Semi-Automated Optimization of the CHARMM36 Lipid Force Field to Include Explicit Treatment of Long-Range Dispersion

Supporting Information

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Table S1. Parameters subject to change for the two optimizations. Atom notations shown in Figure S1. Asterisk sign stands for A/B/C.

Optimization Name	*Global*	*Linkage*
Charges	N, H13*, H14*, H15*, C13, C14, C15, C12, H12*, C11, H11*, P, O13, O14, O11, O12, C1, HA, HB, C2, HS, O21, C21, O22, C22, H2R, H2S, C3, HX, HY, O31, C31, O32, C32, H2X, H2Y	C2, HS, O21, C21, O22, C22, H2R, H2S, C3, HX, HY, O31, C31, O32, C32, H2X, H2Y
ε	N, H13*, H14*, H15*, C13, C14, C15, H12*, C11, H11*, P, O11, O12, O21, C21, O22, O31, C31, C32	O21, O22, O31, C32
$R_{min}/2$	N, H13*, H14*, H15*, C13, C14, C15, H12*, C11, H11*, P, O11, O12, O21, C21, O22, O31, C31, C32	O21, O22, O31, C32

Table S2-a. Rules for charge redistribution for the *Global* optimization. When the charge on the center atom(s) is changed, the opposite change is evenly distributed to the atom(s) to exchange charge with. The transfer of charge is always within an integer charge group defined in CHARMM. Equivalent atomic sites from group 3 and group 4 are listed in the same rows.

center atom(s)	atom(s) to exchange charge with
group 1	
N	C13, C14, C15, C12
H13*, H14*, H15*	H12*
C13, C14, C15	H13*, H14*, H15*
C12	H12*
group 2	
C11	P
H11*	C11
P	O13, O14, O11, O12
O13, O14	O11, O12
O11, O12	C1
C1	HA, HB
group 3 and group 4	
C2	HS
O21 / O31	C2 / C3
C21 / C22	(O21, O22, C22) / (O31, O32, C32)
O22 / O32	C21 / C31
C22 / C32	C21 / C31
(H2R, H2S) / (H2X, H2Y)	C22 / C32
C3	HX, HY

Table S2-b. Rules for charge redistribution for the *Linkage* optimization. The way of exchanging charge is described in the caption of Table S2-a. Equivalent atomic sites from group 3 and group 4 are listed in the same rows.

center atom(s)	atom(s) to exchange charge with
group 3 and group 4	
C2 / C3	O21 / O31
HS	C2
O21 / O31	(C2, C21) / (C3, C31)
C21 / C22	(O21, O22, C22) / (O31, O32, C32)
O22 / O32	(O21, C21, C22) / (O31, C31, C32)
C22 / C32	C21 / C31
(H2R, H2S) / (H2X, H2Y)	C22 / C32

Table S3. Default weight factors for different parameter types in each optimization cycle.

optimization cycle	q	ε	$R_{min}/2$
Global-1	4/e	6/percentage	6/percentage
Global-2	4/e	6/percentage	6/percentage
Global-3	16/e	24/percentage	24/percentage
Linkage-1	4/e	6/percentage	6/percentage
Linkage-2	4/e	6/percentage	6/percentage

Table S4. S_b in eq 5 for each optimization cycle.

optimization cycle	S_b
Global-1	500
Global-2	500
Global-3	2000
Linkage-1	500
Linkage-2	500

Table S5. Partial atomic charges (e) for each optimization cycle. "G" stands for *Global* and "L" stands for *Linkage*.

