

SUPPORTING INFORMATION

“The membrane protein LeuT in micellar systems: Aggregation dynamics and detergent binding to the S2 site”

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SUPPLEMENTAL TABLES:

Table S1:

Number of detergent molecules (N_{DDM}), volumes, and molar concentrations ^a of the detergent in the simulated systems

SIMULATIONS	N_{DDM}	Volume, \AA^3	Molarity, M
246/54	300	5×10^6	0.10
120/174	294	4×10^6	0.12
160/115	275	5×10^6	0.10
246/0	246	3×10^6	0.14
120/115	235	4.7×10^6	0.09
120/41	161	3.5×10^6	0.08
160/0 I	160	3×10^6	0.09
160/0 II	160	3×10^6	0.09

^a – Note that general caution needs to be taken to compare the concentration numbers determined from the simulations and those obtained for the experimental constructs as the simulated and experimental system volumes usually differ substantially.

SUPPLEMENTAL FIGURE CAPTIONS:

Figure S1: Time evolution (after initial equilibration phase) of the number of DDM molecules within 3 Å (*upper panel*) and 5 Å (*lower panel*) of LeuT in different simulations (compare to Figure 3 in the main text).

Figure S2: Time evolution (after initial equilibration phase) of the average number of DDM molecules in the detergent micelle around LeuT (*DM*), in the aggregates bound to *DM* (*BA* and *BM*), and together in *DM*, *BA*, and *BM* from 120/174 (*top*), 120/115 (*middle*), and 120/41 (*bottom*) simulations. For definitions of the various types of aggregates please see Methods in the main text.

Figure S3: Percentage of DDM detergents in *DM*, *BA*, and *BM* (blue line), in *FA* (red line), and in *FM* (black line) as a function of time in 120/174 (*top*), 120/115 (*middle*), and 120/41 (*bottom*) simulations. For definitions of the various types of aggregates please see Methods in the main text.

Figure S4: When DDM molecule penetrates LeuT “from the side”, it establishes first contacts with the transporter through residues located at the extracellular (EC) side of TMH6, and TMH11, before inserting deeper into the S2 site of LeuT. Time evolution (after initial equilibration phase) of the distance between C_α atoms of Phe405 (*black*), Pro241 (*red*), Trp467 (*green*), Val466 (*blue*) residues on LeuT and the center-of-mass of the head group of the penetrating detergent molecule. The profiles were obtained from the 160/115 simulation.

Figure S5: DDM penetration into LeuT “from the top” involves encounters with residues in EC loops 3 and 4 before the detergent takes its final position in the S2 site of the transporter. Time evolution (after initial equilibration phase) of the distance between C_α atom of Glu236 in ECL3 and the center-of-mass of DDM detergent head-group (*black line*), and between C_α atom of Ile314 in ECL4 and DDM hydrocarbon tail (*red line*). The profiles were plotted from the 246/54 simulation.

Figure S6: Characterization of micelle shape by the eccentricity parameter, as a function of time for selected simulations (see Methods in the main text for the eccentricity definition).

