Automatic Non-rigid Histological Image Registration challenge

Jiri Borovec, Jan Kybic, Arrate Muñoz-Barrutia
https://anhir.grand-challenge.org
Organizers

Jiri Borovec
Jan Kybic
A. Muñoz-Barrutia
Ignacio Arganda
Dmitry Sorokin
Alexander Khvostikov
Maria Gloria Bueno Garcia
Motivation

- Consecutive histological slices
- Deformation due to cutting and handling, very thin cuts
- Registration needed to
  - combine information from different stains - protein/antigen colocalization
  - registration for 3D reconstruction

Challenges

- Large size *(most algorithms worked on scaled-down images)*
- Appearance differences
- Repeating structures
- Few unique landmarks
Task statement

- Sets of images
- Non-linear registration of pairs of images
- Submit transformed landmarks coordinates
Dataset overview

- **49 image sets**
  - 5 institutions - CIMA, MMIP, AIDPATH, IBA, RWTH
  - Average 5 images per set with min 3 and max 9
  - 481 image pairs - 230 training and 251 testing

- **8 tissue kinds**
  - Lung lesion, Lung lobes, Mammary glands, Mice kidney, COlon ADenocarcinoma, Gastric mucosa and gastric adenocarcinoma tissue, Human breast & kidney

- **18 different stains**
  - CD1a, CD31, CD4, CD68, CD8, CNEU, Cc10, EBV, ER, HE, HER2, Ki67, MAS, PAS, PASM, PR, Pro-SPC, aSMA

- **Original image sizes from 11k×6k up to 60k×75k pixels**

- **5 resolutions** - 0.174, 0.227, 0.468, 1.274, 2.294, 0.2528 [µm/pixel]
Landmark annotation

- Manual landmark identification using ImageJ
- Average scale used for annotation 25%
- Each image set was annotated once and validated independently
- Annotation time 113 + 106 hours and validation 32 + 5 hours
- 9 annotators and 3 validators

<table>
<thead>
<tr>
<th>Annotations</th>
<th>mean</th>
<th>std</th>
<th>min</th>
<th>max</th>
<th>median</th>
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<td>Images</td>
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<td>1.34</td>
<td>3.0</td>
<td>9.0</td>
<td>5.0</td>
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<td>Landmarks</td>
<td>86.44</td>
<td>28.87</td>
<td>27</td>
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<td>#1 [hours]</td>
<td>2.29</td>
<td>0.82</td>
<td>1.0</td>
<td>4.0</td>
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<td>#2 [hours]</td>
<td>2.16</td>
<td>0.77</td>
<td>1.0</td>
<td>4.0</td>
<td>2.0</td>
</tr>
</tbody>
</table>
Landmark verification

- Validation after fitting an affine transformation
- Co-annotation precision - 0.05% rTRE
Registration pairs

- We provide - all images, landmarks only for "training" images; for a set of 5:
  - 3 training image pairs (green) - with landmarks for both images
  - 6 testing image pairs (red) - with landmarks for one of the images

- Drop “symmetric” registration pairs - bottom left part of the table

<table>
<thead>
<tr>
<th>HE</th>
<th>PR</th>
<th>Ki67</th>
<th>CD31</th>
<th>Cc10</th>
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<tbody>
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<td>HE</td>
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<td>2</td>
<td>3</td>
</tr>
<tr>
<td>PR</td>
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<td>4</td>
<td>5</td>
<td>6</td>
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<tr>
<td>Ki67</td>
<td></td>
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<tr>
<td>CD31</td>
<td></td>
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<tr>
<td>Cc10</td>
<td></td>
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</tbody>
</table>
Evaluation criteria

- **Target registration error (TRE)**
  - $\text{TRE} = d_\rho(x^T_i, x^W_i)$; Euclidean distance between target and warped landmarks; [pixels]
  - Relative TRE (rTRE), TRE normalized by image diagonal [%]

