3rd UK Imaging Facility Manager Meeting 7-8 Jan 2010 Imperial College London: Working group reports

The meeting was attended by ~35 people who made it to London through ice and snow, out of 55 registrations. Roughly 60% were facility people and 40% from companies.

For the first time, we tried break-out sessions on specific topics, which was very productive and popular, see reports below.

A direct outcome of the meeting was a strong interest in a workshop including hands-on training on commercial equipment on high-resolution microscopy. Both facility and company representatives were keen to have one already this summer and offered support, but the location and main organiser is still needed.

Because the meeting is growing in popularity and slowly coming of age, I created a little (very unscientific, non-statistical) survey, to know which way to go next year (at the end of this document).

Talking about next year, thankfully **Rolly Wiegand** has volunteered to organise **next year's meeting in Edinburgh**, so next year the Northerners will have an easier trip. And we even have some interest from Cambridge for the year after.

Working group reports

The working groups at the meeting discussed issues related to new microscopy technologies and issues of facility management. The participants agreed to feed the results directly into the BioimagingUK working groups and use this document as a starting point for further discussions there.

Some working groups (general and specialised facility access) didn't find enough interest at the meeting, so no summary was produced.

Training (chair: Yan Gu, MRC Mill Hill, London)

- issues raised:
  - training courses
  - company involvement
  - funding for training
  - training of staff and supply of new staff
  - modular training could even out different background (physicists, biologists) - basic modules (e.g. optical physics, sample preparation, ...) could bring everybody up to the same level as an entry point for advanced courses; after completing a certain amount of modules, a certificate could be created
  - central website - Oxford already had twice as many registrations as spaces
  - funding for courses - limited to young people, not facility people?

High-throughput microscopy (chair: Nick Barry, Laboratory of Molecular Biology, Cambridge)

- The difference between low throughput (tens of samples with data collection on standard microscopes) and medium throughput (hundreds of samples, multiwell plate format, some degree of automation) is not so big: people already do repetitive experiments that could be automated.
- High-end plate reading instrumentation is entering facilities (e.g. P.March, Manchester)or a closely affiliated facility (e.g. T Self, Nottingham). With the provision of some robotic sample handling and up to medium scale sample numbers, the user can take care of reagents and sample prep. At this level it can function within a well resourced microscopy facility.
- Assay development for HT generally is done via this 'hands-on' route.
- High-throughput is different, with thousands to tens-of-thousands of samples. The whole experimental pipeline needs to be highly automated, with a lot of support/ancillary equipment and in house expertise.
- Setup costs are high, but numbers of data points are huge as well
- Expert support staff is needed, other than the person performing the experiment: biologists, bioinformaticians, statisticians, I.T. people
- Data analysis and bioinformatics are essential,
- Some public domain software is around, what's missing is TRAINING!!
- Some groups report shortfalls with existing data analysis software - method and software development is needed
- Large HTS facilities could save money by buying libraries/reagents in bulk, and could also more easily set up the infrastructure to store them safely. Ultimately a large screen is still expensive
- From the perspective of bringing automated microscopy into wider and more routine use, hardware and software developed for HTS has a lot to offer.

In vivo imaging (Paul Thomas, Univ. East Anglia)

- Cat 3:
  - a Cat 3 facility is needed, has to be central; perhaps, at site that has most safety procedures already in place – *e.g.*, Pirbright (animals) and Rothamsted (plants)
  - but Cat 3 license is always specific for an organism, two Cat 3 experiments can't necessarily share the same space
- general *in vivo* imaging:
  - for general *in vivo* imaging, there are already a large number of facilities across the UK, a central facility doesn't necessarily make much sense for general *in vivo* imaging
  - centres of excellence dedicated for specific methods as set up by the Scottish Universities Life Sciences Alliance (SULSA) might be good – especially to provide access for those sceintists at institutes that have no *in vivo* capability
  - advantage of central facilities rather than local *in vivo* imaging is that *in vivo* and standard microscopy can exclude each other
  - indication on the UK LM facility website of where *in vivo* imaging can be done would go a long way
  - a problem is that a license is linked to experiment and location; if the Home Office would change it so an experiment can be done in any space with dedicated rooms, that would help (Note: Overall disastisfaction with

inconsistency of Home Office inspectors in applying the same rules, and restrictiveness of licenses.)

