Supporting information

The molecular mechanism of conformational changes of the triplet prion fibrils for pH

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Table S1. The structural parameters of HET-s triplet fibrils which are compared with experimental values.

		radius (Å)	rotation/subunit	arc/subunit	pitch length (Å)
pH 2	model¶	21.97	3.12	1.20	361.54
	Experiment [1]	22	3.12	1.20	361
pH 3	Experiment [1]	31	3.37	1.81	335

¶ The structure of pH2 HET-s triplet fibril which is constructed with 2KJ3 according to the experimental structural parameters.

§ The pH3 HET-s triplet fibril is resulted by the conformational changes due to the torsional mode shape of pH2 HET-s triplet fibril.

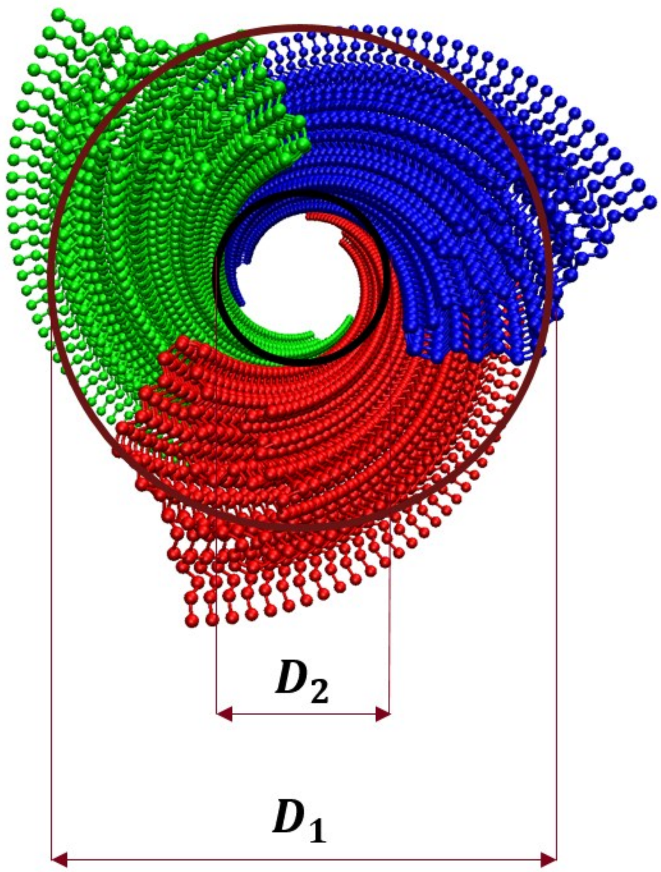

Fig S1. Cross-sectional area of Triplet fibril. D_1, D_2 are the outside and inner side diameter of HET-s triplet fibril. HET-s triplet fibril is regarded as a hollow beam for the calculation of bending rigidity and torsional modulus.

Euler-Bernoulli Beam Model

The equations of motion for bending and torsional mode of a beam is given below.

$$\frac{\partial^2 w(x,t)}{\partial t^2} + \frac{E_B I}{\rho A}\frac{\partial^4 w(x,t)}{\partial x^4} = 0 \quad \text{for bending mode (S1)}$$

$$\frac{\partial^2 \theta(x,t)}{\partial t^2} + \frac{G_T}{\rho}\frac{\partial^2 \theta(x,t)}{\partial x^2} = 0 \quad \text{for torsional mode (S2)}$$

, where w and θ are the transverse displacement for bending mode and torsional mode respectively, $E_B I$ is a bending rigidity, G_T is a torsional modulus. Those values are introduced in the manuscripts. ρ is a mass density and A represents a cross-section area of a fibril. A coordinate of x is defined along the longitudinal direction of HET-s fibril. Let the transverse deflection and torsional angle be defined following form for vibrational motion; $w(x,t) = z(x)\exp\left[i\omega_b t\right]$ and $\theta(x,t) = \varphi(x)exp[i\omega_t t]$, where ω_b and ω_t are representing natural frequencies for bending and torsional modes respectively, $z(x)$ and $\varphi(x)$ are their corresponding eigenmodes. Euler-Bernoulli beam model equations finally can be transformed into following equations.

$$\frac{E_B I}{\rho A}\frac{d^4 z}{dx^4} - {\omega_b}^2 z = 0 \quad \text{for bending mode (S3)}$$

$$\frac{G_T}{\rho}\frac{d^2 \varphi}{dx^2} + {\omega_t}^2 \varphi = 0 \quad \text{for torsional mode (S4)}$$

From Eq. (S3, S4), following equations can be derived[2-5].

$$E_B = \rho\frac{A}{I}(f^B)^2\left(\frac{L}{\alpha}\right)^4 \quad \text{(S5)}$$

$$G_T = \rho(f^T)^2\left(\frac{L}{\pi}\right)^4 \quad \text{(S6)}$$

The bending rigidity and torsional modulus for model 1 was calculated with Eq. S5 and S6.

Timoshenko beam model

The equation for Timoshenko beam model is given below.

$$\delta = \delta_B + \delta_S = \frac{PL^3}{aE_B^0 I} + \frac{cPL}{bG_S A} \quad \text{(S7)}$$

δ is the total bending deflection, δ_B is the deflection due to bending deformation, δ_S is the deflection due to shear deformation, E_B^0 is the length-independent bending elastic modulus, G_S is the intrinsic shear modulus, *I*, *A*, and *L* represent the cross-sectional moment of inertia, the cross-sectional area, and the length, respectively, of an amyloid fibril, *a* and *b* are the boundary-condition-dependent constants, and *c* is a form factor which means a shear coefficient that depends on the cross-sectional shape. A value of 7.5788 was used for a form factor *c*. the total bending deflection can be represented with summation of the bending deformation and shear deformation.

$$form\ factor\ (c) = \frac{\tau_{max}}{\tau_{average}} = \frac{\left(\frac{V \times a \times y}{I \times t}\right)}{\left(\frac{V}{A}\right)} = \frac{a \times y \times A}{I \times t} \tag{S8}$$

, where *V* represents a shear force *a* is an area beyond neutral axis, *y* represents a distance between center of gravity of this area and neutral axis of entire cross-section ,*A* is a total area of section, *I* is a moment of inertia of section, *t* (=$D_2 - D_1$) is a total thickness of gap, and τ is shear stress. Fig. S1.was referred to calculate the form factor (c).

$$E_B = E_B^0\left(1 + \frac{a\ cE_B^0 I}{b G_S A L^2}\right)^{-1} \tag{S9}$$

Eq. S8 can demonstrate the dependence of the bending elastic modulus for the length of HET-s fibrils.

Reference

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