# UV resonance Raman monitors polyglutamine backbone and side chain hydrogen bonding and fibrillization

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## 1. Ψ-angle distribution of Q10

***UVRR spectrum decomposition.*** We used Grams Suite (Version 8.0, Thermo Fisher Scientific, Inc. Waltham, Mass., USA) to model the UVRR spectrum as the sum of Gaussians. The $AmIII^{b}$ region contains no overlapping side chain contributions. The $AmIII_3{}^{b}$ region of non-disaggregated Q10 (NDQ10) in pure water shown in Fig. S1 was fitted to two Gaussians. This resulted in a fitted $AmIII_3{}^{\beta\ b}$ band at 1231 $cm^{-1}$ and an $AmIII_3{}^{T\ b}$ band at 1262 $cm^{-1}$ ($^{b}$ indicates backbone amide vibration). The $AmIII_3{}^{b}$ region of disaggregated Q10 (DQ10) in pure water shown in Fig. S2 was fitted to three Gaussians. This resulted in a fitted $AmIII_3{}^{PPII\ b}$ band at 1243 $cm^{-1}$, an $AmIII_3{}^{2.51\text{-helix}\ b}$ band at 1270 $cm^{-1}$ and an $AmIII_3{}^{T'\ b}$ band at 1207 $cm^{-1}$. (T and T′ refer to different types of turns: Type I, Type III or Type VIII β-turn, and Type I′ or Type III′ β-turn, respectively.)

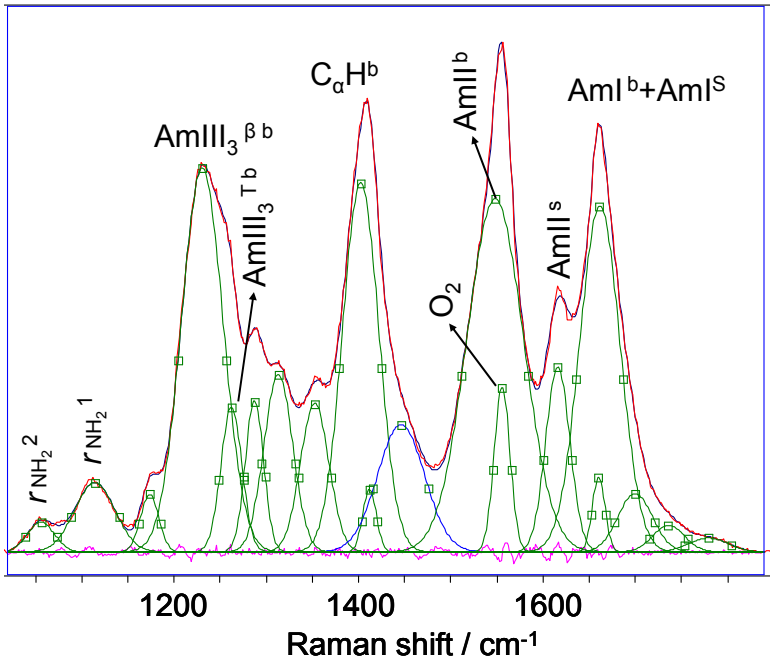


**Figure S1.** Deconvolution of 204 nm UVRR spectrum of the NDQ10 in pure water at 22 $^{0}$C. $^{b}$ indicates backbone amide bands; $^{s}$ indicates side chain amide bands. The $AmI^{b}$ band

overlaps the glutamine side chain AmI$^{s}$ band; the $C_{\alpha}H^{b}$ band overlaps with the side chain AmIII$^{s}$+$\delta_{CH_2}$peak.

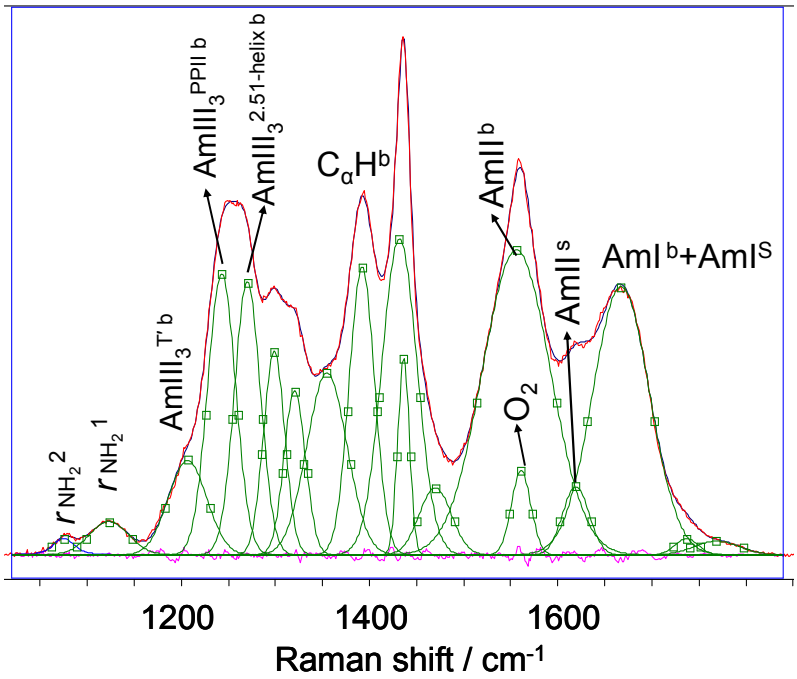


**Figure S2.** Deconvolution of 204 nm UVRR spectrum of the DQ10 at 22 $^{0}$C. $^{b}$ indicates backbone amide bands; $^{s}$ indicates side chain amide bands. The AmI$^{b}$ band overlaps the glutamine side chain AmI$^{s}$ band; the $C_{\alpha}H^{b}$ band overlaps the side chain AmIII$^{s}$+$\delta CH_2$ peak.

