Science Advances
AAAS

advances.sciencemag.org/cgi/content/full/5/3/eaav1850/DC1

Supplementary Materials for

How cardiolipin modulates the dynamics of respiratory complex I

Alexander Jussupow, Andrea Di Luca, Ville R. I. Kaila*

*Corresponding author. Email: ville.kaila@ch.tum.de

Published 20 March 2019, *Sci. Adv.* **5**, eaav1850 (2019)
DOI: 10.1126/sciadv.aav1850

The PDF file includes:

Other Supplementary Material for this manuscript includes the following:

(available at advances.sciencemag.org/cgi/content/full/5/3/eaav1850/DC1)

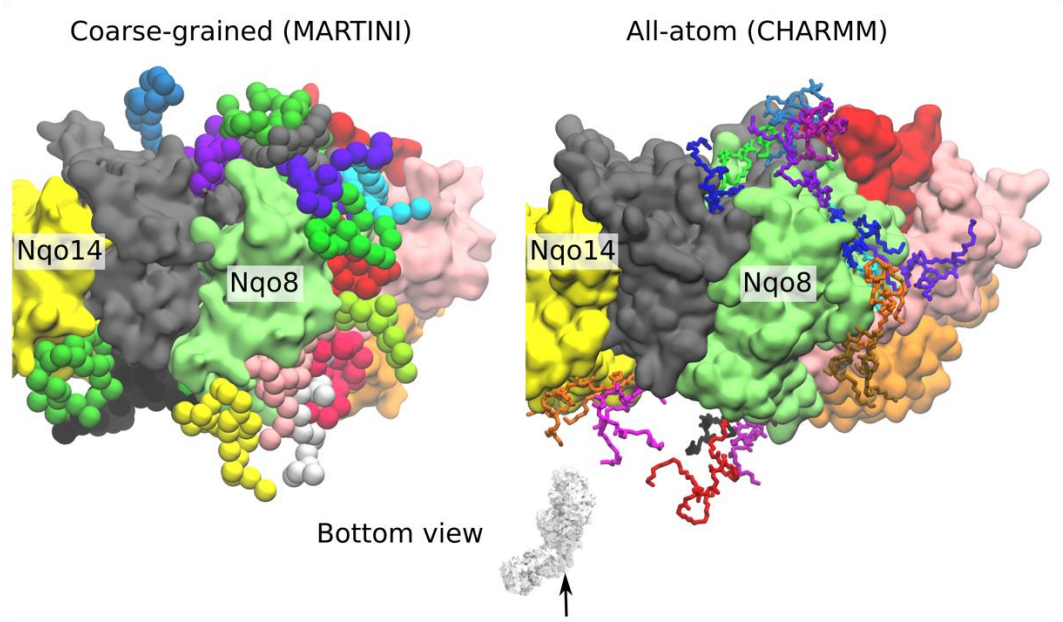


Fig. S1. Comparison of cardiolipin molecules bound to Nqo8 from coarse-grained and atomistic models. Bottom view of the membrane domain of complex I (*inset*). Comparison of cardiolipin molecules (highlighted in different colors for visual clarity) bound to Nqo8, obtained from coarse-grained (MARTINI force field, left) and all-atomistic (CHARMM36 force field, right) models.

