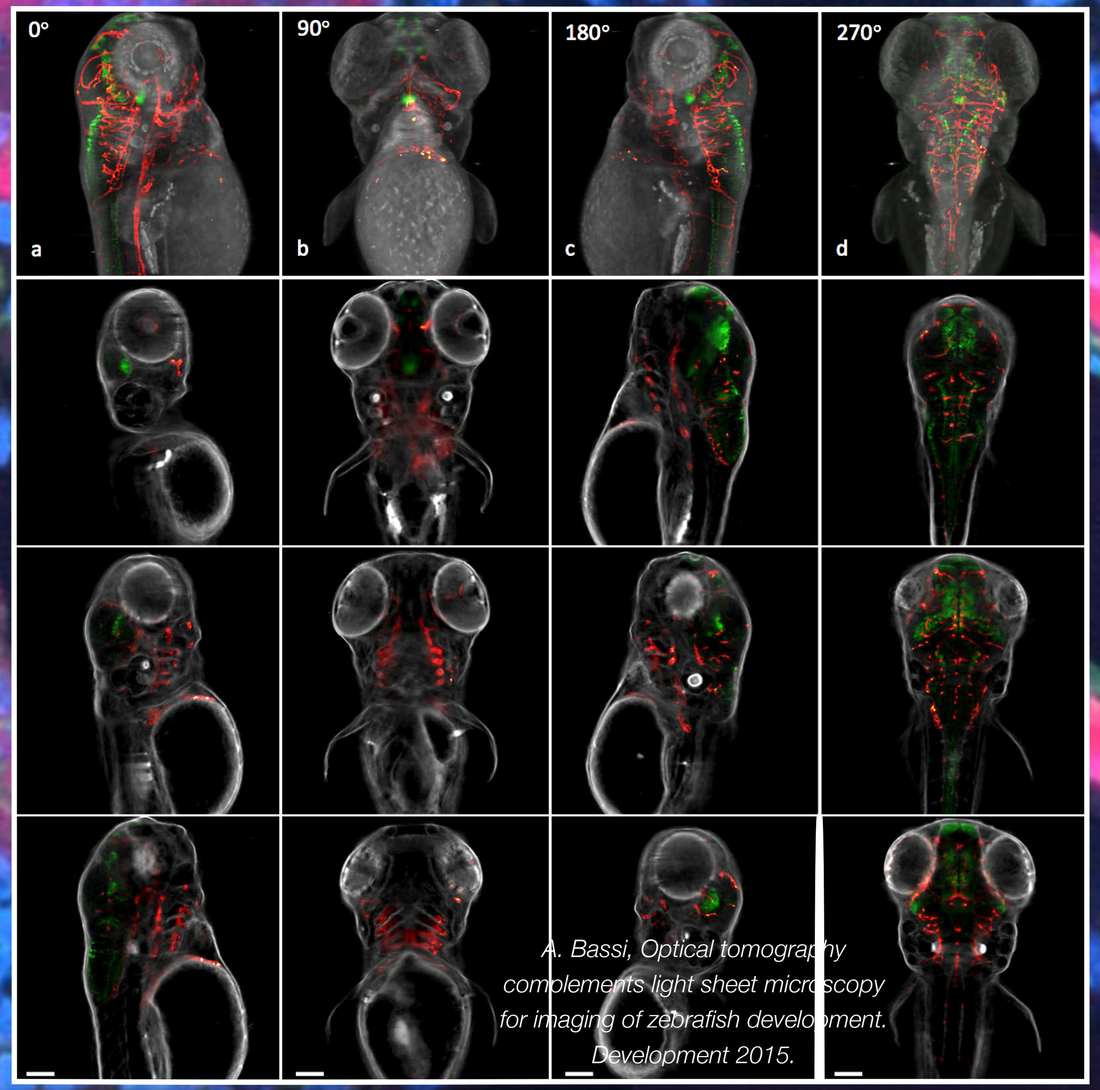
Biochemistry
fluorescence
single-molecule



