

Measuring Circular Dichroism in a Mass Spectrometer

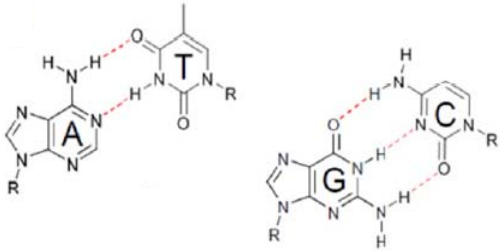
Valérie Gabelica
ARNA & IECB

Frédéric
Rosu

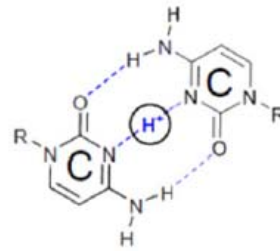
Steven
Daly



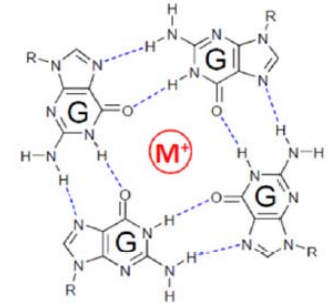
DNA folding and self-assembly



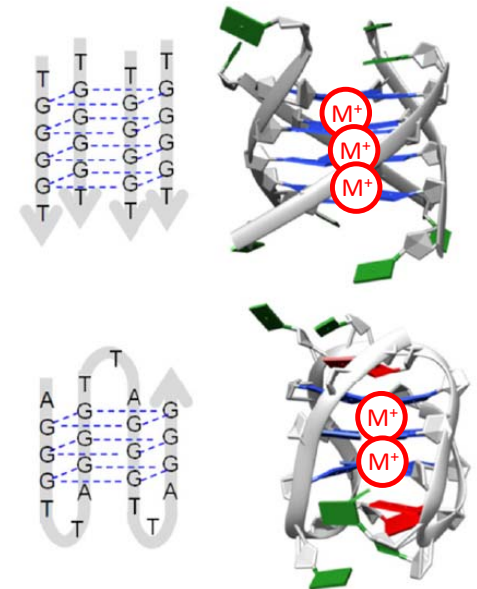
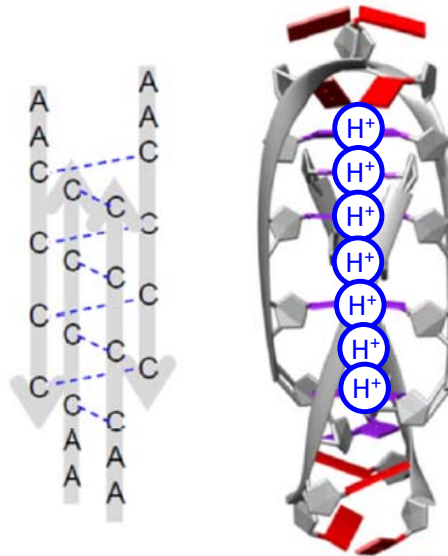
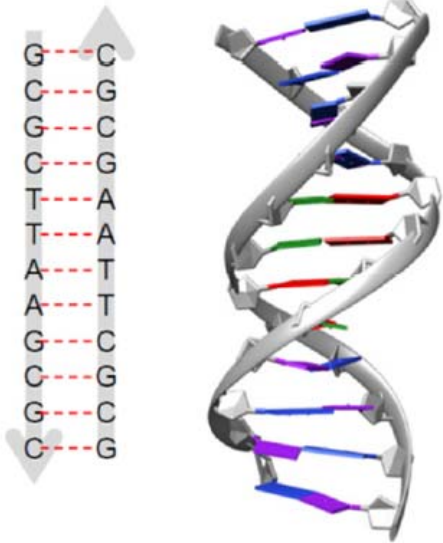
Base pairs
→ double helix



Hemiprotonated cytosine
base pairs → i-motif DNA

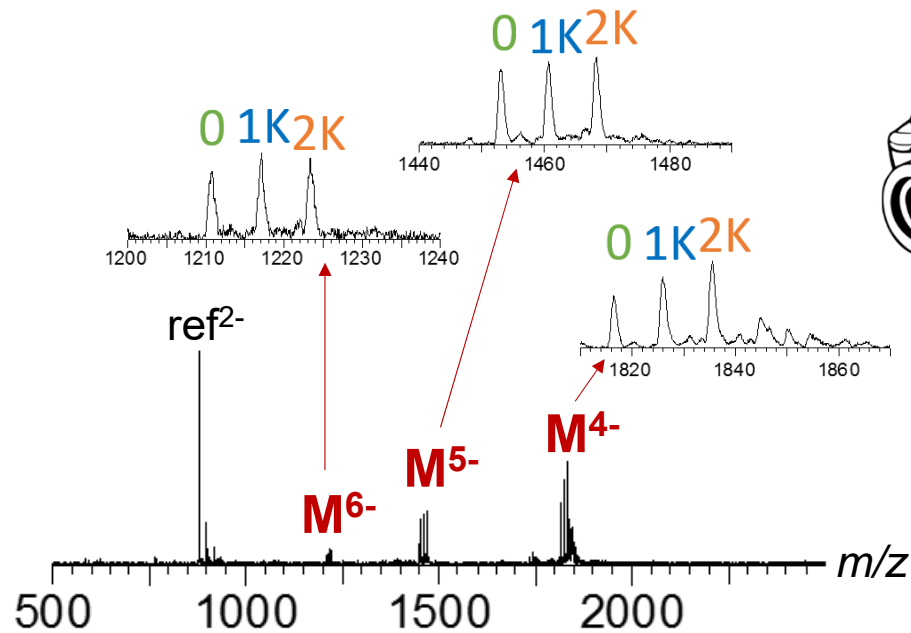
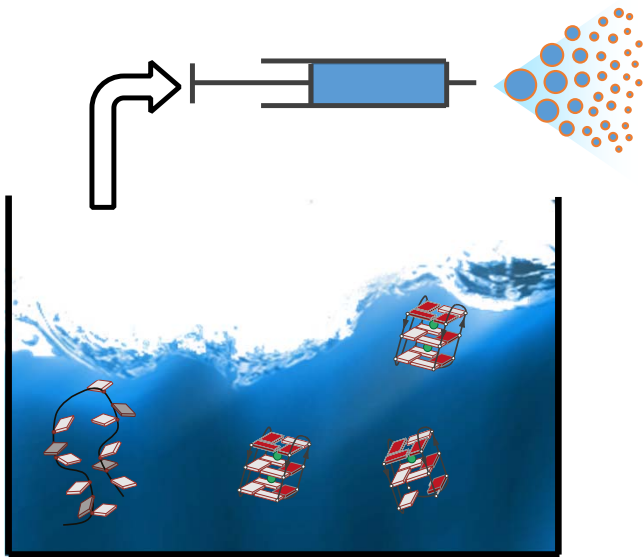