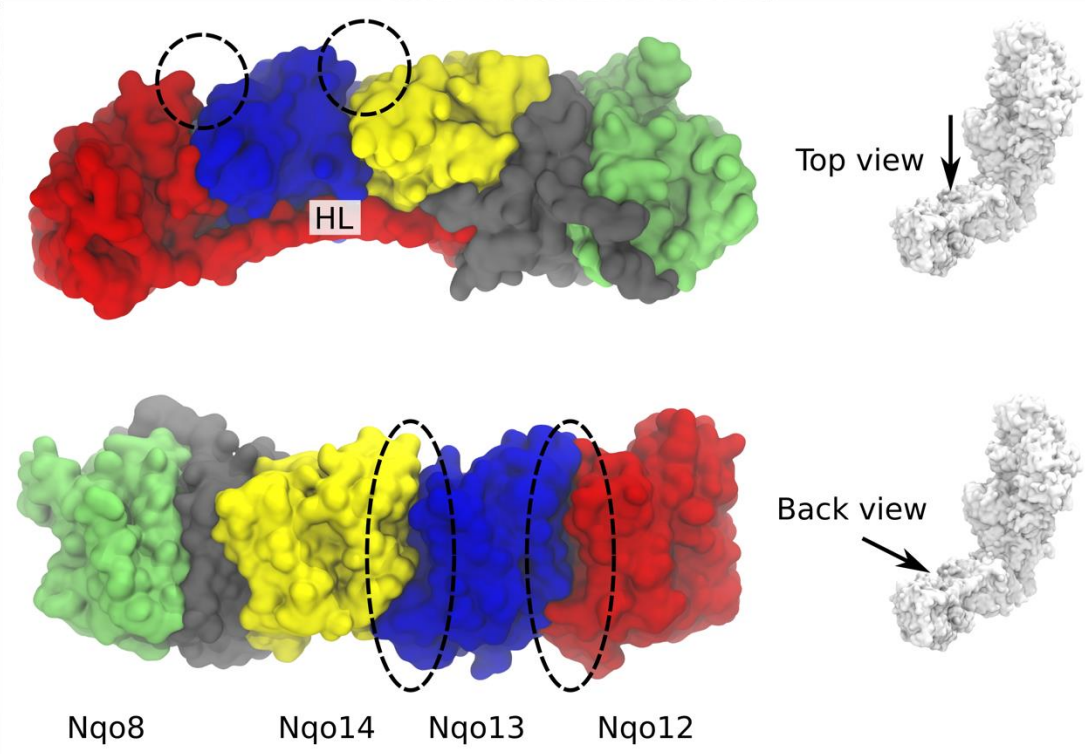


Fig. S2. The structure of the membrane domain of complex I from *T. thermophilus* (PDB ID:4HEA) with predicted cardiolipin binding sites between subunits Nqo12/Nqo13 and Nqo13/Nqo14 marked with dashed circles. The perspective of complex I is shown in the inset on the right.

