Investigating the mechanisms leading to protein aggregation\textsuperscript{1}

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The formation of protein aggregates is a feature of several diseases and is a problem during the manufacture of biopharmaceutical and protein-based food products. During processing, stability may become compromised leading to the condensation of proteins to form non-native aggregates. The aim of this work is to induce aggregation on model proteins by the imposition of a particular stress to evaluate the extent of aggregation and to assess the degree of structural change to the protein. Aggregation of two proteins, lysozyme and bovine serum albumin, has been induced by several mechanisms. Using various techniques (electrophoresis, HPLC, spectroscopic analysis, and microscopic techniques) both the level of aggregation extent of protein unfolding has been investigated for a range of solution conditions. Our results show that the amount of aggregation depends strongly on the mechanism by which non-native aggregation proceeds, and within each mechanism, solution conditions are an important factor. With the exception of aggregation by self-association (which is concentration dependent), the appearance of aggregation is driven by structural changes induced by the applied stress (heat, chemical denaturant, oxidation or contact with a surface).

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