Guanine quartets
→ G-quadruplex



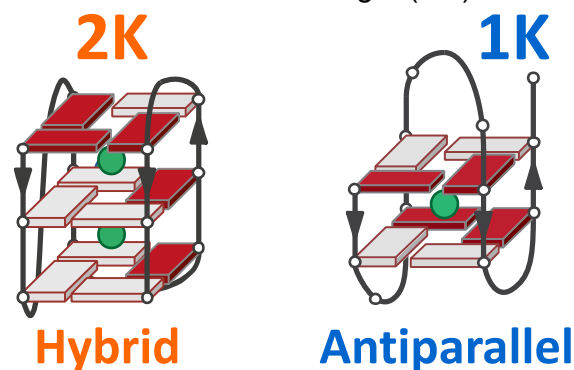
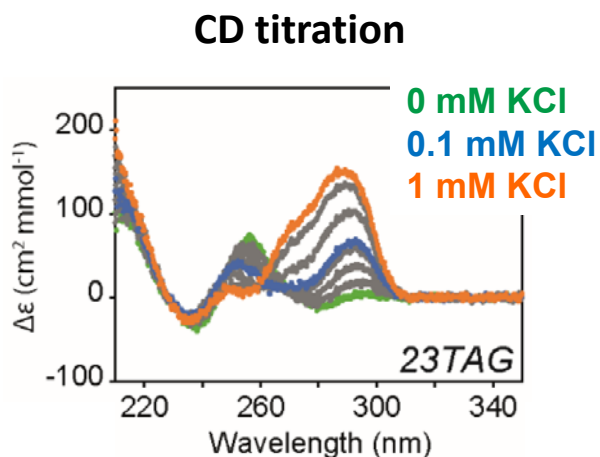
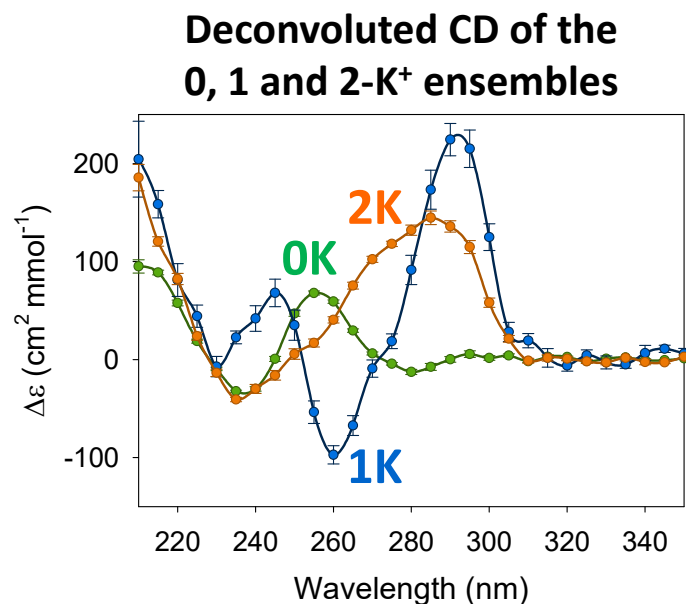
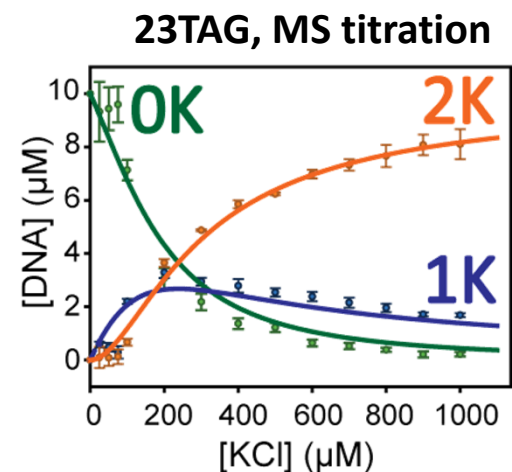
Nucleic Acids Biophysics with Mass Spectrometry

ESI-MS separates and quantifies coexisting solution species



5 μ M dTAGGGTTAGGGTTAGGGTTAGGG
200 μ M KCl
100 mM trimethylammonium acetate

Complementarity between CD spectroscopy and MS

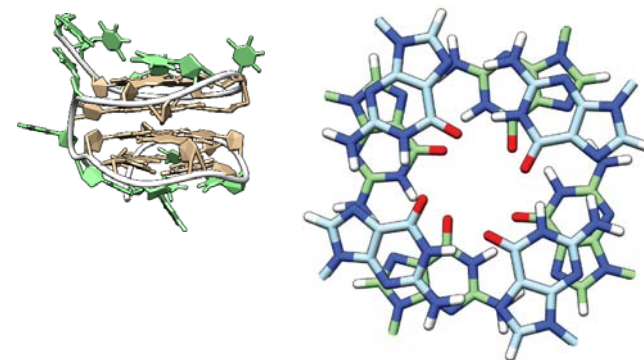
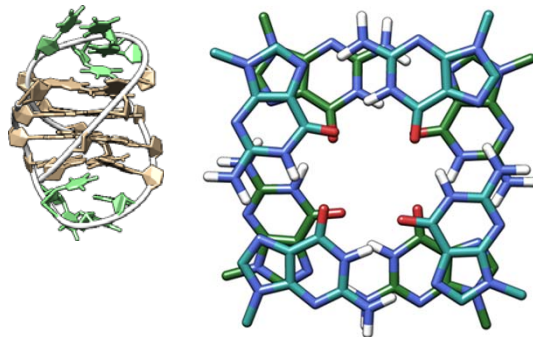
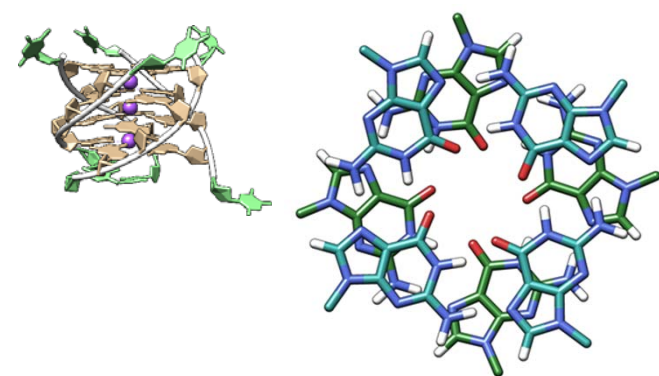


Marchand & Gabelica
Nucleic Acids Res.
(2016) 44, 10999.

