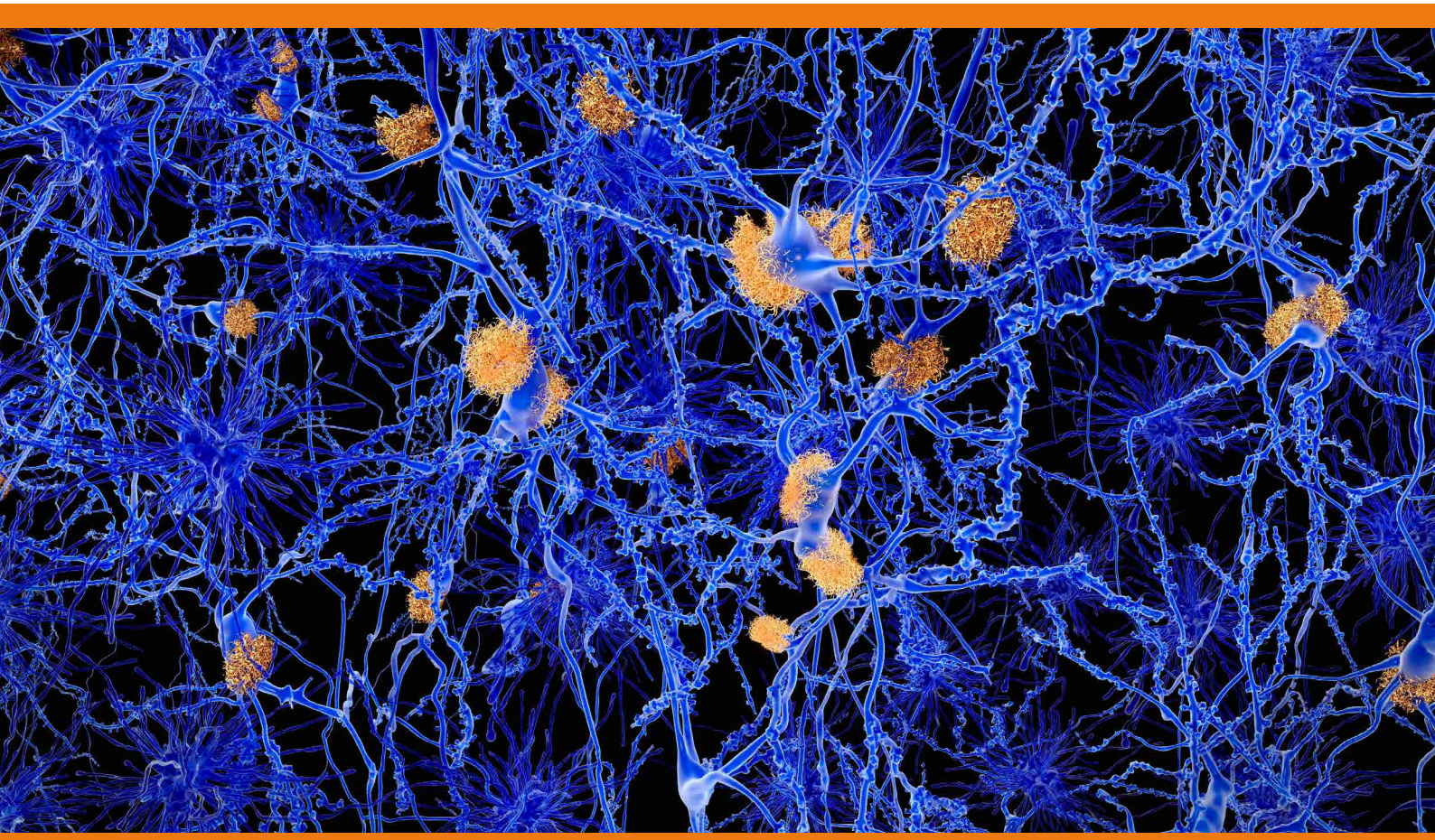
European Metrology Research Programme

Delivering Impact



Surface analysis for Alzheimer's

Modifying or controlling surface chemistry is important in new product development, quality control and research. This is particularly true where functionality of surfaces, thin films and interfaces are key to the application, such as organic solar cells and devices for medical diagnostics.
Surface chemical analysis aims to provide quantitative elemental, chemical state and functional group information from the surface of materials, but requires comparable test data and improved measurement traceability.

