Objects Characterization to Detect Degree of Malignancy in Breast Cancer Histopathology

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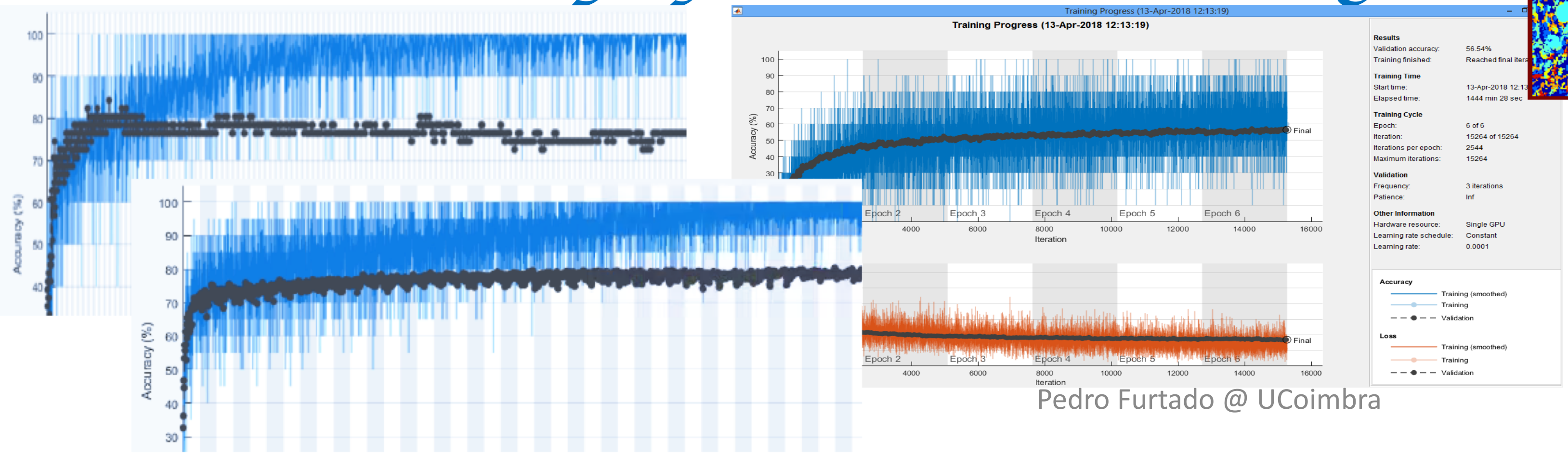
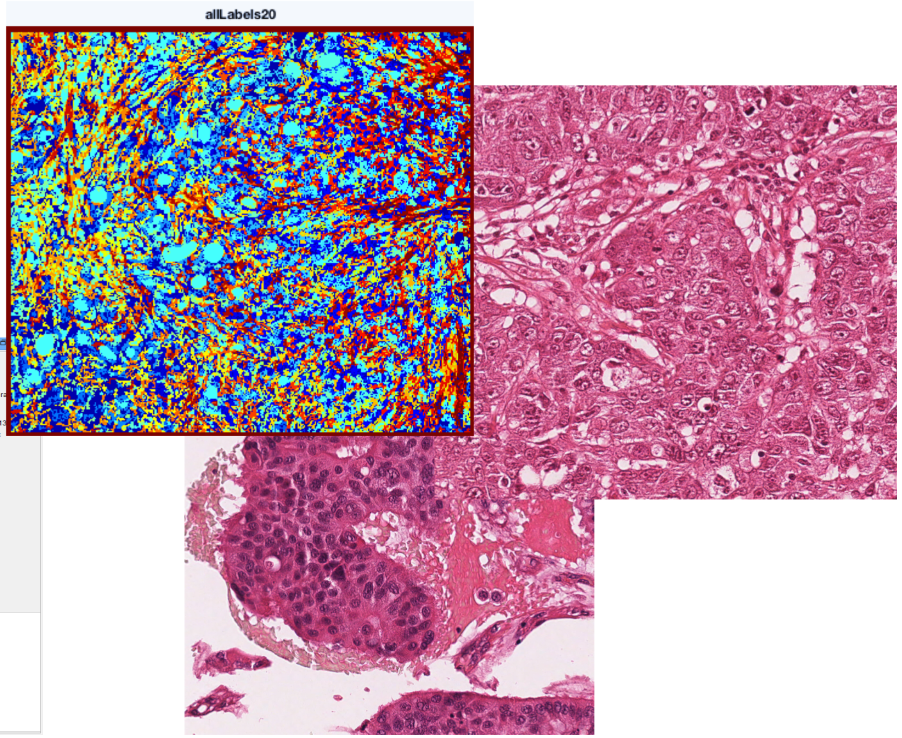
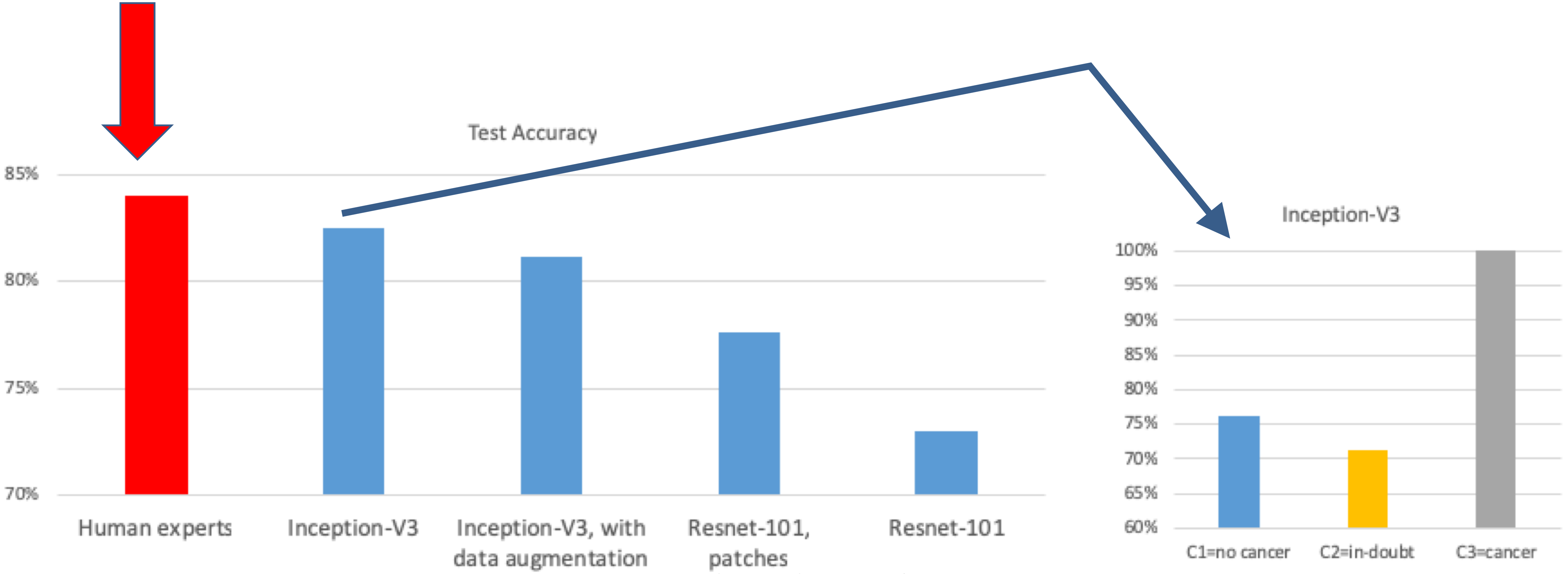




