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Computational Scratch Assay - A New Frontier for Image Analysis: Preliminary Study of Multi-Cellular Segmentation

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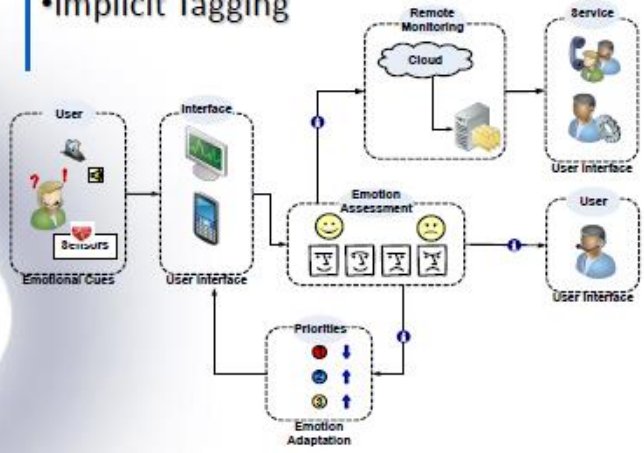
- Digital Camera Processing
- Biomedical Imaging
- Social Signal Processing
- Universal Multimedia Access

Biomedical

- Body Area Networks
- ECG/EEG Analysis
- Ultrasound Signal Processing

Brain-Computer Interface

- Emotion and Cognition Analysis
- Implicit Tagging



Biometrics & Surveillance

- Face Recognition
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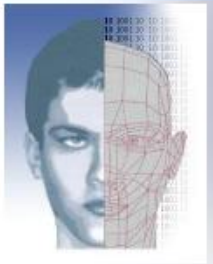
- Privacy Solutions
- Visual Surveillance



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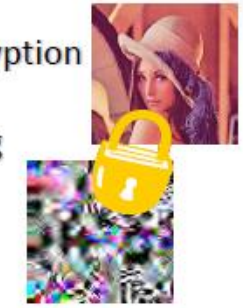
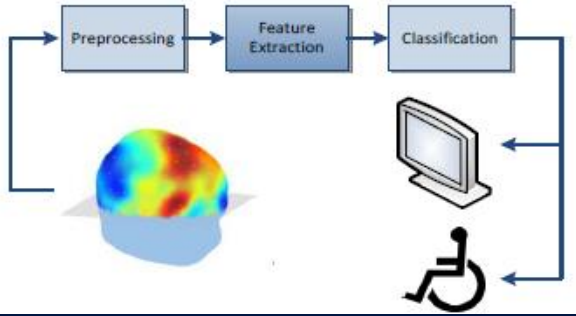
Multimedia Security

- Authentication
- Image & Video Encryption
- Secure Streaming
- Visual Secret Sharing



Social Media

- Biomarker and Neural Feedback
- Rehabilitation & Motor Imagery Detection



Outline

- Computational scratch assay
  - What is scratch assay?
  - What is computational scratch assay?
  - General framework
- Multi-cellular segmentation
  - Prior arts
  - Proposed multi-cellular segmentation algorithm
  - Comparative evaluation
- Conclusion

