Discriminative Semi-Markov Models for Automated Mitotic Phase Labelling

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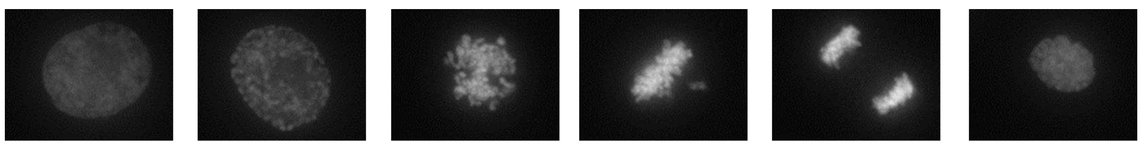
1. Objective

- To automatically identify and track individual cells throughout a time-lapse sequence of fluorescence microscopy images, and to label the mitotic cell cycle phase for each cell at every time point.



Interphase | Prophase | Prometaphase | Metaphase | Anaphase | Telophase

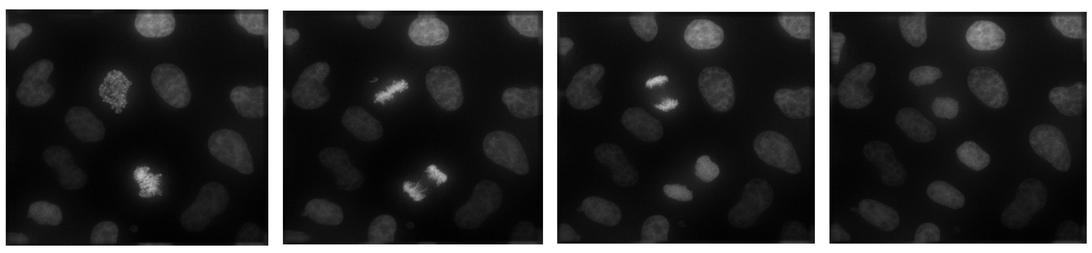
2. Overview

Motivation

- Facilitate automated high-throughput analysis.
- Derive statistics of cellular function.

Data

- 54 image sequences with 650 tracks.
- 23 sequences obtained under conditions in which one of three proteins required for timely progression though mitosis (TACC3, CLTC, or GTSE1) were depleted from cells by RNAi.
- *xy*-resolution 0.2 microns, 1-5 min. temporal resolution, max *z*-projection of a 3D image stack.
- 119 tracks showing at least 3 mitotic phases manually annotated for training/evaluation.
- Sample frames from a sequence:



Novel approach

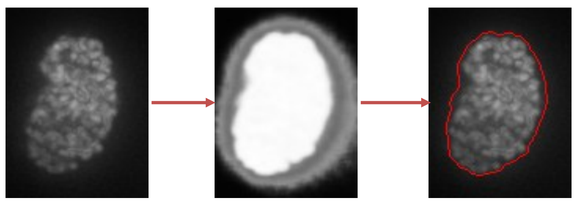
- Existing approaches :
  - **i.** Individual frame classification using SVM, smoothed with HMM.
  - **ii.** Use Dynamic Time Warping (DTW) on temporal signals of features, so that information across time ranges is utilised for labelling [1].
- Our approach: Use a wide margin discriminative Semi-Markov Model [2]. Using temporal features evaluated over the whole of the mitotic phases rather than over single frames, thereby capturing the distinctive behaviour over the phases.

Two Stages

- Segment and track individual cells.
- Label as one of the mitotic phases using Semi-Markov Model.

3. Segmentation & Tracking

- Treated as a two-class classification problem.
- Logistic regression classifier to generate probability map.
- Graph cuts to generate final binary mask.
- Cells tracked using nearest neighbour approach on centroids.



Input image | *Probability map* | *Final segmentation*

4. Semi-Markov Model

- For a given sequence **x**, a Semi-Markov Model finds an optimal segmentation, into temporal segments of frames, **s** = [s_1 … s_n], where each segment s_j is defined by a label and start and end frames.
- Defining a model parameter **w**, and a feature mapping **Φ**(**x**, **s**), the optimal segmentation is then given by:

$$\mathbf{s}^* = \arg\max_{\mathbf{s}} \langle \mathbf{w}, \mathbf{\Phi}(\mathbf{x}, \mathbf{s}) \rangle$$

- The model parameter, **w**, is learnt from a manually annotated training set by solving the regularised optimisation:

$$\min_{\mathbf{w}} \frac{\|\mathbf{w}\|^2}{2} + C \sum \xi_i$$

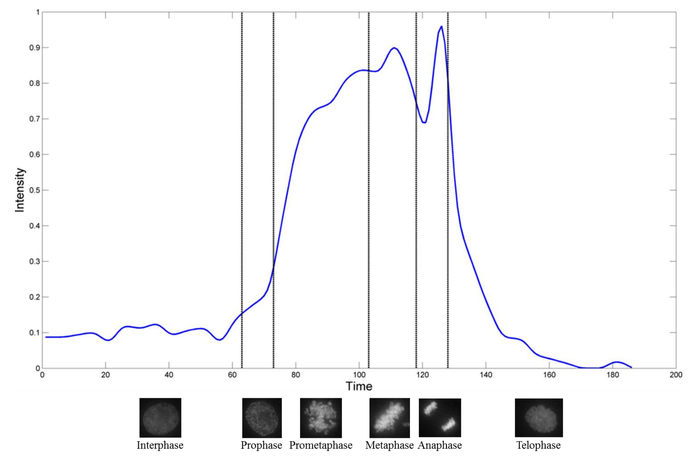
$$\text{s.t.} \langle \mathbf{w}, \Delta\mathbf{\Phi}(\mathbf{x}, \mathbf{s_i}) \rangle > \Delta(\mathbf{s}, \mathbf{s_i}) - \xi_i$$

- We modify the label loss, Δ(**s**,$\mathbf{s}_i$), between the true and predicted segmentations from the original of [2], to be given by the number of misclassified frames, ignoring segment boundary errors within 2 frames of the ground truth, to account for inconsistencies in the annotation.

