Electronic Supplementary Material (ESI) for Nanoscale.

Supporting Information for

Computational investigation on lipid bilayer disruption induced by amphiphilic Janus nanoparticles: combined effect of Janus balance and charged lipid concentration

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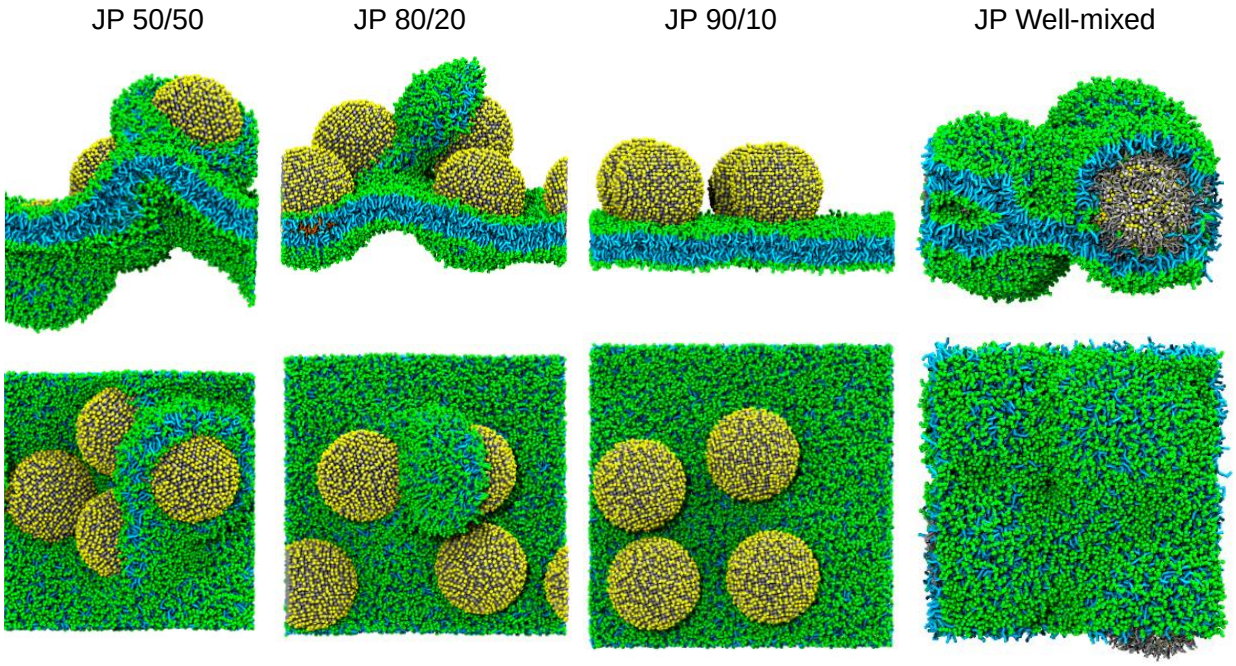

Fig. S1 Multiple Janis NPs with different Janus NP's hydrophobicity interacting with pure DOPC membrane. Membrane's dimension is $35 \times 35 \times 36$ nm^3. The Janus NP diameter is 10 nm. Solvent molecules are included in simulation but are not shown here for clarity.

