

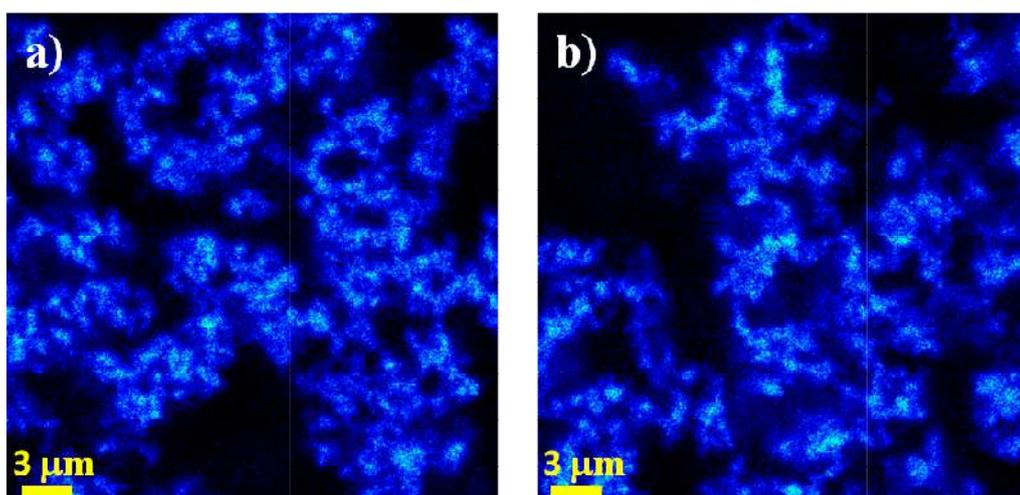
## Back to the Oligomeric State: pH-induced Dissolution of Concanavalin A Amyloid-like Fibrils into Non-Native Oligomers

Maria Grazia Santangelo<sup>\*a</sup>, Vito Foderà<sup>b</sup>, Valeria Militello<sup>a</sup> and Valeria Vetri<sup>\*ac</sup>

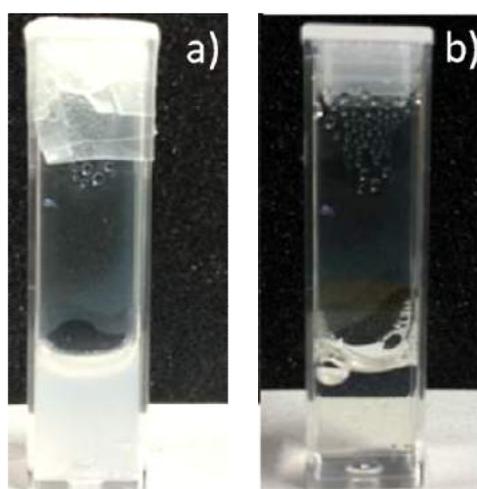
<sup>1</sup> Department of Physics and Chemistry, University of Palermo, Palermo, Italy.

<sup>2</sup> Section for Biologics, Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark.

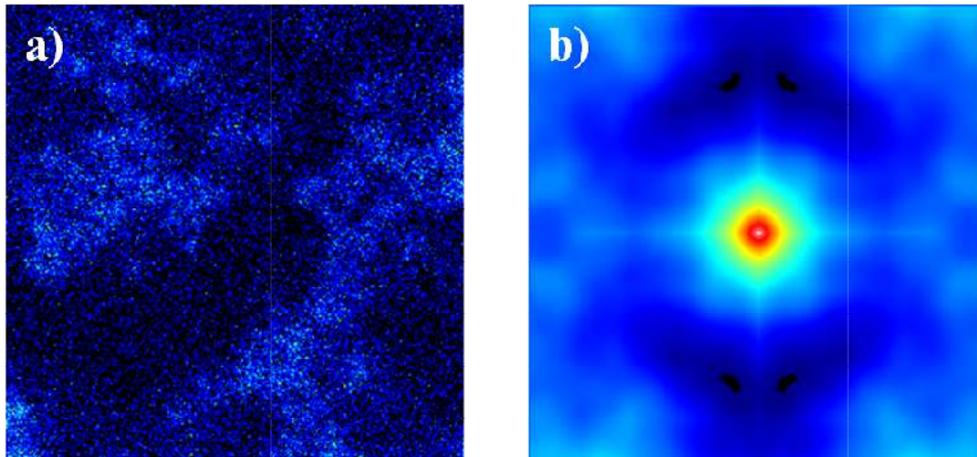
<sup>3</sup> Aten Center, University of Palermo, Palermo, Italy.



