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New developments in the structure analysis of biomolecules using synchrotron-radiation vacuum-ultraviolet circular dichroism

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Circular dichroism (CD) is defined as the difference between the absorption of left- and right-circularly polarized light and is very sensitive to the steric structures of optically active materials such as biomolecules. The CD spectra of biomolecules are measurable at low concentrations under various solvent conditions, which makes CD spectroscopy a powerful technique for analyzing the structures of proteins, saccharides, and DNA in aqueous solution. However, the structural information obtainable from this technique has been limited because a conventional CD instrument using an experimental light source is generally not capable of measuring the CD in the vacuum-ultraviolet (VUV) region below 190nm. Synchrotron radiation (SR) is an excellent high-flux source of photons in the VUV region, and VUVCD spectrophotometers have been constructed using SR to extend the short-wavelength limit of CD spectra. Recently techniques for analyzing the biomolecule VUVCD spectra have been largely developed by the combination with theoretical analysis and bioinformatics, which allowed us to obtain novel structural information of biomolecules based on the high-energy transitions such as acetal and hydroxy groups. In this paper, we show recent progress of SR-VUVCD spectroscopy in the structural analysis of saccharides and proteins.

Monosaccharaides such as D-glucose exhibited the characteristic VUVCD spectra below 190 nm depending on the complicated equilibrium structures between the gauche and trans conformations of hydroxylmethyl group and between the α-/β-anomer configurations of hydroxy group. These spectra were theoretically calculated using a molecular dynamics (MD) simulation and a time-dependent density functional theory. From the comparisons between experimental and theoretical spectra, we revealed the dynamics-structure-hydration relationships of these monosaccharides, which are important factors for understanding their functions such as the molecular recognition and stabilization of proteins. [1, 2] The VUVCD analysis of globular proteins coupled with bioinformatics such as neural-network method allowed us to accurately estimate the contents, numbers of segments, and sequences of α-helix and β-strand structures of proteins. This spectroscopy was applied to the structural analysis of membrane-bound proteins, showing that the numbers of helical segments of the proteins largely increased due to the membrane interaction. The orientations of the helix segments on the membrane surface were determined by the flow linear dichroism apparatus installed in the VUVCD instrument [3] The CD spectrum of amyloid fibrils of β_2-microglobulin core fragments were theoretically calculated using a CD theory and MD simulation, disclosing that the conformations of these fibrils were composed of amyloid accumulations in which the parallel β-sheets stack in an antiparallel manner. [4] These results demonstrate that VUVCD spectroscopy can provide crucial structural information of biomolecules in aqueous solution to open a new field in the structural biology and chemistry.

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