Image Analysis New Frontier: Computational Scratch Assay

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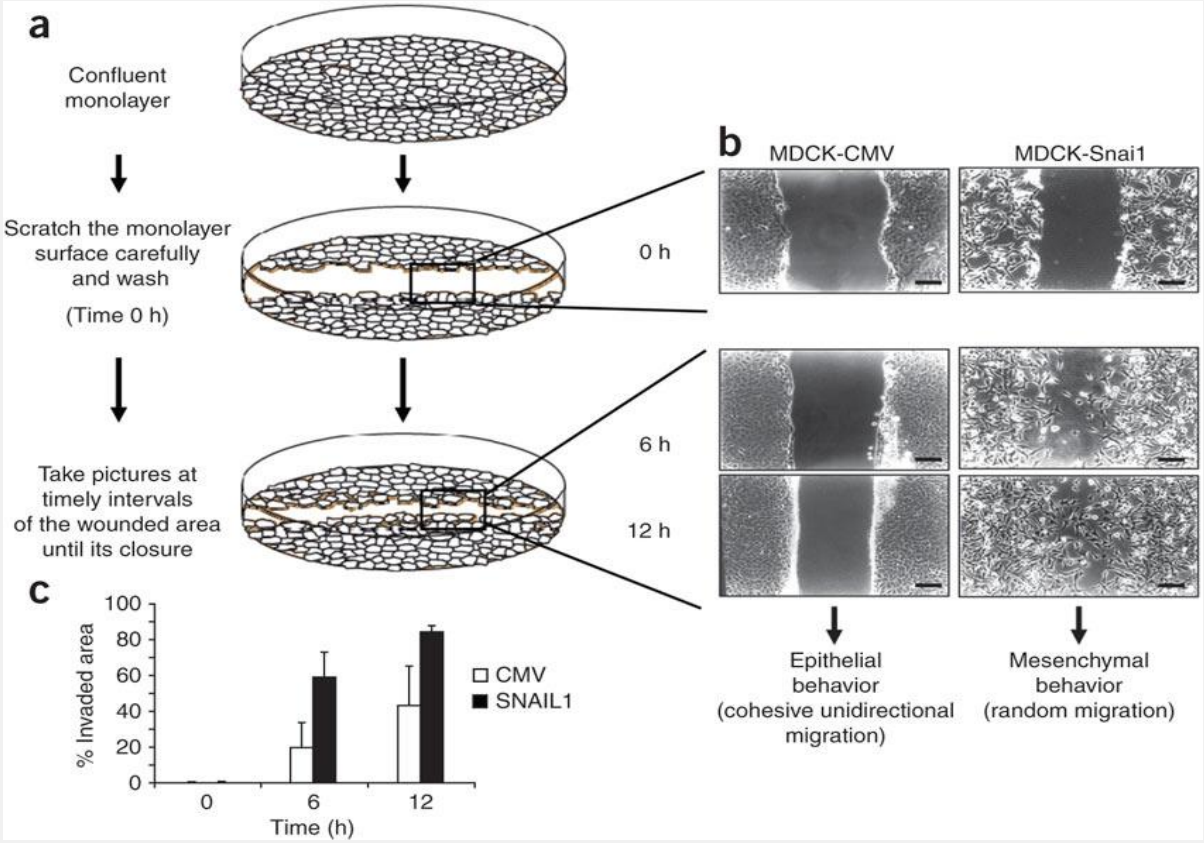
What Is Scratch Assay (SA)?

- SA (or wound healing assay) is a laboratory technique to study cell migration and inter-cell interaction.



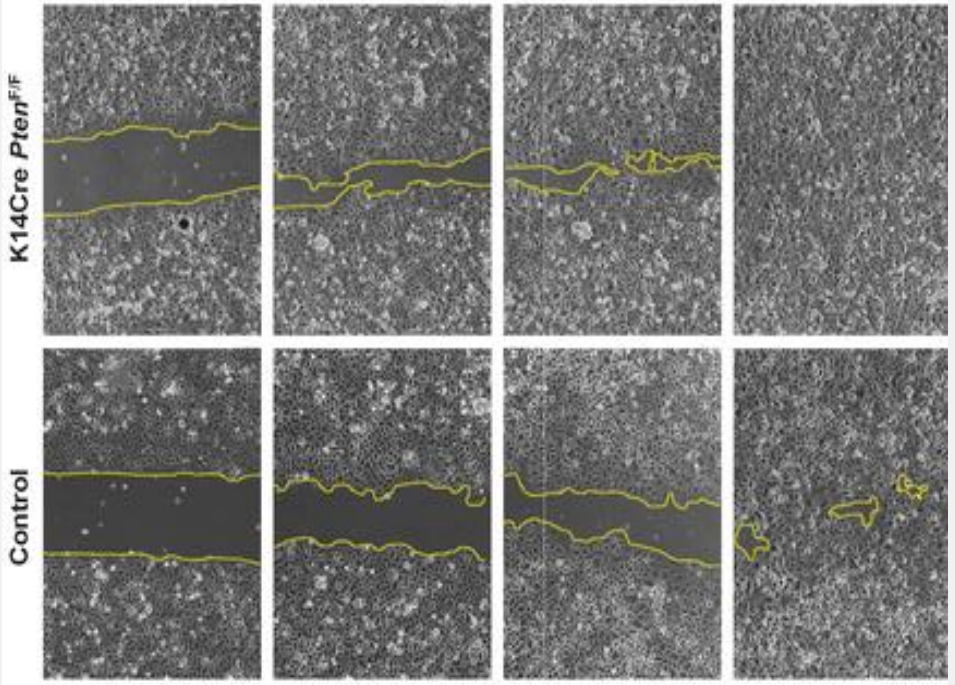
The figure is from Moreno-Bueno et al. “The morphological and molecular features of the epithelial-to-mesenchymal transition”, nature protocols, Oct. 2009.

