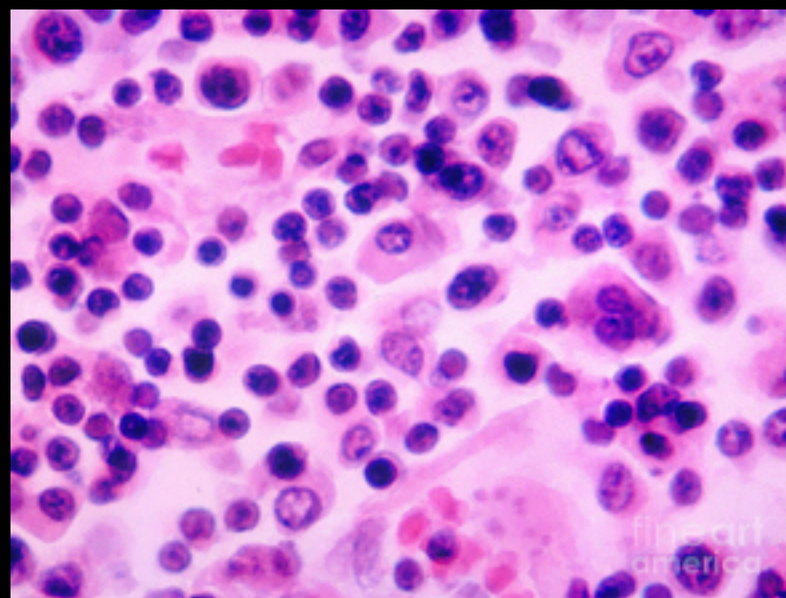
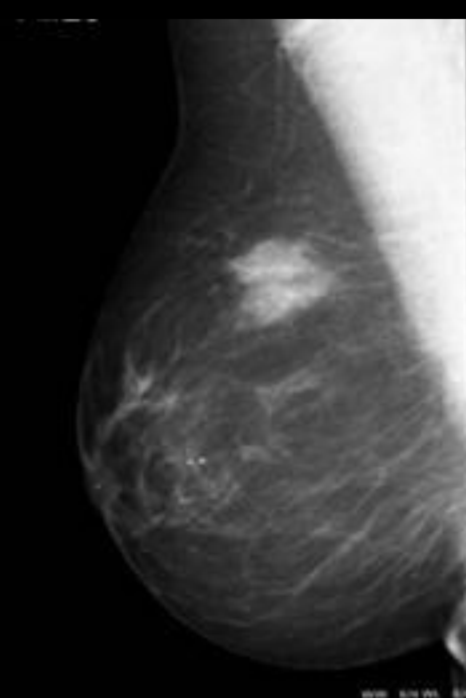
Deep Learning for Biomedical Image Analysis

Fabio A. González
Univ. Nacional de Colombia

Medical Images





In the news…

enlitic

Deep learning technology can save lives by helping detect curable diseases early

Up to Speed on Deep Learning in Medical Imaging

By Isaac Madan and David Dindi

Deep Learning in Healthcare: Challenges and Opportunities

In the news…

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Deep learning technology can save

Deep Learning in Medical Imaging: The Not-so-near Future

Blog | March 11, 2016 | PACS and Informatics

By Nadim Michel Daher

Medical Imaging

By Isaac Madan and David Dindi

Deep Learning in Healthcare: Challenges and Opportunities

Medical Images ≠ Natural Images

- **Natural image analysis:**
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  - Huge volumes available
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- **Medical image analysis:**
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Medical Images ≠ Natural Images

- **Natural image analysis:**
  - Huge volumes available
  - Humans have a natural ability to understand them
  - Cheap annotation
  - Effectivity more important than interpretability
  - Typical resolution 12MP, but lower resolutions enough for analysis.

- **Medical image analysis:**
  - Huge volumes available
  - Understanding require complex training
  - Expensive annotation
  - Interpretability more important than effectivity
  - Large resolution/size images (10^4 MP, 4D, etc)

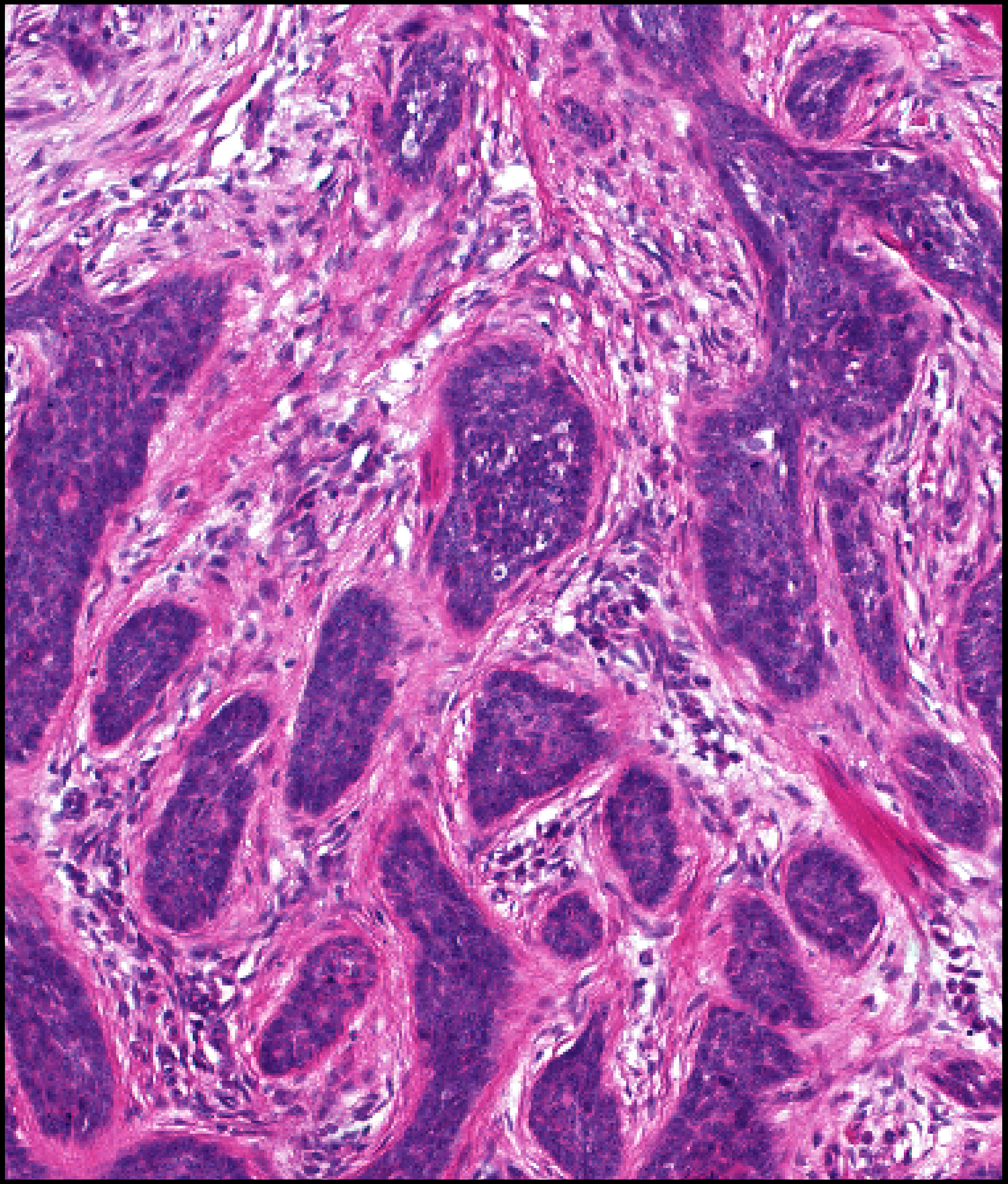
Challenges

- Interpretability
- Involving domain knowledge
- Large sizes/resolutions
- Expensive annotations

Interpretability

Basal cell carcinoma

- BCC is the most common skin cancer.
- Diagnosis is performed by visual inspection of a histopathology slide from a biopsy sample.
- Prognostic is excellent, as long as the appropriate treatment is used in early diagnosis.



Visual variability

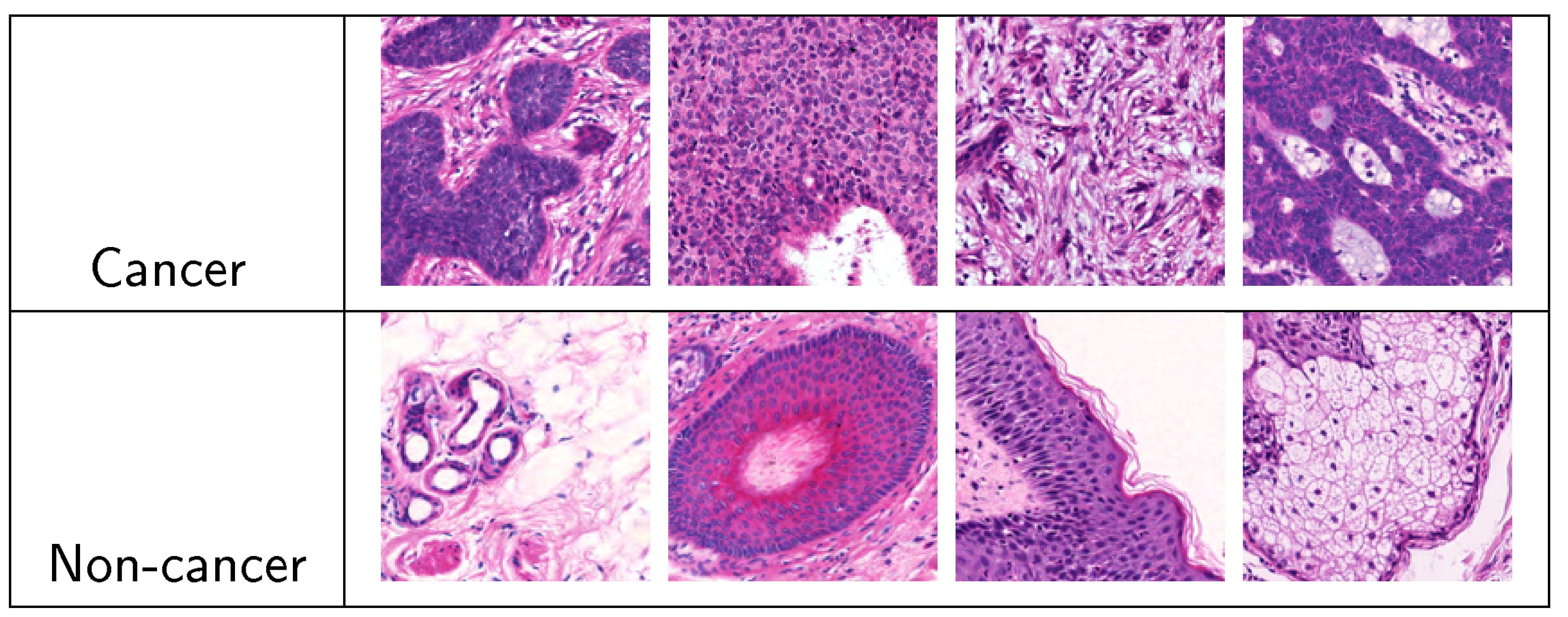
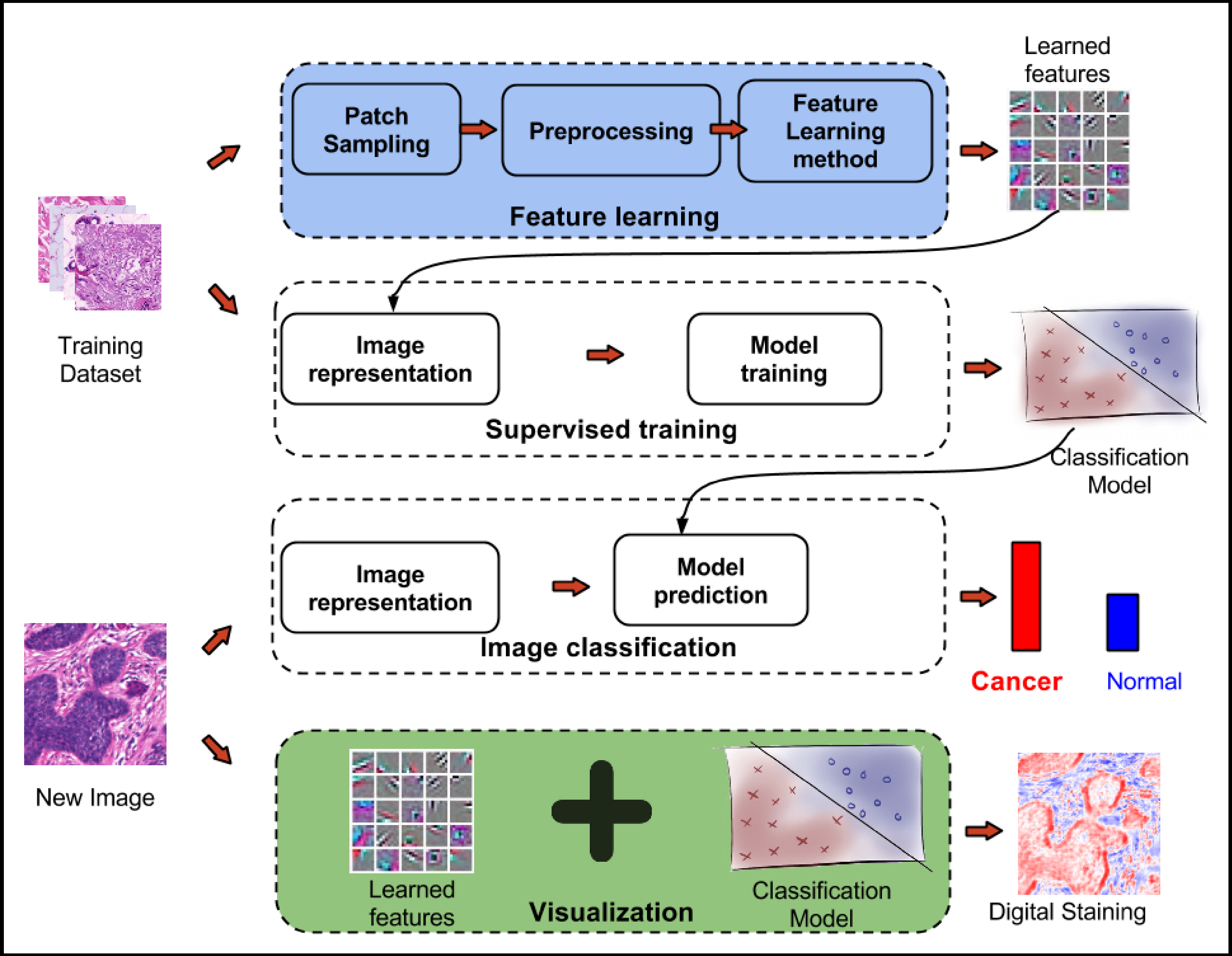
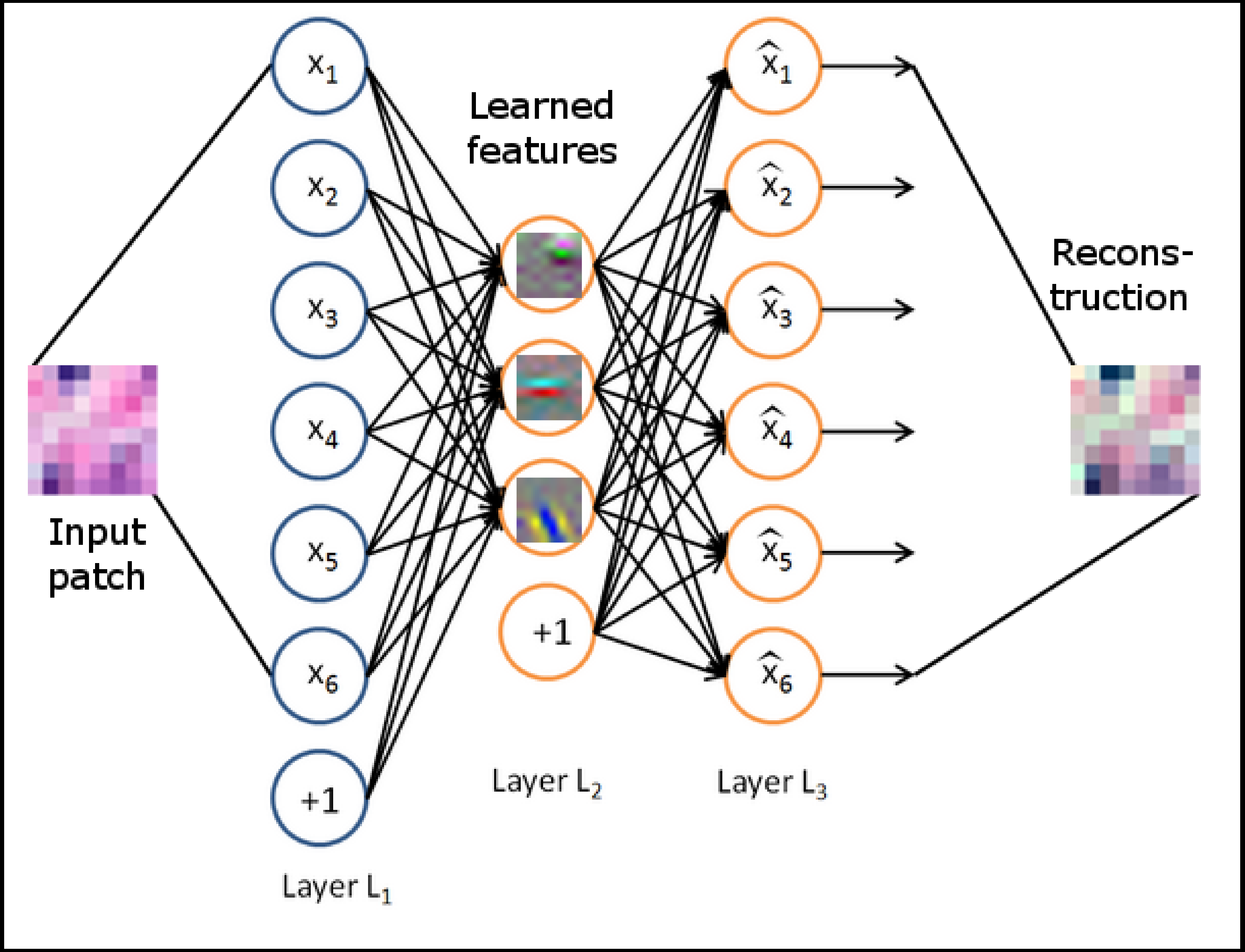


