Supplementary Information for Molecular simulations of DEAH-box helicases reveal control of domain flexibility by ligands: RNA, ATP, ADP, and G-patch proteins

Robert A. Becker and Jochen S. Hub*

Theoretical Physics and Center for Biophysics, Saarland University, Campus E2 6, 66123 Saarbrücken, Germany

E-mail: jochen.hub@uni-saarland.de

Phone: +49 681 302 2740

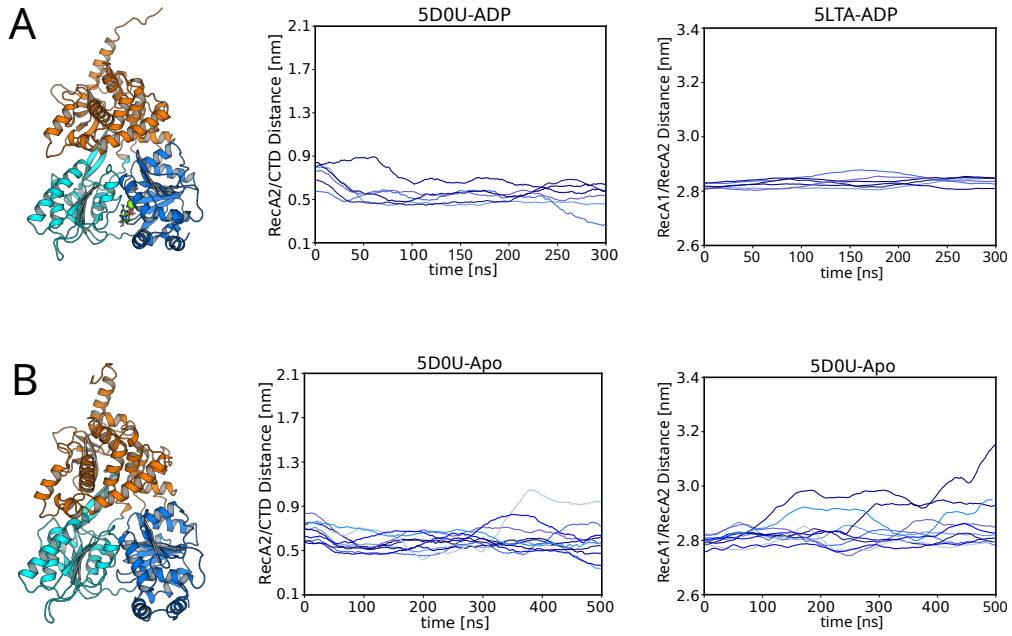

Figure S1: Prp43 simulations starting from the 5D0U structure, analyzed in terms of the RecA2–CTD distance (middle panel) and the RecA1–RecA2 distance (right panel). Lines of different colors represent independent simulations. (A) Prp43•ADP complex of 5D0U, revealing stable domain arrangements. (B) Apo Prp43 derived from 5D0U, revealing decreasing CTD–RecA2 distances with a closed RecA1–RecA2 interface.

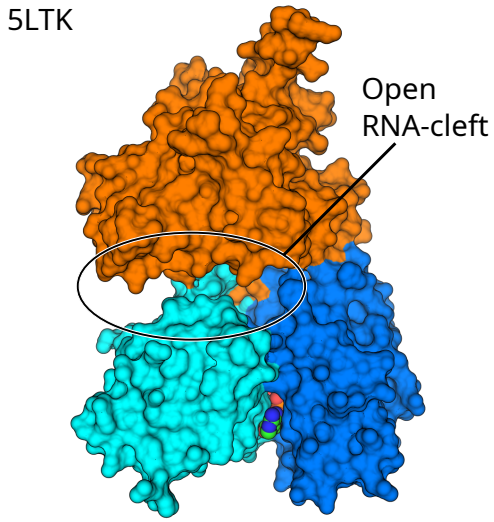

Figure S2: Crystal structure 5LTK exhibiting an open RNA cleft.

