Supplementary Material for

Aggregation versus inclusion complexes to solubilize drugs with Cyclodextrins. A case study using sulphobutylether-β-cyclodextrins and remdesivir

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Table S1.- Average number of clusters for all the molecules, for the CD molecules and for the Remdesivir molecules, determined through the last 100 ns of all the trajectories, together with the corresponding standard deviation values.

CD ID	#REMD	All		CDs		REMD	
		Neutral	Charged	Neutral	Charged	Neutral	Charged
5SBE	1	10.2±1.4	10.2±1.0	10.2±1.4	10.2±1.06	1.0±0.0	1.0±0.0
	2	10.8±1.5	8.01±0.90	10.9±1.4	8.06±0.91	2.0±0.0	2.0±0.0
	4	8.07±0.84	9.5±1.0	8.27±0.94	10.1±1.2	2.85±0.38	2.81±0.39
	8	7.9±1.3	5.4±1.0	8.5±1.4	5.6±1.1	4.1±0.3	5.72±0.58
6SBE	1	10.11±0.86	9.5±1.1	10.11±0.87	9.5±1.1	1.0±0.0	1.0±0.0
	2	11.6±1.4	8.9±1.1	11.7±1.4	8.9±1.1	2.0±0.0	1.0±0.0
	4	8.4±1.3	6.26±0.86	8.8±1.3	6.4±0.89	2.00±0.05	4.0±0.0
	8	10.4±1.1	7.57±0.92	10.8±1.2	7.9±1.2	2.01±0.09	5.02±0.14
7SBE	1	10.95±0.90	11.9±1.3	11.13±0.90	12.0±1.3	1.0±0.0	1.0±0.0
	2	10.05±0.73	9.86±0.68	10.97±0.76	9.90±0.72	1.0±0.0	2.0±0.0
	4	9.9±1.6	8.8±1.3	10.0±1.6	9.4±1.2	3.0±0.0	3.00±0.03
	8	9.98±0.84	8.32±0.57	10.75±0.89	8.52±0.72	3.54±0.50	4.99±0.12

Table S2.- Average number of H-bonds between CDs, between CDs and remdesivir, between CD and water and between remdesivir and water, determined through the last 100 ns of all the trajectories, together with the corresponding standard deviation values. The first and third double columns are normalized by CD molecule while the second and last double columns are normalized by drug molecule.

| CD ID	#REMD	CD-CD		CD-REMD		CD-Water		REMD-Water	
		Neutral	Charged	Neutral	Charged	Neutral	Charged	Neutral	Charged
5SBE	1	3.88±0.45	4.01±0.35	2.68±0.98	5.4±1.1	61.6±1.2	60.8±1.1	3.0±1.3	3.0±1.4
	2	3.80±0.37	4.32±0.38	1.88±0.76	4.42±0.91	61.6±1.1	59.9±1.1	3.5±1.1	5.1±1.0
	4	4.37±0.37	3.72±0.36	2.37±0.54	4.30±0.67	59.7±1.1	60.4±1.1	3.11±0.71	2.71±0.59
	8	3.98±0.36	4.52±0.33	2.25±0.35	4.49±0.43	59.6±1.1	55.9±1.0	3.12±0.48	2.76±0.49
6SBE	1	3.95±0.37	3.87±0.33	1.7±1.1	4.2±1.3	67.1±1.1	66.9±1.1	3.5±1.8	5.5±1.6
	2	3.35±0.39	3.88±0.37	2.37±0.64	4.31±0.76	68.1±1.2	66.6±1.2	3.4±1.0	2.56±0.81
	4	3.90±0.36	4.32±0.36	1.64±0.45	4.57±0.56	66.5±1.1	64.2±1.1	3.31±0.65	2.77±0.65
	8	3.17±0.33	3.71±0.33	1.89±0.39	3.93±0.39	67.5±1.1	64.1±1.0	2.61±0.42	3.76±0.47
7SBE	1	3.38±0.34	3.36±0.51	2.18±0.87	4.3±1.2	73.9±1.1	74.0±1.5	3.3±1.5	2.4±1.3
	2	4.06±0.38	4.04±0.39	2.33±0.56	4.79±0.89	72.2±1.2	71.4±1.3	2.34±0.90	2.56±0.86
	4	3.68±0.37	3.82±0.31	2.05±0.45	3.23±0.56	72.6±1.2	71.2±1.1	2.68±0.63	3.91±0.95
	8	3.41±0.32	3.62±0.32	1.83±0.32	4.10±0.41	72.3±1.1	69.6±1.1	2.98±0.46	2.78±0.47
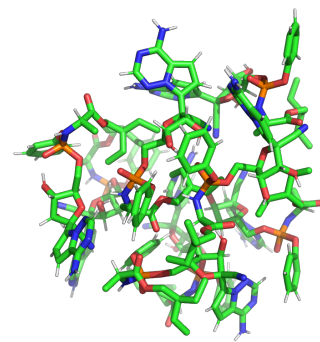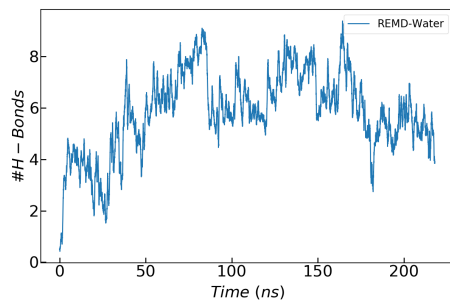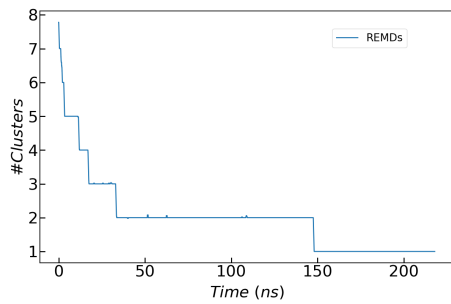
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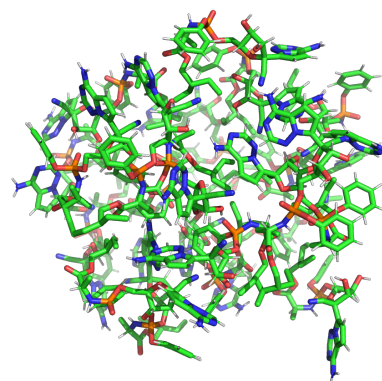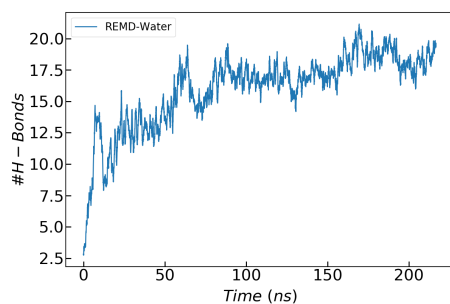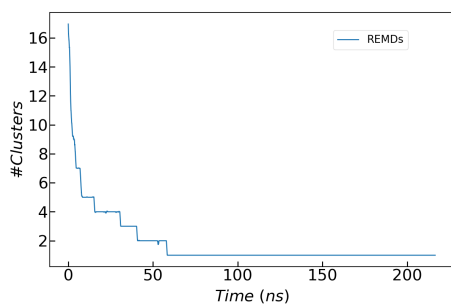
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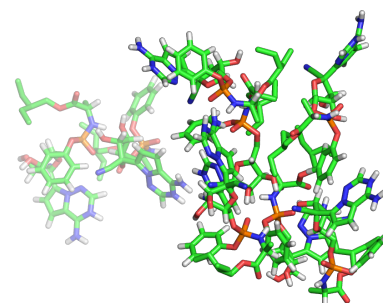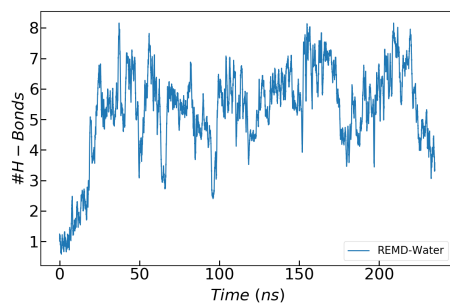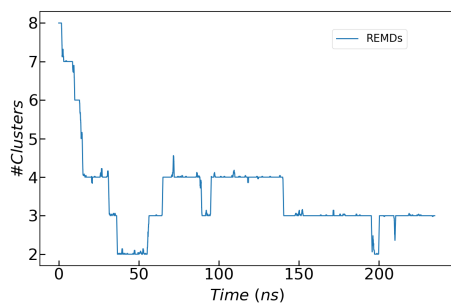
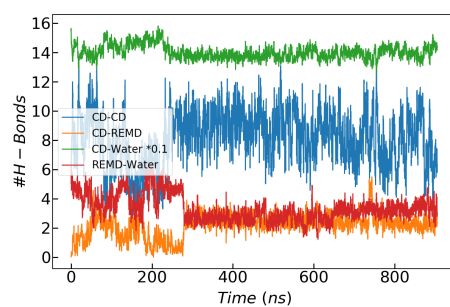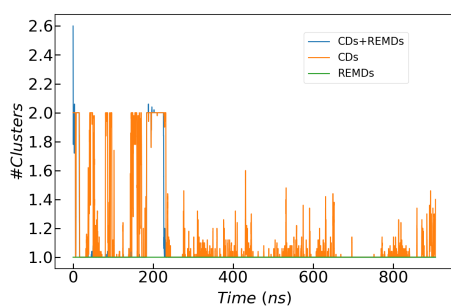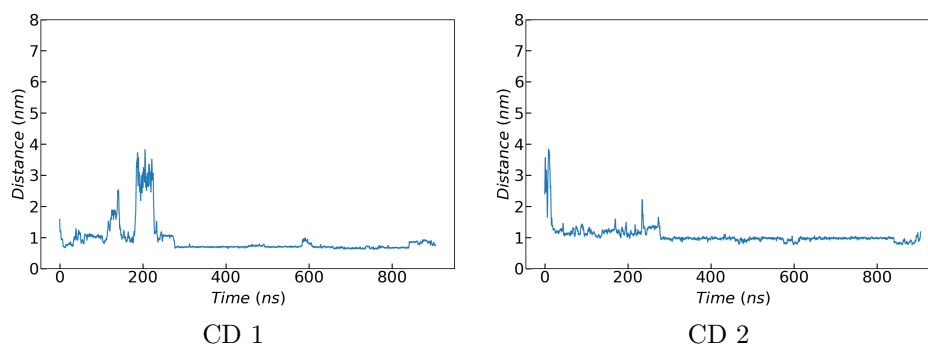8 x Protonated Remdesivir
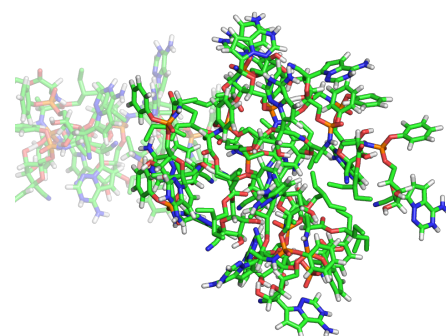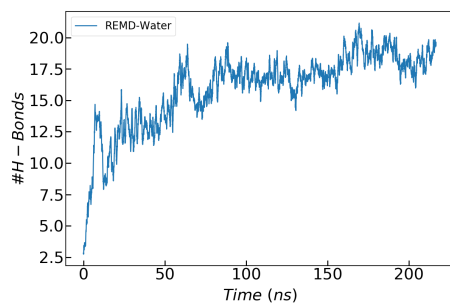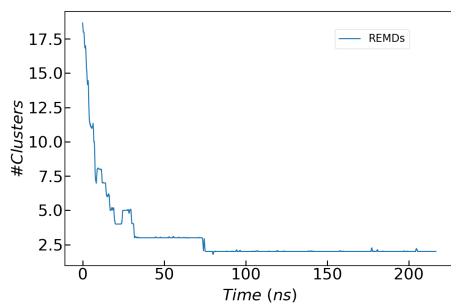
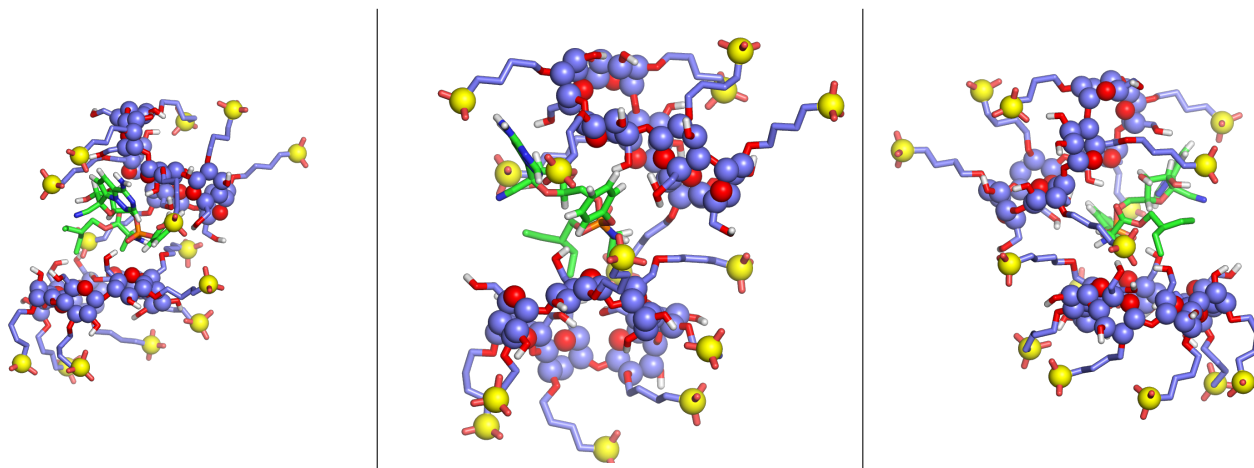20 x Protonated Remdesivir

2 x 7SBE + 1 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:
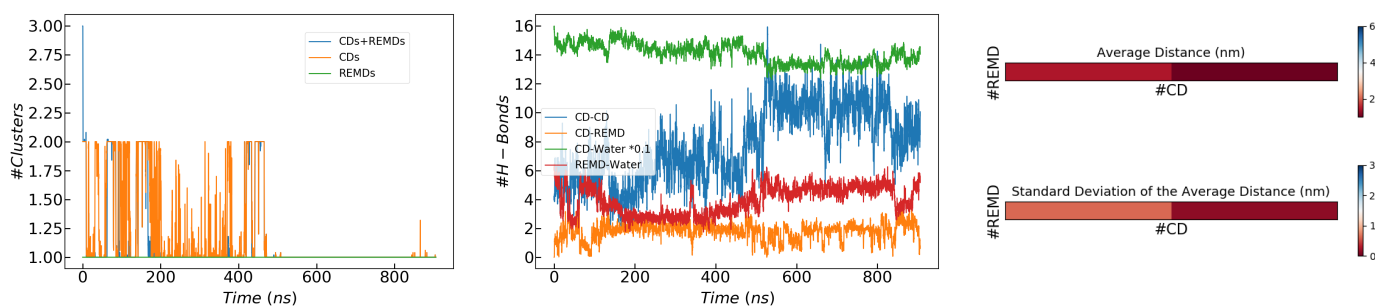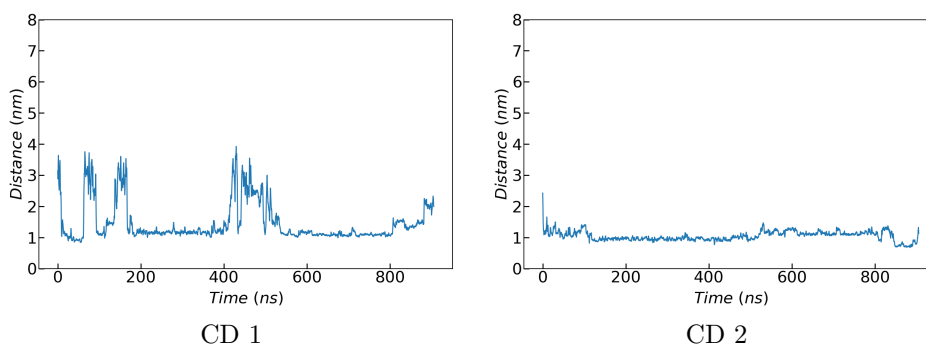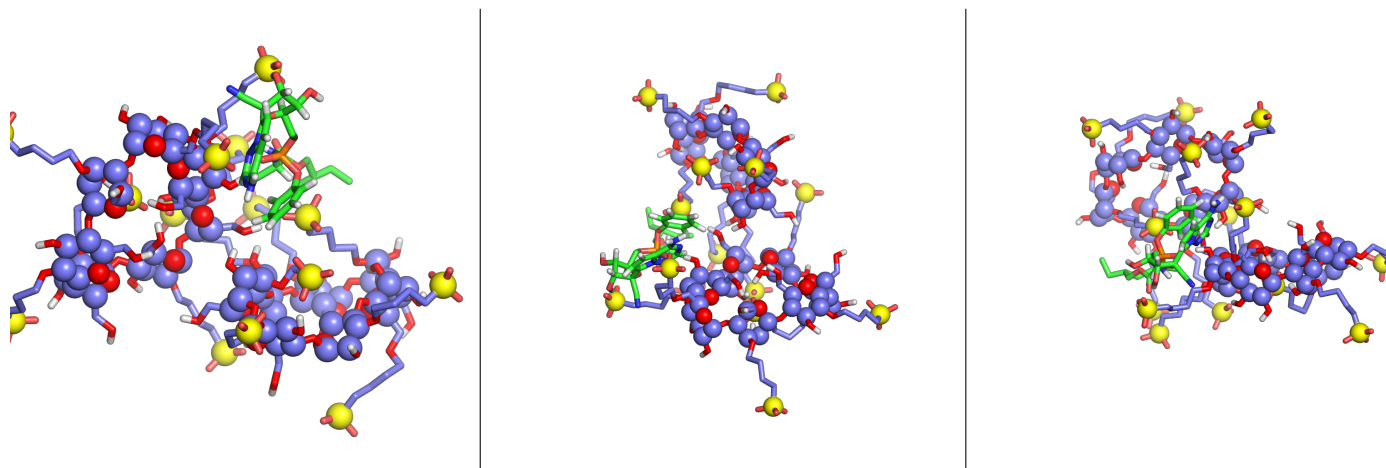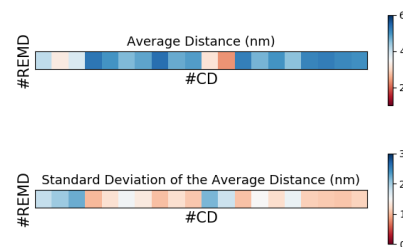

CD 1

CD 2
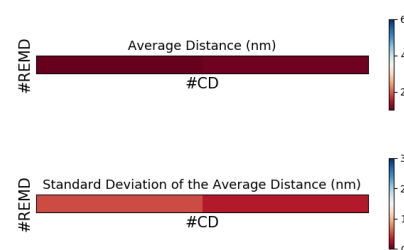
Snapshots taken from the last conformation:

