A Parallelized Molecular Collision Cross Section Package with Optimized Accuracy and Efficiency for Trajectory Method Calculations

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Project Overview

Ion mobility based separation prior to mass spectrometry has become an invaluable tool in the structural elucidation of gas-phase ions and in the characterization of complex mixtures. Application of ion mobility to structural studies requires an accurate methodology to bridge the theoretical modelling of ion geometry with experimental determination; this necessitates a robust evaluation of an ion's collision cross section (CCS). Herein, we present a refined methodology for calculating ion CCS using parallel computing architectures that makes use of atom specific parameters, which we have called MobCal-MPI. Tuning of ion-nitrogen van der Waals potentials on a diverse calibration set of 162 molecules returned a RMSE of 2.60 % in CCS calculations of molecules containing the elements C, H, O, N, F, P, S, Cl, Br, and I. External validation of the ion-nitrogen potential was performed on an additional 50 compounds not present in the calibration set, returning a RMSE of 2.31 % for the CCSs of these compounds, with speedups of up to 64-fold compared the traditional MobCal package. Owing to the use of parameters from the MMFF94 forcefield, the calibration of the van der Waals potential can be extended to other additional atoms defined in the MMFF94 forcefield (*i.e.*, Li, Na, K, Si, Mg, Ca, Fe, Cu, Zn). We expect the work presented here will serve as a foundation for facile determination of molecular CCSs.

The Trajectory Method

Within the trajectory method outlined in the original MobCal implement,[1,2] ion CCSs are evaluated through momentum transfer integrals, which are averaged over all possible velocities and geometries of the ion and buffer gas.

$$\Omega_{avg} = \frac{1}{8\pi^2} \int_0^{2\pi} d\theta \cdot \int_0^{\pi} \sin\varphi \, d\varphi \cdot \int_0^{2\pi} \frac{\pi}{8} \left(\frac{\mu}{k_bT}\right)^3 d\gamma \cdot \int_0^{\infty} g^5 \cdot \exp\left(-\frac{\mu g^2}{2k_bT}\right) dg \cdot \int_0^{\infty} 2b(1 - \cos\chi(\theta,\varphi,\gamma,g,b) \, db$$

Where θ, φ, and γ define the orientation of the ion with respect to the ion-collision gas centre of mass axis, g is the relative velocity, b is the impact parameter, μ is the reduced mass, and χ is the angle at which buffer gas is scattered upon interaction with the ion. Owing to the dependence of χ on molecular orientation and relative velocity, it can only be evaluated numerically.

$$\chi(\theta,\varphi,\gamma,g,b) = (\pi - 2b) \int_{r_{min}}^{\infty} \left[r^2 \sqrt{1 - \frac{b^2}{r^2} - \frac{\Phi(r)}{\frac{1}{2}m_{red} \cdot g^2}} \right]^{-1} dr$$

Gas trajectories are ultimately determined by the intermolecular potential $\Phi(r)$, which is composed of three contributions: van der Waals (V_{vdW}), ion-induced dipole (V_{IID}), and ion-quadrupole (V_{IQ}) interactions.

Optimal performance is obtained when the Exp-6 vdW potential (V_{vdW}) from the MM3 forcefield is used to model trajectories.

$$V_{vdW}(r_i) = \sum_{i=1}^{n} \varepsilon_i \left[1.84 \times 10^5 \exp\left(\frac{12r_i}{r_i}\right) - 2.25 \left(\frac{r_i^*}{r_i}\right)^6 \right]$$

Inclusion of additional potentials beyond the vdW potential enables more accurate description of molecular interactions. These additional terms become increasingly prominent components of the ion-neutral potential as the polarizability of the buffer gas increases (e.g., N_2).

$$V_{IID}(r_i) = -\frac{\alpha}{2} \left(\frac{ze}{n}\right)^2 \left[\left(\sum_{i=1}^{n} \frac{x_i}{r_i^3}\right)^2 + \left(\sum_{i=1}^{n} \frac{y_i}{r_i^3}\right)^2 + \left(\sum_{i=1}^{n} \frac{z_i}{r_i^3}\right)^2 \right] \qquad V_{IQ}(r_{ij}) = \sum_{j=1}^{3} \sum_{i=1}^{n} \frac{z_i z_j e^2}{r_{ij}}$$