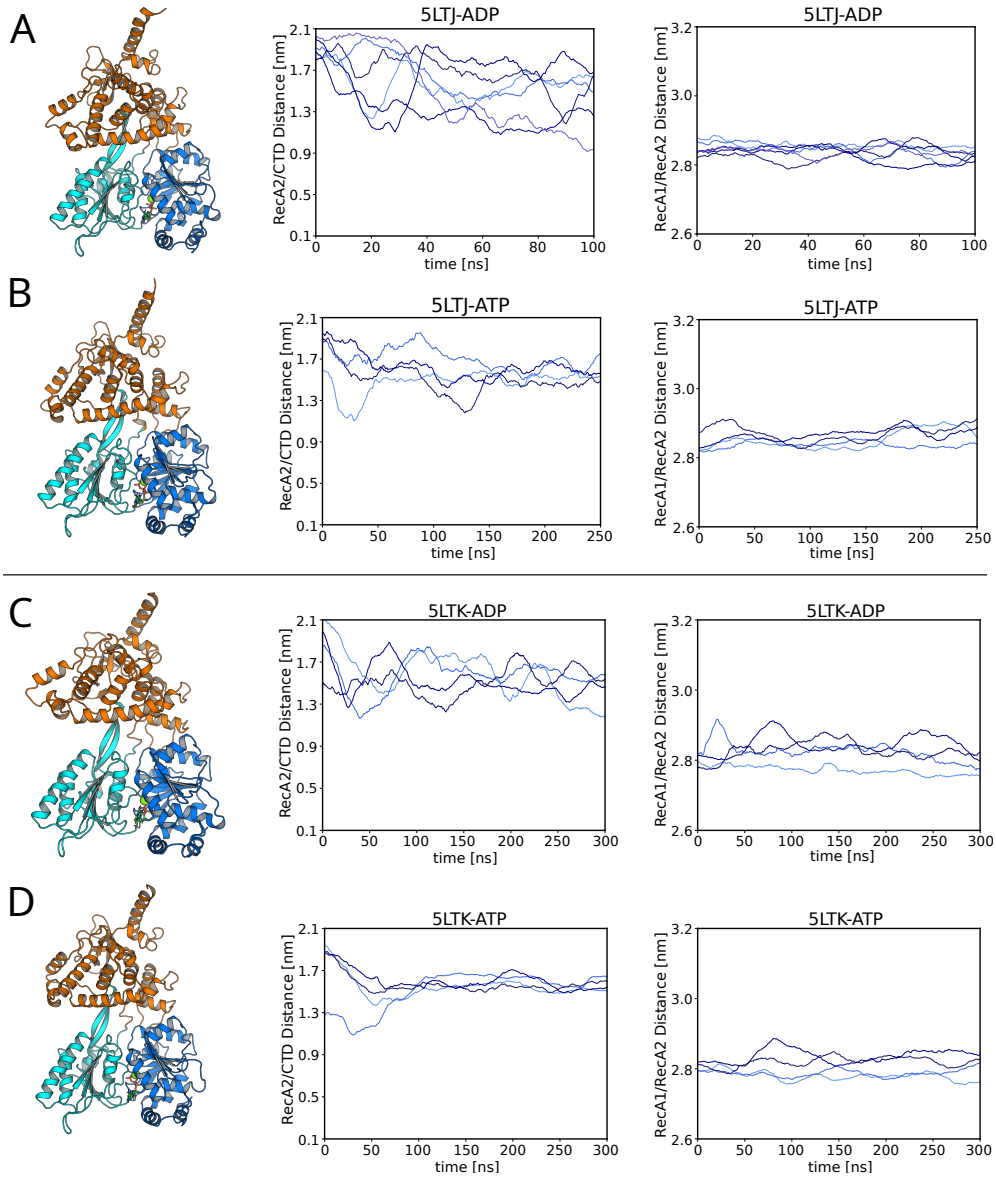

Figure S3: Prp43 simulations starting from the 5LTJ or from the 5LTK structure, analyzed in terms of the RecA2–CTD distance (middle panel) and the RecA1–RecA2 distance (right panel). Lines of different colors represent independent simulations. In all simulations, the RecA1–RecA2 interface is largely stable, whereas the RNA cleft is instable and tends to collapse. (A) Prp43•ADP complex 5LTJ, (B) Prp43•ATP complex of 5LTJ, (C) Prp43•ADP complex of 5LTK, and (D) Prp43•ATP complex of 5LTK

