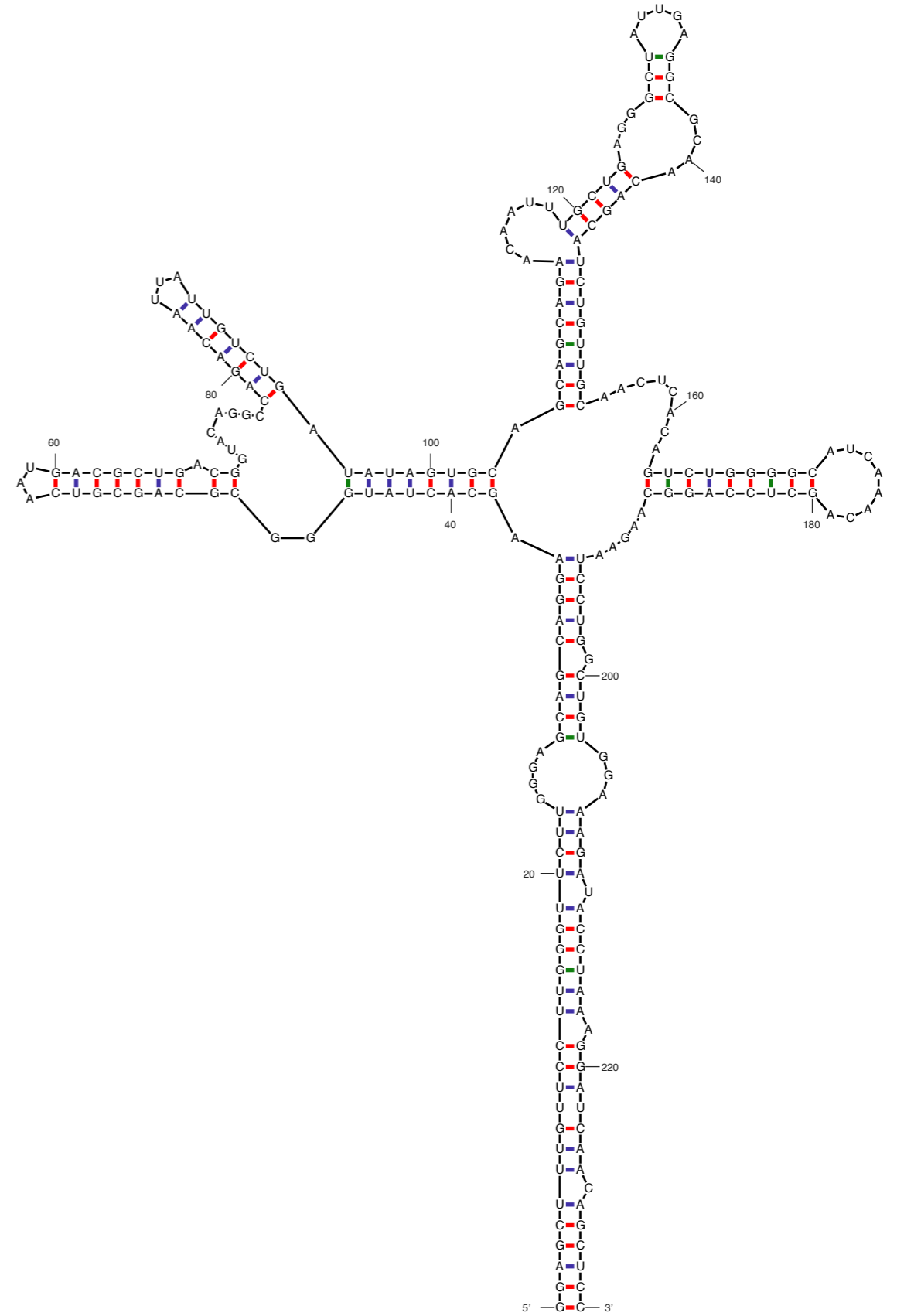
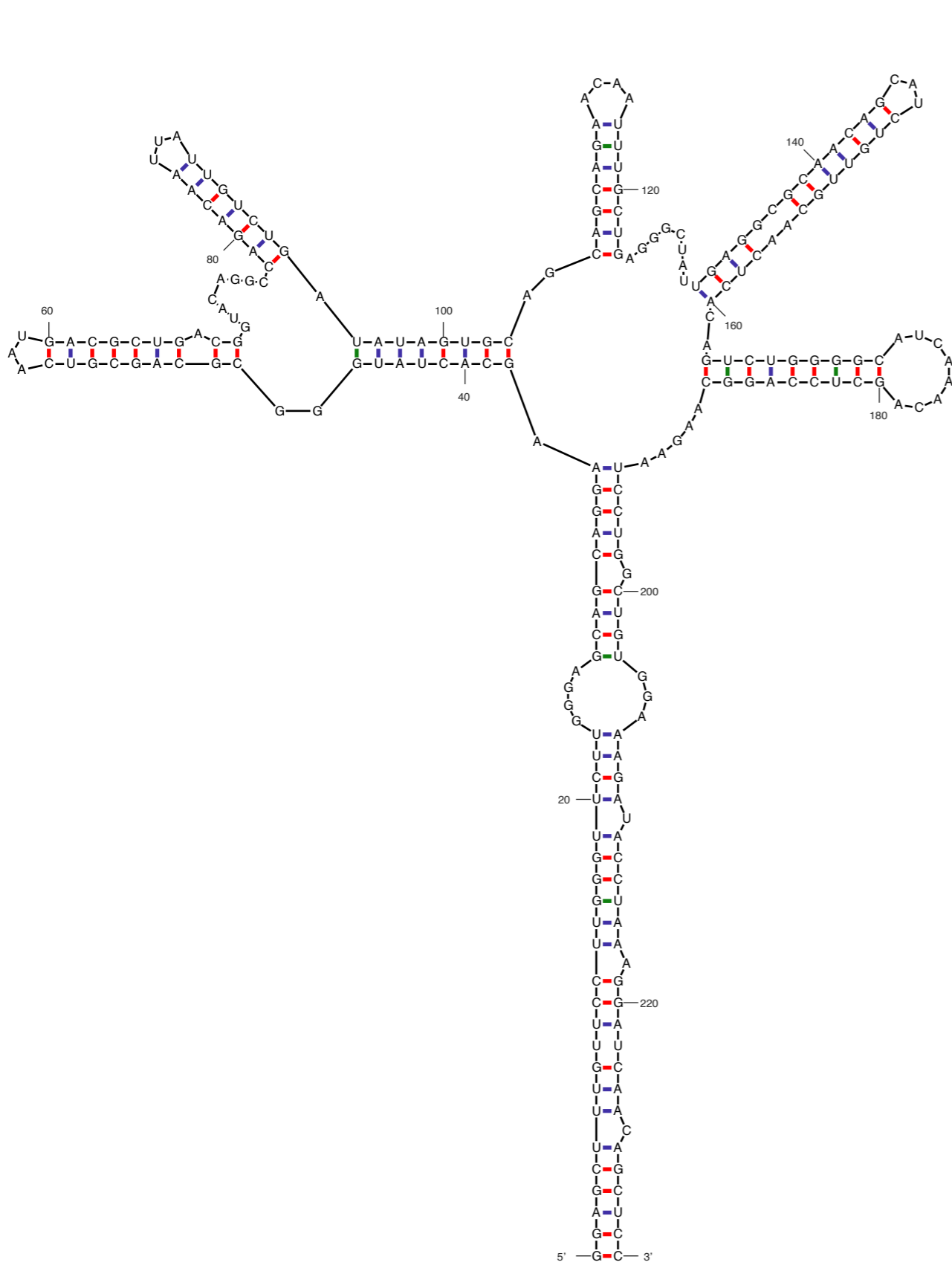
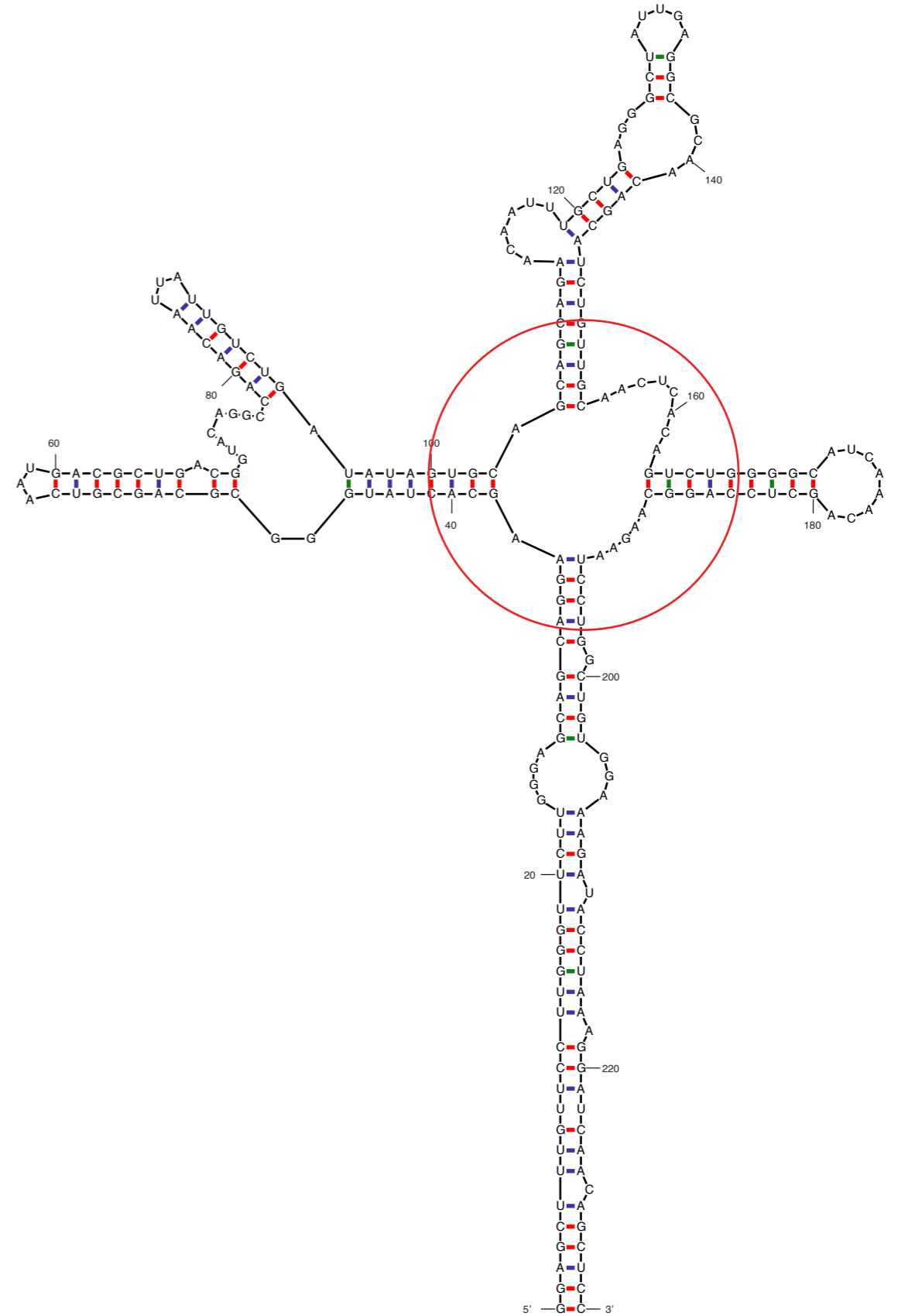
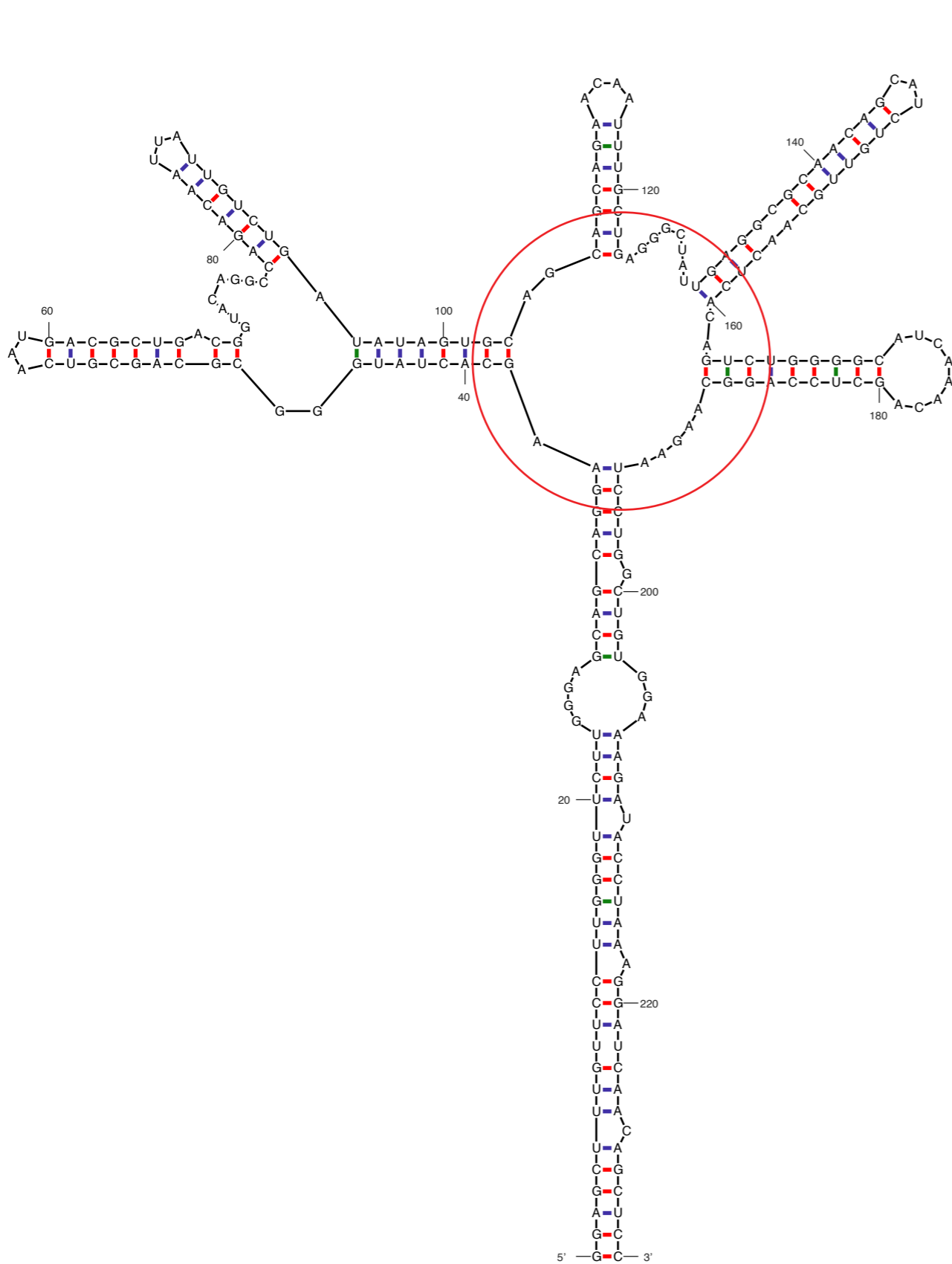


