Supplementary Information

Energetic Mechanism of Cytochrome *c*-Cytochrome *c* Oxidase Electron Transfer Complex Formation under Turnover Condition Revealed by Mutational Effects and Docking Simulation

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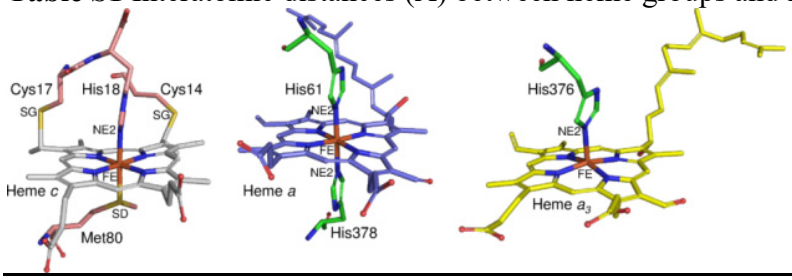
Table S1 Interatomic distances (Å) between heme groups and its ligated amino acid residues



distance[a]	protein (subunit)	observed[b]
Heme *c*@FE···His18@NE2	Cyt *c*	2.02 (0.06)
Heme *c*@FE···Met80@SD	Cyt *c*	2.30 (0.04)
Heme *c*@CAB···Cys14@SG	Cyt *c*	1.89 (0.09)
Heme *c*@CAC···Cys17@SG	Cyt *c*	2.13 (0.14)
Heme *a*@FE···His61@NE2	C*c*O (I)	1.95 (0.08)
Heme *a*@FE···His378@NE2	C*c*O (I)	1.95 (0.06)
Heme a_3@FE···His376@NE2	C*c*O (I)	2.10 (0.11)

[a] See the insert figure.

[b] Average value and standard deviation (in parentheses). These values were obtained from the crystallographic structures of Cyt *c* and C*c*O (PDB codes: 1J3S, 3NWV, 3ZCF, and 3ZOO (Cyt *c*); 1OCR, 1OCZ, 1V54, 1V55, 1OCC, 1OCO, 2Y69, 2ZXW, 2DYR, 2DYS, 2EIJ, 2EIK, 2EIL, 2EIM, 2EIN, 2OCC, 3ABM, 3AG1, 3AG2, 3AG3, 3AG4, 3ASN, 3ASO, 3ABK, and 3ABL (C*c*O)).

Table S2 Energetic contributions of Cyt *c* and each subunit of C*c*O

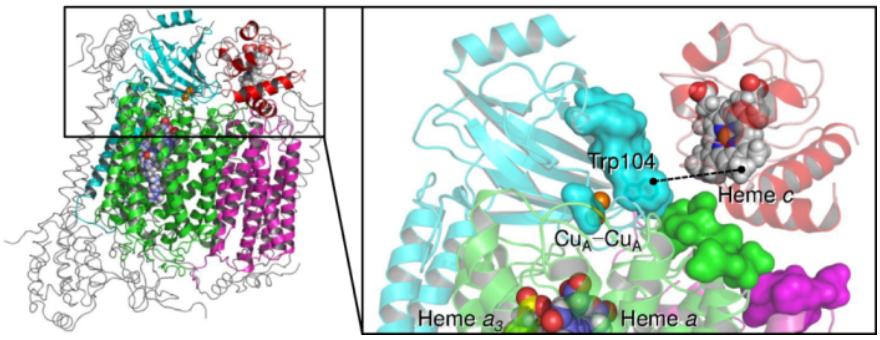
protein (subunit)	ΔE_{vdW}[a]	$\Delta G_{electro}$[a,b]	$\Delta G_{nonpolar}$[a]	ΔG_{tot}[a,c]
wild-type Cyt *c*	−69.7	19.5	−12.5	−62.7
C*c*O (I)	−12.6	−5.6	−1.7	−20.0
C*c*O (II)	−9.7	−5.1	−1.7	−16.5
C*c*O (III)	−3.8	−1.2	−0.6	−5.6
C*c*O (IV–XIII)	−43.6	17.9	−6.7	−32.4

[a] In kcal/mol.