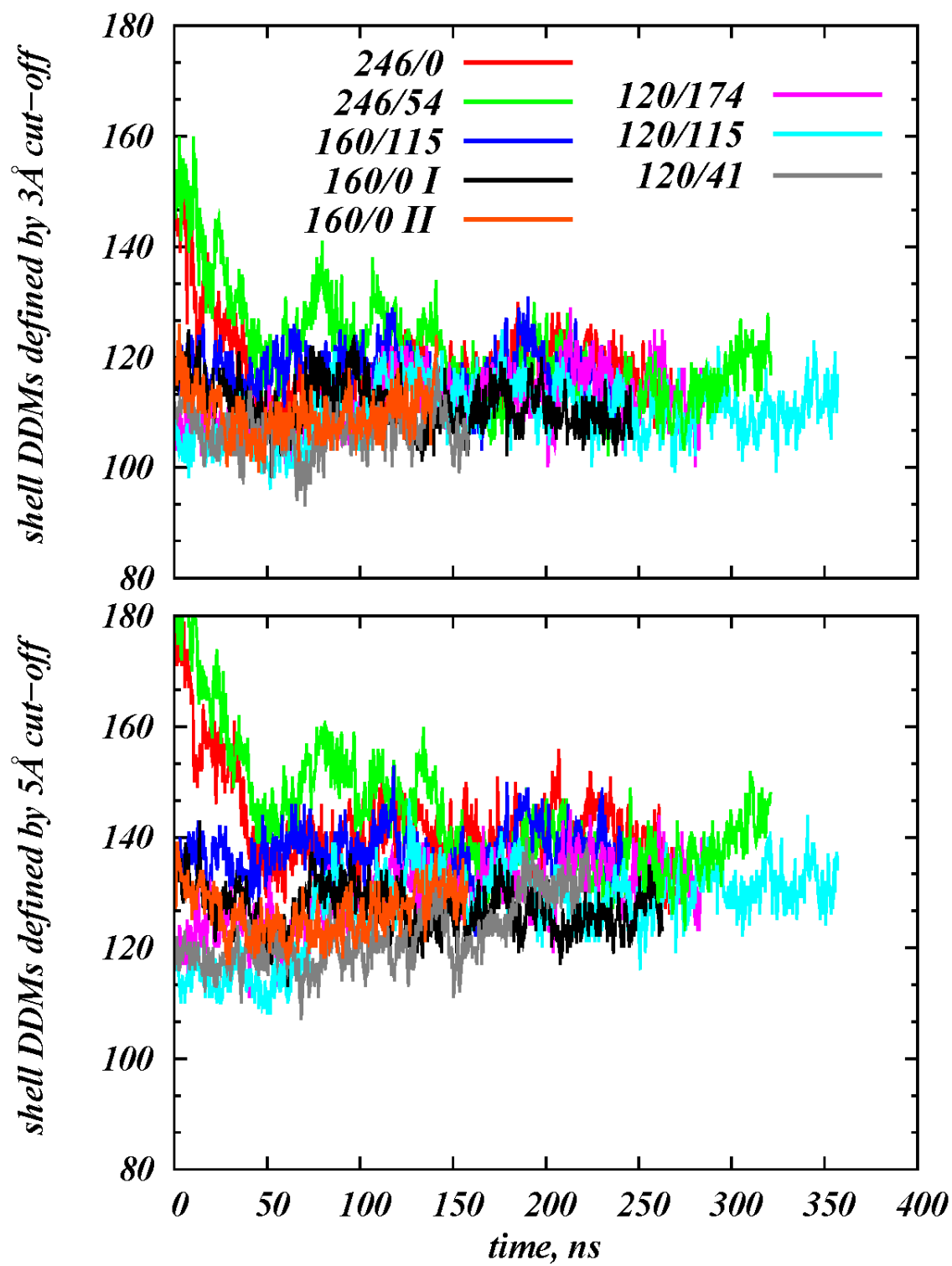


Figure S1

