Imbalanced Domain Generalization for Robust Single Cell Classification in Hematological Cytomorphology

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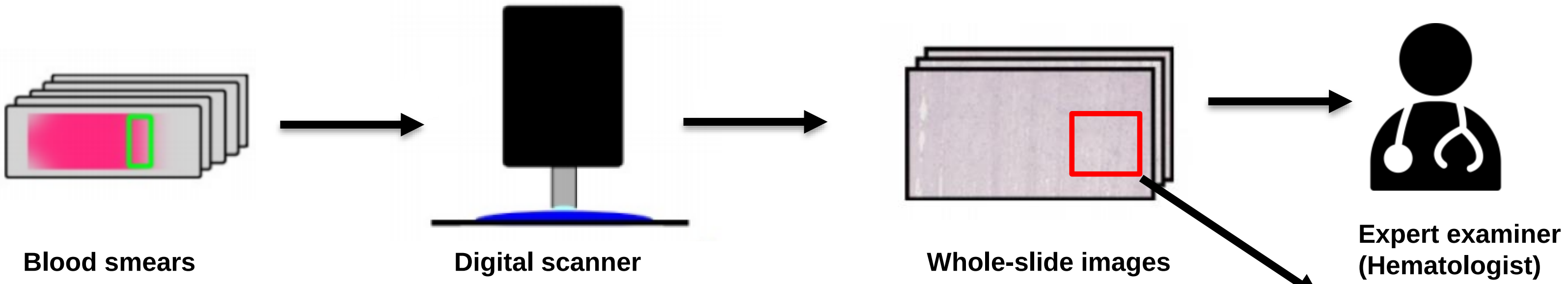
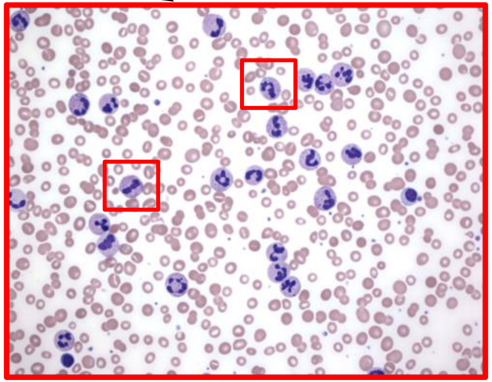
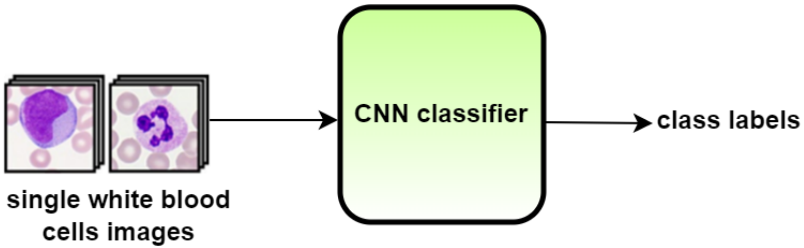
Single white blood cell classification

- Clinical workflow for Acute Myeloid Leukemia (AML) diagnoses (Hematological diagnostics):