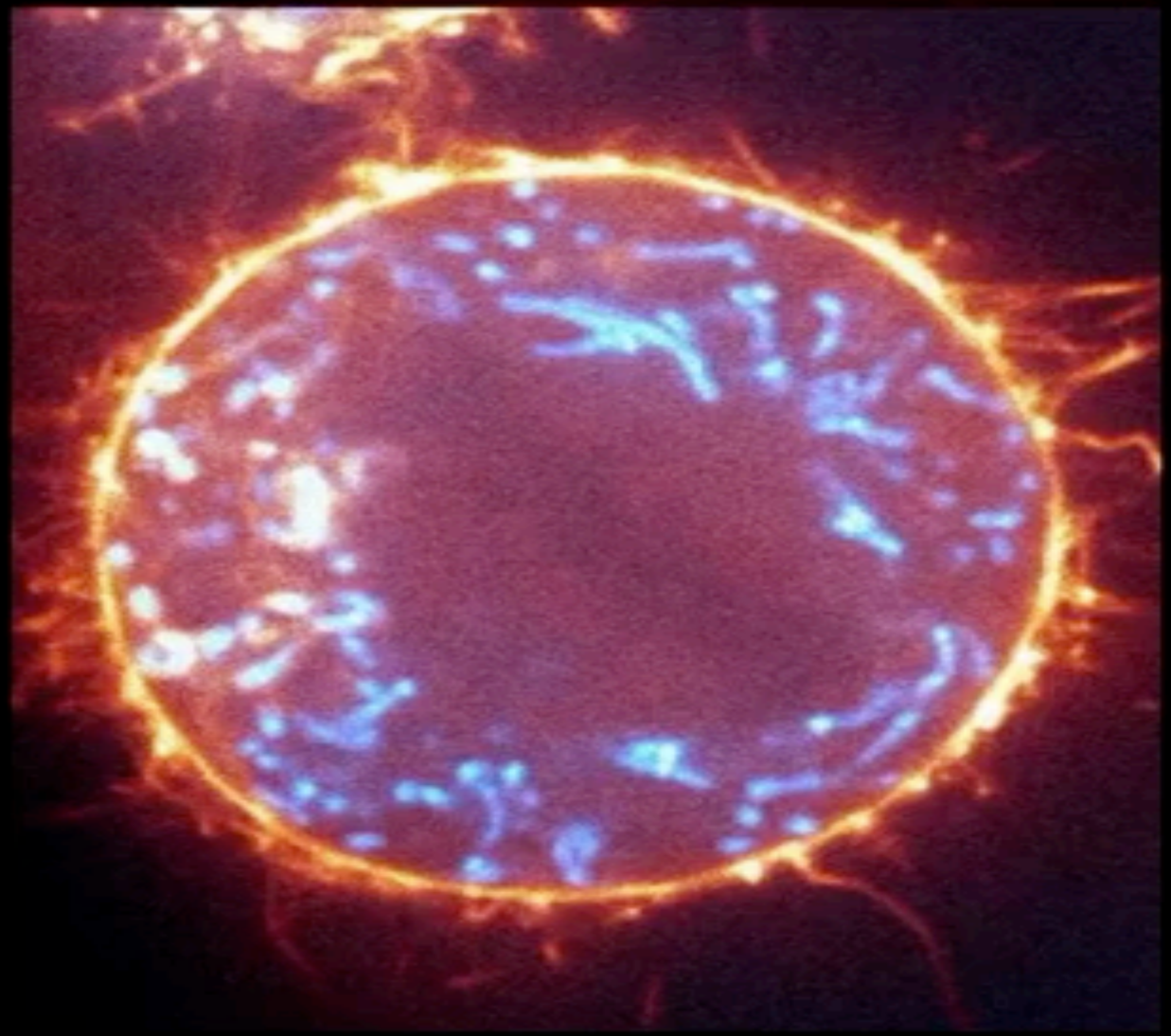
Microscopy
high resolution
time-lapse

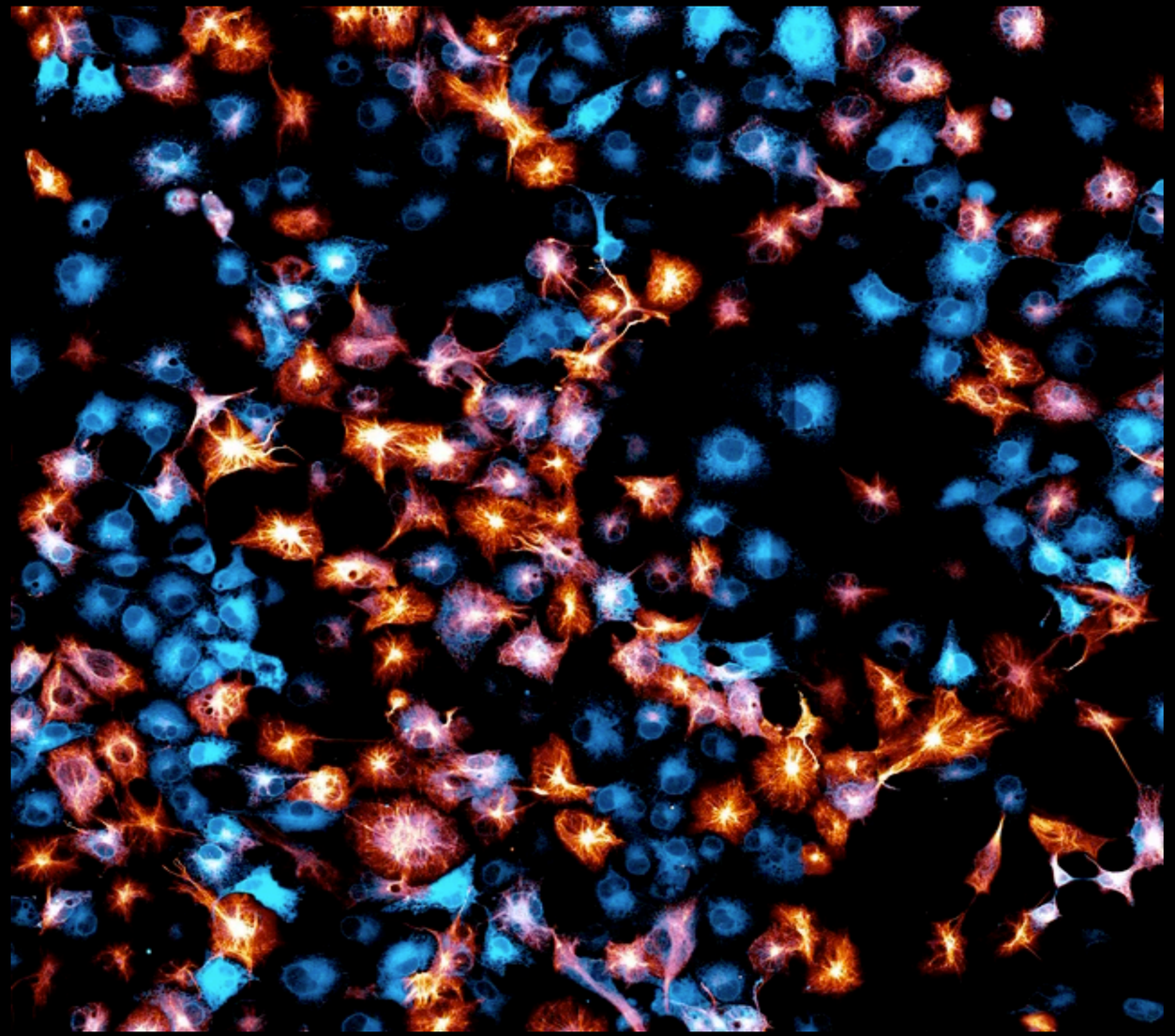
Data
data analysis
machine learning

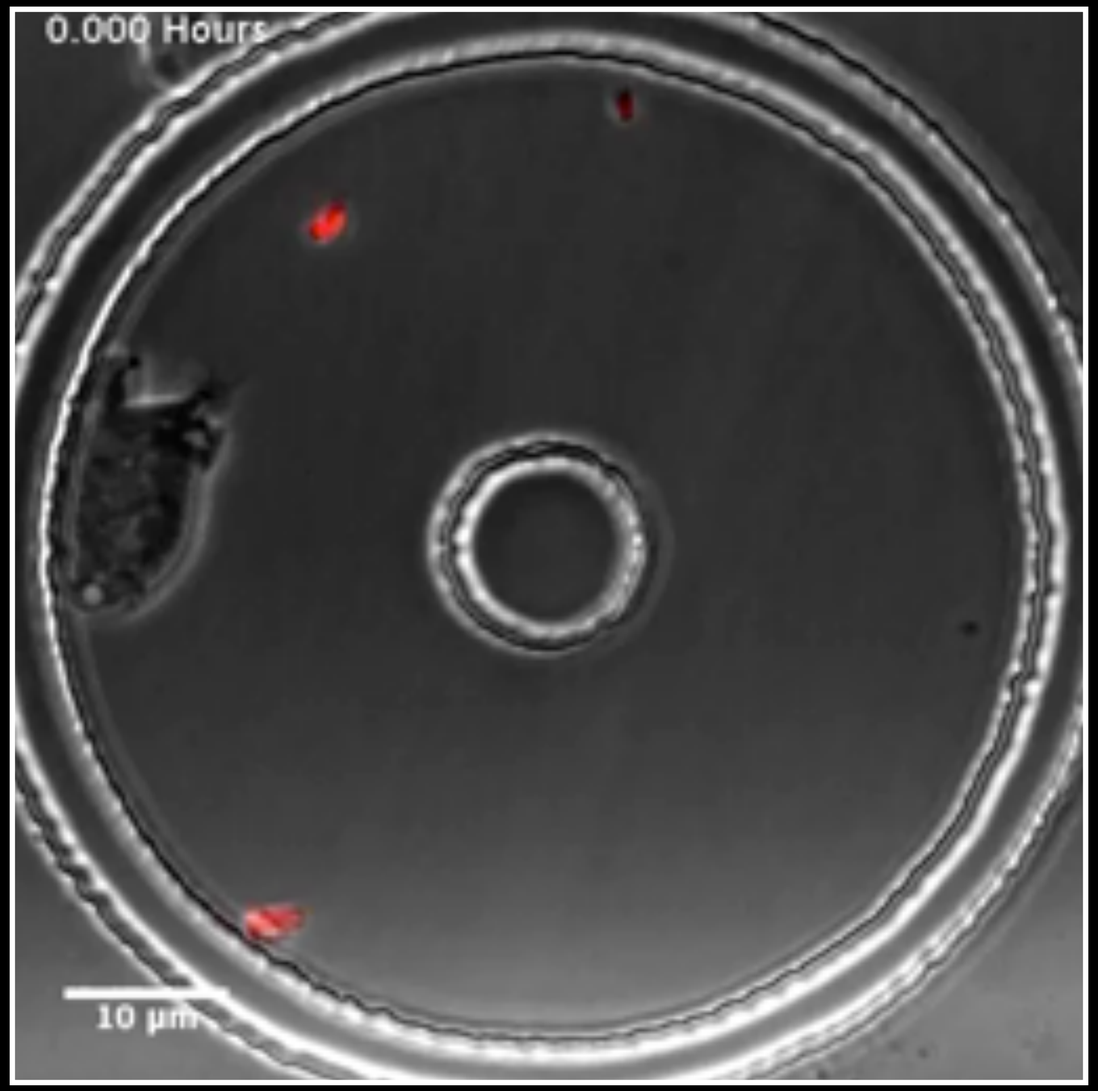




A. Bassi, Optical tomography complements light sheet microscopy for imaging of zebrafish development. Development 2015.



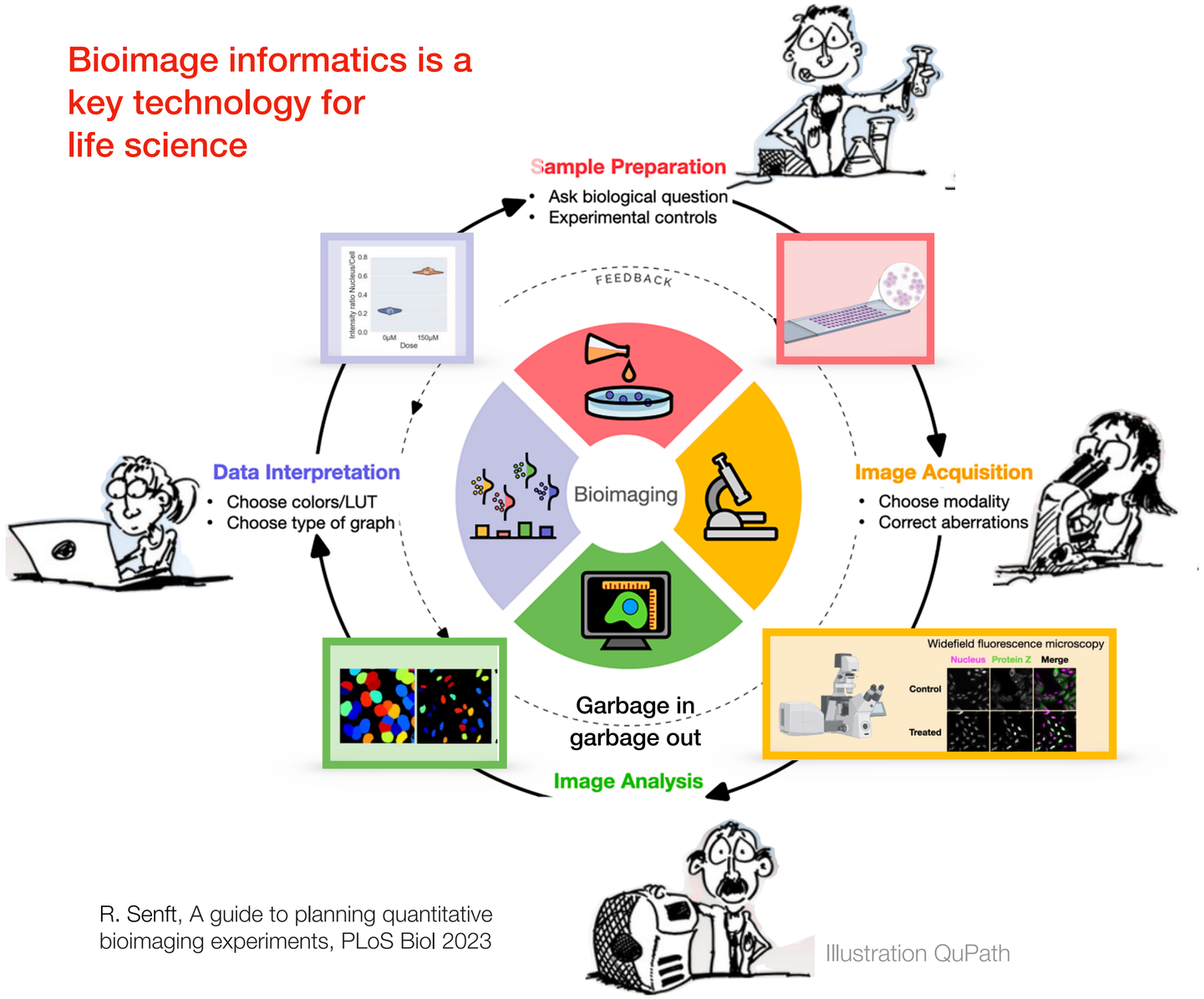




Cell bacteria interaction, phase contrast and fluorescence channel for bacteria
Source: Matthieu Delincé and Chiara Toniolo, McKinney Lab, EPFL

Image-based Studies

Bioimage informatics is a key technology for life science



R. Senft, A guide to planning quantitative bioimaging experiments, PLoS Biol 2023

Illustration QuPath

Why bioimage informatics matters
[Gene Myers 2012|

Vital emerging field

Computational advancements allow to map biological processes [Isabel Kemmer 2023]

New microscope modality

Wide range of imaging modalities from organisms to molecules [Johanna Bischof 2024]

Explosion growth of data

Unprecedented quantity of data and detail of living cells. [Wei Ouyang 2017]

Objective data analysis

Quantitative discipline, made to measure microscopy data [Siân Culley 2023]

Need expertise skills