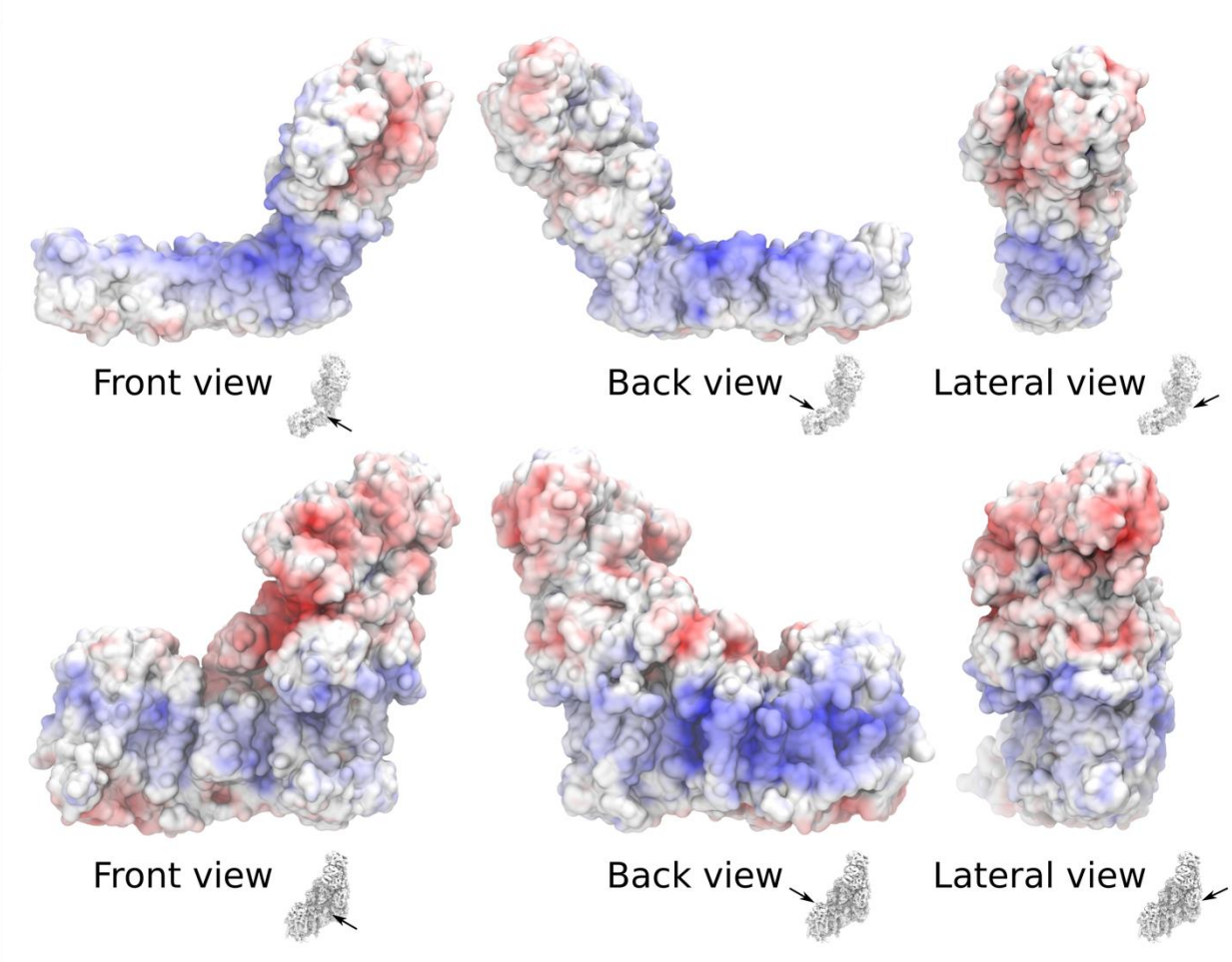


Fig. S3. Electrostatic potential surface of the bacterial and mammalian complex I. The color scale ranges from +10k_BT/e (blue, *ca*. +260 mV) to -10k_BT/e (red, *ca*. -260 mV) at T=298 K. The sites with a positive electrostatic potential correlate well with the cardiolipin binding sites shown in fig. S2. The mammalian and bacterial complex I have a similar potential surface around the membrane domain.

