Understanding Molecular Assembly of Rotaxanes with Machine Learning

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Artificial molecular machines are systems consisting of molecular components designed to imitate the movement of macroscopic machines by receiving an appropriate external stimulus. One strategy that has allowed studying molecular machines' operational principles is mechanically interlocked molecules (MIMs), such as rotaxanes. Atomistic modeling of the assembly process of rotaxane-type systems has been approached with molecular dynamics, metadynamics, nudged elastic band (NEB), and electronic structure calculations. However, applying these methodologies is challenging due to the complexity of the systems and the a priori selection of a collective variable, allowing a coherent reaction coordinate describing the energy change and the assembly process.

In this presentation, we propose a methodology that allows a detailed description of the assembly process in rotaxanes generated from an electrostatically assisted sliding approach (EASA), through a normalized displacement coordinate obtained by combining the image scaling method nudged. elastic band (CINEB) with the potential of the neural network of the ANAKIN-ME family, namely, ANI-1ccx that was trained with the gold standard (CCSD(T)*/CBS), We obtain potential energy barriers of the threading process in good agreement with the free energy barriers reported in the literature. By single-point DFT calculations, we characterize the non-covalent interactions and the steric and electrostatic effects that intervene in the assembly process from the analysis of non-covalent interactions and Shubin Liu's energy decomposition. We argue that combining AI and DFT is a powerful theoretical tool to gain insight into the cumbersome electronic and molecular mechanisms underlying complex molecular processes like chemical assembly.