Acute Lymphoblastic Leukemia Detection Based on Adaptive Unsharpening and Deep Learning

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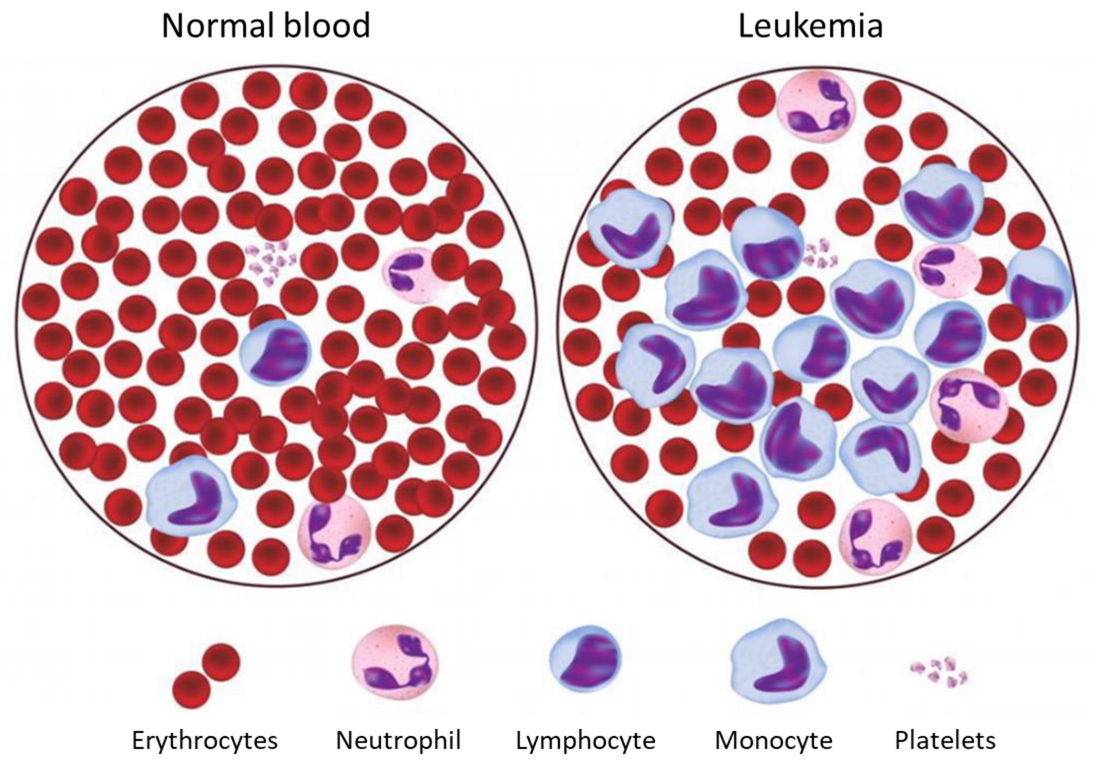
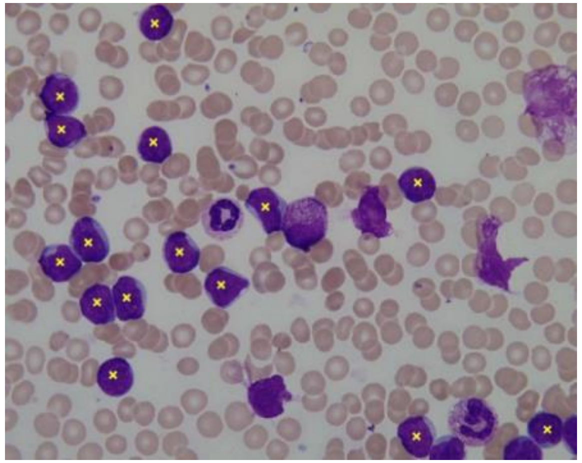
Outline

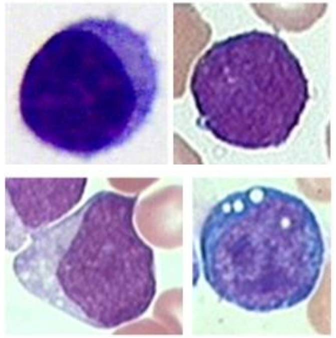
- Introduction
  - Acute Lymphoblastic Leukemia (ALL)
  - Computer Aided Diagnosis (CAD)
  - Deep Learning (DL) for ALL
- Proposed method
- Experimental results
  - Quantitative analysis
  - Qualitative analysis
- Conclusions



Acute Lymphoblastic Leukemia (ALL)