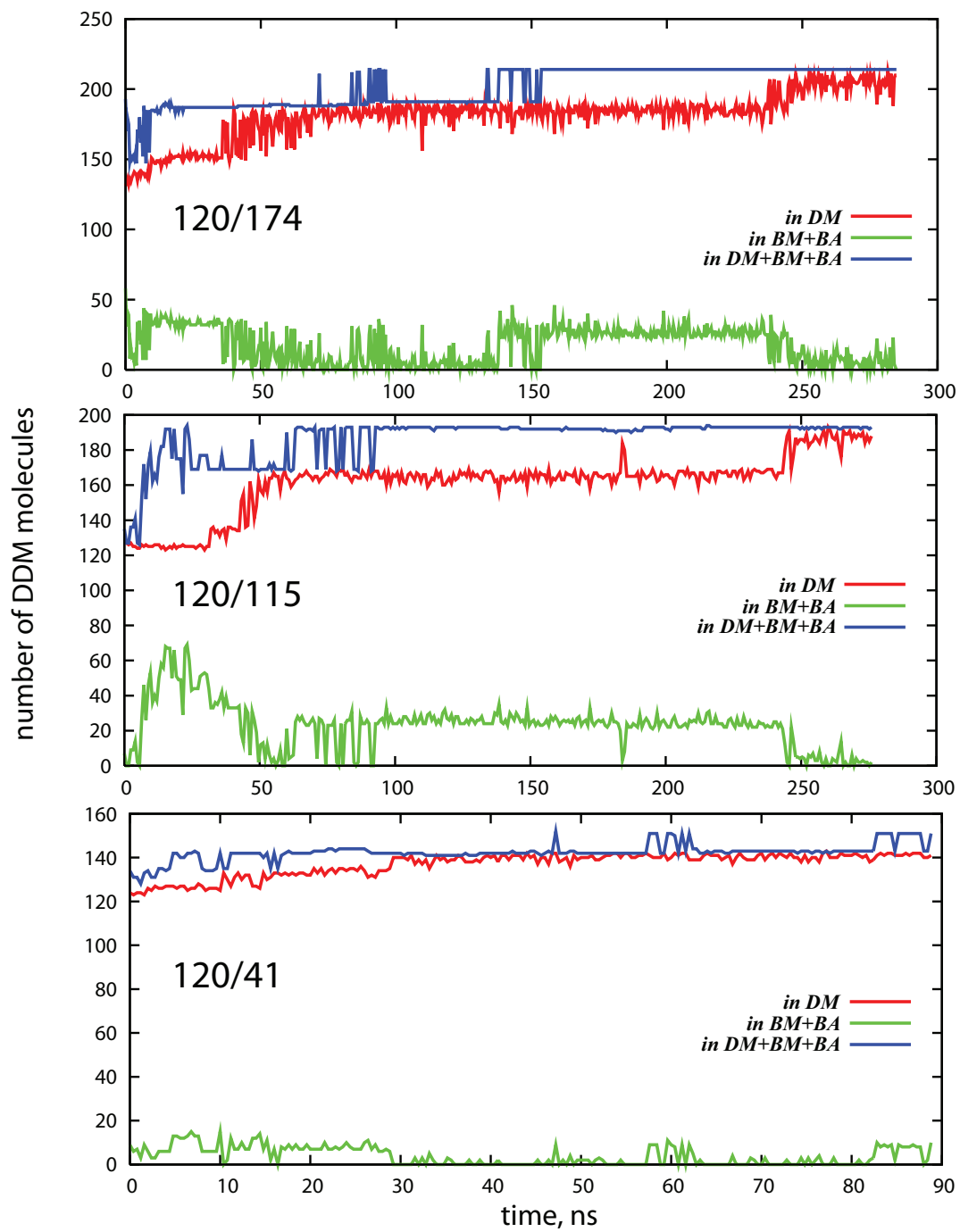


Figure S2

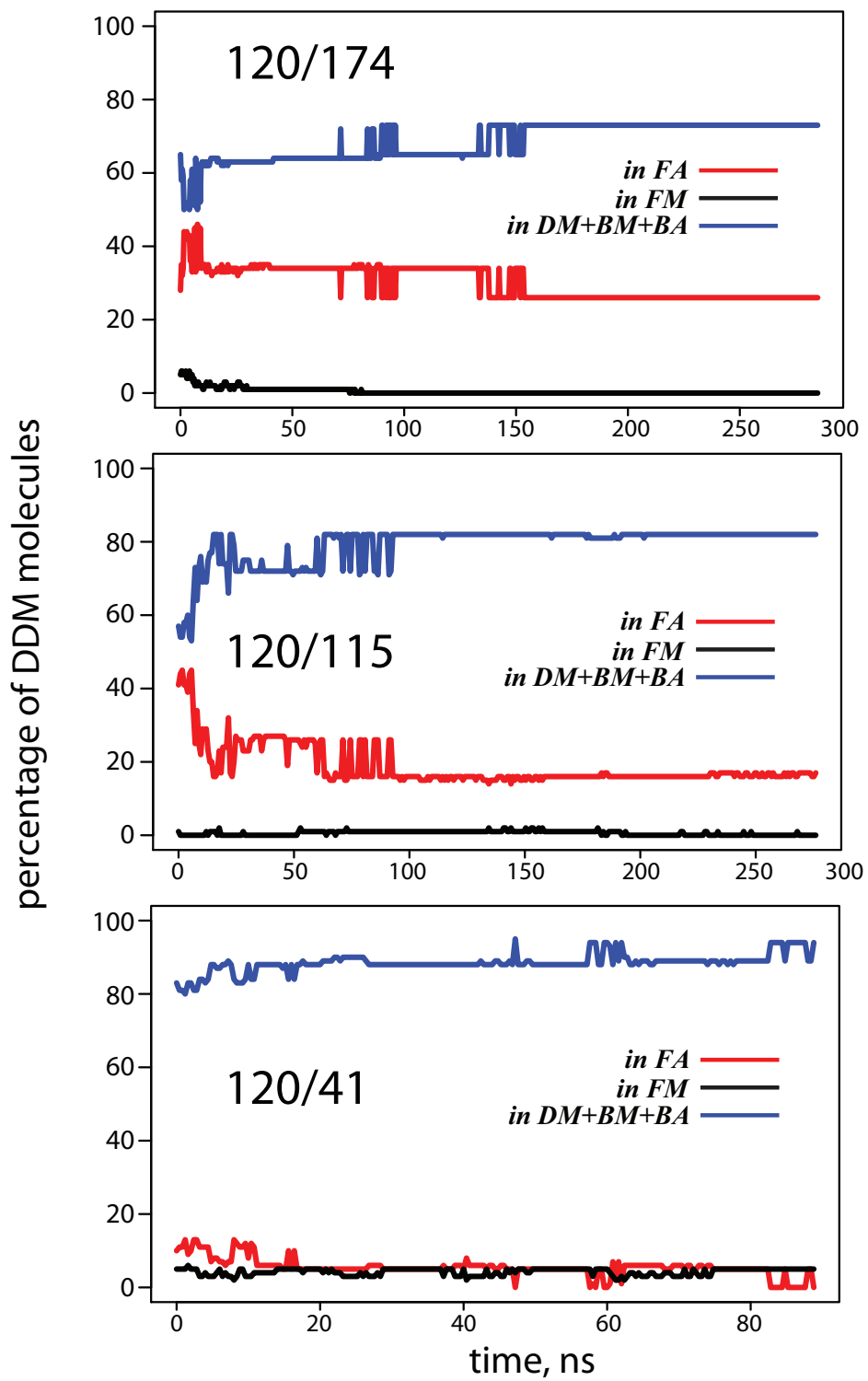