Requires a comprehensive understanding complex workflow [Beth Cimini 2024]

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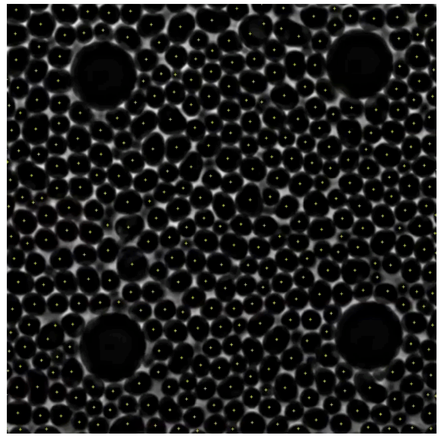
Quantitative Image Analysis

Made to Measure

- **Acquisition** image formation, contrast generation.
- **Analysis** image processing, segmentation, classification

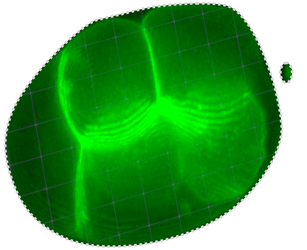
Garbage in -> Garbage out



An introduction to quantifying microscopy data in the life sciences, Siân Culley, Alicia Cuber, Caballero, Jemima Burden, Virginie Uhlmann, Journal of Microscopy 2023

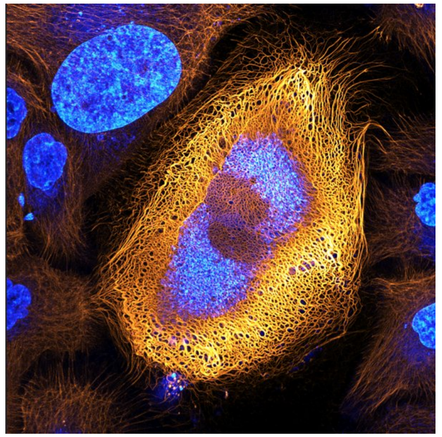
Typical Tasks

- Count cells, measure morphology, classify cells
- Measure the expression of protein (fluorescence)
- Mesure the granularity and texture
- Analyze co-localization, detecting phenotypes
- Identify the interactions, record diffusion dynamics
- Trace over time
- Estimate gowth rate, cell lineage



Bioimage Informatics Span

- **Spatial scales** from single molecules to cells, all to entire multicellular organisms.
- **Time scales** ranging from of ms to days.
- **Multiplexing** visualization of a multitude of sample characteristics in parallel.