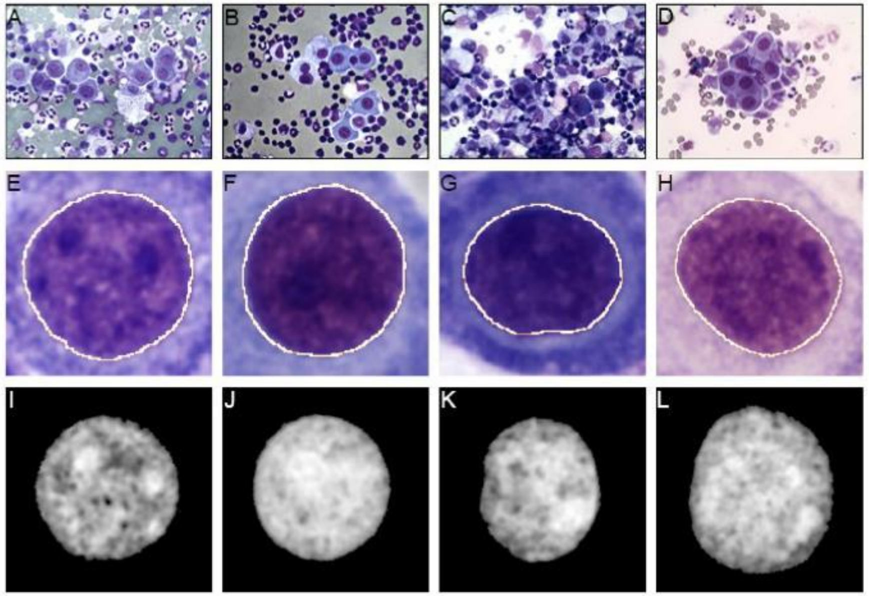
- Disease
  - Affects the blood cells, rapidly spreads
  - Fatal consequences if left untreated
- Diagnosis
  - Experienced pathologist manually inspects white cells in peripheral blood samples identifying the cells with the typical blast morphology
  - **Lymphoblasts**: white cells with an altered morphology
    - Normally present in the bone marrow
    - *An increased number of lymphoblasts in peripheral blood can be associated with ALL*

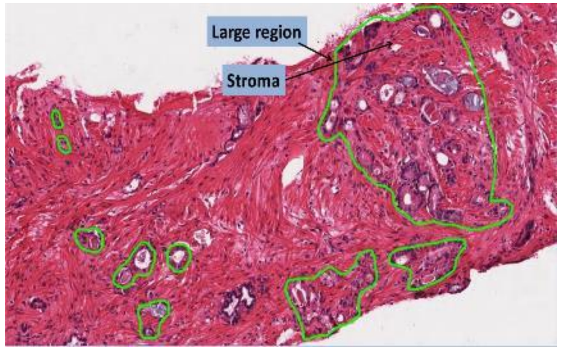


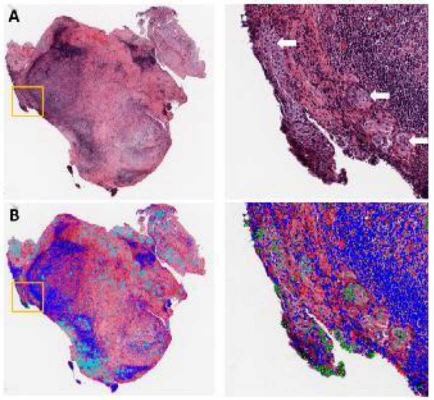


Computer Aided Diagnosis (CAD)

- Partially automate Lymphoblast detection process
  - Image processing
  - Machine Learning (ML)
- Three main categories
  - Handcrafted feature extraction and shallow ML classifier
  - Handcrafted feature extraction and Deep Learning (DL)
  - **Pure DL**

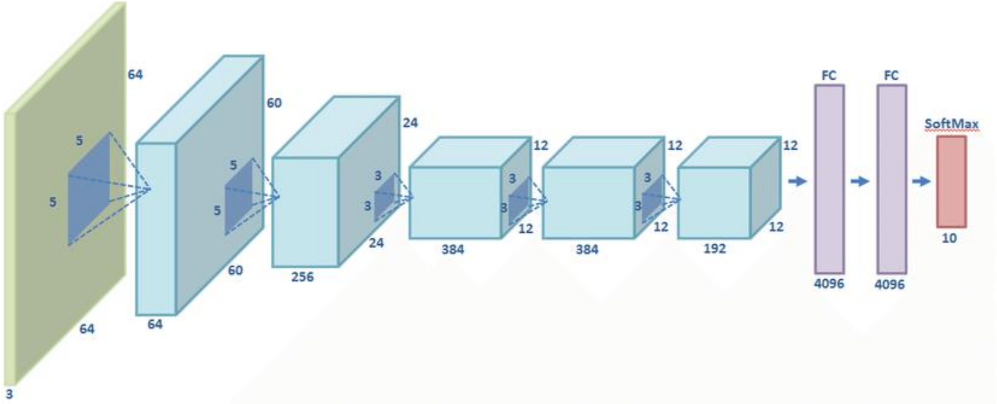




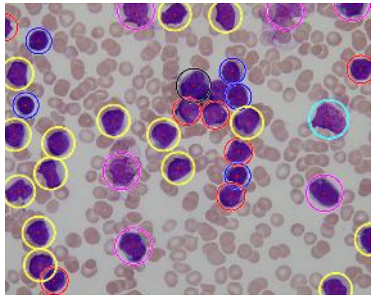


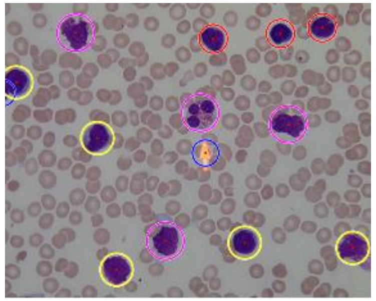
Deep Learning (DL) for ALL

- Deep Learning
  - Automatically learns data representations
  - No need for handcrafted feature extraction
  - *Higher accuracy*