Image analysis framework



Feature learning



Learning strategies

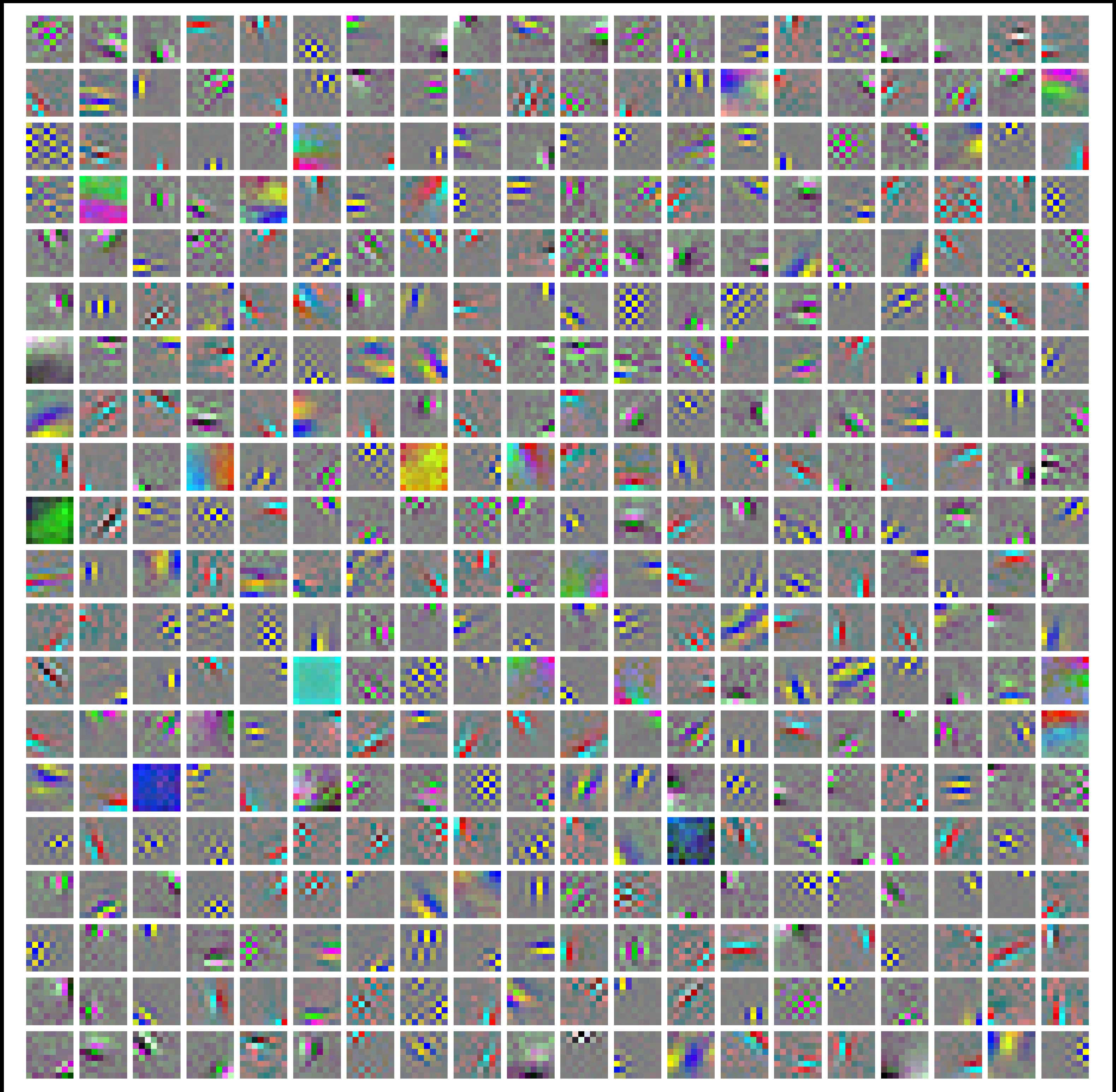
RICA:

$$J(\mathbf{W}) = \mathcal{L}\left(\mathbf{X}, r_{\mathbf{W}}\left(\mathbf{X}\right)\right) + \underbrace{\sum_{i=1}^{m}\sum_{j=1}^{n}\sqrt{\left(\mathbf{W}_j x^{(i)}\right)^2 + \epsilon}}_{\text{Regularization}}$$

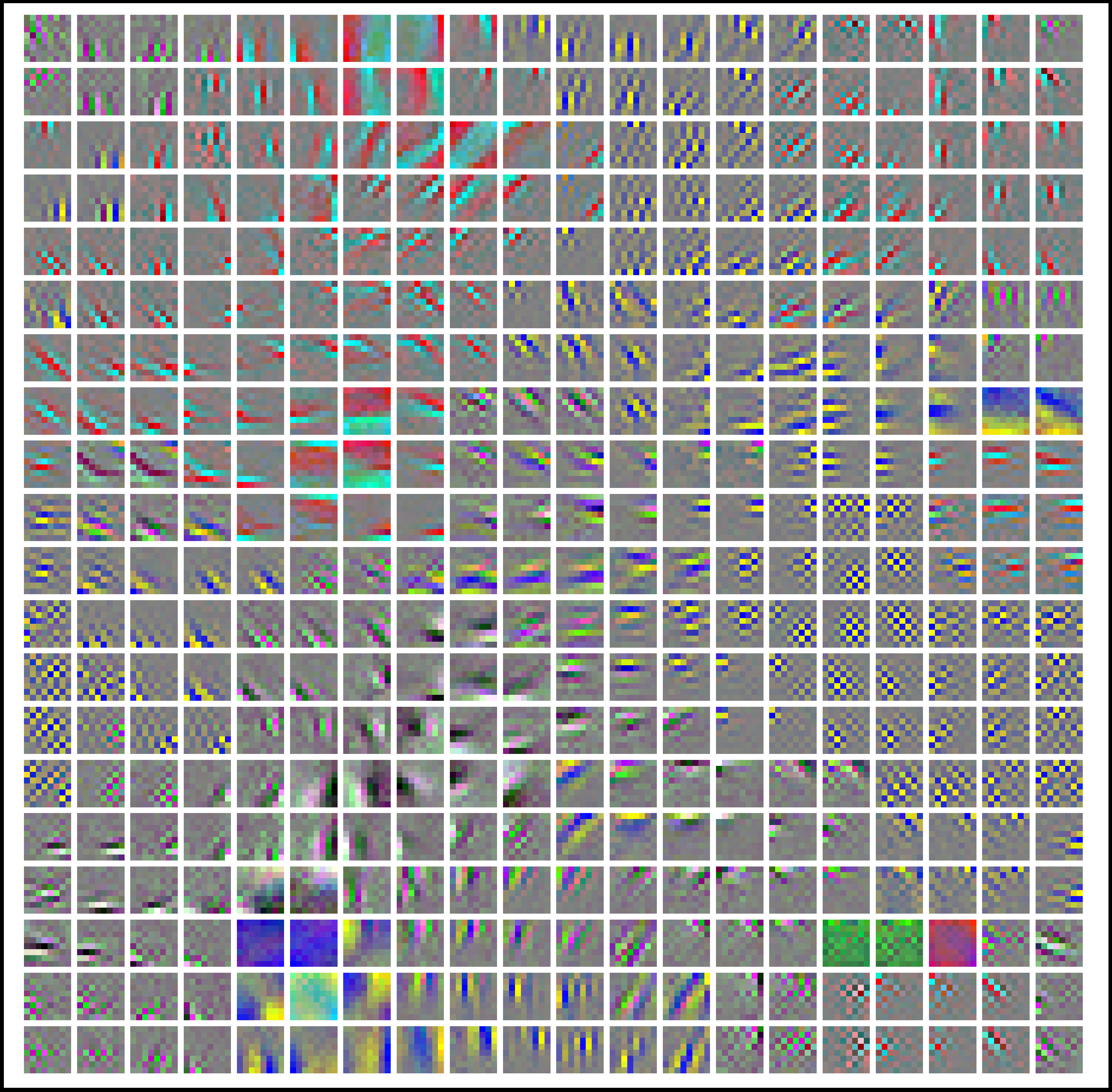
TICA:

$$J(\mathbf{W}) = \mathcal{L}\left(\mathbf{X}, r_{\mathbf{W}}\left(\mathbf{X}\right)\right) + \underbrace{\sum_{i=1}^{m}\sum_{k=1}^{l}\sqrt{\mathbf{H}_k\left(\mathbf{W} x^{(i)}\right)^2 + \epsilon}}_{\text{Regularization}},$$

