Complete kinetochore tracking: tracking kinetochores with machine learning

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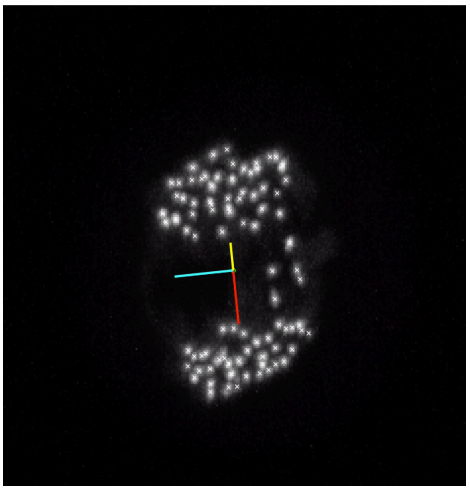
Background

Lattice light sheet microscopy is revolutionizing cell biology since it enables fast, high-resolution extended imaging in three dimensions combined with a drastic reduction in photo-toxicity/ bleaching. However analysis of such data sets still remains a major challenge. Automated tracking of particles in imaging data can reveal quantitative insights into biological mechanisms [1], such as those influencing the mechanics of cell division, which is governed by a protein complex called the kinetochore. Current tracking approaches cannot deal well with the extent of heterogeneity often present in biological data, such as mechanical distortions of an object, or non-specific signal of a fluorescent marker.

Aims and scope of the project



The aim of this project is to leverage the success of machine learning approaches to computer vision [3,4] and improve tracking of kinetochores in live 4D imaging data [2]. This will allow complete analysis of the positions of all 46 chromosomes simultaneously for the first time in human cells. Improving robustness of kinetochore tracking to heterogeneity could open up new datasets for analysis where currently automated tracking is not possible.

In this project, convolutional neural networks (CNNs) will provide detections of particles in each frame of the movie. To link these detected particles between frames, a state space model would provide an appropriate framework, and inference about the system would be achieved via Sequential Monte Carlo (SMC) methods [5]. Alternative approaches, such as solving a linear assignment problem to establish the identity of particles in successive frames, could be driven by the student if preferred.

PhD Projects

1) Extension of tracking framework from mitosis to meiosis, which involves twice as many objects to track, or to multiple fluorescent markers in multiple channels with differing heterogeneity.
2) Modelling of mechanical distortions of kinetochores resulting from incorrect attachment to microtubules (cellular machinery). Automated tracking data of stretched and distorted kinetochores are not currently available, but tracks from the new algorithm could be used to validate any model developed.

External partners

Possibility of partnership with 3i (microscopy company), or with University Hospitals Coventry and Warwickshire (UHCW).

Keywords

Tracking; Machine Learning; Deep Learning; Sequential Monte Carlo; State Space models

References:

[1] Jaqaman et al 2008 Nat Methods https://doi.org/10.1038/nmeth.1237 [2] Armond et al 2016 Bioinformatics https://doi.org/10.1093/bioinformatics/btw087 [3] Newby et al 2018 PNAS https://doi.org/10.1073/pnas.1804420115 [4] Moen et al 2019 Nat Methods https://doi.org/10.1038/s41592-019-0403-1 [5] Naesseth et al 2019 Arxiv arXiv:1903.04797