2 x 7SBE + 1 x Neutral Remdesivir

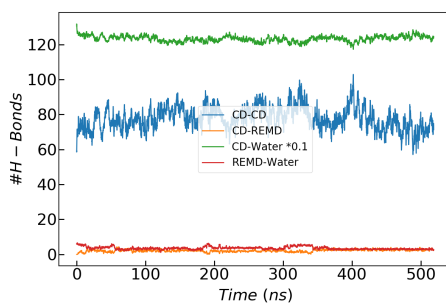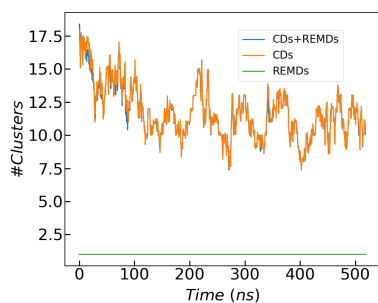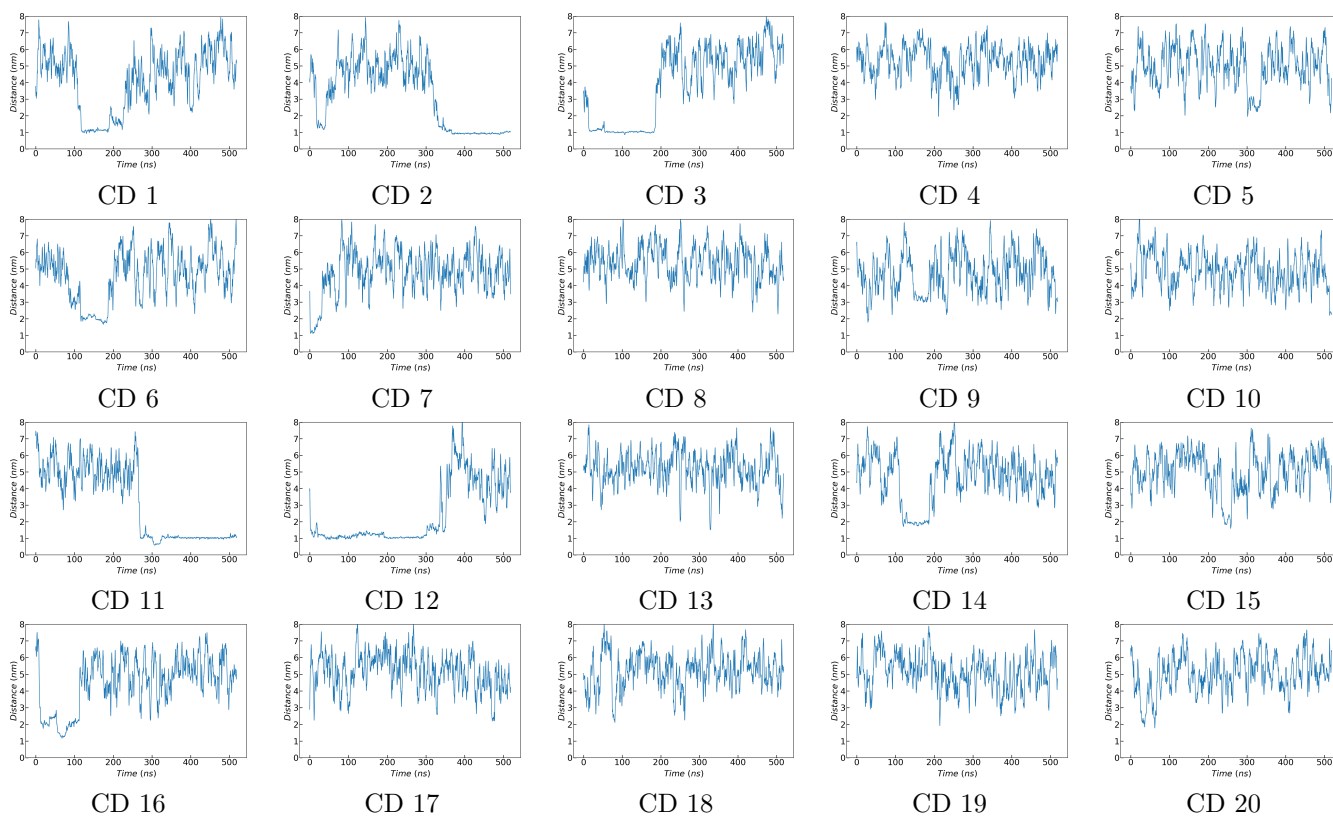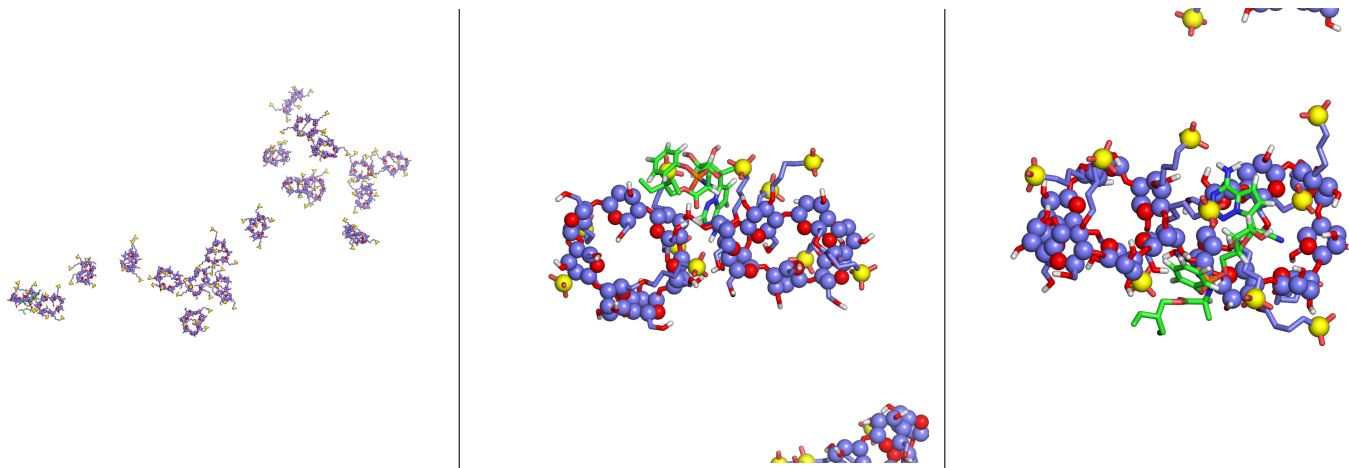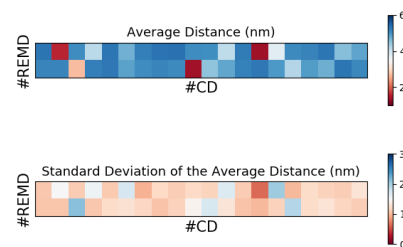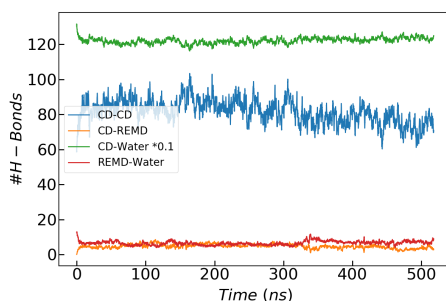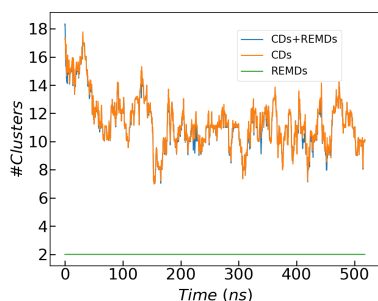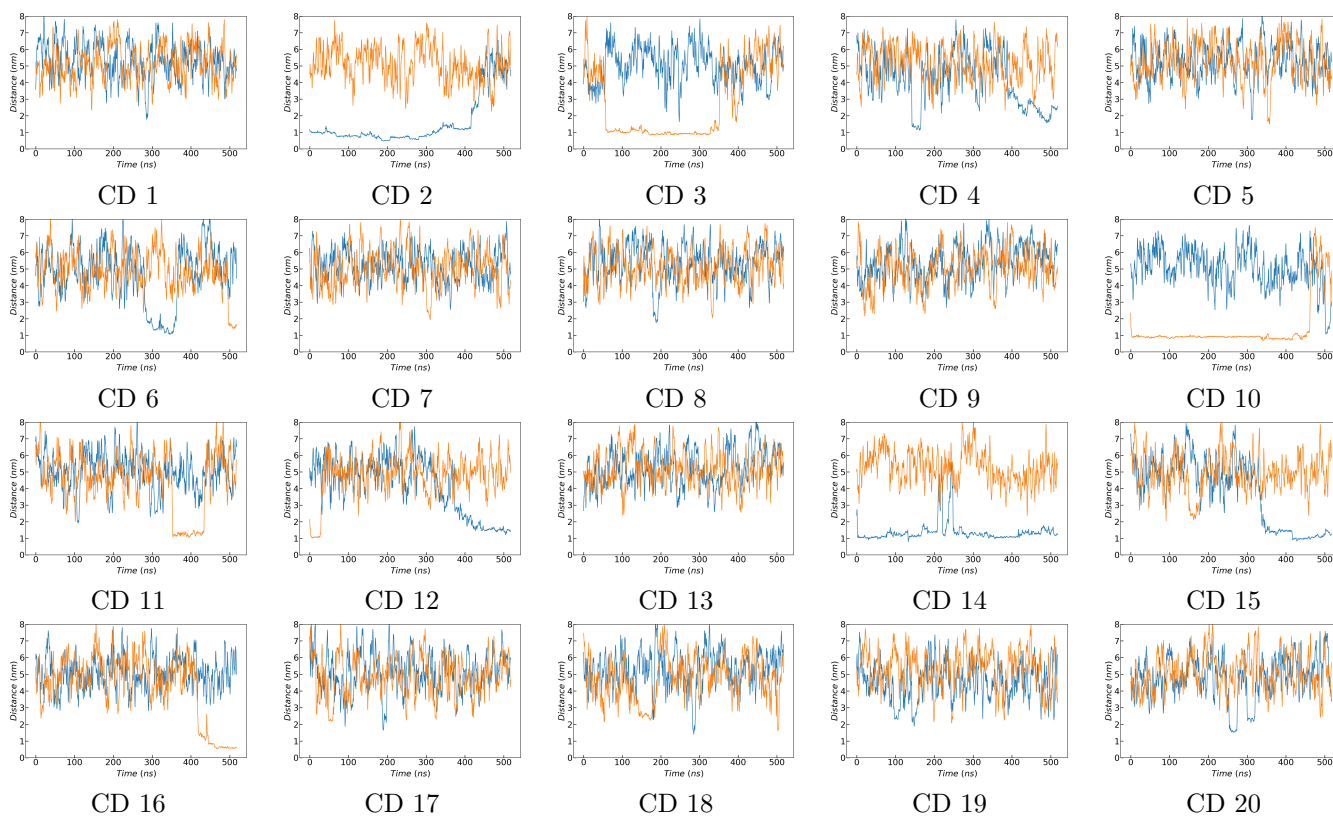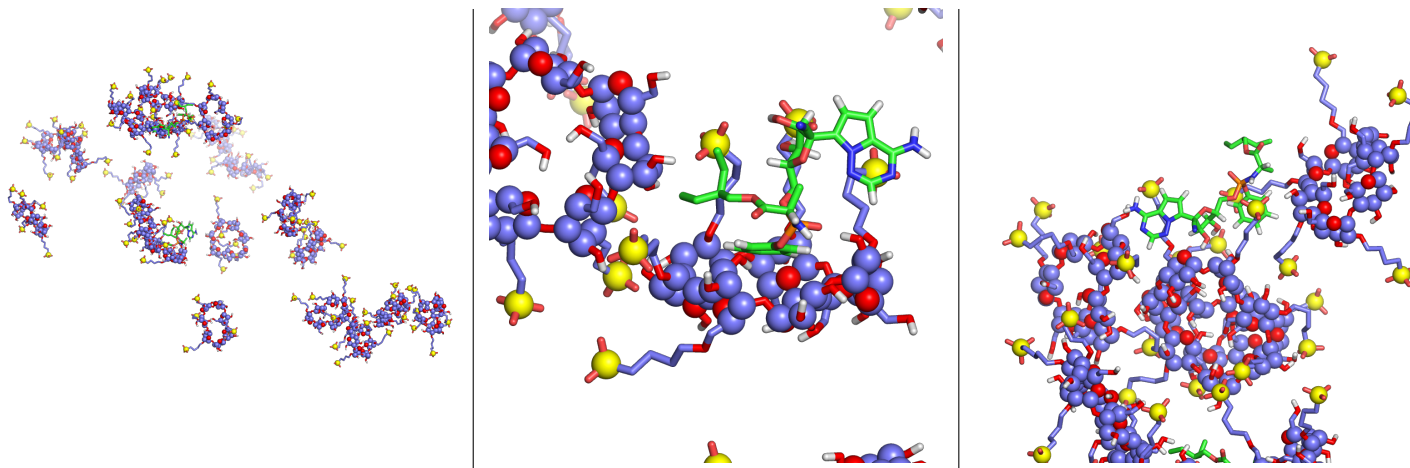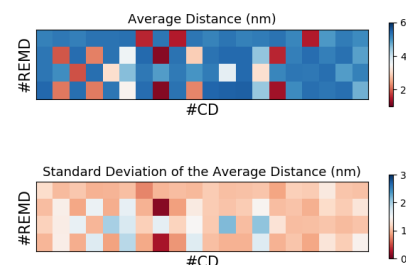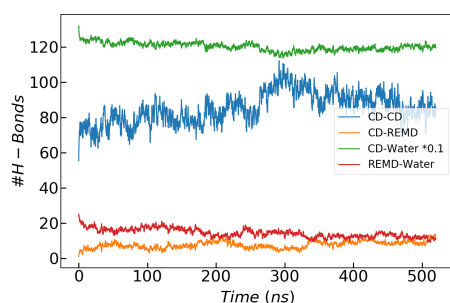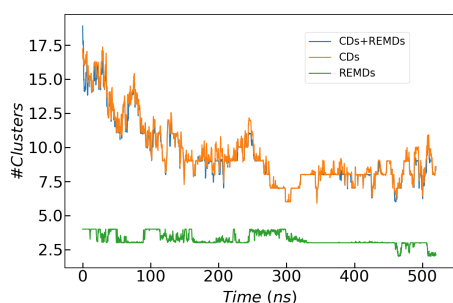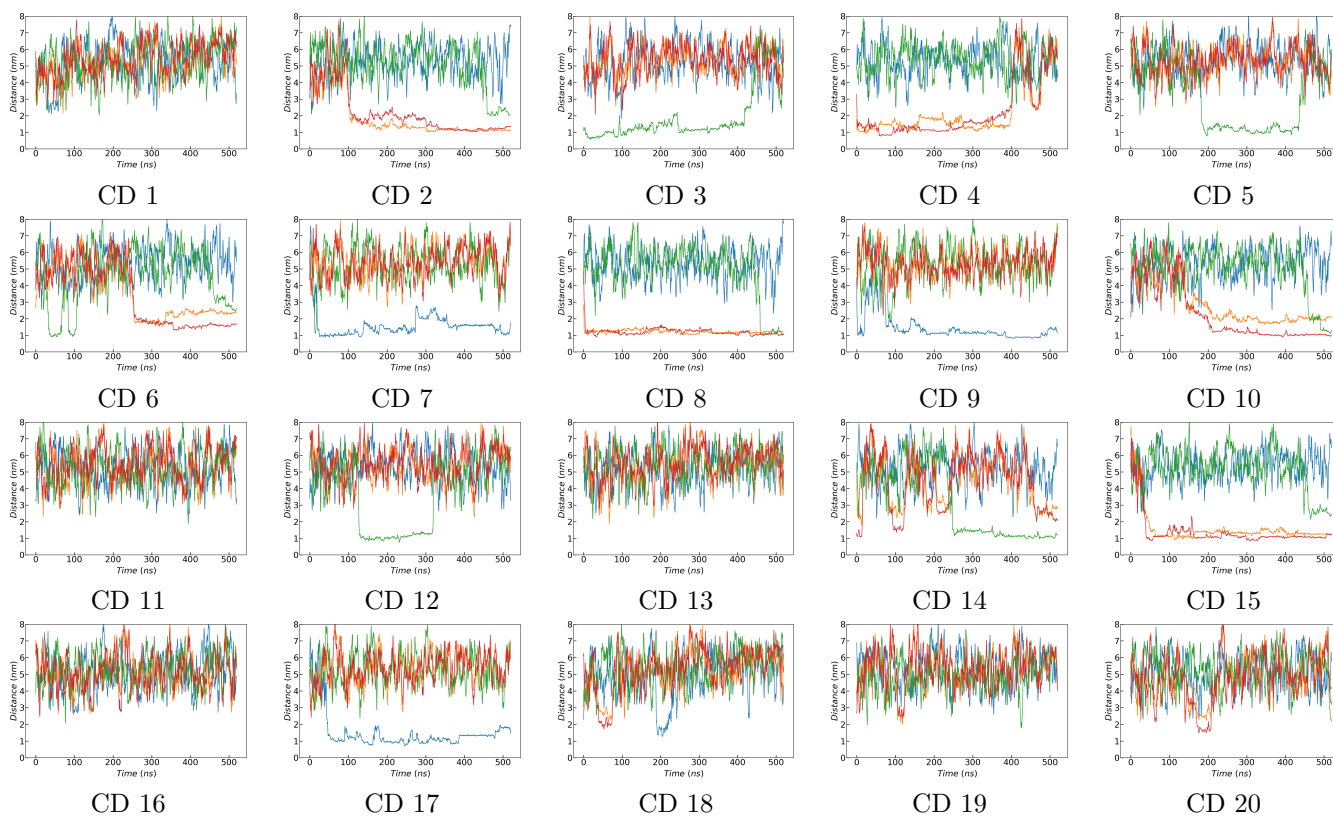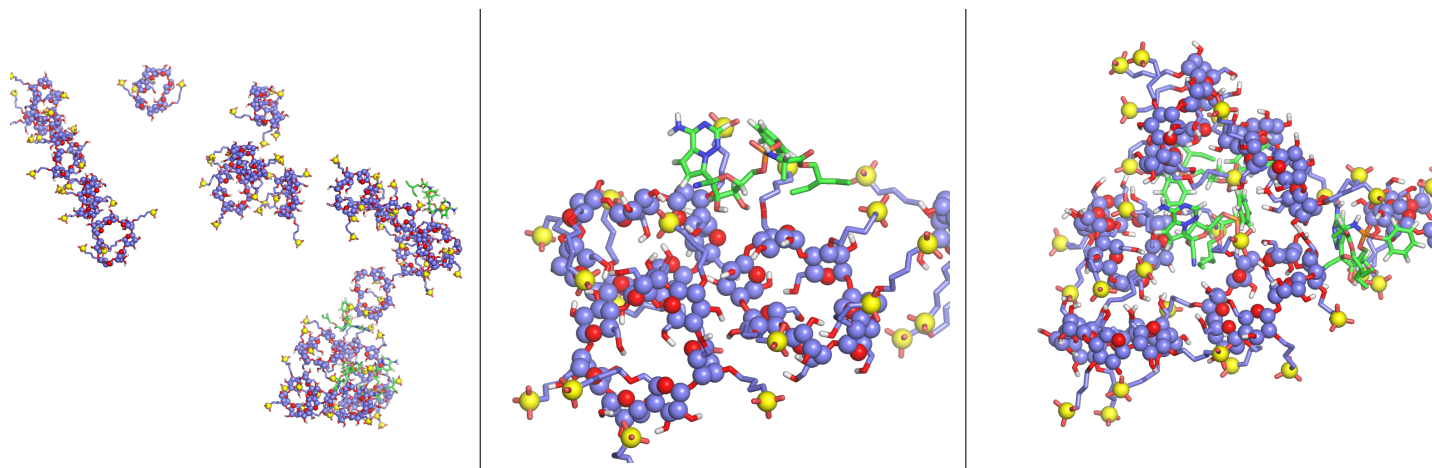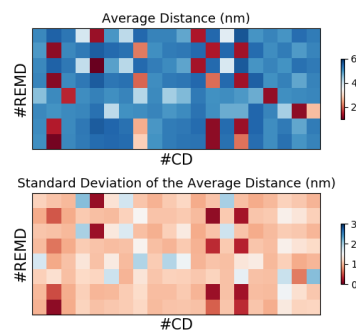Distance between cyclodextrins and remdesivir molecules as a function of time:
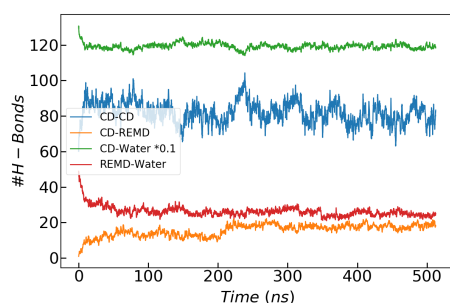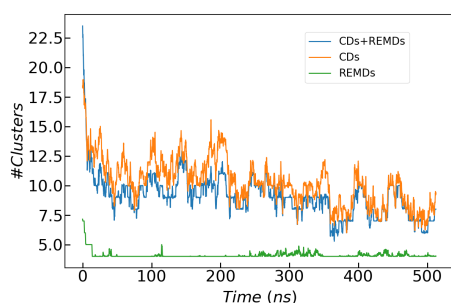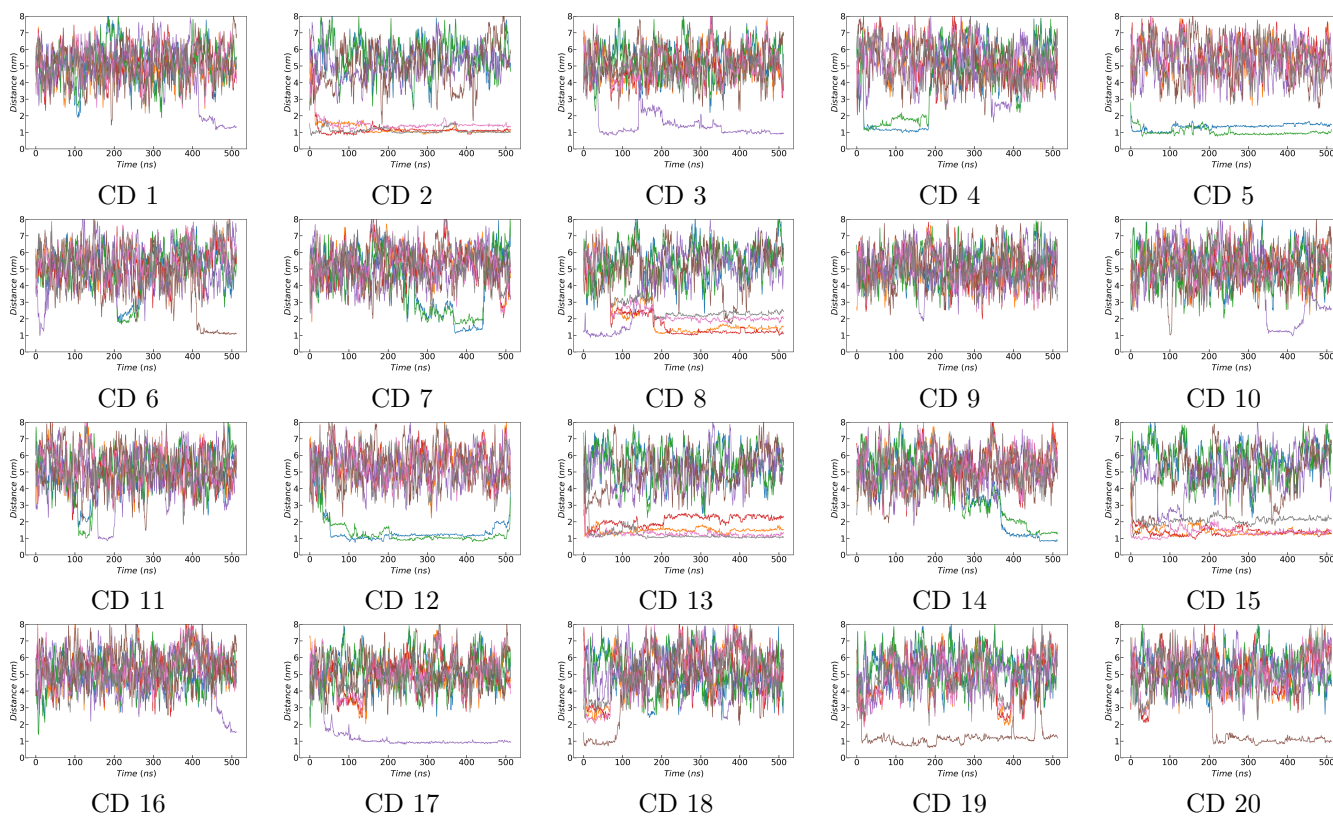

CD 1

CD 2

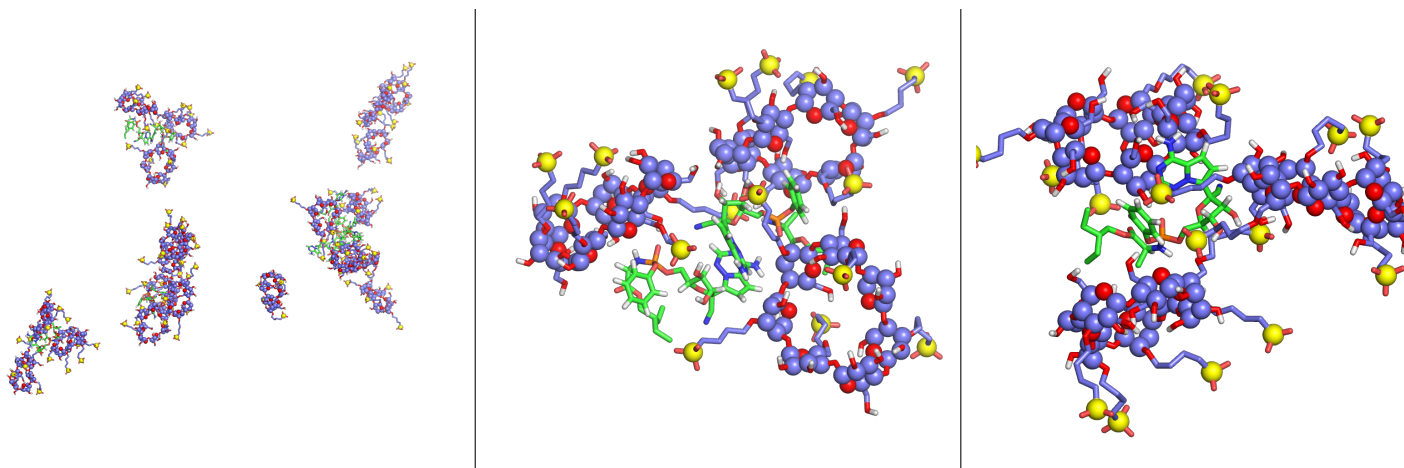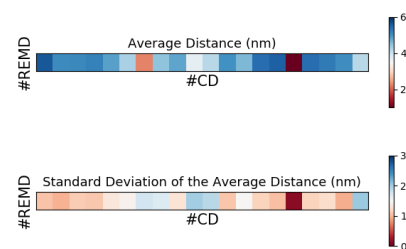

Snapshots taken from the last conformation:

20 x 5SBE + 1 x Neutral Remdesivir

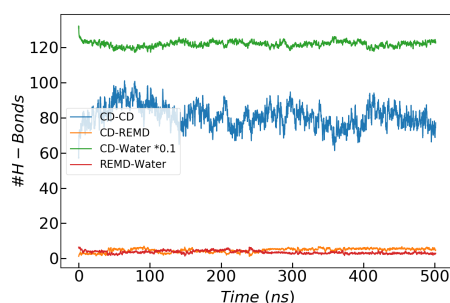Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1 CD 2 CD 3 CD 4 CD 5

CD 6 CD 7 CD 8 CD 9 CD 10

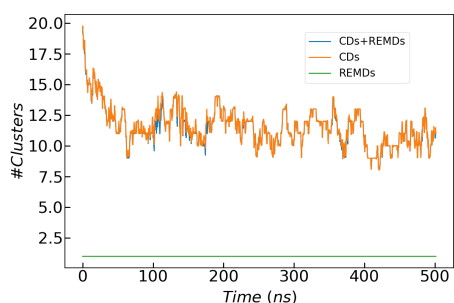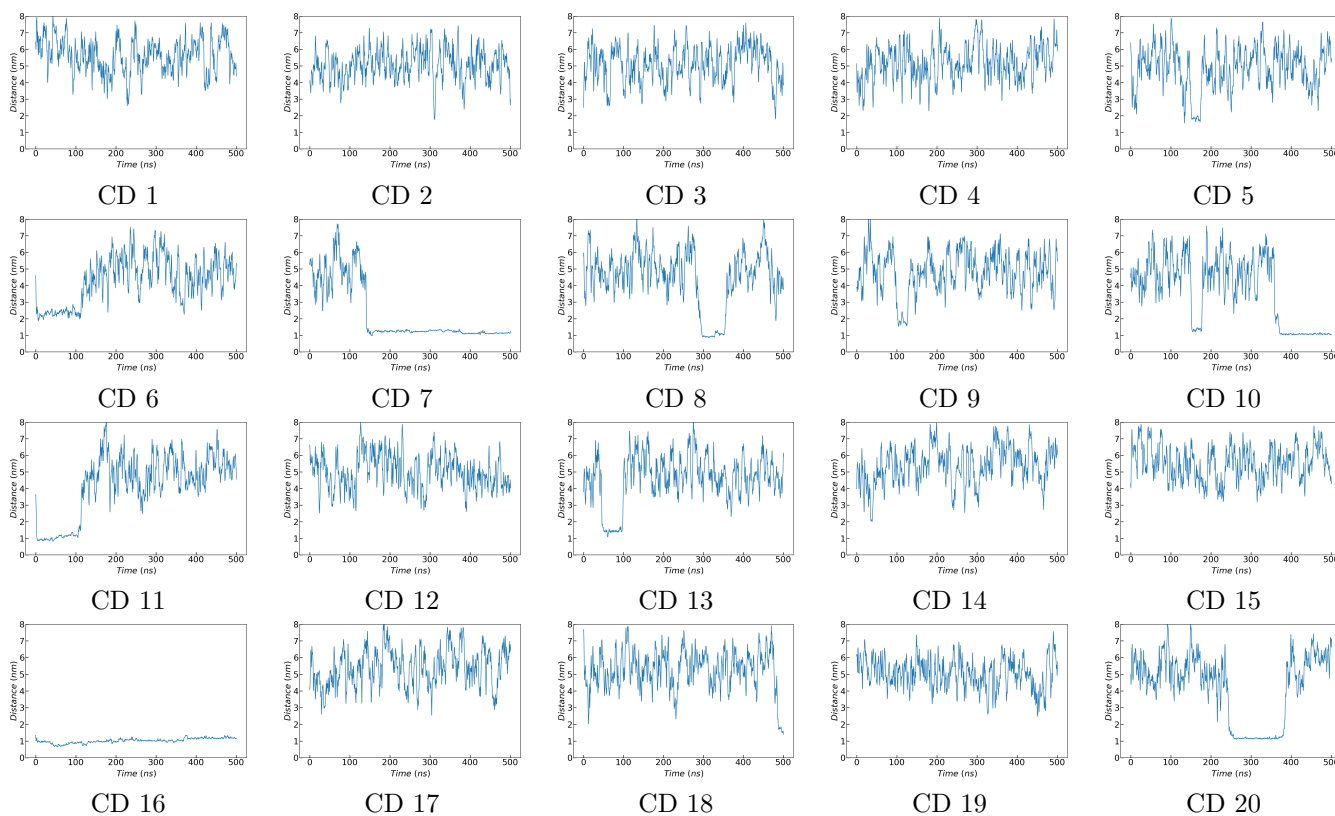CD 11 CD 12 CD 13 CD 14 CD 15

CD 16 CD 17 CD 18 CD 19 CD 20
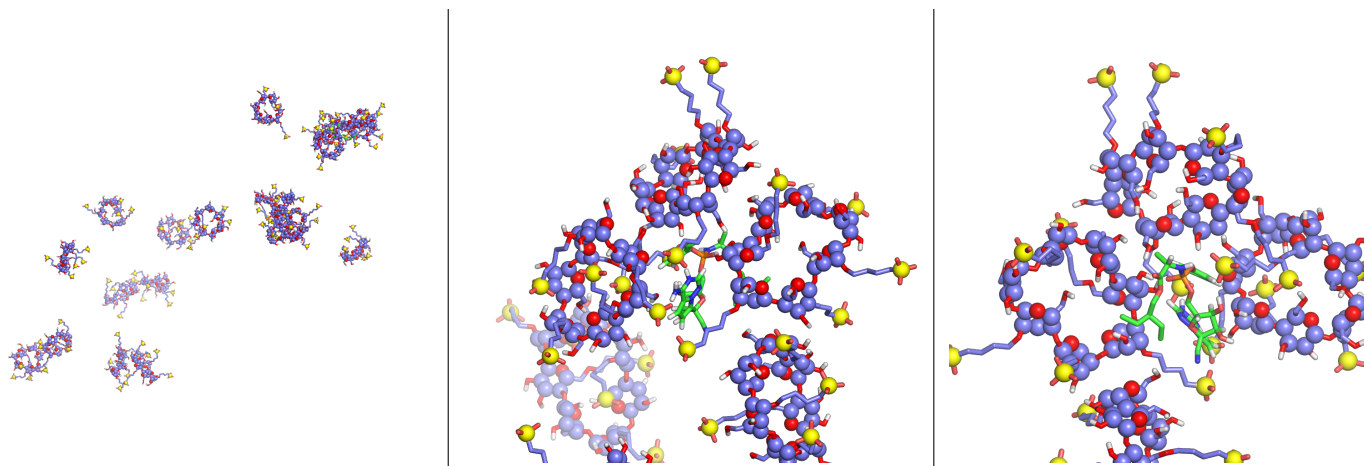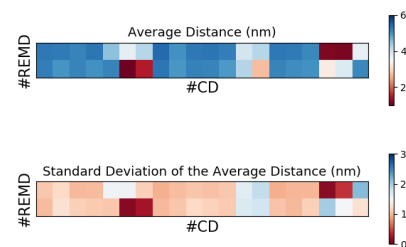

Snapshots taken from the last conformation:

20 x 5SBE + 2 x Neutral Remdesivir

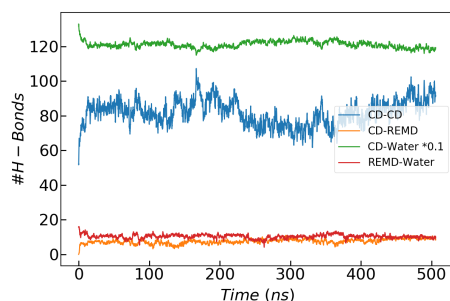Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
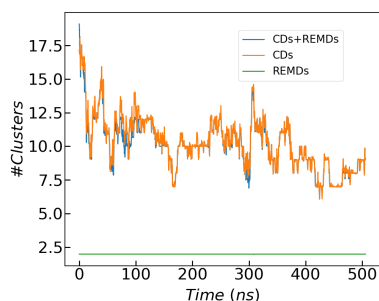
CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 5SBE + 4 x Neutral Remdesivir

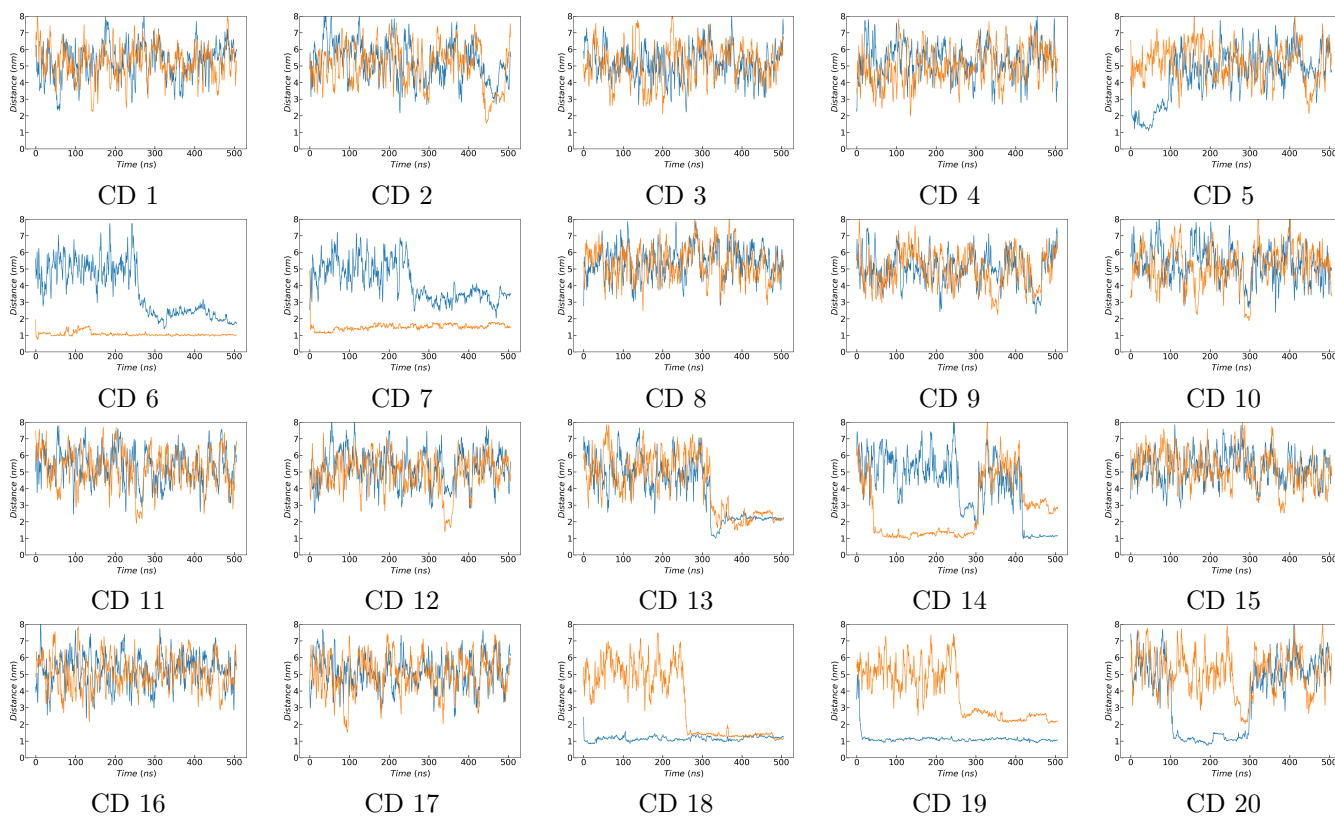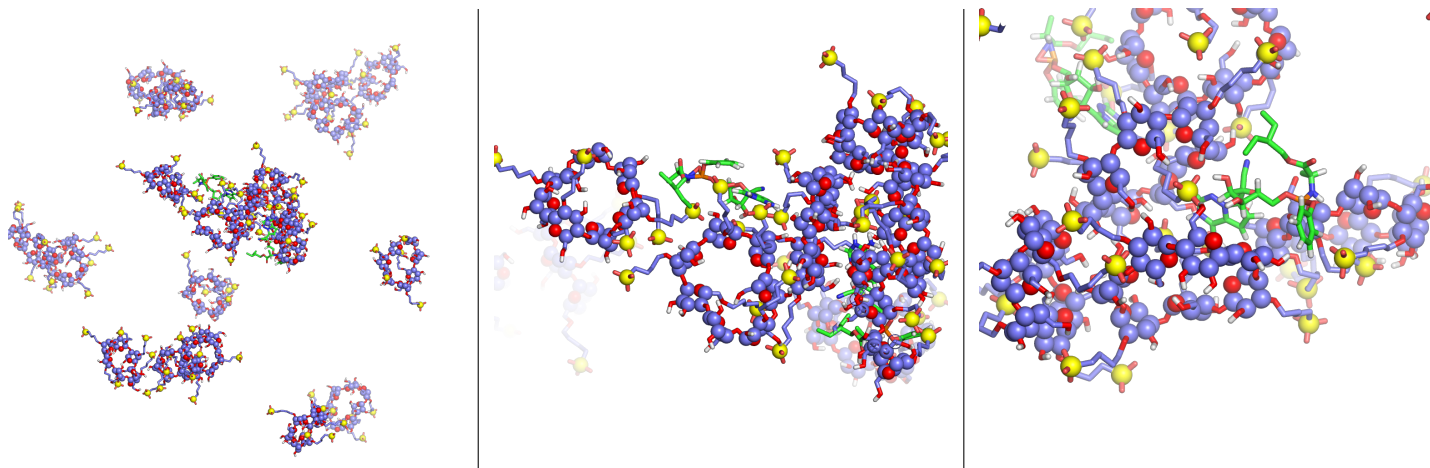Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
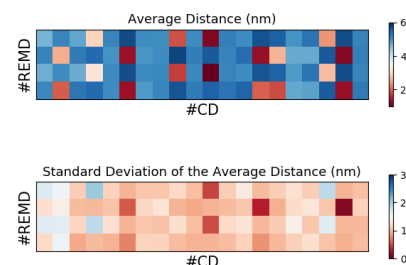
CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 5SBE + 8 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15

CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 5SBE + 1 x Protonated Remdesivir

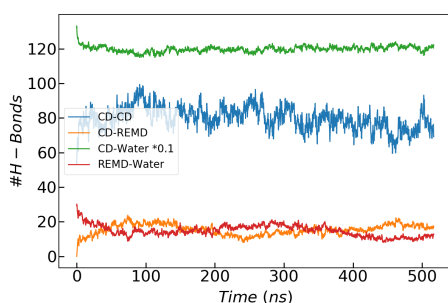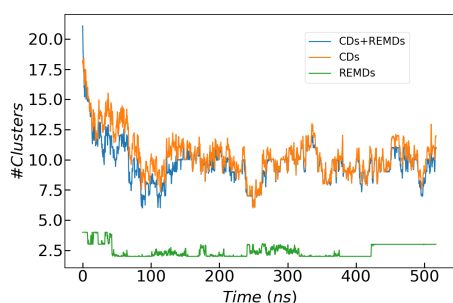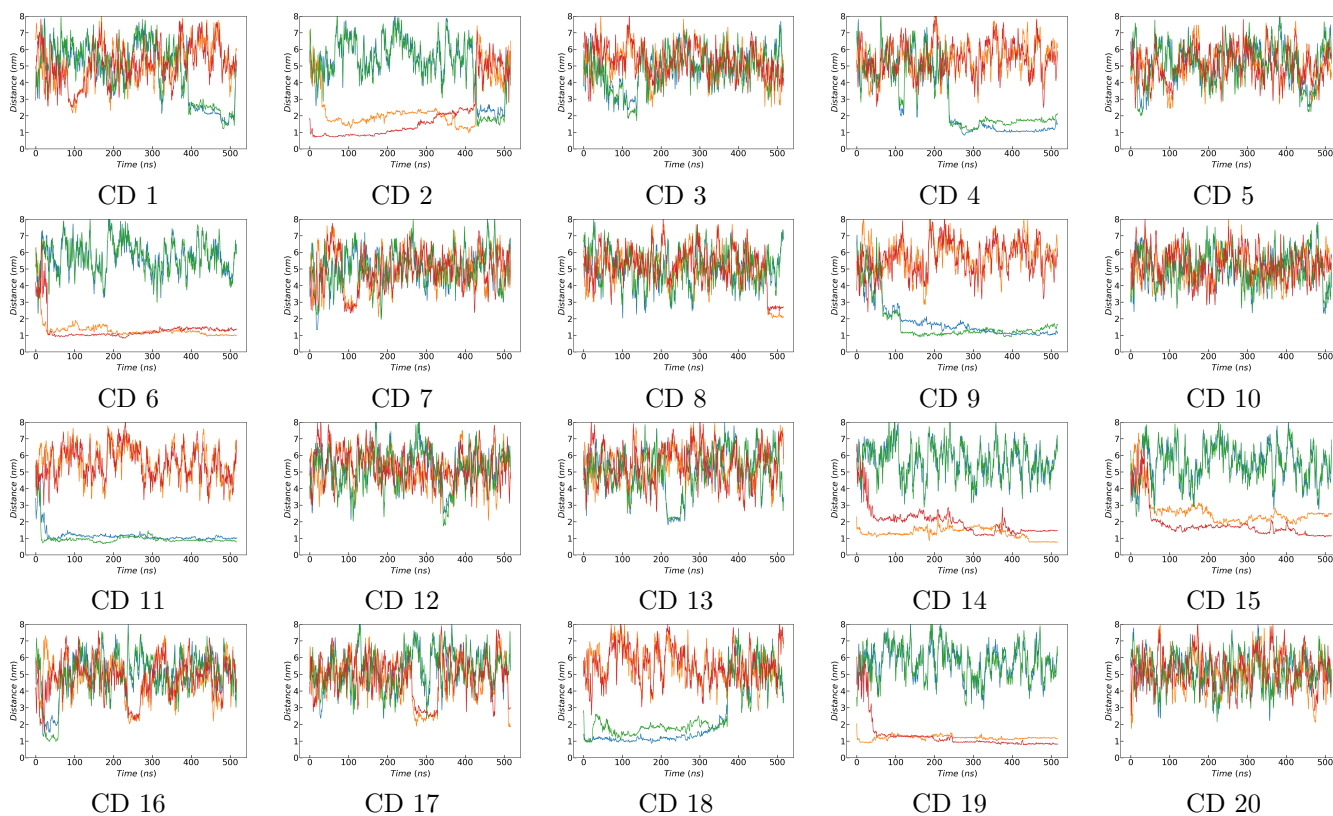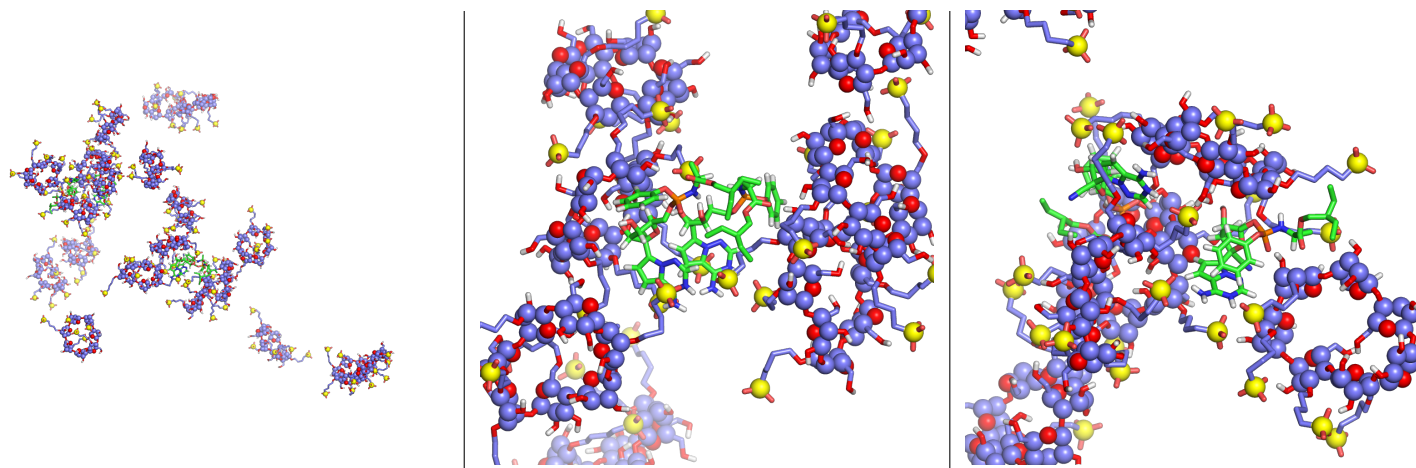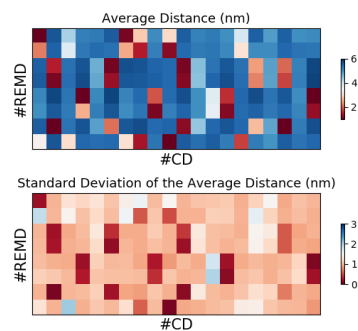Distance between cyclodextrins and remdesivir molecules as a function of time:
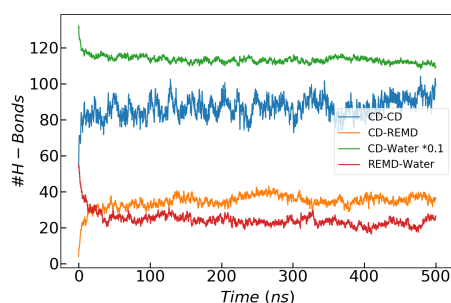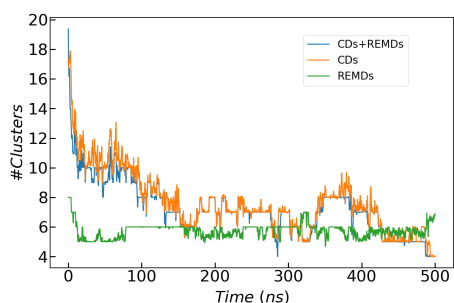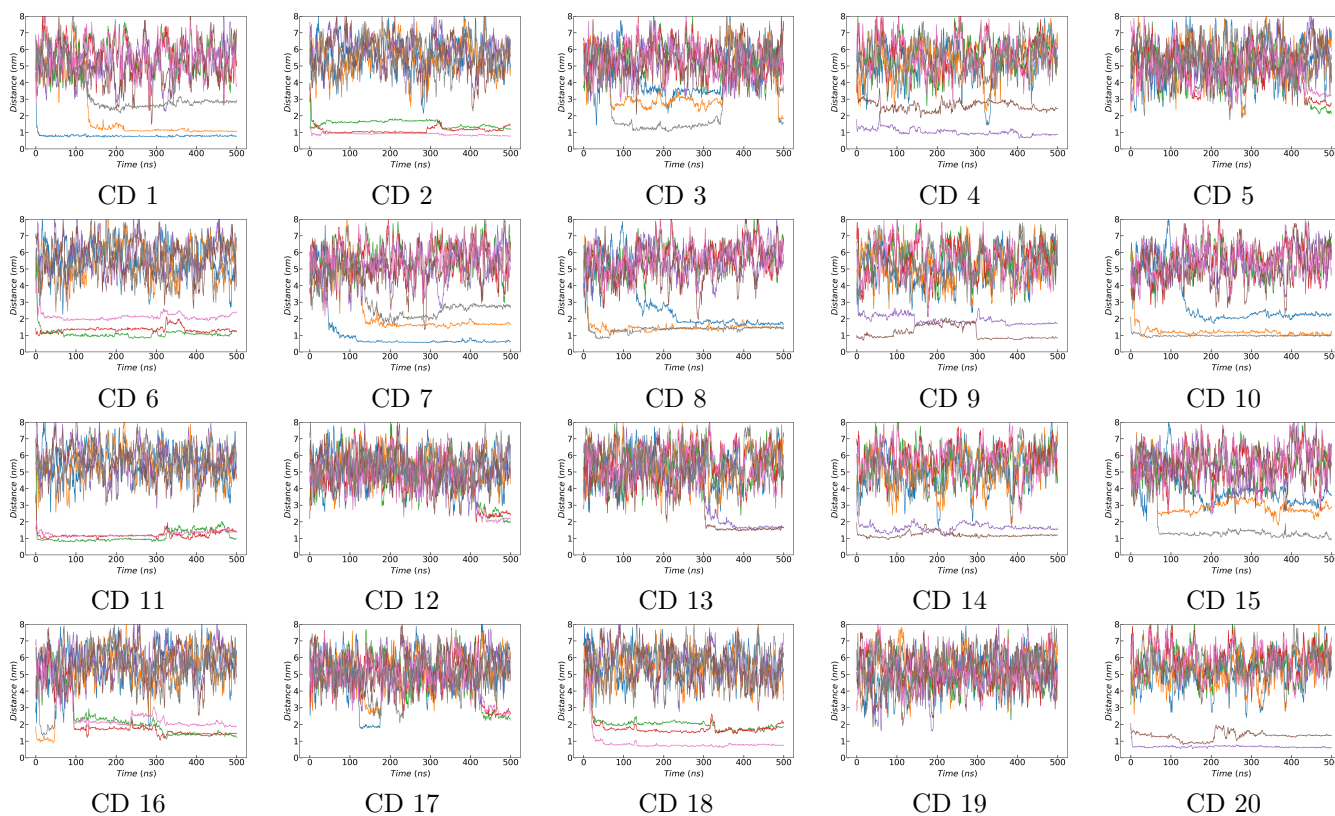