Challenges In Scratch Assay

- Scratch front-edge tracing is a fundamental task in SA.

- SA is time-consuming.
  - ➢ Identifying the front-edge in each images manually.
  - ➢ Using multiple replicates for analysis quality.

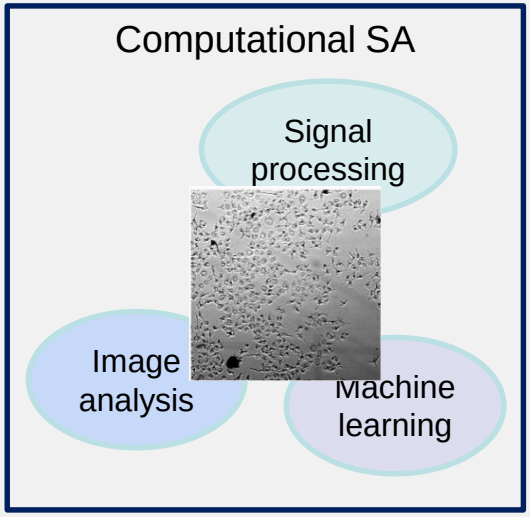
- SA is prone to subjective.



The figure is from Squarize et al. “Accelerated wound healing by mTOR activation in genetically defined mouse models”, PLOS one, May. 2010.

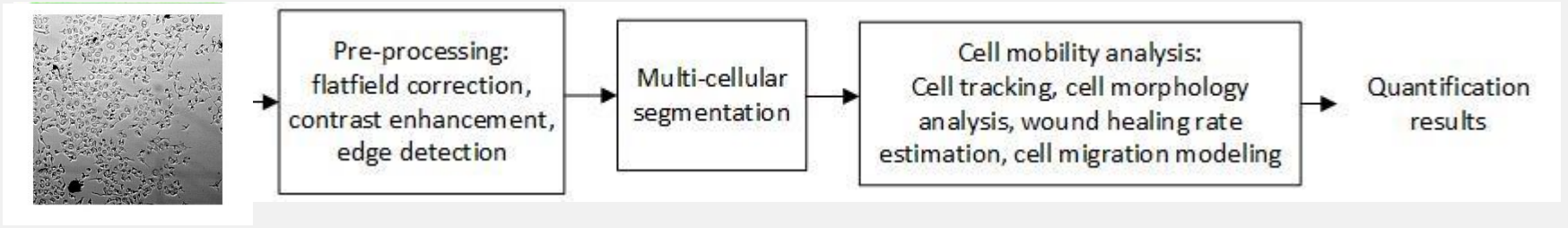
Computational Scratch Assay (CSA)

- CSA exploits advanced techniques to enable computers to do intelligent scratch assay.
  - ➢ Aiming for efficient & reliable analysis.



- CSA is in infancy.
  - ➢ Dedicated algorithms are under-developed.