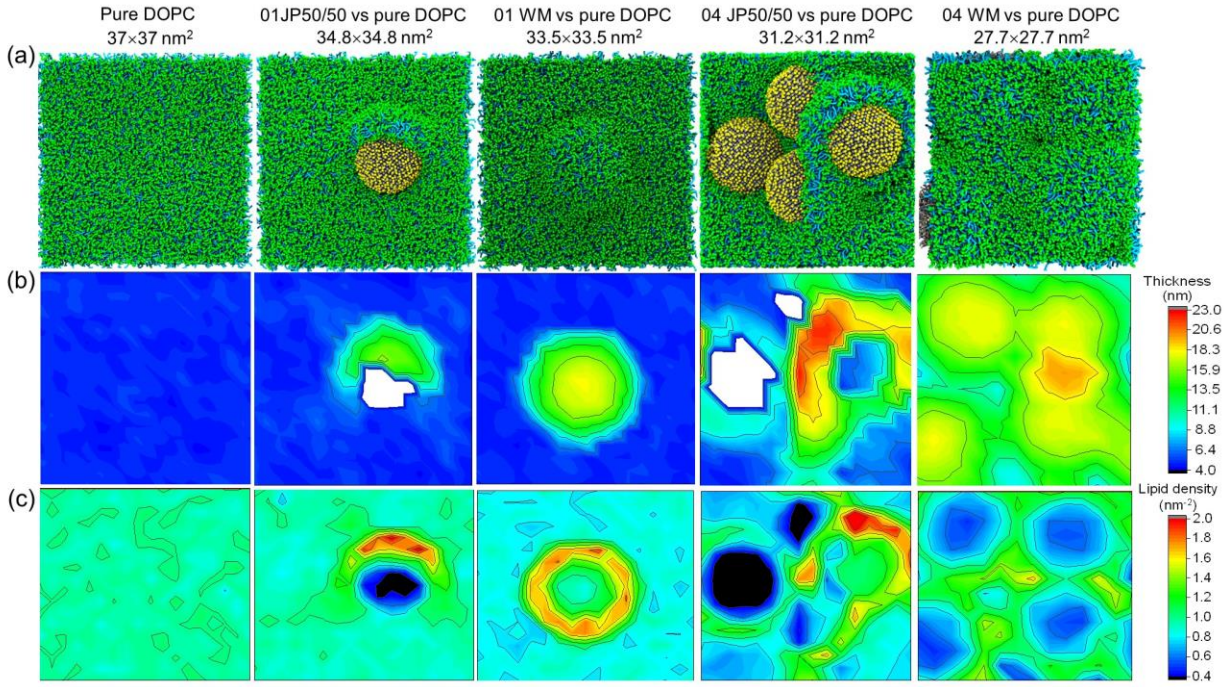

Fig. S2 Comparing membrane disruption ability of JP 50/50 and WM. (a) MD simulation snapshots (top view) of NPs-membrane interactions. From left to right: pure DOPC membrane without NPs, pure DOPC membrane interacting with single JP 50/50 at 200 ns, with single WM NP at 200 ns, with four JP 50/50 at 500 ns and with four WM NPs at 500 ns. (b) Lipid bilayer thickness corresponds to the MD snapshots in (a). The white regions in cases of single JP 50/50 and four JP 50/50 indicating membrane defects (either no lipid heads in top leaflet or bottom leaflet). (c) Lipid density corresponds to the MD snapshots in (a).

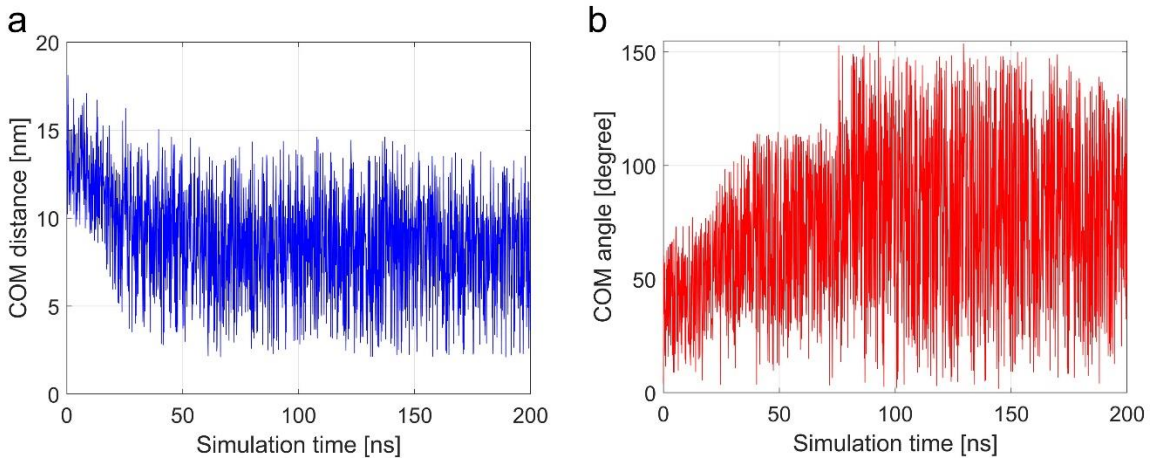

Fig. S3 Collective variables spanning space including (a) COM distance and (b) COM angle during the metadynamics simulation for JP50/50 interacting with DOPC100 membrane.