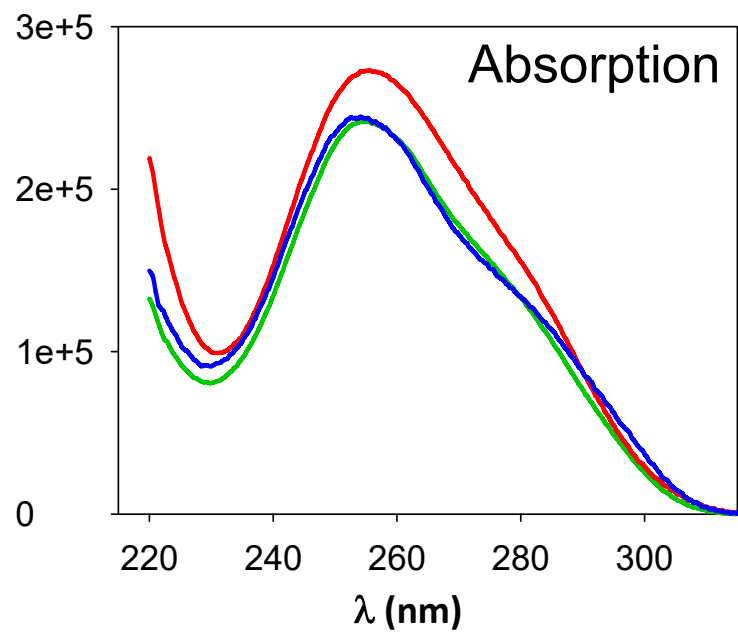
[dTGGGGT]₄

[dGGGGTTTTGGGG]₂

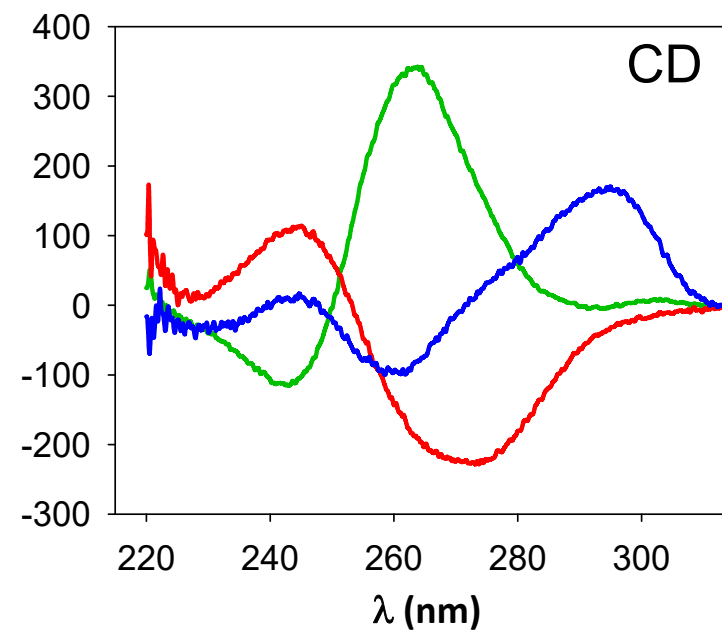
dT(GGT)₄TG(TGG)₃TGTT



ϵ ($M^{-1}cm^{-1}$)

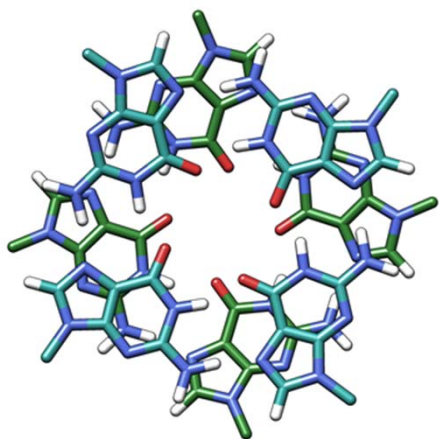


$\Delta\epsilon$ ($M^{-1}cm^{-1}$)

