

Supplementary Information

Tunnel dynamics of quinone derivatives and its coupling to protein conformational rearrangements in respiratory complex I

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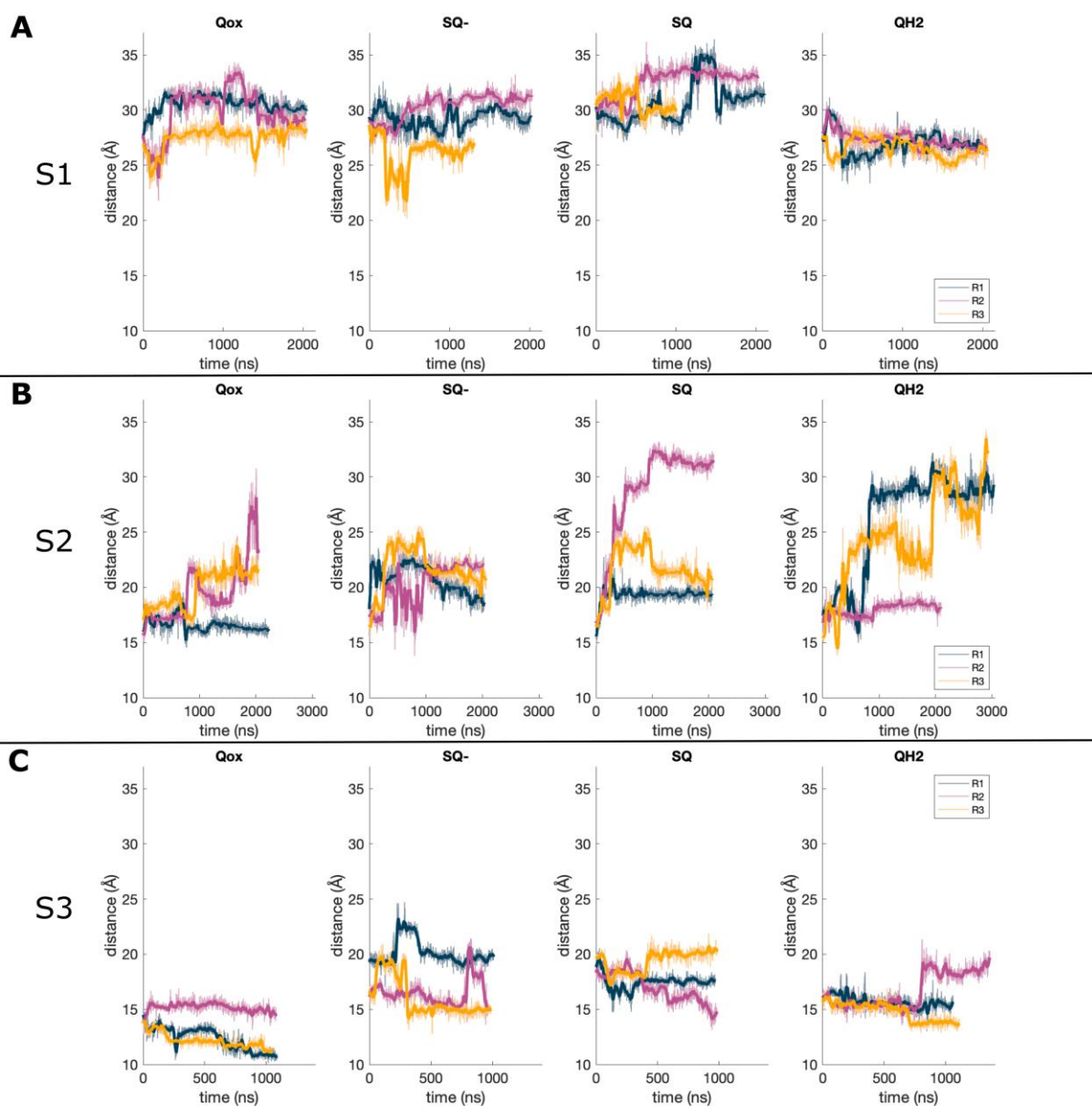


Fig. S1: Distance of Q9 head group (COM) from N2 cluster (COM) over time for S1 (A), S2 (B) and S3 (C) simulations. Different simulation replicas are shown in different colours, and the bold line shows a rolling average based on the previous 20 frames.

