Electron-Nuclear Hyperfine Coupling Simulations with Novel Molecular Dynamics Tools

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Background

Hyperfine coupling is the magnetic interaction between the spin of an unpaired electron and nearby nuclear spins. In liquids, while intermolecular electron-nuclear hyperfine coupling is not directly accessible through experiment, its time evolution is crucial for magnetic resonance methods such as dynamic nuclear polarization (DNP). In this study, we investigate the hyperfine coupling in liquids between a nitroxide radical (TEMPONE) and surrounding molecules of chloroform ($CHCl_3$) and iodobenzene (I-benzene). We employ a dual computational approach utilizing classical molecular dynamics and semi-empirical quantum mechanics, and compare the results.

Methodology

Molecular Dynamics (MD) Simulations

MD simulations allow the investigation of molecular interactions on short timescales (< picoseconds, 10^{-12} s). To perfom the calculations, we used the package *xTB* (*eXtended Tight-Binding*), a family of semi-empirical quantum mechanical methods designed for efficient and accurate calculations of large molecular systems.
Two methods were used:

Classical MD

GFN-FF

- Classical force-field method derived from GFN methodology
- Computationally faster than GFN2-xTB
- Used for larger systems and longer simulations

Semi-Empirical Quantum Mechanics

GFN2

- Semi-empirical quantum mechanical method
- Optimized for accurate geometries, vibrational frequencies, and noncovalent interactions
- Suitable for quantum-based molecular dynamics

System Design: Liquid in a Droplet

We considered a single TEMPONE molecule surrounded by solvent molecules.

