Framework for Multispectral Imaging Application to digital pathology

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Multispectral imaging in pathology

• Brightfield
  • HE stain, Special stains, Immunohistochemistry (IHC) stains
  • Object detection, segmentation
  • Color unmixing – Stain amount image
  • Digital adjustment of staining strength
  • Digital staining

• Fluorescence
  • Simultaneous imaging of multiple markers
  • Cross-talk, auto-fluorescence removal
  • Combined brightfield and fluorescent images
Classification of B lymphocytes without staining

Spectral imaging:

- Nonproducing cells (NP)
- Ab producing cells A (PA)
- Ab producing cells B (PB)

* (Ab: antibody)

Live cell imaging and discrimination without any staining can be achieved using hyperspectral data.

Qualitative evaluation of live cells (eg. activation state of cells) is also possible.

Courtesy of EBA Japan
http://www.ebajapan.jp/English/index.html
General model for multispectral un-mixing

Original

Biomarker 1

Biomarker 2

⋯

Biomarker k

Input device

Multispectral image

Conversion (Un-mixing)

Estimated

Biomarker 1

Biomarker 2

⋯

Biomarker k

PSA, Ki-67, CK-19
HER2, ER, PgR, ...

Keep the original image

Describe the transform
Color unmixing for unwanted fluorescence removal

(Nuclei) (Blue) (Actin-Rhodamine Red) (Red) (Hypericin) (Cyan)
Combination of Fluorescent and HE-stain

HE Staining Process

Fluorescent Image

Registration

HE Color Image

Fluorescent Image + HE Color Image

Registration

Fluorescent Image + H Dye Image

Immunofluorescent Quantification Digital slides (IQD)


Courtesy of Department of Pathology, School of Medicine, Keio University
Solution to color unmixing by ICC v4

- Consider a virtual input device that can directly capture un-mixed biomarker images
- Use DeviceLink profile
Virtual ‘ideal’ input device
that can directly capture un-mixed biomarker images

Original

Biomarker 1

Biomarker 2

⋮

Biomarker k

Virtual Input device

1:1 correspondence

Estimated

Biomarker 1

Biomarker 2

⋮

Biomarker k

(Multispectral image)

Arbitrary combination of biomarker and fluorescence dye

Each channel represents each biomarker expression.

Biomarker image
Solution to color unmixing by iccMAX

• Spectral profiles
• Multi-processing elements
• Application of “Material Connection Space” Profiles
  • MCS connection allowed between source biomarker Material Identification (MID) and destination biomarker Material Visualization (MVIS) profiles

<table>
<thead>
<tr>
<th>Multispectral Device Channels</th>
<th>MID/Input Profile</th>
<th>MCS</th>
<th>MVIS Profile</th>
<th>PCS</th>
<th>Output Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCS Channel Id Tag</td>
<td>BM3</td>
<td>BM8</td>
<td>BM5</td>
<td>BM3</td>
<td>BM2</td>
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<td>BM5</td>
<td>BM1</td>
<td>Ø</td>
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Resulting Channel Connection
Current status

• Investigating the adoption of ICC v4 considering the upper compatibility in iccMax.
• Documentation for implementation to DICOM.
• Planning the test implementation of iccMax MCS approach for investigating its advantage and feasibility.

* We welcome contribution from anyone who can provide sample multispectral fluorescent images.