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**Primary nucleation and linear aggregation: novel methods take us further** GONZALO GARCIA, Department of Chemistry, University of Cambridge — Understanding linear aggregation has long been of interest in the study of proteins, as it is relevant in several human diseases such Alzheimer's Disease. While much work has been carried out experimentally and numerically, relatively little has been done to develop an analytical model for the time evolution and scaling behaviour of such systems. Here, we present a novel mathematical framework, guided by physical insight, for approaching these problems. We then apply this to derive an exact expression for the evolution of the polymer length distribution of an amyloid system, driven by primary nucleation, taking into account both elongation and depolymerisation. This is presented in terms of a perturbative expansion, and is valid for negligible monomer depletion. We then apply a similar framework to solve a similar system that also includes an arbitrary number of conformational intermediates before reaching the final conformation - we uncover the time evolution of the total mass of polymers in the final conformational state, and demonstrate various properties about its time-scaling behaviour. We then apply self-consistent iterative schemes, starting from these solutions, to derive a series of approximate analytical models for these systems, taking monomer depletion into account.

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