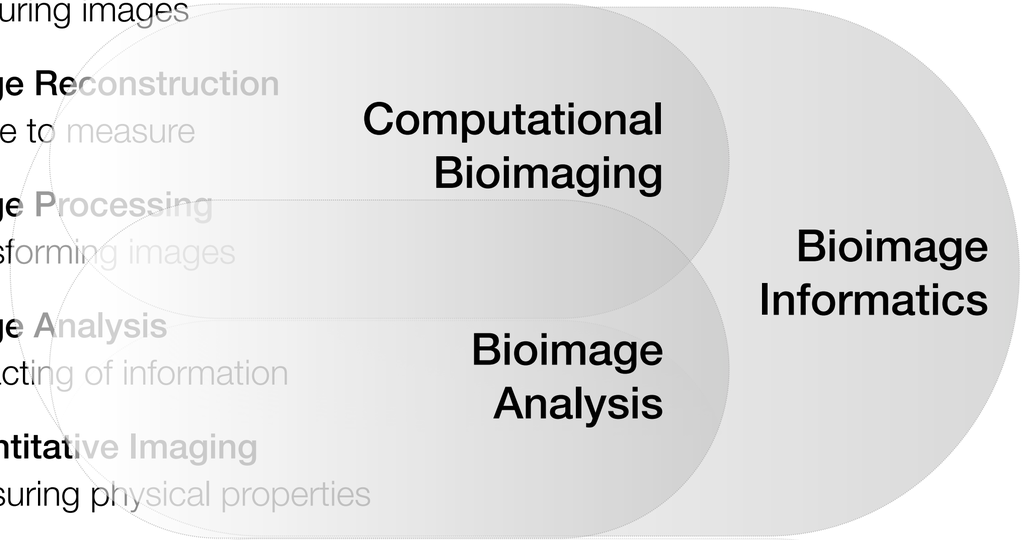


Expectations for Reliable Analysis

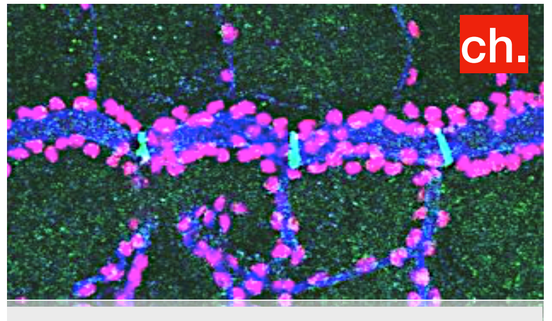
- Quantitative: Minimize bias
- Parameter-Free: Require minimal tuning
- Robust: Handle variations, ensure reproducibility
- Fast: Work efficiently on a laptop
- Practical: 100% accuracy is unrealistic

Digital Imaging Disciplines

- **Imaging**
  Capturing images
- **Image Reconstruction**
  Image to measure
- **Image Processing**
  Transforming images
- **Image Analysis**
  Extracting of information
- **Quantitative Imaging**
  Measuring physical properties
- **Computer Vision**
  Understanding visual information
- **Computer Graphics**
  Synthesizing visual content



Bioimage Analysis

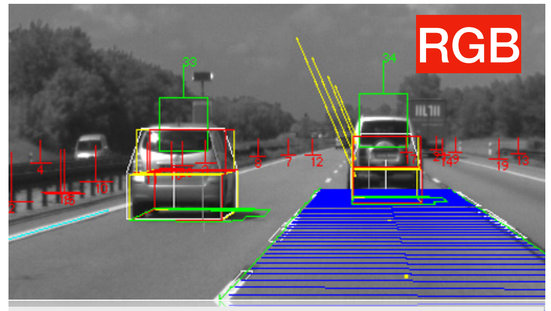


Large number of simple particles

Live cell / interaction / motility

Multiple dimensions

Computer Vision



Human perception modeling

Real-time processing

Well defined shape and geometry

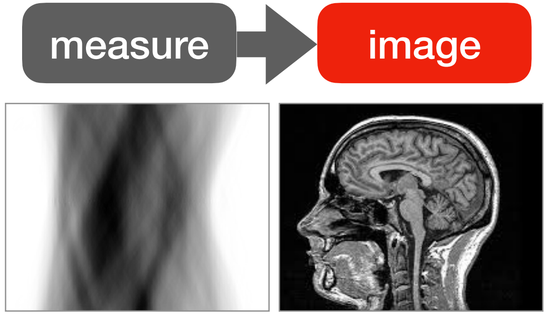


Image Reconstruction

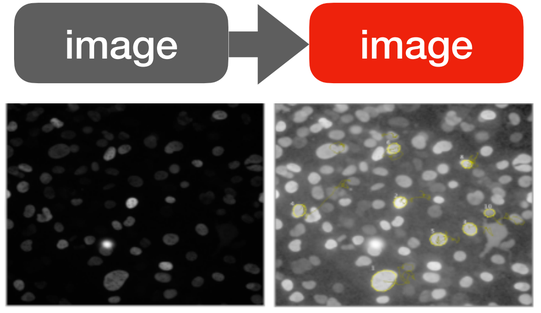


Image Processing

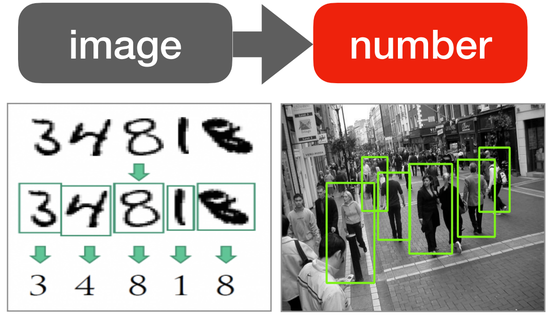


Image Analysis

Methodology

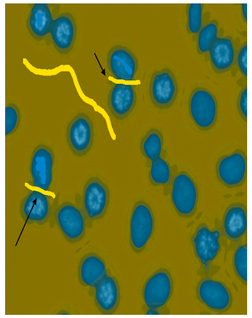
Intensity-based
Ad hoc routines
Aggregation pixels

SIMPLE

Rule-based

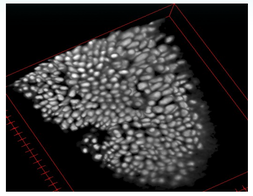
Machine Learning

Pixel classification



PHYSICS-DRIVEN

DATA-DRIVEN



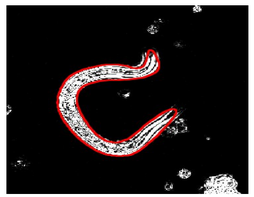
Model-based

Deep Learning

Supervised Learning

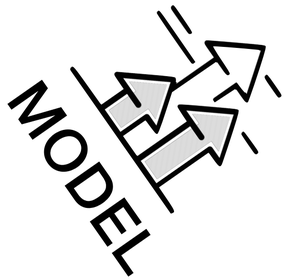
Pre-trained models

Foundation models



Shape model
Acquisition model
Physical model

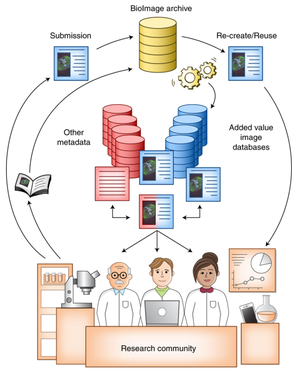
COMPLEX



Bioimage Data

Databases

- Data and metadata
- Annotated data for ML
- Open, re-analysable
- Centralised repositories



A call for public archives for biological image data
Jan Ellenberg et al.
Nature Methods 2018

Building a FAIR image data ecosystem for microscopy communities
Aastha Mathur et al.
J. Histoch Cell Biol 2023

Public repositories of bioimages

BROAD INSTITUTE — https://data.broadinstitute.org/bbbc/

CELL IMAGE LIBRARY — http://www.cellimagelibrary.org/

IDR — http://idr.openmicroscopy.org/
Williams, Nat Methods 2017

EMPIAR — https://www.ebi.ac.uk/pdbe/emdb/empiar
Iudin, EMPIAR. Nucleic Acids Res 2023

CANCER IMAGING ARCHIVE — https://www.cancerimagingarchive.net
Clark, J Digital Imaging 2013

BioImage Archive — https://www.ebi.ac.uk/bioimage-archive/
Hartley, Molecular Biology 2022