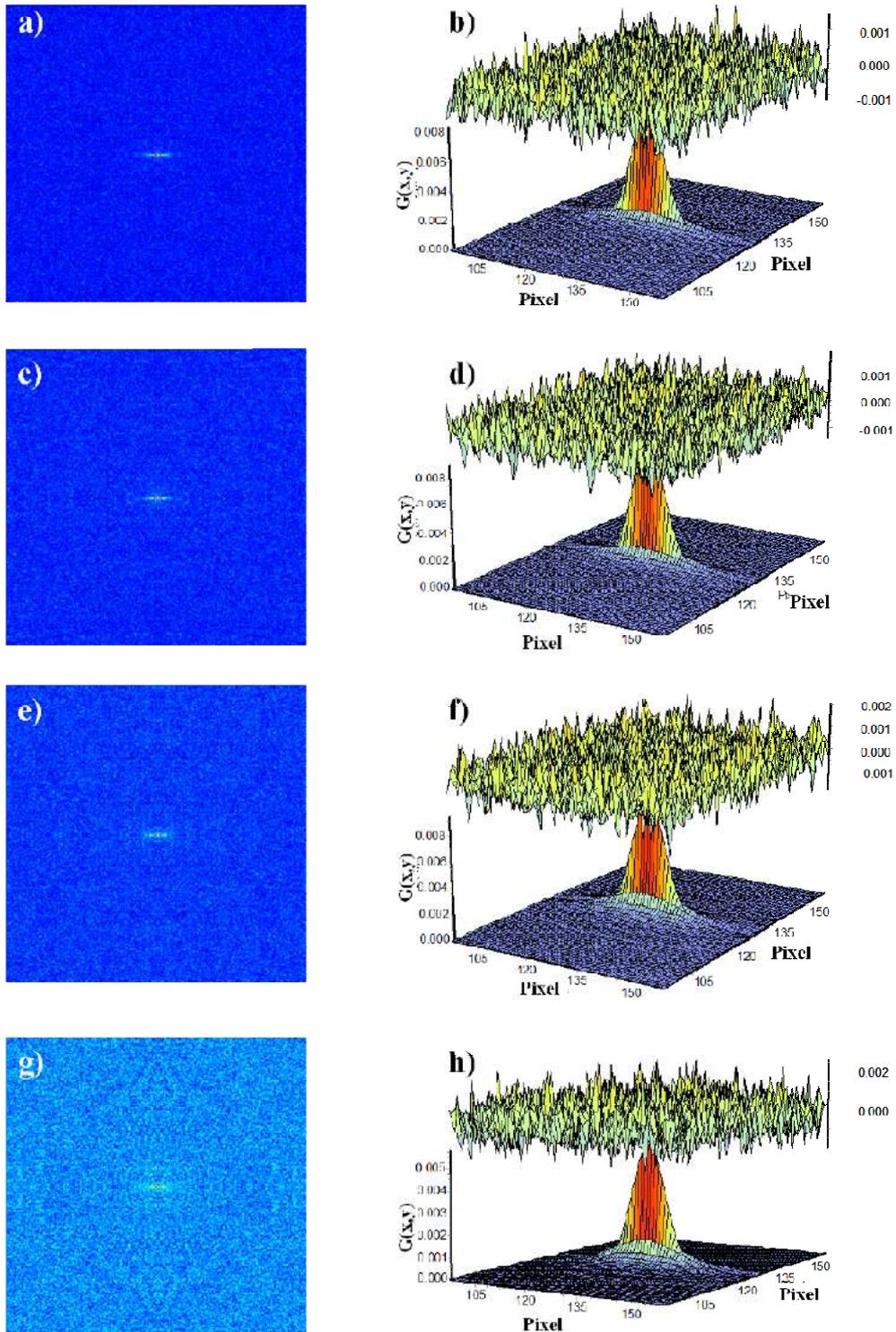
**Figure S1.** Representative 1024×1024 confocal image of fibril-like aggregates obtained by thermal incubation at 60 °C of 8.0 mg/ml ConA sample (pD ~ 2.6) containing ConA-Alexa647 (molar ratio ConA-Alexa/ConA ~ 1/3000) and then titrated with NaOH to change sample pD. a) pD = 5; b) pD = 9. Image size x-y 12.75 μm.



