On the development of a partial vibrational analysis within a QM/MM approach

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In molecular modeling extended systems are often only partially optimized in order to restrict the computational cost. For instance in a first step the whole system is optimized at a low level-of-theory, and in the next step only part of the atoms, usually the chemically active region, is optimized at a high level-of-theory, while atoms in the passive region are kept fixed at their original positions.

However, partially optimized geometries are non-equilibrium structures and the standard normal mode analysis (NMA) shows some serious defects, e.g. spurious imaginary frequencies may appear. In the Partial Hessian Vibrational Analysis [1],[2] these defects are surmounted by giving the fixed part an infinite mass. We propose a new model, the Mobile Block Hessian (MBH) approach, which takes into account the finite mass of the fixed block and avoids the spurious frequencies and the coordinate dependence [3]. The approach was generalized to the case of several mobile blocks. The MBH has been validated by comparing eigenfrequencies and eigenvectors, vibrational entropy and enthalpy, and recently reaction rate constants [4], with remarkably satisfying results.

One of the main advantages is that the implementation of the MBH allows a considerable reduction of computer time [5]. After several tests with smaller QM systems, the method is now also included in the CHARMM package, allowing the simulation of more extended (bio)systems. The next step is combining the MBH approach with QM/MM, currently in a developing stage, which will broaden the range of applications.

MBH in QM/MM is a very promising methodology for extended systems. Whereas a full normal mode analysis is unfeasible even if only the MM part of the system increases, because of the high number of expensive second derivatives of the QM/MM interaction terms in the Hamiltonian, the MBH can considerably reduce this cost, thereby opening the path to vibrational analysis in extended QM/MM systems.

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