Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Electronic Supplementary Information (ESI):

Mechanistic role of nucleobases in self-cleavage catalysis of hairpin ribozyme at ambient versus high-pressure conditions

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Supporting analyses and figures

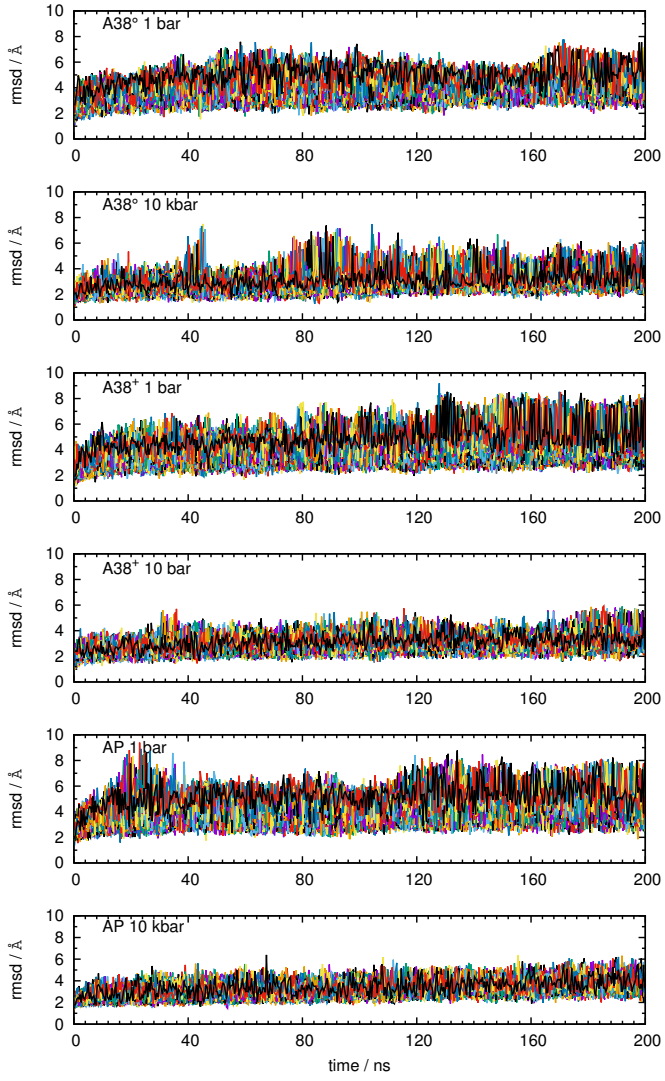

Fig. 1 Root-mean-square deviation (RMSD) of all heavy atoms of the A38°, A38$^+$ and AP states of hairpin ribozyme at 1 bar and 10 kbar and 300 K with respect to its crystal structure (PDB ID: 2OUE based on Ref. 1); a different color is used for each of the 64 replica in the underlying T-REMD simulations which sampled temperatures up to 404 K. There is no abrupt change or significant increase in the RMSD observed which suggests that the ribozyme remains within the docked state in all six system as required for our analyses.