Figure S3

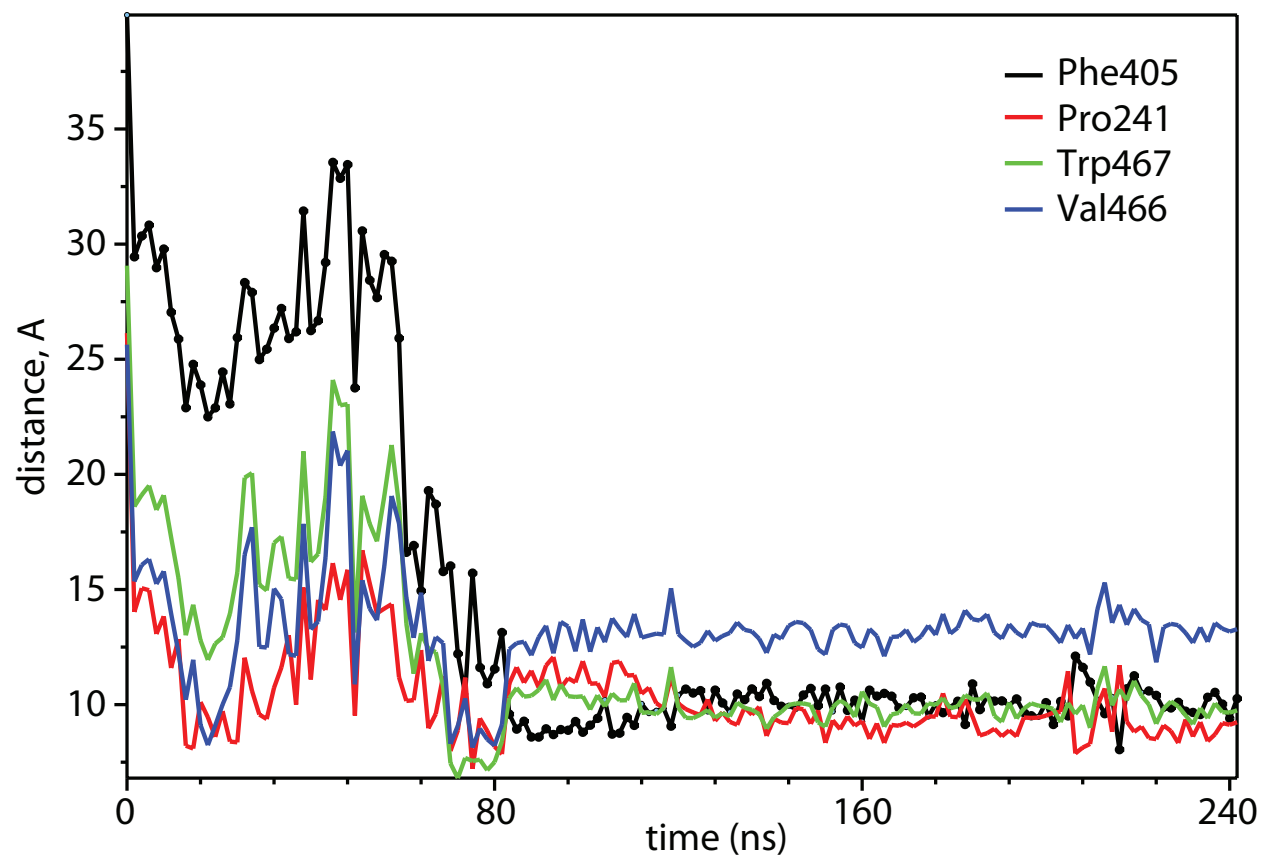


