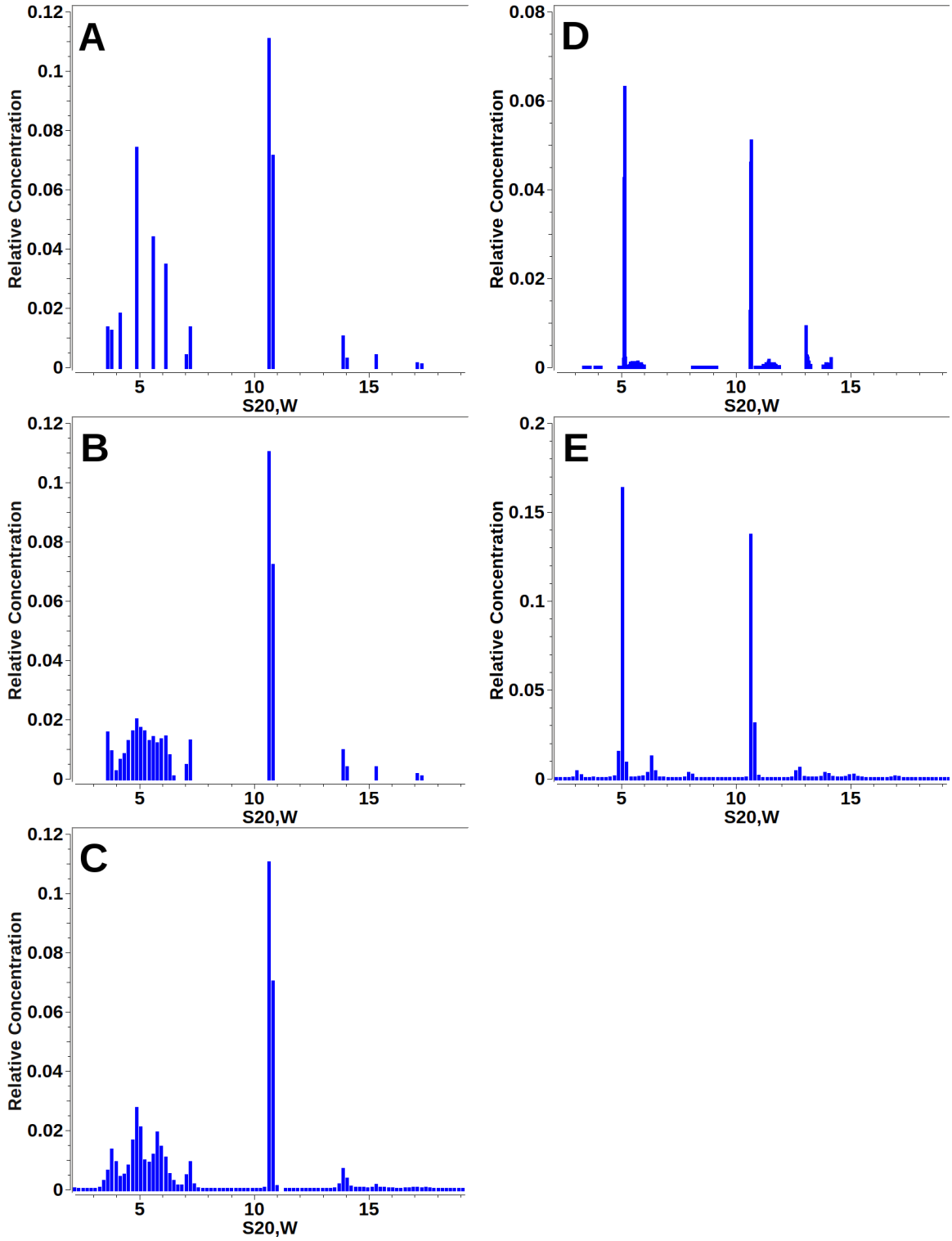
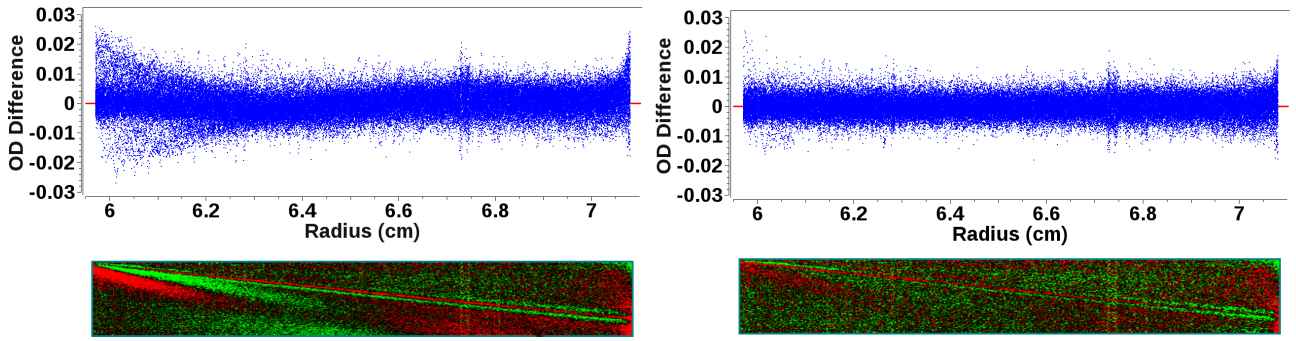
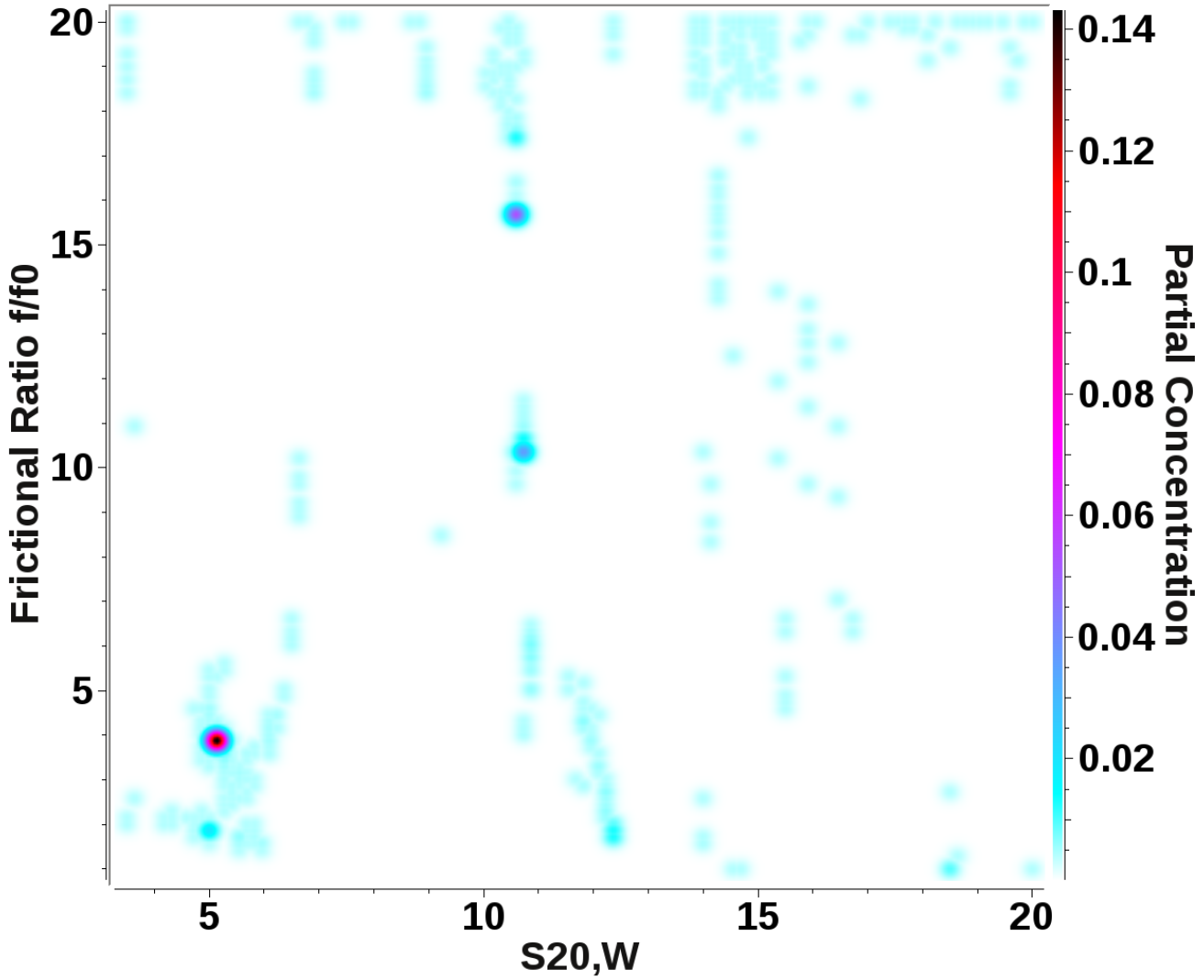
Supplemental Material:



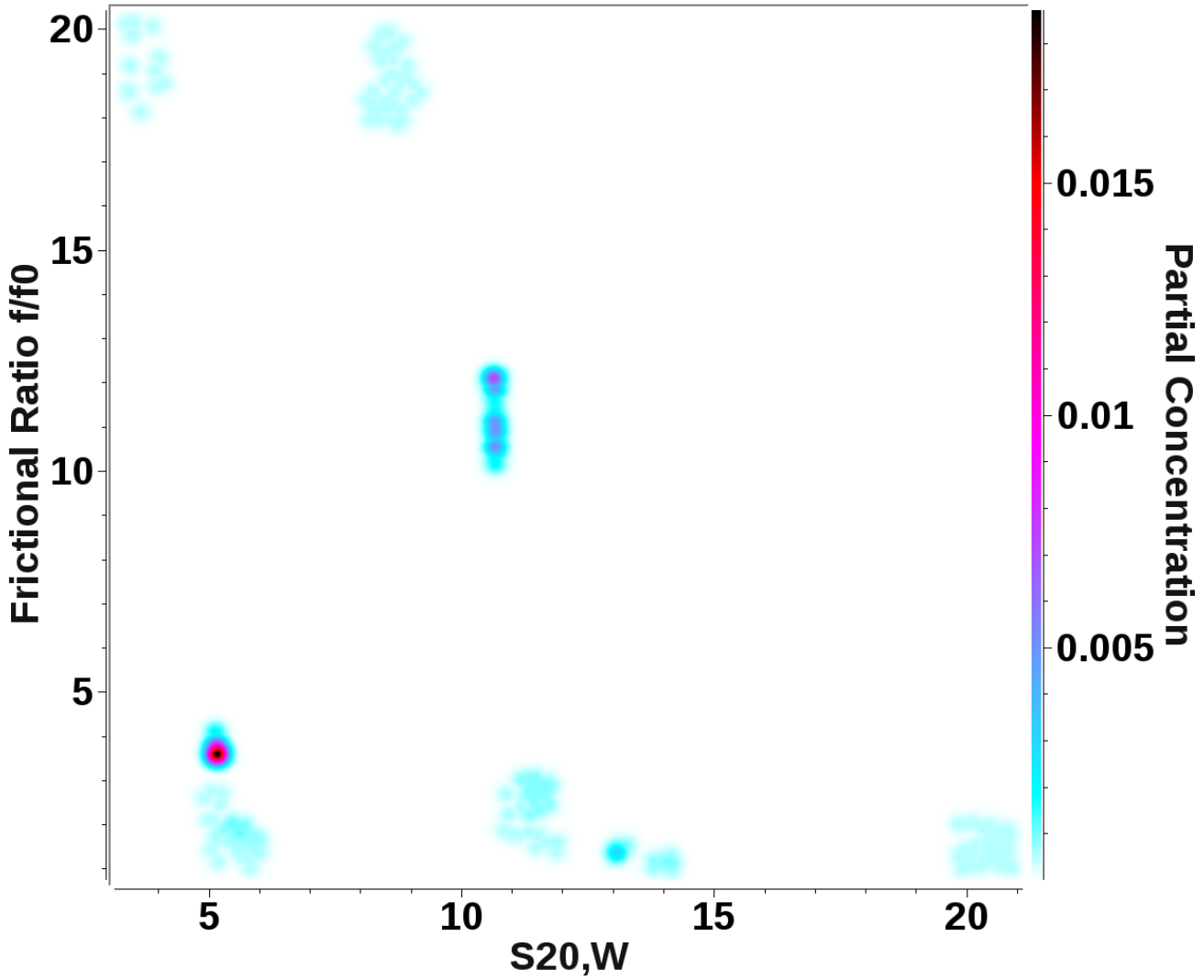
Supplemental_Figure 1: *Histogram plots of data shown in Figure 2B,C.* ***A:****PCSA-HL, without regularization;* ***B:*** *PCSA-HL, with regularization;* ***C:*** *PCSA-HL, Monte Carlo;* ***D:*** *genetic algorithm, Monte Carlo;* ***E:*** *PCSA-SL, Monte Carlo. The PCSA-SL and genetic algorithms produce nearly identical results and avoid the broadening of the 5-S peak.*



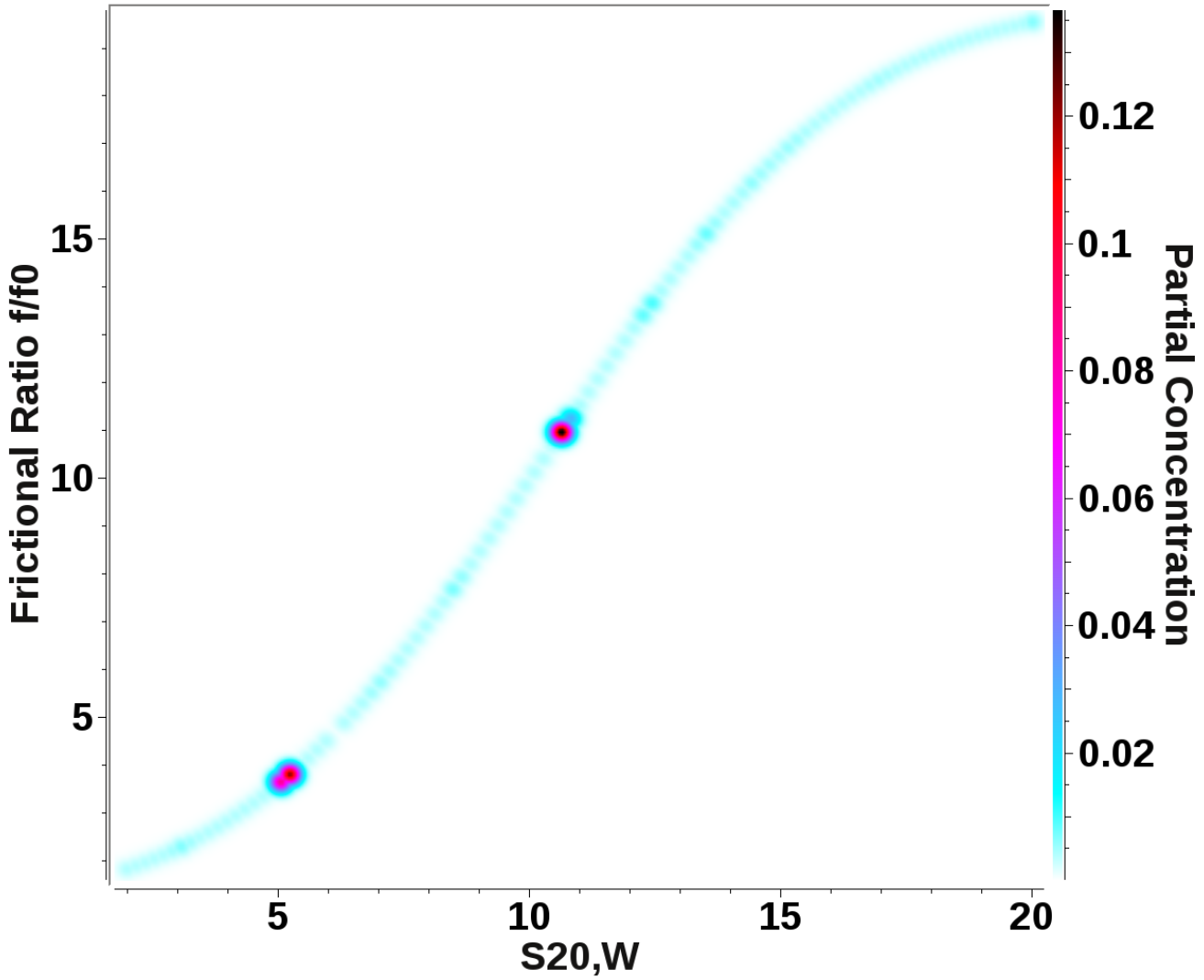
Supplemental_Figure 2: *Residuals for sedimentation velocity whole boundary fitting of two DNA fragments in 1.7 mM NaCl buffer (data from Table 2) for horizontal line (HL) parameterization (left) and straight line (SL) parameterization (right). Bitmaps of the residual pattern are shown on the bottom. The increase