Institute of Molecular and Cell Biology

OUR RESEARCH

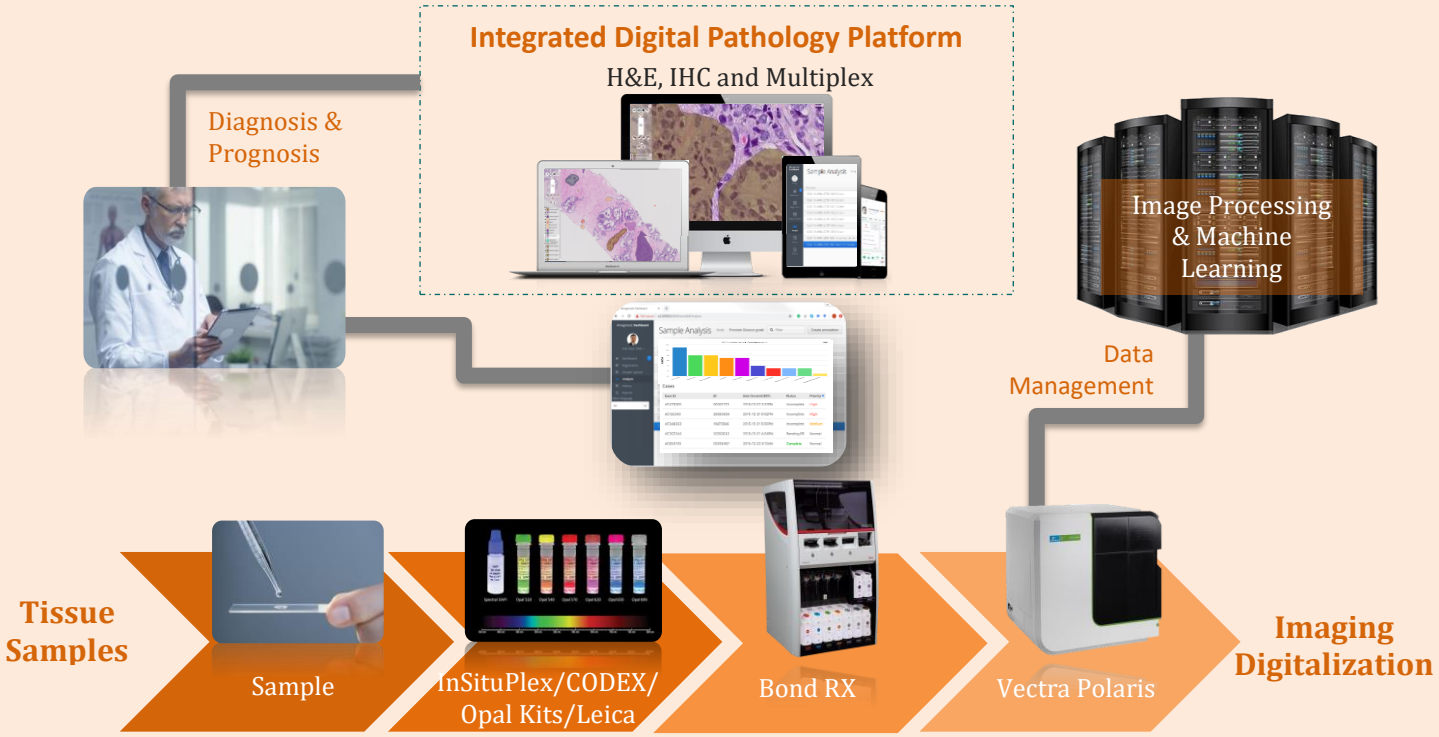
Computational & Molecular Pathology Lab (CMPL)

Our vision and objective is to tailor-make and prototype computational bioimage analysis solutions, including High throughput Screening (HTS) and High Content Screening (HCS), analysis of histology image/stacks in 2D/3D and general bio-image quantification methods. We also focus on developing novel image analysis algorithms for tricky problems in the field.

Our team focuses on the following topics in pathological/biomedical image analysis:

- *Developing novel computational image processing algorithms for basic scientific research, biomedical and drug discovery applications*
- *Developing practical industry-ready software packages for automated image/video analysis to improve clinical practice*
- *Building mathematic models for the classification/prediction using bioimage databases*
- *Developing kernel machine learning and deep learning solutions for big biological/biomedical imaging data.*

IMCB-A!maginostic Joint Service Platform



We offer a complete digital pathology approach from scanning to image analysis. The service platform is unique in that it can optimize pathology workflows, give pathologists and researchers advanced analysis capabilities, and better support clinical decisions and accelerate drug discovery.

