КАТЕДРА МЕТЕОРОЛОГИЯ И ГЕОФИЗИКА
ФИЗИЧЕСКИ ФАКУЛТЕТ - СУ "Св. Кл. Охридски"

Семинар „Кръстанов"

В четвъртък, 24.06.2021, 16:15 ч., онлайн

Проф. Петър Векилов
Houston University

ще изнесе доклад (на български) на тема:

Hematin Crystallization Mechanisms Illuminate the Fight against Malaria

Резюме: Crystallization is the central process of materials synthesis in biological, geological, and extraterrestrial systems. Nature achieves remarkable diversity of shapes, patterns, compositions, and functions of the arising crystalline structures by combining simple strategies to control the number of nucleated crystals and their anisotropic rates of growth. To promote or inhibit crystallization in both natural and engineered environments, soluble foreign compounds are deployed that interact with the solute or the crystal-solution interface. In many cases, two or more modifiers operate in tandem to alter processes of crystallization, yet the fundamental modes of cooperative action are not well understood, mostly because laboratory efforts have focused on crystallization of pure solutes and the effects of single growth modifiers. We examined the molecular mechanisms employed by pairs of inhibitors in blocking the crystallization of hematin. Hematin is a toxic byproduct of hemoglobin digestion in malaria parasites and suppression of its sequestration into inert hemozoin crystals is a favored approach to parasite elimination. Two or more hematin crystallization blockers have been combined in state-of-the-art antimalarial regimens and extensive efforts have failed to deliver molecular-level understanding of the synergy or antagonism between the partner drugs. We demonstrate that drug pairs, whose constituents employ distinct mechanisms of hematin growth inhibition, kink blocking and step pinning, exhibit both synergistic and antagonistic cooperativity depending on the inhibitor combination and applied concentrations. Whereas synergism between two crystal growth modifiers is expected, the antagonistic cooperativity defies current crystal growth models. We demonstrate that kink blockers reduce the line tension of step edges, which facilitates both the nucleation of new crystal layers and step propagation through the gates created by step-pinners. The molecular viewpoint on cooperativity between crystallization modifiers provides guidance on the pairing of modifiers in the synthesis of crystalline materials. The proposed mechanisms suggest strategies to understand and control crystallization in natural and engineered systems, which occurs in complex multicomponent media. In a broader context, our results highlight the complexity of crystal-modifier interactions mediated by the structures and dynamics of the crystal interface.

Nature 577, 497 (2020); J. Biol. Chem. 296, 100123 (2021); PRL 119, 198101 (2017); PNAS 114, 7531 (2017); PNAS 112, 4946 (2015).

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