A GPU ACCELERATED CDMS TRAP TRAJECTORY SIMULATOR AND OPTIMISER

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INTRODUCTION

Charge detection mass spectrometry (CDMS) is an increasingly popular method for the analysis of large and heterogeneous ions. In CDMS single ions are trapped in an electrostatic linear ion trap (ELIT) comprising a detection tube and two ion mirrors. As the ion oscillates through the tube the induced charge on the tube is recorded. From a Fourier Transform (FT) of the transient we obtain the m/z of the ion from the frequency and the charge from the amplitude. Simultaneous measurement of m/z and z allows the mass of the ion to be determined.

Since charge is quantized, reduction of the charge uncertainty to a sufficiently low level (e.g. by reduction in detector noise and long transients) leads to perfect charge accuracy. Mass resolution is therefore limited solely by the m/z resolution of the ELIT. Current CDMS trap geometries have a m/z resolution of ~ 330[1]. For many applications this is sufficient as resolution is limited by sample heterogeneity, nevertheless it is desirable to obtain ELIT geometries with higher m/z resolution.

METHODS

Trajectory simulator

PyCUDA was used to implement a 4^{th} order Runge-Kutta trajectory calculation. Electric fields for a given physical trap geometry are obtained using SIMION® 2020 to solve the Laplace equation, these are then imported into the CUDA® model. Ideal traps have cylindrical symmetry hence we solve for and store 2D fields, for traps with distorted geometries (e.g. mechanically misaligned) we need full 3D field arrays. For the traps simulated here a scale of 0.025mm/gu was found to be sufficient with linear interpolation for the field between grid points.

By default the trajectory solver returns the mean period for single ions to cross the central plane of the trap. Note that we do not simulate a transient and perform an FT, this would be highly inefficient in terms of calculation time and memory usage. For testing or for deeper analysis we can return the plane crossing times or the full trajectory traces of all or a subset of the ions.

To check the validity of using the mean of the crossing period, we used SIMION to simulate a number of 100ms transients. By performing an FT on the transients, and taking the mean of the crossing times, we were able to directly compare the calculated frequencies for each ion trajectory. We used a 4 electrode trap geometry giving an m/z resolution of 600,000 at a mean frequency of 4.8 kHz. Frequency differences of up to 3e-6 kHz were seen, which are negligible at the m/z resolutions we obtain here.

The simulations are run in single ion mode, i.e. we do not consider ion-ion interactions or interference in the induced charge. We also do not consider noise or the sampling resolution of the FT peak. For an ideal on-axis trajectory the m/z of the ion is inversely proportional to the square of the frequency. Variation in the axial KE and radial trajectory of ions leads to deviation from the ideal frequency, the m/z resolution of the trap is therefore the tolerance of the mean frequency to non-ideal ion energies and trajectories. Calculation of the m/z resolution requires simulation of sufficient single ion trajectories to plot an m/z histogram with acceptable statistics.

Speed

Calculation of a 100ms ion trajectory in SIMION on a typical workstation using a single CPU thread took 95 seconds. The CUDA model running on a NVIDIA® GV100 GPU calculated 16,384 100ms trajectories in 480 seconds, giving an approximate speed increase per ion of ~3200 vs a single core, or ~100x vs a typical multi-core workstation.

Optimiser

For a given field array the physical geometry of the electrodes is fixed, parameters that we can vary are the electrode voltages and the tube length. Since the interior of the tube is field-free the length of the tube can be varied analytically, the geometry of the grounded shield is fixed hence varying tube length is effectively varying the separation between the mirrors.

