PATH-zle, an AI-based tool for histopathology Whole Slide Image reconstruction

Gabriele Abbate[1], Bernardo Forni[2/3], Luca Giudici[4], Paola Migliora[4], Luca Mazzucchelli[4], Vittoria Martin[4], Alessandro Giusti[1]

[1]Istituto dalle Molle di Studi sull'Intelligenza Artificiale (IDSIA USI-SUPSI), Lugano, Switzerland; [2]Università della Svizzera Italiana (USI), Lugano, Switzerland; [3]Università di Pavia, Pavia, Italia; [4]Istituto di Diagnostica Integrata della Svizzera Italiana, Clinica di Patologia – EOC, Switzerland

Abstract

Large histopathology specimens are frequently divided across multiple Whole Slide Images, requiring laborious mental reconstruction by pathologists. We introduce PATH-zle, a system that combines AI-driven candidate reconstructions generation with expert validation to reassemble an arbitrary number of tissue fragments. By integrating geometric and visual cues within an interactive interface, PATH-zle enables efficient, accurate reconstruction of high-resolution specimens, addressing key limitations of existing approaches.

Introduction

Digital microscopy is increasingly relevant for the diagnostic workflow in histopathology. The digitization of glass-slide tissue samples into Whole Slide Images (WSIs) enables consistent, reliable, and – potentially – fully automated analyses of samples. However, some specimens are too large to fit in a single slide and must be divided across multiple slides, often 4 or more. When analyzing these, pathologists must mentally reconstruct the architecture of the entire sample while looking at each individual WSI, a time-consuming and difficult process. We report a digital workflow in which the WSIs representing different parts of a specimen can be reassembled to a single large image representing the entire specimen.

The reconstruction task is challenging: a fully manual workflow requires a suitable user interface and is very time consuming, especially when dealing with 4 or more pieces; in contrast, a fully automated workflow is unfeasible, since the correct positioning of the pieces is indicated both by geometrical and visual cues, but these are inherently ambiguous and require validation by a pathologist familiar with the sample. In addition, the extremely high resolution of WSIs (often exceeding 100 gigapixels) introduces substantial computational and usability challenges, requiring specialized software to enable both manual and automated reconstruction. Existing approaches are either fully manual[1] or operate under restrictive assumptions (e.g. being limited to 2- or 4-piece reconstructions or constrained to specific tissue types such as prostate samples[2, 3]).

Methods

PATH-zle implements a workflow that combines AI guidance with human expertise to support the reconstruction of an arbitrary number of tissue fragments from any type of specimen, without imposing domain-specific constraints.

A custom Graphical User Interface supports the following operations: (i) the user selects the case to reconstruct; (ii) the slides are loaded at a low resolution, automatically cropped and binary masked (Figure 1, left image); (iii) the user can correct the cropping if needed (if a slide contains two layers of the same pathology section, the user has to select one); (iv) the program generates a set of candidate solutions automatically, and assigns a score to each of them; (v) the user inspects the proposed solutions sorted by decreasing score (Figure 1, center image); (vi) optionally, the user manually adjust a solution or triggers an automatic bundle adjustment of the selected state (Figure 1, right image); (vii) the selected solution is used to generate the full resolution tiff file of the reconstruction.

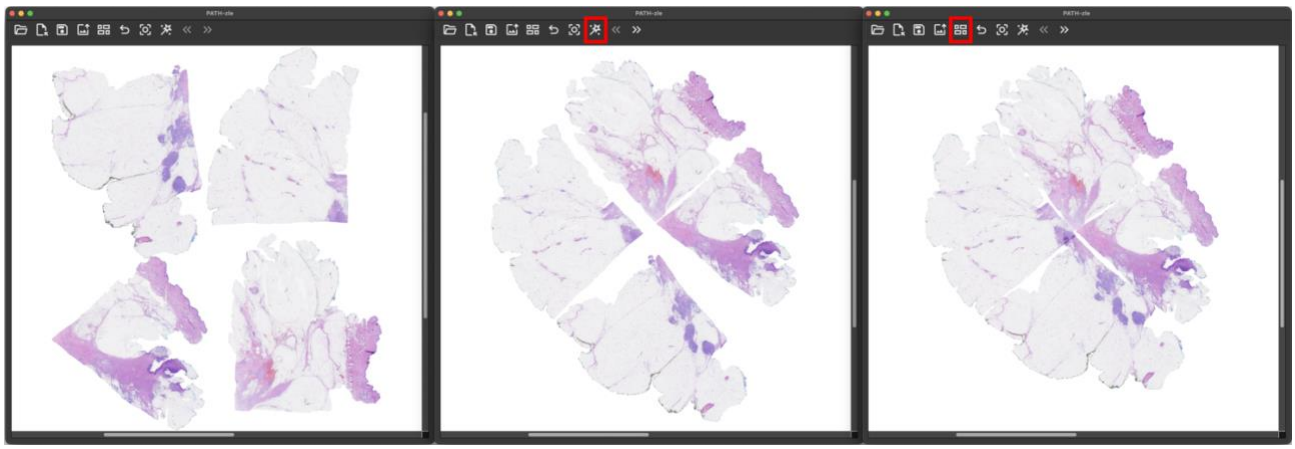

Figure 1. GUI workflow: first, user loads the WSIs (left image); then, they press the "Generate Candidate Solutions" and check the proposed solutions (center image, button highlighted in red): in this case, the first solution is correct; finally, they press the "Bundle Adjust" button to optimize the selected solution (right image, button highlighted in red)