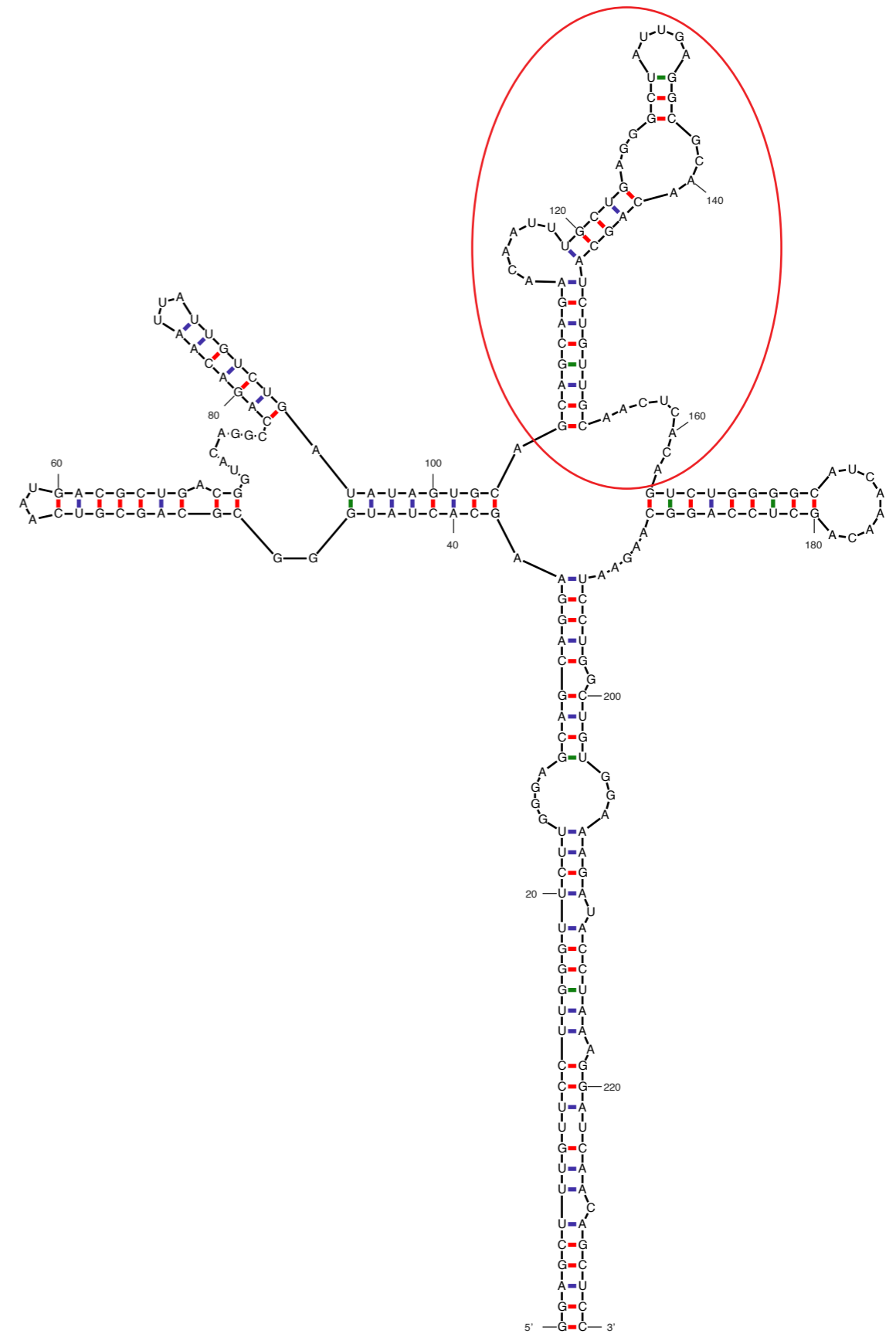
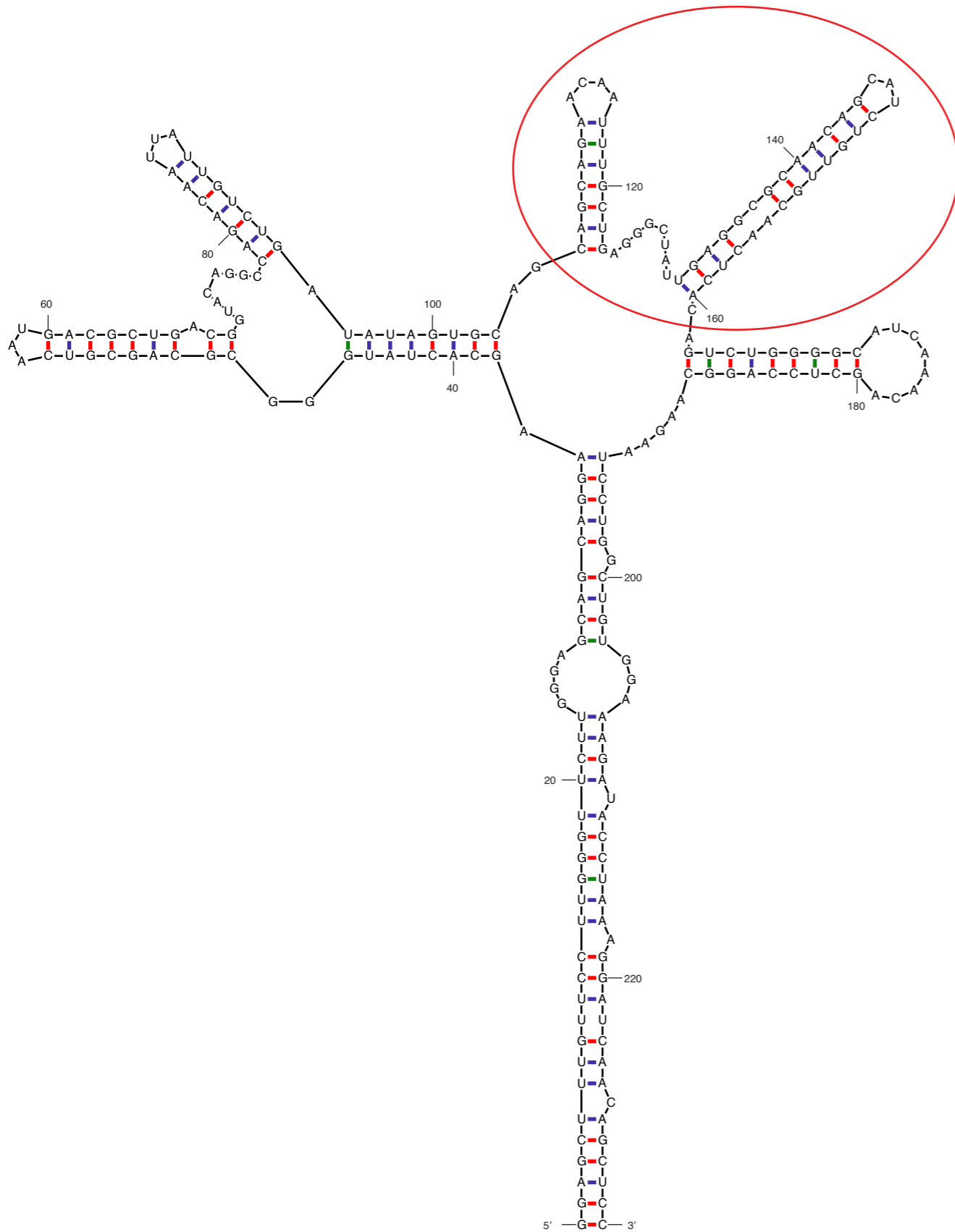
Structure(s) of the RRE and functional implications