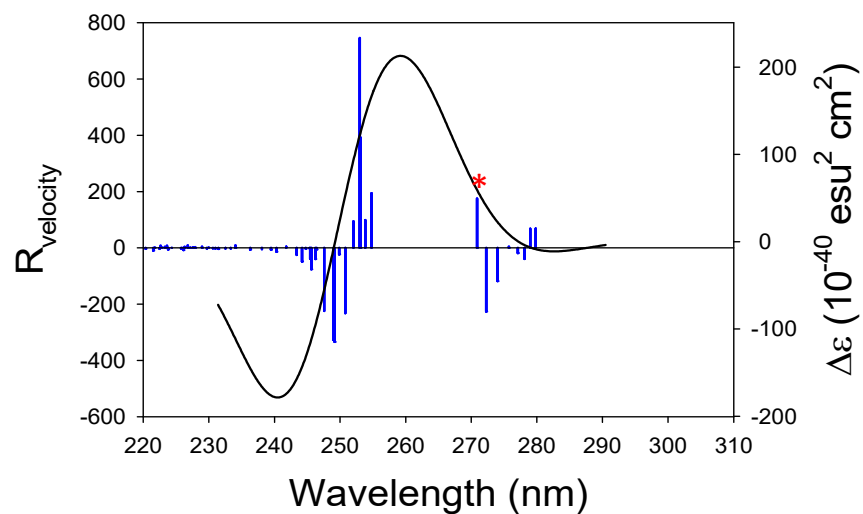
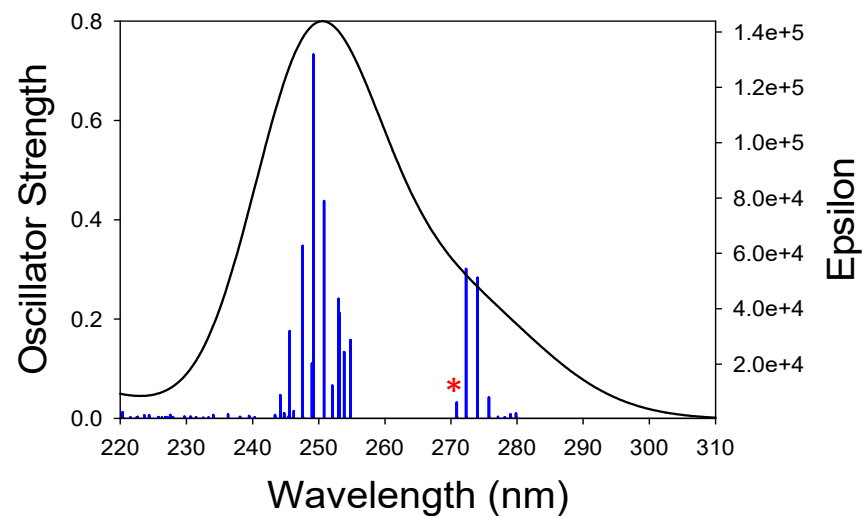


Origin of CD in G-quadruplexes

e.g. homopolar stacking, rotation angle defined by right-handed DNA backbone

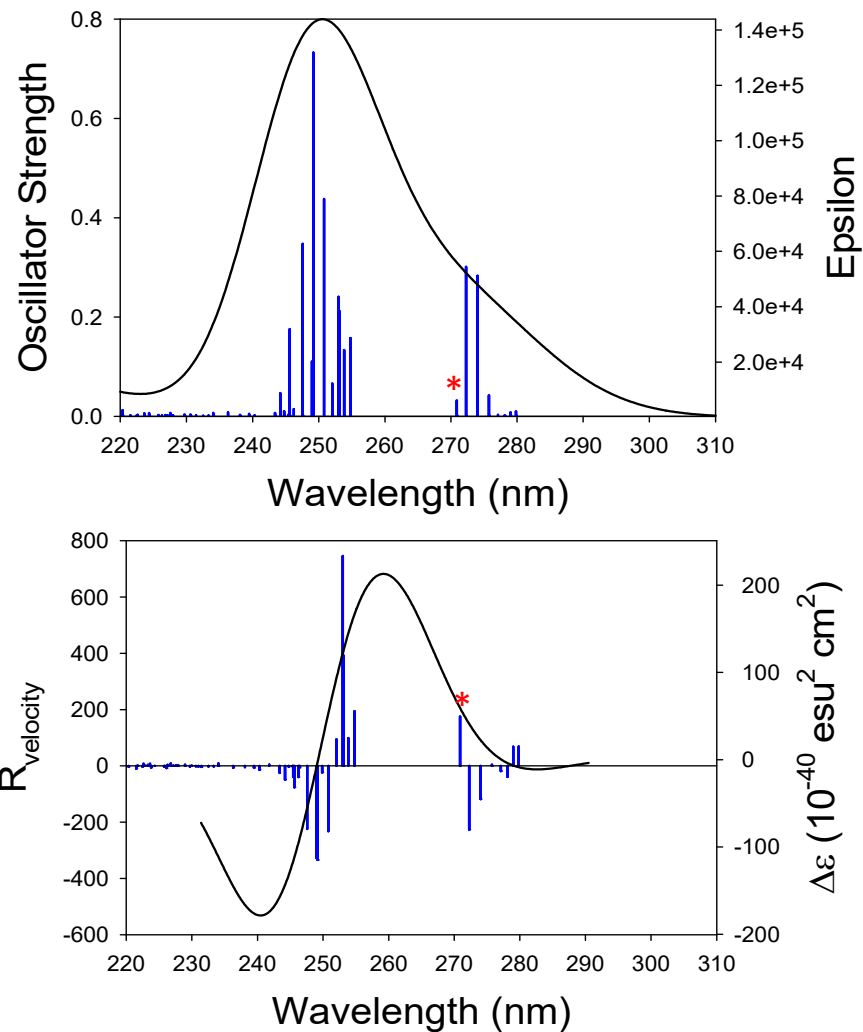
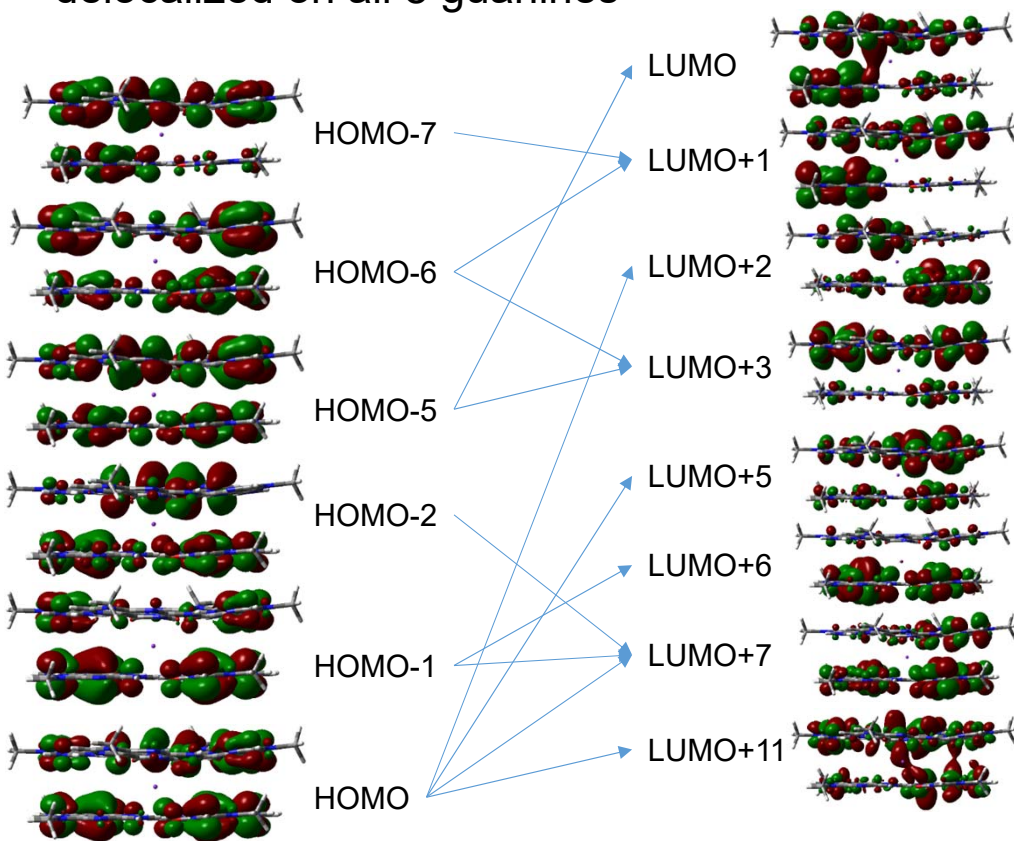


