Exploring macromolecular machine mechanisms with numerical tools

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Abstract

When powered by nucleotide hydrolysis, self-assembled homo-oligomeric complexes can undergo concerted motions that generate mechanical movements of their binding partners. Such mechanisms are notably commonly used to dissociate, translocate or condensate nucleic acid strands. They result from the interplay between atomic level interactions and global assembly organization, over different time-scales. Most often, homo-oligomeric dynamic systems escape experimental characterization, notably due to symmetry breaking. Numerical approaches can then help deciphering the mechanism. I will discuss known cases of cyclic assemblies where coexistence of different interfaces within a same ring-shaped oligomer was associated to sequential stages in the hydrolysis process and I will present how this type of mechanism may apply to so-called collaborative filaments [1] such as the homologous recombination filaments. Our investigations combining coarse-grained docking and high-resolution molecular dynamics simulations indicate the possibility of a weaving-like mechanism that would explain why ATP hydrolysis destabilizes the products of homologous recombination [2].

1. D. Ghosal & J. Löwe (2015) Collaborative protein filaments, EMBO J, 34, 2312
2. C. Danilowicz, L. Hermans, V. Coljee, C. Prévost and M. Prentiss (2017) ATP hydrolysis provides functions that promote rejection of pairings between different copies of long repeated sequences. Nucleic Acids Res 45, 8448-8462

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