Cancer-grading, hystopathology images, mytos atypia public dataset

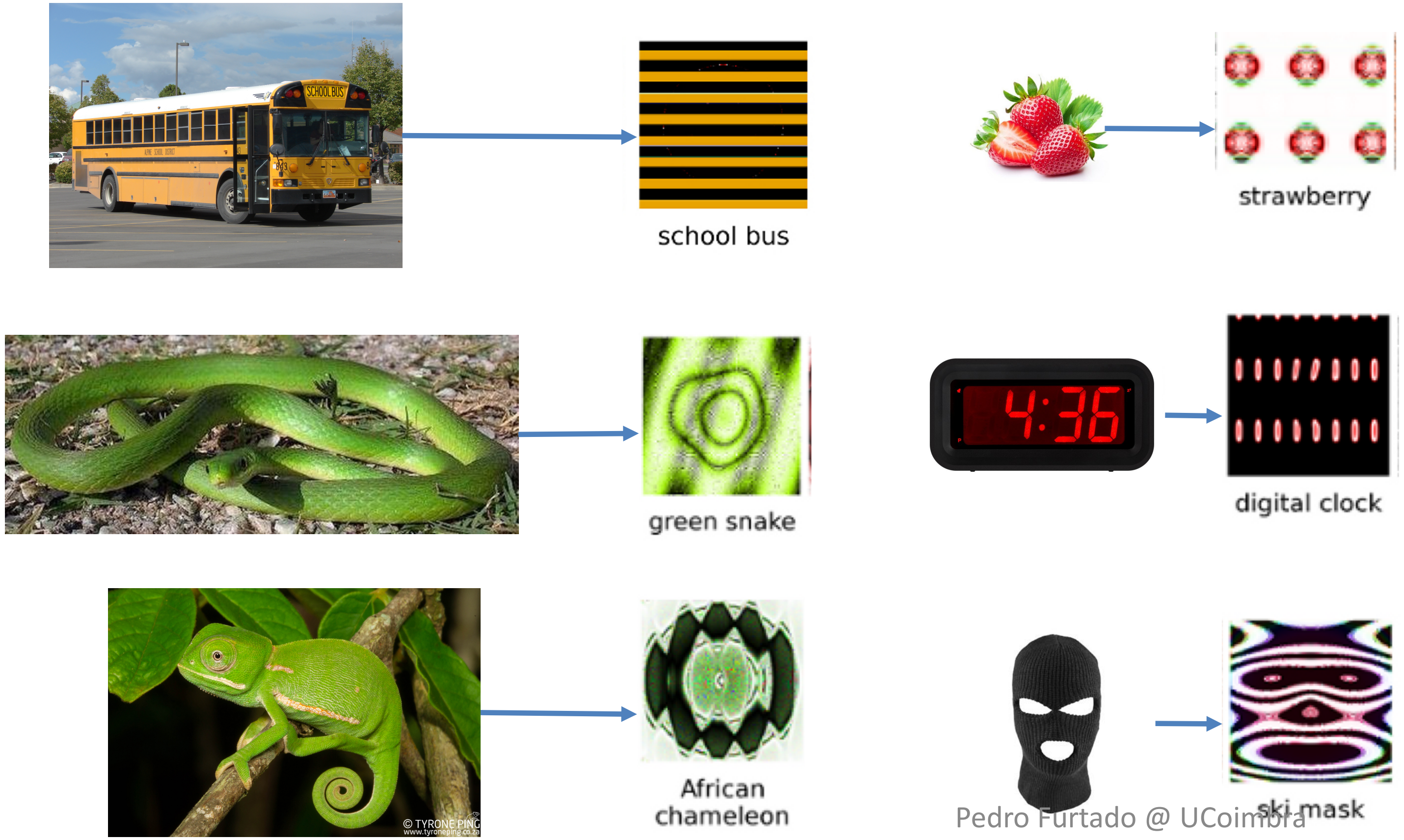
- CNNs are easy to use and very accurate...
- But they need tons of labelled data...
- AND perhaps human experts detect details and variations well...



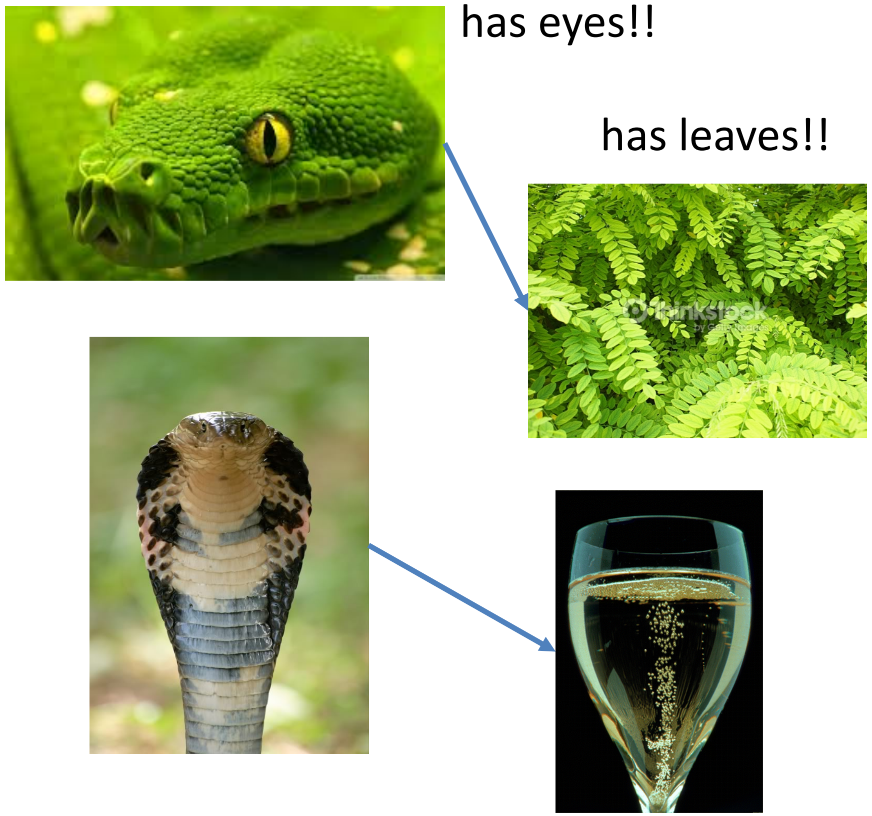
And some funny CNN problems?

in: Nguyen A, Yosinski J, Clune J. Deep Neural Networks are Easily Fooled: High Confidence Predictions for Unrecognizable Images. In Computer Vision and Pattern Recognition (CVPR '15), IEEE, 2015.

The **mean DNN confidence scores for these images is 99.12%** for the listed class, meaning that the DNN believes with near-certainty that the image is that type of thing.



Some examples we got sometime ago:



Some non-CNN work had TOP ACCURACIES

- **E.g. Breast Cancer Wisconsin (Diagnostic) Data Set**
  - Measured Geometries
  - Involved some human intervention

!!Precision 97%, recall 97%!!

Cell characteristics:
a) radius, perimeter, area
b) texture (standard deviation of gray-scale values)
e) smoothness (local variation in radius lengths)
f) compactness (perimeter^2 / area - 1.0)
g) concavity (severity of concave portions of the contour)
h) concave points (number of concave portions of the contour)
i) symmetry
...

Classificador	Precisão	Recall
BayesNet	96.7%	97.3%
NaiveBayes	95.4%	96.2%
LibSVM	95.0%	96.2%
Logistic	96.3%	96.3%
MultilayerPerceptron	94.8%	95.1%
SimpleLogistic	95.8%	95.6%
supportVector.PolyKernel	96.7%	96.9%
Nearest Neighbour 1	94.9%	94.6%
KStar	95.4%	94.7%
AdaBoost	94.5%	94.4%
J48	94.2%	94.2%
RandomForest	96.1%	96.3%
RadomTree	92.5%	92.1%

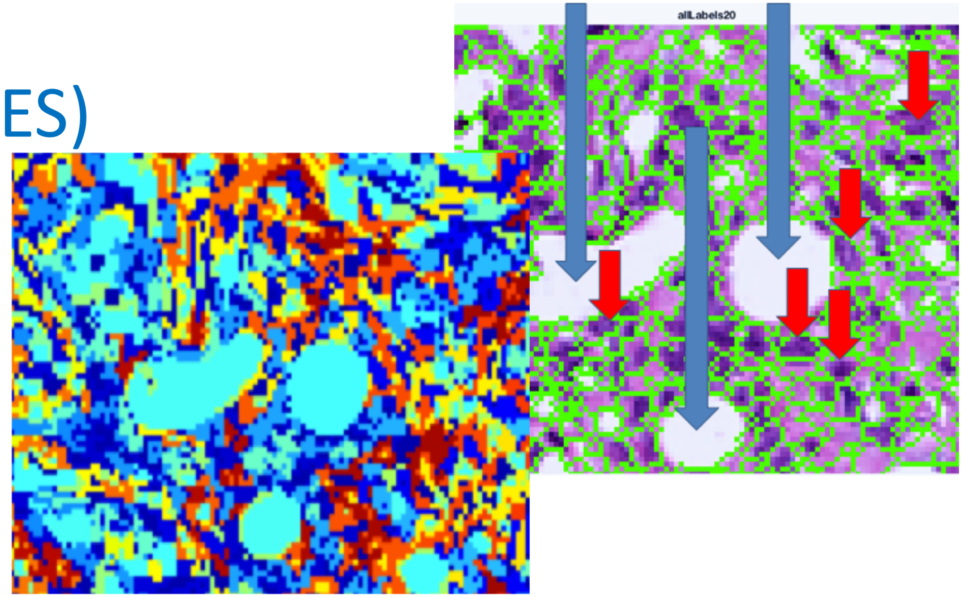
[2] W.H. Wolberg, W.N. Street, D.M. Heisey, and O.L. Mangasarian. Computer-derived nuclear features distinguish malignant from benign breast cytology. Human Pathology, 26:792--796, 1995.

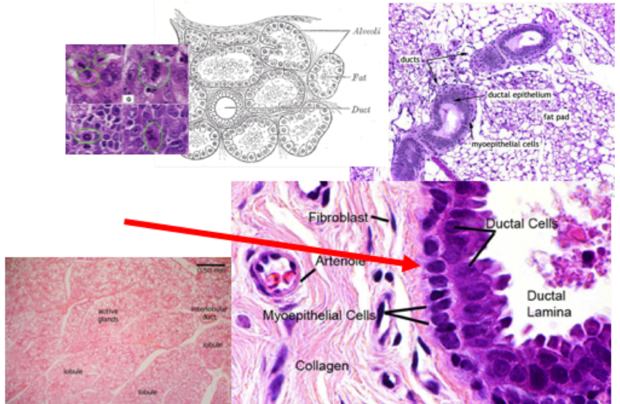
OBI= object-based identification

Structures have characteristic props in healthy versus ill tissue

Automate:

1. Discriminate objs into types (SEMANTIC ENTITIES)
2. Characterize objs and object types adequately
3. Characterize normality/abnormality from that
4. Use that for better detection from images





