Pathology Image Informatics Platform (PathIIP)

PIs: Anant Madabhushi (CWRU), Anne Martel (UToronto), Metin Gurcan (Wake Forest)

Year 3 Update

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UB School of Medicine and Biomedical Sciences
University at Buffalo The State University of New York

Develop a digital pathology platform to facilitate wider adoption of whole slide imaging and the use of digital pathology analysis by the cancer research community.

Platform will support:

- Visualization of WSIs from multiple vendors
- Annotation tools for pathologists
- Plug in architecture to allow integration of algorithms
- Multimodality support

- Creation of an archive of richly annotated datasets
- Evaluation and validation of algorithms on benchmarked datasets

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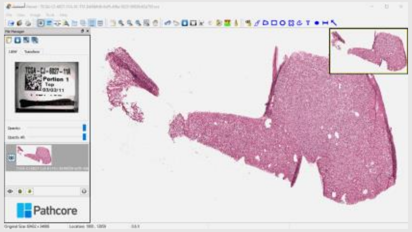
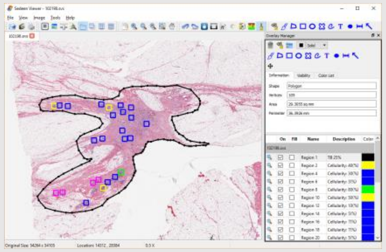
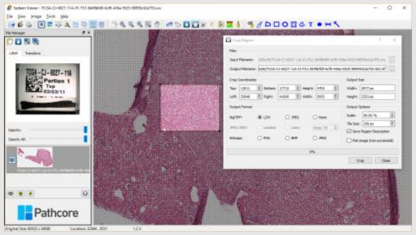
WSI viewer



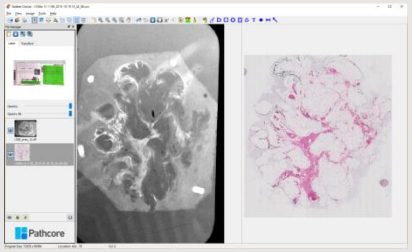
Annotation Tools

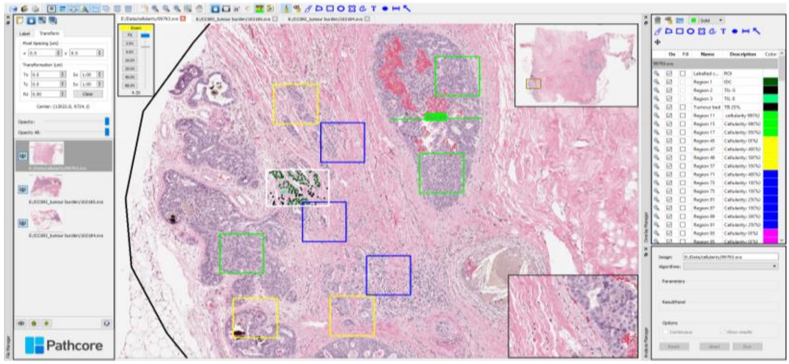


Conversion and crop tools



Multimodality imaging

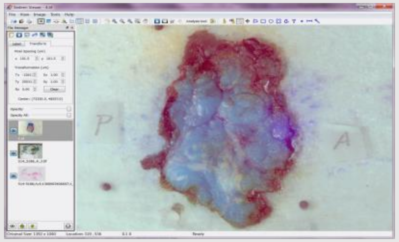


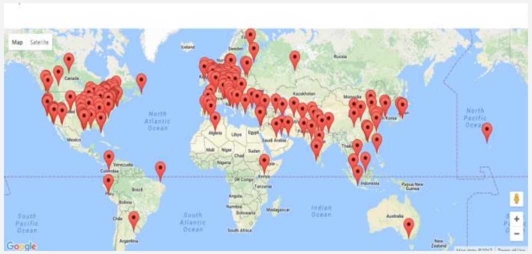


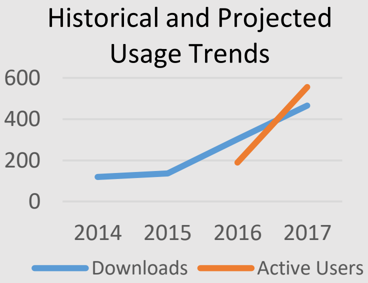
File formats supported:

Aperio (.svs)
Hamamatsu (.vms, .vmu, .ndpi)
Leica (.scn)
MIRAX (.mrxs)
Sakura (.svslide v2.6)
Generic tiled TIFF (.tif)
Generic BigTIFF (.tif)
Generic JPEG 2000 (.jp2, .jpc)
DICOM (.dcm)

Manual registration







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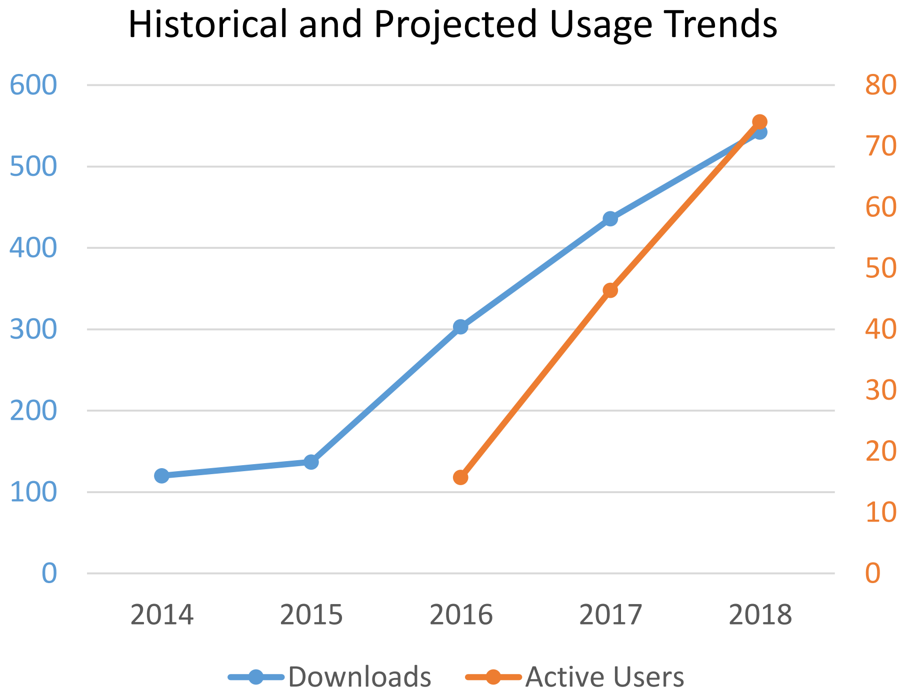
Sedeen Viewer

Sedeen Viewer Statistics

- Updates and releases
    - 2015: 2 updates
    - 2016: 3 updates
    - 2017: 5 updates
    - 2018: 2 updates (Jan-Mar)