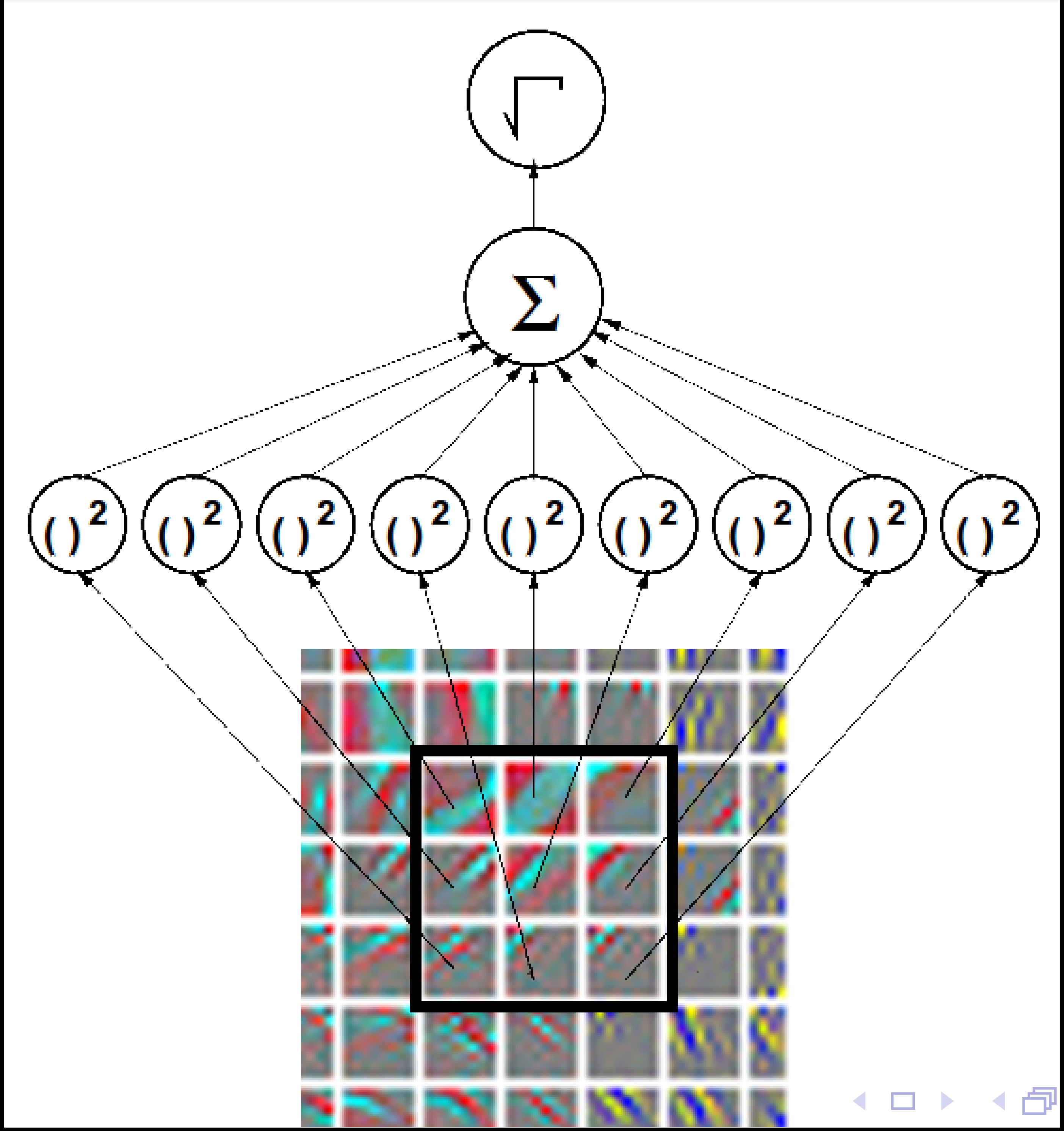
RICA features



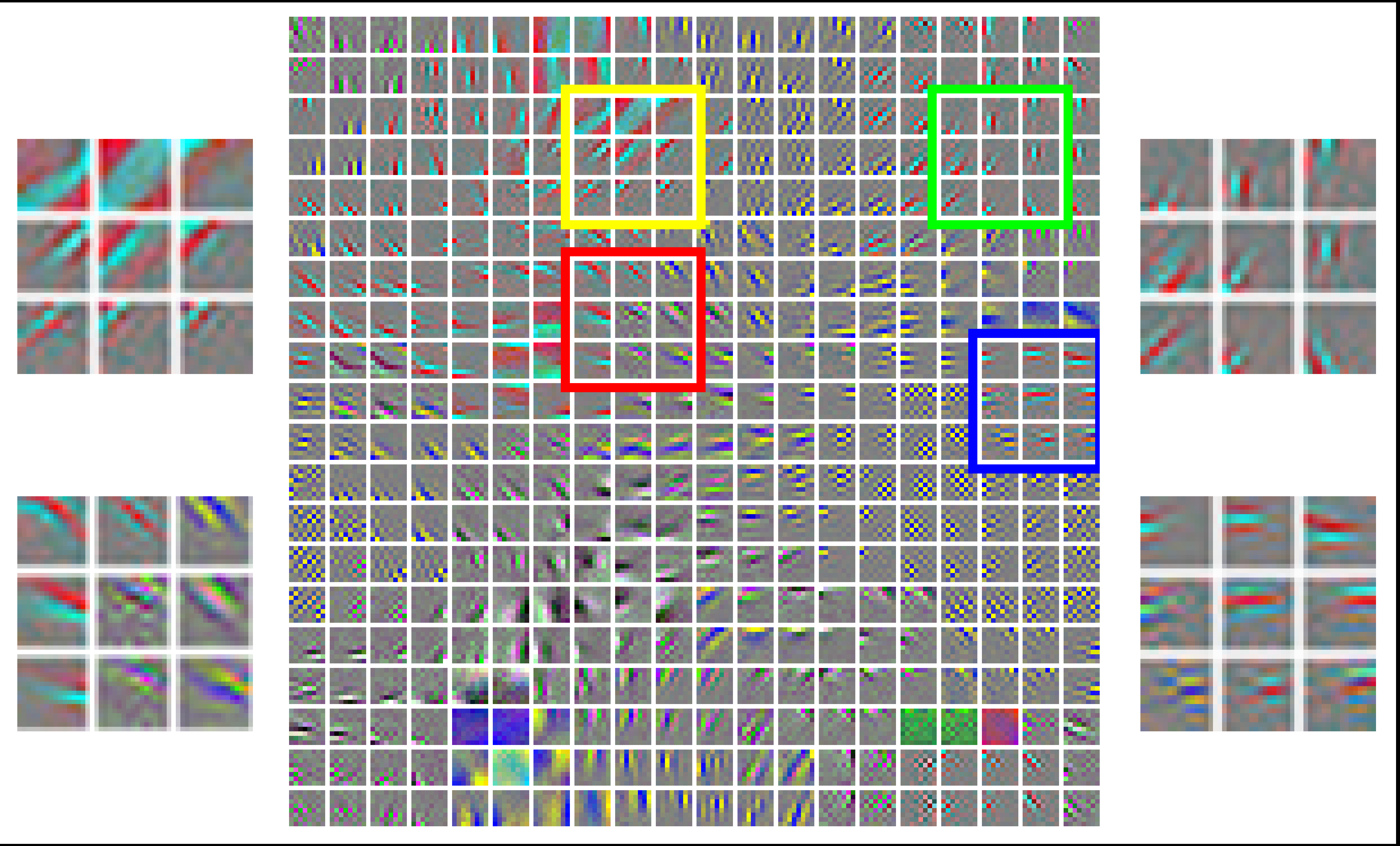
TICA features



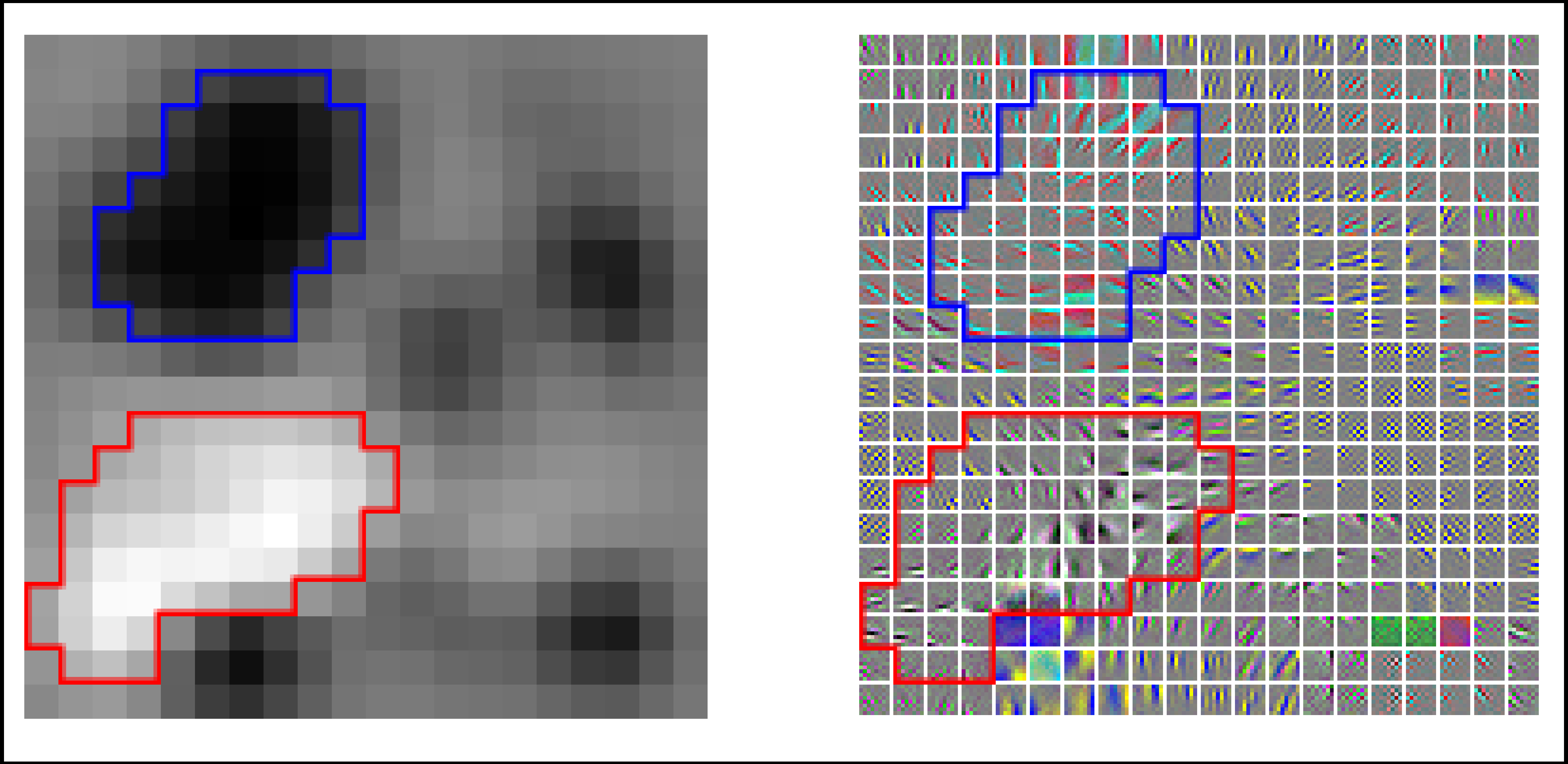
Topographic representation



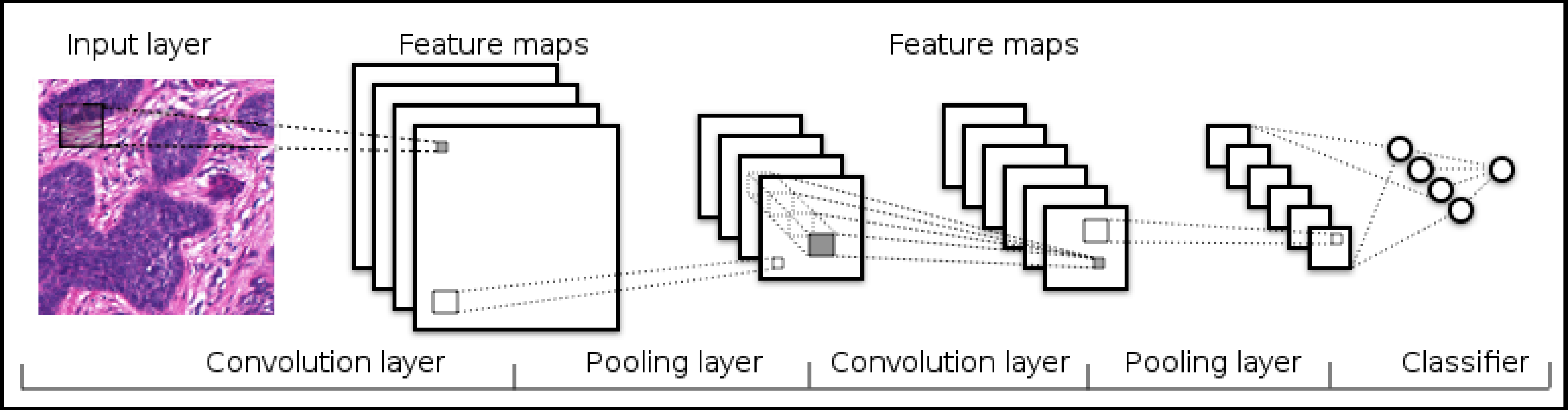
Invariant features



Unsupervised discrimination



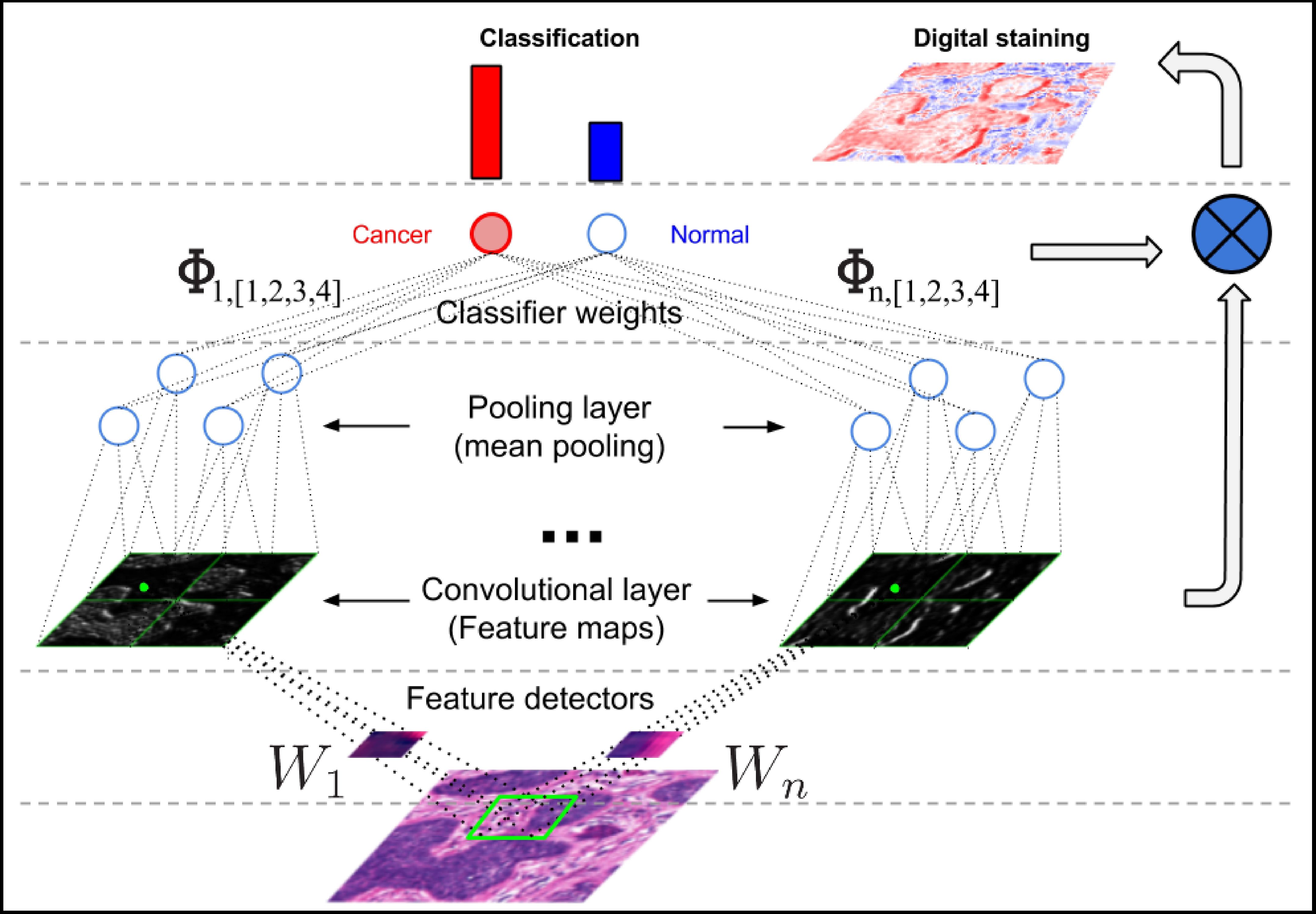
Classification



Classification results

Representation	Accuracy	F-Score	BAC
TICA combined layers	**0.944 +/- 0.025**	**0.925 +/- 0.031**	**0.941 +/- 0.027**
RICA combined layers	0.935 +/- 0.025	0.912 +/- 0.026	0.931 +/- 0.023
AE combined layers	0.933 +/- 0.026	0.908 +/- 0.029	0.926 +/- 0.025
TICA Second layer	0.937 +/- 0.015	0.913 +/- 0.020	0.931 +/- 0.017
AE Second layer	0.916 +/- 0.034	0.886 +/- 0.039	0.907 +/- 0.031
TICA First Layer	0.936 +/- 0.022	0.914 +/- 0.027	0.933 +/- 0.020
RICA First Layer	0.926 +/- 0.029	0.899 +/- 0.033	0.920 +/- 0.032
AE First Layer	0.925 +/- 0.027	0.899 +/- 0.027	0.917 +/- 0.024
(BOF) ColorDCT-400	***0.891 +/- 0.023***	***0.851 +/- 0.027***	***0.883 +/- 0.024***
(BOF) Haar-400	***0.796 +/- 0.026***	***0.708 +/- 0.031***	***0.772 +/- 0.026***

Digital staining



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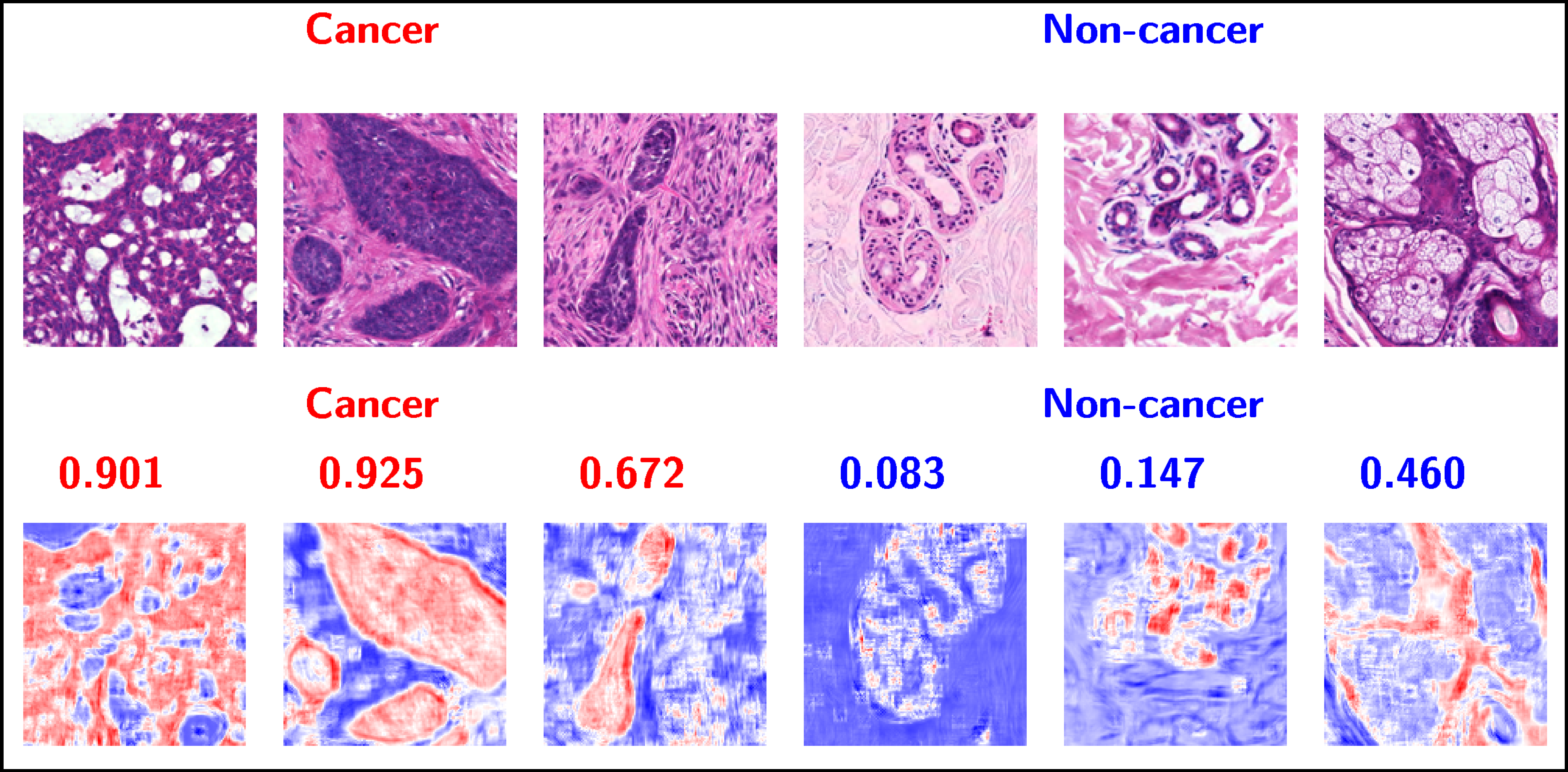