The MMFF94 forcefield assigns vdW parameters for each unique atom type (*i.e.*, H bonded to carbon *versus* oxygen), which are then fit to experimental CCSs by application of uniform scaling factors ρ_{ener} and ρ_{dist}.

$$\varepsilon_{i \, scaled} = \varepsilon_i \cdot \rho_{ener} \qquad\qquad r_i^*{}_{scaled} = r_i^* \cdot \rho_{dist}$$

Fitting van der Waals Potentials and Parallelization

Scaling factors (ρ_{ener} and ρ_{dist}) are determined by fitting to experimental CCS of 162 unique species, which have been conformationally explored through molecular dynamics searches, and geometrically refined using DFT. Fitting of vdW potentials was externally validated on an additional 50 compounds not present in the calibration set. Overall, modification of the original trajectory method code yields speedups of up to 64-fold upon deployment on 32 cores, with a RMSE of 2.6%.
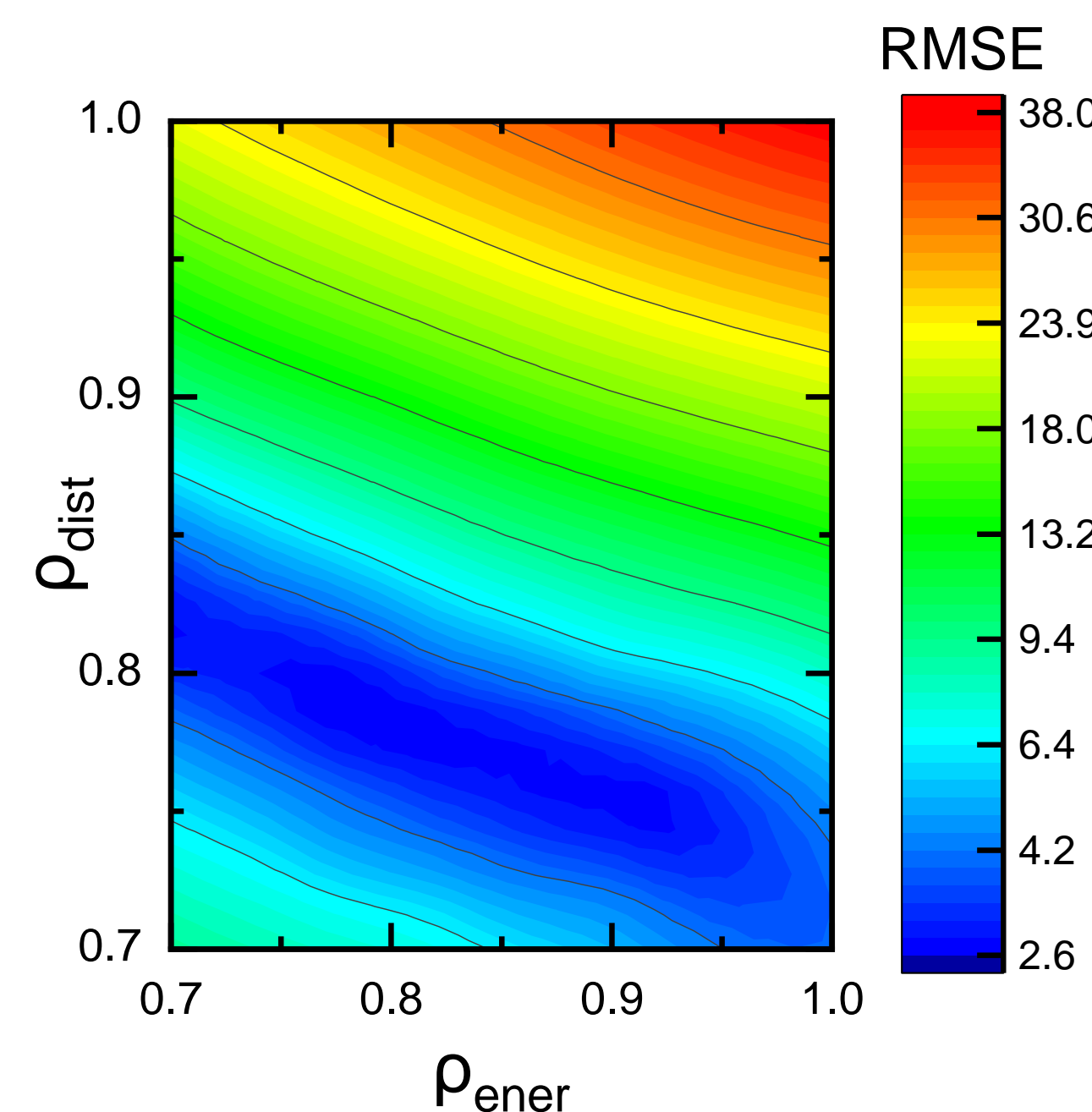
Figure 1. RMSE contours of the calibration set as specific combinations of the scaling parameters ρ_{dist} and ρ_{ener}.