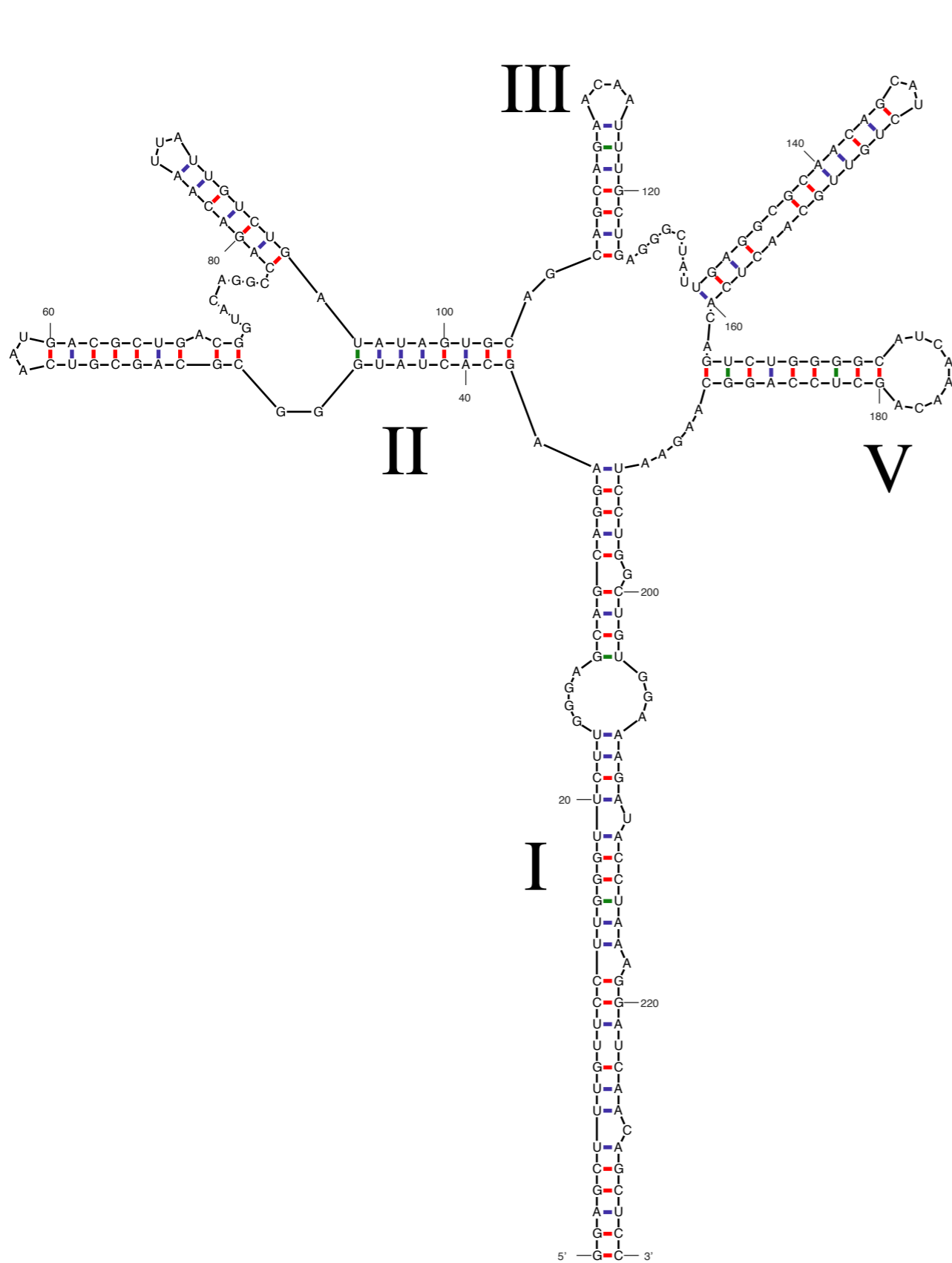
Structure(s) of the RRE and functional implications



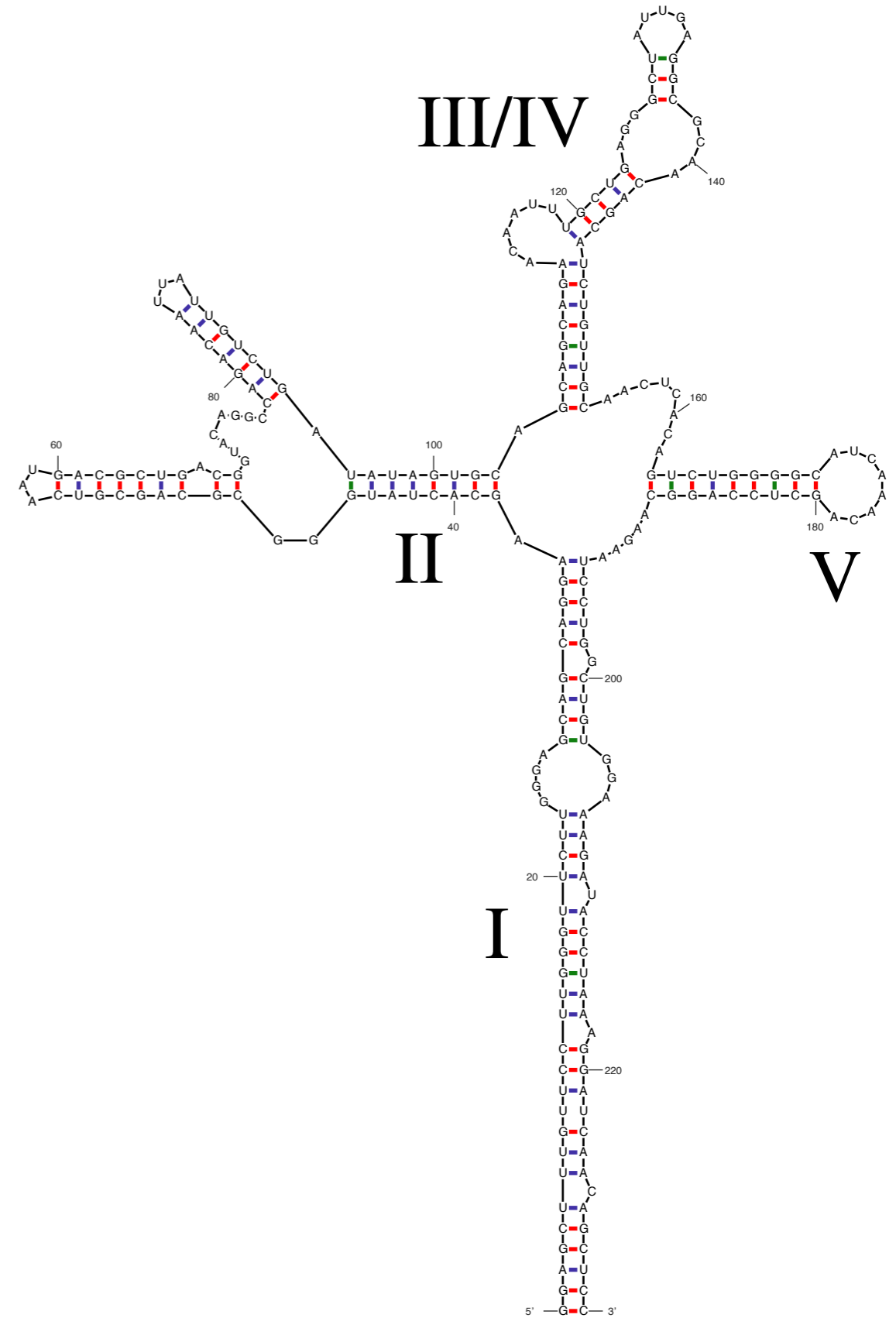
Structure(s) of the RRE and functional implications



Structure(s) of the RRE and functional implications



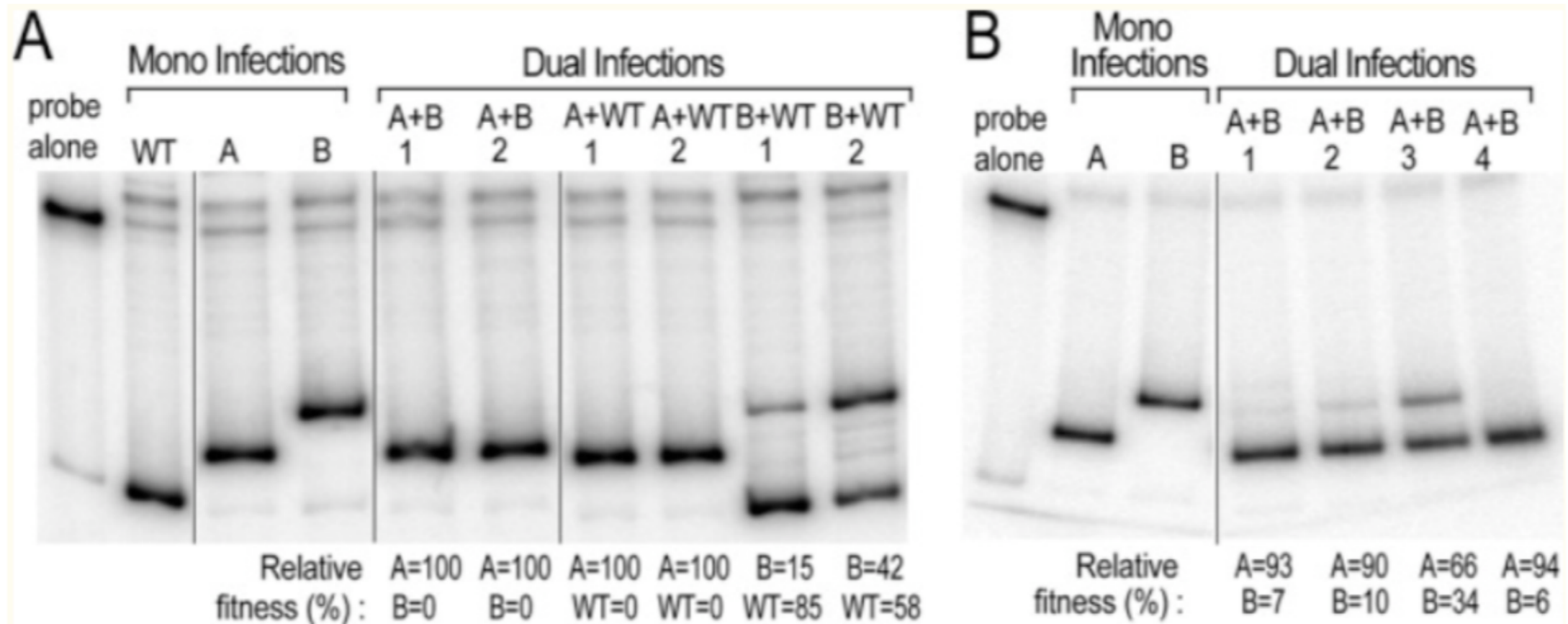
"5 stem"



"4 stem"

Does conformation matter?

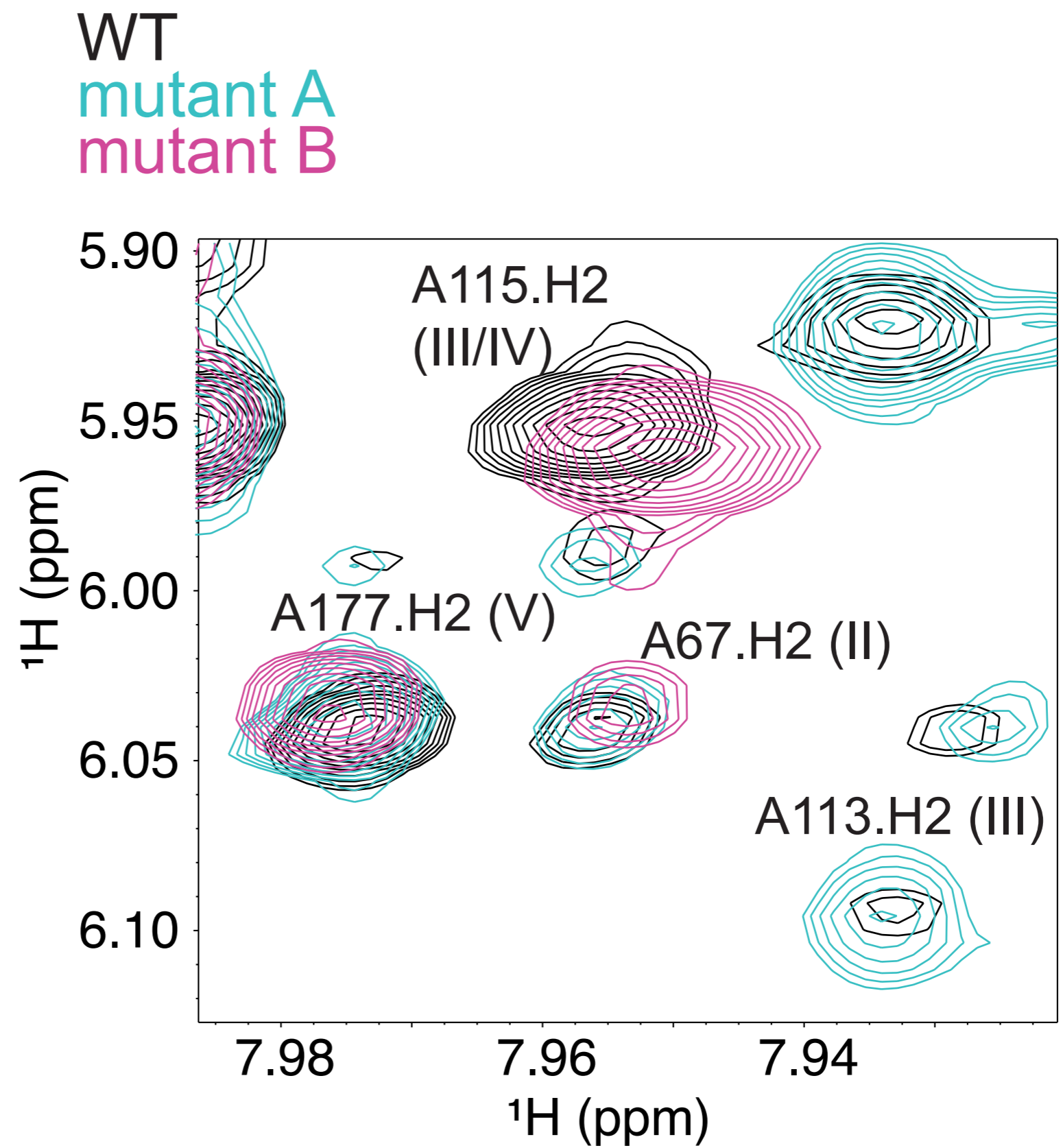
- local structure of high affinity Rev binding sites not perturbed