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A Deep Learning Architecture for Image Representation, Visual Interpretability and Automated Basal-Cell Carcinoma Cancer Detection

Angel Alfonso Cruz-Roa[1], John Edison Arevalo Ovalle[1], Anant Madabhushi[2], and Fabio Augusto González Osorio[1]

[1] MindLab Research Group, Universidad Nacional de Colombia, Bogotá, Colombia
[2] Dept. of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, USA

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Artificial Intelligence in Medicine

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An unsupervised feature learning framework for basal cell carcinoma image analysis

John Arevalo[a], Angel Cruz-Roa[a], Viviana Arias[b], Eduardo Romero[c], Fabio A. González[a,*]

[a] *Machine Learning, Perception and Discovery Lab, Systems and Computer Engineering Department, Universidad Nacional de Colombia, Faculty of Engineering, Cra 30 No 45 03-Ciudad Universitaria, Building 453 Office 114, Bogotá DC, Colombia*
[b] *Pathology Department, Universidad Nacional de Colombia, Faculty of Medicine, Cra 30 No 45 03-Ciudad Universitaria, Bogotá DC, Colombia*
[c] *Computer Imaging & Medical Applications Laboratory, Universidad Nacional de Colombia, Faculty of Medicine, Cra 30 No 45 03-Ciudad Universitaria, Bogotá DC, Colombia*

Involving Domain Knowledge

Handcrafted/learned feature fusion

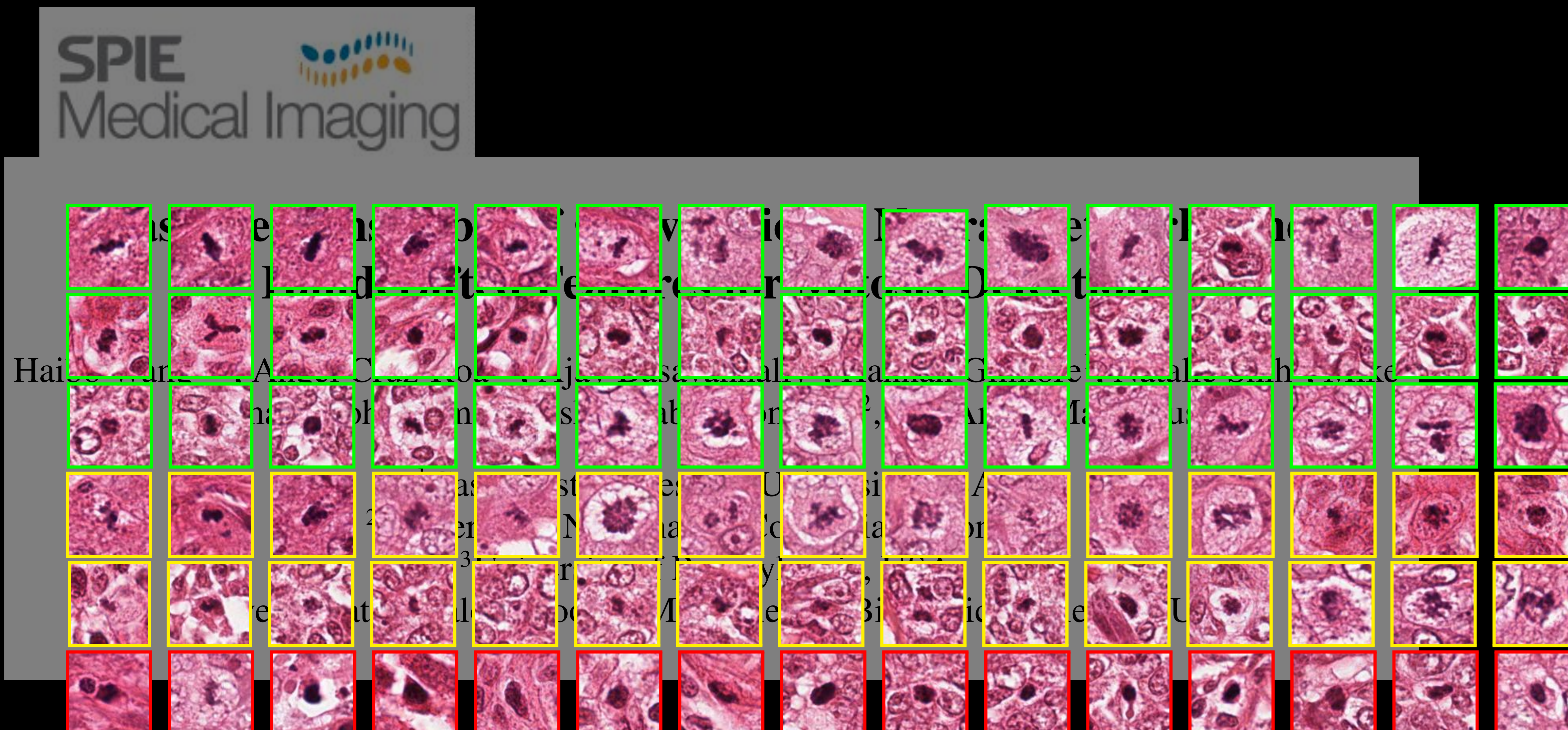
SPIE Medical Imaging

Cascaded Ensemble of Convolutional Neural Networks and Handcrafted Features for Mitosis Detection

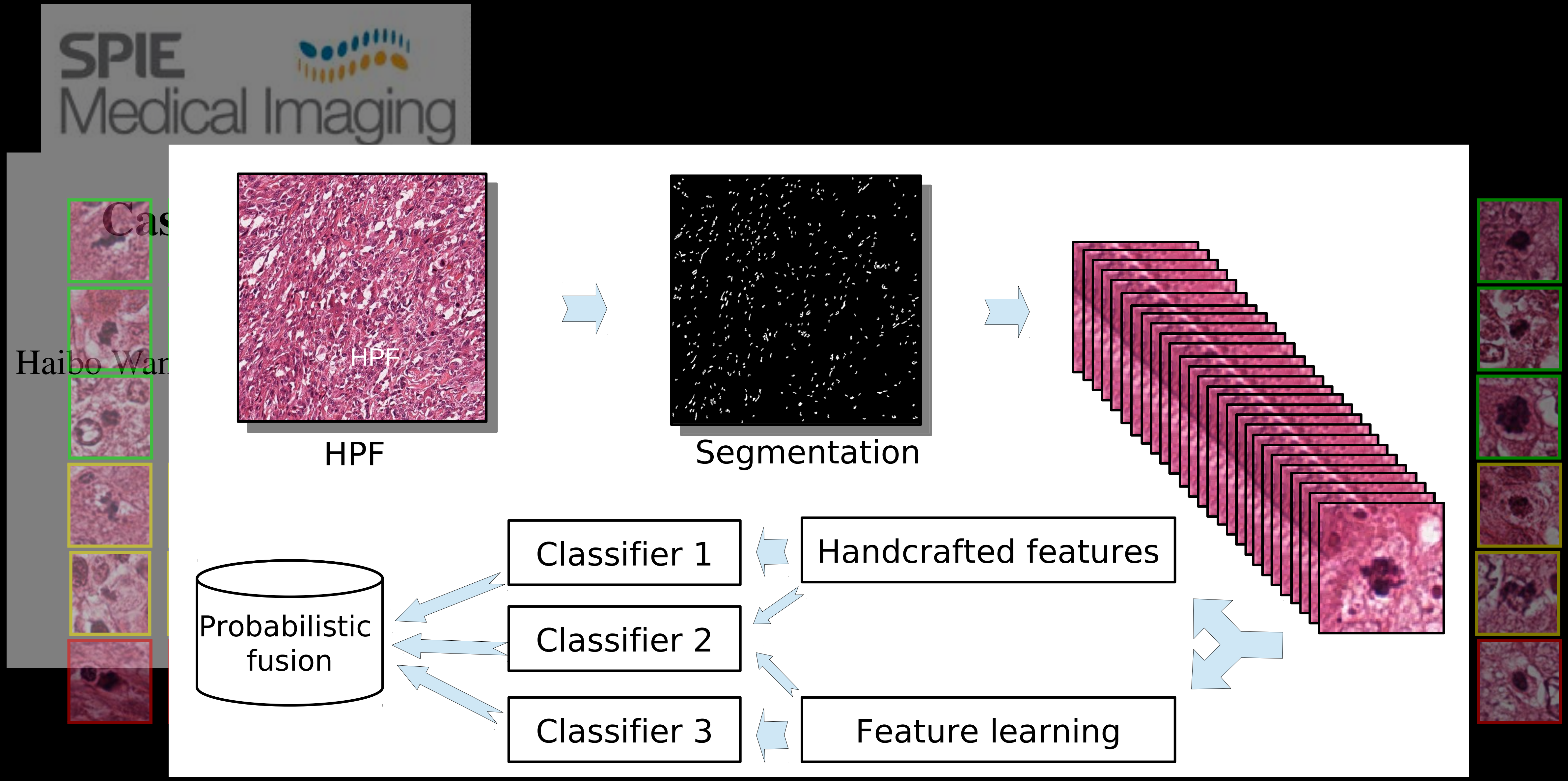
Haibo Wang *ǂ, Angel Cruz-Roa*[2], Ajay Basavanhally[1], Hannah Gilmore[1], Natalie Shih[3], Mike Feldman[3], John Tomaszewski[4], Fabio Gonzalez[2], and Anant Madabhushi[1]

[1]Case Western Reserve University, USA
[2]Universidad Nacional de Colombia, Colombia
[3]University of Pennsylvania, USA
[4]University at Buffalo School of Medicine and Biomedical Sciences, USA

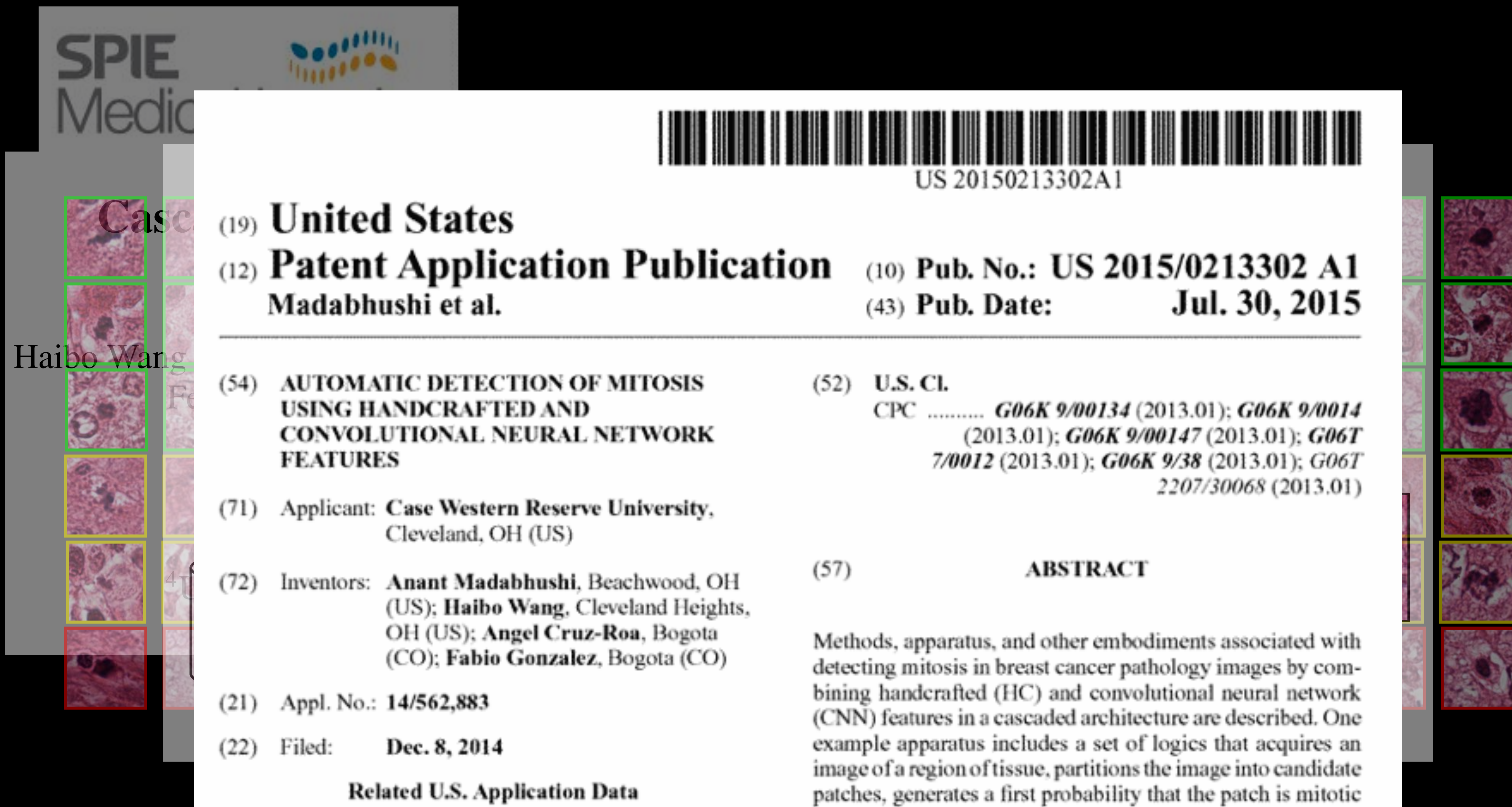
Handcrafted/learned feature fusion



Handcrafted/learned feature fusion



Handcrafted/learned feature fusion



US 20150213302A1

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(12) **Patent Application Publication**
Madabhushi et al.