- **2018 usage is projected based on statistics gathered up to March 15, 2018**
- **Active user counts presents the monthly average for the calendar year**

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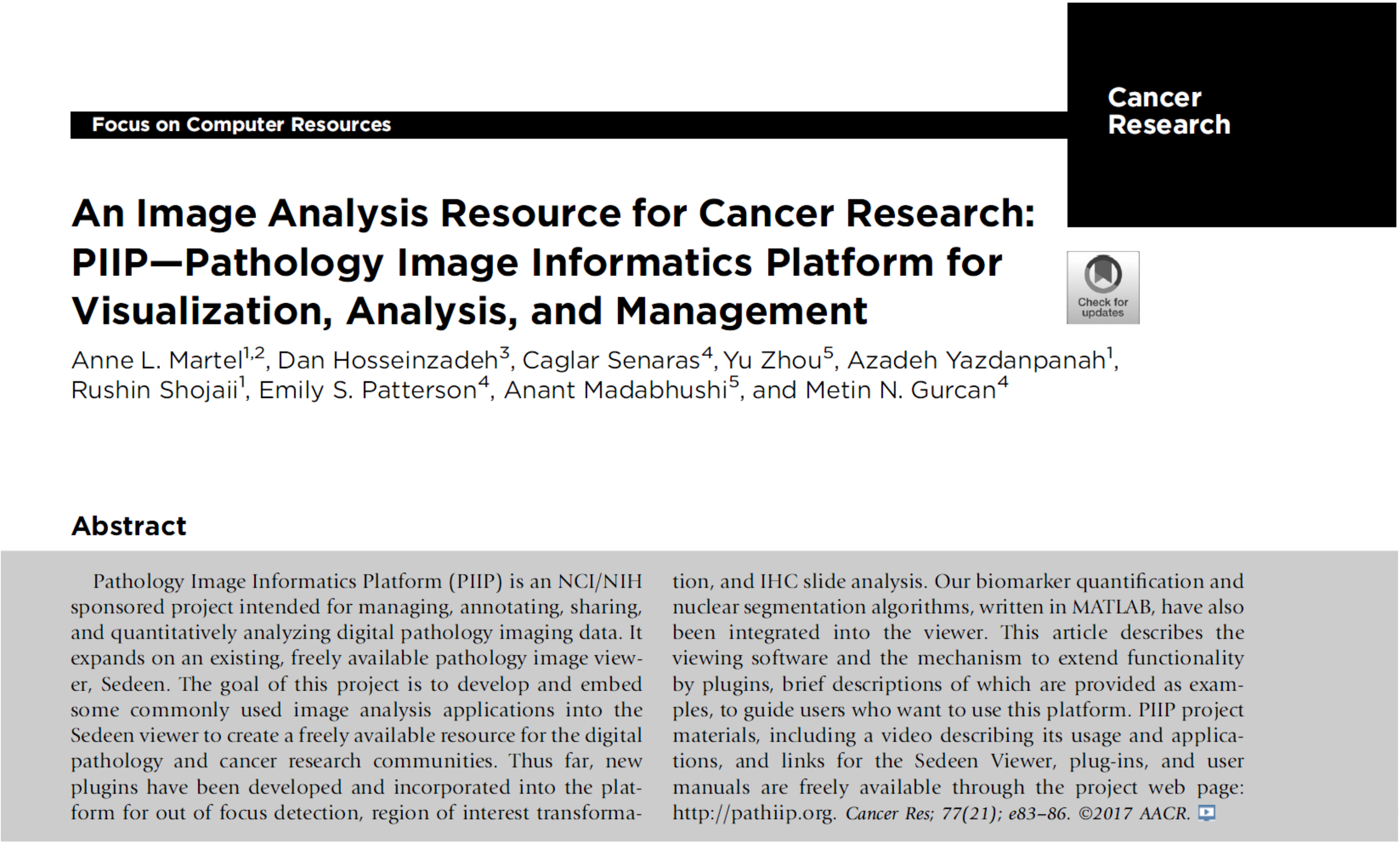
Dissemination

- Tutorials
    - Live at SPIE Medical Imaging 2018

- Platform
    - Platform description in **Cancer Research, 2017**
        - Martel AL, Hosseinzadeh D, Senaras C, Zhou Y, Yazanpanah A, Shojaii R, Patterson ES, Madadhushi A, Gurcan MN, “An image analysis resource for Cancer Research: PIIP – Pathology Image Informatics Platform for visualization, analysis, and management,” Cancer Research, 2017. Vol. 77, no. 21, pp. e83-e86, DOI: 10.1158/0008-5472.CAN-17-0323 Published November 2017.

Platform Description Published in 2017



Focus on Computer Resources

Cancer Research

An Image Analysis Resource for Cancer Research: PIIP—Pathology Image Informatics Platform for Visualization, Analysis, and Management

Anne L. Martel[1,2], Dan Hosseinzadeh[3], Caglar Senaras[4], Yu Zhou[5], Azadeh Yazdanpanah[1], Rushin Shojaii[1], Emily S. Patterson[4], Anant Madabhushi[5], and Metin N. Gurcan[4]

Abstract

Pathology Image Informatics Platform (PIIP) is an NCI/NIH sponsored project intended for managing, annotating, sharing, and quantitatively analyzing digital pathology imaging data. It expands on an existing, freely available pathology image viewer, Sedeen. The goal of this project is to develop and embed some commonly used image analysis applications into the Sedeen viewer to create a freely available resource for the digital pathology and cancer research communities. Thus far, new plugins have been developed and incorporated into the platform for out of focus detection, region of interest transformation, and IHC slide analysis. Our biomarker quantification and nuclear segmentation algorithms, written in MATLAB, have also been integrated into the viewer. This article describes the viewing software and the mechanism to extend functionality by plugins, brief descriptions of which are provided as examples, to guide users who want to use this platform. PIIP project materials, including a video describing its usage and applications, and links for the Sedeen Viewer, plug-ins, and user manuals are freely available through the project web page: http://pathiip.org. *Cancer Res; 77(21); e83–86. ©2017 AACR.*

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SPIE Medical Imaging 2018

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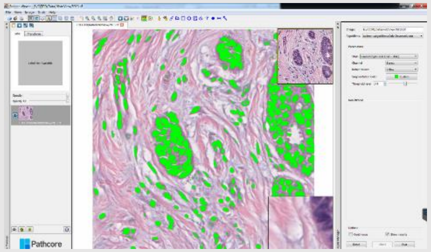
Progress