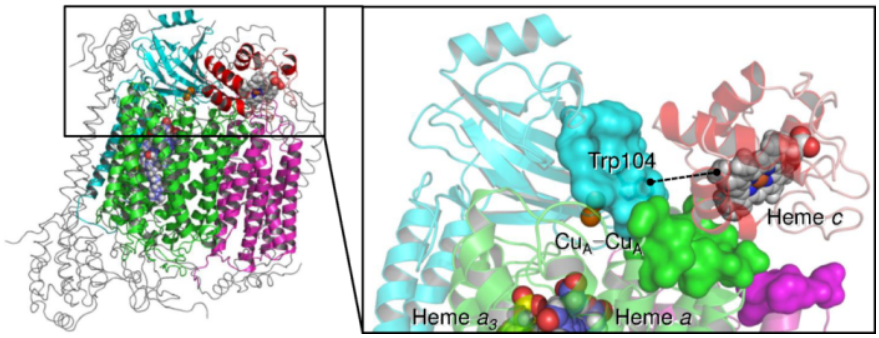
[b] $\Delta E_{coul} + \Delta G_{polar}$.

[c] $\Delta E_{vdW} + \Delta E_{coul} + \Delta G_{polar} + \Delta G_{nonpolar}$.

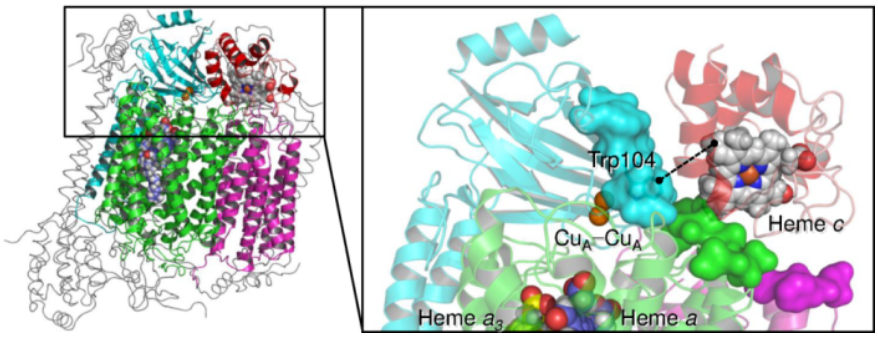
(a) Pose 1



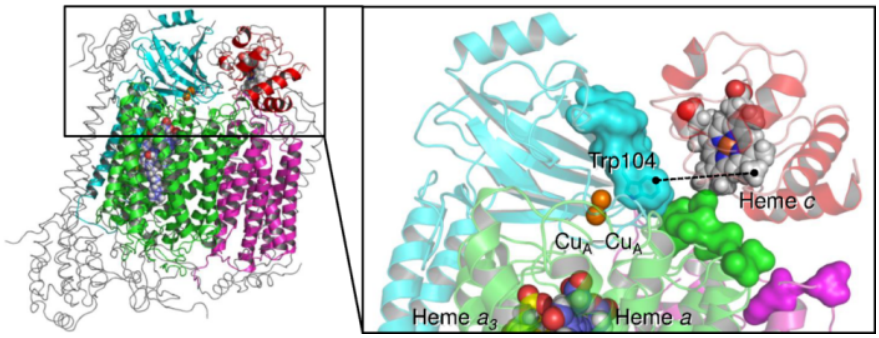
(b) Pose 6



(c) Pose 10



(d) Pose 11



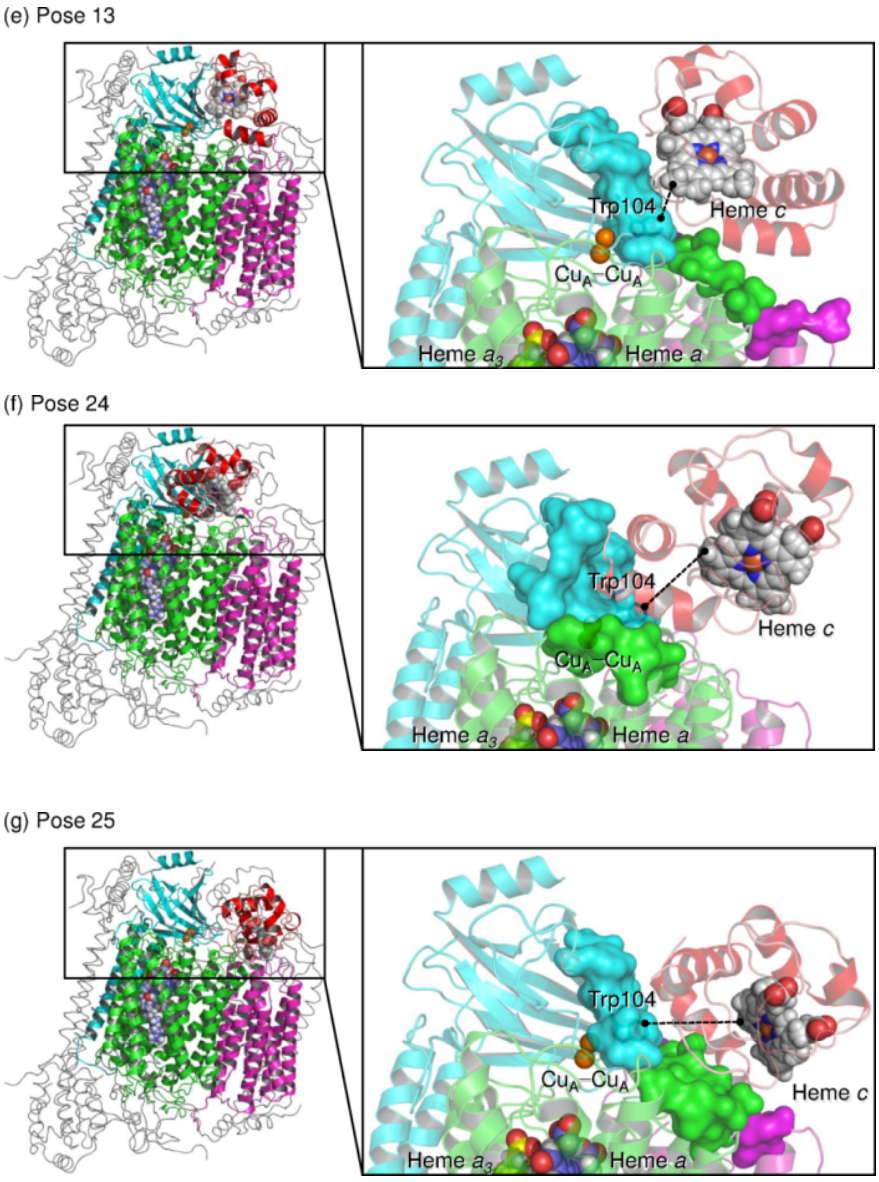


Figure S1 Predicted binding interfaces of the Cyt *c*−C*c*O complexes of poses (a) 1, (b) 6, (c) 10, (d) 11, (e) 13, (f) 24, and (g) 25. The contact residues