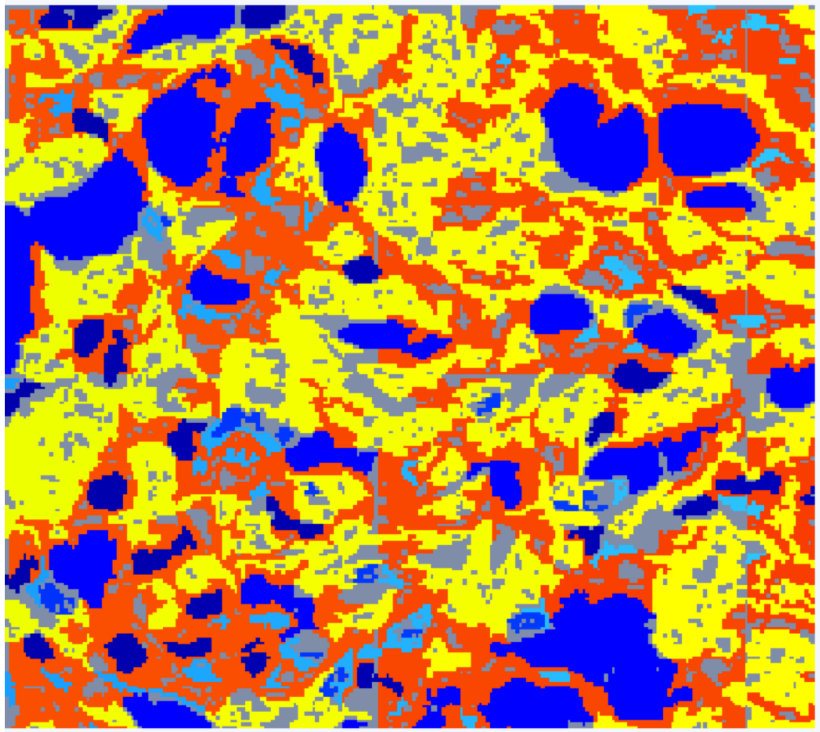
There is LOTS OS SEMANTICS in breast hysto

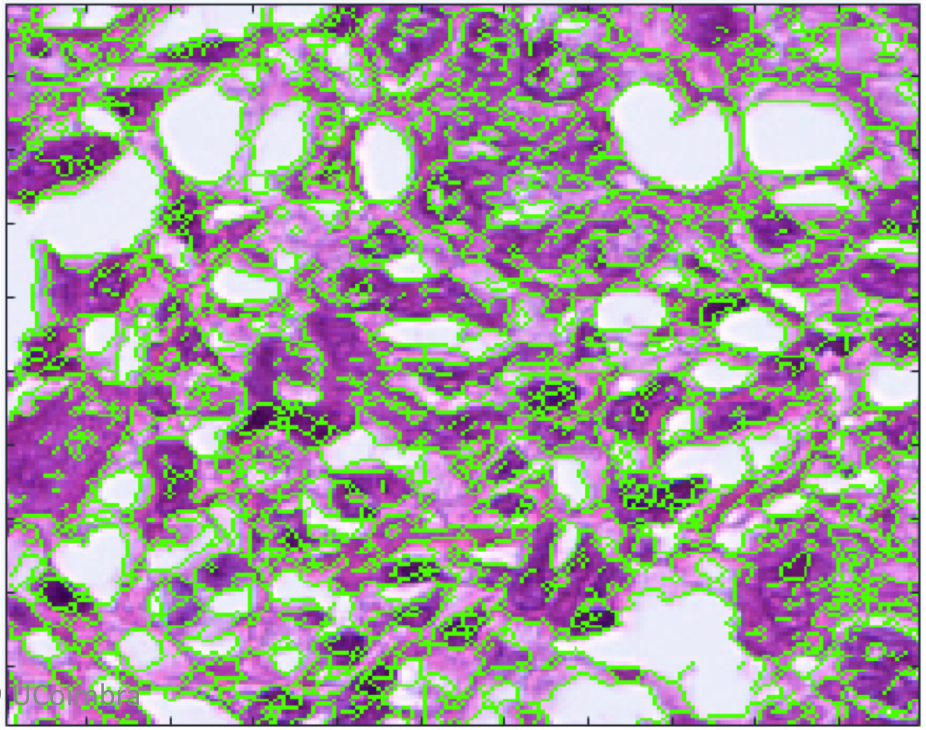
Lots of specific simple and composite objects/structures

Lots of atypia conditions

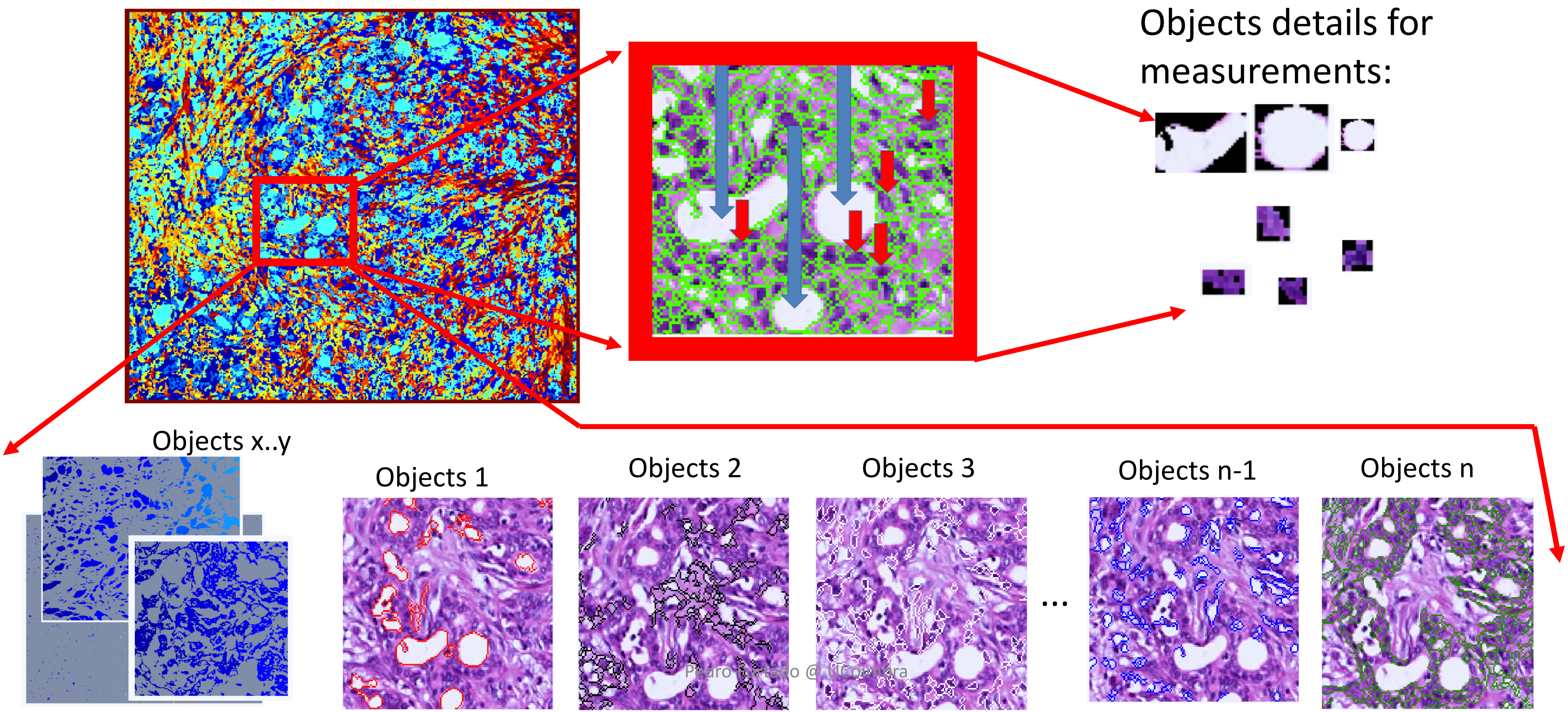
1. discriminate objects/structures

In image/images





Segment, label and separate into types



2. Object type characterization...

Capture characteristics

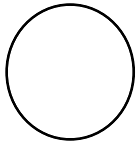
- Vacuoles, Adipocits
- Mammarian cells
- Clusters of cells
- Interstitial Tissue
- Other Cells
- ...

Characteristics are captured by features…

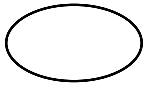
- Instead of low-level, try to capture shape, geom, texture semantics
- Some features are very “descriptive”
  - e.g. characterize shape based on slope and slope derivative

