Mimicking biological chirality process

Background

Chirality is one of the most fascinating natural phenomena, leading to a specific handedness of biological structures, and directing the biochemistry to choose a specific homochirality in life processes. Nature is able to mysteriously translate molecular chirality into selective left- or right-handed homochirality at various structural levels of organisms. Tobacco mosaic virus (TMV) provides an exquisite example of chiral self-assembly in natural systems. In TMV the whole virion is a right-handed nucleoprotein helix, composed of a single type of protein subunits closely packed in a regular helical capsid, interpenetrated by a strand of RNA. A remarkable feature of this self-assembled TMV is the ability of the virus to destabilize the capsid structure once inside the host cell, and release the genetic material for subsequent infection. Anionic amino acids, in particular, multiple glutamate (Glu) residues play an important role in disrupting the chirality of the TMV capsid superstructure.

Problems/Issues

Several attempts have been made to design chiral chemical architectures with an effort to mimic the function and geometry of complex biological systems using molecular self-assembly. However, none of these systems has been able to mimic the inherent complexity of even the simplest biological organisms, such as TMV inherent dynamic nature of non-covalent interactions, accompanied with their susceptibility to manipulation using physical and chemical stimuli may offer an idealistic avenue to mimic the complexity of chirality-directed biological self-assembly.

Mimicking natural phenomenon with small organic molecule

Herein, we report for the first time synthesis of naphthalenediimide appended L-glutamate (part of TMV) i.e. NDI-L-Glu that self-assembles into chiral supramolecular structures. Specifically, NDI-L-Glu shows a mixture of left- and right-handed helices under physiological conditions, and any deviation from the ambient biochemical environment has a remarkable influence on the chirality of these structures. For instance, acidic environments shift the helicity to left-handedness while the alkaline conditions reversed the helical structures to right-handedness, thereby mimicking the molecular virulence mechanism of tobacco mosaic virus (TMV). The chirality of these supramolecular assemblies can also be controllably tuned by using temperature as an external stimulus, allowing reversible flip of helicity.

Another well-known example in the human body is **sickle cell anaemia** that is caused by the replacement of glutamate with valine in the β-globin chain of haemoglobin, leading to protein aggregation. As such, our current work demonstrates that akin to the biological systems, the **NDI-L-Glu** complex is not only able to self-assemble into chiral supramolecular helices under physiological conditions; but also the deviation from the physiological environment leads to reversible chiral transformation in the supramolecular superstructures.

Conclusion

The supramolecular system studied here offers for the first time not only the more in-depth experimental understanding of chirality, but also provides a unique way to control the helical assemblies by changing the pH and temperature stimuli. In addition, the present system offers a new and simple approach to the design of new chiral supramolecular polymers, which can provide a good illustration of chirality control with right and left handed preference by either controlling pH or temperature.

Future benefits of the system

These tunable chiral assemblies may find applications in challenging areas, such as, purifying racemic mixtures of commercially important drugs, detecting subtle changes in the spatio-temporatal configuration of biomolecules during disease progression, obtaining more in-depth mechanistic understanding of host-pathogen interactions, and engineering environmentally-responsive macroscopic chiral objects. These new findings will have high impact to a wide range of disciplines across supramolecular chemistry, chirality, biochemistry, molecular pathogenesis, nanomedicine, and engineering.