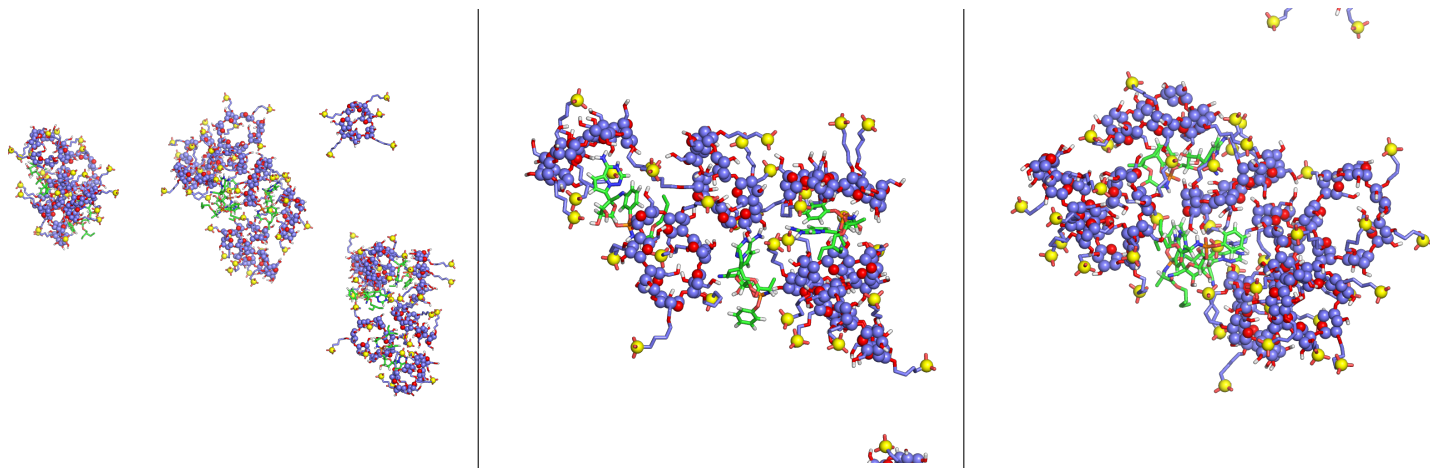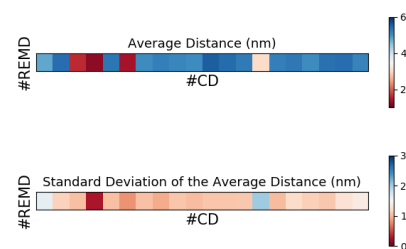Snapshots taken from the last conformation:

20 x 5SBE + 2 x Protonated Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15

CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 5SBE + 4 x Protonated Remdesivir

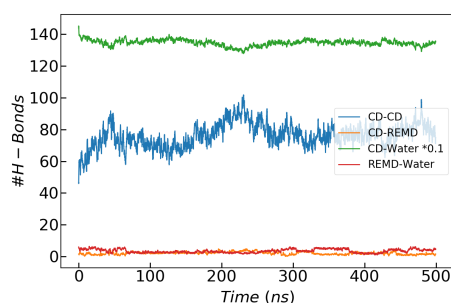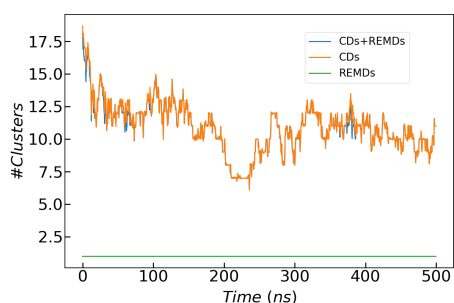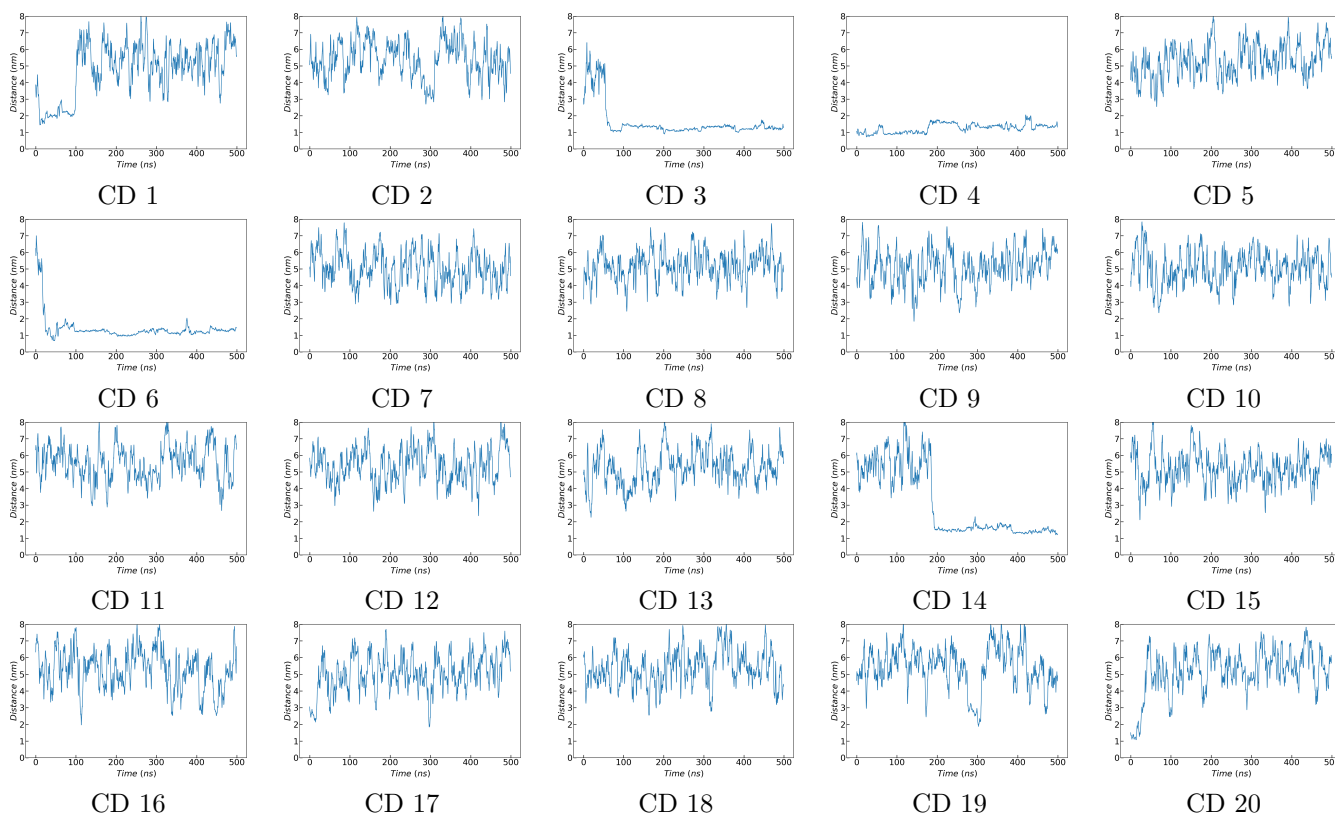Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1 CD 2 CD 3 CD 4 CD 5

CD 6 CD 7 CD 8 CD 9 CD 10

CD 11 CD 12 CD 13 CD 14 CD 15

CD 16 CD 17 CD 18 CD 19 CD 20

Snapshots taken from the last conformation:

20 x 5SBE + 8 x Protonated Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1　　CD 2　　CD 3　　CD 4　　CD 5

CD 6　　CD 7　　CD 8　　CD 9　　CD 10

CD 11　　CD 12　　CD 13　　CD 14　　CD 15

CD 16　　CD 17　　CD 18　　CD 19　　CD 20

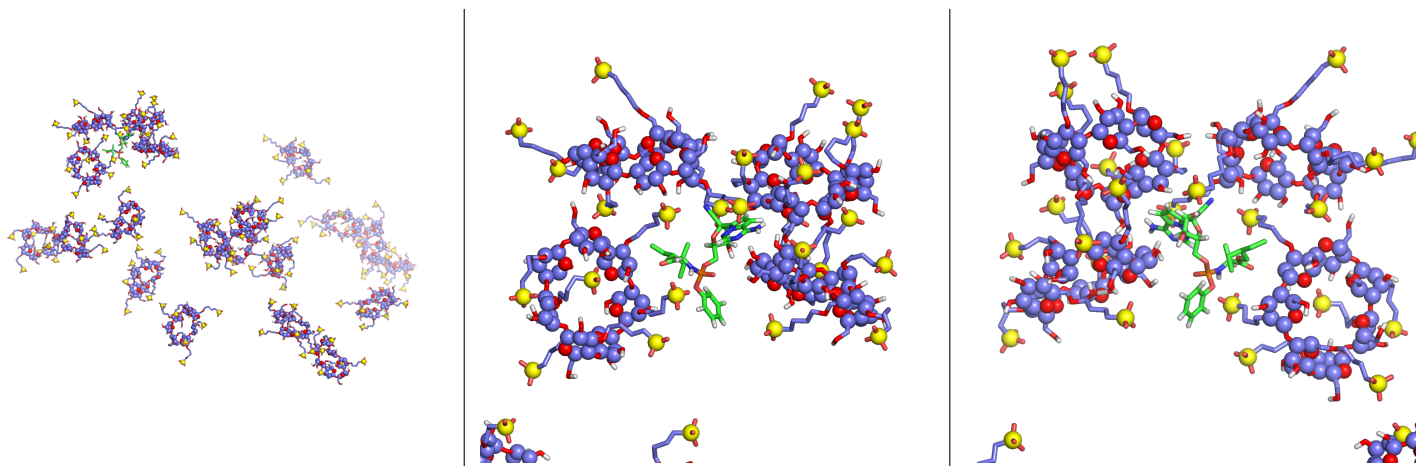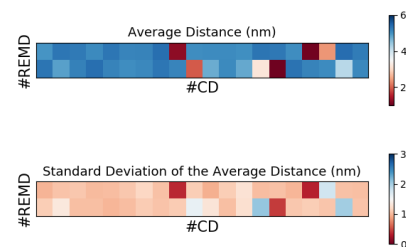Snapshots taken from the last conformation:

20 x 6SBE + 1 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:
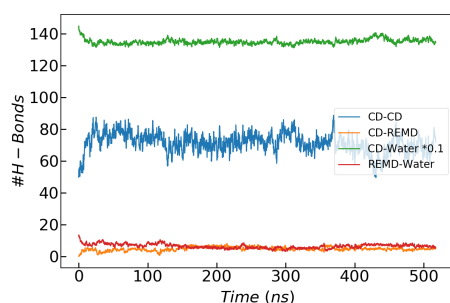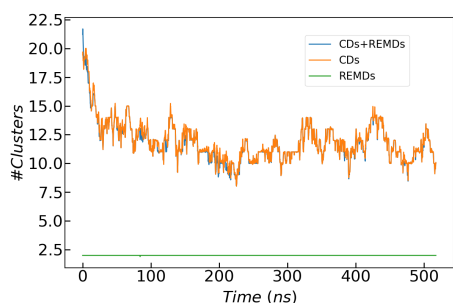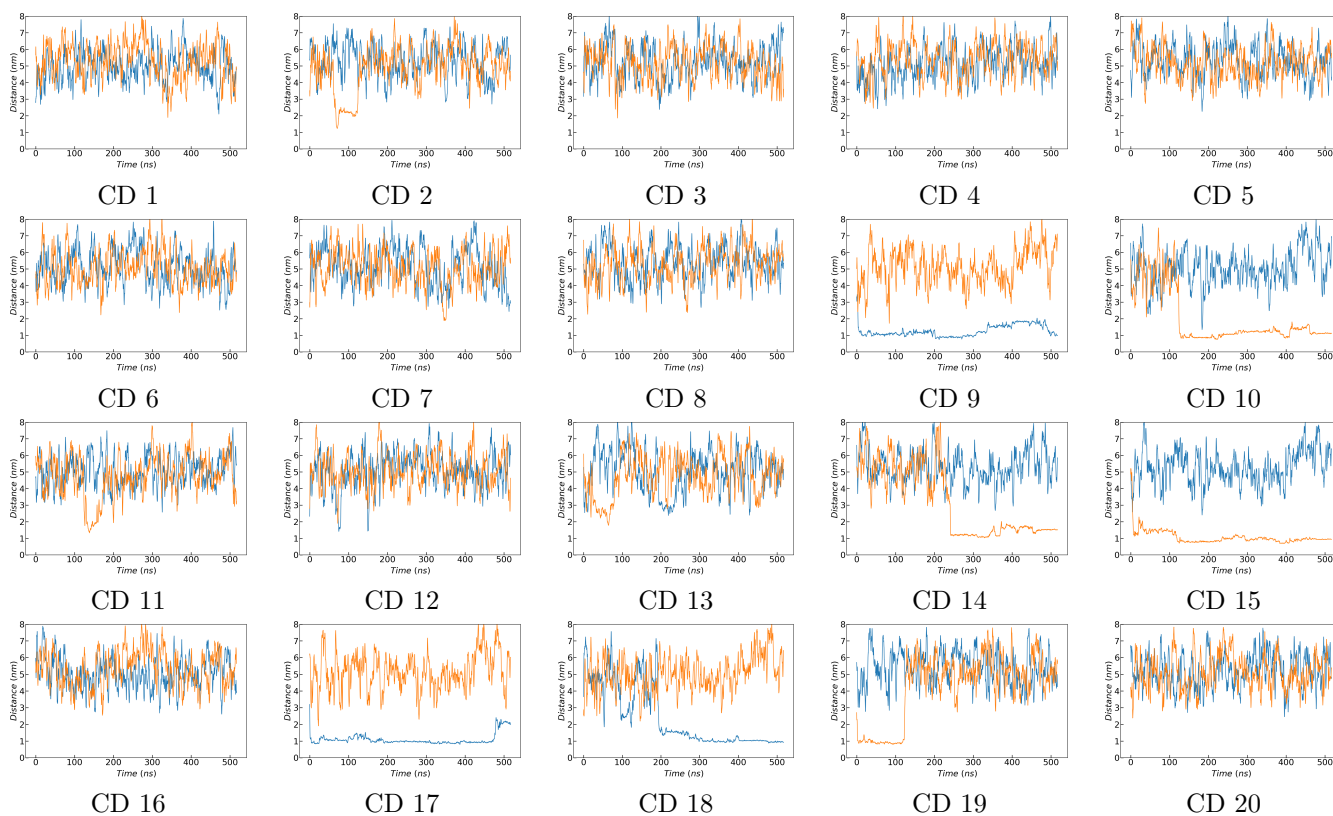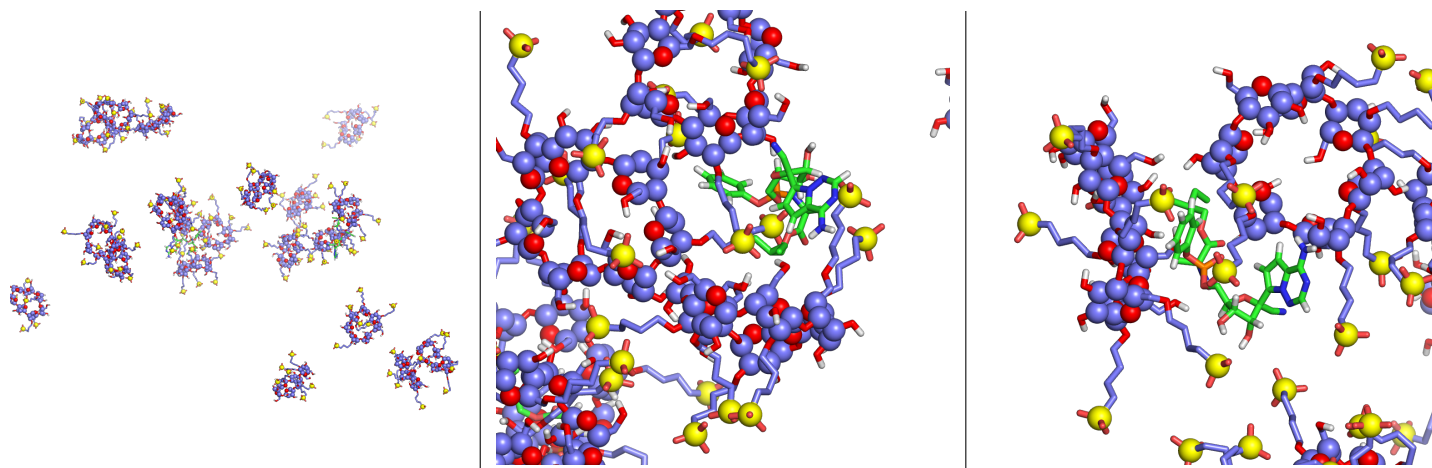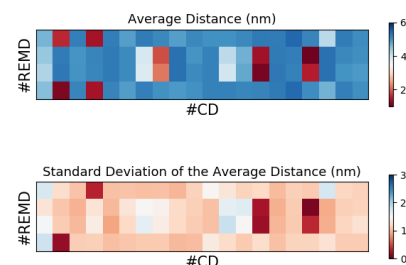

Snapshots taken from the last conformation:

20 x 6SBE + 2 x Neutral Remdesivir

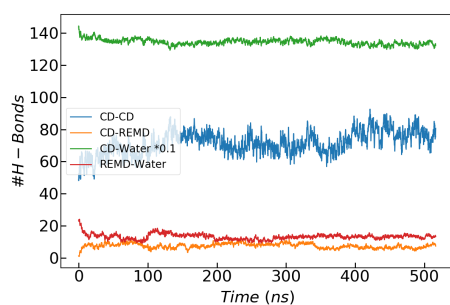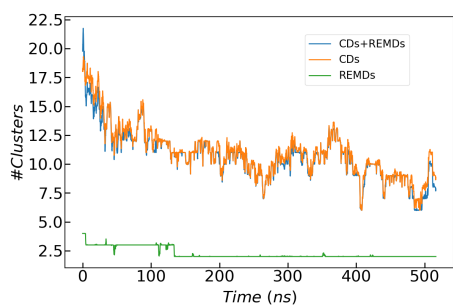Distance between cyclodextrins and remdesivir molecules as a function of time:
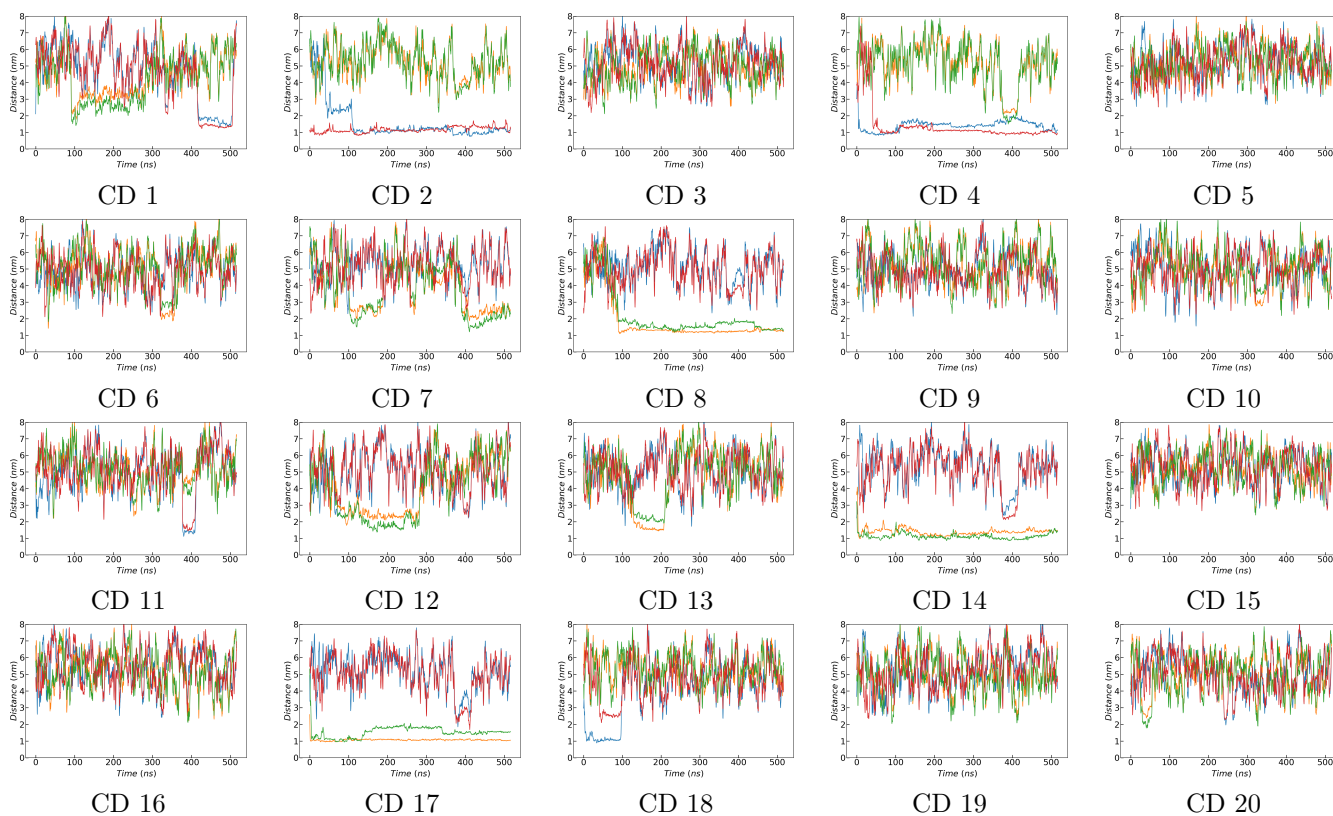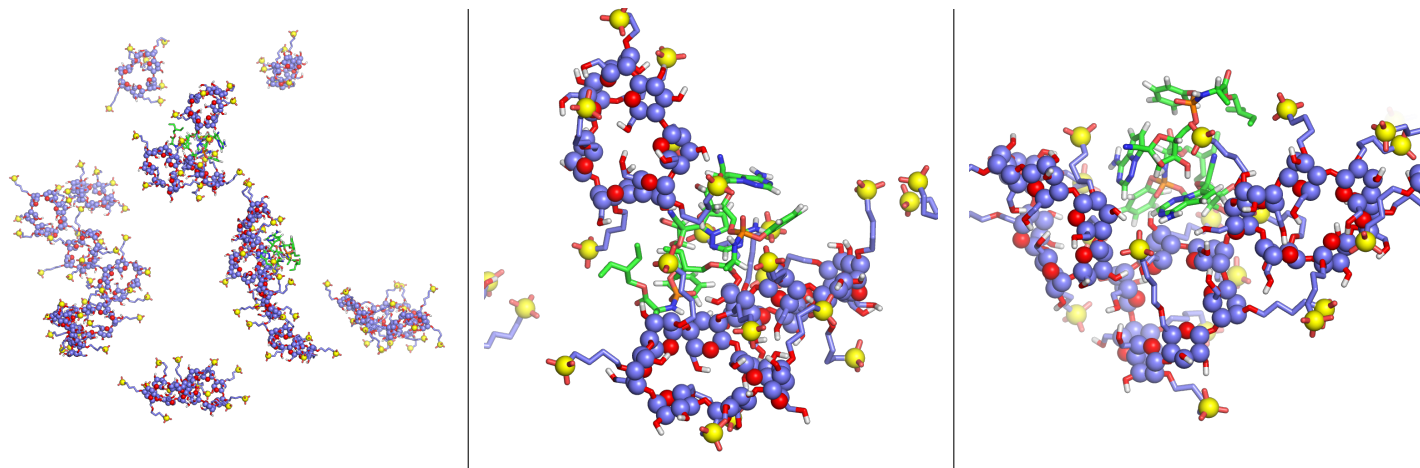

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15

CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 6SBE + 4 x Neutral Remdesivir

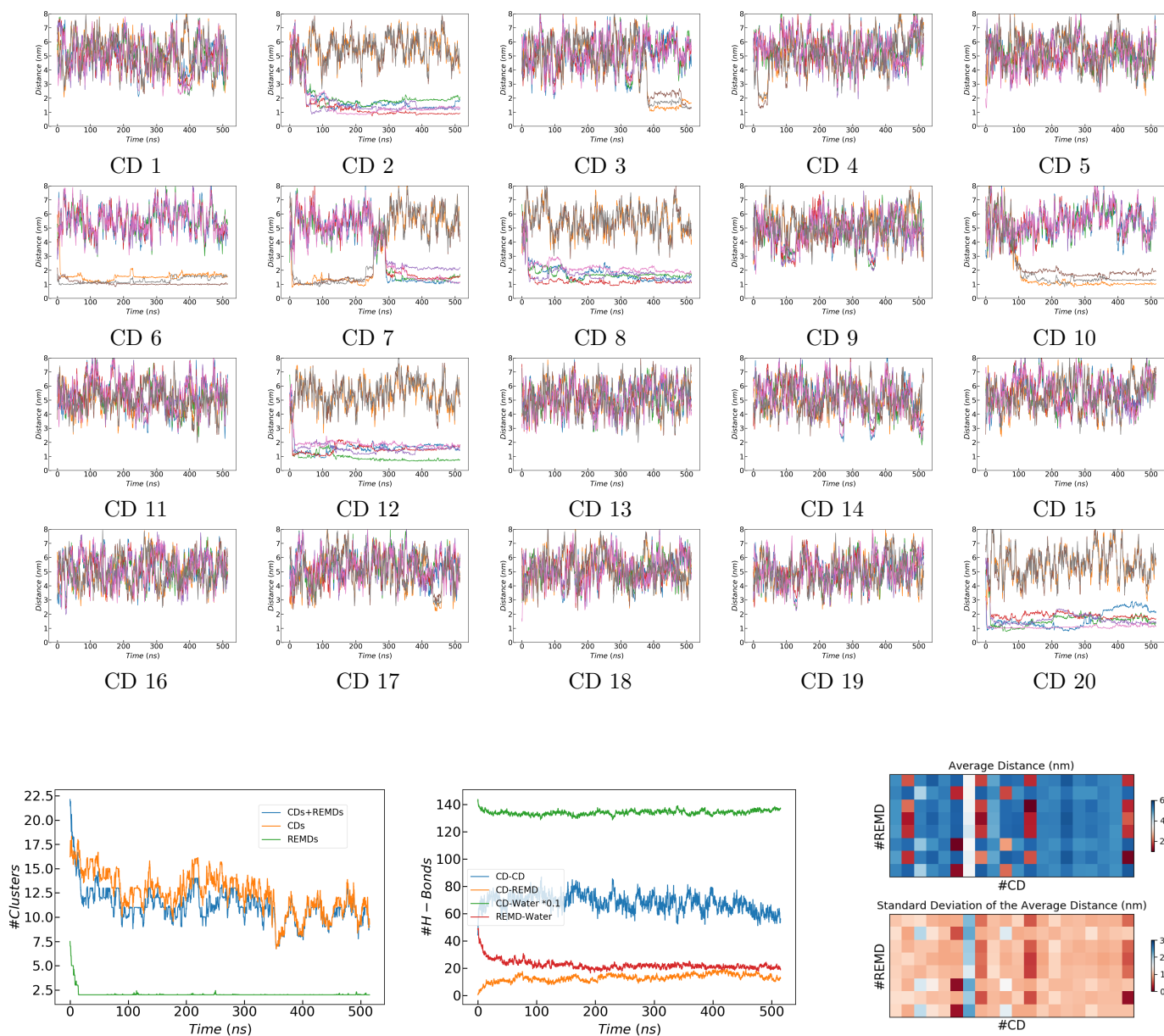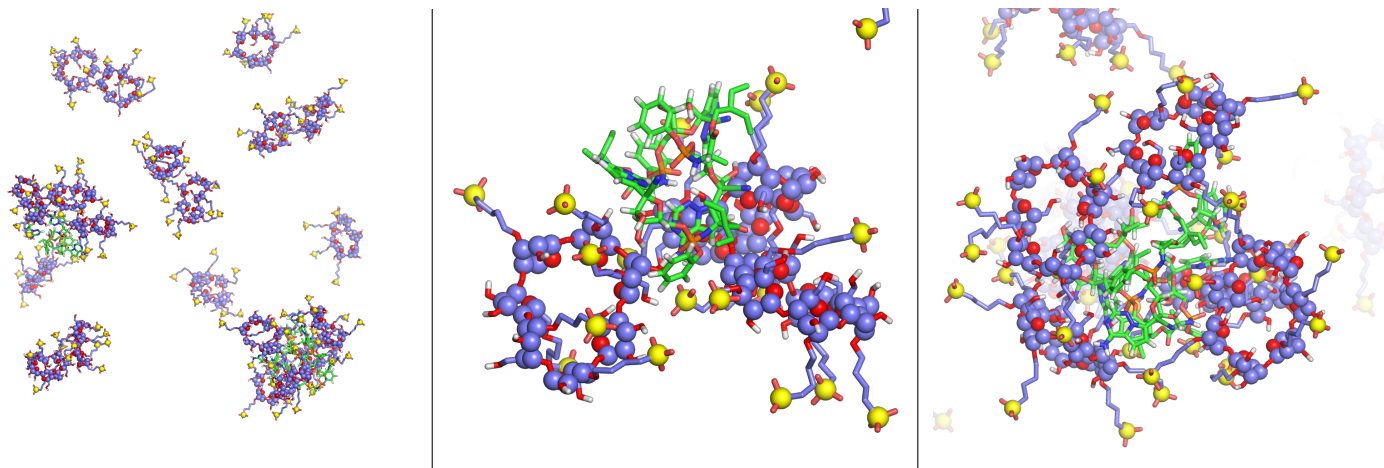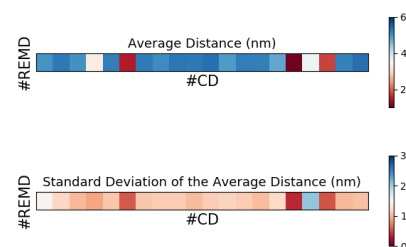Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15

CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 6SBE + 8 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
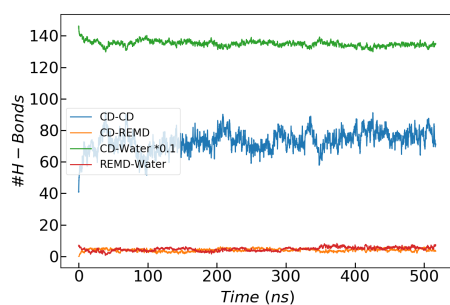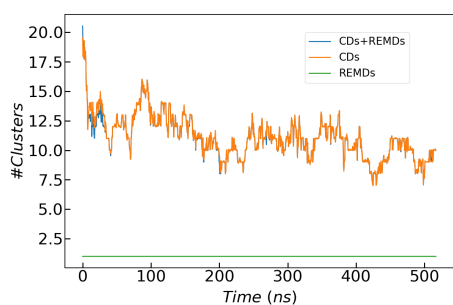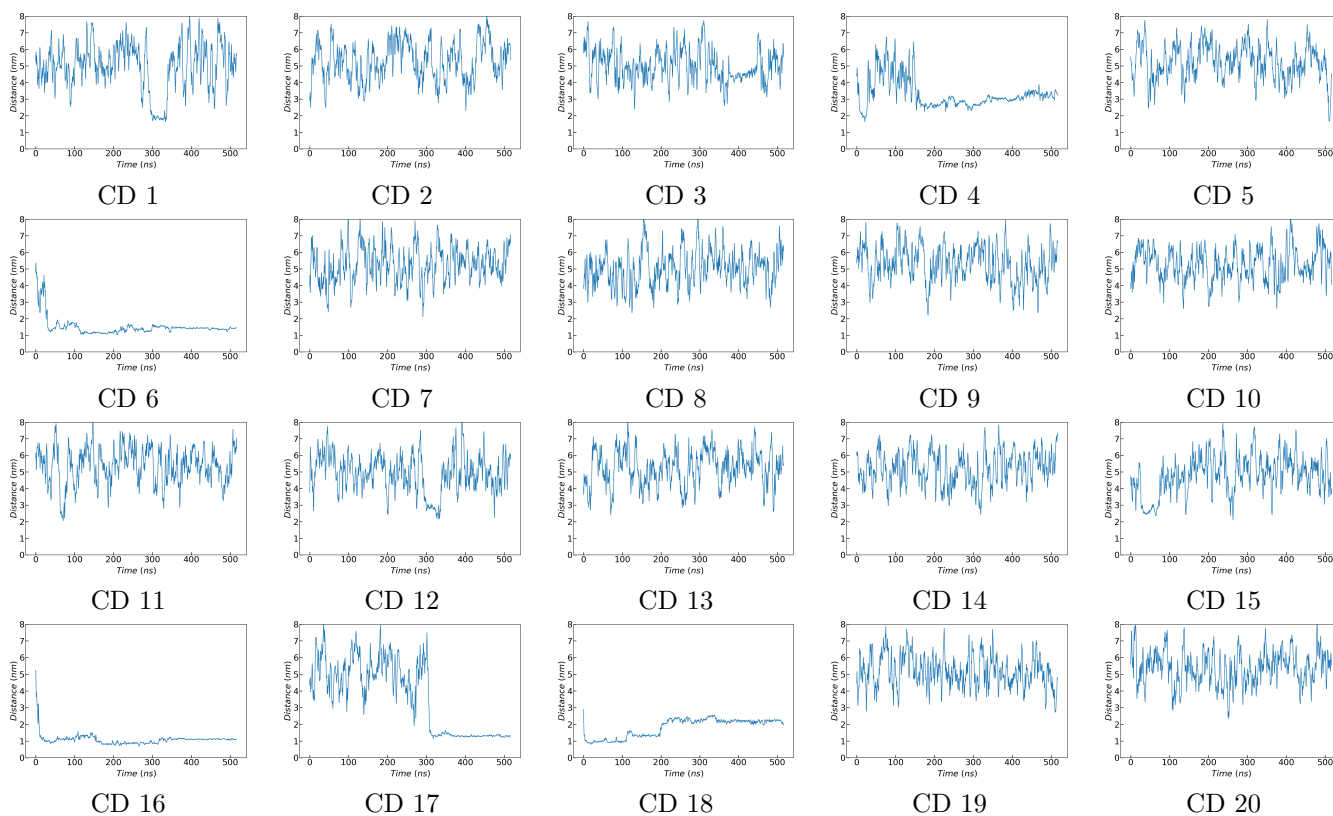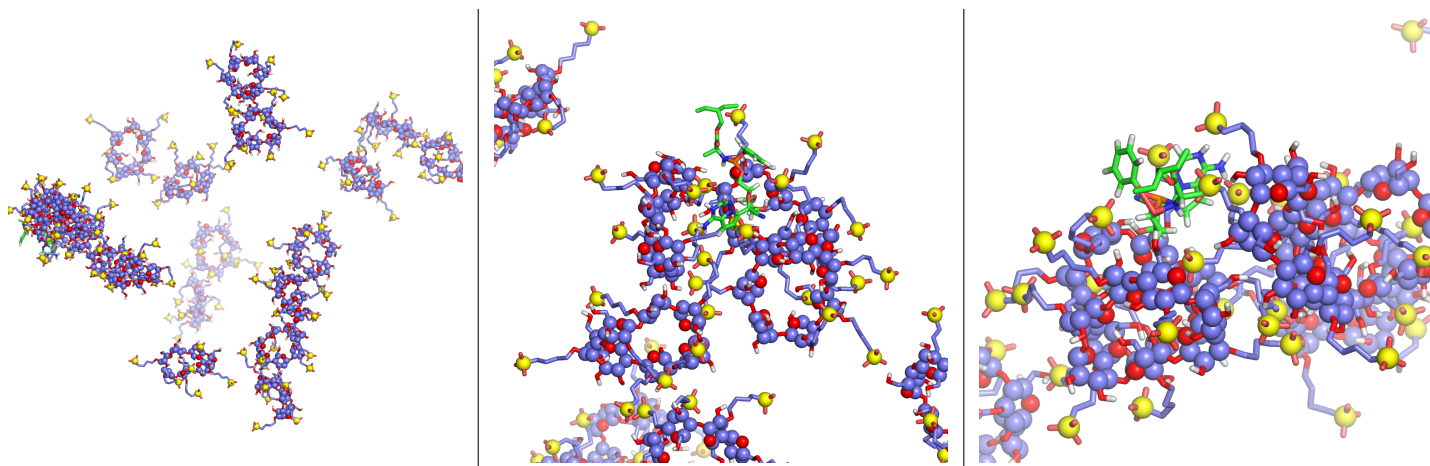
CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 6SBE + 1 x Protonated Remdesivir

