From All Atom to Coarse Grain: Molecular Dynamic Simulation of Imprinting Process on a Silica Xerogel

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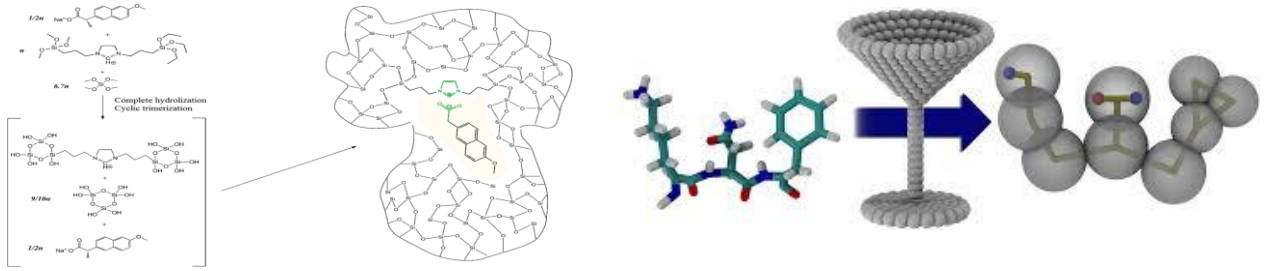
Abstract

Molecular imprinted polymers (MIP) are used in very different fields such as solid-phase extraction, enantiomer separations, drug delivery, drug discovery, and so on. Sol-gel polycondensation technique is one of the most promising approach since MIP produced with this technique has been proved to present several advantages such as physical robustness, long shelf life, simple preparation, great selectivity, etc. The most widely used precursors for preparing sol−gel materials have been silicon alkoxides, such as tetramethoxysilane (TMOS) or tetraethoxysilane (TEOS). Molecular Dynamics simulation of these systems are quite complexes and time expensive. Due to this, Martini Coarse Grain (CG) force field is an interesting approach that may be able to overcome limitation of classical approaches.

Introduction and Objectives

Molecular imprinting is an emerging technique inspired on natural molecular recognition, which allows the production of tailored recognition sites that will favourably interact with pre-determined compounds. In essence, the fabrication of molecularly imprinted materials starts with the interaction between the template and complementary functional monomers and continues with the polymerization of this conjugate with cross-linkers in an appropriate solvent (the porogen)[1]. Finally, the template molecule is removed from the matrix, leaving behind binding sites that fit the template molecule in size, shape and functionality. On the other hand, the Martini force field is a coarse-grain (CG) force field suited for molecular dynamics simulations of biomolecular systems [2]. The model uses a four-to-one mapping, i.e. on average four heavy atoms and associated hydrogens are represented by a single interaction center. The main aim of this study is to perform a molecular dynamic (MD) simulation of a complex system in order to study both, the imprinting effect of the Naproxen and the formation of the silica backbone.



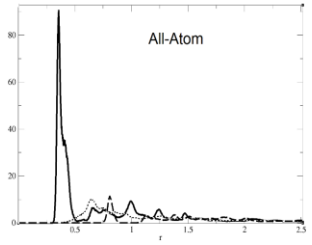
Methodology

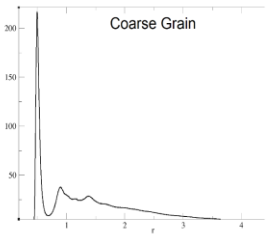
Molecular dynamics simulations were performed using Gromacs4 package. The simulation was performed for a period of 1μs using classical Martini mdp settings. Analysis of the results was performed using the tools included in the Gromacs package by means of RDF analysis.

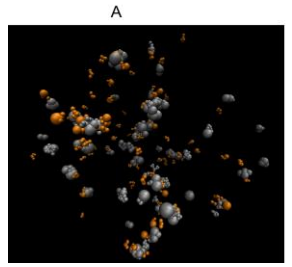
Results

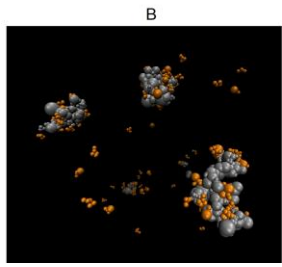
The main aim of this study was to start simulating the imprinting effect of the Naproxen (NAP) on a silica gel backbone (DHI). In addition, we also aimed at simulating the polycondensation effect typical of these polymers. We already simulated this system using an all-atom approach and thus, this study was aimed at parametrized this system using the Martini coarse-grain force field. Regarding the imprinting effect, preliminary results show that the NAP is strongly interacting with the DHI. This result is in line with the all-atom simulations and thus, may be used as a first confirmation that the system is working correctly. These results are reported on the **Figure 1**.

Finally, regarding the polycondensation effect, first analysis may suggest that this approach is suitable to simulate the growing of this kind of silica polymers. In fact, as reported in the Figure 2, we can how the backbone is growing during the simulation. In the Figure 2A we reported the initial state of the system, while on the Figure 2B we reported the final state of the system. It is straightforward how DHI monomers, reported in silver color, are highly associated at the end of the simulation, forming large aggregates. In addition, we reported also the NAP, in orange, in order to check the aggregation with the DHI.









References

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2. Marrink, S. J.; Risselada, H. J.; Yefimov, S.; Tieleman, D. P.; de Vries, A. H., The MARTINI Force Field: Coarse Grained Model for Biomolecular Simulations. The Journal of Physical Chemistry B 2007, 111 (27), 7812-7824