Bio21 Molecular Science and Biotechnology Institute

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Platform Technologies

Platform technologies make biotechnology work. They help us understand the composition, structure and interaction of molecules, and use this knowledge in fundamental research and industrial applications of biological processes.

The remarkable recent advances in instrumentation and computing have delivered today's platform technologies which allow us to answer questions that we previously couldn't even ask. They are as much about skilled people and expertise as equipment. The Bio21 Institute embraces a range of molecular technologies. The platforms and expertise that we have invested in reflects our research priorities. We have concentrated our investments in a select few major areas of technology of strategic importance, but which are not affordable by individual research groups or disciplines. Each facility is accessible to outside academic and industry research groups. We have been supported in this endeavour by University of Melbourne, Victorian Government and Commonwealth Government funds.

We work in partnership with academia and industry to extend the commercialisation of our discoveries and ensure that we have access to state-of-the-art technologies. Once it is completed, we will also work closely with the Australian Synchrotron, one of the most powerful and versatile of platform technologies.

Nuclear Magnetic Resonance (NMR) facility: NMR spectroscopy determines the structures of molecules ranging from small chemicals to macromolecular proteins and nucleic acids. It is particularly useful for the analysis of proteins that cannot be crystallised, and for investigating interactions between proteins, biological membranes, and ligands, including potential new drugs. The Institute's substantial NMR facility, affectionately referred to as the NMR Cave, is led by several of Australia's foremost protein and biomembrane NMR experts, Paul Gooley, Frances Separovic, Terry Mulhern (Bio21 Institute) and Ray Norton (WEHI).

The Institute's primary uses of NMR are investigating the structures of potential drug and pesticide targets, protein pharmaceuticals, and include metabolite biomarkers of disease, as well as the interactions of proteins with their specific ligands (including candidate drugs) and, where relevant, their target membranes. The Institute's NMR capability is also of fundamental importance to a range of analytical and synthetic chemistry applications.

The NMR facility houses nine instruments, including six previously owned U of M and WEHI instruments and three new U of M instruments. The latest acquisitions are the massive 800MHz high-field NMR spectrometer equipped with cryoprobe technology and the 600MHz solid state NMR instrument. This aggregation of major NMR instruments in a single facility provides a unique resource for basic and applied research and serves as a magnet for recruiting expert scientists and attracting academic research and industry collaborations.

Mass spectrometry: This long standing core analytical chemistry platform has in recent years become the cornerstone platform for proteomics and metabolomics. Proteomics allows us to determine the structure and regulation of individual proteins. Metabolomics defines the chemical state of cells and changes in cell metabolism that occur in response to regulators, stress and test compounds and other perturbations, for example genetic modification.

The Institute has 12 mass spectrometers covering a broad range of applications, including:

- High accuracy determination of molecular mass of naturally occurring proteins, nucleic acids and metabolites, as well as chemically synthesised molecules
- Protein sequencing by fragmentation analysis

- Detection of individual molecular species in molecular profiling of cells and animal test systems
- Validation of chemical synthesis and definition of chemically diverse metabolites requiring a variety of ionization techniques.

Nanobiotech clean room and high resolution microscopy facility: Nanotechnology is an emerging field considered to likely have a major impact on medicine, agriculture and the environment and generate substantial economic benefits within the next decade. Essential requirements are clean rooms for assembly of nanostructures and electron microscopes (EMs) for imaging the molecular structures, microanalysis (metal ions) of complex materials and nanofabrication of fluidics systems.

The $10M Bio21 Institute Nanobiotech facility was jointly funded by the University of Melbourne and the State Government. This new facility is designed for physical sciences, life sciences and engineering applications. Equipment includes:

- Focused ion beam scanning & field emission gun-equipped transmission EMs for materials science applications
- Cryo EM for imaging large biological complexes within their cellular environments, as well as for determining the 3-dimensional structures of large proteins
- Scanning EMs equipment with cryo-stages and Raman optics EM for imaging of biological material
- Atomic Force-field microcscopy (AFM) for investigating the topography and chemical environment of a range of biological and chemical surfaces
- High-resolution confocal laser scanning microscope for imaging entities within live cells.

The nanotech facility will be used for:

- preparing functional protein chips, protein-based biosensors and other polymeric structures with biomedical applications
- preparing clean proteins for incorporation into small drug delivery devices
- developing biosensors for environmental testing.

Bio-molecular interaction analysis facility: In living systems, the interactions between molecules are as important as the molecules themselves. The Institute has a range of new biophysical technologies that allow us to measure these interactions quantitatively as well as qualitatively, including:

- analytical ultracentrifugation
- micro-calorimetry
- plasmon resonance spectroscopy
- fluorescence spectrometry
- circular dichroism spectrometry.

These capabilities are fundamental to drug discovery where the affinity of candidate drugs for their targets and the consequences of these interactions for protein subunit structure and conformation are critical information.

Synthetic chemistry: The ability to make molecules, including candidate drugs, is a key capability of the Institute. Eight research groups within the Institute are dedicated to "synthetic chemistry". Supported by a comprehensive range of synthetic and analytical equipment, they have capabilities to make molecules ranging from polymers to peptides, sugars to small molecule candidate drugs.

Animal models for disease: Animal models for disease are vital for understanding the impact of potential new drugs and the role of cell signalling systems in living organisms. The Institute has a $700m^2$ rodent house and Drosophila breeding facility for these purposes.

The rodent facility includes clean room breeding facilities and general experimental working areas and will accommodate a range of mouse and rat models used by resident Institute and external researchers. In addition to environmental biotech applications, the Drosophila facility is a resource for investigating functions of counterparts of human cell signaling components.

Bioinformatics: Computational analysis of patterns and similarities in gene and protein sequences, molecular modeling of proteins and the integration of transcriptome, proteome and metabolome profiles are fundamental requirements for contemporary biotechnology. The Institute is building capability in this area in collaboration with Bio21 partners.