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# What Happens to DNA Duplexes in the Gas Phase?

Massimiliano Porrini,<sup>1,2</sup> Frédéric Rosu<sup>3</sup> & Valérie Gabelica<sup>1,2</sup>

<sup>1</sup>Univ. Bordeaux, IECB, ARNA Laboratory, F-33600 Pessac, France, <sup>2</sup>Inserm, U869, ARNA Laboratory, F-33000 Bordeaux, France, <sup>3</sup>CNRS UMS 3033, IECB, University of Bordeaux, F-33600 Pessac, France.

## Key findings

→ It is generally believed that DNA double helix is maintained from solution to the gas phase [1-5].

- [1] Schnier, (...) & Williams, (1998) *JACS*, 120, 9605.
- [2] Gabelica & De Pauw (2002) *IJMS*, 219, 251.
- [3] Rueda (...) & Orozco (2003). *JACS*, 125, 8007.
- [4] Gidden (...) & Bowers (2004) *JACS*, 126, 15132.
- [5] Baker & Bowers, (2007) *JASMS*, 18, 1188.



→ In contrast, we found that **(12-mer)<sub>2</sub> duplexes sprayed from physiological conditions** (predominant charge: 5-) have **much lower CCS than expected** from either a B-helix or an A-helix.

→ The compact duplex DNA gas-phase structure at low charge states most probably involves **zipping of the major groove** due to self-solvation (extra H-bonds formed between phosphates).