atom name	atom type	original	G-1	G-2	G-3	L-1	L-2
N	NTL	-0.60	-0.5959	-0.6030	-0.6030	-0.6	-0.6
C13	CTL5	-0.35	-0.3468	-0.3451	-0.3451	-0.35	-0.35
H13A	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
H13B	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
H13C	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
C14	CTL5	-0.35	-0.3468	-0.3451	-0.3451	-0.35	-0.35
H14A	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
H14B	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
H14C	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
C15	CTL5	-0.35	-0.3468	-0.3451	-0.3451	-0.35	-0.35
H15A	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
H15B	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
H15C	HL	0.25	0.2506	0.2542	0.2542	0.25	0.25
C12	CTL2	-0.10	-0.0680	-0.0551	-0.0551	-0.1	-0.1
H12A	HL	0.25	0.2245	0.2027	0.2027	0.25	0.25
H12B	HL	0.25	0.2245	0.2027	0.2027	0.25	0.25
C11	CTL2	-0.08	-0.0914	-0.0726	-0.0793	-0.08	-0.08
H11A	HAL2	0.09	0.0869	0.0687	0.0664	0.09	0.09
H11B	HAL2	0.09	0.0869	0.0687	0.0664	0.09	0.09
P	PL	1.50	1.5149	1.5229	1.5308	1.5	1.5
O13	O2L	-0.78	-0.7898	-0.7874	-0.7816	-0.78	-0.78
O14	O2L	-0.78	-0.7898	-0.7874	-0.7816	-0.78	-0.78
O11	OSLP	-0.57	-0.5423	-0.5295	-0.5307	-0.57	-0.57
O12	OSLP	-0.57	-0.5423	-0.5295	-0.5307	-0.57	-0.57
C1	CTL2	-0.08	-0.1001	-0.1484	-0.1481	-0.08	-0.08
HA	HAL2	0.09	0.0834	0.0972	0.0942	0.09	0.09
HB	HAL2	0.09	0.0834	0.0972	0.0942	0.09	0.09
C2	CTL1	0.17	0.1412	0.1020	0.0988	0.1638	0.1339
HS	HAL1	0.09	0.1188	0.1580	0.1626	0.1092	0.1023
O21	OSL	-0.49	-0.4904	-0.4904	-0.4919	-0.4992	-0.4739
C21	CL	0.90	0.8793	0.8604	0.8579	0.8669	0.8445
O22	OBL	-0.63	-0.6507	-0.6607	-0.6560	-0.6391	-0.6272
C22	CTL2	-0.22	-0.1770	-0.1555	-0.1565	-0.1873	-0.1652
H2R	HAL2	0.09	0.0894	0.0931	0.0926	0.0928	0.0928
H2S	HAL2	0.09	0.0894	0.0931	0.0926	0.0928	0.0928
C3	CTL2	0.08	0.0830	0.1125	0.1139	0.1026	0.0302
HX	HAL2	0.09	0.0885	0.0738	0.0738	0.0852	0.1030

HY	HAL2	0.09	0.0885	0.0738	0.0738	0.0852	0.1030
O31	OSL	-0.49	-0.4904	-0.4904	-0.4919	-0.4992	-0.4739
C31	CL	0.90	0.8793	0.8604	0.8579	0.8669	0.8445
O32	OBL	-0.63	-0.6507	-0.6607	-0.6560	-0.6391	-0.6272
C32	CTL2	-0.22	-0.1770	-0.1555	-0.1565	-0.1873	-0.1652
H2X	HAL2	0.09	0.0894	0.0931	0.0926	0.0928	0.0928
H2Y	HAL2	0.09	0.0894	0.0931	0.0926	0.0928	0.0928

Table S6. ε (kcal/mol) for each optimization cycle. "G" stands for *Global* and "L" stands for *Linkage*. For the *Linkage* optimization, changed parameters are emphasized in **bold**.

atom name	atom type	original	G-1	G-2	G-3	L-1	L-2
N	NTL	-0.2000	-0.2000	-0.2000	-0.2000	-0.2000	-0.2000
C13	CTL5	-0.0800	-0.0800	-0.0800	-0.0800	-0.0800	-0.0800
H13A	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
H13B	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
H13C	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
C14	CTL5	-0.0800	-0.0800	-0.0800	-0.0800	-0.0800	-0.0800
H14A	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
H14B	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
H14C	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
C15	CTL5	-0.0800	-0.0800	-0.0800	-0.0800	-0.0800	-0.0800
H15A	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
H15B	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
H15C	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
C12	CTL2	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560
H12A	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
H12B	HL	-0.0460	-0.0457	-0.0455	-0.0455	-0.0460	-0.0460
C11	CTL2	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560
H11A	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
H11B	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
P	PL	-0.5850	-0.5850	-0.5850	-0.5850	-0.5850	-0.5850
O13	O2L	-0.1200	-0.1196	-0.1194	-0.1194	-0.1200	-0.1200
O14	O2L	-0.1200	-0.1196	-0.1194	-0.1194	-0.1200	-0.1200
O11	OSLP	-0.1000	-0.0996	-0.0996	-0.0996	-0.1000	-0.1000
O12	OSLP	-0.1000	-0.0996	-0.0996	-0.0996	-0.1000	-0.1000
C1	CTL2	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560
HA	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
HB	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
C2	CTL1	-0.0200	-0.0200	-0.0200	-0.0200	-0.0200	-0.0200
HS	HAL1	-0.0220	-0.0220	-0.0220	-0.0220	-0.0220	-0.0220
O21	OSL	-0.1000	-0.0995	-0.0991	-0.0991	-0.1000	-0.1000
C21	CL	-0.0700	-0.0696	-0.0693	-0.0693	-0.0700	-0.0700
O22	OBL	-0.1200	-0.1189	-0.1185	-0.1185	**-0.1192**	**-0.1192**
C22	CTL2	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560
H2R	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
H2S	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
C3	CTL2	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560
HX	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280

