MOL2NET, International Conference Series on Multidisciplinary Sciences

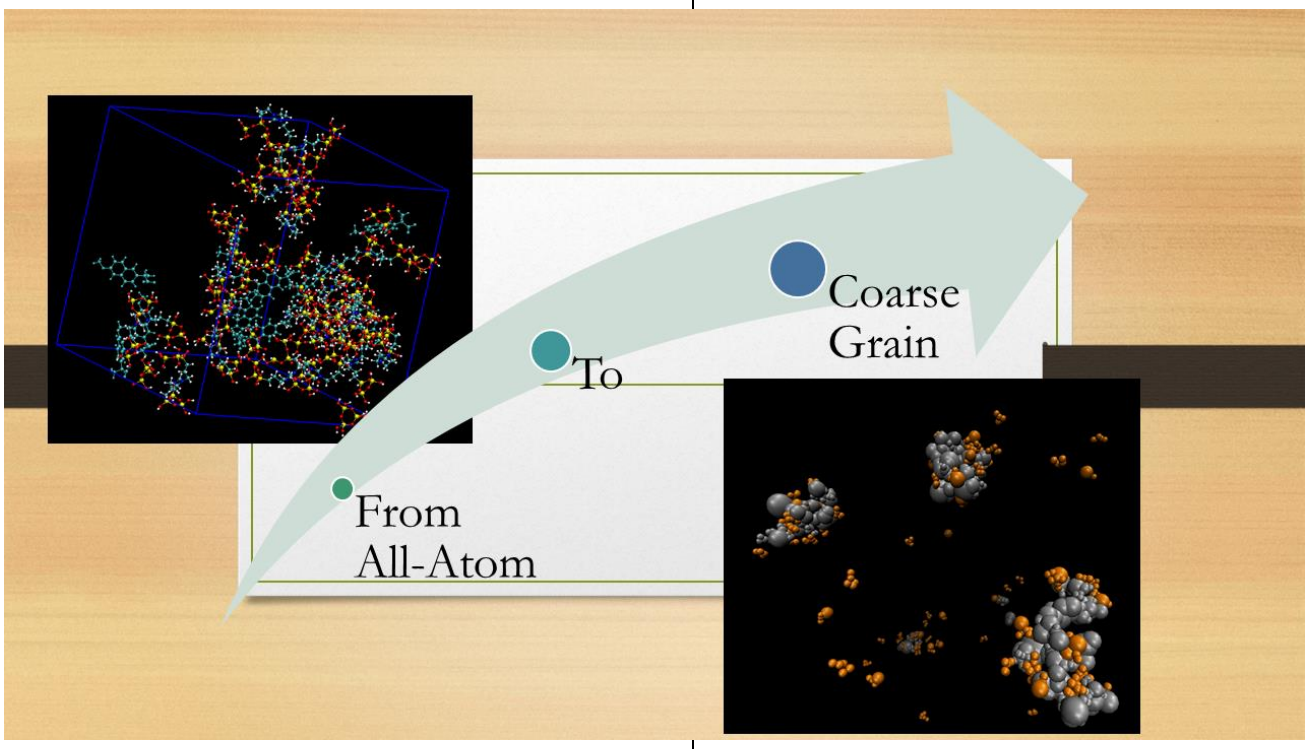
From All Atom to Coarse Grain: Molecular Dynamic Simulation of Imprinting Process on a Silica Xerogel

Riccardo Concu [a] *, *Maria Natalia Dias Soeiro Cordeiro* [a]

[a] *LAQV@REQUIMTE/Department of Chemistry and Biochemistry, Faculty of Sciences, University of Porto, 4169-007 Porto, Portugal*

.
.
.

Graphical Abstract



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. Due to this, different techniques have been investigated in the past few years. In this contest, sol-gel polycondensation technique is an interesting alternative 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). In a recent paper for the first time, we simulated a complex sol-gel system aimed at preparing the (S)-naproxen-imprinted xerogel with an explicit representation of all the ionic species at pH 9. With that simulation we were able to undercover the molecular mechanism behind the imprinting process. However, the simulation ran for only 100ns and we were unable to simulate other important process such as the polymer formation. One possible solution is to move on to a coarse-grain (CG) simulation based on the Martini force field. 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. One of the main advantages of this approach is that larger systems may be simulated for longer time. Due to this, the main aim of this study is the simulation of the molecular imprinting process using the Martini force field, in order to simulate all the relevant aspects occurring during the imprinting and polycondensation process.

Introduction

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). Finally, the template molecule is removed from the matrix, leaving behind binding sites that fit the template molecule in size, shape and functionality. These cavities are then capable to preferentially recognize and rebind the imprinted molecule. [1] One of the most promising way to produce molecular imprinted polymers is thorough the application of the sol-gel process. The latter can be described as follows: in an aqueous solution (in the presence of a co-solvent to prevent immiscibility) metal alkoxides (M-OR) are hydrolysed to produce M-OH groups, which will then go under condensation reactions to form a -M-O-M- network that is the foundation of the growing three-dimensional gel structure. Both base- or acid-catalysed hydrolysis and condensation reactions occur at the same time. During the time required for these reactions to take place the viscosity of the solution gradually increases, and when drying occurs at ambient conditions the resultant material is denominated xerogel. Books by Brinker and Scherer or Wright and Sommerdijk are recommended for further reading about the physical and chemical principles of sol-gel processing.[2] This process is usually times consuming and due to this its simulation is a challenging task.