5. Features

Simple features

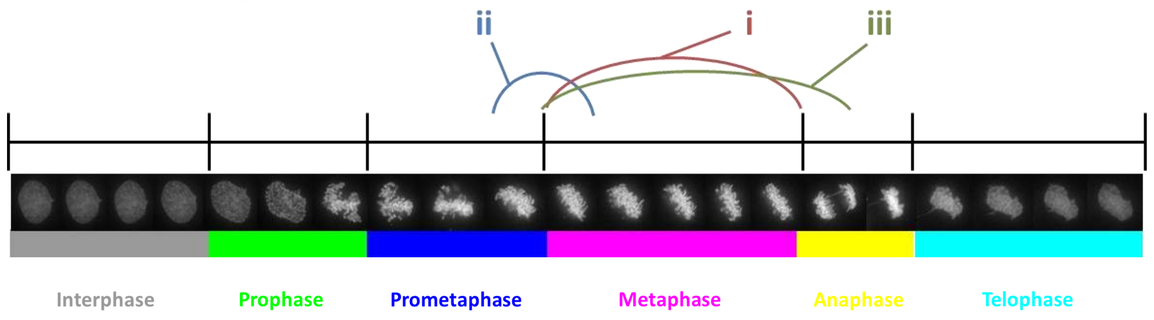
- Features: for each temporal sample record maximum pixel intensity, with temporal gradients at two scales to give context.
- These simple features show distinct variations in each phase.
- Encoding: feature values are discretized into evenly spaced bins using soft assignment.



Feature Mapping

The feature mapping, **Φ**(**x**, **s**), consists of a concatenation of 3 features:

- **i. Segment level feature.** Captures characteristics of the signal over the segment as a whole, evaluated between the start and end points.
- **ii. Segment boundary feature.** Captures information about the transition into a segment. Evaluated from a local window centered on the start frame.
- **iii. Neighbouring segment feature.** Captures correlation between neighbouring segments, thus learning allowed transitions.



6. Results

Evaluation

- Class confusion matrices.
- Per-class accuracy: mean of confusion matrix diagonal.
- Scores affected by phases as short as 1-2 frames — allow ±1, ±2 frames slack.

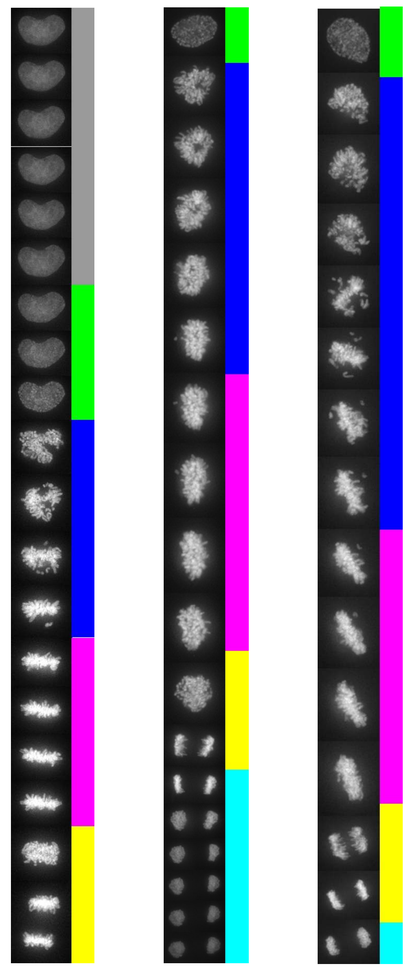
	Interphase & Telophase	Prophase	Prometaphase	Metaphase	Anaphase
Interphase & Telophase	0.96				
Prophase	0.17	0.73	0.10		
Prometaphase			0.80	0.16	
Metaphase			0.12	0.81	0.07
Anaphase	0.12			0.06	0.82

(a) Exact match. Mean per-class accuracy: 0.82

0.97				
0.09	0.91			
		0.87	0.10	
		0.04	0.95	
				0.98

(b) ±2 frames. Mean per-class accuracy: 0.94

Model	Exact	±1 frame	±2 frames
DTW	0.76	0.87	0.90
SMM [2] loss	0.80	0.89	0.91
SMM our loss	**0.82**	**0.91**	**0.94**



7. References

[1] A. El-Labban, A. Zisserman, Y. Toyoda, A. W. Bird, and A. Hyman, "Dynamic time warping for automated cell cycle labelling," in MIAAB, 2011.

[2] Q. Shi, L. Cheng, L. Wang, and A. J. Smola, "Human action segmentation and recognition using discriminative Semi-Markov models," in IJCV, 2011.