TD-DFT, 130 states
M06-2X/6-31G* GD3
Energy scaling factor: 0.88

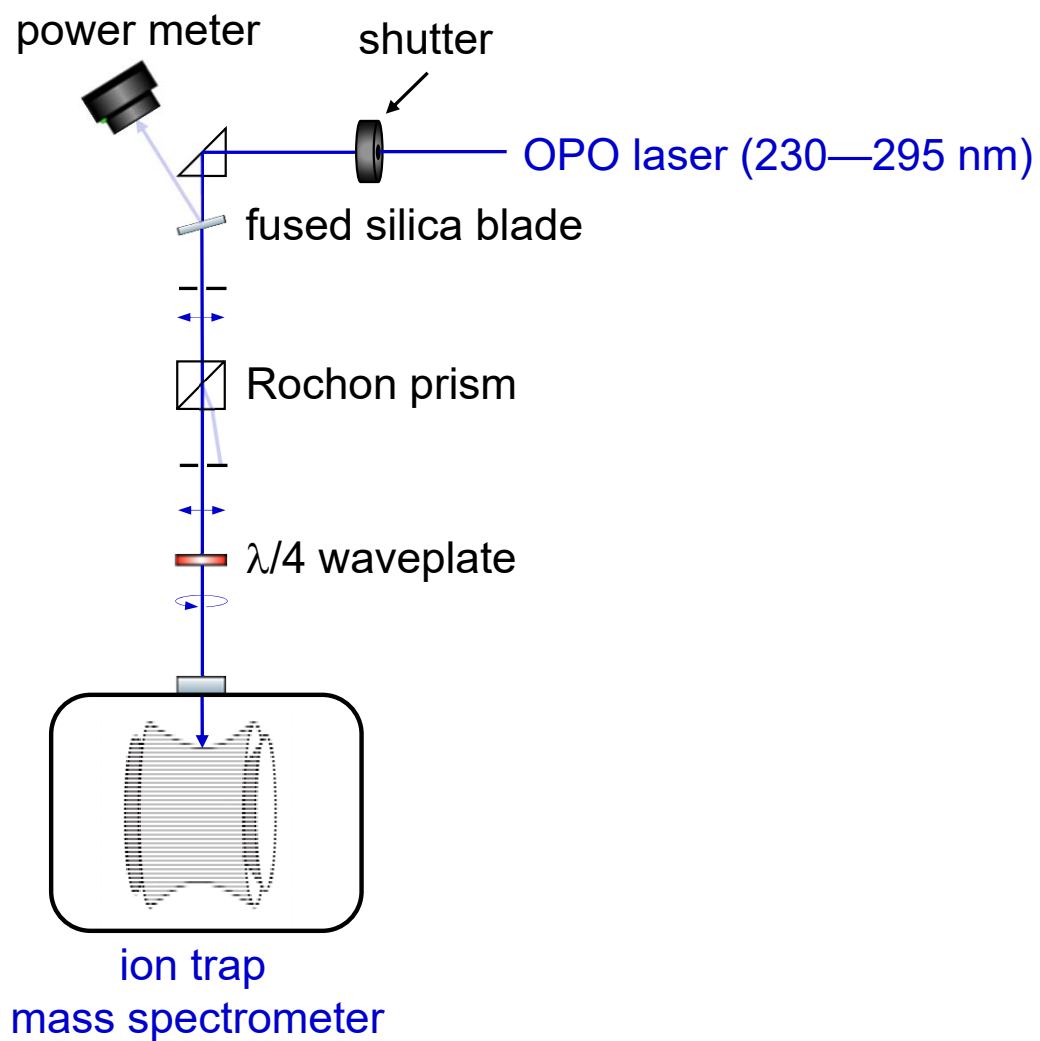
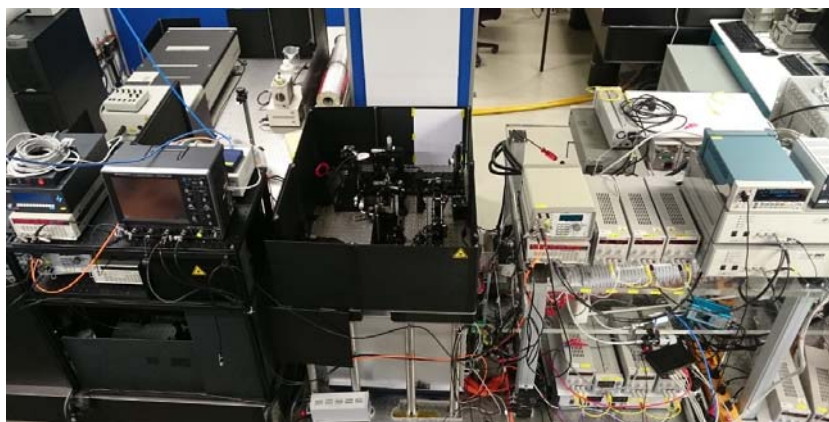


Origin of CD in G-quadruplexes

270 nm transition*:
Many molecular orbitals involved,
delocalized on all 8 guanines