slope is constant

d slope is ~ 0

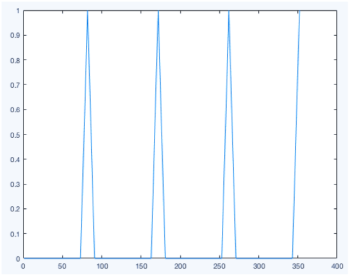


(dslope= slope change) is constant



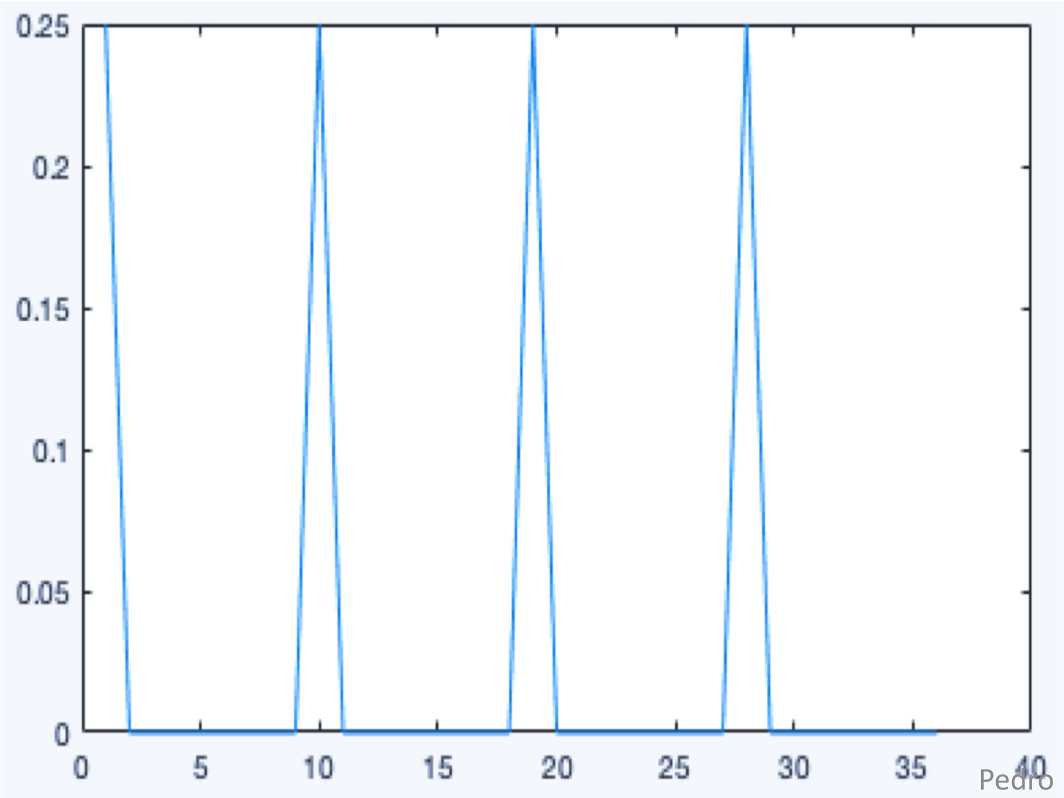
slope:

slope:

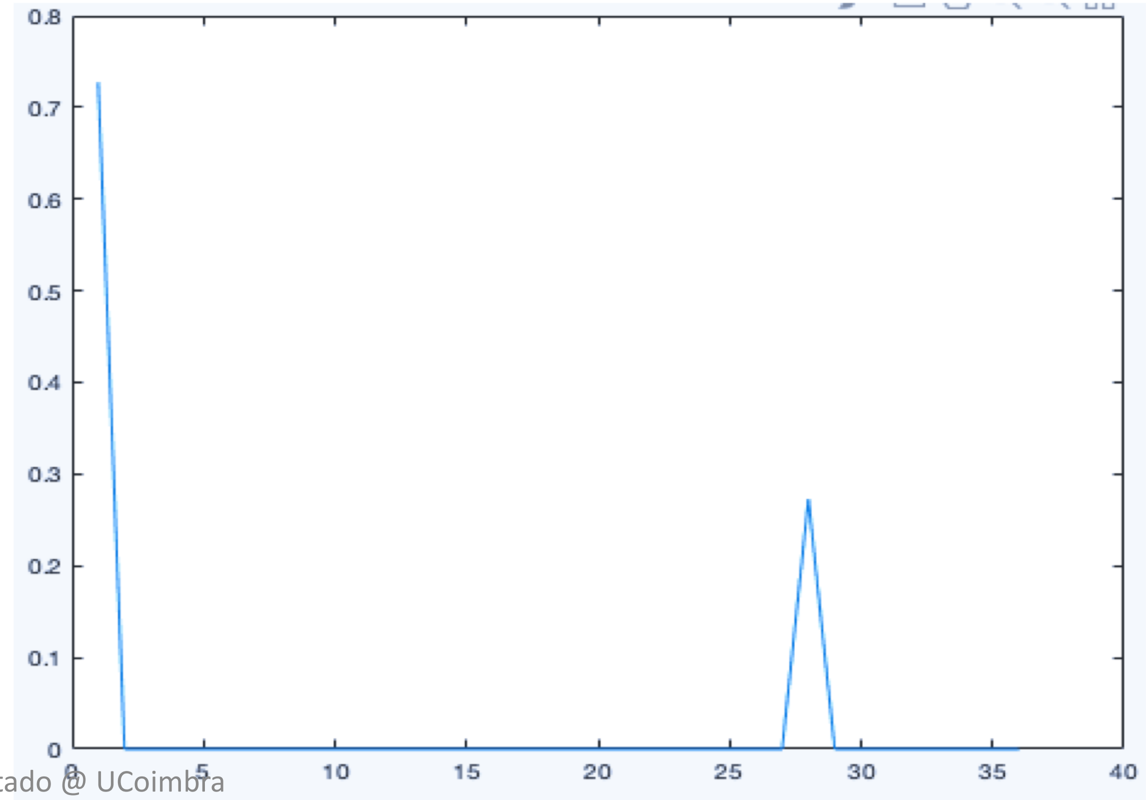


Shape slope/dslope histograms & seqs

Slope histogram and sequence



Dslope histogram and sequence

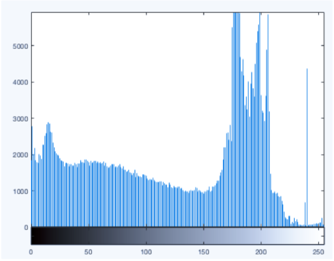


Features=measures can completely characterize regions

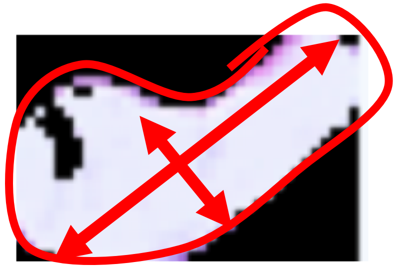
~600 feature values => NCGTS

Feature types:

- **N**umber per unit area
- **C**olour histograms (r,g,b,L,a,b,gray)



- **G**eometry (shape generic)
  - Area, Solidity, mAxis, MAxis, Eccentricity, ConvexArea, Extent



- **T**exture =
  - gray-level co-occurrence matrix, co-occurence properties with rotation invariance
  - colour-spatial distance "texture" 2D histogram

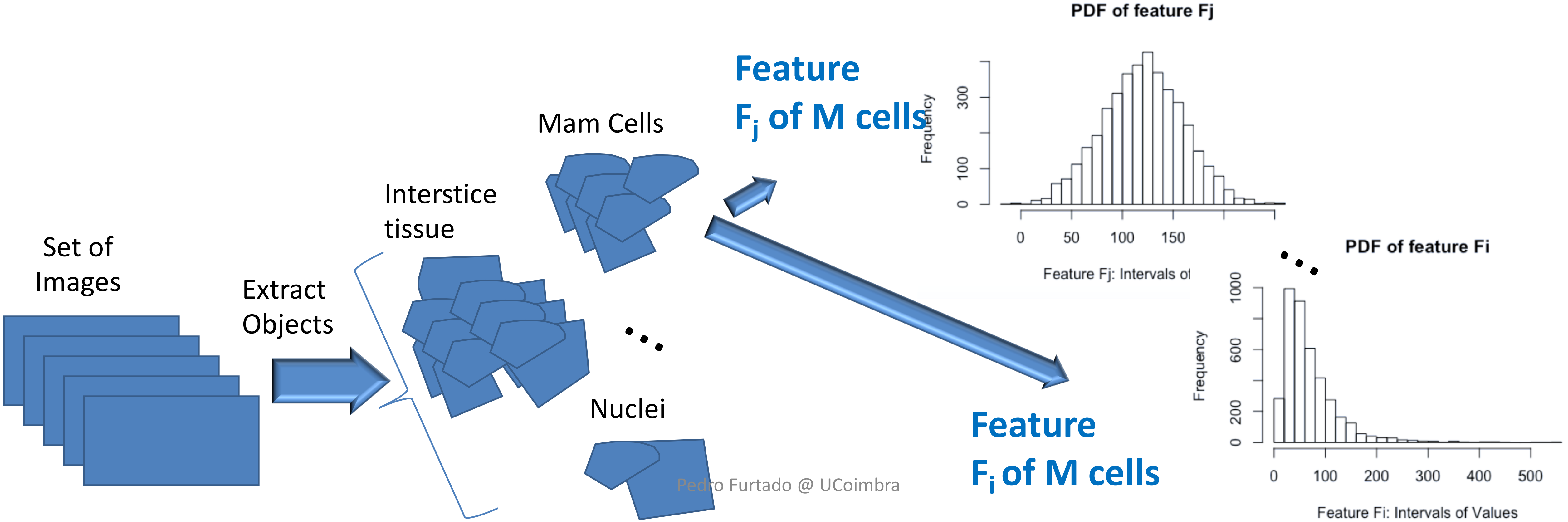
- **S**hapes =
  - Histograms of slopes, dSlopes and ddSlopes (variation of slopes in consecutive edge points)
  - 2D histograms (slope, dslope, ddslope) X spatial distance
  - Slope sequence histograms Slope sequences + histograms of slopes sequences

3. Characterize Normality/Abnormality...

Classes distinguish disease conditions

How to characterize OBJ (e.g. Mammarian Cells)

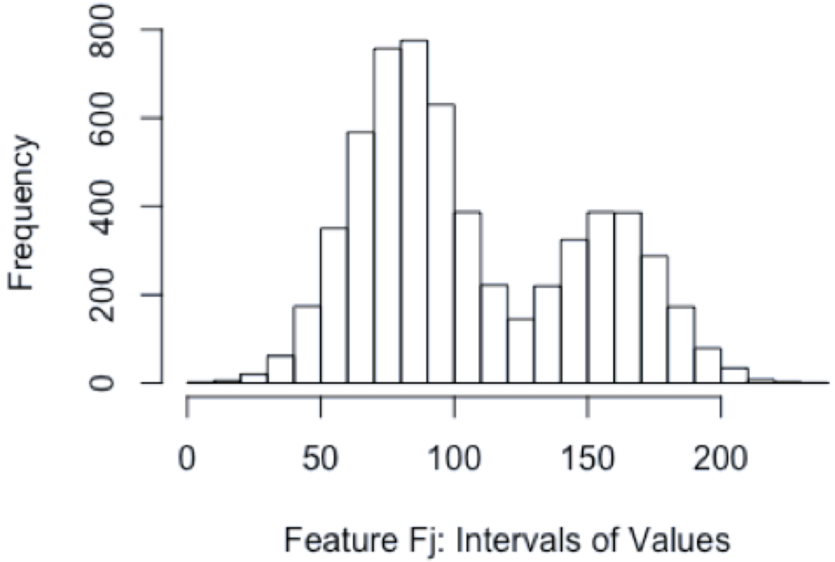
- Based on a transformation:
- Get distribution of each feature value: (PDF) => histogram



How to characterize degree of disease?

