Imbalanced Domain Generalization for Robust Single Cell Classification in Hematological Cytomorphology

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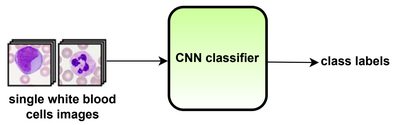
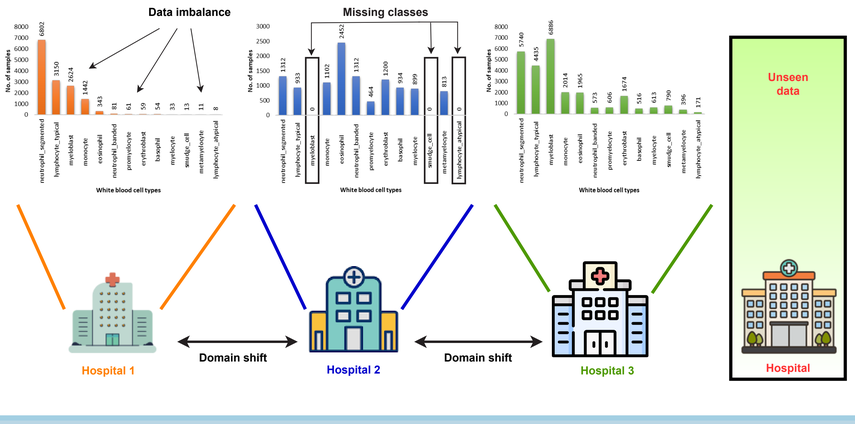
Problem Formulation

Problem: Cytomorphology as a image classification problem.

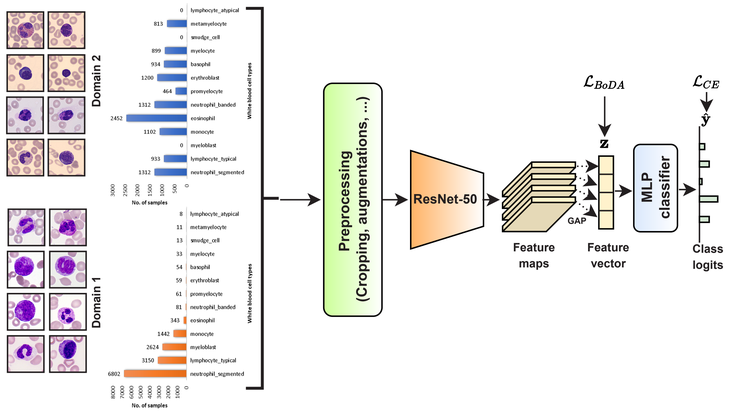


Goal: Train a robust classifier for unseen target data of white blood cell classification by addressing cross-domain data imbalance and domain shifts.



Network Training

Approach:



Training Loss:

$$\mathcal{L} = \arg\min_{\boldsymbol{\theta}} \mathcal{L}_{\mathrm{CE}} + \lambda \mathcal{L}_{\mathrm{BoDA}}$$

Standard cross-entropy (CE) applied to output layer:

$$\mathcal{L}_{CE}(\hat{\mathbf{y}}, \mathbf{y}) = -\frac{1}{N}\sum_{n=1}^{N} \mathbf{y}_n \log \hat{\mathbf{y}}_n + (1-\mathbf{y}_n)\log(1-\hat{\mathbf{y}}_n)$$

Balanced Domain-Class Distribution Alignment (BoDA) loss to tackle the data imbalance across domain-class pairs, which is applied to the latent features:

$$\mathcal{L}_{BoDA}(\mathbf{z}, \boldsymbol{\psi}) = \sum_{\mathbf{z}_i \in \mathcal{Z}} \frac{-1}{|\mathcal{D}|-1} \sum_{d \in \mathcal{D} \setminus \{d_i\}} \log \frac{\exp\left(-\boldsymbol{w}_{d_i,c_i}^{d,c_i}\, \hat{\mathrm{d}}(\mathbf{z}_i, \boldsymbol{\psi}_{d,c_i})\right)}{\sum_{(d',c') \in \mathcal{M} \setminus \{(d_i,c_i)\}} \exp\left(-\boldsymbol{w}_{d_i,c_i}^{d',c'}\, \hat{\mathrm{d}}(\mathbf{z}_i, \boldsymbol{\psi}_{d',c'})\right)}$$

Positive cross-domain pairs

Negative cross-class pairs

Data and Experimental Results

Datasets: Statistics and properties of the three datasets used in our experiments.