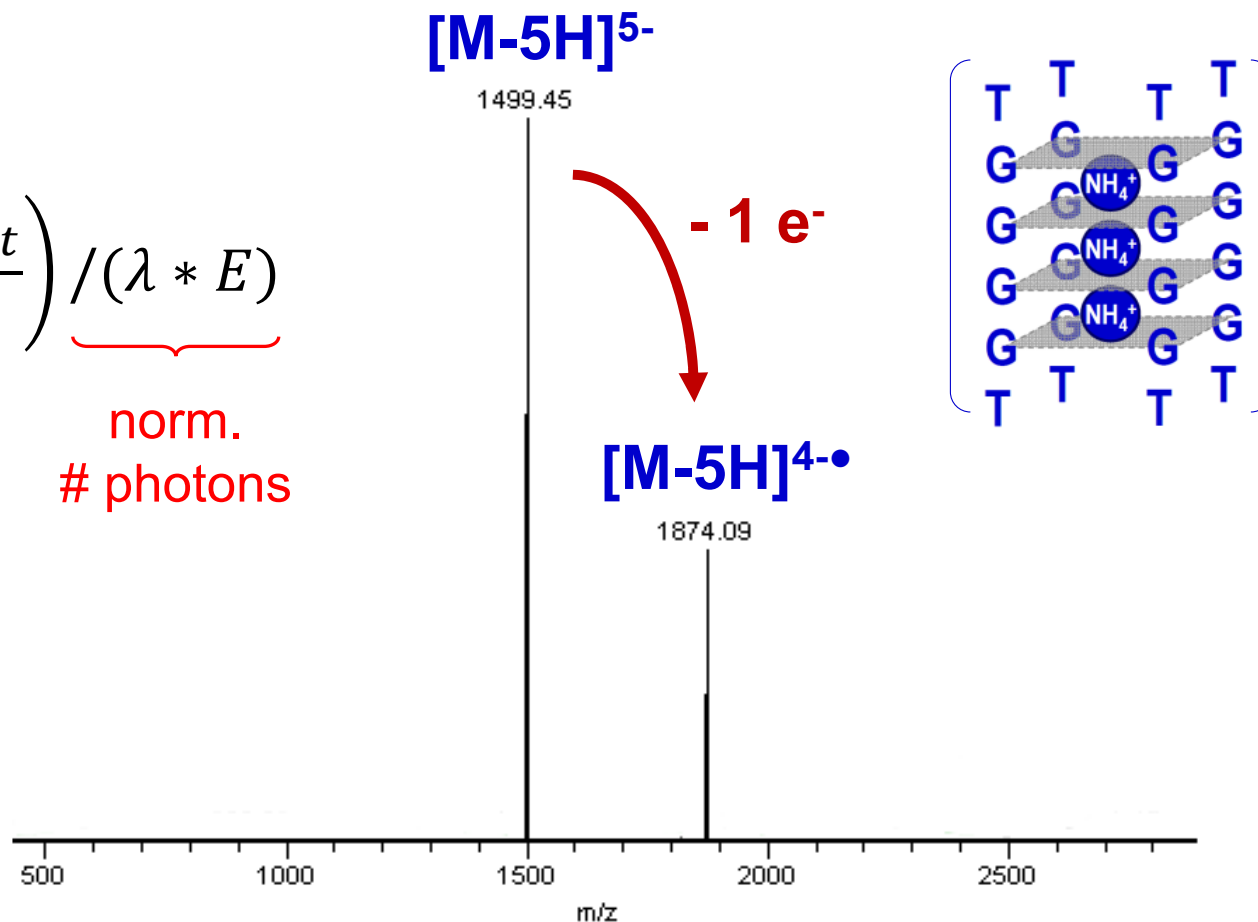


« 2-in-1 » Circular dichroism mass spectrometry

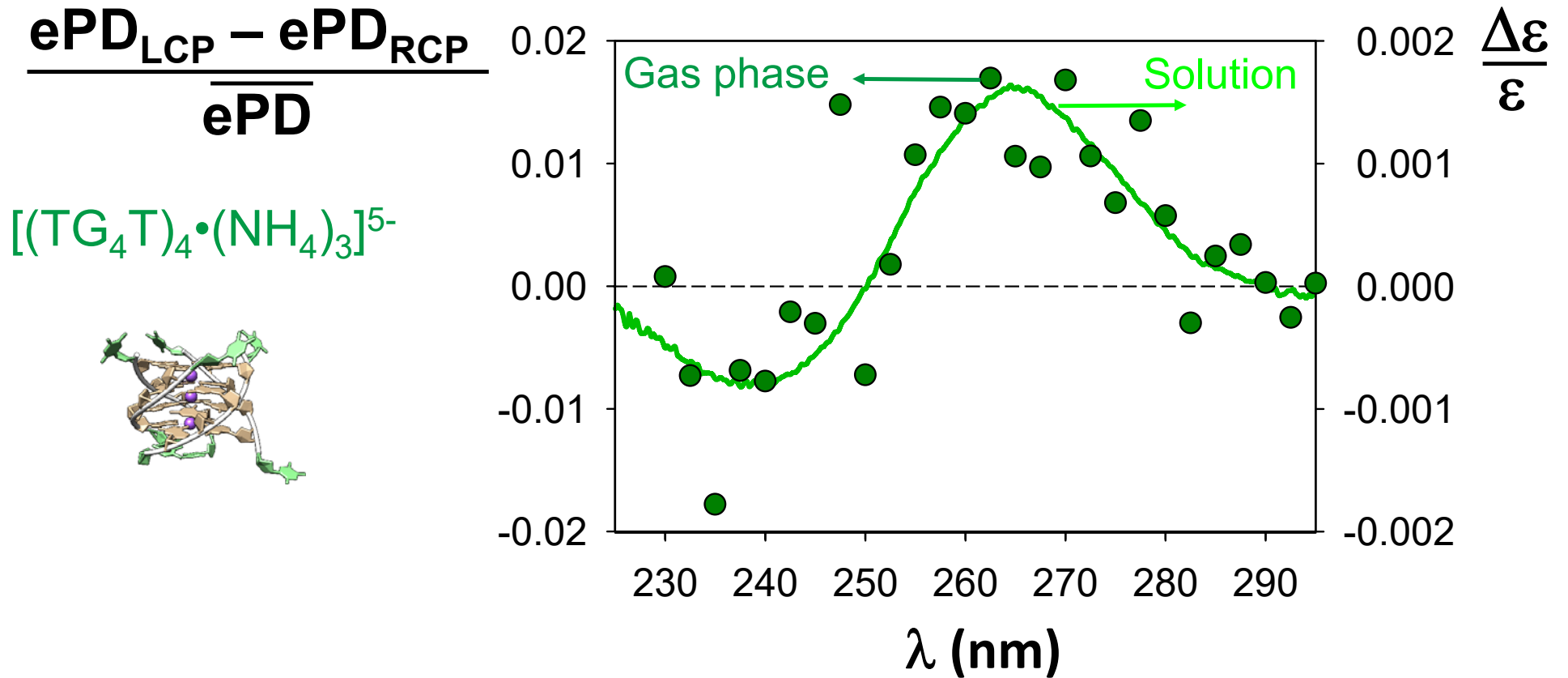


Electronic Action Spectroscopy of Gas-Phase DNA

