Supplemental for "Dynamics of Lipids, Cholesterol, and Transmembrane α-Helices from Microsecond Molecular Dynamics Simulations"

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Table 1: Rotational diffusion coefficients (10^{-2} rad^2/ns)

system		**WT1**	**WT2**	**R694L**
protein		0.04	0.02	0.01
DPPC	UL	0.98	0.31	0.19
	LL	0.73	0.17	0.087
cholesterol	UL	24.4	12.8	1.44
	LL	22.0	11.1	6.91
temperature (K)		306.7 $\pm$1.22	302.6 $\pm$1.22	302.2 $\pm$1.24

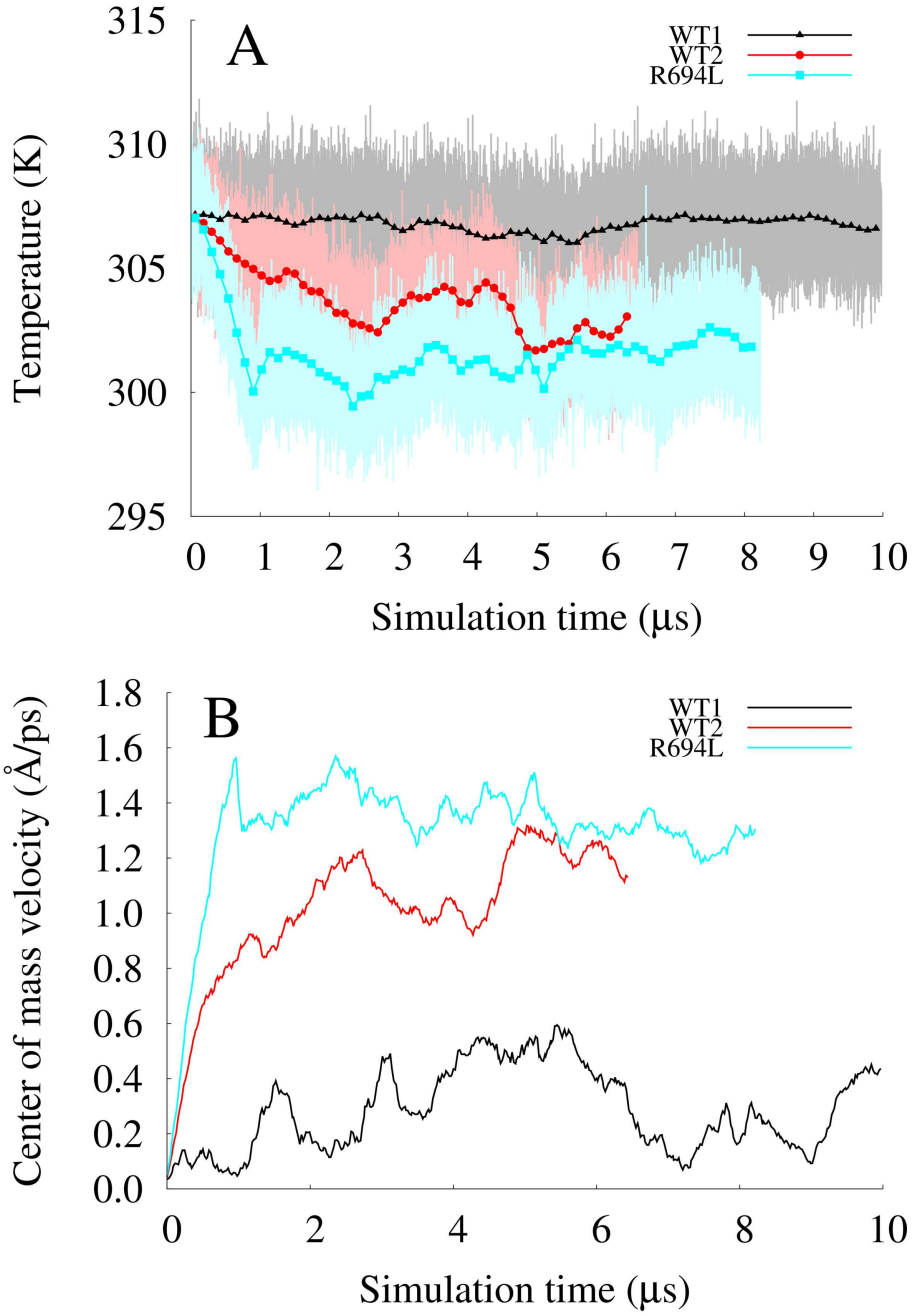

Figure 1: (A) Simulation temperature (K) over time for WT1, WT2, and R694L. (B) System center of mass velocity over time.