- State of the art of DL for ALL
  - Strive towards higher classification accuracy
    - More efficient learning procedures
    - Original network architectures
  - **However, no method deals with ALL data analysis**
    - No focus or quality analysis
    - No preprocessing algorithm



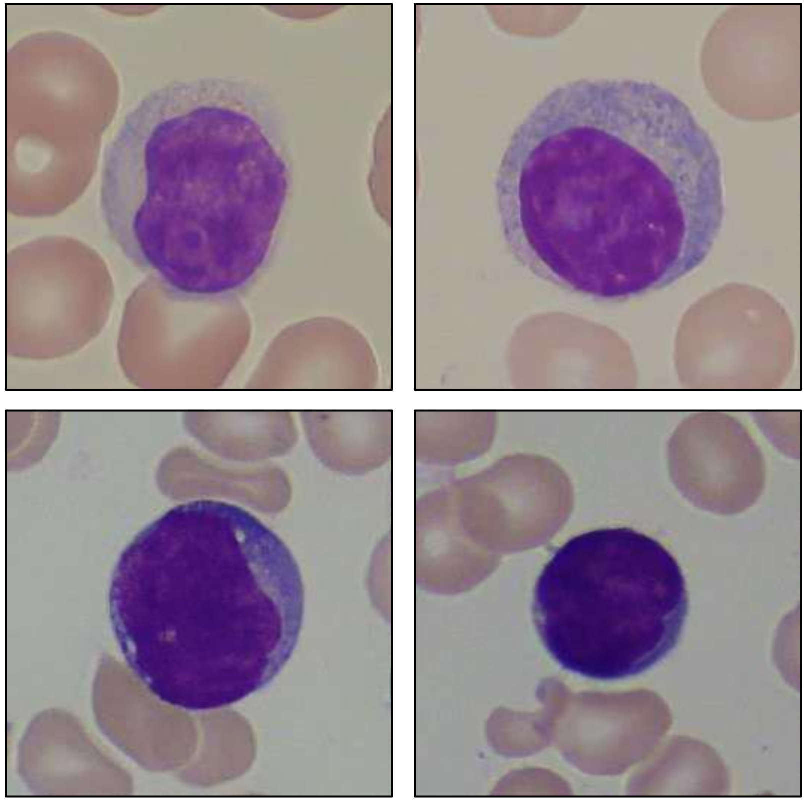


Proposed Method (1/2)

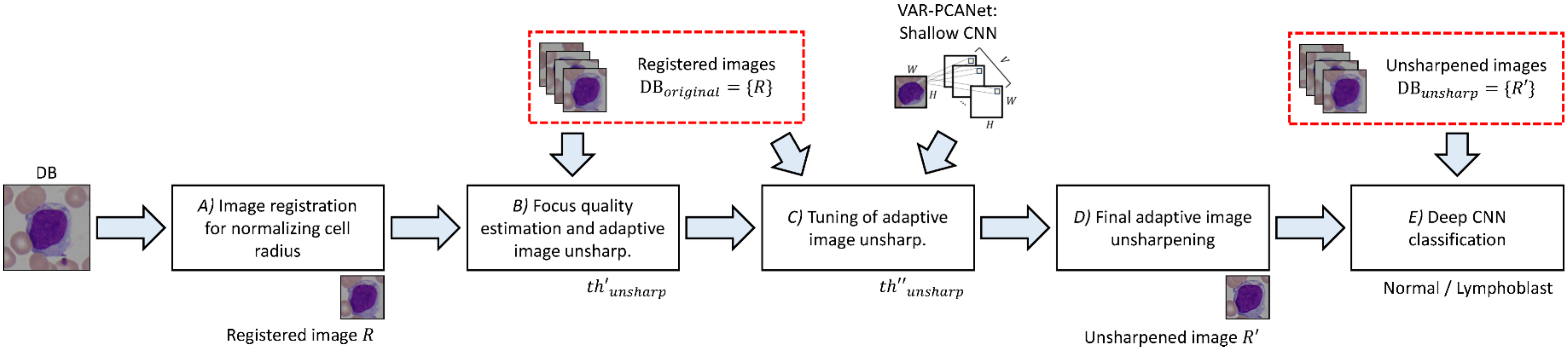
- First DL-based method for lymphoblast detection that analyzes ALL data
  - **Focus** quality estimation
  - Adaptive **unsharpening**
  - White blood cell classification using **CNNs**
    - *0: «normal»*
    - *1: «lymphoblast»*

Normal

Lymphoblast



Proposed Method (2/2)