Optimisation of trap voltages and tube length was performed using a modified Nelder-Mead simplex algorithm[2]. An outline of an optimiser run is given here:

1. Initial guess values for the parameters are selected via uniform distributions over selected ranges. A small packet of ions is run for each guess value, only those solutions where at least 95% of ions are stable are retained.
2. Each optimiser thread runs the simplex algorithm until the termination criteria is reached. The algorithm can optionally be restarted with a new simplex generated around the optimised result.
3. When the optimiser thread has run the final pass of the simplex algorithm a new stable solution is selected and we return to step 2 above.
4. New stable solutions are generated as in step 1 when the pool of available stable solutions is exhausted.

Typically a packet of 1000 ions was used to give sufficiently good statistics, the initial conditions for these ions were retained and used for all optimiser runs. With 16,384 GPU threads, we can run 16 parallel optimiser threads.

The usual objective function was the m/z resolution calculated assuming a Gaussian peak, with a penalty applied for solutions less than 100% stable. Optimising directly on, e.g., the FWHM resolution leads to higher FWHM resolutions at the cost of peak shape. Other options include constraining the duty cycle (time in tube vs time out of tube) and enforcing 2-pass y-position point-parallel focusing.

For optimisation the scan time was 2 passes across the central plane, while this is short in terms of testing stability (i.e. we can have unstable trajectories that survive for 2 passes) we have found that optimised (i.e. high resolution) solutions tend to exhibit good stability. Once we have obtained optimised solutions they are re-run with larger packets of ions over longer scan times to ensure they remain well behaved.

Initial phase space

As is typical for m/z analysers the performance of an ELIT is dependent on the initial position and velocity spreads (phase space) of the incoming ion beam. We have performed SIMION simulation of upstream optics comprising a high pressure segmented quadrupole, low pressure segmented quadrupole and focusing lenses to allow estimation of reasonable values for the initial phase space.

For ions of mass 500kDa and z=+40, simulated ion packets at the trap centre have axial KE σ=0.1eV/z, radial (x/y) position σ=0.15mm, radial angle σ=0.1deg (Gaussian distributions). The optics simulated here have yet to be experimentally verified, the phase space values given above would lead to a m/z resolution of 1100 for the current 3 electrode trap geometry, significantly higher than the 350 seen experimentally.

Adjusting the phase space to more conservative σ values of 0.3eV/z, 0.3mm, 0.2 deg gives the expected resolution of 350 for the 3 electrode trap, we therefore use these phase space values unless otherwise noted.

The existing 3 electrode trap is tuned for ions with an axial energy of 130eV/z, to allow direct comparison we have retained this energy for all the trap optimisation here. In practice it may be beneficial to increase the axial KE, raising the frequency of oscillation can be advantageous, and depending on the upstream optics the proportional axial KE spread may be reduced.

RESULTS

Current 3 electrode trap

Figure 1A shows the geometry of the current 3 electrode trap. The angled electrode nearest to the detection tube is a shield electrode at the same potential as the tube, typically at ground. A SIMION ion trajectory is shown starting from the centre of the trap at +0.5mm y, with the nominal axial energy (130eV/z), for 10 passes across the central plane. **Figure 1B** shows an expanded view of the trajectory, we can see that the ion takes multiple different paths through the device, i.e. we are far from exhibiting point-to-parallel focusing. **Figure 1C** shows the axial field, in this geometry we have no accelerating lens elements.

