Representation learning for histopathology image analysis

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Outline

Histology and Histopathology

Histology

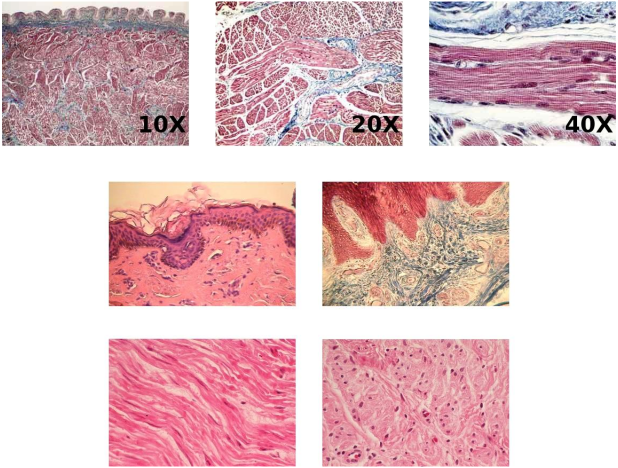
"Histology is the study of the tissues of the body and how these tissues are arranged to constitute organs " *Junqueira, 2009*

Histopathology

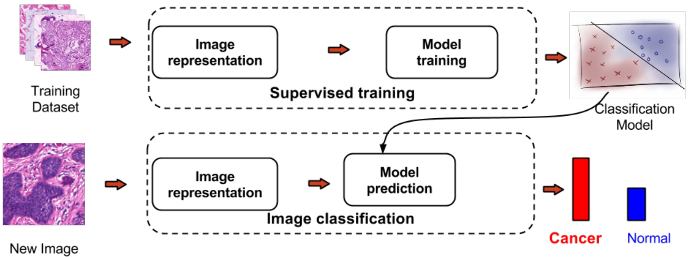
It refers to the microscopic examination of tissue in order to study the manifestations of disease.

Histology image acquisition

Histology visual variability



Learning-based automatic image analysis



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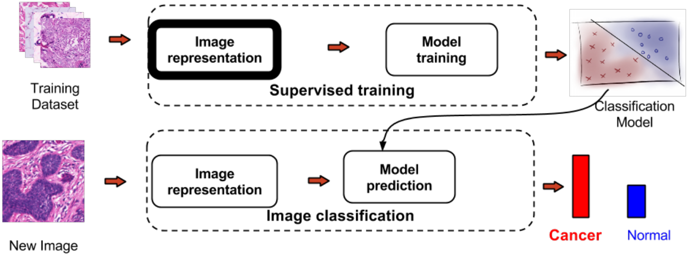

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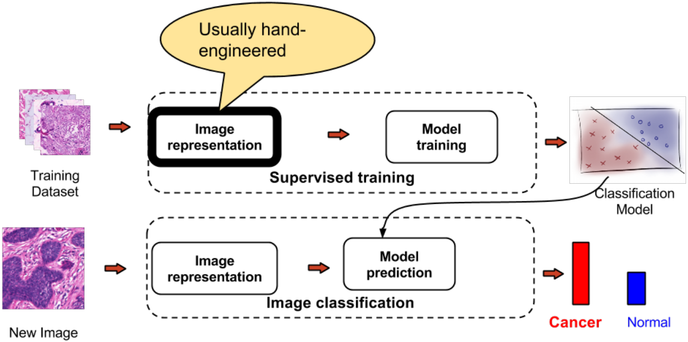


Learning-based automatic image analysis

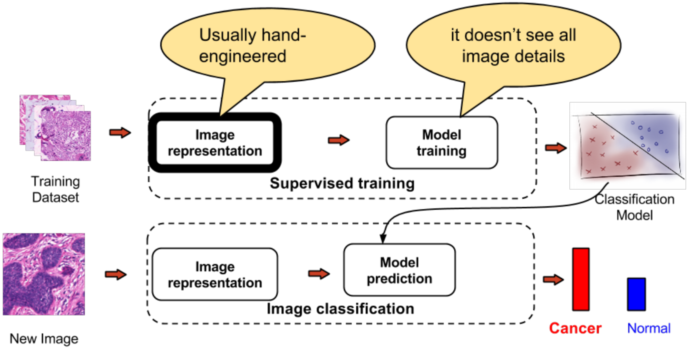
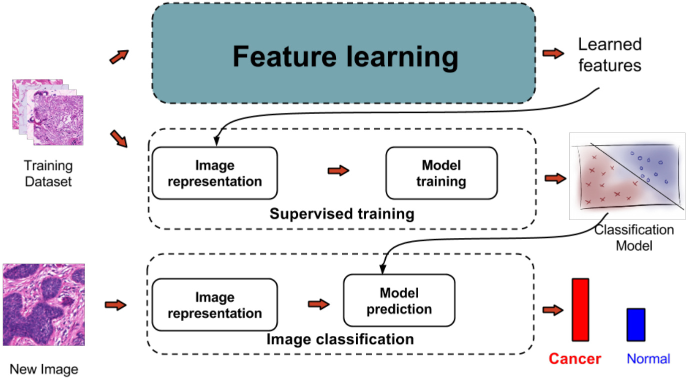


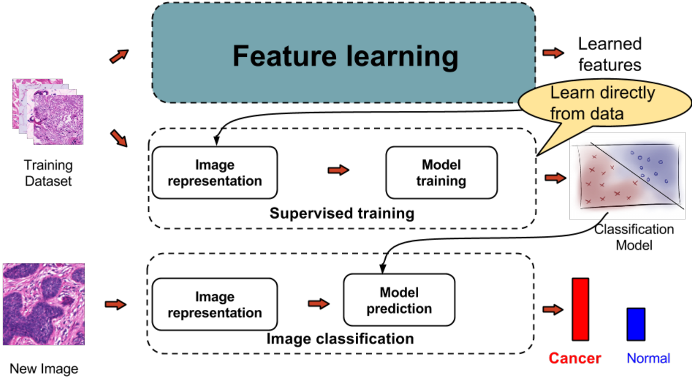
Image representation

- Transformations of the data that make it easier **to extract useful information** when building classifiers or other predictors.
- Classic representations (e.g. Fourier analysis) that are fixed based on some general theoretical criteria **completely ignore** what kind of data is being analyzed.
- Hand-engineered representations that are devised to solve a particular problem **are manually engineered** by an expert.
- "We do not believe that there could be a single set of features which would be optimal for all kinds of images" *Hyvärinen, 2009 (NIS)*
- In contrast, an adaptive (learned) representation is one that does not attempt to represent all possible kinds of data; instead, **the representation is adapted** to a particular kind of data.

