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Structural Dynamics of β-Lactoglobulin in the Interaction Processes with Sodium Dodecyl Sulfate Micelles Observed by Time-Resolved Vacuum-Ultraviolet Circular Dichroism

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Structural transition of proteins induced by the membrane interaction alter their biological function. Hence, the structural dynamics in the membrane-interaction processes is key information to elucidating the mechanisms of expressed function. While vacuum-ultraviolet circular dichroism (VUVCD) spectroscopy has been widely applied to the studies of membrane-bound structures of proteins[1,2], the previous investigations were limited to the static conditions (before and after membrane interaction). To address this, we developed a time-resolved VUVCD (TR-VUVCD) method, enabling real-time observation of structural dynamics[3]. This study analyzed the interaction processes between β-lactoglobulin (bLG) and sodium dodecyl sulfate (SDS) micelles using TR-VUVCD and molecular dynamics (MD) simulations. First, we obtained a TRCD dataset in the 178–260 nm wavelength range within one second, which reflected the structural transitions of bLG due to the SDS interaction. Our analysis identified a single intermediate state, revealing a step-by-step transition of the native (N-) state → intermediate (I-) state → micelle-bound (M-) state. Secondary structure analysis showed that the I-state formed six helices, which were extended and stabilized in the M-state. Second, we conducted the MD simulations to confirm the binding potential of these helices to the micelle surface. Our analysis on the physicochemical properties (charge, hydrophobicity) of each helix and MD-derived parameters such as peptide-micelle distance, hydrogen bonding, and micelle penetration, characterized the key driving forces on the interactions, in which electrostatic interactions contributed at the initial stage (I-state) while hydrophobic interactions played a significant role in stabilizing the final structure (M-state). These results demonstrate that TR-VUVCD combined with MD simulations is a powerful method for characterizing protein dynamics in the processes of membrane interaction, contributing to a deeper understanding of the mechanism of function expression at molecular level.

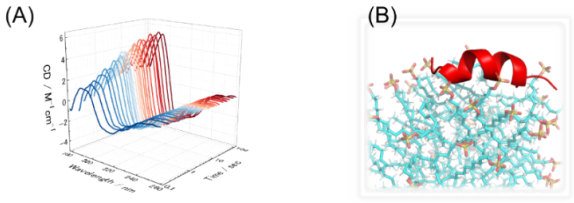

FIGURE. (A) TR-VUVCD data sets in the interaction process between bLG and SDS micelle. (B) The snapshot of MD simulation using Amber program.

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