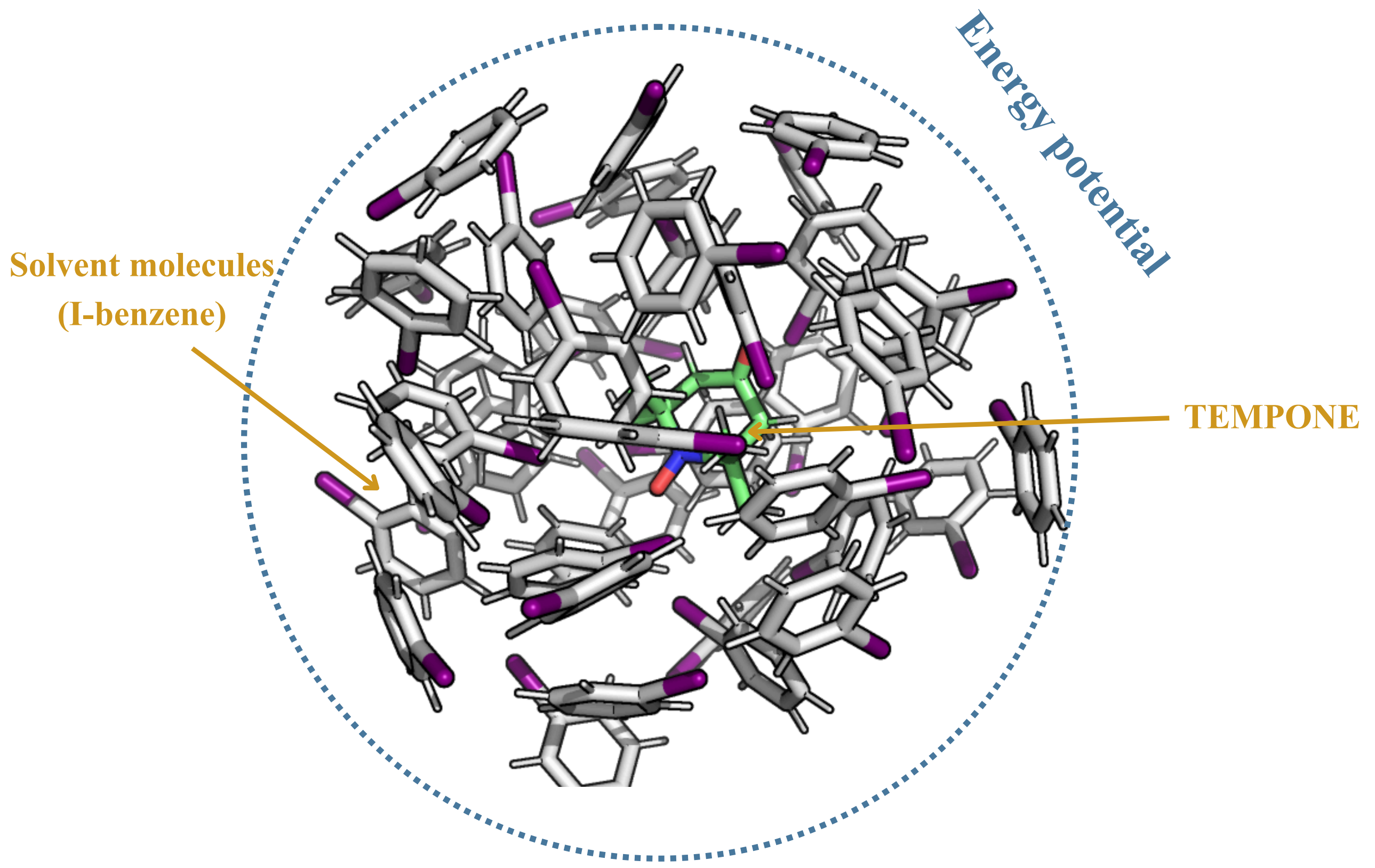


Figure 1. Liquid in a droplet. A finite droplet of I-Benzene solvent with a TEMPONE radical in the center, confined by an energy potential boundary.

- The liquid is confined in a finite droplet with TEMPONE at the center.
- The amount of solvent molecules in each system was computed based on solvent density, molecular weight, and droplet size in angstroms.
- An energy potential boundary was applied to confine the molecules in the droplet.
- System size was limited to ensure reasonable computational times (< 7 days).

Computational Steps

1. **Build individual molecules** in a molecular builder (*Avogadro*).
2. **Optimize the static geometry** of each molecule using quantum chemistry (*xTB*).
3. **Construct droplets** of solvents-TEMPONE with molecular builder (*Packmol*).
4. **Pre-optimization** of the static geometry of the droplets with quantum chemistry tools (*xTB*).

