Supplementary Information for Protonation Dynamics in the K-channel of Cytochrome c Oxidase estimated from Molecular Dynamics Simulations

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Conformational analysis

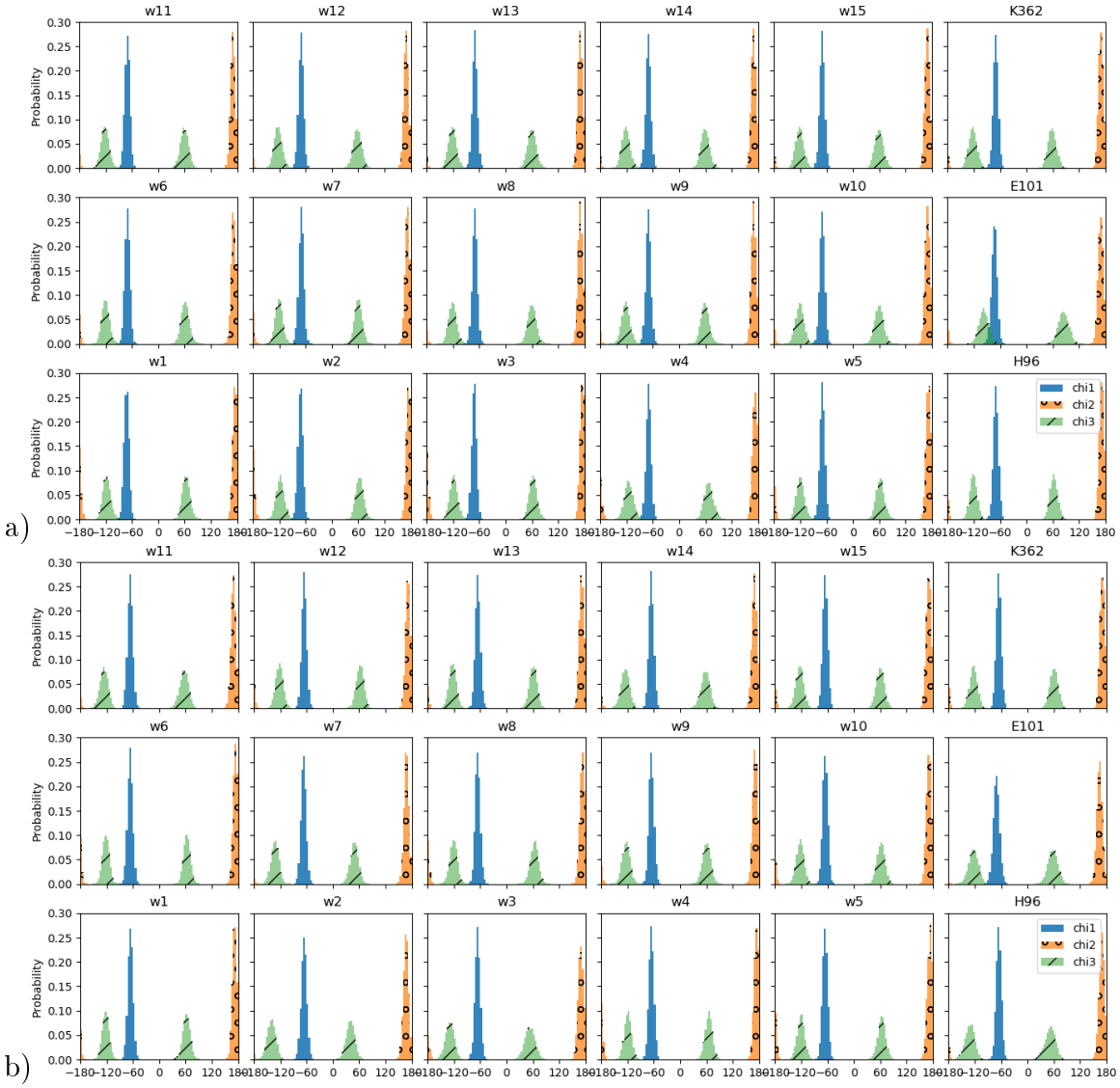

Figure S1: Distribution of side chain dihedral angles, χ_1,χ_2, and χ_3 of residue E101 in the MD simulations with the excess proton located at different sites. a) Simulations of the reduced model based on a snapshot with K362 in an "up" position, b) simulations of the reduced model based on a snapshot with K362 in a "down" position.