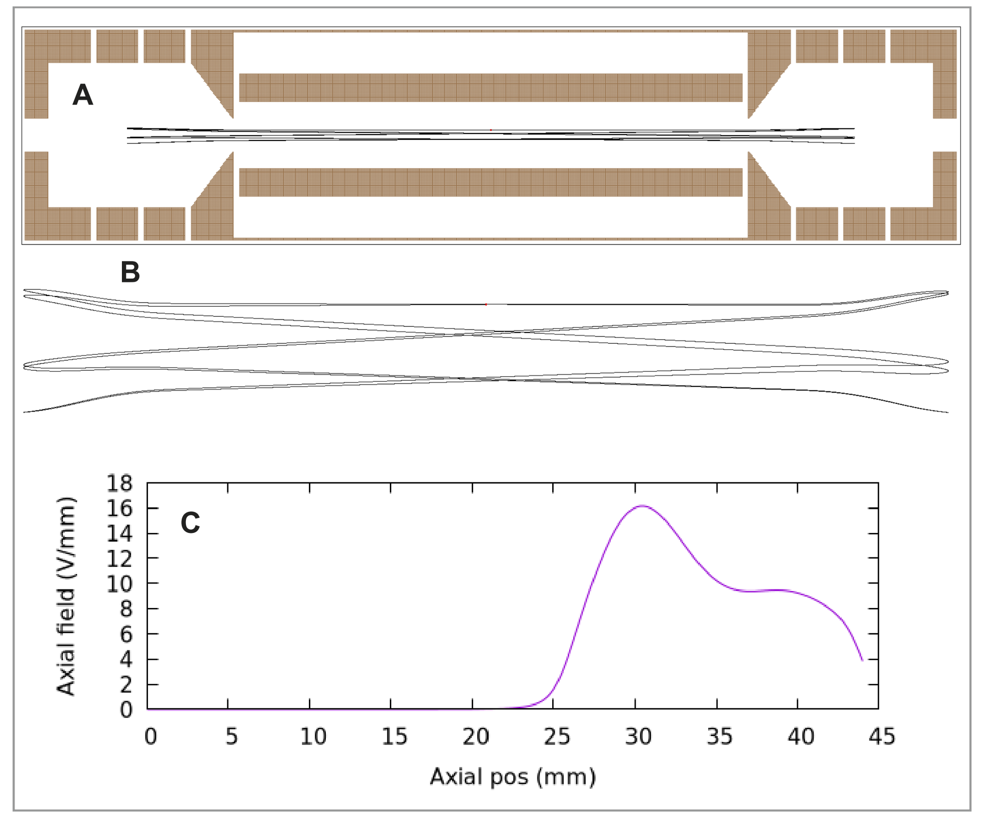

Figure 1. *A - SIMION geometry for the current 3 electrode trap, also shown is a 10 pass trajectory with initial y=0.5mm. B - expanded view of the trajectory. C - on-axis axial field.*

Optimiser results

It is known from MR-TOF design that mirrors with an accelerating lens at their entrance lead to improved spatial focusing[3], therefore we have chosen to examine candidate geometries with 4 electrodes. Since we only optimise for voltages and tube length selection of a physical geometry is an iterative process of trial and error.

Figure 2 shows an example of the optimiser output for two candidate geometries, in these geometries the first three electrodes are 12mm or 14mm and the final electrode is 8mm. Tube length and the four electrode voltages were allowed to vary in the optimisation, the plot shows m/z resolution vs tube length. Many of the optimiser runs converge to local optima that are far from the best solution, this is dependent on the ranges used to bound the initial guess values. We are clearly able to find optimal solutions for each geometry however, with an ideal tube length of 155mm / 175mm for the 12mm / 14mm geometries respectively.

