The resolution revolution reaches India

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Historically, India has had a strong presence in development and structure determination by X-ray crystallography with the likes of Sir CV Raman and GN Ramachandran laying the foundation and grooming generations of scientists particularly in small molecule crystallography. Macromolecular crystallography also started relatively earlier in India compared with other developing countries with M. Vijayan setting up a protein structure program at the Molecular Biophysics Unit at the Indian Institute of Science, Bangalore. This was quickly followed by KK Kannan setting up a facility at the Bhabha Atomic Research Center in Mumbai. However, India lost the edge when synchrotrons came into play and did not catch up with the corresponding revolution in structure determination methods. While recent agreements with ESRF, Grenoble, and Elettra in Trieste provide access to synchrotrons, the lack of one within the country has significantly affected the Indian structural biology community.

The developments in the last few years in electron cryo-microscopy (bright source, better vacuum, detector detectors, automation, and sophisticated software) have dramatically facilitated structure determinations of biomolecules such that side chains can be visualized easily, and resolution between 2 and 3.5 Å are now routinely obtained, with few structures determined to as high as 1.5 Å. Venki Ramakrishnan, who visits India ever so often in December/January and actively engages with younger generation of scientists, had initially proposed the idea that India should invest in a high-end microscopy facility to one of us (Satyajit Mayor), who was the Director of the National Center for Biological Sciences and the Institute for Stem Cell Science and Regenerative Medicine, Bangalore,

and to K. Vijayaraghavan the Secretary of Department of Biotechnology at that time. This was in 2013 just before the “resolution revolution” and Venki Ramakrishnan presented the unpublished work from his group on the Mitochondrial Ribosome structure.

This idea was taken seriously and work on preparing a proposal to the Department of Biotechnology for funding started immediately. The idea was to set up a center in India that would be the equivalent of the synchrotron for crystallography. The facility ideally would have a high-end 300 kV microscope with state of the art detectors and a screening microscope. The hope was that as Indian structural biologists begin to use this, there will be more screening microscopes around the country and grids that were screened and ready for data collection would be brought to the National facility for data collection.

The first proposal was submitted in July 2014. After much deliberation and a few rounds of consultation with the DBT and constant support from both Venki Ramakrishnan and Richard Henderson at the LMB, Cambridge, in Sept. 2016, the Department of Biotechnology sanctioned the purchase and installation of the 300 kV electron cryo-microscope in the Bangalore Life Science cluster campus.

In the fall of 2013, the Institute for Stem Cell Science and Regenerative Medicine started construction of its new building within the Bangalore Life Science Cluster. This was a very good coincidence. The leadership of the cluster had a great vision on the future of the cryoEM and in the basement of the new building built two large rooms for microscopes and two control rooms for operation. In fact, the preparation for the room had started even before the sanction was made. An order was placed for the Titan Krios 300 kV microscope along with all other accessories including high-performance computing in Feb. 2, 2017. The leadership also managed to convince Dr. Vinothkumar who was working with Richard Henderson at the MRC to join the campus and set up the facility. He joined in July 2017 just as the microscope arrived and immediately, Vinoth and the local engineer Vikas Jois started the installation. The installed working microscope was handed over for testing and data collection around Sept. 2017. The speed of

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installation was possible because of the planning of the building for the microscope and with the help of the support staff from the Bangalore cluster.

Data collection started immediately and now in a year, several structures have been determined and ready to be communicated. An international advisory committee chaired by Richard Henderson sets the overall policy for the use of the national facility. Access to the facility is provided through a portal <http://ecryom.instem.res.in/>. Users apply for time and the proposals are evaluated by a committee. If the project is approved, time is provided at no cost to the users. The cost for the first round has been covered by a generous grant from the Department of Biotechnology, Government of India. Several national users and a few international users have so far collected data on the microscope. Vinoth not only does his own work but helps collect data and train users who come for data collection from all over India. The facility has held two hands-on workshops and several meetings to get people the information on the capabilities of the instrument including single particle cryoEM, tomography, and electron diffraction.

The good news is that there is a continued investment of screening microscopes by the Indian funding agencies—there is already one at the Indian Institute of Science, a second one at the Regional Center of Biotechnology in the National Capital Region, and hopefully more are coming. The ball is now in the court of Indian structural biologists; can they leverage these resources to get back to the top of the table in structural biology? Only time will tell.

Compliance with ethical standards

Conflict of interest S. Ramaswamy declares that he has no conflict of interest. Satyajit Mayor declares that he has no conflict of interest. Kutti R. Vinothkumar declares that he has no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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