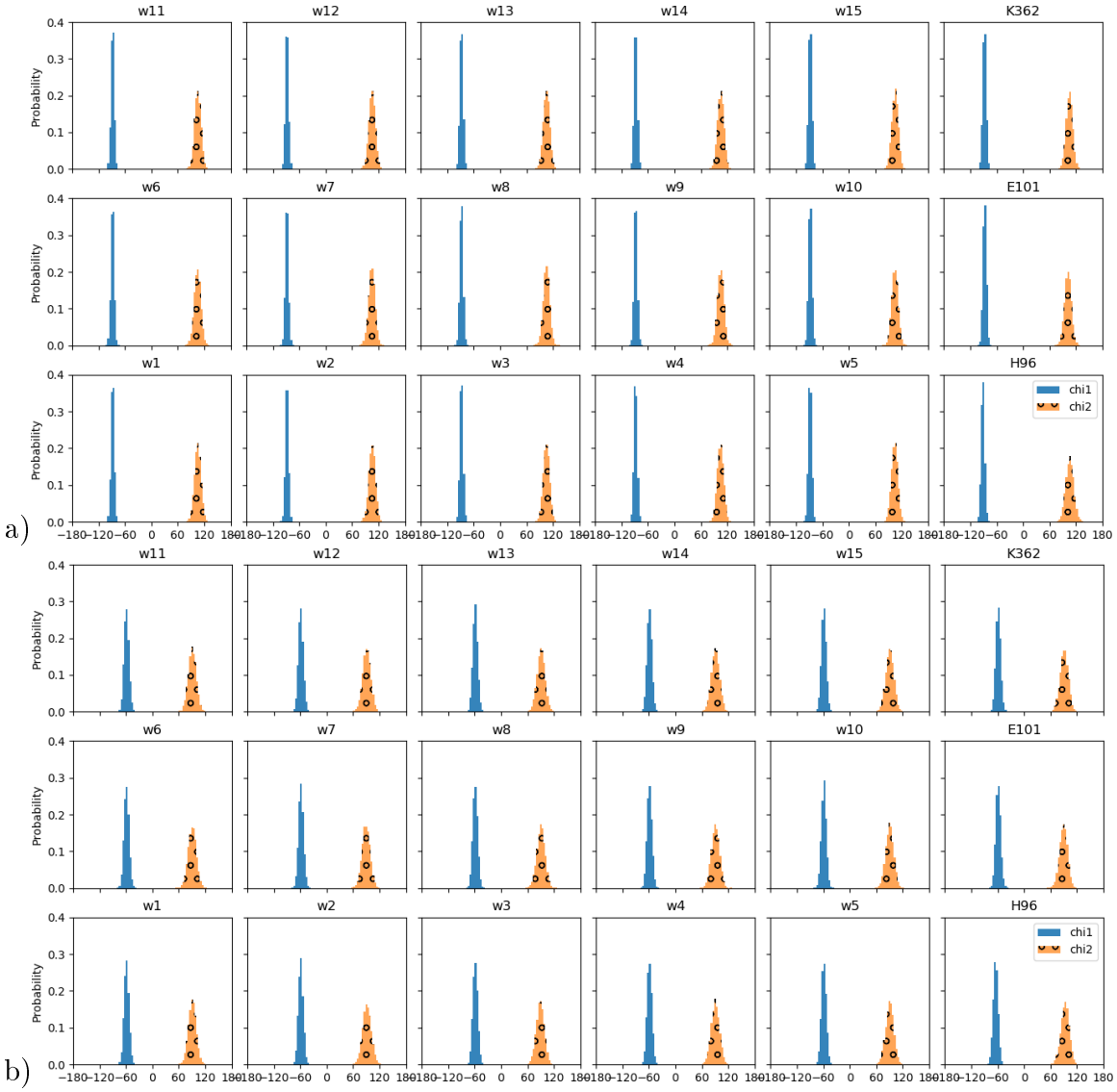

Figure S2: Distribution of side chain dihedral angles, χ_1 and χ_2 of residue H96 in the MD simulations with the excess proton located at different sites. a) Simulations of the reduced model based on a snapshot with K362 in an "up" position, b) simulations of the reduced model based on a snapshot with K362 in a "down" position.

Table S1: Average positions of oxygen atom OH of Y288, the nitrogen atom NZ of K362, the CD atom of E101, and the CE1 atom of H96.Simulations of the reduced model based on a snapshot with K362 in an "up" position, b) simulations of the reduced model based on a snapshot with K362 in a "down" position.

