ipal
Image & Pervasive Access Lab

IMAGE AND PERVASIVE ACCESS LAB

Since 1998 …

ipal
Image & Pervasive Access Lab

www.ipal.cnrs.fr

cnrs
A*STAR Institute for Infocomm Research
UNIVERSITE JOSEPH FOURIER
NUS National University of Singapore
MINES TELECOM INSTITUT Mines-Télécom
UPMC SORBONNE UNIVERSITÉS

History and Evolution

1998-2007

IPAL
Image Processing and Application Lab
EP 1956 & FRE CNRS 2339

Image Processing
Image Indexing and Retrieval
Image and 3D Perception
Video Indexing and Retrieval

BUILDING CONFIDENCE

2007-2011

IPAL
Image Perception, Access & Language
UMI CNRS 2955

Content-Based Image/Information Retrieval
Multilingual Access to Multimodal Images
Mobile Information Access
Medical Image Analysis, Indexing, Retrieval

BENCHMARKING AND INNOVATION

2011-2015

IPAL
Image & Pervasive Access Lab
UMI CNRS 2955

Biomedical Image Understanding
Formal Methods and Model Checking
3D Visual Objects Streaming
Visual Memory Extension
Ambient Assistive Living

EXCELLENCE AND IMPACT

Our supporting Partners

- National University of Singapore (NUS)
- Institute for Infocomm Research (I^2R) Agency for Science Research and Technology (A*STAR)
- Centre National de la Recherche Scientifique (CNRS)
- Université Pierre et Marie Curie, Sorbonne Universités
- Institut Mines-Télécom
- Université Joseph Fourier, Grenoble 1

Role of IPAL

Scientific bridge between Singapore / ASEAN and France / EU

Role of IPAL

MAJOR IMPACTS

- Inspire scientific breakthrough by a new way of thinking : mixing Asian and European scientific research approaches
- Research Incubation Unit - future French/ASEAN sc. leaders
- Research HUB for French and ASEAN countries
- Translational research support for ASEAN emerging economies
- Accelerate innovative technologies maturation and deployment in a dynamic Singaporean and ASEAN environment
- Better understand each-other philosophy, culture, way of life

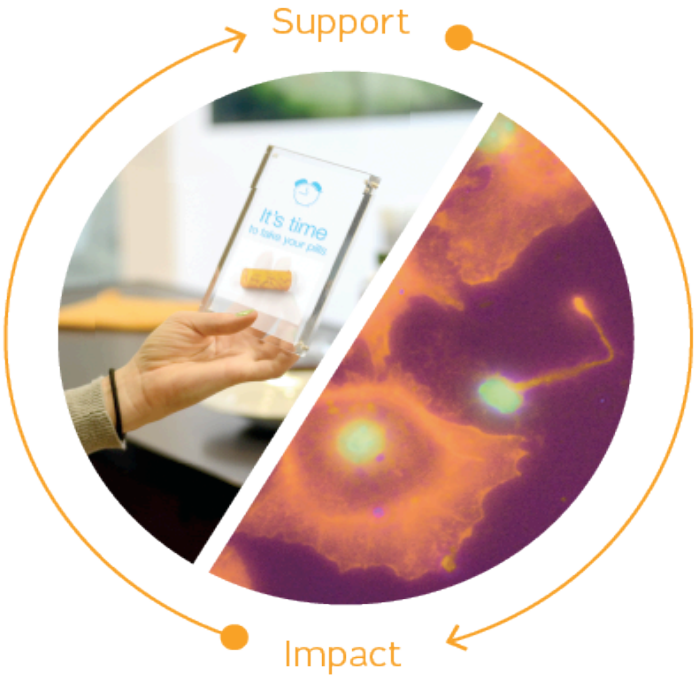
Research Themes / Focuses

Wellness

PAWM

Pervasive Access and Wellbeing Management

AAL - Ambient Assistive Living and Mobile Information Access



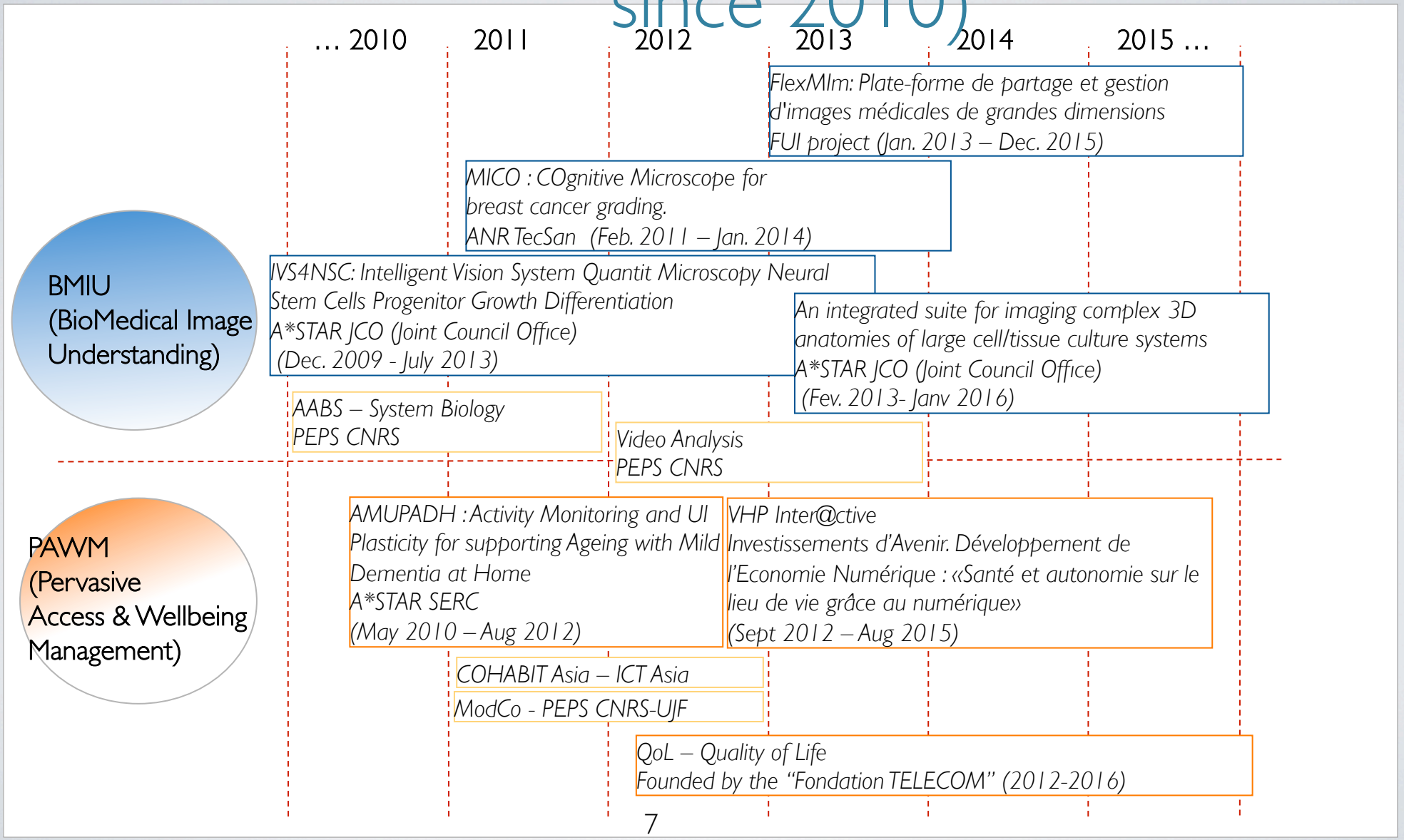
Healthcare

BMIU

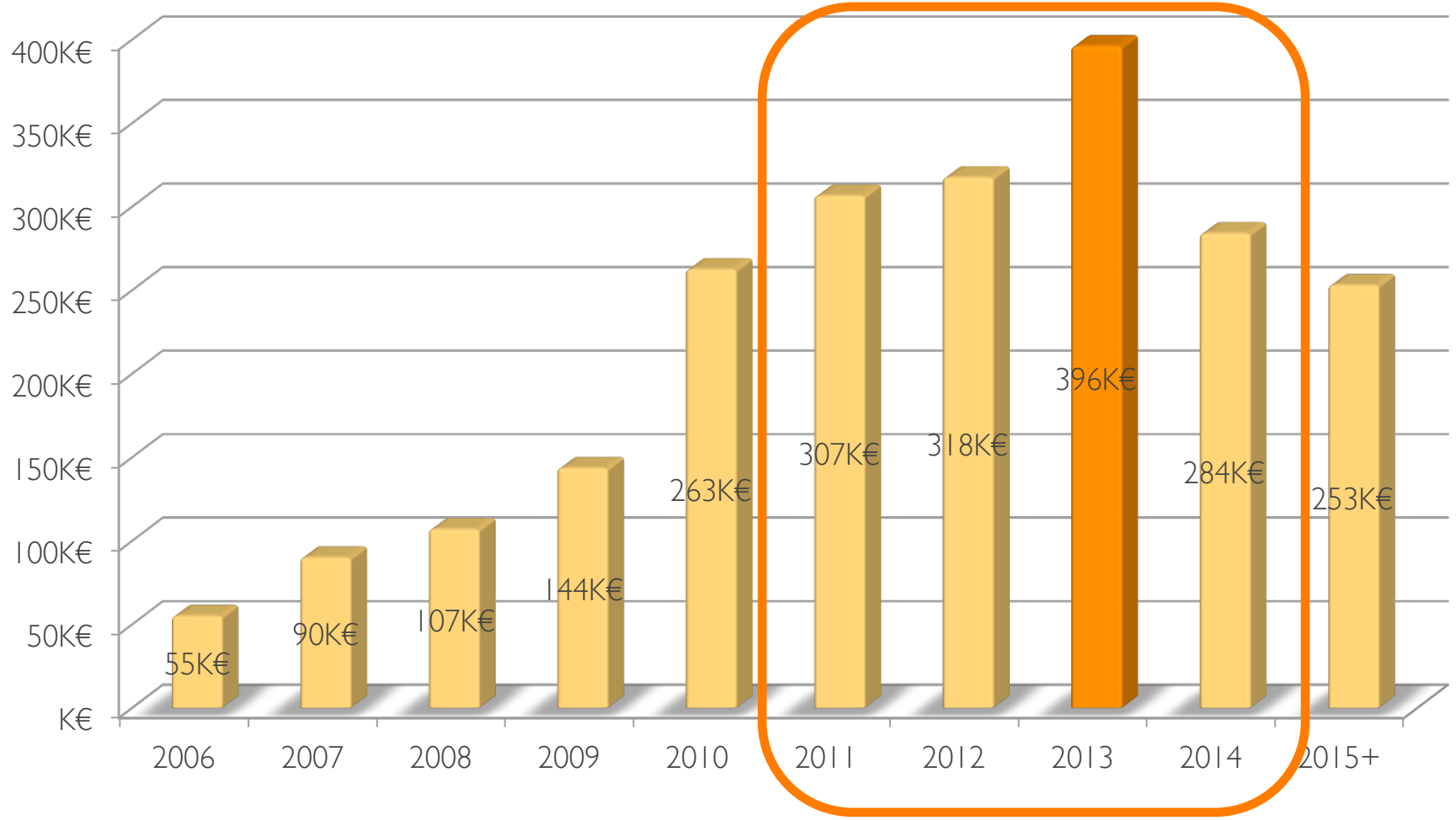
BioMedical Image Understanding

BioMedical Images
Pervasive Exploration and Modeling for Prognosis and Treatment Assistance

Recent Competitive Projects (6 M€ - total research budget since 2010)

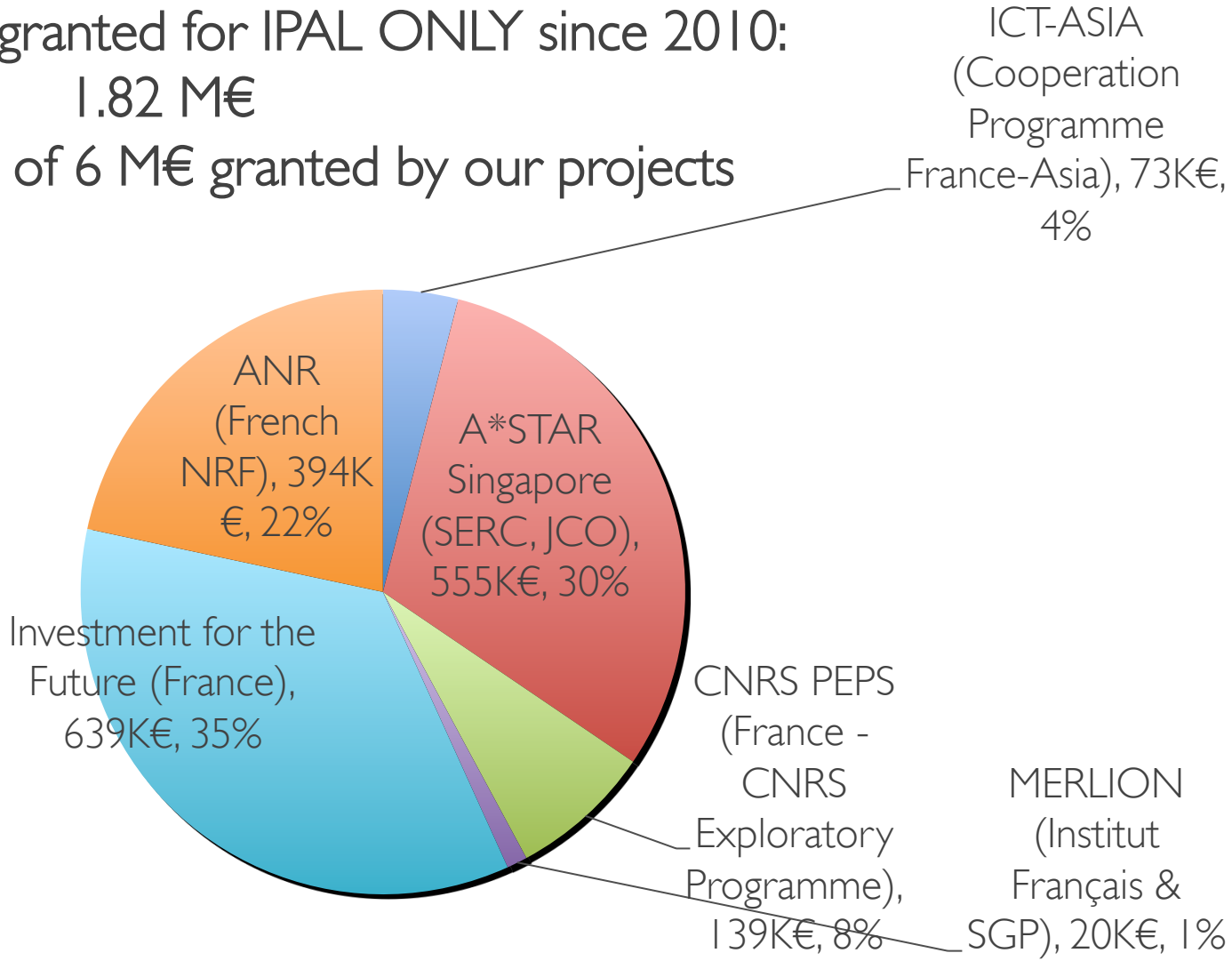


IPAL external funding per year (since 2006)