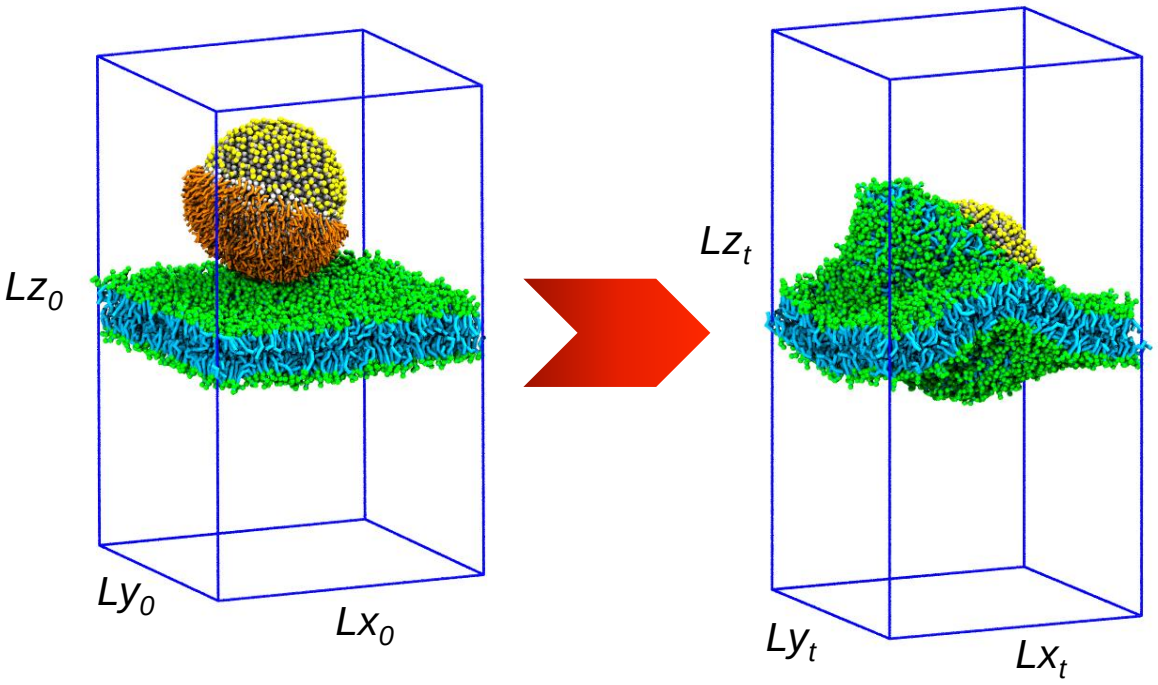

Fig. S4 Calculation of reduction in membrane projection area induced by Janus NPs. Lx_0, Ly_0 and Lz_0 are dimensions of the initial simulation box in *x*, *y* and *z* directions, respectively. Similarly, Lx_t, Ly_t and Lz_t are dimensions of the simulation box in x, y and z directions at time *t*, respectively. The area reduction is calculated as $\frac{A_t - A_0}{A_0} \times 100\%$, where $A_0 = Lx_0 \times Ly_0$ is the initial membrane area and $A_t = Lx_t \times Ly_t$ is the membrane area at time *t*. Initial membrane dimension is ~22 × 22 nm^2. The Janus NP diameter is 10 nm. Solvent molecules are included in simulation but are not shown here for clarity.

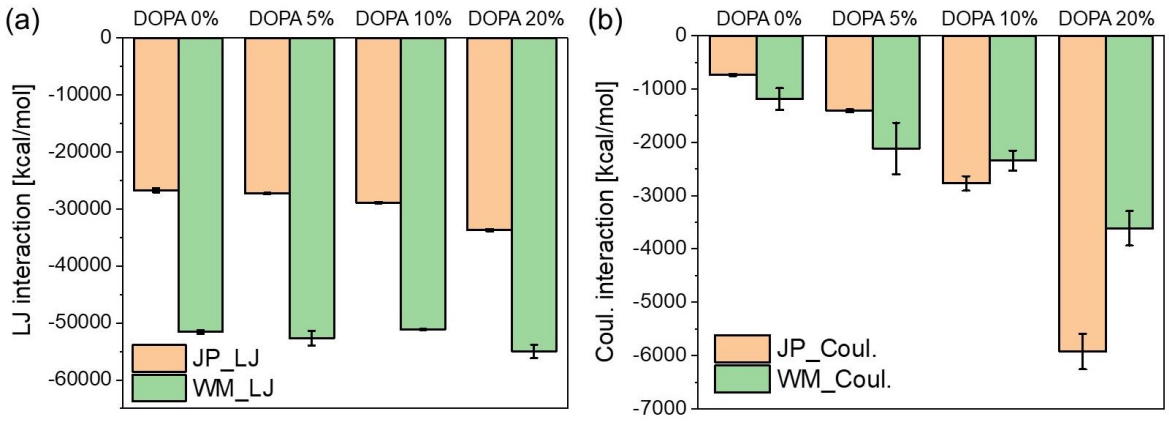

Fig. S5 Comparing interaction with DOPA membranes between JP 50/50 and WM NP after 200 ns. (a) Average hydrophobic (LJ) and (b) electrostatic (Coulomb) interaction energy as a function of DOPA concentration from 0 to 20% molar concentration.

