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Dynamic renormalisation group reveals sequential mechanism of the secondary nucleation of proteins THOMAS MICHAELS, PAOLO AROSIO, TUOMAS KNOWLES, University of Cambridge — Secondary nucleation has emerged as a key process in the self-assembly of amyloid fibrils associated with a number of neurodegenerative disorders. Secondary nucleation conceptually involves both aggregates and monomers, but a variety of ways exist, in which this process may occur. Elucidation of this complex mechanism using experimental data represents a theoretical challenge. A systematic coarse-graining procedure inspired by the renormalisation group is used to bridge the length- and timescale gaps between detailed microscopic descriptions and the processes observed in experiments. Various mechanisms of secondary nucleation are discussed at different levels of coarse graining and compact terms in the master equation are generated, that provide a single-step description of this process. This treatment is general and allows to test assumptions regarding mechanisms at the microscopic level and to filter their effect on the kinetics at the macroscopic scale. By analysing data from the polymerisation of amylin, we conclude that pre-critical nuclei in islet amyloid polypeptides stay attached to the aggregates during the process of secondary nucleation.

Thomas Michaels
University of Cambridge

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