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Lymphocyte Mimicry Correction via Region-Level Tissue Reasoning and Unbalanced Optimal Transport
Supplementary Material

A MLLM Prompting Protocol

Claude Sonnet 4.5 is queried once per (ROI, tissue) block in a single-turn multimodal dialog. The system and user prompts below are reproduced verbatim from the production pipeline.

Tissue-label mapping. The placeholder `{label_description}` in the user message is filled by matching the tissue index parsed from the (ROI, tissue) PNG filename to: T1 `invasive_tumor`, T2 `tumor_stroma`, T3 `in_situ_tumor`, T4 `benign_glands`, T5 `necrosis`, T6 `inflamed_stroma`, T7 `other_tissue`.

System message (sent once per query as the `system` field):

> *LYMPHOCYTE ASSESSMENT*
>
> *CRITICAL INSTRUCTION: "Presence Probability" is based primarily on ANATOMICAL CONCEPT and strict definitions (are lymphocytes within the defined compartment based on anatomical boundaries?) — Other fields (Density, Pattern, Description) are based on VISUAL OBSERVATION combined with anatomical context (what do you see and how much?)*

The anatomy-vs-visual split reduces hallucination: anatomical compartment knowledge drives the binary presence call; visual evidence drives the quantitative density estimate.

User message (multimodal: one PNG of the ROI with the target tissue outlined in blue contour, plus the text below):

```
TASK: Analyze lymphocytes in the blue-outlined region
(labeled as {label_description}):

- Presence Probability (0.00-1.00):
[likelihood based on ANATOMICAL DEFINITION]
- Density (if lymphocytes exist):
[category with % range -- VISUAL assessment]
• Rare: <5%   • Low: 5-20%
• Moderate: 20-40%   • High: 40-70%
• Very high: >70%
- Density by area (if lymphocytes exist): [%]
- Density by cell count (if lymphocytes exist): [%]
- Rationale: [explanation for probability assessment]
- Predominant location (if lymphocytes exist):
[where most lymphocytes are]
- Overall pattern (if lymphocytes exist):
[distribution -- VISUAL]
- Clinical interpretation: [significance]
```

```
- Overall confidence (0.00-1.00):
[confidence in entire assessment]

OUTPUT REQUIREMENT: Provide your response in structured JSON format.
```

Representative assistant response (T6 inflamed stroma, TIGER training set):

```
{
"Presence Probability": 0.95,
"Density": {"category": "High", "range_percent": "40-70%"},
"Density by area": 52,
"Density by cell count": 58,
"Rationale": "The blue-outlined region exhibits clear lymphocytic
infiltrate with characteristic small round nuclei and high
nuclear-to-cytoplasmic ratio. Anatomically, this region is
identified as inflamed tumor stroma, where lymphocyte
infiltration is expected.",
"Overall confidence": 0.85
}
```

B Per-Subtype MAE

Table 1. Per-ROI MAE by tissue subtype (TCGA-BRCA test; lymphocytes per ROI), point estimate with 95% bootstrap CI [low, high] (N=1000, ROI-level resampling). Due to wide, overlapping CIs in the small-n subtypes (T4 n=19, T5 n=58, T3 n=73), we do not bold a single per-tissue-subtype winner. PanopTILs attains the lowest MAE in sparse-positive epithelial subtypes (T1, T3–T5, T7) by its tendency to suppress positive predictions everywhere, whereas Loki-OT is lowest in T2 and lower than PanopTILs in the lymphocyte-dense T6, consistent with its lower patient-level MAE.

Tissue subtype (n)	Lizard	PanopTILs	Context-soft	Loki-OT
T1 Invasive tumor (1108)	5.24 [4.83,5.69]	1.14 [.96,1.34]	3.69 [3.38,4.01]	2.63 [2.41,2.86]
T2 Tumor-assoc. stroma (1169)	2.51 [2.34,2.70]	2.09 [1.91,2.28]	2.35 [2.18,2.55]	1.96 [1.80,2.12]
T3 In-situ tumor (73)	3.58 [2.38,5.01]	0.67 [.25,1.22]	2.05 [1.45,2.84]	1.25 [.85,1.71]
T4 Healthy glands (19)	3.47 [1.84,5.95]	0.84 [.16,1.79]	1.84 [.47,4.05]	1.32 [.32,2.84]
T5 Necrosis (58)	2.84 [1.57,4.91]	0.28 [.14,.45]	3.21 [1.62,5.79]	1.74 [.98,2.91]
T6 Inflamed stroma (624)	6.54 [5.97,7.15]	8.68 [7.94,9.54]	6.54 [5.96,7.16]	6.70 [6.11,7.36]
T7 Rest (103)	0.51 [.35,.69]	0.29 [.18,.41]	0.41 [.26,.59]	0.31 [.19,.44]