fig S1

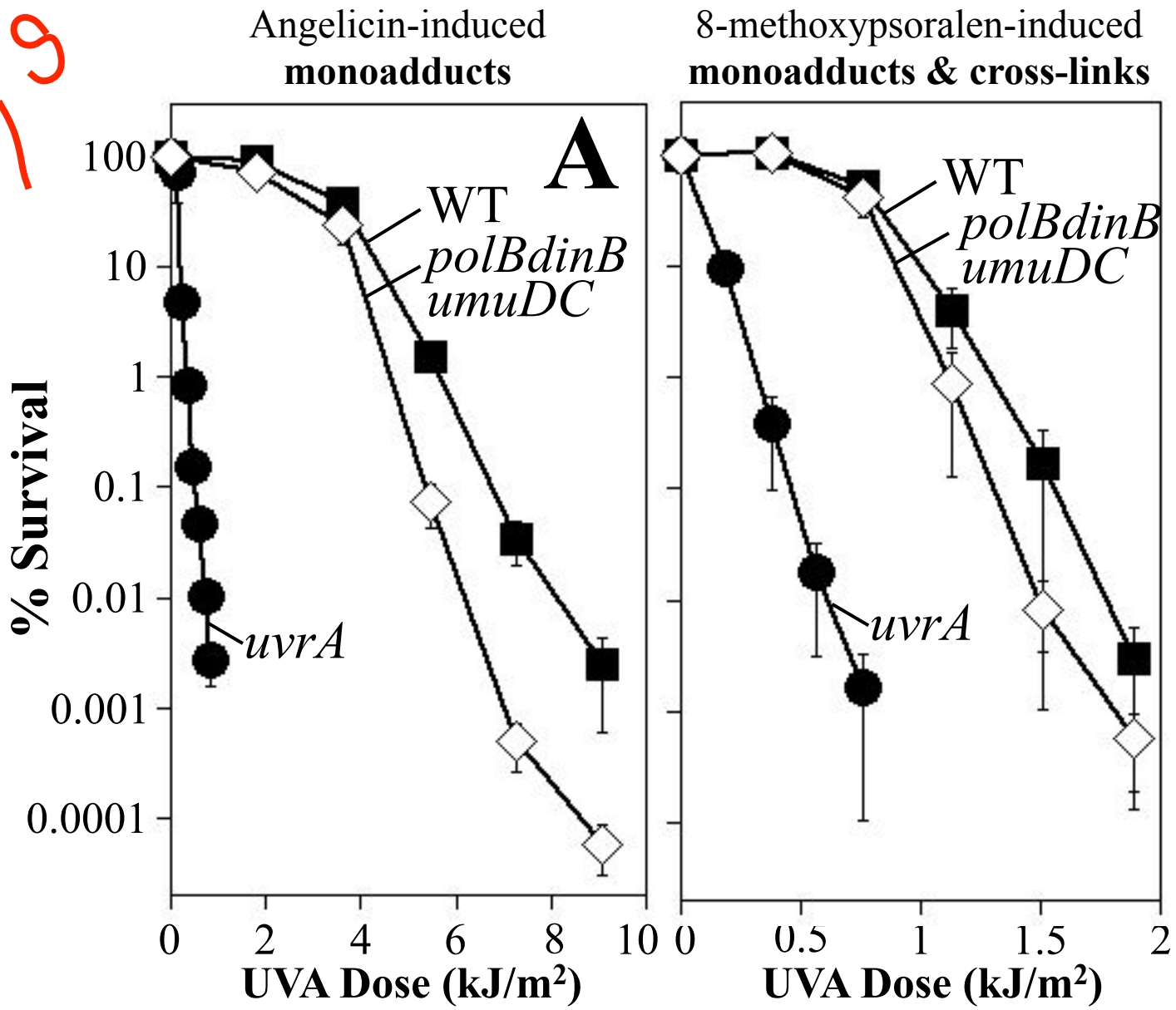

Figure S1. The translesion DNA polymerases do not contribute to survival in the presence of 8-methoxypsoralen-induced DNA interstrand cross-links in non-replicating cells. Subcultures of all strains were grown for 24 hours prior to treatment. The survival of WT (filled squares), uvrA (filled circles), and polB dinB umuDC (open diamonds) mutants following UVA irradiation in the presence of A) 40 µg/mL angelicin or B) 10 µg/mL 8-methoxypsoralen is plotted. Plots represent the average of at least 3 experiments. Error bars represent standard error of the mean. WT and uvrA from Fig 2 shown for comparison.