HY	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
O31	OSL	-0.1000	-0.0995	-0.0991	-0.0991	-0.1000	-0.1000
C31	CL	-0.0700	-0.0696	-0.0693	-0.0693	-0.0700	-0.0700
O32	OBL	-0.1200	-0.1189	-0.1185	-0.1185	**-0.1192**	**-0.1192**
C32	CTL2	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560	-0.0560
H2X	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280
H2Y	HAL2	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280	-0.0280

Table S7. $R_{min}/2$ (Å) for each optimization cycle. "G" stands for *Global* and "L" stands for *Linkage*. For the *Linkage* optimization, changed parameters are emphasized in **bold**.

atom name	atom type	original	G-1	G-2	G-3	L-1	L-2
N	NTL	1.850	1.8500	1.8500	1.8500	1.8500	1.8500
C13	CTL5	2.060	2.0600	2.0600	2.0600	2.0600	2.0600
H13A	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
H13B	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
H13C	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
C14	CTL5	2.060	2.0600	2.0600	2.0600	2.0600	2.0600
H14A	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
H14B	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
H14C	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
C15	CTL5	2.060	2.0600	2.0600	2.0600	2.0600	2.0600
H15A	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
H15B	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
H15C	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
C12	CTL2	2.010	2.0100	2.0100	2.0100	2.0100	2.0100
H12A	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
H12B	HL	0.700	0.6951	0.6951	0.6951	0.7000	0.7000
C11	CTL2	2.010	2.0100	2.0100	2.0100	2.0100	2.0100
H11A	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
H11B	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
P	PL	2.150	2.1500	2.1500	2.1500	2.1500	2.1500
O13	O2L	1.700	1.7516	1.7914	1.7000	1.7000	1.7000
O14	O2L	1.700	1.7516	1.7914	1.7000	1.7000	1.7000
O11	OSLP	1.650	1.6500	1.7094	1.7139	1.6500	1.6500
O12	OSLP	1.650	1.6500	1.7094	1.7139	1.6500	1.6500
C1	CTL2	2.010	2.0100	2.0100	2.0100	2.0100	2.0100
HA	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
HB	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
C2	CTL1	2.275	2.2750	2.2750	2.2750	2.2750	2.2750
HS	HAL1	1.320	1.3200	1.3200	1.3200	1.3200	1.3200
O21	OSL	1.650	1.6434	1.6132	1.6380	**1.6809**	**1.6809**
C21	CL	2.000	1.9848	1.9804	1.9750	2.0000	2.0000
O22	OBL	1.700	1.6735	1.6686	1.6789	**1.6621**	**1.6470**
C22	CTL2	2.010	2.0100	2.0100	2.0100	2.0100	2.0100
H2R	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
H2S	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
C3	CTL2	2.010	2.0100	2.0100	2.0100	2.0100	2.0100
HX	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400

HY	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
O31	OSL	1.650	1.6434	1.6132	1.6380	**1.6809**	**1.6809**
C31	CL	2.000	1.9848	1.9804	1.9750	2.0000	2.0000
O32	OBL	1.700	1.6735	1.6686	1.6789	**1.6621**	**1.6470**
C32	CTL2	2.010	2.0100	2.0100	2.0100	2.0100	2.0100
H2X	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400
H2Y	HAL2	1.340	1.3400	1.3400	1.3400	1.3400	1.3400

Table S8. Real-space cutoff (R_{cut}) dependence of A_l for DPPC bilayer at 323.15 K. Standard errors shown in parentheses.