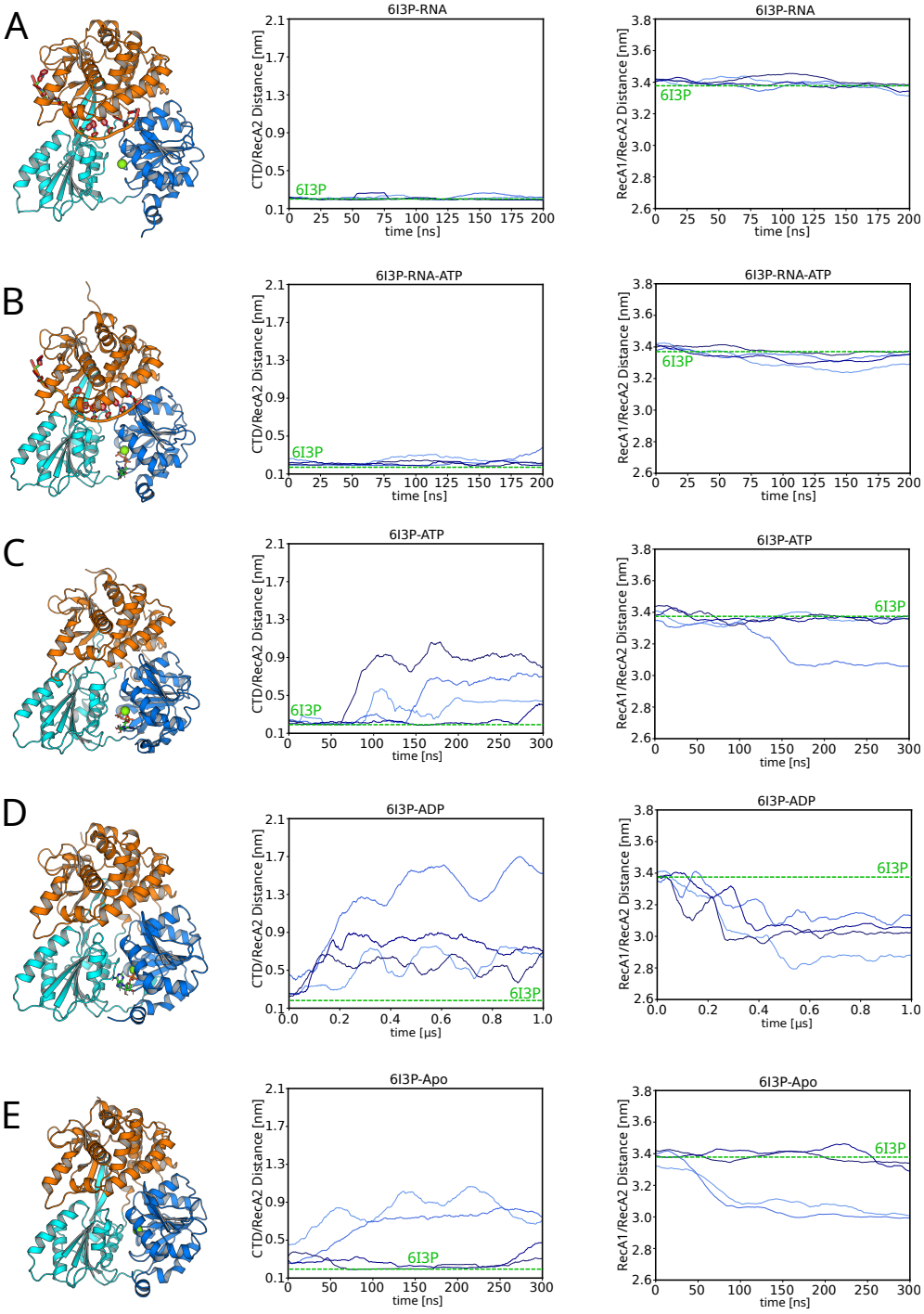

Figure S4: Prp22 simulations starting from the 6I3P structure, analyzed in terms of the RecA2–CTD distance (middle panel) and the RecA1–RecA2 distance (right panel). Lines of different colors represent independent simulations. (A) Prp22•RNA complex, in a largely stable conformation. (B) Prp22•RNA•ATP complex, corresponding to the crystal conformation, revealing only minor domain fluctuations over 200ns. (C) Prp22•ATP complex, revealing increasing CTD–RecA2 distances with a stable RecA1–RecA2 distance, except for one simulation. (D) Prp22•ADP complex, revealing increasing CTD–RecA2 distances with partly closing RecA1–RecA2 interfaces. (E) Apo Prp22, revealing strongly fluctuating CTD and RecA2 domains. Furthermore, the RecA1 domains fluctuates heavily during two simulations.