***AmIII$_3^b$ band deconvolution.*** We assume that the inhomogeneously broadened experimentally measured AmIII$_3^{b}$ band profile derives from different conformations and can be modeled by the sum of Lorentzian bands.[1] We deconvoluted each of the AmIII$_3^{b}$ bands from the Fig. S1-S2 fit into the sum of Lorentzian bands with homogeneous line widths $\Gamma$ with different center frequencies $ve_i$:

$$A(\nu) = \pi^{-1} \sum_{i=1}^{M} L_i \cdot \frac{\Gamma^2}{\Gamma^2 + (\nu - ve_i)^2} \qquad (1)$$

where $L_i$ is the probability for a band to occur at frequency $ve_i$.

***Quantitative correlation between the Ψ-angle and the AmIII$_3$ frequency.*** Equations exist that correlate the Ψ angle to the AmIII$_3$ frequency,[2] thus allowing the calculation of the Ψ-angle distributions.[3] The Ψ-angle distribution for PPII-like and 2.5$_1$-helix-like conformations were calculated using the following expression for peptide bonds fully exposed to water:[2]

$$\nu_{AmIII_3}(\Psi,t) = 1256 \ \ cm^{-1} - 54 \ \ cm^{-1} \cdot \sin(\Psi + 26^o) - 0.11 \frac{cm^{-1}}{^oC} t \quad (2)$$

The Ψ-angle distribution for the β-sheet was calculated by using the following expression for peptide bonds forming two-end-on peptide bond-peptide bond hydrogen bonds:[2]

$$\nu_{AmIII_3}(\Psi) = 1244 \ \ cm^{-1} - 54 \ \ cm^{-1} \cdot \sin(\Psi + 26^o) \quad (3)$$

The Ψ-angle distributions for Type I or Type III or Type VIII β turns and Type I′ or Type III′ β turns were calculated by using the average expression for peptide bonds with different possible hydrogen bonding patterns:[2]

$$\nu_{AmIII_3}(\Psi,t) = 1250 \ \ cm^{-1} - 54 \ \ cm^{-1} \cdot \sin(\Psi + 26^o) - 0.06 \frac{cm^{-1}}{^oC} t \quad (4)$$

These equations correlating the $AmIII_3$ frequency with the Ψ-angle ignore the more modest Φ-angle dependencies.[4] The estimated error of this determination is suggested to be $< \pm 14^o$.[2]

## 2. CD spectra of Q10 solutions by using different solvents for disaggregation

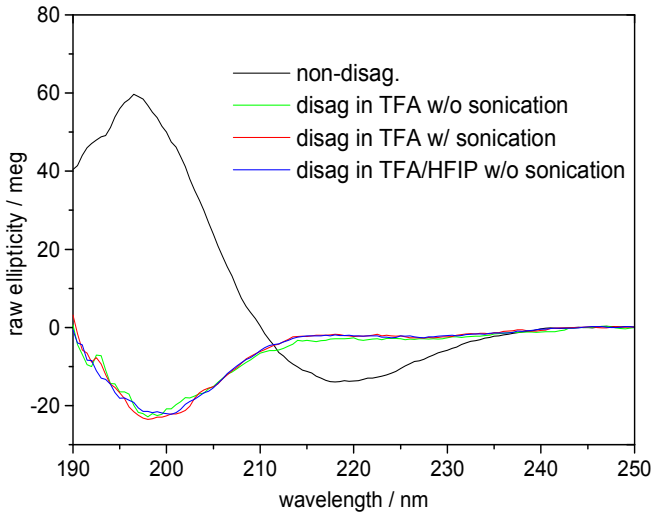


**Figure S3**. CD spectra of 1 mg/ml NDQ10 (black) and DQ10 in pure water at 22 $^oC$. Disaggregation using TFA with (red), and without (green) sonication, and using 1:1 TFA/HFIP mixture without sonication (blue) give rise to essentially identical CD spectra. The peptide solutions were not centrifuged.

Fig. S3 shows the CD spectra of DQ10 solutions using different solvents for disaggregation. The CD spectrum of Q10 using TFA for disaggregation without sonication (Fig. S3, green) shows a very slight negative ellipticity at ~ 220 nm and a strong negative band at 200 nm, indicative of extended conformations.[5-7] The CD spectra of solutions without sonication are essentially identical to those with sonication (Fig. S3, red), indicating that sonication is not required. The TFA disaggregated CD spectrum is identical to the TFA/HFIP mixture disaggregated spectrum (Fig. 3S, blue), indicating that TFA alone dissolves Q10 aggregates.

**3. Electron micrographs of NDQ10 in pure water at short time incubation**

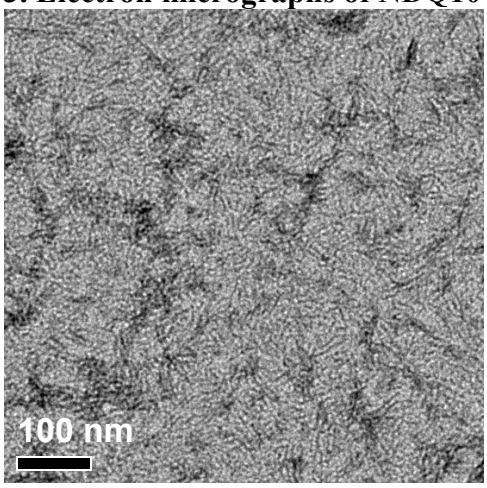


Figure S4: Electron micrographs of NDQ10 in pure water at short time incubation.

**References:**

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