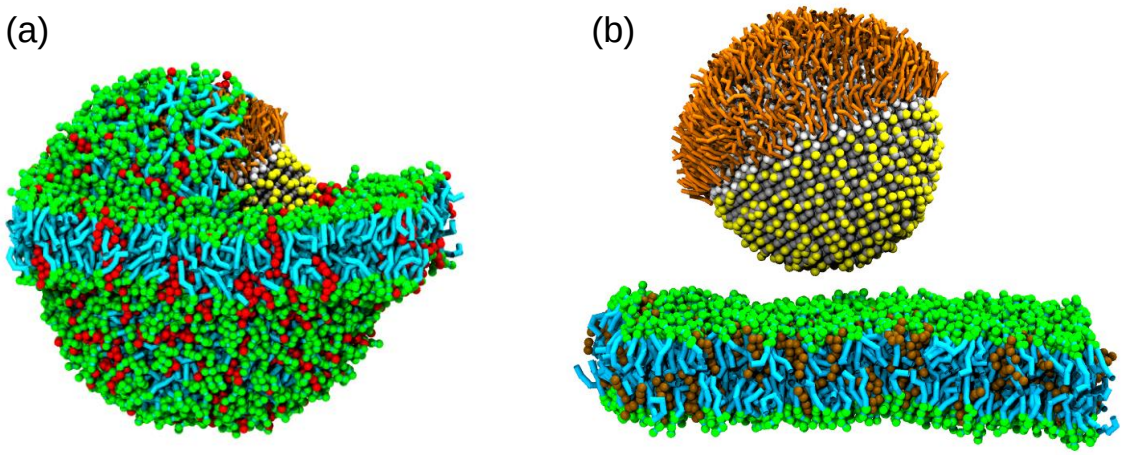

Fig. S6 Positive hemisphere facing the membranes. (a) Negatively charged membrane (20% DOPA); (b) Positively charged membrane (20% DOTAP) after 100 ns MD simulations.

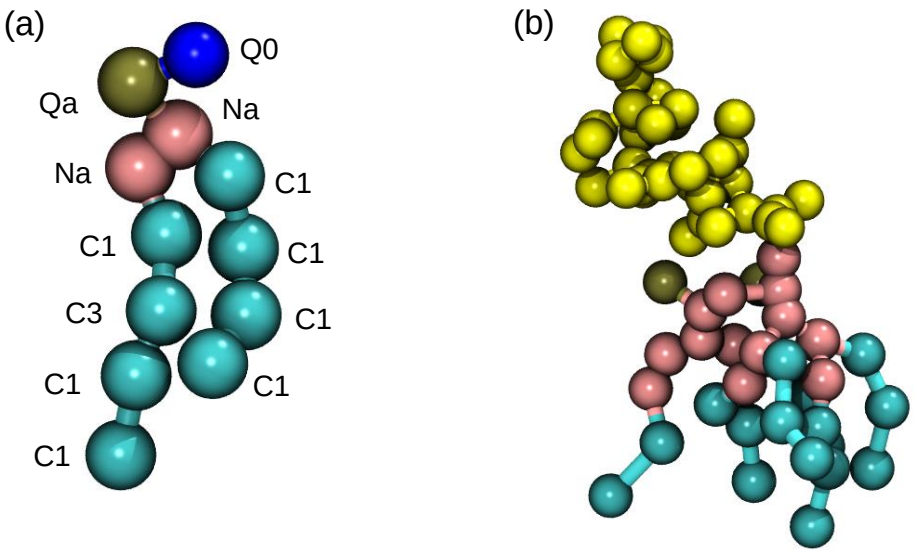

Fig. S7 Coarse-grained representation for (a) POPC and (b) LPS. Details of LPS beads are in **Table S1**. For LPS, hydrocarbon tails are cyan, the lipid A head group is pink, phosphate groups are brown, and the remaining outer and inner core saccharides are yellow.