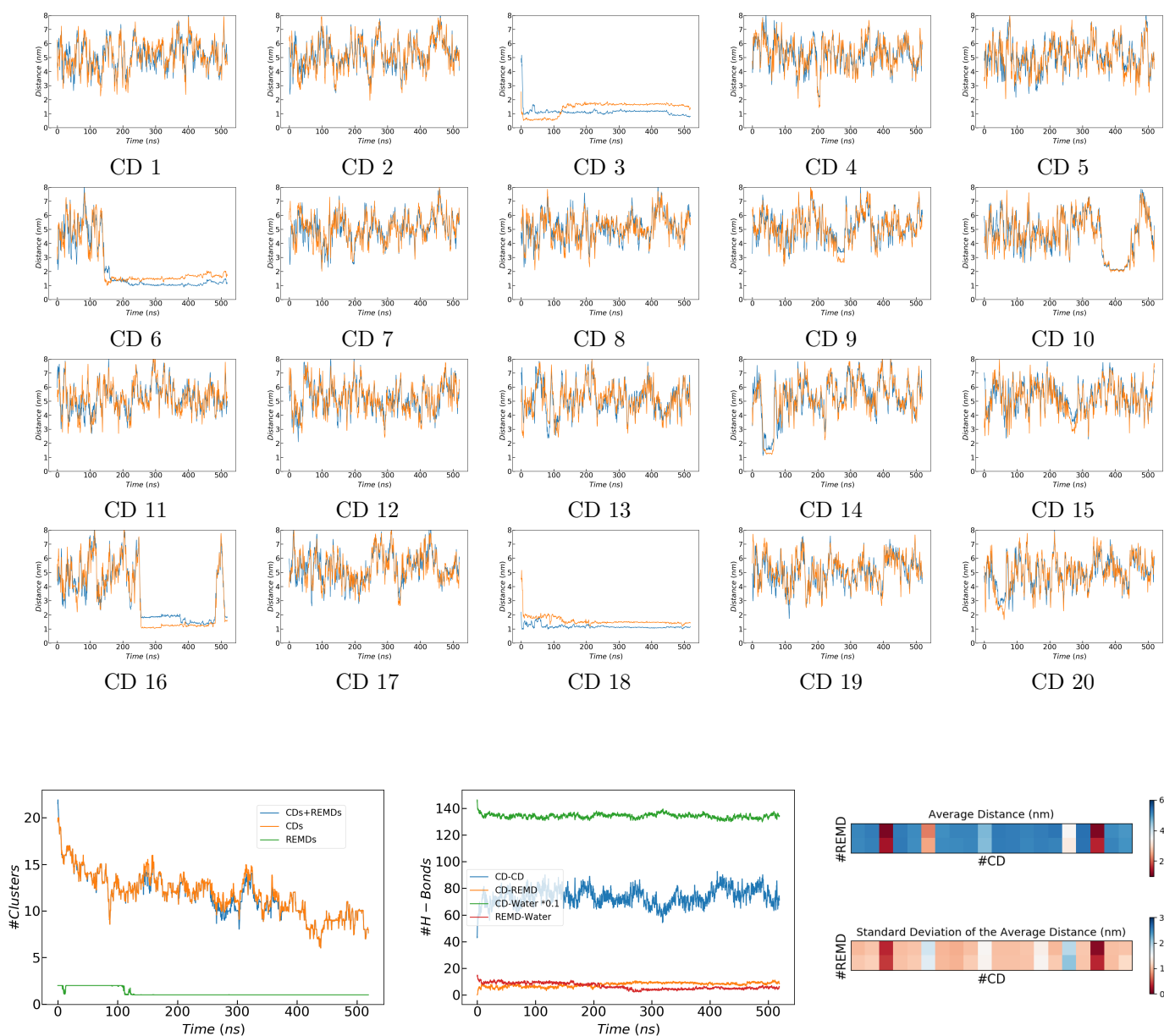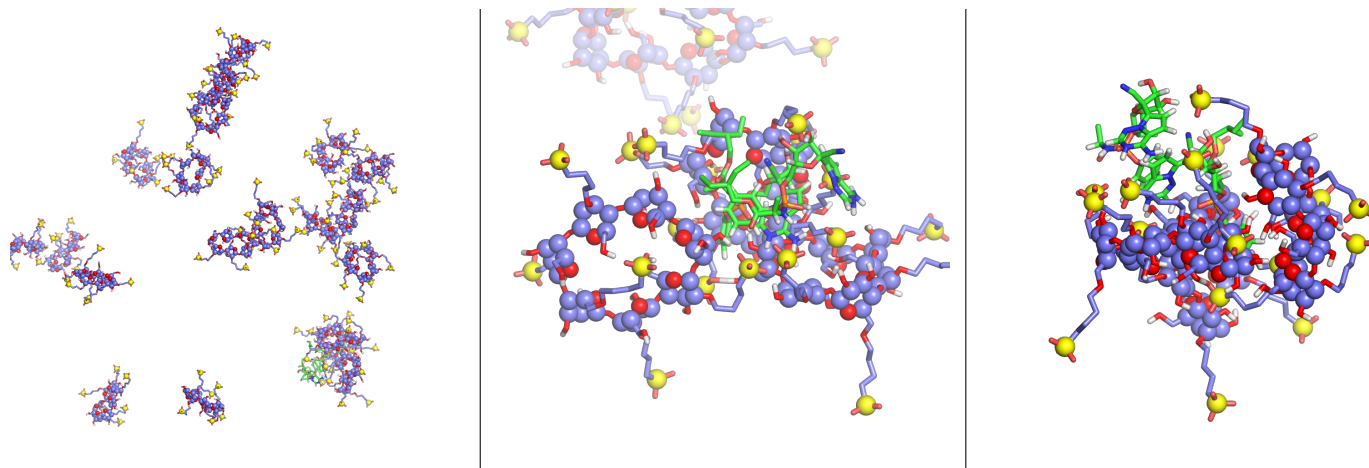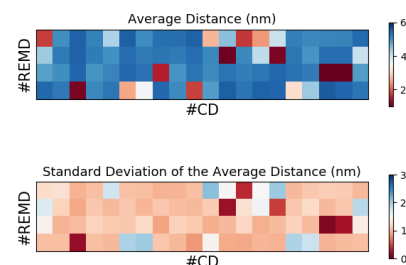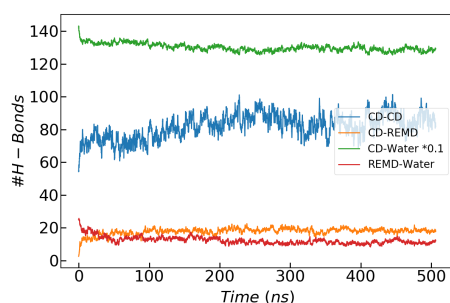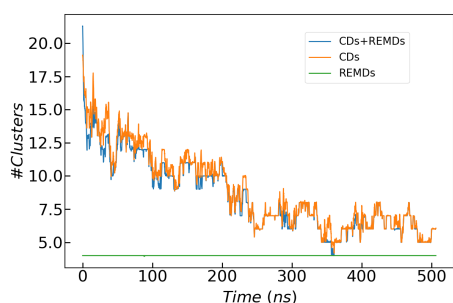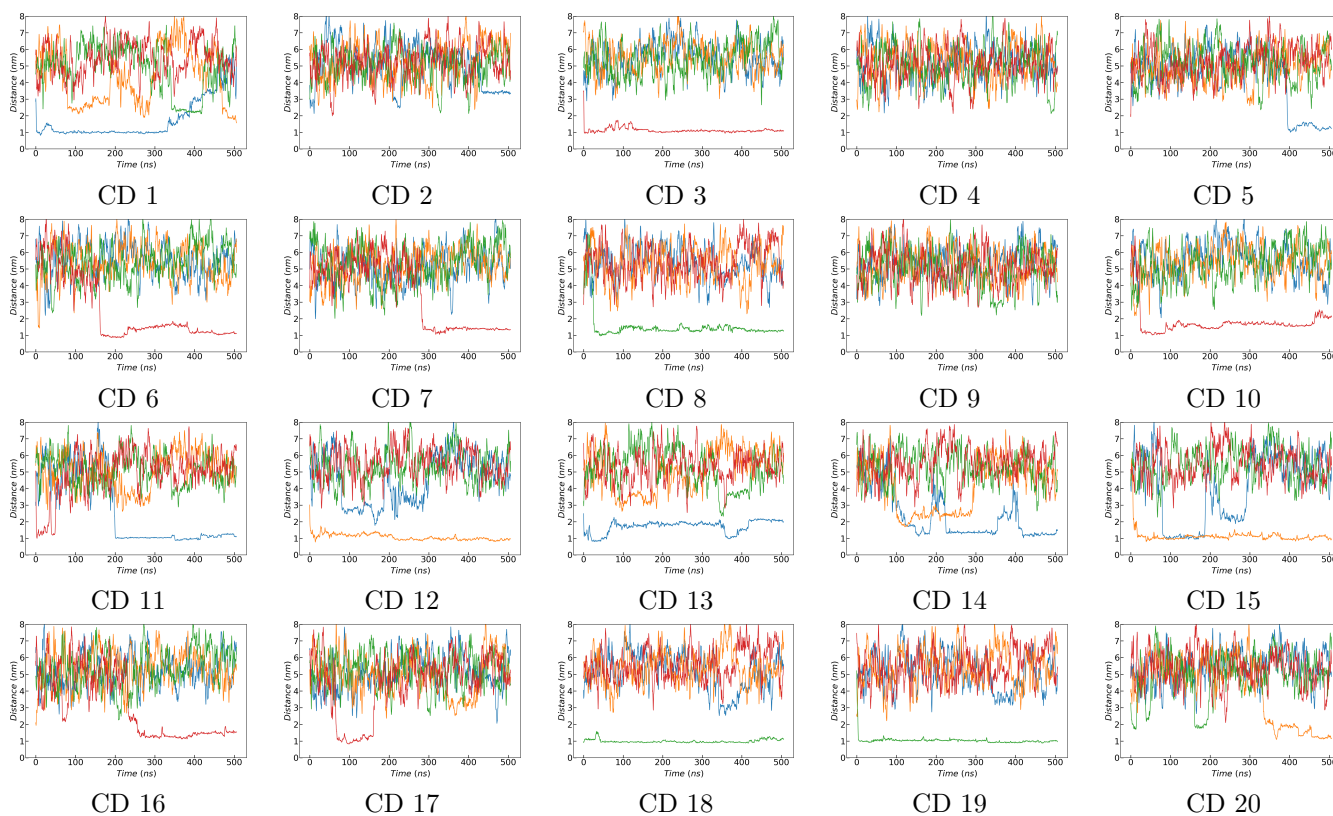Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1 CD 2 CD 3 CD 4 CD 5

CD 6 CD 7 CD 8 CD 9 CD 10

CD 11 CD 12 CD 13 CD 14 CD 15

CD 16 CD 17 CD 18 CD 19 CD 20

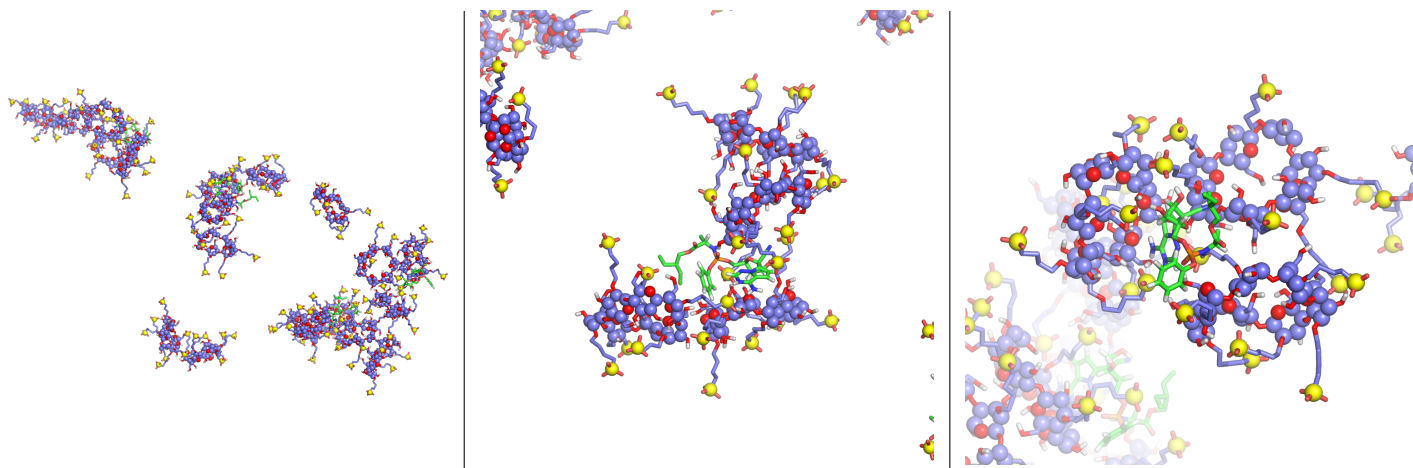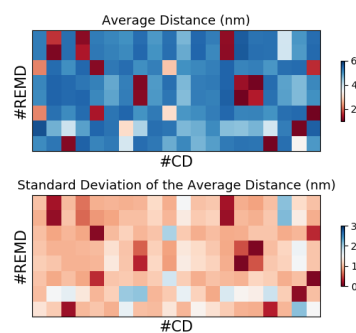Snapshots taken from the last conformation:

20 x 6SBE + 2 x Protonated Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:


CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15

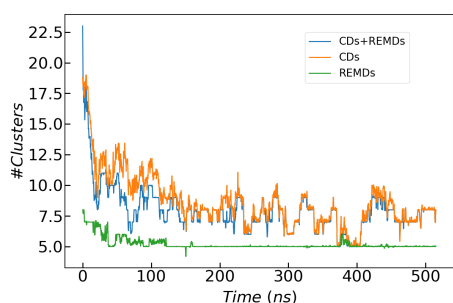CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 6SBE + 4 x Protonated Remdesivir

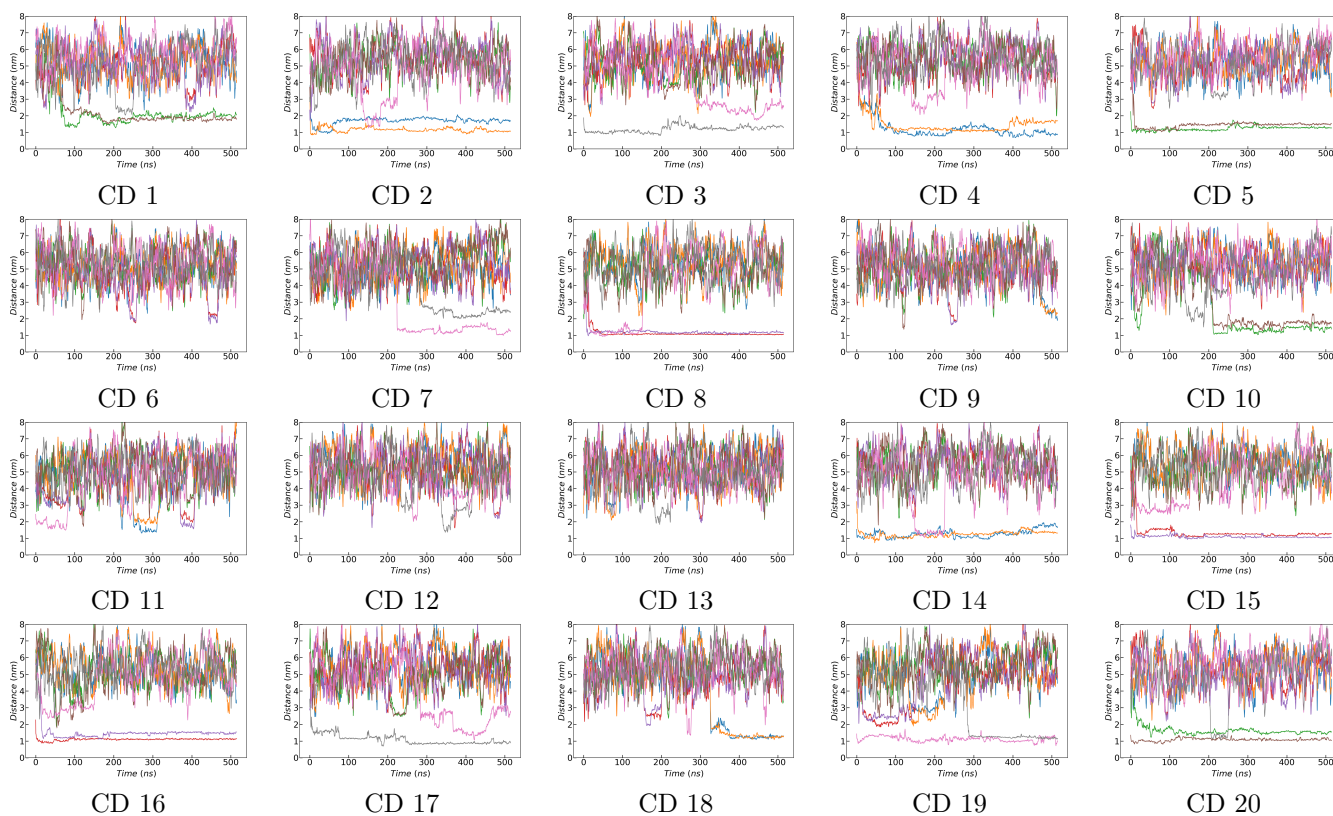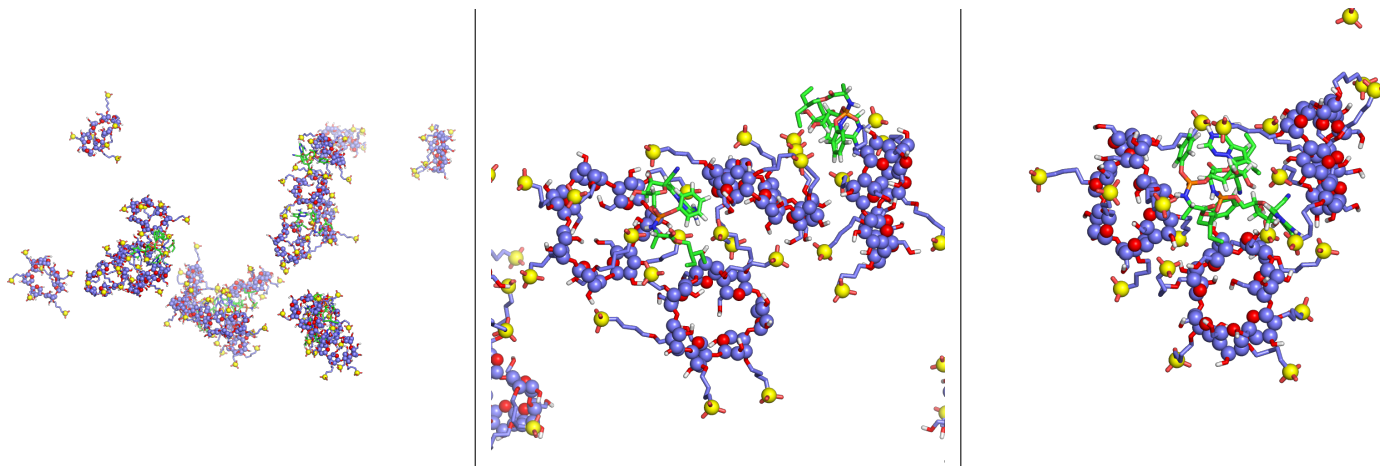Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
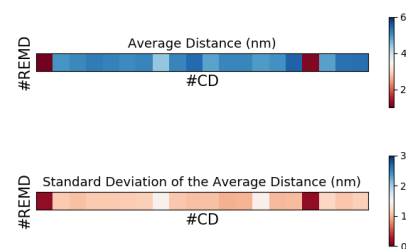
CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 6SBE + 8 x Protonated Remdesivir

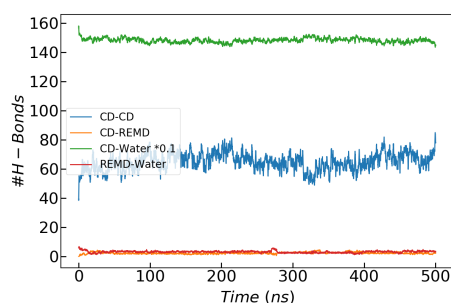Distance between cyclodextrins and remdesivir molecules as a function of time:
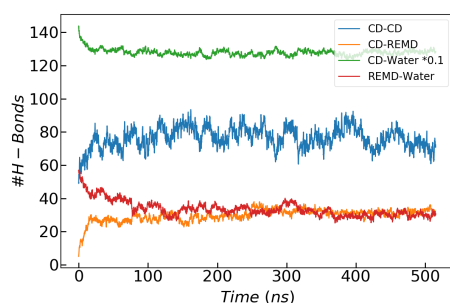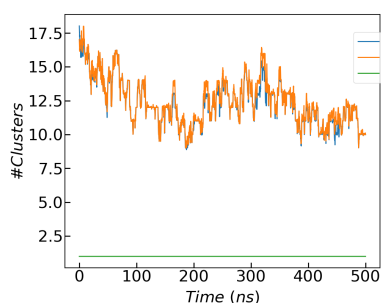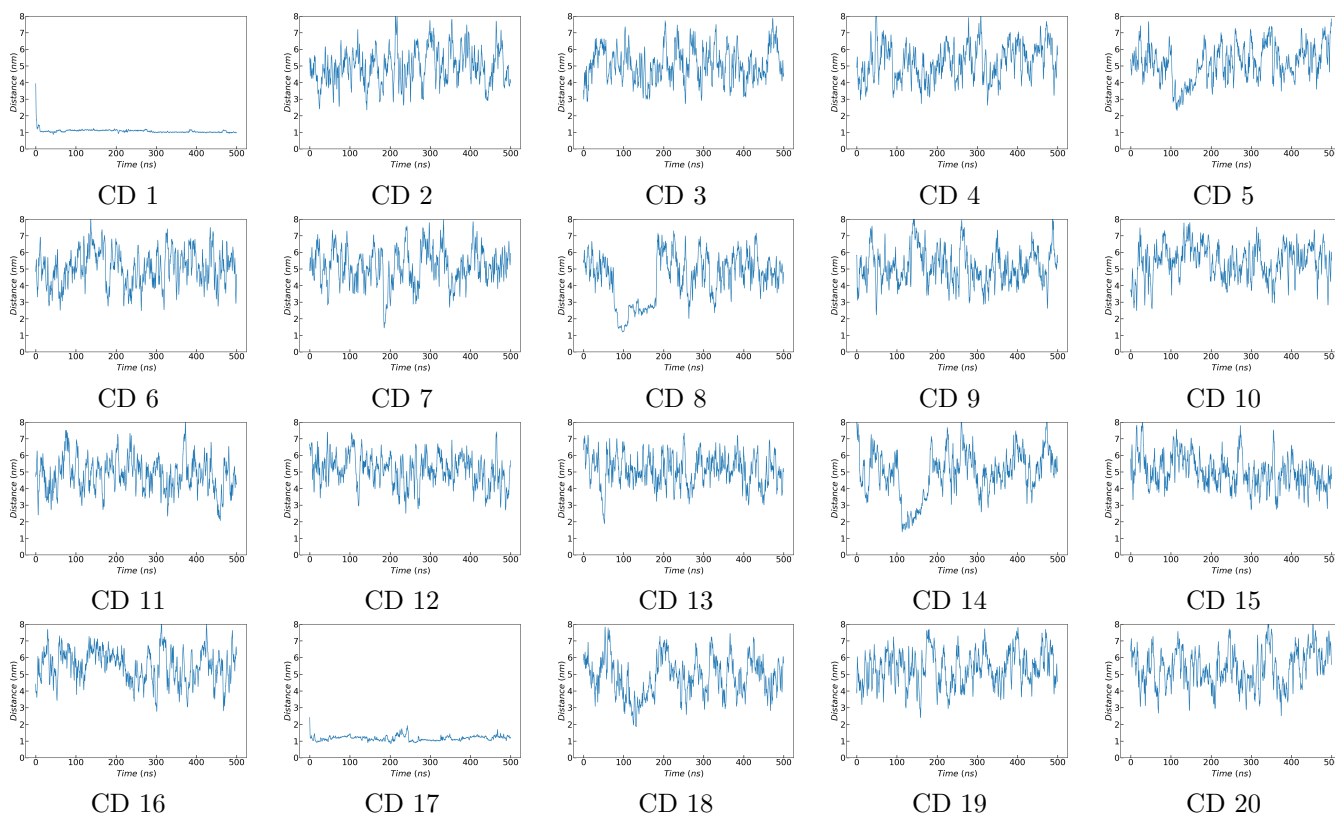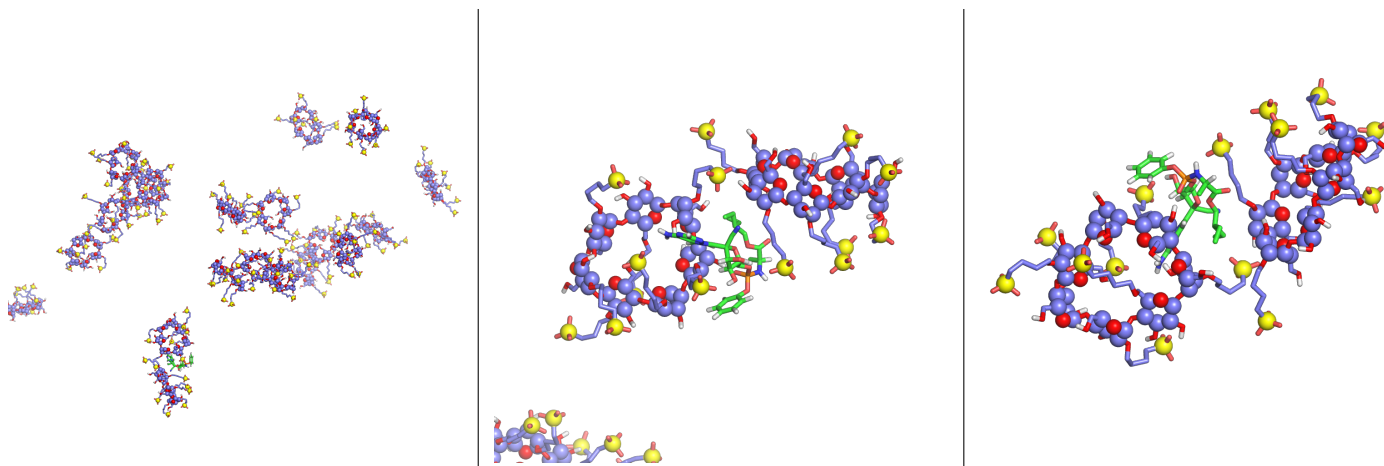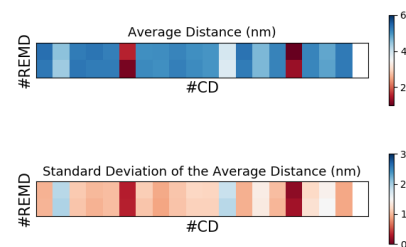

Snapshots taken from the last conformation:

20 x 7SBE + 1 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:
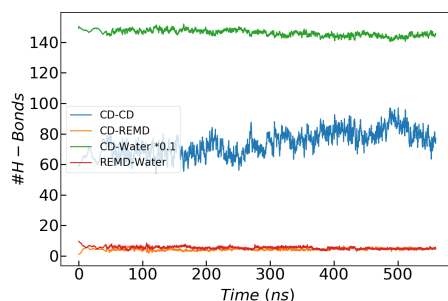