- General analysis pipeline:



Preliminary Study: Multi-Cellular Segmentation

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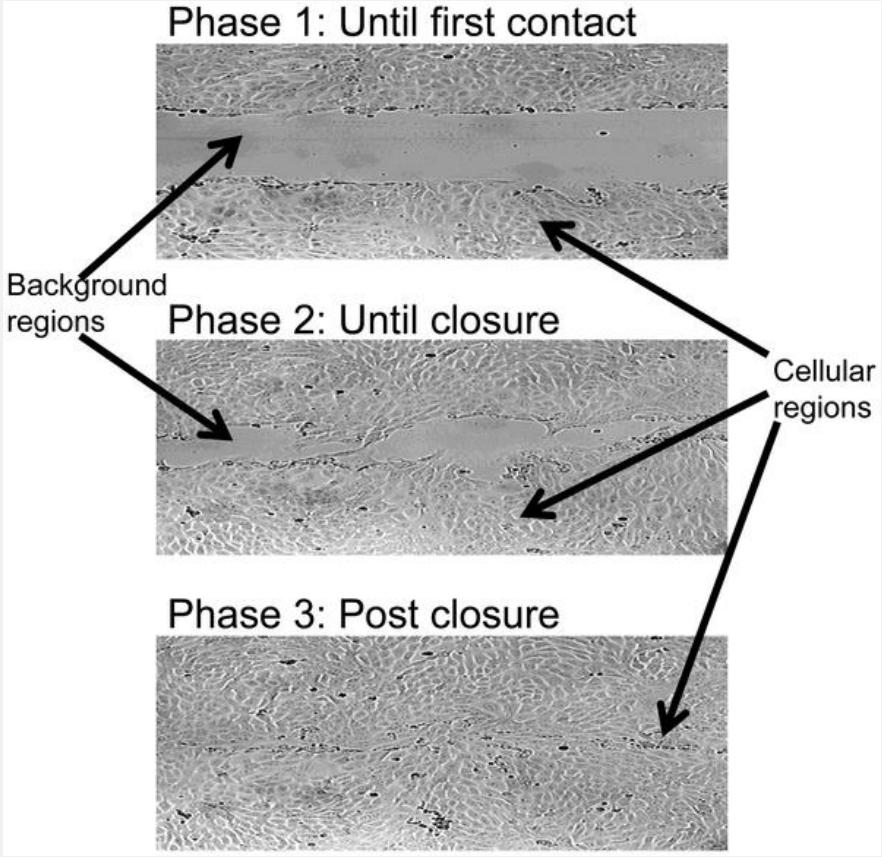
Multi-Cellular Segmentation

- Goal: dividing an image into wound(background) regions & cell-populated areas.
  - No need to segment single cell
- Challenges:
  - High variability in imaging condition.
  - Irregular scratch front-edge due to cells' different mitigation rates.



The figure is from Zaritsky et al. "Emergency of HGF/SF-induced coordinated cellular motility", PLOS one, Sept. 2012.