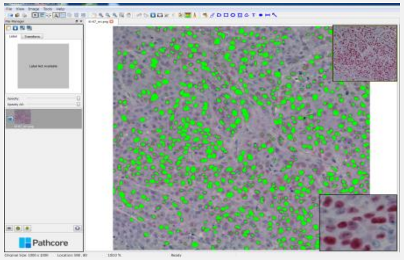
- Software release
  - 7 releases during from Jan 2017 – March 2018
  - 4 plugins developed and released (open source)
- Recent improvements
  - Added support for Visual Studio 2015 and 2017
    - Now compatible with modern deep learning frameworks
  - Added x64bit architecture support
  - Add more input parameters
    - FileDialog input
  - Added more image formats
    - PerkinElmer QpTiff, Olympus VSI, Omnyx JP2, Motic SVS
  - Improved support for Matlab-based plugins

PIIP algorithms & plugins

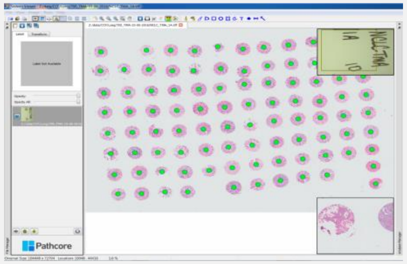
Color Normalization



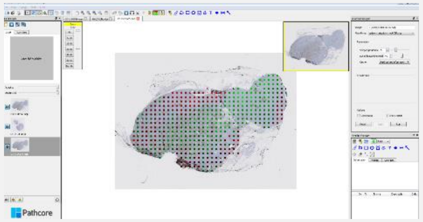
Biomarker Quantification

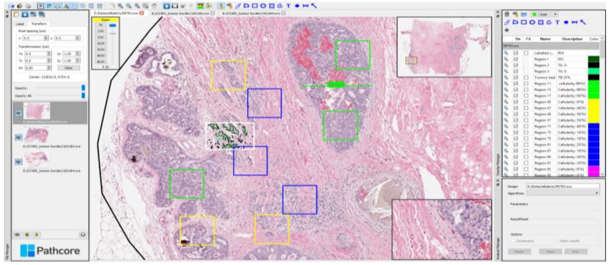


Auto TMA spot extraction

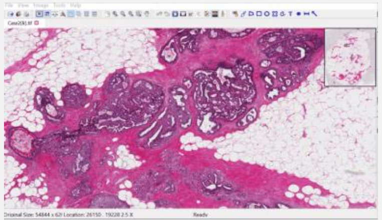


Out of Focus Detection

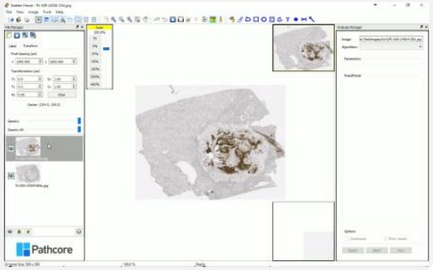




Stain Analysis

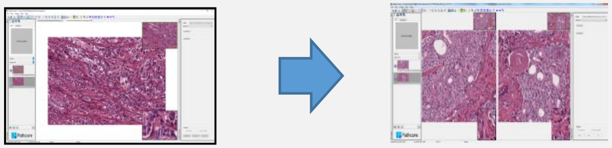


Automatic registration

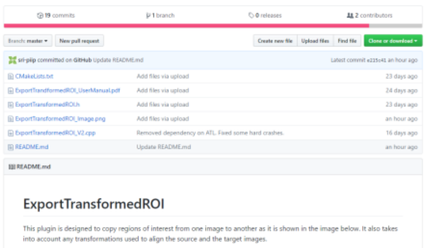


Human Factors Engineering

- Understanding cognitive challenges informs use cases
- Identifying useful leverage points and 'design seeds'
- Improving usability by modifying interface



Opensource - Github



sri-piip committed on GitHub Update README.md — Latest commit e215c41 an hour ago

CMakeLists.txt	Add files via upload	23 days ago
ExportTrandformedROI_UserManual.pdf	Add files via upload	24 days ago
ExportTransformedROI.h	Add files via upload	23 days ago
ExportTransformedROI_Image.png	Add files via upload	an hour ago
ExportTransformedROI_V2.cpp	Removed dependency on ATL. Fixed some hard crashes.	16 days ago
README.md	Update README.md	an hour ago

README.md

ExportTransformedROI

This plugin is designed to copy regions of interest from one image to another as it is shown in the image below. It also takes into account any transformations used to align the source and the target images.

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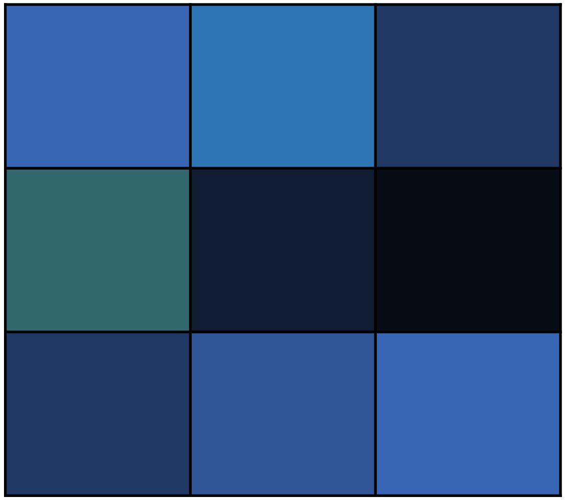
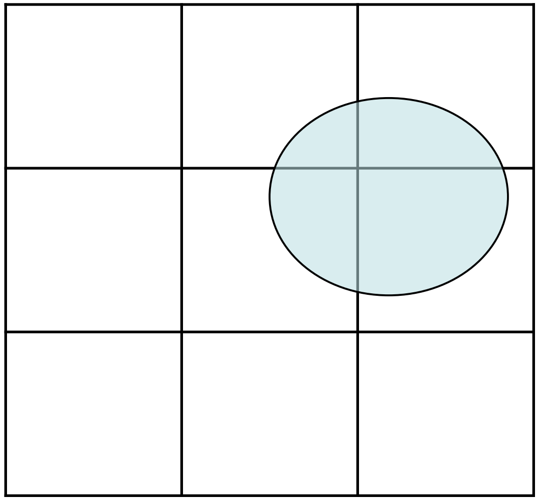
Plugins and the SDK

- Written in C++
- Support for ITK and openCV
- CMake is used for compilation, doxygen documentation
- Algorithm developer is shielded from details of file structure
- SDK provides utilities to efficiently access pixel data



Tile access – colour manipulation



Pixel access – morphology

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Plugins and the SDK

- Pipeline consists of a chain of kernels
- Kernel objects carry out specific tasks
- Each kernel may have parameters which can be set using controls exposed in the user interface
- Kernels can also access image metadata

Source Image → Color Selection → Thresholding → Morphology Closing → Cache → Output Image