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
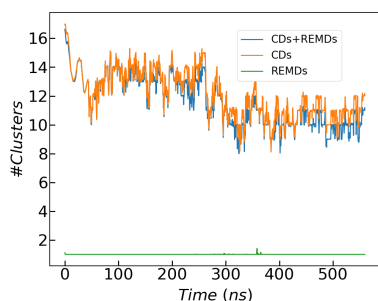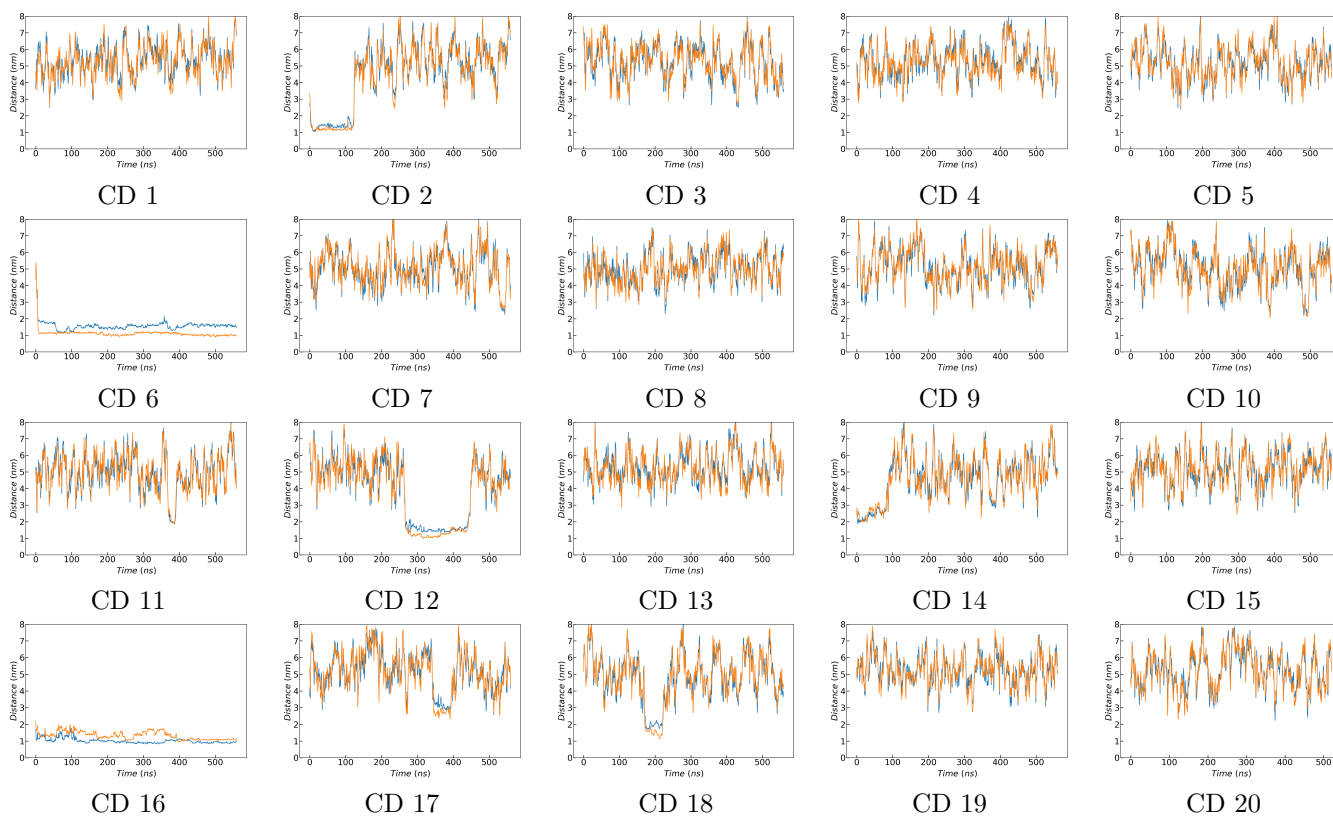
CD 16   CD 17   CD 18   CD 19   CD 20

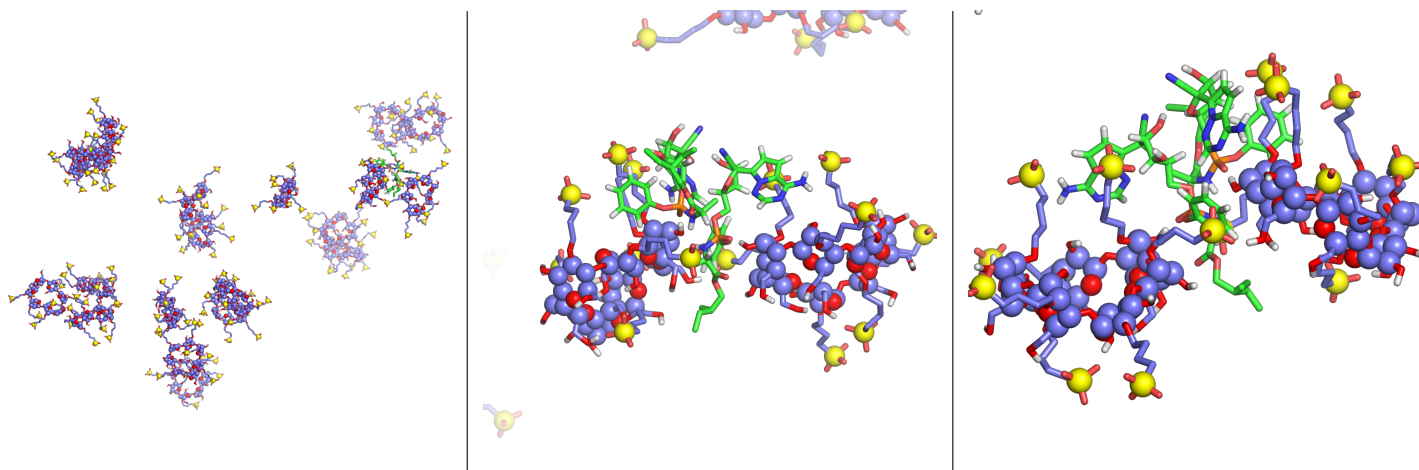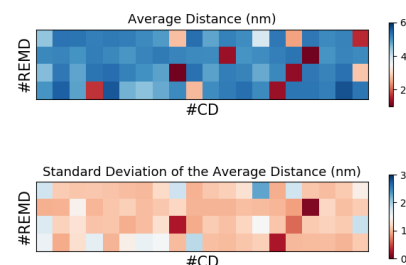Snapshots taken from the last conformation:

20 x 7SBE + 2 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
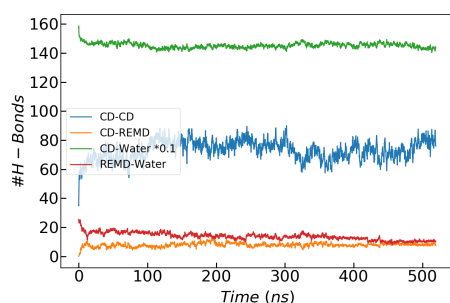
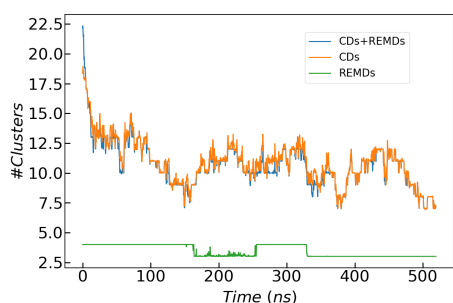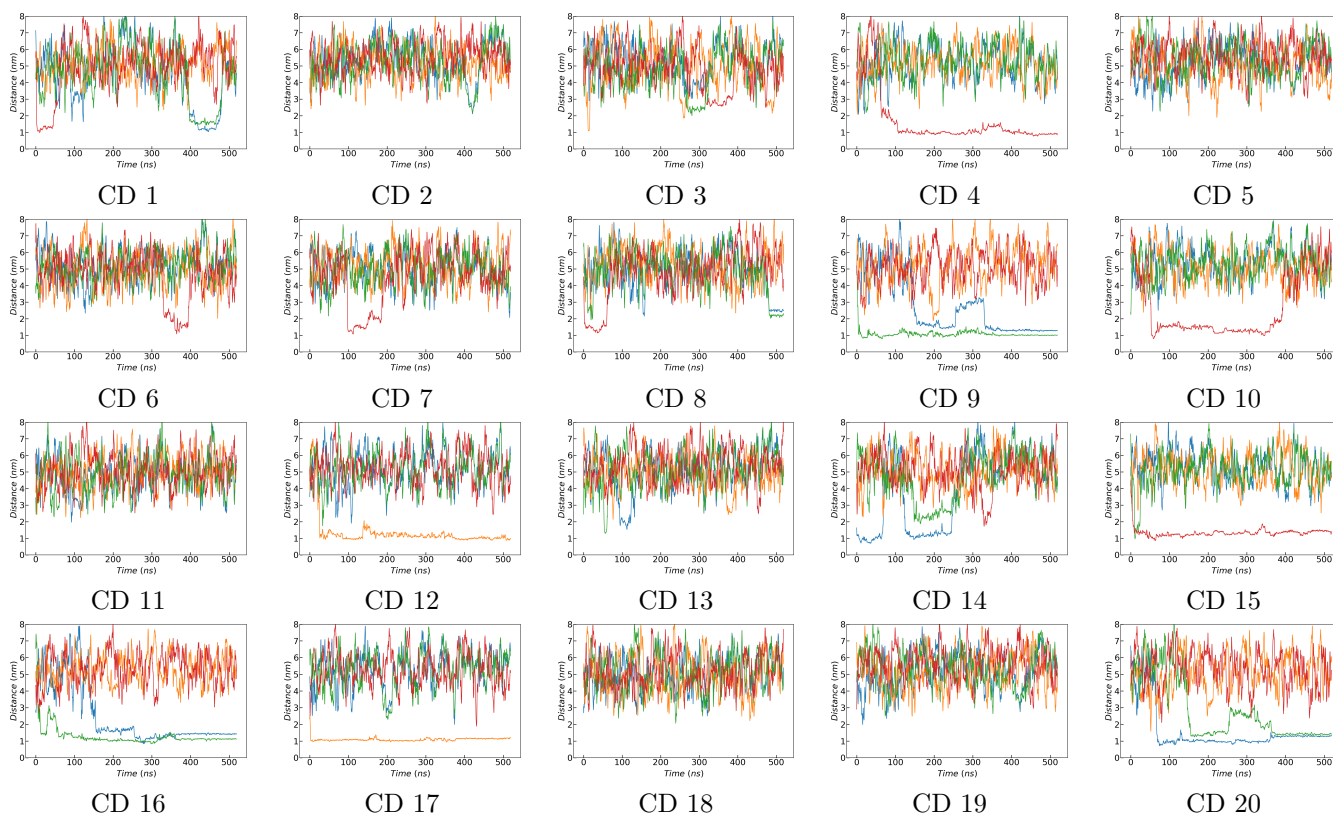CD 16   CD 17   CD 18   CD 19   CD 20
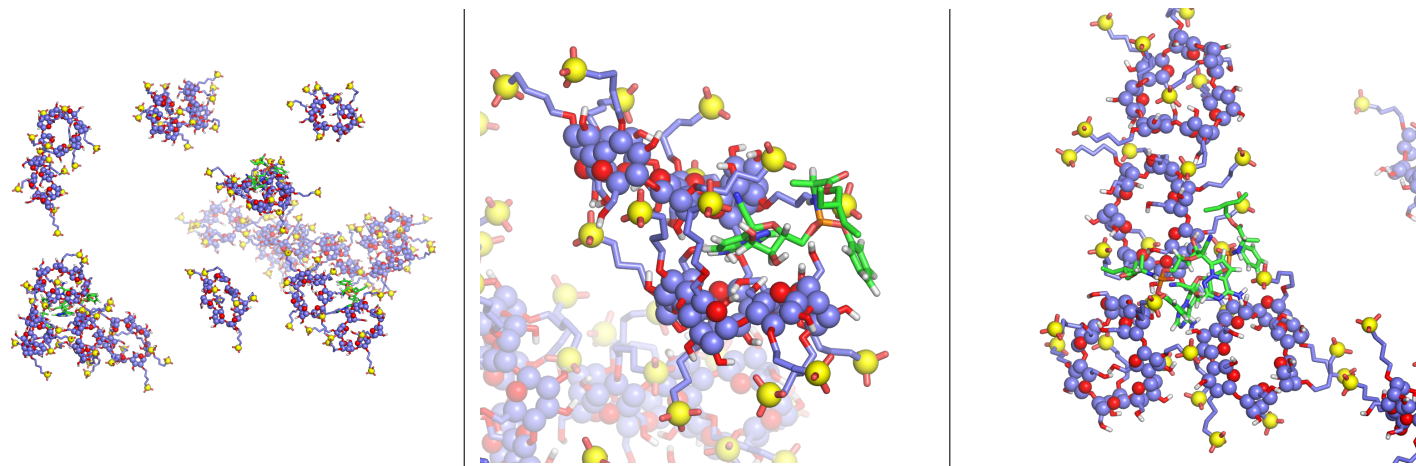

Snapshots taken from the last conformation:

20 x 7SBE + 4 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

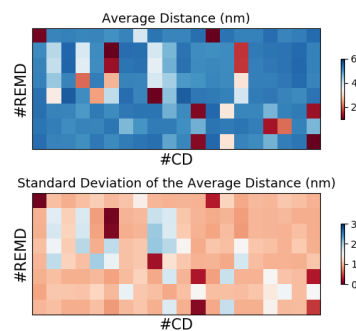CD 11   CD 12   CD 13   CD 14   CD 15
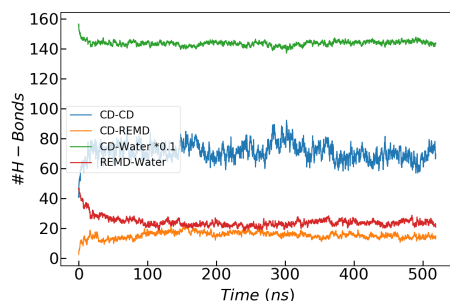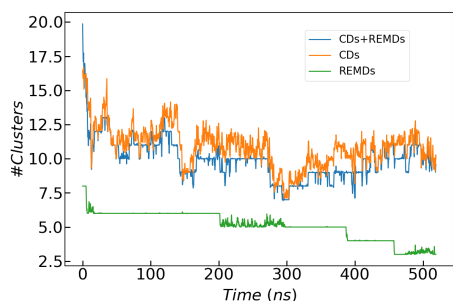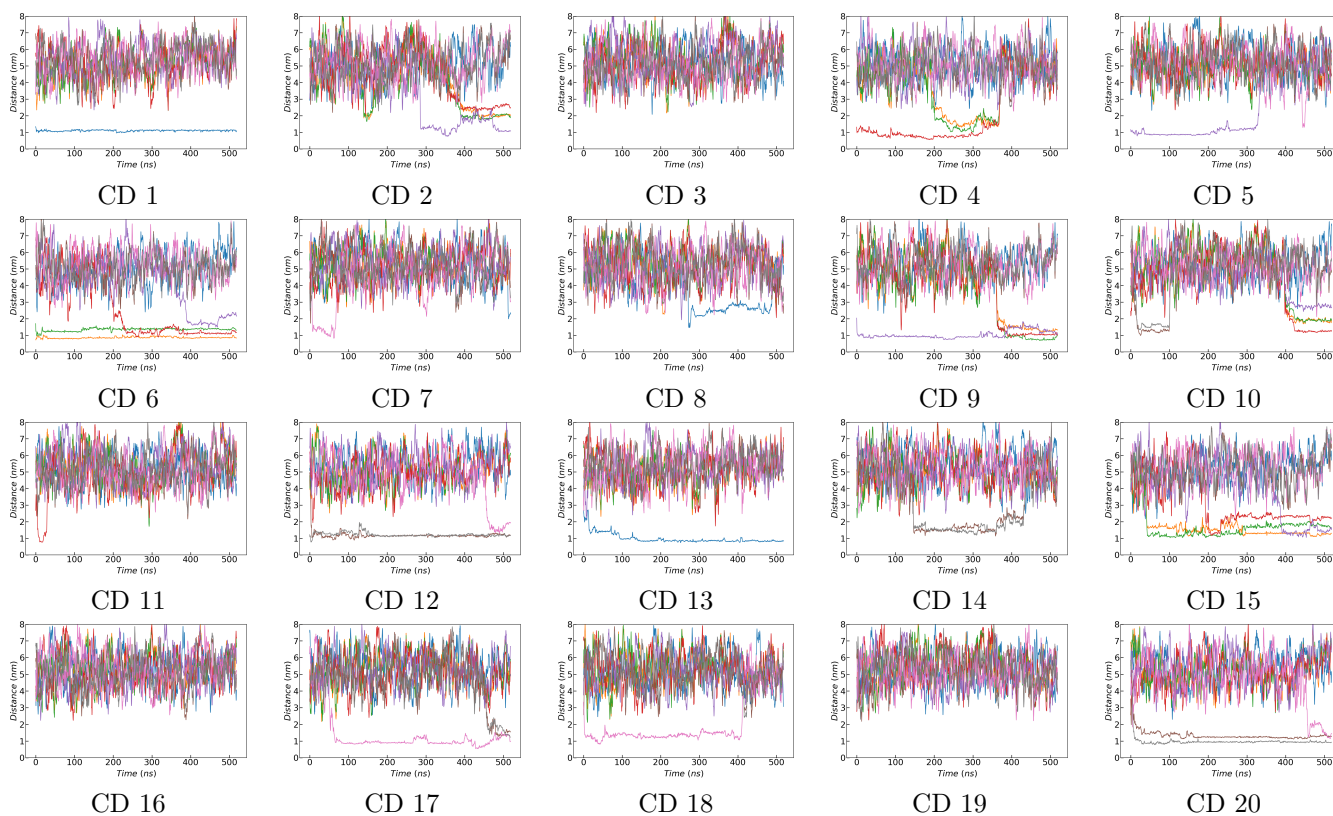
CD 16   CD 17   CD 18   CD 19   CD 20

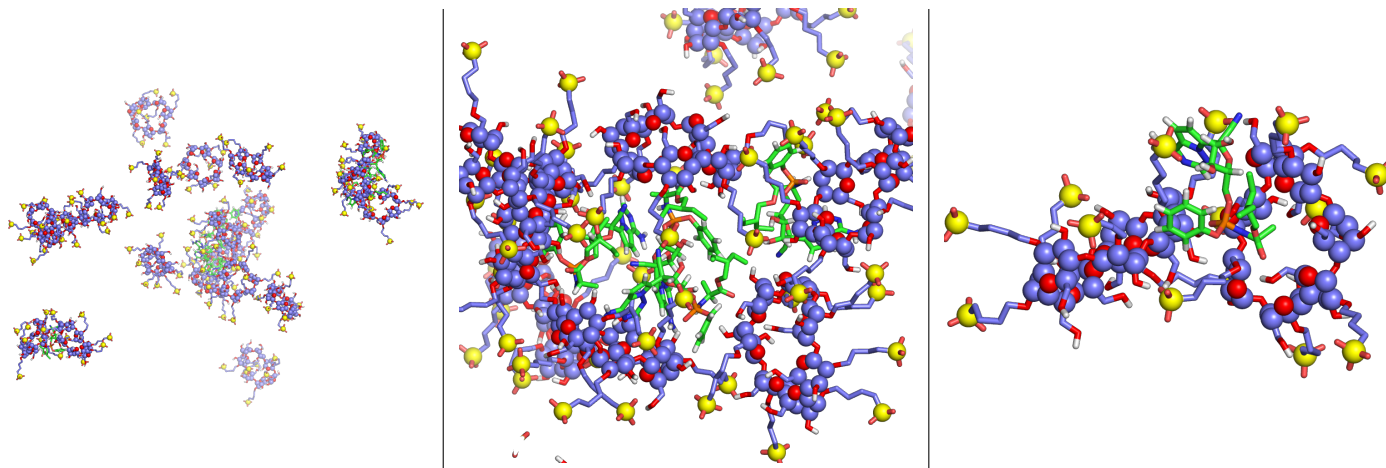Snapshots taken from the last conformation:

20 x 7SBE + 8 x Neutral Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

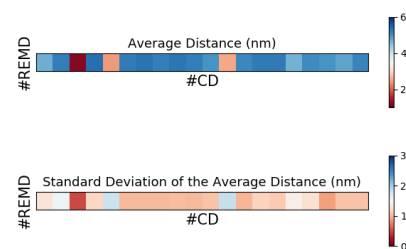CD 11   CD 12   CD 13   CD 14   CD 15
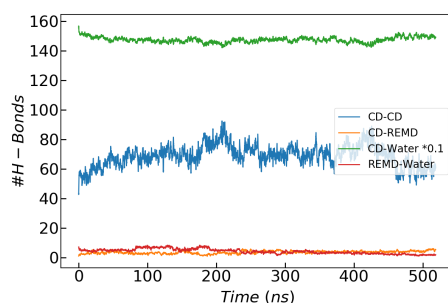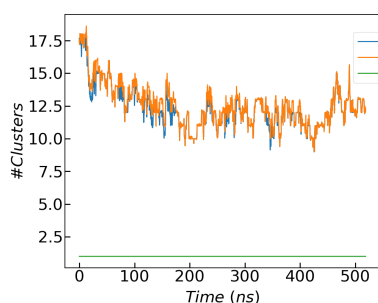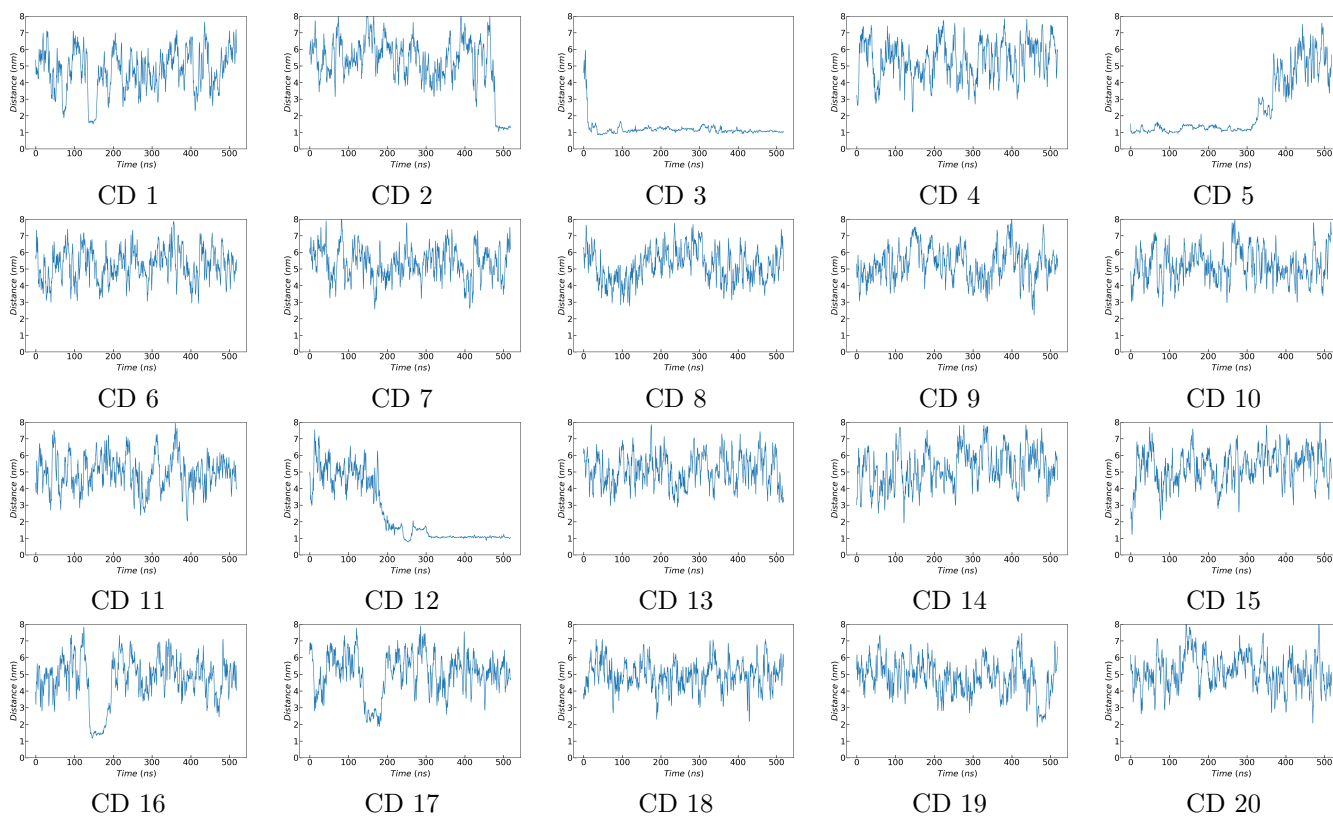
CD 16   CD 17   CD 18   CD 19   CD 20

