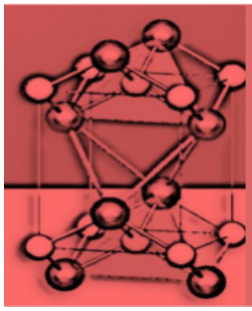

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QM-MM simulations using the ANI machine learning potential: assessment of embedding schemes

J.S. Grassano [a, b], J.A. Semelak [a,b], M.C. Gonzalez Lebrero [a,b], A. Roitberg [c], D.A. Estrin [a, b],

[a] *INQUIMAE, CONICET, UBA, Argentina.*

[b] *DQIAQF, Facultad de Ciencias Exactas y Naturales UBA, Argentina.*

[c] *Department of Chemistry, University of Florida, USA.*

email:

Introduction: Multiscale quantum (QM-MM) schemes, which consist of describing one portion of the system with quantum mechanics and the other using classical force fields, are ideal tools to describe chemical processes in complex environments, such as proteins or solutions. The computational cost of performing QM-MM simulations is mainly determined by the computational cost of the QM calculation and the extent of sampling necessary to describe the system. This makes QM-MM simulations very demanding from a computational point of view. For alleviating this issue, in this work we present a scheme in which the QM region is described by using the ANI machine learning approach developed in the University of Florida in A. Roitberg's group, which provides results of QM quality at a much lower computational cost.

The key issue of the implementation consists in modeling the coupling QM-MM contribution. This interaction is typically computed using an electrostatic embedding approach in which the QM density is calculated in the presence of the MM electrical field. In order to be able to use the ANI approximation to the QM energy, a simpler mechanical embedding scheme is proposed, in which the QM-MM coupling energy is computed by using a set of point charges on the QM(ANI) region. In addition, we propose a correction that includes the polarizability of the QM subsystem by the presence of the field generated by the MM subsystem.

Results : For validating the scheme, we employed a set of molecules, structural isomers of 18 amino acid species, which were extracted from the ANI-1x database. The species were solvated with 4000 water molecules and 100 ps long classical molecular dynamics simulations were performed to relax the solvent and generate representative solvated structures.

The results suggest that, in general terms, the mechanical embedding approach succeeds in reproducing the benchmark term given by an electrostatic embedding scheme using DFT. The quality of the approximation depends strongly on the charge partitioning scheme used. A substantial improvement was demonstrated by implementing the correction for atomic polarizability. The QM(ANI)-MM scheme was tested by performing MD simulations of several small species in different solvents, and computing the IR spectrum using the Fourier transform of the dipole autocorrelation function.

[1]. Smith, J. S., et al, Chemical Science, 2017, 8(4) 3192-3203.

[2]. Smith, J. S., et al., Scientific Data, 2020, 7(1)1-10.