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Supplementary Material

Explicit-pH Coarse-Grained Molecular Dynamics Simulations Enable Insights into Restructuring of Intestinal Colloidal Aggregates with Permeation Enhancers

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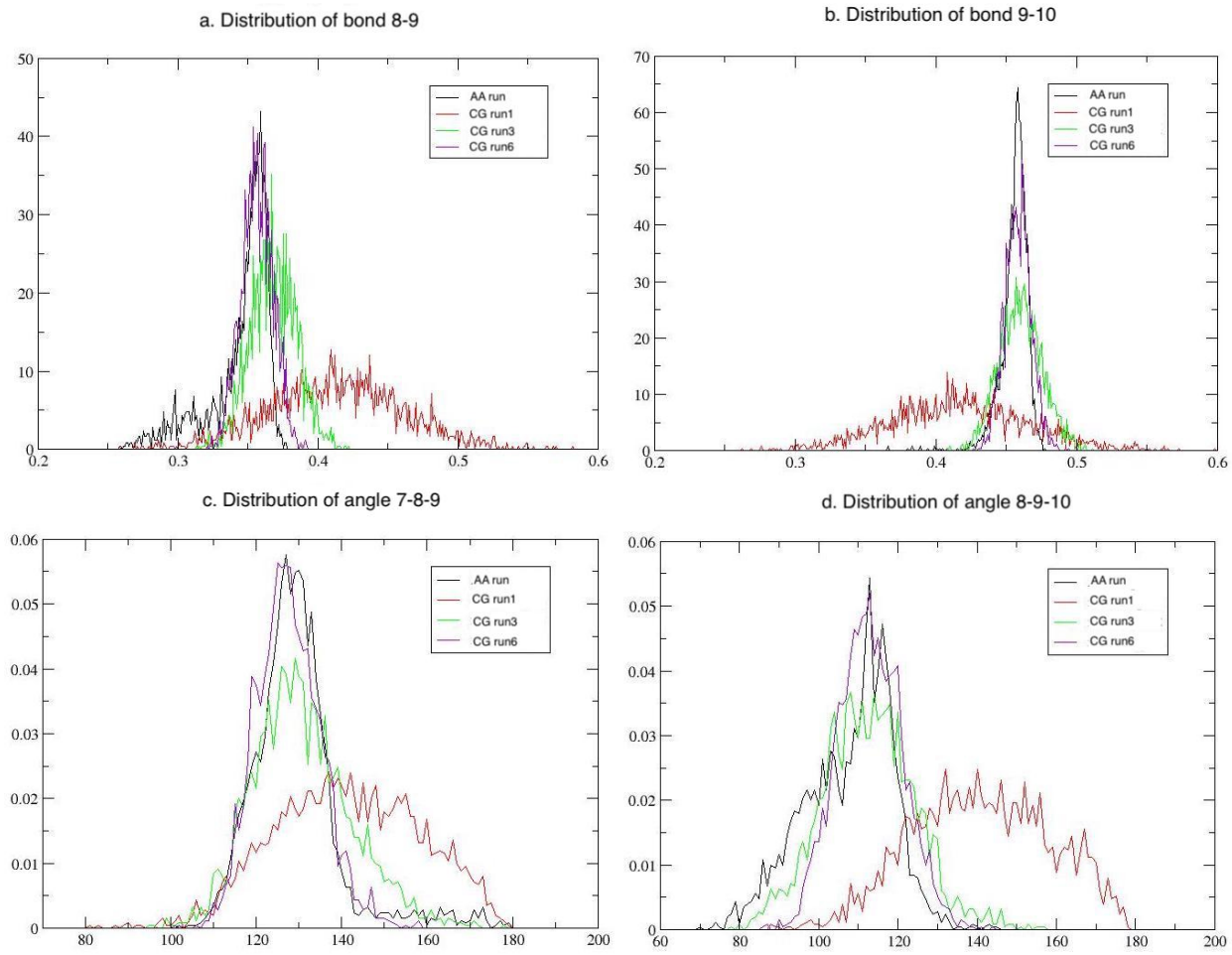

Figure S1. Histograms of AA and CG bond lengths and angles for **a)** bond 8-9, **b)** bond 9-10, **c)** angle 7-8-9, and **d)** angle 8-9-10 for a different CG-optimization runs (1, 3 and 6). Black line is the reference AA distributions, CG run 1 is the red line, CG run 3 is the green line, and CG run 6 is colored in violet in all plots. Figures generated by XMGRACE.