A) Image registration

B) Focus quality estimation and adaptive image unsharpening

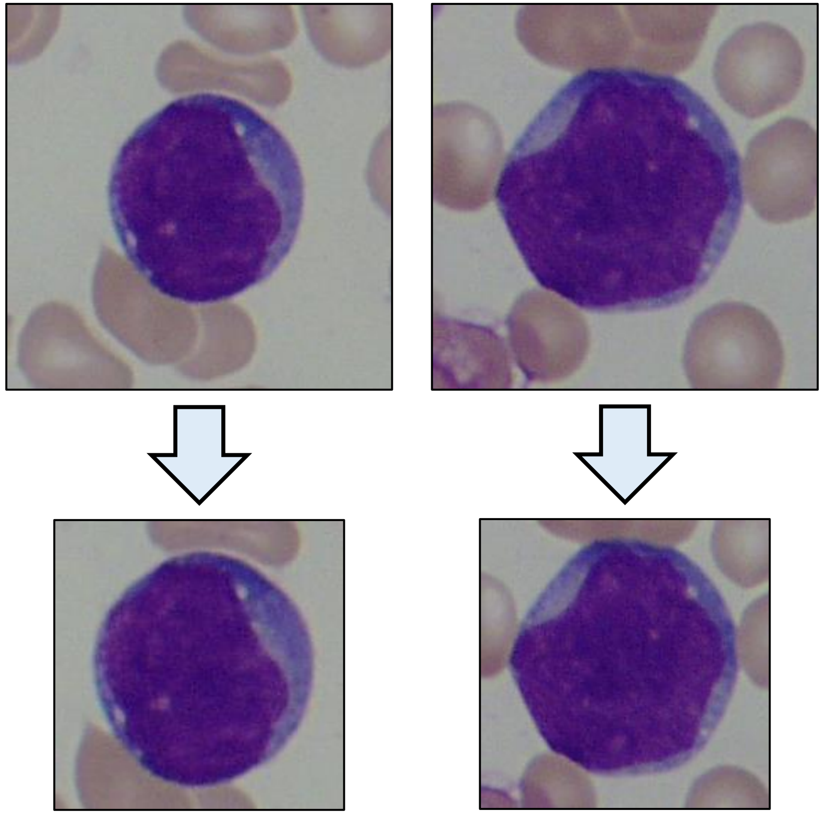
C) Shallow CNNs for tuning of adaptive image unsharpening

D) Final adaptive image unsharpening

E) Deep CNN classification

Image Registration

- Color normalization and grayscale conversion
- M_{thresh} = Otsu's binarization
- M_{fcm} = Fuzzy C-means clustering
  - Discard largest class (background)
- $M = M_{thresh} + M_{fcm}$
  - Extraction of largest CC
- Active contour refinement
- Ellipse fitting
  - Center of ellipse: c_x, c_y
  - Axes of ellipse: a_{max}, a_{min}
- Extraction of ROI centered on c_x, c_y, with size $1.5 \cdot a_{min}$

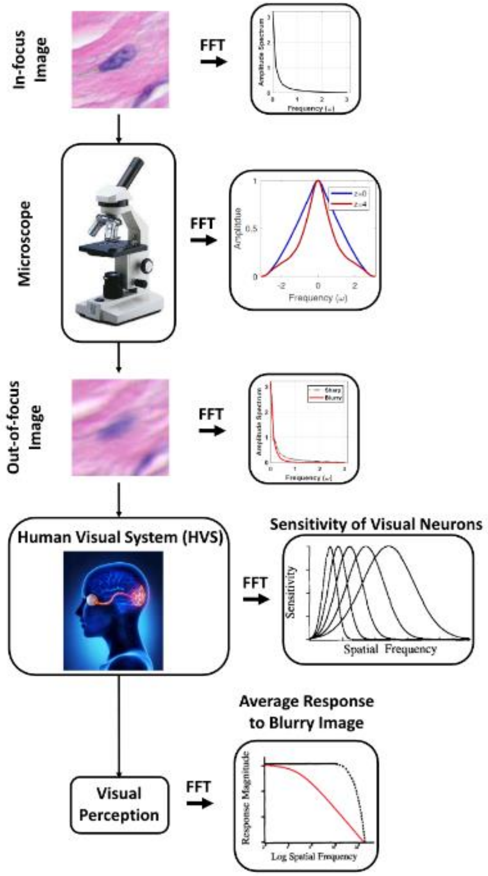


Focus Quality Estimation and Adaptive Image Unsharpening (1/2)

- Estimation of focus quality
  - FQPath method
    - Decomposes the input image using a visual sensitivity-like FIR filter corresponding to the out-of-focus lens
    - Extracts high order statistical moment features to quantize the image sharpness level
    - Vector of focus qualities $\mathbf{f} = [f_1, f_2, \dots, f_N]$
- Estimation of data bias
  - Correlation coefficient between $\mathbf{f}$ and vector of labels $\mathbf{l}$:

$$b = \mathrm{corrcoeff}(\mathbf{f}, \mathbf{l})$$

  - **Significant data bias: $|b| > 50\%$**

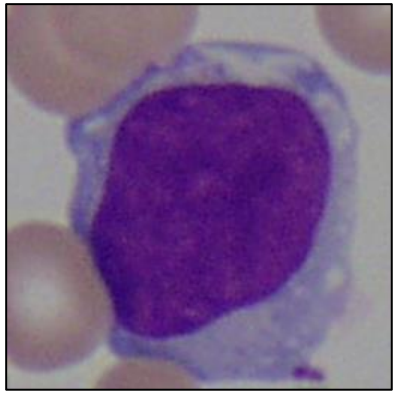


M. S. Hosseini, J. A. Z. Brawley-Hayes, Y. Zhang, L. Chan, K. N. Plataniotis and S. Damaskinos, "Focus Quality Assessment of High-Throughput Whole Slide Imaging in Digital Pathology," in IEEE Transactions on Medical Imaging, vol. 39, no. 1, pp. 62-74, Jan. 2020, doi: 10.1109/TMI.2019.2919722.