Large Data

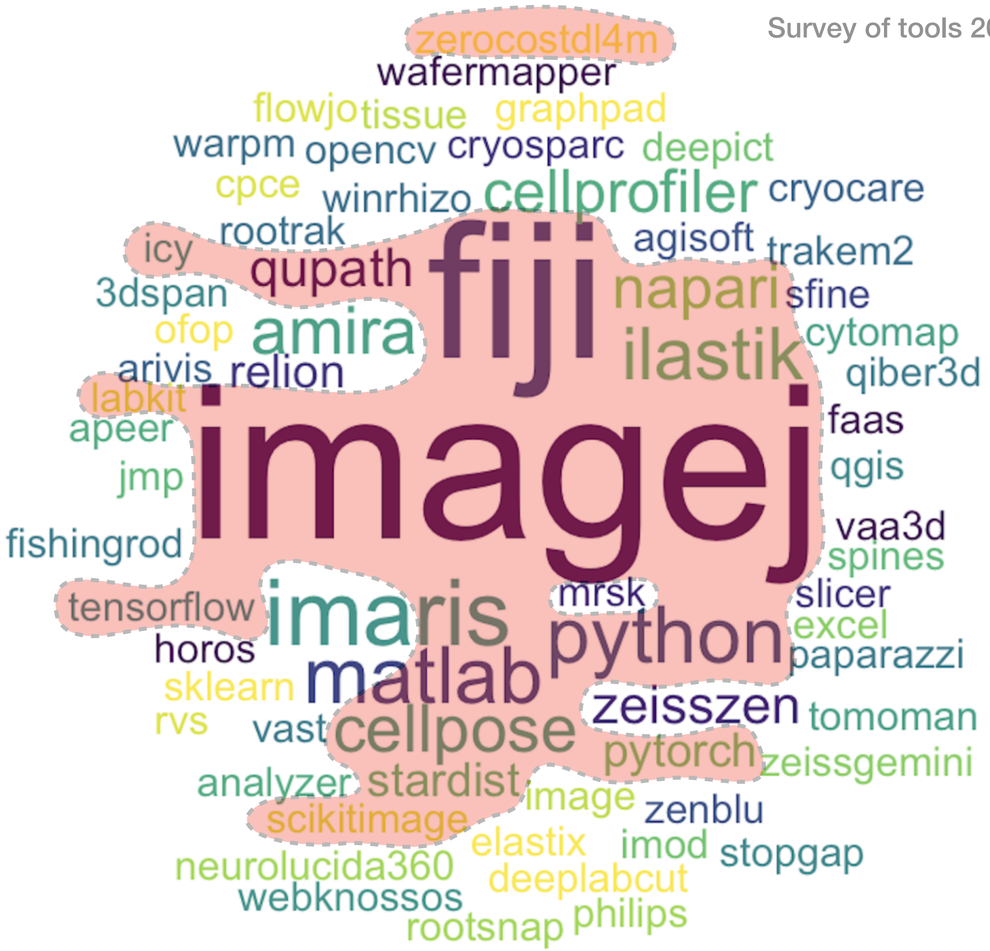
- 🔴 Storage
- ⏱ Transfer
- ✗ Share and annotation
- ⏱ Simple processing
- ⏱ Visualization

Pre-trained DL models

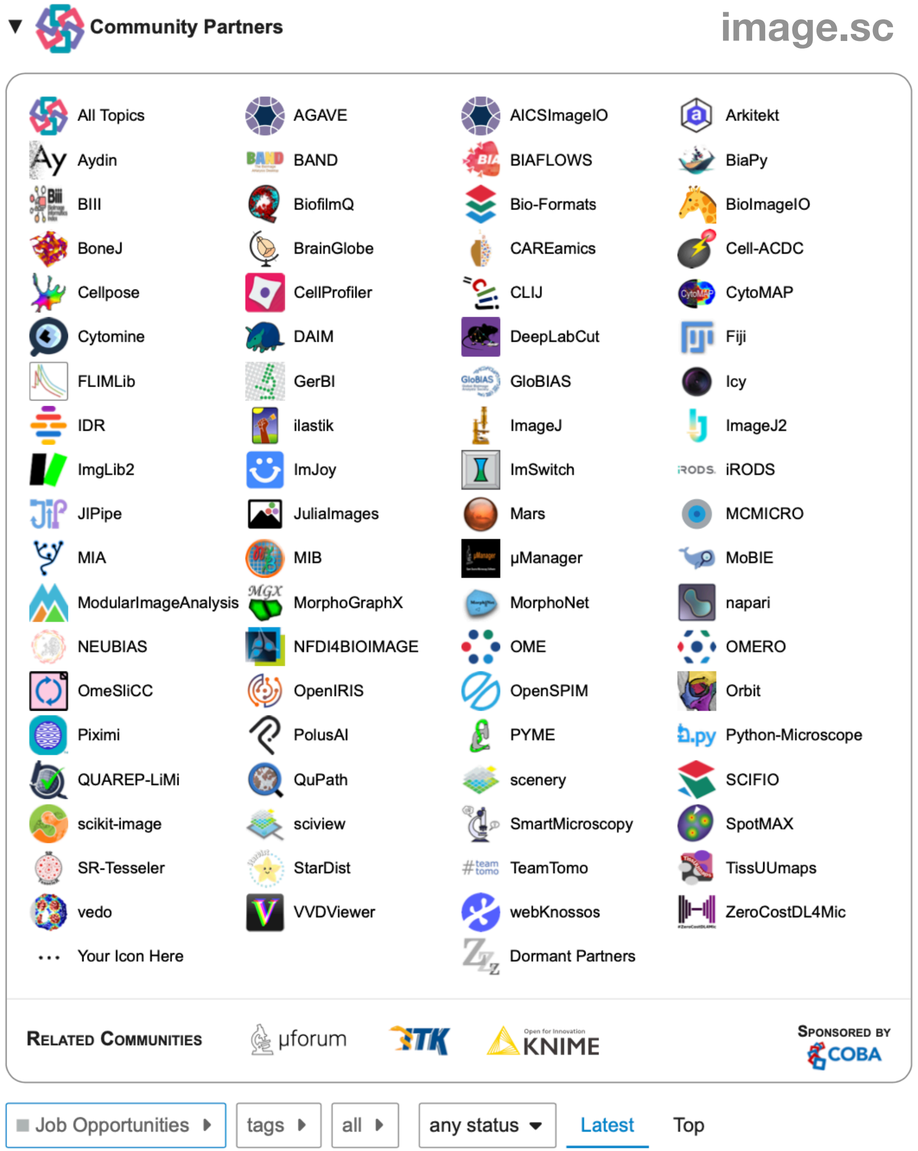
http://bioimage.org/
Trained Models Zoo

http://cellpose.org/
Cellpose for Cell Segmentation

Software Tools



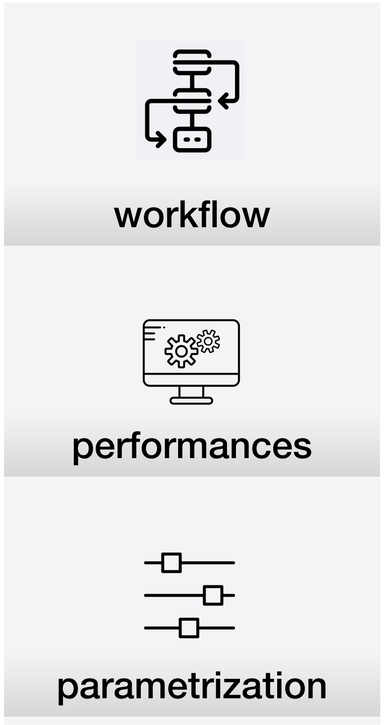
A Hitchhiker's guide through the bio-image analysis software universe
Robert Haase, FEBS 2022



Coding

When no standard tool solve your image analysis problem

- Automation, speed up, many images
- Non-human bias
- Reproducibility, documentation



Which language?	Java	python	MATLAB
Open-source	✓	✓	✗
Efficiency	✓	✓	▲
For the end-user			
Multiple OS	✓	✓	✓
Installation	✓	✗	✓
GUI	✓	✗	✗
For the developper			
Learning curve	▲	▲	▲
Prototyping	✗	✓	✓
Imaging libraries	✓	✓	▲
ML frameworks	✗	✓	✗