"up"	Y288	T359	K362	S365	E101	H96
w15	24.2±0.2	19.3±0.2	17.2±0.6	8.1±0.2	2.4±0.1	2.9±0.1
w14	24.3±0.2	19.6±0.2	18.1±0.2	8.2±0.2	2.4±0.1	2.9±0.1
w13	24.3±0.2	19.6±0.2	17.3±0.6	8.2±0.2	2.4±0.1	2.9±0.1
w12	24.3±0.2	19.3±0.3	17.7±0.3	8.2±0.2	2.4±0.1	2.9±0.1
w11	24.3±0.2	19.1±0.2	17.3±0.5	8.1±0.2	2.4±0.1	2.9±0.1
w10	24.3±0.2	19.1±0.2	17.3±0.4	8.1±0.2	2.4±0.1	2.9±0.1
w9	24.3±0.2	19.6±0.2	17.9±0.2	8.2±0.2	2.4±0.1	2.9±0.1
w8	24.3±0.2	19.4±0.3	16.6±0.8	8.2±0.2	2.4±0.1	2.9±0.1
w7	24.3±0.2	19.0±0.2	15.9±1.0	8.2±0.2	2.5±0.1	2.9±0.1
w6	24.3±0.2	19.5±0.2	18.0±0.4	8.3±0.2	2.5±0.1	2.9±0.1
w5	24.3±0.2	19.3±0.3	16.6±0.8	8.2±0.3	2.5±0.1	2.9±0.1
w4	24.3±0.2	19.1±0.2	16.2±0.5	8.1±0.2	2.5±0.1	2.9±0.1
w3	24.3±0.2	19.1±0.2	16.4±0.7	8.2±0.2	2.6±0.1	2.9±0.1
w2	24.3±0.2	19.3±0.2	16.3±0.9	8.3±0.2	2.6±0.1	2.9±0.1
w1	24.3±0.2	19.2±0.2	17.3±0.4	8.2±0.2	2.6±0.1	2.9±0.1
K362	24.3±0.2	19.1±0.2	17.4±0.3	8.2±0.2	2.4±0.1	2.9±0.1
E101	24.3±0.2	19.3±0.2	17.5±0.2	8.2±0.2	2.6±0.1	2.9±0.1
H96	24.3±0.2	19.0±0.2	17.0±0.4	8.2±0.2	2.5±0.1	3.0±0.1

"down"	Y288	T359	K362	S365	E101	H96
w15	26.0±0.2	19.5±0.2	17.4±0.7	8.8±0.4	2.4±0.1	0.8±0.1
w14	26.0±0.2	19.5±0.2	17.4±0.5	8.9±0.2	2.5±0.1	0.8±0.1
w13	26.0±0.1	19.4±0.2	17.4±0.5	9.0±0.2	2.5±0.1	0.8±0.1
w12	26.1±0.1	19.4±0.1	17.9±0.4	8.9±0.3	2.5±0.1	0.8±0.1
w11	26.0±0.1	19.4±0.1	16.9±1.0	9.0±0.2	2.4±0.1	0.8±0.1
w10	26.1±0.1	19.4±0.1	17.2±0.5	8.9±0.2	2.5±0.1	0.8±0.1
w9	26.1±0.1	19.4±0.1	16.0±0.4	9.0±0.2	2.5±0.1	0.8±0.1
w8	26.1±0.1	19.4±0.1	16.5±0.5	8.9±0.3	2.5±0.1	0.8±0.1
w7	26.0±0.1	19.4±0.1	17.6±0.4	8.9±0.3	2.6±0.1	0.8±0.1
w6	26.1±0.1	19.4±0.1	17.2±0.6	8.9±0.3	2.6±0.1	0.8±0.2
w5	26.1±0.1	19.4±0.1	17.6±0.2	9.3±0.2	2.6±0.1	0.8±0.1
w4	26.1±0.1	19.3±0.1	17.2±0.7	9.1±0.2	2.6±0.1	0.8±0.2
w3	26.1±0.1	19.4±0.1	17.6±0.5	9.1±0.2	2.5±0.2	0.8±0.1
w2	26.1±0.1	19.4±0.1	17.4±0.4	9.0±0.2	2.4±0.1	0.8±0.2
w1	26.0±0.1	19.4±0.1	17.3±0.5	9.0±0.2	2.4±0.1	0.8±0.1
K362	26.1±0.1	19.4±0.1	16.5±0.2	9.0±0.2	2.5±0.1	0.8±0.1
E101	26.0±0.1	19.4±0.1	17.7±0.5	9.0±0.2	2.6±0.1	0.8±0.1
H96	26.0±0.1	19.5±0.2	17.6±0.6	8.7±0.4	2.4±0.1	1.0±0.2