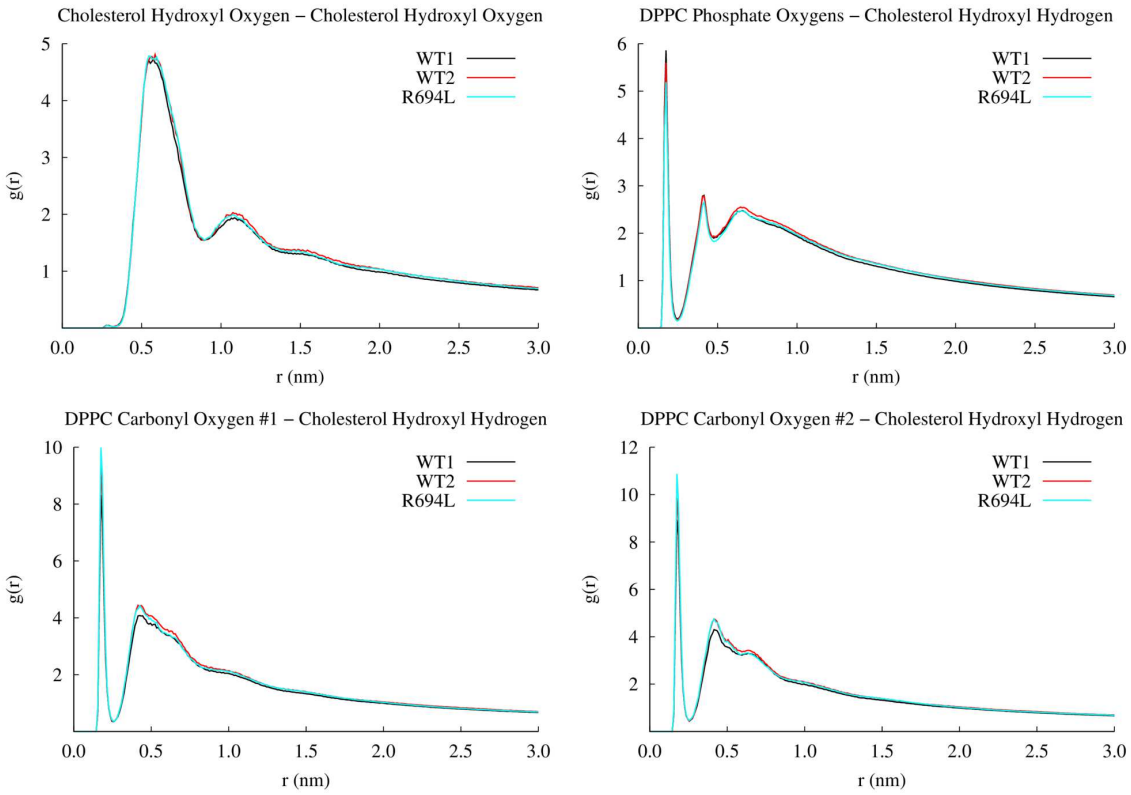

Figure 2: Radial distribution function for cholesterol hydroxyl oxygen with respect to itself and cholesterol hydroxyl hydrogen with respect to either the lipid phosphate oxygen atoms or the lipid carbonyl oxygen atoms for WT1, WT2, and R694L.