Figure S4

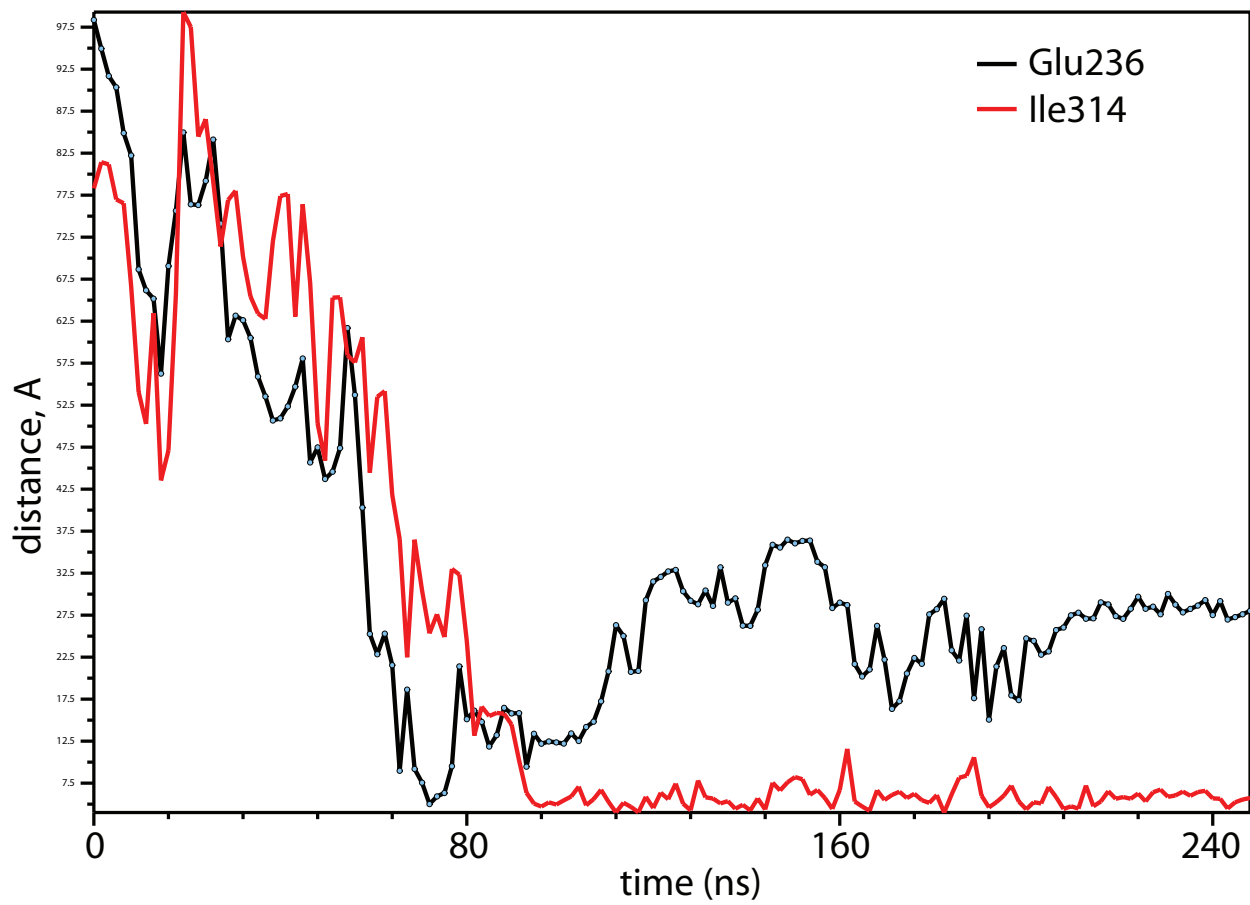


