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| **Title** | **Network Reactivity Dictated by Confined Size Selectivity (CONFINET)** |
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| # months (min.3) | 3 |

**Project description (2 page max):**

**State of the art**. One of the key chemistry challenges in the 21st century is to master chemical reactivity molecular network events. Great inspiration comes from reactions occurring in biological systems where high reactivity is often accompanied with sequence-derived reactions governed by an extraordinary level of substrate selectivity. These features have sparked interest in the engineering of artificial supramolecular structures able to mimic these functions. In particular, the compartmentalization within cavities typical of enzymes has been the source of inspiration to build-up tailored environments wherein reactions can proceed isolated from others in bulk solution and to be able to select molecules based not only on their functions but also in their molecular size. These discrete nanospaces offer the possibility to gain control over the reactivity by virtue of substrate pre-organisation, higher relative concentrations of the reactants, and stabilisation of the transition states. Since the pioneering works on carcerands, supramolecular confined systems have led to many interesting applications, such as separation, chemical sensing, drug delivery and signal transduction. However, the main playground arena for confined nanospaces has been catalysis. Beside the variety of reactions which have been reported, noteworthy are the numerous examples regarding the utilization of well-defined nano-spaces to engender new transformations and generate molecules otherwise difficult to obtain. In this context, while ionic and pericyclic reactivities have been largely investigated, the perform sequence of reactions dictated by the molecular size has not been reported. However, this type of network reactivity has nowadays all the possibilities to be investigated and performed with the aim to better understand reactivity of complex systems and to obtain novel types of selectivity.

Within this context, the proponent has in recent years developed a large variety of molecular confined environments, which have been prepared and used for molecular recognition.[1] More recently, in collaboration with the co-proponent, who has strong expertise in electrochemically mediated atom transfer radical polymerization,[2] preliminary unpublished studies have shown the capability of these systems to furnish catalyzed polymerization dictated by molecular size.

**Objectives**: The main objective of CONFINET is to tame network reactivity of a series of molecular cages able to catalyze carbon centered radicals. This will be performed exploiting molecular size selectivity of the recently reported nanospaces. To this end, the project will generate essential new knowledge, novel tools and data to fill the gaps between two of the forefront chemical research areas: confinement, complex network reactivity and radical chemistry. Main objectives are: i) to develop a series of cage catalytic system able to perform in sequence (stereo)-selective radical reactions taking advantage of confinement. We expect also synergistic effects in terms of: TOF, product selectivity, atom efficiency and catalyst stability compared to traditional approaches; ii) to reveal potential and limitations in the exploitation of active metal sites embedded in a confined space synergically exploiting the recognition properties peculiar of nanospaces and iii) to link together the knowledge present in electrochemical and photochemical catalysis, supramolecular chemistry, synthesis and theoretical chemistry to tackle a problem of paramount importance. These results will be obtained: preparing novel (chiral) containers exploiting them in combined radical reactivities activated electrochemically: atom transfer radical polymerisation (e-ATRP) and atom transfer radical addition and cyclisation (ATRA and ATRC).

**Methods** CONFINET is planned for a duration of 3 years and the work plan has been organized combining the possibility to prepare a large variety of chiral catalytic confined structures of increasing size which can be alternatively and iteratively tested in different types of combined reactivities. CONFINET synthetic plan will be divided in three stages according to the complexity of the investigated structures which will be in the order: i) sample reference complexes to test the reactivity, ii) single cages reactivity, iii) combined cage differing in size reactivity iv) combined different metal/size cages reactivity. Molecular architectures design and preparation will be iterative allowing the project to test continuously the catalytic performances. Cyclisation and Polymerisation reactivities will be the mainly investigated reactivities.



**Figure 1**. Example of combined cage/metal size driven reactivity.

**References**

[1] C. Bravin, E. Badetti, F. A. Scaramuzzo, G. Licini, C. Zonta *J. Am. Chem. Soc*. **2017**, *139*, 6456. C. Bravin, E. Badetti, R. Puttreddy, F. Pan, K. Rissanen, G. Licini, C. Zonta *Chem. Eur. J.* **2018**, *24*, 2936. C. Bravin, G. Licini, C. A. Hunter, C. Zonta *Chem. Sci.* **2019**, *10*, 1466. C. Bravin, A. Guidetti, G. Licini, C. Zonta *Chem. Sci*. **2019**, *10*, 3523. C. Bravin, G. Mason, G. Licini, C. Zonta *J. Am. Chem. Soc*. **2019**, *141*, 30, 1196. F. Begato, G. Licini, C. Zonta *Angew. Chem. Int. Ed.* **2023**, e202311153. F. Begato, R. Penasa, K. Wurst, G. Licini, C. Zonta *Angew. Chem. Int. Ed.* **2023**, e202304490.

[2] M. Fantin, A. A. Isse, A. Venzo, A. Gennaro, K. Matyjaszewski *J. Am. Chem. Soc*. **2016**, *138*, 7216. P. Chmielarz, M. Fantin, S. Park, A. A. Isse, A. Gennaro, A. J. D. Magenau, A. Sobkowiak, K. Matyjaszewski *Prog. Polym. Sci.* **2017**, *69*, 47.