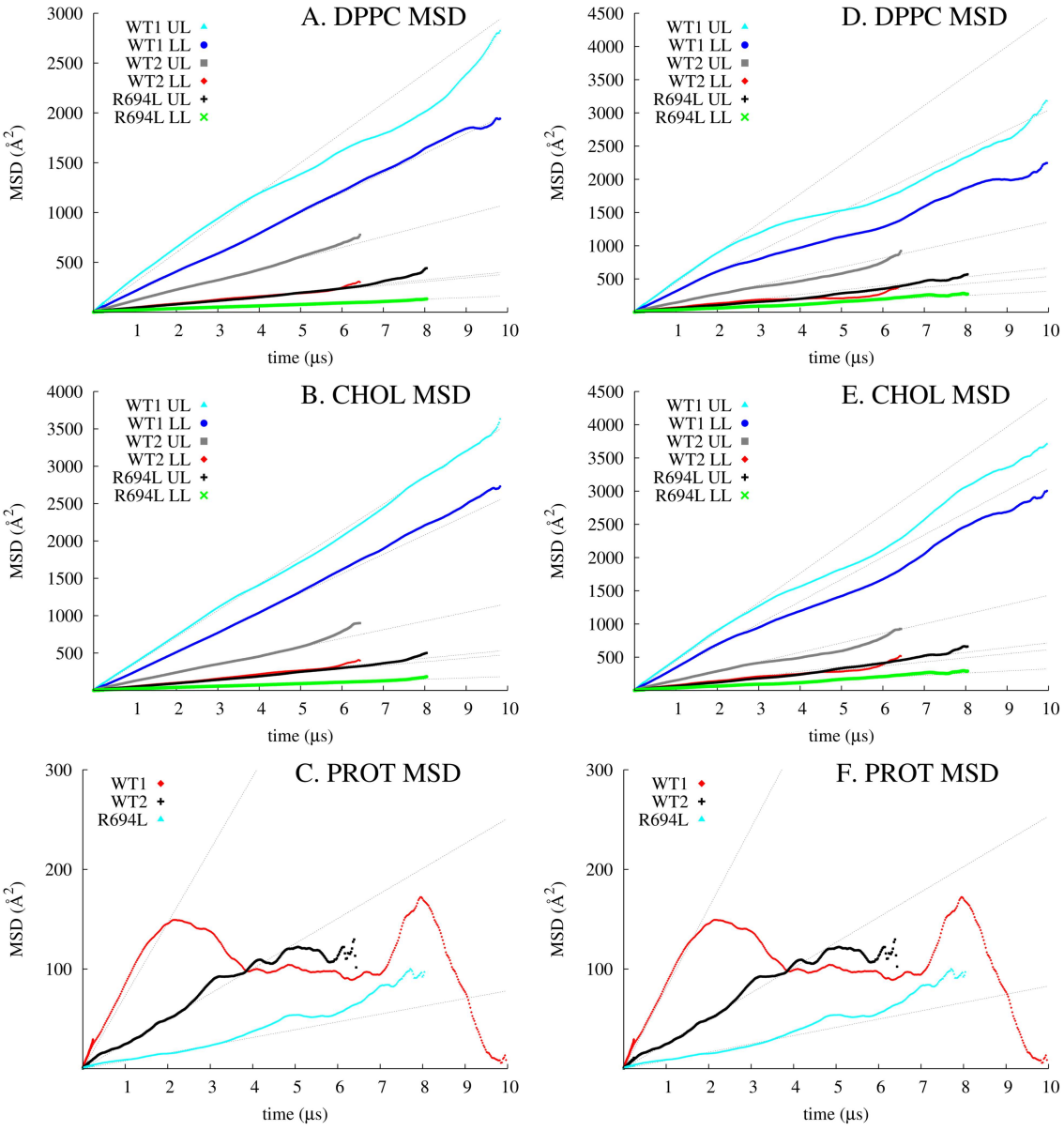

Figure 3: Plots of mean-squared displacements vs time for DPPC, cholesterol (excluding flip-flops), and the gp41 TM α-helix for measurements after monolayer COM removal in A, B, and C and after bilayer COM removal in D, E, F. Dashed lines show best fits of $4D_{i,\mathrm{lat}}t$ for A) $1< t <5$ μs, B) $1< t <5$ μs, C) $0.1< t <2.5$ μs, D) $1< t <2.5$ μs, E) $1< t <3$ μs, F) $0.1< t <2.5$ μs to extract the translational diffusion constant. In A, B, D, E, "UL" and "LL" refer to upper and lower leaflets, respectively. (C) and (F) both show a sudden drop in diffusivity from 10^3 to 10^4 due to the lack of statistics for the peptide at long timescales.