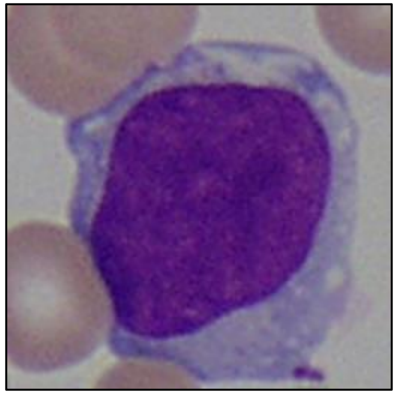
Focus Quality Estimation and Adaptive Image Unsharpening (2/2)

- **Adaptive** unsharpening
  - Improving focus quality for each image until it reaches the threshold $th_{unsharp}$
    - The threshold is uniquely computed *for each training* subset
    - Determines which focus the images should have
  - Unsharp masking
    - Gaussian kernel with standard deviation σ_i
    - σ_i is adaptively estimated *for each image* to reach the focus quality $th_{unsharp}$
    - $\sigma_i = \arg\min_{\sigma}(f_i - th_{unsharp})$
  - Threshold is computed to minimize the data bias:
    - $th_{unsharp} = \arg\min(|b|)$

Original

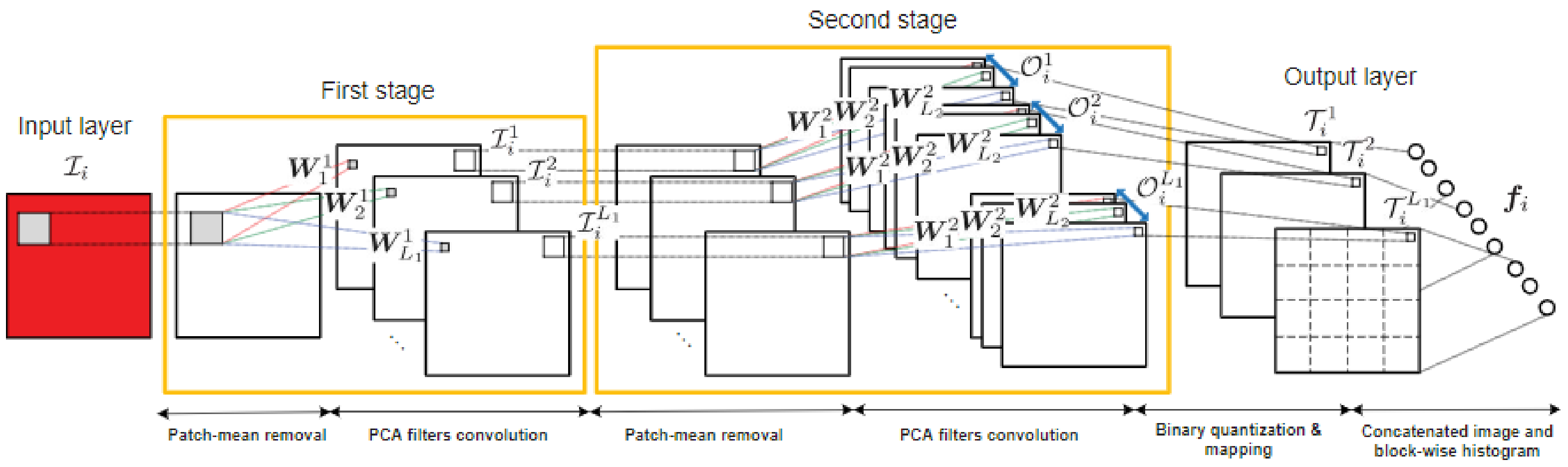


Unsharpened



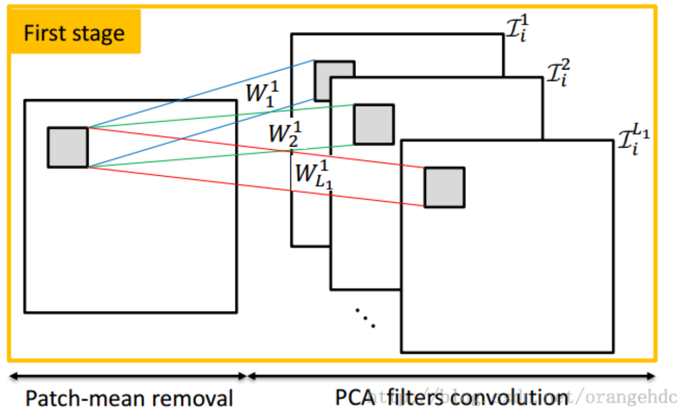
Shallow CNNs for Tuning of Adaptive Image Unsharpening (1/2)

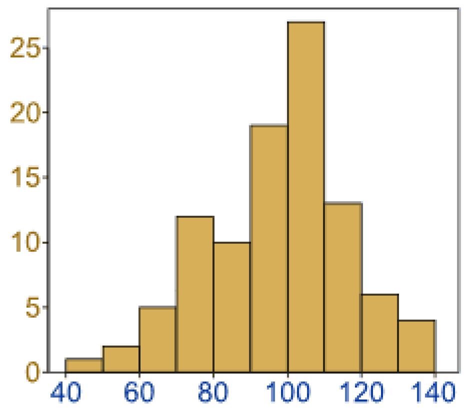
- Tuning of $th_{unsharp}$ using a *shallow CNN*
  - Train a CNN on the unsharpened samples
  - Varying $th_{unsharp} \pm 10\%$
  - Considering the value for which the CNN obtains the best classification accuracy