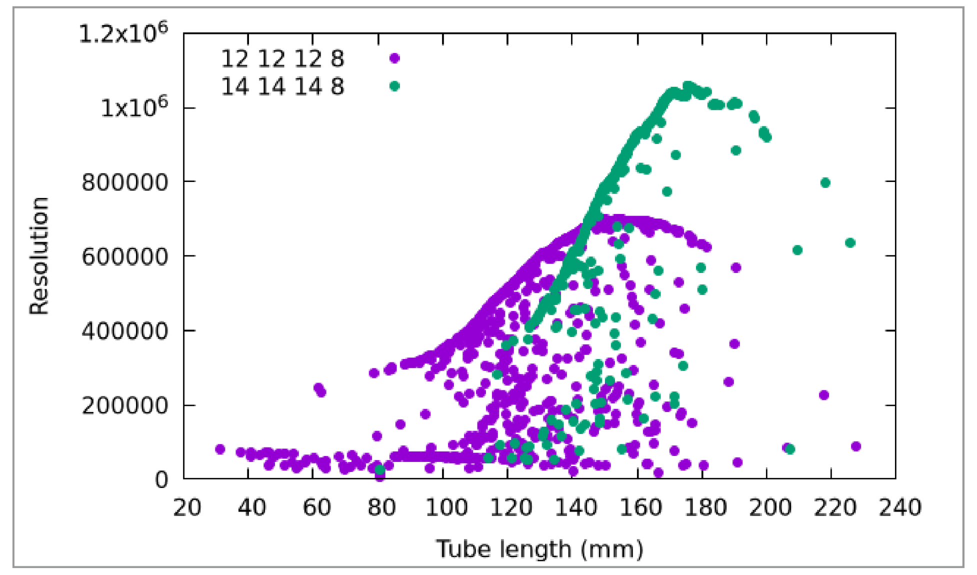

Figure 2. *Resolution vs tube length for optimised solutions obtained for the 12mm and 14mm 4 electrode trap geometries.*

The resolution of the optimal solution for the 14mm electrode geometry is ~1.7x higher than that for the optimal 12mm solution. Physical geometry optimisation thus far has been carried out as a process of manual iteration. We can envisage automating this process with, for example, a simple pattern search applied to the electrode lengths. We would then run the optimiser for a given geometry until sufficient solutions are obtained such that we can be confident we have found the optimum. The physical geometry would then be iterated according to the pattern search and the optimiser re-run.

These results demonstrate a general feature of these trap geometries: while the exact physical geometry does affect the best solution we can obtain there is a wide range of geometries for which we can obtain high resolutions. In other words trap resolution is relatively weakly dependent on the physical electrode structure as long as we tune the voltages and mirror separation.

High resolution solutions

Selecting one of the optimal resolution 155mm tube solutions for the 12mm electrode geometry, we show in **Figure 3A** a 10 pass trajectory with initial y=+0.5mm. This trajectory is shown in an expanded view in **Figure 3B**, the axial electric field is shown in **Figure 3C**.

A notable feature of the trajectory is that we have approximate point-to-parallel focusing, this is known to be a desirable property of high resolution MR-TOF solutions[3]. The objective function for the voltage optimisation was m/z resolution and stability over 2 passes, we did not explicitly optimise for point-to-parallel focusing.