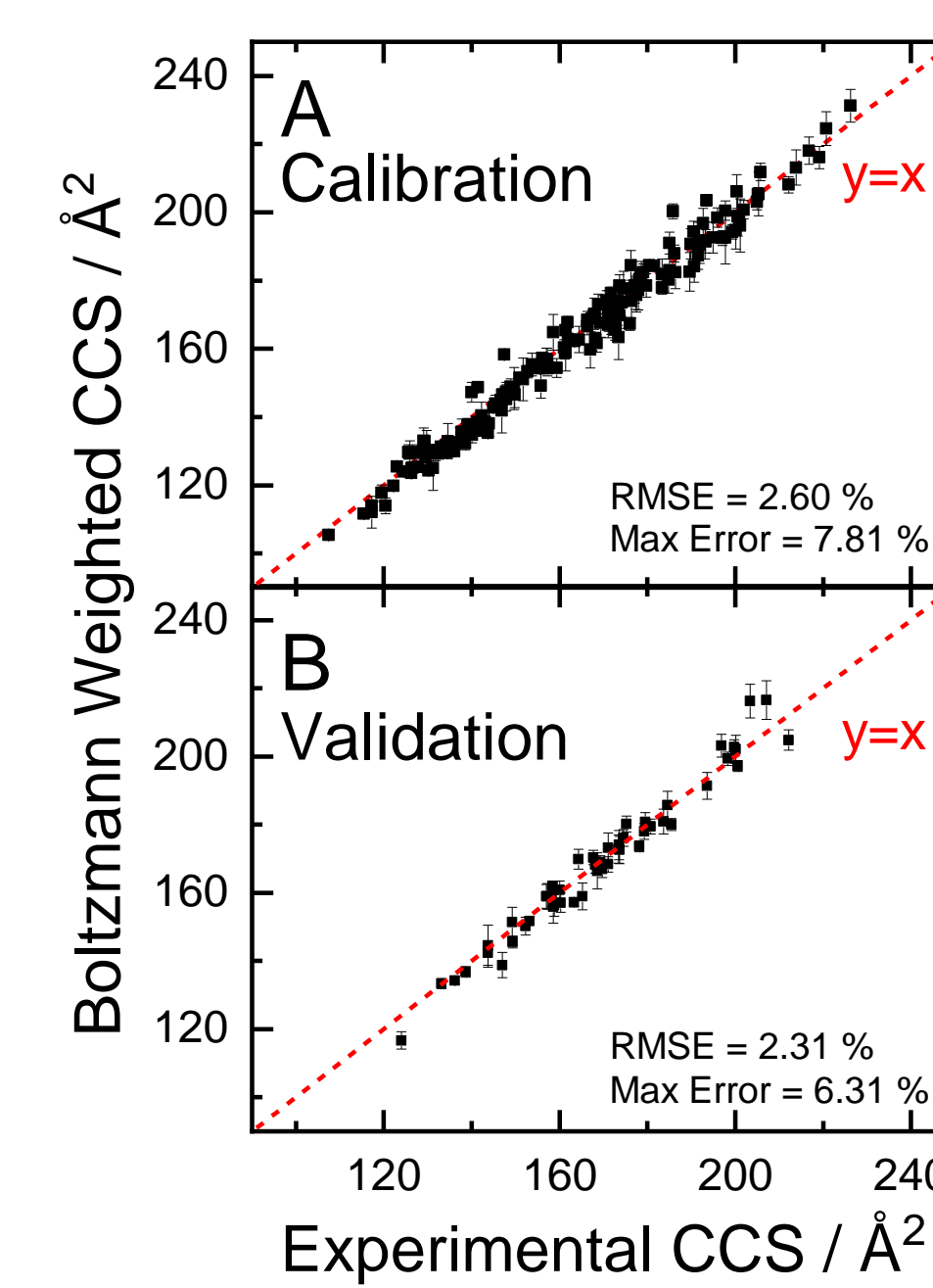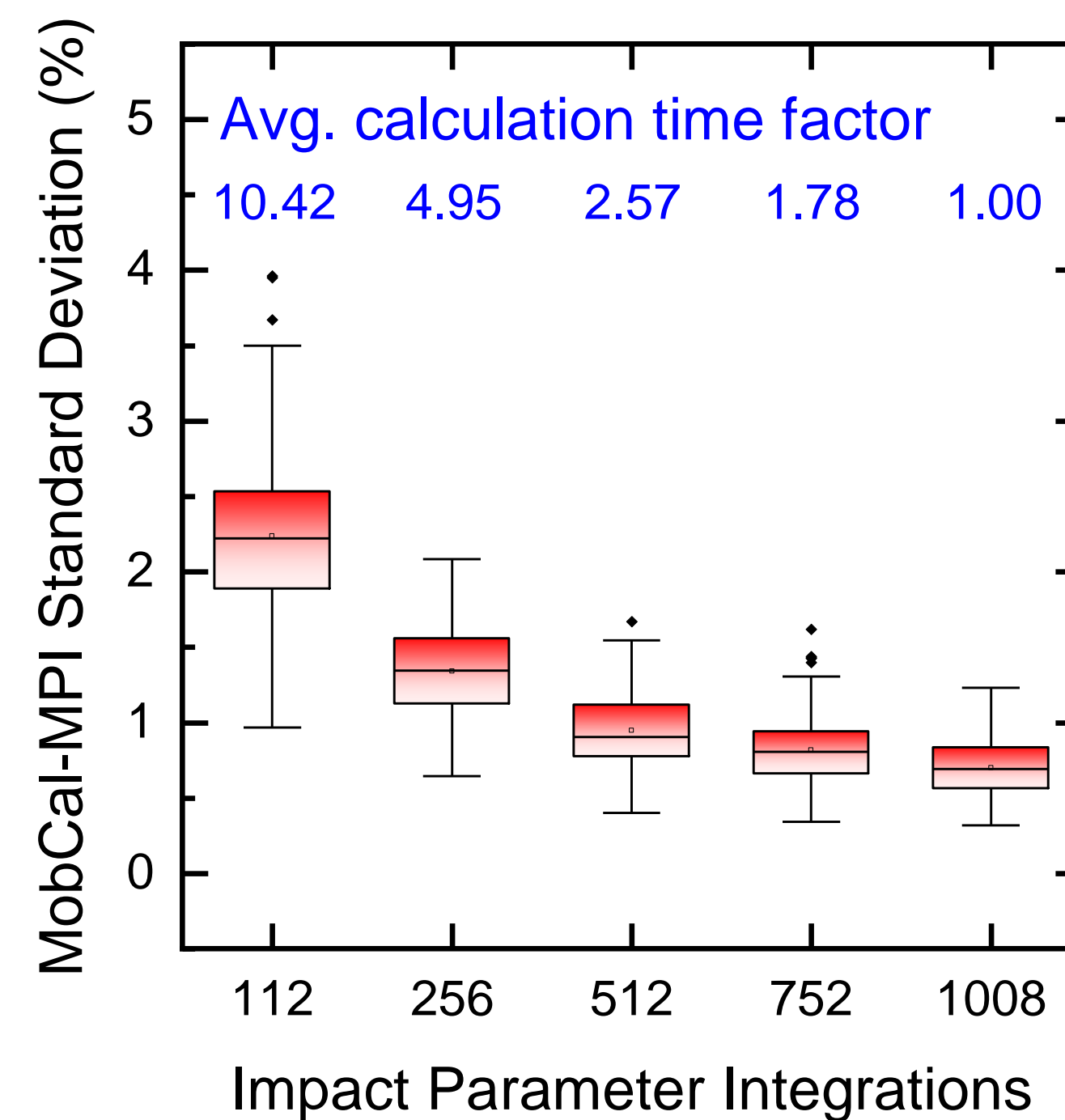
Figure 2. Comparison of Boltzmann-weighted CCSs from the calibration set (**A**) and validation set (**B**) to experiment.
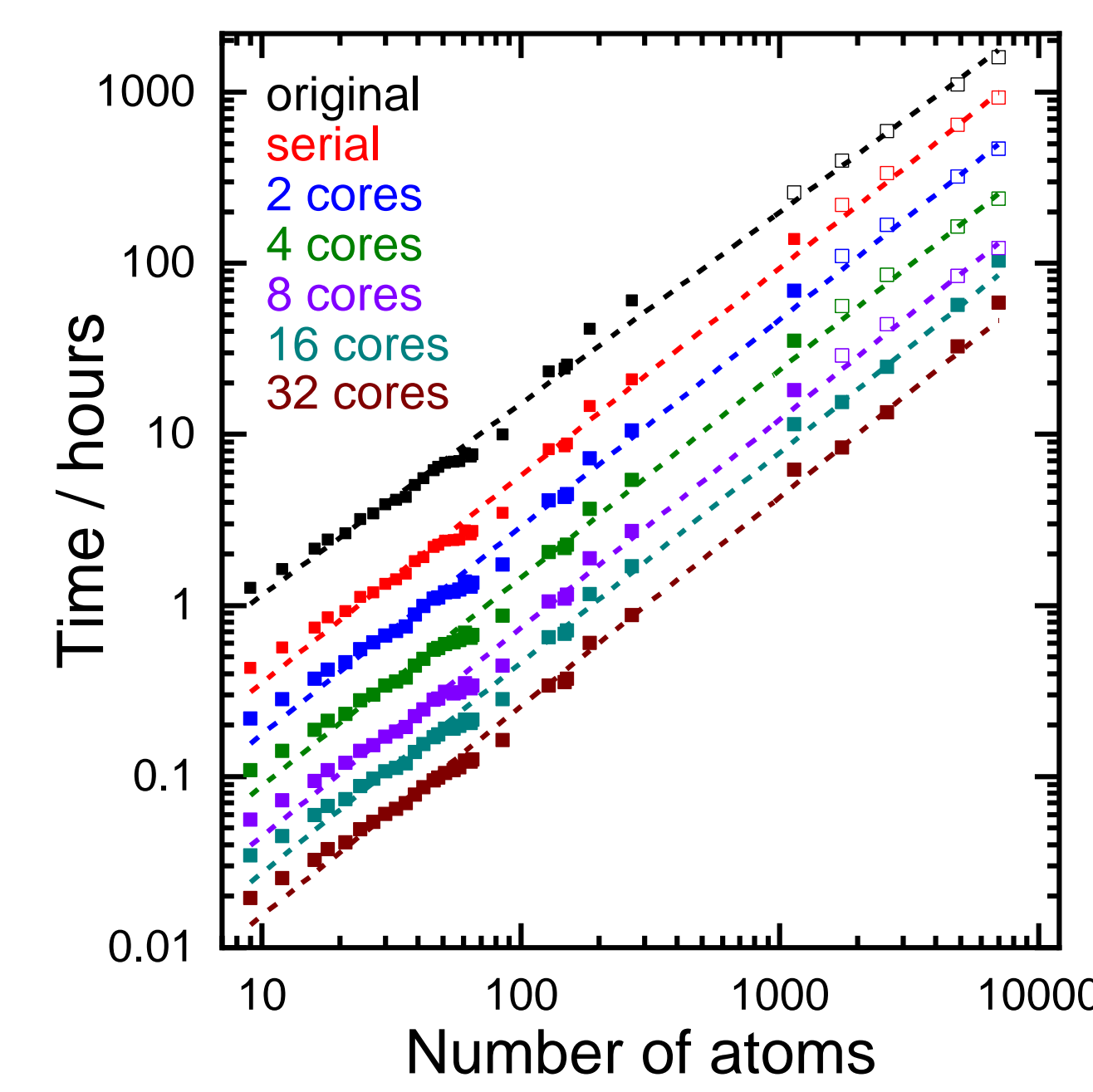
Figure 3. Total execution times for species ranging in size from 9 to 7029 atoms on various core allocations.