Prior Arts

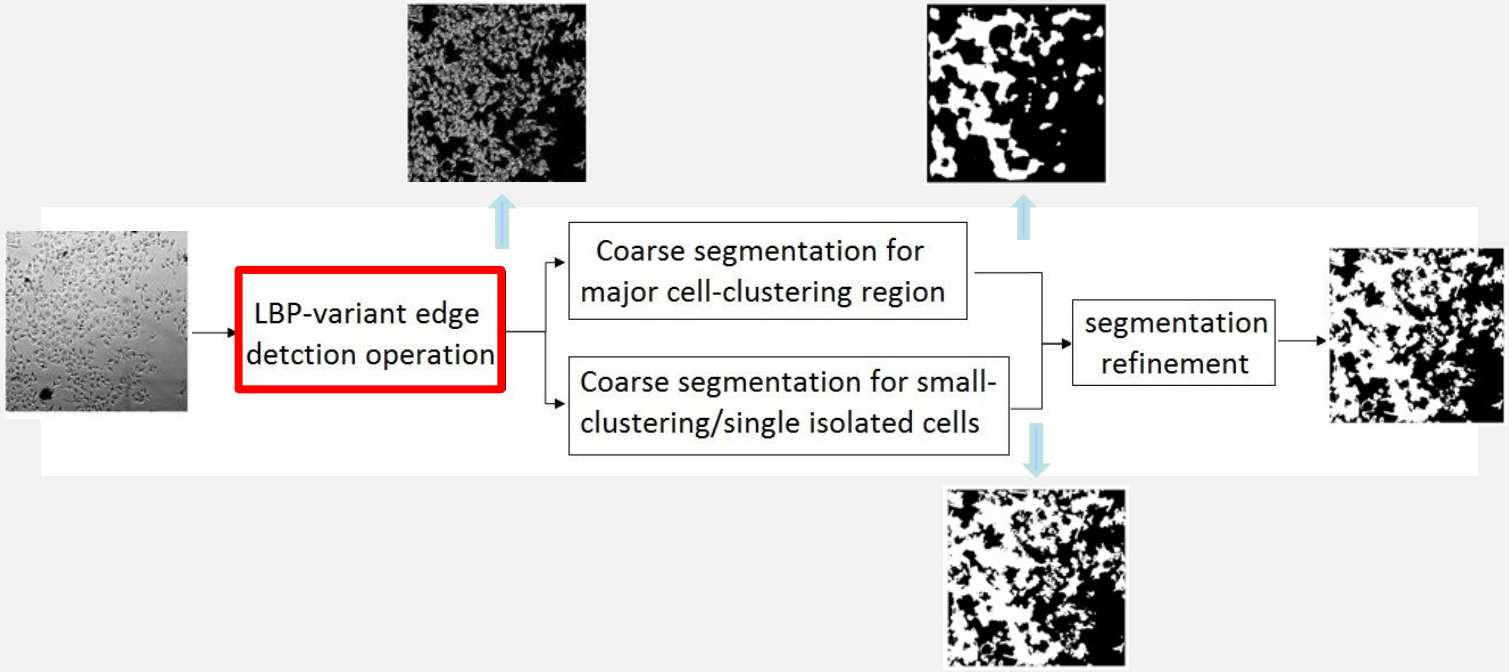
Representative methods	Category	Key techniques	Performance ranking [4]
TScratch [1]	Unsupervised	Discrete curvelet transform + thresholding	3
Topman's [2]	Unsupervised	Intensity standard deviation + parallel filtering + thresholding	1
NultiCellSeg [3]	Supervised	Intensity gradient + support vector machine + graph cut based segmentation	2

- All have poor performances in scatter sassy of the public BBBC multi-cellular segmentation benchmark [4].

[1] Geback et al., "Tscratch: a novel and simple software tool for automated analysis of mono-layer wound healing assays", Bio Techniques, Apr. 2009.
[2]Topman et al., "A standardized objective method for continuously measuring the kinematics of cultures covering a mechanically damaged site", Medical Engineering & Physics, May 2011.
[3] Zaritsky et al., "Cell motility dynamics: a novel segmentation algorithm to quantify multi-cellular bright field microscopy images", PLOS One, Nov. 2011.
[4] Zaritsky et al., "Benchmark for multi-cellular segmentation of bright field microscopy images", BMC Bioinformatics, 2013.