(10) **Pub. No.: US 2015/0213302 A1**
(43) **Pub. Date: Jul. 30, 2015**

(54) **AUTOMATIC DETECTION OF MITOSIS USING HANDCRAFTED AND CONVOLUTIONAL NEURAL NETWORK FEATURES**

(71) Applicant: **Case Western Reserve University**, Cleveland, OH (US)

(72) Inventors: **Anant Madabhushi**, Beachwood, OH (US); **Haibo Wang**, Cleveland Heights, OH (US); **Angel Cruz-Roa**, Bogota (CO); **Fabio Gonzalez**, Bogota (CO)

(21) Appl. No.: **14/562,883**

(22) Filed: **Dec. 8, 2014**

Related U.S. Application Data

(52) **U.S. Cl.**
CPC ***G06K 9/00134*** (2013.01); ***G06K 9/0014*** (2013.01); ***G06K 9/00147*** (2013.01); ***G06T 7/0012*** (2013.01); ***G06K 9/38*** (2013.01); *G06T 2207/30068* (2013.01)

(57) **ABSTRACT**

Methods, apparatus, and other embodiments associated with detecting mitosis in breast cancer pathology images by combining handcrafted (HC) and convolutional neural network (CNN) features in a cascaded architecture are described. One example apparatus includes a set of logics that acquires an image of a region of tissue, partitions the image into candidate patches, generates a first probability that the patch is mitotic

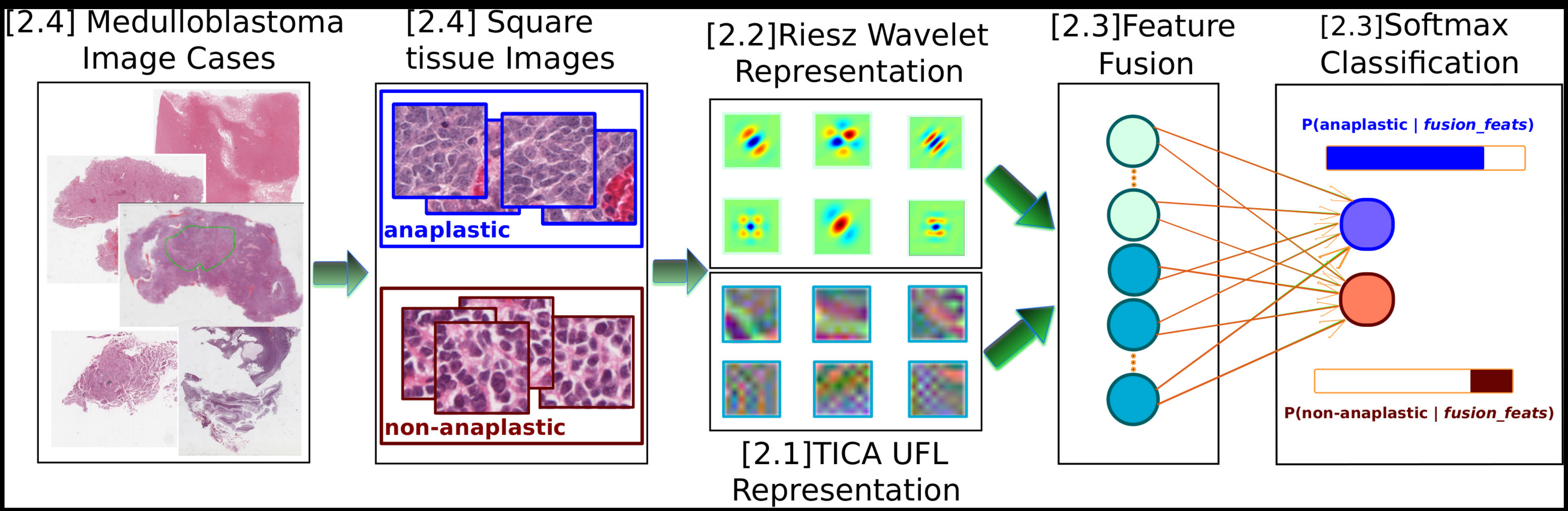
Handcrafted/learned feature fusion

Combining Unsupervised Feature Learning and Riesz Wavelets for Histopathology Image Representation: Application to Identifying Anaplastic Medulloblastoma

Sebastian Otálora[1], Angel Cruz-Roa[1], John Arevalo[1], Manfredo Atzori[2], Anant Madabhushi[3], Alexander R. Judkins[4], Fabio González[1], Henning Müller[2], and Adrien Depeursinge[2,5]

[1] Universidad Nacional de Colombia, Bogotá, Colombia
[2] University of Applied Sciences Western Switzerland (HES-SO)
[3] Case Western Reserve University, Cleveland, OH, USA
[4] St. Jude Childrens Research Hospital from Memphis, TN, USA
[5] Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland

Handcrafted/learned feature fusion

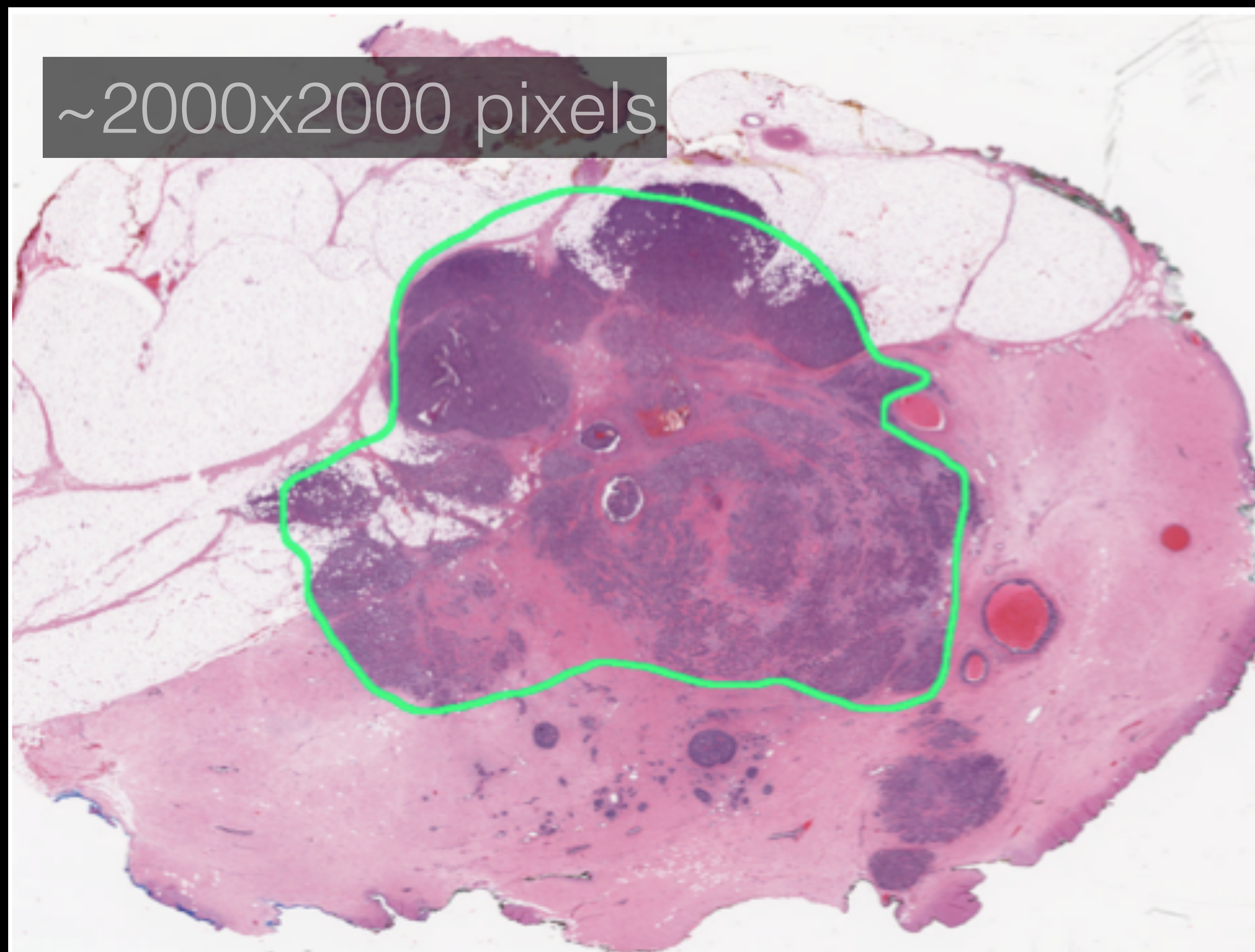


Handcrafted/learned feature fusion

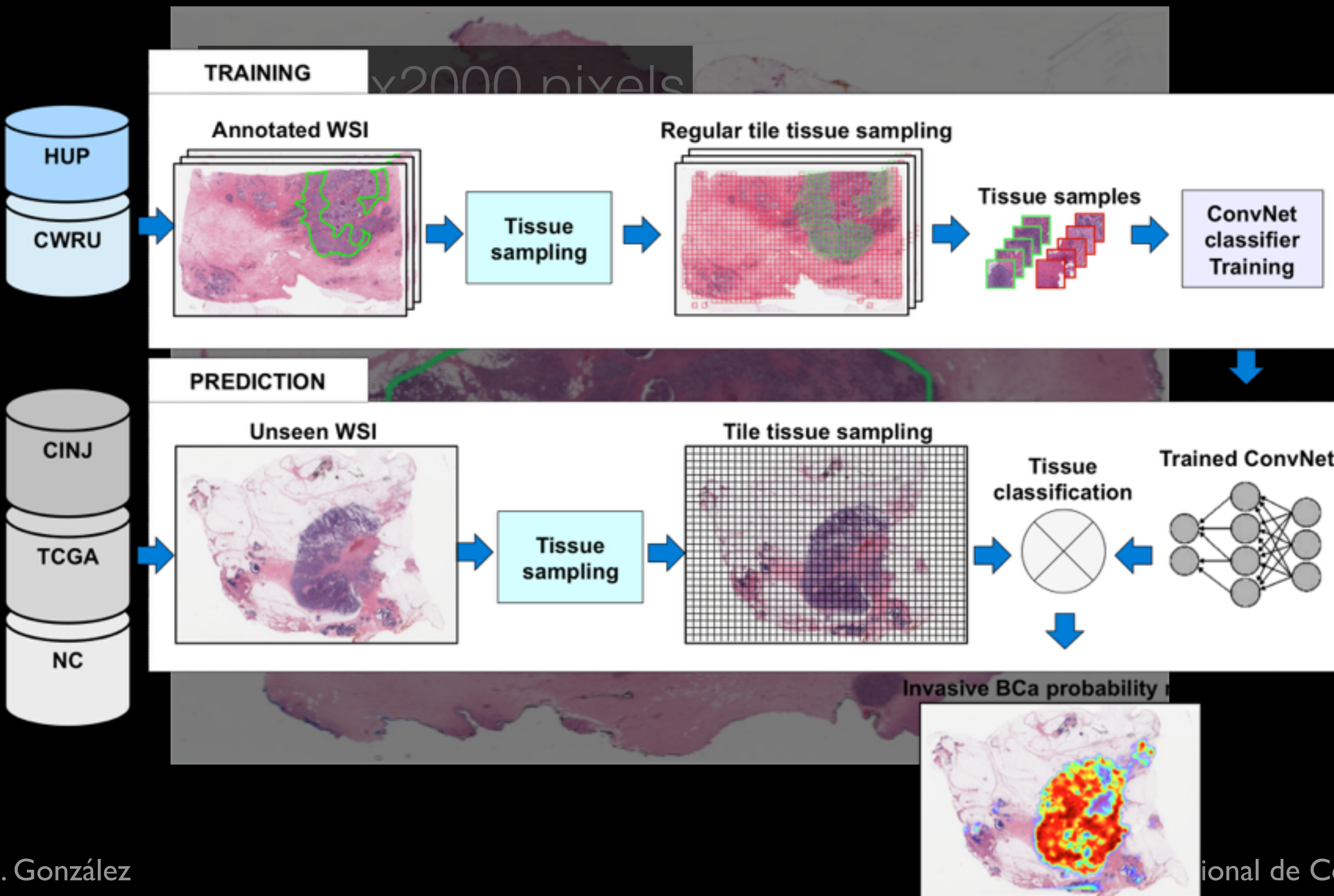
Method	**Accuracy**	**Sensitivity**	**Specificity**
$TICA$ + Riesz$[N_3^1, N_2^2, N_1^2]$	**0.997 +/- 0.002**	**0.995 +/- 0.004**	**1 +/- 0**
$TICA$[9]	0.972 +/- 0.018	0.977 +/- 0.021	0.967 +/- 0.031
Riesz $[N_3^1, N_2^2, N_1^2]$	0.964 +/- 0.038	0.999 +/- 0.001	0.932 +/- 0.07
Riesz $[N_3^1]$	0.958 +/- 0.062	0.963 +/- 0.05	0.916 +/- 0.125
Riesz $[N_2^2]$	0.94 +/- 0.02	0.94 +/- 0.02	0.3 +/- 0.04
CNN[9]	0.90 +/- 0.1	0.89 +/- 0.18	0.9 +/- 0.0.3
sAE[9]	0.90	0.87	0.93
BOF + $A2NMF$ (Haar) [10]	0.87	0.86	0.87
Riesz $[N_1^2]$	0.85 +/- 0.23	0.9 +/- 0.15	0.7 +/- 0.47
BOF + K - NN (Haar) [2]	0.80	-	-
BOF + K - NN (MR8)[2]	0.62	-	-

Efficient Analysis of Large Resolution Images

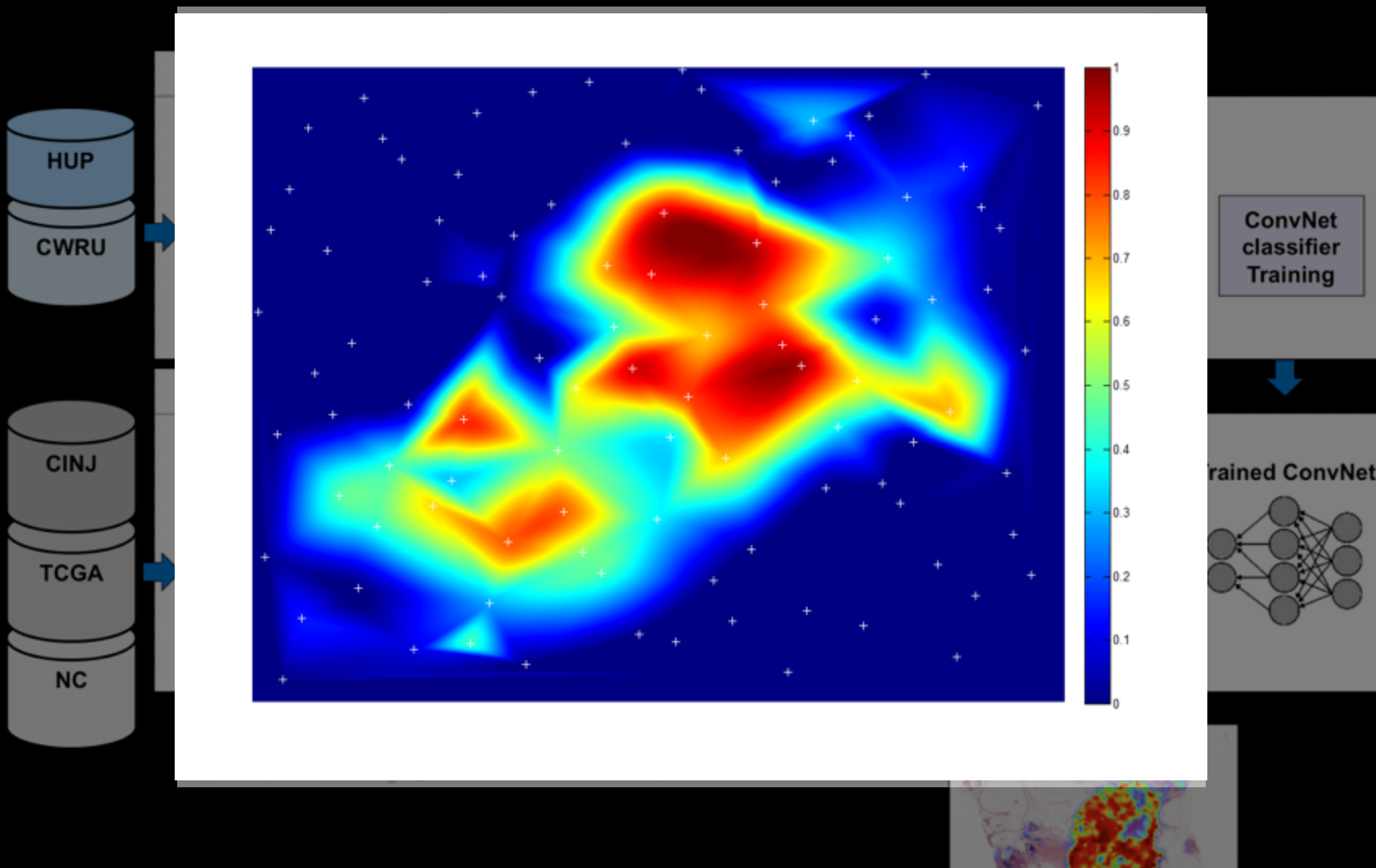
Efficient DL over whole slide pathology images