Service available are:

- Specimen preparation and staining with fully automatic multiplex IHC stainer.
- Provides whole slide imaging scans and tissue microarrays (TMA) imaging scans.
- Available staining methods are InSituPlex Kit (Ultivue) and Opal Kit (Perkin Elmer).
- Hematoxylin and eosin (H & E) brightfield scanning objectives with 20x or 40x magnifications.
- Immunohistochemistry (IHC) brightfield scanning objectives with 20x or 40x magnifications.
- Multiple fluorescence immunohistochemistry (IHC) scans with 20x or 40x magnification of objective lens.
- Perform quantitative cell phenotyping analysis on multiplex images.
- Perform quantitative positive cell analysis on immunohistochemistry brightfield images.

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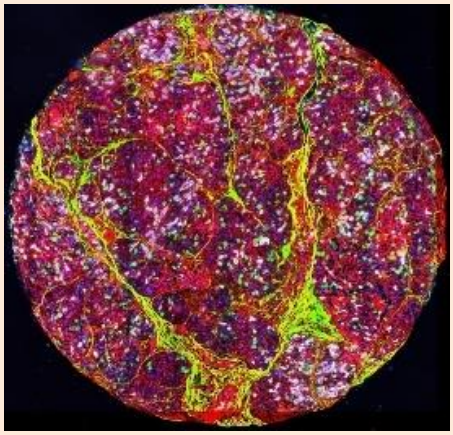
We have developed and proposed a digital pathology annotation platform to realize the concept of pathologist-AI interaction. The platform provides a highly interactive visual viewer and annotation tools to perform annotation tasks. AiHistoNote is developed for human elements. The modern look and style can improve readability and navigation.

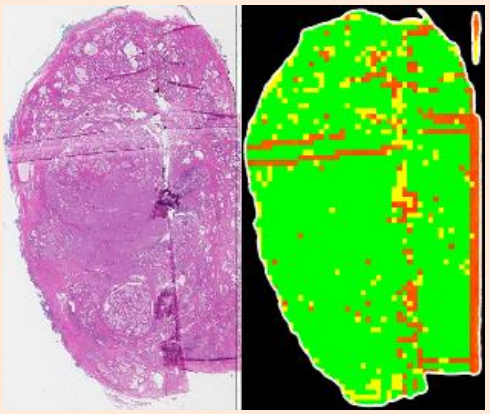
Therefore, it can enhance intuitive interaction and the efficient workflows. Senior pathologists at the National University Hospital of Singapore (NUHS) have used the platform to test and perform annotation tasks.

A!HISTONOTE H&E ANNOTATION & LEARNING TOOLS

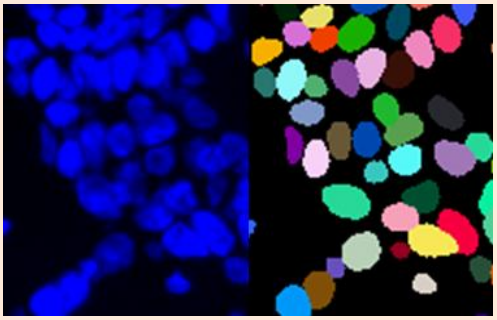


Multiplexed image of the tumour immuno-stromal microenvironment of triple negative breast cancer. Green cells: CD8 T cells, White cells: CD20 B cells, Pink nuclear cells: Regulatory T cells, Light red cells: Tumour cells, Green fibres: Stromal collagen. Red cells and green fibres were imaged on Genesis 200. Featured in The Straits Times, 16th December 2016, Beautiful Science section.

Fully Automated Quality Control of Whole Slide Images (H&E, 20X):
Digitalization of Pathology slides is the first crucial step for data archiving, remote pathology diagnosis, education, and the future development of computational analysis/diagnosis in clinical pathology. Here is a comprehensive solution to address WSI quality control requirements.



Nuclei Segmentation on Whole Slide Image of prostate (DAPI, 20X): Deep Learning Architecture allows for an accurate segmentation of clustered nuclei. An accurate nuclei segmentation pipeline is the cornerstone of cell-by-cell analysis and spatial distribution of biomarkers in Digital Pathology.