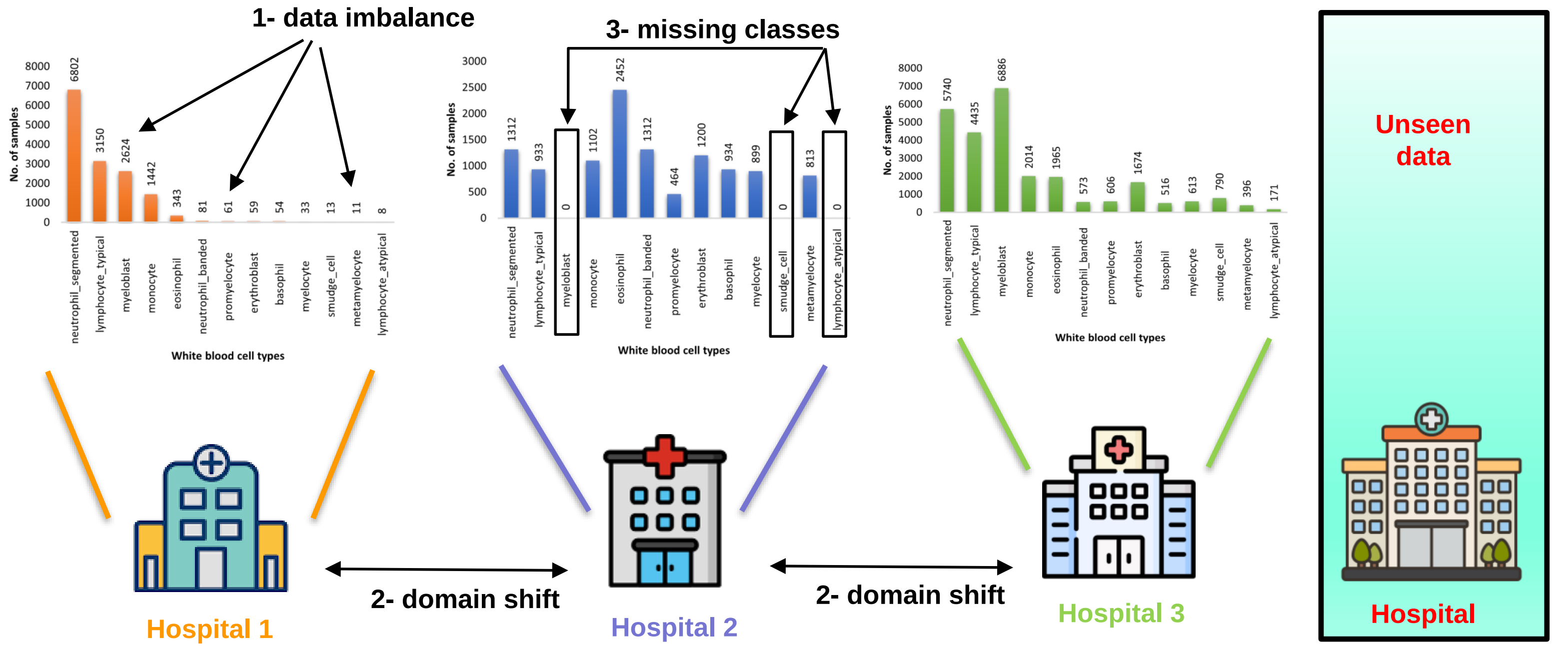


- Cytomorphology as an image classification problem:



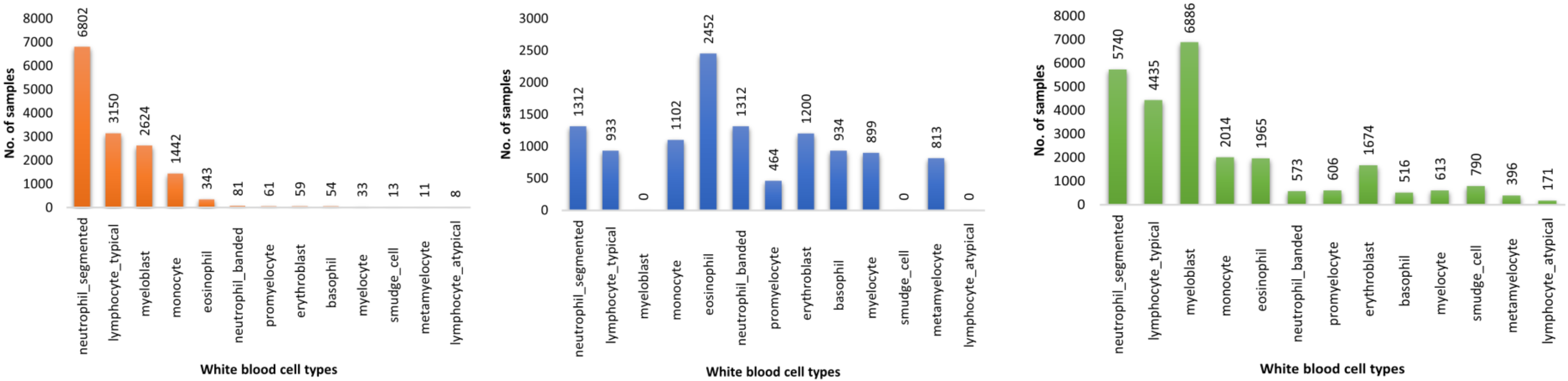
Robust single white blood cell Classification