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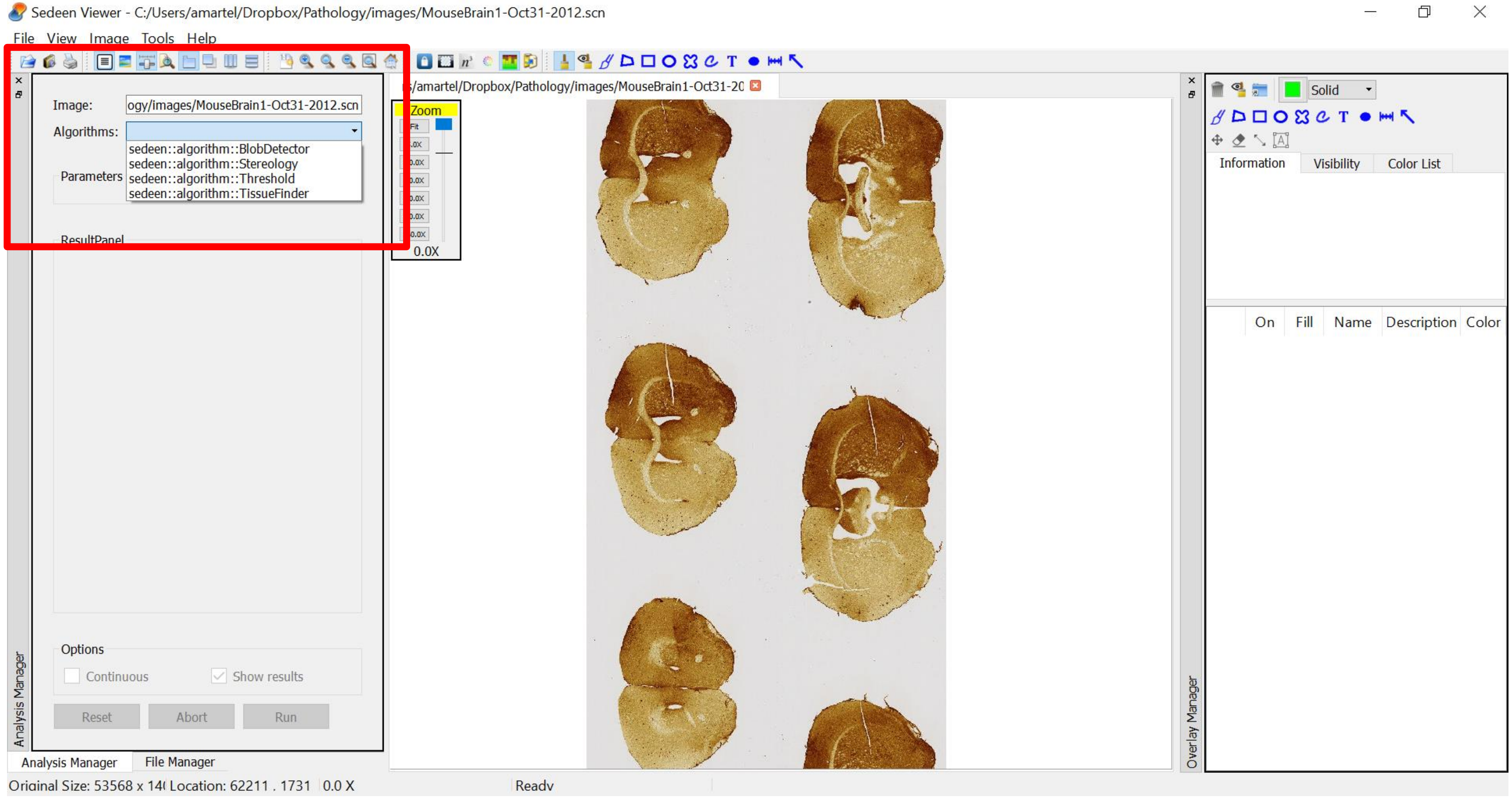
Example plugin: tissue finder



Sedeen Viewer - C:/Users/amartel/Dropbox/Pathology/images/MouseBrain1-Oct31-2012.scn

Image: ogy/images/MouseBrain1-Oct31-2012.scn

Algorithms:

- sedeen::algorithm::BlobDetector
- sedeen::algorithm::Stereology
- sedeen::algorithm::Threshold
- sedeen::algorithm::TissueFinder

Options

☐ Continuous ☑ Show results

Original Size: 53568 x 14(Location: 62211 . 1731 0.0 X Ready

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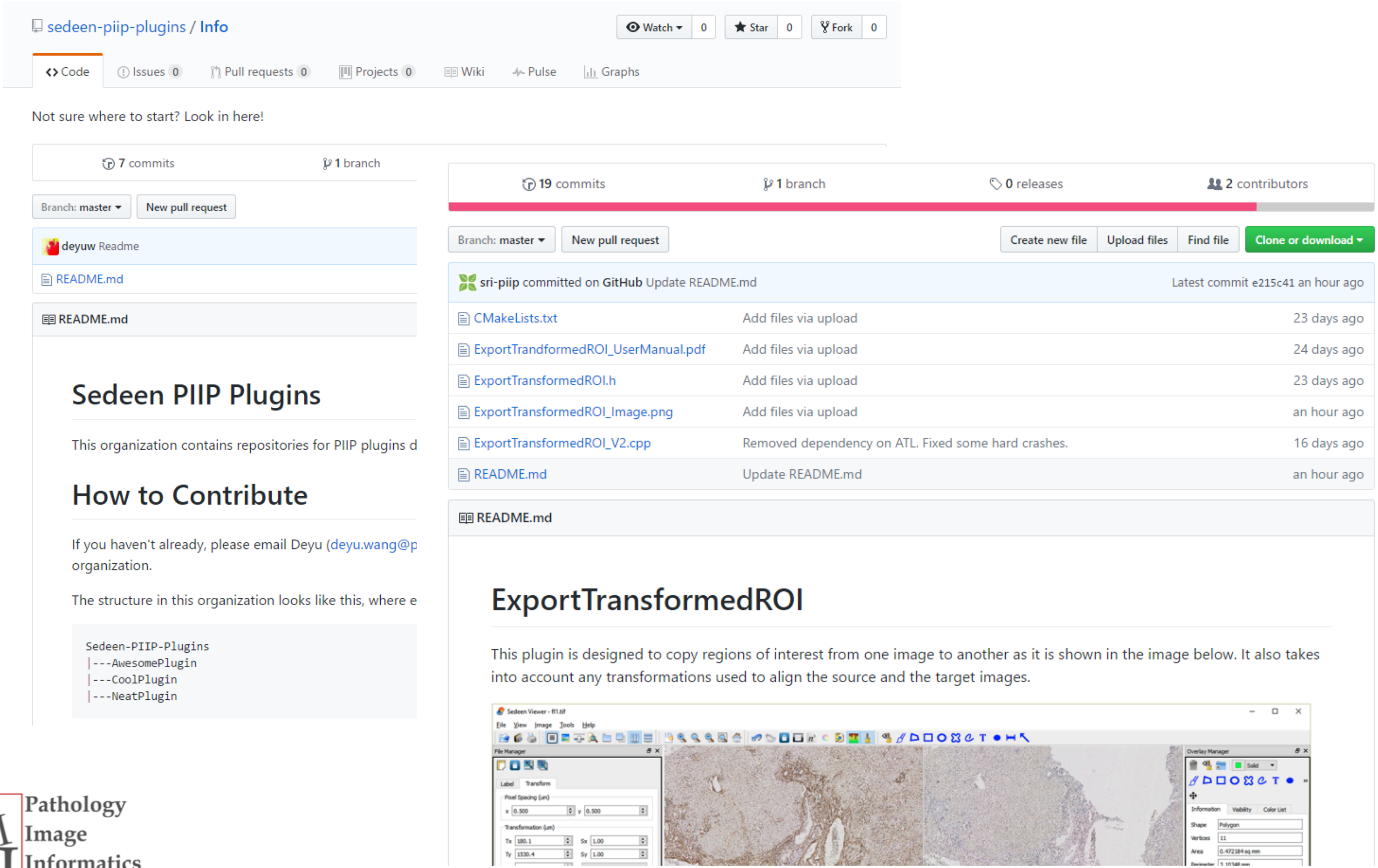
Plugins loaded from a drop down menu