- an idea for the UK LM facility website would be for facility managers to indicate their willingness to provide help and advice (applies to other areas of expertise as well as *in vivo*)

Funding & sustainability (Lucy Collinson, CRUK London)

- direct funding for open access facilities, incl. service contracts and support staff, rather than via research groups, would be more efficient (better usage of equipment) and induce a change of mentality(no protectiveness and secrecy)
- imaging inventory:
  - an inventory of facilities across UK would be good, as information for all scientists what's available and for universities and funding agencies to dedicate funding
  - this should include a wishlist for equipment
  - this could be built from the facility website currently hosted by York
- balance small - medium - national facilities needs to be discussed (so large central facilities don't take money away from established local ones)
- specialised equipment and pre-commercial novel technology:
  - dedicated funding for specialised equipment and pre-commercial novel technology is needed, to promote development
  - how can companies be involved, mixed open licence / commercial licence model for technology, as it is already established for software?
  - could companies save money by sharing development costs with funding bodies, which in exchange get the final product cheaper?
- currently, equipment funding is channelled via project grants, but the most efficient use of equipment is outside / across single projects - different metrics to review funding for facilities are needed
- bulk service contracts between research councils and companies would make service contracts cheaper for facilities, but the number of service contracts most likely higher and more predictable for companies

Software & data (Paul Thomas, Univ. East Anglia)

- overwhelming support for a single, standardised file format from users and from companies developing image-analysis software, but problem would be to get the image-acquisition companies to adopt a single file format
- one objection raised by image-acquisition companies was that the present OME-TIFF format may not include all the necessary meta-data
- general support for an on-line, centralised database for published images that includes the original images (as JCB DataViewer, but global)
- this database would be useful for validation of data by peers, and would also enable software developers to check new algorithms on "standard" datasets
- less enthusiasm for the OME database (Omero), some had tried it and failed to get it to work, and so were disinclined to try again despite assurances from people with newer installations that it was now much improved
- some non-users of Omero were not convinced that it would be useful to them; however, present users argued that it enabled better organisation of large amounts of data, and simpler access to archived images – perhaps, the biggest

impetus to uptake will come if the centralised database is implemented, and funders begin to seriously apply their own rules for data archiving and access
- uptake of Omero might be greater if it was simpler to install and had more image analysis tools
- a separate issue was how, and to which degree, can experimental (as opposed to image) meta-data be standardised and saved (*e.g.*, sample preparation, organism, tissue, ...)
- software training would be good; especially, for open-source software (ImageJ, Omero); although, it was pointed out that RMS runs image processing workshops every year (June) – and this includes ImageJ
- Question: do facility managers support Omero? Answer not clear, because hardly anyone actually uses it, comes down to 'if it works, yes'
- idea for next year's meeting: Omero workshop

High-resolution microscopy (Rolly Wiegand, Univ. Edinburgh)

- Over the last 3 years, a range of novel microscopic techniques have become available that circumnavigate the limitations as defined by Abbe's law of diffraction-limited resolution of optical microscopy, thus providing 'super-resolution'. These new approaches were discussed and here a short summary of the methods is given:
  - Structured illumination microscopy (SIM)(OMX / Zeiss PAL-M):
    - ~2x increased XYZ resolution (~100 nm lateral, 250 nm axial)
    - too slow for live cell imaging in SIM mode
    - limited penetration depth (< 20 μm)
    - strong signal necessary (photobleaching might be a problem)
    - costs are high, therefore only affordable for large facilities/institutes (at present Oxford and SULSA/Dundee)
    - no multi-colour image acquisition in high resolution mode (grid wavelength-dependent, can't be easily realigned)
    - Zeiss PAL-M has added functionality of PALM and costs might be slightly lower
  - 4Pi:
    - Leica have discontinued the system and vast operational problems strongly suggest that this technology is not feasible for practical use
  - Stimulated depletion microscopy (STED):
    - 3x increased resolution in XY (~75 nm), no improvement in Z, yet
    - Leica have multiphoton and continuous wave version available
    - purely optical, so no computing involved, but fluorophores need to tolerate high (depletion) laser power and many excitation / depletion cycles
    - modular system allows use of standard scanning systems and thus combined functionality and lower costs
    - acquisition speed as for SIM relatively slow
    - so far only single channel acquisition, but a two-channel solution is under development for the MP-system
    - CW-system allows the use of standard fluorophores and provides less problems with photobleaching