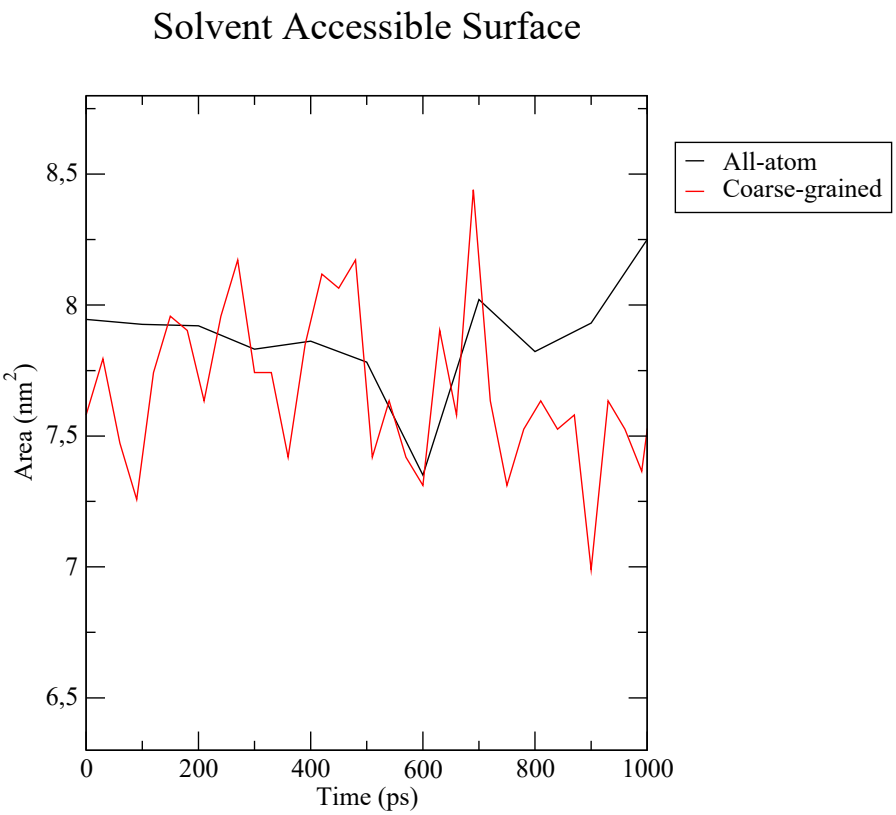

Figure S2. Time-evolution of solvent accessible surface area for the reference all-atom and coarse-grained versions of taurocholate. The coarse-grained simulation was sampled more frequently as part of the parametrization process Figure generated by XMGRACE.

Table S1. Different Non-Bonded Interaction Parameters with Neutral Beads for the taurocholate titratable beads which is defined as SP6_2.0.

Titratable Taurocholate Bead	Neutral Beads	σ	ε
SP6_2.0	C1	0.473	1.28
SP6_2.0	C4	0.430	1.93
SP6_2.0	C4h	0.430	1.93
SP6_2.0	X2	0.430	2.32
SP6_2.0	N4a	0.430	2.92
SP6_2.0	SN4a	0.410	2.35
SP6_2.0	SC3	0.418	1.40
SP6_2.0	SC2	0.418	1.40
SP6_2.0	SX2	0.410	1.91
SP6_2.0	TN3d	0.365	1.75
SP6_2.0	TC5	0.394	1.29
SP6_2.0	TC4	0.404	1.13
SP6_2.0	TC2	0.409	1.08
SP6_2.0	SC6	0.410	1.91
SP6_2.0	SC5	0.410	1.75
SP6_2.0	P3	0.430	3.97
SP6_2.0	SN6	0.410	2.84
SP6_2.0	SP1	0.410	3.55
SP6_2.0	SP3	0.410	3.55

Table S2. pH dependent interaction parameters with water for the taurocholate titratable bead SP6_2.0.