in subunits I, II, and III of C*c*O are represented in green, cyan, and magenta surfaces, respectively. Dashed lines indicate the heme *c*−Trp104 distances.

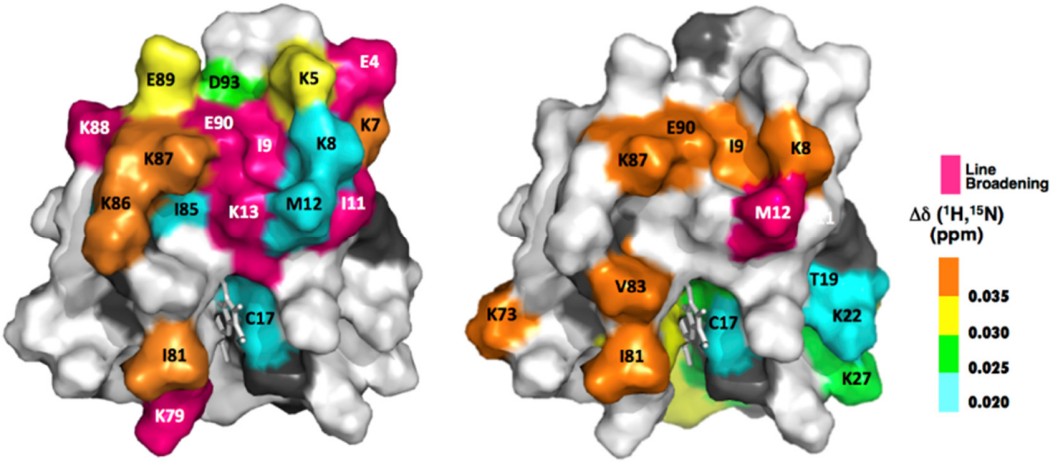


Figure S2. C*c*O interaction site on wild type and Lys-13 → Leu mutant Cyt *c*. Wild type (left) and Lys13 → Leu mutant Cyt *c* (right). The amino acid residues showing significant chemical shift perturbations associated with the binding C*c*O ($\Delta\delta > 0.020$ or line broadening) are highlighted.