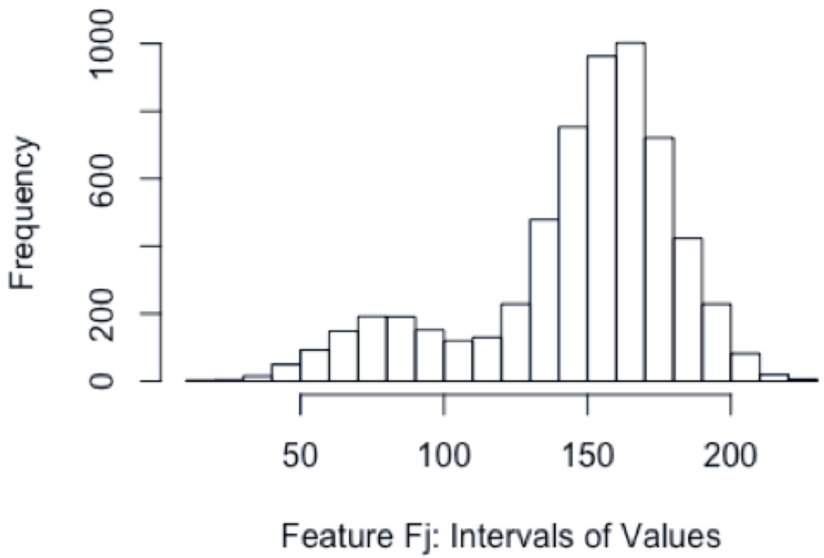
- Variations in distribution (PDF) (normal/abnormal, degree)
  - e.g. “Sizes, shapes, textures, density of each type of object

PDF of value F_j in normal images



≠

PDF of value F_j in cancer images



Which translates to …

- Detecting which distribution details distinguish better the degree of disease

Which translates to …

- Keeping histogram intervals with TOP degree of correlation to class = degree

Which is done by…

- Data reduction indepedently for each OBJ TYPE

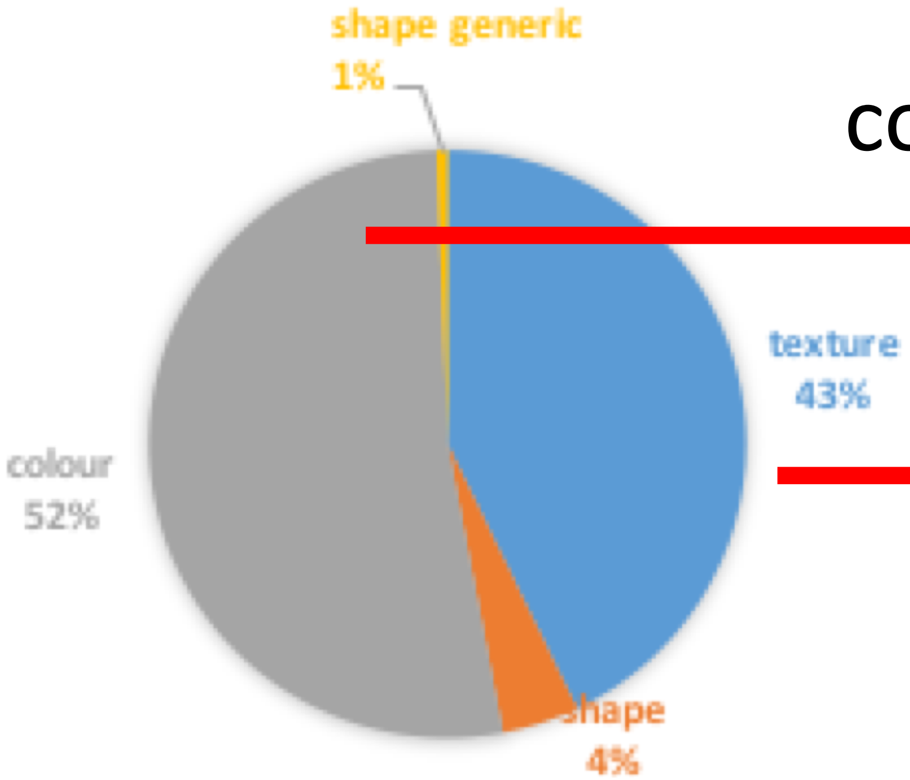
Data reduction …

- Reduce huge amount of feature values ~72000 (72K)
  - Each feature value (600) for each object type (6) has 20 histo intervals (PDF)
- Approach: CORRELATION
  - Keep top corr with the class = degree of malignancy
  - Drop 1 of redundant = highly correlated pairs
- Runtime optimized alg was needed
  - Corr with class **=> O(n)**
  - Pair-wise corr non-class **=> $O(n^2)$**

Also tested PCA and others,
Corr was the best

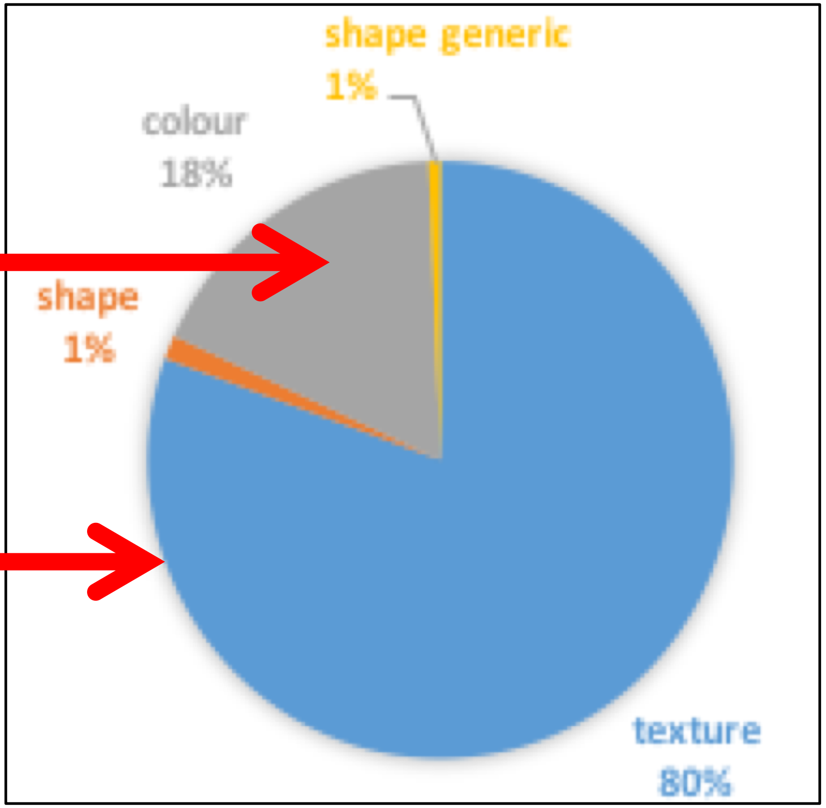
Unsurprisingly, Texture in Interstitial Tissue helps a lot detecting abnormality!

All objs	Interstitial Tissue



colour - 30%

Texture + 40%



Unsurprisingly, Shape+geo X Cells (also texture) helps a lot detecting abnormality!

All objs	Mammarian cells

4. Create a Classifier for malignancy

- Training Dataset was labeled by medical doctors
- Create a classifier (random forests, neural net, logit,...)