Proposed Multi-Cellular Segmentation

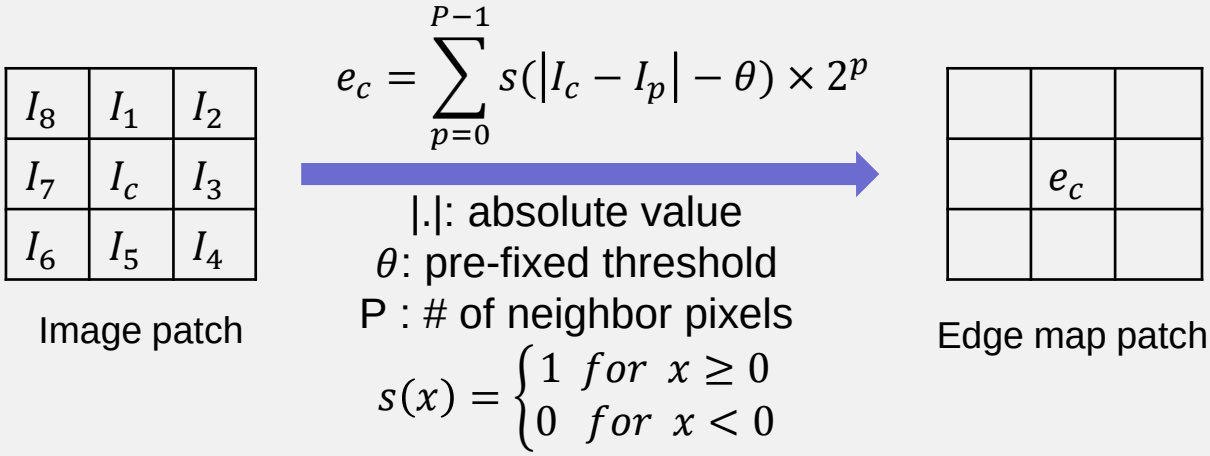
- Block diagram of the proposed method



- ➢ Introducing a LBP-variant edge detector for edge extraction.
- ➢ Adopting the parallel filtering structure in Topman's method for coarse segmentation.

LBP-Variant Edge Detector

- The first attempt to adopt the LBP paradigm for edge information extraction.

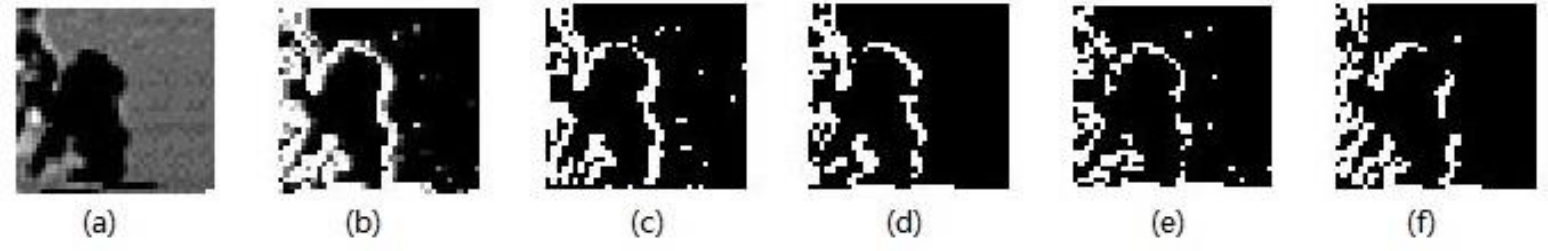


- Selection of threshold θ
  - A large threshold extracts strong edges.
  - A small threshold generates a fine edge map.

Properties of LBP-Variant Edge Detector

- Insensitivity to small intensity change
  - Obtained results are robust to non-uniform imaging illumination.

- Direction-aware property
  - Given e_c, information of edge orientations at pixel c can be uniquely determined.
  - Example: for image (a), edges along different orientation (c)-(f) can be uniquely retrieved from the obtained edge map (b).

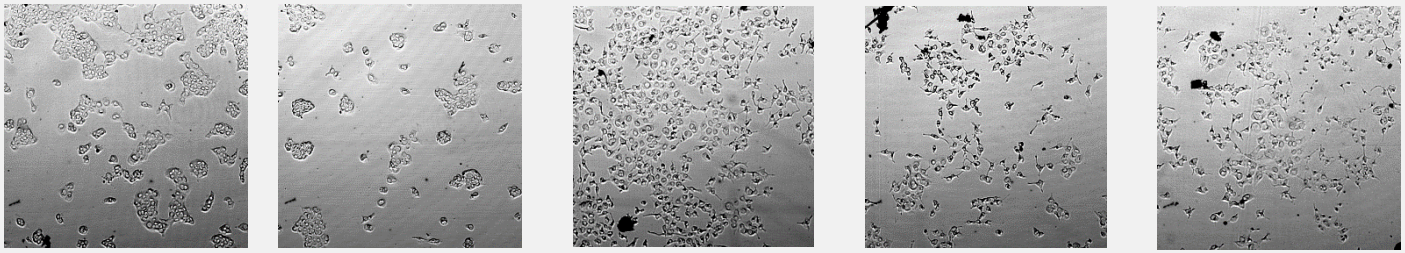


Experimentation

Objective: to evaluate the proposed method

Experimental setup

- Data set: BBBC multi-cellular segmentation benchmark
  - 5 8-bit grayscale scatter images with segmentation ground truth



- Methods for comparison:
  - Tscratch [1], Topman's [2], MultiCellSeg [3]
- Evaluation metric: F-measure= $\frac{2precision \cdot recall}{precision+recall}$

[1] Geback et al., "Tscratch: a novel and simple software tool for automated analysis of mono-layer wound healing assays", Bio Techniques, Apr. 2009.