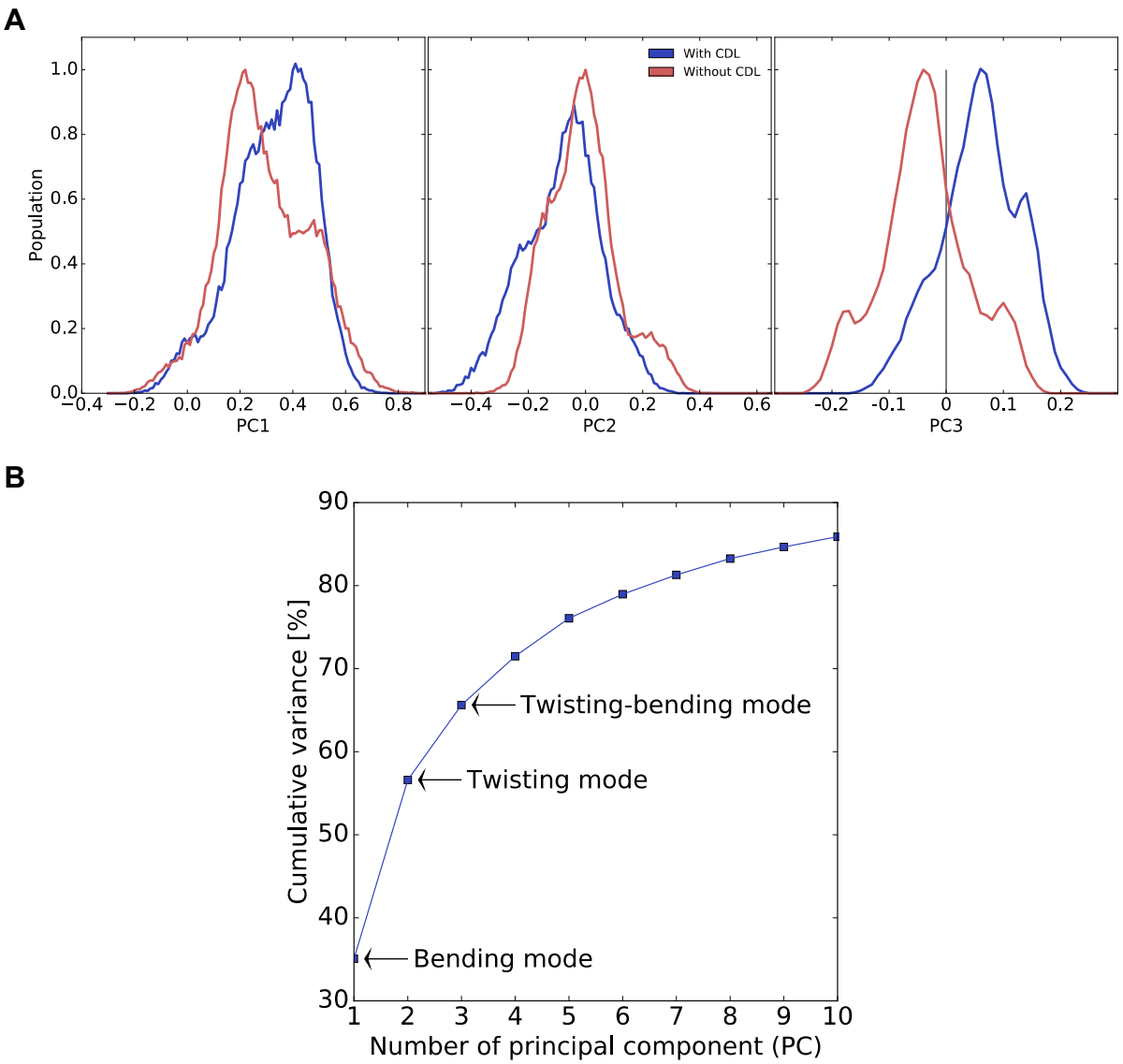


Fig. S4. Global motion of complex I with and without cardiolipin. A) Sampling the conformational space of all simulations along the bending (PC1), twisting (PC2), and coupled twisting-bending motion (PC3). Simulations with cardiolipin are shown in blue, and without cardiolipin in red. **B**) Cumulative variance of the principal component analysis. The first three principal components capture 65% of the total variance and account for around 2/3 of the total dynamics of complex I.