On the other hand, the Martini force field is a coarse-grain (CG) force field suited for molecular dynamics simulations of biomolecular systems. 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. In order to keep the model simple, only four main types of interaction sites are defined: polar, non-polar, apolar, and charged. Each particle type has a number of subtypes, which allow for an accurate representation of the chemical nature of the underlying atomistic structure[3]. One of the biggest advantages of this approach is that allow very long simulations in a shorter period of time. In fact, it is reported that may speed-up simulations up to 10 times.

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.

.

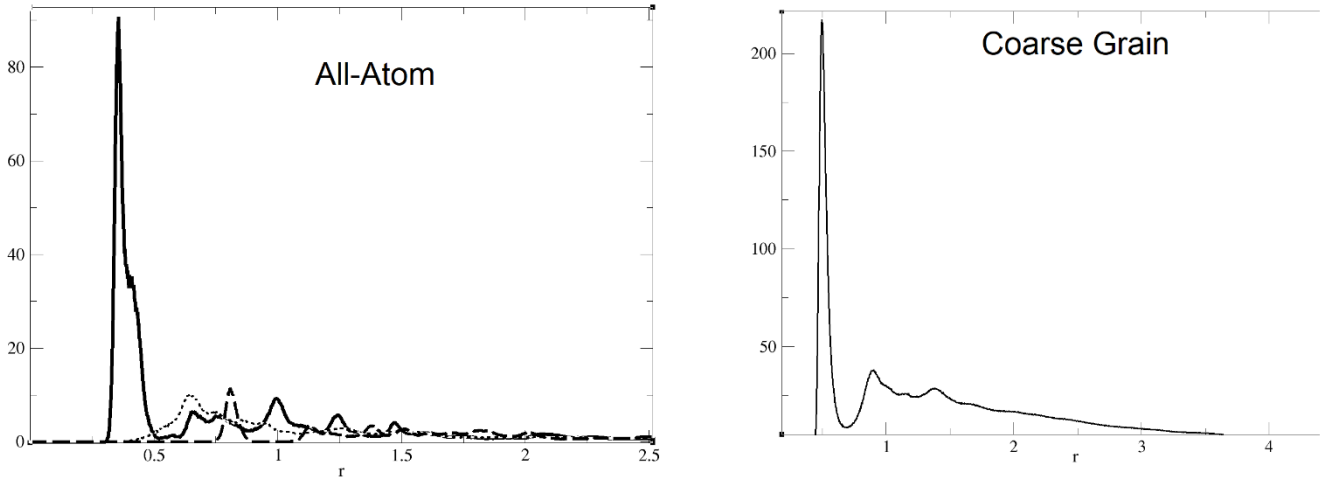
Materials and Methods

Molecular dynamics simulations were performed using Gromacs[4] 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[4] package by means of RDF analysis.

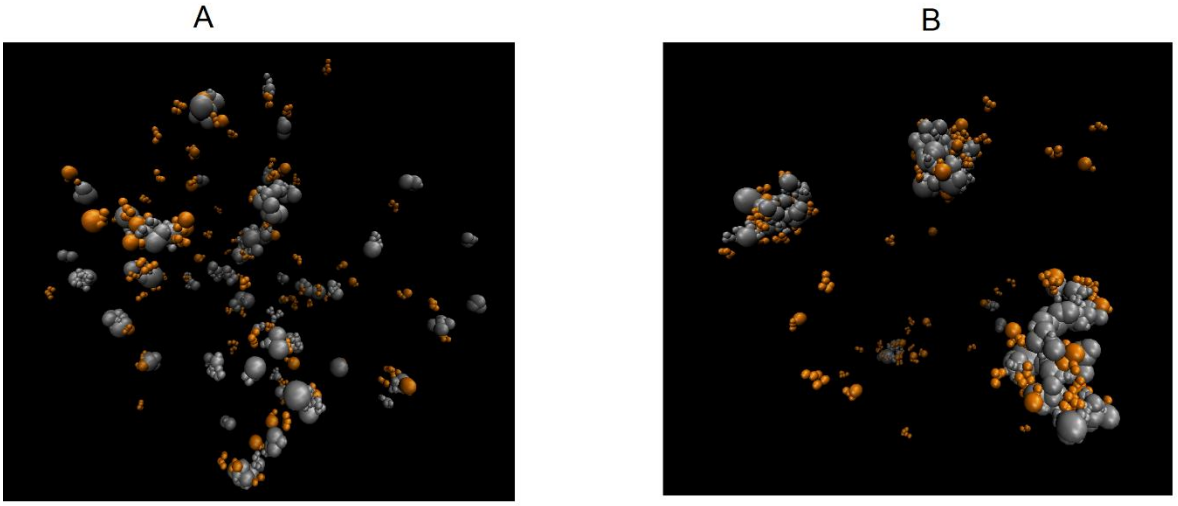
.

Results and Discussion

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.



.

Conclusions

This study was aimed at firstly check if the parametrization we did of the original all-atoms was correct. We checked the first results comparing the all-atom simulation with the Martini CG force field. Results suggest the parametrization was correctly performed and thus, confirming we may use this approach to simulate both, the imprinting effect and the silica backbone polycondensation

.

References

.

.

1. Zaidi, S. A., Molecular imprinting polymers and their composites: a promising material for diverse applications. *Biomaterials Science* **2017,** *5* (3), 388-402.

2. Concu, R.; Ornelas, M.; Azenha, M., Molecularly imprinted sol-gel materials for medical applications. *Curr Top Med Chem* **2015,** *15* (3), 199-222.
3. 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.
4. Berendsen, H. J. C.; van der Spoel, D.; van Drunen, R., GROMACS: A message-passing parallel molecular dynamics implementation. *Computer Physics Communications* **1995,** *91* (1), 43-56.