R_{cut} (Å)	16	14	12	10	9	8	6
A_l (Å^2)	62.7 (0.3)	62.4 (0.2)	63.0 (0.4)	62.8 (0.3)	62.4 (0.3)	62.6 (0.3)	64.0 (0.3)

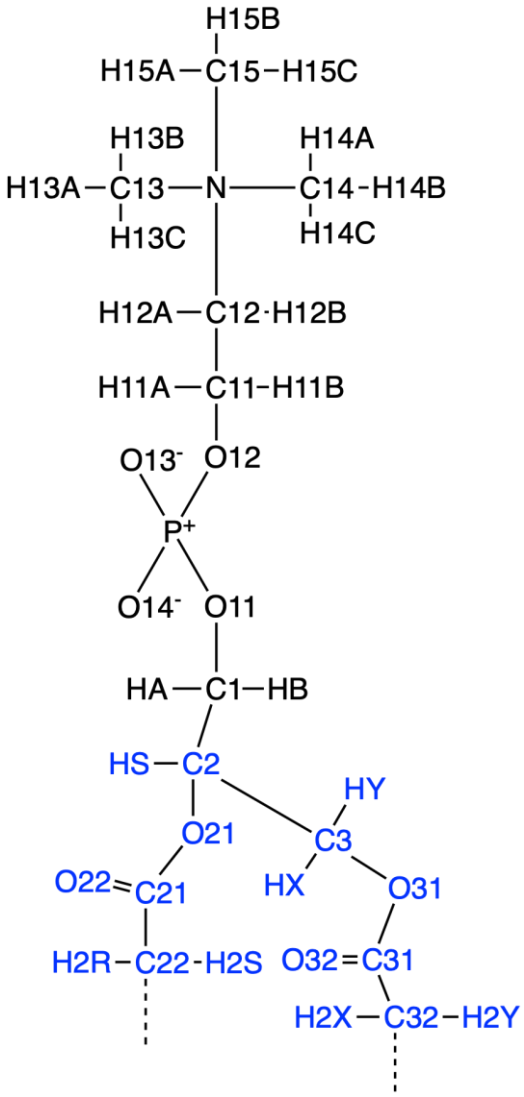


Figure S1. Atom naming of the head group for phosphatidylcholines. The blue part highlights the atoms parametrized in *Linkage*.