- **Criteria**
  - Average $\text{dataset}$ Rank Median $\text{image}$ rTRE - winning criteria
  - Average $\text{dataset}$ Median $\text{image}$ rTRE - automatic leaderboard
  - Average $\text{dataset}$ Robustness - $\text{avg}_\text{image} \text{TRE}_{\text{final}} < \text{avg}_\text{image} \text{TRE}_{\text{initial}}$
  - Normalized execution time [minutes]
  - Median $\text{dataset}$ Median $\text{image}$ rTRE
Implementation (web & frameworks)

- Hosting web and evaluation
  - [https://anhir.grand-challenge.org](https://anhir.grand-challenge.org)
- Dataset: histology landmarks
  - [https://borda.github.io/dataset-histology-landmarks](https://borda.github.io/dataset-histology-landmarks)
- BIRL: Benchmark on Image Registration methods with Landmark validation
  - [https://borda.github.io/BIRL](https://borda.github.io/BIRL)
Statistics of the participants

- Participants counts
  - 256 joined
  - 250 data downloads
  - 11 submitting
  - 6 invited to ISBI’19 workshop

- Geographical distribution
  - 32 countries
  - 162 institutions
  - 143 departments
Submissions over time

The time is the count to deadline in days
Timeline: Avg. Median rTRE

![Timeline Graph]

- Users: Mohammed, zsyzzsoft, zhaoshuaibit, punithakumar, HistoReg, pszma2, delamoer, baihaozi12, IMW, masi, Borda, nick.weiss, Ludovic_Venet, PMG_Shuai

- Ranking: D12, D11, D10, D9, D8, D7, D6, D5, D4, D3, D2, D1, D0

- Deadline_days: 12, 10, 8, 6, 4, 2, 0

- Average-Median rTRE: 0.10, 0.08, 0.06, 0.04, 0.02, 0.00
Robustness
Execution time [minutes/image pair]
Leaderboard

### Results

<table>
<thead>
<tr>
<th>#</th>
<th>User (Team)</th>
<th>Created</th>
<th>TRRE</th>
<th>Time</th>
<th>Robustness</th>
<th>Comment</th>
<th>Publication</th>
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<tbody>
<tr>
<td>1</td>
<td>HistoReg</td>
<td>31 March 2019</td>
<td>0.00279</td>
<td>1.45119</td>
<td>1.00000</td>
<td>final_40_40_6_5</td>
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<tr>
<td>2</td>
<td>zhaoessahei (CASIA-Genwis)</td>
<td>1 April 2019</td>
<td>0.00347</td>
<td>6.09852</td>
<td>0.99792</td>
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<td>3</td>
<td>IMW (AGH UST)</td>
<td>31 March 2019</td>
<td>0.00300</td>
<td>6.86368</td>
<td>0.99792</td>
<td>Maybe a final submission.</td>
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<td>4</td>
<td>nick.weiss (Fraunhofer MEVIS)</td>
<td>29 March 2019</td>
<td>0.00385</td>
<td>1.14539</td>
<td>0.99792</td>
<td>Weakly supervised test</td>
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<td>5</td>
<td>zsyszsoft</td>
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<td>delamoer</td>
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<td>0.00462</td>
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<td>7</td>
<td>maci (Blomage Informatics Tampere)</td>
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<td>0.00873</td>
<td>9.62843</td>
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<td>8</td>
<td>pszma2 (NMPN)</td>
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<td>0.02071</td>
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<td>9</td>
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<td>puntiahakumar</td>
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<td>0.05497</td>
<td>1.47093</td>
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</table>

Showing 1 to 10 of 10 entries.

Only the best published result for each participant is listed.
Median rTRE, evaluation vs. training
Execution time, evaluation vs. training

[minutes per image pair]

- HistoReg
- Mohammed
- bUnwarpJ
- delamoer
- IMW
- masi
- nick.weiss
- pszma2
- punithakumar
- rNfityReg
- zhaoshuaibit
- zsyzzsoft

Execution times range from a few minutes to over 30 minutes per image pair.
Max rTRE, evaluation vs. training

Maximal rTRE from each image reg. pair

![Chart showing Max rTRE from each image registration pair](image)
Ranks of median rTRE, evaluation vs. training
Results

Weakness = - Robustness

Smaller is better
Ranks by criterion
Avg. & Median
Ranks by criterion, eval vs train
Avg. Median rTRE by tissue type
Avg. Robustness by tissue type
# Participants presentations

