Computational single-cell classification using deep learning on bright-field and phase images

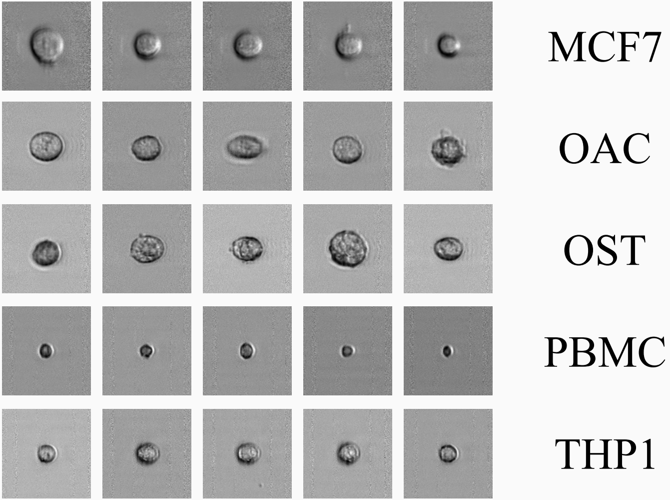
Nan Meng, Hayden K.-H. So, Edmund Y. Lam

Imaging Systems Laboratory,
Department of Electrical and Electronic Engineering,
University of Hong Kong

http://www.eee.hku.hk/isl

15th IAPR International Conference on Machine Vision Applications

In a nutshell



Ultrafast imaging

Enabling technology #1: Time-stretch imaging

Asymmetric-detection time-stretch optical microscopy (ATOM) for obtaining label-free, high-contrast image of the transparent cells at ultrahigh speed, and with sub-cellular resolution.

Figure: Photo of an ATOM system.

Ultrafast imaging

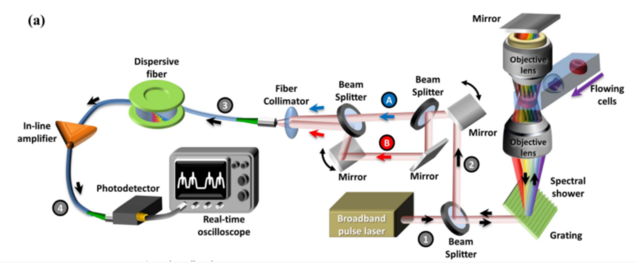


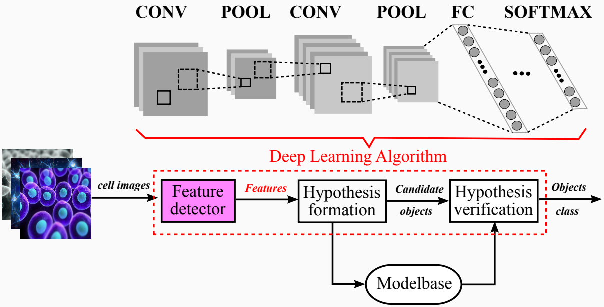
Figure: General schematic of an ATOM system.

- Top speed: $\approx 30,000$ images per second
- Original image resolution: 84×305
- Pixel superresolution gives: 305×305
- Four bright-field images captured concurrently
- Data rate: $30000 \times 84 \times 305 \times 4 \approx 3.1\,\text{GB/s}$
- Detection mechanism: line by line via XXXXXX
- Cell flow: optofluidic system

Cell classification

Enabling technology #2: Deep learning for image classification

- Cell classification (phenotype): identify some specific cells among many different cells based on image analysis techniques.
- **Data-driven** methods for object classification.
- **Automatically** extract features to identify different types of cells.



Introduction

Deep learning breaks the desired complicated mapping into a series of nested simple mappings, each described by a different layer of the model.

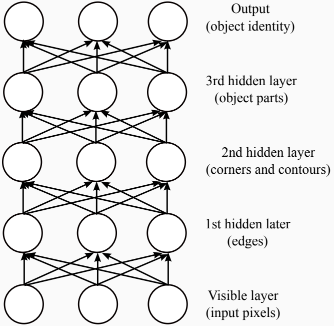


Figure: Deep learning framework.

- The input is presented at the **visible layer**.
- A series of **hidden layers** extracts increasingly abstract features from the image.
- Finally, the last layer learns descriptions of the image in terms of the **object parts** and use them to recognize objects.

Network Design

Convolutional Neural Network (CNN)

We explore a systematic way to design the network and tune the structure to obtain a robust model to avoid overfitting.

