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Neutron scattering explains how myoglobin can perform without water

Understanding will help protein's potential application in biochemical gas sensors or in state-of-the-art wound dressing

Proteins do not need to be surrounded by water to carry out their vital biological functions, according to scientists from the Institut de Biologie Structurale (IBS) in Grenoble, the University of Bristol, the Australian National University, the Institut Laue Langevin and the Forschungszentrum Jülich, in Germany. In a new paper published in the Journal of the American Chemical Society, the team used a state of the art neutron scattering technique to demonstrate that when myoglobin, an oxygen-binding protein found in the muscle tissue of vertebrates, is enclosed in a sheath of surfactant molecules, it moves in the same way as when it is surrounded by water. These motions are essential if a protein is to perform its biological function, and their findings make proteins a viable material for use in new wound dressings or even as chemical gas sensors.

Water is the natural environment for soluble proteins and an integral part of their structures which allows them to carry out their specific function. It had been perceived for many years that proteins required water or another solvent in order to function. But in 2010, the Bristol team proved that by grafting polymer chains onto the protein surface, it was possible to produce solvent- and water-free myoglobin liquids that could still perform their biological roles. Scientists have now demonstrated that protein dynamics is the reason why.

Myoglobin is common to almost all mammals and responsible for the red colour of raw meat. Like all soluble proteins, its surface is covered with water molecules. In this study researchers wanted to assess whether the protein structure could still move and continue to bind oxygen if all the water was completely removed and replaced by synthetic molecules.

The team analysed three samples, a wet sample (the protein in water), a dry sample (the dehydrated protein) and a dry protein-polymer hybrid sample where the water molecules had been replaced by synthetically crafted polyethylene glycol-based polymer surfactant molecules. Using a technique called incoherent neutron scattering at the Institut Laue Langevin (ILL) in Grenoble, France, and at the Jülich Centre for Neutron Science at FRMII, Garching, Germany, the team was able to monitor the motions in the protein and in the polymer surfactant separately. This separation has been made possible by specific labelling, carried out in a dedicated deuteration laboratory at the ILL, by which either polymer or protein motions are masked by replacing hydrogen with its heavier isotope, deuterium. What they found was that the myoglobin molecules surrounded by polymer moved just as well as the wet sample, and that the dry sample had very little mobility.

Knowing that proteins can function outside of water opens them up to use in real life applications because it shows that there are other alternatives if water is unavailable. Examples of where they could be used include biochemical gas sensors, as myoglobin can bind carbon monoxide molecules. Another potential application is in the development of new wound dressings, where the liquid protein could be applied either internally and

externally to the wound to reduce healing time by supplying oxygen or other essential chemicals to the damaged tissue.

Adam Perriman of the University of Bristol said:

'These discoveries have increased our fundamental understanding of proteins and how they behave, which could create many new opportunities for their application in industrial processing and in medical technologies. The fact that our proteins can happily perform their function outside of water, a substance generally thought to be vital for life, really drives home just how robust these biological nanomachines are. '

Martin Weik of the Institut de Biologie Structurale explained:

'Neutron scattering techniques are excellent for studying the dynamics of proteins and of their environment. The world class neutron scattering facilities at the ILL and the FRM II allow us to analyse how proteins move, thus complementing the single snapshots of their structures provided by crystallography.'

Earlier this month, Martin Weik and colleagues from the IBS, the ILL, the University of California, the Australian Institute of Science and Technology Organisation and the Jülich Centre for Neutron Science at FRMII, applied these techniques to an intrinsically disordered protein (IDP) called tau, to try and understand how its flexibility and its interactions with water differ from ordered proteins such as myoglobin.

They found that the coupling of the disordered tau protein with water motions was much tighter than for folded proteins. IDPs are of significant interest in a medical context because they can aggregate and cluster together to create the amyloid fibrils behind neuro-degenerative diseases such as Parkinson's and Alzheimer's. Whilst the ordered structure of folded proteins makes it possible to develop drugs that fit into the protein like a key in a lock, the conformational variability of an intrinsically disordered protein like tau makes it more difficult. A more in-depth understanding of their dynamics is required and the discovery of tight coupling with water motions is a significant step forward.

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Notes to editors

1. About ILL – the Institut Laue-Langevin (ILL) is an international research centre based in Grenoble, France. It has led the world in neutron-scattering science and technology for almost 40 years, since experiments began in 1972. ILL operates one of the most intense neutron sources in the world, feeding beams of neutrons to a suite of 40 high-performance instruments that are constantly upgraded. Each year 1,200 researchers from over 40 countries visit ILL to conduct research into condensed matter physics, (green) chemistry, biology, nuclear physics, and

materials science. The UK, along with France and Germany is an associate and major funder of the ILL.

2. The University of Bristol is consistently ranked among the leaders in UK higher education. Research-intensive and with an international reputation for quality and innovation, the University has 17,000 students from over 100 countries, together with more than 5,500 staff. In terms of the number of applications per undergraduate place, Bristol is one of the most popular universities in the country.

The University was founded in 1876 and was granted its Royal Charter in 1909. It was the first university in England to admit women on the same basis as men. It is located in the heart of the city from which it grew, but is now a significant player on the world stage as well as a major force in the economic, social and cultural life of Bristol and South West England.

3. Forschungszentrum Jülich pursues cutting-edge interdisciplinary research addressing pressing issues facing society today while at the same time developing key technologies for tomorrow. Research focuses on the areas of health, energy and environment, and information technology. The cooperation of the researchers at Jülich is characterized by outstanding expertise and infrastructure in physics, materials science, nanotechnology, and supercomputing. With a staff of about 4700, Jülich – a member of the Helmholtz Association – is one of the large research centres in Europe.

The Jülich Centre for Neutron Science (JCNS) develops and operates neutron scattering instruments at some of the best neutron sources worldwide. In-house research focuses on “correlated electron systems and nanomagnetism” as well as “soft matter and biophysics”. In these areas of expertise, JCNS offers expert support on world-class instruments with a specialized sample environment and ancillary laboratory access to external users.