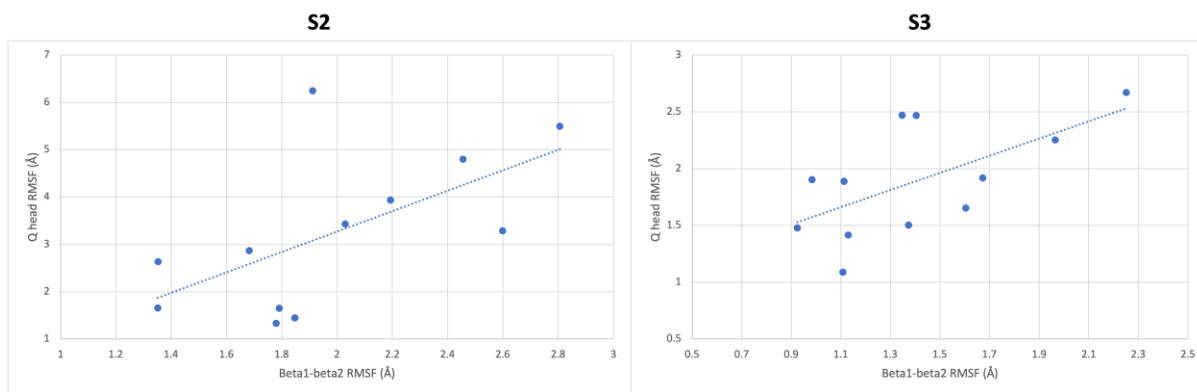


Figure S2 – Scatter plot of RMSF values of CA atoms of β 1- β 2^{NDUFS2} loop and Q head atoms for S2 and S3 simulations.