No cancer

In-Doubt

Cancer

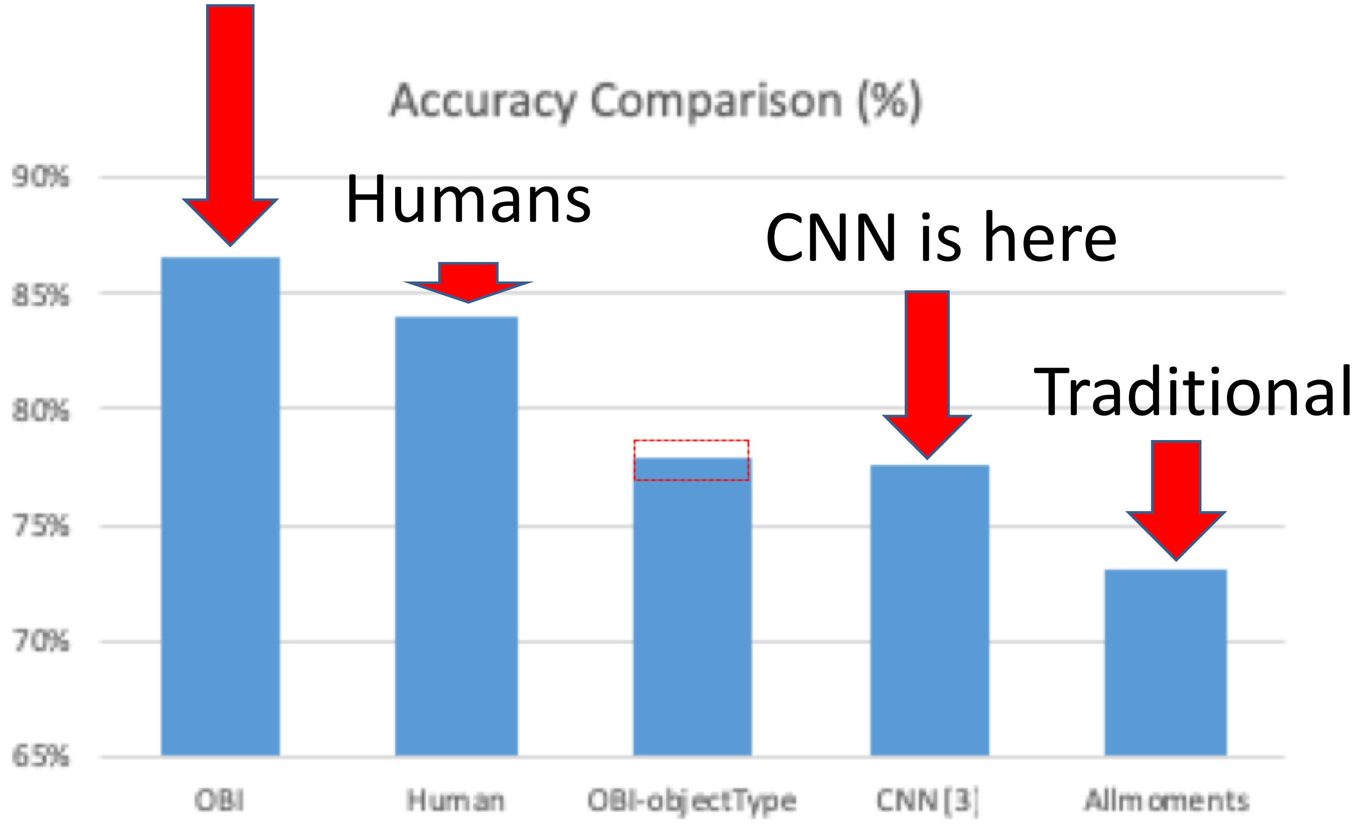
Model (maths) 

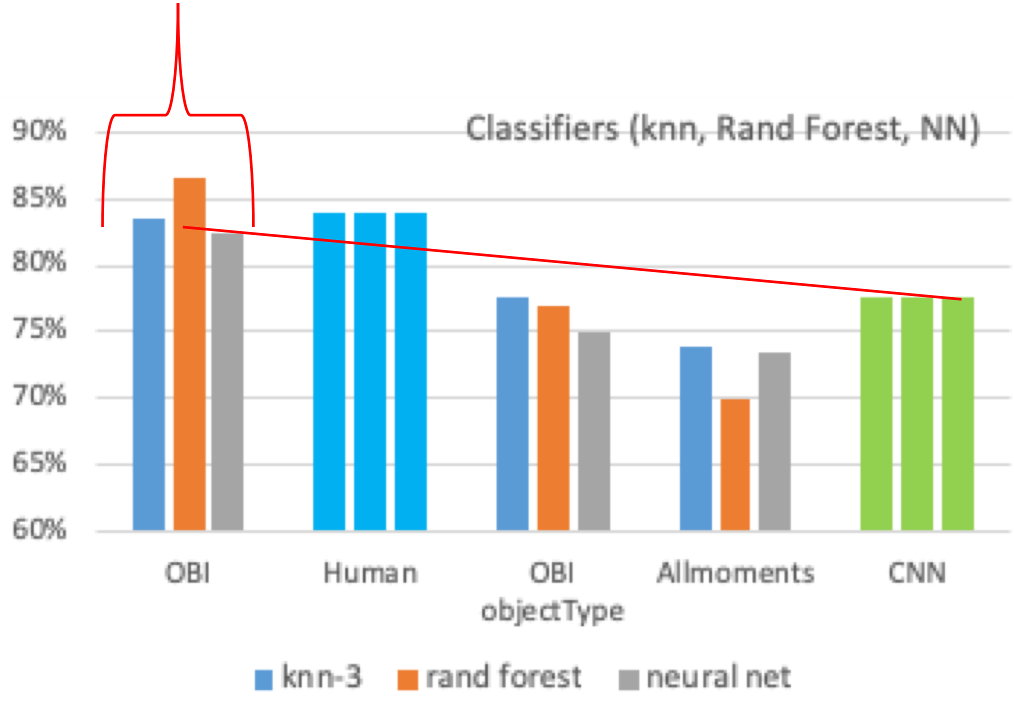
e.g.
Neural network
K-nn
Random Forest
Bayes net
...

Results (mytos atypia dataset 1136 frames)

Small variation with diferent classifier models, still best

OBI (proposed) had best accuracy



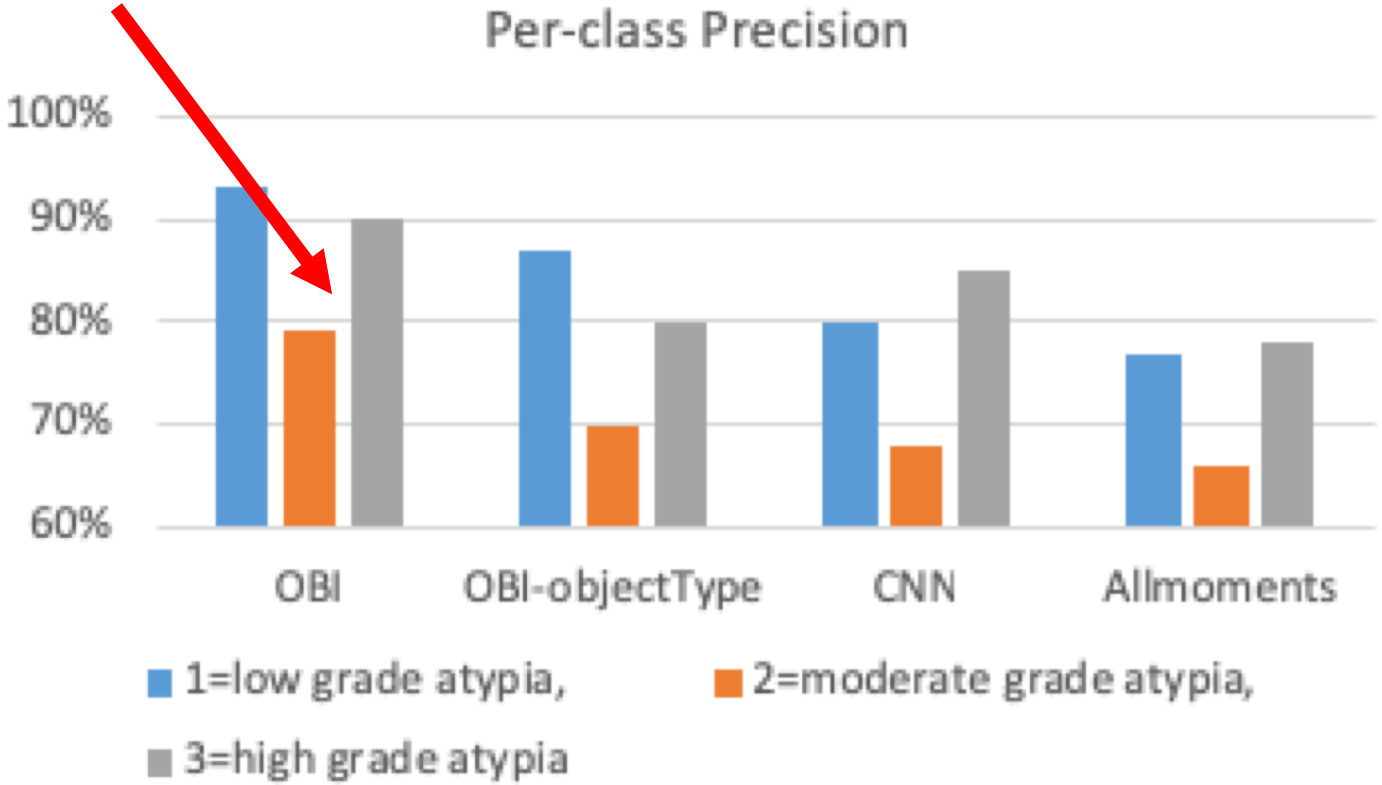


[3] Recognition rates with MITOS-ATYPIA-14 by using CNN features. by Kenji Watanabe
Takumi Kobayashi, Toshikazu Wada

Detail: Per-class precision

OBI (proposal) had best accuracy on each degree (class)

Class 2 = moderate grade atypia, is the most difficult and lowers overall accuracy

