Supplementary information

## Probing physical properties of amyloid fibrils using nanofluidic channels

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## Applicability of the Odijk theory

The extension of a semiflexible polymer in the Odijk regime is given by Eq. 1 of the main text as a function of the contour length L, the the width of the channel in direction i,  $D_i$ , and the persistence length, P. In theory, the validity of the Odijk regime requires simultaneously satisfying two strong inequalities. First, the channel size must be small compared to the persistence length,  $D_i \ll P$ , such that the configuration of the chain consists of a series of deflection segments with characteristic length  $\lambda = D^{2/3}P^{1/3}$ .<sup>1</sup> Second, the contour length must be small compared to the global persistence length, ideal semiflexible polymer, and numerical results for g(D/P) are available in the literature.<sup>3, 4</sup> This second restriction ensures that excluded volume interactions between distal segments of the chain are negligible. Since the global persistence length increases exponentially as the channel size becomes smaller than the persistence length, satisfying the first inequality is usually sufficient. In rectangular channels, where  $D_1 \neq D_2$ , application of Eq. 1 requires that the conditions for the Odijk regime be satisfied for both  $D_1$  and  $D_2$  because the derivation of Eq. 1 is based on the existence of independent, persistent random walks in the two confined directions.<sup>5, 6</sup>

Since our experiments are intended to provide a measure of the persistence length, we need to check the validity of the Odijk regime self-consistently by first fitting the data to Eq. 1 compute L and P, and then checking to see whether the results satisfy the conditions for the Odijk regime. While the Odijk theory is only strictly valid in the strong inequality limit, simulations of semiflexible polymers with a very wide range of stiffness indicate that Eq. S1 holds until  $D \approx 2P$ .<sup>4</sup> For the smaller channel depth,  $D_1 = 300$  nm, this condition is met for all persistence lengths reported in Figure 3 of the main text. However, using  $P \approx 1$  µm as an approximate lower bound for those persistence lengths, the most aggressive application of Eq. S1 to the data should be limited to  $D_2 < 2000$  nm. To be somewhat more conservative, our analysis (see Figure S2 for an example) only uses the data up to  $D_2 = 1500$  nm.

For the situation where  $D \approx P$ , it may be the case that  $L \approx g$  for short fibrils because g is approaching P as well.<sup>3</sup> In this case, visual inspection of the kymographs is sufficient to ensure that the chain is not backfolded; backfolding would lead to regions of the kymograph with twice the intensity of the remainder of the chain and are readily identifiable.<sup>7</sup> If the absence of any folds, Eq. 1 may be used even if the probability of forming such a fold is not exponentially small.



**Figure S1.** Optical microscope image of the nanochannels on  $SiO_2$ . Image on the left with markers on the side show the width of the nanochannels at designated locations. The scale bar is 50  $\mu$ m. Image on the right is at a higher magnification, showing the smooth transition between regions of different widths. The scale bar is 10  $\mu$ m.



**Figure S2.** a) The change in extension with channel width for a single  $A\beta(1-42)$  amyloid fibril. The solid black line is the fit to Equation 1. The dashed red line shows the fit when the extension in the 2.4 and 3 µm wide channels are considered. b) The change in extension with channel width for a single  $\alpha$ -syn amyloid fibril. The solid black line is a fit to Equation 1. The dashed red line shows the fit when the extension in the 2.4 and 3 µm wide channels are included.



**Figure S3.** Histogram of persistence lengths for  $A\beta(1-42)$  amyloid fibrils showing two populations.



Figure S4. Absorbance of ATTO488, labeled and unlabeled  $\alpha$ -syn.



Figure S5. Histogram of intensity and contour length of a) for A $\beta$ (1-42) and b)  $\alpha$ -syn amyloid fibril.



**Figure S6.** Relationships between contour length and fluorescence intensity per length unit for single amyloid fibrils. a) Scatter plots of contour length versus fluorescence intensity for A $\beta$ (1-42), b)  $\alpha$ -syn amyloid fibril.

## **Supporting Videos**

Videos shows A $\beta$ -42 and  $\alpha$ -synuclein fibrils at different confinements.

## References

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