Hydrogen Bonds

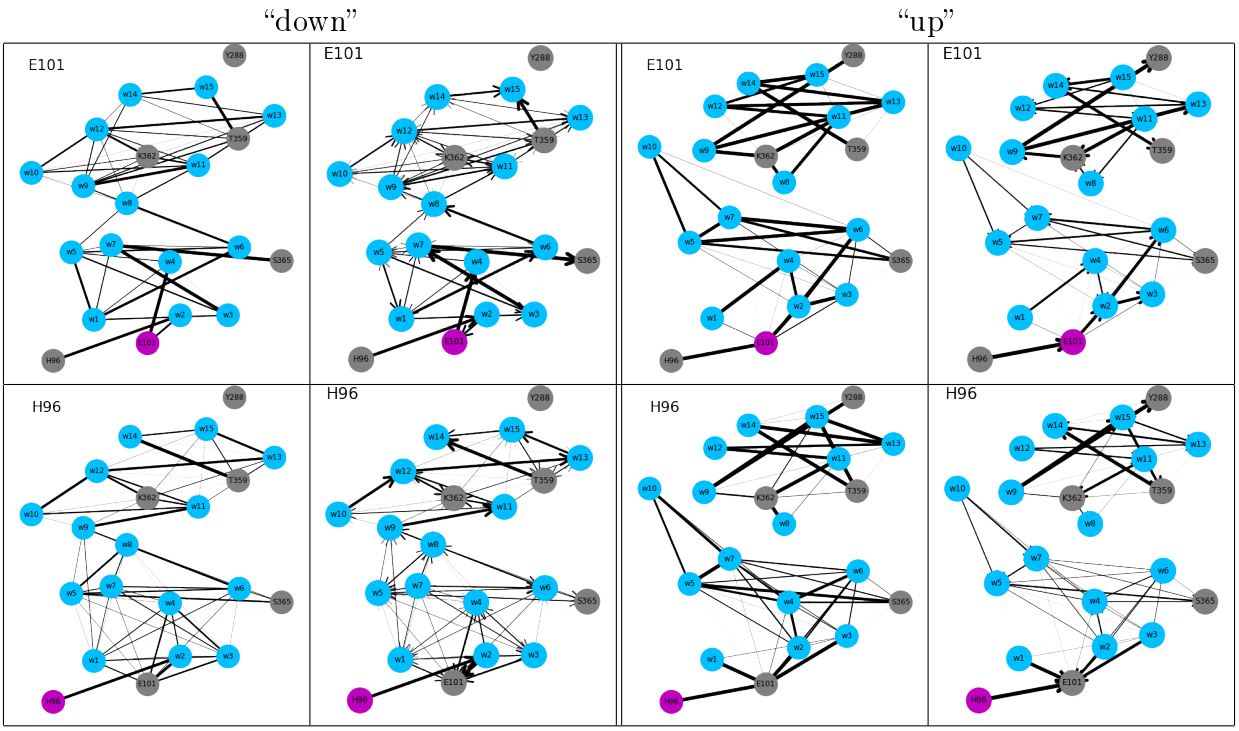

Figure S3: Undirected and directed hydrogen-bond networks of simulations with H96 or E101 protonated, started from a snapshot with K362 in a "down" or an "up" conformation, respectively. The nodes of the network are the protein residues (in grey) Y288, T359, K362, S365, H96, or E101, and the fifteen water molecules (in blue) in the channel. The residue carrying the excess proton is highlighted in magenta. Edges of the network correspond to hydrogen bonds, shown as lines for undirected and as arrows pointing from donor to acceptor residue for directed networks. The thickness of the lines indicate the probability of the hydrogen bonds.