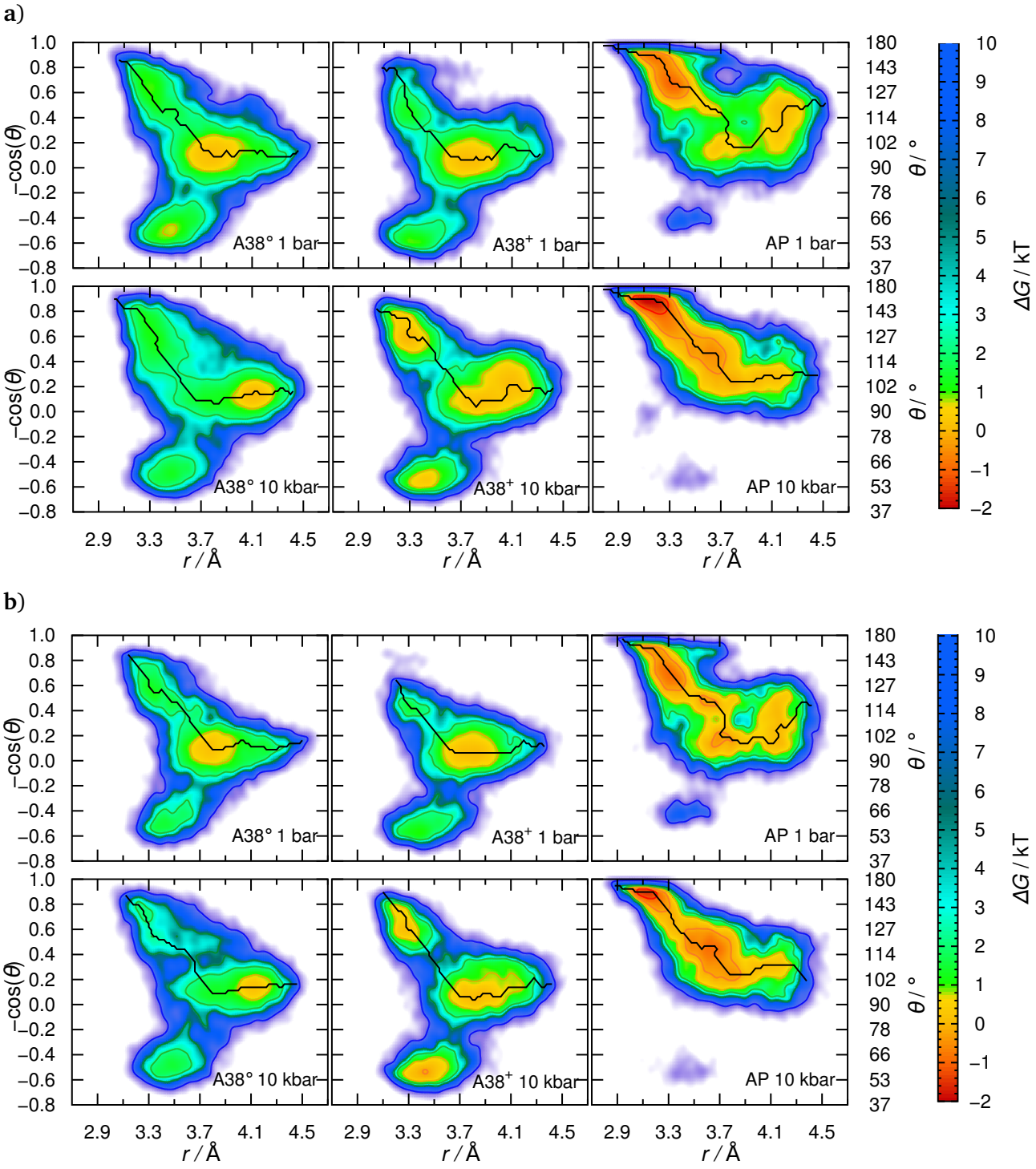

Fig. 2 Gibbs free energy landscapes of the A38°, A38$^+$, and AP states of the hairpin ribozyme both at 1 bar and 10 kbar by considering (a) full simulation time, and (b) the second half of the simulation time (see Fig. 5 of the main text for more information). The free energy landscapes of (a) both at 1 bar and 10 kbar are qualitatively similar to their corresponding counterparts in (b) thus confirming the convergence.

