Multivalent probes as a versatile tool for efficient, selective and tunable supramolecular assembly

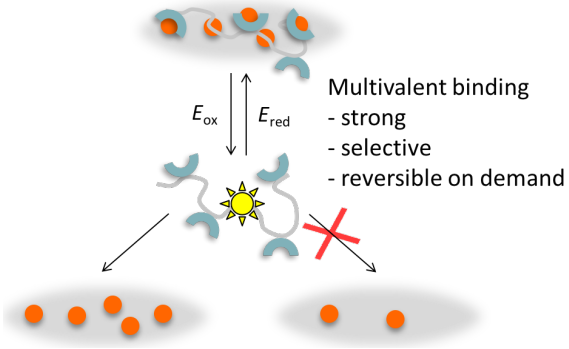
G.V. Dubacheva[1,2,5*], T. Curk[3], R. Auzély[4], L. Guerente[5], P. Labbé[5], D. Frenkel[3], R.P. Richter[2,5]

[1]*PPSM, CNRS, ENS Cachan - Université Paris-Saclay, France*
[2]*CIC biomaGUNE, San Sebastian, Spain*
[3]*Department of Chemistry, University of Cambridge, United Kingdom*
[4]*Centre de Recherches sur les Macromolécules Végétales, CNRS, Grenoble, France*
[5]*Département de Chimie Moléculaire, Université Grenoble Alpes, CNRS, Grenoble, France*

**galina.dubacheva@ens-cachan.fr*

The design of stable supramolecular assemblies, while tuning their selectivity and reversibility remains challenging. We demonstrate that this can be achieved using multivalent interactions, where ligands and receptors interact collectively [1-5]. While the multiple binding of ligand/receptor pairs provides high binding strength to the assembly, it can still be disassembled by breaking each ligand/receptor complex independently [1-3]. In addition, the efficiency of multivalent binding can be designed to sharply depend on the ligand/receptor density, enabling high targeting selectivity [4,5].

Several examples will be presented. First, we show that self-assemblies of polymers and proteins at functional interfaces can be switched on/off using redox-active β-cyclodextrin/ferrocene interactions [1-3]. Then, building upon β-cyclodextrin/guest chemistry, we develop well-defined and highly tunable model systems to study multivalent binding at interfaces, including naturally occurring cases (e.g. hyaluronan-cell binding) [4,5]. We demonstrate experimentally that multivalent probes can distinguish sharply surfaces with different receptor densities [4], and that this superselective behaviour can be adjusted to a desired range of receptor densities by tuning molecular characteristics of the probes (valency, affinity, etc.) [5]. The effect of lateral mobility of surface binding sites on multivalent binding will also be discussed.



Theoretical modelling and simulations support experimental results and point that superselectivity is indeed a consequence of multivalency.

Our approach lays the foundation for the new generation of analytical, diagnostic, and therapeutic probes. It should be instructive for the rational design of polymers and other types of multivalent scaffolds currently used in nanomedicine such as nanoparticles, nanocapsules and liposomes [6]. Moreover, the obtained insights enhance our understanding of naturally occurring multivalent interactions [7].

Acknowledgements The financial support of CNRS, Marie Curie Career Integration Grant ("CELLMULTIVINT" PCIG09-GA-2011-29380) and ANR (08-BLAN-0097 "E-DETACHPEM").

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