pH	Titratable taurocholate bead	Water bead	σ	ε
3.00	SP6_2.0	WNT	0.425	1.00
3.25	SP6_2.0	WNT	0.425	3.25
3.50	SP6_2.0	WNT	0.425	4.50
4.00	SP6_2.0	WNT	0.425	5.75
4.25	SP6_2.0	WNT	0.425	7.00
4.50	SP6_2.0	WNT	0.425	10.00
4.75	SP6_2.0	WNT	0.425	13.00
5.00	SP6_2.0	WNT	0.425	16.00
5.25	SP6_2.0	WNT	0.425	19.00
5.50	SP6_2.0	WNT	0.425	21.00
5.75	SP6_2.0	WNT	0.425	22.00
6.00	SP6_2.0	WNT	0.425	23.00
6.25	SP6_2.0	WNT	0.425	23.00
6.75	SP6_2.0	WNT	0.425	23.00
7.00	SP6_2.0	WNT	0.425	23.00
7.25	SP6_2.0	WNT	0.425	23.00
7.50	SP6_2.0	WNT	0.425	23.00
7.75	SP6_2.0	WNT	0.425	23.00
8.00	SP6_2.0	WNT	0.425	23.00

Table S3. Other interaction parameters for the taurocholate titratable bead SP6_2.0

Interaction Parameters with Proton of the Titratable Model			
Titratable Taurocholate Bead	**Proton Beads**	σ	ε
SP6_2.0	POS	0.295	1.00
Self-Interaction Parameters			
Titratable Taurocholate Bead	**Proton Beads**	σ	ε
SP6_2.0	SP6_2.0	0.410	1.00
Non-Bonded Interaction Parameters with Charged Beads			
Titratable Taurocholate Bead	**Charged Beads**	σ	ε
SP6_2.0	Q1p	0.430	2.40
SP6_2.0	Q5n	0.430	2.80
Non-Bonded Interaction Parameters With Another Titratable Bead			
Titratable Taurocholate Bead	**Titratable Acid Beads**	σ	ε
SP6_2.0	P2_4.8	0.430	1.00

Table S4. List of the simulated systems and the number of the all the molecules inserted into the simulation box.

System Number	Description	Number of Different Molecules used in the Simulations
1	FaSSIF with 20 mM caprate at pH 3	Water—129408, taurocholate—28, DLiPC—7, caprate—188, sodium ion—216
2	FaSSIF with 20 mM caprate at pH 5	
3	FaSSIF with 20 mM caprate at pH 8	
4	FeSSIF with 20 mM caprate at pH 3	Water—129408, taurocholate—141, DLiPC—35, caprate—188, sodium ion—329
5	FeSSIF with 20 mM caprate at pH 5	
6	FeSSIF with 20 mM caprate at pH 8	
7	FaSSIF with 20 mM SNAC at pH 3	Water—129408, taurocholate—28, DLiPC—7, SNAC—188, sodium ion—216
8	FaSSIF with 20 mM SNAC at pH 5	
9	FaSSIF with 20 mM SNAC at pH 8	
10	FeSSIF with 20 mM SNAC at pH 3	Water—129408, taurocholate—141, DLiPC—35, SNAC—188, sodium ion—329
11	FeSSIF with 20 mM SNAC at pH 5	
12	FeSSIF with 20 mM SNAC at pH 8	
13	FaSSIF with 100 mM caprate at pH 3	Water—129408, taurocholate—28, DLiPC—7, caprate—940, sodium ion—968
14	FaSSIF with 100 mM caprate at pH 5	
15	FaSSIF with 100 mM caprate at pH 8	
16	FeSSIF with 100 mM caprate at pH 3	Water—129408, taurocholate—141, DLiPC—35, caprate—940, sodium ion—1081
17	FeSSIF with 100 mM caprate at pH 5	
18	FeSSIF with 100 mM caprate at pH 8	
19	FaSSIF with 100 mM SNAC at pH 3	Water—129408, taurocholate—28, DLiPC—7, SNAC—940, sodium ion—968
20	FaSSIF with 100 mM SNAC at pH 5	
21	FaSSIF with 100 mM SNAC at pH 8	
22	FeSSIF with 100 mM SNAC at pH 3	Water—129408, taurocholate—141, DLiPC—35, SNAC—940, sodium ion—1081
23	FeSSIF with 100 mM SNAC at pH 5	
24	FeSSIF with 100 mM SNAC at pH 8	