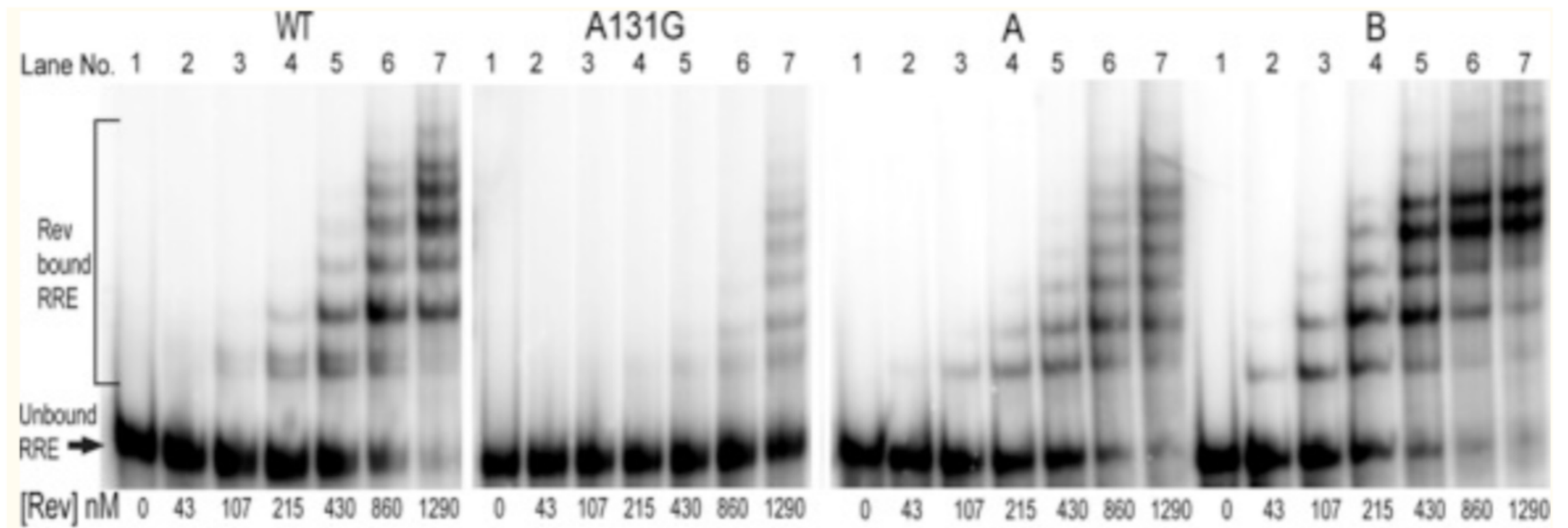
Competition growth experiments demonstrate a replicative advantage for virus containing a 5 SL RRE

Sherpa, C., *et al. Nucleic Acids Research*, 2015, 43 (9), 4676-4686.

Mutants recapitulate WT folds

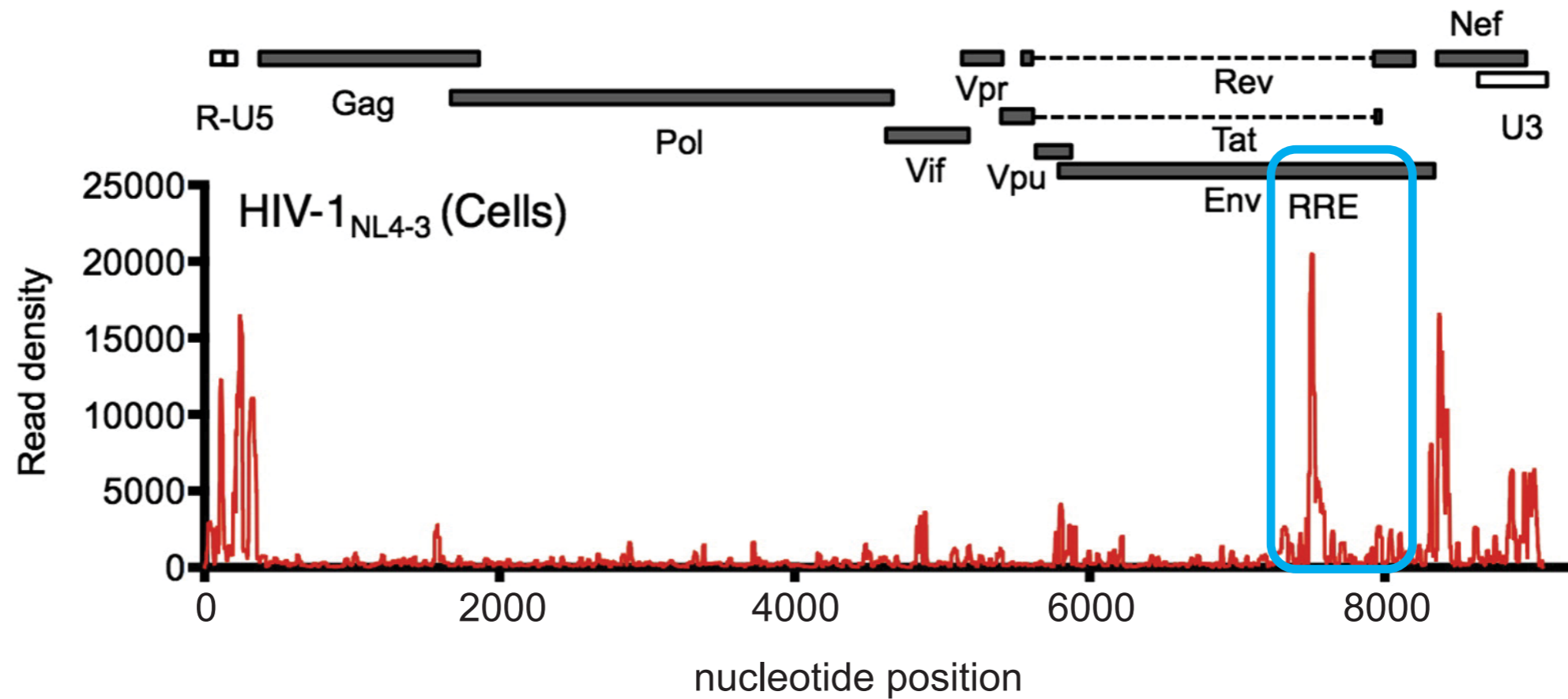


Primary binding of Rev to the RRE and multimerization are largely unaffected by conformation



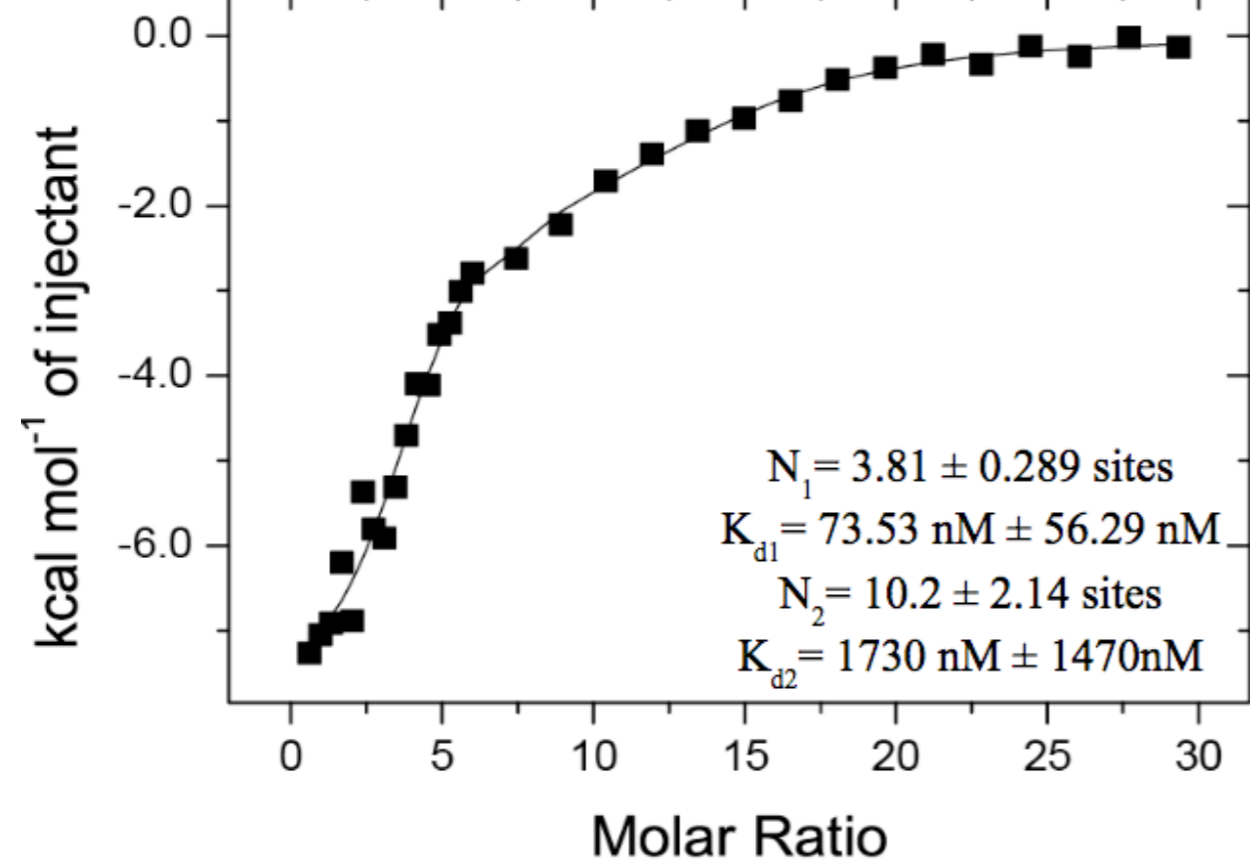
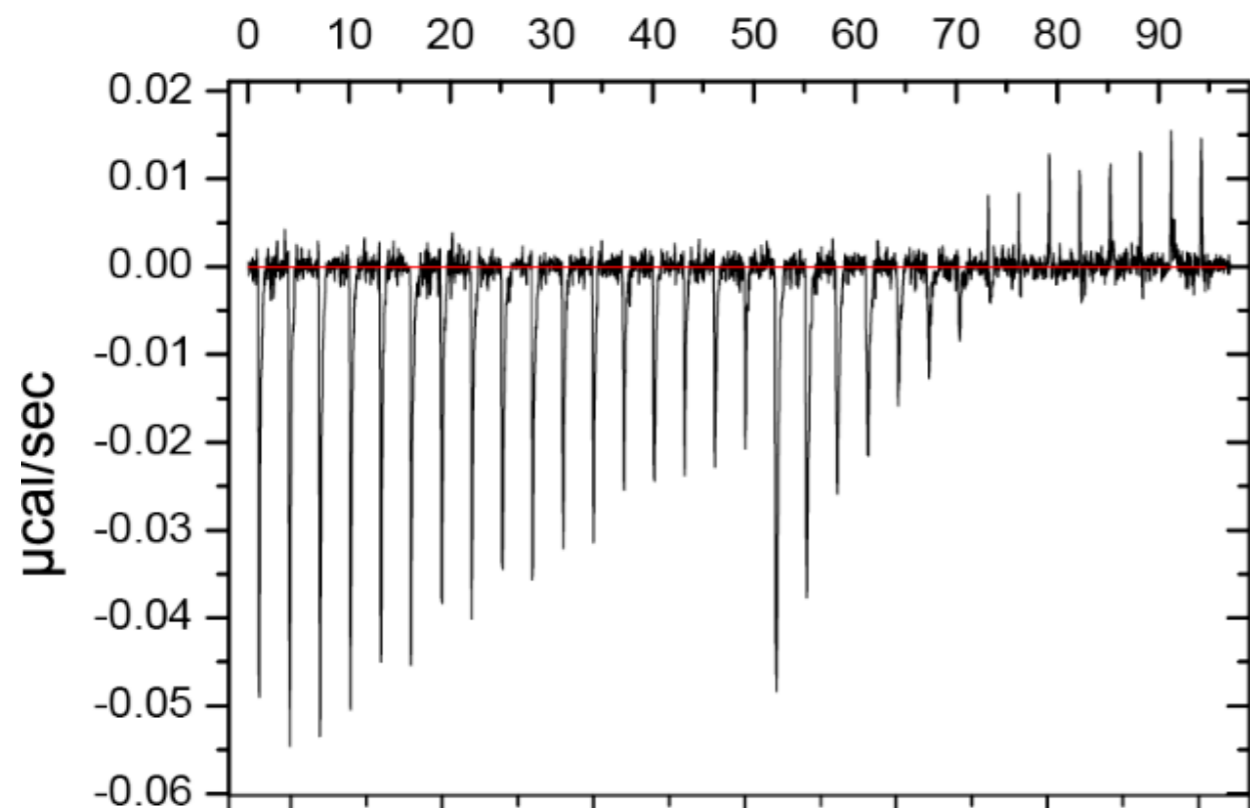
Sherpa, C., *et al. Nucleic Acids Research*, 2015, 43 (9), 4676-4686.

