Normal modes in partially optimized molecular systems: the Mobile Block Hessian (MBH) 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 shows some serious defects. The Cartesian Hessian has only 3 zero-eigenvalues instead of 6, implying that the rotational invariance is not manifest anymore. Spurious imaginary frequencies appear. Moreover the eigenvalues of the Hessian are coordinate dependent.

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. Comparison of MBH with another promising partial Hessian method, the Vibrational Subsystem Analysis [5], shows that both models are essentially different, and a combination of MBH and VSA is one of the future possibilities.

One of the main advantages is that the implementation of the MBH allows a considerable reduction of computer time [6]. After several tests with smaller QM systems, the method is now included in the CHARMM package, allowing the simulation of
more extended biosystems such as amylose or insulin. Work is in progress to exploit this computational profit by combining MBH with QM/MM models, which will broaden the range of applications.