Imaging informatics at Medicines Discovery Catapult

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Medicines discovery is changing. Imaging is an invaluable tool and is used throughout the drug discovery process, from advanced microscopy at the early stages through to translational imaging in later stages and during clinical trials.

We assist UK innovators in all aspects of accelerating drug discovery from experimental design, conducting experiments and performing cutting edge data analysis.

We are part of a highly interdisciplinary and collaborative team. The imaging informatics team is expanding, with experience in a range of image processing techniques to facilitate cross-modality analysis, manage large datasets and develop bespoke advanced workflows.

Some areas of interests are image reconstruction, enhancement and analysis, for example segmentation and characterisation of an object of interest, co-localisation studies and quantification of drug uptake.

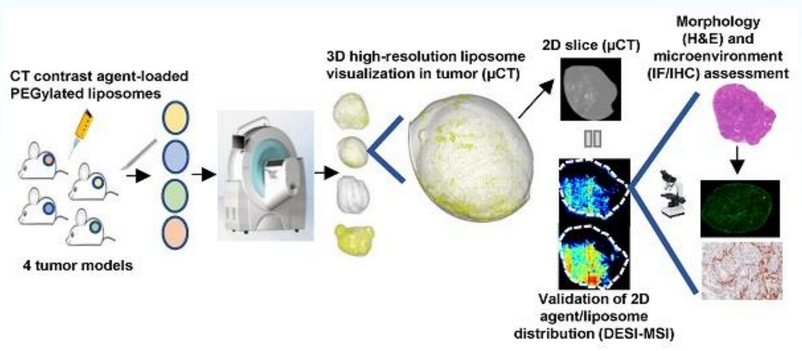
We aspire to work to FAIR data principles [1] and place special emphasis on the integrated use of state-of-the-art open-source software tools to create modular and sharable workflows to increase reproducibility.

Finally, as partners in the QuPharma Innovate UK project, we are exploring how quantum computing will impact the drug discovery process.

Here we show some examples of our work and ask: how can we help you?

Nanomedicines Delivery – Bespoke Data Analysis

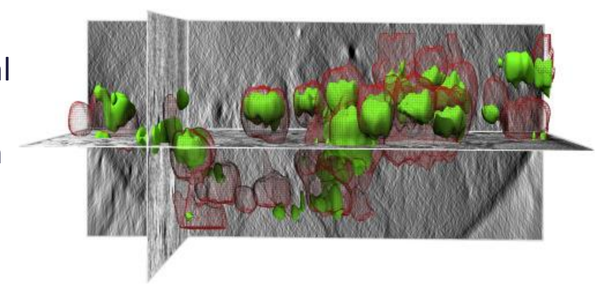
We have experience of characterising the intra-tumoural delivery of medicine by X-ray CT and other imaging technique as illustrated below [2].



We continue to work with partners in this domain, and keep refining the range of biological questions we can answer.

Correlation of cryoSIM and X-ray Microscopy

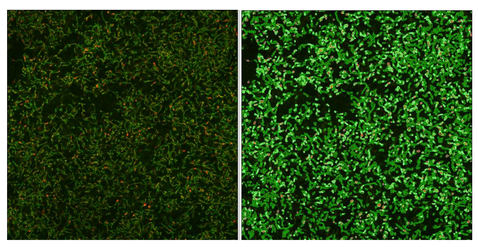
- Correlation is important to gain further information on the biological function and structure.
- A protocol has been developed with a case study using data from Beamline B24 at Diamond Light Source using X-ray absorption contrast imaging and cryo structured illumination microscopy [3,4].



Correlated image of an area of a U2OS cell taken using cryoSIM and cryoSXT, which has been infected with reovirus (shown in green) [5]

Automatic Biofilm Viability Quantification

- Determining the viability of bacterial biofilms is important for testing the mode of action or efficacy of a new antimicrobial.
- Traditional microbiology methods are laborious and resource intensive.
- A Fiji macro was developed to automatically calculate the percentage of live and dead bacteria from confocal microscopy images [6]

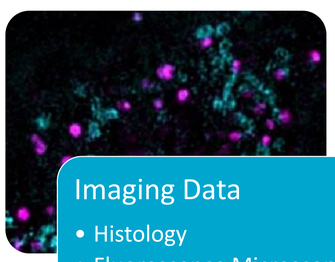


(a) *Streptococcus sanguinis* biofilm grown for 48h, stained using the LIVE/DEAD stain and imaged with confocal microscopy. (b) our macro which automatically detects live bacteria (outlined in green) and dead bacteria (outlined in white)

Working Across Imaging Modalities

The use of open source software tools helps us to maximise our contribution to a wide range of imaging activities. Further examples are:

- Implementation of good data management practices. This underpins the automation of tasks where possible, including QC checks and connecting a sample's data across imaging modalities.
- Optimisation of the definition of regions of interests on microscopic images of tissue samples prior to the capture of the **(spatial) transcriptomics** signatures in each region.
- For tissue sections, the spatial registration of data from **digital pathology** and **mass spectrometry imaging**.
- Building our **single molecule localisation microscopy** (SMLM) capability, making use of the quickly expanding suite of analysis tools.



Imaging Data
- Histology
- Fluorescence Microscopy
- Pre-clinical Imaging

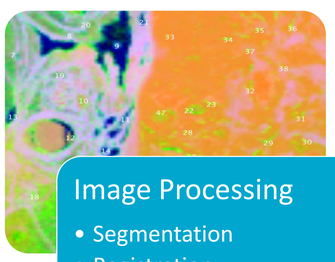
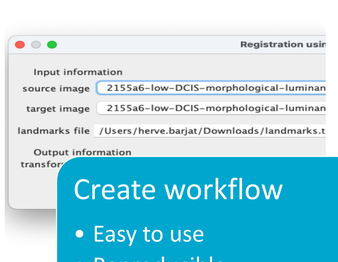
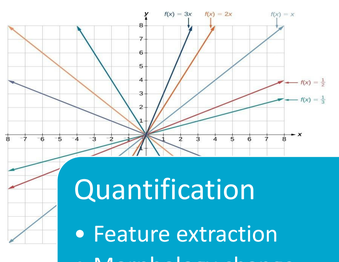


Image Processing
- Segmentation
- Registration
- Correlation
- Tracking
- Colocalization

Using state of the art image analysis developments
- Deep learning
- Fiji plugins
- Python/R packages



Create workflow
- Easy to use
- Reproducible
- Accurate
- Automated



Quantification
- Feature extraction
- Morphology change measurements
- Clustering

References

[1] Wilkinson, Mark D. et al. "The FAIR Guiding Principles for scientific data management and stewardship." Scientific Data 3.1 (2016).
[2] Moss, Jennifer et al. "High-resolution 3D visualization of nanomedicine distribution in tumors." Theranostics 10.2 (2020): 880-897.
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[4] Vyas, Nina et al. "Protocol for image registration of correlative soft X-ray tomography and super-resolution structured illumination microscopy images." *STAR protocols* 2.2 (2021): 100529.
[5] Kounatidis, Ilias et al. "3D correlative cryo-structured illumination fluorescence and soft X-ray microscopy elucidates reovirus intracellular release pathway." *Cell* 182.2 (2020): 515-530.
[6] Mountcastle, Sophie E. et al. "Biofilm viability checker: An open-source tool for automated biofilm viability analysis from confocal microscopy images." *npj Biofilms and Microbiomes* 7.1 (2021): 44.

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