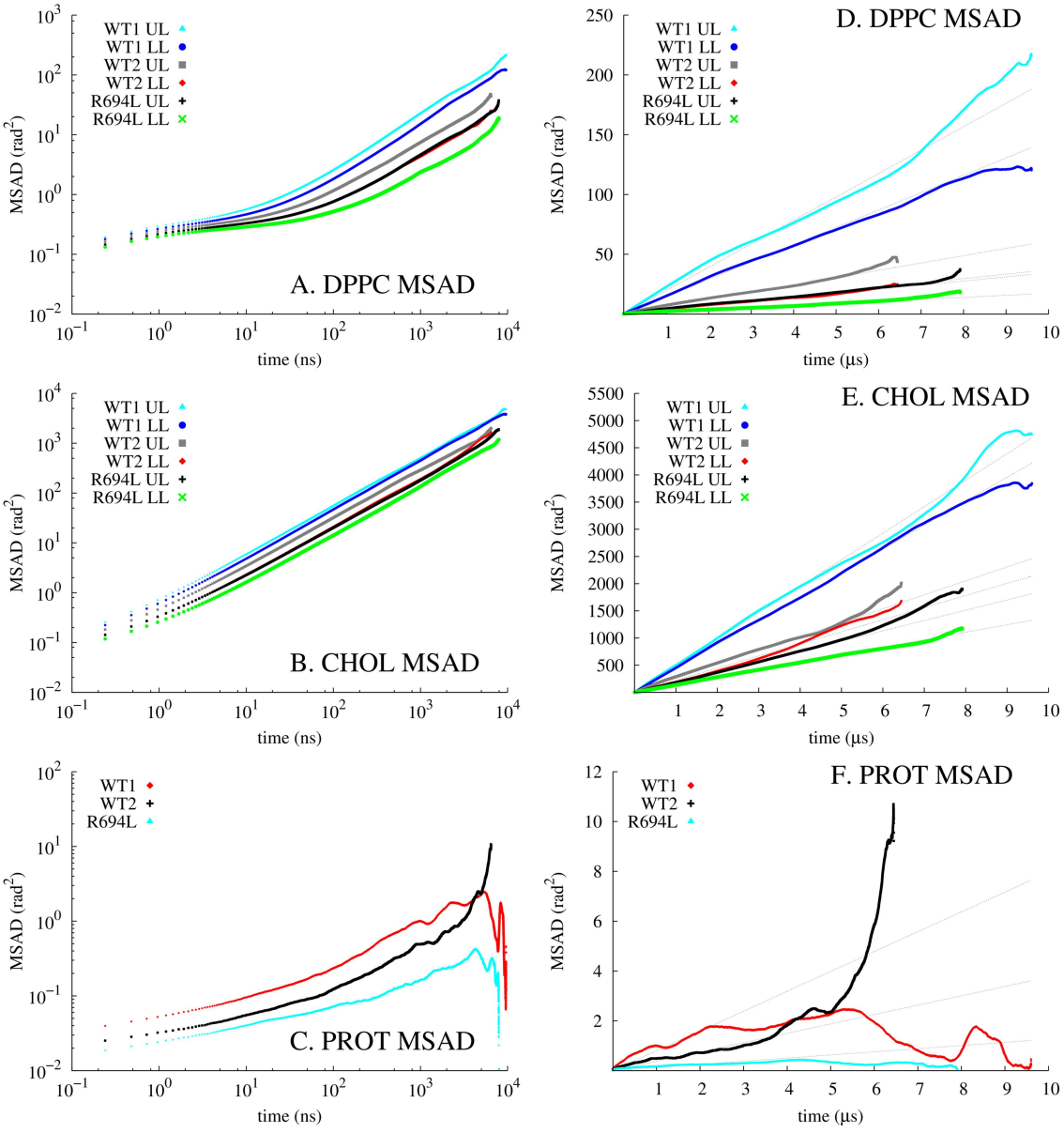

Figure 4: Orientational mean-squared displacements vs time for DPPC, cholesterol (excluding flip-flops), and the gp41 TM α-helix in log-log plots (A, B, C). Dashed lines show best fits of $2D_{i,\mathrm{rot}}t$ for D) $1< t <5$ μs, E) $1< t <5$ μs, F) $0.1< t <2.5$ μs to extract the rotational diffusion constant. In A, B, D, E, "UL" and "LL" refer to upper and lower leaflets, respectively. (C) and (F) both show a sudden drop in diffusivity from 10^3 to 10^4 due to the lack of statistics for the peptide at long timescales.

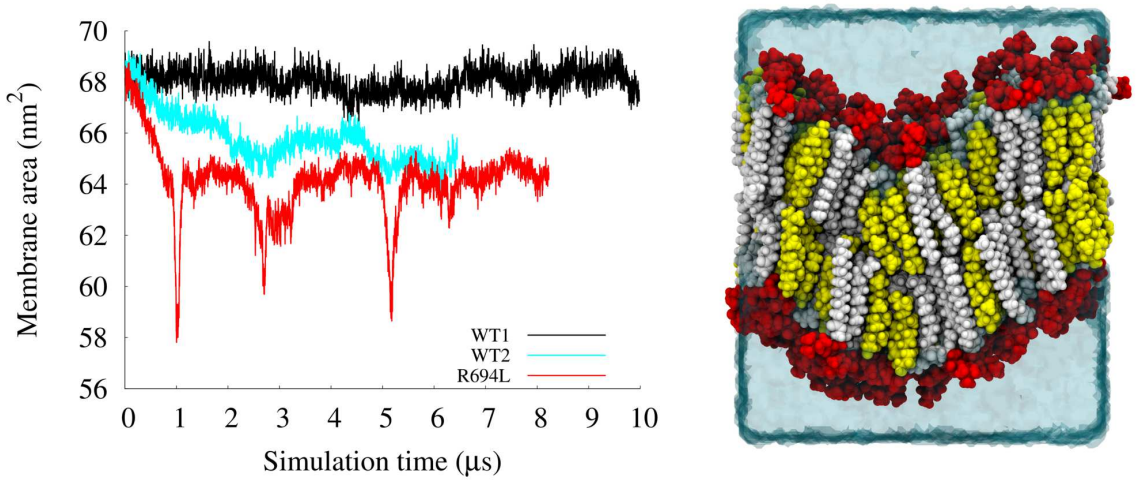

Figure 5: Left, total unit cell area during μs simulations. Right, snapshot of R694L with undulation motion: cholesterol in yellow, water in cyan, lipid headgroups in red, lipid tails in white.