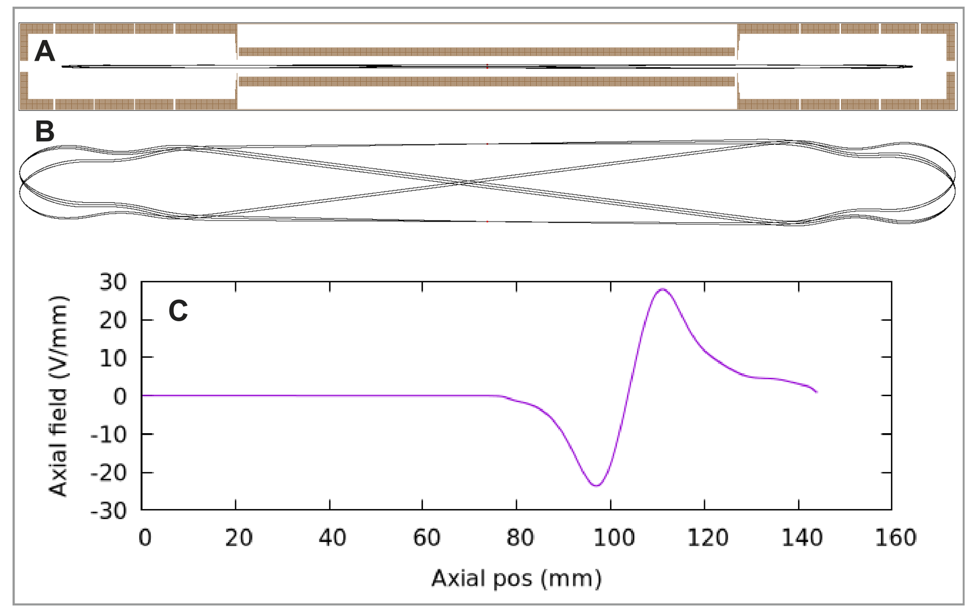

Figure 3. *A - SIMION geometry for a 4 electrode trap, electrode lengths of 12,12,12 and 8mm, 155mm tube. Also shown is a 10 pass trajectory for a high resolution solution, with initial y=0.5mm. B - expanded view of the trajectory. C - on-axis axial field.*

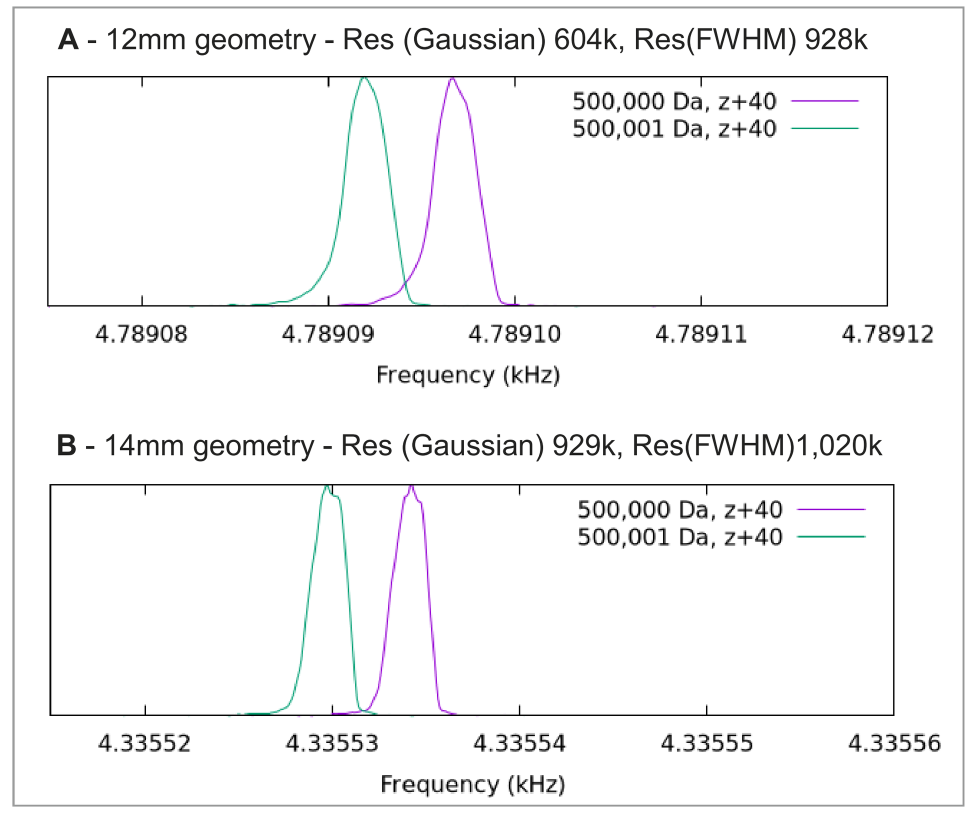

Figure 4. *Histograms of mean oscillation frequency for ions of mass 500,000 and 500,001 Da, z+40, for 4 electrode traps with A - 12mm geometry, B - 14mm geometry.*

Figure 4 shows frequency histograms for high resolution solutions for the 12 and 14mm geometries, for ions of m500,000 and 500,001 z+40. The FWHM resolutions for the two geometries are similar, however the 14mm geometry exhibits better peak shape. The low frequency tails on the 12mm solution limit the Gaussian resolution.

