Towards a roadmap for Biomedical Electron Microscopy within the Bioimaging UK framework.

Through several rounds of consultation and incorporation of interest from different EM communities (e.g. structural biology and cell biology EM), the following plan has been developed to fulfil the needs of the general UK Biomedical EM community for the period up to 2020.

We envision a 3-tiered structure based upon the complexity of the technique, the need for expert support, and especially the (running) costs of the instruments.

- National facilities:

National facilities provide access to newly-developed technology and/ or equipment that is so expensive that few systems can be acquired nationally. Currently we foresee the need for 2 (or 1 integrated) large-scale institutes that would provide instruments and expert support. Funding for these resources should be at a national level and access charges should be subsidized (similar to synchrotron at Diamond).

1. High-Resolution TEM – focusing on 300kV microscopes for cryo EM and electron tomography. This will be the prime resource for structural biology (single particle EM and cryo tomography) and will include 3D cellular EM. A proposal has already been submitted to construct a national facility at Diamond, which is currently under discussion with the funding bodies (Wellcome).

2. Volume SEM – automated physical sectioning and imaging within the SEM chamber over hundreds of microns^3 at nanometer resolution. This technology is suited to acquire lower resolution, high volume information from cells and tissues. Instruments such as Focused Ion Beam SEM (FIB/SEM) and Serial Block Face SEM (SBF/SEM or 3View) could run in a 24/7acquisition mode producing large datasets. This could be run largely as a remote service, and would require expertise in sample processing, data acquisition, image analysis and large-scale data storage and handling. This is a fast-developing field with new, expensive microscopes coming to market in quick succession. This Facility is under discussion and it must be emphasized that rather than going for the highest resolution, the aim is to provide volume information within the tissue reference space.

- Centres of Excellence:

Centres of excellence provide access to cutting edge technology that does not necessarily require extremely expensive equipment but rather very skilled staff that are able to perform and support the execution of experiments. These types of technologies are not used on a day-to-day basis in biomedical research but do require dedicated equipment. A bundling of resources in a limited number of centres across the UK would provide a very cost-effective model. Such centres should also provide training for new researchers in the field and in that way allow the dissemination of the technology to other institutes. Funding for this type of centre should be at a national

level with application, for instance, as a distributed network to the Science and Technology Facilities Council (STFC).

1. Correlative Light and Electron Microscopy (CLEM) - distributed network across the UK, providing expertise, training, and access. These types of center need to be associated with down and upstream technologies (e.g. different types of light microscopy, culture facilities, and sample preparation).

2. Cellular Electron Tomography - Room temperature Electron Tomography is a very valuable research technique that not always requires the highest resolution instruments but does need dedicated staff, especially for the data analysis.

3. Analysis Electron Microscopy – More and more the application of what traditionally were considered material science EM techniques is applied to biomedical questions as well. Technologies such as EDX, STEM, SIMS, GIF, and EELS have already shown their use but they are not applied widely mainly because of the unfamiliarity with the technology.

- University and Research Institute EM facilities:

Existing local facilities will still serve the vast majority of EM projects as they are based on routine applications (SEM / TEM). These types of facilities are critical for biomedical research as they provide all the groundwork and therefore provision of lower-end instruments and upgrades must be protected. We emphasise that the above-mentioned National facilities and centers of excellence do not preclude other facilities from performing or acquiring such high-end technologies, rather, they act as a resource to researchers that do not have access to those technologies at their home institute because of the expense of the technology or the lack of expertise.