github.com/sedeen-piip-plugins/



Not sure where to start? Look in here!

deyuw Readme

README.md

README.md

Sedeen PIIP Plugins

This organization contains repositories for PIIP plugins d

How to Contribute

If you haven't already, please email Deyu (deyu.wang@p
organization.

The structure in this organization looks like this, where e

```
Sedeen-PIIP-Plugins
|---AwesomePlugin
|---CoolPlugin
|---NeatPlugin
```

sri-piip committed on GitHub Update README.md — Latest commit e215c41 an hour ago

CMakeLists.txt	Add files via upload	23 days ago
ExportTrandformedROI_UserManual.pdf	Add files via upload	24 days ago
ExportTransformedROI.h	Add files via upload	23 days ago
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README.md

ExportTransformedROI

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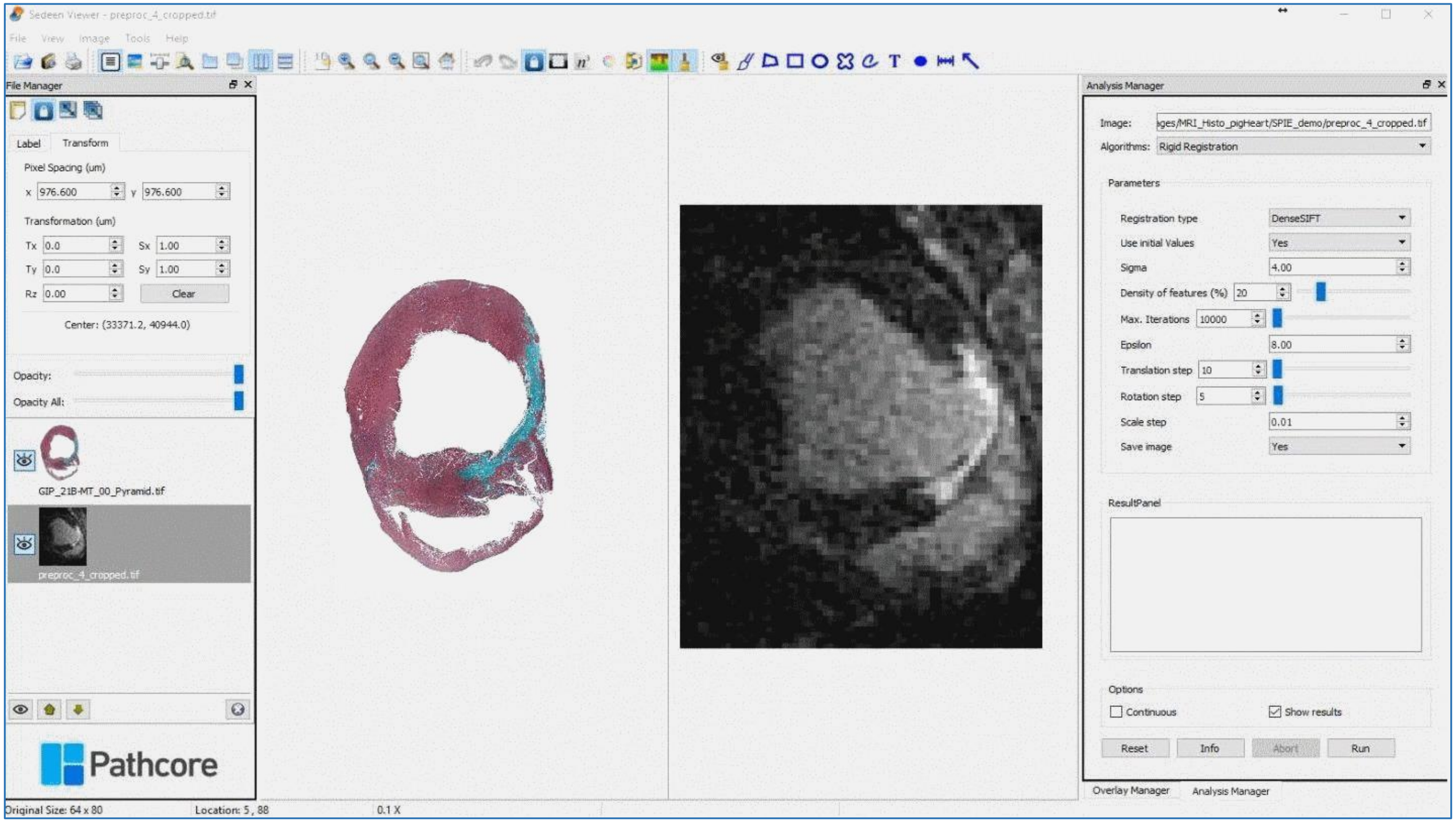
Rigid registration and Export Transformed ROI Plugins for Radiology Pathology Fusion



Pixel Spacing (um)

x 976.600 y 976.600

Transformation (um)

Tx 0.0 Sx 1.00

Ty 0.0 Sy 1.00

Rz 0.00 Clear

Center: (33371.2, 40944.0)

Image: ages/MRI_Histo_pigHeart/SPIE_demo/preproc_4_cropped.tif

Algorithms: Rigid Registration

Parameters	
Registration type	DenseSIFT
Use initial Values	Yes
Sigma	4.00
Density of features (%)	20
Max. Iterations	10000
Epsilon	8.00
Translation step	10
Rotation step	5
Scale step	0.01
Save image	Yes