Efficient DL over whole slide pathology images



Efficient DL over whole slide pathology images



Efficient DL over whole slide pathology images

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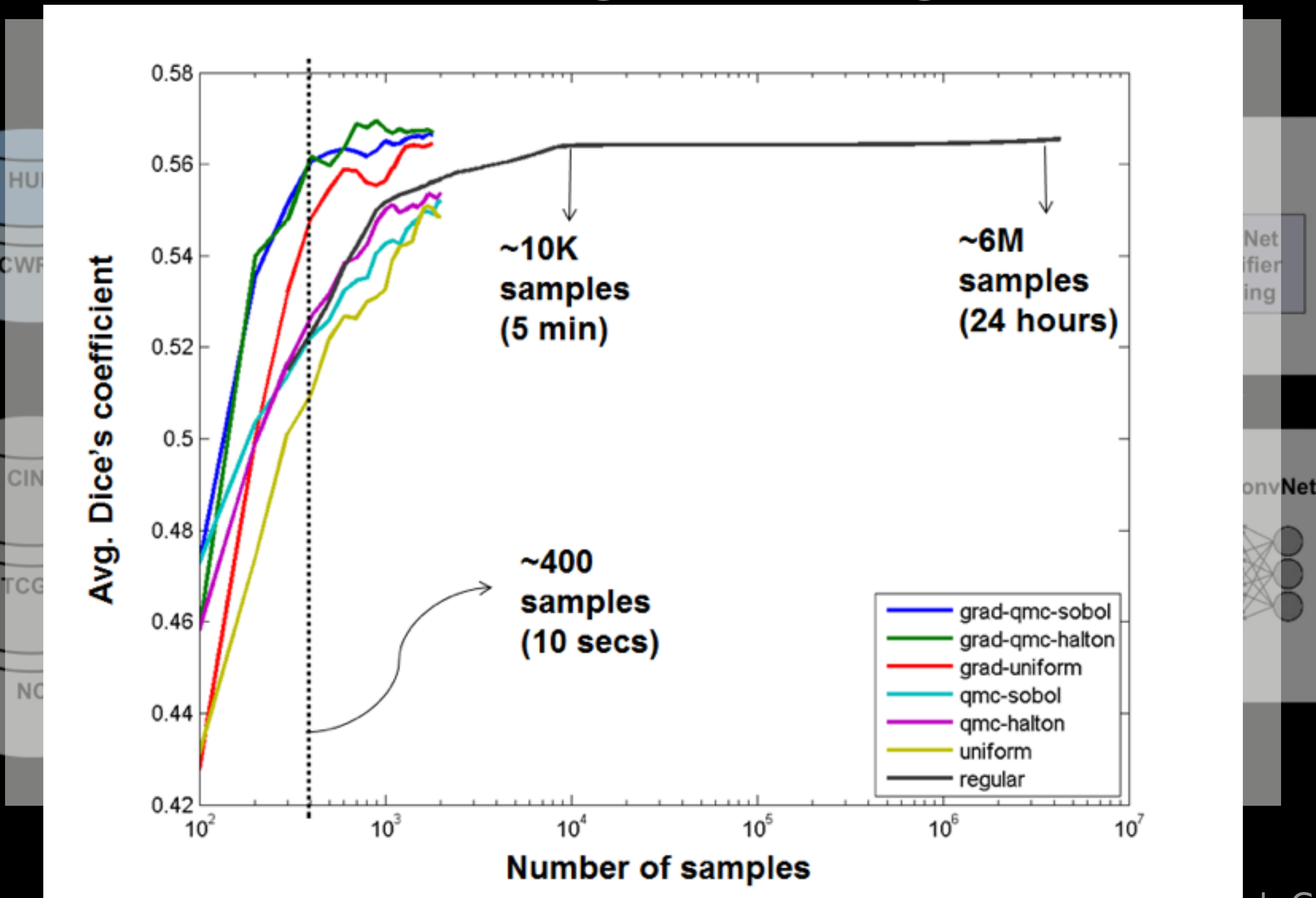
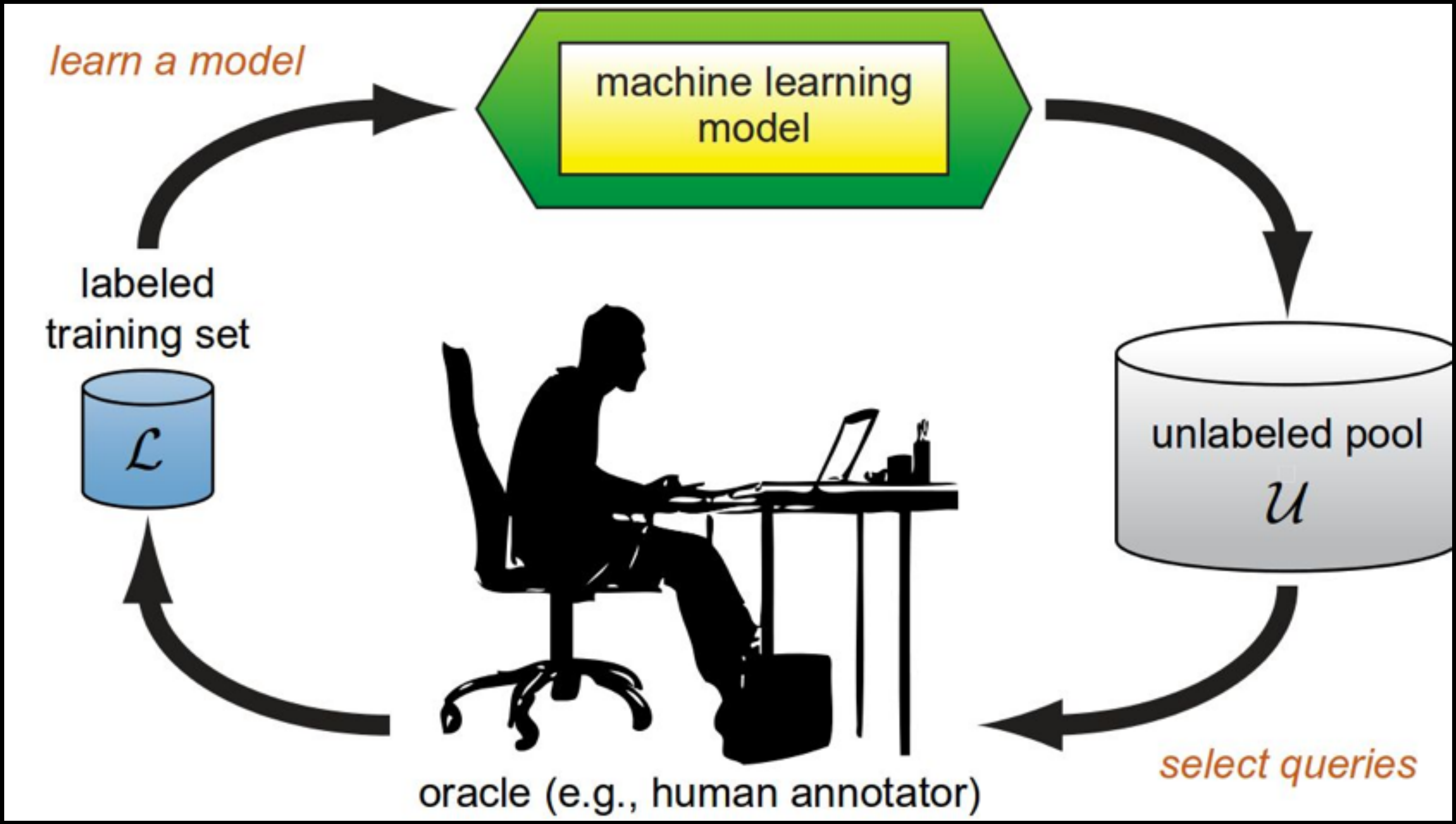
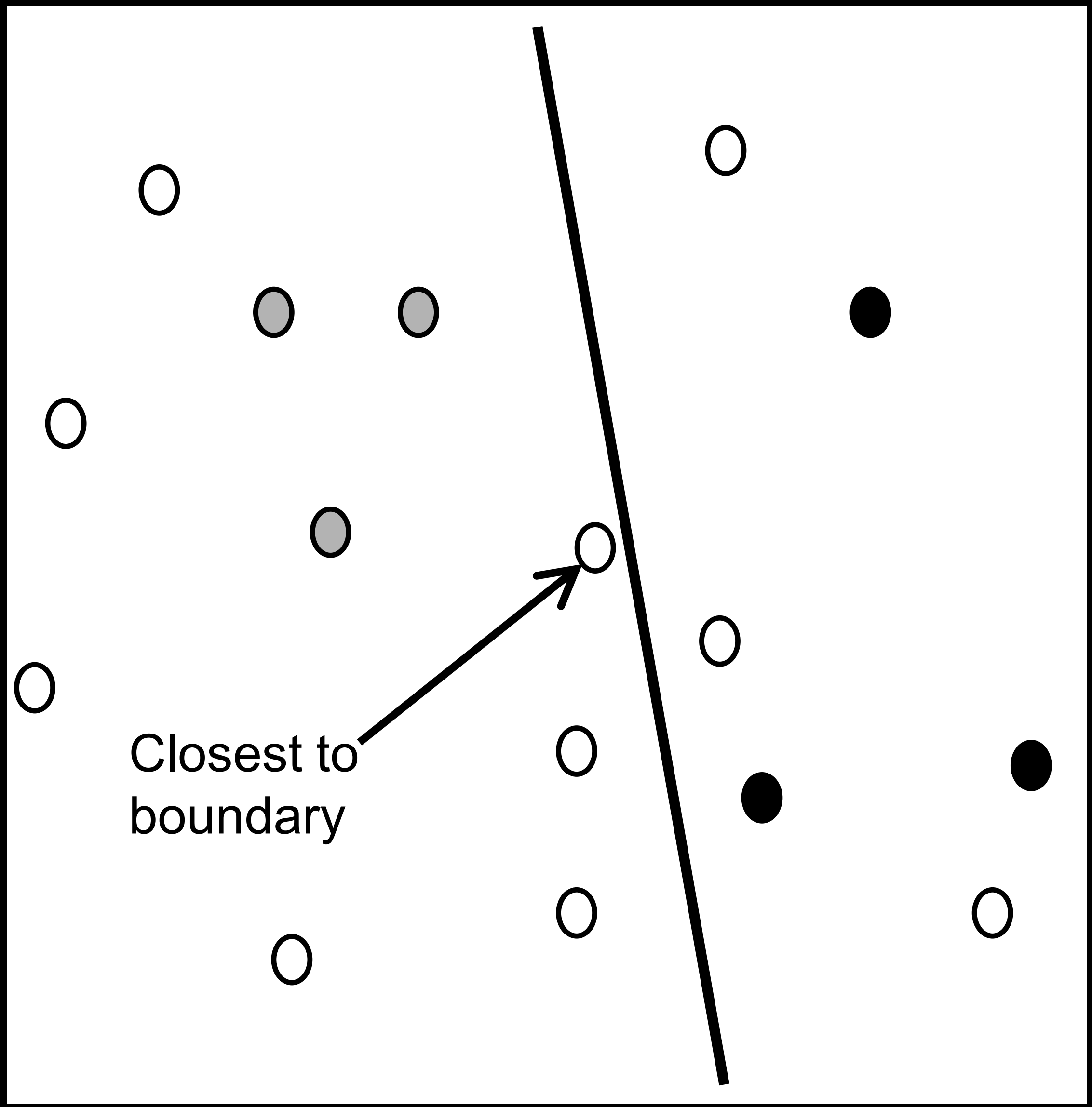