IPAL External Competitive Funding Ratio (since 2010)

Competitive budget granted for IPAL ONLY since 2010:
1.82 M€
out from a TOTAL of 6 M€ granted by our projects



COGNITIVE VIRTUAL MICROSCOPY FOR BREAST CANCER GRADING IN HISTOPATHOLOGY

WHOLE SLIDE IMAGE EXPLORATION USING A SYMBOLIC COGNITIVE VISION APPROACH

Daniel RACOCEANU

http://www.comp.nus.edu.sg/~danielr/

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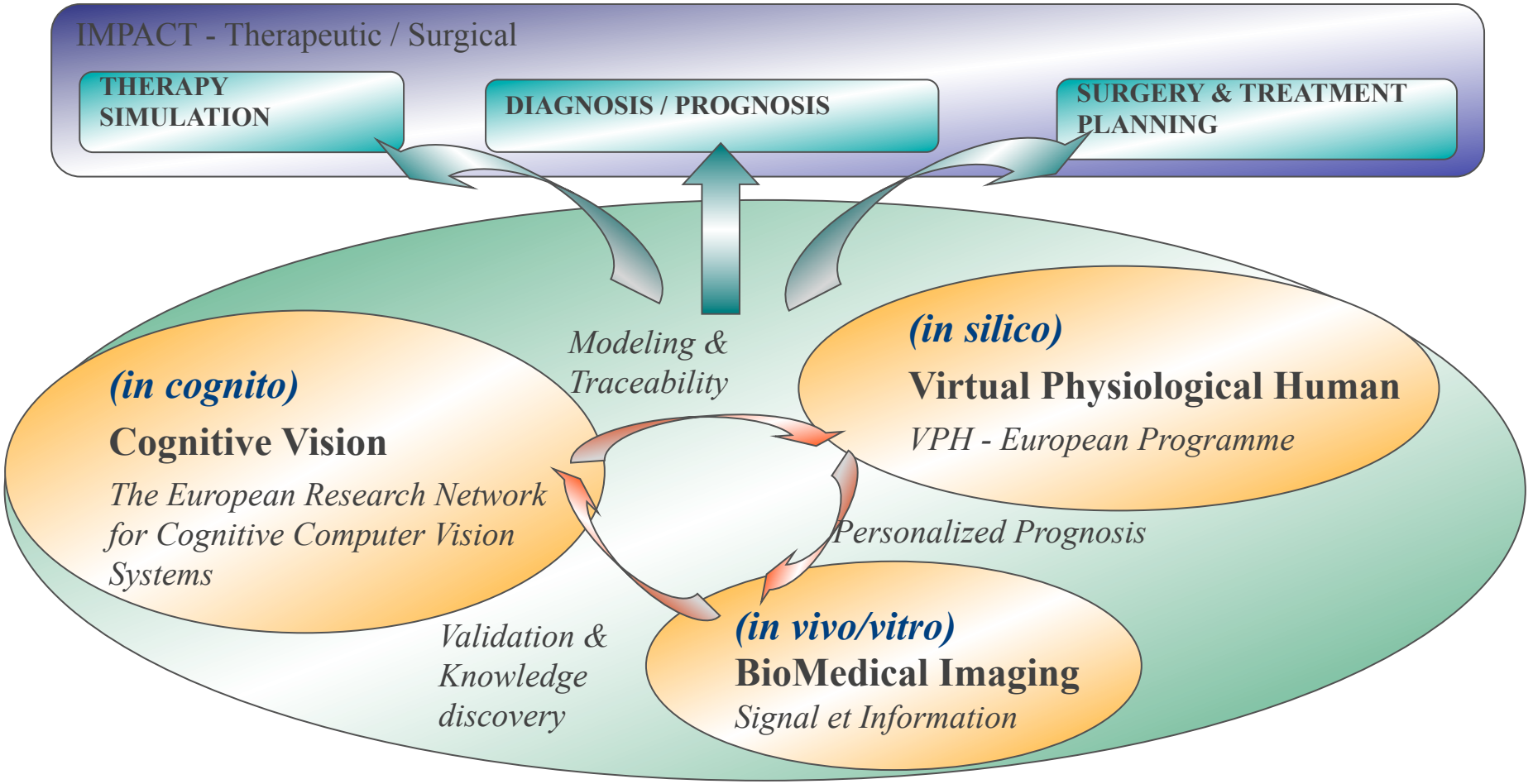
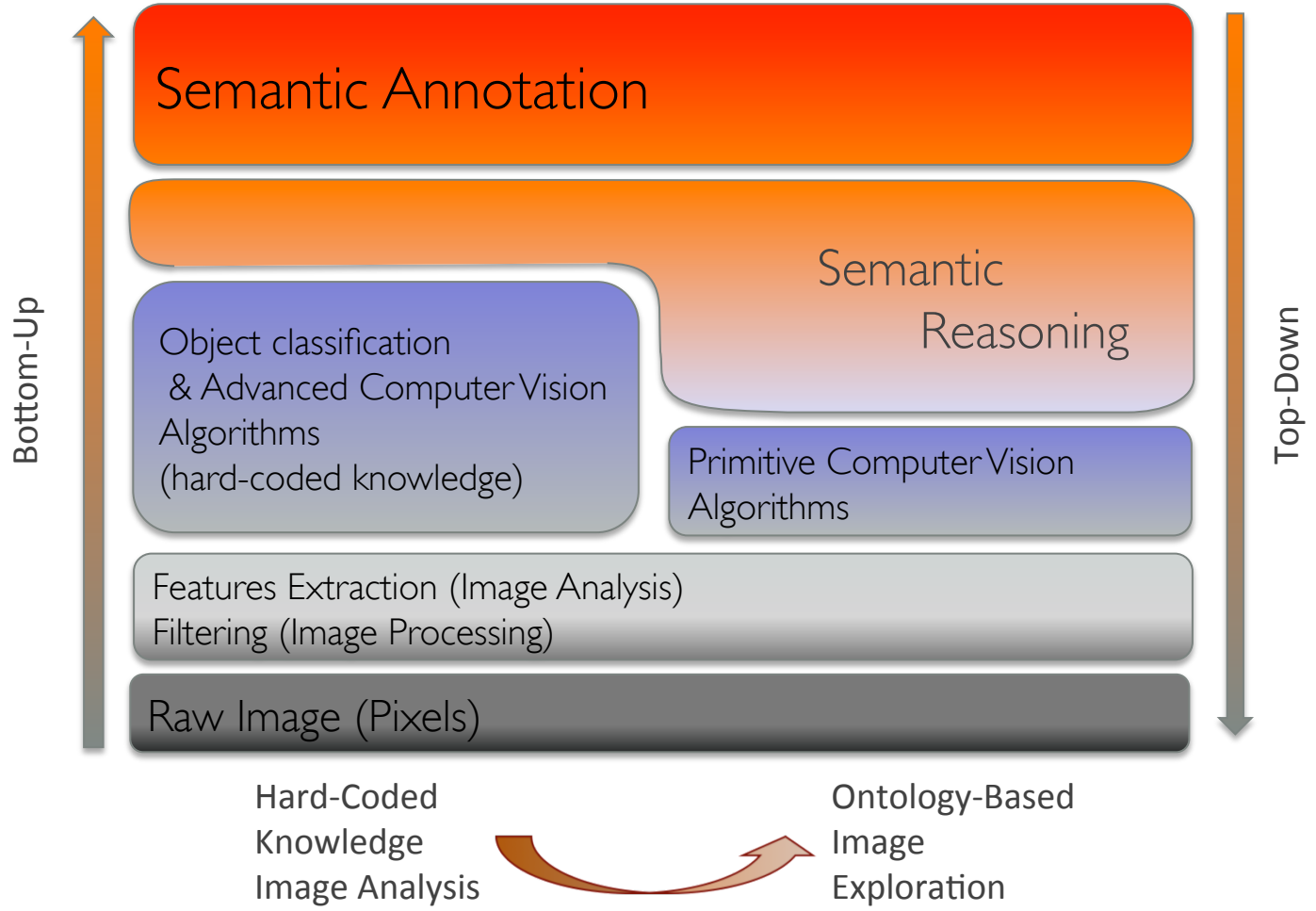
Scientific Challenges

BIOMEDICAL IMAGE UNDERSTANDING

BMIU Framework



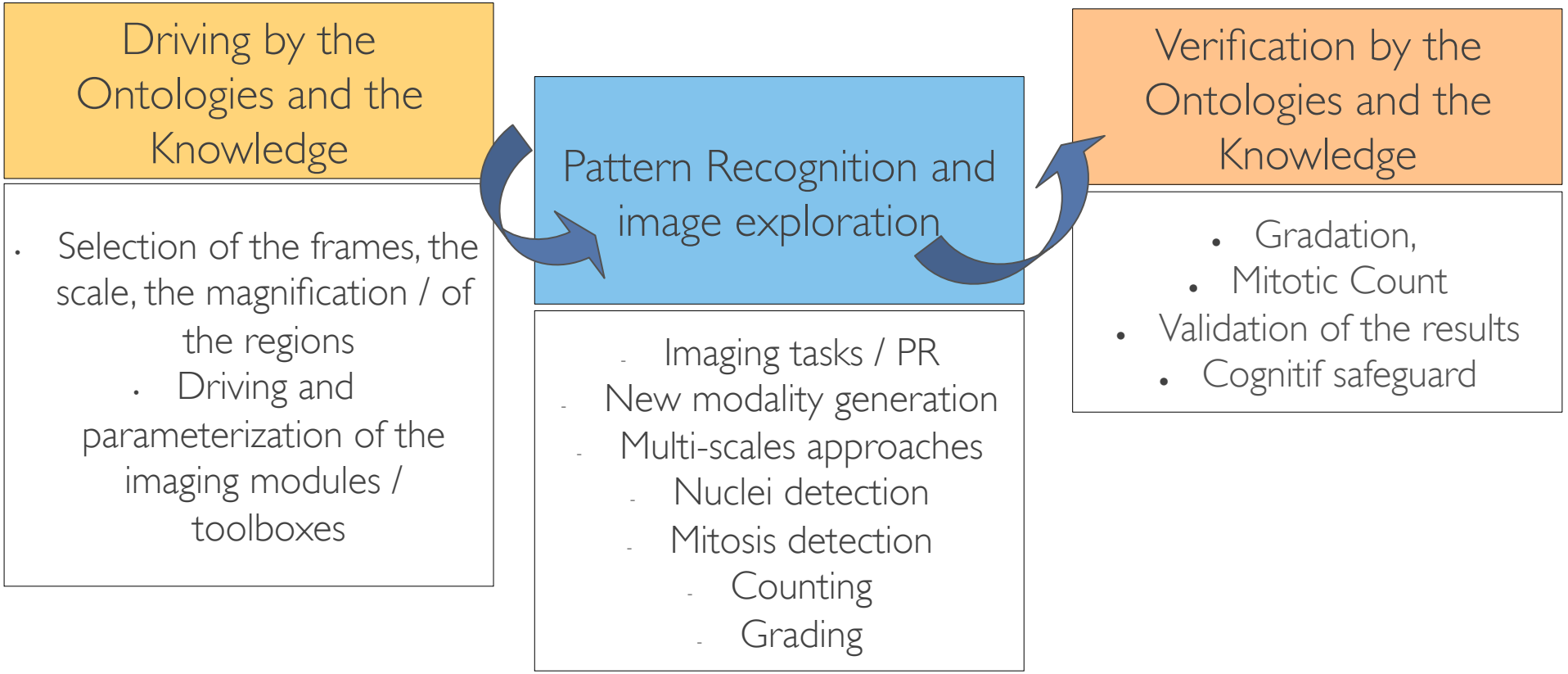
Origin of the challenge: From Hard-Coded to Semantic-Based Image Exploration



Interaction between ontologies and images

Coupling between knowledge and pattern recognition

- Role sharing and interaction between the AI and Pattern Recognition approaches

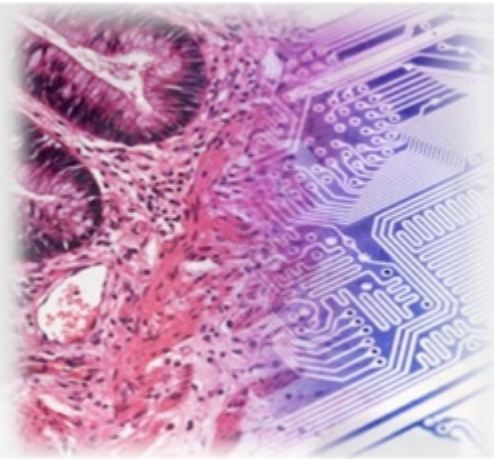


IPAL/BMIU

MICO (ANR TecSan 2011-2014)
COgnitive virtual MIcroscopy for digital pathology

Challenge of the digital pathology

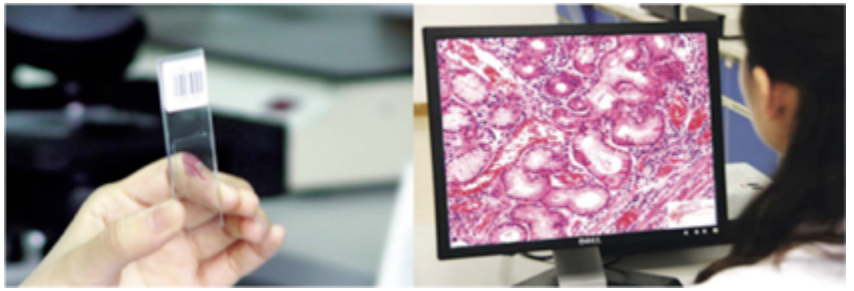
- The future of the pathology will need to be
  - Ethical: traceability / reference / validation
  - Dynamic: predictability / morphogenesis