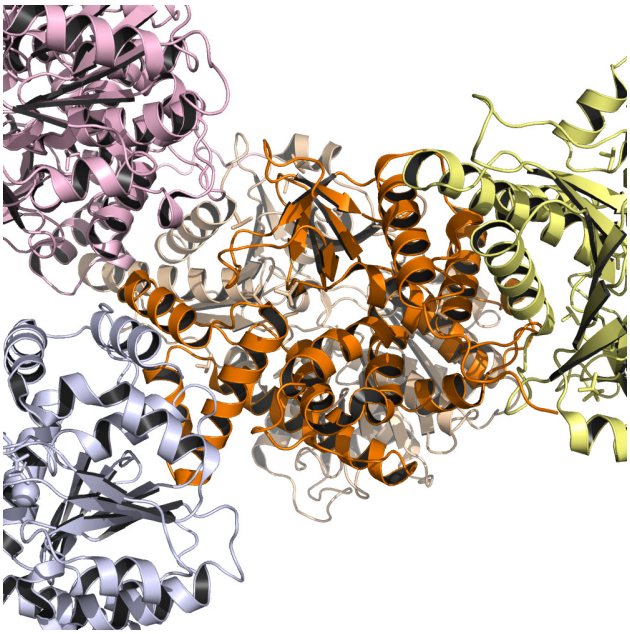

Figure S5: Crystal contacts of the Prp43 C-terminal domain in the 5D0U structure (orange cartoon) with three neighboring symmetry mates (pink, blue, and yellow cartoon). RecA1 and RecA2 domains are shown in the background as brown cartoon.

Supplementary Methods

Modeling of missing residues with Modeller

Prp22. The missing residues of the 6I3P crystal structure were added using the following Python script together with the following alignment files using Modeller.[1]

```
>>alignment.ali
>P1;prp22-rna
structureX:/path-to-pdb/Prp22-RNA-4.pdb:547:D:1178:D::::
NMSIKEQRESLPVFQFRDQIIQAVKDNQILIVVGETGSGKTTQVTQYLAEAGFTKYGMIGCTQPRRV
AAVSVAKRVAEEVGCQLGQEVGYTIRFEDVTSPATKIKYMTDGMLQREILMDPDLKRYSVIMLDEAH
ERTIATDVLFALLKKTVKRRPDLKVIVTSATLDAEKFSEYFNSCPIFTIPGRTFPVEILYSREPEPD
YLEAALTTVMQIHLTEPPGDILVFLTGQEEIDTACEILYERMKALGPSVPELIILPIYSALPSEMQS
RIFEPAPPGSRKVVIATNIAETSITIDYIYYVVDPGFVKQNAYDPKLGMDSLVVTPISQAQANQRAG
RAGRTGPGKCFRLYTEAAYQSEMLPTTIPDIQRQNLANTILLLKAMGINDLLRFDFMDPPPVNTMLT
ALEELYALGALDDEGLLTRLGRKMADFPMEPSLSKVLIASVDKGCSDEMVTIVSMLNLQQIFYRPKD
KQQQADQKKAKFHDPTGDHLTLLNVYNAWKNSGYSNAWCFENYIQARAMRRARDVRQQIVKIMERHR
HPIISCGRDTDKIRQALCAGFFRNTARKDP--GYKTLTEGTPVYLHPSSALFGKQAEWVLYHELVLT
TKEYMHFTTAIEPKWLVEAAPTFFKLAPT*

>P1;prp22-rna_fill
sequence:::::::::
NMSIKEQRESLPVFQFRDQIIQAVKDNQILIVVGETGSGKTTQVTQYLAEAGFTKYGMIGCTQPRRV
AAVSVAKRVAEEVGCQLGQEVGYTIRFEDVTSPATKIKYMTDGMLQREILMDPDLKRYSVIMLDEAH
ERTIATDVLFALLKKTVKRRPDLKVIVTSATLDAEKFSEYFNSCPIFTIPGRTFPVEILYSREPEPD
YLEAALTTVMQIHLTEPPGDILVFLTGQEEIDTACEILYERMKALGPSVPELIILPIYSALPSEMQS
RIFEPAPPGSRKVVIATNIAETSITIDYIYYVVDPGFVKQNAYDPKLGMDSLVVTPISQAQANQRAG
RAGRTGPGKCFRLYTEAAYQSEMLPTTIPDIQRQNLANTILLLKAMGINDLLRFDFMDPPPVNTMLT
ALEELYALGALDDEGLLTRLGRKMADFPMEPSLSKVLIASVDKGCSDEMVTIVSMLNLQQIFYRPKD
KQQQADQKKAKFHDPTGDHLTLLNVYNAWKNSGYSNAWCFENYIQARAMRRARDVRQQIVKIMERHR
HPIISCGRDTDKIRQALCAGFFRNTARKDPQEGYKTLTEGTPVYLHPSSALFGKQAEWVLYHELVLT
TKEYMHFTTAIEPKWLVEAAPTFFKLAPT*

>>alignment.py

from modeller import *
from modeller.automodel import *

log.verbose()
env = environ()

env.io.atom_files_directory = ['.', 'Prp22-RNA-4.pdb']

a = loopmodel(env, alnfile = 'alignment.ali',
              knowns = 'prp22-rna', sequence = 'prp22-rna_fill')
a.starting_model = 1
a.ending_model   = 1

a.loop.starting_model = 1
a.loop.ending_model   = 2
```

```
a.loop.md_level       = refine.fast

a.make()
```