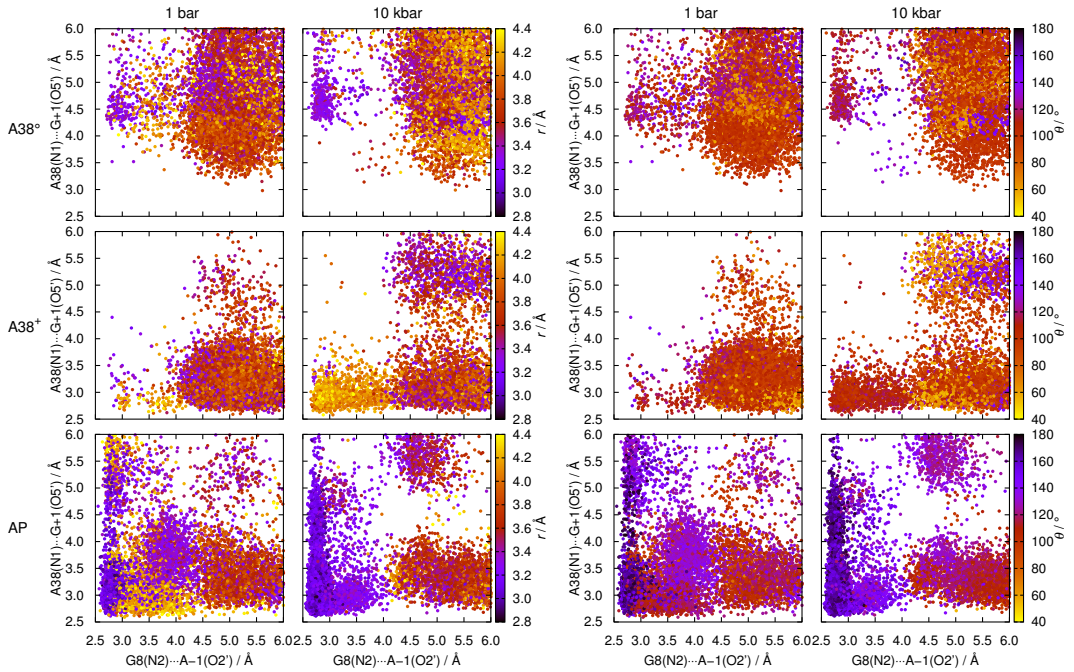

Fig. 3 Three-dimensional structural correlations between the G8(N2)···A-1(O2′) and A38(N1)···G+1(O5′) distances (where small values indicate hydrogen bonding w.r.t. O2′ and O5′ , respectively) and the O2′ – P distance r (left part of the figure) as well as the attack angle θ (right part of the figure) at 1 bar and 10 kbar (according to the topmost line) at 300 K, see Fig. 3b and Fig. 4 of the main text for site labels and structures. The r and θ values at a given point in the (x,y)-plane spanned by G8(N2)···A-1(O2′) and A38(N1)···G+1(O5′) are provided in terms of the color bars as defined at the respective right axes, thus dark (violet/blue) colors encode the preferred inline attack arrangement realized when r is small and θ is close to $180°$. The panels from top to bottom correspond to the A38°, A38$^+$ and AP states, respectively, as indicated. The same correlation analysis involving G8(N1)···A-1(O2′) is shown in Fig. 8 of the main text.

References

1 J. Salter, J. Krucinska, S. Alam, V. Grum-Tokars and J. E. Wedekind, *Biochemistry*, 2006, **45**, 686–700.

Preparation files for protonated A38 nucleobase and the cleavage site of AP

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% % % % % % % % % % % % % % % % % % % % % % % % % % % % % % % % % % % % %
[ bondedtypes ]
;
; RAP is Adenine protonated at N1 with charges from JPCB 2010, 114, 6642-6652.
;
; RAA is Adenine deprotonated at 2-O', O2' is changed to O2a
; GAA is Guanidine phosphate protonated at proR oxygen., O2P is changed O2n
;
;
[ RAP ]
 [ atoms ]
     P    P          1.16620    1
   O1P    O2        -0.77600    2
   O2P    O2        -0.77600    3
   O5'    OS        -0.49890    4
   C5'    CI         0.05580    5
  H5'1    H1         0.06790    6
  H5'2    H1         0.06790    7
   C4'    CT         0.10650    8
   H4'    H1         0.11740    9
   O4'    OS        -0.35480   10
   C1'    CT         0.12970   11
   H1'    H2         0.20070   12
    N9    N*        -0.05320   13
    C8    C5         0.14120   14
    H8    H5         0.20080   15
    N7    NB        -0.53300   16
    C5    CB         0.26130   17
    C6    CA         0.27480   18
    N6    N2        -0.72510   19
   H61    H          0.42820   20
   H62    H          0.42820   21
    N1    NA        -0.26040   22
    HN1   H          0.35660   23
    C2    CQ         0.19640   24
    H2    H5         0.18890   25
    N3    NC        -0.44310   26
    C4    CB         0.32400   27
   C3'    CT         0.20220   28
   H3'    H1         0.06150   29
   C2'    CT         0.06700   30
  H2'1    H1         0.09720   31
   O2'    OH        -0.61390   32
  HO'2    HO         0.41860   33
   O3'    OS        -0.52460   34
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 [ bonds ]
    P   O1P
    P   O2P
    P   O5'
   O5'   C5'
   C5'  H5'1
   C5'  H5'2
   C5'   C4'
   C4'   H4'
   C4'   O4'
   C4'   C3'
   O4'   C1'
   C1'   H1'
   C1'    N9
   C1'   C2'
    N9    C8
    N9    C4
    C8    H8
    C8    N7
    N7    C5
    C5    C6
    C5    C4
    C6    N6
    C6    N1
    N6   H61
    N6   H62
    N1    C2
   HN1    N1
    C2    H2
    C2    N3
    N3    C4
   C3'   H3'
   C3'   C2'
   C3'   O3'
   C2'  H2'1
   C2'   O2'
   O2'  HO'2
  -O3'     P
 [ impropers ]
    C4    C8    N9   C1'
    C6   H61    N6   H62
    N9    N7    C8    H8
    N1    N3    C2    H2
    C5    N6    C6    N1
    C6    C2    N1   HN1

