300 keV microscope Tender specification

Background
The University of Glasgow is aiming to purchase a fully automated 300 keV cryo-transmission electron microscope to service the structural biology communities of Scotland. The instrument will be installed in the Sir Michael Stoker building at the Garscube campus and will become the front-line instrument for the Scottish Macromolecular Imaging Centre. Importantly, a critical requirement of funding is that this instrument must be delivered before the end of March 2018

Summary of requirements.
The microscope should have a field-emission gun (FEG) and operate at multiple accelerating voltages up to 300 keV. A fully automated system to load frozen-hydrated specimens into the stage should be designed to minimise the risk of specimen contamination. The tool should have phase-plates comprising a continuous carbon film, along with software capable of regenerating the phase-shift during unattended operation. Full automation for both single particle and tomography data collection should be implemented in a robust and user-friendly software environment. An energy filter, capable of excluding inelastically scattered electrons for zero-loss imaging should be present and capable of operating in a user-friendly manner and without inducing image magnification anisotropy. A counting direct detection camera should be included that is capable of recording data that has at least a 50% DQE at half-Nyquist and 40% DQE at 75% Nyquist.

Technical Specifications

Column
M - The microscope should be housed in an enclosure that ensures a stable operating environment for the column.

M - The microscope should have an oil-free vacuum system, capable of delivering cryo-imaging over > 3 days with negligible contamination (please give details of vacuum system and contamination rates). Scoring: ≤ 0.8Å/hour – 3 points; ≤ 1Å/hour – 2 points; ≤1.5Å/hour - 1 point; > 1.5Å/hour – 0 points.

M - The microscope should have either Schottky or cold field emission source – please give details of energy spread. Scoring: ≤0.4 eV – 3 points; ≤0.8 eV – 2 points; ≤1.2 eV – 1 point; >1.2 eV – 0 points.
If a cold field-emission source is specified ‘flashing’ of the source should be fully integrated into all automated data collection software– please provide details of source stability.
The source should have a long working lifetime; please provide details of expected lifetime and replacement time and cost.

D - The microscope should operate at multiple accelerating voltages – with appropriate stored alignments, up to and including 300 keV – please specify (one point for every additional stored AccV – up to 3)

M - The condenser lens system should provide for multiple parallel illumination settings such that images of single R1.2/1.3 or R2/2 Quantifoil holes or smaller sub-areas may be recorded without irradiating surrounding areas.

M - The lens-system should deliver excellent stability and minimal hysteresis.

M - The optical system should provide for excellent point-resolution with a pole-piece optimised for cryogenic and high-tilt operation (please specify) score by point resolution (<=1.5 angstroms 3 points <=2 angstroms 2 points <=2.5 angstroms 1 point >2.51 angstroms 0 points)

Stage

M - The specimen stage area should have an anti-contamination system to support imaging of cold specimens for > 3 days with negligible contamination. Scoring: ≤ 0.8Å/hour – 3 points; ≤ 1Å/hour – 2 points; ≤1.5Å/hour - 1 point; > 1.5Å/hour – 0 points.

M - The specimen stage should provide for stable cryogenic imaging over ≤ 3 days having computer controlled auto-filling of the cryogen dewar – control of which may be accessed by automated single particle and tomography data collection software.

M - The microscope should have a ROBUST and RELIABLE liquid-nitrogen cooled auto-loader system that allows for computer controlled specimen exchange and minimises specimen contamination.

M – The microscope should be supplied with all necessary components to run the auto-loader – including liquid nitrogen pressure vessels and consumables for at least 500 samples.

M - The stage should give excellent drift performance – please specify X and Y drift values at ~100K.
Score ≤ 5 angstroms/minute – 3 points; ≤10 angstroms/minute - 2 points; ≤20 angstroms/minute – 1 point; >20 angstroms/minute – 0 points.
Score for each axis.

D - The stage should provide for computer controlled dual-axis tilting for electron tomography. Specify tilt-range in X and Y (71-80 3 points 61-70 2 points 51-60 1 point).

Phase plates

M - The microscope should be provided with phase plates for in-focus high-contrast imaging. These should comprise a continuous carbon film in which generation of a phase-shift can be fully automated in both single-particle and tomography data collection regimes.

Please give full metrics to indicate the stability and longevity of the phase-shift (ideally a plot), the number of locations on a carbon-film that may be used, the expected life-span of a phase plate and the cost of replacement (score stable phase shift achieved: ≥ 1 hour – 3 points ≥; ½ hour - 2 points; < ½ hour - 0 points – score life span of phase plate: >6 months 3 points; 3-6 months - 2 points; <3 months - 0 points – score replacement cost <=£5k 3 points 5-10k 2points 10-15k 1 point > 15k 0 points)

Energy filter

M - The microscope should be equipped with an energy filter capable of delivering zero-loss imaging without inducing image distortion.

