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THE UNIVERSITY  
OF QUEENSLAND

Flagship: High-throughput cryo-TEM facility

## Unique high-throughput cryo-transmission electron microscopy (TEM) facility for structural analysis

*The University of Queensland's cryo-TEM facility has the latest technologies, including ultrahigh-resolution CCD cameras, a new TEM and specialist cryo-holders, creating a world-leading platform for high-throughput structure determination.*

#### Scientific Drivers

Future advances in bioscience and nanomaterials research will depend heavily on the ability to link structure to function and particularly how individual molecular machinery components fit together into dynamic macromolecular assemblies. Atomic-resolution structure determination of protein complexes and other macromolecular assemblies, including whole viruses, is one of the great challenges of cell biology, proteomics and structural biology. A high-throughput cryo-TEM platform is the only possible tool for achieving this. It will lead to the elucidation of the three-dimensional structure of entire cells with sufficient resolution to examine the arrangement and interactions of internal macromolecular complexes.

With the expanding interest in nanotechnology, the cryo-TEM is also well positioned to make an impact in this field. Understanding the structure of complex 3-D structures of inorganic materials provides valuable insights to the next generation of materials with applications across a wide range of disciplines.

Examples of the types of work that this facility enables include:

- Determining how the 3-D biology of the human islet/ beta cell relates to the development, physiology and

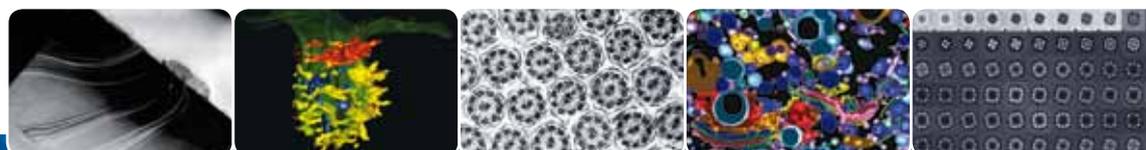
dysfunction of the human endocrine pancreas and its role in diabetes.

- Characterising caveolae by using electron tomography and immunolabelling methods. Caveolae have been linked to cancer, cholesterol regulation and muscular dystrophy.
- Revealing the structure of membrane proteins to assist in the design of new and highly specific drugs.
- Developing an understanding of the nature and structure of nanometre-scale materials, which have application in medicine, in energy production, and in opto-electronic projects.

With the ability to probe the molecular basis of disease, this platform advances National Research Priority 2, in particular, but it also contributes to National Research Priority 3 in the area of biotechnology.

#### Capabilities and the National Research Capacity

The cryo-TEM facility at the University of Queensland is the only fully established life-sciences facility in Australia or New Zealand capable of collecting and processing atomic-resolution images at low temperatures ( $-160^{\circ}\text{C}$ ), as well as undertaking 3-D electron tomography of organelles, cells and tissues at ambient and low temperatures. As such, it is one of only a



handful of similar facilities in the world. NCRIS investment is creating a high-throughput platform capable of the high output essential to make genuine inroads into key questions in molecular biology, medicine and biotechnology. The system offers Australian researchers a quantum leap in technology and productivity for the emerging techniques of electron tomography and electron crystallography. The demand is increasing significantly for rapid elucidation of molecular structures, especially in systems where crystal growth is difficult. Techniques in which images of a large number of randomly oriented 'particles' are assembled into 3-D structures are providing molecular biologists with a fast means of obtaining structural information.

The high-throughput system is sited in custom-built laboratories within the Australian Institute for Bioengineering and Nanotechnology (AIBN) and the Queensland Biosciences Precinct (QBP). Practically,

this places the instruments within easy reach of associated equipment and laboratories for sample preparation and screening. Scientifically, this builds on the unparalleled experience within the Centre for Microscopy and Microanalysis in cryo-electron microscopy, particularly the recent developments in rapid image-processing pipelines for single particle analysis, electron crystallography and electron tomography. Moreover, it provides easy access for the approximately 1000 researchers from the Institute for Molecular Bioscience, the AIBN, and the Queensland Brain Institute (QBI) as well as interstate users. Since its inception, a large number of national and international research projects have been undertaken at the facility.

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