Available online at www.sciencedirect.com
ScienceDirect
Physica B 385–386 (2006) 865–867
PHYSICA B
www.elsevier.com/locate/physb

Contrast variation SANS for the solution structure of the β-amyloid peptide 1–40 influenced by SDS surfactants

U.-Ser Jeng[a], Tsang-Lang Lin[b,*], J.M. Lin[b], Derek L. Ho[c]

[a]National Synchrotron Radiation Research Center, Hsinchu 30076, Taiwan
[b]Department of Engineering and System Science, National Tsing Hua University, 101, Sec. 2, Kuang Fu Road, Hsinchu 30043, Taiwan
[c]National Institute of Standards and Technology, Gaithersburg, MD 02899, USA

Abstract

Using small-angle neutron scattering (SANS), we have studied the suppression of fibril formation of β-amyloid peptide (A_β), a 1–40 amino acid peptide fragment derived from proteolytic cleavage of a large amyloid precursor protein, by an ionic surfactant, SDS. In comparison with the pure peptide in aqueous solutions which forms long and thin fibrils, A_β forms smaller complex with SDS, which hinders partially the growth of long fibrils. With a selected deuteration of SDS for a contrast variation in SANS, we have extracted the structural information of the SDS/peptide complex, including a short rod-like shape, size, and an association ratio between SDS and the peptide.

PACS: 87.15.Nn

Keywords: SANS; Amyloid peptide; SDS; Complex aggregate

1. Introduction

The β-amyloid peptide (A_β), of 1–40 amino acids, fragment derived from proteolytic cleavage of a large amyloid precursor protein folds into a random coil, β-helix, or oligomeric β-sheet structure in aqueous solutions. Without buffering, A_β evolves into a β-sheet structure, and further forms fibril that can possibly deposit on membranes, as that found in the Alzheimer disease. A pioneer work using small-angle neutron scattering (SANS) and small-angle X-ray scattering for the structure of pure A_β aggregates was done by Thiyagarajan et al. [1]. Here, we study the suppression effect on the fibril structure of β-amyloid by an inhibitor, an ionic surfactant sodium dodecyl sulfate (SDS). Using SANS, we have found a suppression effect of long fibril aggregates of A_β in aqueous solutions with SDS. Substituting SDS with deuterated SDS (d-SDS) in the system for a contrast variation, we have identified the formation of peptide–surfactant complex. Using a model analysis for the contrast SANS data, we are able to extract a detailed structural information of the peptide/surfactant complex.

2. Scattering model and contrast variation

Small-angle scattering profiles for colloidal aggregates of a monodisperse size can be modeled as [2]

$$I(Q) = I_o P(Q) S(Q), \tag{1}$$

where $P(Q)$ is the normalized form factor with $P(0) = 1$ and $S(Q)$ is the structure factor. The scattering wave vector Q is defined by $4\pi \sin(\theta/2)/\lambda$, with θ and λ the scattering angle and wavelength of incident neutrons, respectively. The forward scattering, $I_o(Q = 0) = n_p(\rho - \rho_w)^2 V^2$, is determined by the number density n_p and the volume V of the scattering particles. The scattering-length-density for the particles and the solvent are denoted by ρ and ρ_w, respectively. For homogeneous rod-like particles of radius a and length L, the spatial-orientation averaged form

*Corresponding author. Tel.: +886 3 5742671; fax: +886 3 5728445.
E-mail addresses: usjeng@nsrrc.org.tw (U.-S. Jeng), tllin@mx.nthu.edu.tw (T.-L. Lin).

0921-4526/$ - see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.physb.2006.05.128

factor is

$$\tilde{P}(Q) = \int_0^1 \left| \frac{2J_1(v)}{v} \frac{\sin(w)}{w} \right|^2 \mathrm{d}\mu, \quad (2)$$

with $v = Qa(1-\mu^2)^{1/2}$, $w = (1/2)QL\mu$, and the first-order Bessel function J_1 [2].

For particles which form larger network or porous domains of fractal-like characteristics, a pair correlation function for the particles in the fractal domains

$$g(r) \propto r^{D-d} \exp(-r/\xi) \quad (3)$$

may be constructed to account for the fractal structure of a fractal dimensional D [3]. In Eq. (3), the characteristic cut-off length ξ defines loosely the fractal region $\sim 2\xi$. A structural factor for the fractal domains

$$S(Q) = 1 + \frac{1}{(QR)^D} \frac{D\Gamma(D-1)}{(1+D(\xi)^{-2})^{(D-1)/2}} \times \sin[(D-1)\tan^{-1}(Q\xi)] \quad (4)$$

can be obtained from the Fourier transform of Eq. (3) [3]. Here, an equivalent radius R for a rod-like particle of radius a and length L can be derived on the basis of the equivalent volume constrain ($4/3\pi R^3 = \pi a^2 L$).

