Reconstruction of 3-D Histology Images by Simultaneous Deformable Registration

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Motivation

Creation of geometrically coherent 3-D histological volumes from serial 2-D sections is difficult due to sectioning process introducing artifacts and distortions (holes, folding, tears)

Current approaches:

- Registration between consecutive sections [e.g. Cifor et al, 2009]
  Problem: Drifts in stack direction
- Registration of sections to external reference (e.g. block-face) images [e.g. Bardinet et al, 2002]
  Problem: Smaller resolution, structural homogeneity between consecutive sections not guaranteed

Our approach: Registration of histological sections *simultaneously* to their corresponding reference images *and* to their neighboring sections

Problem Formulation

Given a set of histology images $\mathcal{I} = \{\mathcal{I}_1, \ldots, \mathcal{I}_n\}$ and their corresponding block-face images $\mathcal{J} = \{\mathcal{J}_1, \ldots, \mathcal{J}_n\}$, we seek a set of sufficiently smooth transformations $\mathbf{T} = \{T_1, \ldots, T_n\}$, which align each $\mathcal{I}_i$ to $\mathcal{J}_i$ and to its adjacent neighbors $\mathcal{I}_{i-1}, \mathcal{I}_{i+1}$:

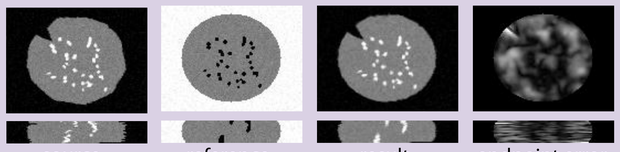
$$\mathbf{T}^* = \arg\min_{\mathbf{T}} \mathbf{E}_R(\mathcal{I}, \mathcal{J}, \mathbf{T}) + \mathbf{E}_C(\mathcal{I}, \mathbf{T}) + \mathbf{E}_S(\mathbf{T})$$

$\mathbf{E}_R(\mathcal{I}, \mathcal{J}, \mathbf{T})$: energy between histology images and block-face images
$\mathbf{E}_C(\mathcal{I}, \mathbf{T})$: energy between consecutive histology slices
$\mathbf{E}_S(\mathbf{T})$: independent *in-plane* regularizer

Evaluation

Synthetic data:

- Including tubular structures, tearing, random FFDs, staining, intensity variability, Gaussian noise
- Quantitative evaluation

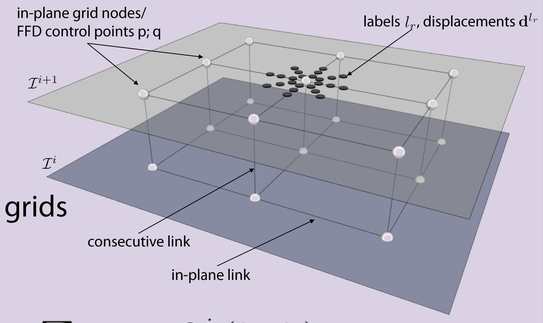


Real data:

- Rat kidney, HE staining
- 580 sections of 9 µm thickness

Markov Random Fields for Simultaneous Registration

- Uniform 2-D free-form deformation (FFD) grid for each T_i
- MRF [Glocker et al, 2008]: Assignment of a node to each control point of an FFD grid $\mathcal{G}^i$
- Creation of links between neighboring in-plane control points and neighbors in consecutive FFD grids
- Minimization of MRF energy $\mathbf{E}$ for labeling l



$$\mathbf{E}(\mathbf{l}) = \sum_{i=1}^{n} \sum_{\mathbf{p}\in\mathcal{G}^i} \Theta_R^i(l_\mathbf{p}) + \gamma \sum_{i=1}^{n-1} \sum_{\substack{\mathbf{p}\in\mathcal{G}^i,\\ \mathbf{q}\in\mathcal{G}^{i+1}}} \Theta_C^{i,i+1}(l_\mathbf{p}, l_\mathbf{q}) + \lambda \sum_{i=1}^{n} \sum_{\mathbf{p}\in\mathcal{G}^i} \sum_{\mathbf{r}\in\mathcal{N}(\mathbf{p})} \Theta_S^i(l_\mathbf{p}, l_\mathbf{r})$$

with weighting factors γ, λ, the set of in-plane neighbors $\mathcal{N}$ of control point $\mathbf{p}$, and costs

$$\Theta_R^i(l_\mathbf{p}) = \int_{\Omega_i} \eta(\mathbf{x}, \mathbf{p}) D_1(\mathcal{I}_i(\mathbf{x} + \mathbf{d}_{l_\mathbf{p}})), \mathcal{J}_i(\mathbf{x}))d\mathbf{x}$$

$$\Theta_C^{i,i+1}(l_\mathbf{p}, l_\mathbf{q}) = \int_{\Omega_i} \eta(\mathbf{x}, \mathbf{p})\eta(\mathbf{x}, \mathbf{q}) D_2(\mathcal{I}_i(\mathbf{x} + \mathbf{d}_{l_\mathbf{p}}), \mathcal{I}_{i+1}(\mathbf{x} + \mathbf{d}_{l_\mathbf{q}}))d\mathbf{x}$$

$$\Theta_S^i(l_\mathbf{p}, l_\mathbf{r}) = \int_{\Omega_i} R(\mathbf{d}_{l_\mathbf{p}}, \mathbf{d}_{l_\mathbf{r}})d\mathbf{x}$$

where D_1 and D_2 are dissimilarity measures using normalized mutual information and normalized crossed correlation, the regularizer R uses the squared difference between displacement vectors, and η controls the influence of a control point to a pixel

Conclusion

- Fully automatic reconstruction of 3-D histology stacks
- Geometrical coherence by simultaneous registration approach
- Increased accuracy and robustness against artifacts

Results

method	error measure AE	EE	IE	NE
initial alignment	50.84	1.57	26.06	13.28
histology-to-block-face registration	36.26 (+28.68%)	1.22 (+22.29%)	17.70 (+32.08%)	9.13 (+31.25%)
consecutive registration	57.41 (-12.92%)	1.91 (-21.66%)	25.76 (+1.15%)	12.35 (+7.00%)
sequential approach	36.56 (+28.09%)	1.23 (+21.66%)	24.97 (+4.18%)	11.72 (+11.75%)
simultaneous approach	34.30 (+32.53%)	1.17 (+25.48%)	16.69 (+35.96%)	8.66 (+34.79%)

AE: relative angular error
EE: absolute endpoint error
IE: interpolation error
NE: normalized IE

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