Feature learning-based image analysis

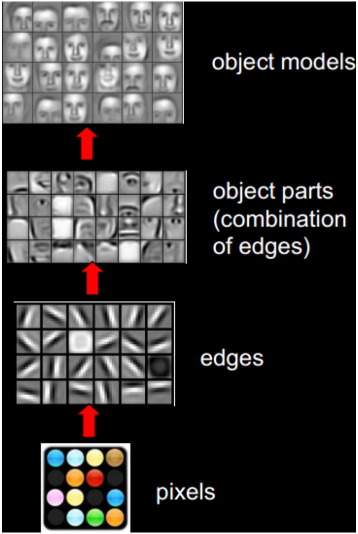


Feature learning-based image analysis



Unsupervised Feature Learning and Deep Learning

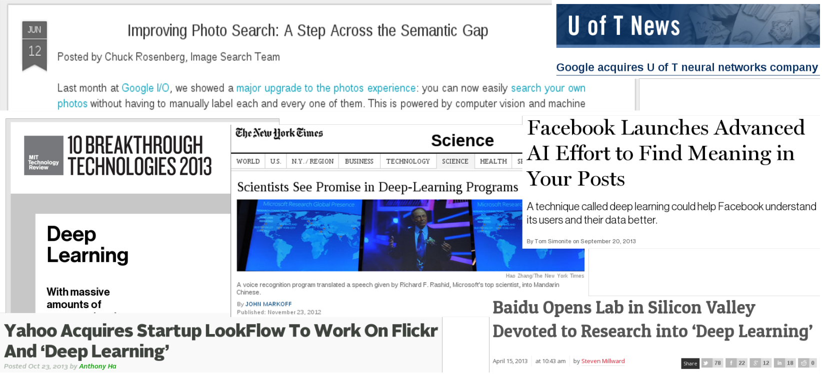
- Deep learning architectures mimic the hierarchical structure of visual system.
- Successive layers learn more complex features based on basic features from the previous layer.



[Lee et. at. 2009, ICML]

Unsupervised feature learning and deep learning

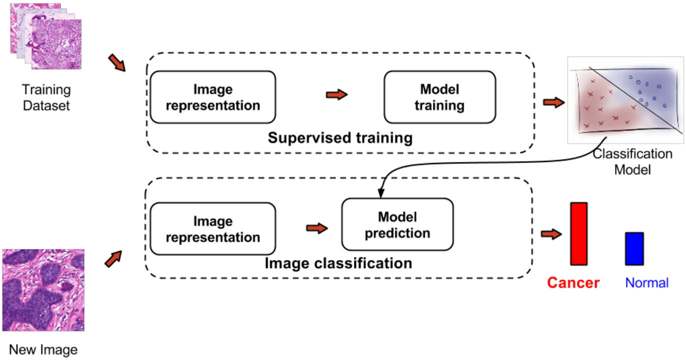
Deep learning is attracting much attention both from the academic and industrial communities mainly because of their success in several areas.



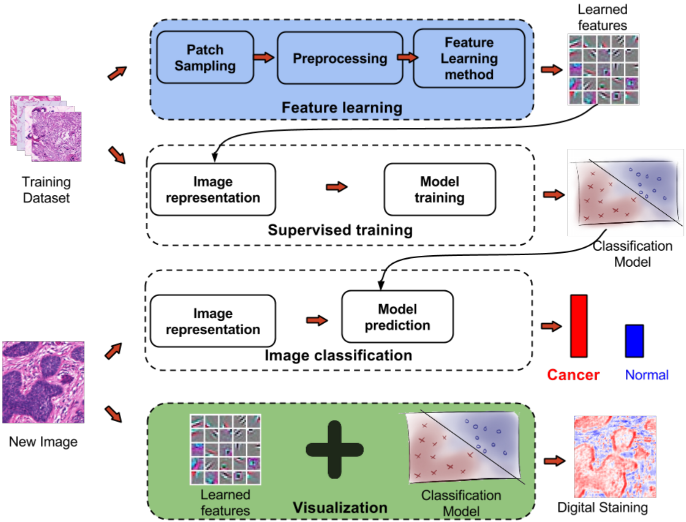
Research questions

- *Does a feature learning approach successfully work in histopathology image classification?*
- *If so, how the criteria used by a classifier can be visualized to support the decision made by such classifier?*