<table>
<thead>
<tr>
<th>Time</th>
<th>Authors</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:45</td>
<td>organizers</td>
<td><em>Introduction, challenge description and some statistics</em></td>
</tr>
<tr>
<td>15:00</td>
<td>Nazanin Tahmasebi, Michelle Noga, and</td>
<td>Cascaded Rigid Multi-Resolution and Moving Mesh Image Registration</td>
</tr>
<tr>
<td></td>
<td>Kumaradevan Punithakumar</td>
<td>Frameworks for Histological Image Registration</td>
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<tr>
<td>15:20</td>
<td>Masi Valkonen, Kimmo Kartasalo, Leena</td>
<td>Stain invariant elastic registration of histological sections</td>
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<tr>
<td></td>
<td>Latonen, Pekka Ruusuvuori</td>
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<tr>
<td>15:40</td>
<td>Yu Xiang</td>
<td>Stain deconvolution based pathological image registration</td>
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<tr>
<td>16:00</td>
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<td><em>coffee break</em></td>
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<tr>
<td>16:30</td>
<td>Johannes Lotz, Nick Weiss and Stefan</td>
<td>Robust, fast and accurate: A 3-step method for automatic histological</td>
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<td>Heldmann</td>
<td>image registration</td>
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<tr>
<td>16:50</td>
<td>Marek Wodzinski and Andrzej Skalski</td>
<td>Automatic nonrigid histological image registration with adaptive</td>
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<td></td>
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<td>multistep algorithm</td>
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<td>17:10</td>
<td>Ludovic Venet, Sarthak Pati, Paul</td>
<td>Accurate and robust alignment of variable-stained histological images</td>
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<td></td>
<td>Yushkevich,Spyridon Bakas</td>
<td>using a general-purpose greedy diffeomorphic registration tool</td>
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<tr>
<td>17:30</td>
<td>organizers</td>
<td><em>prize giving ceremony, closing remarks</em></td>
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<tr>
<td>17:40</td>
<td>organizers</td>
<td><em>article planning (by invitation, for active participants)</em></td>
</tr>
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</table>
Final results
AND THE WINNERS ARE...
The ANHIR challenge organizers recognize the team formed by

Marek Wodzinski, Andrzej Skalski

as the final #3 ranked team in the image registration competition.


The organizers

April 11, 2019
The ANHIR challenge organizers recognize the team formed by
Ludovic Venet, Sarthak Pati, Paul Yushkevich, Spyridon Bakas
as the final #2 ranked team in the image registration competition.

J. Borovec, J. Kybic, A. Muñoz-Barrutia, I. Arganda-Carreras,
D. Sorokin, A.- Khvostikov, M. G. Bueno Garcia

The organizers

April 11, 2019
The ANHIR challenge organizers recognize the team formed by

Johannes Lotz, Nick Weiss, Stefan Heldmann

as the final #1 ranked team in the image registration competition.

J. Borovec, J. Kybic, A. Muñoz-Barrutia, I. Arganda-Carreras,
D. Sorokin, A.- Khvostikov, M. G. Bueno Garcia

The organizers

April 11, 2019

Sponsored by:
Final results
## Final results

<table>
<thead>
<tr>
<th></th>
<th>Avg-Median-rTRE</th>
<th>Avg-Norm-Time</th>
<th>Avg-Rank-Median-rTRE</th>
<th>Avg-Robustness</th>
<th>Median-Median-rTRE</th>
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<td>evaluation</td>
<td>training</td>
<td>evaluation</td>
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Closing remarks

- Picture time
- Future of the challenge
  - Re-opening submission with extended metrics
  - Future editions
- Journal publication
- Sponsors
ANNOUNCEMENTS

- Workshop on Biomedical Image Registration

- Special issue on Computer Vision methods for Microscopy

- COST action COMULIS (www.comulis.eu)

Research Topic

Computer Vision Methods for Microscopy

Frontiers in
Robotics and AI
Robot and Machine Vision

Frontiers in
ICT
Computer Vision and Image Analysis