PhD in Chemical Sciences

Advanced Course

Chirality and Chiral discrimination

The course is dedicated to the understanding of the concepts and consequences of molecular chirality and to illustrate some of the most advanced topics in this area, including several important applications at the industrial level, in biological as well as material chemistry research, and in organic synthesis.

Bibliographic material and references for further study of these subjects will be provided.

The course is composed by 6 lectures of 2-hour time, distributed over two weeks, for a total of 12 hours, corresponding to 1.5 CFU. Students will get credits according to their attendance to the lectures and a score based on a final exam.

The lecture titles and contents are:

1-Life, the Universe and… Chirality.

Chirality can be defined in several ways depending on the context in which this term is used; some definitions will be given, including topological chirality and 'true and false chirality' as proposed by L.Barron. Chirality has many implications in understanding the fundamentals of matter composition and of origin of life. These will be described and consequences of chirality in living systems and thus in drug development will be discussed.

2-Chiral separations

Methodologies used in the lab and in the industrial sector for the separation of chiral molecules will be described. Crystallization procedures and strategies, and enzymatic processes will be first considered. The principles of chiral chromatography techniques and the most used chiral stationary phases for GC and HPLC and CE will be presented.

3-Chiral analysis by non-chromatographic methods

Non-chromatographic methods for rapid screening of enantiomeric excess will be discussed, in particular with MS and spectroscopic methods using 'pseudoenantiomers', and chiral molecular sensors will be highlighted.

4-The quest for absolute asymmetric synthesis

Highly efficient enantioselective syntheses are nowadays available and are presented as an introduction. Principles enabling absolute asymmetric synthesis using only achiral reagents and external biases will be discussed and linked to the possible origin of biological homochirality. Non-linearity in chiral catalysis will be introduced, as a method for amplification of chirality. The Kagan model will be presented and examples from the literature will be discussed. Self-catalytic non-linear reactions will be discussed in details, in particular the Soai reaction and similar ones.

5-Chirality in supramolecular systems

The possibility to use non-covalent interactions to generate chirality from achiral objects is a very interesting approach, which has been utilized to generate supramolecular chiral architectures from tiny amounts of chiral molecules or dopants. The consequences of this approach in polymer and material chemistry will be analyzed, with several examples, in particular in the fields of molecular-motors and nanofabrication.

6- Chirality in biomolecular systems

Biomolecular objects exploit the same supramolecular interactions and are therefore subjected to similar behavior: this will be illustrated by examples concerning biomimetic macromolecules. Finally, the effect of chirality in the interaction of synthetic products with bio-macromolecules, in particular with DNA, and consequences in molecular biology and biotechnology will be discussed. Models mimicking the origin of Biological chirality will be discussed.

The lectures will be held by Prof. Roberto Corradini, and are based on his experience in the field of chirality, in particular of chiral discrimination using chromatographic techniques, development of enantioselective sensors, and study of the role of chirality in DNA binding, which is testified by several peer-reviewed papers in international journals on this subject (listed below) and which has been awarded with the 2015 research prize for 'Organic Chemistry in its aspects of structural determination and molecular interactions" by the Division of organic Chemistry of the Italian Chemical Society. RC has also been in the Organizing Committee and scientific manager of the17-Symposium on Chirality ISCD-17, Parma, September 2005, and has been member of the Editorial Board of the Journal *Chirality (Wiley-VCH)* in the years 2010 - 2015.

RC has published a total of 148 articles in international peer-reviewed papers, and 14 book chapters in internationally distributed books. He has been invited in many international symposia, including 3 dedicated to chirality, and one dedicated to drug development.

List of lecturer's relevant publications on the subject:

General reviews.

Topics in Current Chemistry **2011**. 300: 175–216; *Curr. Topics Med. Chem.,* **2007**, *7*, 681-694; *Chirality*, **2007**, *19*, **269-294;**

Research Papers.

Sci Rep. **2017**, *7*, 42799; *Supramolecular Chem* **2017**; *29*, 784-795; *Org. Lett.* **2016**, 18, 5452-5455; *Chirality*, **2015,** *27*, 864-874; *ChemBiochem* **2012**, *13*, 1327 – 1337; *Chirality* **2010** , 22, E161-E172; *Macromolecules* **2010***, 43, 2692–270; Chirality*. **2009,** *21,* 245-253; *Nucleic Acid Res.* **2008***, 36,* 1464-1471; *J Incl Phenom Macrocycl Chem* **2007,** *57*, 625-630; *J Mater Chem* **2005**, *15*, 2741-2746; *Chem Eur J* , **2004**, *10*, 2749-2758.; *J. Mol. Rec.* **2004** *17*, 76-84; *Tetrahedron Asymm* , **2002**, *13*, 1629-1636

Book chapers.

(2014) Chiral PNAs with constrained open-chain backbones in : “Peptide Nucleic Acids: Methods and Protocols, Second Edition” P. E. Nielsen and D. H. Appella Editors, Humana Press, 2014, Chapter 3 pages 19-35; Electronic Circular Dichroism of Peptide Nucleic acids and their analogues in “Advances in Chiroptical Methods” (Editors: Nina Berova, Prasad Polavarapu, Koji Nakanishi, and Robert W. Woody) Volume 2. Chapter 2.IV.5, John Wiley and Sons Inc, (United States). Pages 587-614; Control of Helical Handedness in DNA and PNA Nanostructures, in, “DNA Nanotechnology: Methods and Protocols” Giampaolo Zuccheri and Bruno Samorì (eds.), Methods in Molecular Biology, vol. 749, DOI 10.1007/978-1-61779-142-0_6, Springer Science+Business Media; Enantioselective Separation of Amino Acids and Hydroxy Acids by Ligand Exchange with Copper(II) Complexes in HPLC (Chiral Eluent) and Fast Sensing Systems. In: SUBRAMANIAN G. Chiral Separation Techniques. (pp. 301-331).