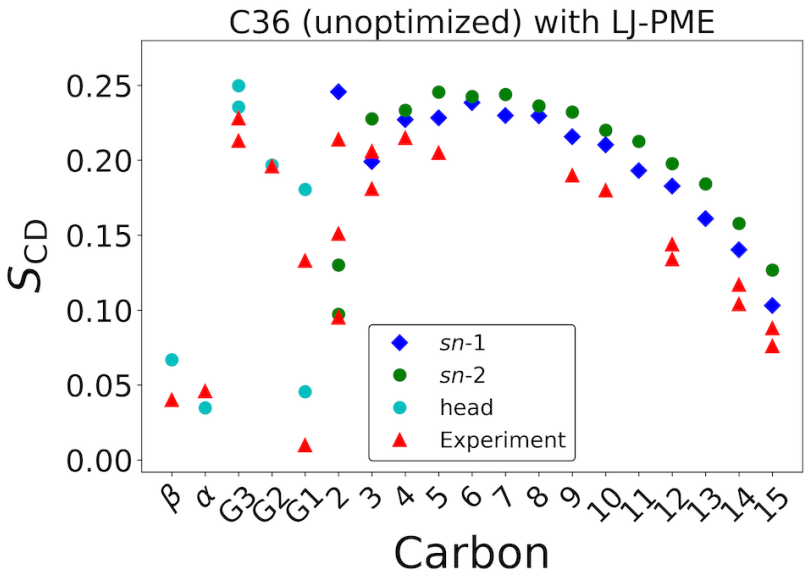
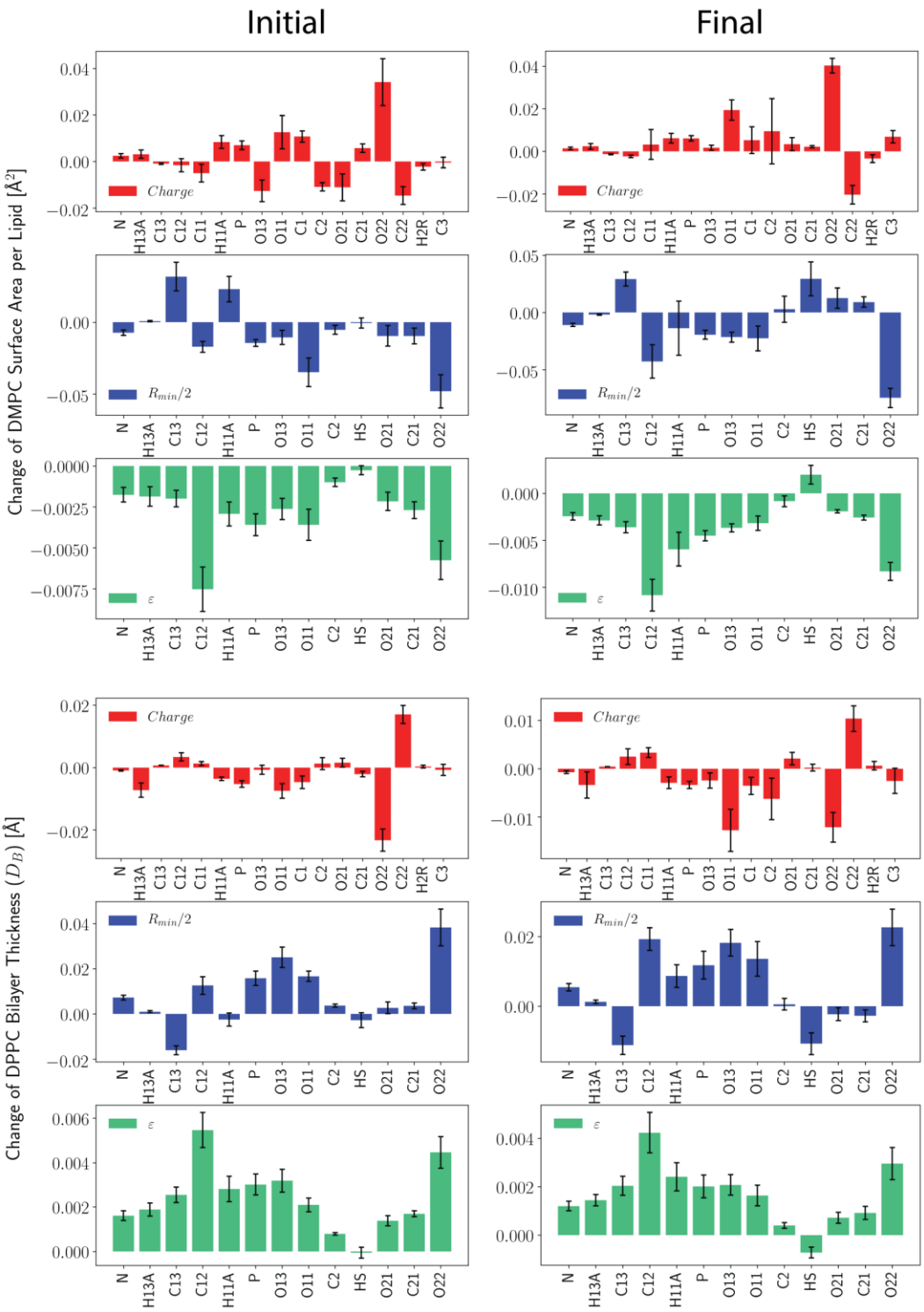


Figure S2. Deuterium order parameters of DPPC bilayer at 323.15 K (unoptimized).