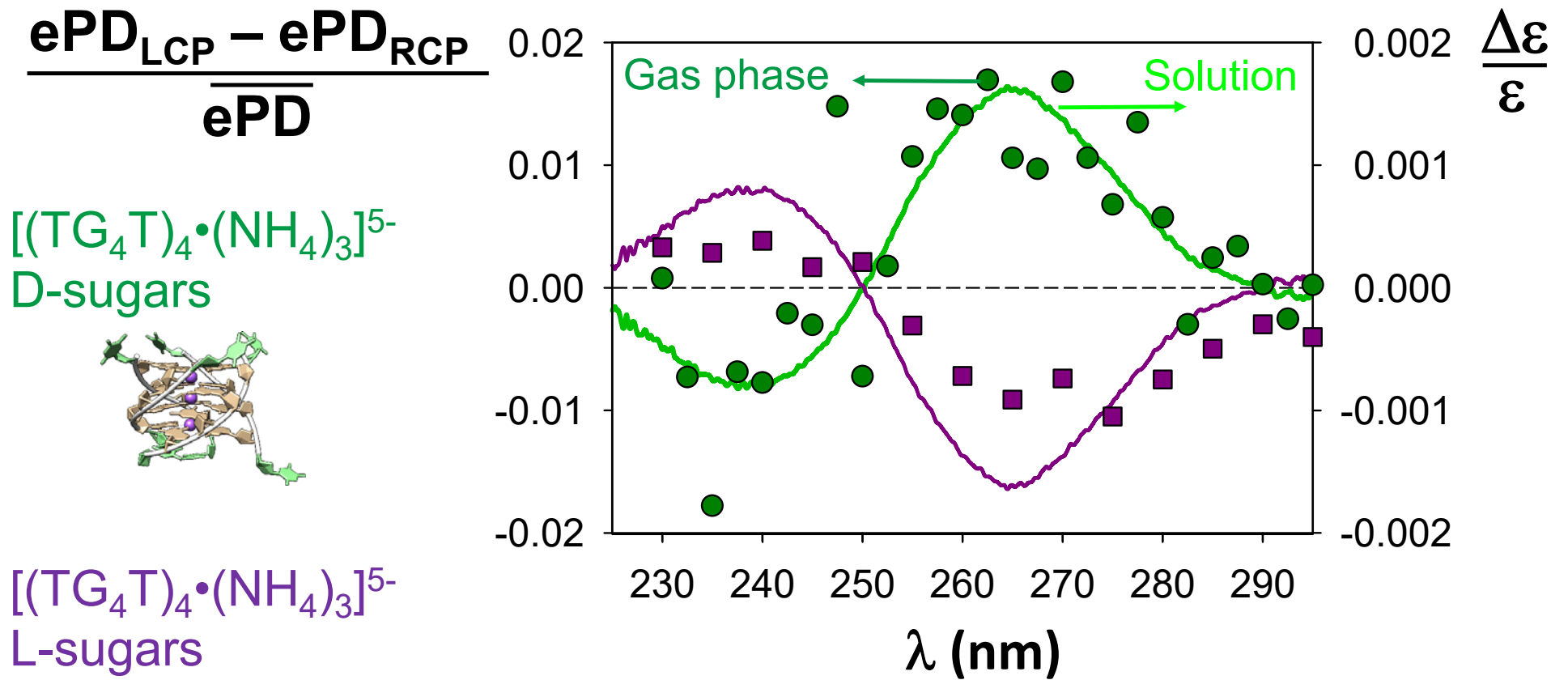
$$ePD = -\log\left(\frac{I_{parent}}{I_{total}}\right) / \underbrace{(\lambda * E)}_{\substack{\text{norm.} \\ \# \text{ photons}}}$$