Software Packages in Java

ImageJ
NIH
Vanilla version

ImageJ2
Loci
Integration in scijava

ICY
Pasteur Institute

QuPath
Pete Blankhead

Software Packages in Python

NAPARI
Biohub

scikit-image
image processing in python

TensorFlow

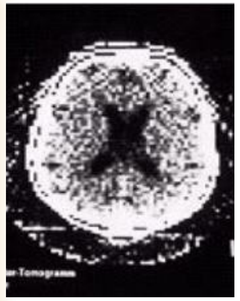
jupyter

OpenCV

PyTorch

Nobel Prizes

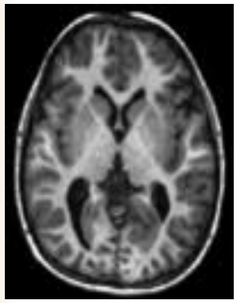
Röntgen
X-rays



Bloch, Purcell
Nuclear Magnetic (NMR)

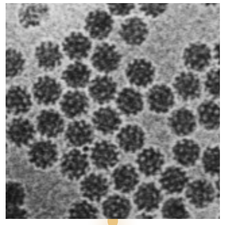
Cormack, Hounsfield
Computed tomography

Ernst
NMR spectroscopy



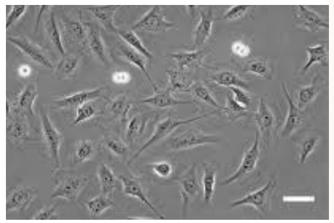
Lauterbur, Mansfield
MRI

Dubochet, Franck, Henderson
Cryo-electron microscopy

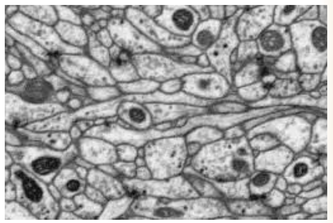


1901 · 1952 · 1953 · 1979 · 1986 · 1991 · 2003 · 2008 · 2014 · 2017

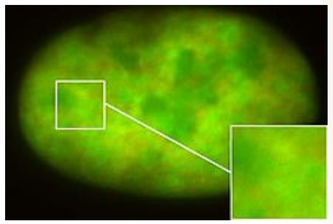
Zernike
Phase contrast



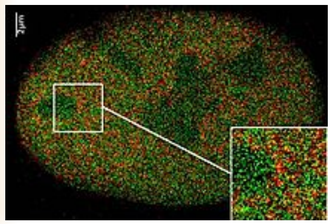
Ruska
Electron microscopy



Shimomura,Chalfie, Tsien
Fluorescent protein



Betzig, Hell, Moerner
Super-resolution



Bioimage Analysts

New Profession

An bioimage analyst uses existing tools or assembles tools or develop new algorithms in workflow.

By understanding the biological question, the image acquisition, the algorithms and the code, the bioimage analyst is a designer of bioimage applications.

Bioimage Analysis Societies

GLOBAL BIOIMAGING growing collaboration

BioImaging North America

Latin America Bioimaging

African BioImaging Consortium

QUAREP-LiMi

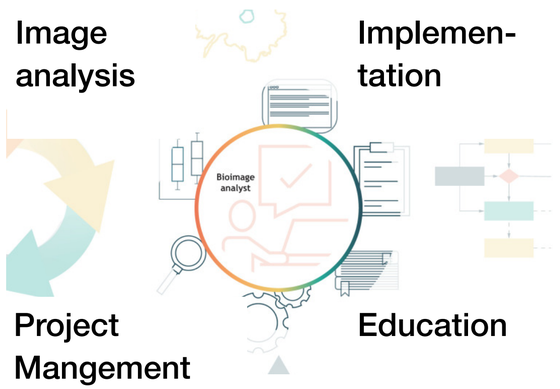
SWISS BIAS

EURO BIOIMAGING

FRANCE-BIOIMAGING

German BioImaging Gesellschaft für Mikroskopie und Bildanalyse

AI4Life



The crucial role of bioimage analysts in scientific research and publication
Beth A Cimini, J Cell Sci. 2024

Associate Software Engineer: Free and Open-source Biological Imaging Software

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il y a 11 heures · À plein temps

Postuler sur Trabajo.org - S...

Description du poste

The University of Basel is seeking an experienced Senior Bioimaging Specialist to join its prestigious Imaging Core Facility (IMCF). The ideal candidate will have a strong background in bioimage analysis and possess excellent communication skills.

About the Role

• Develop and implement advanced image processing pipelines using popular toolkits like ImageJ/Fiji, Python, QuPath, and Imaris.

• Provide user support and training on image analysis topics, working closely with scientists and researchers.

Typical tasks include:

- User support and training with image analysis related topics.
- Development and implementation of image / data processing pipelines, mostly based on scripting common bioimaging toolkits like ImageJ/Fiji, Python (Cellpose, Stardist, Scikit-image, Napari), QuPath, Ilastik, Imaris etc.
- Work in close collaboration in a versatile team with members experienced image analysis and advanced light microscopy.

Multiple positions in the Bioimaging Core of Leuven microscopy	N	0	13d
Multiple opportunities at the Broad Imaging Platform (Cambridge, MA, USA) cellprofiler	R	1	16d
Bioimage analysis position at IMCF, Biozentrum, Basel		0	17d
Software developer for OME-Zarr at German BioImaging (Germany/remote)		2	18d
Opening for Senior Expert Data Science / Imaging @ NIBR (Basel, Switzerland) novartis		0	Oct 2024
Image analysis fellowship opportunities x-ray, em		0	Oct 2024
Freelance Opportunity: OMERO-ARC-Converter Project – Apply by October 17, 2024 omero	P	0	Oct 2024
2 PhD opportunities in Machine Learning at SciLifeLab and KTH, Sweden	G	0	Oct 2024
Post-Doc in Advanced Fluorescence Microscopy @CCMAR Portugal fiji, napari, fluorescence, zen, lightsheet, immunofluorescence	T	0	Oct 2024
Associate Professor Empire Innovations Program/Cluster Hire with the focus on Biological Imaging, Biosensors, Cell Dynamics Analysis, and Optogenetics	M	0	Oct 2024
Postdoc vacancy available at UCL - Machine Learning for Multi-scale, Correlative, Biomedical Imaging		0	Oct 2024
Job offer AI expert at CNIO Spain		0	Oct 2024
Two open positions at the SciLifeLab Bioimage Informatics Unit - BIIF		1	Oct 2024
Bioinformatician with focus on research support within image analysis - Sweden fiji, cellprofiler, qupath, python, tissuumaps		1	Sep 2024

