

Self-Assembly of Functional Metabolites and Metabolite Derivatives into Supramolecular Architectures with Unique physicochemical Properties

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Abstract

Metabolites are essential for the normal operation of cells and fulfill various physiological functions. It was recently found that within several metabolic disorders, the associated metabolites can self-assemble to generate amyloid-like structures, similar to canonical protein amyloids that have a role in neurodegenerative disorders. Yet, protein assemblies with typical amyloid characteristics are also known to have physiological functions. In addition, many non-natural proteins and peptides presenting amyloidal properties have been used for the fabrication of functional nanomaterials. Similarly, functional metabolite assemblies are also found in nature, demonstrating various physiological roles. A notable example is the structural color formed by guanine crystals or fluorescent crystals in feline eyes responsible for enhanced night vision. Moreover, some metabolites have been used for the in vitro fabrication of functional materials, such as glycine crystals presenting remarkable piezoelectric properties or indigo films used to assemble organic semiconductive electronic devices.

Following these studies, we aimed to explore the ability of different metabolites and derivatives to self-assemble into ordered functional structures and examine their physicochemical properties. Specifically, we were interested in nucleobases and nucleobase-containing molecules as supramolecular motifs. This interest is supported by previous studies showing the ability of nucleobases containing molecules to self-assemble into functional supramolecular structures with unique features such as intrinsic fluorescence, structural coloration and more. We believe that this study is not only important in order to understand the role of these metabolites in normal physiology and pathology, but also paves a new route in exploring the fabrication of organic, bio-compatible, functional materials .

To achieve these goals, we began by identifying a library of nucleobases and exploring their physicochemical properties. We were able to show that nucleobase

crystals demonstrate intrinsic fluorescence in the visible range and that fluorescence spectra are excitation-emission dependent. Importantly, we demonstrated that intrinsic fluorescence is associated with the formation of a supramolecular fluorophore. These observations are uncommon in the field of organic supramolecular materials and could have implications in fields such as therapeutics of metabolic disorders and materials science.

Alongside the study of intrinsic fluorescence of nucleobase crystals, we have studied riboflavin, vitamin B₂, the reflecting material in the eyes of animals such as cats and lemurs which is responsible for their enhanced night vision. Our study aimed to explore the crystallization of riboflavin to understand its structural-property relationships. We discovered two different crystal structures (solvate and non-solvate) that were solved in different methods, single-crystal X-ray diffraction and Powder X-ray diffraction (PXRD) analysis. Next, we explored the physical properties of these bio-inspired crystals. We found that riboflavin solvate crystals present structural flexibility and can twist and bend depending on the surface they are deposited on. This observation led us to investigate their electromechanical properties. Combining experimental and theoretical approach we were able to rationalize this unique behavior. In addition, we explored the optical properties of riboflavin non-solvated crystals. Giving its biological role as a reflecting material we examined the refractive index of the crystals. For this purpose, we applied experimental and computational methods. The values for the refractive index of riboflavin were not as high as other reported biomolecules found in optically active systems in animals such as guanine and isoxanthopterin. This was explained by the close examination of the crystal packing and hydrogen bond motifs.

Lastly, co-assembly provides a promising approach to further expand structural and functional complexity in supramolecular materials. By using our knowledge regarding the self-assembly of riboflavin and nucleobases, we demonstrated that co-assembly of riboflavin and nucleobase 2,6-diaminopurine results in urchin-like structures with superhydrophilic nature. This is in contrast with their monomeric counterparts. This superwetting behavior is associated with both the surface hydrophilic groups and the nano-scale roughness of the urchin-like structure,

highlighting again the importance of co-assembly in generating diverse functionality in supramolecular structures.

Overall, these insights advance metabolite-based material design by understanding electronic, mechanical, and chemical properties and structure-function relationships, bridging the gap between synthetic and natural materials for advancements in nanotechnology applications and beyond.