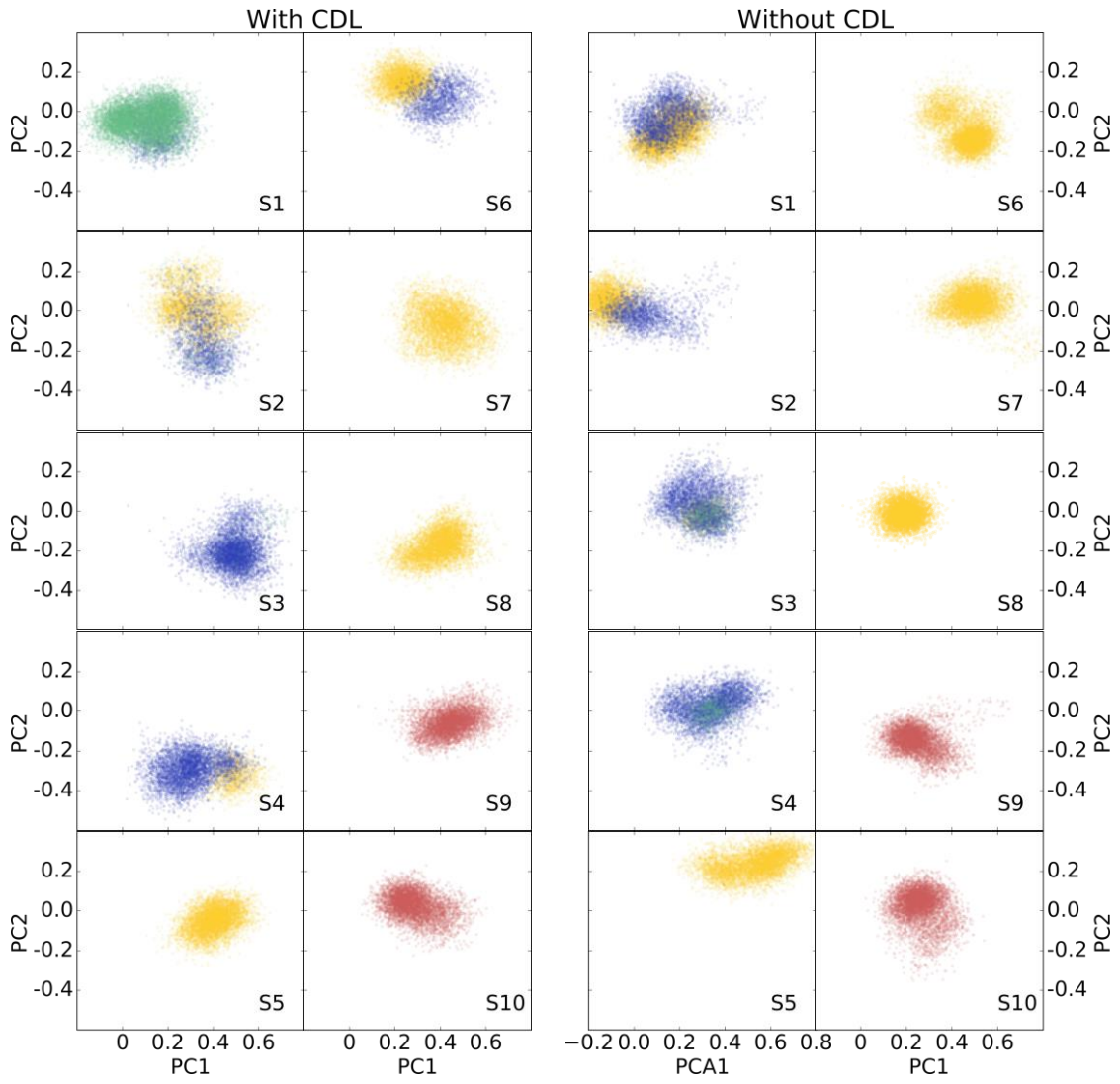


Fig. S5. Projection of complex I dynamics with and without cardiolipin along the bending (PC1) and twisting (PC2) modes for each individual coarse-grained simulation (see table S1). The color scale is the same as the one shown in Fig. 4 (main text) indicating the quinone position: no Q (in red); Q in the lower site (in yellow) and Q in upper sites (in blue and green).

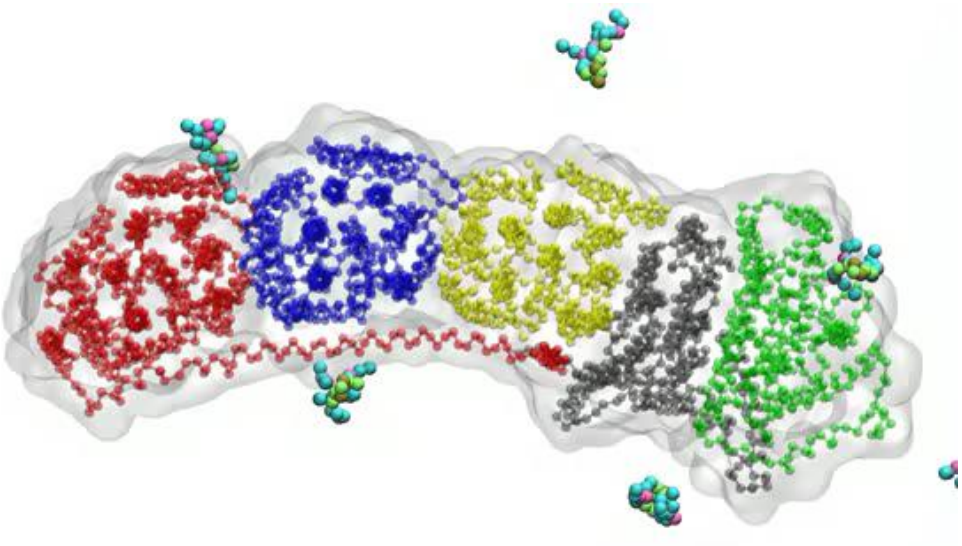
Table S1. Overview of all coarse-grained MD simulations. The table shows the simulation time and starting quinone position in all coarse-grained simulations.

