High-speed Recognition of Micro-array Genomic Images Using Multi-scale Representations

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INTRODUCTION

- This project is part of the Northeast Structural Genomics Consortium (NESG). The goal of this consortium is to develop efficient and integrated technologies for high-throughput (HTP) protein production and 3D structure determination.
- This project focuses on the design of an image analysis system to classify protein crystal structures in a production oriented environment.
- The method performs classification of microscopic images as clear droplets versus non-clear droplets (precipitates and crystals).
- Using expert classification for ground truth, current results show high classification accuracy with a large image datasets.

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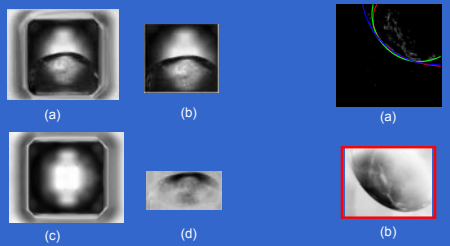
METHODOLOGY

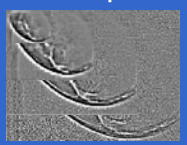
1. Preprocessing of Microscopic Images



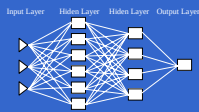
(a) Original image with an oil droplet containing precipitates. (b) Cropped image with Radon transform. (c) Background image acquired without drops. (d) Pre-processed image with Ellipsoidal Hough transform.

(a) Ellipsoidal Hough transform [1] to detect the three most probable ellipses, plotted over the edge map of the pre-filtered image. (b) Pre-processed image cropped with the minimal rectangular area encompassing the three ellipses.

2. Feature Extraction with Laplacian Pyramidal Expansion [2]



3. Classification with a Feed-Forward Neural Network



4. We used the quantitative shape descriptions of a first-order histogram combined with the power spectrum and autocorrelation information:

$$\text{Mean:} \quad S_M = \bar{b} = \sum_{b=0}^{L-1} bP(b)$$

$$\text{Standard Deviation:} \quad S_D = \left[\sum_{b=0}^{L-1} (b-\bar{b})^2 P(b)\right]^{1/2}$$

$$\text{Skewness:} \quad S_S = \frac{1}{\sigma_b^3}\sum_{b=0}^{L-1} (b-\bar{b})^3 P(b)$$

$$\text{Kurtosis:} \quad S_K = \frac{1}{\sigma_b^4}\sum_{b=0}^{L-1} (b-\bar{b})^4 P(b) - 3$$

$$\text{Energy:} \quad S_E = \sum_{b=0}^{L-1} [P(b)]^2$$

$$\text{Entropy:} \quad S_E = -\sum_{b=0}^{L-1} P(b)\log_2[P(b)]$$

$$\text{Power:} \quad S_P = \sum_{i=1}^{L} fft(\mathrm{Im})^2$$

$$\text{Autocorrelation:} \quad S_A = \sum_{r=1}^{L}\sum_{i=1}^{L} \mathrm{Im}(i)\cdot\mathrm{Im}(r+i)$$

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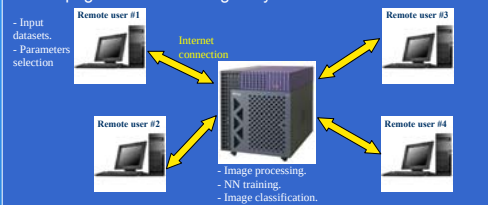
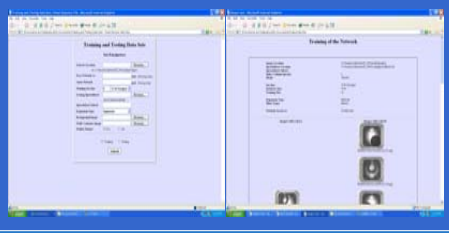
METHODOLOGY

5. Remote Application Server

Web page interface managed by a Matlab© Server.





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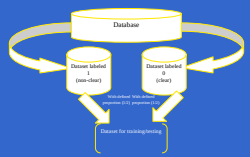
DATA

1. Microscopic images were acquired with a CCD camera under robotic control.
2. Gray scale 8-bits images saved in tiff format.
3. Image Database of 5,000 manually classified images:
   - 2500 drops containing precipitates and/or crystals.
   - 2500 clear drops (clear, skin, etc)



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DISCUSSION

- Introduction of robotic manipulation of the crystals for HTP protein production requires the automation of image analysis of crystallization experiments for classification of solution content.
- The proposed feed forward neural network showed promising results in classifying microscopic images.
- Most features of representation were computed from Laplacian pyramid expansion histograms. The histogram made the features invariant to orientation which was a desirable feature in order to be able to characterize the diversity and complexity of precipitate appearances.
- The Laplacian expansion provided a representation of the image edge and texture patterns at different scales with extremely fast implementation.

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RESULTS

1. Classification with the Image Database

►Image Features for Neural Network

Quantitative shape descriptions of a first-order Laplacian pyramid coefficients histogram combined with the power spectrum and autocorrelation information.

8 statistics for each Laplacian coefficient subset with totally 5 subsets. (8*5=40)

► Binary classification

0 = clear drop, 1 = not a clear drop

► Training data set

100, 500, 1000, 1500, 2000, 2500, 3000, 3500 images

1/2 clear drops, 1/2 drops with precipitates/crystals

► Testing experiments

200 images with precipitates/crystals: TP = 90%.

200 images with clear drops: TN = 92%.

► Definition of the classification system

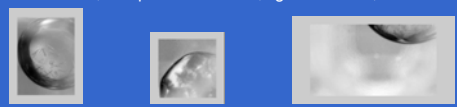
Accuracy = (TP+TN)/2 = 91%

TP= True Possitive (Percentage) = Correctly classified images with precipitates or crystals/ Total images with precipitates or crystals*100%

TN = True Negative (Percentage) = Correctly classified images with clear drops/Total images with clear drops*100%

2. Examples of Misclassified Images

Skin effects, complex boundaries, light reflection, etc.



Small bubble size, no sharp gradient, background influence, etc.

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CONCLUSION

- We are working on further classification of the microscopic image database to separate crystals from precipitates.
- A parallel task of this project includes the creation of a web-based infrastructure for testing and development. An experimental test-bed for crystallization screening is currently under development.

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REFERENCES

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