Any effect on Gag interaction?



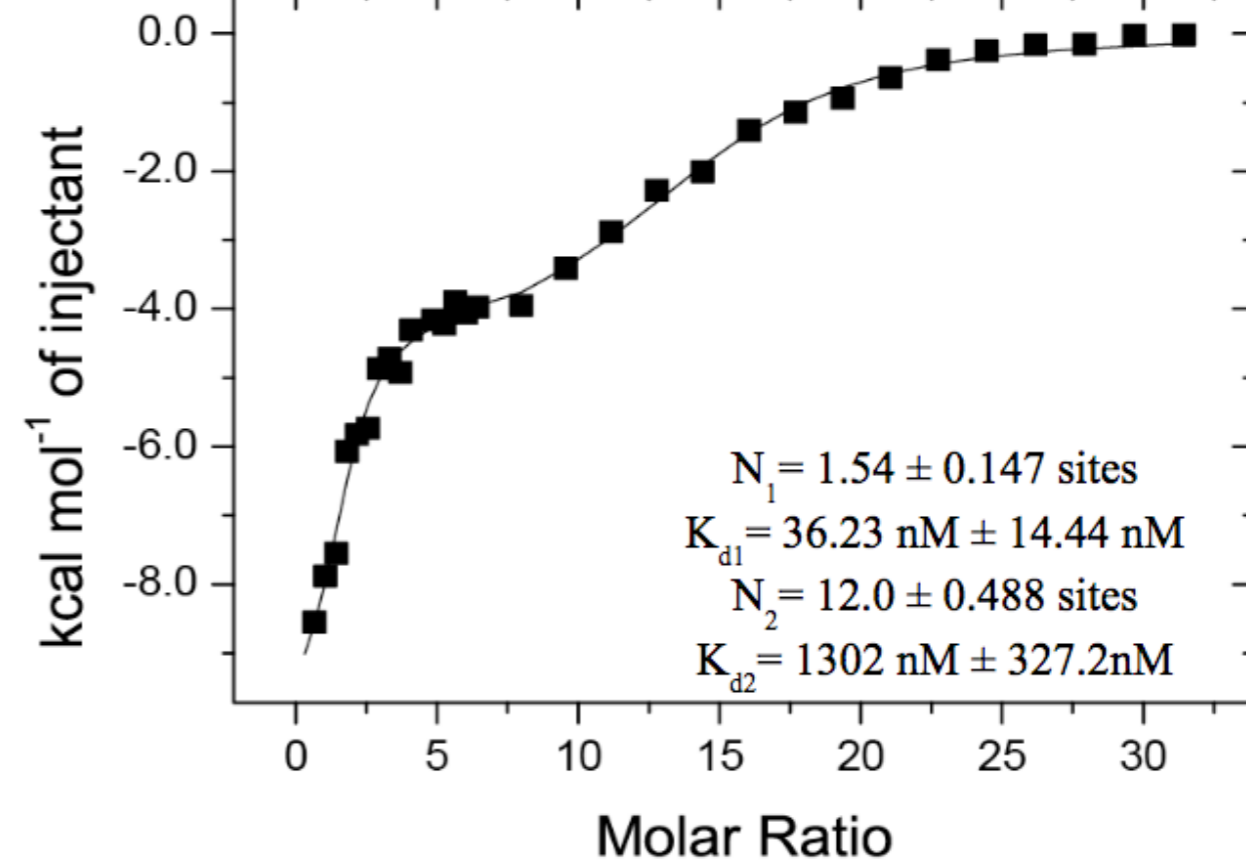
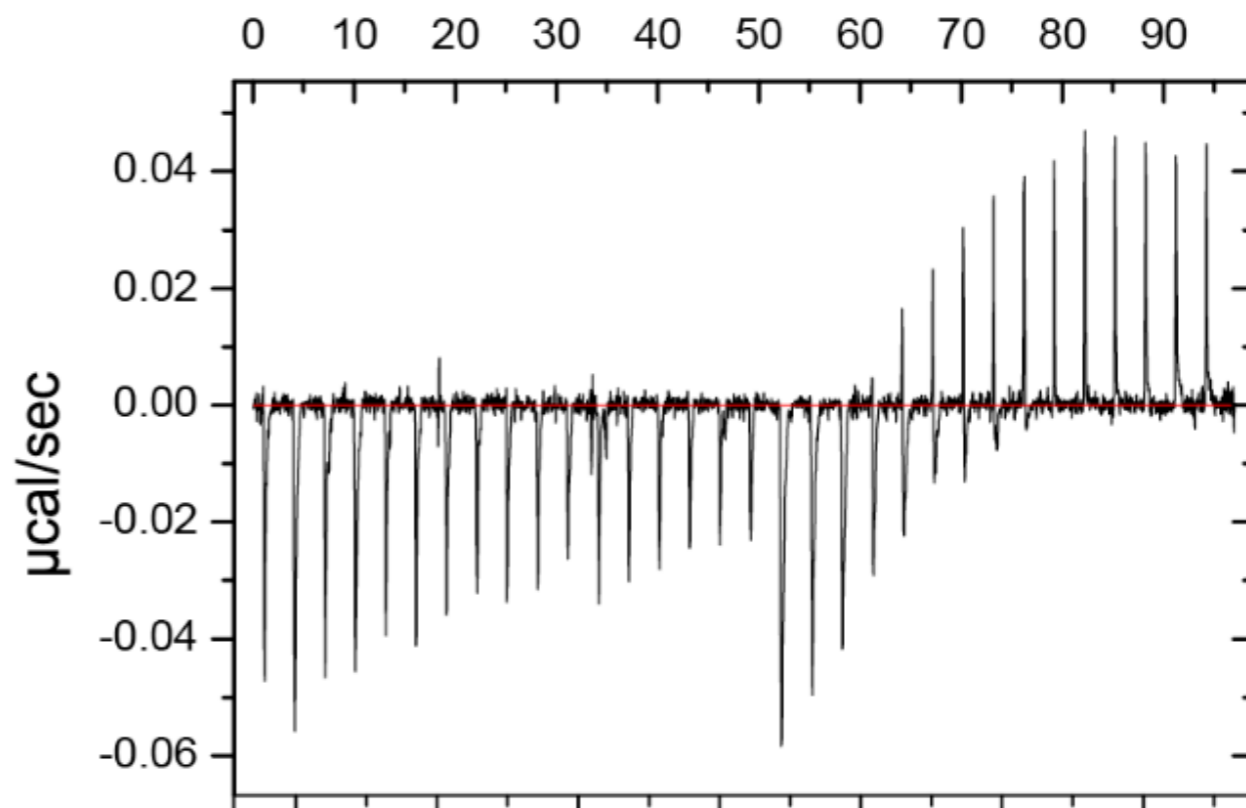
NC to RRE mutA

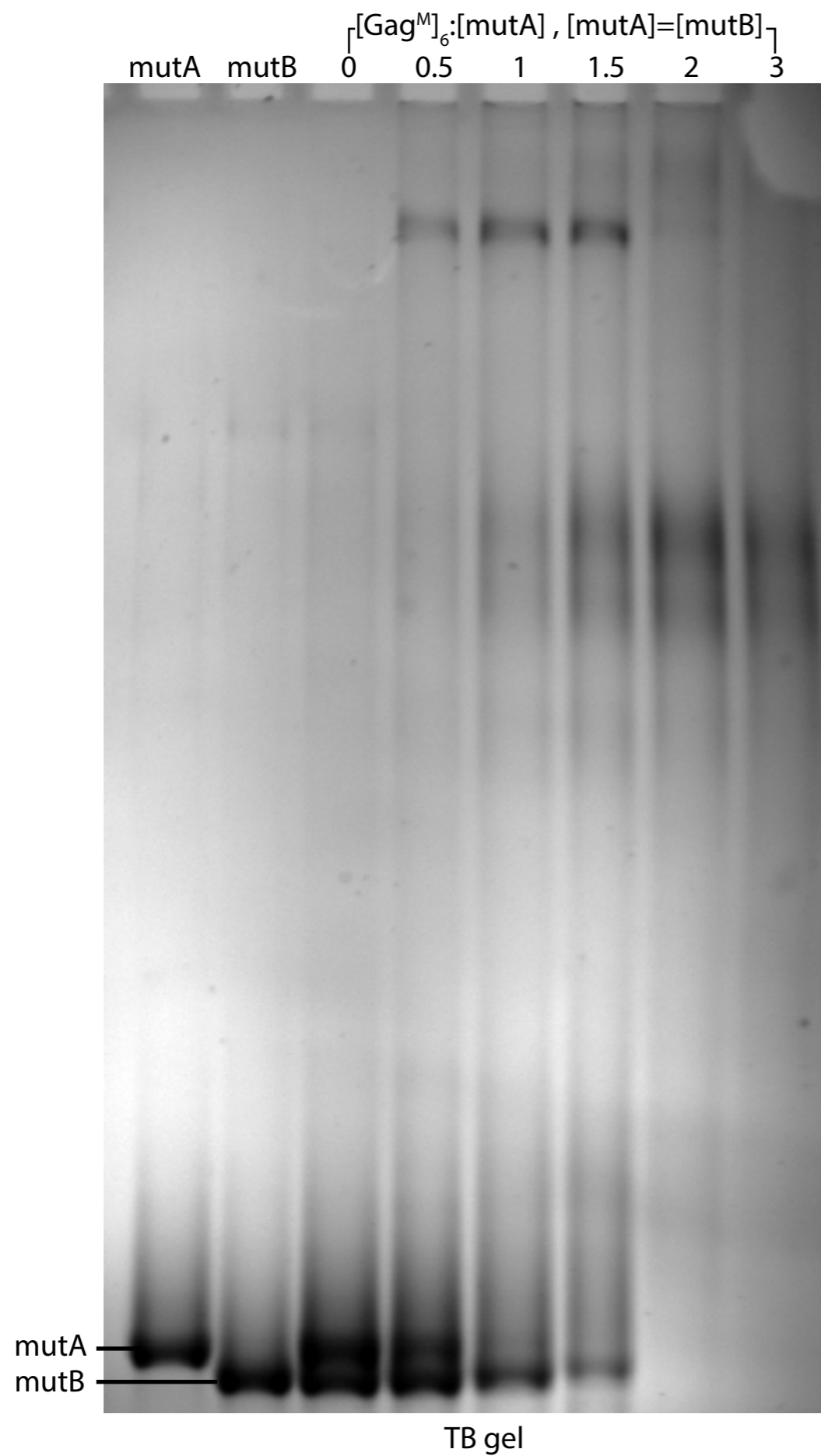
Time (min)



