Mathematical Imaging Methods for Mitosis Analysis in Cancer Research

Big Data, Multimodality & Dynamic Models in Biomedical Imaging

Isaac Newton Institute, Cambridge

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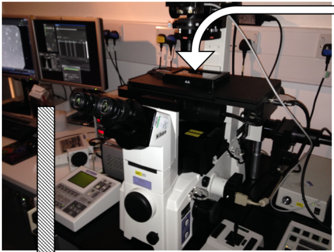
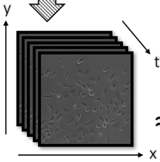
A Typical Data Set

Experimental Set-Up

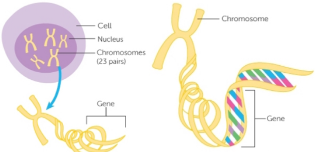




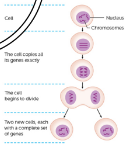
Phase Contrast Microscope

$\approx 1000^3$

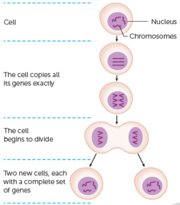
Cell Culture

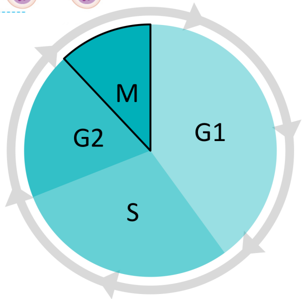


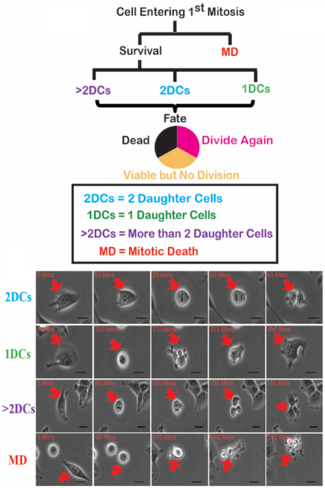
Treatment with anti-mitotic drugs (chemotherapy)



Determination of **mitosis duration** and **cell fate distribution**

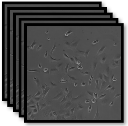




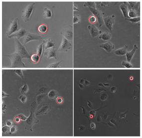


Jennifer Harrington, CRUK CI

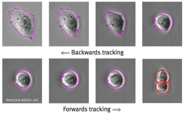
Summary of Mitosis Analysis Framework

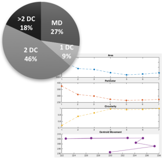


1 Mitosis Detection

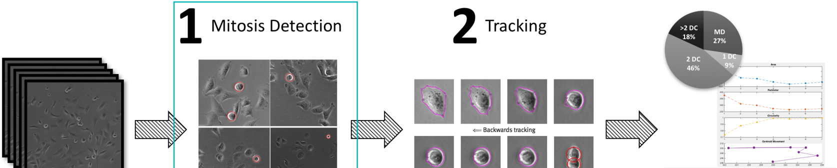


2 Tracking





	Control			Treatment 1			Treatment 2		
	1	2	3	4	5	6	7	8	9
Number of events	27	21	43	29	21	32	34	15	35
Avg mitosis duration (min)	101	86	80	77	107	106	110	53	111
Total avg mitosis duration	89			97			91		



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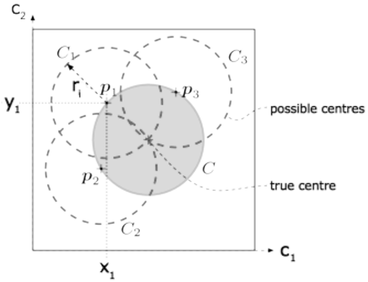
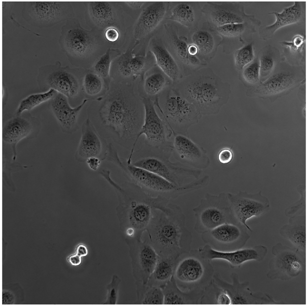
Mitosis Detection by Circular Hough Transform

The **Circular Hough Transform** is defined as a path integral along a circle:

$$CHT(f(c,r)) = \int_{\partial B_r(c)} f(y)\, d\sigma(y).$$





References: [Hough 1962], [Duda and Hart 1972]

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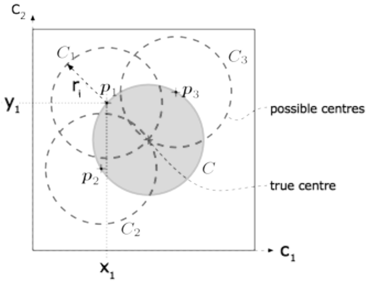