DHX15. The missing residues of the 6SH7 crystal structure were modeled using the following Python script together with the following alignment files using Modeller.[1]

```
>>alignment.ali
>P1;DHX15
structureX:/path-to-pdb/6sh7.pdb:109:A:789:A::::
HMLEQCINPFTNLPHTPRYYDILKKRLQLPVWEYKDRFTDILVRHQSFVLVGETGSGKTTQIPQWCVE
YMRSLPGPKRGVACTQPRRVAAMSVAQRVADEMDVMLGQEVGYSIRFEDCSSAKTILKYMTDGMLLRE
AMNDPLLERYGVIILDEAHERTLATDILMGVLKEVVRQRSDLKVIVMSATLDAGKFQIYFDNCPLLTI
PGRTHPVEIFYTPEPERDYLEAAIRTVIQIHMCEEEEGDLLLFLTGQEEIDEACKRIKREVDD-----
---KIIPLYSTLPPQQQQRIFEPPP------AIGRKVVVSTNIAETSLTI--VVFVIDPGFAKQKVYN
PRIRVESLLVTAISKASAQQRAGRAGRTRPGKCFRLYTEKAYKTEMQDNTYPEILRSNLGSVVLQLKK
LGIDDLVHFDFMDPPAPETLMRALELLNYLAALNDDGDLTELGSMMAEFPLDPQLAKMVIASCDYNCS
NEVLSITAMLSVPQCFVRPTEAKKAADEAKMRFAHIDGDHLTLLNVYHAFKQNHESVQWCYDNFINYR
SLMSADNVRQQLSRIMDRFNLPRRSTDFTSRDYYINIRKALVTGYFMQVAHLERTGHYLTVKDNQVVQ
LHPSTVLDHKPEWVLYNEFVLTTKNYIRTCTDIKPEWLVKIAPQYYDMSNFPQCEAKRQLDRIIAKLQ
S*

>P1;DHX15-fill
sequence:::::::::
HMLEQCINPFTNLPHTPRYYDILKKRLQLPVWEYKDRFTDILVRHQSFVLVGETGSGKTTQIPQWCVE
YMRSLPGPKRGVACTQPRRVAAMSVAQRVADEMDVMLGQEVGYSIRFEDCSSAKTILKYMTDGMLLRE
AMNDPLLERYGVIILDEAHERTLATDILMGVLKEVVRQRSDLKVIVMSATLDAGKFQIYFDNCPLLTI
PGRTHPVEIFYTPEPERDYLEAAIRTVIQIHMCEEEEGDLLLFLTGQEEIDEACKRIKREVDDLGPEV
GDIKIIPLYSTLPPQQQQRIFEPPPPKKQNGAIGRKVVVSTNIAETSLTIDGVVFVIDPGFAKQKVYN
PRIRVESLLVTAISKASAQQRAGRAGRTRPGKCFRLYTEKAYKTEMQDNTYPEILRSNLGSVVLQLKK
LGIDDLVHFDFMDPPAPETLMRALELLNYLAALNDDGDLTELGSMMAEFPLDPQLAKMVIASCDYNCS
NEVLSITAMLSVPQCFVRPTEAKKAADEAKMRFAHIDGDHLTLLNVYHAFKQNHESVQWCYDNFINYR
SLMSADNVRQQLSRIMDRFNLPRRSTDFTSRDYYINIRKALVTGYFMQVAHLERTGHYLTVKDNQVVQ
LHPSTVLDHKPEWVLYNEFVLTTKNYIRTCTDIKPEWLVKIAPQYYDMSNFPQCEAKRQLDRIIAKLQ
S*
```

```
>> alignment.py
from modeller import *
from modeller.automodel import *

log.verbose()
env = environ()

env.io.atom_files_directory = ['.', '6sh7.pdb']

a = loopmodel(env, alnfile = 'alignment.ali',
              knowns = 'DHX15', sequence = 'DHX15-fill',
              assess_methods=(assess.DOPE,
                              assess.GA341),
              loop_assess_methods=(assess.DOPE,
                              assess.GA341))
a.starting_model = 1
```

```
a.ending_model   = 2

a.loop.starting_model = 1
a.loop.ending_model   = 5
a.loop.md_level       = refine.fast

a.make()
```

References

(1) Webb, B.; Sali, A. Protein Structure Modeling with MODELLER. *Prot. Struct. Predict.* **2014**, 1–15.