**Figure S2.** a) Image of cuvette containing fibril-like aggregates obtained by thermal incubation at 60 °C of 8.0 mg/ml ConA sample (pD ~ 2.6). b) Image of the same sample in a) when the pD value was titrated to pD ~ 12.



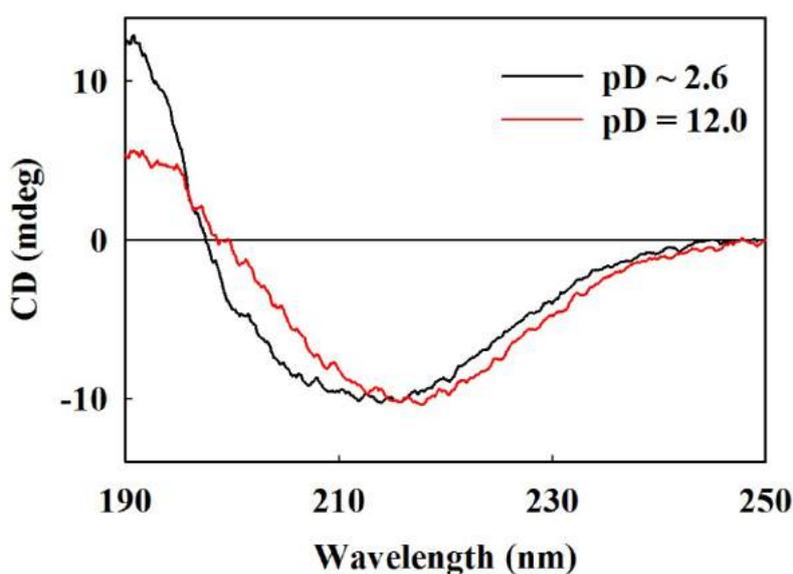
**Figure S3.** a) Representative 256x256 image, from an image stacks for RICS analysis, of fibril-like aggregates obtained by thermal incubation at 60 °C of 8.0 mg/ml ConA sample (pD ~ 2.6) containing Con A-Alexa647 (molar ratio ConA-Alexa/ConA ~ 1/3000). b) RICS function obtained from the analysis of the image stacks in panel a). For this sample a fitting of the correlation function using the diffusion model is not possible [Digman, M.A. et al 2005, Digman, M.A. et al 2009].



**Figure S4.** Spatial autocorrelation (RICS) function measured for 8.0 mg/ml ConA sample ( $pD \sim 2.6$ ) containing ConA-Alexa647 (molar ratio ConA-Alexa/ConA  $\sim 1/3000$ ) and then titrated with NaOH to change sample pD, and the corresponding fits of the correlation functions. a-b)  $pD = 3$ ,  $D = 46 \pm 2 \mu\text{m}^2/\text{s}$ ; c-d)  $pD = 5$ ,  $D = 43 \pm 2 \mu\text{m}^2/\text{s}$ ; e-f)  $pD = 9$ ,  $D = 31.2 \pm 1.5 \mu\text{m}^2/\text{s}$ ; g-h)  $pD = 12$ ,  $D = 28 \pm 2 \mu\text{m}^2/\text{s}$ .

## Circular Dichroism

Circular dichroism (CD) spectra were recorded, using a 0.5 mm quartz cuvette, on a J-815 spectropolarimeter (Jasco, J-715) equipped with a Jasco PCT 348 WI temperature controller. The spectra were acquired with the average of 10 scans (1 nm bandwidth, 1 s response, 50 nm/min scan rate, 0.1 nm data pitch) and baseline-corrected by subtracting a buffer spectrum. To perform CD measurements, F-ConA samples at different pD have been diluted in deuterated solution with 0.1 M NaCl to obtain a final concentration of about 0.008 mg/ml. The Far-UV CD spectrum of mature fibril-like aggregates of ConA at pD ~ 2.6 (black line Figure S5) is characterized by a prominent peak at 215 nm that indicates the presence of  $\beta$ -aggregate structures [Vetri et al. 2007]. After the adding of few  $\mu$ l of NaOH to the same sample to change the pD (red line Figure S5), the Far-UV CD spectrum changes toward a typical ConA  $\beta$ -native profile. However, a decrease of the signal at lower wavelengths (region around 190 nm) is also observed indicating formation of random coil structures [Kelly et al. 2005].



**Figure S5.** Far-UV CD spectra a sample containing mature fibrils of ConA obtained after 300 minutes of thermal incubation at 60 °C ( $c = 8$  mg/ml) at pD ~ 2.6 (black line) and after the adding of few  $\mu$ l of NaOH (pD = 12; red line).

## References

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