☐ Continuous ☑ Show results

Original Size: 64 x 80 Location: 5 , 88 0.1 X

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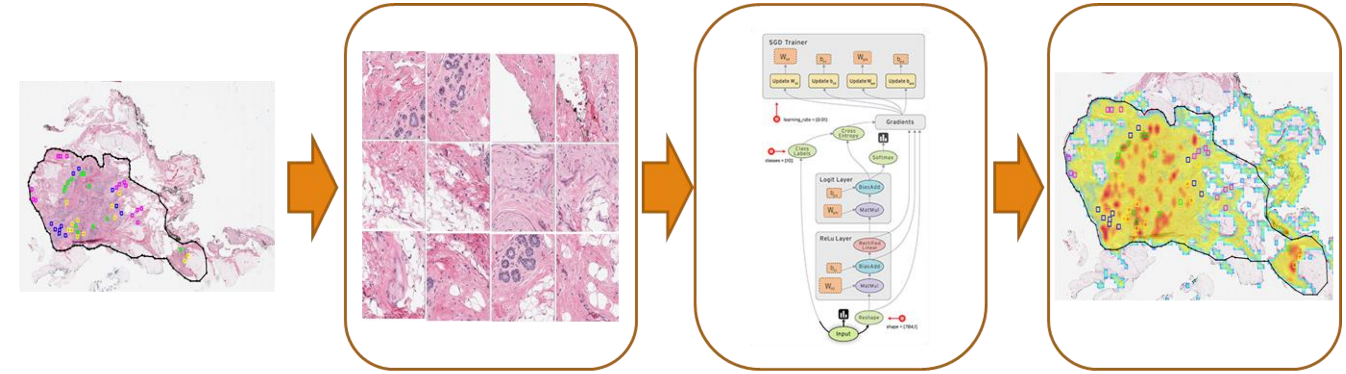
Deploying Machine Learning Models

- ☐ Aim to develop an end-to-end pipeline to deploy machine learning models using Sedeen SDK.
- ☐ Designed to facilitate the testing of pre-trained models
- ☐ This project was developed based on Tensorflow C++ API, Boost C++ Library, and Keras (for Python scripting).



Typical Digital Pathology Image | TileExtraction Plugin | MLModelDeployer Plugin | ColorMap Plugin

Deployment pipeline: This figure demonstrates the deployment pipeline. Please refer to PIIP repository at https://github.com/sedeen-piip-plugins for more information regarding the plugins.

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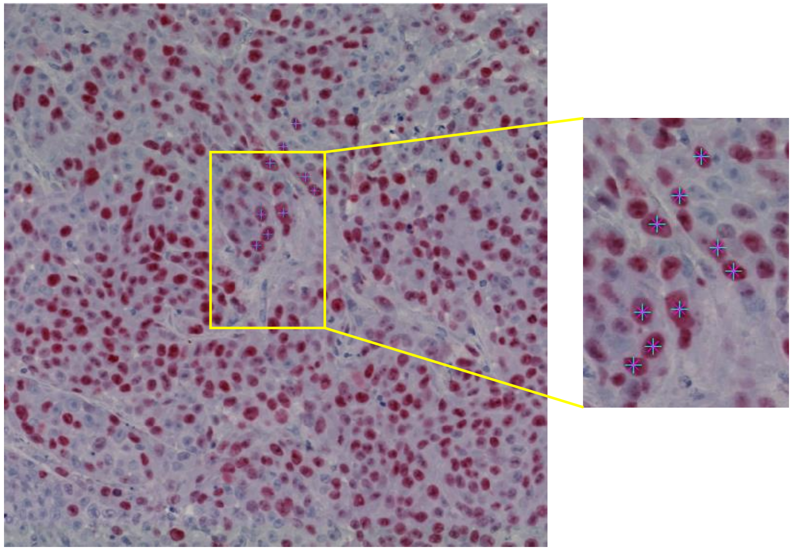
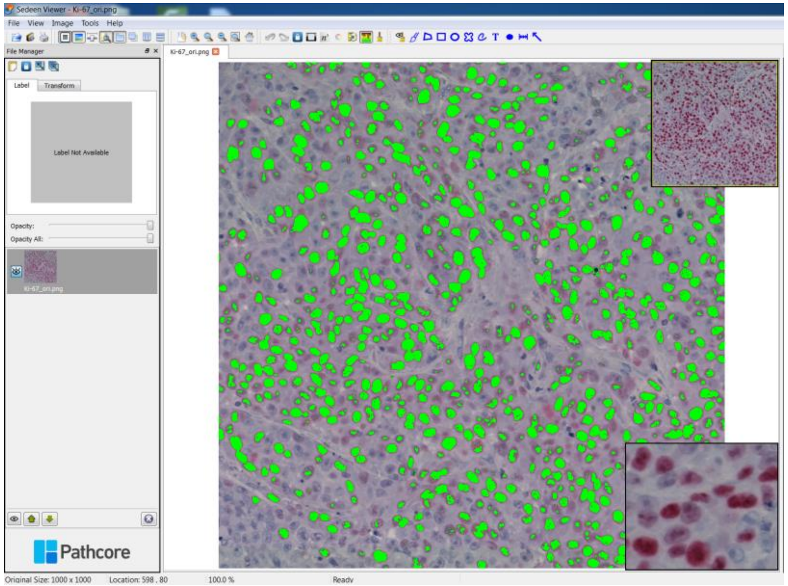
HNCut Plugin

- Hierarchical Normalized Cuts (HNCut) algorithm [1] combines the normalized cuts algorithm with mean shift clustering. HNCut can help pathologists to both quantify and annotate immunohistochemically stained slides by allowing them to identify all pixels that fit within a specific color space. The approach is minimally interactive, requiring the user to select just a few representative pixels from the color region of interest.



(a) The user randomly selects a few representative points.



(b) HNCut helps to quantify Ki-67 stained tumor nuclei based on the selected points.