Shallow CNNs for Tuning of Adaptive Image Unsharpening (2/2)

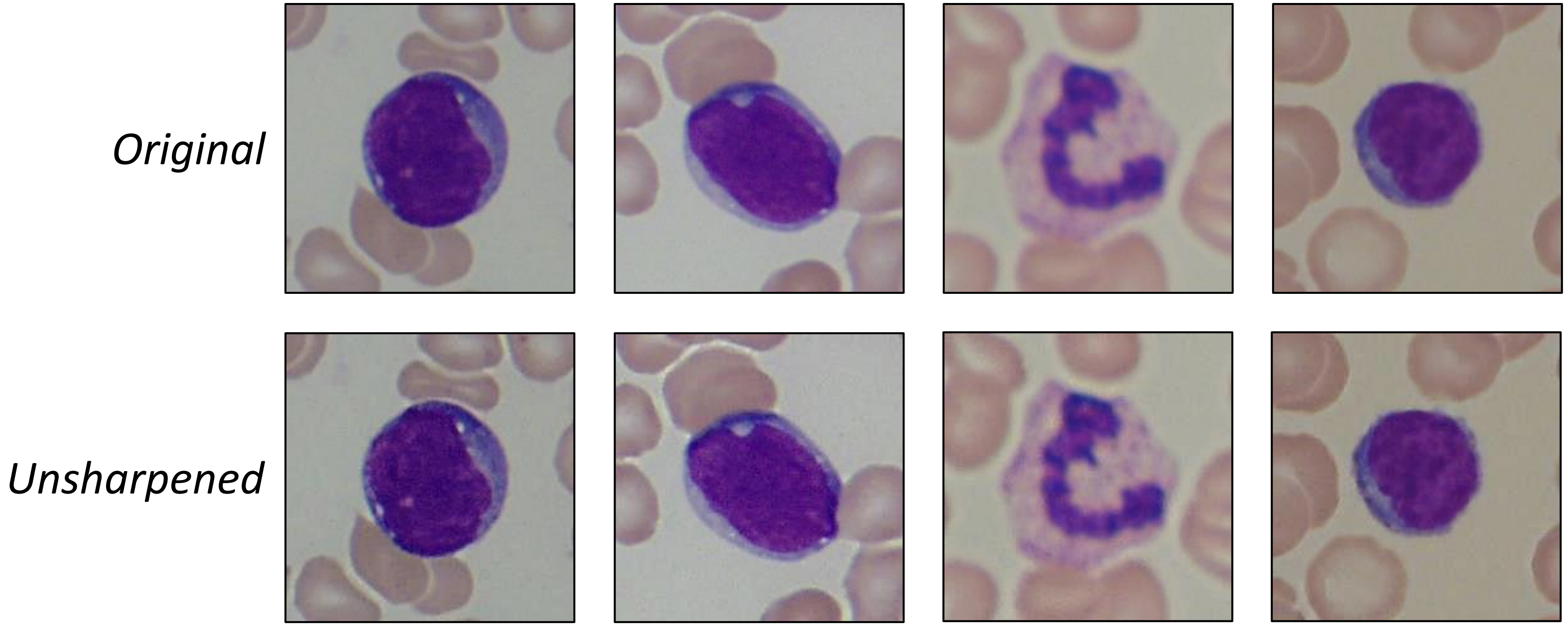
- Shallow CNN: **VAR-PCANet**
  - High-accuracy baseline in several fields
  - 1 layer
  - Filters are computed as eigenvectors of input data
    - **Number of filters V adaptively estimated** to preserve a percentage th_{var} of variance of input data
    - $V = \arg\min_V \left(\left(\sum_{v=1}^{V} \lambda_v\right) - th_{var}\right)$
  - Feed-forward design
  - Extracts a feature vector
    - Compare samples in the feature space
    - Classification with Nearest Neighbor (1-NN) classifier
      - No training
      - Output only depends on the feature vector





