Our preliminary results find growth rates greater than previously observed by DIC microscopy. We can also measure the growth rate of bundles by observing a mass of fibers that subsequently grow along the channel, and these grow at rates comparable to those determined by DIC microscopy. Implications of the measurements and the method will be discussed.

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A Unified Theory of Liquid-Liquid Demixing and Polymer Formation Kinetics

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Sickle hemoglobin is a natural hemoglobin mutation with a hydrophobic replacement of a charged aminoacid on the molecular surface. This leads to aggregation into rigid helical structures (''polymerization''), the underlying cause of sickle cell disease. It has also been shown that polymerization occurs in close correspondence with the phase transition of liquid-liquid demixing , or with the critically diverging fluctuations of local concentration occurring in its proximity. Due to this correspondence, polymerization kinetics remarkably appear to exhibit, with respect to demixing temperature, the same universal scaling features shown by amplitudes and lifetimes of fluctuations occurring in proximity of phase transitions. Thus, it is important to understand the relation between polymer formation and liquid-liquid demuxing (LLD). Nucleation kinetics have been described by a relatively complete theory, that until now does not include LLD. We present here a way to incorporate LLD seamlessly into such theory, so as to have a description in terms of the concurrence and interaction of the two processes. In addition, we present new light scattering data supporting the theory. The theory provides a more in-depth understanding of aggregation and crystallization.

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Amyloid-like Aggregation Of A Human Apolipoprotein A-I Variant

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Amyloidosis are characterized by extra cellular deposits of anomalous fibrilar proteins. Human apolipoprotein A-I (apoA-I) is not normally involved within these pathologies. However, one case of severe amyloidosis associated with atherosclerosis was observed when apoA-I shows a deletion of a lysine residue in a central region of the protein (apoA-I Lys107-0). In order to get insight on the local cellular environment that promotes this anomalous aggregation, we studied the folding of the deletion mutant, as compared with wild type apoA-I (Wt). Analysis of chemical denaturation and by using hydrostatic pressure show that apoA-I Lys107-0 is more unstable and has a stronger tendency to form β sheet structure as incubation time increases, specially at acidic pH. Under these conditions, mutant denaturation is less cooperative, suggesting intermediate states folding. In order to confirm that these states prone protein aggregation, we followed protein folding by two-Photon Fluorescence Correlation Spectroscopy. Our results clearly show that, even at very low concentrations, protein aggregation is detected, under acidic conditions, after incubation for a few hours at 37°C. Interestingly, also Wt suffers conformational chances that favor some insoluble states. These results suggest that the anomalous aggregation of apoA-I Lys 107-0, is mediated by intermediate folded states and β sheet conformation, induced by an acidic pH. Protein misfolding is concentration-dependent, but can occur under diluted solutions. We discuss our results in terms of the pathological landscape of atherosclerosis.

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Endogenous Formaldehyde Is Related To Sporadic Alzheimer's Disease

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Formaldehyde is produced in human body at every moment. Our previous work has showed that formaldehyde at a low concentration induces tau protein to misfolding and aggregation, resulting in cytotoxicity to SH-SY5Y cells and rat hippocampus cells[1,2]. Therefore, concentrations of endogenous formaldehyde of human have been investigated to suggest that endogenous formaldehyde plays an important role in the pathology of sporadic Alzheimer's disease. Investigation of 420 Chinese people of different ages shows that blood formaldehyde is increased with aging (over 60 years old). The human blood formaldehyde is dynamically kept approximately around 0.087 ± 0.014 mM under physiological conditions. The endogenous formaldehyde is gradually increased and accumulated in human body especially in the central nerve system as aging, resulting in chronic aldehyde damage to human brain including white matter and grey matter. The chronic aldehyde damage is thought as one of the important factors related to sporadic neurodegeneration. According to this viewpoint, clinical investigation has been carried out that the concentration of morning uric formaldehyde is found to be positively related to the degree of dementia: the more severe the dementia, the higher the concentration of uric formaldehyde of the patients. Furthermore, to regulate endogenous formaldehyde as clinical treatment (methods or drugs) for Alzheimer's patients is suggested in the light of this work.

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Intramolecular Diffusion of the Amyloidgenic Protein HypF

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The mechanism of amyloid fibril aggregation is as fundamental a process in protein dynamics as folding. Our goal of studying the N terminal domain of E.coli HypF (HypF-N) is to seek the intrinsic intramolecular properties of amyloidgenic proteins. We measured two mutants (W81F and W27F) using Trp-Cys contact quenching to explore the microsecond loop formation of two chain segments of HypF (27-65 and 65-81). Using Szabo, Schulten and Schulten theory and a worm-like chain model to determine an effective intramolecular diffusion coefficient, *D,* we observed different behaviors for these two segments. The short loop (C65-W81) collapsed into a very vicious and compact state under low denaturant conditions while the long loop (W27-C65) is relatively more diffusive. Finally chronological measurements in 3%-6% (v/v) TFE (trifluoroethanol) show that the long loop appears to become unstructured and highly diffusive before aggregating.

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Amyloid Formation By Peptides From Yeast Adhesins

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Candida albicans adhesins bind to peptides and lead to cell aggregation with amyloid properties. We therefore searched in other fungal adhesins for β-aggregation forming sequences with the TANGO algorithm and synthesized three peptides. The *C. albicans* Als5 peptide, SNG (SNGIVIVATTRTV), has a 90% β-aggregation potential and forms amyloids (Otoo, et al, Euk. Cell, 7(5): 776-782, 2008). The two additional peptides, from *C. albicans* Eap1 adhesin (HTA VTTGVTIITVTTND) and *Saccharomyces cerevisiae* Flo1 adhesin (TDETVIV IRTP), have aggregation potentials of 90% and 42% respectively, and were studied for amyloid formation.

Peptide interactions were analyzed by circular dichroism (CD), absorbance and fluorescence spectroscopy to monitor secondary structure and amyloid formation. CD spectra showed unstructured random coil for both Eap1 and Flo1 peptides in buffer, changing to β-aggregate with an ellipticity minimum at 230-235nm after stirring to induce amyloid formation. The stirred solutions of both Flo1 and Eap1 peptides showed an increase in Congo Red absorbance with a shoulder near 550nm and also had enhanced thioflavin-T fluorescence. Thioflavin-T emission intensity is much greater when it is bound to amyloids and the emission spectra of both amyloid peptides show a significant fluorescence intensity increase. These results with the Flo1 and Eap1 peptides suggest a change from non-amyloid characteristics when initially dissolved in buffer to amyloid formation with stirring. Therefore, sequences from two additional adhesins show conformational changes leading to amyloid formation.

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Conformational Instability, Aggregation, and Hydrogel formation of a 16-Residue Alanine-Based Peptide in Aqueous Media

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