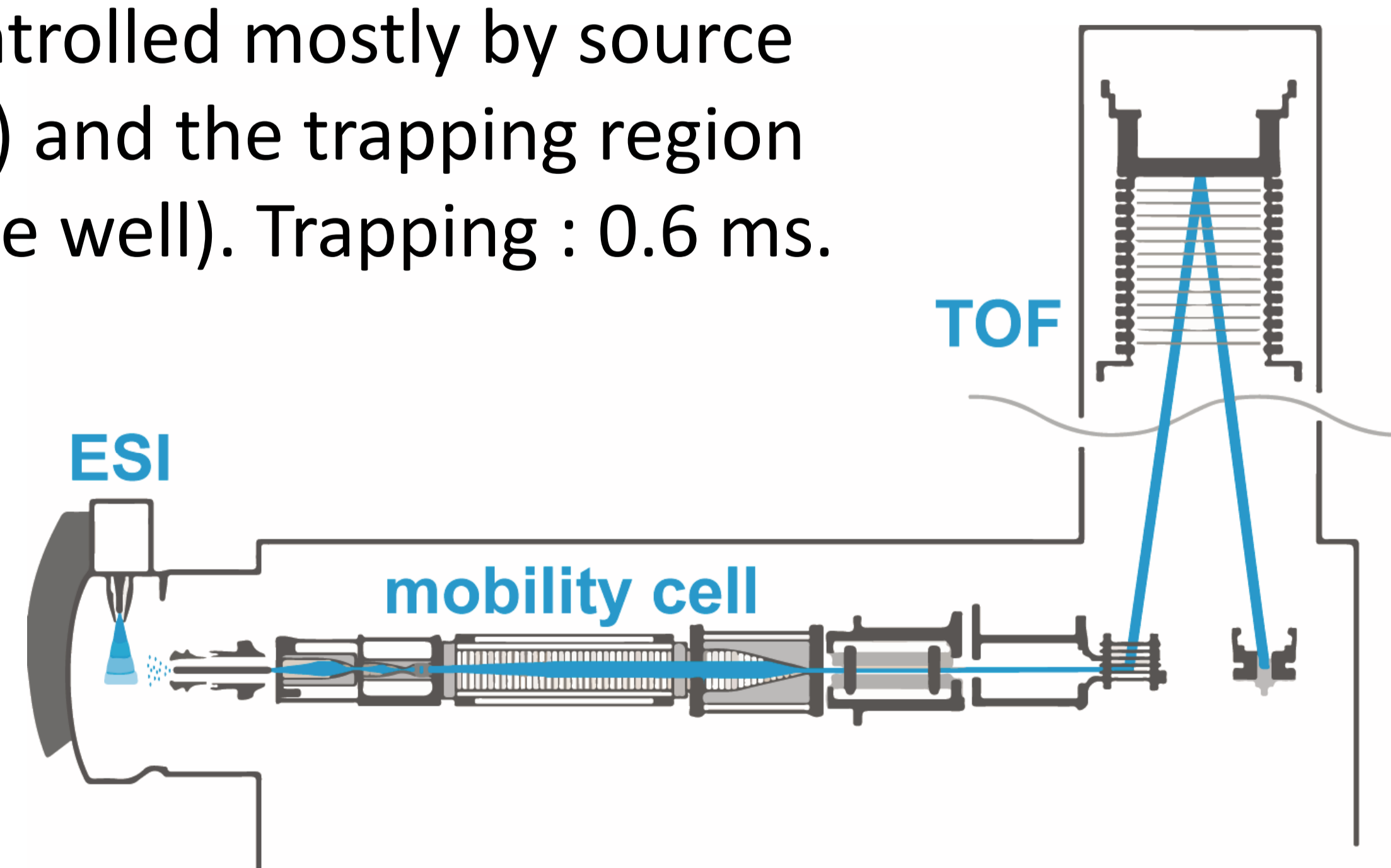
## Ion mobility experiments

→ DNA strands from Eurogentec, annealed in 100 mM NH<sub>4</sub>OAc, injected at 20 μM duplex, no organic co-solvents.

→ Agilent 6560 IMS-Q-TOF (drift tube IMS)

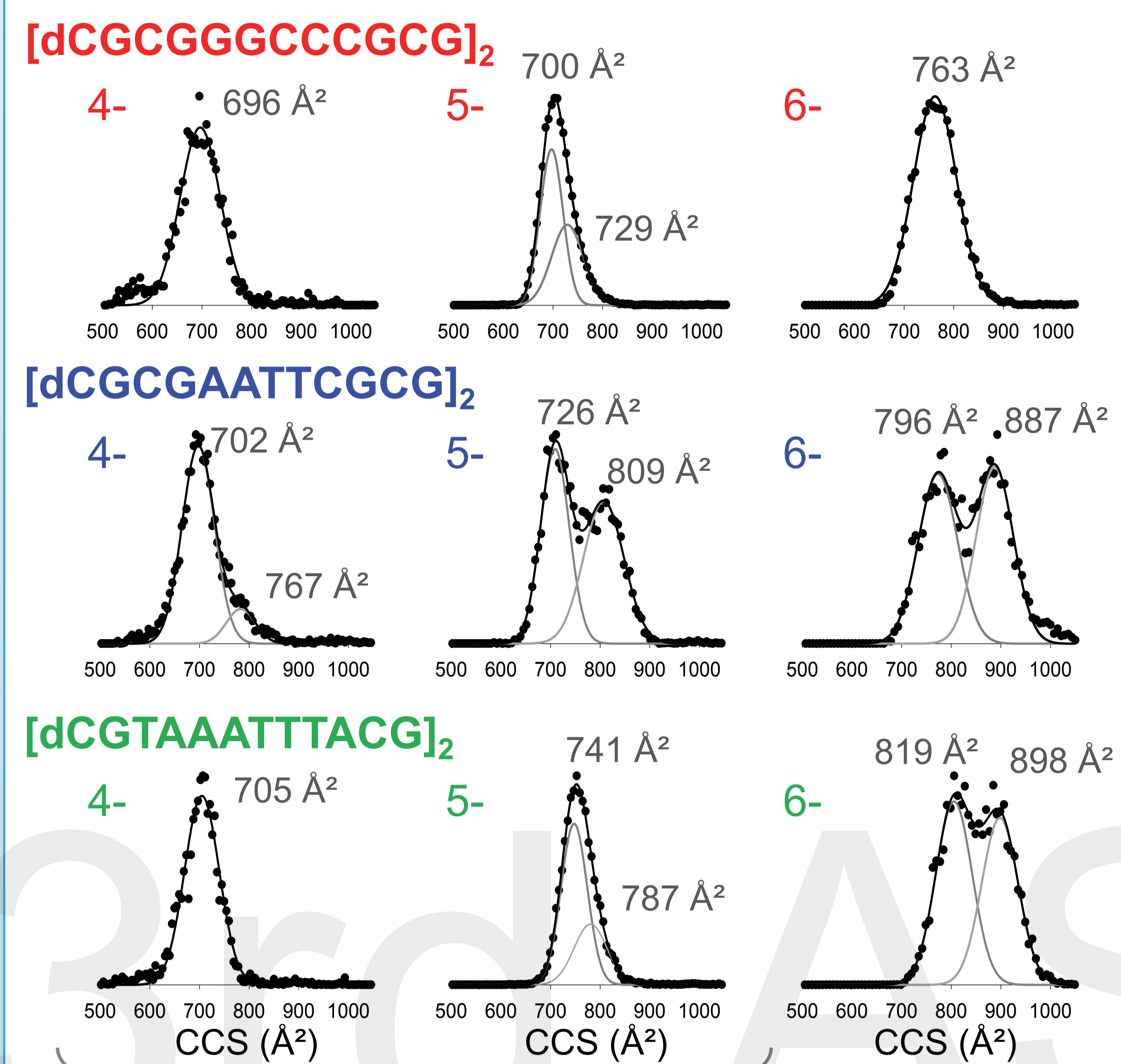
→ DTIMS operated in Helium, p = 3.85 mbar, T = 296 K.