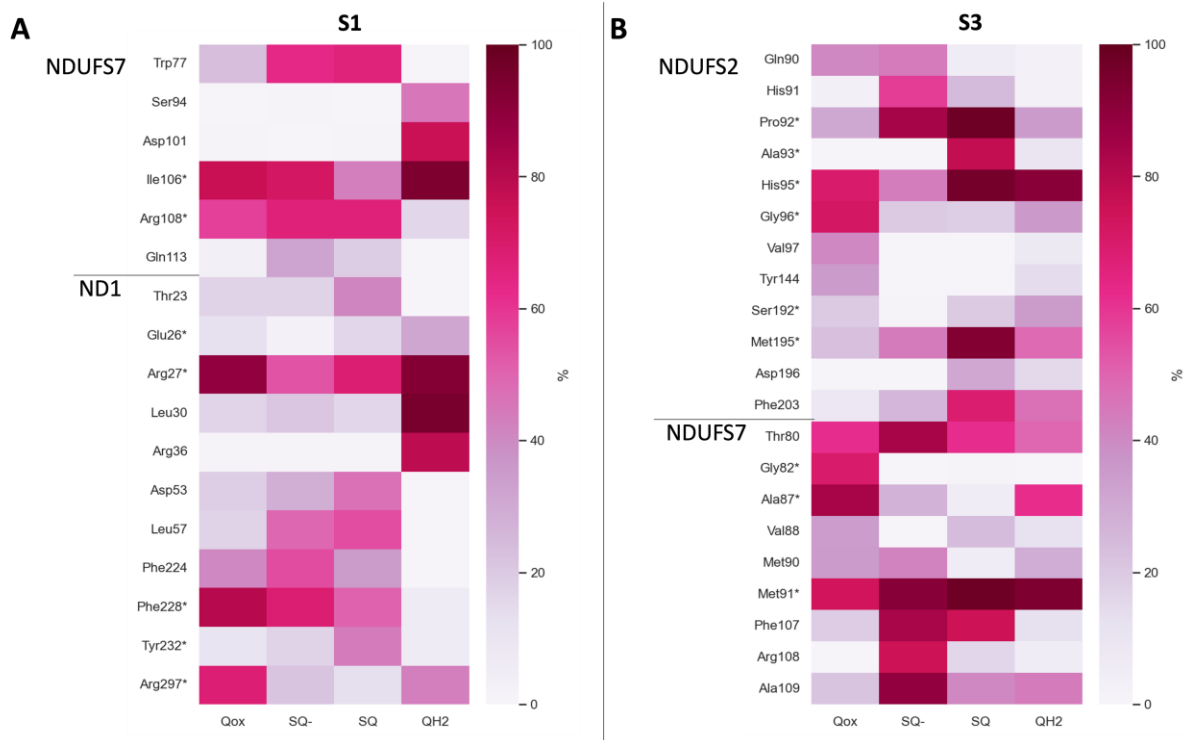


Figure S3 – Interactions between Q head group and protein residues in S1 simulations based on structure PDB 6RFR (A) and in S3 simulations based on high resolution structure PDB 7O6Y (B). The asterisk (*) denotes interactions between the Q head group and protein residues present in the respective structure.

