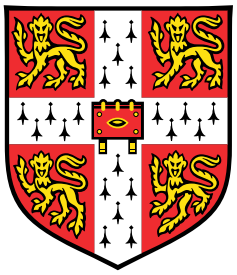
# Hardware, software and applications of super-resolution microscopy



**Marcus Fantham**

Supervisor: Prof. Clemens F. Kaminski

Department of Chemical Engineering and Biotechnology
University of Cambridge

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# Declaration

I hereby declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except as specified in the text and Acknowledgements. This dissertation contains fewer than 65,000 words including appendices, bibliography, footnotes, tables and equations and has fewer than 150 figures.

Marcus Fantham
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This work details the development of two tools, and demonstrates their applications to answer biological questions.

Chapter 2 describes LAG SIM, a versatile and user-friendly structured illumination microscope, capable of imaging in multiple colours at 11 Hz with a resolution of 80 nm. Data can be captured and reconstructed with minimal training, allowing the microscope to be used for a wide variety of biological investigations. A collection of case-study experiments is presented, which can be used as a resource for new users to find the optimal set-up to answer their biological question.

Chapter 3 presents my new volumetric rendering program, FPBioimage, which runs in a web browser. In combination with a suite of additional software built to complement the main tool, FPBioimage makes sharing and publishing 3D volumetric data a one-click process. With a focus on creating a tool that is intuitive and easy to use, researchers around the world can now immediately view their colleagues experimental results, even when separated by thousands of miles.

Chapter 4 shows an application of these two tools for novel cancer treatments based on metal organic frameworks (MOFs). The large pore size of these crystalline materials allows them to be loaded with drugs which would otherwise be degraded in extracellular space, for example siRNA. Experiments show that MOF complexes are successfully endocytosed by the cell, and can therefore be used as effective drug delivery systems, with the potential of treating a wide range of cancers.

Chapter 5 utilises fast, high resolution TIRF SIM to reveal a new phenomenon in the endoplasmic reticulum (ER). Evidence is presented for tubule pinching, which generates non-diffusive directed flow. Computational modelling reveals that pinching reduces the time taken for molecules to travel through the network up to $3\times$ compared to Brownian particle motion. This contribution to the community's fundamental understanding of cell biology will further assist the effort to find cures for the wide range of diseases associated with ER malfunction.

# List of code snippets

# List of publications

David Holcman, Pierre Parutto, Joseph E Chambers, **Marcus Fantham**, Laurence J Young, Stefan J Marciniak, Clemens F Kaminski, David Ron, and Edward Avezov. Single particle trajectories reveal active endoplasmic reticulum luminal flow. *Nature cell biology*, 20:1118–1125, 2018.

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Peyman Z Moghadam, Timur Islamoglu, Subhadip Goswami, Jason Exley, **Marcus Fantham**, Clemens F Kaminski, Randall Q Snurr, Omar K Farha, and David Fairen-Jimenez. Computer-aided discovery of a metal–organic framework with superior oxygen uptake. *Nature communications*, 9(1):1378, 2018.

Michelle H Teplensky, **Marcus Fantham**, Peng Li, Timothy C Wang, Joshua P Mehta, Laurence J Young, Peyman Z Moghadam, Joseph T Hupp, Omar K Farha, Clemens F Kaminski, and David Fairen-Jimenez. Temperature treatment of highly porous zirconium-containing metal–organic frameworks extends drug delivery release. *Journal of the American Chemical Society*, 139(22):7522–7532, 2017.

**Marcus Fantham** and Clemens F Kaminski. A new online tool for visualization of volumetric data. *Nature Photonics*, 11(2):69, 2017.