- **Key challenges for robust classification:**



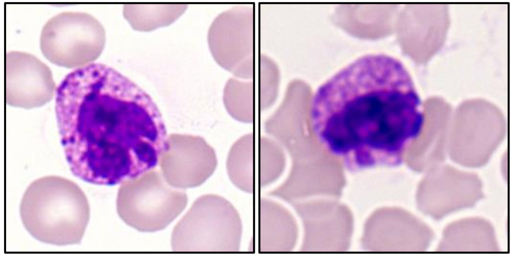
Challenge # 1: Data imbalance

- **In-domain and across domains data imbalance:**
  - **Data imbalance** is an intrinsic problem in **medical data**.
  - Learning **domains** naturally **differ** in their **label distributions**.
  - Domains can have **(severe) class imbalance** (long-tailed distribution) within each domain.



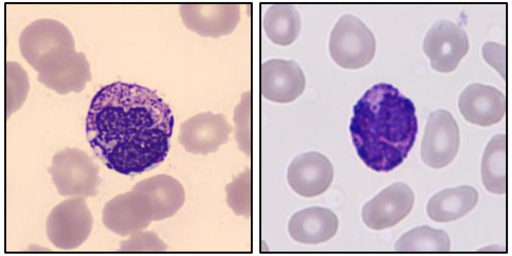
Challenge # 2: Domain shift

- **Domain shift within and across domains:**
  - **Data distribution shifts** can have due to **different staining procedures**, **different scanners** or **acquisition protocols (i.e., background light, focus)**, **different magnifications** / **resolutions**, and **variations** in **clinical centers** or **patients**.
  - **Domains** can have **different distribution-shift** within a domain and across domains.



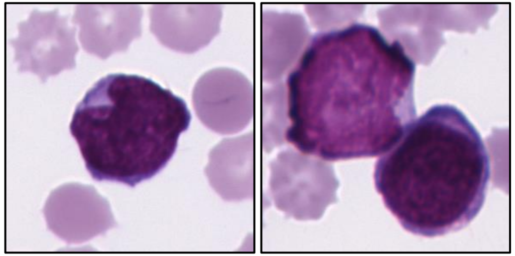
Mat_19

- 14681 samples
- 400x400x3 pixels
- 29.0 µm x 29.0 µm
- = 13.8 pixels/micron
- 13 classes



Ace_20

- 11421 samples
- 360x363x3 pixels
- 36.0 µm x 36.3 µm
- = 10 pixels/micron
- 10 classes