    - easy to operate by standard user

- Statistical methods (PALM, STORM, ...):
    - 3-4x increased resolution in XY, no improvement in Z in basic mode, therefore most applications combine it with TIRFM so far
    - modified methods (e.g. astigmatic optics with 3D STORM, de-focussing or double-lens systems (iPALM)) allow ~3x increased resolution in Z as well
    - relatively easy and cheap to implement on a standard high-end widefield system
    - needs either switchable/activatable fluorophores or special reducing conditions for ground-state depletion of standard fluorophores (so far limited to fixed samples)
    - requires very stable, high precision stage and environmental conditions
    - high computational demand for data processing
    - first publication of two-channel image acquisition
    - can be combined with standard widefield image acquisition/deconvolution to add information from a different spectral channel at 'normal' resolution

- a discussion platform and workshop would be desirable
- a workshop has been proposed and initiated:
    - invited speakers could be :
        - PALM / STORM: Sam Hess, Eric Betzig, Jennifer Lippincott-Schwartz
        - STED: Stefan Hell or colleages
        - switchable proteins: Uli Nienhaus, S Jakobs
        - application of the techniques above: Anne King and/or Ian Dobbie (OMX), Christina Flors (TIRF-PALM, ground-state depletion microscopy), ...
        - microscope companies at the meeting (Zeiss and Leica) are happy to provide their demo equipment (Zeiss: PAL-M, Leica: STED, Olympus: Cell R system capable of TIRF-PALM , other widefield system suppliers for PALM?); this would allow to compare all techniques with the same sample side by side
        - location to be decided, if the OMX system is to be used, it would have to be in Oxford or Dundee, because it can't be transported
    - a good date would be beginning of July, after the equipment is used at Microscience

- The feasibility of a central research and development facility for super-resolution microscopy was discussed (desirable but presumably impossible to fund and administer).

- Due to the increasing demand in computing power, data management and storage capacity, the improvement of local IT infrastructure and collaboration with computing experts seems to be the way forward for central imaging facilities (see also break-away session 'Software and Data').

Participant's feedback

Because in its 3rd year the meeting has started to get even more interest, and we had covered the most basic and obvious facility topics, I asked people for feedback on the current form, and 12 have responded. The details are below, they can be summarised as follows:

- pretty much everyone finds this meeting very useful
- the break-out sessions about dedicated topics have been successful, but more time for plenary discussions would be good
- the current format of half-days with an overnight stay seems to be a good option, although with more topics coming up, two nights have been proposed to avoid rushing through discussions
- everyone agrees that it's great to meet very informally in a small group, yet it's difficult to say how to keep the format without excluding people
- it was not obvious when we started our facility manager meetings in which form and number company representatives would participate, and how that could affect the outcome; luckily, companies have showed big interest, and all participants feel that they integrate seamlessly and are a valuable contribution to the general discussions (direct feedback, technical updates, ...); and by the way – the 17% not answering that question were polite company reps