Expensive Annotations

Active learning

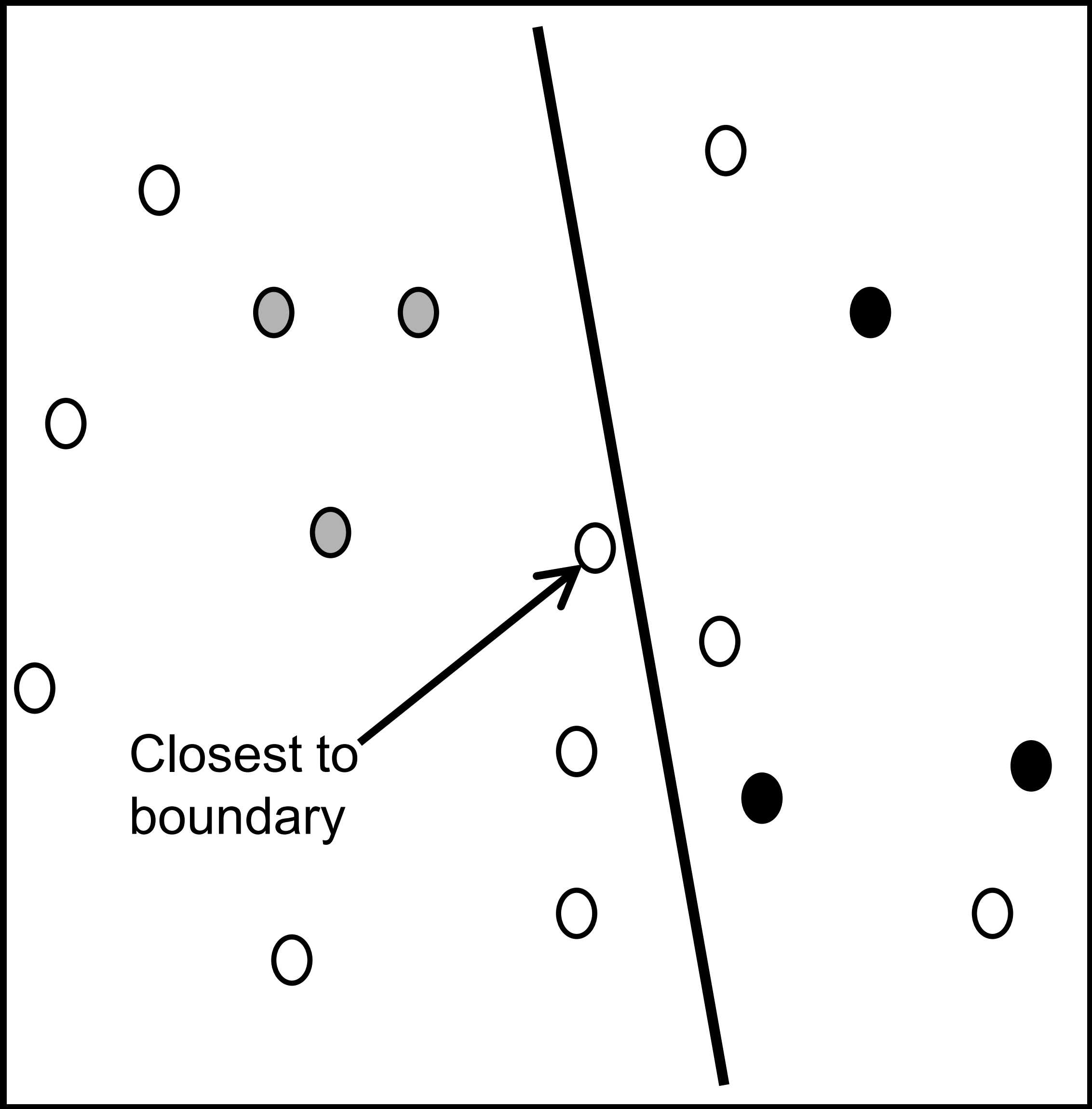


Query Selection Strategy

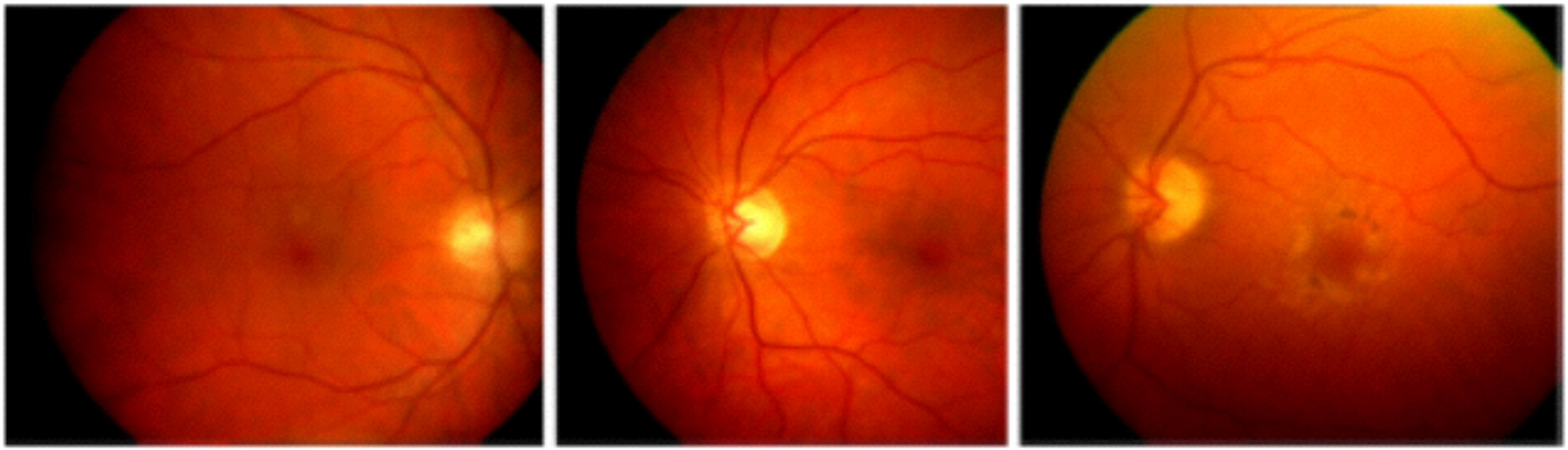


Query Selection Strategy

- Uncertainty sampling
- Query by committee
- Expected model change
- Expected error reduction
- Variance reduction



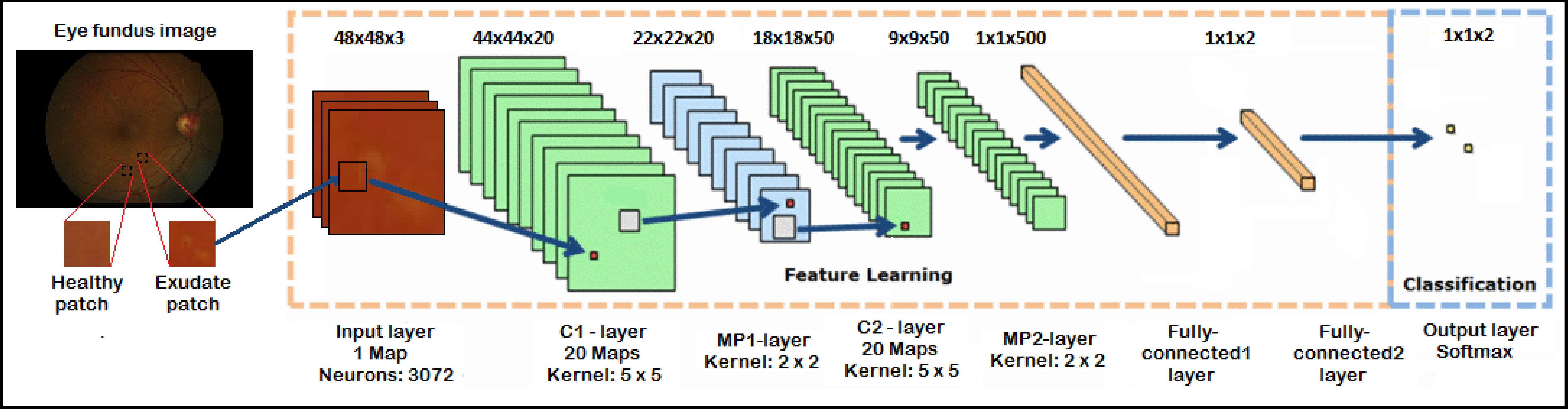
Exudate detection in eye fondus images with CNNs



(a) (b) (c)

Exudate detection in eye fondus images with CNNs

Exudate detection in eye fundus images with CNNs



How to apply active learning?

- Which active learning strategy? It must be efficient and compatible with CNN training.
- Patch level classification model.
- Image level annotation.

Expected gradient length

$$\theta = \theta - \eta \nabla J_i(\theta)$$

Expected gradient length

$$\theta = \theta - \eta \nabla J_i(\theta)$$

$$\Phi(x^i) = \sum_{j=1}^{c} p(y^i = j | x^i) \|\nabla J_i(\theta)\|$$

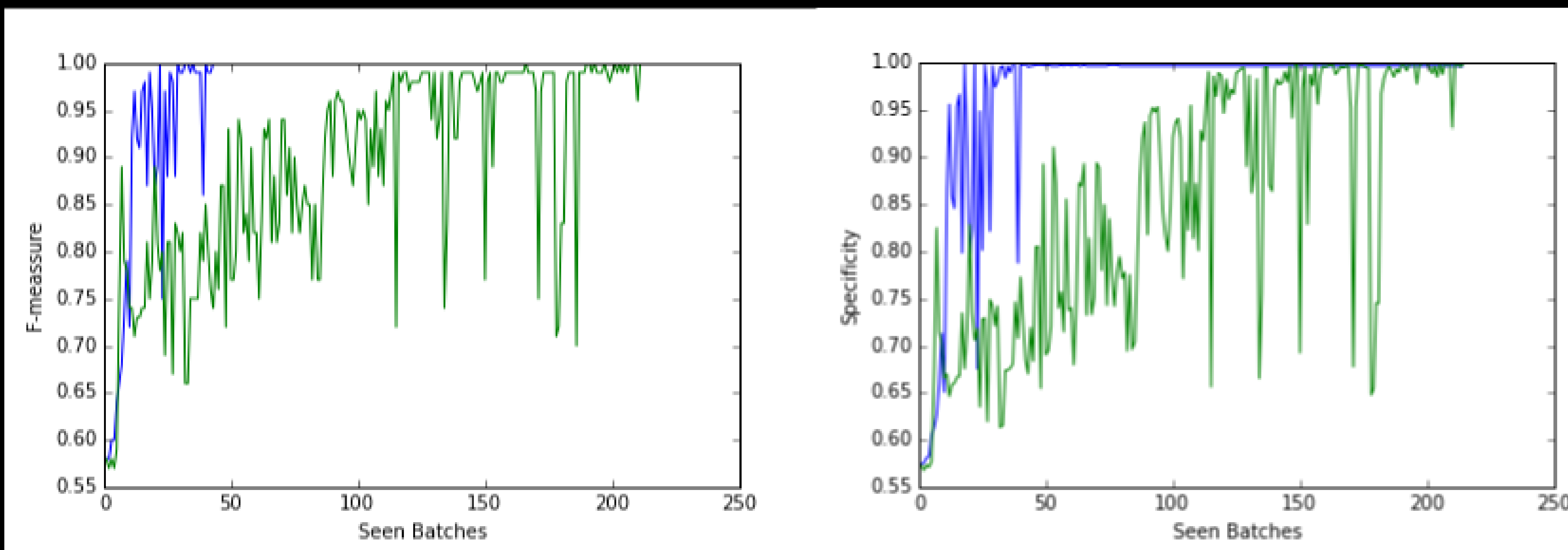
EGL at patch level

Algorithm 1 EGL for Active Selection of patches in a Convolutional Neural Network

Require: Patches Dataset $\mathscr{L}$, Initial Trained Model $\mathbf{M}$, Number k of most informative patches

```
while not converged do
    Create and shuffle batches from 𝓛
    for each batch do
        Compute Φ(x) using M, ∀x ∈ batch
    end for
    Sort all the Φ Values and return the higher k corresponding samples 𝓛_k
    Update M using 𝓛' ∪ 𝓛_k
end while
```

Patch-level results (EGL vs random selection)



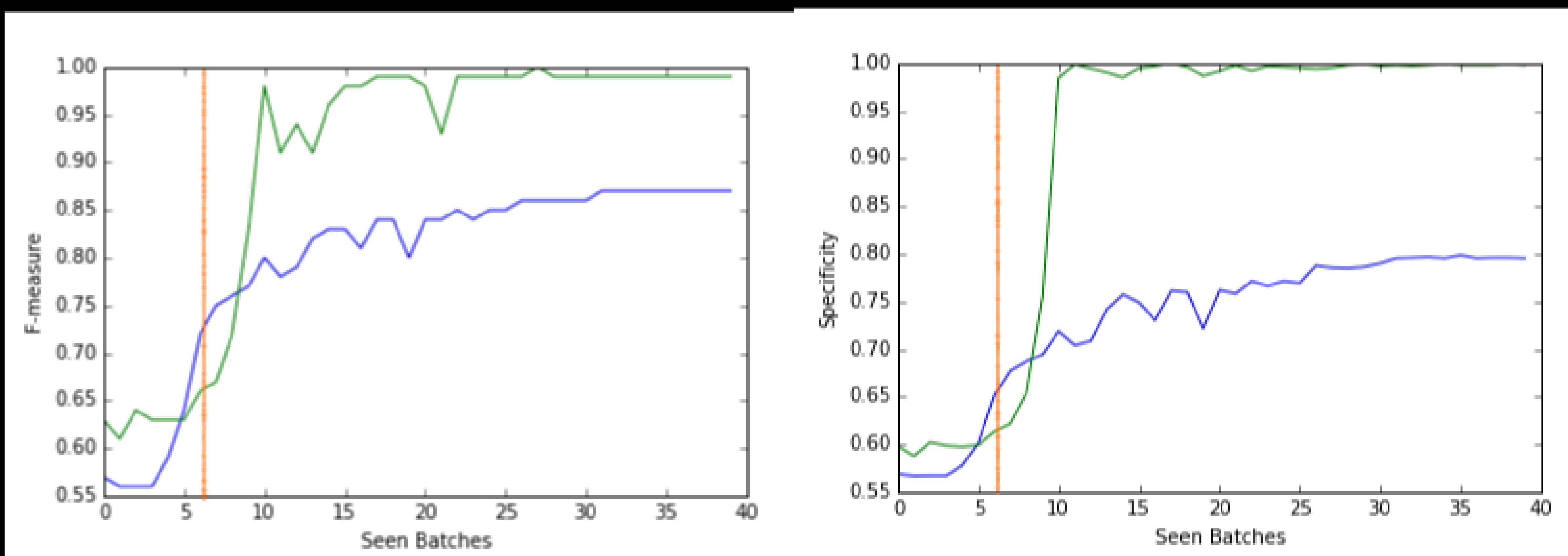
EGL at image level

Algorithm 2 EGL for Active Selection of images in a Convolutional Neural Network

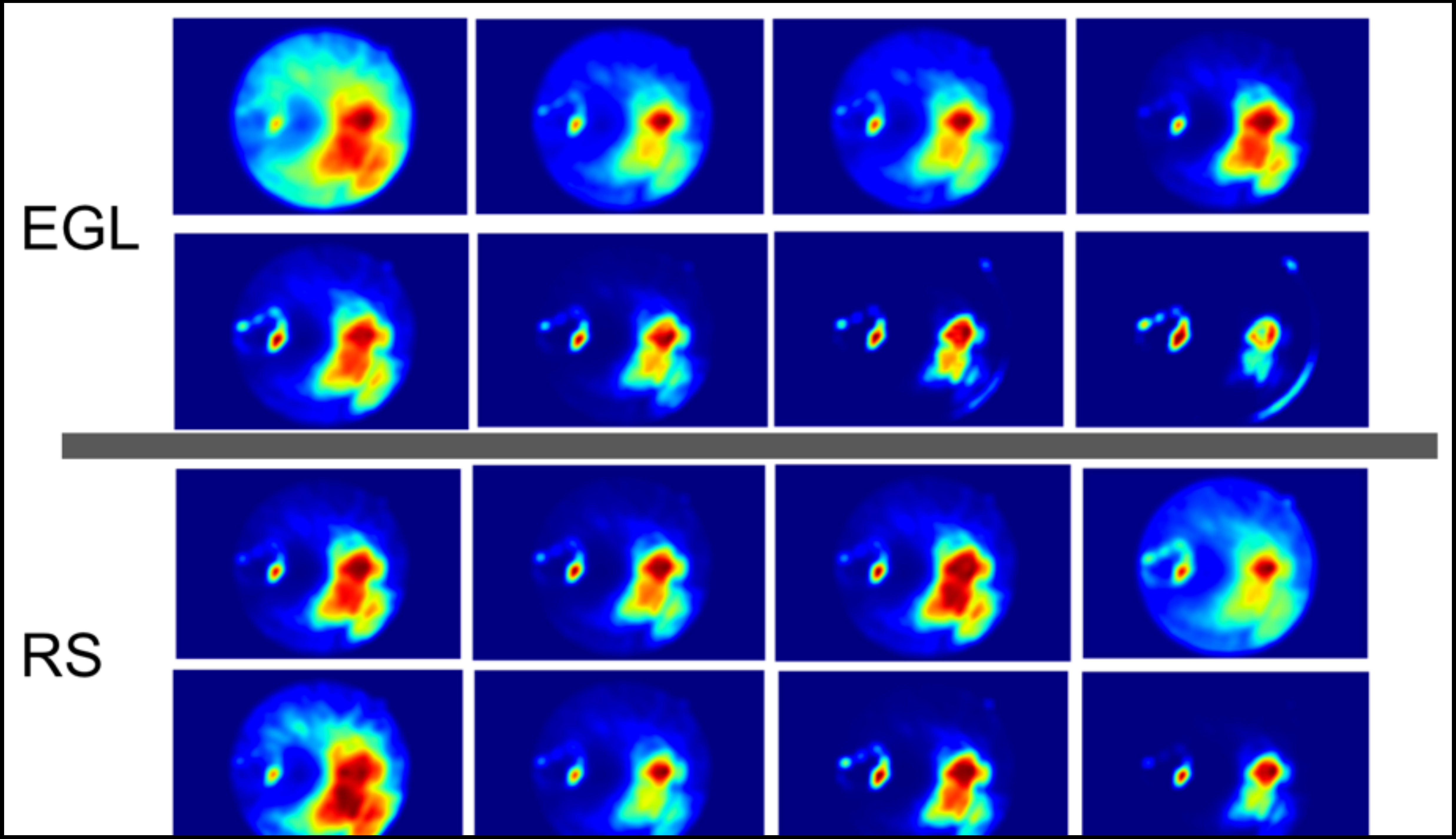
Require: Training Images Set $\mathscr{T}$, Patches Dataset $\mathscr{L}$, Number μ of initial images to look

Select an initial set $\mathscr{T}_\mu$ of images randomly
Train Initial Model $\mathbf{M}$ using the ground truth patches from the μ images
while not converged **do**
  for each image in $\mathscr{T} \setminus \mathscr{T}_\mu$ **do**
    Patchify image and compute $\sigma_{image} = \sum_{patch \in image} \Phi(patch)$, using $\mathbf{M}$
  end for
  Sort all the σ_{image} values and return $\mathscr{I}_{max}$, the image with higher sum
  $\mathscr{T}_\mu = \mathscr{T}_\mu \cup \mathscr{I}_{max}$
  $\mathscr{L}_\mu = \{ \text{ patch} \in \mathscr{L}_{\mathscr{I}}, \forall \mathscr{I} \in \mathscr{T}_\mu \}$
  Update $\mathbf{M}$ with k selected patches using Algorithm 1 and the patches in $\mathscr{L}_\mu$
end while