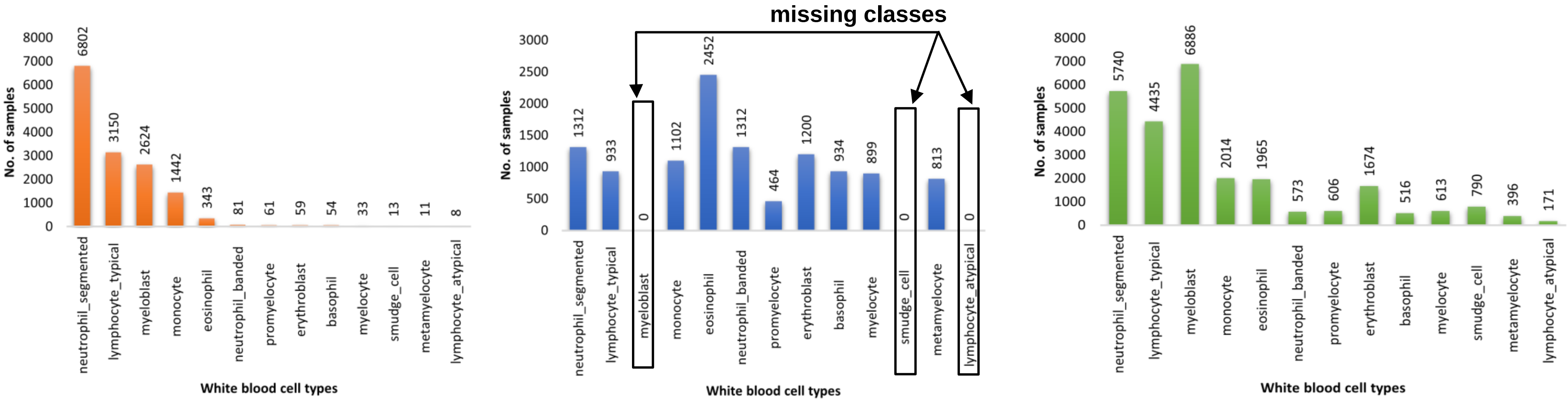


MLL_20

- 26379 samples
- 288x288x3 pixels
- 25.0 µm x 25.0 µm
- = 11.52 pixels/micron
- 13 classes