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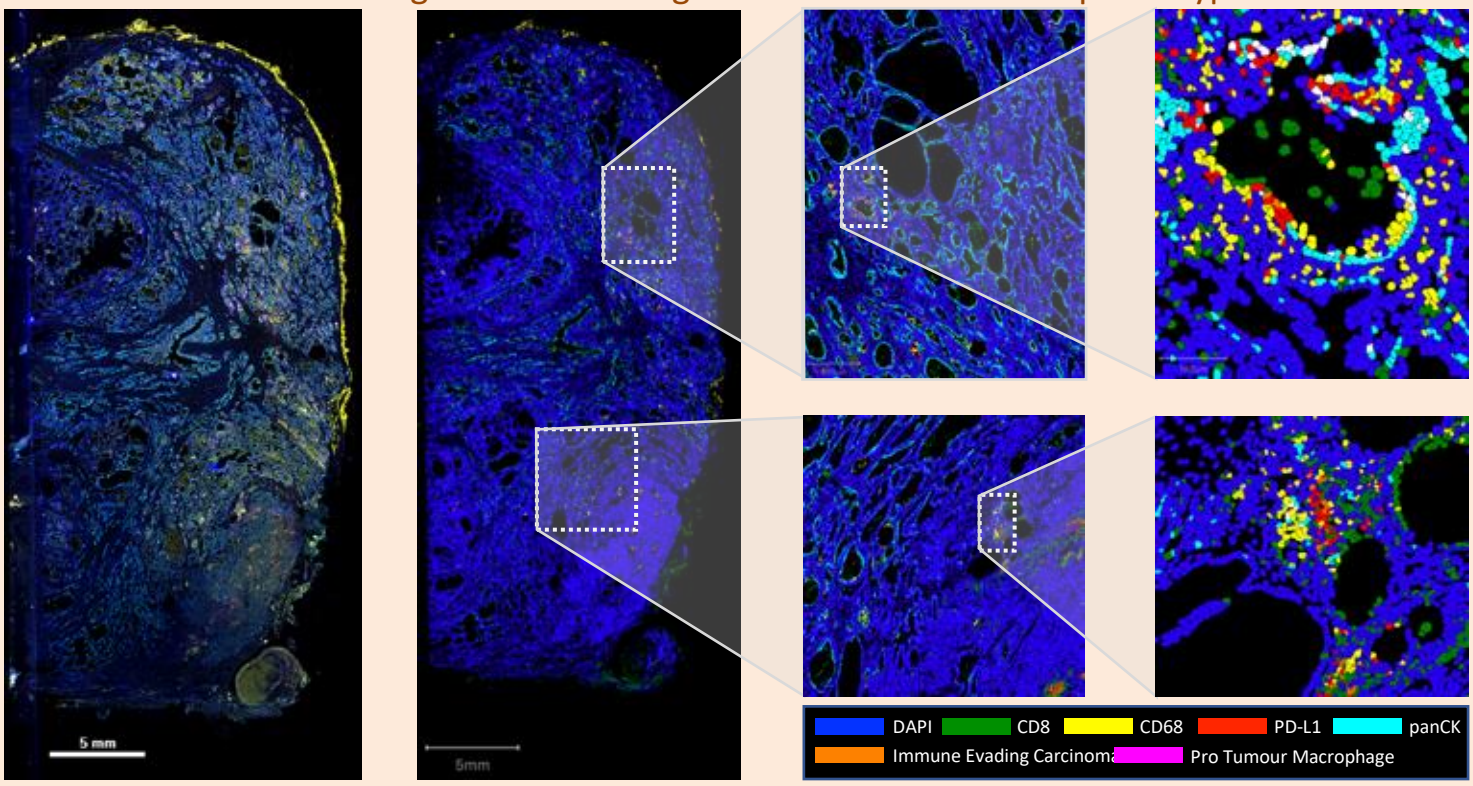
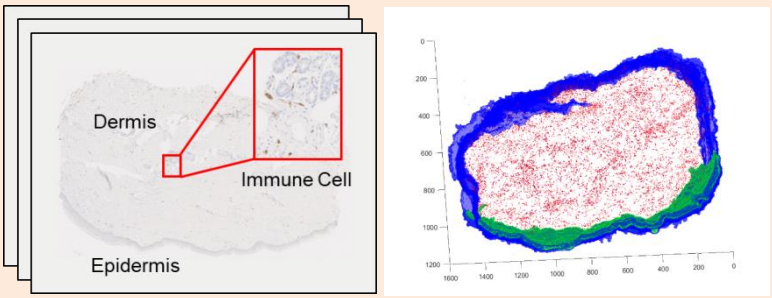
PD-L1 Image with nuclei segmentation and detected phenotypes



