Measuring

Sydney Mass Spectrometry

Proteomics, metabolomics and lipidomics analysis

Sydney Mass Spectrometry provides state-of-the-art tools and expertise for proteomics, metabolomics and mass spectrometry imaging for the life and biomedical science communities.

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Evaluating deep learning for protein analysis

Challenge

Proteins are the core building blocks of life, performing a diverse array of essential functions through an almost infinite variety of shapes and structures. Some proteins work in isolation, and others work in conjunction with other proteins. When protein-protein interactions go astray, it can lead to devastating effects such as Creutzfeldt-Jakob disease (CJD), a neurodegenerative affliction resulting in dementia and death. Therefore, mapping protein structures and protein-protein interactions is of critical importance in the study of many biological processes in health and disease.

In 2021, a neural-network-based deep-learning algorithm called AlphaFold was released, transforming protein structure prediction by allowing researchers to predict the structure of almost any protein from its sequence alone. However, learning material for the model is scarce, as only 6% of human protein-protein interactions have experimentally determined structures. This means that the accuracy of its predictions for protein complexes (and those of its successor, AlphaFold 2) is unclear.

Research

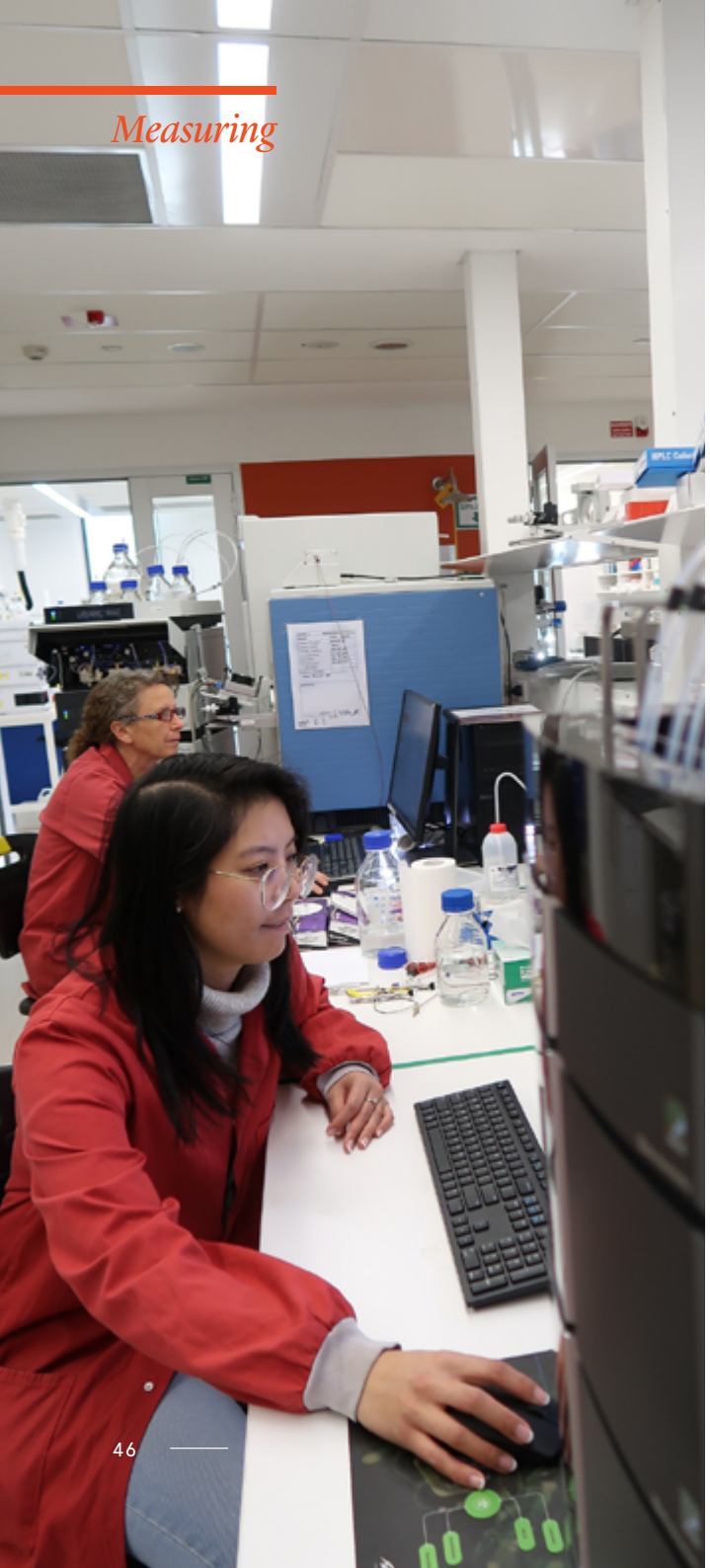
To address this challenge, Dr Jason Low (School of Life and Environmental Sciences, Faculty of Science) and his team began a large-scale cross-linking mass spectrometry project, with the aim of providing a deep-coverage characterisation of cultured human cell lines. This work was made possible by the latest generation of mass spectrometers at Sydney Mass Spectrometry, and the proteomics and mass spectrometry expertise of Angela Connolly and the proteomics team.

