<u>Research summary –functional metabolite assemblies</u>

Metabolites are essential for the normal operation of cells and fulfill various physiological functions.[1-3] It was recently found that in 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.[4,5] Yet, 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.[6-8] Similarly, functional metabolite assemblies are also found in nature, demonstrating various physiological roles. Moreover, some metabolites have been used for the *in vitro* fabrication of functional materials in the file nanotecnology.[9]

Supramolecular architectures or aggregates of metabolite assemblies such as nucleobases adenine and uracil were reported to have amyloid-like properties and play a key role in metabolic disorders. But nucleobases such as guanine and other metabolites like pteridines and small vitamins are also frequently found in photonic structures in biological systems. Therefor the main objective of my research is to explore the ability of these metabolites, to self-assemble into ordered structures and examine their physicochemical properties with the emphasis of their optical properties. We believe that this is not only important in order to understand their role in normal physiology and pathology, but also paves a new route in exploring the fabrication of organic, bio-compatible materials.

In my research, I have presented a library of nucleobases and explored their physiochemical properties. I have demonstrated the ability of nucleobases building blocks to self - assemble into ordered architectures. The optical properties of the characterized nucleobases assemblies are especially intriguing. Specifically, the excitation-dependent emission is unique for such organic supramolecular materials. The wide spectral range of some nucleobases may be useful for the fabrication of organic optical devices. These findings can also be applied to understand and maybe manipulate the self-association and aggregation of nucleobases metabolites in human diseases. Next, we explored other metabolites with potential to be implemented in bio-inspired self-assembly. We have identified riboflavin, vitamin B2, which is known to be the reflecting material in eyes of animal such as cats and lemurs, as a metabolite able to self-assemble under different conditions giving rise to different morphologies. We were able to form ordered single crystals and solve the crystal structure which was never reported before. We have also began to explore the optical properties of the crystal and are aiming to construct a retro-reflecting device from these structures as well as try to enrich the properties using the co-assembly approach. Lastly, we began exploring the self-assembly of xanthopterin. This metabolite belong to the pteridine family and was reported to act as a light-harvesting molecule that transform light into electrical energy. This May explain the insects increased activity when light intensity is greater. We are currently interested in finding a relationship between the structure of the assemblies of xanthopterin and their function by extracting the pigment from the animal and studying its physicochemical properties. This may lead us to be able to fabricate a bio-inspired solar cell.

To conclude, self-assembly of metabolites presents a new avenue in the construction of biological and bioinspired materials. Although metabolites are often overlooked as building blocks for self-assembly processes, their versatile physical properties, inherent biocompatibility, biodegradability, and low costs make them promising candidates for diverse applications, from the fabrication of optical materials to high-performance electronics. Moreover, basic research of the complex architectures spontaneously generated by various metabolites, both in health and disease, can lead to more profound understanding of their diversified roles, as well as to the development of novel therapeutics for numerous metabolic disorders.

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