Optimizing Calculation Parameters

An additional factor regarding the accuracy of the CCS calculations stems from the trajectory method itself. Optimization of the number of impact parameter integrations shows that variance in a MobCal-MPI measurement is substantial below 512 grid points.

CCS calculations can vary dramatically when alternative charge schemes are used. In this regard, V_{IID} and V_{IQ} terms should incorporate charges from electrostatic potential mapping (*e.g.*, MK, ChelpG) for optimal accuracy.

Figure 4. Effect of the frequency of impact parameter integration points on standard deviation and calculation time.
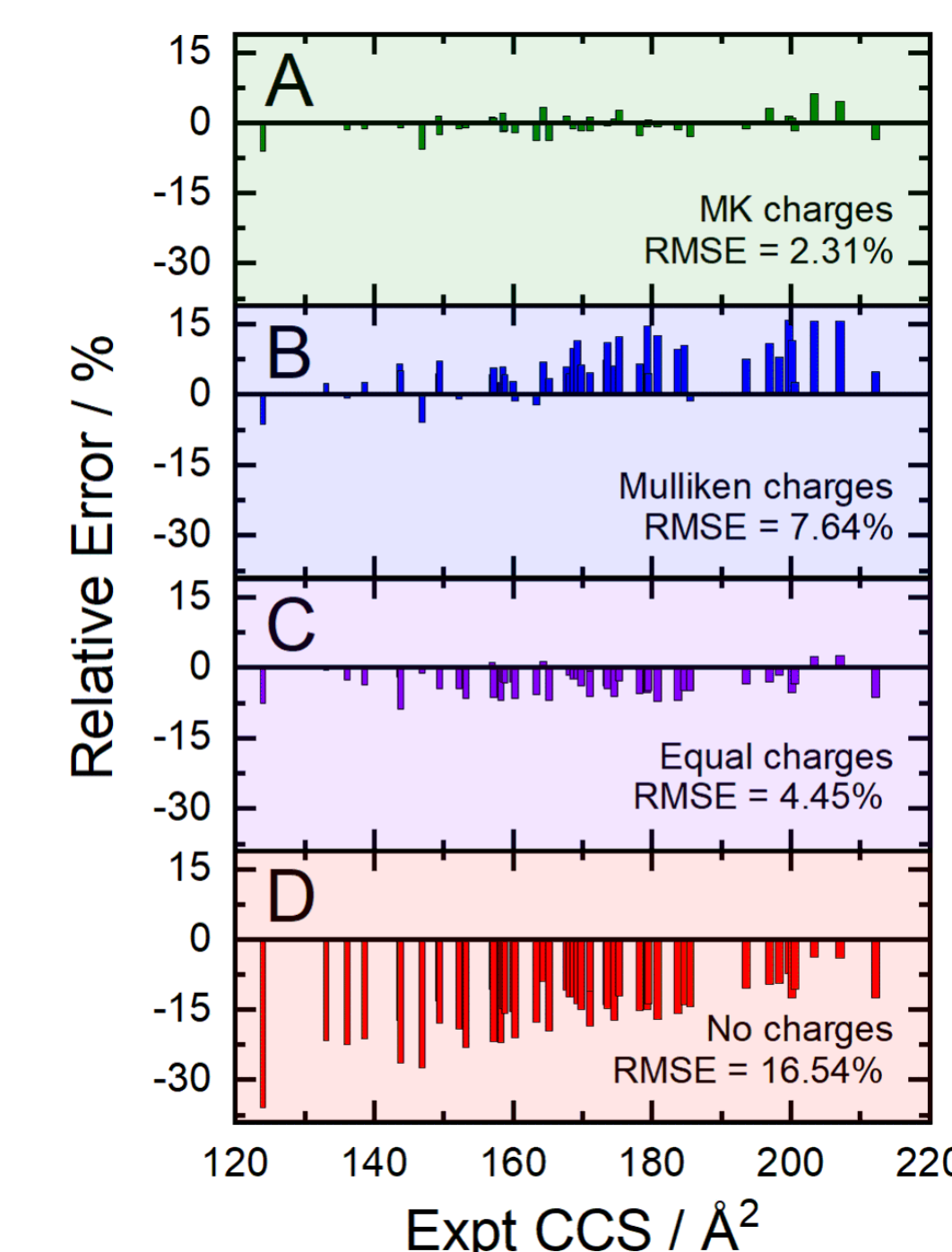
Figure 5. Relative error (%) associated with assignment of partial charges by various methodologies.

Concluding Remarks and Future Directions

Scaling factors are determined for vdW parameters outlined in the MMFF94 forcefield. Parallelization of MobCal-MPI provides a fast, nearly universal method for CCS calculation of molecules composed of the common elements. Future implements will encompass an automated pipeline capable of structure PES exploration, refinement, and CCS calculation.

References and Acknowledgements

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2 T. Wyttenbach, G. Von Helden, J. J. Batka, D. Carlat and M. T. Bowers, *J. Am. Soc. Mass Spectrom.*, 1997, **8**, 275–282.