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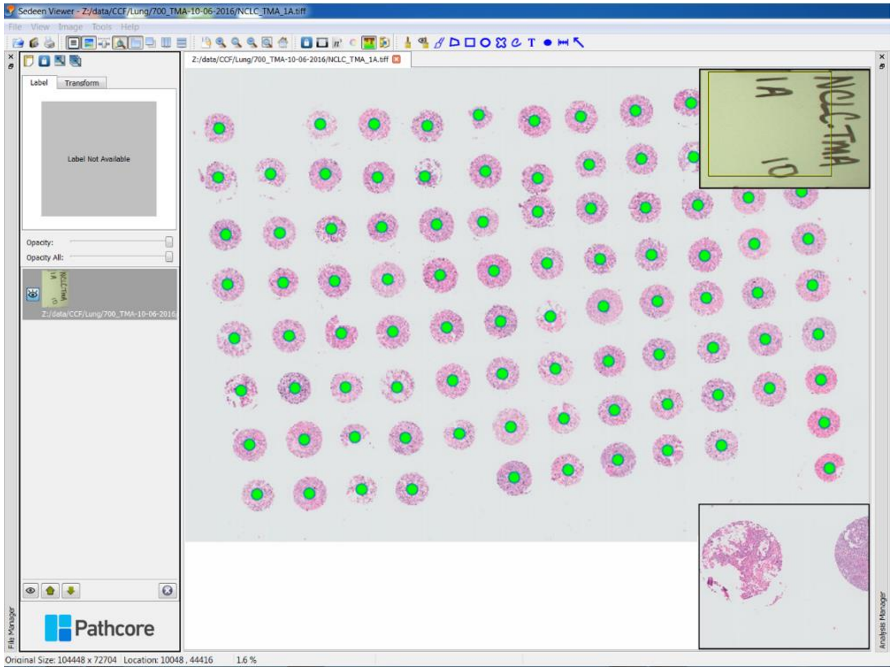
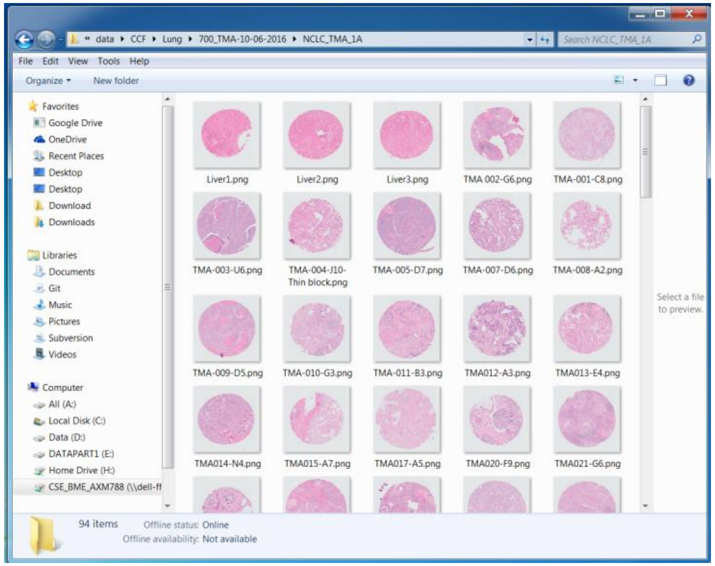
[1] Janowczyk, A. et al ., Hierarchical normalized cuts: Unsupervised segmentation of vascular biomarkers from ovarian cancer tissue microarrays. In: Medical Image Computing and Computer-Assisted Intervention: MICCAI 2009. LNCS, vol. 5761, pp. 230–238. Springer, Heidelberg (2009).

TMA Spot Extraction Plugin

- Color deconvolution algorithm is applied to the down sampled whole slide image to find the regions, which have the most, signal intensities to hematoxylin and eosin (H&E) stain. Then, circular Hough transform based algorithm was iteratively used to detect the only circular regions as tissue samples.



(a) Result of automatic TMA spot extraction in Sedeen Viewer. The detected spots are labeled in green dots.



(b) Extracted spots are saved as 2,000 x 2,000 png images (b)

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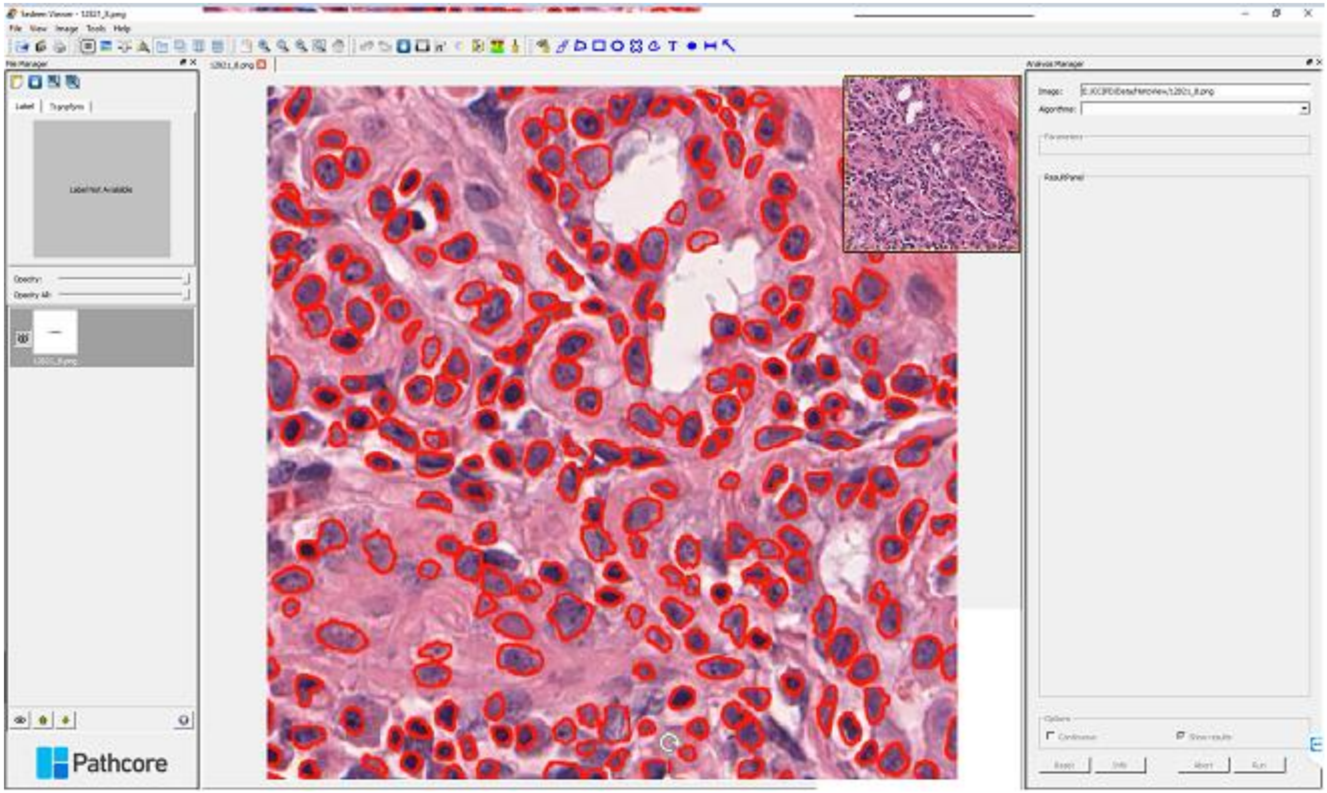
Marker-controlled Watershed Segmentation Plugin

- This unsupervised automatic method applies color deconvolution and morphological operations to the digital pathology images, followed by the fast radial symmetry transform to obtain the candidate nuclei locations, which act as markers for a marker-controlled watershed segmentation.



(a) Nuclei segmentation using Veta watershed segmentation algorithm.