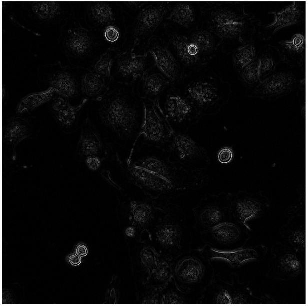

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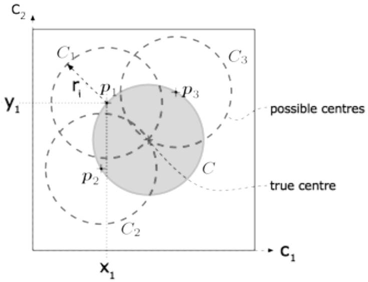

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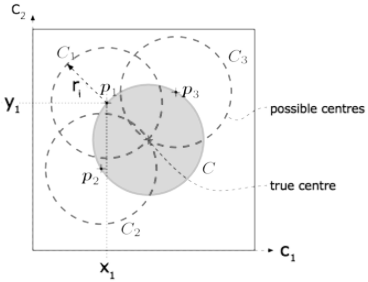

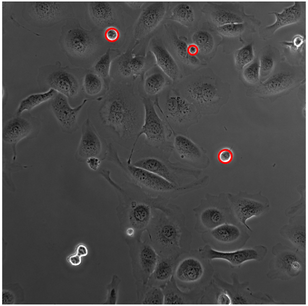

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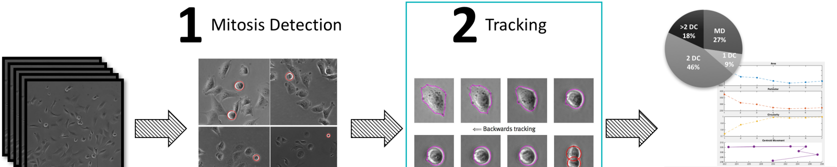

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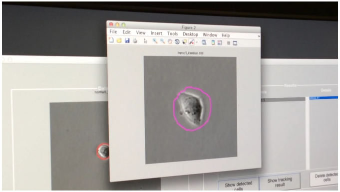
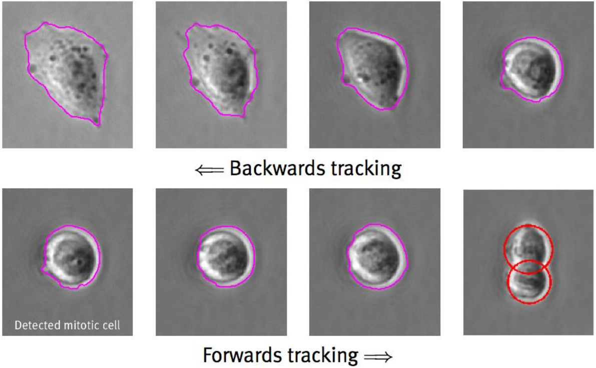
Tracking


File Edit View Insert Tools Desktop Window Help
Show detected cells
Show tracking result


⟸ Backwards tracking
Detected mitotic cell
Forwards tracking ⟹

Variational Segmentation Model

$$
\begin{aligned}
&E(\phi, c_1, c_2) \\
&= \underbrace{\lambda_1 \int_\Omega (c_1 - |v|)^2 \left(1 - H(\phi(x))\right) dx + \lambda_2 \int_\Omega (c_2 - |v|)^2 H(\phi(x))\, dx}_{\text{partition into two regions with different normal velocities}} \\
&\quad + \underbrace{\mu \int_\Omega |\nabla H(\phi(x))|\, dx}_{\text{small contour length}} + \underbrace{\nu \int_\Omega g(f(x))\, |\nabla H(\phi(x))|\, dx}_{\text{stop contour at edges based on local std}} \\
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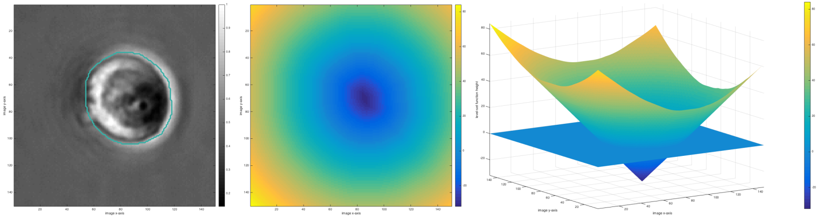

$$\phi(x) \begin{cases} < 0, & \text{if } x \text{ is inside of the contour,} \\ = 0, & \text{if } x \text{ lies on the contour,} \\ > 0, & \text{if } x \text{ is outside of the contour.} \end{cases}$$

$$H(\phi) \begin{cases} = 0, & \text{if } \phi \leq 0, \\ = 1, & \text{if } \phi > 0. \end{cases}$$