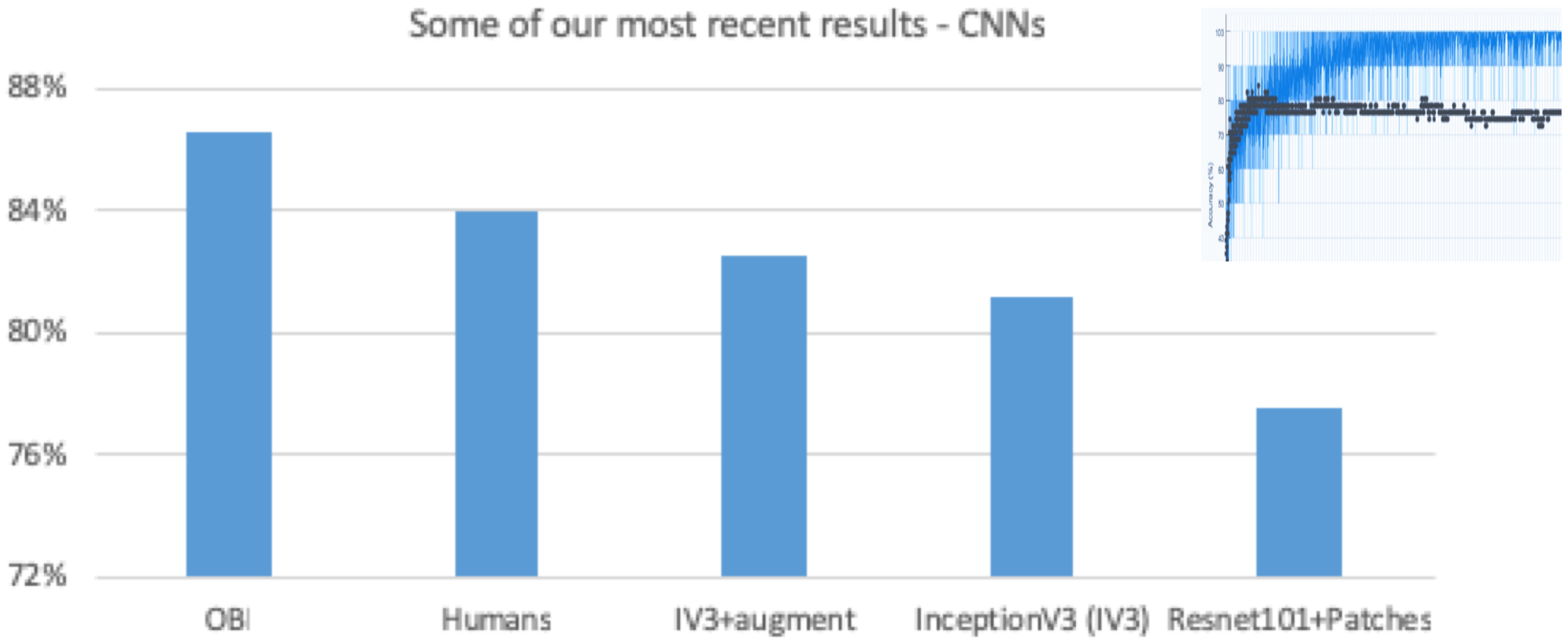


- Variations with the data

Variation	Accuracy
OBI	86,50%
OBI 2 classes	91%
OBI no balancing	95%

After this work, we continued experimenting…

- More comparison with CNNs ...included transfer L, patching and augmentation
- CNNs improved, but still below OBI



Conclusions

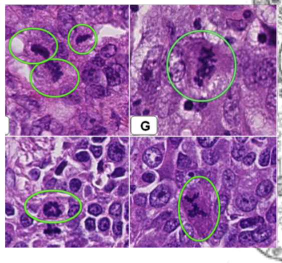
- OBI (the proposal) is able to achieve top accuracy on the tested problema
- Completely automatic
- Characterize structures
- Detect variations to detect degree of malignancy/atypia
- This can be improved a lot further => FUTURE= increase use of semantic structures

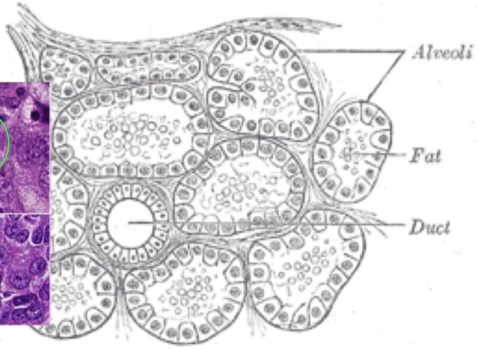
Our future work on this…

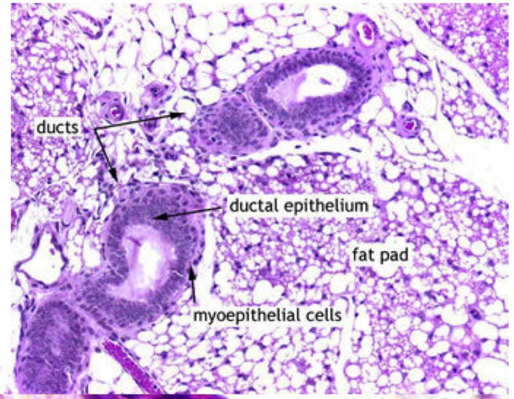
- Further domain knowledge => identify complex structures and normal VS disease VARs -> need pathologist
- Improve segmentation, add elicitation of complex structures
- Speedup feature extract and characterization
- Merge this with Deep Learning

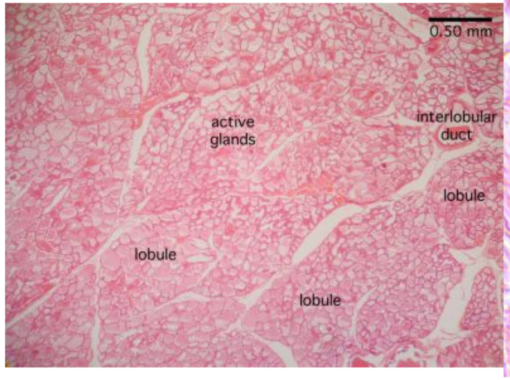
There is a lot more Semantics to explore ...

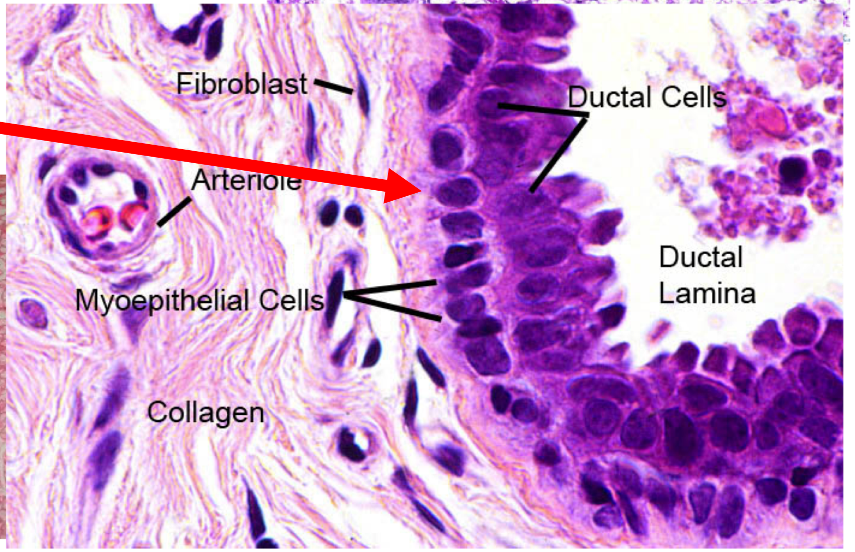
- Object types = structures
  - cell, cell nucleous, cytoplasm, membrane
  - cell nucleous mytosis (division into 2)
    mytosis phases: metaphase, anaphase, telophase
  - ducts, lobules, alveoli
  - mamarian cells, lymphocites
  - ductal cells
  - inner cuboidal epithelial + outer layer myoepithelial cells
  - interstitial tissue
  - vacuoles, adipose tissue











- More specific identification of atypia
  - Ductal hyperplasia
  - Atypical ductal hyperplasia
  - Ductal carcinoma in-situ (dcis)
  - DCIS with microinvasion
  - Invasive ductal cancer

Thank you!

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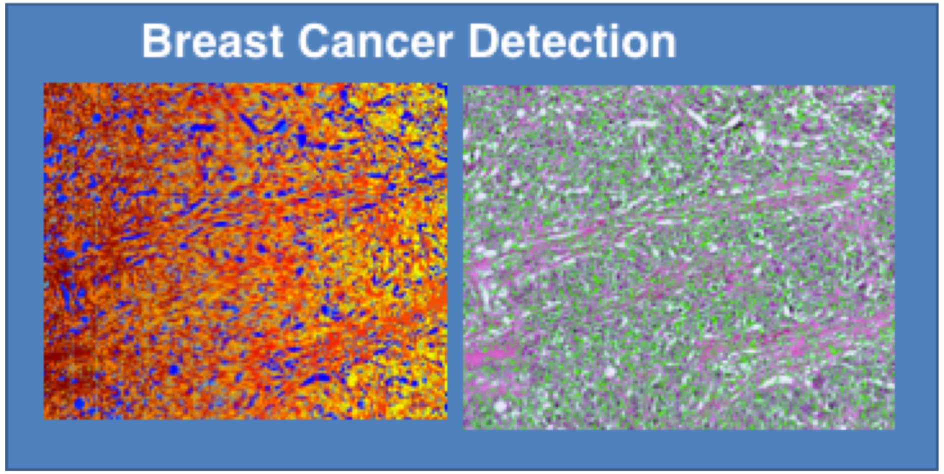
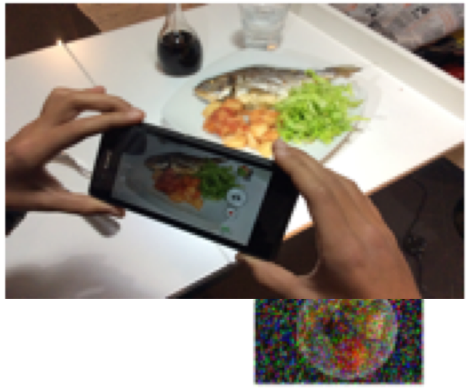
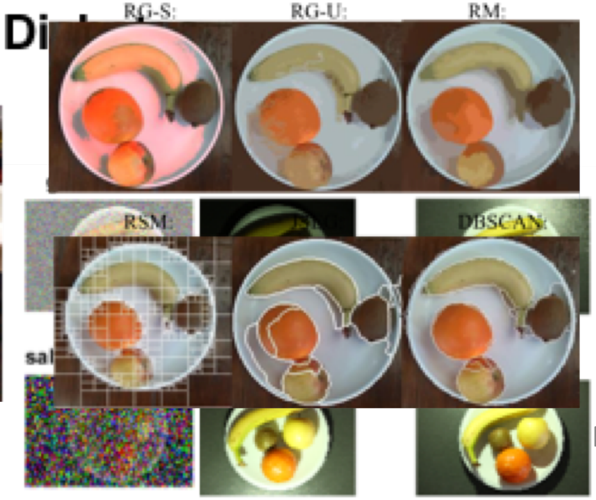