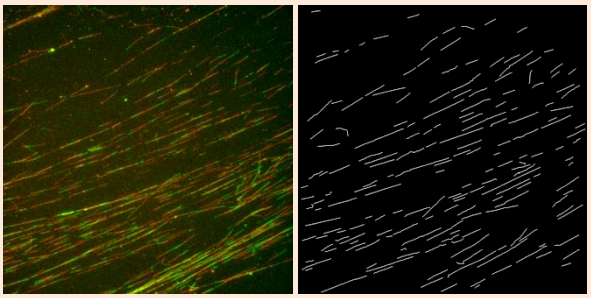
PD-L1 Whole Slide

Nuclei Segmentation with detected Phenotypes

Automated tumor-microenvironment analysis using multiplexed fluorescence imaging for Prostate Cancer. The whole slide image has been scanned using Ulti-Mapper I/O PD-L1 Kit. This WSI is processed using our in-house image analysis and quantification pipeline for immuno-phenotype quantification. Our method can analyse the tissue structure(s) at local (region-wise within WSI) and global (across multiple WSI) scales.



Semi-automatic skin tissue immune cell profiling solution. The quantitative 3D skin model can assist pathologists to have better understanding of immune cell spatial distribution in skin tissue. Figure: Continuous skin slices and reconstructed 3D skin model (green: epidermis, blue: dermis, red: immune cell).



Fully automatic DNA fiber analysis algorithm using DNA fluorescence image. It can provide accurate and unbiased DNA detection and quantification, and its processing speed is 10 to 100 times faster than manual solutions. Figure: DNA fluorescence image and DNA detection result.

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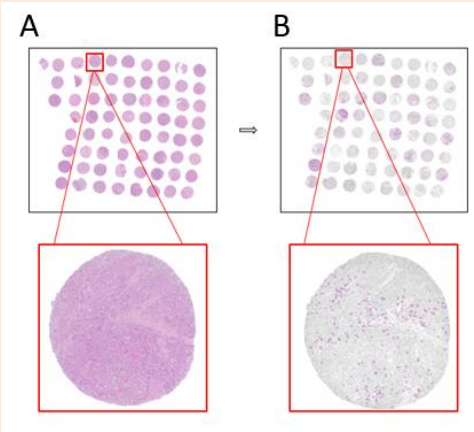
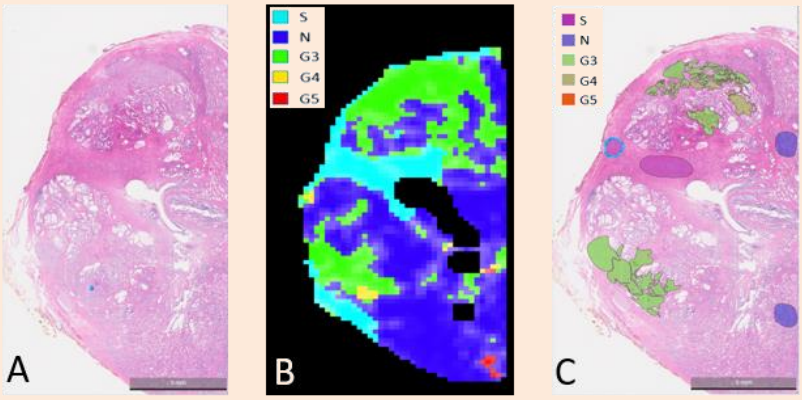
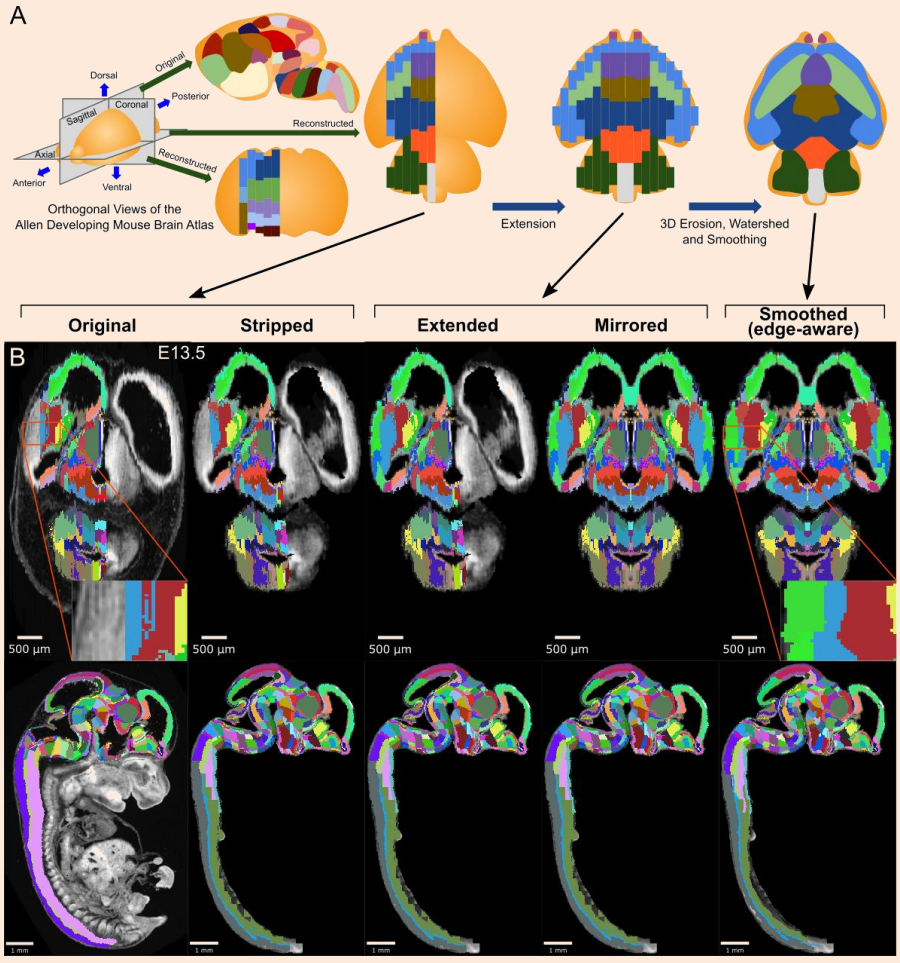