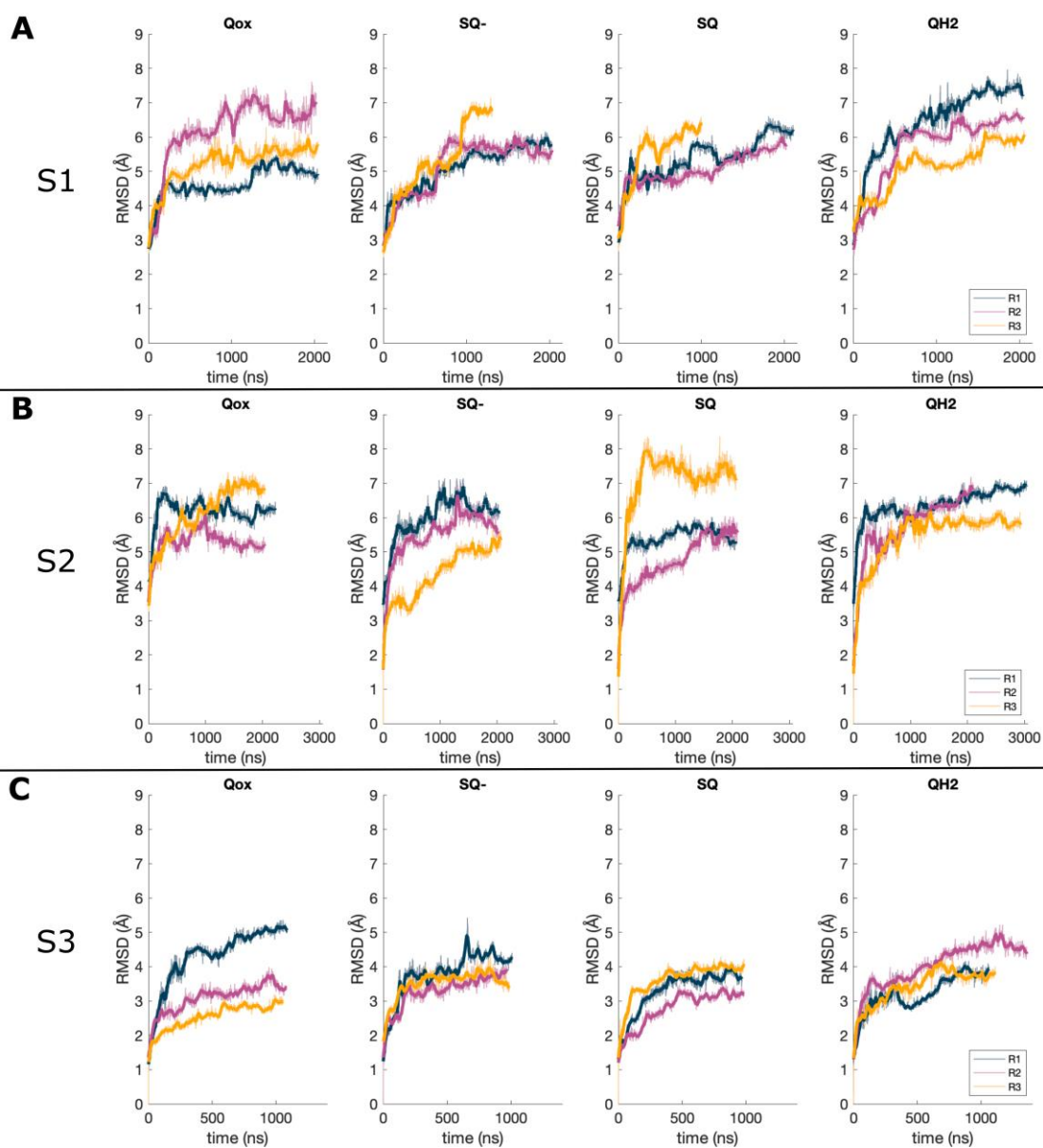


Fig. S4: RMSD of CA atoms over time for S1 (A), S2 (B) and S3 (C) simulations. Different simulation replicas are shown in different colours, and the bold line shows a rolling average based on the previous 20 frames.

		Conservation	Mutation data
NDUFS2	His91	Conserved	H91A – reduced activity
	Pro92	Conserved	
	Ala93	Partly conserved	
	Ala94	Partly conserved	A94I – decreased activity
	His95	Conserved	H95A – decreased activity
	Gly96	Conserved	
	Met195	Partly conserved	M195F – decreased activity
	Leu200	Partly conserved	
	Phe203	Partly conserved	F203W – increased activity
	Leu204	Partly conserved	
	Phe207	Conserved	F207W – decreased activity
NDUFS7	Trp77	Conserved	W77A/I/E – decreased activity
	Thr80	Partly conserved	
	Ala87	Partly conserved	
	Val88	Partly conserved	V88L/M/F – decreased activity
	Met90	Conserved	M90A/E – decreased activity
	Met91	Partly conserved	M91C/K – decreased activity
	Ser94	Partly conserved	S94A – no effect
	Asp101	Partly conserved	D101A – decreased activity
	Ile105	Partly conserved	I105A – no effect
	Ile106	Partly conserved	I106F/A – decreased activity
	Phe107	Partly conserved	F107A/P – decreased activity
	Arg108	Conserved	R108A/E – decreased activity
	Ala109	Partly conserved	A109G/S/C/L – decreased activity
	Asp115	Conserved	D115N – decreased activity
ND1	Thr23	Partly conserved	

	Glu26	Conserved	E24K – human disease
	Arg27	Conserved	R25Q – human disease
	Leu30	Partly conserved	
	Arg36	Conserved	R34H – human disease
	Asp53	Conserved	D62E – <i>P. denitrificans</i> - decreased activity
	Lys56	Conserved	K67A - <i>P. denitrificans</i> - decreased activity
	Leu57	Partly conserved	
	Arg199	Conserved	R195Q – human disease
	Asp203	Conserved	D213A/E/N – <i>E. coli</i> – decreased activity
	Glu206	Conserved	E216A – <i>E. coli</i> – decreased activity
	Phe224	Partly conserved	
	Phe228	Partly conserved	
	Tyr232	Conserved	
	Ile294	Partly conserved	
	Arg297	Conserved	R291A – <i>E. coli</i> – decreased activity

Table S1 - List of residues mentioned in the current work, along with their conservation and mutation data (if available). Mutation data for NDUFS2 is taken from (Angerer et al., 2012), for NDUFS7 from (Fendel, Tocilescu, Kerscher, & Brandt, 2008; Garofano, Zwicker, Kerscher, Okun, & Brandt, 2003; Yoga et al., 2019) and for ND1 from (Baradaran, Berrisford, Minhas, & Sazanov, 2013).

Ion pair	6GCS		7O6Y	
	Qox (stay)	QH2 (move)	Qox	QH2
R108 ... E206	Closed	Open	Open	Open
R199 ... E206	Mostly open	Mostly closed	Open	Mostly open
R297 ... E206	Mostly closed	Mostly open	Closed	Open
R297 ... D203	Mixed	Closed	Open	Open
R27 ... D101	Open	Closed	Mixed	Mixed
K56 ... D115	Mostly closed	Mostly open	Closed	Closed

Table S2 – Ion pairs identified to change with Q diffusion in the Q tunnel in S2 and S3 simulations. Data is shown for both Qox and QH2 species. See also main text Fig. 4. Closed was defined as the distance between Arg:CZ, Lys:NZ, Glu:CD, and Asp:CG atoms being < 5.5 Å.

References

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