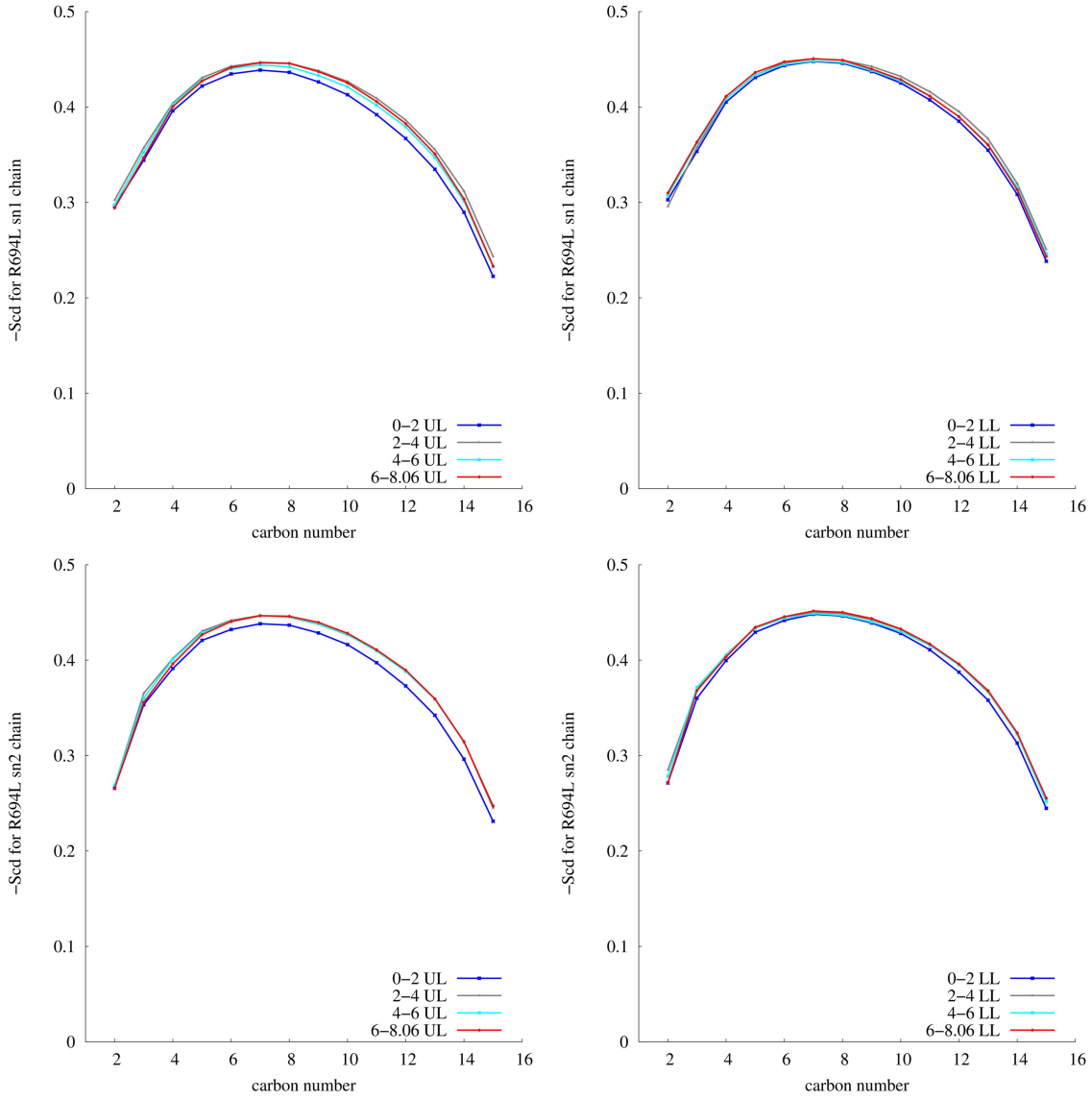

Figure 6: DPPC tail order parameters (sn1 and sn2) vs carbon atom index every 2 μs for upper and lower leaflets of R694L.