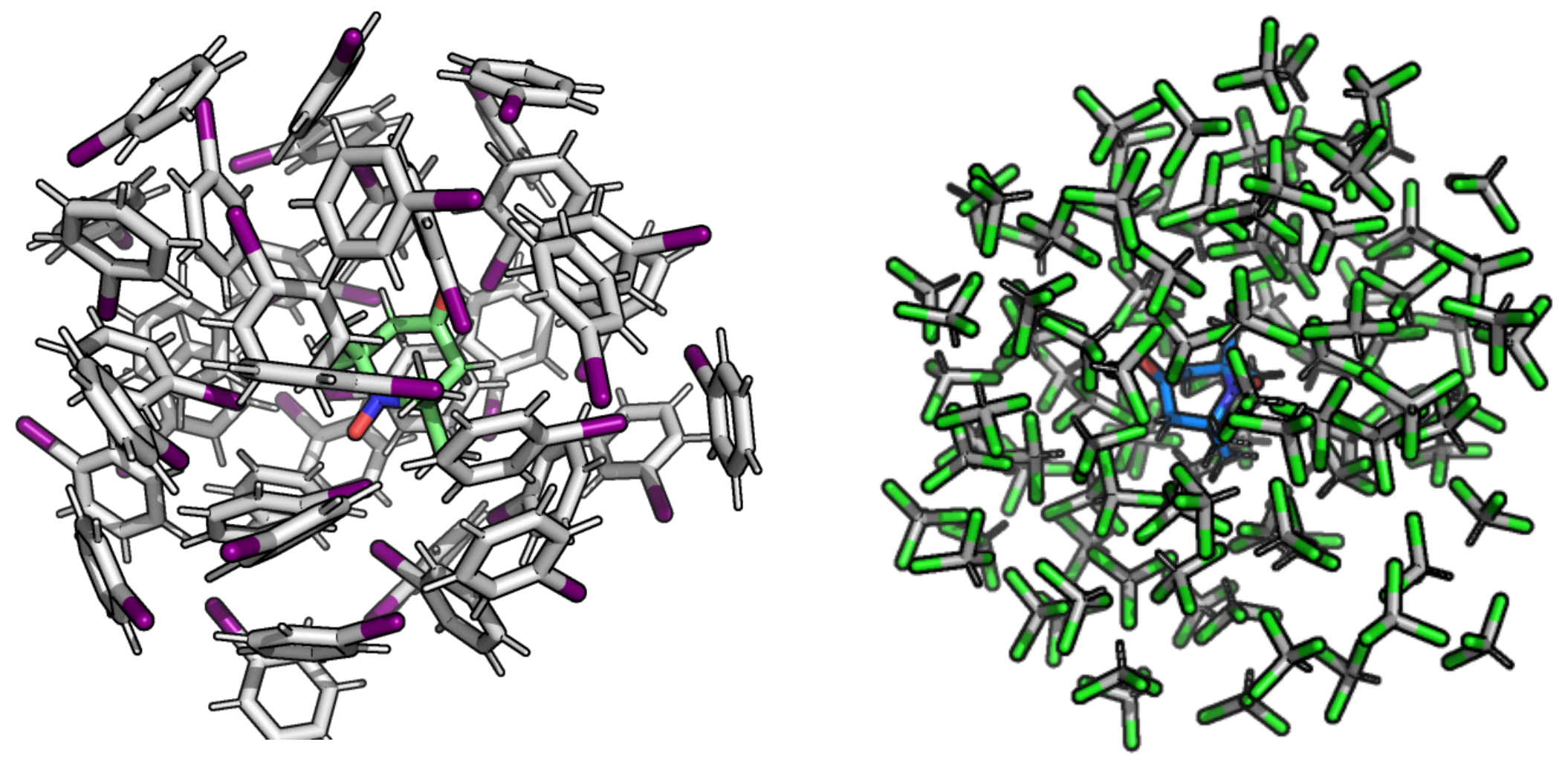


Figure 2. Droplets. Finite droplets of I-Benzene and chloroform solvent with a TEMPONE radical in the center.

5. **Define MD input** parameters (time span, time steps, energy potential).

I-benzene + TEMPONE

- Boundary radius: 12 Å
- Temperature: 298 K
- Simulation time: 100 ps
- Time step: 1.0

$CHCl_3$ + TEMPONE

- Boundary radius: 15 Å
- Temperature: 298 K
- Simulation time: 100 ps
- Time step: 1.0

6. **Run MD** simulations using *GFN-FF* and *GFN2*.

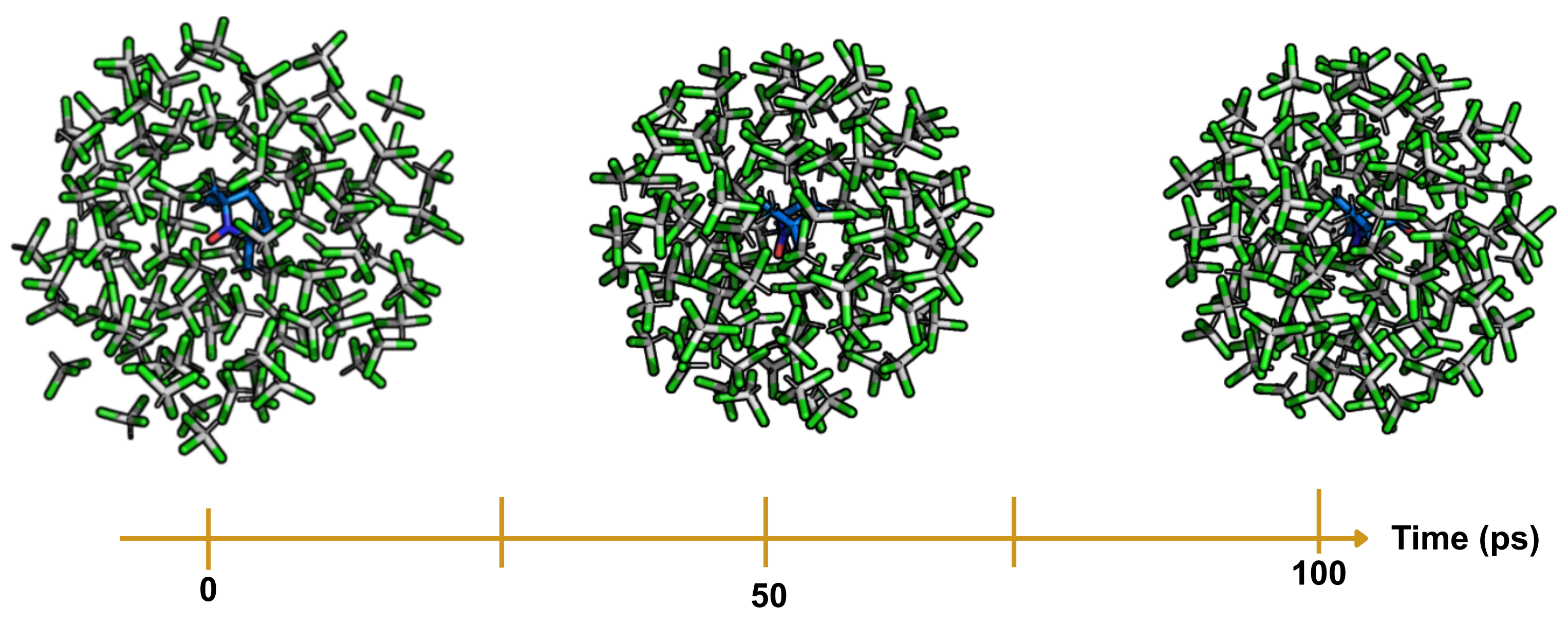


Figure 3. Time evolution of the droplet through an MD run. The droplet of $CHCl_3$ and TEMPONE is visualized at three different time frames: t=0, t=50 ps, and t=100 ps.