[2]Topman et al., "A standardized objective method for continuously measuring the kinematics of cultures covering a mechanically damaged site", Medical Engineering & Physics, May 2011.

[3] Zaritsky et al., "Cell motility dynamics: a novel segmentation algorithm to quantify multi-cellular bright field microscopy images", PLOS One, Nov. 2011.

Experimentation Results

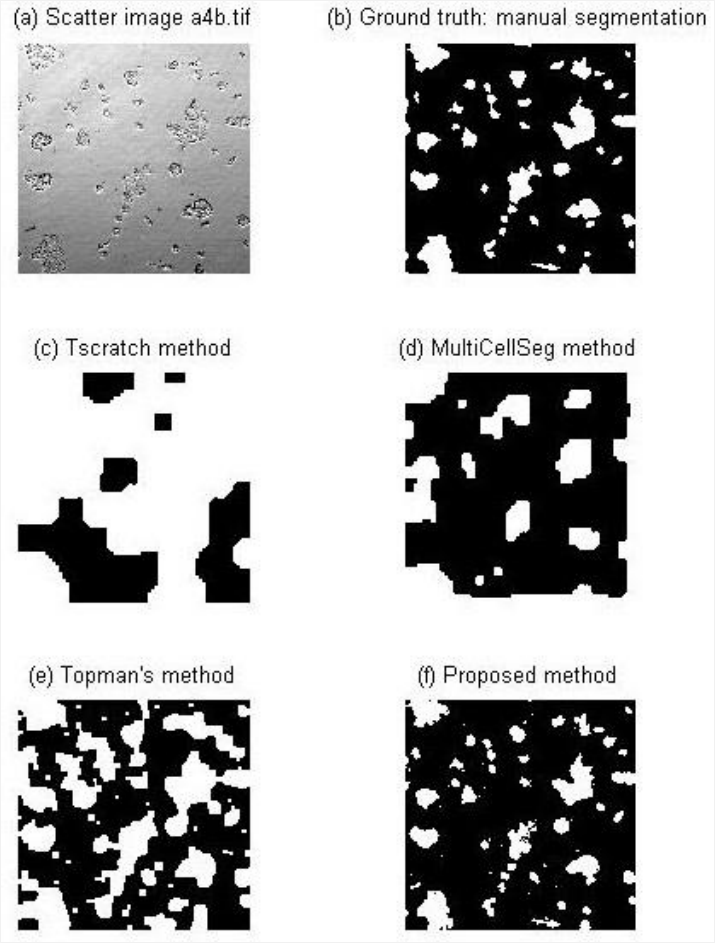
Statistics of multi-cellular segmentation over the BBBC scatter images

Algorithm	Mean F-measure	Median F-measure
TScratch	0.514±0.164	0.536
MultiCellSeg	0.611±0.107	0.587
Topman's	0.647±0.086	0.616
Proposed *	0.858±0.042	0.861

- Due to the edge detector's insensitivity to non-uniform imaging illumination, the proposed method achieve more accurate segmentation than the Topman's method.

* The results are generated with threshold $\theta = 25$ in the proposed method.

Example



Conclusions

- Computational scratch assay is a new frontier in image analysis research.
  - We hoped this study would encourage more researchers to contribute this research realm.

- We presented a very preliminary study on multi-cellular segmentation in scratch images.
  - A LBP-variant edge detector was introduced, which was capable of preserving edge information along various orientations.
  - Multi-cellular segmentation is much improved in the public BBBC scatter image set.

Thank you very much for your attention.

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