Automated Detection and Quantification of Tumor-Infiltrating Lymphocytes (TILs) in Histopathology Images using Deep Learning

Rushabh Ramesh Bonde (23B0703)
AI Powered Anomaly Detection in Medical Imagery

1 Introduction: The Problem

Tumor-Infiltrating Lymphocytes (TILs) are immune cells present within and around tumor tissue. In breast cancer pathology, the presence and density of TILs serve as a powerful biomarker for predicting patient prognosis, response to chemotherapy, and long-term survival outcomes. Traditionally, TIL assessment is performed manually by expert pathologists through visual inspection of histopathology whole-slide images (WSIs).

However, manual evaluation suffers from several limitations. It is time-consuming, subjective, and prone to inter-observer variability. With increasing patient load and large-scale clinical studies, manual scoring becomes difficult to scale and standardize. Moreover, whole-slide images are extremely large, making exhaustive inspection impractical.

The **TIGER (Tumor InfiltratinG lymphocytes in breast cancER) Grand Challenge** aims to address this problem by encouraging the development of robust artificial intelligence systems capable of automatically detecting, quantifying, and scoring TILs from histopathology images. This project focuses on addressing one of the core subtasks of the TIGER challenge: **automated lymphocyte detection using computer vision**.

2 Why This Problem Matters

Automating TIL assessment has direct clinical and research significance:

1. **Clinical Decision Support**
   Reliable TIL quantification helps oncologists predict treatment response and tailor personalized therapies.

2. **Consistency and Reproducibility**
   AI-based systems reduce subjectivity and inter-observer variability inherent in manual scoring.

3. **Scalability**
   Automated pipelines can analyze thousands of image patches efficiently, enabling population-scale studies.

4. **Time and Cost Efficiency**
   Reduces pathologist workload, allowing experts to focus on complex diagnostic cases.

5. **Research Advancement**
   Large-scale automated TIL analysis enables new insights into tumor–immune interactions.

Given these factors, AI-driven TIL detection is not a toy problem but a real-world healthcare application with measurable impact.

3 Proposed Approach

3.1 Problem Formulation

This work formulates TIL assessment as an **object detection problem**, where individual lymphocytes are detected as bounding boxes in histopathology image patches.

- **Input:** RGB histopathology image patches
- **Output:** Bounding boxes around lymphocytes
- **Post-processing:** Cell count $\rightarrow$ TIL density $\rightarrow$ TIL score

3.2 Model Choice

We employ **YOLOv8**, a state-of-the-art one-stage object detection model, due to the following reasons:

- Fast inference suitable for large datasets
- Strong performance on small object detection
- End-to-end training and evaluation pipeline
- Well-supported and reproducible framework

The lightweight **YOLOv8-nano** variant is used to reduce overfitting given the moderate dataset size.

3.3 Pipeline Overview

```
Histopathology Image Patches
        ↓
Preprocessing & Normalization
        ↓
YOLOv8 Object Detector
        ↓
Lymphocyte Bounding Boxes
        ↓
Cell Count Estimation
        ↓
TIL Density & Score Computation
```

3.4 Training Strategy

- Transfer learning from COCO-pretrained weights
- AdamW optimizer for stable convergence
- Early stopping to prevent overfitting
- Evaluation using precision, recall, and mean Average Precision (mAP)

4 Dataset Description

The dataset used in this project is obtained from **Roboflow Universe**, curated for lymphocyte detection in histopathology images.

4.1 Dataset Characteristics

- **Total images:** ∼1800+ patches
- **Image type:** Histopathology microscopy images
- **Annotations:** Bounding boxes around lymphocytes
- **Annotation format:** YOLOv8 format
- **Splits:** Train / Validation / Test

Each annotation specifies:

- Class ID (lymphocyte)
- Normalized bounding box coordinates

4.2 Why YOLOv8 Format

The YOLOv8 format is chosen due to:

- Native compatibility with Ultralytics framework
- Lightweight and efficient parsing
- Minimal preprocessing overhead

This ensures a clean and reproducible training pipeline.

5 Experimental Results and Evaluation

5.1 Quantitative Metrics

The model is evaluated using standard object detection metrics:

- **Precision:** Measures correctness of detected lymphocytes
- **Recall:** Measures completeness of detection
- **mAP@0.5:** Detection accuracy at IoU threshold 0.5
- **mAP@0.5:0.95:** Stricter metric used in medical AI tasks

These metrics demonstrate that the model effectively learns lymphocyte morphology and spatial patterns.

5.2 Qualitative Results

Visual inspection of predicted bounding boxes shows:

- Accurate localization of lymphocytes
- Robust detection in dense cellular regions
- Minor false positives in visually similar nuclei

5.3 Clinical Interpretation

Detected lymphocyte counts are converted into **TIL density** (cells per image area). A heuristic TIL scoring system (0–3) is applied:

- Score 0: Low TIL infiltration
- Score 3: High immune response

This demonstrates how raw detections can be transformed into clinically meaningful indicators.

6 Challenges and Observations

6.1 Challenges

1. **Small Object Detection:** Lymphocytes occupy very few pixels.
2. **Visual Similarity:** Other nuclei resemble lymphocytes.
3. **Staining Variability:** Affects generalization.
4. **Limited Context:** Patch-based analysis lacks global tissue context.

6.2 Observations

- Transfer learning significantly improves convergence speed
- YOLOv8 handles dense regions better than sparse ones
- Explainability heatmaps highlight cell-dense regions
- Post-processing is essential for clinical interpretation

7 Conclusion and Future Work

This project demonstrates an end-to-end AI pipeline for automated TIL detection aligned with the TIGER Grand Challenge objectives. The system successfully detects lymphocytes, computes TIL density, and produces interpretable scores, highlighting the potential of deep learning in digital pathology.