7. **Calculate the hyperfine coupling** constants between the unpaired electron of the radical and the carbon atom of the three closest solvent molecules in each time frame (*Orca* simulation program). For the I-benzene, we considered the *ipso* C atom (C1).

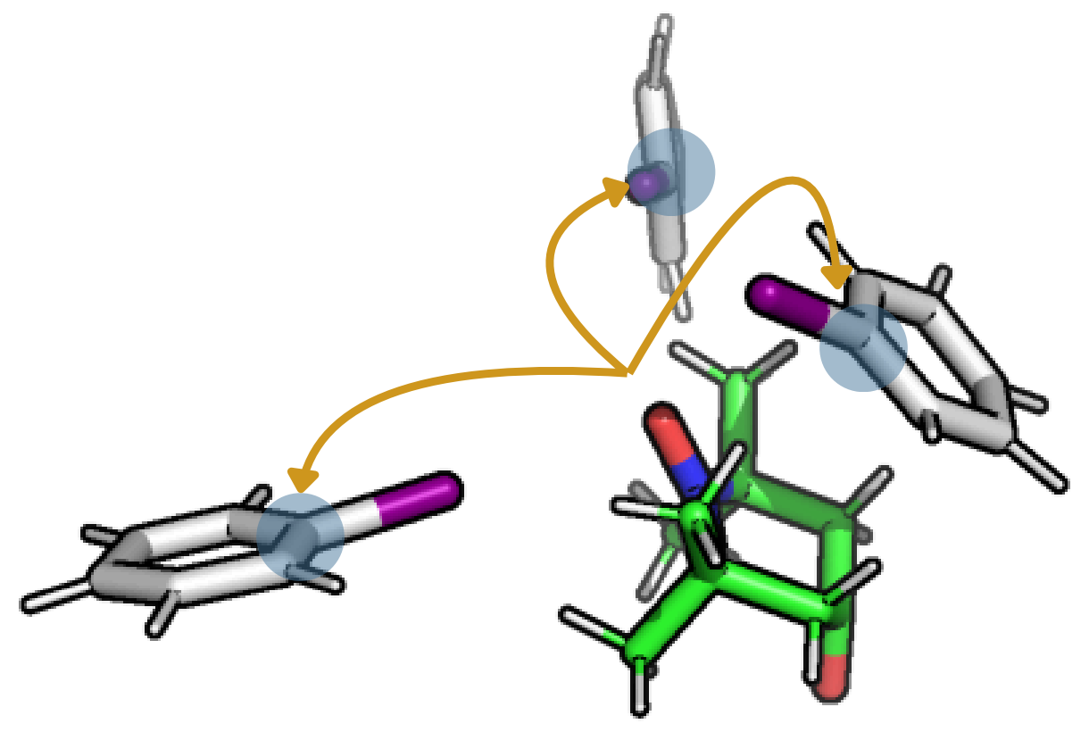
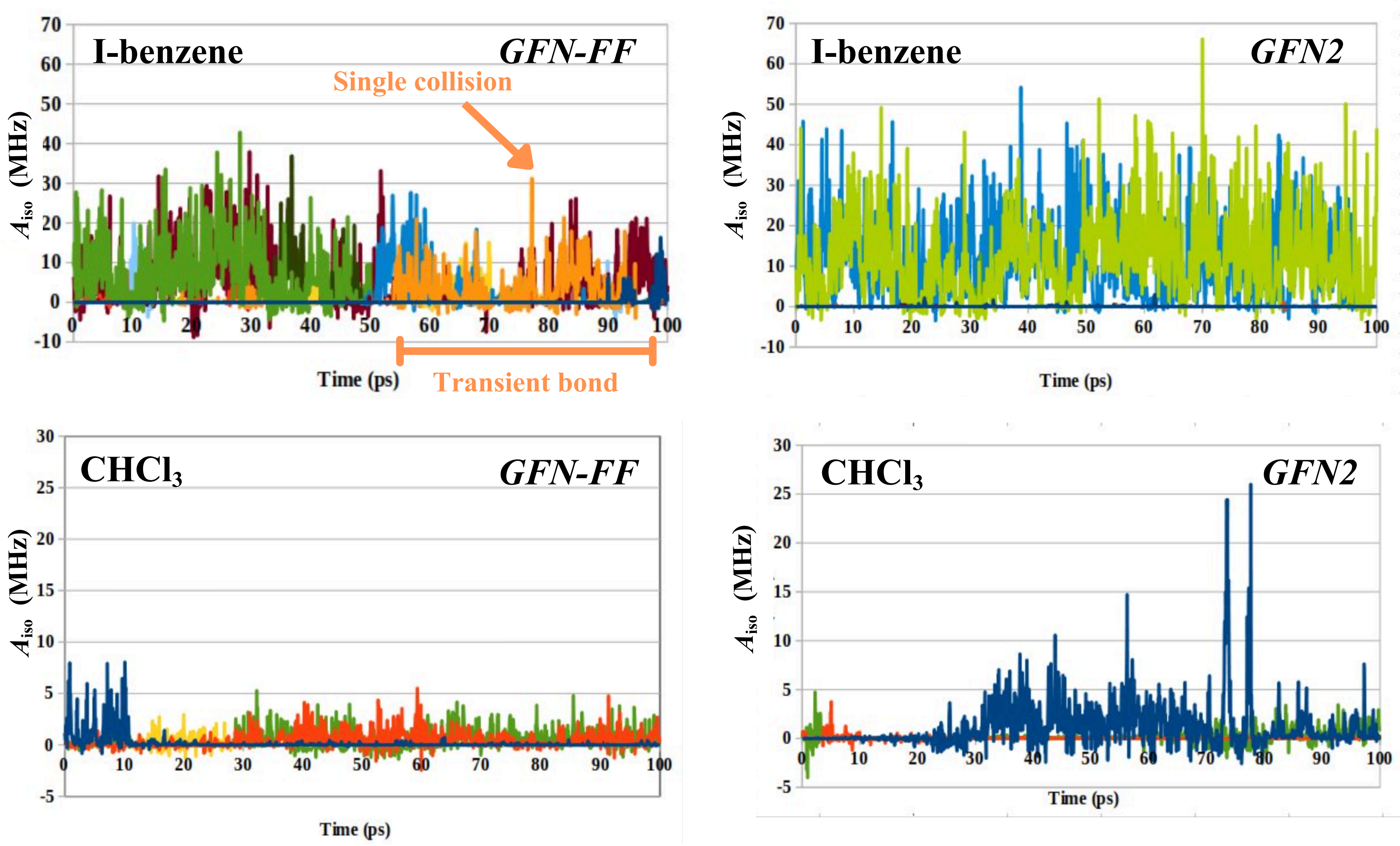