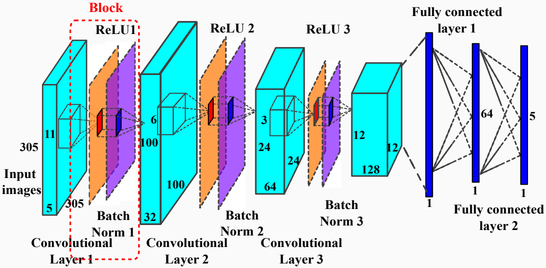
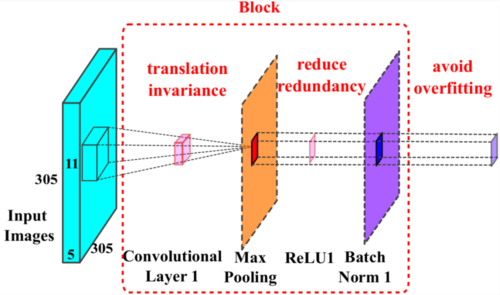


Figure: Our proposed CNN-based framework.

Network Design

Building blocks

- **Convolution layer** extracts robust features for translation and rotation variations.
- **Pooling layer** makes the output less redundant.
- **Batch normalization layer** is effective to avoid overfitting.

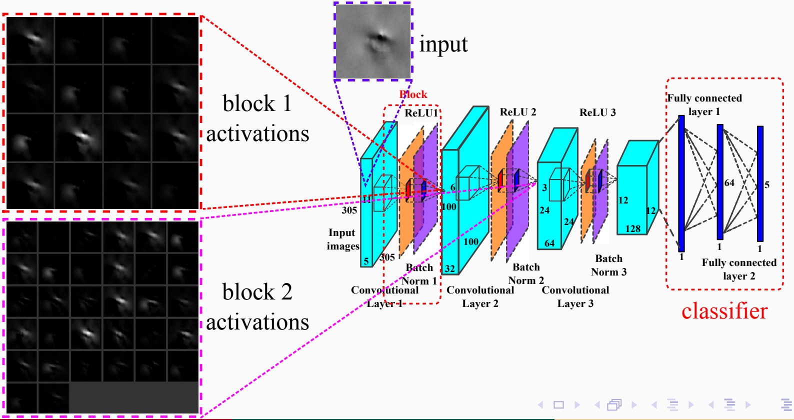


- Combine these three connected layers as a basic feature extraction unit, what we call a "block".
- Cascade multiple blocks to get the final framework.

Network Design

Cascading the blocks

1. Deep learning models can extract high-level features.
2. Higher layers are more likely to extract abstract and invariant features.



Channel Augmentation

Bright-field and phase images

Bright-field imaging is a technique where light from the specimen and its surroundings is collected to form an image against a bright background.

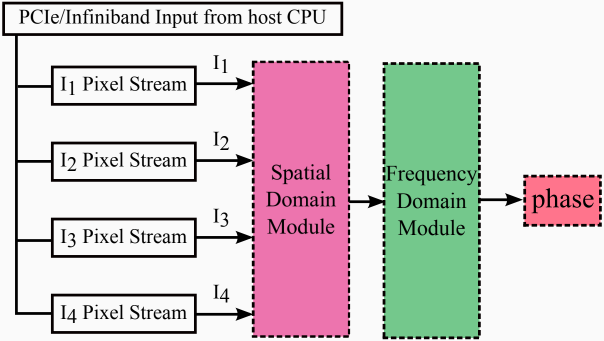


Figure: System Architecture.

Channel Augmentation

Computation of phase image $\phi(x, y)$:

$$\phi(x, y) = \mathrm{Im}\left[\mathcal{F}^{-1}\begin{Bmatrix} C, & \kappa_x = \kappa_y = 0 \\ \frac{\mathcal{F}\{G(x,y)\cdot \mathrm{FOV}\}}{2\pi\cdot(\kappa_x + i\kappa_y)}, & \text{otherwise} \end{Bmatrix}\right] \tag{1}$$

$\nabla\phi_x$ and $\nabla\phi_y$: local phase shift

$G(x, y) = \nabla\phi_x + i \cdot \nabla\phi_y$

$\mathcal{F}$ and $\mathcal{F}^{-1}$: Forward and inverse Fourier transforms

$(\kappa_x + i\kappa_y)$: Fourier spatial frequencies normalized as a linear ramp

C : An arbitrary integration constant

FOV : image field of view expressed in physical units

Channel Augmentation

Generating the phase image aims to enrich information of each individual sample without increasing the size of the dataset used for training.

