Case Study

Medical Research Council Selects Wyatt Technology Instrumentation to Perform Breakthrough Research into Human Health and Disease

Summary

The Medical Research Council (MRC) Laboratory of Molecular Biology (LMB) has long been a world-class research laboratory. The LMB's primary goal is to understand biological processes at the molecular level, through the application of methods drawn from physics, chemistry and genetics. This quest extends from structural studies of individual macromolecules, through their interactions and beyond to the functioning of subcellular systems, cells and multicellular systems in whole organisms. MRC LMB adopted Wyatt Technology instrumentation as part of its ultimate aim to equip its facilities with cutting-edge tools for research and to use the knowledge obtained to tackle specific problems in human health and disease.

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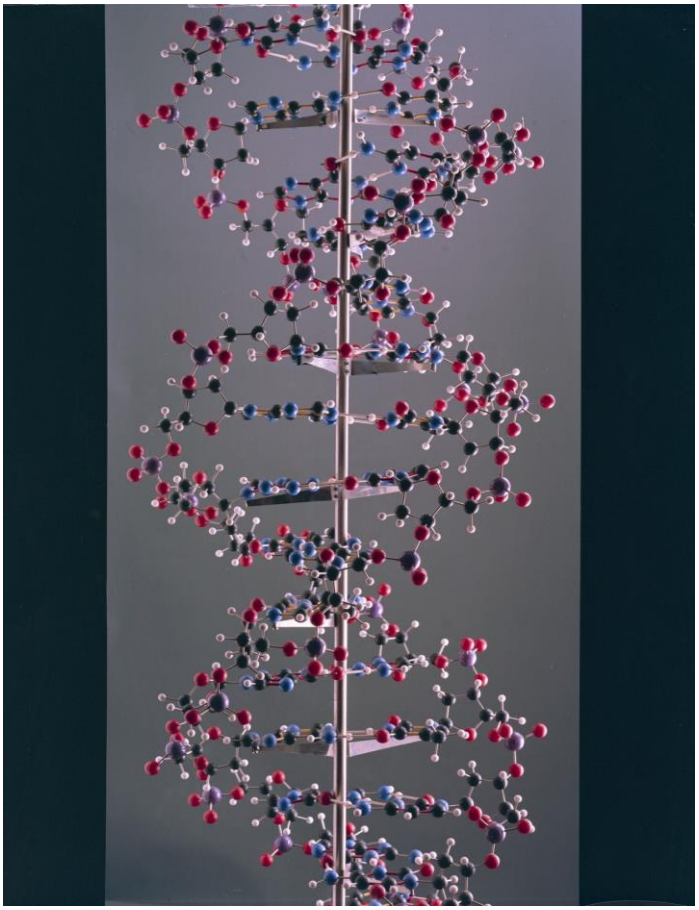
WYATT TECHNOLOGY

I. Profile

In 1947, the MRC set up a 'Unit for Research on the Molecular Structure of Biological Systems' using X-ray diffraction to study proteins. The unit quickly diversified into other areas, including the structure of DNA, mechanism of muscle contraction and the structure of viruses. Realizing the potential for medical applications, the MRC provided a new building for the unit, and in 1962 the LMB was opened on the site of the Addenbrooke's Hospital in Cambridge, UK.

The LMB is one of the birthplaces of modern molecular biology. Many techniques were pioneered at the laboratory, most notably methods for determining the three-dimensional structure of proteins and DNA sequencing. Whole genome sequencing was initiated at the LMB. Another landmark discovery was the invention of monoclonal antibodies.

LMB is funded by the MRC, the UK's leading publicly funded biomedical research organization, dedicated to improving human health through excellent science. The Laboratory today houses over 400 scientists and supporting staff, with about 320 directly carrying out research in more than 50 groups.



II. Challenge

The research at LMB covers a wide range of molecular biology, including structural determination of biological "machines" by X-ray crystallography and cryo-electron microscopy, computational biology and biology of immunity and cancer. It also focuses on intercellular signalling, membrane trafficking and advanced optical microscopy of live cells, molecular origins of neurodegenerative diseases, synthetic biology, selection technologies and in vitro evolution. There is emphasis on the development of new technologies, the study of basic biological processes and the use of this knowledge to tackle specific problems in human health and disease, including the development of new therapeutic agents.

With the aim of establishing best-in-class research facilities, the LMB outlined a requirement to invest in accurate and reliable instrumentation in order to better characterize proteins. The new technology would be based in the biophysics facilities, which support and collaborate in breakthrough research to solve unanswered questions in structural biology. This research can lead to potential applications in human health, requiring high quality instrumentation.

Biophysics is an interdisciplinary science that applies theories and methods from the physical sciences to questions in biology. Biophysical techniques can contribute to all areas of structural biology from expression and purification issues through to high resolution structure and can probe interactions and biology from single molecules through to whole cells. These methods have been central to the success of many research programs in the LMB.