Please indicate guaranteed magnification anisotropy across the field of view of the largest supplied detector (score <=0.5% 3 points 0.51-1% 2 points > 1% 0 points).

M - The energy filter operation should be fully and reliably integrated into both automated single particle and tomography data collection software.

Detectors

M - The microscope should be fitted with a direct-detection device type camera capable of delivering high-frame rates suitable for electron counting (counting must be implemented).

IMPORTANT – Each camera will be scored individually and the top scoring camera will be used to judge each tender. In the case of super-resolution mode cameras, they will be scored twice – for super-resolution and whole-pixel measurements (thus for DQE measurements made in super-resolution mode they should be a function of the interpolated Nyquist limit).

Please give DQE measurements in counting and integrating modes at:
0, 0.5 and 0.8 of Nyquist.
Score at 0 of Nyquist for counting mode:
0.9-1.0 3 points, 0.8-0.89 2 points 0.7-0.79 1 point < 0.69 0 points.
Score at 0.5 and 0.8 of Nyquist for counting mode
>0.6 3 points, 0.5-0.59 2 points 0.4-0.49 1 point <0.39 0 points.
Score at 0.5 and 0.8 of Nyquist for integrating mode
>0.6 3 points, 0.5-0.59 2 points 0.4-0.49 1 point <0.39 0 points.

Please give frame rate for counting over an area of ~16 MP or more.
Score
>300 fps – 3 points
200-300 fps – 2 points
100-200 fps – 1 point
<100 fps – 0 points

Please give the detector size – If the detector allows for super-resolution imaging please give DQE values for this mode as well.

Score
>60 MP 3 points
40-60 MP 2 points

14-40 MP 1 point
<14 MP 0 points

Software
M - The microscope should have user-friendly software for basic operation and fully automated data collection in both single-particle and tomography projects.

D – The software should allow remote monitoring and operation of the instrument and data collection.

D - Microscope operation should be through stable software, on a stable OS platform. In the event that the OS is deprecated, then software upgrade should be made an NO COST as long as the microscope is maintained under standard service contract or warranty. This is to ensure that network access is maintained – allowing operators to manage both the microscope and data collection remotely. (5 points for free software upgrade)

Single particle data collection software. Software should be present which integrates with all DDD detectors present and the microscope to deliver robust automated single-particle data collection.

This system should be capable of collecting a full or partial montage of the specimen grid at sufficient magnification to assess ice quality in < 1 hour.
M – partial montage
D – full montage

M - Data should be collected on vitreous specimens under low-dose conditions, capturing images from regularly arrayed holes in the carbon support film.

M - Excellent operator control over data collection parameters should allow for manual selection of regions of interest and:

D - if necessary selection/deselection of individual holes. – 3 points if possible in automated data collection mode.

M – Software should provide for robust z-height and focussing (with specification of a range of defocus values)

M – Software should reliably capture images of the identified holes.

Tomography data collection software. Software should be present which integrates with all DDD detectors present and the microscope to deliver robust automated cryo-tomography data collection.

This system should be capable of collecting a full or partial montage of the specimen grid at sufficient magnification to assess ice quality and identify regions of interest in < 1 hour.
M – partial montage
D – full montage

M – Once ROIs are identified software should automatically move the specimen stage to ROIs and reliably capture tilt-series while unattended.

M – Software should provide for robust setting of eucentric height and focussing.

D – In addition to single direction tilt (e.g. -70-+70) software should allow for multiple tilt-series acquisition schemes
Scoring
3 points for multiple schemes - oscillating tilt angles, e.g. 0, +3, -3, +6, -6 etc. and bidirectional acquisition starting at non-zero value as well as at zero.
2 points for multiple schemes - bidirectional acquisition starting at non-zero value as well as at zero.
1 point for bidirectional acquisition starting at zero.

Installation, Engineering support and sign off

M Delivery and installation should commence before the 30th March 2018.
D Delivery as early as possible after order is placed (assuming the customer has prepared the site).

Give projected date of delivery (points for sooner)
3 points before September 2017
2 points before November 2017
1 point before February 2017

M - The instrument should be provided with a UPS that will support in the event of a power failure for up to 15 minutes – allowing safe transition to local generator supply. The UPS should also smooth the power supply to protect against dips or surges in power supply.

M - The instrument including all detectors should be fully supported including all parts for a period of not less than five years. Please give cost of 5 year service contract.

M - A competent engineer should be onsite within 24 hours of notification of an instrument failure that has prevented data collection.

D - A competent engineer should be onsite within 48 hours of notification of a failure or issue with non-critical systems.

M -Sign off and final payment will follow completion of installation including all software, demonstration of having achieved specification and delivery of training to relevant staff.

M - The microscope must have demonstrated reliable performance over at least one month period, including successful calculation of a ≤3.6Å resolution structure from a test specimen such as beta-galactosidase following fully automated data collection, as well as successful unattended acquisition of at least ten tilt-series – with phase plates, in one imaging session.