Mathematical Imaging Methods for Mitosis Analysis in Live-Cell Phase Contrast Microscopy

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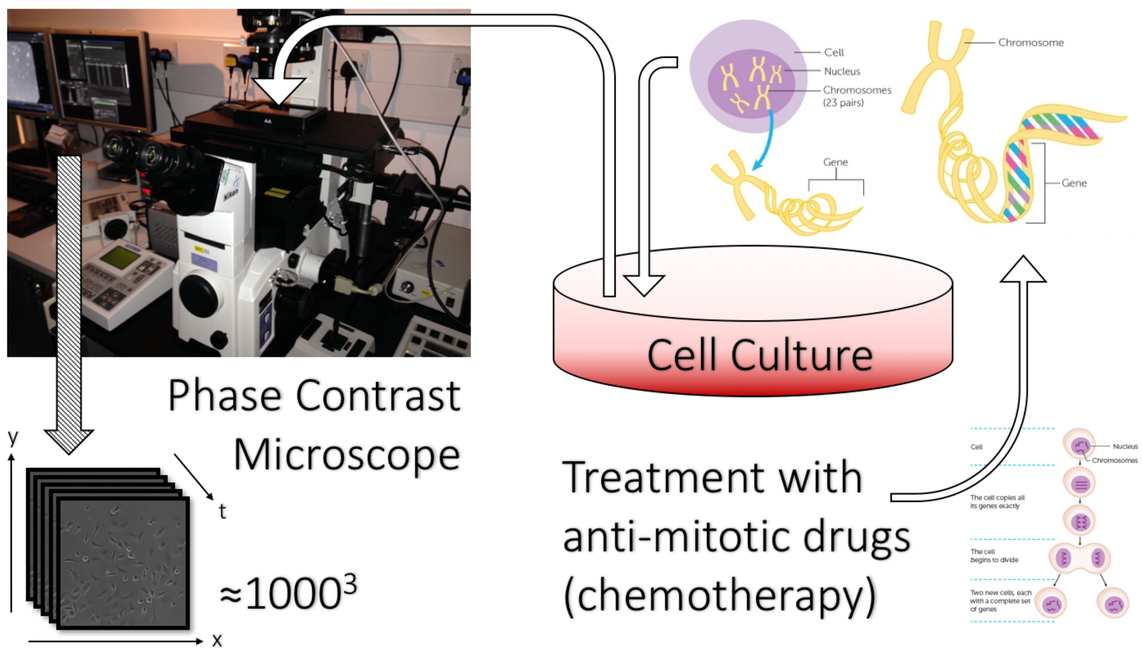
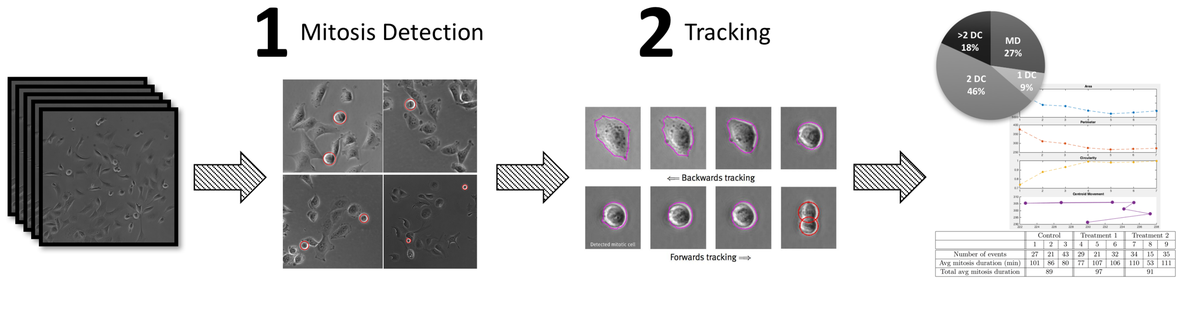
Motivation