Figure 4. Interaction between TEMPONE and the closest I-Benzene solvent molecules. Cutout of TEMPONE and the three closest I-benzene molecules from one of the frames obtained with the MD run. The arrows represent the hyperfine coupling, while the circles mark the *ipso* C atoms.

Results and Discussion

Hyperfine coupling vs time

The hyperfine coupling (measured in MHz) is plotted as a function of time (in picoseconds) for the investigted systems. Each color trace represents a single solvent molecule (I-benzene or $CHCl_3$) and each spike represents a molecular collision between the radical and the solvent molecule.



Transient bonds between radical and solvent last tens of picoseconds.

Short molecular collisions (< 1 ps) modulate the hyperfine coupling.

Differences between *GFN-FF* and *GFN2*

- *GFN-FF* methodology shows 4-7 different solvent molecules forming **transient bonds** with the TEMPONE radical; on the contrary, *GFN2* shows fewer molecules forming transient bonds with the radical (2-3) but with longer duration (~100 ps) with relatively high peaks, the highest being just below 70 MHz, indicating interactions where the hyperfine coupling is very prominent.
- The **hyperfine coupling values** are consistently larger when simulating with *GFN2* (up to 70 MHz) than with *GFN-FF* (up to 40 MHz)

Conclusions and Future Development

- The two MD computational methods show substantial differences in the dynamics of the solvent/radical interaction.
- While *GFN-FF* (classical MD) qualitatively agrees with results published with similar methods, it is not clear if the simulations performed with *GFN2* (semi-empirical quantum mechanics) suffer from artifacts or grasp additional features of the process.
- More work is ongoing to assess the viability of this methodology with more solvents and radicals.

References

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