Applying microfluidic techniques in quantitative studies of protein aggregation

THERESE HERLING, University of Cambridge — Protein aggregation and fibrillation is involved in a number of devastating diseases, of which we have a limited understanding at present. Microfluidic techniques can be used in developing quantitative assays to study individual aspects of protein aggregation. Under certain conditions bovine insulin aggregates to give spherulites; spherical structures with fibrils growing and branching out from a central core. Drawing a parallel to actin polymerisation of the cell’s cytoskeleton, fibril growth generates force. The force generated by polymerisation at fibril ends during spherulite growth can be measured in a microfluidic environment (TPJ Knowles et al, PNAS, 2009). By measuring the bending of four polydimethylsiloxane walls by a growing spherulite positioned in the centre, the force generated by polymerisation at fibril termini can be calculated. By growing the spherulites with a constant flow of monomer, the maximum force able to be generated by fibril growth, the stall force, can be calculated. This gives insight into the energy landscape of protein aggregation.

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