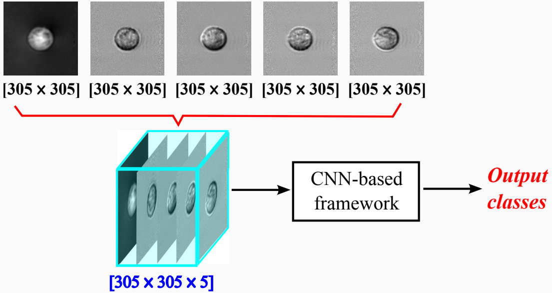


Figure: Channel augmentation **cascades** several relevant images together to enrich information.

Results

Channel Augmentation is efficient for cell classification problem.

- Different channel images provide competitive information.
- Channel images contain better features than phase image.
- Cascading channel and phase images achieves best classification.

Aspects	Average Accuracy	
	validation	test
channel 1	0.94	0.94
channel 2	0.96	0.95
channel 3	0.94	0.96
channel 4	0.94	0.92
channel 1-4	0.96	0.93
phase only	0.93	0.90
channel 1-4 & phase	**0.97**	**0.97**

Table: Classification accuracy with different channel augmentation strategies.

Results

The **Precision** of each class of testset

- Different channels perform discriminatively on specific type of cells.
- Model preforms best after channel augmentation.

$$\text{precision} = \frac{\mathrm{tp}}{\mathrm{tp} + \mathrm{fp}}$$

tp : true positive

fp : false positive

Table: Precision of test

Aspects	Precision of each class **test**				
	THP1	OAC	MCF7	PBMC	OST
channel 1	0.8429	0.9551	**1.000**	0.8795	**1.000**
channel 2	0.9296	0.9872	0.9868	0.8588	0.9889
channel 3	0.9444	0.9753	**1.000**	0.9255	0.9753
channel 4	0.7838	0.9773	0.9880	0.8462	0.9870
channel 1-4	**1.000**	0.9859	0.9767	0.7907	0.9259
phase	0.8571	0.9167	0.9870	0.8642	0.8642
channel 1-4 &phase	**1.000**	**1.000**	0.9524	**0.9351**	0.9324

Results

The **Recall** of each class of testset

- Different channels perform discriminatively on specific type of cells.
- Model preforms best after channel augmentation.

$$\text{recall} = \frac{\mathrm{tp}}{\mathrm{tp} + \mathrm{fn}}$$

tp : true positive

fn : false negative

Table: Recall of test

Aspects	Recall of each class **test**				
	THP1	OAC	MCF7	PBMC	OST
channel 1	0.8551	**1.000**	0.9634	0.9012	0.9518
channel 2	0.8354	0.9872	**1.000**	**0.9359**	0.9889
channel 3	0.8947	0.9875	**1.000**	0.9355	**1.000**
channel 4	0.7945	**1.000**	**1.000**	0.8048	0.9870
channel 1-4	**0.9870**	0.9859	0.9882	0.9189	0.8065
phase	0.8571	0.8652	**1.000**	0.8642	0.9091
channel 1-4 &phase	0.9756	0.9770	**1.000**	0.9351	0.9324

Results

The F1 score of each class of testset.

- Different channels perform discriminatively on specific type of cells.
- Model preforms best after channel augmentation.

$$F_1 = 2 \times \frac{\text{precision} \cdot \text{recall}}{\text{precision} + \text{recall}}$$

Table: F1 score of test

Aspects	F1 score of each class **test**				
	THP1	OAC	MCF7	PBMC	OST
channel 1	0.85	0.98	0.98	0.89	0.98
channel 2	0.88	0.99	0.99	0.90	0.99
channel 3	0.92	0.98	**1.0**	0.93	0.99
channel 4	0.79	0.99	0.99	0.83	**0.99**
channel 1-4	0.99	0.98	0.98	0.85	0.86
phase	0.87	0.90	0.99	0.88	0.89
channel 1-4 &phase	**0.99**	**1.0**	0.99	**0.95**	0.94

Conclusions and Future Work

Some conclusions:

- CNN-based models after careful design can have strong capacities to learn **representational features**, which further improve the classification accuracy
- **Channel augmentation** strategy via cascading several relevant images is effective for the network to learn good representations in cell classification task

Future work:

- Investigate further the abilities of CNN-based models to extract representational features
- Explore strategies for network design to extract resolution invariant features

Acknowledgment

This work was supported in part by

- National Natural Science Foundation of China (NSFC)/RGC under Hong Kong Research Grants Council (NHKU714/13)
- Hong Kong Research Grants Council General Research Fund (17245716)
- Croucher Innovation Award