Attention-Based Multiple Instance Learning for Cellularity Estimation in Bone Marrow Core Biopsies

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Abstract

Estimation of cellularity in bone marrow tissue specimens is a routine task, useful in the diagnosis and monitoring of hematologic diseases. In this work we train a weakly supervised regressor on a large dataset of bone marrow biopsy slides with LLM parsed cellularity estimates from case reports. We utilize attention-based multiple instance learning and a DINOv2 vision transformer model. The model is trained and validated on a set of over 5600 bone marrow biposy slide scans achieving a R^2 of 0.776 on our test set.

Keywords: Bone Marrow, Core Biopsy Cellularity, Attention-Based Multiple-Instance Learning, DINOv2

1. Introduction

Automated methods for measuring the cellularity in bone marrow core biopsies show promise for improving the accuracy and workflow of pathologists. Overwhelmingly these have utilized segmentation which requires time-consuming annotation effort and naturally limits the dataset size which can be created for the task (D'Abbronzo et al., 2024; van Eekelen et al., 2024; Lin et al., 2024; Sarkis et al., 2023; Hatayama et al., 2023; Shiffman et al., 2023; Eekelen et al., 2022; Brück et al., 2021; van Eekelen, 2020; Nielsen et al., 2019; Hagiya et al., 2018).

In this study we make use of an attention-based multiple instance regressor and a DINOv2 vision transformer fine-tuned on an in-house dataset to estimate cellularity in bone marrow core biopsies (Ilse et al., 2018; Oquab et al., 2024). To build this dataset we leveraged a large language model (LLM) to parse pathology case reports and extract cellularity estimates (Touvron et al., 2023; Grattafiori et al., 2024). From this we trained a model on 2892 scans with a test validation set of 2889 bone marrow biopsy scans and analyze its performance.

2. Method and Dataset

Cellularity, reported as percentages, were extracted automatically from pathology report text using Ollama, an open-source implementation of the Llama family of LLMs, and the llama3.1:70B model (Touvron et al., 2023; Grattafiori et al., 2024). To be consistent with single-value cellularity values extracted from the reports, reports indicating a range for cellularity, such as "50% to 60% cellularity" were averaged (e.g., 55%).

With our archive of hematopathology slides currently being scanned, we are able to utilize cases from 2019 to early 2023 for which we have whole slide images (WSIs) available. We use the pyvips library to resize WSI to a consistent 2.0 microns per pixel (MPP, approximately 5x objective magnification) and pre-extract 224x224 tiles after we eliminate background tiles via HSV colorspace filtering. We split the images by time into even train and test datasets.

From the pre-extracted set of tiles, we chose a "bag" size of 256 tiles per WSI, which are randomly sampled from the pre-extracted set of tiles. These are embedded with a frozen weights from a DINOv2 vision transformer (ViT) model that was trained on a large private set of tiles, which we've extracted from our archive of WSI (Oquab et al., 2024). We combine the embedding vectors via an attention-based pooling method similar to the approach in Ilse et al. (2018). The pooled embedding representation is then classified via a single linear layer and sigmoid activation for a WSI-level cellularity estimate. We train this model using the AdamW optimizer and a very standard training loop. During inference we resample the bag for each WSI ten to twenty times, which allows us to estimate a type of mean and standard deviation estimate of the cellularity prediction for each WSI, though this is less important with larger choice of bag size.

3. Results and Discussion

Our model achieves an R^2 of 0.776 (see figure 1) on our test set which suggests that this approach is able to learn cellularity estimation. We find that it performs well on the middle range of cellularity estimates, but struggles with the low and high ends of the cellularity spectrum where we have fewer cases, which can be seen in figure 1. We saw an increase in performance over an initial model when we switched to using our own fine-tuned model weights for image embedding versus the publicly available UNI2 weights and increased the bag size of instances, which we document in table 1 (Chen et al., 2024).

Table 1: Comparison of DINOv2 trained on an internal WSI tile dataset vs public UNI2 weights

Weights	**Result (R^2)**	Inference Samples	Bag Size
UNI2	0.7239	20	16
ARUP	0.7760	10	256

Human leading digit preference is visible in the combing patterns visible in both figures 1 & 2, with only only a handful of target labels having a value that is not a multiple of ten or five.

While we achieved good initial results, we believe improvement over this performance is possible as we identified several points of error and noise in our process which we intend to address with continued work. These include errors in LLM parsing of reports, bad scans included in training and test sets, better background tile filtering, as well as many other potential improvements to the model architecture and training process. Individual feature ablation of the backbone image embedding vs other parameters such as bag size would allow us to more concretely determine the effect size of these parameters.

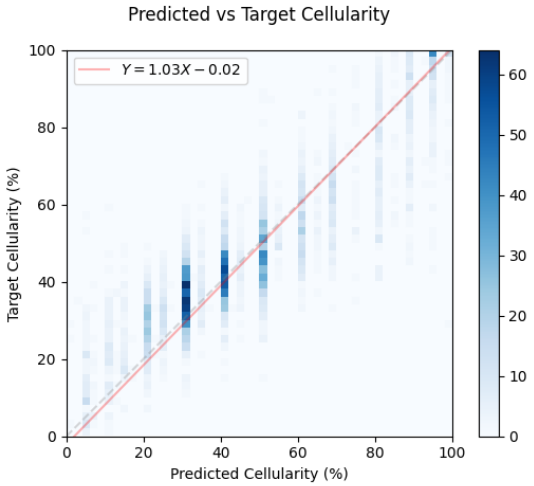

Figure 1: Heatmap of predicted vs ground truth results. On the test set we achieve an R^2 measure of 0.776.

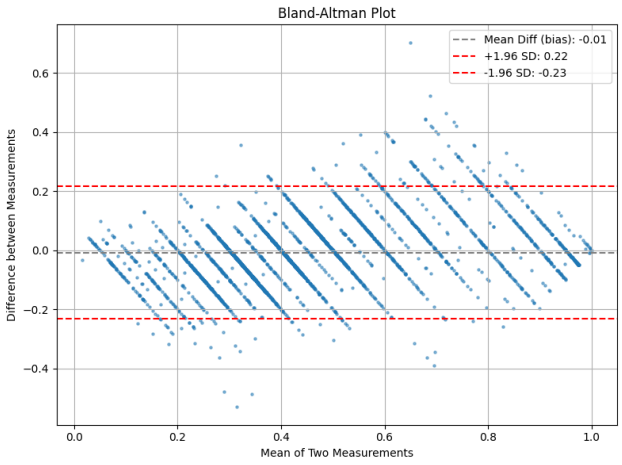

Figure 2: Bland-Altman plot of predicted vs ground truth results.

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