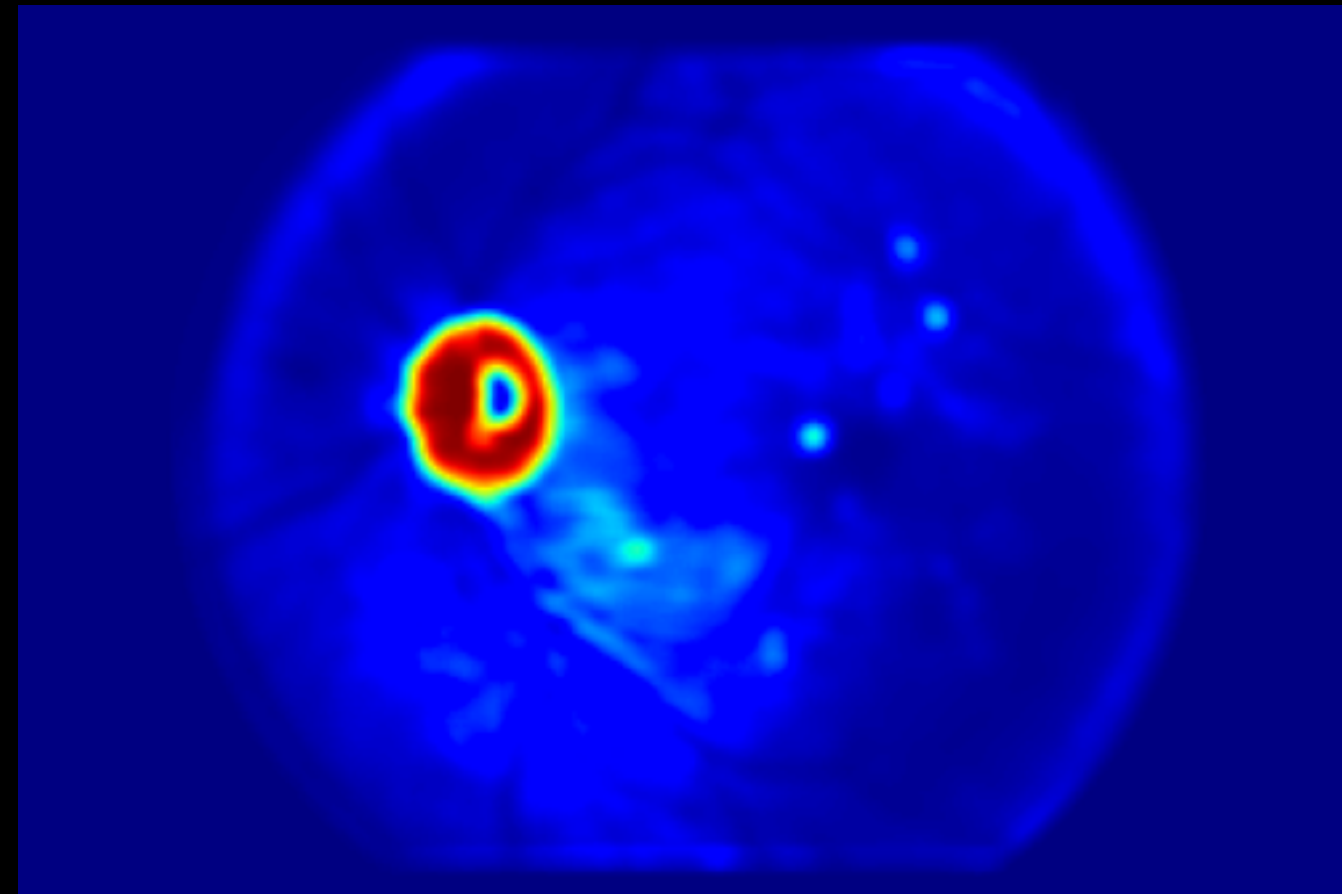
Image-level results (EGL vs random selection)

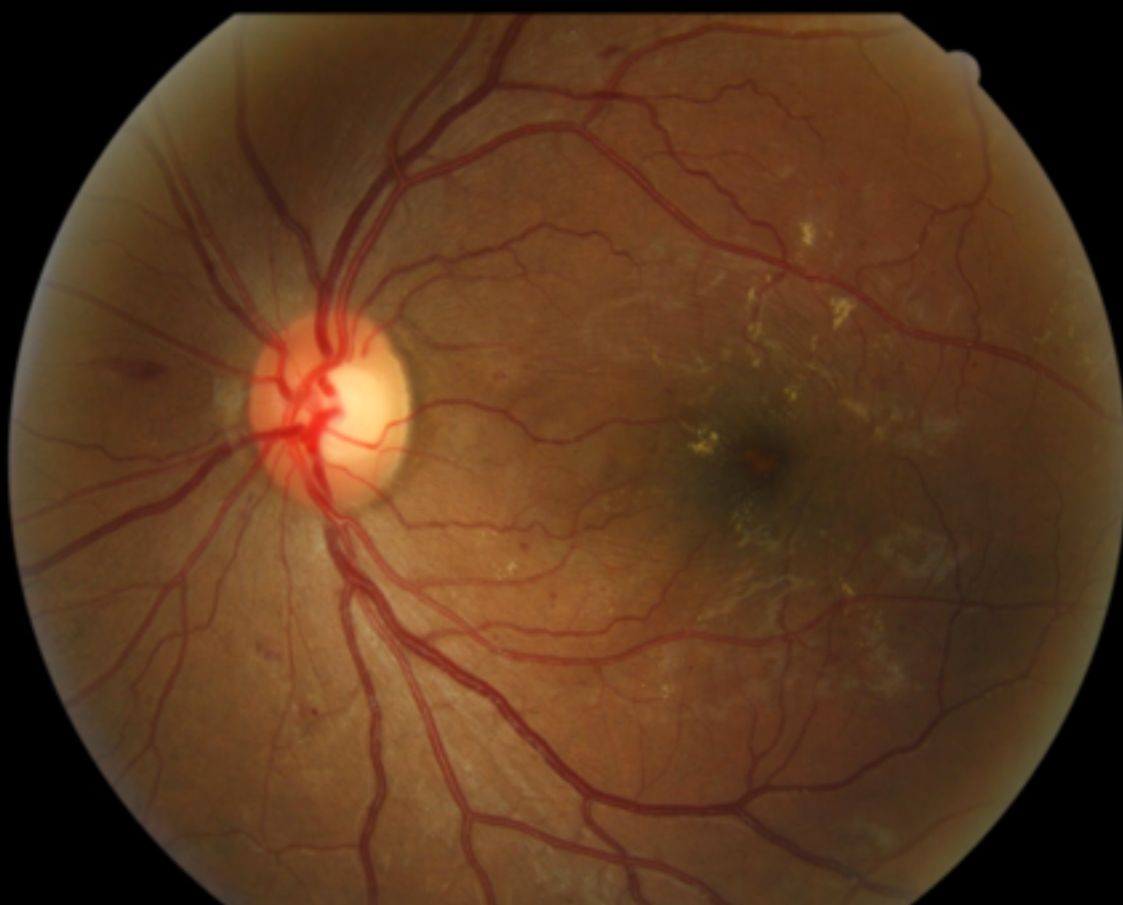


Prediction through time

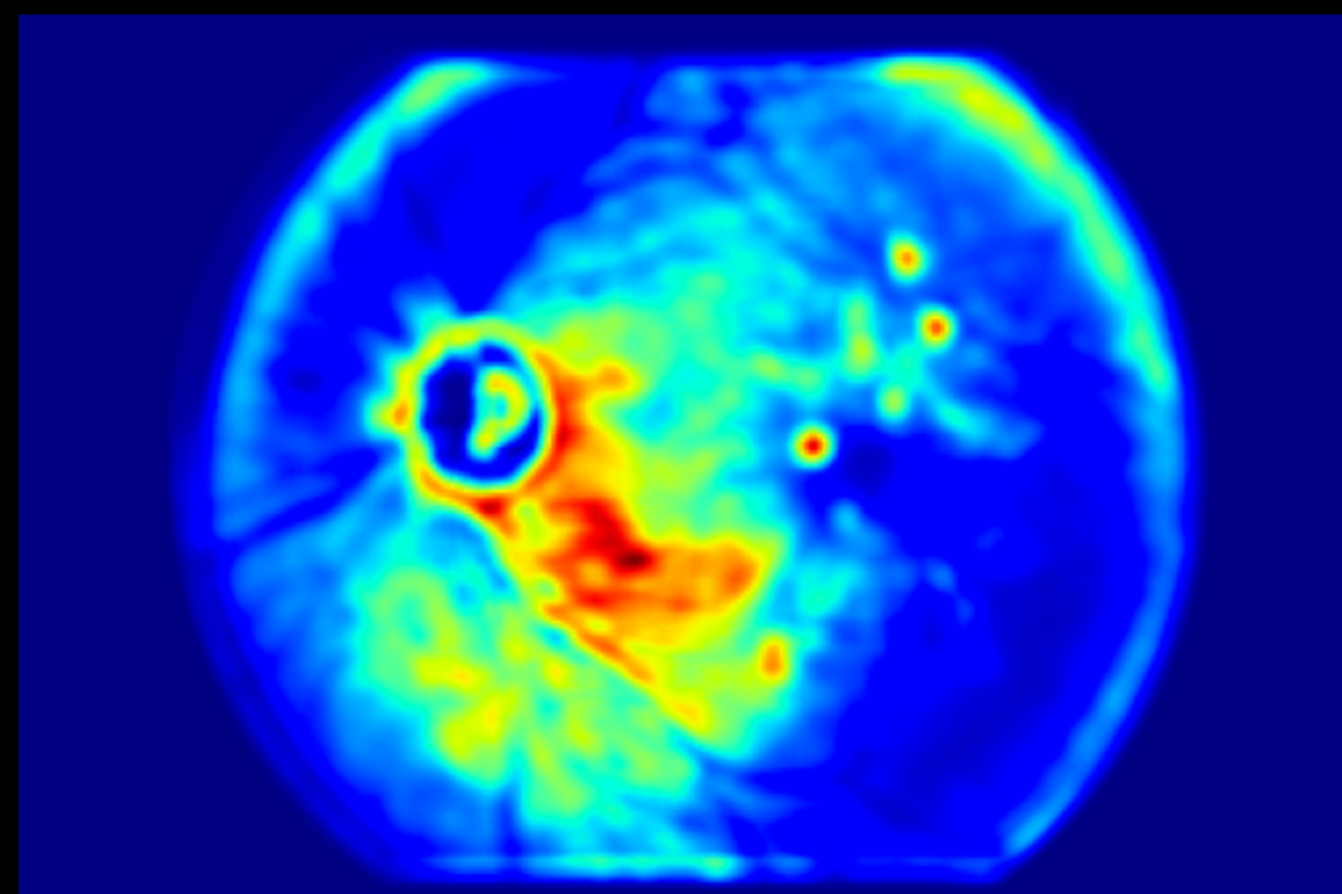


Current model prediction





Expected gradient length



The Team

mind LAB
machine learning
perception and discovery

The Team

Alexis Carrillo
Andrés Esteban Paez
Angel Cruz
Andrés Castillo
Andrés Jaque
Andrés Rosso
Camilo Pino
Claudia Becerra
Fabián Paez
Felipe Baquero
Fredy Díaz
Gustavo Bula
Germán Sosa
Hugo Castellanos
Ingrid Suárez
John Arévalo
Jorge Vanegas
Jorge Camargo

Jorge Mario Carrasco
Joseph Alejandro Gallego
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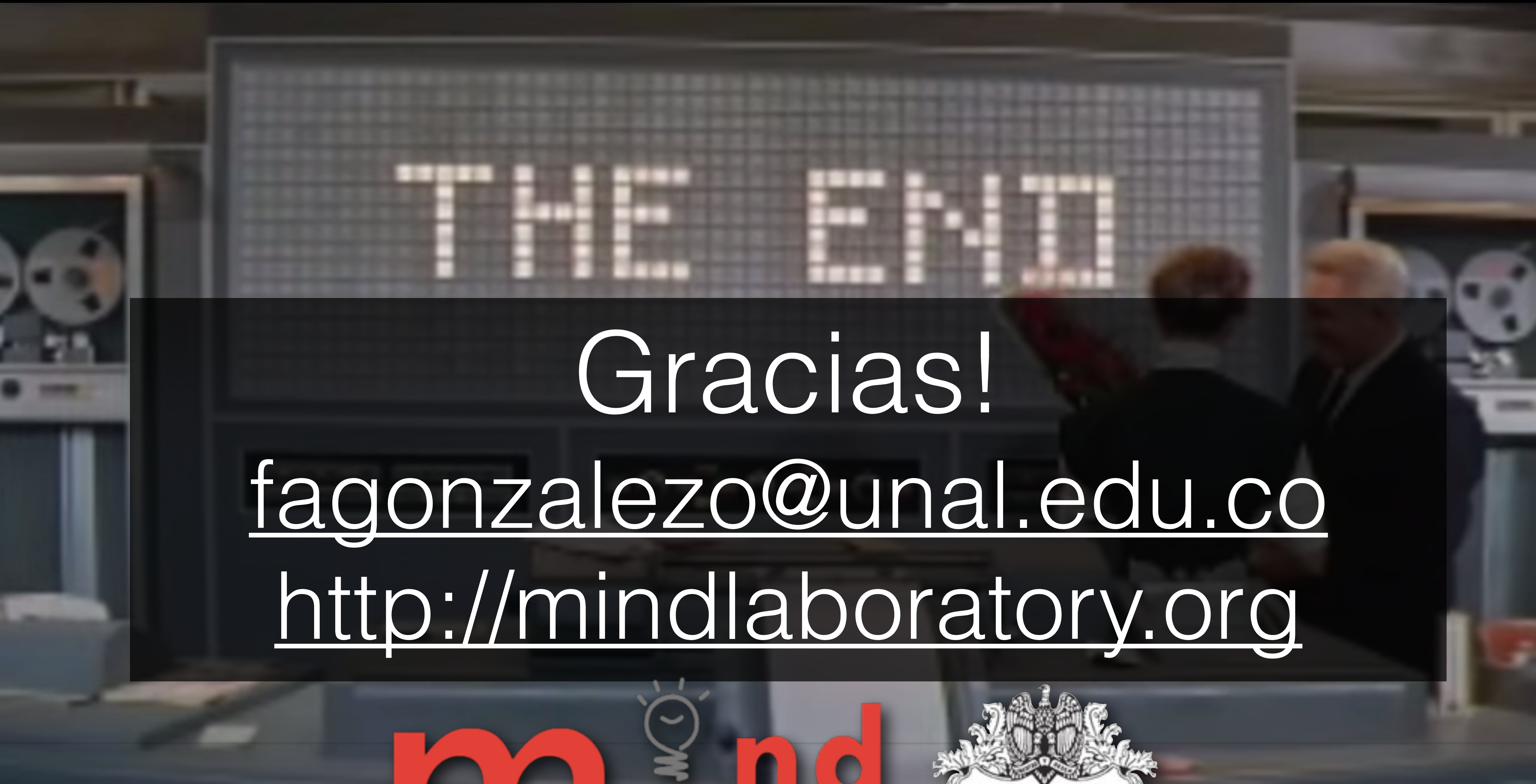
Juan Carlos Caicedo
Juan Sebastián Otálora
Katherine Rozo
Lady Viviana Beltrán
Lina Rosales
Luis Alejandro Riveros
Miguel Chitiva
Óscar Paruma
Óscar Perdomo
Raúl Ramos
Roger Guzmán
Santiago Pérez
Sergio Jiménez
Susana Sánchez
Sebastián Sierra



Gracias!

fagonzalezo@unal.edu.co

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