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Theoretical Study of Interactions between Drugs and Metal-Organic Frameworks

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Abstract: In the last two decades a new material class, now called Metal-Organic Framework (MOF), arose and rapidly became eligible for a wide range of applications, especially in fields related to gas selection and storing [1-3]. Beyond its great values of superficial area and pore volume, MOFs might have its chemical functionality modified, which make them a good alternative for drug delivering as well [4]. However there is none theoretical works that explore the reaction details between MOF, drug and the media in which these reactions occur. Thus the objective of the project is to study the interactions between the MOF Zeolitic Imidazolate Framework (ZIF-8), water and the pharmacological agents theophylline, caffeine and diprofylline, through Monte Carlo (MC) and Molecular Dynamics (MD) simulations. Understanding how systems composed by these substances behaves at the microscopic level may bring insights for interpretation of the experimental results already available.

Key-words: molecular simulation, metal-organic framework, drug delivery

Introduction: Metal-Organic Frameworks constitute a class of materials made by metallic nuclei linked by organic molecules, which forms crystalline structures with permanent porous. MOFs have many desirable features for fields related to porous media: large porous, great superficial areas, low density and thermal stability. Additionally, the uncountable combinations of ionic nucleus and organic ligand makes possible produce MOFs with properties commonly sought for biomedical applications such as high hydrothermal stability and low toxicity [5] . Such features can be used to make MOFs with pores able to store drugs and release them on controlled basis, or even for produce MOFs made of therapeutic compounds, which also can be disassembled in a controlled manner. Regarding the first possibility, MIL-100, MIL-101, MIL-53 and ZIF-8 are examples of MOFs that are stable on environments that simulates human physiology [6, 7].

Methodology: In order to develop low-cost processing methodologies for studying MOFs with potential for drug loader, this project has two milestones: first check how suitable the available ZIF-8 force fields are for the systems we intend to study. Since they was originally developed aiming the gas storing properties of ZIF-8 [8, 9], it is necessary to verify what happens on calculations of hydrated environments. At this stage all simulations will be performed by the MC molecular simulation software DICE [10]. Once that is done, the second milestone is to simulate MOF-drug systems in water. Beyond the MC approach, these systems will be simulated by MD as well through

Gromacs. Accompanying this process will be the development of tools able to facilitate the peripheral steps to the simulation, such as the handling of atomic coordinate files which will originate the simulations inputs, and specific data scraping from simulation outputs.

Perspectives: This project is being developed in collaboration with the Fundamental Chemistry Department, Federal University of Pernambuco (DQF/UFPE), which already has experimental data collected. Then as soon as all simulations has been finished, it will be possible confront them with the measurements as a means for checking the plausibility of the calculations and, ideally, searching for clues about the prospects of ZIF-8 as a drug carrier . It is also expected that the used methods become reproducible so that other MOFs of biomedical interest can be studied, in particular those which the DQF/UFPE is able to synthesize.

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