Semi-automated Mitosis Detection for Breast Cancer Histopathology Image. Pathologists can easily count the number of mitotic figures based on our detection result. (A) Original TMA image. (B) Visualization of the generated binary mask, which shows most of the mitotic figures.



Automated Gleason Grading for Prostate Cancer Histopathology Image. The solution will assist pathologists to calculate the Gleason Score for the diagnosis of Prostate Cancer(A) Original Whole slide image in testing set. (B) Heat map generated by our model (cyan: stroma, blue: normal, green: Gleason 3, yellow: Gleason 4, red: Gleason 5). (C) Ground truth annotated by pathologists from NUH.



3D Atlas Construction and Optimization Pipeline. (A) 2D-derived atlases, such as those in the Allen Developing Mouse Brain Atlas (ADMBA), are smooth and consistent in the sagittal plane in which they were annotated. However, in the 3D reconstructions of these 2D sagittal planes, the coronal and axial planes reveal missing sections and jagged edges. To improve their performance for annotating 3D data, the lateral edges are extended to complete the labeled hemisphere. A 3D rotation is applied to bring the brain parallel to the image borders, then both the completed hemisphere labels and underlying microscopy sections are mirrored across the sagittal midline to complete coverage in the opposite hemisphere. To improve anatomical registration, the labels are each eroded and re-grown through a 3D watershed, guided by the anatomical edge map. To smooth the final product, labels are iteratively filtered with a morphological filter. (B) The pipeline illustrated in axial (top) and sagittal (bottom) views on the ADMBA E13.5 atlas