→ Softness controlled mostly by source (fragmentor) and the trapping region (height of the well). Trapping : 0.6 ms.

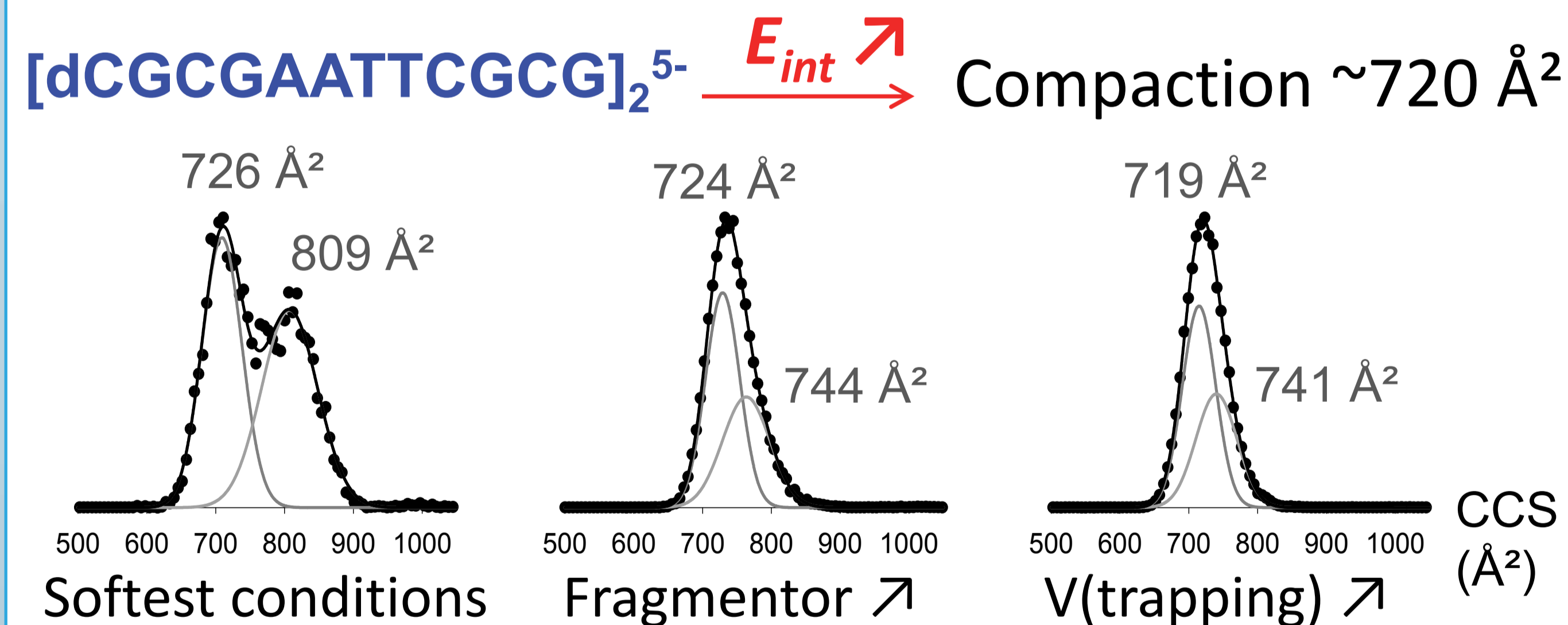


→ In those conditions, IMS performance tested on [TG<sub>4</sub>T]<sub>4</sub><sup>5-</sup> model is: resolution = 41, CCS accuracy better than 1%.