Proton transfer

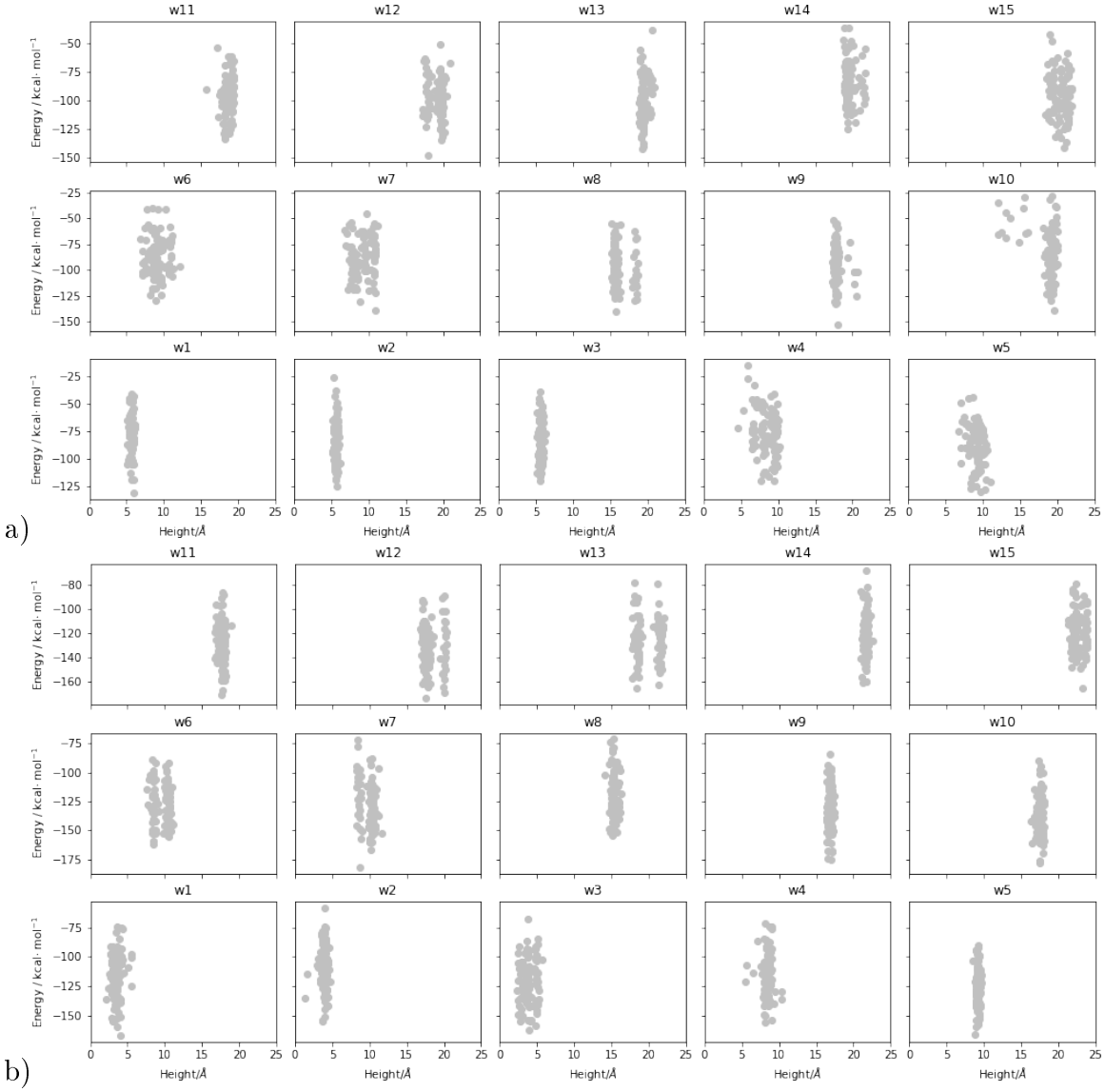

Figure S4: Energies of the snapshots used for crossing attempts vs. height of the protonated water molecules' oxygen atoms.a) Simulations of the reduced model based on a snapshot with K362 in an "up" position, b) simulations of the reduced model based on a snapshot with K362 in a "down" position.