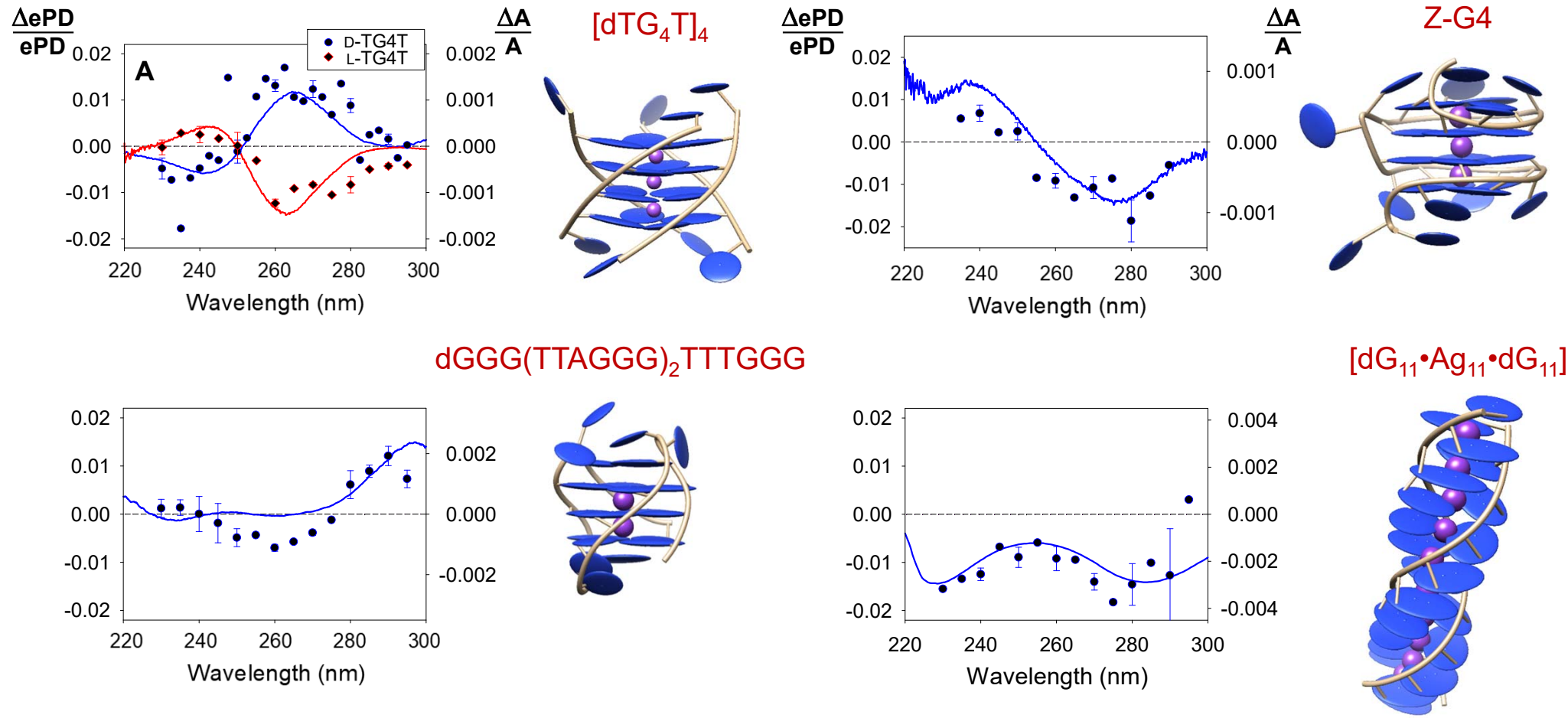
CD Spectroscopy of $[\text{dTG}_4\text{T}]_4$ G-quadruplex DNA



CD Spectroscopy of $[\text{dTG}_4\text{T}]_4$ G-quadruplex DNA

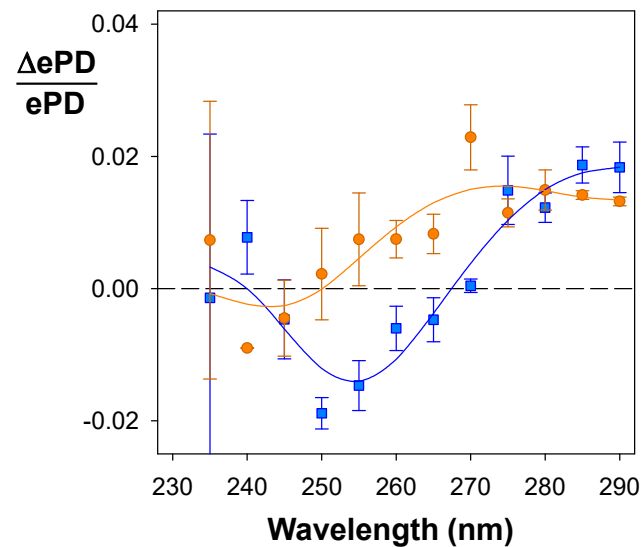
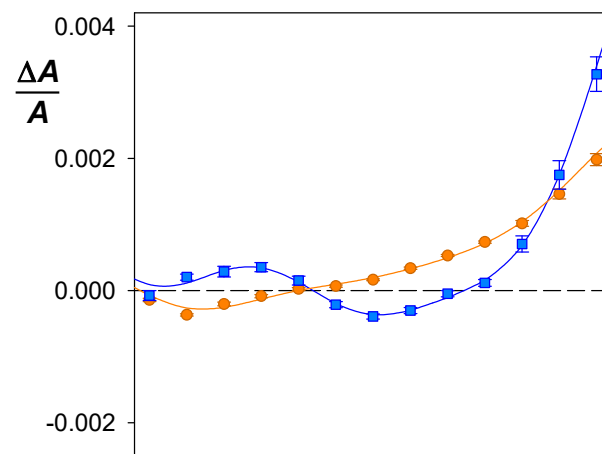
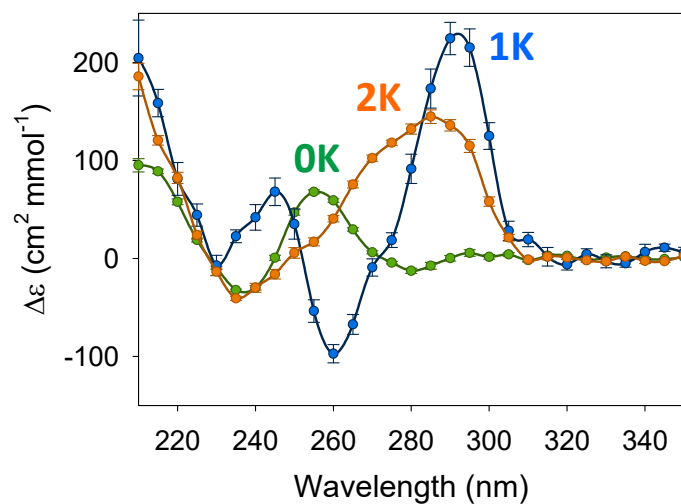
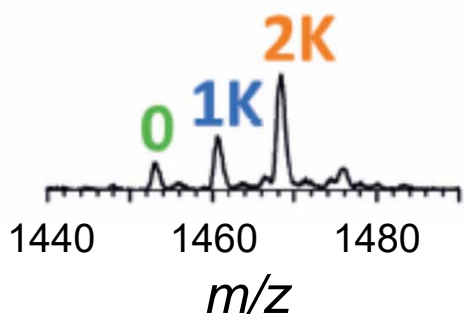


Gas-phase spectra (dots) resemble solution spectra (lines)



Daly, Rosu & Gabelica, *Science* (2020) 368, 1465

CD of isolated complexes



What made CD action spectroscopy feasible:

- **Paul trap** configuration to avoid reflexions and preserve the **circular light polarization**
- ePD on polyanions to have a **monophotonic action** and good statistics
- **Electron photodetachment** on nucleic acids responded particularly well to the CD effect