- The revolution of the digital pathology
  - The pathology is fundamentally cognitive
    (slides / signs reading / interpretation)
  - We need cognitive tools for digital pathology
  - New laws on the telemedecine / telepathology
  - Evolution of the DICOM standard (supplements 122, 145)
  - New generation of PACS

Objectives of the MICO project

- Accompany the evolution towards the numerical pathology
  - Augmented Microscopy: cognitive exploration, traceability
- By the breast cancer, towards the cancer grading in histopathology
  - Acquire a methodology
  - Define a formalism
  - Effective efficient cognitive approach
  - Test, validate and integrate the technologies in clinical environment

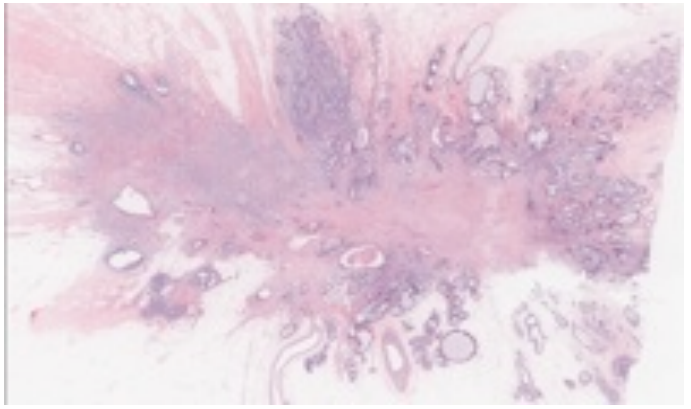


- Augmented microscopy for high-content imaging
  - A generic challenge in biomedical imaging

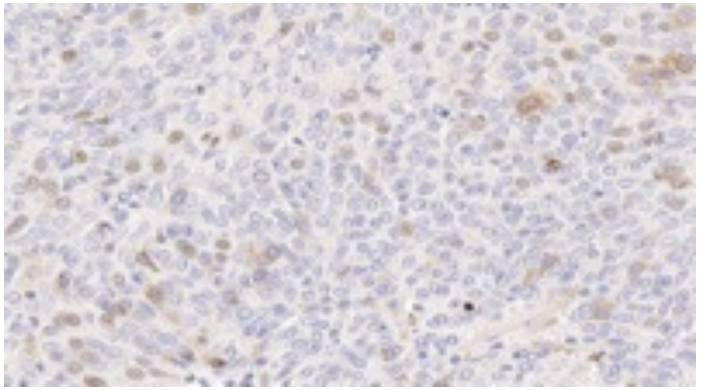
Grading Process

Breast Cancer – Canalar Carcinoma (80%)

- H&E staining - Hematoxylin-eosin staining
  - Architecture evaluation
  - Mitotic count
  - Nuclear polymorphism



- IHC – Immunohistochemistry – Analysis of Hormone Receptors
  - Nuclear labeling
    - KI-67 Proliferation Index
    - ER, Estrogen Receptor
    - PR, Progesterone Receptor
  - Cytoplasm and cellular membrane
    - HER2/neu, Epidermal Growth Factor Receptor



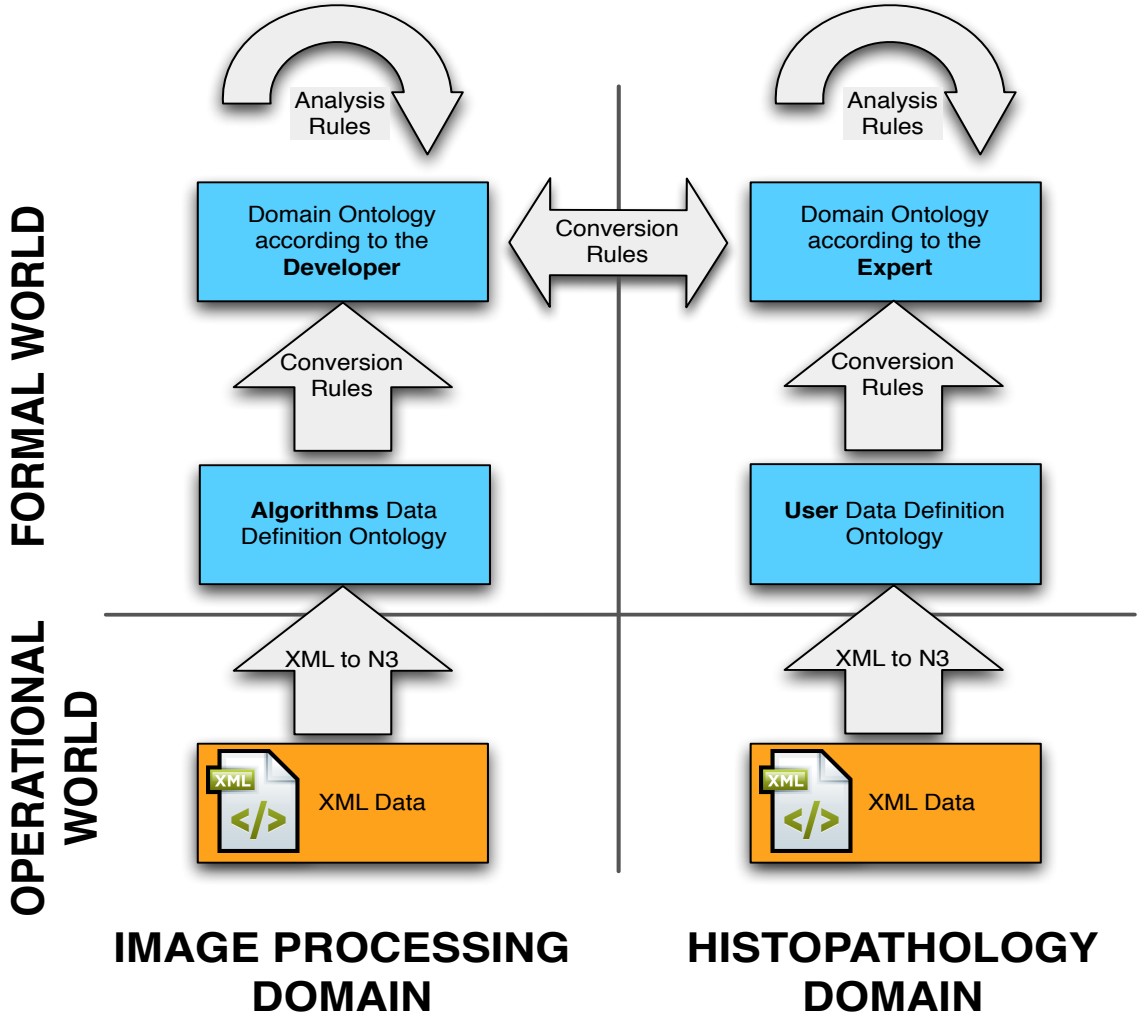
Symbolic Cognitive Vision

- Cognitive vision
  - Symbolic / Semantic
  - Connexionnist
- Our approach (ANR TecSan MICO project): symbolic approach
  - Close to the medical interpretation of the pathologist
  - Ontological references (SNOMED-CT / ADICAP *)

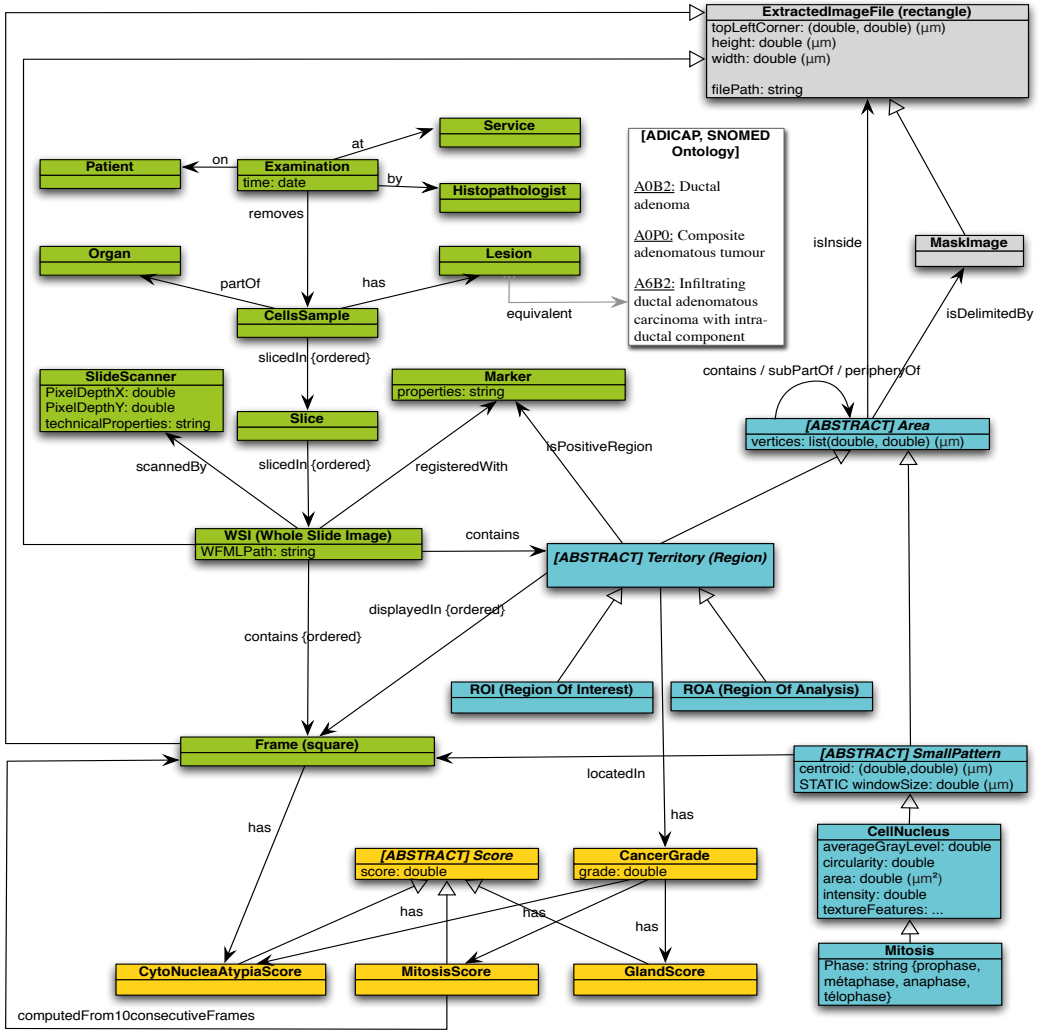
MICO Platform : A semantic approach

- Traceability
  - MICO platform is aimed to help histopathologists to take decisions by providing statements about medical cases, its decisions should obviously provide traceability. Semantic reasoning takes place in a formal world, each inference is proven: each decision is proven.
- System understanding & Decision support
  - Tedious and time consuming tasks. User in the loop.
- Flexibility and maintenance
  - With a full semantic approach, all the facts and processes are expressed in an open manner. They are also fully described and therefore easily understood. Compared to "hard coded" systems, semantic systems are more flexible and easier to maintain.
- Technology acceptance
  - Semantic web technologies helps the user to understand what the system truly does, and therefore increase its perceived ease of use. By increasing the system perceived ease of use and its perceived usefulness, this approach will probably help the user to accept technology.
- Improved image processing
  - Expert knowledge used to guide image processing algorithms, target interesting spots in order to spare as much processing power as possible and to make the overall gradation faster. ONTOLOGY AT THE HELM.