NC to RRE mutB

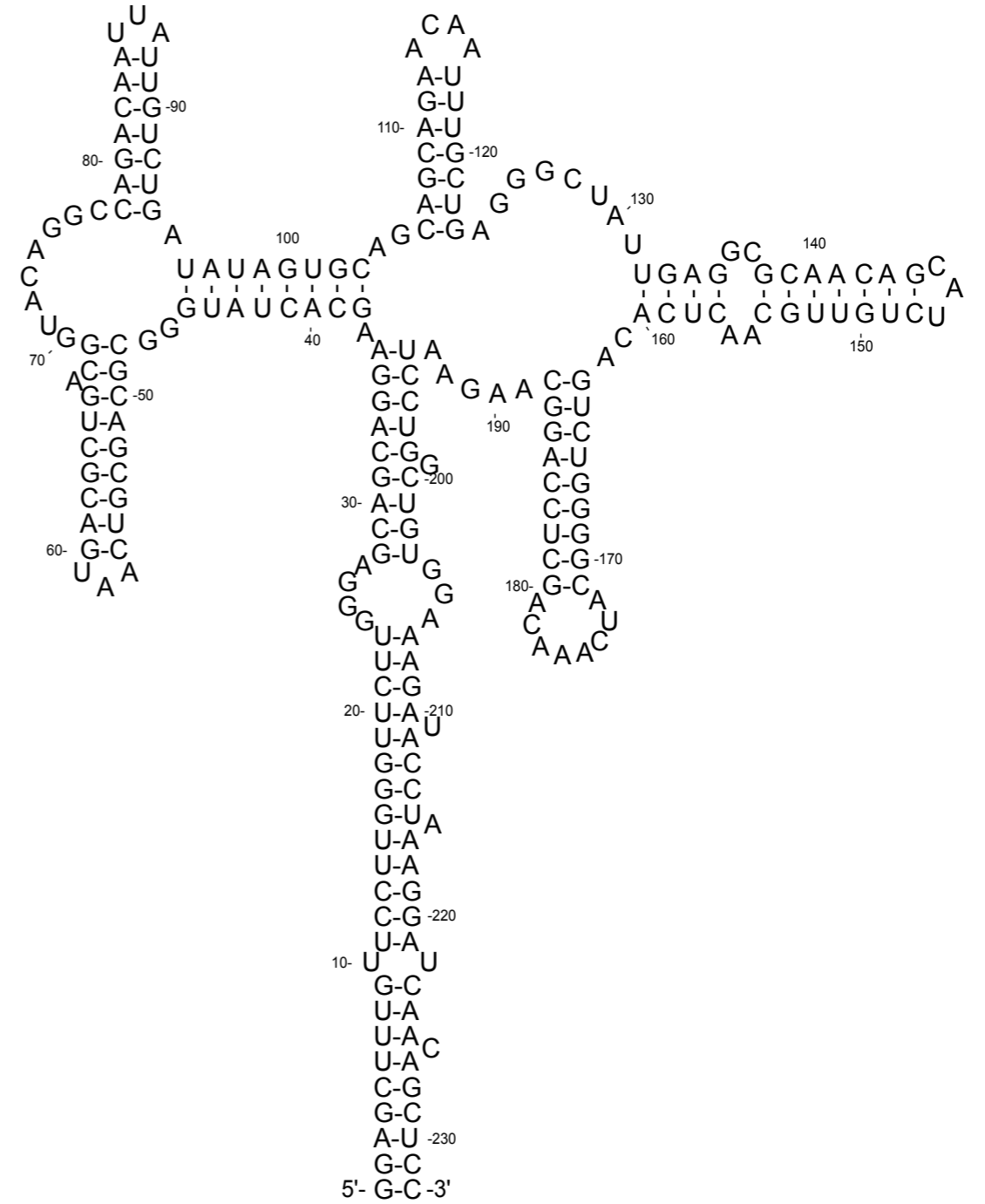
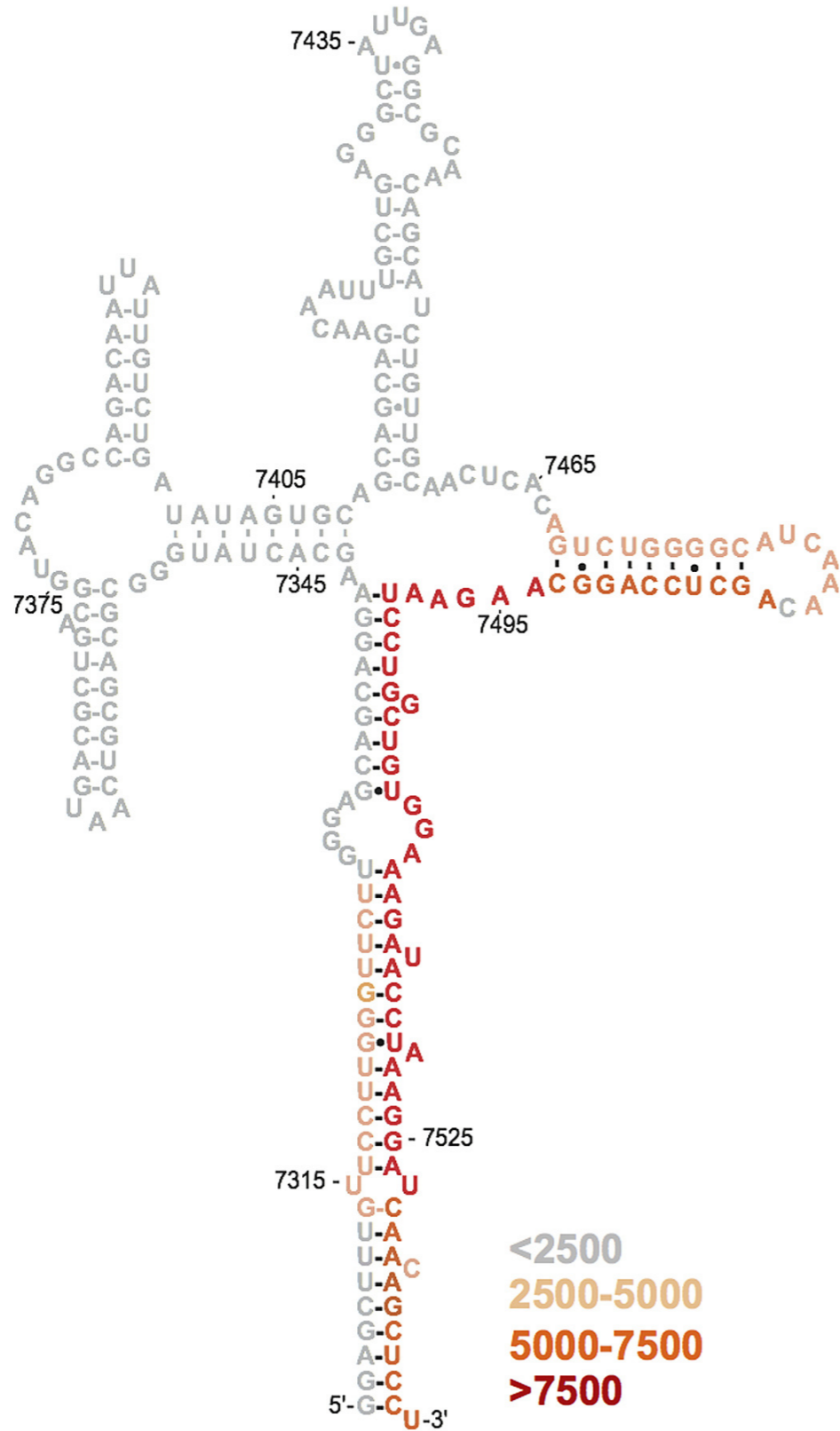
Time (min)