## DT-IMS experimental results



→ Native charge states are very compact (< 800 Å<sup>2</sup>)

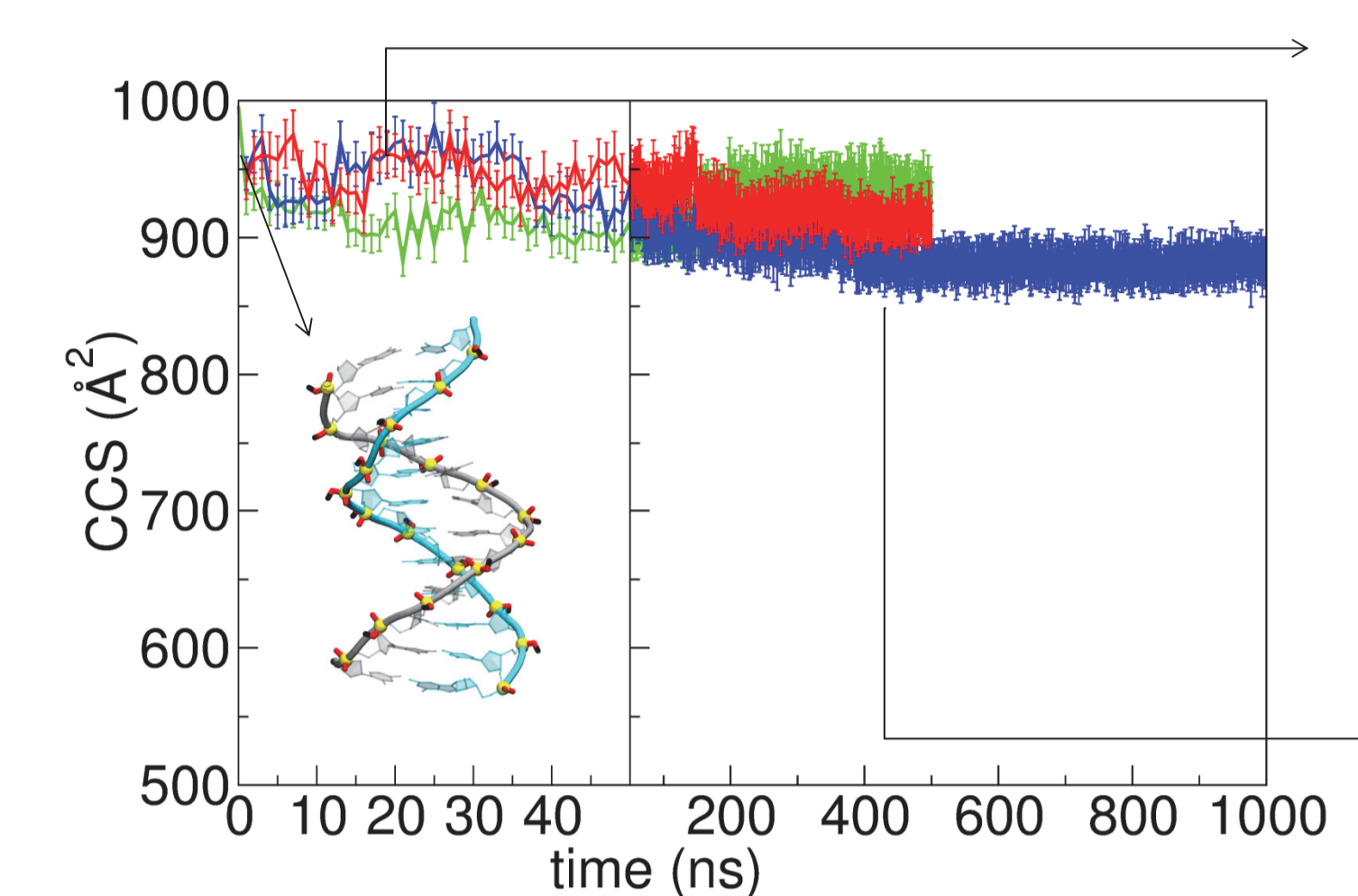


## Molecular modeling details

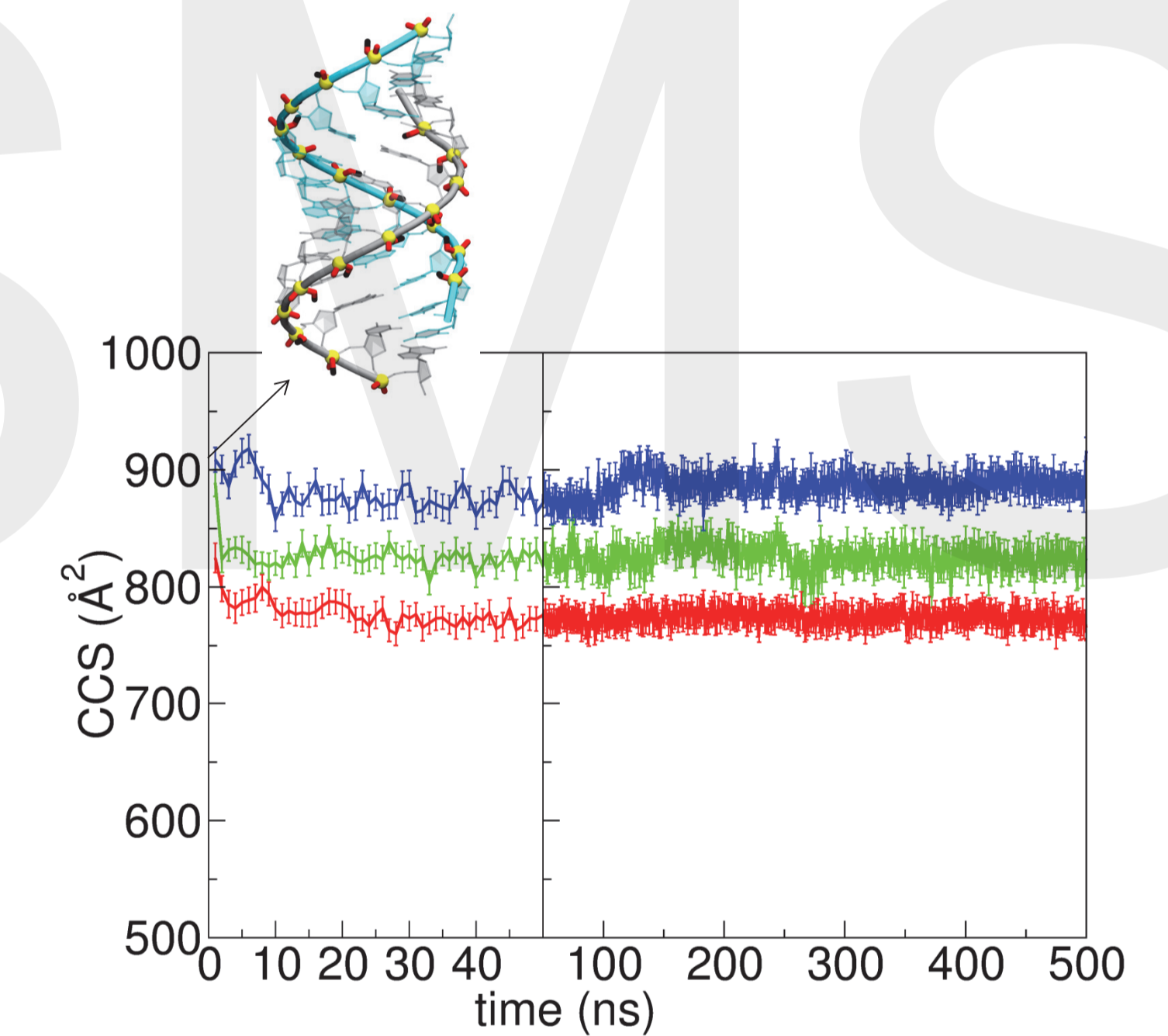
- Amber, parmBCS1 ff (Orozco *et al.*), *pmemd* module in solution, *sander* module in vacuo.
- Lowest energy protonation isomers compatible with 5- charge state were selected.
- Simulated annealing (globular conformations): 60 ps at 550 K, cooling to 0K, minimization.
- Major groove zipping: minimization with restrained H-bonds, then 1 μs free in gas phase.
- CCS Calc: EHSSrot, radii param of Siu *et al.*