MICO Ontologies

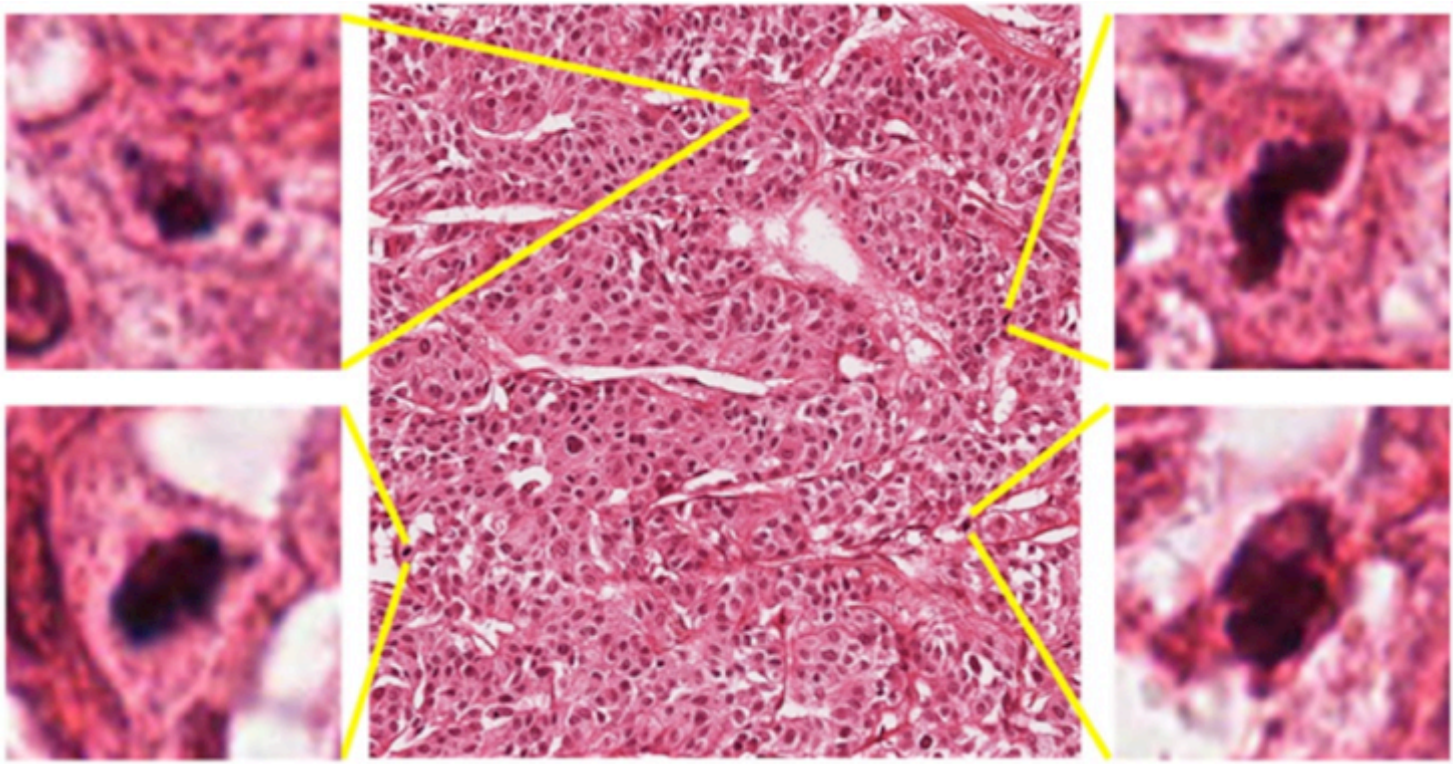


MICO conceptual graph

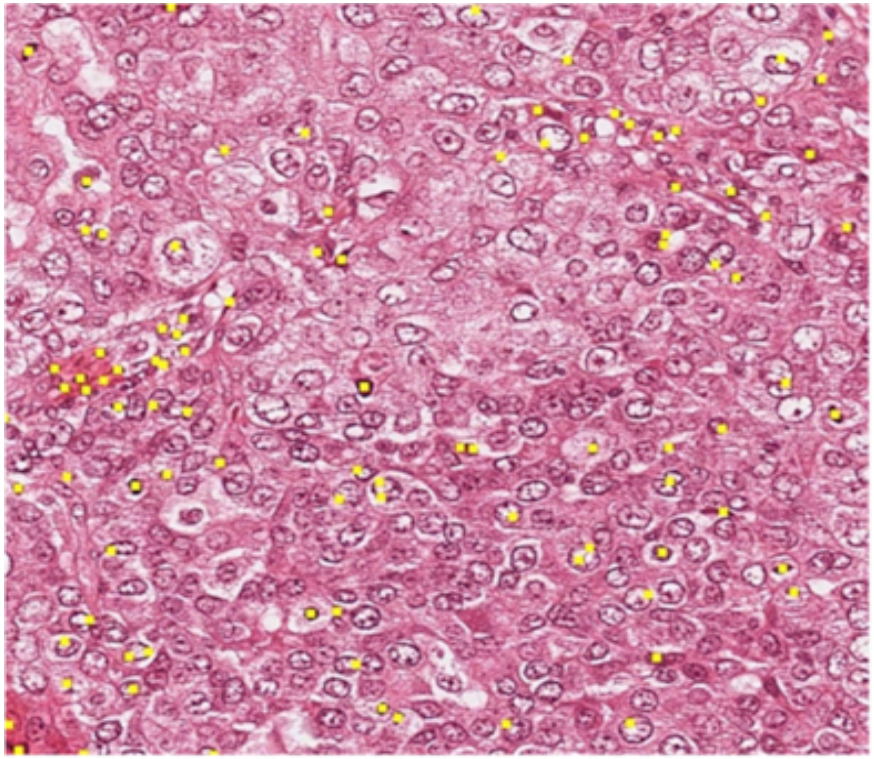


Challenge of the Automatic Mitotic Detection

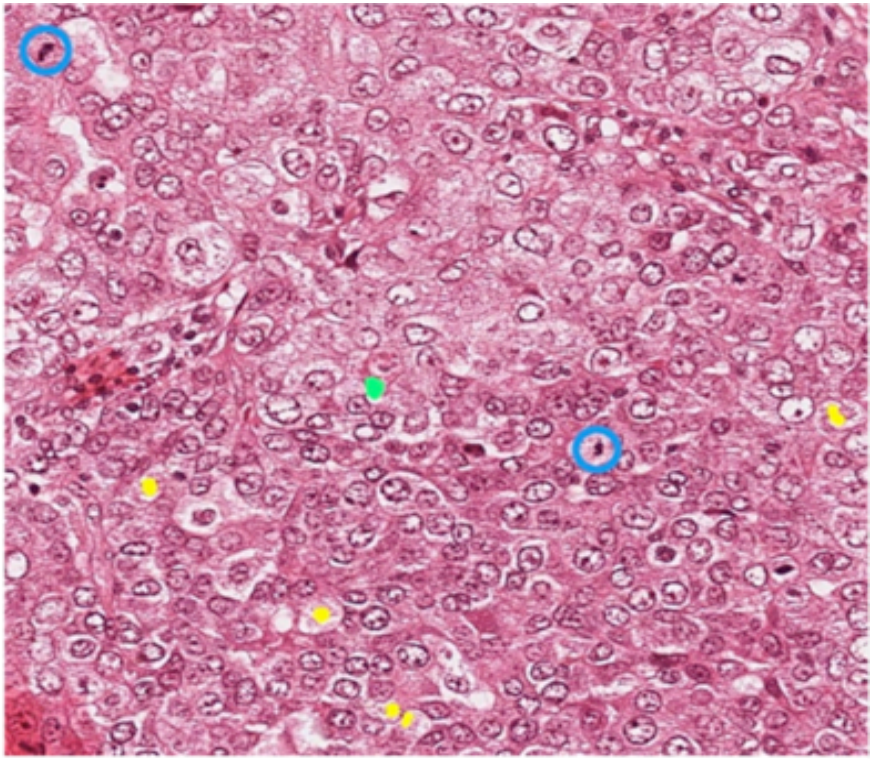
- Variation in shape and size,
- Variation in pixel intensity,
- Few mitosis per frame,
- Similarity with other types of objects (e.g., apoptosis, necrosis, dust particles, lymphocytes, etc)



Mitotic Detection Results



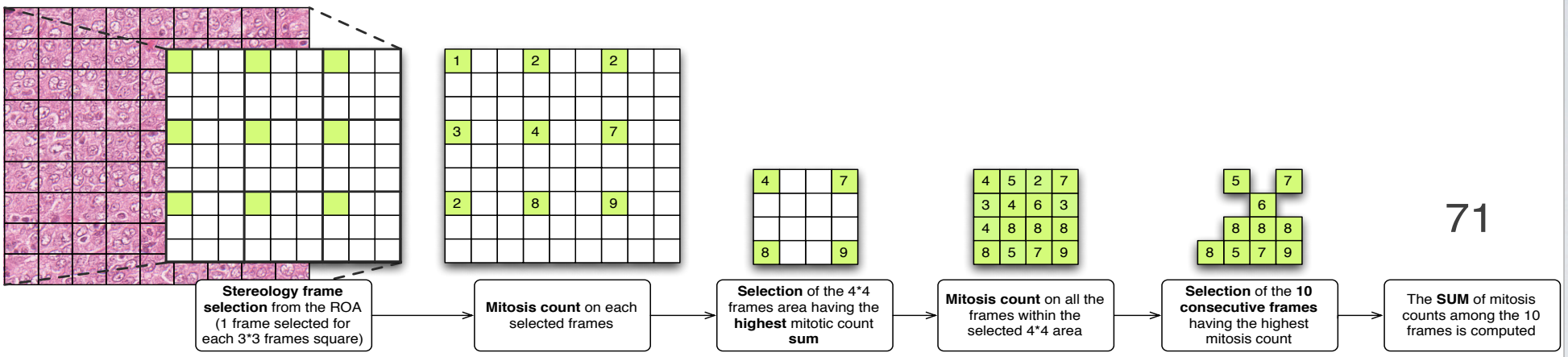
Candidate Detection: Yellow spots highlight candidate for Mitosis



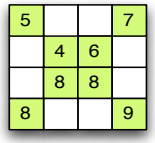
Candidate Classification: The yellow colour for true positives, green for false positive and the blue for false negatives

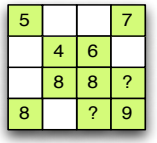
Grading strategy

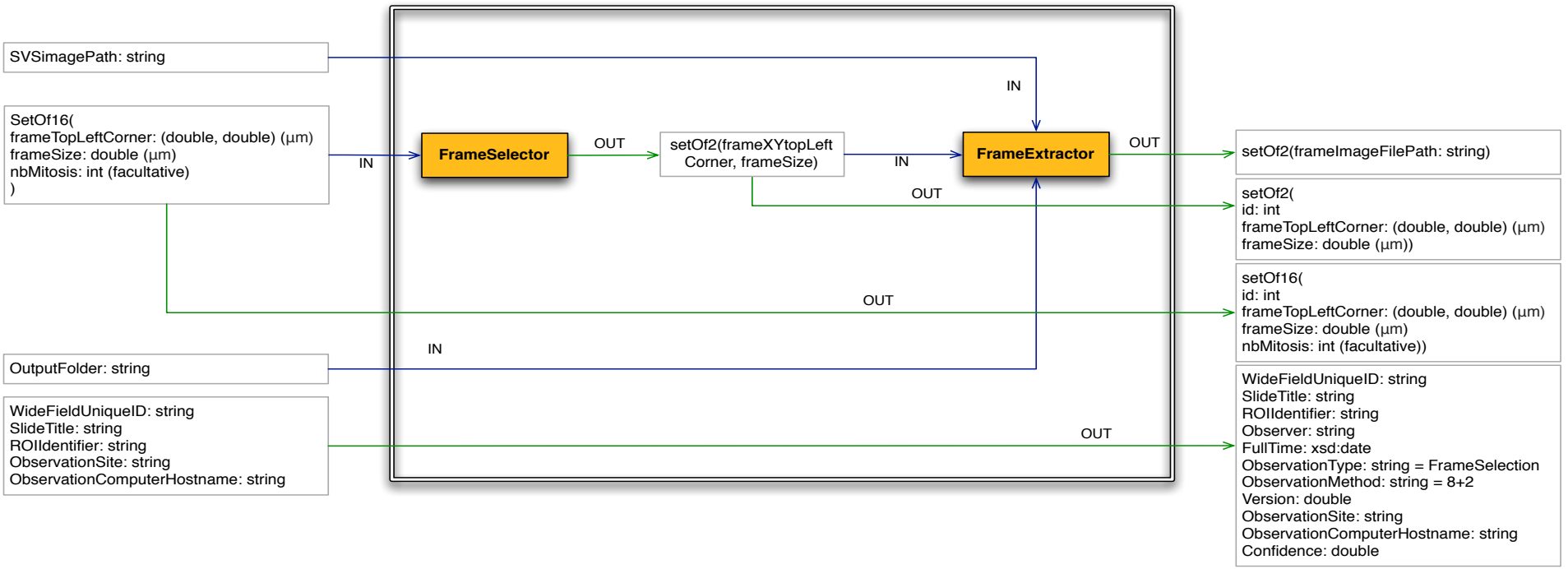
- Mitosis analysis algorithm



FrameSelector 8+2





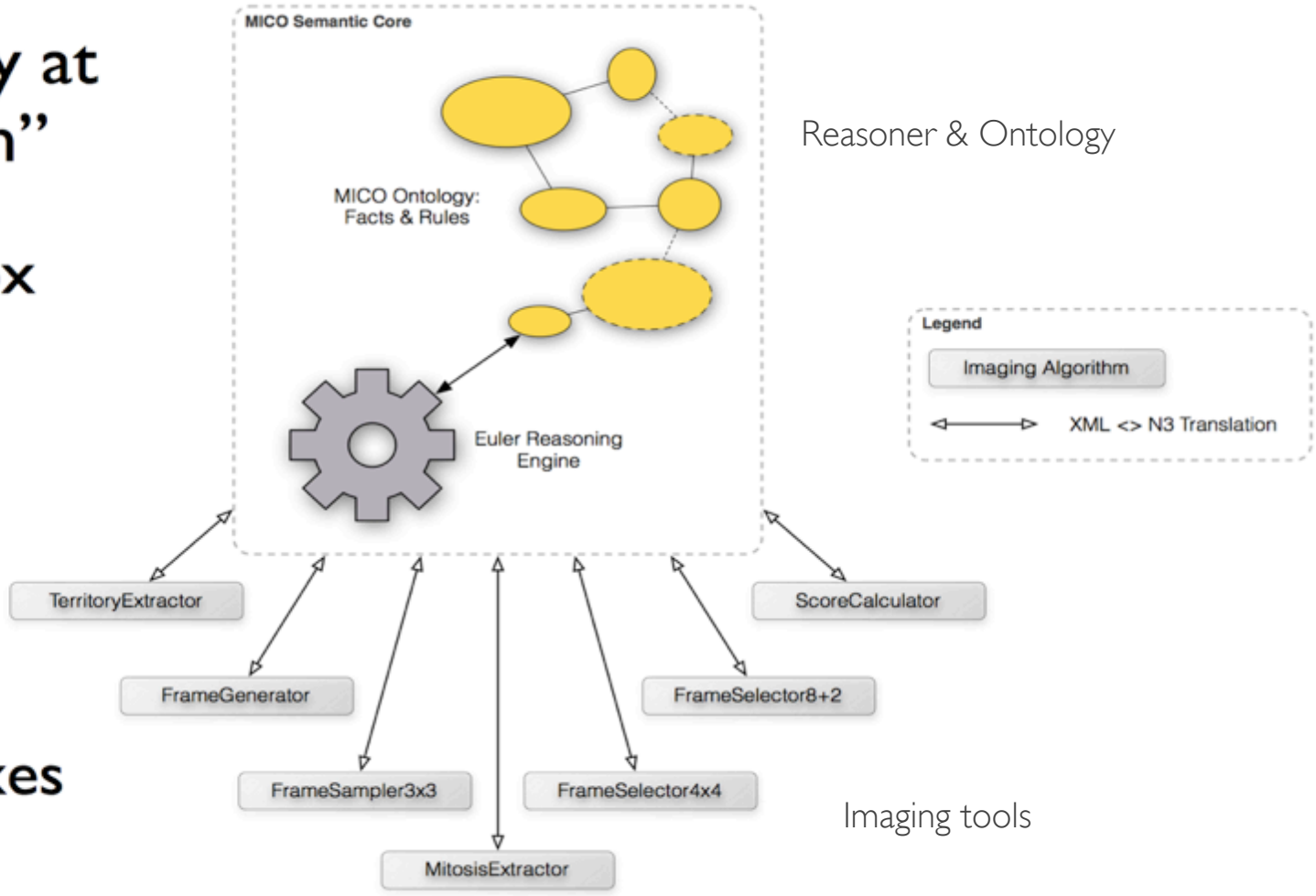


Cognitive-visual whole slide image exploration

"Ontology at the helm"

