Large-scale automated identification of mouse brain cells in confocal light sheet microscopy images

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http://bioinformatics.oxfordjournals.org/content/30/17/i587
Transgenic mouse cerebellum at the micron scale
(Slivestri et al., 2012)

Goal in this work: identification of all Purkinje soma in the whole cerebellum
Cell identification challenges

- Most existing tools designed to work with small/medium scale images
- Whole mouse cerebellum image: 120 GVoxel
- Over 200,000 Purkinje cells
- Wild variability, even locally within a single image
Mean shift cell identification

Soma center: center of “mass” of a set of voxels (a cluster)
Mean shift cell identification

One cluster for each soma!
Mean shift cell identification

Step 1: **Background removal** (max-entropy, 2 thresholds)
Mean shift cell identification

Step 2: **Seeding** (local maxima + average intensity in a ball of radius \( r \) above the background threshold)
Mean shift cell identification

2 parameters: *Seed ball radius* and *mean shift bandwidth*
Mean-shift on raw images

Test set: 56 hand-labeled substracks, 4138 soma centers

Precision
F1-Measure
Recall

Roughly the radius of smallest soma

Radius of the seed ball
Mean-shift on raw images

Test set: 56 hand-labeled substracks, 4138 soma centers

Mean shift kernel bandwidth

Precision
F1-measure
Recall

Roughly the radius of smallest soma
Semantic deconvolution as supervised learning

No cell segmentation, just use centers!
How to do semantic deconvolution

• Naive idea:
  • Use 3D patches of size $s$ as input to a neural net
  • Classify each voxel as soma vs non-soma
  • Running time: for an image of size $n$ it takes $O(hn^3s^3)$ when using a one-layer net with $h$ units
Our approach

- Predict $s^3$ voxels simultaneously in $O(2hn^3s^3)$ using a network with $s^3$ outputs.

- Using a stride of $d$ when moving the patch we may speedup the computation significantly $O(2hn^3s^3/d^3)$, e.g. for $d=4$ we get a 32x speedup over the naive approach.
Mean-shift on semantically deconvolved images

![Graph showing precision, recall, and F1-measure for different mean shift kernel bandwidths. The x-axis represents the mean shift kernel bandwidth, ranging from 3 to 7. The y-axis represents values from 0.3 to 1.0. There are two sets of data points: one for before and one for after processing. The precision, recall, and F1-measure values are indicated by different markers and lines.](image-url)
Mean-shift on semantically deconvolved images

Performance measures

- Recall
- F1-Measure
- Precision

Radius of the seed ball

<table>
<thead>
<tr>
<th>Radius of the seed ball</th>
<th>Before</th>
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Can we do better than F1=0.93?

- The cerebellum cortex folds into folia, i.e. manifolds
- Isolated / off-manifold predictions: mostly false positives
- Estimate manifold distance: charted Isomap + LOWESS
The filter gains 3 points of F1, halving false positive rate
A digital map of the whole mouse cerebellum
Conclusions

• Combination of three core ideas:
  • **Mean shift** clustering (F1=0.77)
  • Supervised **semantic deconvolution** (F1=0.93)
  • **Manifold modeling** (F1=0.96)

• Highly effective, performance not far from the intrinsic noise level (disagreement between two human labelings has F1=0.98)

• Suitable to **parallel processing** at several levels