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Flow induced protein nucleation: Insulin oligomerization under shear. ANDREW DEXTER, ALI AZADANI, MIRCO SORCI, GEORGES BELFORT, AMIR HIRSA, Rensselaer Polytechnic Institute — A large number of diseases are associated with protein aggregation and misfolding, such as Alzheimer's, Parkinson's and human prion diseases such as Creutzveld-Jakob disease. Characteristic of these diseases is the presence of amyloid fibrils and their precursors, oligomers and protofibrils. Considerable evidence exists that a shearing flow strongly influences amyloid formation both in vitro and in vivo. Furthermore, the stability of protein-based pharmaceuticals is essential for conventional therapeutic preparations and drug delivery systems. By studying the nucleation and growth of insulin fibrils in a well-defined flow system, we expect to identify the flow conditions that impact protein aggregation kinetics and which lead to protein destabilization. The present flow system consists of an annular region bounded by stationary inner and outer cylinders and is driven by rotation of the floor. Preliminary results indicate that a continuous shearing flow can accelerate the aggregation process. The interfacial shear viscosity was found to drastically increase during aggregation and appears to be a useful parameter to probe protein oligomerization and the effects of flow.

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