Simulation	Quinone starting position	Simulation time [μs]
With cardiolipin		
S1	middle	101.27
S2	middle	54.46
S3	middle	52.13
S4	middle	50.26
S5	lower	52.87
S6	lower	54.88
S7	lower	53.56
S8	lower	53.68
S9	No Q	56.28
S10	No Q	52.03
	Total:	581.42
Without cardiolipin		
S1	middle	101.19
S2	middle	54.38
S3	middle	54.44
S4	middle	51.15
S5	lower	57.29
S6	lower	57.88
S7	lower	56.10
S8	lower	60.45
S9	No Q	51.23
S10	No Q	56.49
	Total:	599.60

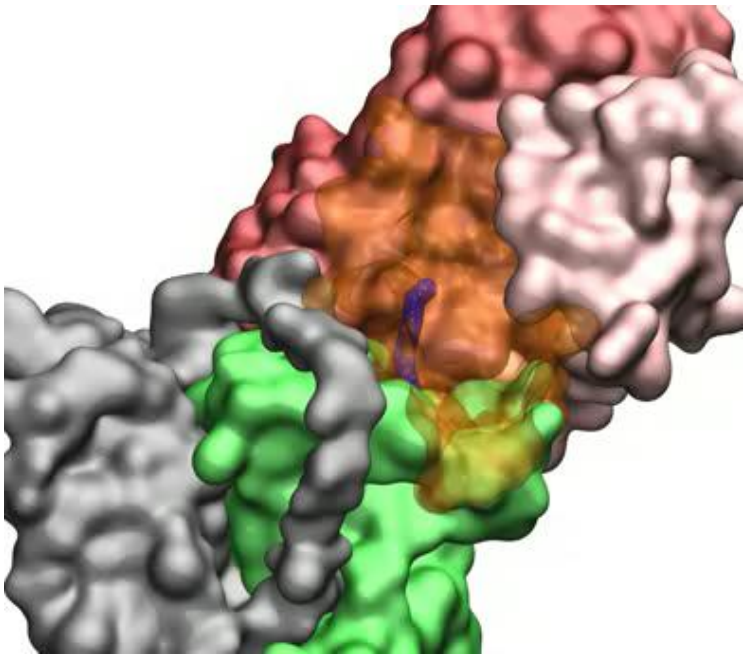
Table S2. Residues within 3 Å of putative channels 1 and 2 (*cf.* Fig. 4) that are identified in the channel analysis during >25% of the simulation trajectory ("Occupancy"). Residues that are within the Q-tunnel are excluded.

Subunit	Residue	Amino acid	Occupancy [%]
Channel 1			
Nqo6	95	Val	99.8
Nqo6	91	Val	97.4
Nqo6	94	Arg	95.9
Nqo7	45	Glu	90.2
Nqo6	98	Gln	84.7
Nqo4	31	Gly	62.3
Nqo7	43	Pro	62.1
Nqo7	46	Ser	50.1
Nqo7	42	Met	36.0
Nqo4	42	Arg	33.4
Nqo4	29	Asn	31.2
Nqo6	92	Met	25.5
Channel 2			
Nqo4	151	Arg	99.1
Nqo4	148	Tyr	88.0
Nqo9	21	Pro	87.4
Nqo9	22	Val	86.0
Nqo9	23	Thr	65.6
Nqo4	149	Ala	50.6
Nqo6	56	Ala	42.9
Nqo9	25	Pro	31.9
Nqo6	57	Arg	27.4

Partially conserved residues	Fully conserved residues	Exposed residues in the deactive state of the mammalian complex I



Movie S1. Cardiolipin binding to complex I from a coarse-grained simulation trajectory (simulation S1, table S1). Cardiolipin is shown in CPK representation and Nqo12 (in red), Nqo13 (in blue), Nqo14 (in yellow), Nqo9/10/11 (in gray), Nqo8 (in green). POPC and POPE lipids are not shown for clarity.



Movie S2. Cardiolipin-induced channel formation dynamics. Channel 1 (in red) and channel 2 (in green) connecting the N-side with the Q tunnel are strongly enhanced by cardiolipin (see Fig. 4 of the main text).