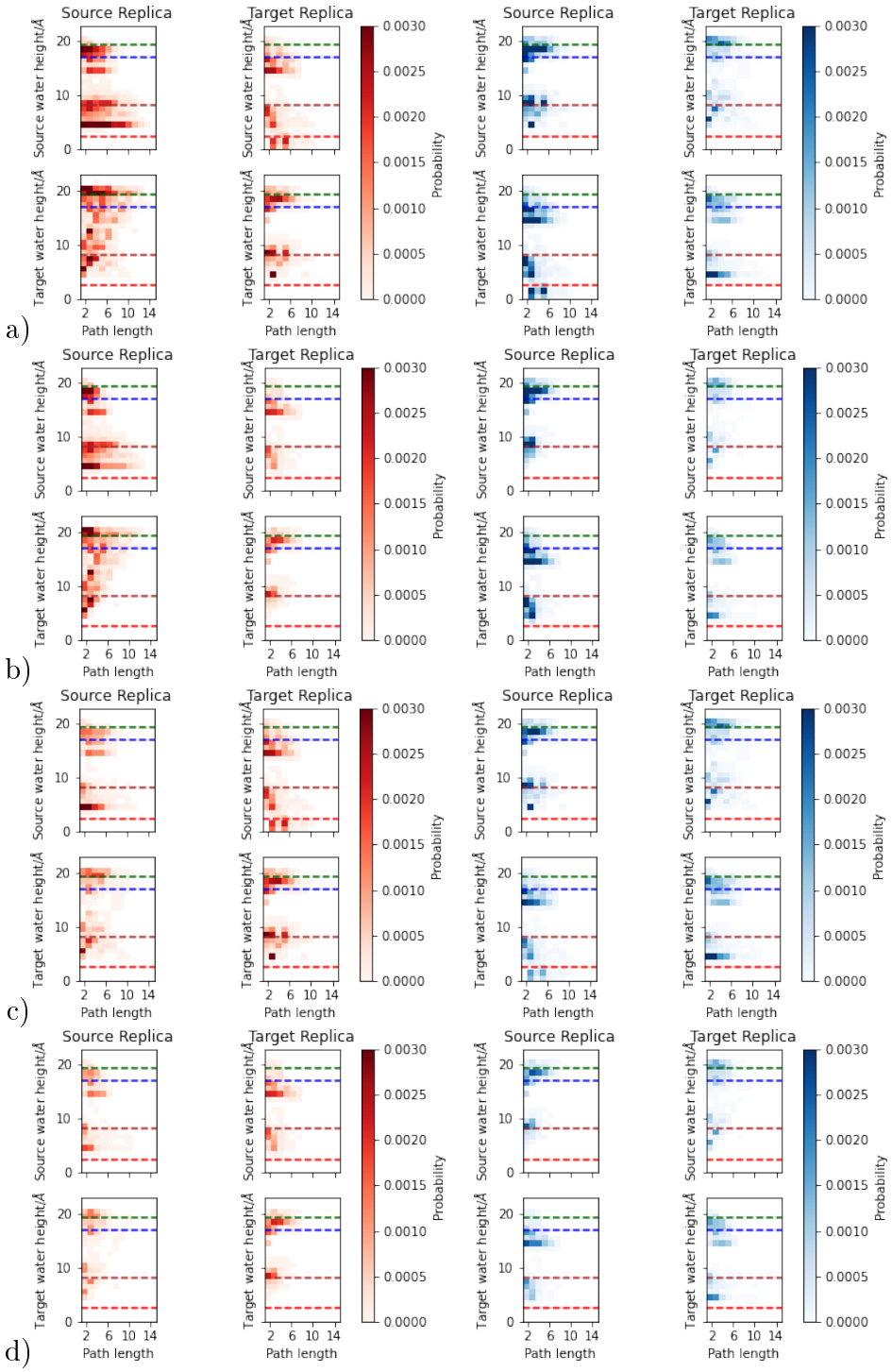

Figure S5: Position-dependent acceptance for proton exchange in "up" models as function of the transition step size as measured by the length of the hydrogen-bonded chain. Left: "upwards" (direction from H96 to Y288) transitons, right: "downwards" (direction from Y288 to H96) transitions. Dashed lines indicate the average position of protein residues E101 (red), S365 (brown), K362 (blue), and T359 (green). a) existence of a hydrogen-bonded connection in the source replica, b) existence of a directed hydrogen-bonded connection in the source replica, c) existence of a directed hydrogen-bonded connection in the source replica, and d) existence of a directed hydrogen-bonded connection in the source and target replica as additional criterion.