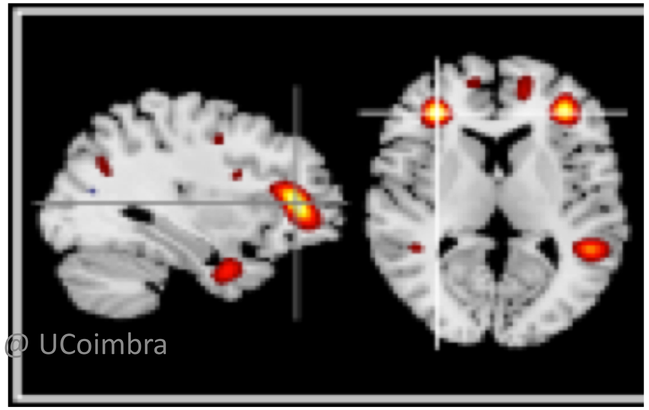
Automated CHC In Self-management Of Di



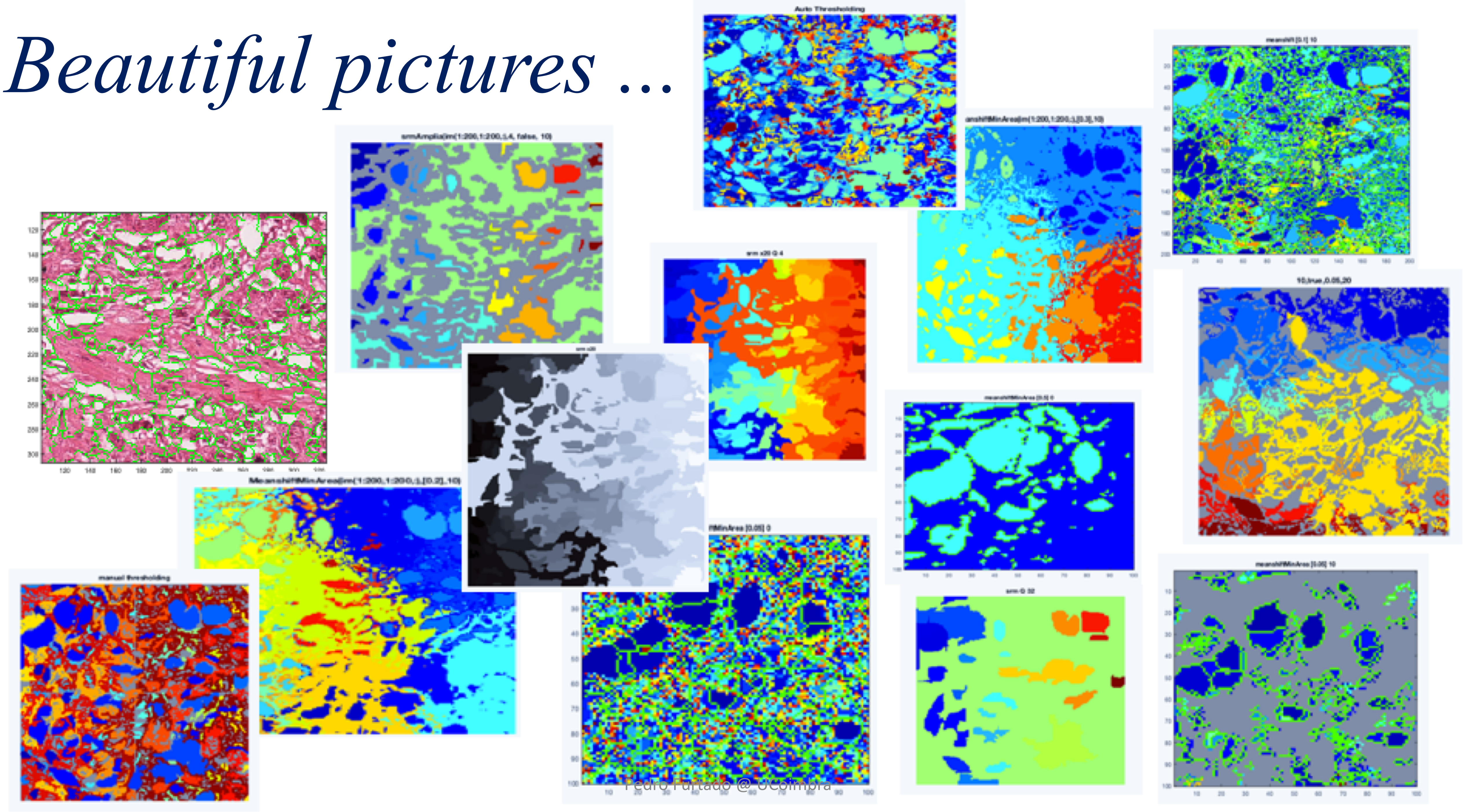
Food segmentation



Seizures Detection



Beautiful pictures …



Appendix

Setup:
Dataset

Mytos-Atypia

284x4 RGB frames at X20 magnification.
Nuclear atypia score 1=low grade atypia, 2=moderate grade atypia, 3=high grade atypia.

Score given independently by two different senior pathologists. There were some frames for which the pathologists disagree and gave a different score.

Methods tried

- OBI = our approach = object-based identification
- allMoments = Standard classification pipeline
- Human = classification done by humans
- OBI-objectType = OBI with just one of the object types

Execution time problems (again)

Example nr of regions for segmentation in image = 3400

- time PreProcess Colour:1.8231 secs
- time extract Colour:3.7685 secs -> 0.93 secs
- time extract GLCM: 29.0835 secs-> 13.6 secs
- time extract tDSD Texture:3.3383 secs -> 2.44 secs
- time extract Shape: 16.8656 secs -> 12.9 secs

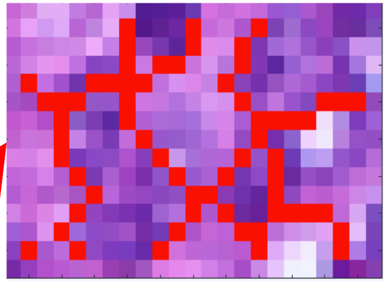
~ **54 secs** per image, just for feature extraction **=> 23 secs**

- CONCLUSIONS:
- We had to cut a huge lot of detail everywhere for processing time

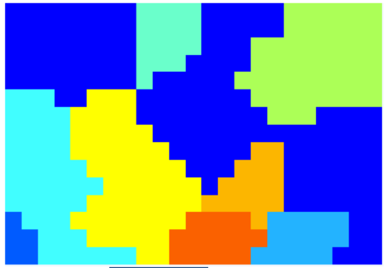
MacBook Pro, MacOS Sierra 10.12, 2,5 GHz Intel Core i5, 16GB RAM, SSD

*We also want to add **later** (computation-hard):*

- Complex Objects, Groups, topology, neighborhood, spatial relations ...
  - e.g. spatial characteristics of invasive carcinoma
  - e.g. cell has a nucleous, cytoplasm and a membrane=> id cells



slicDbscan



Extract complex objs, topology relations

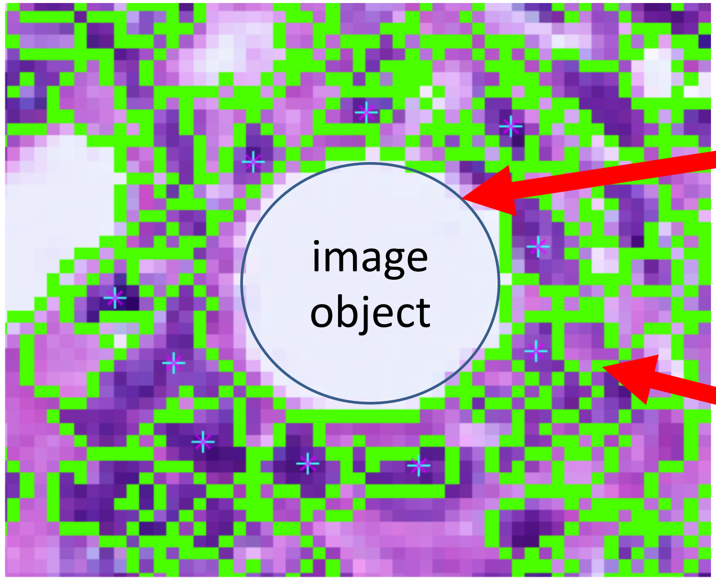


image object features

close neighborhood, layout, obj relations features