Dataset	# classes	Image size	Image resolution	Single cell images
`Matek_19` [1]	13	$400 \times 400 \times 3$	$29.0\,\mu m \times 29.0\,\mu m$ $= 13.8$ pixels/micron	14681
`Acevedo_20` [2]	10	$360 \times 363 \times 3$	$36.0\,\mu m \times 36.3\,\mu m$ $= 10$ pixels/micron	11421
`INT_20`	13	$288 \times 288 \times 3$	$25.0\,\mu m \times 25.0\,\mu m$ $= 11.52$ pixels/micron	26379

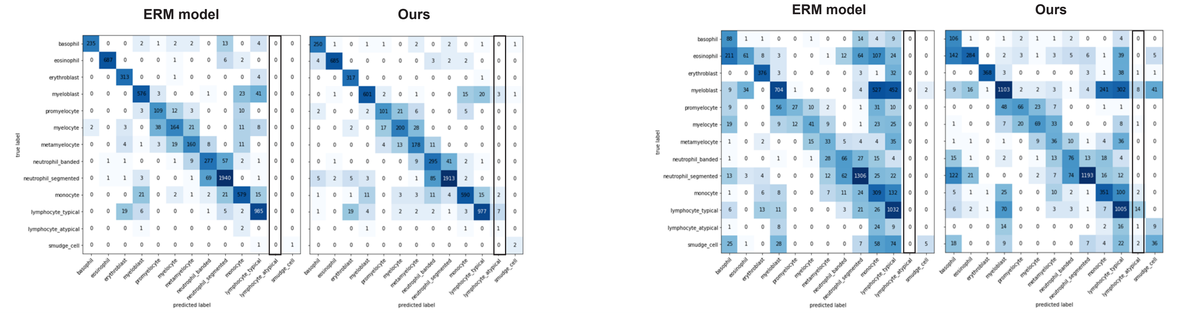
Quantitative Results:

- Imbalanced domain generalization classification results (mean±std) determined by five-fold cross-validation on Acevedo_20 & Matek_19 validation sets and INT_20 testset (unseen domain). Our base-line model is ResNet50, pretrained on ImageNet.

Methods	F1-micro↑	F1-macro↑
ERM [3]	**0.93** ±0.01	0.77 ±0.02
DANN [4]	0.87 ±0.03	0.67 ±0.04
CORAL (current SOTA DG) [5]	0.92 ±0.01	0.76 ±0.03
Ours	**0.93** ±0.01	**0.78** ±0.05
Ours^{+}	0.90 ±0.02	0.76 ±0.04

Methods	F1-micro↑	F1-macro↑
ERM [3]	0.64 ±0.03	0.40 ±0.05
DANN [4]	0.59 ±0.07	0.35 ±0.06
CORAL (current SOTA DG) [5]	**0.66** ±0.03	0.43 ±0.03
Ours	**0.66** ±0.05	0.43 ±0.06
Ours^{+}	0.59 ±0.09	**0.46** ±0.08

- Confusion matrices show an improved classification of cells from the lowly populated **lymphocyte_atypical** class with our method compared to the standard ERM model on validation and test set, respectively.



Conclusions

- We develop a robust CNN model for out-of-distribution generalization in hematological cytomorphology classification that tackles three main challenges: data imbalance, domain shifts, and missing classes.
- Our work shows how biological, epidemiological, and technical variabilities in hematologic single white blood cell classification can be addressed for training classifiers.

References

[1] C. Matek, S. Schwarz, K. Spiekermann, and C. Marr, "Human-level recognition of blast cells in acute myeloid leukaemia with convolutional neural networks," *Nature Machine Intelligence*, 2019.

[2] A. Acevedo, A. Merino, S. Alférez, Á. Molina, L. Boldú, and J. Rodellar, "A dataset of microscopic peripheral blood cell images for development of automatic recognition systems," *Data in brief*.

[3] V. N. Vapnik, "An overview of statistical learning theory," *IEEE transactions on neural networks*, 1999.

[4] Y. Ganin, E. Ustinova, H. Ajakan, P. Germain, H. Larochelle, F. Laviolette, M. Marchand, and V. Lempitsky, "Domain-adversarial training of neural networks," *The journal of machine learning research*, 2016.

[5] B. Sun and K. Saenko, "Deep coral: Correlation alignment for deep domain adaptation," in *ECCV*, 2016.