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What Happens to DNA Duplexes in the Gas Phase?

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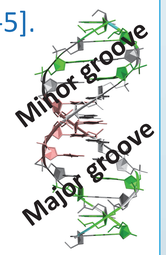
Key findings

→ 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 **$(12\text{-mer})_2$ 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).

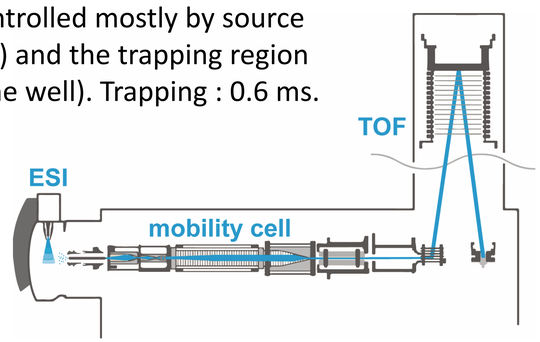
Ion mobility experiments

→ DNA strands from Eurogentec, annealed in 100 mM NH_4OAc, 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 $[TG_4T]_4^{5-}$ model is: resolution = 41, CCS accuracy better than 1%.

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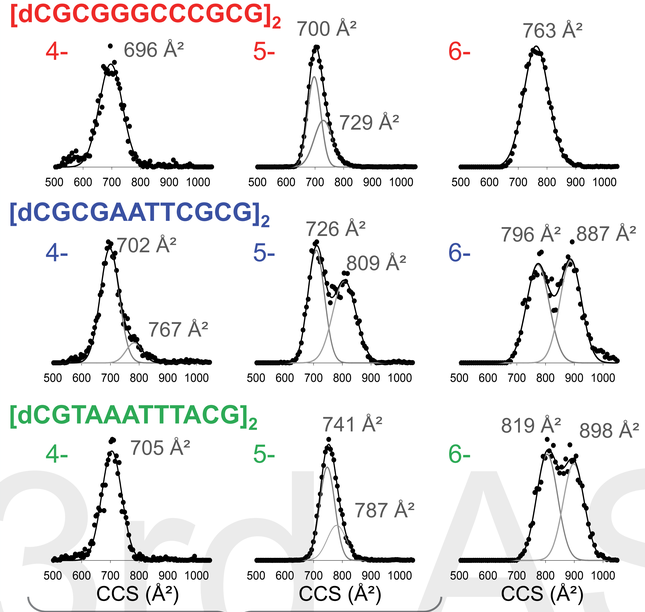
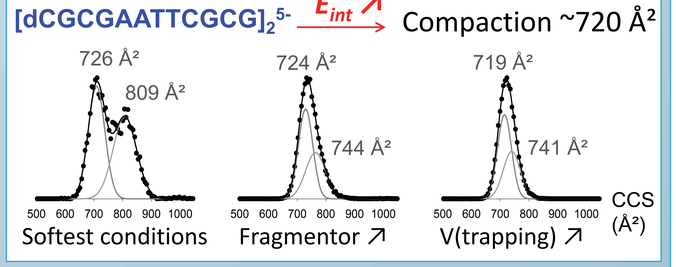
DT-IMS experimental results



→ Native charge states are very compact (< 800 Å²)



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.

