SUPPLEMENTARY INFORMATION

Phosphodiester cleavage in ribonuclease H occurs via an associative two-metal-aided catalytic mechanism

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CLASSICAL MD SIMULATIONS

The system was immersed in a box of water molecules (37,000 atoms) of edge 66×74×76 $Å^3$, in a 10 mM buffer of NaCl. A time step set of 1.5 fs was used. Hydrogen atoms were added assuming standard bond lengths and were constrained to their equilibrium position with the SHAKE algorithm. The system was coupled in the NPT ensemble to a Berendsen thermostat at 298 K and barostat at 1 atm. Periodic boundary conditions were applied to the system. PME method was used to evaluate long-range electrostatic interactions, and a cutoff of 12 Å was used to account for the van der Waals interactions. Ad-hoc parameterization of the active site, as reported in Ref. 23 of the manuscript.
Further details in Ref. 23 of the manuscript.

Figures

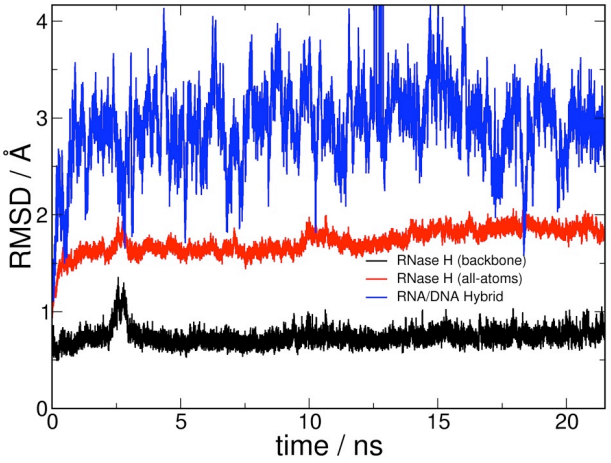

Fig1_suppinfo Along the ~25 ns classical MD simulation, the RMSD of the RNase H backbone (all) atoms fluctuates around a value of 0.7 (1.8) Å, while the substrate fluctuates around 3.2 Å maintaining unaltered interactions with the enzyme, with respect to the crystal structure. Further details in Ref. 23 of the manuscript.

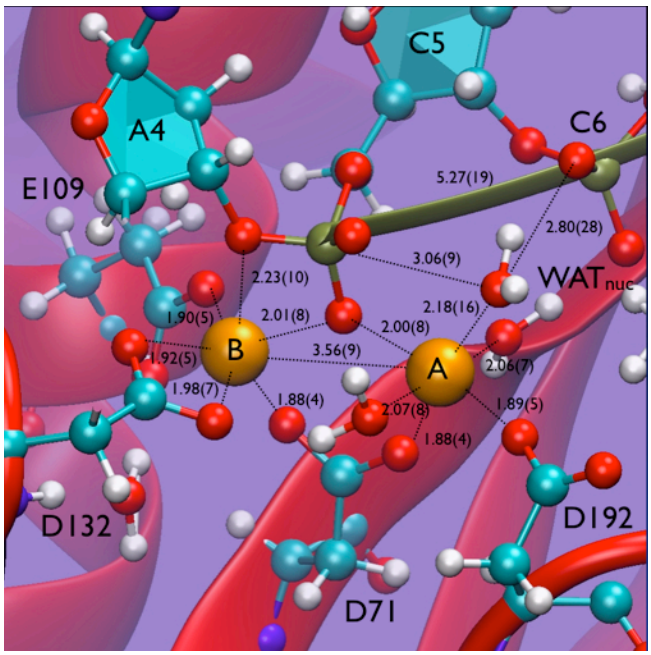

Fig2_suppinfo RNase H catalytic site. Orange spheres indicate the two Mg^{2+} cations. Average length of relevant distances is reported, calculated along the ~25 classical MD simulations. Further details in Ref. 23 of the manuscript.

Table

Atom	δq	q^{eff}	q^{*}_{AMBER}
Mg1-Mg2	-0.25	1.75	2.00
Oδ1-2(Asp71)	0.05	-0.74	-0.80
Oδ1(Asp132)	0.07	-0.73	-0.80
Oδ1(Asp192)	0.15	-0.65	-0.80
Oε1-2(Glu109)	0.05	-0.78	-0.82
O3'(A-RNA)	0.05	-0.47	-0.52
OP1(C-RNA)	0.03	-0.75	-0.78
O(Wat)	0.00	-0.83	-0.83

Table1_suppinfo. Corrected charges for metal ions and ligands with respect to AMBER RESP charges. Further details in Ref. 23 of the manuscript.