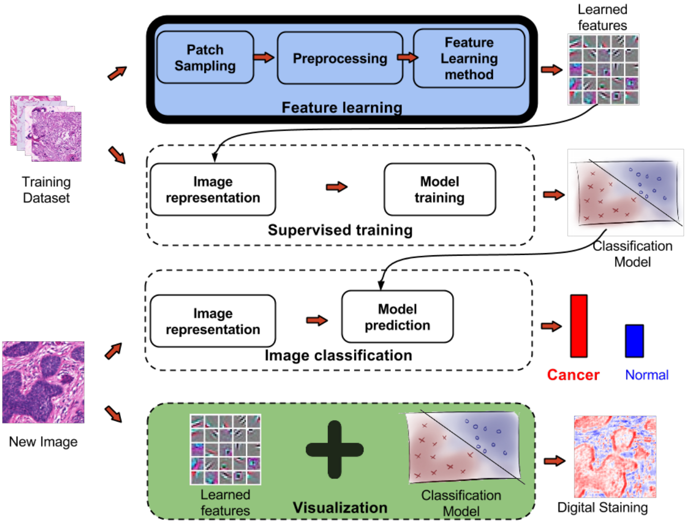
Learning-based automatic image analysis



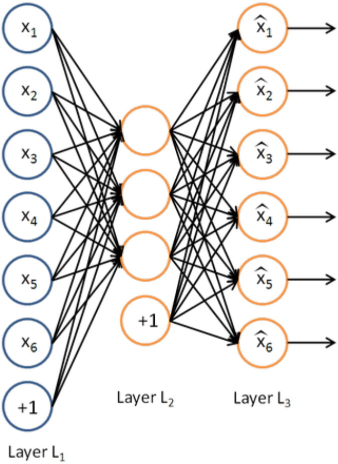
Overall proposed framework



Feature learning

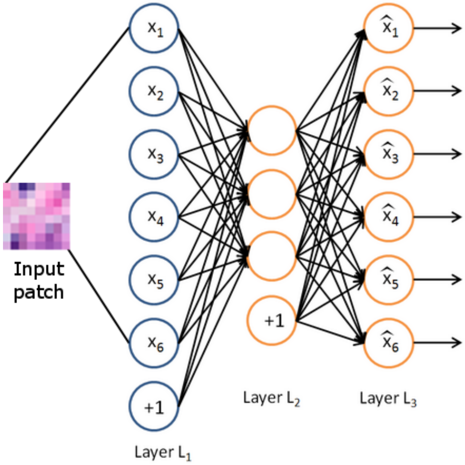


Autoencoders



$$r_{\Theta}(\mathbf{X}) = g(f(\mathbf{X})) \approx \mathbf{X},$$

Autoencoders



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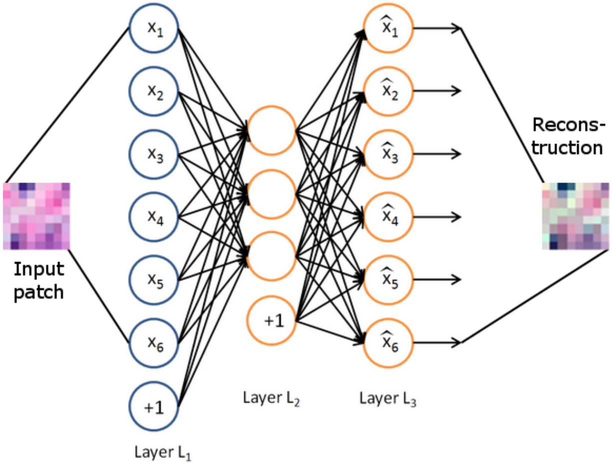
Autoencoders



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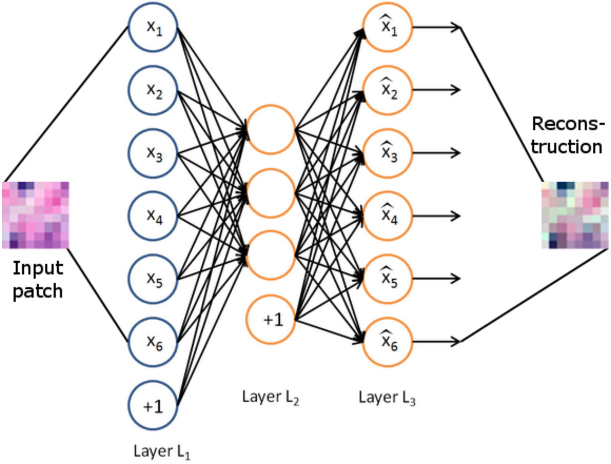
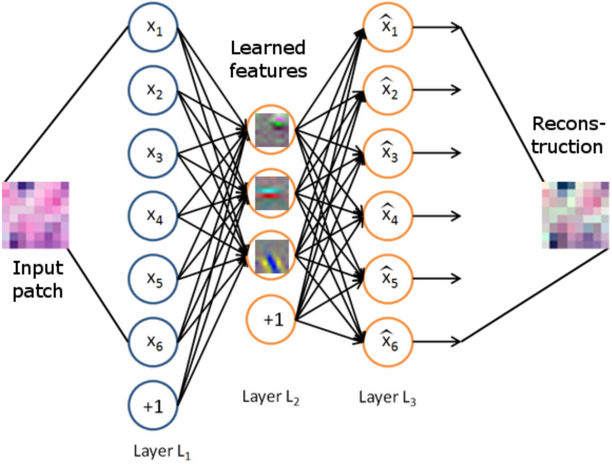
Autoencoders



$$J(\Theta) = \mathcal{L}\left(\mathbf{X}, r_{\Theta}\left(\mathbf{X}\right)\right) + \mathcal{R}\left(\mathbf{X}, \Theta\right),$$

Autoencoders



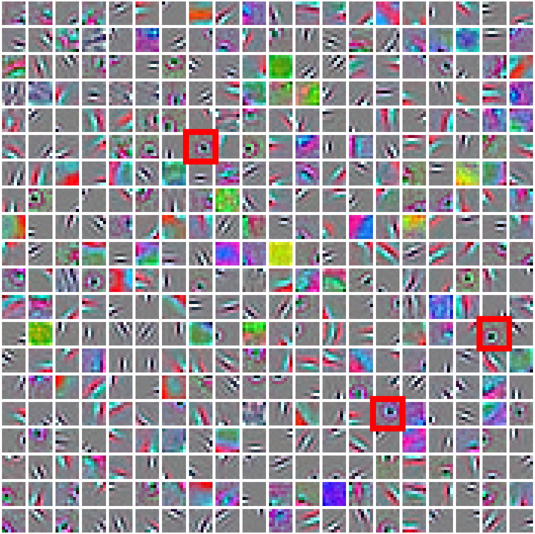
$$J(\Theta) = \mathcal{L}\left(\mathbf{X}, r_{\Theta}\left(\mathbf{X}\right)\right) + \mathcal{R}\left(\mathbf{X}, \Theta\right),$$

Sparse autoencoders (sAE)