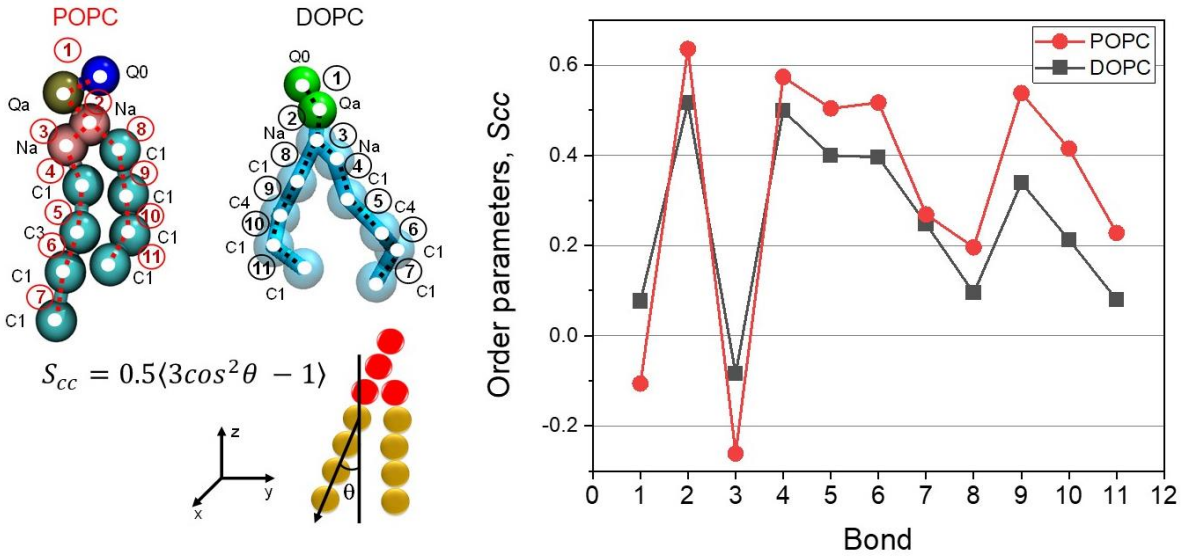

Fig. S8 Average order parameters of the main lipids in LPS/POPC membrane (POPC) and DOPC lipids in pure DOPC membrane where POPC lipids show higher order parameters for the hydrophobic tails compared to that of DOPC lipids in the pure DOPC membrane.

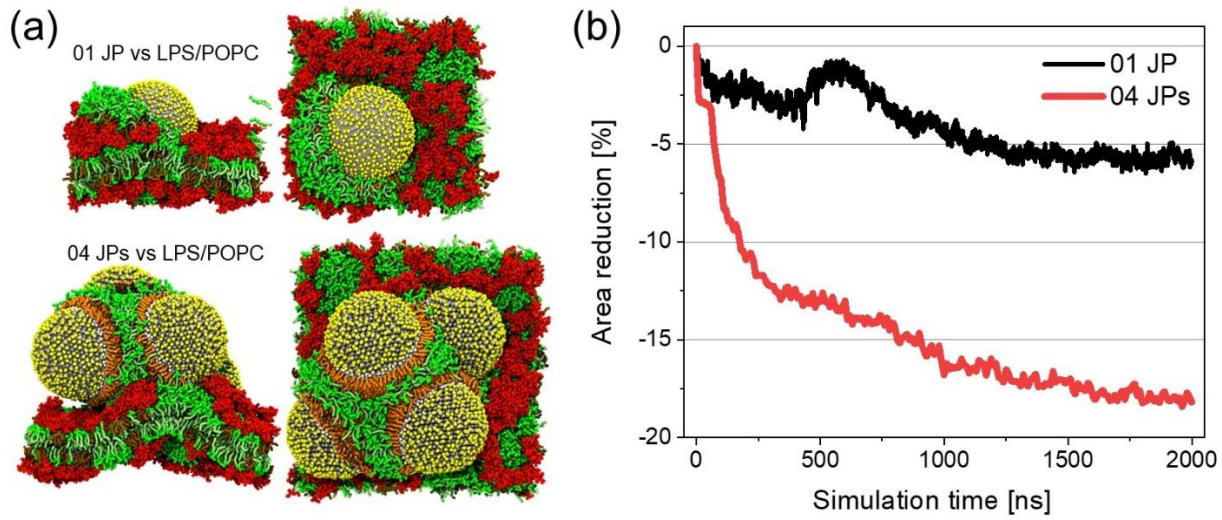

Fig. S9 Comparing single JP with multiple JPs effect on LPS/POPC membrane disruptions. (a) Snapshots of MD simulations of 01 JP 50/50 and 04 JP 50/50 NPs interacting with 20% LPS/POPC membrane after 2 μs. (b) Membrane area reduction induced by 01 JP 50/50 and 04 JP 50/50 NPs over the course of simulations. The membrane dimensions are 23 × 23 nm^2 and 30 × 30 nm^2 for interacting with 01 and 04 JP 50/50 NPs, respectively. Solvent molecules are included in the simulation but are not shown here for clarity.