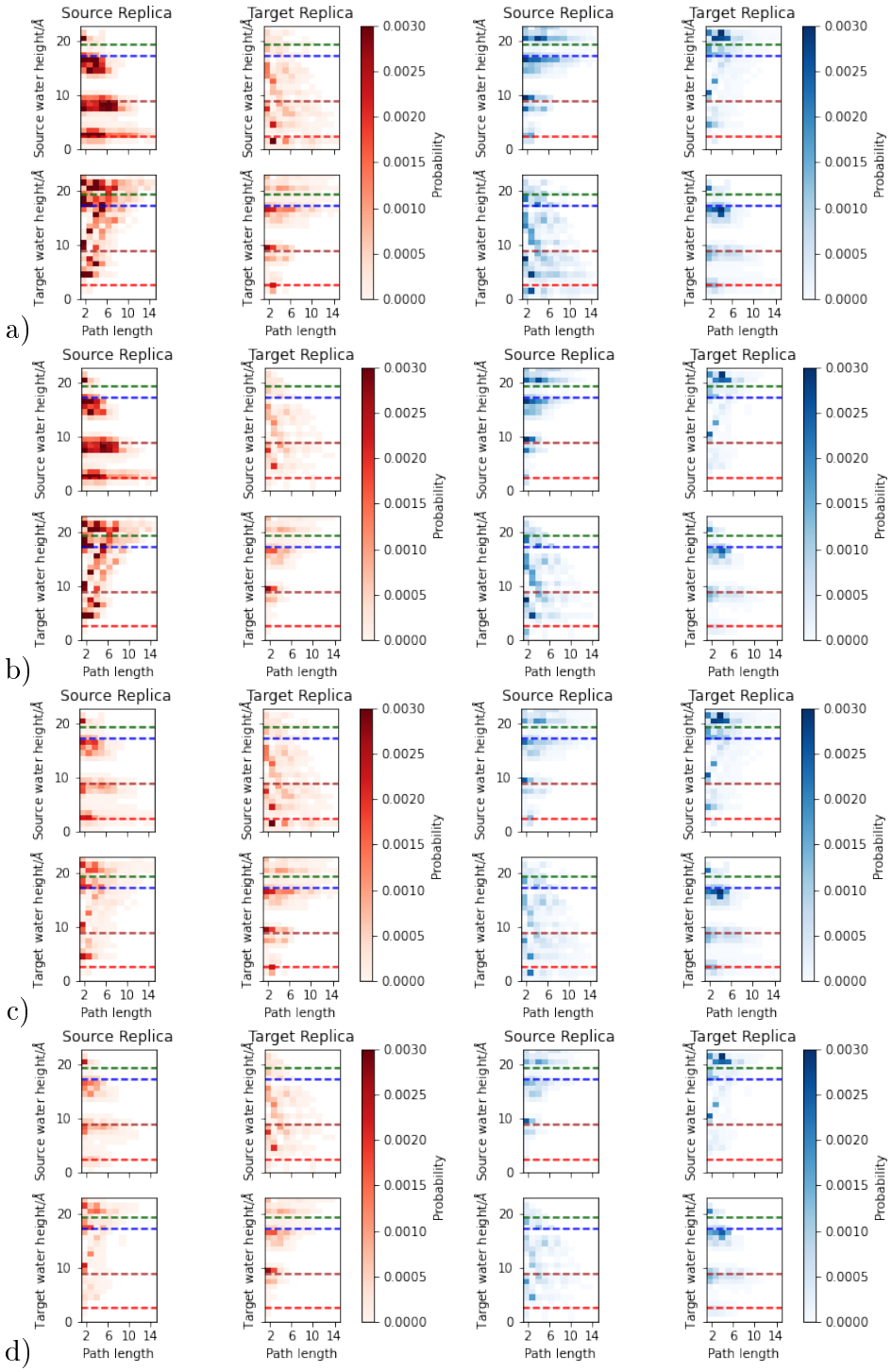

Figure S6: Position-dependent acceptance for proton exchange in "down" models as function of the transition step size as measured by the length of the hydrogen-bonded chain. Left: "upwards" (direction from H96 to Y288) transitons, right: "downwards" (direction from Y288 to H96) transitions. Dashed lines indicate the average position of protein residues E101 (red), S365 (brown), K362 (blue), and T359 (green). a) existence of a hydrogen-bonded connection in the source replica, b) existence of a directed hydrogen-bonded connection in the source replica, c) existence of a directed hydrogen-bonded connection in the source replica, and d) existence of a directed hydrogen-bonded connection in the source and target replica as additional criterion.