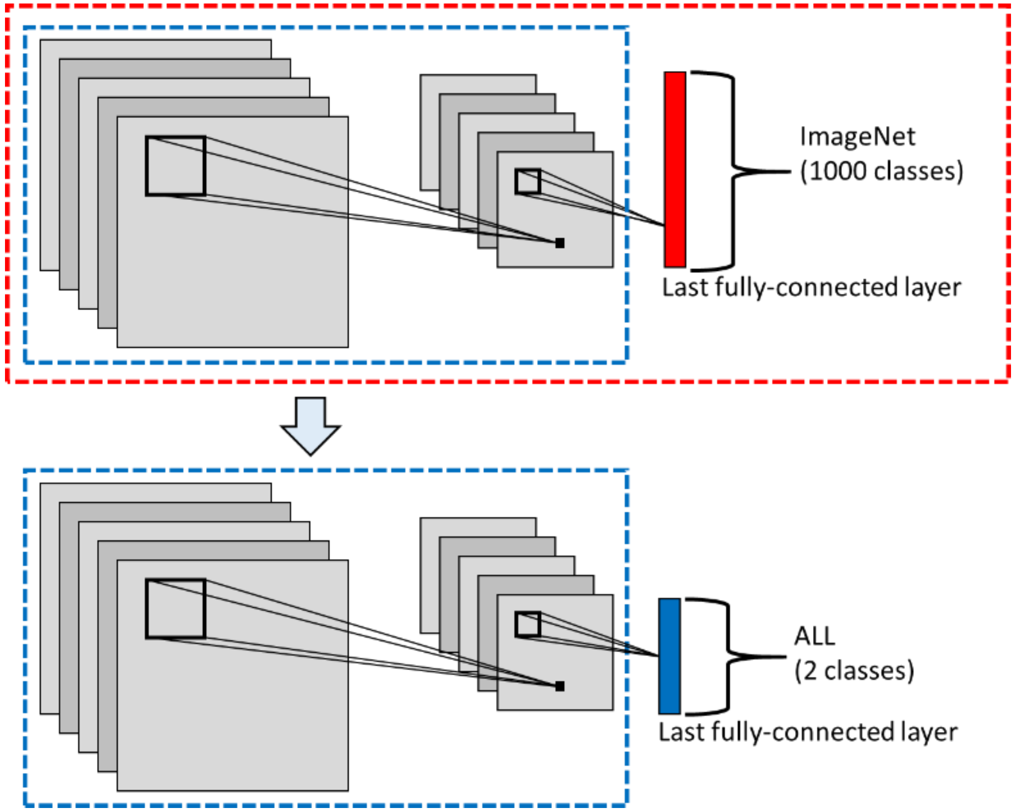
Final Adaptive Image Unsharpening

- Application of tuned threshold $th_{unsharp}$
  - Both training and testing subsets
  - Set of unsharpened images $DB_{unsharp}$



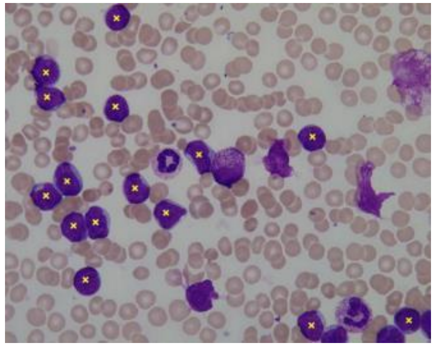
Deep CNN Classification

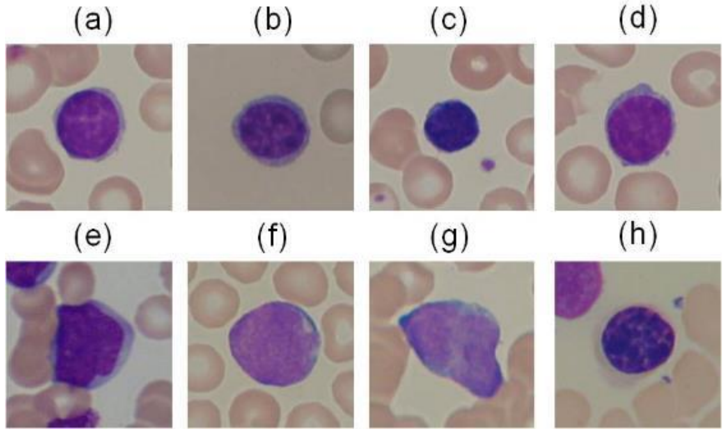
- Pre-trained CNN
  - Limited number of samples
  - Substitute last layer
    - 1000 classes (ImageNet) → 2 classes (ALL)
    - (0: *"normal"*; 1: *"lymphoblast")*
  - Fine tuning on the ALL database
    - Train on the training subset
    - Inference on the testing subset



Experimental Results

- Database
  - ALL-IDB2 dataset
  - 260 images of white cells, each with binary label
    - (0: *"normal"*; 1: *"lymphoblast"*)
  - Cropped to show only region around the cell
- Evaluation procedure
  - N-fold validation ($N = 2$) repeated 10 times, results averaged
  - Apply the proposed methodology on the training subset
    - Estimate $th_{unsharp}$, perform the final unsharpening, train the Deep CNN on $DB_{unsharp}$
    - Apply Deep CNN to perform the classification on the testing subset of $DB_{unsharp}$