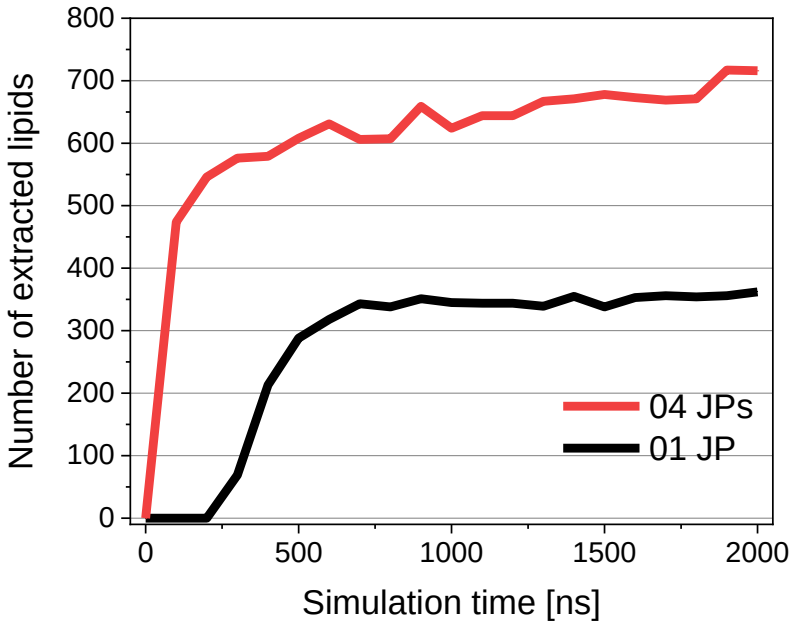

Fig. S10 Number of extracted lipids induced by 01 and 04 JP 50/50 NPs over the course of simulations.

Table S1 CG beads of LPS from CHARM-GUI.

No.	Bead type	Bead name	Bead charge
1	Qa	PO1	-2
2	P2	GM1	0
3	Nda	GM2	0
4	P1	GM3	0
5	P2	GM4	0
6	P1	GM5	0
7	Nda	GM6	0
8	Qa	PO2	-2
9	Na	GL1	0
10	Na	GL2	0
11	C1	C1A	0
12	C1	C2A	0
13	C1	C3A	0
14	C1	C1B	0
15	C1	C2B	0
16	C1	C3B	0
17	Na	GL3	0
18	Na	GL4	0
19	C1	C1C	0
20	C1	C2C	0
21	C1	C3C	0
22	C1	C1D	0
23	C1	C2D	0
24	C1	C3D	0
25	Na	GL5	0
26	Nda	GL6	0
27	C1	C1E	0
28	C1	C2E	0

29	Na	GL7	0
30	Nda	GL8	0
31	C1	C1F	0
32	C1	C2F	0
33	Qa	S01	-1
34	SC1	S02	0
35	SN0	S03	0
36	P2	S04	0
37	P4	S05	0
38	SC1	S06	0
39	P2	S07	0
40	SN0	S08	0
41	P4	S09	0
42	Qa	S10	-1
43	SP1	S11	0
44	SN0	S12	0
45	P1	S13	0
46	P4	S14	0
47	Qa	S15	-2
48	SP1	S16	0
49	SN0	S17	0
50	P2	S18	0
51	Qa	S19	-2
52	SN0	S20	0
53	SC1	S21	0
54	SN0	S22	0
55	P2	S23	0
56	P4	S24	0
57	SP1	S25	0
58	P1	S26	0

59	P4	S27	0
60	SP1	S28	0
61	P1	S29	0
62	P4	S30	0
63	SP1	S31	0
64	P4	S32	0
65	P1	S33	0
66	SP1	S34	0
67	P1	S35	0
68	P4	S36	0
69	SP1	S37	0
70	P1	S38	0
71	P4	S39	0