Automatic Human Embryonic Stem Cell Detection By Spatial Information and Mixture of Gaussians

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SUMMARY

Problem:

To detect stem cells and cell colonies in microscopy images automatically. It is needed to study the effects of chemical agents on Human Embryonic Stem Cells (HESCs), and to understand the dynamics of stem cells.

Approach:

1. Exploit spatial information from median filter responses to enhance the performance of the mixture of Gaussians to model the gray scale distribution in an image for cell colony detection.
2. Optimize the solution with spatial detail obtained at various scales.
3. Identify stem cell colonies and individual cells in each colony.

CHALLENGES

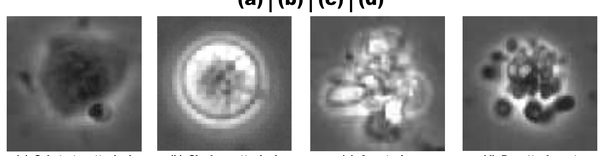
General Challenges:

1. Low contrast between cell, cell colony and background regions.
2. Low signal-to-noise (SNR) in the phase contrast microscopy images.
3. High topological complexity of cell shapes.

Challenges for Automatic Detection:

1. Cell in (a) is similar to the background in intensity and is usually surrounded by a low intensity halo.
2. Cell in (b) is brighter and similar to the halo in intensity.
3. Cell in (c) is bright and shows random blebbing.
4. Cell in (d) is darker when blebbing and is surrounded by a recognizable halo.

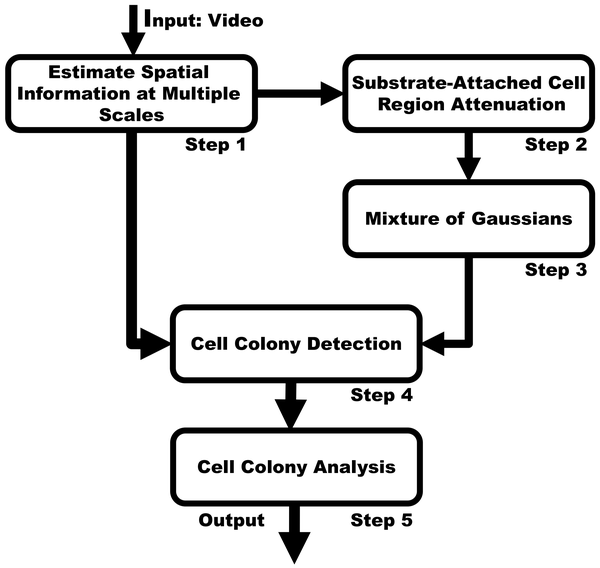
(a) | (b) | (c) | (d)



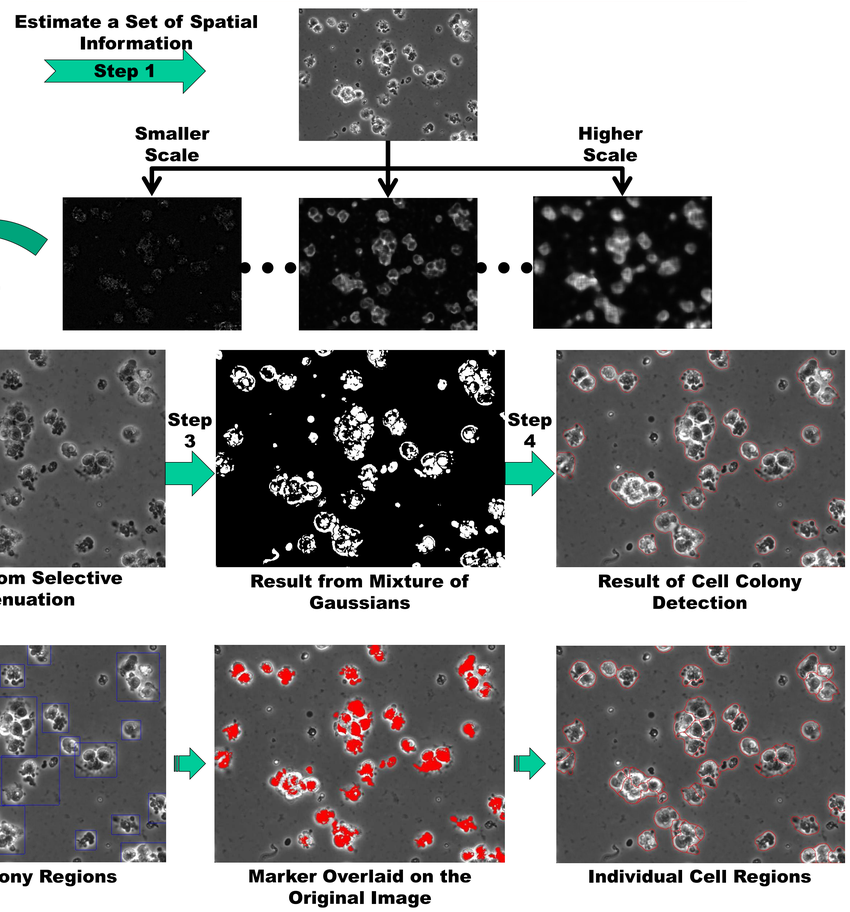
(a). Substrate- attached Cell | (b). Single unattached Cell | (c). Apoptosis | (d). Pre-attachment behavior