Initial
Final
Change of DMPC Surface Area per Lipid [Å^2]
Change of DPPC Bilayer Thickness (D_B) [Å]
Charge
$R_{min}/2$
ε
N H13A C13 C12 C11 H11A P O13 O11 C1 C2 O21 C21 O22 C22 H2R C3
N H13A C13 C12 H11A P O13 O11 C2 HS O21 C21 O22

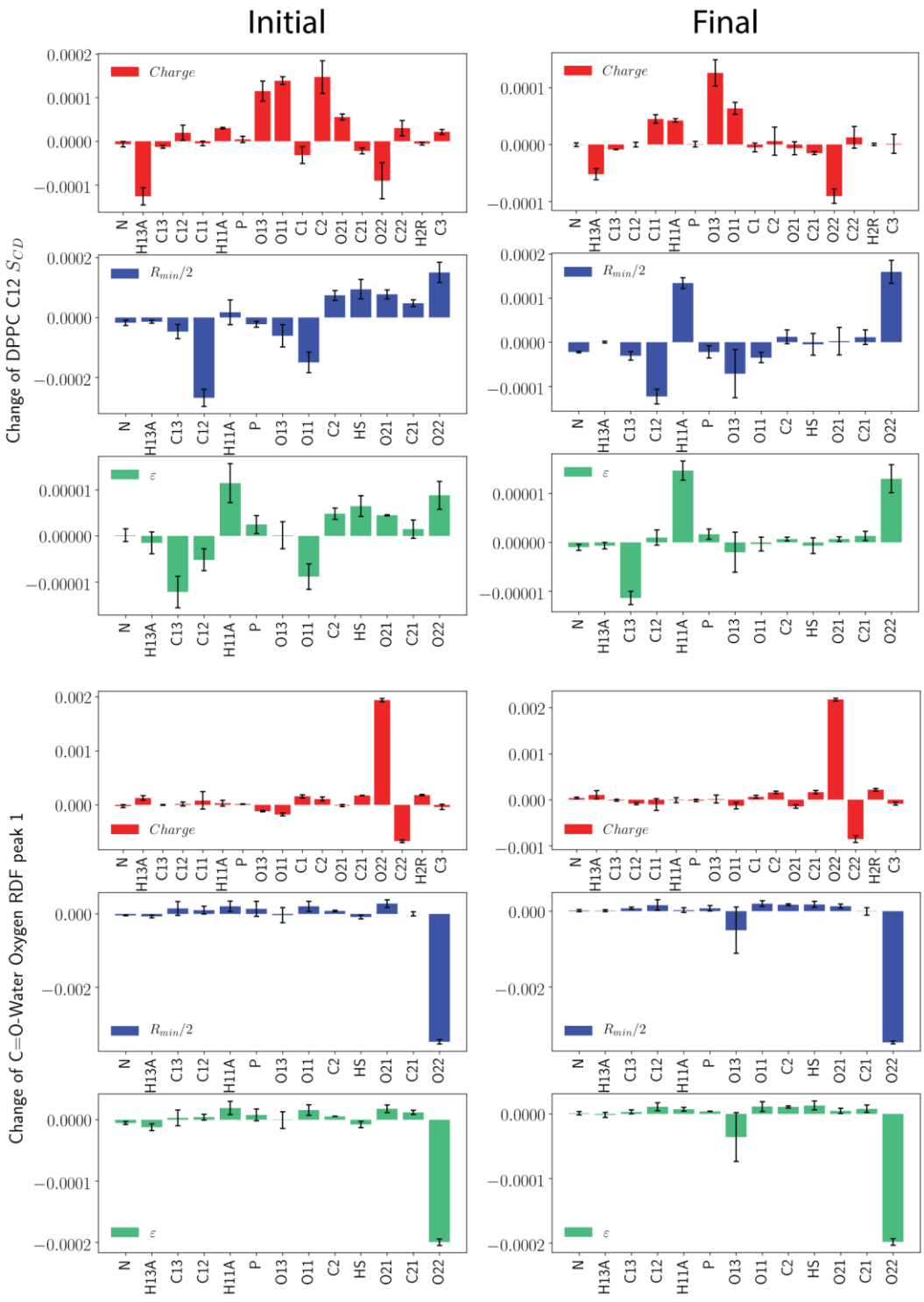


Figure S3. Parameter sensitivities for selected properties from the *Global* optimization. Standard deviations evaluated from trajectory blocks shown in black line with caps. The perturbation sizes used are 0.001 e (absolute value) for partial charge and 0.1% of the original parameter for $R_{min}/2$ and ε.