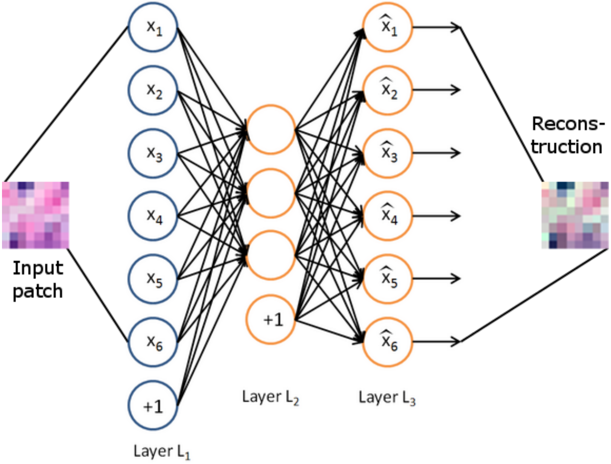
$$J(\mathbf{W}) = \underbrace{\frac{1}{2}\sum_{i=1}^{m}\left\| r_{\Theta}(x^{(i)}) - x^{(i)} \right\|_2^2}_{\text{Reconstruction}} + \underbrace{\beta \sum_{j=1}^{n} KL\left(\rho \| \hat{\rho}_j\right)}_{\text{Sparsity constraint}} + \underbrace{\frac{\gamma}{2}\left(\|\mathbf{W}\|_F^2 + \|\mathbf{W}'\|_F^2\right)}_{\text{regularization}}$$

- It is an unconstrained problem which can be solved using gradient-based methods.

detectors learned with sAE



RICA



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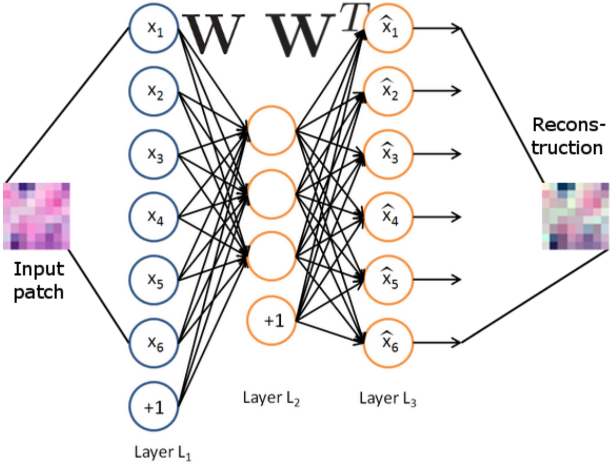
RICA



$$J(\Theta) = \mathcal{L}\left(\mathbf{X}, r_\Theta\left(\mathbf{X}\right)\right) + \mathcal{R}\left(\mathbf{X}, \Theta\right),$$

Reconstruct Independent Component Analysis (RICA)

$$J(\mathbf{W}) = \underbrace{\frac{\lambda}{m}\sum_{i=1}^{m}\left\|\mathbf{W}^T\mathbf{W}x^{(i)} - x^{(i)}\right\|_2^2}_{\text{Reconstruction}} + \underbrace{\sum_{i=1}^{m}\sum_{j=1}^{n}\sqrt{\left(\mathbf{W}_j x^{(i)}\right)^2 + \epsilon}}_{\text{Regularization}}$$

- It is an unconstrained problem which can be solved using gradient-based methods.
- Only one hyperparameter to adjust.

Moving to topographic representation

RICA:

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

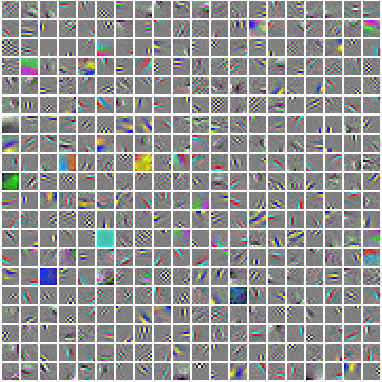
TICA:

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

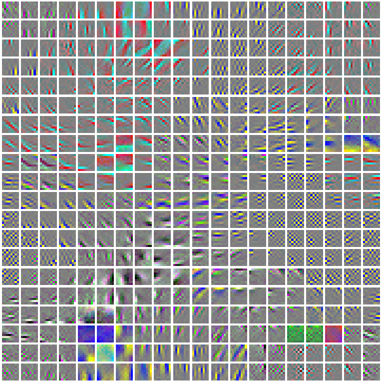
This is also an unconstrained problem which can be solved using gradient-based methods.

Learned features

RICA

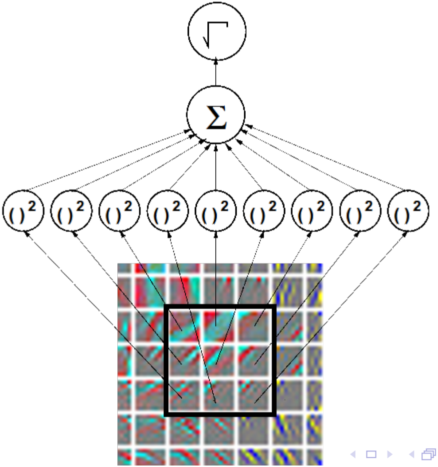


TICA



Topographic Representation

Grouping adjacent features together in the smoothed L_1 norm penalty make that their activations be similar yielding to invariant properties.