TECHNICAL APPROACH

- Obtain spatial information at multiple scales by varying the size of median filters. (Step 1)
- Perform a selective attenuation on the original image. (Step 2)
- Carry out mixture of Gaussians analysis. (Step 3)
- Find the optimal solution for cell colony regions. (Step 4)
- Detect and analyze colony and individual cell regions. (Step 5)



EXAMPLE OF PROCESS



EXPERIMENTAL RESULTS

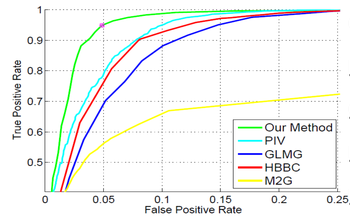
Experiment 1: Data Collection

1. Collected six videos of Human Embryonic Stem Cells with the BioStation IM.
2. The videos were captured under an objective of 20x with a 800x600 resolution; a frame was taken every two minutes.

Experiment 2: Performance Comparison

Comparison with Four Other Methods for a single Frame:

ROC Plot



Comparison with Four Other Methods are:

PIV: Pixel Intensity Variance

GLMG: Gray Level Magnitude Gradient

HBBC: Histogram Based Bayesian Classifier

M2G : Mixture of two Gaussians

Comparisons for Six Videos:

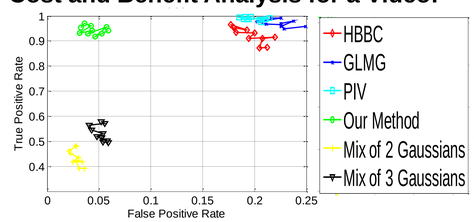
Average Accuracy

Video	HBBC	GLMG	PIV	M2G	M3G	Our app.
1	0.8251	0.8122	0.8369	0.8703	0.8695	**0.9534**
2	0.7628	0.8214	0.8528	0.8017	0.8201	**0.9311**
3	0.8584	0.8102	0.8449	0.9116	0.9039	**0.9562**
4	0.8768	0.8613	0.8556	0.9308	0.9175	**0.9482**
5	0.8913	0.8577	0.8708	0.9272	0.9174	**0.9491**
6	0.8631	0.8172	0.8332	0.9116	0.8988	**0.9571**

Average False Discovery Rate

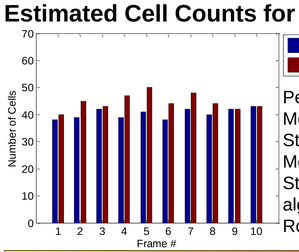
Video	HBBC	GLMG	PIV	M2G	M3G	Our app.
1	0.4745	0.4944	0.4605	0.2116	0.2894	**0.1612**
2	0.4792	0.4054	0.3620	0.2065	0.2345	**0.1732**
3	0.4635	0.5377	0.4868	0.2585	0.3211	**0.2006**
4	0.4698	0.4996	0.5097	0.2704	0.3484	**0.2661**
5	0.4058	0.4743	0.4508	0.2341	0.3043	**0.2335**
6	0.4204	0.4939	0.4705	0.2267	0.3021	**0.1724**

Cost and Benefit Analysis for a Video:



1. The True Positive Rate tells the sensitivity of each method.
2. The False Positive Rate tells the fall out of each method.
3. Our method has above 90% true positive rate while gives less than 7% false positive rate.

Estimated Cell Counts for a Video:



Performance (Average Over 10 Frames):
Mean of cell count in ground truth = 40.40
Standard deviation of cell count in ground truth = 1.84
Mean of cell count by automatic algorithm = 44.60
Standard deviation of cell count by automatic algorithm=2.99
Root Mean Square Error = 4.20

CONCLUSIONS/FUTURE WORK

- The method yields better detection result than the other four methods and has higher performance in the ROC plot.
- The method gives high average accuracy while has low average false discovery rate.
- The cell counts given by the method are similar to the actual cell counts.
- Future work will focus on classification, tracking and obtaining a lineage map for stem cells.

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