# Cocrystal formation and crystal polymorph selection by patchy particles

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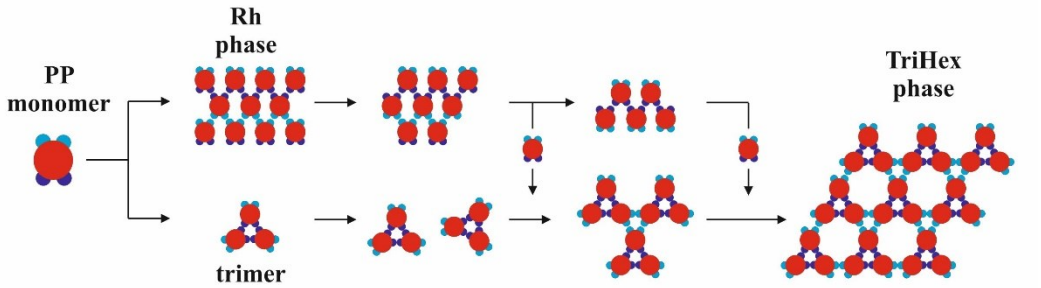
Both crystal polymorph selection and cocrystal formation are processes of particular interest to the pharmaceutical industry, proteins and colloidal crystals. To mimic the molecular scale processes of polymorph selection and cocrystal formation, we use 2D Monte Carlo simulations and a computational model with short-range attraction for "protein-like" patchy particles (PPs) of a specific patch geometry, bond width and bond strength. The polymorph selection is established in a narrow temperature range where part of PPs monomers arrange initially in a rapidly growing unstable rhombohedral lattice (Rh). Stable trimers form simultaneously from the monomers remaining in the solution and monomers released from the Rh lattice. These trimers serve as building blocks of a more stable Kagome trihexagonal lattice (TriHex), appearing after a prolonged simulation time [1]. Slight "modification" in the patch geometry is used to introduce two types of PPs, which are able to form two-component cocrystal. The final cocrystal Kagome like structure is preceded by formation of two types of trimers involving strong bonds only, or mixed trimers of strong and weak bonds. The mixed trimers serve as building blocks for the finally generated Kagome patchy cocrystal [2]. The step-by step process governing the polymorph selection and cocrystal formation is discussed in details, concerning the temperature interval, concentrations of PPs, the specific patch geometry and patch anisotropy as well.




Schematic representation of the polymorph selection: from monomers to coexistence of metastable Rh phase and trimers and final stable TriHex phase.

**References**

[1] Ranguelov B and Nanev Ch. 2D monte carlo simulation of patchy particles association and protein crystal polymorph selection. Crystals. 2019; 9 (10), art. no. 508.
[2] Ranguelov B and Nanev Ch. 2D Monte Carlo Simulation of Cocrystal Formation Using Patchy Particles. Crystals. 2022; 12 (10), art. no. 1457.