Out of Focus Detector

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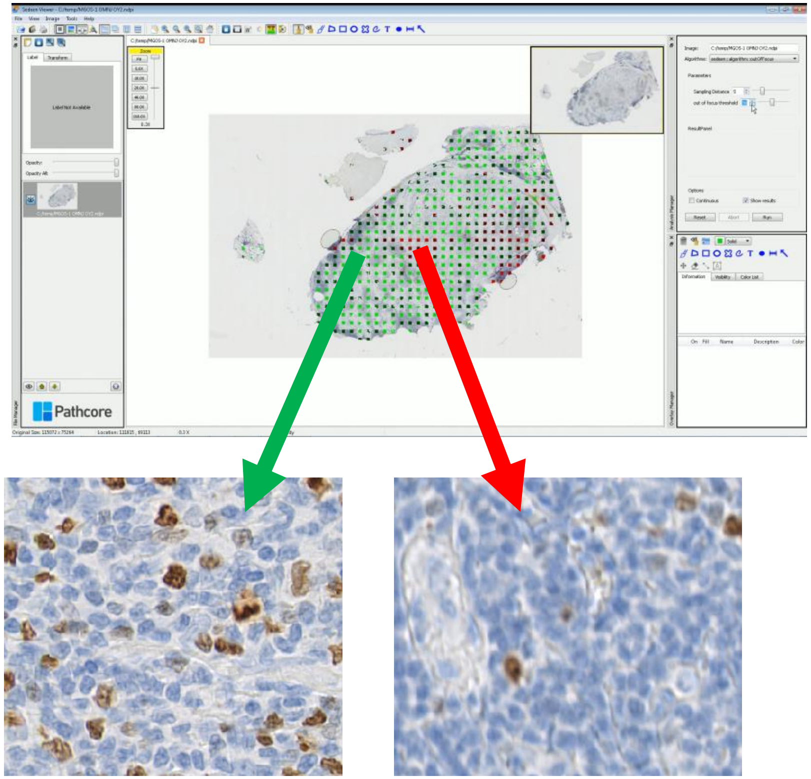
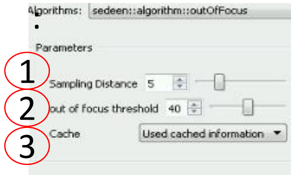


Function: The plugin scans the whole digital slide and finds out of focus regions.

Input: whole histopathology slide

Parameters

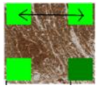

Algorithms: sedeen::algorithm::outOfFocus

Parameters

① Sampling Distance 5

② out of focus threshold 40

③ Cache Used cached information

① 

② Acceptable image quality

③ Save temporary results and use them when changing “out of focus threshold”

Output: Image quality mask.

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Task	**Deliverables**	**Y1**	**Y2**	**Y3**	**Y4**	**Y5**
Improve Plugin Framework	New version released Dec 2016, 4 updates in 2017, distribution mechanism established	🟩	🟩	🟩		
Documentation and Training	SDK documented, 2 training sessions for developers	🟩	🟩	🟩	▨	▨
Add existing algorithms	Cell segmentation, stain normalization, out of focus detection, biomarker quantification, TMA spots extraction	🟩	🟩	🟩	▨	▨
Rad-pathology co-reg	Automatic pipeline established	🟩	🟩	🟩	▨	▨
Algorithm Evaluation				▨	▨	▨
Create image repository	Pathcore Web made available	🟩	🟩	🟩		
Accrual of annotated WSIs	Collection of Ki67 WSIs in progress	🟩	🟩	▨	▨	▨
Otology creation	J Biomed Inform publication on QHIO	🟩	🟩	🟩	▨	
Conference Demos	SPIE 2018 presentation on PIIP			🟩	▨	▨
HCI feedback	Report on GUI from HCI expert		🟩	▨	▨	▨
Organize Grand Challenge					▨	▨

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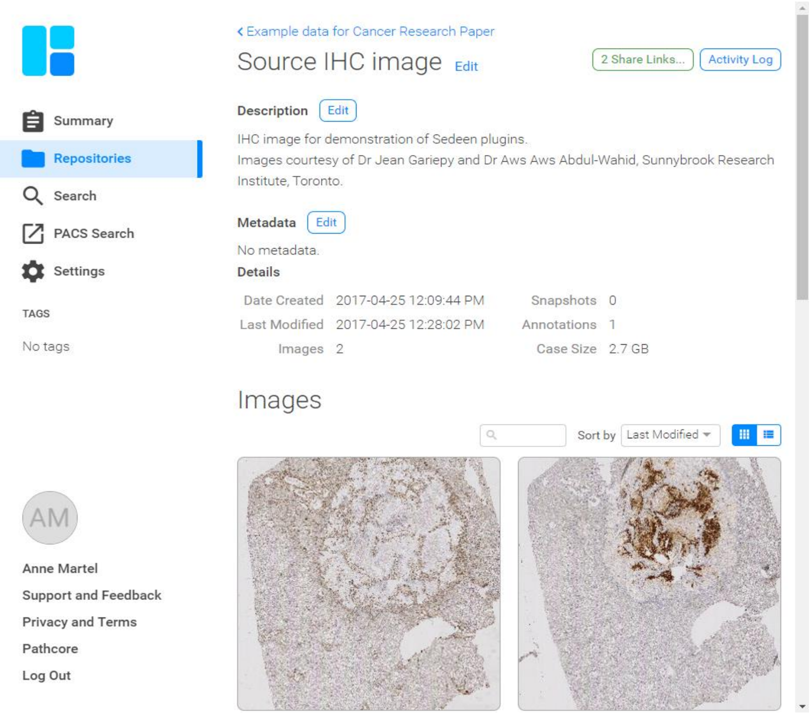
In the pipeline….

- Improved support for Matlab routines
- Mechanism to call Python procedures from plugin
- Distributing SDK to a wider research community
- MacOS and linux versions
- Support for web based image tile servers
- Collection of datasets for validation
- To integrate deep learning frame work into Sedeen

Curated Datasets

- Collect image databases
- Richly annotated by pathologists
- Develop ontologies
- Benchmark datasets



‹ Example data for Cancer Research Paper

Source IHC image

Description

IHC image for demonstration of Sedeen plugins.
Images courtesy of Dr Jean Gariepy and Dr Aws Aws Abdul-Wahid, Sunnybrook Research Institute, Toronto.

Metadata

No metadata.

Details

Date Created 2017-04-25 12:09:44 PM
Last Modified 2017-04-25 12:28:02 PM
Images 2
Snapshots 0
Annotations 1
Case Size 2.7 GB

Images

Images and annotations made available through PathcoreFlow™

Ulysses Balis, MD

Michael Feldman, MD, PhD

John Tomaszewski, MD, MASCP

Pathcore

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University *of* Pennsylvania

Sunnybrook
Research Institute

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