Ethics in Image Analysis

Image Manipulation

Guidelines

Keeping raw data, open data

No image compression

Simple adjustment acceptable

Cropping acceptable

Digital filtering is not encouraged

Combining images if no hiding

No local alteration

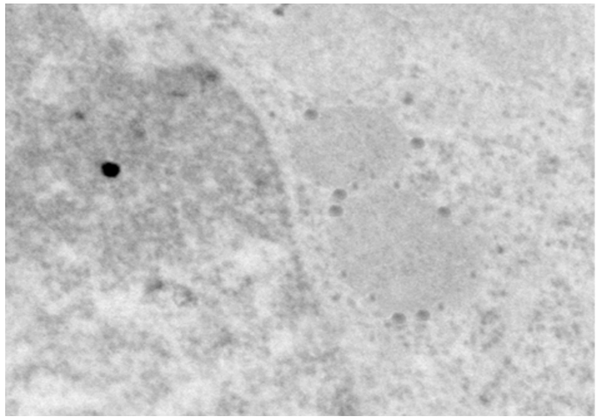
Compare in the same conditions

Image should be documented

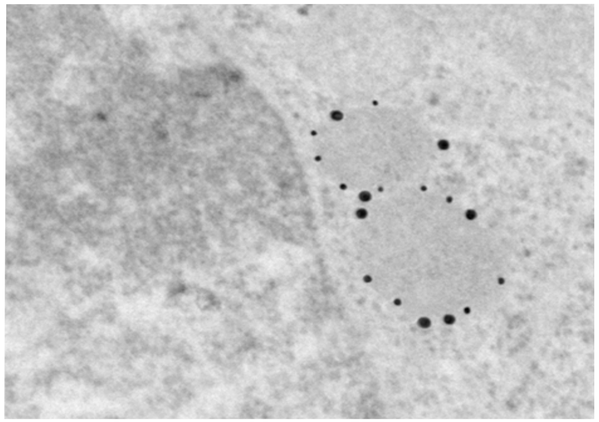
Reporting the analysis script

What's in a picture? The temptation of image manipulation
Mike Rossner 2004

Manipulation and misconduct
C. Blatt, Plant Physiology, 2013

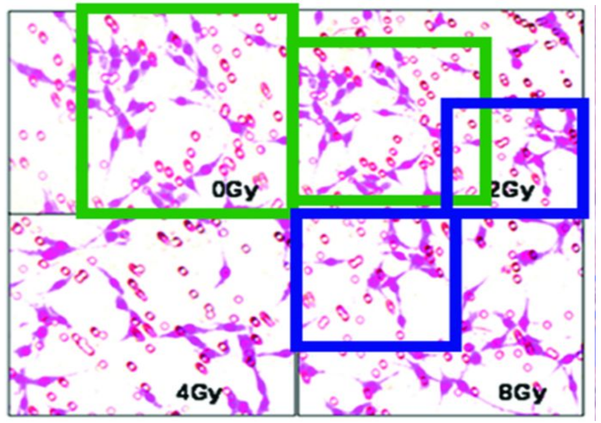


Original



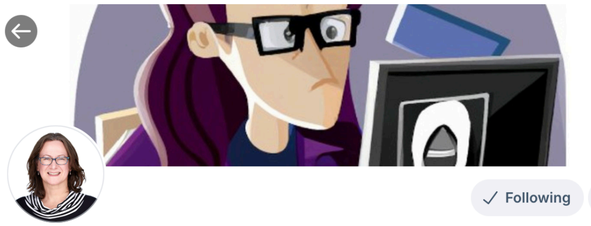
Manipulated

Science Integrity



Avoiding twisted pixels
D. Cromey, 2010

Mishandling and Misconducts
K. Miura, S. Nørrelykke, 2021



The super-spotter of duplicated images in science papers

The prevalence of inappropriate image duplication in biomedical research publications
Bik, E. (2016).

Responsable Imaging

Good Practices

Code
Open-source, versioning, test
➜ Git

Data
Accessible
Meta-data
➜ Zenodo

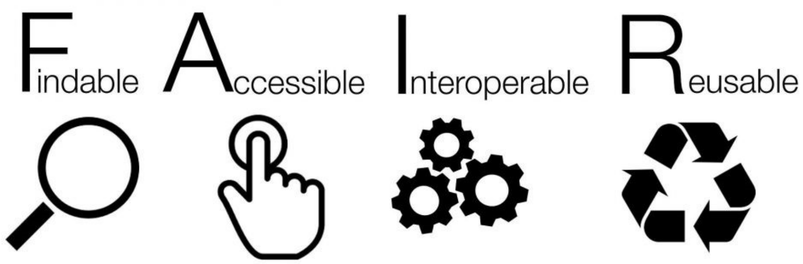
Results
Open Access
publication

Illustration from the online book
The Turing Way

Software usability

Bioimage informatics: usability is essential
P. Paul-Gilloteaux, PLoS, 2023
A call for bioimaging software usability
Carpenter A, Nat. Meth. 2012

Open Science



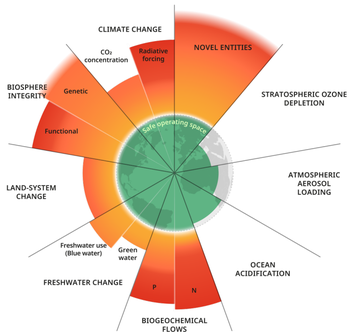
Building a FAIR image data ecosystem for microscopy communities
Aastha Mathur, Histochem Cell Biol. 2023

Sustainability

Overshot of the planetary boundaries

Digital: Life-span cycle of equipments (gray energy)

➜ green-algorithms.org



EPFL

Bioimage Informatics

Daniel Sage & Arne Seitz

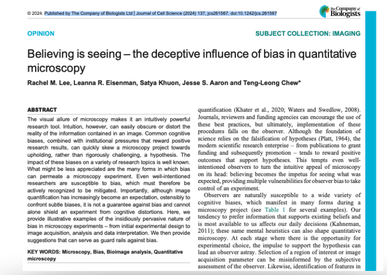
Extra Material

Human Factors

Human Bias

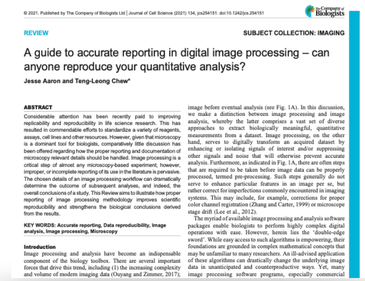
Believing is seeing – the deceptive influence of bias in quantitative microscopy
R. M. Lee et al.

Journal of Cell Science 2024



A guide to accurate reporting in digital image processing
J. Aaron and T.-L. Chew

Journal of Cell Science 2024

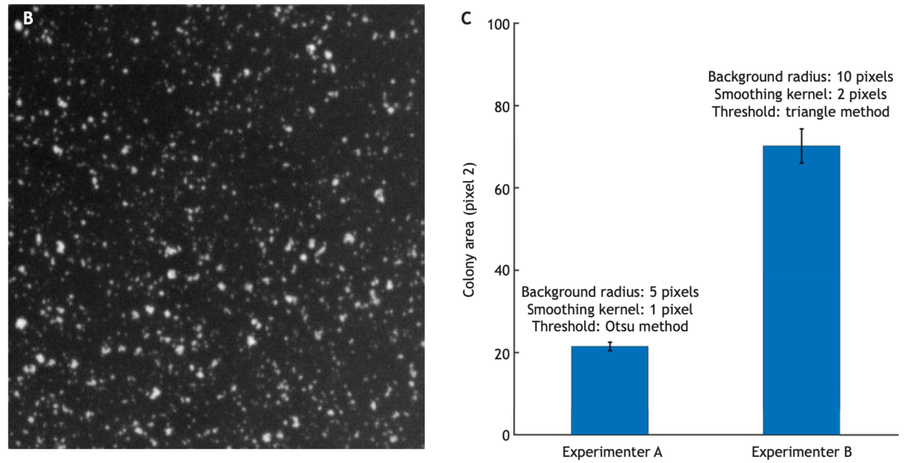


Cognitive Bias

Clustering illusion	Seeing groups as significant when they are random
Color perception	Illusions due to misleading perception of colors
Confirmation bias	Favoring information that supports existing beliefs
Congruence bias	Not testing alternative hypotheses for the observed data
Contrast effect	Over- or under-estimating a feature based on surroundings
Illusory correlation	Seeing a relationship where there is no correlation
Pareidolia	Seeing patterns that do not exist
Publication bias	Withholding negative results from publication
Recency bias	Giving greater weight to more recent observations
Selection bias	Focusing on a sample that is not representative
Survivorship bias	Overlooking data that does not survive a selection process

Reproducibility

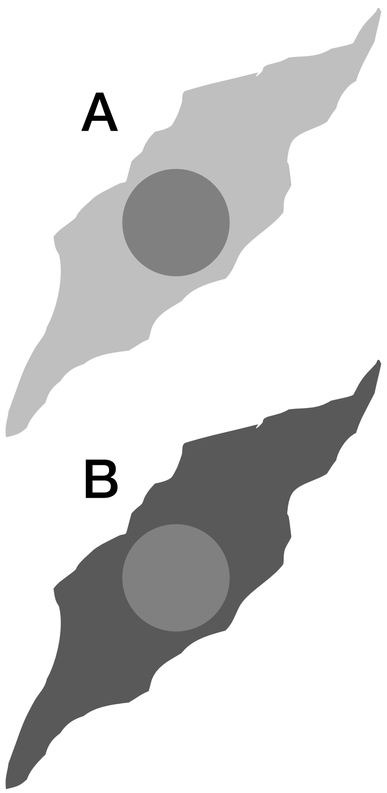
Can anyone reproduce your quantitative analysis?