[ RAA ]
 [ atoms ]
```

```
    P     P            1.16620     1
  O1P     O2          -0.77600     2
  O2P     O2          -0.77600     3
  O5'     OS          -0.49890     4
  C5'     CI           0.05580     5
 H5'1     H1           0.06790     6
 H5'2     H1           0.06790     7
  C4'     CT           0.10650     8
  H4'     H1           0.11740     9
  O4'     OS          -0.35480    10
  C1'     CT           0.03940    11
  H1'     H2           0.20070    12
   N9     N*          -0.02510    13
   C8     C5           0.20060    14
   H8     H5           0.15530    15
   N7     NB          -0.60730    16
   C5     CB           0.05150    17
   C6     CA           0.70090    18
   N6     N2          -0.90190    19
  H61     H            0.41150    20
  H62     H            0.41150    21
   N1     NC          -0.76150    22
   C2     CQ           0.58750    23
   H2     H5           0.04730    24
   N3     NC          -0.69970    25
   C4     CB           0.30530    26
  C3'     CT           0.20220    27
  H3'     H1           0.06150    28
  C2'     CT           0.06700    29
 H2'1     H1           0.09720    30
  O2a     O2          -0.77600    31
  O3'     OS          -0.52460    32
[ bonds ]
    P   O1P
    P   O2P
    P   O5'
  O5'   C5'
  C5'  H5'1
  C5'  H5'2
  C5'   C4'
  C4'   H4'
  C4'   O4'
  C4'   C3'
  O4'   C1'
  C1'   H1'
  C1'    N9
  C1'   C2'
   N9    C8
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    N9    C4
    C8    H8
    C8    N7
    N7    C5
    C5    C6
    C5    C4
    C6    N6
    C6    N1
    N6   H61
    N6   H62
    N1    C2
    C2    H2
    C2    N3
    N3    C4
   C3'   H3'
   C3'   C2'
   C3'   O3'
   C2'  H2'1
   C2'   O2a
  -O3'     P
 [ impropers ]
    C4    C8    N9   C1'
    C6   H61    N6   H62
    N9    N7    C8    H8
    N1    N3    C2    H2
    C5    N6    C6    N1

[ GAA ]
 [ atoms ]
     P    P            1.16620     1
   O1P    O2          -0.77600     2
   O2n    OH          -0.61390     3
   HOP    HX           0.41860     4
   O5'    OS          -0.49890     5
   C5'    CI           0.05580     6
  H5'1    H1           0.06790     7
  H5'2    H1           0.06790     8
   C4'    CT           0.10650     9
   H4'    H1           0.11740    10
   O4'    OS          -0.35480    11
   C1'    CT           0.01910    12
   H1'    H2           0.20060    13
    N9    N*           0.04920    14
    C8    CP           0.13740    15
    H8    H5           0.16400    16
    N7    NB          -0.57090    17
    C5    CB           0.17440    18
    C6    C            0.47700    19
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    O6     O            -0.55970    20
    N1     NA           -0.47870    21
    H1     H             0.34240    22
    C2     CA            0.76570    23
    N2     N2           -0.96720    24
   H21     H             0.43640    25
   H22     H             0.43640    26
    N3     NC           -0.63230    27
    C4     CB            0.12220    28
   C3'     CT            0.20220    29
   H3'     H1            0.06150    30
   C2'     CT            0.06700    31
  H2'1     H1            0.09720    32
   O2'     OH           -0.61390    33
  HO'2     HO            0.41860    34
   O3'     OS           -0.52460    35
[ bonds ]
     P    O1P
     P    O2n
   HOP    O2n
     P    O5'
   O5'    C5'
   C5'   H5'1
   C5'   H5'2
   C5'    C4'
   C4'    H4'
   C4'    O4'
   C4'    C3'
   O4'    C1'
   C1'    H1'
   C1'     N9
   C1'    C2'
    N9     C8
    N9     C4
    C8     H8
    C8     N7
    N7     C5
    C5     C6
    C5     C4
    C6     O6
    C6     N1
    N1     H1
    N1     C2
    C2     N2
    C2     N3
    N2    H21
    N2    H22
    N3     C4
```

```
   C3'   H3'
   C3'   C2'
   C3'   O3'
   C2'  H2'1
   C2'   O2'
   O2'  HO'2
  -O3'     P
 [ impropers ]
    C4    C8    N9   C1'
    C5    N1    C6    O6
    C6    C2    N1    H1
    C2   H21    N2   H22
    N9    N7    C8    H8
    N2    N1    C2    N3

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