For a complex aggregate containing N_p and N_s numbers of amyloid peptides and SDS molecules, the forward scattering can be further expressed as

$$I_o = n_p[N_p(b_p - \rho_w V_p) + N_s(b_s - \rho_w V_s)]^2, \quad (5)$$

with b_p, b_s and V_p, V_s denote, respectively, the scattering lengths and volumes for A_β and SDS [1]. Assuming most of the A_β monomers aggregate, we have $n_p = C_p/N_p$ determined by the concentration, C_p, of A_β in the solution. With two sets of contrast SANS data measured for the amyloid peptide solutions mixed with SDS and d-SDS, respectively, two different I_o in Eq. (5) can be obtained with $b_s = 160 \times 10^{-6}$ Å for SDS and $b_s = 2762 \times 10^{-6}$ Å for d-SDS, providing a non-trivial value of N_s. Using the two I_o obtained from the two sets of contrast data with A_β/SDS and A_β/d-SDS in Eq. (5), we can determine an association ratio μ between the peptide and SDS, with

$$\mu = N_s/N_p = A(\chi - 1)/(\chi B_d - B), \quad (6)$$

where the intensity ratio $\chi = \pm[I_{o\text{-sds}}/I_{o\text{-d-sds}}]^{1/2}$, $A = b_p - \rho_w V_p$, $B_d = b_{s\text{-d-sds}} - \rho_w V_s$, and $B = b_{s\text{-sds}} - \rho_w V_s$. The aggregation numbers can, thus, be expressed in terms of μ, with

$$N_p = (I_{o\text{-sds}}/n_p)^{1/2}/(A + \mu B)$$

and

$$N_s = \mu(I_{o\text{-sds}}/n_p)^{1/2}/(A + \mu B) \quad (\text{or } N_s = \mu N_p). \quad (7)$$

In Eq. (5), the relevant amyloid peptide volume of 5473 Å^3 can be estimated from the individual amino acids in the peptide [4], while the dry volume $V_s = 404$ Å^3 of SDS adapted from Sheu et al. [5]. The scattering length $b_s = 16622.8 \times 10^{-6}$ Å for the amyloid peptide and $\rho_w = 6.33 \times 10^{-6}$ Å^{-2} (98% deuterated water) for the D_2O solvent in Eq. (5) can also be calculated from the molecular formulae. Note, in calculating the b_s, we have taken in account the small portion of H–D exchange effect between the amino acids of the peptide and the deuterated solvent D_2O, as mentioned by Jacrot [4].

3. Experimental section

β-amyloid peptide (A_β), 1–40 amino acid peptide of a molecular weight of $M_w = 4329.8$ g/mole was purchased from Sigma. After being dissolved in hexafluoroisopropanol (HFIP) and incubated for 12 h at room temperature, the sample was retrieved by lyophilization, as a form of monomers. The sample then was added with D_2O for three sample solutions of 0.5 mg/ml (0.12 mM) amyloid peptide. Two of the sample solutions were added with 6.0 mM SDS and 6.0 mM d-SDS, respectively. After waiting for 72 h for A_β aggregation, the samples were measured by SANS.

SANS measurements were conducted at an ambient temperature on the 30-m SANS spectrometer at NIST, USA. The sample solutions were sealed in quartz cell of 5-mm thickness. With 5-Å neutrons and two sample-to-detector distances, 2.5 and 15 m respectively, data collected covered a Q-range of 0.002–0.3 Å^{-1}. The SANS data collected were corrected for transmission, background, and pixel sensitivity of the 2-D detector, and averaged into 1-D function $I(Q)$. Data were further scaled to the absolute intensity for the scattering cross section per unit sample volume, of an unit of cm^{-1} [6].

4. Result and discussion

Fig. 1 shows the SANS data for the D_2O solutions of 0.12 mM amyloid peptide, and the same peptide solutions mixed with 6 mM SDS and 6 mM d-SDS, respectively. In the lower-Q region (0.002–0.01 Å^{-1}), the pure peptide solution demonstrates a power-law scattering of $I(Q) \propto Q^{-4}$, indicating a boundary scattering from large fibril aggregate (the fibrils were confirmed in our AFM result). For the mixtures with SDS, the large particle scattering is reduced by more than 50%. Presumably, less number of large A_β aggregates are formed due to the intervening of SDS in the solution. On the other hand, in the Q region $\geqslant 0.01$ Å^{-1}, the scattering is more pronounced for the A_β solution with the presence of SDS, revealing a more abundant small aggregates, compared to the pure peptide solution. Substituting SDS by d-SDS, the significantly lowered scattering in the same scattering region strongly suggests that the smaller aggregates are indeed complex aggregates of A_β/SDS. And the contrast between the complex aggregates and D_2O ($\rho = 6.4 \times 10^{-6}$ Å^{-2}) is lowered significantly due to the substitution of SDS ($\rho = 0.4 \times 10^{-6}$ Å^{-2}) with d-SDS ($\rho = 6.8 \times 10^{-6}$ Å^{-2}), since the peptide has also a small ρ of 0.3×10^{-6} Å^{-2}. Here, we have intentionally used a small surfactant concentration below the critical micelle concentration (8 mM) of SDS, to avoid the formation of SDS micelles,