## Modeling of DNA duplex gas-phase structure

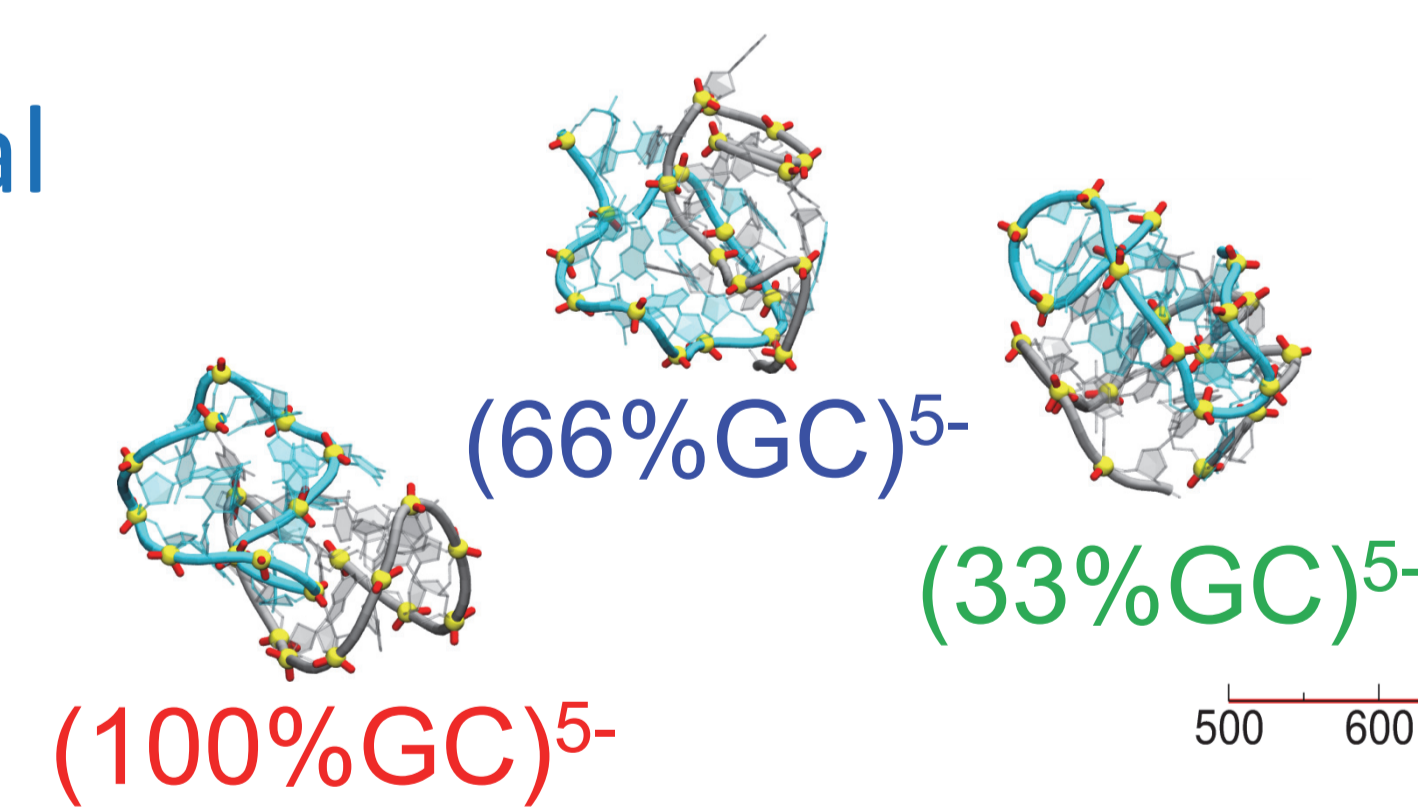
▶ **MD starting from B-helix?** Zipping of minor groove due to phosphate self-solvation. No match with experiment.



▶ **A-helix?** Better trend, but no quantitative match for native charge states 4- and 5-. Could be OK for 6-.



▶ **Globular?** Correct size but original H-bonding or stacking not preserved (contradicts past MS/MS results).



▶ **Major groove-zipped conformation?** Stable in the gas phase and has a CCS compatible with experiment on 4- and 5- ions.