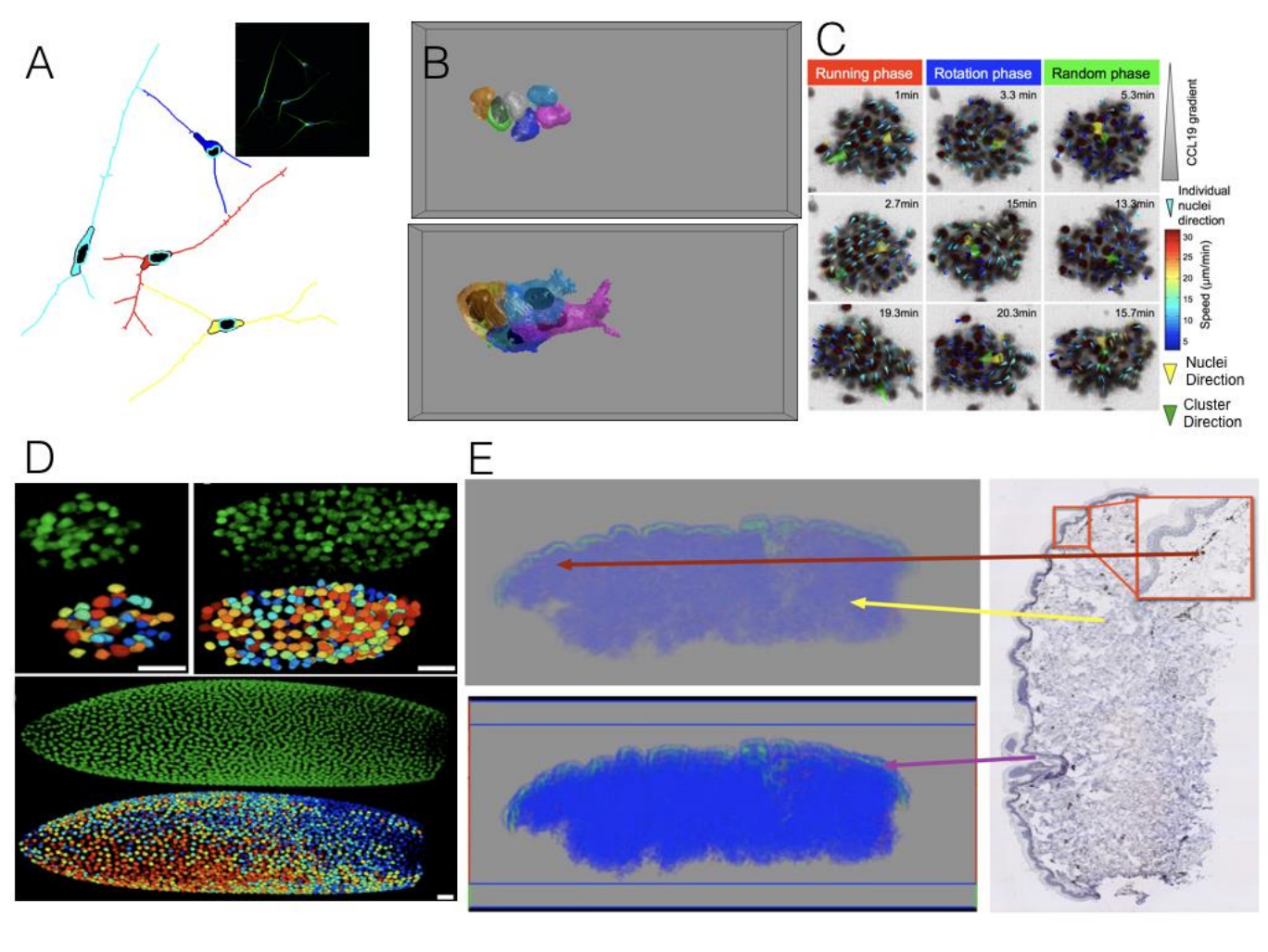


Figure 1. Image Analysis of different applications. (A) Segmented and traced neurite with crossing and touching [4]. (B). Segmented and tracking migrating border cells/nuclei with different cell identities in different colors. Two polar cells are in light and dark gray (Top). Reconstructed migrating cell surfaces in 3-D with nuclei in black and surface color representing the cell identities(Bottom). (C) Examples of the running, rotation, and random phases of a representative JVM3 cell cluster migrating along a 0–500 ng/ml CCL19 gradient. Thin color-coded arrows indicate individual nuclei directions over 20 s intervals. The large yellow arrow indicates the mean direction of the nuclei whereas the green arrow indicates the cluster direction. The length of the large green arrow indicates the value of group polarization. (D) 3D Segmentation of *Neurosphere*, *C.elegans* embryo and *Drosophila* embryo. 3D view of original images are shown in green and segmented results are shown by color coded objects (blue to red correspond at small to large volume). (E). 3D reconstruction of the skin samples with epidermis (green), dermis (blue) and T cells (brown in the zoom-in region).