Aim: Determination of average mitosis durations and cell fate distributions

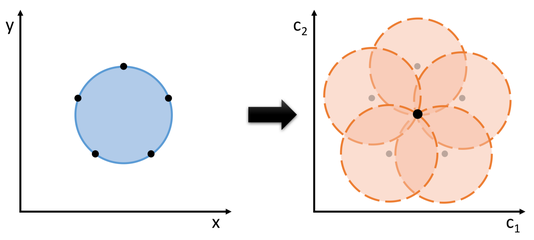
MitosisAnalyser

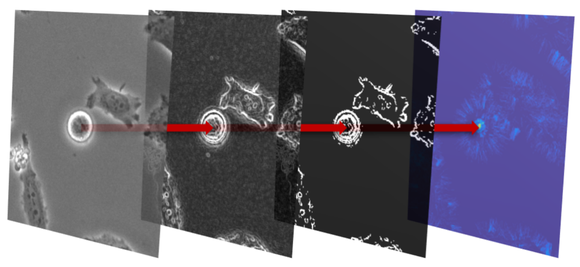


	Control			Treatment 1			Treatment 2		
	1	2	3	4	5	6	7	8	9
Number of events	27	21	43	29	21	32	34	15	35
Avg mitosis duration (min)	101	86	80	77	107	106	110	53	111
Total avg mitosis duration	89			97			91		

1 Mitosis Detection

- We are using the circular Hough transform, which is an object recognition method for circles in images, in order to detect circularly-shaped mitotic cells
- During this procedure, cell locations are determined from maxima of the circular Hough transform applied to an edge map of the underlying image



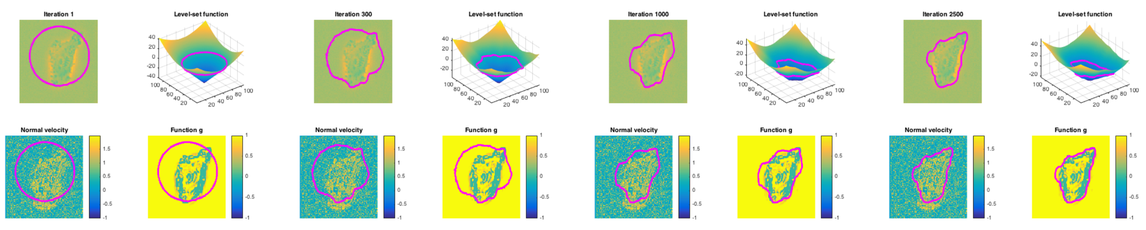


2 Tracking

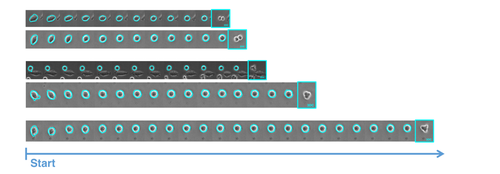
- The circular contour obtained in Step 1 is used as an initialisation for the segmentation in Step 2, where cells are first tracked backwards in time until the beginning and subsequently forwards in time until the end of mitosis
- Using variational and level-set methods, we aim at minimising the following energy functional incorporating information on the tracking contour evolution, which shall lead to coincidence of the contour with the cell membrane:

$$\underbrace{\lambda_1 \int_\Omega (c_1 - |v|)^2 (1 - H(\phi(x)))\, dx + \lambda_2 \int_\Omega (c_2 - |v|)^2 H(\phi(x))\, dx}_{\text{partition into two regions with different normal velocities}} + \underbrace{\mu \int_\Omega |\nabla H(\phi(x))|\, dx}_{\text{small contour length}}$$

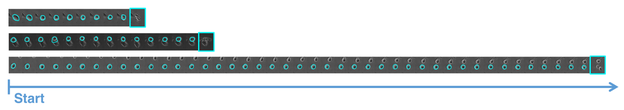
$$+ \underbrace{\nu \int_\Omega g(f(x))\, |\nabla H(\phi(x))|\, dx}_{\text{stop contour at edges based on loc std}} + \underbrace{\omega \frac{1}{2} \max\left\{ \int_\Omega (1 - H(\phi(x)))\, dx - t_{\text{area}}, 0 \right\}^2}_{\text{keep area above threshold}} \rightarrow \min_{\phi, c_1, c_2}$$



Results

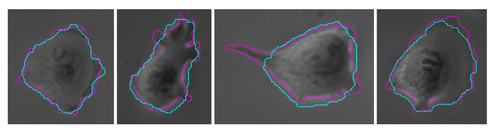


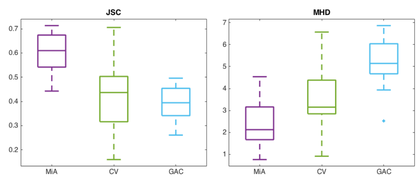
	DMSO	25nM MLN	0.75nM P	30nM P	Combined
Events	44	75	10	35	43
AMD	58	73	68	116	105