in RMSD for HL parameterization is significant, with non-random residual patterns especially evident for the poorly fitted slower sedimenting component near the meniscus.*



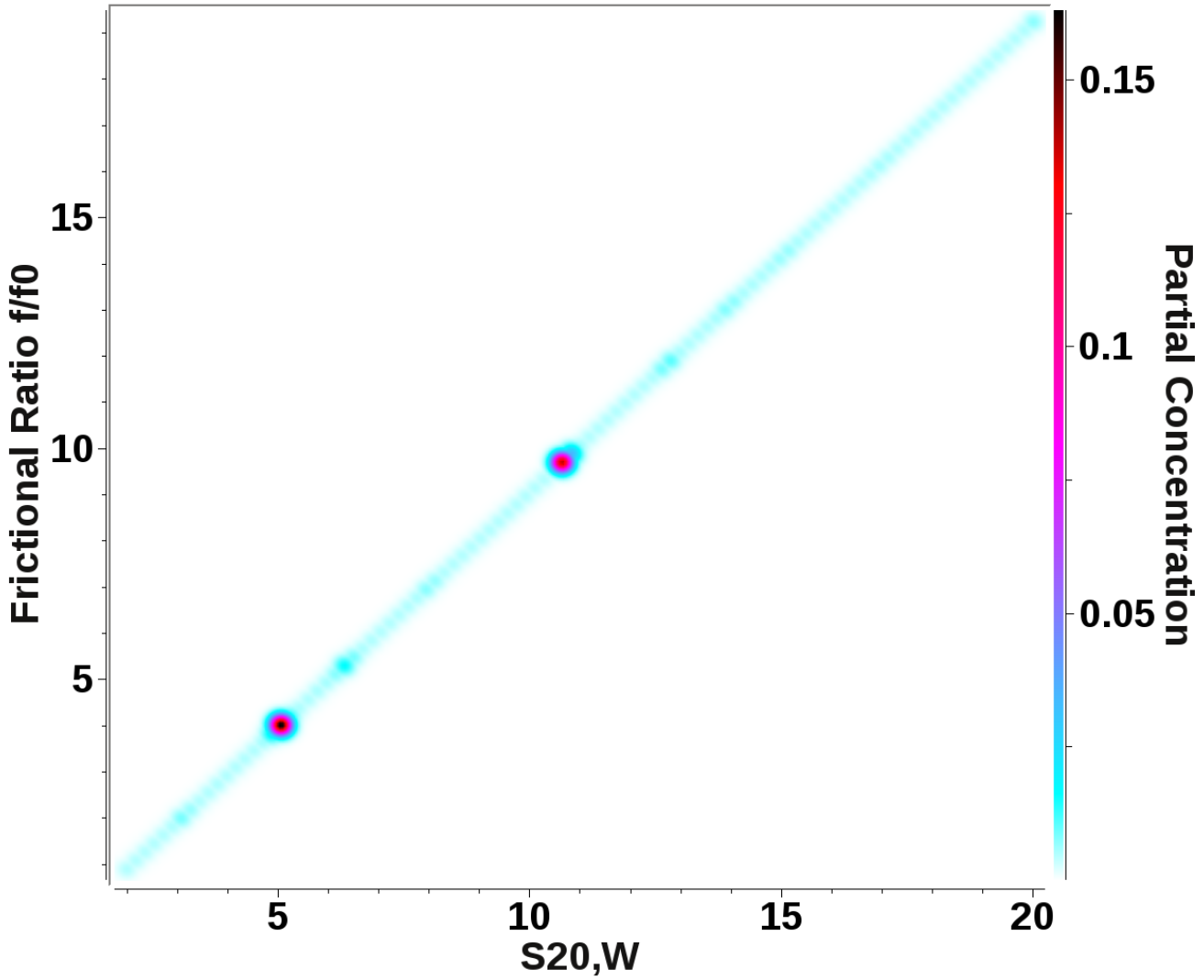
Supplemental_Figure 3: *2DSA with a 100 iteration Monte Carlo analysis of 1.7 mM NaCl DNA sample (compare Table 2)*



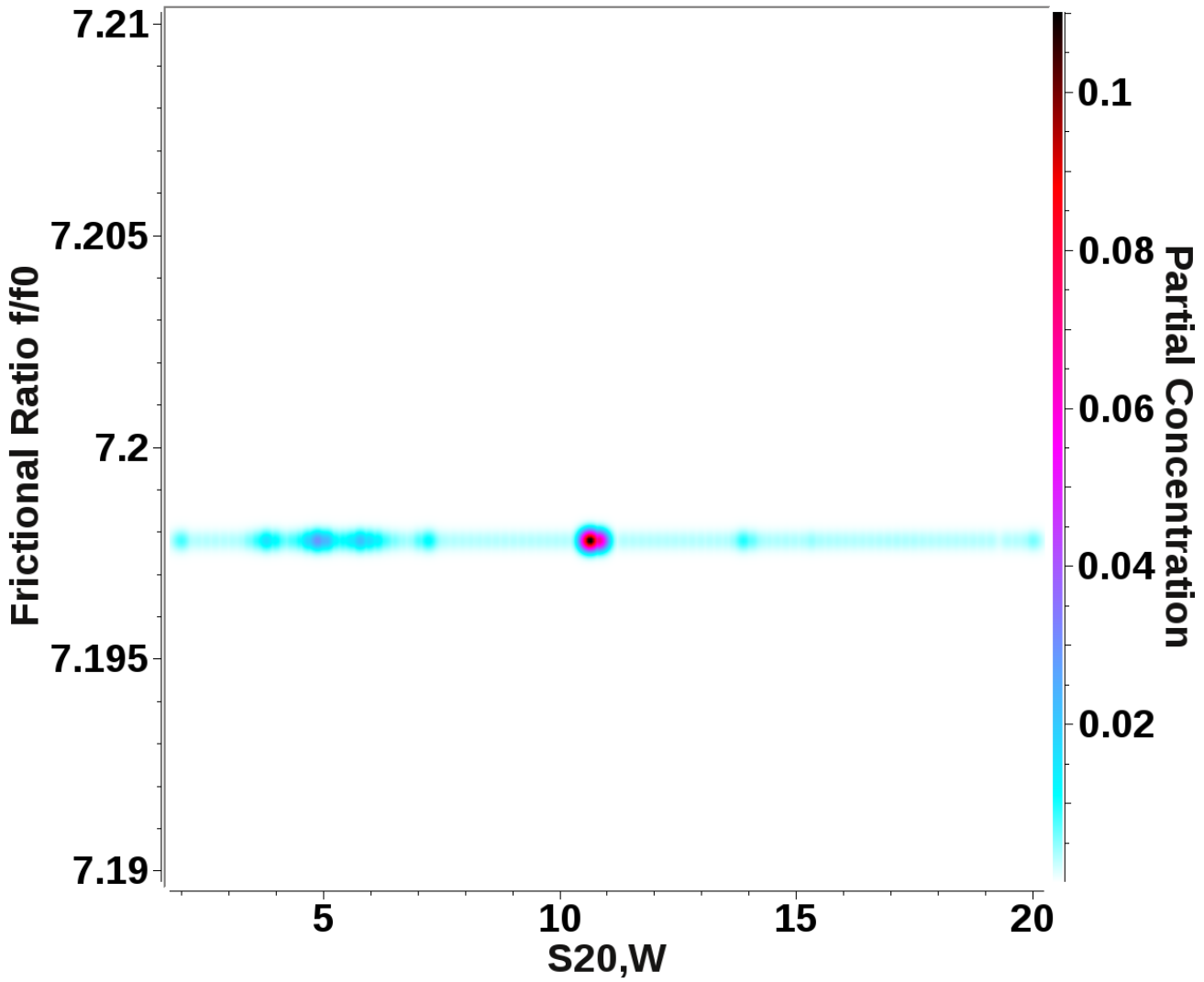
Supplemental_Figure 4: *Genetic algorithm with a 100 iteration Monte Carlo analysis of 1.7 mM NaCl DNA sample (compare Table 2).*



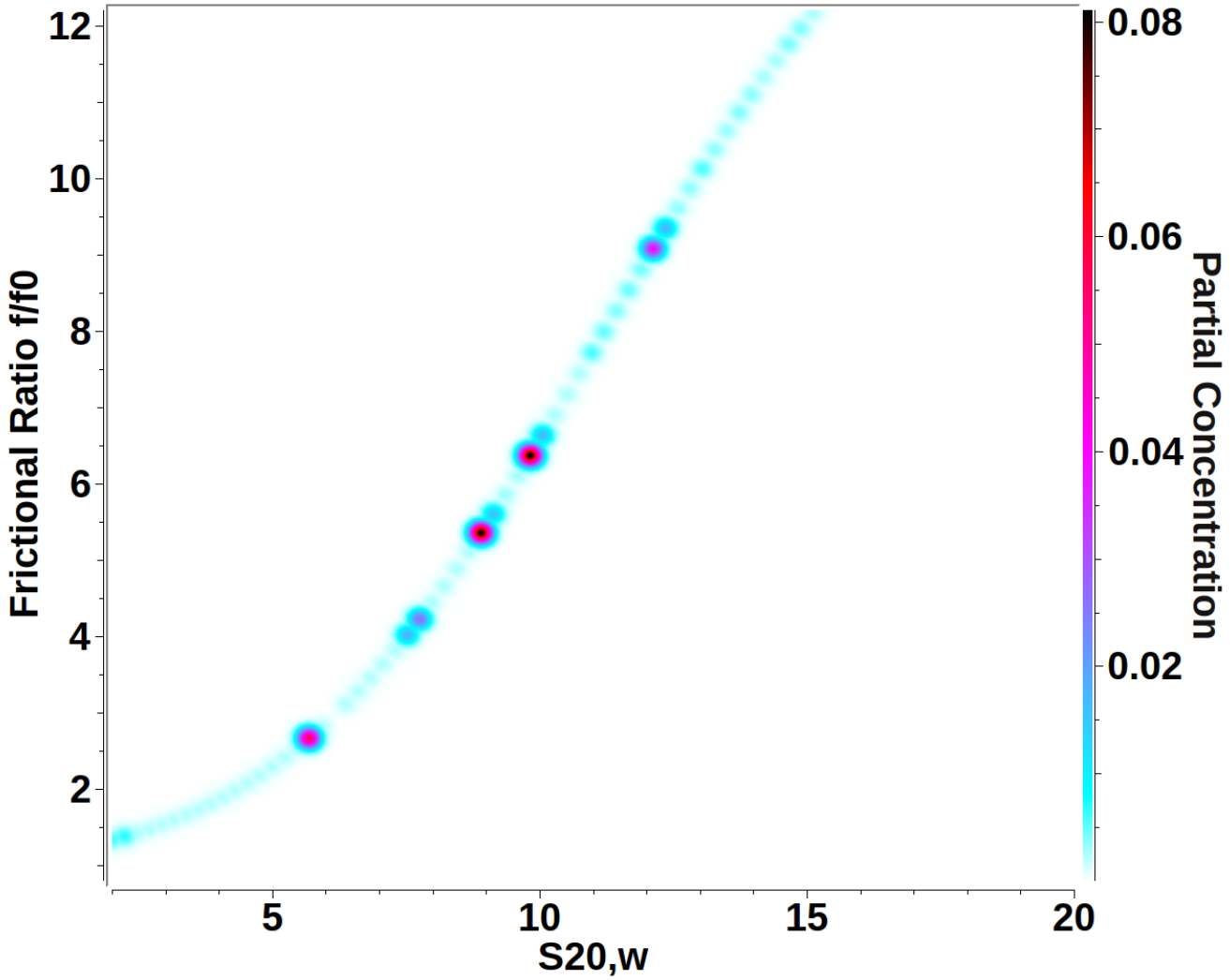
Supplemental_Figure 5: *PCSA increasing sigmoid parameterization with a 100 iteration Monte Carlo analysis of 1.7 mM NaCl DNA sample (compare Table 2).*



Supplemental_Figure 6: *PCSA straight line parameterization with a 100 iteration Monte Carlo analysis of 1.7 mM NaCl DNA sample (compare Table 2).*



