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Interfacial-shear induces protein amyloid fibrils[1] HANNAH MIDDLESTEAD, NICHOLAS DEBONO, ADITYA RAGHUNANDAN, AMIR HIRSA, Rensselaer Polytechnic Institute — The formation of amyloid fibril plaques and the accumulation of such material in vivo is the hallmark of many disorders including Alzheimers and type-II diabetes. Fibril formation can be induced by several factors including changes to pH and temperature conditions. However, the role of the dominant and most varying physiological factors of fluid flow and shear at hydrophobic interfaces in amyloidogenesis remain poorly understood. Proteins adsorbed at the air/liquid interface are also subjected to significant hydrodynamic stresses during bioprocessing and drug delivery, which leads to unwarranted denaturation/aggregation and loss in efficacy. We report on the kinetics of fibril formation in human recombinant insulin solutions sheared in a knife-edge surface viscometer using fixed time-point ThT fluorescence and native-protein absorbance assays across a wide range of concentrations and rotation rates. We identify differences in the morphology of the fibril structures formed at the air/liquid interface and in the bulk at different stages of pre-fibrils and fibril growth. This is key to elucidating the aggregation pathway and toxicity of shear-induced denaturation and protein fibril formation.

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