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Aggregation of model amyloid insulin protein in crowding environments and under ac-electric fields ZHONGLI ZHENG, BENXIN JING, University of Notre Dame, BRIAN MURRAY, MIRCO SORCI, GEORGES BELFORT, Rensselaer Polytechnic Institute, Y. ELAINE ZHU, University of Notre Dame — In vitro experiments have been widely used to characterize the misfolding/unfolding pathway characteristic of amylodogenic proteins. Conversion from natively folded amyloidogenic proteins to oligomers via nucleation is the accepted path to fibril formation upon heating over a certain lag time period. In this work, we investigate the effect of crowing environment and external electric fields on the pathway and kinetics of insulin, a well-established amyloid model protein by single fluorescence spectroscopy and imaging. With added co-solutes, such as glycerol and polyvinylpyrrolidone (PVP), to mimic the cellular crowding environments, we have observed that the lag time can be significantly prolonged. The lag time increases with increasing co-solute concentration, yet showing little dependence on solution viscosity. Conversely, applied ac-electric fields can considerably shorten the lag timewhen a critical ac-voltage is exceeded. The strong dependence of lag time on ac-frequency over a narrow range of 500 Hz-5 kHz indicates the effect of ac-electroosmosis on the diffusion controlled process of insulin nucleation. Yet, no conformational structure is detected with insulin under applied ac-fields, suggesting the equivalence of ac-polarization to the conventional thermal activation process for insulin aggregation. These finding suggest that at least the aggregation kinetics of insulin can be altered by local solution condition or external stimuli, which gives new insight to the treatment of amyloid related diseases.

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