Supplemental_Figure 7: *PCSA horizontal line parameterization with a 100 iteration Monte Carlo analysis of 1.7 mM NaCl DNA sample (compare Table 2).*



Supplemental_Figure 8: *5-fragment DNA digest shown in Figure 7 analyzed with the PCSA using an increasing sigmoid functional form, producing a very similar pattern as the straight line method shown in Figure 7.*

Variations	Time	Refinements	RMSD	Threads	LM Iterations	Speedup
10	1m.34s	1	0.0054185	1	0	1
10	0m.17s	1	0.0054185	8	0	5.5
12	2m.16s	1	0.0054143	1	0	1
12	0m.24s	1	0.0054143	8	0	5.25
10	4m.48s	3	0.0054129	1	0	1
10	0m.51s	3	0.0054127	8	0	5.7
10	4m.56s	3	0.0054124	1	12	1
10	0m.59s	3	0.0054124	8	12	5.0
10	1m.55s	1	0.0054124	1	24	1
10	0m.40s	1	0.0054124	8	24	2.9
5	0m.49s	1	0.0054124	1	36	1
5	0m.42s	1	0.0054124	8	36	1.2
11	2m.08s	1	0.0054124	1	18	1
11	0m.33s	1	0.0054124	8	18	3.9

Supplemental_Table 1: *PCSA performance analysis for a 20,000 point absorbance sedimentation velocity dataset using a 100 point s-value resolution