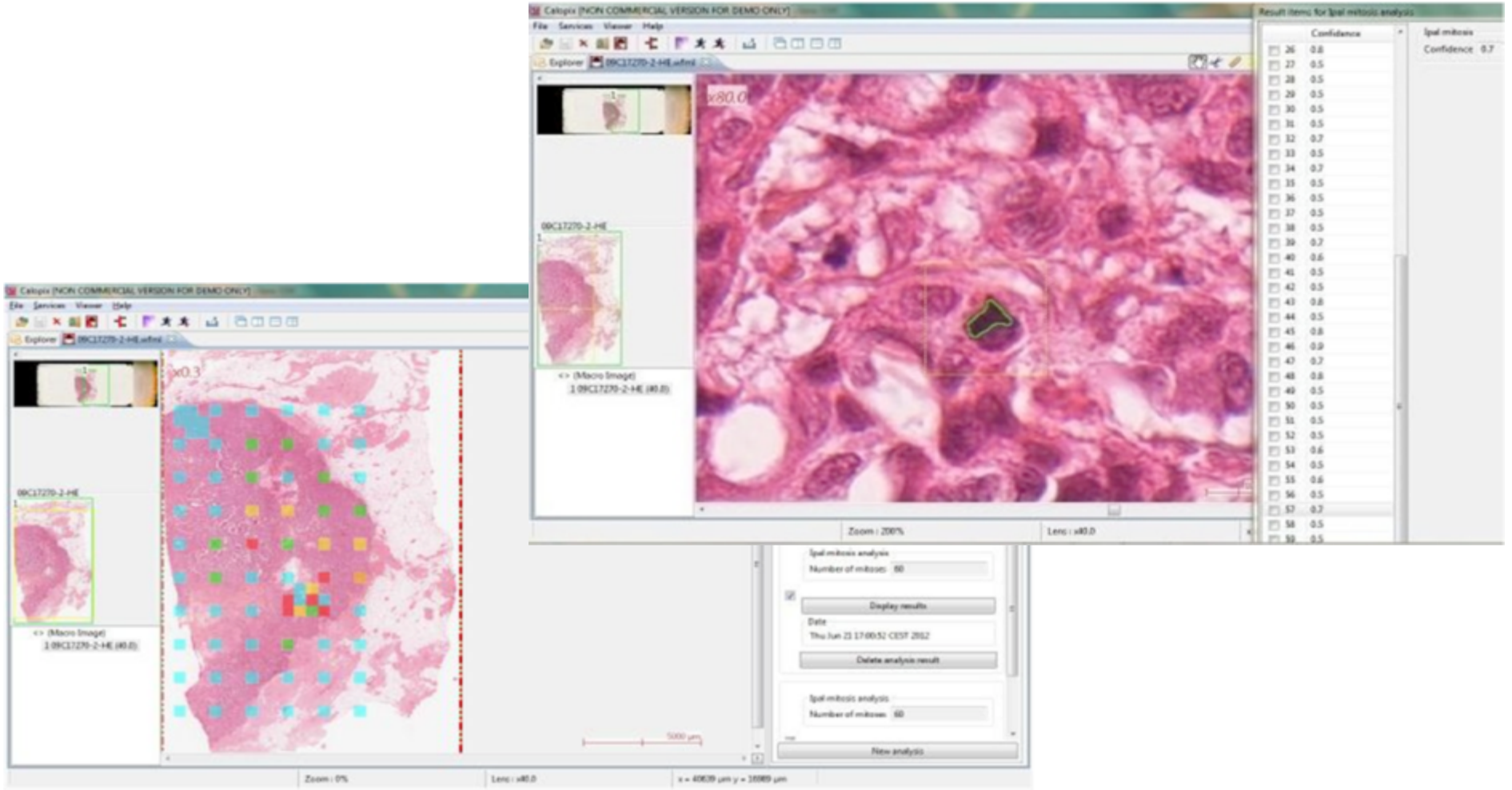
Glass box

Black boxes

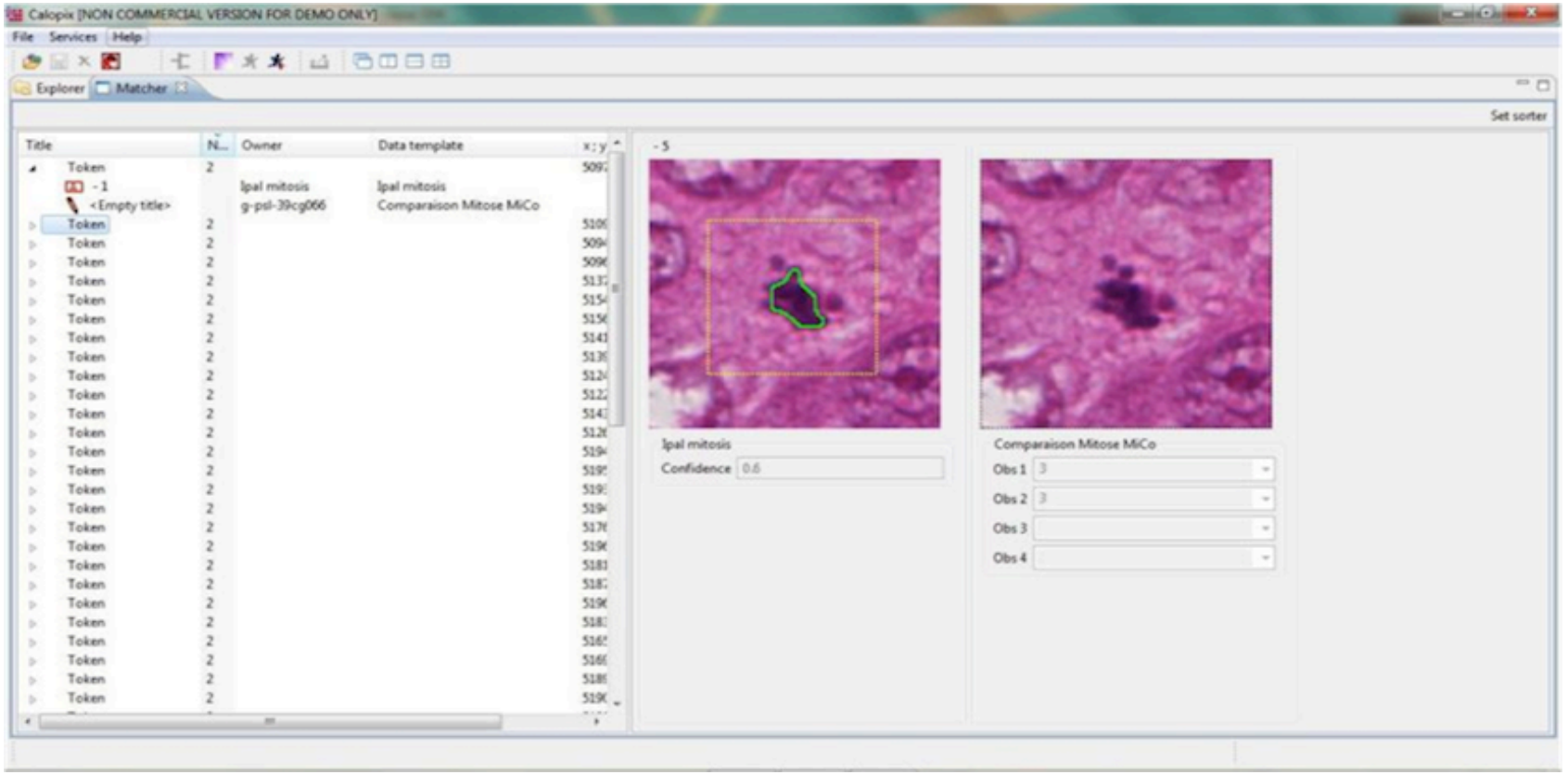


Assistants numériques

- Reconnaissance de formes



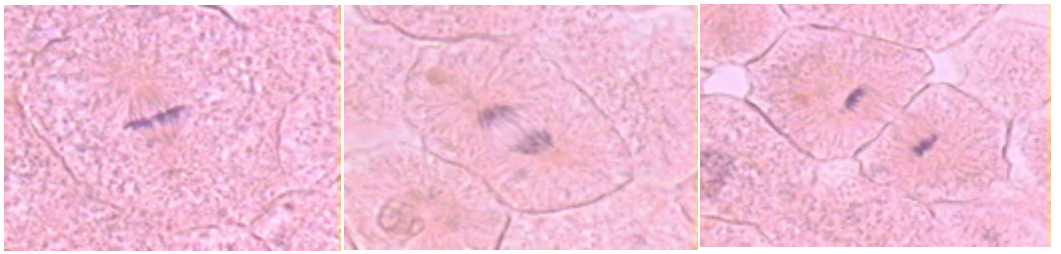
- «Match» de cohérence des informations produites



MITOSIS DETECTION INTERNATIONAL BENCHMARKING @ ICPR 2012

initiative leaded by IPAL

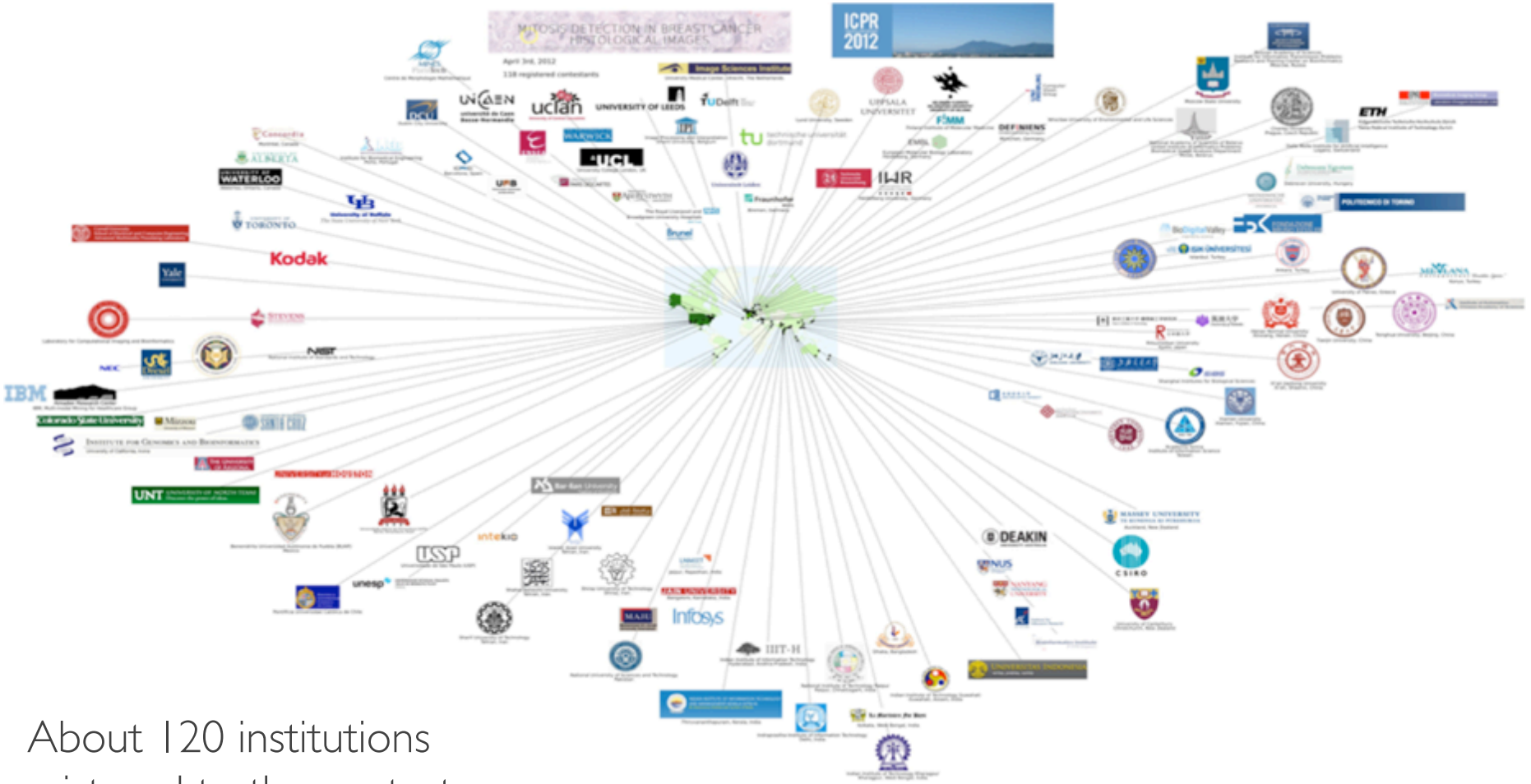
- Organized by IPAL, La Pitié Hospital, TRIBVN, Ohio Univ
  - ICPR 2012, November 11, 2012, Tsukuba, Japan
  - URL: http://ipal.cnrs.fr/ICPR2012/