Phase space effects

The optimal resolution 4 electrode solutions shown here have greatly extended tube lengths, >150mm, vs the 50mm of the 3 electrode trap. The grounded shield aperture at either end of the tube places physical constraints on the angular acceptance of the trap. For the 3 electrode trap, trajectories starting at the centre with angles up to ~2 degrees pass through the aperture, for the 4 electrode traps shown here we are limited to 1.3 to 1.5 degrees of acceptance (this includes widening the grounded shield aperture to 2mm radius vs 1.65mm radius in the 3 electrode trap). Note that the phase space values we are using here have an angular spread well within these bounds.

To illustrate the importance of the initial phase space **Figure 5** shows optimiser results for the 12mm geometry for the default phase space, for a tight phase space (σ 0.2eV/z, 0.2mm, 0.13deg), and a wide phase space (σ 0.45eV/z, 0.45mm, 0.3deg). The optimal resolution we can obtain is strongly dependent on the phase space, 700k for the default, rising to over 2e6 for the tight phase space, and dropping to 200k for the wide phase space. Note that the optimal solutions obtained depend on the phase space used in the optimiser, an optimal solution obtained for one phase space will likely be sub-optimal for a different phase space.

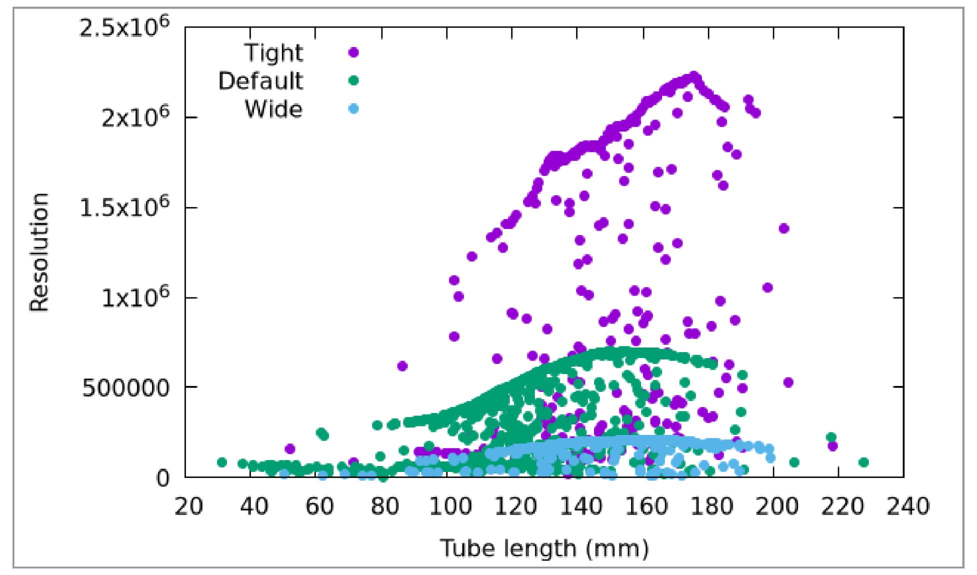

Figure 5. *Resolution vs tube length for optimised solutions obtained for the 12mm 4 electrode trap geometry, for default, tight and wide initial phase space.*

