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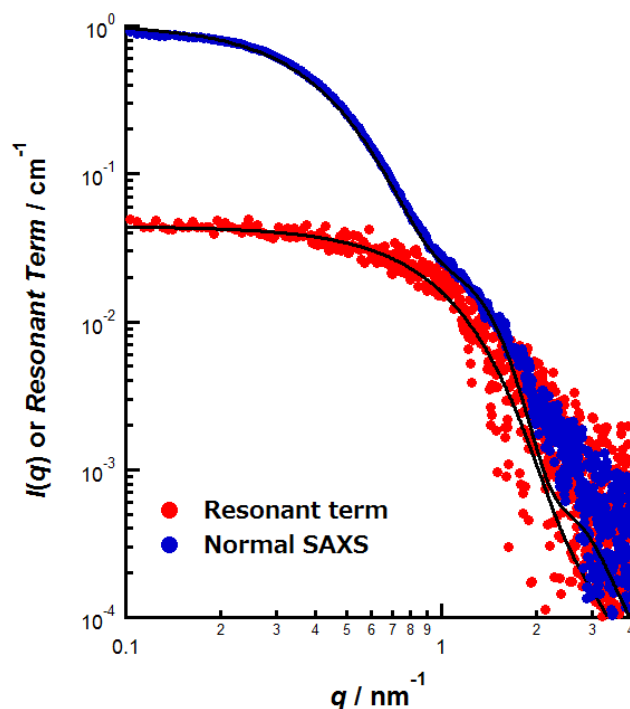
ASAXS Study on Spatial Distribution of Hydrophobic Compounds in Polymer Micelles

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In drug delivery system (DDS) using polymer micelles as drug carrier, DDS properties are related to spatial distribution of drug compounds in the micelles [1]. Because the spatial distribution of drug compounds should strongly depend on interactions and solubility of drug compounds in the micelles, elucidation of the relation between chemical structures of drug compounds and their spatial distribution in the micelle is much important. Thus, in this study, we examine to elucidate the relation between chemical features and spatial distribution of drug compounds in polymer micelles by using anomalous small-angle X-ray scattering (ASAXS). To apply the ASAXS near bromine K-edge for analysis [2] of spatial distribution of drug compounds in polymer micelles, we employ 4 different bromine-labeled hydrophobic compounds as model drug compounds and polymer micelles composed of poly(dimethylaminoethyl methacrylate)-block-poly(methyl methacrylate) (PDMAEMA-b-PMMA). Figure shows SAXS and resonant term obtained from ASAXS near bromine K-edge for the polymer micelles containing 9-bromofluorene (BrF). The domain size estimated from the resonant term is much smaller than that of hydrophobic PMMA core of the micelle. Therefore, When BrF, which is highly hydrophobic and scarcely dissolved in hydrophobic PMMA, is incorporated in the polymer micelle, BrF forms small droplet in the hydrophobic core composed of PMMA. For the micelles incorporating bromobenzene, which as similar properties of BrF, similar result is obtained. On the other hand, 4-bromobenzyl alcohol and ethyl 2-bromoethyl propionate, which are miscible with PMMA, are homogeneously dispersed in the PMMA core of the micelles. These results indicate that highly hydrophobic compounds forms small droplet in hydrophobic core, and introduction of polarity to the compounds causes expansion of the area existing the hydrophobic compounds in polymer micelle.

[1] I. Akiba, N. Terada, S. Hashida, K. Sakurai, T. Sato, K. Shiraishi, M. Yokoyama, H. Masunaga, H. Ogawa, K. Ito, N. Yagi, *Langmuir*, 2010, 26, 7544-7551., [2] I. Akiba, A. Takechi, M. Sakou, M. Handa, Y. Shinohara, N. Yagi, K. Sakurai, *Macromolecules*, 2012, 45, 6150-6157,



Keywords: Polymer micelle, Drug delivery system, Anomalous small-angle X-ray scattering