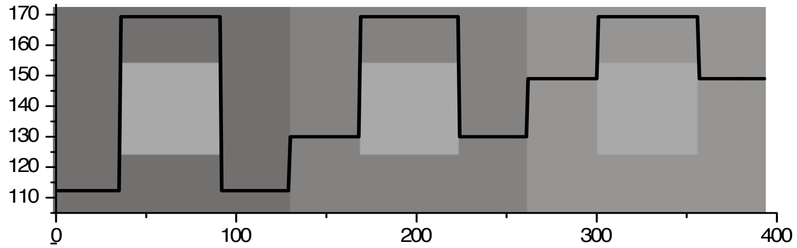


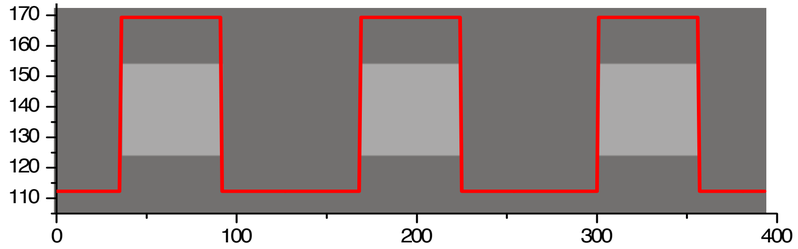
Human Perception

HUMAN INTERPRETATION IS BIASED BY TO THE CONTEXT

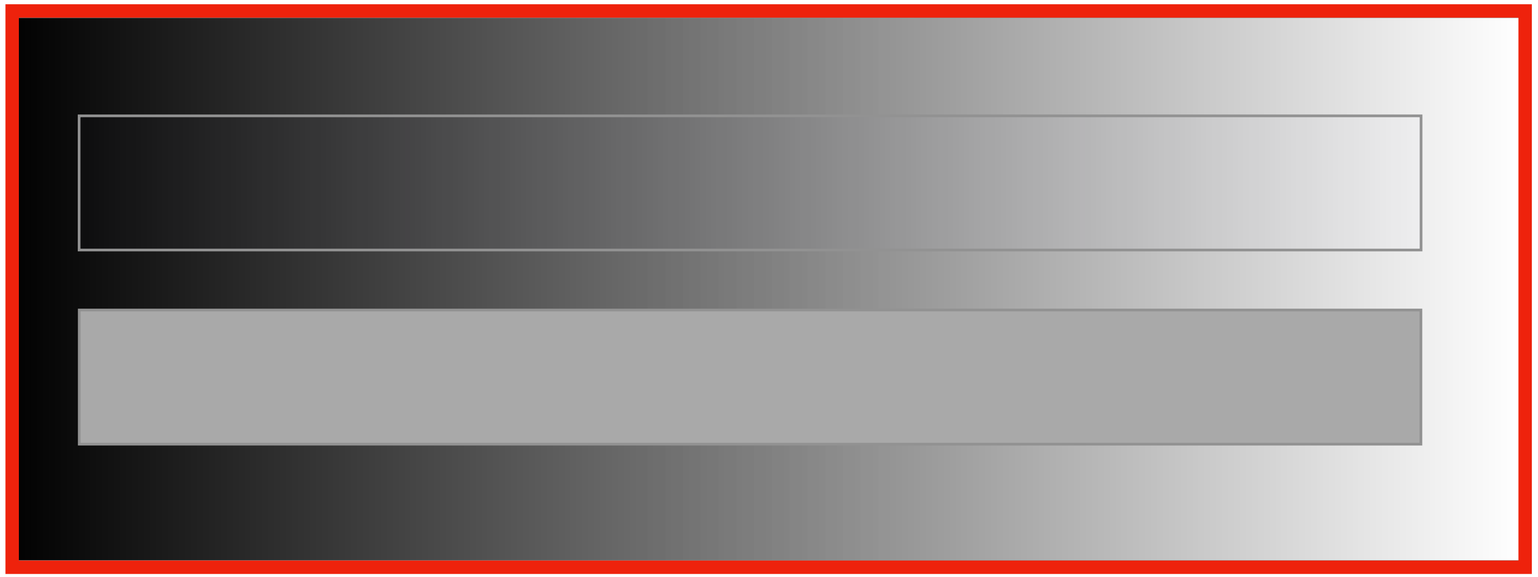
Which disk is brighter?





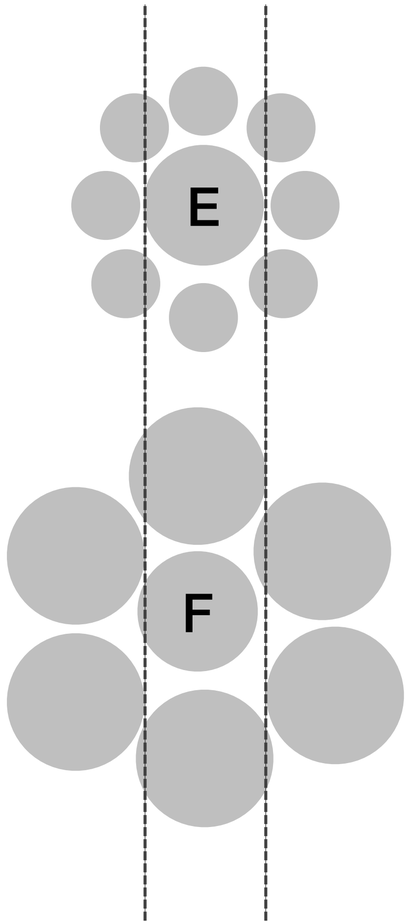


Which bar has a gradient?



Human Interpretation

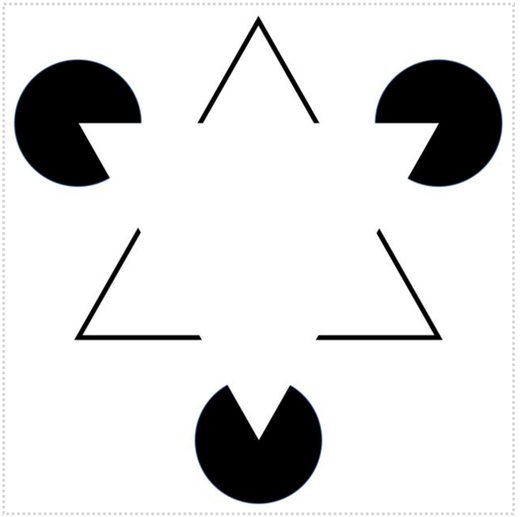
Which disk is larger?

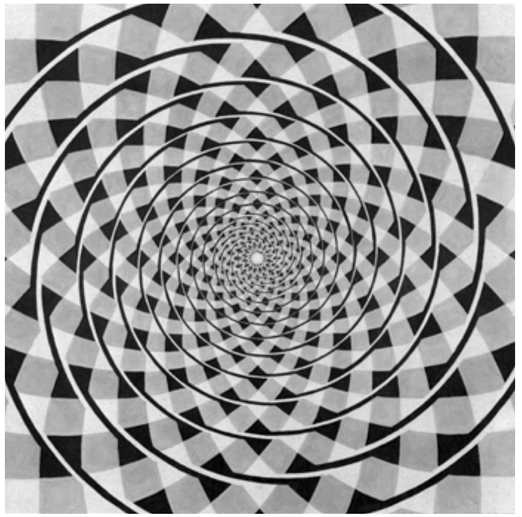


SEEING IS BELIEVING, QUANTIFYING IS SCIENCE

Hallucination

Seeing the scientific image, John C. Russ www.drjohnruss.com





Interpretation

Seeing is believing? Alison J. North Journal of Cell Biology 2006