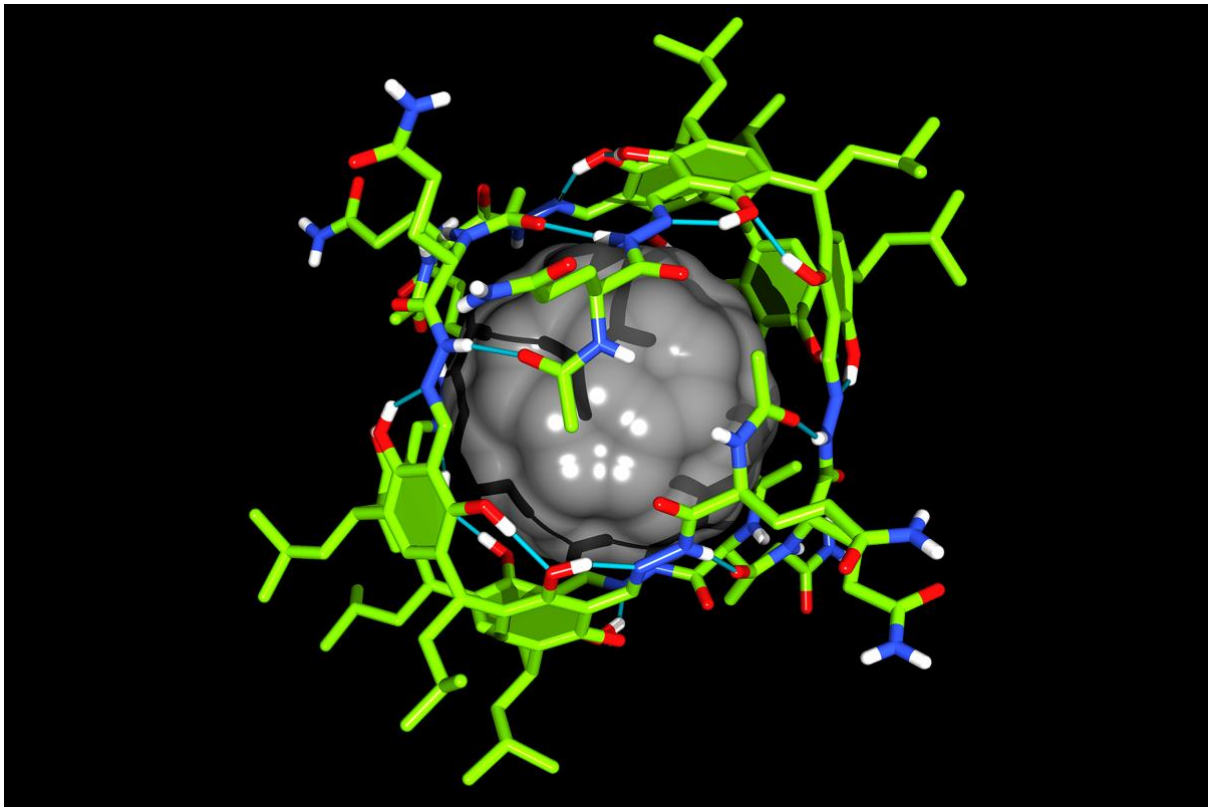
To assemble or not to assemble...



Motivation behind the research

Our research focuses on creation of capsules of the nanometer-size that feature a set of useful properties including porosity, chirality, biocompatibility, dynamic character, functionality and stability in very highly competitive environments (water and polar solvents). Such capsules are promising candidates as drug delivery containers or as highly specific nanoreactors for asymmetric reactions. However, their assembly presents a substantial challenge, mainly because some of the desired features are contradictory, for example dynamic character and simultaneously high stability. Therefore, synthesis of such systems requires a precise balance of numerous covalent and non-covalent forces between all interacting molecules, including also surrounding solvent molecules. In our work we aim at balancing of hydrogen bonding and hydrophobic interactions so that we can assemble capsules that are stable yet dynamic in polar environment.

The Discovery

We take an inspiration from a protein world and use peptides and their very precise binding motifs for self-assembly of functional, chiral and biocompatible capsules in relatively non-competitive solvents. However, we have found that, as the polarity of environment increases, such binding motifs alone are not sufficient for effective self-assembly. Therefore, we have employed additional forces - hydrophobic interactions - that are not so precise but provide a required strength. Together, these forces enabled us to produce chiral, biomolecule-based capsules that are stable in polar environment yet, due to their non-covalent structure they remain dynamic.

Being more specific: we started with an attachment of hydrophilic amino acids, histidine and glutamine, to a vase-shaped macrocycle (resorcin[4]arene) resulting in formation of a hemisphere-shaped cavitands. Despite the presence of numerous hydrogen-bonding sites, these cavitands do not self-assemble into capsules in polar environment (dimethyl sulfoxide, methanol). However, when their synthesis is performed in the presence of fullerene, the cavitands wrap around this hydrophobic template and form dimeric non-covalent capsules. What is important, the templated capsules are precisely arranged by means of hydrogen-bonding motifs in a very competitive environment. These hydrogen bonding motifs are not effective alone, but with additional hydrophobic stabilization by fullerene they become very effective even in polar solvents. All the species, assembled or not, have been thoroughly characterized by means of NMR (nuclear magnetic resonance), MS (mass spectrometry) and CD (circular dichroism). Summing up, our studies have shown that a combination of the more precise but weak interaction (hydrogen bonding) with the less precise but stronger interaction (hydrophobic effect) allows for stabilization of ordered molecular capsules (and probably many more species of this type) in very demanding environments.

Study Limitations:

Aqueous environment is a default for biologists, but it is a kind of 'Holy Grail' for supramolecular chemists. The limitation of the current design so far is that our templated capsules don't dissolve in water. So, we are not there yet, but…

The Future

… our initial results with macrocycles that are more hydrophilic indicate that analogous approach is also effective in water. So, we are almost there…

Research Article: The templation effect as a driving force for the self-assembly of hydrogen-bonded peptidic capsules in competitive media, Org. Biomol. Chem., 2017.