- Key information :
  - Multimodal data :
    - Fast scanners (Aperio & Hamamatsu)
    - Multispectral Multifocal Microscopy
  - March 31st, 2012: submit a paper about the proposed method to ICPR 2012
  - April 27th, 2012: submit an abstract (1 page) of their method.
  - August 1st, 2012: evaluation data set available.
  - September 10th, 2012: deadline for participants to send their results.
  - November 11th, 2012: mitosis detection contest meeting will take place during ICPR 2012 in Tsukuba, Japan. Contestants will make a short presentation of their method and results.
  - Special issue in JPI - Journal Pathology Informatics – March 2013

MITOS @ ICPR 2012

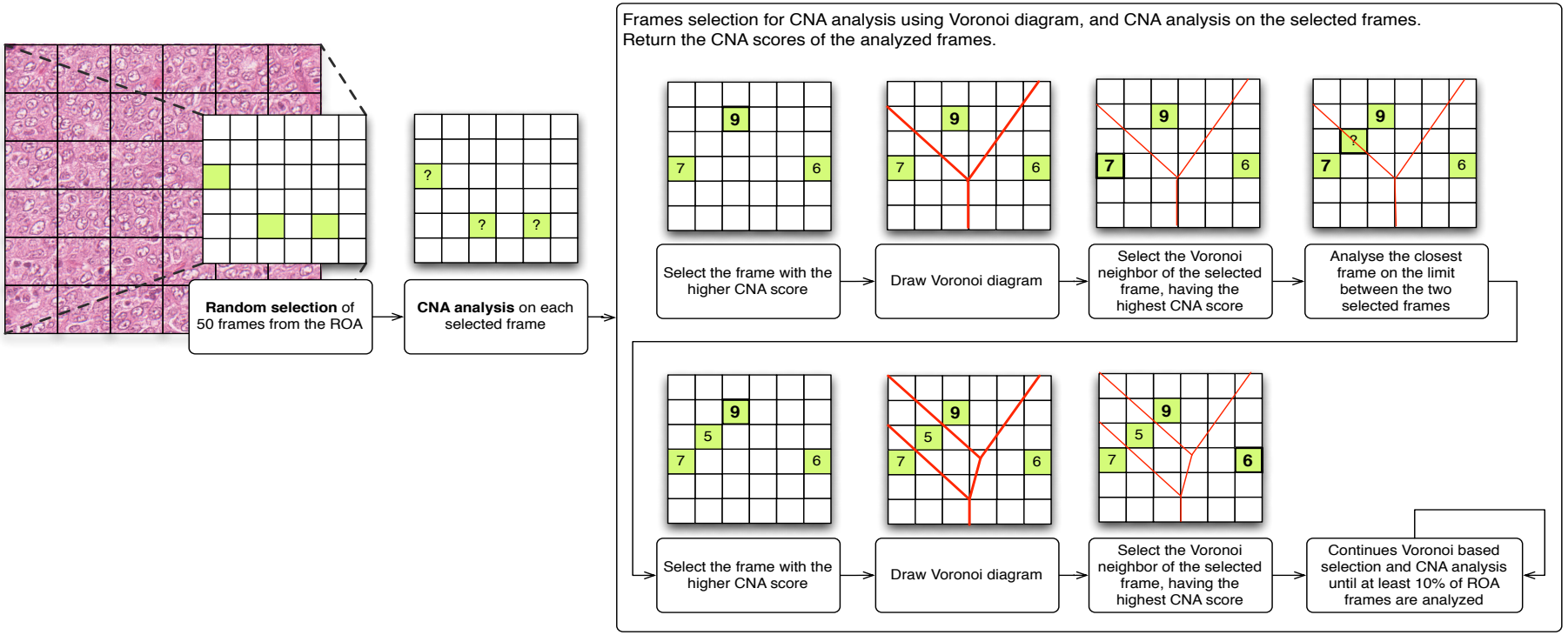
Participants to the international benchmark



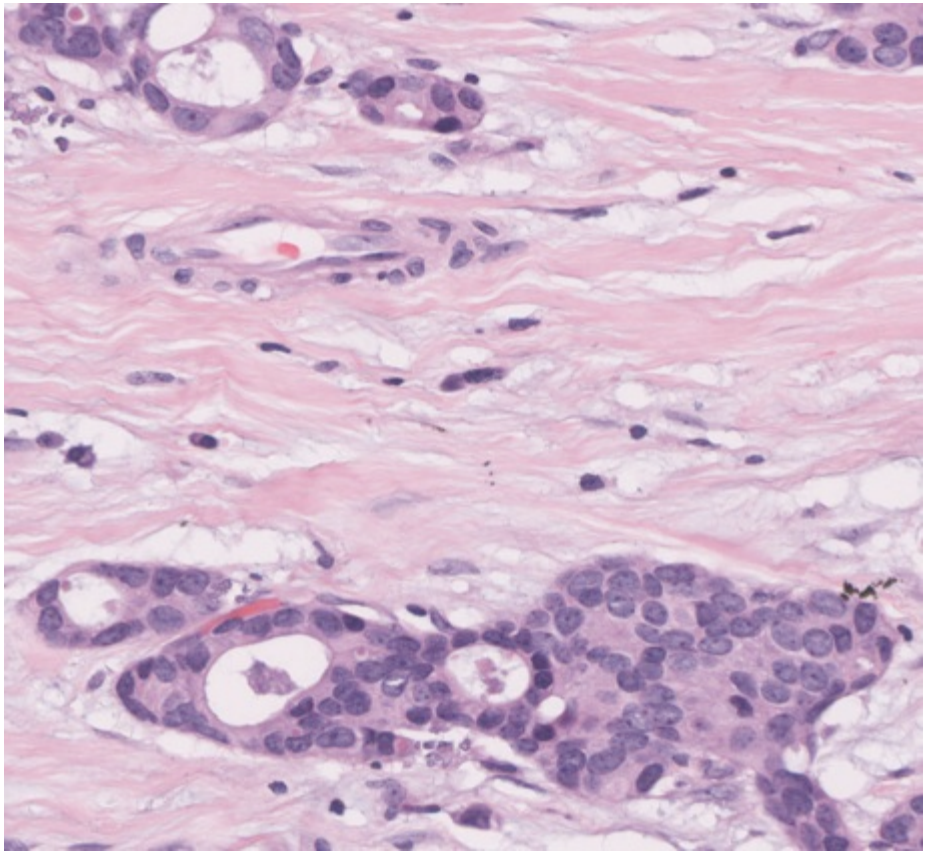
About 120 institutions registered to the contest

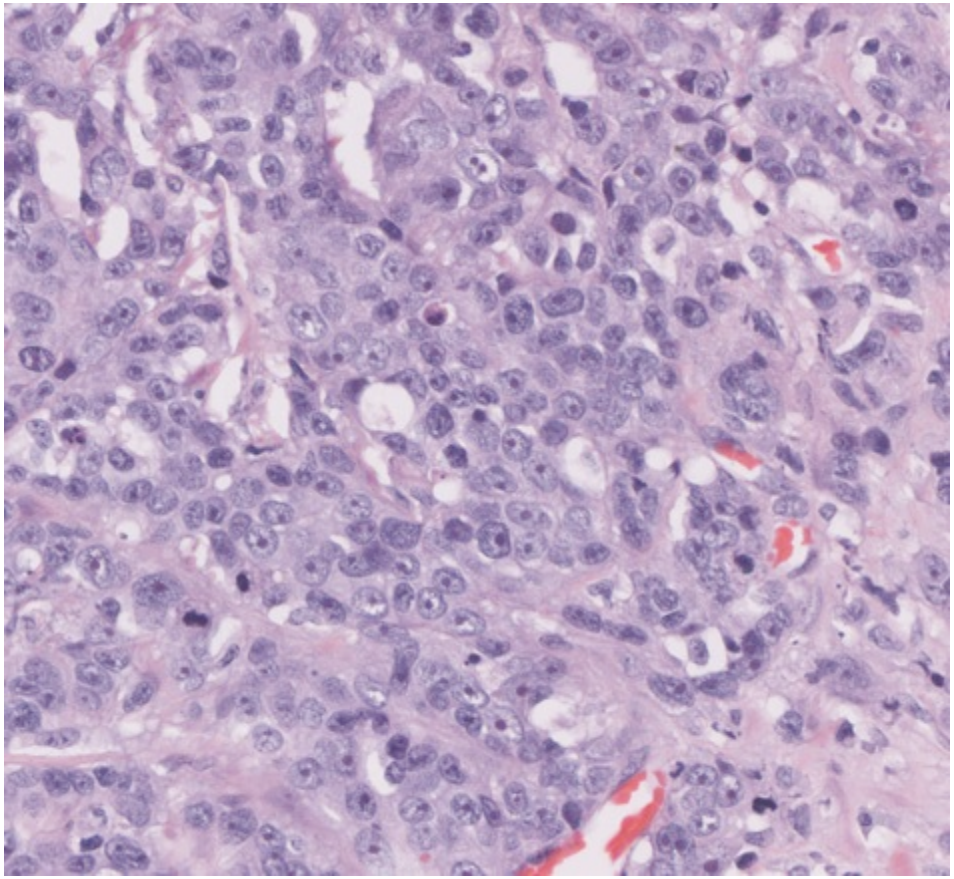
Grading strategy

- Nuclear polymorphism analysis algorithm



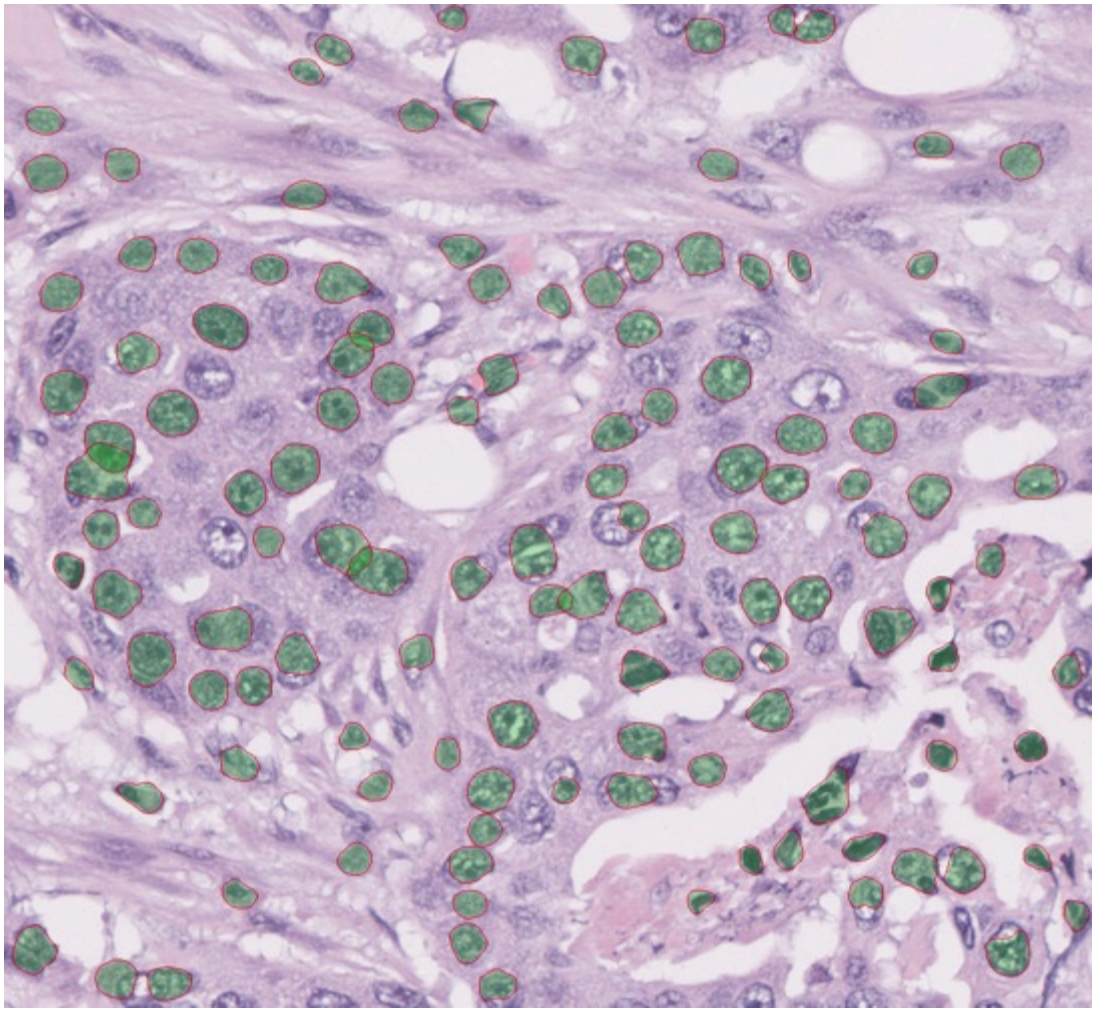
H&E stained surgical breast images
40x magnification





1024×1024 frames where the nuclei have been manually delineated by pathologists

Nuclei extraction challenges



Score 3

Problems:
- Nuclei non-homogeneity
- Nuclei vary a lot in terms of size, shape and cytoplasm homogeneity

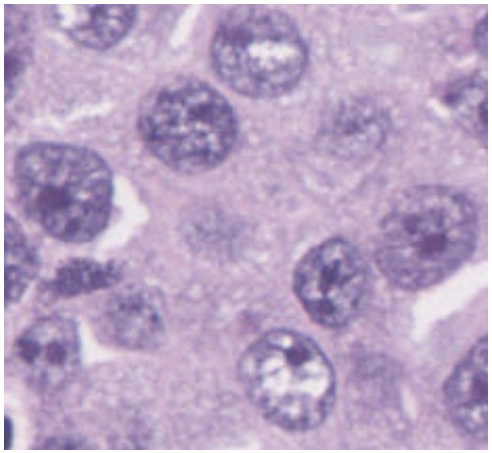
Nuclei non-homogeneity

- Create a new image modality using a machine learning based method using
  - colour
  - texture,
  - scale information,

