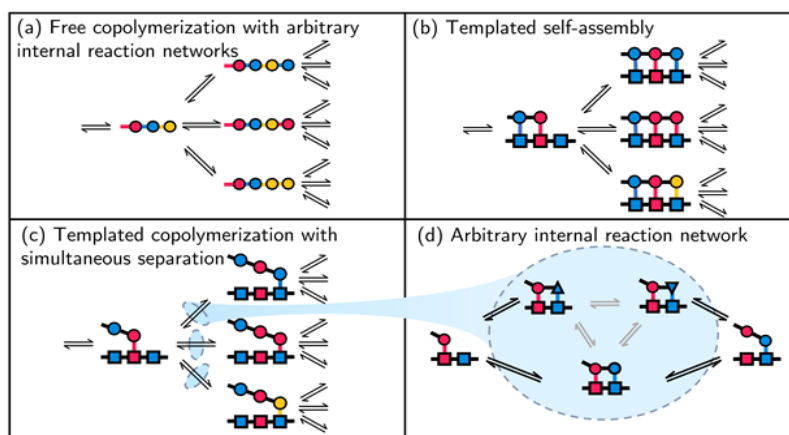


A universal method for analysing copolymer growth

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Copolymers are polymers consisting of more than one type of monomer and are ubiquitous in biology, including, for example, DNA, RNA and proteins. Producing copolymers with a specific sequence is thermodynamically challenging, and in living systems copolymers without repetitive sequences are typically produced with the aid of a template copolymer. Templated copolymerisation reactions often feature complicated pathways with multiple sub-steps in order to ensure accurate reproduction of the sequence encoded in the template. Information is embedded in the sequence of monomers of these copolymers; this information is transferred through templated copolymerisation, and used to direct molecular folding and cellular function in the vital processes of transcription, translation and replication. In this work, we consider a general class of copolymerisation models in which monomers are added to or removed from the end of a growing polymer via an arbitrary Markovian reaction network. Such a class of models can be used to study both non-templated and templated copolymerisation. Hitherto, analysis of these models has either required restrictive assumptions, such as irreversibility, or brute force simulation. We introduce a methodology that allows for properties such as the sequence distribution, polymerisation speed and entropy production to be obtained either analytically or via simple numerical calculations. This methodology makes use of techniques from absorbing Markov chains, graph theory and statistical mechanics in order to map the complex copolymerisation process onto a simpler coarse-grained process that may then be solved. Crucially, using our method, fine-grained, kinetic details of the full process, such as time spent and work done, are not lost and may be inferred exactly from using the solution to the coarse-grained process. With access to these kinetic and thermodynamic quantities, we study trade-offs between accuracy, speed and the thermodynamic cost of copolymerisation systems, and define the efficiency with which work is converted to accuracy of the copolymer. Interesting properties of these copolymerisation systems emerge from this analysis. For example, there exists a minimum driving required to create copolymers; below this driving the copolymerisation process stalls. For some systems, this stall point corresponds to equilibrium; in general, however, the stall point need not be at equilibrium. This stall point cannot be accessed directly by simulation, as simulation time diverges at this point, but can be analysed straight-forwardly within our framework. Finally, we demonstrate the power of our method by analysing a family of previously intractable Hopfield-style kinetic proofreading mechanisms embedded in a copolymerisation process, and show that our method particularly excels when analysing reaction networks with recursive structures.



References

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