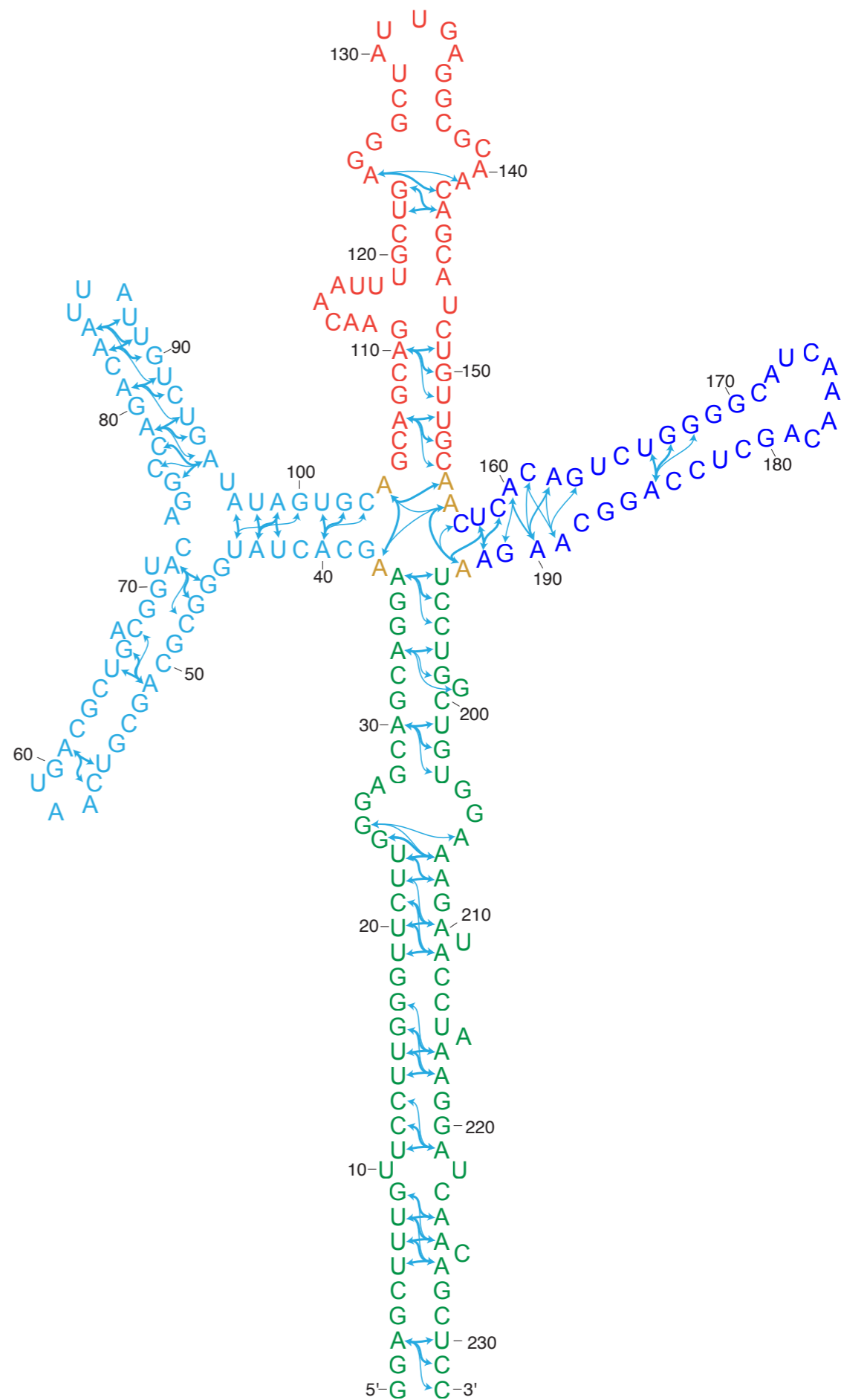
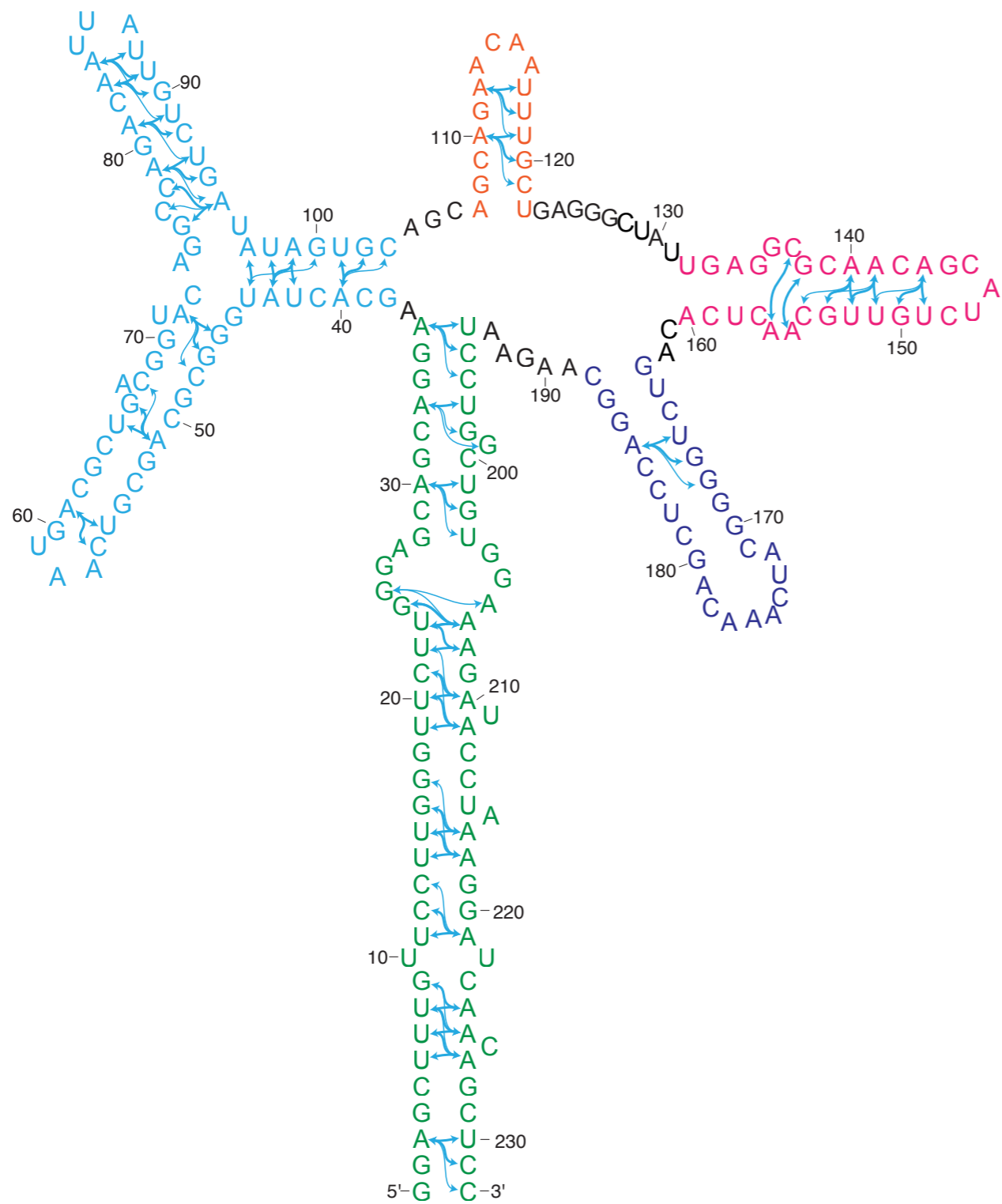


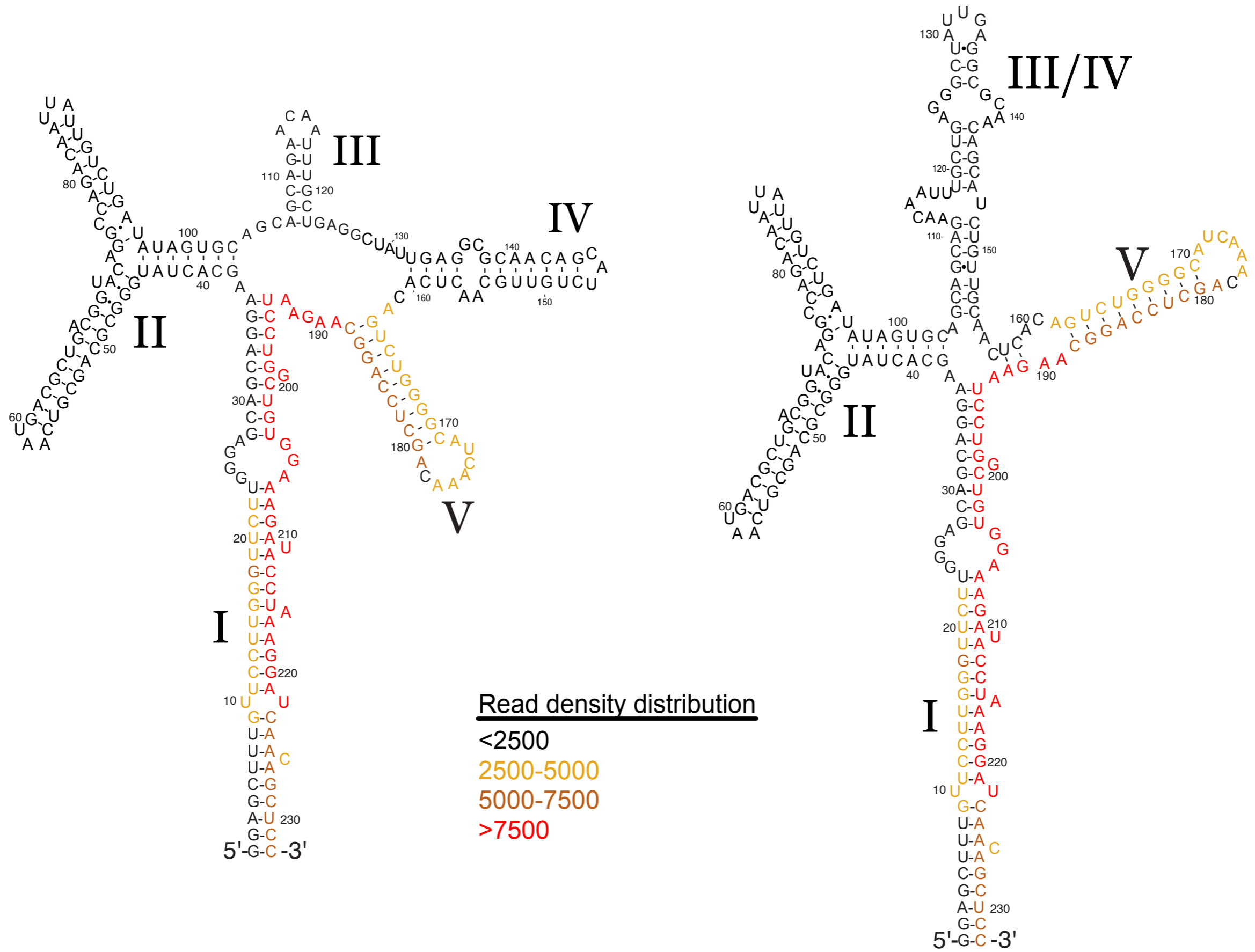


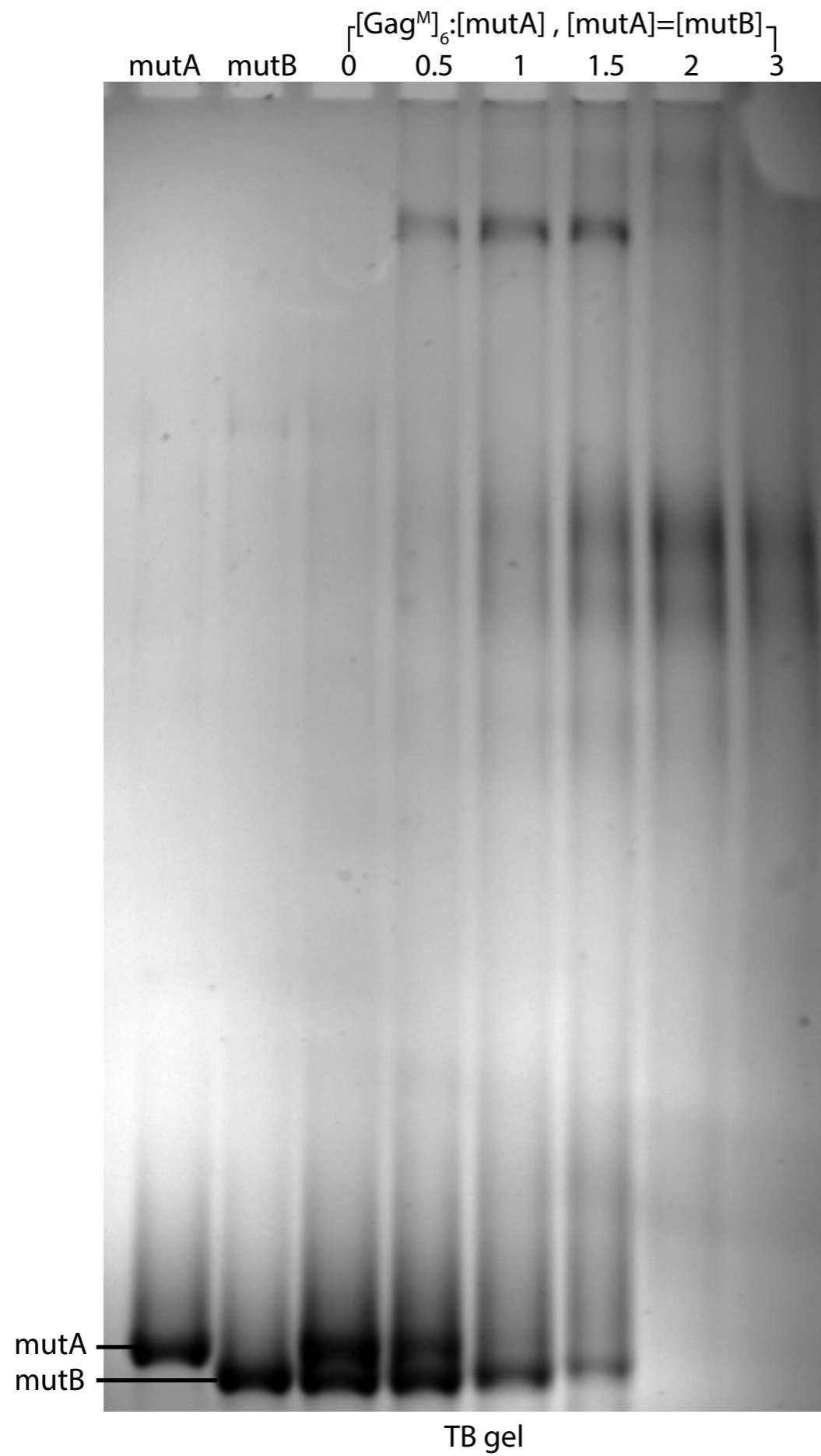
$[Gag^M]_6$ is a Gag mimetic consisting of a hexameric coiled coil chimera with CActd-SP1-NC