setting and the straight-line functional form. All calculations were performed on a Dell Inspiron 1732 laptop equipped with an Intel I7 processor and 8 GB RAM. The effect of different analysis settings on the speed of convergence is shown. The following trends are observed: When Levenberg-Marquardt refinement was used, the solution converged reliably to the same, lowest RMSD observed during all trials. The number of Levenberg-Marquardt iterations required for convergence depended on the resolution of the parameter grid for the functional form. Additional grid refinements provided an initial improvement in RMSD, which reduced the number of Levenberg-Marquardt iterations. RMSDs obtained with grid refinements approached the RMSD value obtained with Levenberg-Marquardt iterations, with variations only in the fifth significant digit. Since grid refinements can be parallelized, additional threads accelerate the calculations most when the number of Levenberg-Marquardt iterations is smallest, since Levenberg-Marquardt iterations are evaluated sequentially. For reference, the RMSD from the 2DSA was 0.0053679. For this dataset, the optimal solution was reached fastest when multi-threading was used, and when using an intermediate grid resolution setting. For a single thread calculation, the fastest execution speed was obtained when a relatively coarse grid was used and more time was spent in the Levenberg-Marquardt iterations, where multi-threading has no advantage. The trends observed here are typical, but execution time will vary with hardware, dataset size, and desired optimization level. In general, RMSDs obtained from fits without Levenberg-Marquardt iterations vary only in the fourth significant digit, a small penalty for significant speedup realized when multiple processors are available. A 2-fold increase in memory was