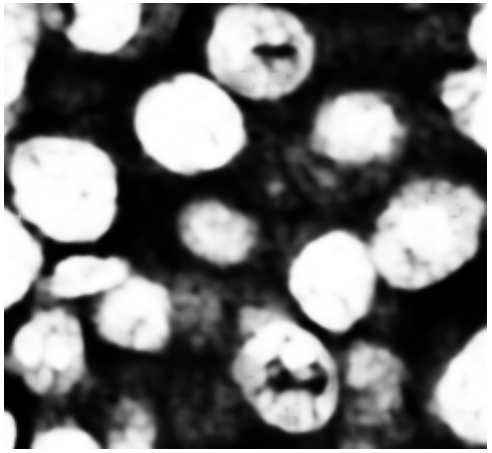
in order to improve the accuracy of nuclei extraction

Probabilistic Image Modality

- Probability Map
- The resulting 180-dimensional feature vector X is used to compute the probability p(X) of each pixel to belong to a cell nuclei

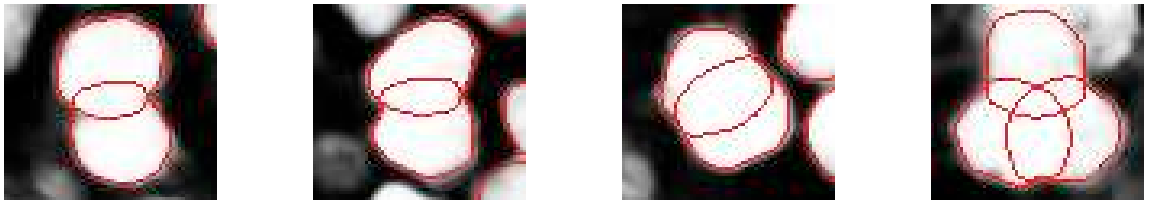


Original H&E image



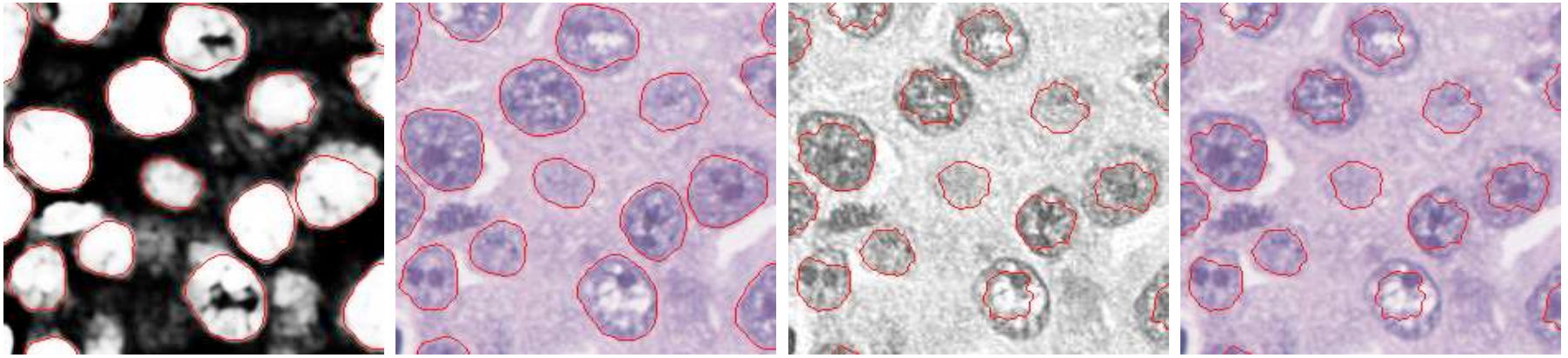
Obtained image modality

Nuclei Segmentation use of the probabilistic modality and of the Marked Point Process



(a) (b) (c) (d)

Figure 4: The shape prior information allows to extract the overlapping nuclei.

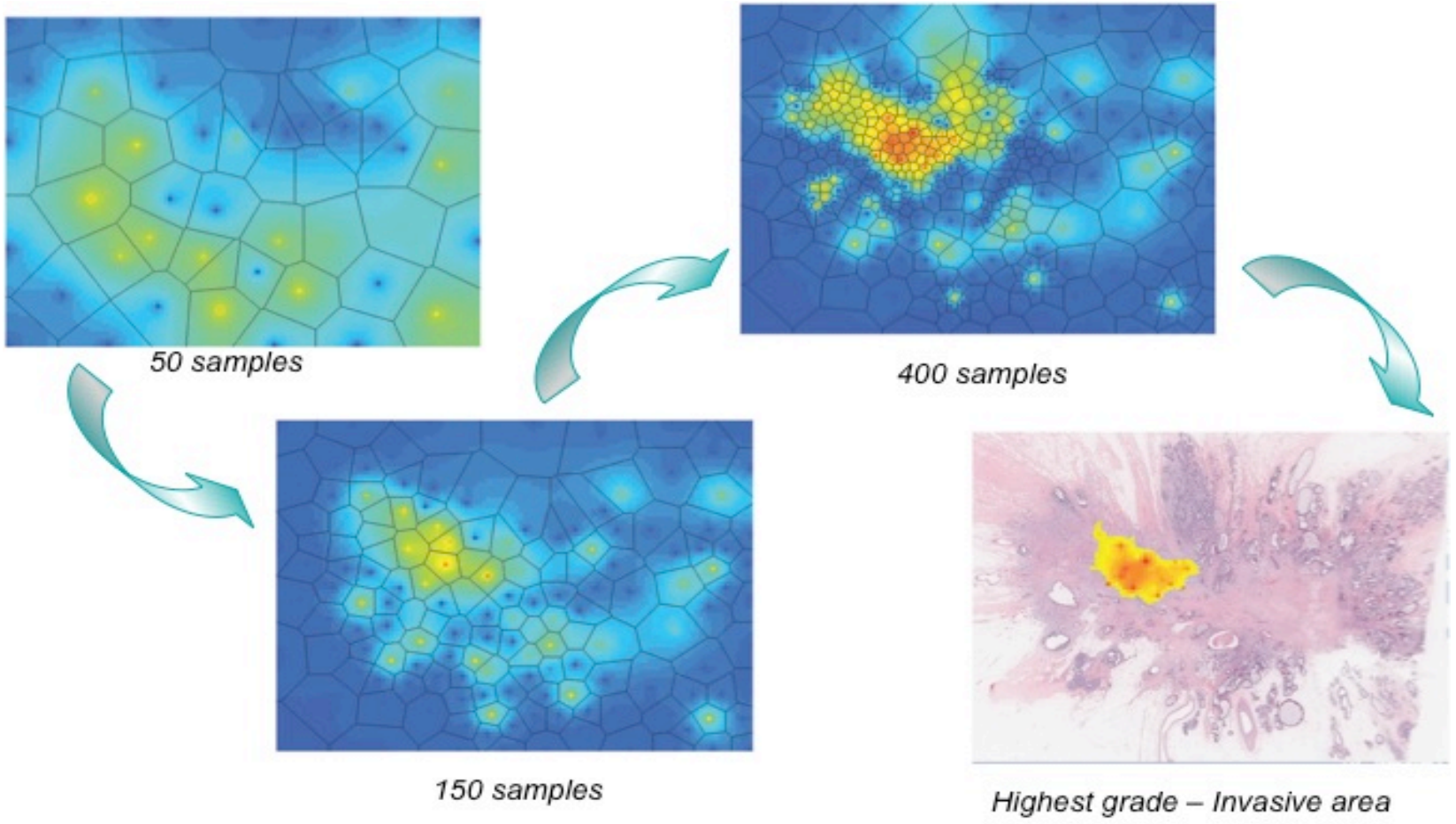


(a) Probability map (b) Corresponding H&E stained image (c) Haematoxilin image (d) Corresponding H&E stained image

Figure 5: Illustration of the extraction results : (a-b) is obtained using the probability map and (c-d) is obtained using the haematoxilin channel after the image color deconvolution.

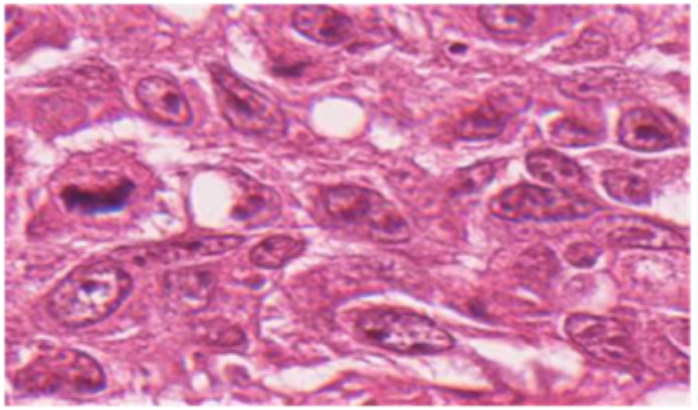
Cell Nuclei Extraction from Breast Cancer Histopathology Images Using Color, Texture, Scale and Shape Information, European Congress on Telepathology and 5th International Congress on Virtual Microscopy, June 2012.

WSI efficient BCG using dynamic sampling involving Voronoi Diagrams

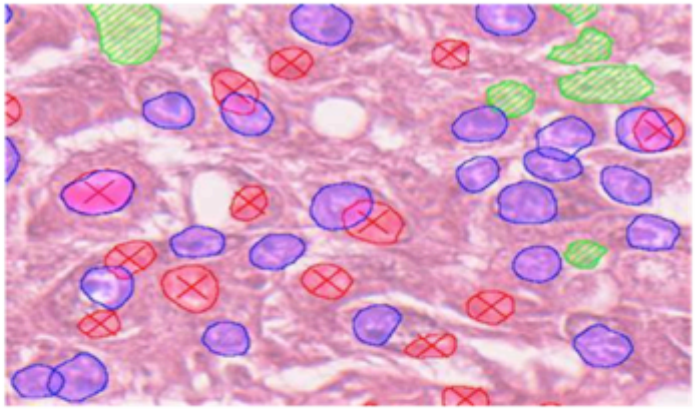


An Exploration Scheme for Large Images: application to Breast Cancer Grading, ICPR 2010