The LMB has world class facilities for biophysical techniques including analytical ultracentrifugation (AUC), isothermal titration calorimetry (ITC), differential scanning calorimetry (DSC), circular dichroism (CD), linear dichroism (LD), size exclusion chromatography – multi-angle light scattering (SEC-MALS), quasi-elastic light scattering (QELS), surface plasmon resonance (SPR), fluorescence and most recently microscale thermophoresis (MST). In addition, the LMB has a number of in-house instruments for performing the latest cutting edge techniques in rapid reaction kinetics or single molecule spectroscopy.

New technology was specifically needed in order to characterize proteins in terms of their mass, levels of association and physical properties (such as radius of gyration and hydrodynamic radius). These simple parameters measured on molecules in solution are often key to any structural biology initiative and give information about why systems may not crystallize and how this can be overcome. The addition of other proteins, ligands and cosolvents (detergents) can affect these properties and this may be fundamental to mechanistic interpretation. The instrumentation would also need to measure hydrodynamic radius in order to benchmark other techniques where molecular diffusional properties are used.

III. The Solution

After viewing a demonstration of Wyatt Technology SEC-MALS with online QELs instrumentation and sampling the company's field-flow fractionation (FFF) technology, the researchers within the LMB were impressed by the quality of the instrumentation, the quality of the data and the knowledge and helpfulness of the Wyatt Technology team.

Dr. Chris Johnson, Senior Investigator Scientist at the LMB explains: "Wyatt Technology's instrumentation was very impressive and performed well on a wide variety of test systems that we examined straight out of the box. The UK representative that we dealt with was also very helpful and clearly highly knowledgeable."

The Wyatt Technology Eclipse FFF system, Optilab rEX online refractive index (RI) detector and DAWN HELEOS with online QELS were implemented by the LMB extremely quickly and are currently being used to characterize proteins within a wide range of applications.

Dr. Johnson added, "The demand for the technique has been sufficient that a second SEC-MALS system has been installed in the Biophysics facilities at LMB."

IV. Realizing the Benefits

As an example, Wyatt Technology's MALS detectors were used by the LMB in a recent landmark study that transforms the previous scientific understanding of immunity to viral diseases such as the common cold, AIDS, 'winter vomiting' and gastroenteritis. Such viruses are among the hardest diseases to treat and are adept at avoiding recognition by changing their molecular patterns. Antibodies were originally thought to only offer extracellular protection and were helpless against the virus once it had entered the cytosol of a cell. However, the new study utilizing Wyatt Technology instrumentation shows that antibodies remain attached to viruses after cell infection and provide effective antiviral immunity.

The DAWN HELEOS II instrument coupled to the Optilab rEX online refractive index detector were used to identify the positive interaction between a cytosolic Immunoglobulin G (IgG) receptor, tripartite motif-containing 21 (TRIM21) and IgG. Scientists discovered that TRIM 21 binds to antibodies with a higher affinity than any other IgG receptor in the human body and once activated begins to rapidly degrade virions in the cytosol, neutralizing the infection.

Wyatt Technology instrumentation is designed to improve accuracy and precision, delivering high quality data. The Eclipse FFF system provides flexibility, speed and ease-of-use, while offering the ability to separate both soluble and colloidal components over a wide size range at ultra-high resolutions. Many time-consuming sample preparation steps are also eliminated, simplifying analyses. In addition, the DAWN HELEOS with online QELS provides sensitivity for the measurement of absolute molecular weight and size, and the conformation of macromolecules in solution. The Optilab rEX offers improved temperature stability, 256 times the detection power and up to 50 times the dynamic range of other RI detectors on the market.

"During the installation process and ongoing after-sales support, we have received excellent service from Wyatt Technology in both the UK and the US," comments Dr. Johnson. Included with the purchase, researchers from the LMB were invited by Wyatt Technology to attend its well-known Light Scattering University (LSU) training. Held in Santa Barbara, LSU aims to demystify light scattering and explain how to get the most out of Wyatt Technology instrumentation.

"The LSU was an excellent course which is best attended after some month's practical use of the instrumentation," explains Dr. Johnson. "We have found Wyatt Technology to be one of the best, if not the best, companies to deal with within the industry."

V. Conclusions

Due to the vital research conducted within the LMB, best in class instrumentation was required to characterize proteins in a reliable manner. Wyatt Technology's SEC-MALS, FFF and online refractive index technology have proven to deliver quality data and researchers have been able to make significant advancements towards understanding immunity to viral diseases.

"Wyatt Technology is definitely the leader in the field of light scattering", continues Dr. Johnson. "From a performance and technical standpoint as well as from an after sales and support angle, Wyatt Technology has excelled. In protein chemistry, Wyatt Technology instrumentation coupled to SEC is a powerful tool to determine particle mass, purity and even shape."

The MRC celebrated its Centenary in 2013, when the LMB moved to a new, world-class £200m laboratory building - the flagship development on the newly expanded Cambridge Biomedical Campus. The scientists working in the new building now have access to cutting-edge instruments and an abundance of innovative new technologies to help them achieve their own goals and contribute to the continuing success of the LMB in understanding all aspects of life at the molecular level. Since implementation, Wyatt Technology's instrumentation has provided high quality results, coupled with invaluable customer service and training to optimize the LMB's use of light scattering to advance research in human health and disease.