The living as reaction media: towards the development of bio-specific and chemo-switchable therapeutic agents.

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The development of chemical reactions that are compatible with biological media has attracted increasing attention over the past decade. These reactions, qualified as bio-orthogonal when they can take place in a complex biological medium without distorting it, or as bio-specific when they touch only a precise part of it, opened the door to new methods of exploring complex phenomenon. Progress in controlling these bio-functional reactions quickly helped to increase the significance of the studies from *in vitro* model to cellular environments and finally to living organisms. Further integration of such chemistry driven endeavor to therapeutic approaches contributed to the birth of chemical-biology.
Taking advantage of imaging and bio-analytic methods we have developed original chemometric methodologies to figure the bio-response profile of bond-forming and bond-breaking chemical reactions.
By applying this methodology, we were able to characterize novel functional groups that exhibit a clean activation profile but also to uncover unexpected bio-specificity. We will focus on recent results obtained on functional groups that undergo cleavage in response to biothiols or bioacidity miss regulation.
As part of the study to be presented we will also show that it is possible, through a bio-orthogonal reaction, to alter the molecular structure of a drug after its administration in live animal. This strategy allowed to switch a compound from a bioactive state to a bio-inert state and concomitantly to switch from a long circulating to a fast excretion compound. This case-study illustrates the need of integrating into the periphery of chemistry a variety of knowledge and technologies from different research area i.e. analytical chemistry, medicinal chemistry, pharmacology, metabolomics, cell biology, development of animal models.