Overall proposed framework

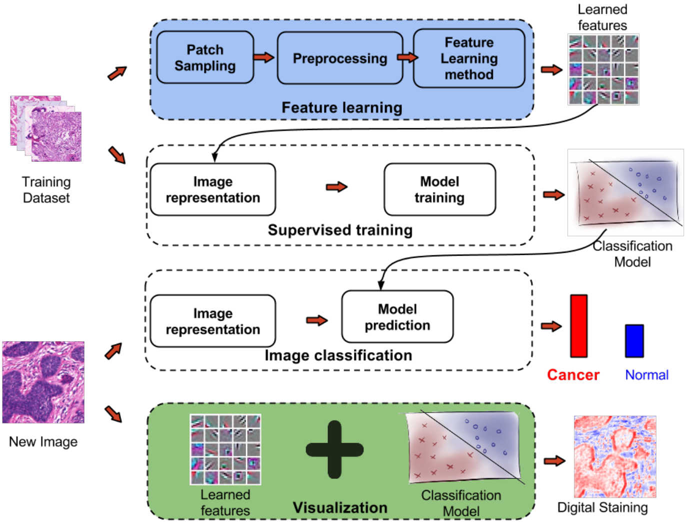
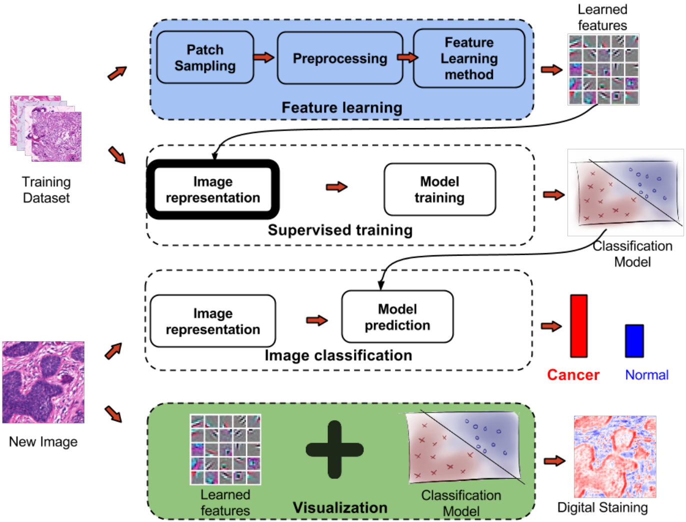
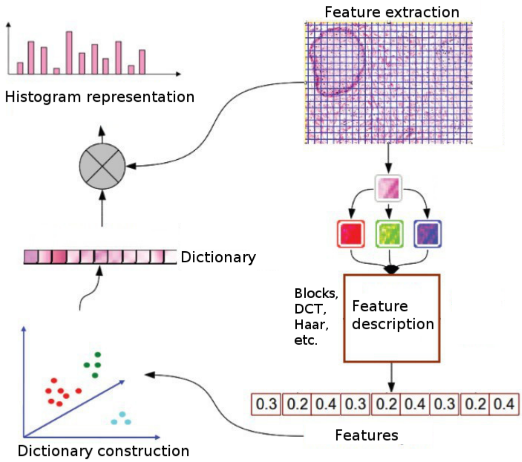


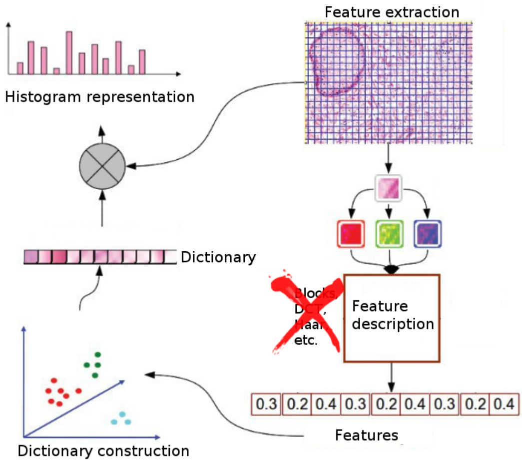
Image representation



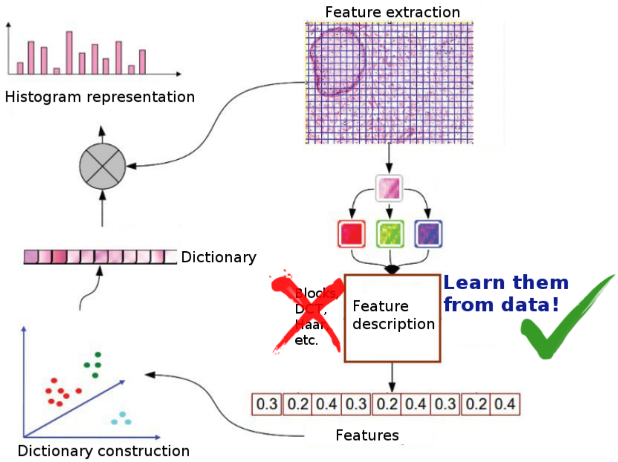
Bag-of-features (BOF) image representation