Europe's National Measurement Institutes working together

The European Metrology Research Programme (EMRP) brings together National Measurement Institutes in 23 countries to address key measurement challenges at a European level. It supports collaborative research to ensure that measurement science meets the future needs of industry and wider society.

Challenge

There are many different methods to analyse surfaces and interfaces, each with advantages and disadvantages. Imaging plays a key role in medical research and drug discovery, identifying the spatial distribution of particles, locating drug targets, and assessing drug distribution. This type of analysis depends on reliable comparison between different techniques, and developments here can result in more data, gathered more quickly, and in some cases analysis that was not previously possible.

One of these surface analytical techniques, time-of-flight secondary ion mass spectrometry (ToF-SIMS), has advantages including high sensitivity and the ability to achieve high spatial resolution. However, ToF-SIMS generally cannot be used to produce quantitative analyses and traceability is not well-established. This hinders its wider use in understanding the causes of diseases and drug uptake within the body. Being able to traceably apply ToF-SIMS to biological samples would improve confidence in results and support a broad range of research, including into Alzheimer's disease.

Solution

The EMRP project *Traceable quantitative surface chemical analysis for industrial applications* worked on the identification of low concentrations of surface peptides or proteins using liposomes. This involved the introduction of a new diagnostic tissue labelling method for ToF-SIMS, which was traceably linked to an established fluorescent analysis technique.

ToF-SIMS can quantitatively identify different proteins and peptides in a single analysis by using biological labels. Liposomes have enabled ToF-SIMS to be used to simultaneously measure multiple surface sites in a single analysis, introducing the possibility of screening for many different functional entities - proteins, peptides, and DNA in each measurement. Mapping the position of specific peptides simultaneously with other molecules that cannot be located using conventional protein marker imaging, provides information about lipid-protein interactions which are key in understanding the mechanisms of neurodegeneration associated with Alzheimer's disease.

The benefits of ToF-SIMS, including its superior spatial resolution and the use of samples that are freeze-dried without the need for complex and time consuming preparation, can now be deployed traceably and with confidence for quantitative analysis to identify the location of specific entities on a sample's surface.

Impact

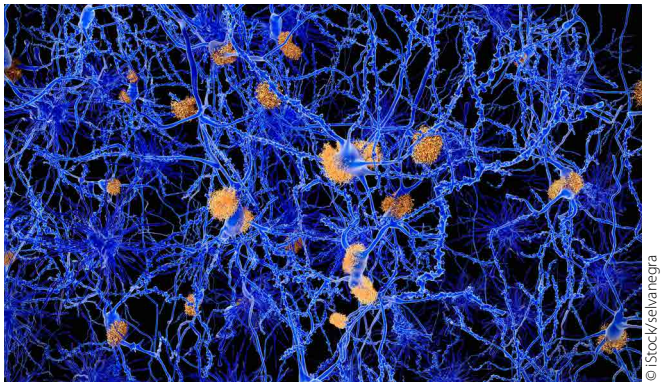
SP Technical Research Institute of Sweden was one of the first to use this technique in determining the amount and location of specific liposome sites on tissue sample surfaces. This is part of their investigations into the formation of Alzheimer's plaques and tangles. Plaques occur in brain regions where nerve degeneration has occurred due to the disease, and mapping these regions promotes understanding of the mechanisms involved. Studying these characteristic features of Alzheimer's with greater confidence, and particularly focussing on the spatial localisation of specific peptide deposits will aid research into causes of this disease.

Analysing a single sample to simultaneously look for multiple features means more samples can be studied in greater detail. Samples can now generate more data faster than previously possible, speeding up tissue sample analysis, and reducing costs. Medical researchers can now have greater confidence in using comparable ToF-SIMS data to support their research, contributing to understanding the causes of diseases and drug uptake within the body.

Traceable quantitative surface chemical analysis for industrial applications

Surface chemical measurements have provided a foundation for the development of products in many sectors including chemicals, fuels, semiconductor devices and biomedical devices. However, an improved metrological infrastructure is now needed for continued product development and quality control by European manufacturers.

The EMRP project *Traceable quantitative surface chemical analysis for industrial applications* has addressed this by developing new certified reference materials and methods to improve analytical instrumentation traceability. As a result of the project, instrument manufacturers and researchers can have greater confidence in the comparability of surface chemical analysis results. This will speed the introduction of complex measurement techniques such as EPMA EDS, the use of Argon cluster sputtering for the analysis of layered organic films and the use of XPS and ToF-SIMS to perform multiple species analyses in a single biological sample measurement.



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