The proposed method generates solutions for a given N-piece specimen by evaluating the placement of pairs of pieces. For each pair, we consider up to 32 distinct placements and rank them based on: (a) geometric criteria, such as minimizing the area of the convex hull of their union, and minimizing the area of their intersection; and (b) visual matching of the tissue colors and patterns across the seam. Candidate solutions of the N pieces are incrementally built by combining high-ranking pairs. The solutions are ordered according to the same criteria mentioned above, with highly similar solutions suppressed to facilitate inspection.

Results

We analyzed 30 cases containing between 2 and 4 pieces each. For all specimens, the solutions are generated in less than 5 seconds. In 25 cases (83%), the correct reconstruction was found within the first 5 proposed solutions.

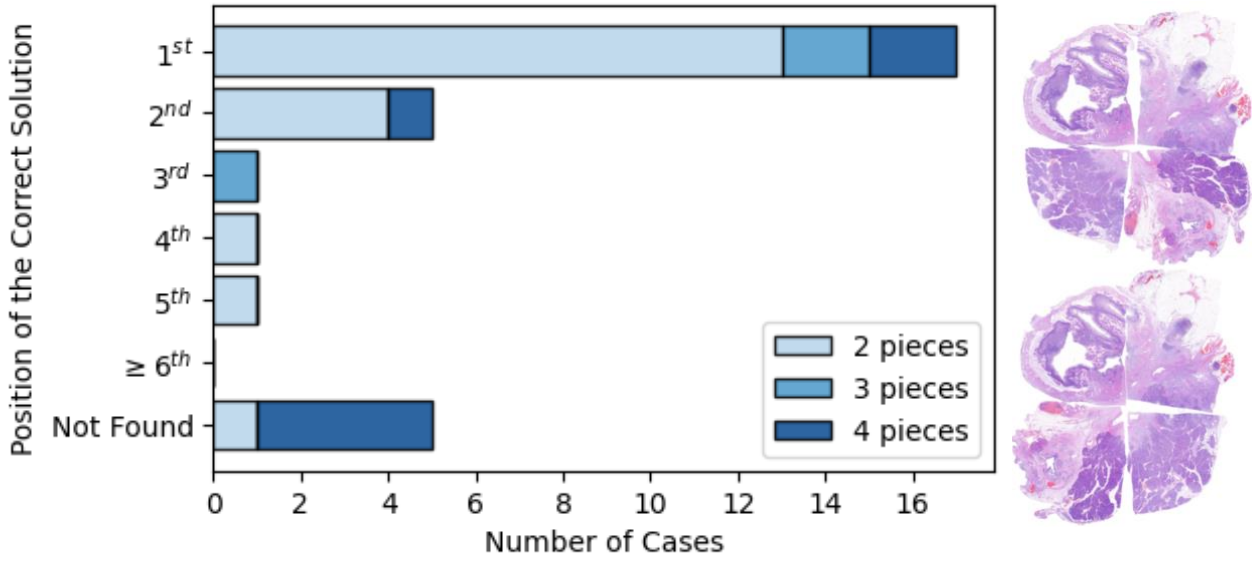

Figure 2. Rank distribution of correct solutions found by PATH-zle (left); with a sample where the correct reconstruction is ranked in 2nd position (right): the top image displays the incorrect first proposal, while the bottom image displays the correct second solution.

Discussion and Conclusions

PATH-zle demonstrates that a semi-automated approach is a viable and efficient solution for the complex task of WSI reconstruction. The workflow significantly reduces manual burden on pathologists while retaining necessary human validation.

References

1. Chappelow J, Tomaszewski JE, Feldman M, et al. HistoStitcher(©): an interactive program for accurate and rapid reconstruction of digitized whole histological sections from tissue fragments. *Computerized Medical Imaging and Graphic*. 2011. doi:10.1016/j.compmedimag.2011.01.010.
2. Penzias G, Janowczyk A, Singanamalli A, et al. AutoStitcher: An Automated Program for Efficient and Robust Reconstruction of Digitized Whole Histological Sections from Tissue Fragments. *Scientific Report*. 2016; doi: 10.1038/srep29906.
3. Schouten D, van der Laak J, van Ginneken B, et al. Full resolution reconstruction of whole-mount sections from digitized individual tissue fragments. *Scientific Report.* 2024; doi:10.1038/s41598-024-52007-5