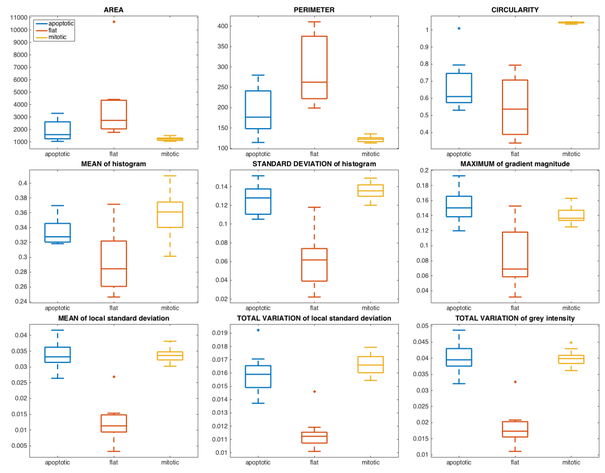


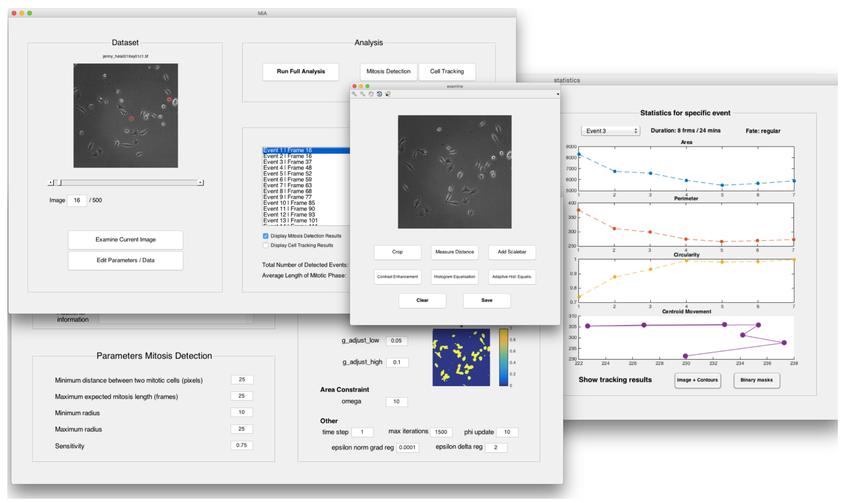
	DMSO control			3nM paclitaxel			30nM paclitaxel		
	Pos 1	Pos 2	Pos 3	Pos 4	Pos 5	Pos 6	Pos 7	Pos 8	Pos 9
Events	14	11	13	12	8	19	10	13	35
AMD	51	41	60	52	88	94	146	104	112
Total AMD	51			78			121		

Left: Phase contrast microscopy experiment with HeLa Aur A cells
Right: Multi-modality experiment with FUCCI-expressing MIA PaCa-2 cells









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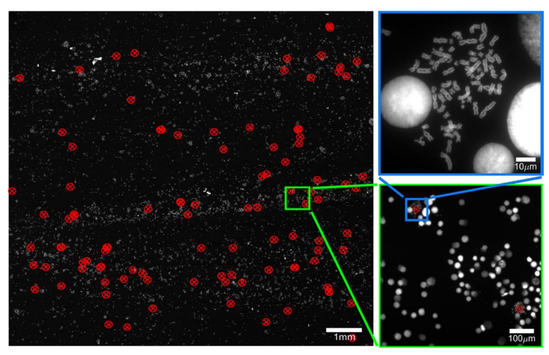
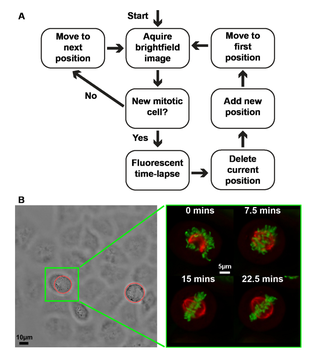
Outlook: Multi-Modal On-Line Processing





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