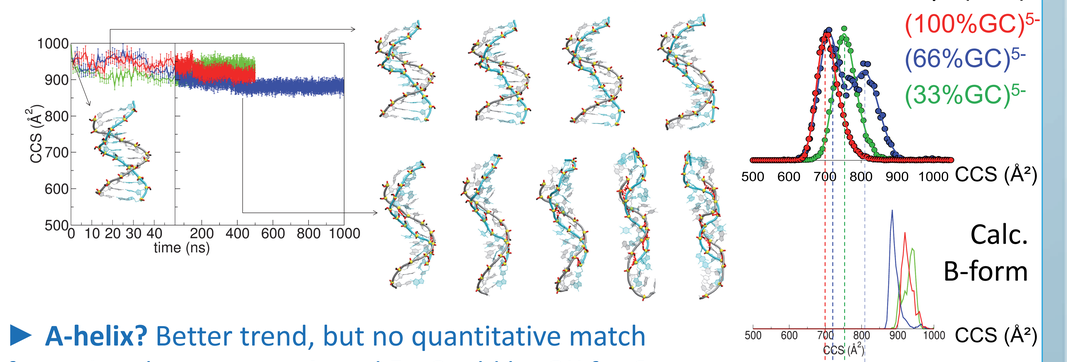
→ Simulated annealing (globular conformations): 60 ps at 550 K, cooling to 0K, minimization.

→ Major groove zipping: minimization with restrained H-bonds, then 1 µs free in gas phase.

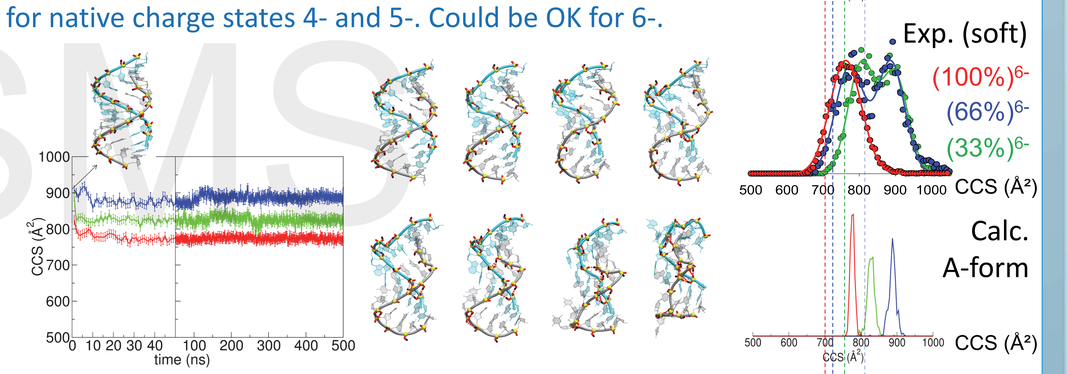
→ CCS Calc: EHSSrot, radii param of Siu *et al.*

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.

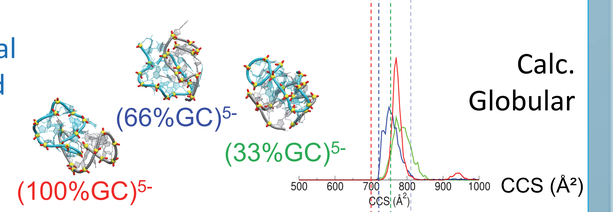
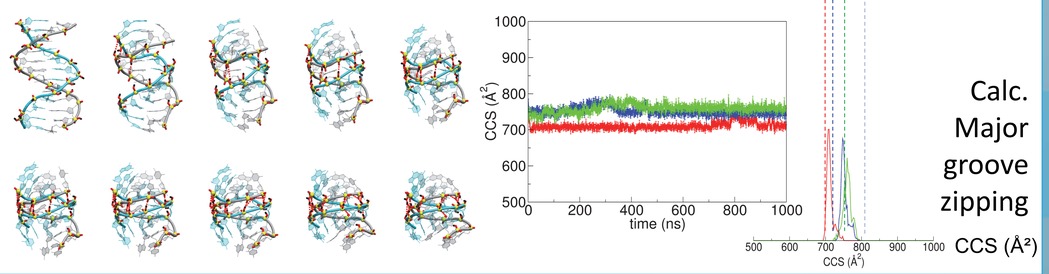


► **A-helix?** Better trend, but no quantitative match for native charge states 4- and 5-. Could be OK for 6-.



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

Simulated annealing →



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