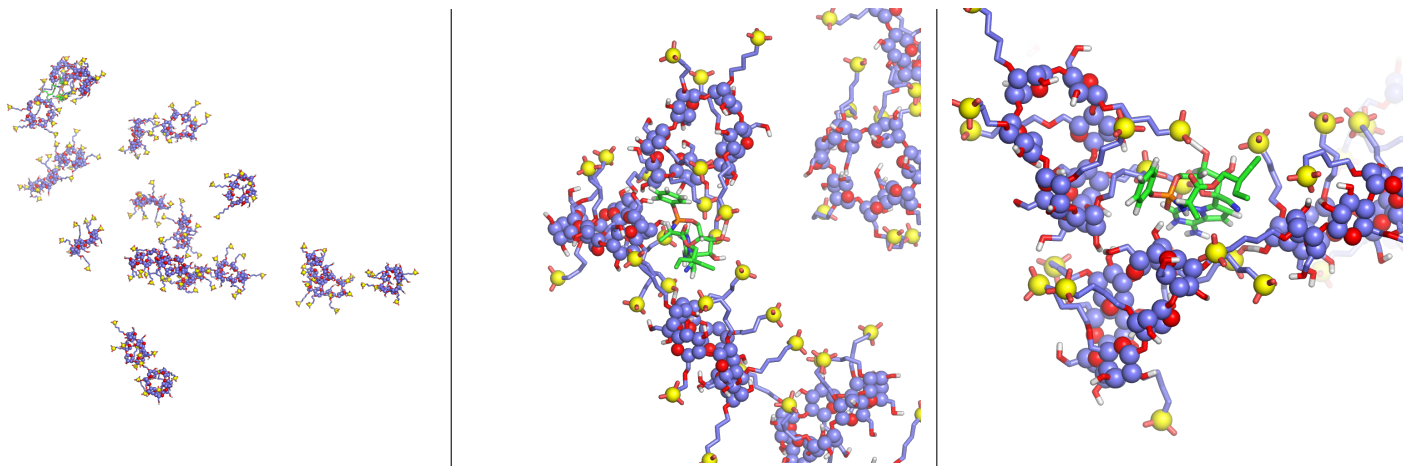Snapshots taken from the last conformation:

20 x 7SBE + 1 x Protonated Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
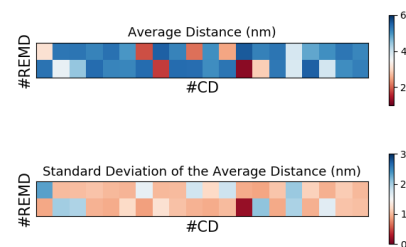
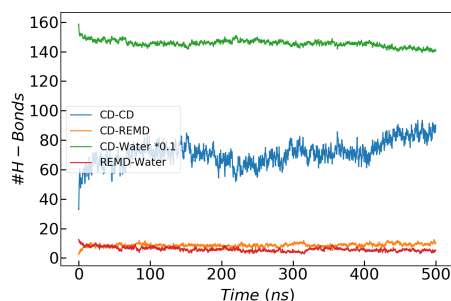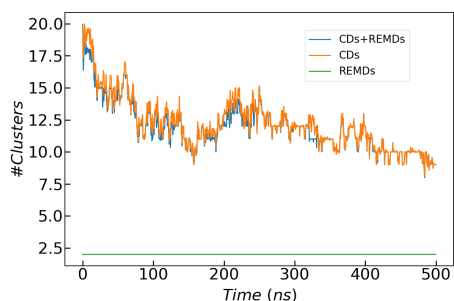CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 7SBE + 2 x Protonated Remdesivir

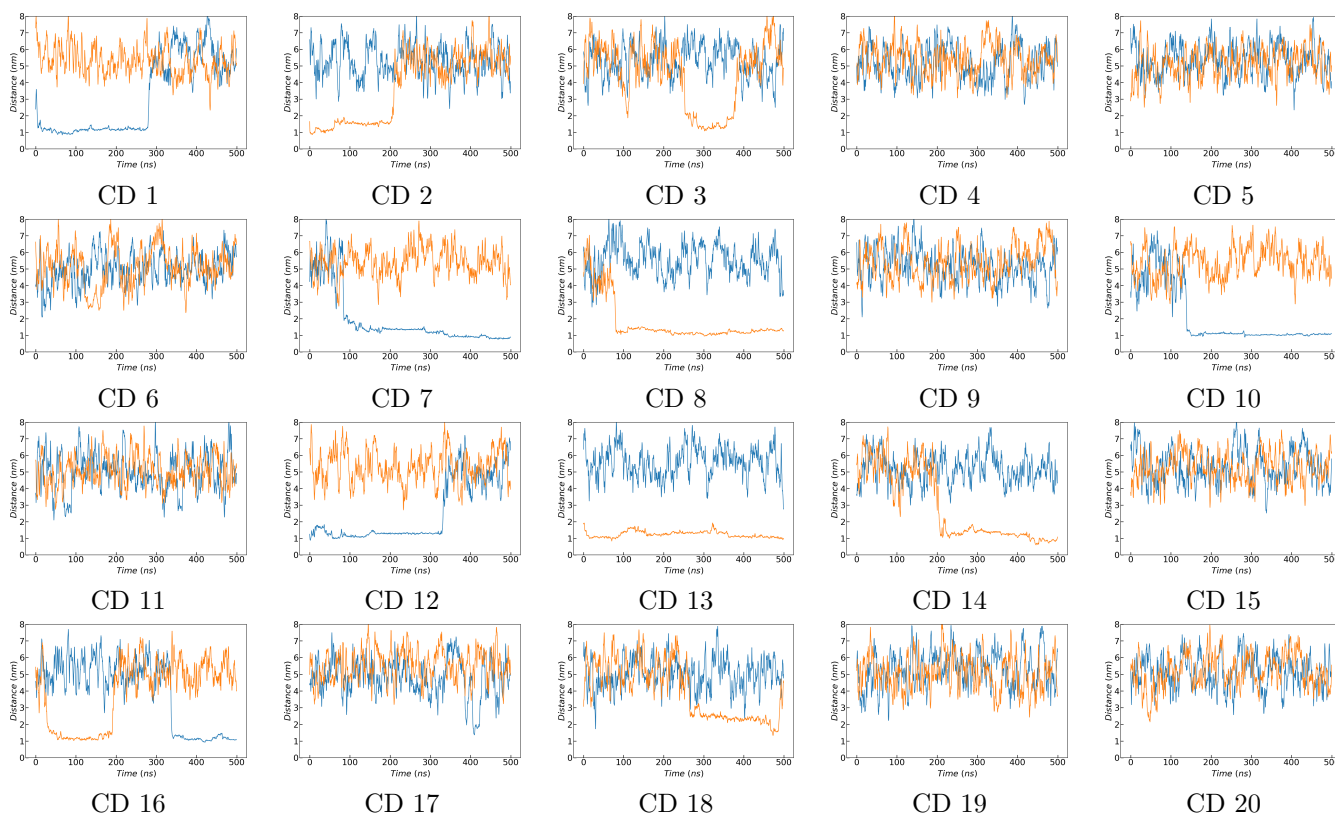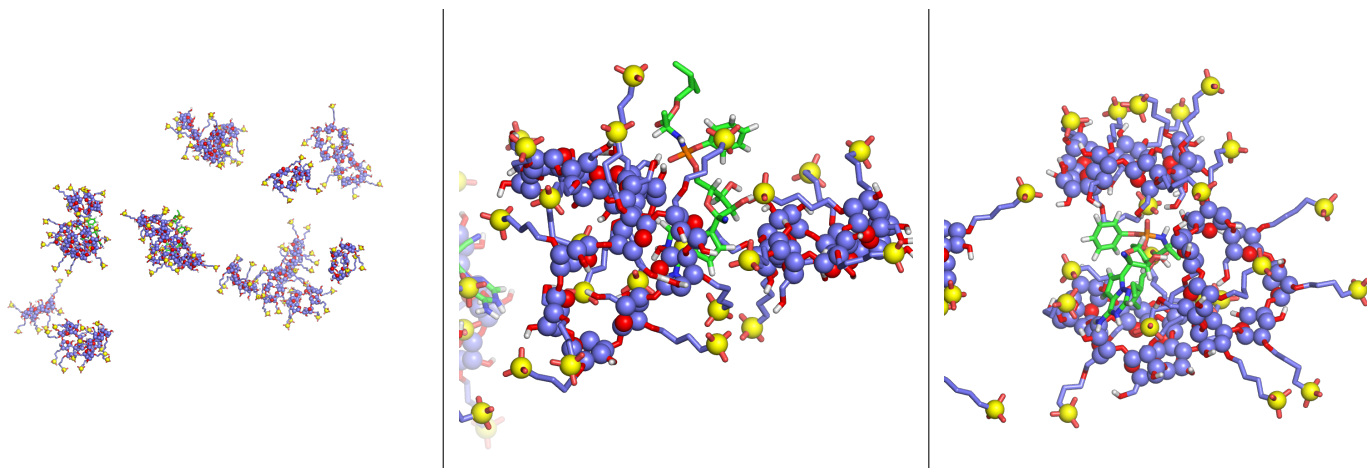Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1 CD 2 CD 3 CD 4 CD 5

CD 6 CD 7 CD 8 CD 9 CD 10

CD 11 CD 12 CD 13 CD 14 CD 15
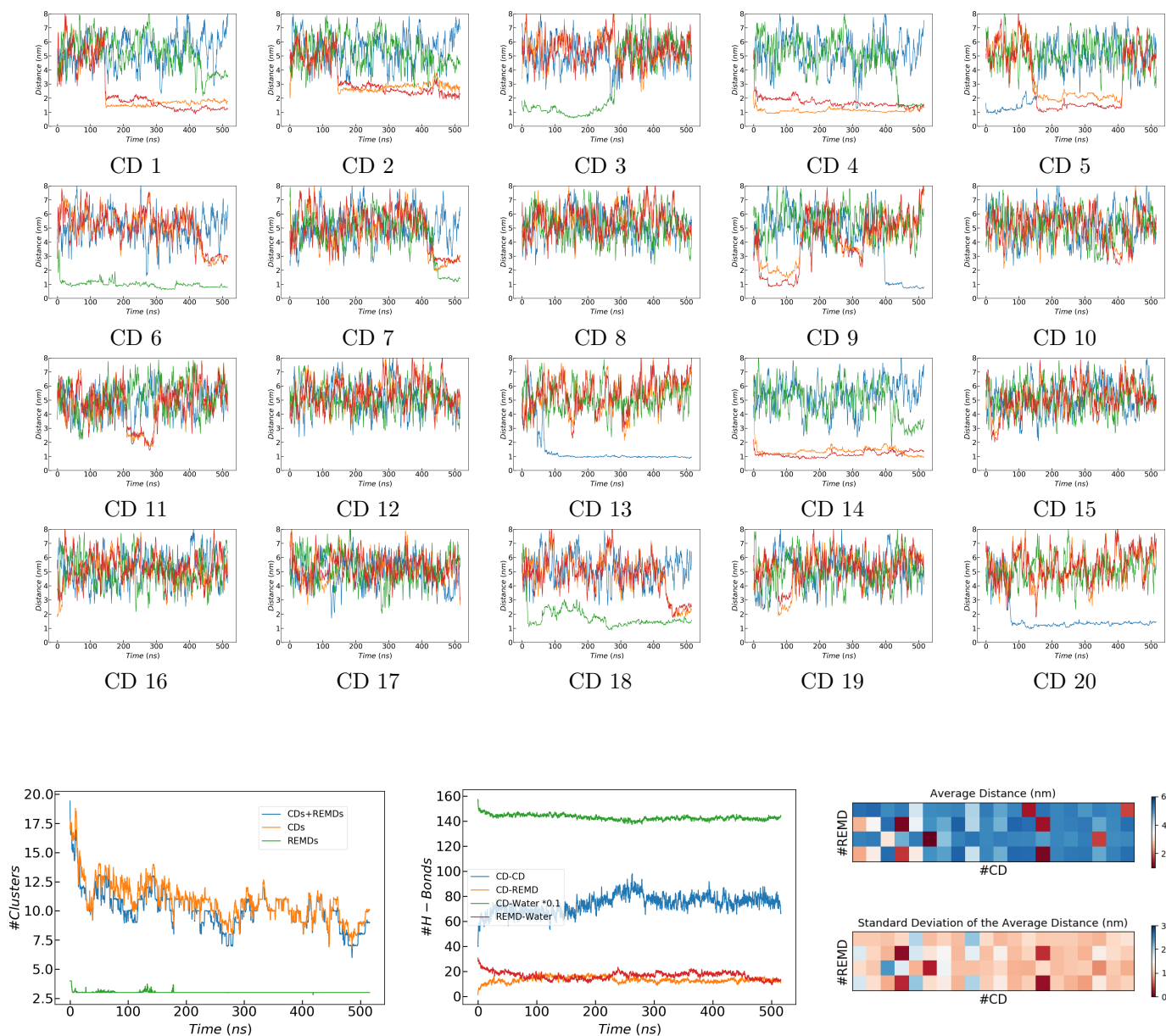
CD 16 CD 17 CD 18 CD 19 CD 20

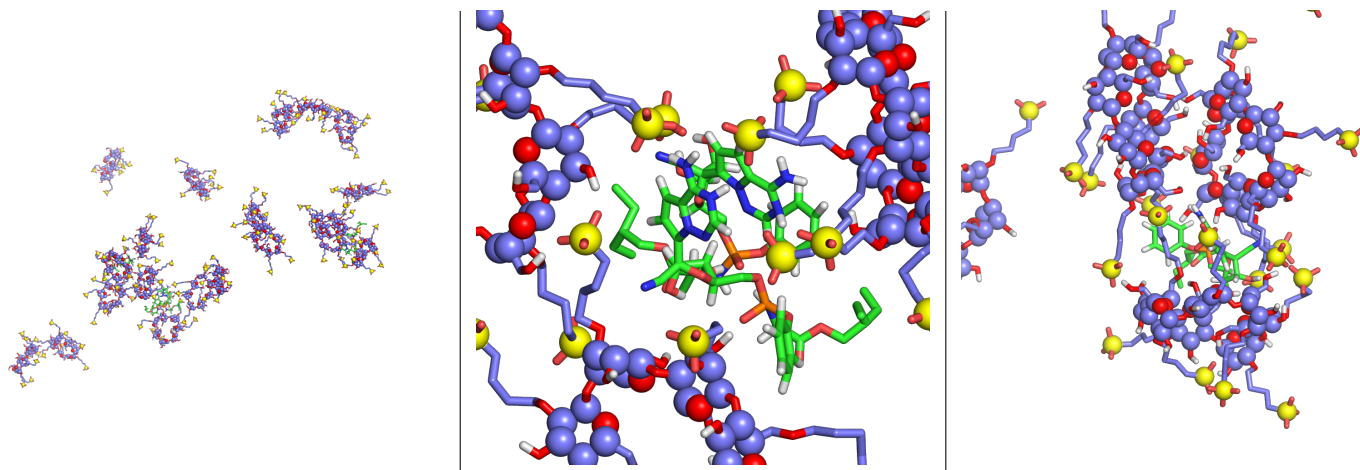Snapshots taken from the last conformation:

20 x 7SBE + 4 x Protonated Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

CD 1   CD 2   CD 3   CD 4   CD 5

CD 6   CD 7   CD 8   CD 9   CD 10

CD 11   CD 12   CD 13   CD 14   CD 15
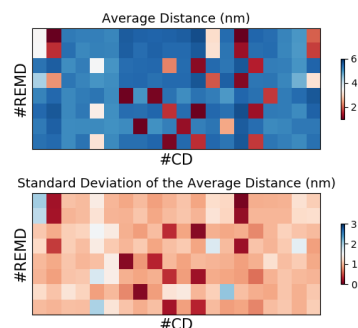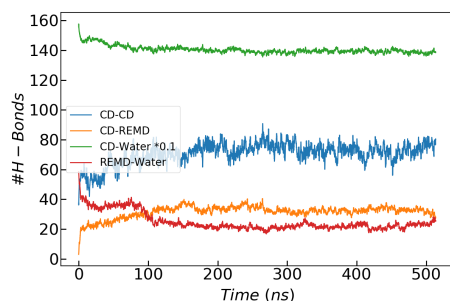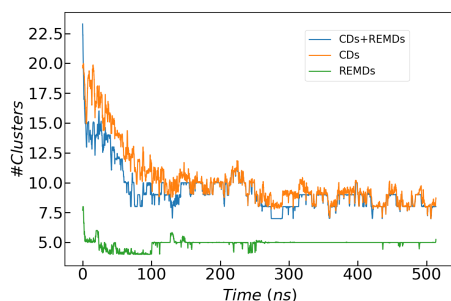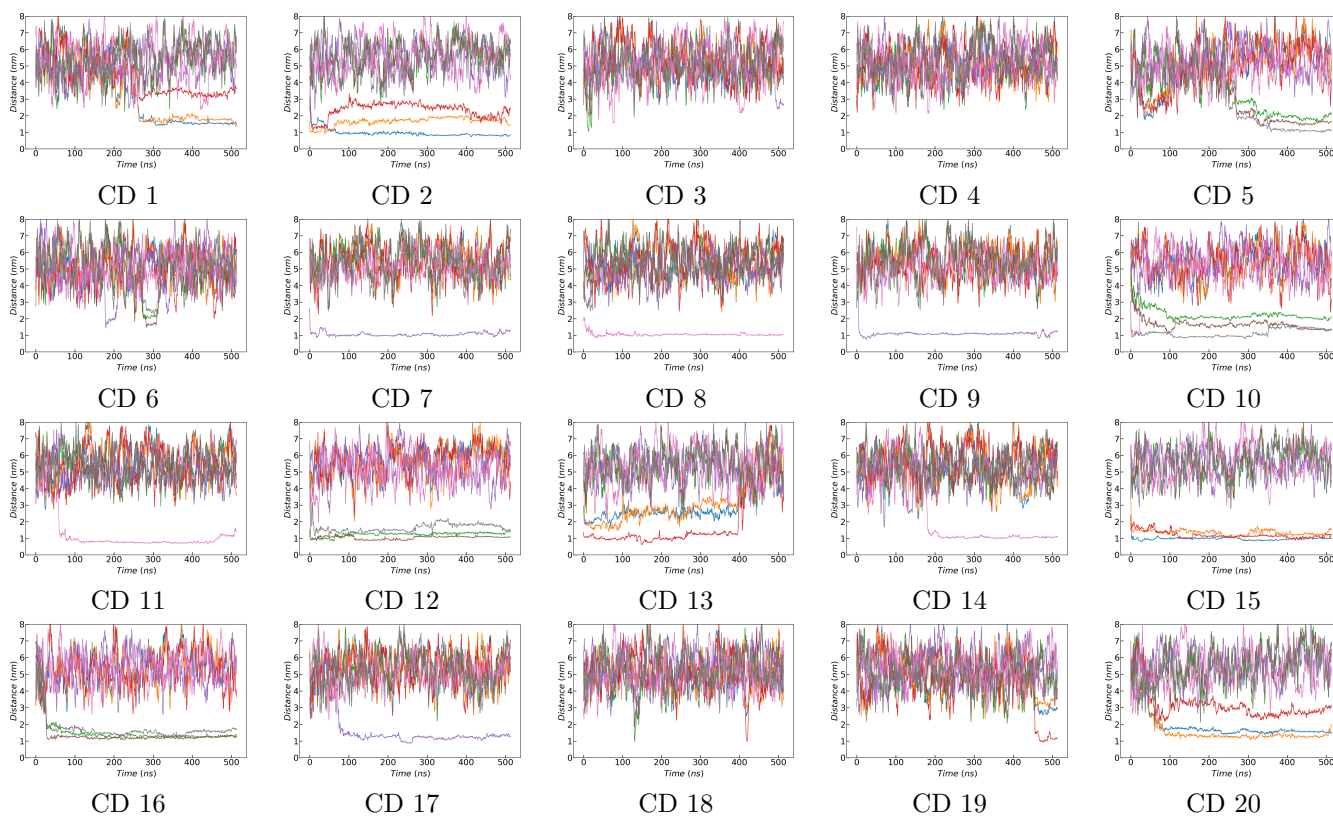
CD 16   CD 17   CD 18   CD 19   CD 20

Snapshots taken from the last conformation:

20 x 7SBE + 8 x Protonated Remdesivir

Distance between cyclodextrins and remdesivir molecules as a function of time:

Snapshots taken from the last conformation: