# Phase behaviour and transitions in complex biological systems

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## Introduction

My research is focused on the application of theoretical computational tools developed in soft condensed matter physics to investigate the phase behaviour and transitions of complex systems of biomolecules. The research highlights in the year 2013 was our reconsideration of nucleation theory to describe amyloid fibrils nucleation.

## Confounding the paradigm: peculiarities of amyloid fibril nucleation

Fibrils of amyloid proteins are currently of great interest because of their involvement in various amyloid-related diseases and nanotechnological products. In a recent kinetic Monte Carlo simulation study [Cabriolu, R., Kashchiev D., Auer, S. (2012) *J. Chem. Phys.*, 137, 204903], we found that our simulation data for the rate of amyloid fibril nucleation occurring by direct polymerization of monomeric protein could not be described adequately by nucleation theory. It turned out that the process occurred in a peculiar way, thus confounding the nucleation paradigm and demanding a new theoretical treatment. In the present study, we reconsider the theoretical approach to nucleation of amyloid fibrils and derive new expressions for the stationary rate of the process. As these expressions provide a remarkably good description of the simulation data, using them, we propose a theoretical dependence of the amyloid-$\beta_{40}$ fibril nucleation rate on the concentration of monomeric protein in the solution. This dependence reveals the existence of a threshold concentration below which the fibril nucleation in small enough solution volumes is practically arrested, and above which the process occurs vigorously, because then each monomeric protein in the solution acts as fibril nucleus. The presented expressions for the threshold concentration and for the dependence of the fibril nucleation rate on the concentration of monomeric protein can be a valuable guide in designing new therapeutic and/or technological strategies for prevention or stimulation of amyloid fibril formation.

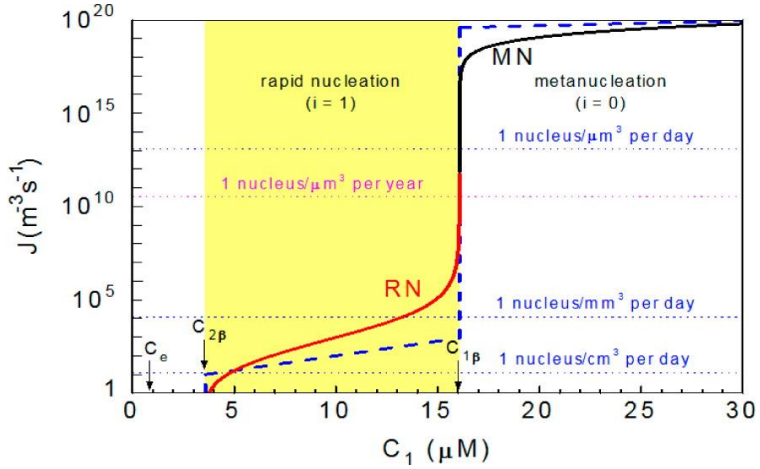


**Figure 1:** illustration of the sharp jump of the nucleation rate of amyloid fibrils at a certain threshold concentration.

## Publications

Kashchiev, D., Cabriolu, R. & Auer, S. (2013) Confounding the paradigm: peculiarities of amyloid fibril nucleation. *J. Am. Chem. Soc.* **135**: 1531-1539.

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**Collaborators**
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