Invisible Deuterated Detergents for Membrane Protein SANS Investigations

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Membrane proteins constitute more than 50% of all drug targets. Yet, they continue to present considerable challenges to the field of structural biology. The use of small-angle neutron scattering (SANS) and the contrast match-point of a detergent to study membrane protein structures is a powerful and a well-known technique. However,a common feature for all previous studies is that they rely on commercially available hydrogenated detergents or fully deuterated detergents. This is reflected in the resulting scattering data, which represent the multiple contrasts of the entire detergent-membrane protein complex due to the differences in excess scattering length density of the hydrophobic and hydrophilic parts of the detergents. This effect, mainly present at q-values,is difficult to disentangle from the signal from the membrane protein and significantly limits the resolution that can be obtained. In addition, the overall match-point of the commercially available detergents is generally different from that of 100% D2O, hence leading to a large incoherent background signal from the hydrogen in the buffer. In the present study, the use of detergents for structural elucidation of membrane protein was taken one step further; fully match-out deuterated versions of two commonly used detergents OG and DDM with varying deuteration levels in the heads and the tails were synthesized to reduce the signal of the detergent to background level. By doing so, current optimized protocols for handling a specific membrane protein could directly be adapted for a membrane protein sample for structural studies. This method does not rely on the expensive and time-consuming approach of producing perdeuterated membrane proteins or deuterated lipids in vivo.