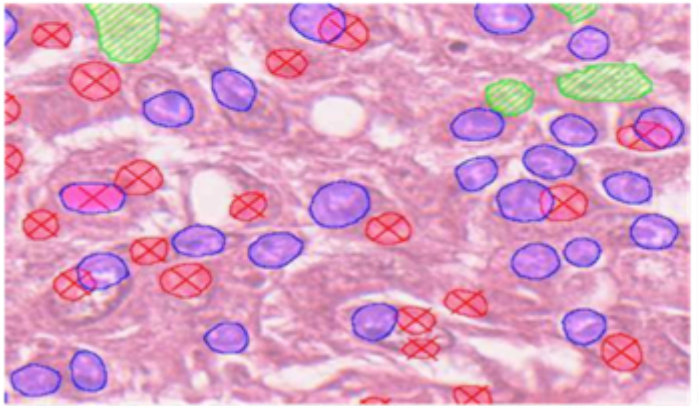
Various MPP versions



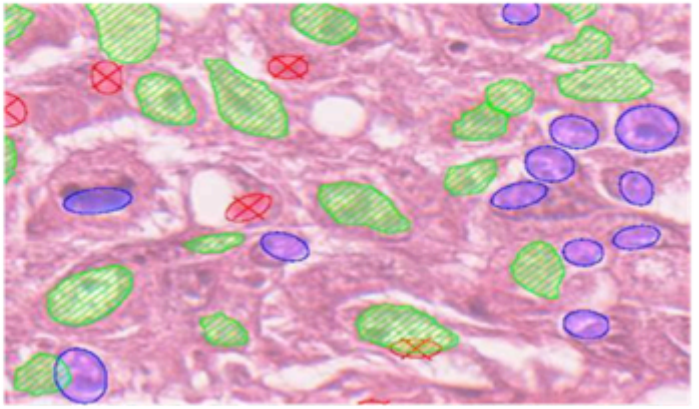
(a) H&E breast cancer surgical slide



(b) Results of Arbitrarily-Shaped Object MPP with a large radius range



(c) Results of Arbitrarily-Shaped Object MPP with a small radius range

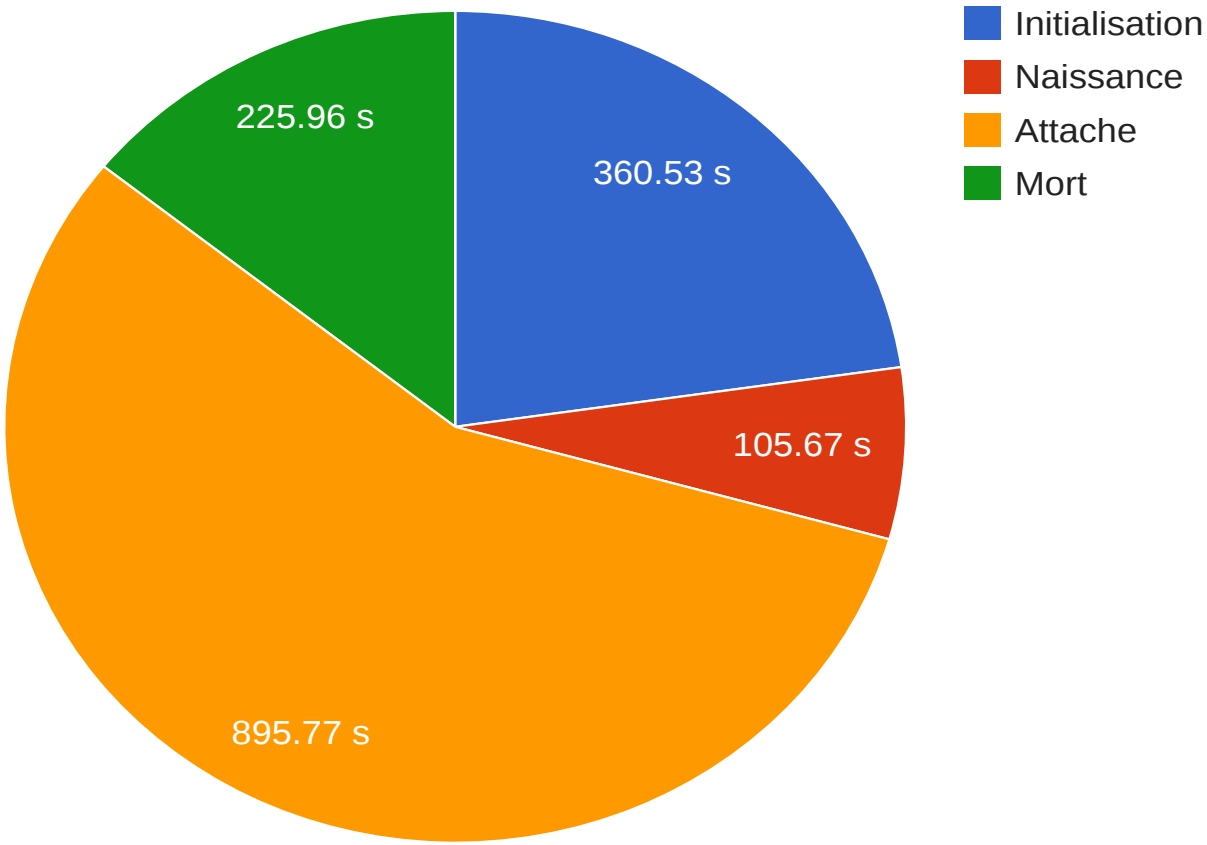


(d) Results of Elliptically-Shaped Object MPP

Figure 3: Comparing results on a single H&E image of high grade

Sequential algorithm: computation time

- Processing time ratio



Quantitative results on grades 1 and 3

Image	Method	Manually	Detected	Matched	F. P.	F. N.	Jaccard	F-measure
01	ASO	171	89	77	12	94	0.42	0.59
01	ASO_small	171	130	110	20	61	0.58	0.73
01	ESO	171	174	134	40	37	0.64	0.78
02	ASO	133	276	109	167	24	0.36	0.53
02	ASO_small	133	323	116	207	17	0.34	0.51
02	ESO	133	134	66	68	67	0.33	0.49

Table 1: Quantitative results on a H&E image 01 of grade 1 and 02 of grade 3

$$F\text{-}measure = \frac{2 \cdot \mathrm{TP}}{(2 \cdot \mathrm{TP} + \mathrm{FN} + \mathrm{FP})}$$

$$Jaccard\ index = \frac{\mathrm{TP}}{(\mathrm{TP} + \mathrm{FN} + \mathrm{FP})}$$

Performances of the Parallel Algorithm

Computation time in seconds on 3326x2971 pixel image:

[s]	Initialization	Birth	Energy	Death	Total
Sequential	360.53	105.67	895.77	225.96	1583.02
Multi-core	37.34	19.96	156.73	31.23	244.17
GPU	2.52	2.41	94.98	36.36	136.37

Acceleration ratio:

	Initialization	Birth	Energy	Death	Total
Multi-core	9.65	5.25	5.67	7.18	6.48
GPU	142.95	44.19	9.49	6.25	11.61

SYSTEMATIC

MEDICEN PARIS REGION

IPAL/BMIU

FlexMIm (Grand Emprunt, FUI project 2013-2016)

Collaborative Telepathology based on semantic imaging

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Next step : FlexMIm translational project

- Treats the user needs, expressed by anatomo-pathologists, in a context of decrease of their demography and increase of the number of medical acts
- Provide the pathologists with tools increasing their cooperative (initial tele-diagnostic, tele-expertise, e-learning) and collaborative capabilities, based on whole slide imaging technologies
- Develop and setup cognitive algorithms, driven by medical knowledge models (image exploration and cancer grading rules, annotation procedures, valid medical ontologies), to identify specific regions of interest for pathological analysis/grading
- Provide innovative, effective solutions to manage and manipulate WSI according to the used devices and networks. Provide intelligent algorithms allowing fluid data sharing and exchange via telecommunication network in the «Télépathologie Ile de France» cluster.
- Annotation and enrichment tools using medical databases and ontologies, by bringing closer the imaging and patient data.
- "Télépathologie Ile de France" evaluates and validates efficient/effective cooperative and collaborative process proposed by FlexMIm, focusing on the anatomopathological imaging, in order to reach concrete clinical use and dissemination, by formalizing a professional reference.

Etablissements impliqués et lien avec l'ARS

27 établissements impliqués dans FlexMIm dont 17 établissements impliqués dans ARSIF

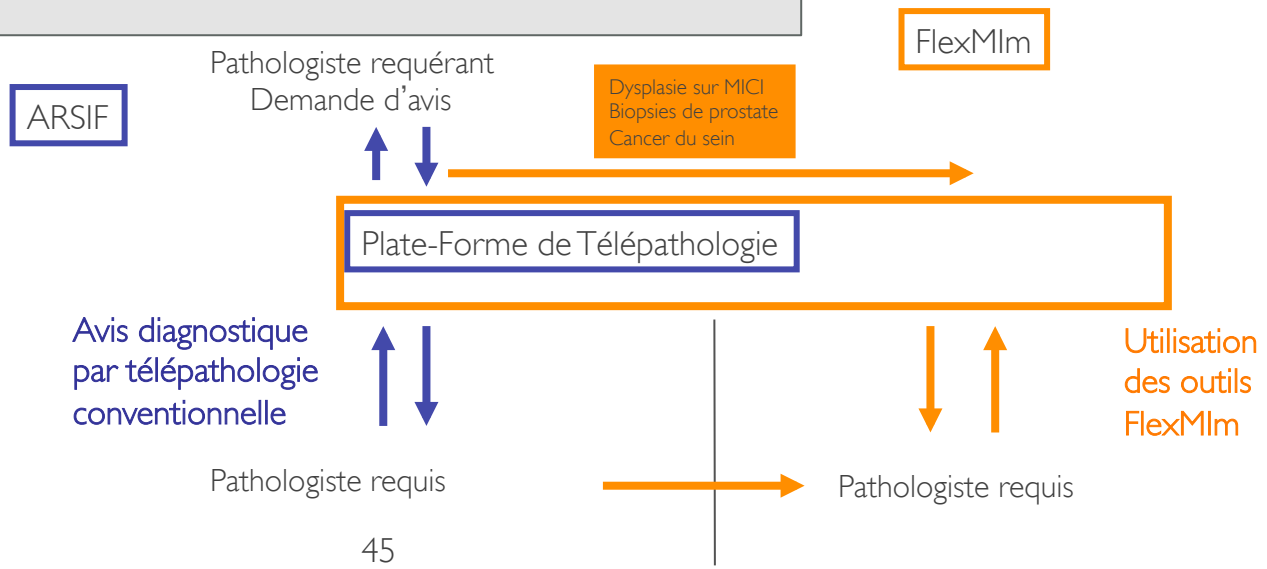
CHU APHP
CHU Ambroise Paré
CHU Antoine Béclère
CHU Bicêtre-Paul Brousse
CHU Bichat
CHU Cochin
CHU HEGP
CHU Henri Mondor
CHU Jean Verdier
CHU Necker
CHU Pitié Salpétrière
CHU Robert Debré
CHU Saint Louis
CHU Saint-Antoine
CHU Trousseau

CHG
CHG Eaubonne
GHI Le Raincy-Montfermeil
CHG Pontoise
CHG Villeneuve St-Georges
CHG Versailles

ESPIC
Hôpital Foch
Hôpital St Joseph

CLCC
Institut Gustave Roussy
Institut Curie

Secteur libéral
ACP Bièvres
Cabinet Tolbiac
Cabinet de Pathologie Amiens
Cabinet de Pathologie Compiègne



Valeur technologique et innovation

1 ▪ Un workflow exploitant le Cloud pour gérer, analyser et partager des données médicales de taille grandissante : → simplification de l'exploitation, services additionnels, contrôle de la qualité

2

3 ▪ Des algorithmes permettant de pré-analyser la qualité d'une lame virtuelle → pour permettre l'interprétation des lames

4 ▪ Des algorithmes de compression validés par les pathologistes → pour assurer une visualisation fluide et fiable sur stations de travail et mobiles

Pour une plate-forme d'échanges multi-thématiques entre pathologistes (unique en France)

Vers une plate-forme d'échanges mais aussi d'aide automatique au diagnostic ou à l'établissement de scores pronostiques dans les cancers

IPAL/BMIU

A*STAR JCO IAMS (2013-2016)

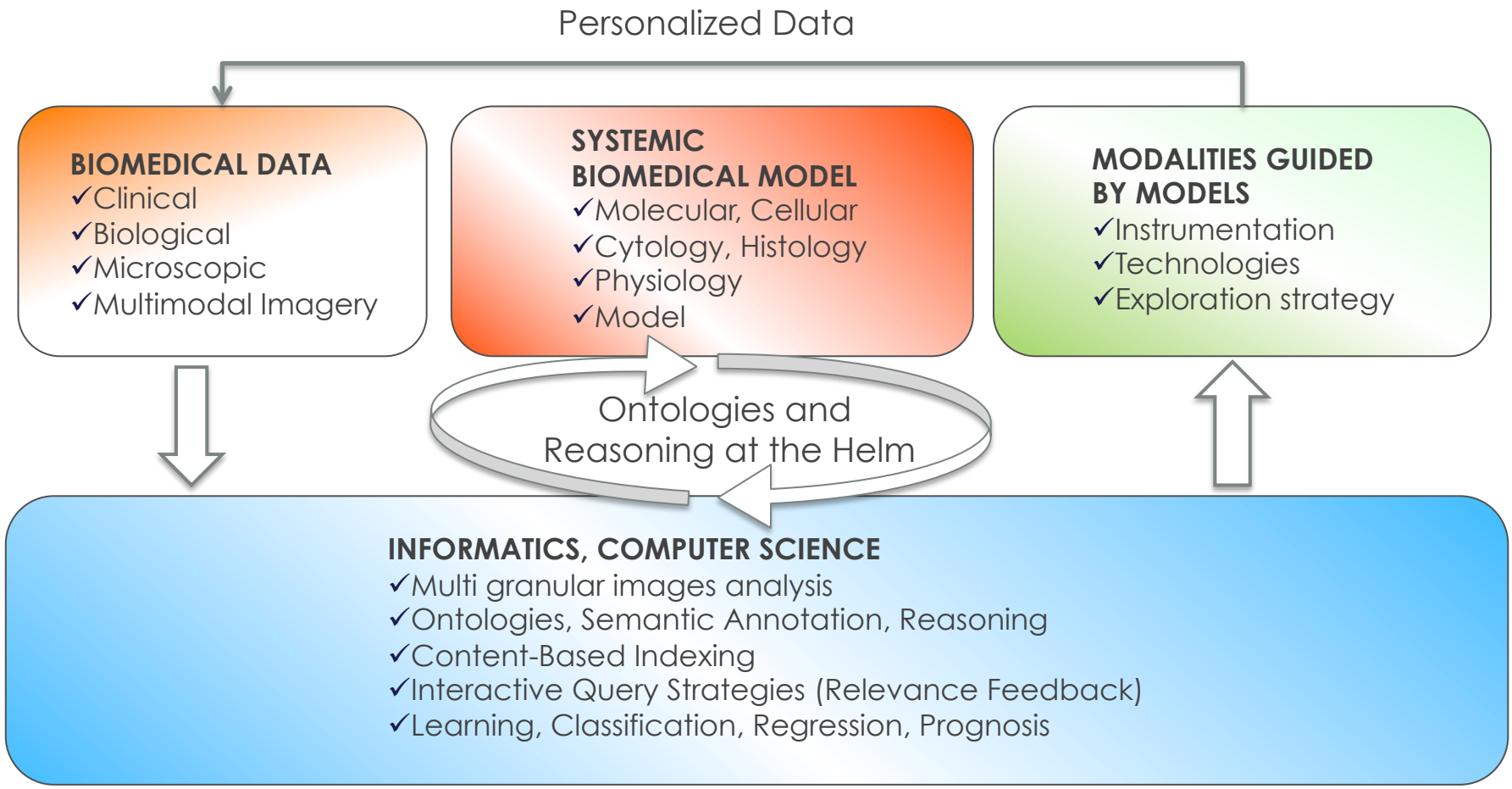
Integrated Autonomous Microscopy Systems: "Imaging anatomies of complex 3D cell culture systems"

IAMS: Executive summary

- Specific aims:
  - Suite of automated microscopy systems that can perform experiments automatically for a contiguous period of several days or weeks. Complex 3D cell cultures.
- Hypotheses:
  - Enable biological experiments (otherwise currently impossible to perform) to be carried out systematically. We will provide enabling technologies to progress biological studies on 3D cell cultures and to advance new pharmaceutical development.
- Methodology:
  - Human neural stem cells, neurospheres, reconstructed skin and intestinal spheroids/crypts. Assortment of microscopy techniques, which includes light sheet, confocal, super-resolution

Perspective: Integrated Microscopy Mining

- Combine microscopic exploration with symbolic and quantitative models and modalities



Acknowledgement

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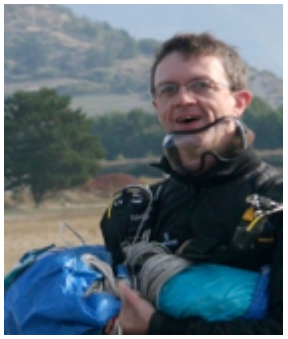

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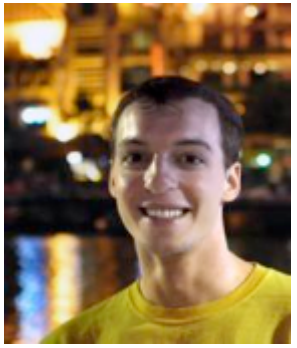
M. Christophe AVENEL, LIP6/UPMC

- M. Humayun IRSHAD, IPAL/UJF

- M. Olivier MORERE, IPAL/CNRS-A*STAR



Prof. Frédérique CAPRON, Hospital Pitié -Salpêtrière, Paris

- Dr Jacques KLOSSA, TRIBVN