observed when the number of threads were quadrupled. Runs executed with one thread required an average of 79 MB, while runs performed with 8 threads needed an average of 318 MB of RAM. The column labeled "Speedup" indicates the speedup observed when eight threads are used compared to identical parameterization with one thread.*

Model:	$s_{20,W}$ (sec)	$D_{20,W}$ (cm^2/sec)	f/f_0	$\bar{\nu}$ (ml/mg)	MW (kDa)
Fibrinogen, monomer	7.28466e-13	2.56171e-07	2.0300	0.719	245.55
Fibrinogen, dimer	1.02062e-12	1.79455e-07	2.3000	0.719	491.10
Fibrinogen, trimer	1.20156e-12	1.40846e-07	2.5600	0.719	736.65
Fibrinogen, tetramer	1.31673e-12	1.15758e-07	2.8300	0.719	982.21
Fibrinogen, pentamer	1.38593e-12	9.74709e-08	3.1200	0.719	1,227.75

Supplemental_Table 2: *Hydrodynamic and molecular parameters for simulated fibrinogen oligomers*

	f/f$_0$						Molar Mass						Partial Concentration					
	40 krpm			60 krpm			40 krpm			60 krpm			40 krpm			60 krpm		
	GA	IS	HL	GA	IS	HL	GA	IS	HL	GA	IS	HL	GA	IS	HL	GA	IS	HL
1	0.4	6.2	33.4	-0.6	0.9	28.9	-0.6	9.4	54.5	-0.9	1.5	46.7	0.2	-0.8	-3.0	0.3	0.0	-0.1
2	-0.8	11.4	17.8	3.0	8.8	13.8	-1.1	17.3	27.2	4.7	13.6	21.5	0.3	-2.5	-3.5	0.2	0.5	0.4
3	0.5	10.7	5.8	1.2	9.9	2.3	0.7	16.5	6.5	2.1	15.8	3.5	-1.2	2.3	-43.5	2.1	3.6	-1.4
4	-2.3	6.0	-4.5	-0.4	6.5	-8.1	-3.4	8.3	-13.9	-0.1	10.4	-13.1	4.6	-24.2	-41.4	9.5	-2.0	-22.8
5	6.7	-0.3	-15.2	12.1	0.3	-19.2	-4.1	-1.0	-26.2	19.4	0.7	-31.3	-4.2	19.2	63.1	-13.8	-3.3	19.5
av	2.2	6.9	15.3	3.5	5.3	14.5	3.3	10.5	25.7	5.4	8.4	23.2	2.1	9.8	30.9	5.2	1.9	8.8

Supplemental_Table 3: *Accuracy comparison between genetic algorithms (GA), PCSA-IS (IS) and PCSA-HL (HL) for recovering the frictional ratio, molar mass and partial concentration for the five simulated fibrinogen oligomers for 40 and 60 krpm simulations. Shown are the percentage differences between the observed values from each method, and the actual values that were simulated (compare Supplemental_Table 2 for target values). Smaller numbers indicate a better agreement with the simulated data. 0.5% random noise were added to the simulated data to approximate experimental conditions observed in the instrument. Values highlighted in green represent the best fit of the three methods. Overall averages (av) for each category and method are shown in the last row. Percent RMSD deviations from the simulated RMSD value (0.005 OD) for each method at 40 krpm were 0.0% (GA), +0.3516 % (IS), +2.957% (HL), and at 60 krpm were +0.3594% (GA), +0.4496 (IS) and +2.4422% (HL). This matches well with the overall error rate for the three methods, which where 3.62 % (GA), 7.13% (IS), and 19.73% (HL). The 20 krpm results are not listed since neither method was able to resolve the two most closely spaced species, the tetramer and pentamer at 20 krpm.*