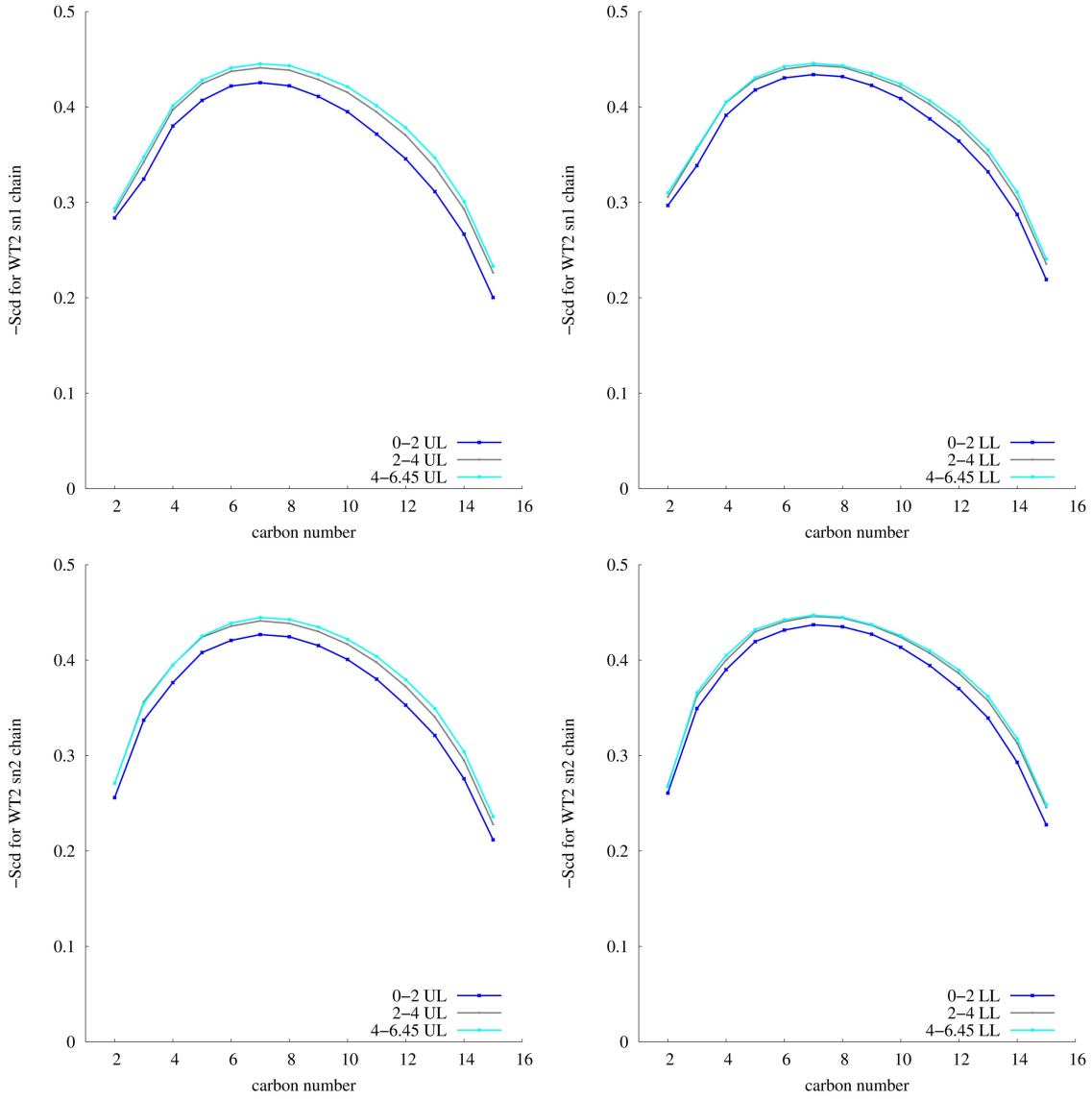

Figure 7: DPPC tail order parameters (sn1 and sn2) vs carbon atom index every 2 μs for upper and lower leaflets of WT2.