Results

Published in *Proceedings of the National Academy of Sciences*, the project yielded in the largest-ever cross-linking mass spectrometry dataset, which has been a powerful asset in evaluating, validating and supporting structures modelled using machine-based learning programs such as AlphaFold. The dataset represents a significant leap for the field of functional proteomics and interactomics, as it will enable the identification of protein-protein interactions that are upregulated or downregulated in a disease, potentially leading to the design of more targeted approaches to cure or treat illness.

Funding sources include:

- Australian Research Council
- National Computational Infrastructure
- National Health and Medical Research Council of Australia
- NSW State Government
- UNSW Sydney



Combating chronic disease with nutrition

Challenge

Diabetes, obesity, and cardiovascular disease are major health concerns in Australia and elsewhere, leading to a high rate of morbidity and mortality. Professor Stephen Simpson AC (School of Life and Environmental Sciences, Faculty of Science; Academic Director, Charles Perkins Centre; Executive Director, Obesity Australia) and colleagues have been investigating the intersection between Western diets and their health implications.

Research

Professor Simpson is a globally recognised entomologist and nutritional biologist who co-developed an integrative modelling framework for nutrition known as the Geometric Framework. Building on this work, he and his team wanted to determine whether changes in the macronutrient composition of the diet could potentially enhance lifespan and improve metabolic health during middle age in animal models.

Sydney Mass Spectrometry has one of the largest collections of liquid-chromatography mass spectrometry available to academic researchers in the country. Offering excellent capabilities and capacity, Sydney Mass Spectrometry assisted the research team in processing hundreds of samples from their landmark study of 33 isocaloric diets on 700 mice to quantify a variety of metabolites. The work was enabled by targeted metabolomics specialist Dr Atul Bhatnagar and the metabolomics team from Sydney Mass Spectrometry utilising the QTRAP mass spectrometer platforms.

Results

The study, published in *Nature Metabolism*, led to insights on how different carbohydrate types can have a profound effect on metabolic health. For example, they found that a low-protein high-carbohydrate diet can result in improved glycaemic status, plasma biochemistry, metabolic status and gut microbiota health if complex carbohydrates rather than simple carbohydrates are used. These findings suggest that nuanced nutritional advice may lead to better outcomes than simply recommending calorie-restricted diets, charting a course to address population health burdens.

Funding sources include:

- Ageing and Alzheimers Institute
- Australian Research Council
- Diabetes Australia
- National Health and Medical Research Council of Australia

Linking the gut microbiome and auto-immune disease

Challenge

Autoimmune diseases such as rheumatoid arthritis, multiple sclerosis or coeliac disease are chronic conditions that affect 3–5% of the general population. While these conditions have been linked to environmental factors, there is growing evidence that gut dysbiosis contributes to onset and severity. Could a healthy gut microbiome help treat autoimmune disease?

Research

Advances in understanding of host-microbiota interactions have highlighted that metabolites, especially short-chain fatty acids, released by gut bacteria play a key role in immune cell development and function. Research by Professor Laurence Macia (School of Medical Sciences, Faculty of Medicine and Health) and others has shown that short-chain fatty acids are central players in immune tolerance as they promote the activation of anti-inflammatory regulatory T cells.

Professor Macia coordinated a study to elucidate the immunosuppressive mechanism of short-chain fatty acid acetate. Using a QTRAP 5500 mass spectrometer, and with the assistance of the Sydney Mass Spectrometry metabolomics team led by Dr Lake Ee Quek, the researchers used stable isotope labelled acetate to show how acetate stimulated the production of anti-inflammatory cytokine interleukin-10 in B cells.

Results

The findings were published in a recent *Journal of Clinical Investigation* paper, and may explain the rise in inflammatory diseases in fiber-underconsuming Western populations. The study highlighted how a healthy gut microbiome can combat chronic inflammation, opening a path for safe and cost-effective dietary intervention to tackle autoimmune disease.

Funding sources include:

- Australian Research Council
- Cancer Institute NSW
- Cooper Foundation
- National Health and Medical Research Council
- The Medical Foundation of the University of Sydney
- University of Sydney

Below: Source: Daïen et al., JCI Insight. 2021 Apr 8; 6 (7): e144156.