	a	b	c
1. We've had this **2 half-day format** twice now, do you like it? *(a) it is ideal (b) 1/2 day would be enough (c) 2 days would be better*	100.0%	0.0%	0.0%
2. Did you like the idea of **short technical reports** by facility people? *(a) yes (b) don't know (c) no*	91.7%	8.3%	0.0%
3. Did you like the idea of **short technical updates by company people** (camera technology)? *(a) yes (b) don't know (c) no*	91.7%	0.0%	0.0%
4. Did you like the **break-out groups**? *(a) yes (b) don't know (c) no*	66.7%	33.3%	0.0%
5. Was the number of **sessions** (two) ok? *(a) two is perfect (b) one would be enough (c) "more would be better (could participate on more topics)"*	83.3%	0.0%	16.7%
6. Was the number of **topics** (nine) ok? *(a) yes (b) don't know (c) no*	58.3%	25.0%	8.3%
7. Was the time for **plenary discussions** ok? *(a) yes (b) too short (c) too long*	58.3%	25.0%	8.3%
8. This year we had 57 registrations (up from 27 last year), but (because of the weather) only ~35 were present at any time. Should the **number of participants** be limited? To which number? *(a) No, everyone should be allowed to attend (b) max 40 (c) max 60)*	75.0%	16.7%	8.3%
9. How do you feel about **company people** being part of the meeting? *(a) perfect as it is (b) not enough (c) too many*	83.3%	0.0%	0.0%
10. In the Doodle poll, most people seemed to be available in the first full week of January Thu-Fri, are this the **ideal time of the year and days of the week** for you? *(If not, please use comment box below)* (a) yes (b) don't care (c) no	50.0%	25.0%	25.0%
11. Do you think you **will attend again** next year? *(a) yes (b) don't know (c) no*	100.0%	0.0%	0.0%

Other comments:

- So difficult to have an open discussion with everyone at the same time, the breakout groups really helped in this as groups of 10 work well. The summary session could do with a time limit per topic as 80% of time is spent on one topic and then the other 4 squeezed into a few minutes. However, this may reflect the interst in that topic. It's clear that databases is a major topic and maybe should have its own meeting or session. Would it make sense to increase the length of the meeting to 2nights (1full day and 2 half days to allow for more in depth discussions? I really enjoyed the meeting and got a lot out of it so thank you for all of your hard work.
- ad Q10 (: I think the first week in the year might not be ideal for everybody. Some people use the Xmas break for extended holidays, in particular people from abroad working in the UK. Also, Sundays, Mondays and Fridays are bad days for travel within the UK. Tickets are a lot more expensive, reservations more difficult to get and planes and trains are over-crowded, in particular if you travel between London and the North/Scotland.
- I think the general format works well and the break-out sessions are a good idea as it gives everyone a chance to contribute. A few short (5-10 min) presentations from selected companies on their new technologies might be a good idea as it would help inform us (the Facility managers) of new developments and give the companies some tangible reward for their sponsorship. Maybe some kind of case studies would provide a good platform for discussion e.g. one of the facility managers gives an overview of how their Facility is organised and used.
- Travelling on a Friday over a long distance can be expensive, how about the beginning of the second full week in January?
- I think holding the meeting a little later in the year would be a good idea to avoid adverse weather conditions and increase the availability of those who normally have an extended Christmas break.
- Break-out sessions could be shorter (45 min), with more time for summary discussions (1.5 hr). Number of topics could be reduced to 6. The number of attendees was about right; perhaps, limit could be kept at 40 by allowing only 1 person from each facility or company?
- The only problem I found with the break-out groups is that I wanted to go to more than one that were running at the same time. Would folk like more commercial updates?
- I think the break out sessions could be shorter, say one hour maximum, to allow more time for the plenary discussions, or for the possibility of additional break out sessions (depending on concensus) within the 2 day meeting format)
- 2. Short reports similar to the one on Multi-photon specification are of great benefit.
- 3. Same goes for the camera talk, pity he didn't have more time.
- 4. Not so sure about breakout groups, maybe it was different for others but for the groups I was in, we talked as a group and then it was pretty much all said again in the session following. Breakout may be good to get discussion started but should be shorter so that real debate takes place with everyone present.
- 8. It would be a pity to exclude people who are actually running or trying to set up facilities.
- 9. As it happened this year, company participation was most useful and was not simply treated as a sales opportunity. Any chance of getting participation from funding bodies since they need to know what happens to the equipment they fund and how the money might be better used?

- 10. A good time to hold it (and it does not snow most years) since it is quiet at work while things are still getting started again and hotels/trains have plenty of room.

2 February 2010, Martin Spitaler