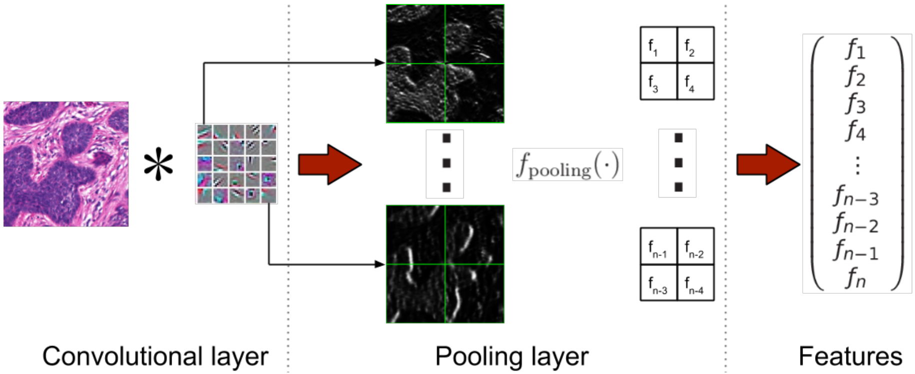
BOF image representation



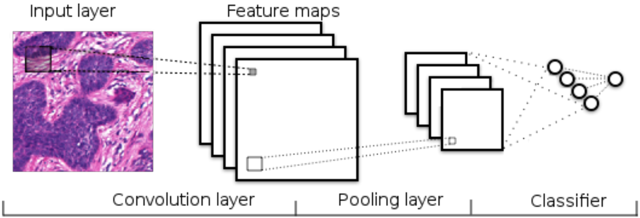
BOF image representation



Convolutional neural networks (CNN) image representation



Convolutional neural networks (CNN) image representation



Deep CNN image representation

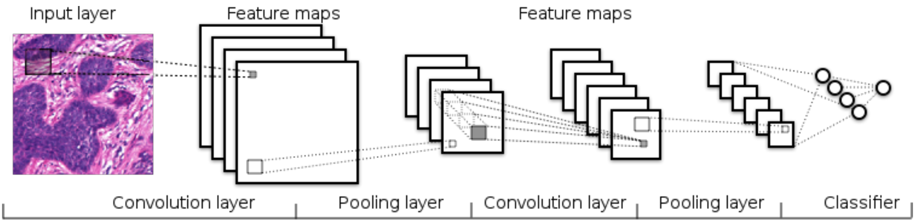
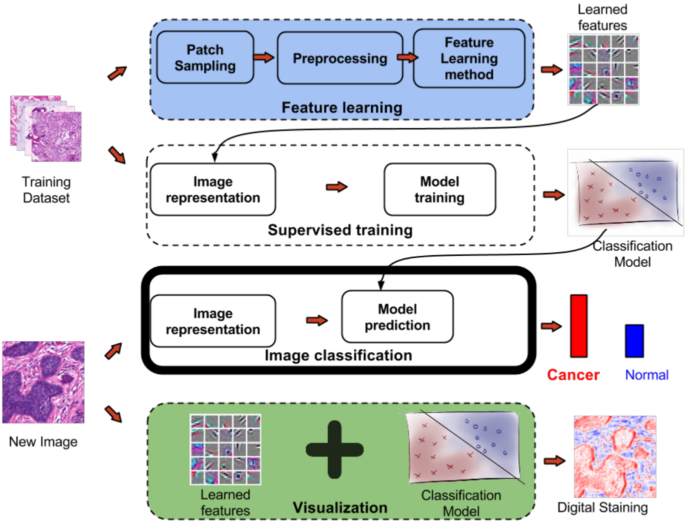
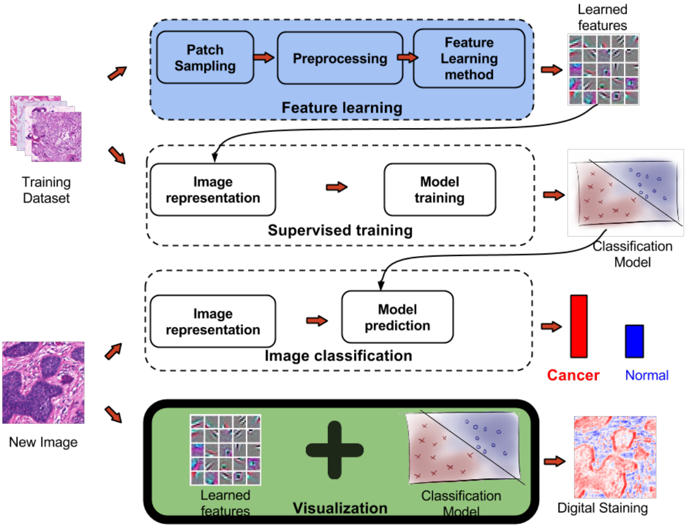


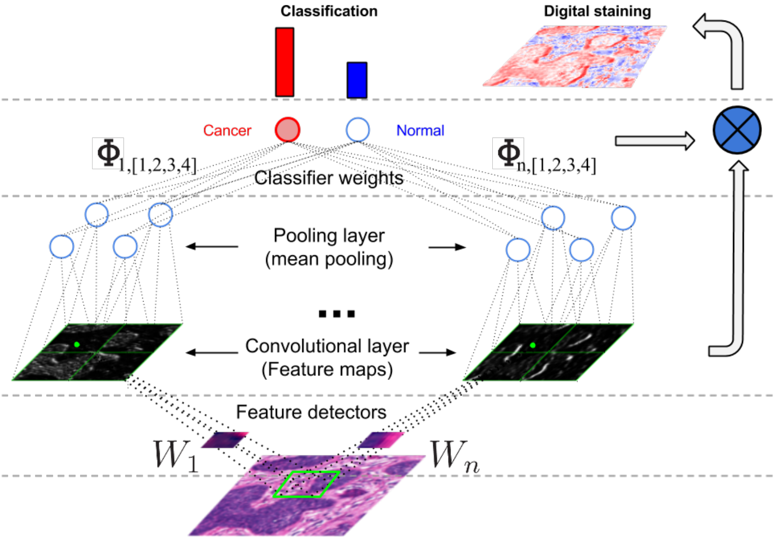
Image classification



Visualization

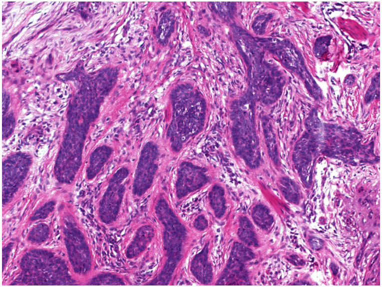


Visualization



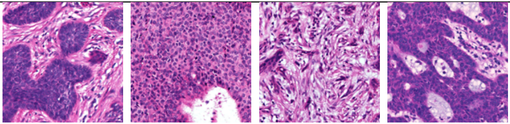
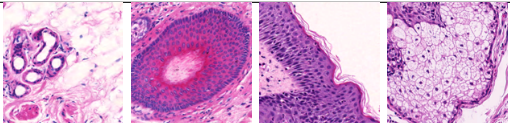
Basal Cell Carcinoma (BCC) Case study

- BCC is the most common skin cancer.
- It may cause significant tissue damage, destruction and disfigurement.
- The 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.



The challenge: Visual variability

BCC images have the high variability of biological structures associated to different morphology and architectural arrangements of cells in cancer or non-cancer tissues.