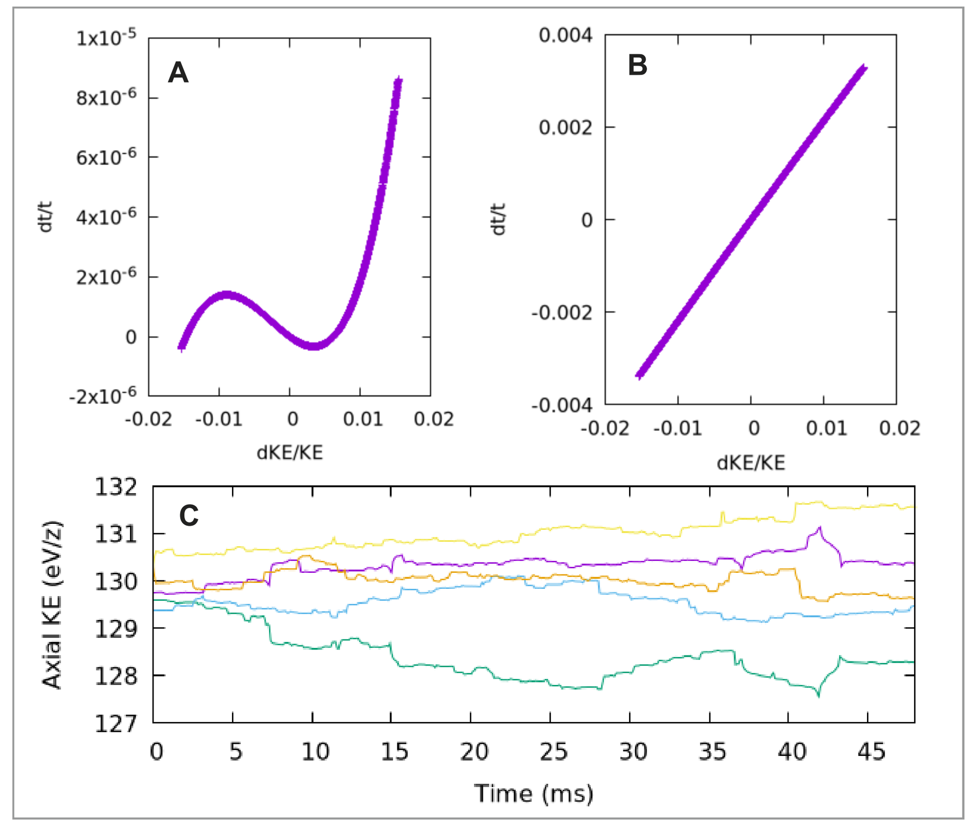

Figure 6. *Flight time deviation vs axial KE deviation for A - 3 electrode trap, B - optimised 4 electrode trap, 12mm geometry. C - Axial KE vs time for five z+200 ions trapped in a 3 electrode trap with space charge modelled via Coulombic repulsion.*

One factor limiting the speed of CDMS is the requirement to analyse single ions. Space charge interaction between multiple highly charged ions lead to shifts in the axial KE of the ions and hence degradation of the m/z resolution. **Figure 6** plots cross time period deviation vs axial KE deviation (+/- 2eV) for otherwise ideal ion trajectories in the 3 electrode trap (**6A**) and in the 12mm optimised 4 electrode trap (**6B**). As expected the higher resolution trap is much more tolerant to variation in axial KE vs the significant linear dependence seen in the 3 electrode trap. **Figure 6C** plots the evolution of axial KE in a SIMION simulation with five z+200 ions in a 3 electrode trap, space charge effects calculated via Coulombic repulsion. We see KE shifts in the order of a few eV/z, sufficient to drop the m/z resolution of the 3 electrode trap to less than 100. This ability to tolerate axial KE shifts should allow higher resolution traps to be operated in multiple ion trapping mode without excessive loss of m/z resolution. This demonstrates the potential utility of higher resolution trap designs even where the single ion resolution is limited by sample heterogeneity.

CONCLUSION

- **We have developed a GPU accelerated trajectory simulator and optimiser for the design of electrostatic linear ion traps.**
- **Trajectory calculation speed ~100x faster than a typical workstation.**
- **Optimisation of voltages and mirror separation for a fixed electrode geometry can be rapidly accomplished.**
- **We show ELIT geometries with m/z resolutions over three orders greater than current CDMS trap designs.**
- **Improved tolerance to axial KE shifts offers the possibility of multiple ion analysis while maintaining m/z resolution.**

References

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