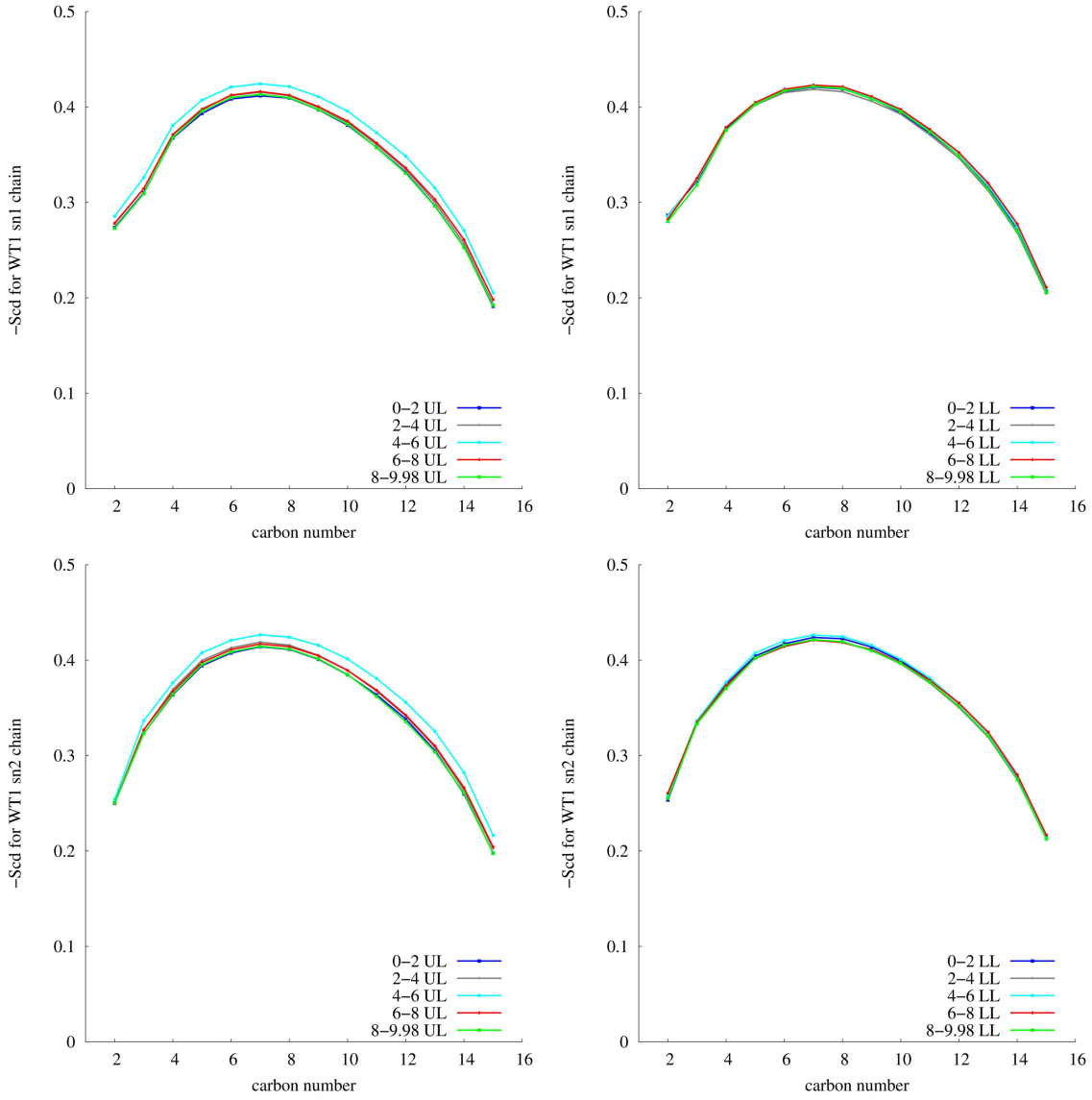

Figure 8: DPPC tail order parameters (sn1 and sn2) vs carbon atom index every 2 μs for upper and lower leaflets of WT1.

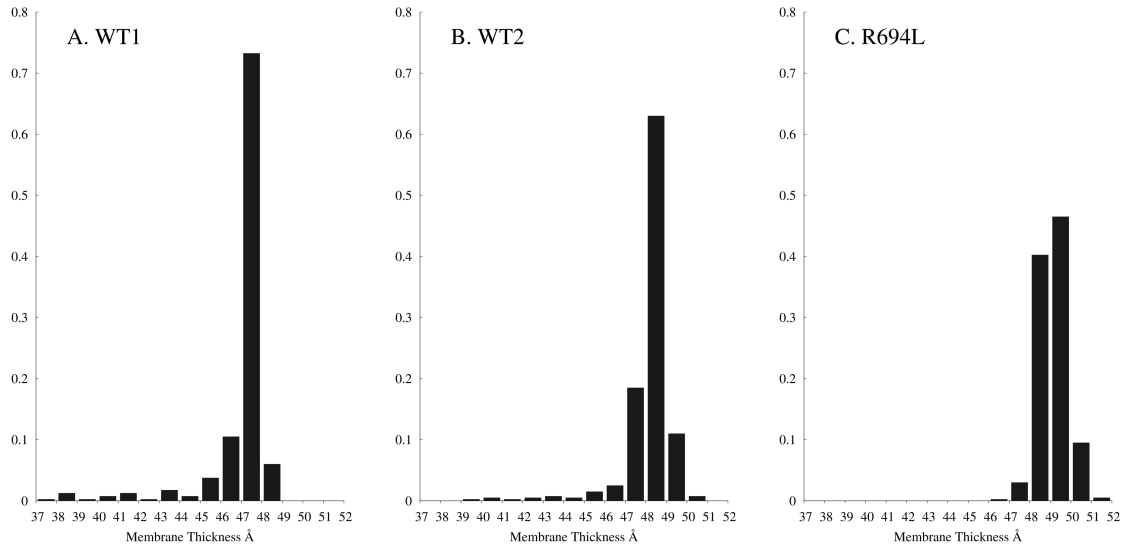

Figure 9: Histograms of average membrane thickness in 4 x 4 $Å^2$ patches for WT1, WT2, and R694L systems.