Cancer	
Non-cancer	

Experimental evaluation

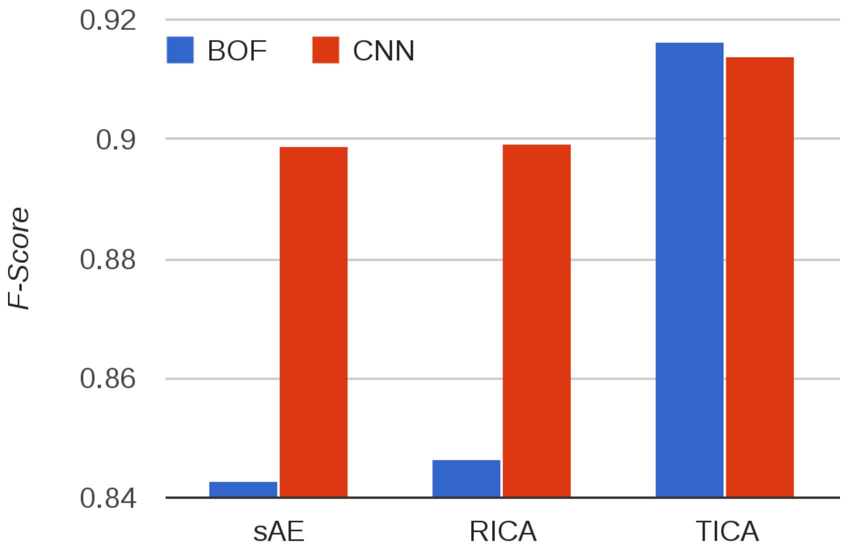
- **1417** color images, (150×150 pixels at 10X), manually annotated by a pathologist (**518** **cancer**, **899** **non-cancer**)
- Experiments were performed on a 5-fold cross validation scheme with stratified sampling.

	Accuracy F-Score Balanced Acc.	Image representation		
		Bag of features	CNN	
			one layer	deep
Patch representation	Haar	Baseline		
	DCT	Baseline		
	sAE			
	RICA			
	TICA			

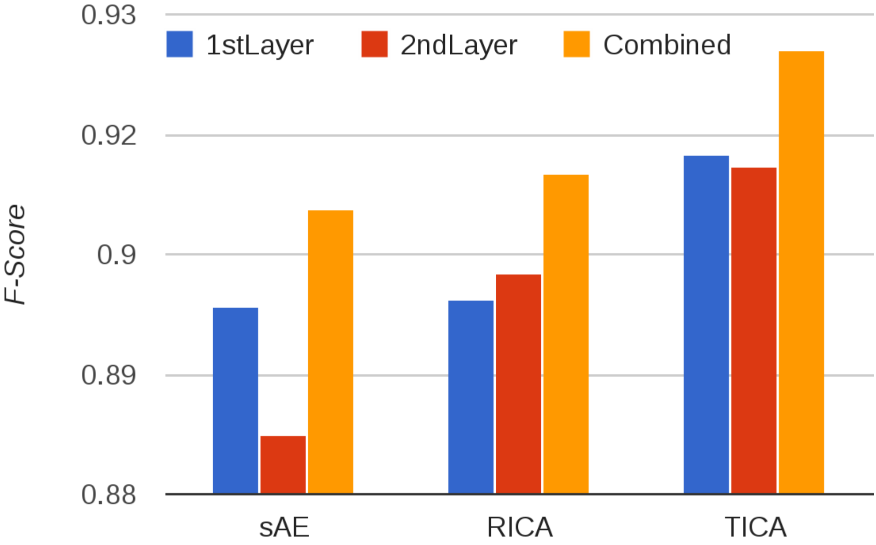
Canonical features vs Learned features

Feature	Accuracy	F-Score	BAC
Haar	0.796 +/- 0.026	0.708 +/- 0.031	0.772 +/- 0.026
DCT	0.891 +/- 0.023	0.851 +/- 0.027	0.883 +/- 0.024
sAE	0.925 +/- 0.027	0.899 +/- 0.027	0.917 +/- 0.024
RICA	0.926 +/- 0.029	0.899 +/- 0.033	0.920 +/- 0.032
TICA	0.936 +/- 0.022	0.914 +/- 0.027	0.933 +/- 0.020

