Multi-modality – Paul and Lucy

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Discussion topic: What is the demand for a UK infrastructure for correlative and multimodal imaging, and what are the details that should be considered?

- What is the research question? This needs to be answered by end user communities to be able to assess demand
- What are the scales involved, from sample size to feature resolution?
- What are the types of information that need to be correlated, e.g. the connectomics community require the addition of e.g. electrical and calcium signals on top of brain ultrastructure
- Are infectious agents involved and therefore containment required?
- Will the multimodal experiments require whole animal imaging facilities?
- What are the imaging modalities that need to be correlated?
    - Fluorescence microscopy
    - X-ray
    - nanoSIMS
    - FIB-SEM
- How do we image large intact samples with fluorescent labels
    - Light sheet microscopy/ brain saw
    - Serial sectioning of light sheet imaged samples
    - Correlation of light sheet with vEM
    - Light sheet and multiphoton for large pathology samples in clinical research
- Where should facilities be housed?
    - For containment, spread facilities geographically for safety
    - For some sample prep workflows, initial fixation can be done locally. For complex sample prep, specialist centres might be needed, especially when working with regulated specimens.
    - Some CMI pipelines can be close to end users, others may need to be more centralised, consider several levels.
    - The synchrotron model has specific time-limited calls which mean that the end user has to build a concise proposal, and this is supported by beamline scientists. This model could be considered for a CMI NF. Synchrotrons also have BAG vs rapid access portals.
- DATA is critical

    - Correlative and multimodal data overlay is non-trivial. There must be end user support for data processing, analysis, handling, interpretation, sharing…
- TRAINING is critical
- Should the focus be on instrument development for multimodal approaches (where possible) or on combining data types from different instruments? Or both?
- How can we bring communities together to forge collaboration – e.g. spatial omics and imaging specialists; cryoCLEM and vEM; medical imaging?

Identify at least 1 obstacle to try and overcome (don't just say lack of funding, be specific) and 1 action point to address it

- Access to containment facilities for CMI for pathogens and animal models e.g. mice? Solution could be a roving facility to bring equipment close to the experiment.
- General access modes for CMI pipelines, user support in getting started, troubleshooting. Triaging at entry point with user advice is critical. A good facility will facilitate fast pipelines and return of results, and will combine a broad range of expertise to focus on specific end user research.

Generate a WIBGI (Wouldn't It Be Great If) wishlist (don't say more funding, be specific)

- Wouldn't it be like Christmas if…a research scientist anywhere in the UK could approach their local imaging facility and together connect with a UK CMI National Facility to get advice on CMI experiments that could be applied to their research question, followed by assistance in preparing, imaging and analysing the data, and returning quantifiable data for analysis by the end user.

OTHER DISCUSSION POINTS:

Value

- Lack of access, lack of time and lack of expertise can affect whether a local facility can handle a CMI pipeline. Users might get pointed to other facilities that have the CMI expertise and instruments.
- Local facility experts should be engaged in the whole process of a project moving through the NF.

Engagement of local facilities in the infrastructure

- Local light microscopy expertise and equipment is essential.
- The EM facility is often the entry point for a CMI pipeline, who then engage the LM facility to design the upstream imaging protocols.

Support for end users

- Initial portal and discussion with CMI experts is an essential first step, this team can advise on preliminary data that could be collected locally to support the application.
- Ensure that the research question is properly focused by an expert team as it comes into the NF.
- End users may have expert support or they may not - different levels of user support will be needed at first contact.

Cost

- Would funding agencies pay for an expert team at the head of the portal in some form?
- Consider how POP is funded.
- Paying for the experiments is a challenge.
- For new users - how long will it take and how much will it cost?
- Chicken and egg of idea and money to try it.

Training

- Education of end users and facility leads and teams about CMI pipelines and what they can do is essential.
- NF can act as a hub for training local facility staff to be able to use CMI pipelines on local equipment.

Design of the National Facility

- Proof of principle (POP) data collection to show end users what is possible is important.
- Full service is good.
- For single vs distributed, be careful not to undermine local facilities and their costing and sustainability.
- It cannot be funded just by an equipment call, because if you have the machines you still might not be able to link them together to form a CMI pipeline.
- Most local users won't need all of the instruments that are needed to build a CMI pipeline, just some of them.

Engagement

- Good communication is essential due to the complex workflows
- Engage with industry early enough to travel on the journey together with instrument automation/ data technologies.
- Bring sample prep expertise and microscope manufacturers together.
- Forum for discussion.
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Measuring success

- Once the NF is in place, how do you recognise when you have reached saturation - metrics!