HIV-1_{NL4-3} RRE









Directions

Identify further high affinity binding sites by mutagenesis

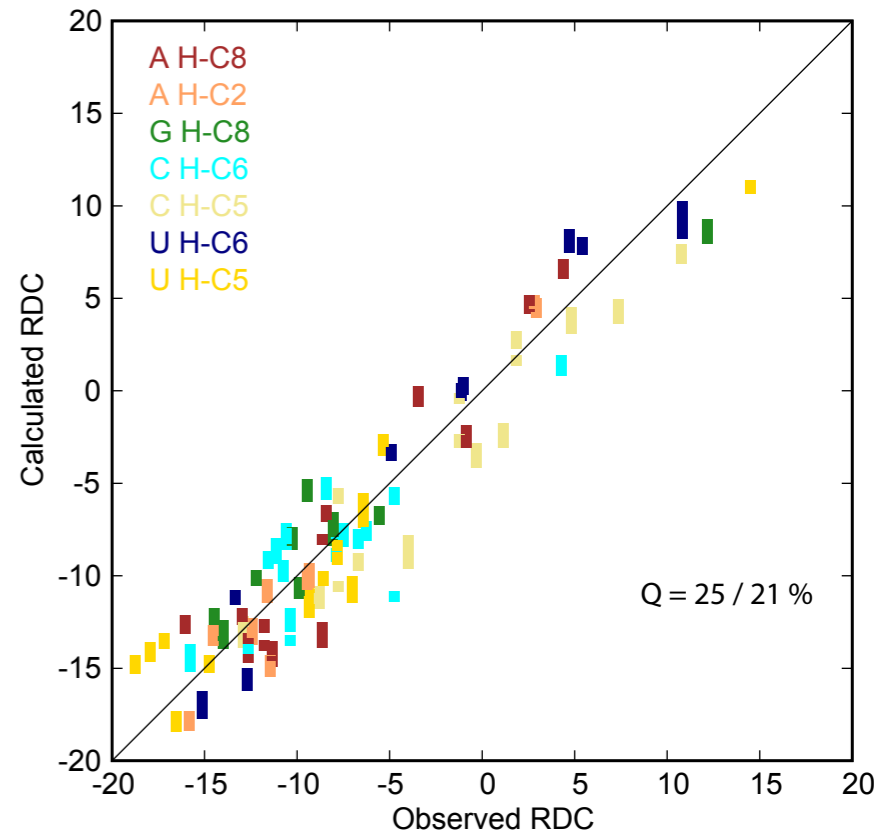
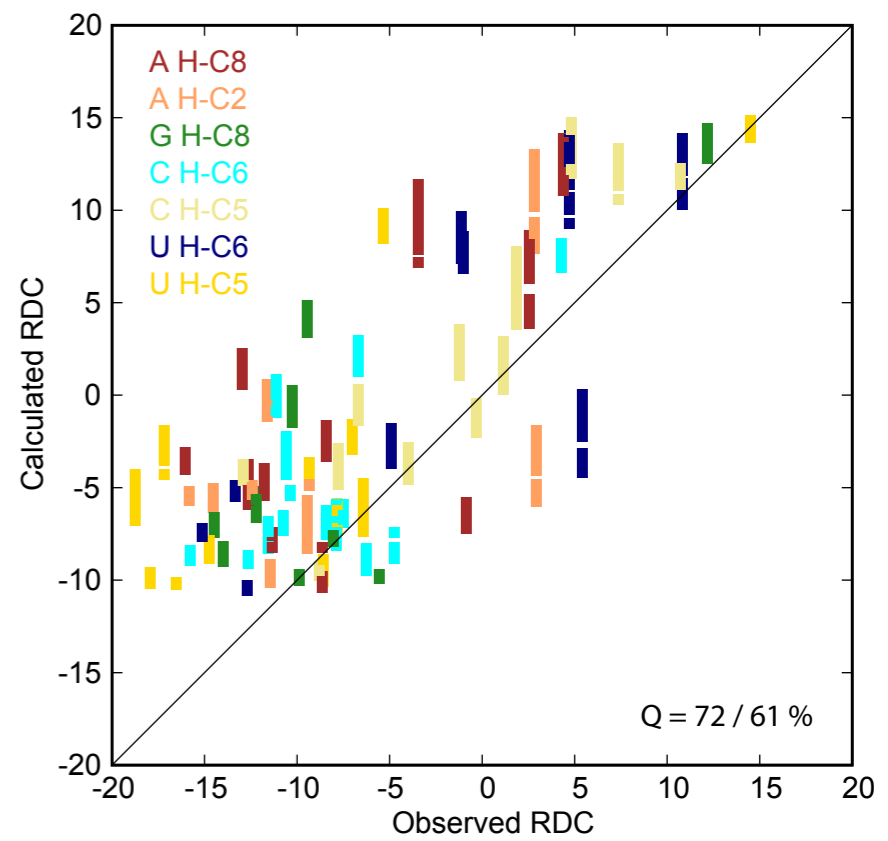
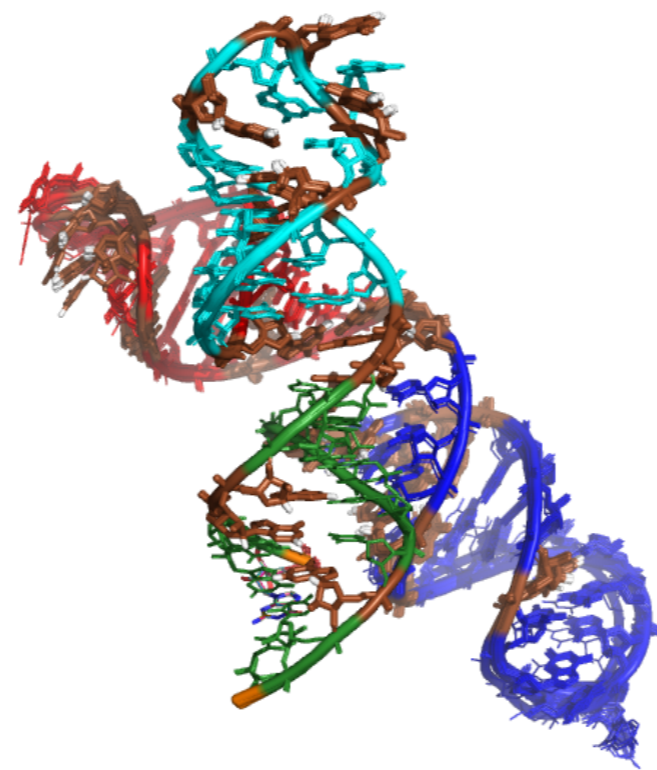
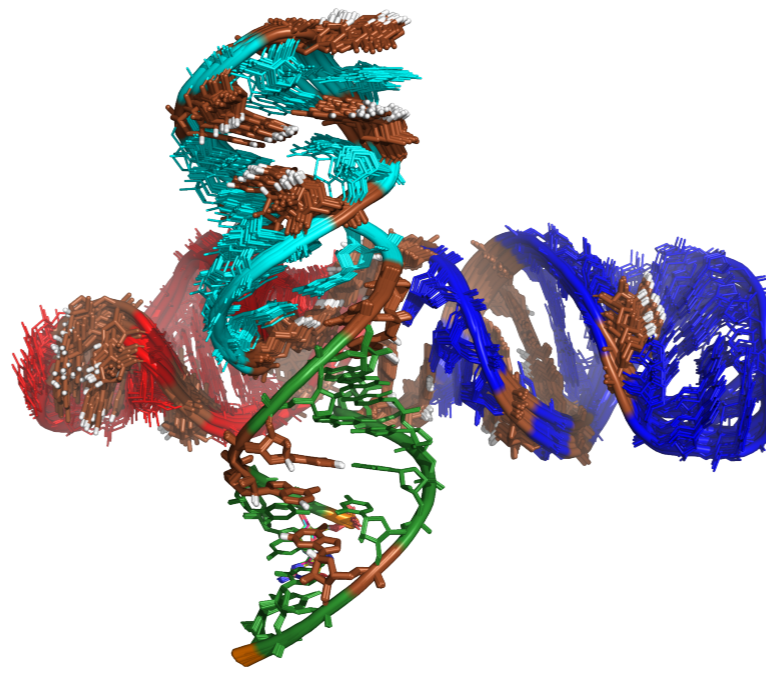
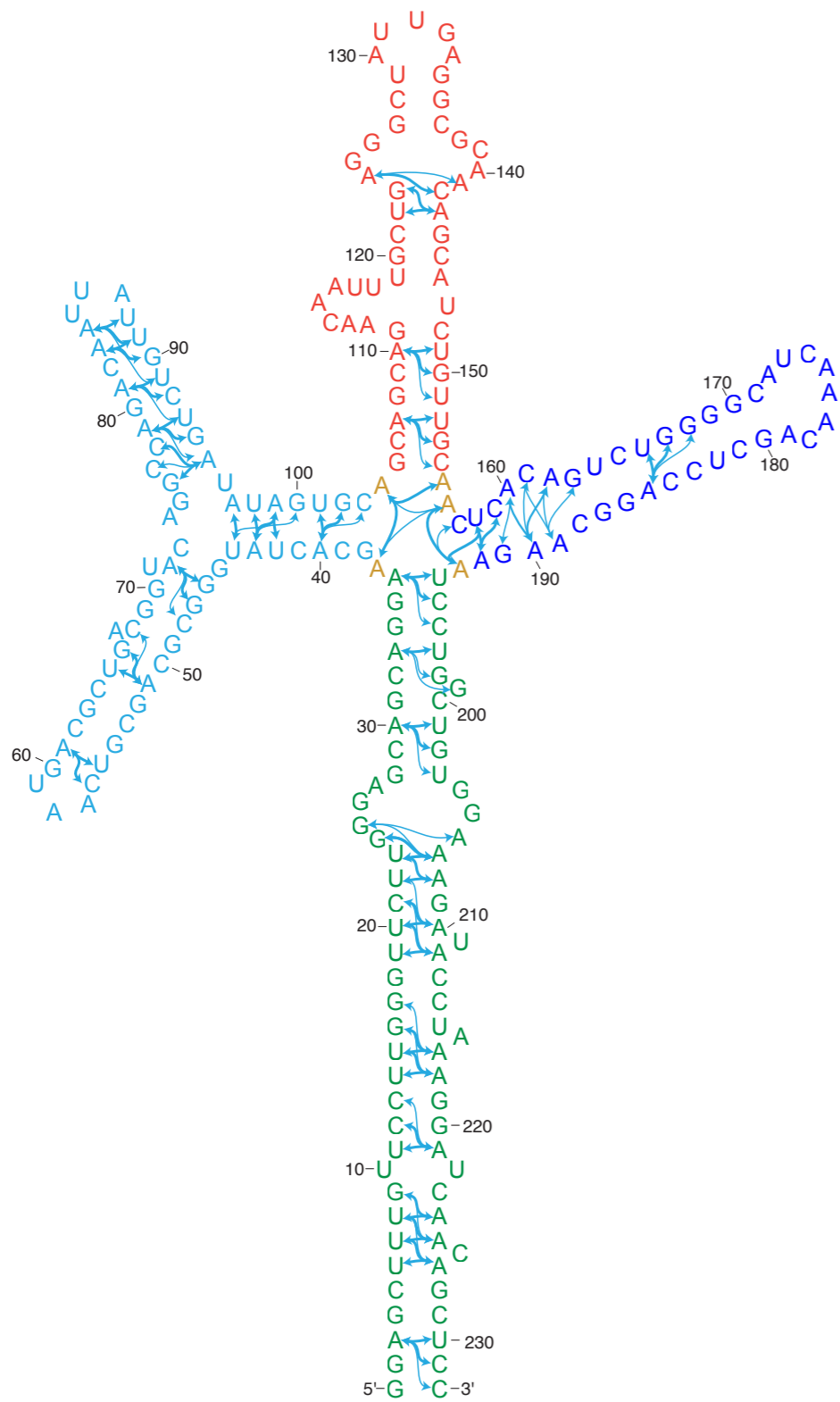
- target bulge guanosines
- test with Gag mimetics in competition

CLIP experiments with RRE mutants

- does Gag selectively bind 5 stem conformer in vivo?

Finalize structural characterization of both conformers

- including 5 stem conformer in high $[Mg^{2+}]$



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The rest of the lab



hhmi

CRNA

NIH National Institutes of Health



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