BOF representation vs CNN representation



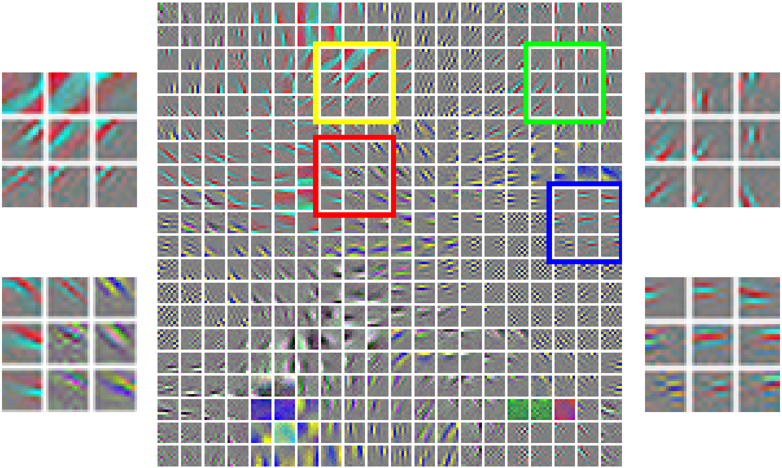
Stacked representation



Overall classification results

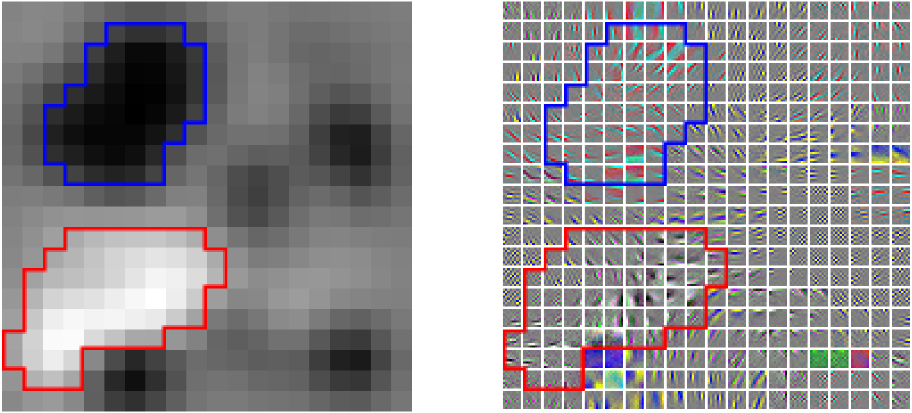
Representation	Accuracy	F-Score	BAC
TICA combined layers	**0.944 +/- 0.025**	**0.925 +/- 0.031**	**0.941 +/- 0.027**
RICA combined layers	0.935 +/- 0.025	0.912 +/- 0.026	0.931 +/- 0.023
AE combined layers	0.933 +/- 0.026	0.908 +/- 0.029	0.926 +/- 0.025
TICA Second layer	0.937 +/- 0.015	0.913 +/- 0.020	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***

Invariant features



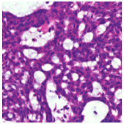
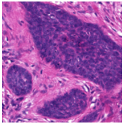
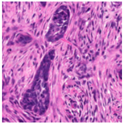
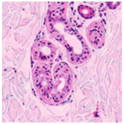
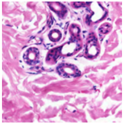
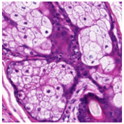
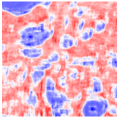
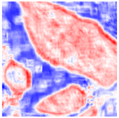
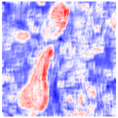
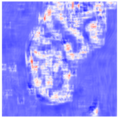
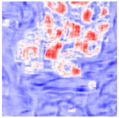
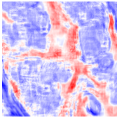
TICA model was able to detect translational, color , scale and rotational invariances.

Topographic organization

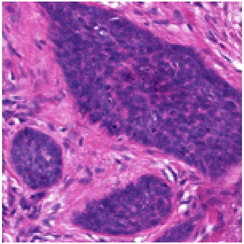


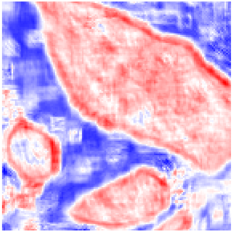
Softmax weights mapped back to topographic organization (left) and learned features(right) highlighting Cancer and Non-cancer classes.

Digital staining

True class		Cancer			Non-cancer	
Input image						
Prediction		Cancer			Non-cancer	
Probability	0.901	0.925	0.672	0.083	0.147	0.460
Digital staining						

Digital staining





Pathologist concept

The digitally stained image highlights two main criteria to perform diagnosis: *cell proliferation* and *peripheral palisade*.

Conclusions

- The results showed that, in general, features learned from data performed better than traditional hand-engineered features for the BCC detection task.
- The proposed method is able to capture and organize relevant patterns of each class *totally unsupervised*.
- Invariance properties considerably improved classification performance with respect to current state-of-the-art approaches.
- The interpretation stage of the proposed framework allows to understand why the classifier assigns a concept to a particular image.
- Learned features and visualization results are consistent with the nature of the problem.

Contributions I

1. **John Arevalo**, Angel Cruz-Roa, and Fabio A. González. Hybrid image representation learning model with invariant features for basal cell carcinoma detection. In The 9th International Seminar on Medical Information Processing and Analysis, volume 8922, 2013. doi: 10.1117/12.2035530 [1].
2. **John Arevalo**, Angel Cruz-Roa, and Fabio González. Histopathology image representation for automatic analysis: A state-of-the-art. Manuscript submitted for publication in Revista de la facultad de medicina, Universidad Militar Nueva Granada 2013 [2].
3. **John Arevalo**, Angel Cruz-Roa, Viviana Arias, Eduardo Romero, and Fabio González. An unsupervised feature learning framework for basal cell carcinoma image analysis. Computerized Medical Imaging and Graphics, 2014. Manuscript prepared for submission to the "Computational Medical Imaging and Graphics" journal.[3].

Contributions II

4. Angel Cruz-Roa, **John Arevalo**, Anant Madabhushi, and Fabio González. A deep learning architecture for image representation, visual interpretability and automated basal-cell carcinoma cancer detection. In Medical Image Computing and Computer-Assisted Intervention - MICCAI 2013, volume 8150 of Lecture Notes in Computer Science, pages editors, 403-410. Springer Berlin Heidelberg, 2013[4].
5. Angel Cruz-Roa, **John Arevalo** and Fabio González. Prediction of Morphometric Measures from Bag-of-Features Image Representation of Cervix Cancer Cells. In The 8th International Seminar on Medical Information Processing and Analysis, 2012[5].

Contributions III

6. Andrea Rueda, **John Arevalo**, Angel Cruz, Eduardo Romero, and Fabio González. Bag of features for automatic classification of Alzheimer's disease in magnetic resonance images. In Progress in Pattern Recognition, Image Analysis, Computer Vision, and Applications, volume 7441 of Lecture Notes in Computer Science, pages 559-566. Springer Berlin Heidelberg, 2012 [6].
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Contributions IV

8. Raul Ramos, **John Arevalo**, and Fabio Gonzalez. Learning a bag of features representation of the Human Protein Atlas on the cloud. In 6a Conferencia Latinoamericana de Computación de Alto Rendimiento, 2013. [8].
9. Raul Ramos-Pollan, Fabio Gonzalez, J.C. Caicedo, Angel Cruz-Roa, J.E. Camargo, J.A. Vanegas, S.A. Perez, J.D. Bermeo, J.S. Otalora, P.K. Rozo, and **John Arevalo**. Bigs: A framework for large-scale image processing and analysis over distributed and heterogeneous computing resources. In E-Science (e-Science), 2012 IEEE 8th International Conference on, pages 18, 2012. [9].

Thank you for your attention!!

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