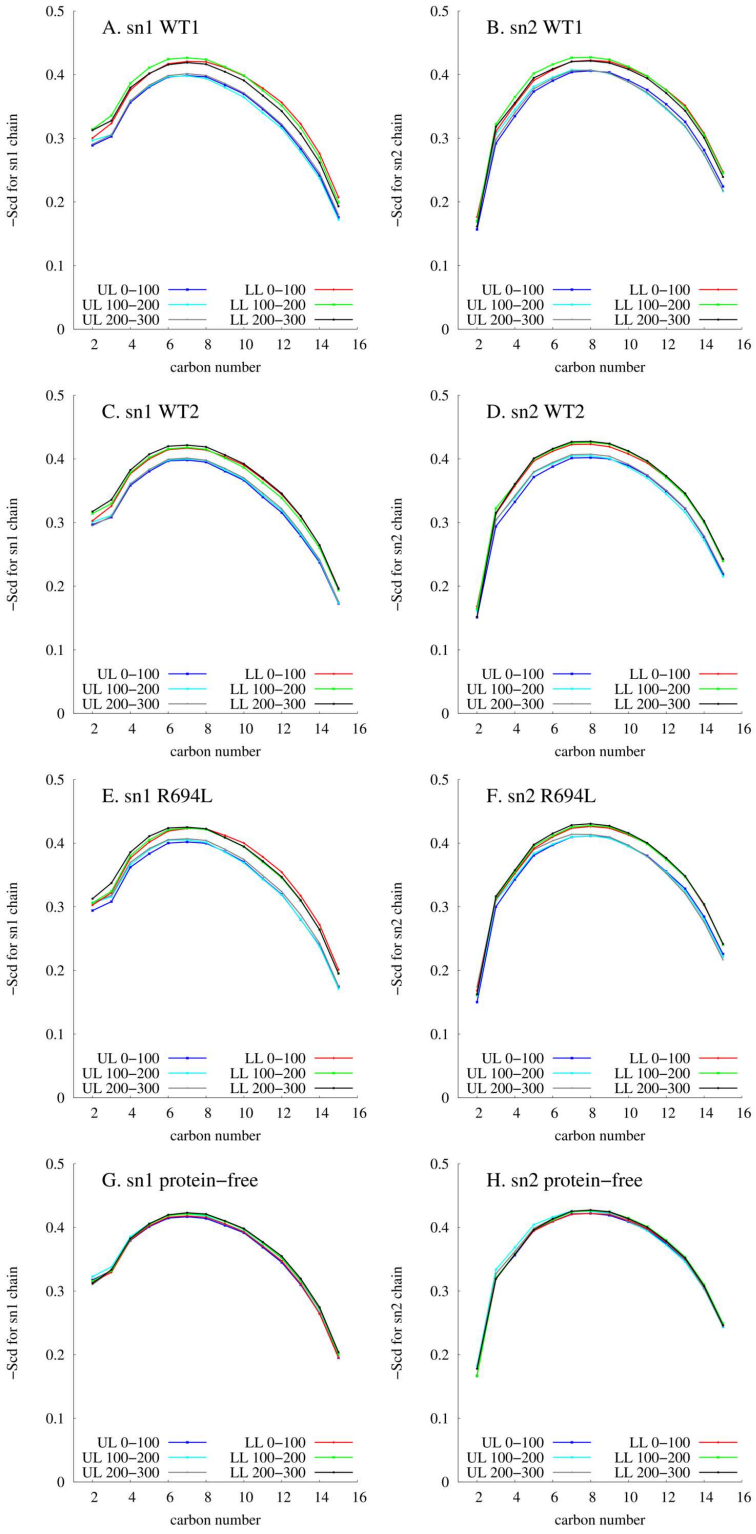

Figure 10: Previous (300 ns) DPPC order parameters for each chain, averaged over 100 ns intervals. “UL” and “LL” refer to upper and lower leaflets, respectively.

Anton software version 2.6.4 configuration parameters for WT1

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anton = {
    chem = {
        Escale = "1000."
        FmaxSeparation = "2.0"
        Fscale = "3000."
        Tempmax = "350"
        maxBondLength = "4.0"
        max_strain = "0.1"
        r_over_sigmamin = "0.60"
        rmin = "0.9"
    }
    run_options = {
        cm_port = "37907"
        ganglia_addr = "log.anton.desres.deshaw.com"
        jobid = "105239"
        jobstep_id = "105239"
    }
    tune = {
        BumpyBoxDelta = "1.535"
        BumpyN = "8"
        DistNumSubboxesX = "1"
        DistNumSubboxesY = "1"
        DistNumSubboxesZ = "2"
        NumSubboxesX = "1"
        NumSubboxesY = "2"
        NumSubboxesZ = "2"
        PacketsPerSubboxPerCore = "5"
        check_overflow = "true"
        checkpoint = {
            first = "0"
            interval = "1200"
            on_last_timestep = "true"
            outdir = "checkpoint.atr"
        }
        go_verbosity = "0"
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        last_time = "Inf"
        machine_size = ["8" "8" "8"]
        optional = {
            AllowDRAMMode = "false"
            BondChunksPerNode = "1"
        }
        regenerateBondProgram = "true"
        trajectory = {
            first = "0"
            format = "dtr"
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            periodicfix = "true"
            write_velocity = "true"
```

```
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    }
}
boot = {
    file = "WT_final.dms"
}
force = {
    nonbonded = {
        electrostatic = {
            type = "ewald"
        }
        far = {
            n_k = ["64" "64" "64"]
            r_spread = "6.654"
            sigma = "1.9987426757812492"
            sigma_s = "1.3295978613281245"
            type = "gse"
        }
        r_cut = "9.0"
        r_lazy = "9.5"
    }
}
global_cell = {
    r_clone = "7.008"
}
integrator = {
    Multigrator = {
        barostat = {
            MTK = {
                T_ref = "310"
                tau = "0.0416667"
                thermostat = {
                    NoseHoover = {
                        chain = {
                            mts = "1"
                            tau = ["0.0416667" "0.0416667" "0.0416667"]
                        }
                    }
                    type = "NoseHoover"
                }
            }
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            type = "MTK"
        }
        nve = {
            PLS = {
                number_of_stages = "3"
            }
            type = "Verlet"
        }
        thermostat = {
            NoseHoover = {
                chains = [{
                    mts = "1"
```

```
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            }]
            use_molecular_ke = "true"
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        type = "NoseHoover"
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}
NH_NVT = {
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        mts = "2"
        tau = ["1." "1." "1."]
    }]
    thermostat_molecular_ke = "true"
}
V_NVE = {
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dt = "0.0020"
pressure = {
    isotropy = "semi_isotropic"
    max_margin_contraction = "0.9"
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}
remove_com_motion = "false"
respa = {
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temperature = [{
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type = "Multigrator"
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