Calixarene-based ratiometric array for the sensing of polycationic peptides in solution and in artificial membranes

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Supramolecular chemistry has shown great potential for the development of new assays in biological applications, from sensing to actuators and drug delivery agents, by taking advantage of their easier synthesis processes, self-assembly and stimuli-responsive properties associated with the non-covalent linkage prevalent in these systems. These properties are an advantage for sensing applications due to the reversible nature of non-covalent interactions, allowing for detection of fluctuations in a biological system. Macrocycles are an example of a class of molecules that are often used as receptor moieties in sensors due to their inherent affinity towards relevant biological targets and, in some cases, their ease of functionalization to design novel specificity.

Two projects will be the focus of this presentation. The first consists of the design of a calixarene sensor family, monofunctionalized with variable length aliphatic linkers, connecting the receptor moiety with a pyrene reporter. Application of this family of sensors in an aggregation-based array sensing assay has been successful with the ability to distinguish oligoarginines with two to eight arginine residues. The second project aimed at the development of a heteroternary host:guest:host complex applied in a dual displacement assay for the orthogonal sensing of two different analytes. This takes advantage of the cooperative binding found between Cucurbit[7]uril (CB7) and Stoddart's Blue Box (BB) in the presence of a guest that allows their alignment. Using a family of dyes know to bind to CB7, it was found that BB binds to the CB7:dye complex with μM affinity instead of the mM affinity it usually bind to the individual components. A dual displacement assay was successfully developed for the detection of naproxene and the peptide Phe-Gly-Gly, leading to respectively turn-on and turn-off fluorescence signals, for the distinct binding events.