Figure S5

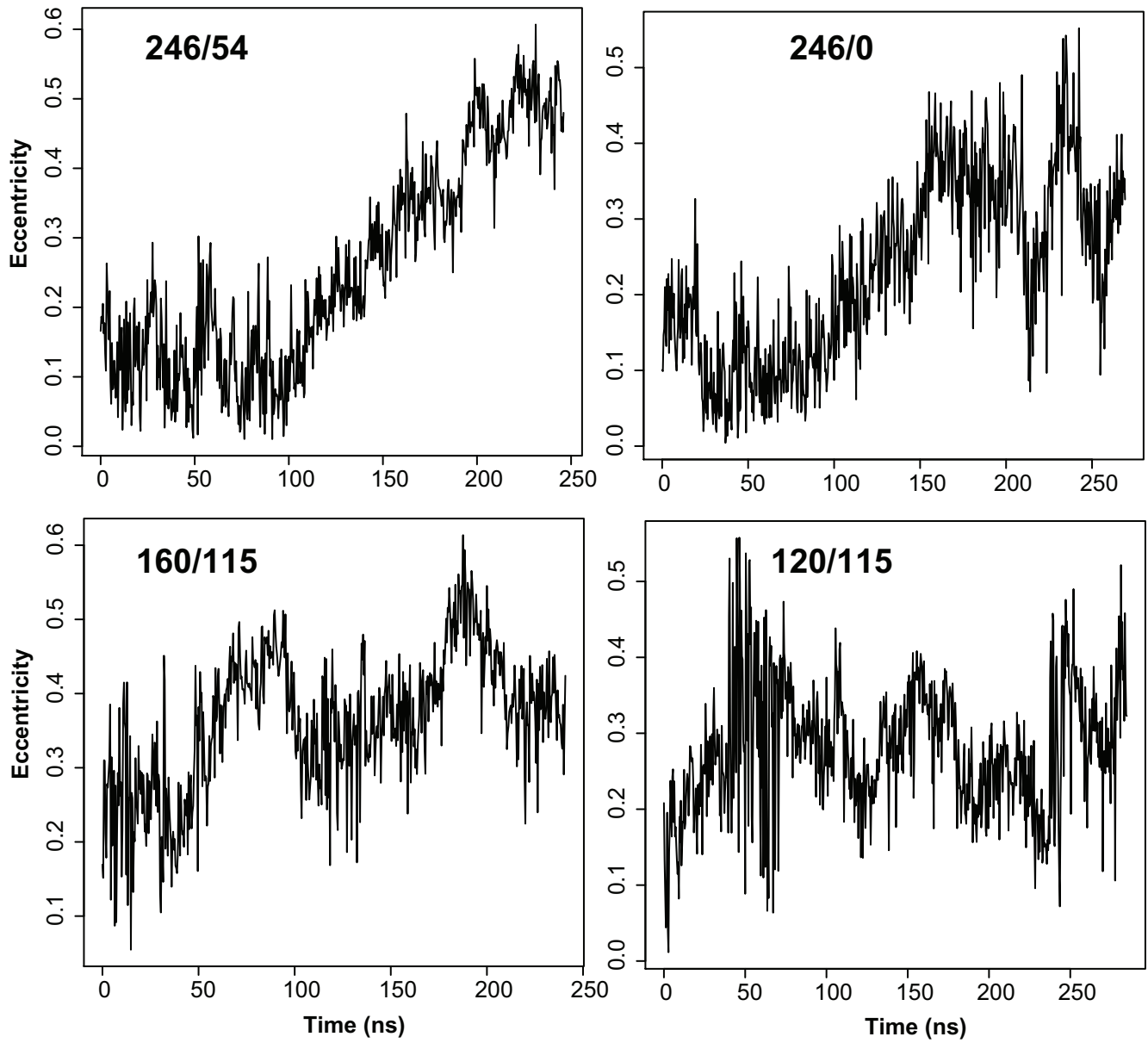


Figure S6