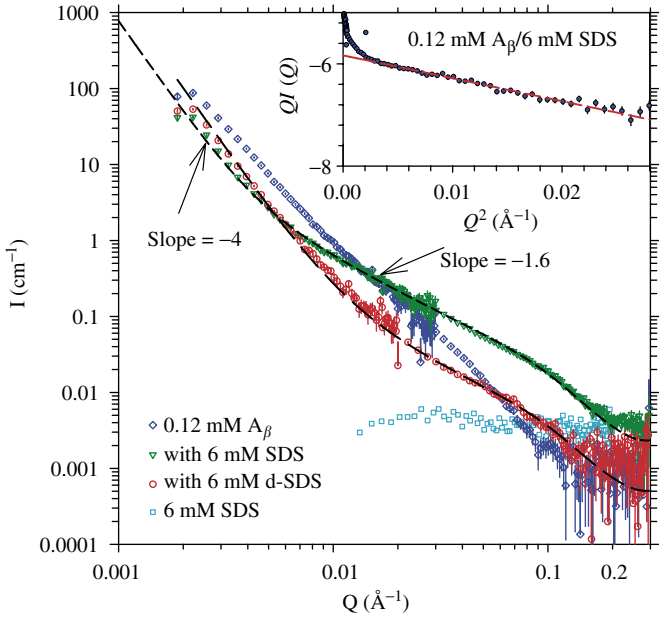

Fig. 1. SANS data for the aqueous solutions of 0.12 mM amyloid peptide. Data for the solutions mixed with 6 mM SDS and 6 mM d-SDS are respectively fitted using the model described in the text. SANS data for a solution of 6 mM SDS are also shown. Inset shows the Kratky–Porod approximation (dashed line) for the SANS data of the A_β/SDS solution.

and thereby eliminate efficiently the scattering contribution from the SDS micelles as can be seen in Fig. 1.

For the SANS data of the A_β/SDS solution, the data in the region $Q > 0.07\,\text{Å}^{-1}$ (dominated by the form factor scattering) can be fitted with the Kratky–Porod approximation (the dotted line in the inset of Fig. 1), indicating a rod-like shape. A rod radius $r = 14\,\text{Å}$ can be extracted from the Kratky–Porod approximation for the complex aggregates [2]. Whereas in the intermediate-Q region ($0.01\,\text{Å}^{-1} \leqslant Q \leqslant 0.07\,\text{Å}^{-1}$), data show a power-law scattering of $I(Q) \propto Q^{-1.6}$, implying a mass fractal domains formed by the rod-like aggregates [3]. Using the rod-like form factor $P(Q)$ and the mass fractal structural factor $S(Q)$ described previously, we can fit both sets of the contrast data (dashed curves in Fig. 1) well, with the common structural parameters $r = 13.4$ and $L = 49\,\text{Å}$ for the rod complex, and $\xi = 427\,\text{Å}$ and $D = 1.58$ for the fractal domains formed by the rods. In the fitting curve, we have included the Q^{-4} contribution by the large A_β fibrils.

Since some of the A_β monomers form fibrils, the concentration n_p of the complex A_β/SDS cannot be determined concretely. We have difficulty in extracting the absolute aggregation numbers N_p and N_s of the complex. Nevertheless, an association ratio $\mu = N_s/N_p = 30$ can still be obtained according to Eq. (6), using the two fitted $I_o(0)$ for the two contrast solutions.

5. Conclusions

We have found that SDS can suppress the fibril structure of β-amyloid peptide, via the formation of small peptide/SDS complex in aqueous solutions. The suppression effect is expected to be enhanced with SDS micelles when a larger SDS concentration is used, as indicated by Marcinowski et al. [7].

Acknowledgments

We acknowledge the support of the NIST for the SANS beam time. The work was partially supported by the NSC under Grant nos. NSC-93-2112-M-213-011 (U. Jeng), NSC91-2113-M-007-037 (T.-L. Lin).

References

[1] P. Thiyagarajan, T.S. Burkoth, V. Urban, S. Seifert, T.L.S. Benzinger, D.M. Morgan, D. Gordan, S.C. Meredith, D.C. Lynn, J. Appl. Crystallogr. 33 (2000) 535.
[2] T.-L. Lin, S.-H. Chen, N.E. Gabiel, M.F. Robert, J. Am. Chem. Soc. 108 (1986) 3499.
[3] S.-H. Chen, J. Teixeira, Phys. Rev. Lett. 57 (1986) 2583.
[4] B. Jacrot, Rep. Prog. Phys. 39 (1976) 911.
[5] E.Y. Sheu, S.H. Chen, J. Phys. Chem. 92 (1988) 4466.
[6] C.J. Glinka, J.G. Barker, B. Hammouda, S. Krueger, J.J. Moyer, W.J. Orts, J. Appl. Crystallogr. 31 (1998) 430.
[7] K.J. Marcinowski, H. Shao, E.L. Clancy, M.G. Zagorski, J. Am. Chem. Soc. 120 (1998) 11082.