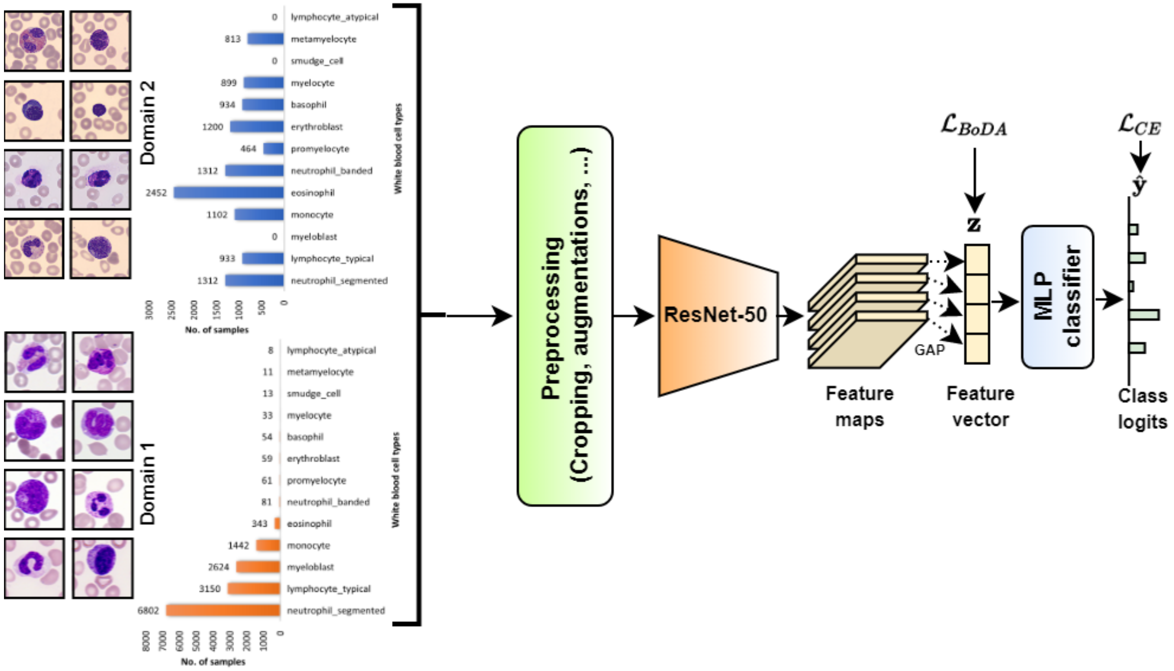
Challenge # 3: Missing classes

- **In-domain Missing classes:**
  - In **certain domain**, we have **no data** at all for **certain classes**.
  - The **classifier** should also be **generalized** to the **unseen classes** as well.
  - Sometimes **divergent labels distribution** (Forward/backward LT) across domain can also occur to make the problem more complex.



Proposed Methodology

- **Training setup of our robust WBC classification approach:**



Proposed Methodology

- **Network 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 [5] (**BoDA**) loss to tackle the data imbalance across domain-class pairs, which is applied to the latent features:

Positive cross-domain pairs

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

Negative cross-class pairs

Robust classification results

- **Results comparison:**

Table 1: Imbalanced DG classification results (mean±std) determined by five-fold cross-validation on Acevedo_20 and Matek_19 validation-sets. Our base-line model is ResNet50, pretrained on ImageNet.

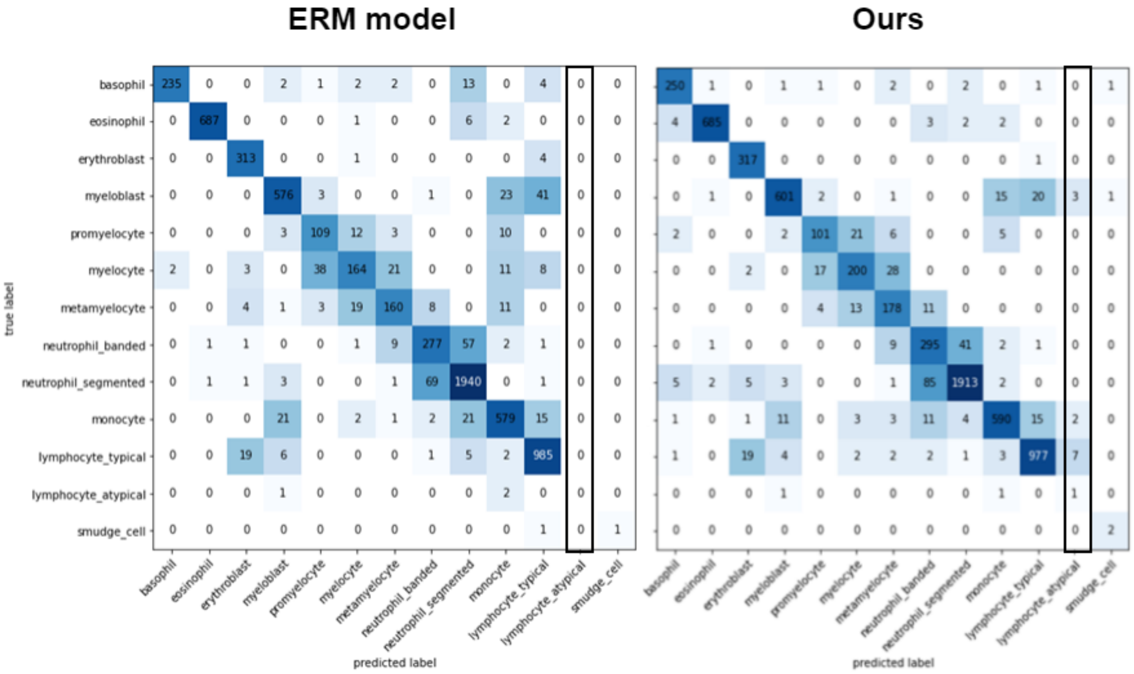
Methods	**F1-micro↑**	**F1-macro↑**
ERM (Vapnik, 1999)	**0.93** ±0.01	0.77 ±0.02
DANN (Ganin et al., 2016)	0.87 ±0.03	0.67 ±0.04
CORAL (current SOTA DG) (Sun & Saenko, 2016)	0.92 ±0.01	0.76 ±0.03
Ours	**0.93** ±0.01	**0.78** ±0.05
Ours^{+}	0.90 ±0.02	0.76 ±0.04

Table 2: Imbalanced DG classification results (mean±std) determined by five-fold cross-validation on INT_20 testset (unseen domain). Our base-line model is ResNet50, pretrained on ImageNet.