Variational Segmentation Model

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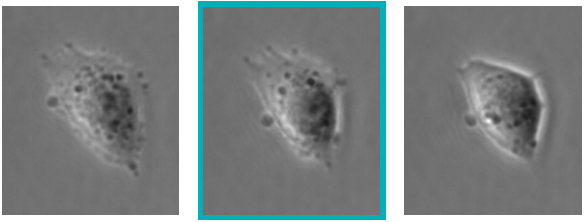

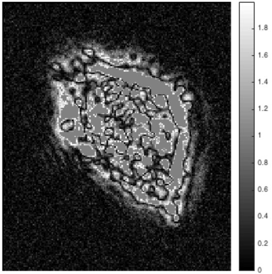

$|v| \approx \frac{\left|\frac{\partial}{\partial t} f(x,t)\right|}{|\nabla f(x,t)|_\varepsilon}$ absolute value of the **normal velocity**

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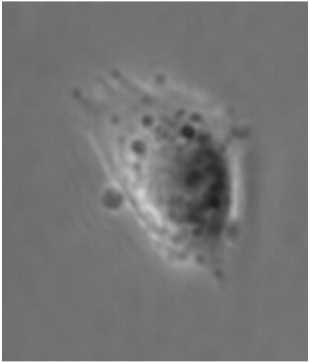
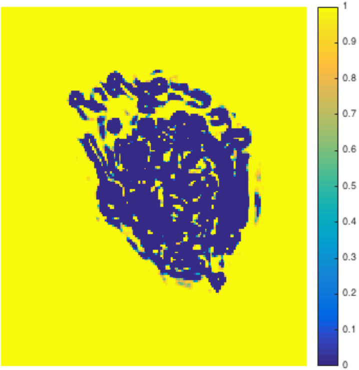
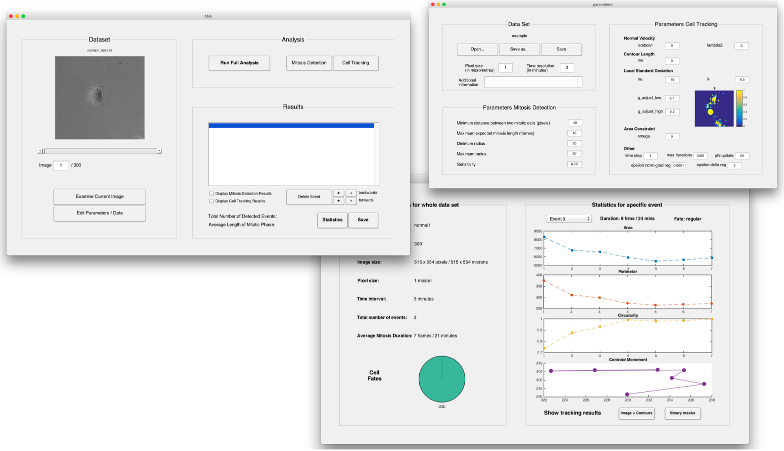


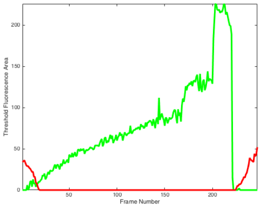


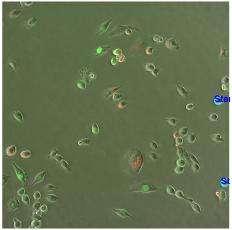
MitosisAnalyser: MATLAB® Graphical User Interface



Example: Multi-Modal Experiment

Phase contrast data + two fluorescent channels (**F**luorescent **U**biquitination-based **C**ell **C**ycle **I**ndicator)





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Future Work

- Incorporating modelling of cell motion (membrane evolution), ideally from round to flat state in backwards tracking, in a realistic and physically meaningful way
- Bilevel learning of the motion model and the segmentation parameters

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- Multi-modal on-line processing during image acquisition by combining mitosis detection performed on phase contrast data with higher resolution analysis on fluorescence microscopy images
- Sparsity-enforcing regularisation incorporating shape information

Thank you very much for your attention!

Are there any questions?

Contact: jg704@cam.ac.uk

CAMBRIDGE IMAGE ANALYSIS
DAMTP - UNIVERSITY OF CAMBRIDGE

http://www.damtp.cam.ac.uk/research/cia/
http://www.lightmicroscopy.cruk.cam.ac.uk
http://www.images.group.cam.ac.uk

Cambridge Biomedical Research Centre
NHS
National Institute for Health Research

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- Möller, M., Burger, M., Dieterich, P., & Schwab, A. (2014). A framework for automated cell tracking in phase contrast microscopic videos based on normal velocities. *Journal of Visual Communication and Image Representation, 25*(2), 396-409.