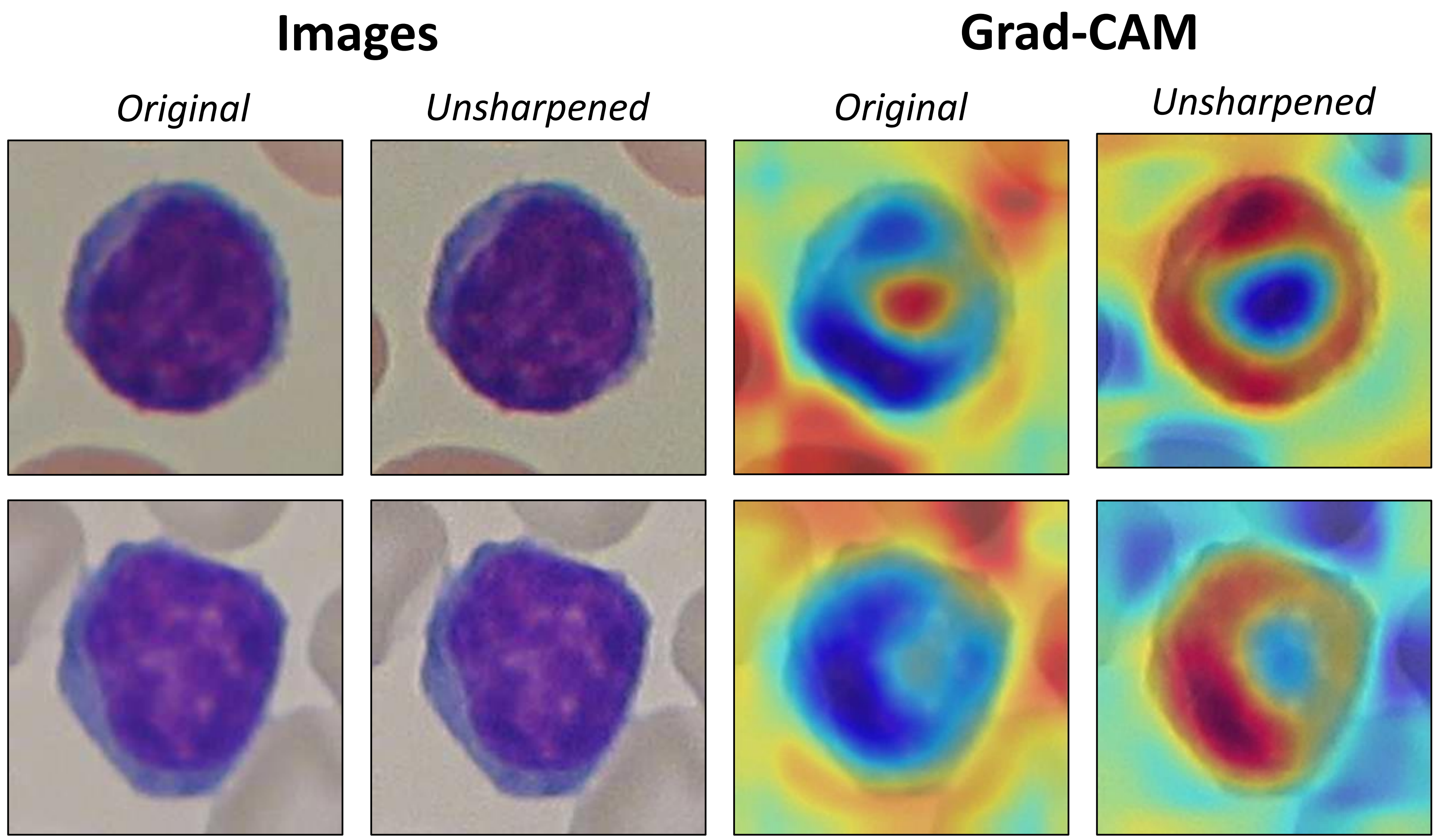


R. D. Labati, V. Piuri and F. Scotti, "All-IDB: The acute lymphoblastic leukemia image database for image processing," 2011 18th IEEE International Conference on Image Processing, Brussels, Belgium, 2011, pp. 2045-2048, doi: 10.1109/ICIP.2011.6115881. https://homes.di.unimi.it/scotti/all/

Quantitative Analysis

Original		Unsharp	
Deep CNN	Accuracy (%) $(Mean_{Std})$	Deep CNN	Accuracy (%) $(Mean_{Std})$
AlexNet	$93.76_{2.06}$	AlexNet	$95.07_{1.85}$
VGG16	$95.30_{2.52}$	**VGG16**	$\mathbf{96.84_{1.27}}$
VGG19	$95.38_{2.05}$	VGG19	$95.53_{1.57}$
ResNet18	$96.00_{1.01}$	ResNet18	$96.00_{1.13}$
ResNet50	$96.00_{1.48}$	ResNet50	$96.69_{1.49}$
ResNet101	$95.53_{1.97}$	ResNet101	$96.00_{1.87}$
DenseNet201	$96.76_{1.48}$	DenseNet201	$96.69_{1.14}$

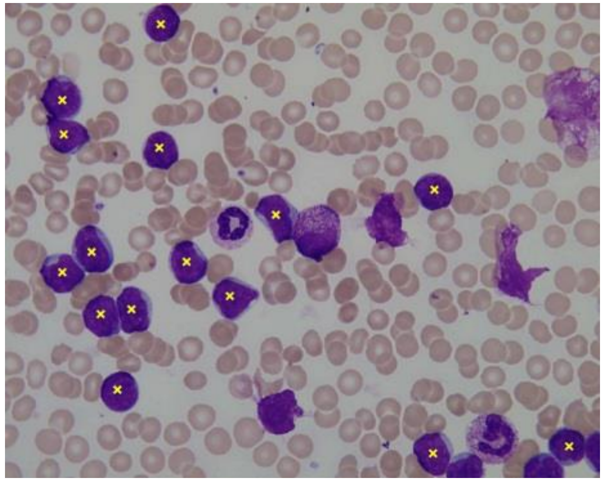
Qualitative Analysis



Conclusions

- First ML-based for focus quality estimation, adaptive unsharpening, and classification of ALL blood samples
  - Improve sharpness of images prior to classification
  - Shallow CNN to tune the unsharpening parameters
  - Adaptively reducing bias between quality and label
- Experiments show increase in classification accuracy using state-of-the-art pretrained CNNs
- Future works
  - Databases with more samples
  - Different DL architectures

Thank you for your kind attention!



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