Methods	**F1-micro↑**	**F1-macro↑**
ERM (Vapnik, 1999)	0.64 ±0.03	0.40 ±0.05
DANN (Ganin et al., 2016)	0.59 ±0.07	0.35 ±0.06
CORAL (current SOTA DG) (Sun & Saenko, 2016)	**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

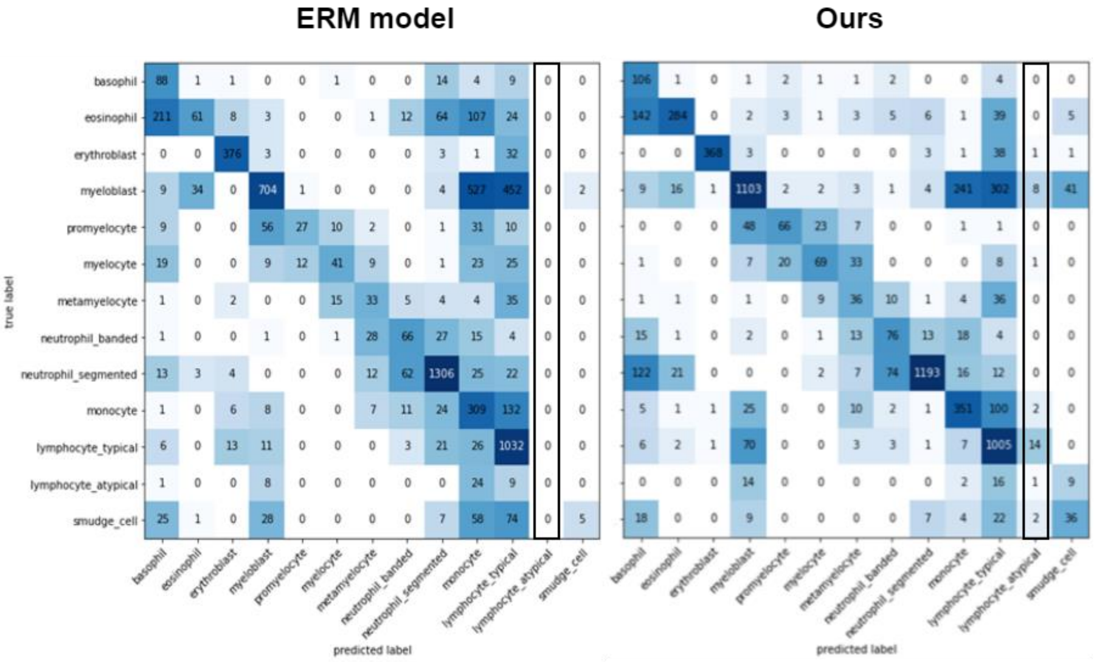
Robust classification results

- **Results comparison:**
  - **Confusion Matrix Comparison: Mat_Ace valset**



Robust classification results

- **Results comparison:**
  - **Confusion Matrix Comparison: MLL_20 testset (unseen)**



Conclusion

- 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**.

- We show how existing **pre-trained deep models** can be improved for distinct domains by **optimizing** the **loss function** in the **latent feature space** and **output logits** of the network.

- Our work shows how **biological**, **epidemiological**, and **technical variabilities** in hematologic single white blood cell classification can be addressed for training **robust classifiers**.

References

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Thanks!
Q&A?