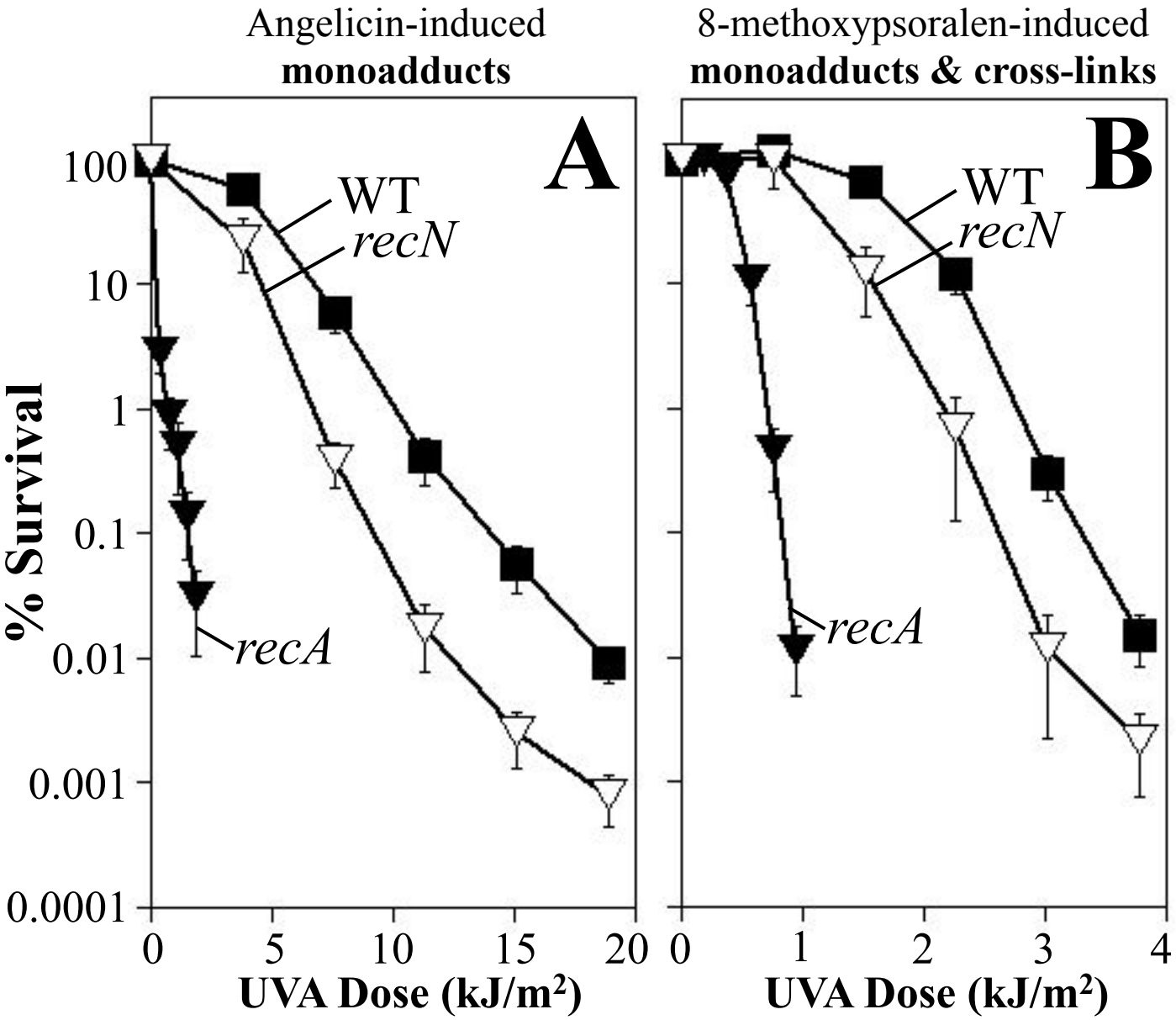

Figure S2. recN, which is required for resistance to double-strand breaks, does not contribute to survival in the presence of DNA interstrand cross-links in non-replicating cells. Subcultures of all strains were grown for 24 hours prior to treatment. . The survival of WT (filled squares), recA (filled triangles), and recN (open triangles) mutants following UVA irradiation in the presence of A) 40 µg/mL angelicin or B) 10 µg/mL 8-methoxypsoralen is plotted. Plots represent the average of at least 3 experiments. Error bars represent standard error of the mean. WT from Fig 2 shown for comparison.

figS2

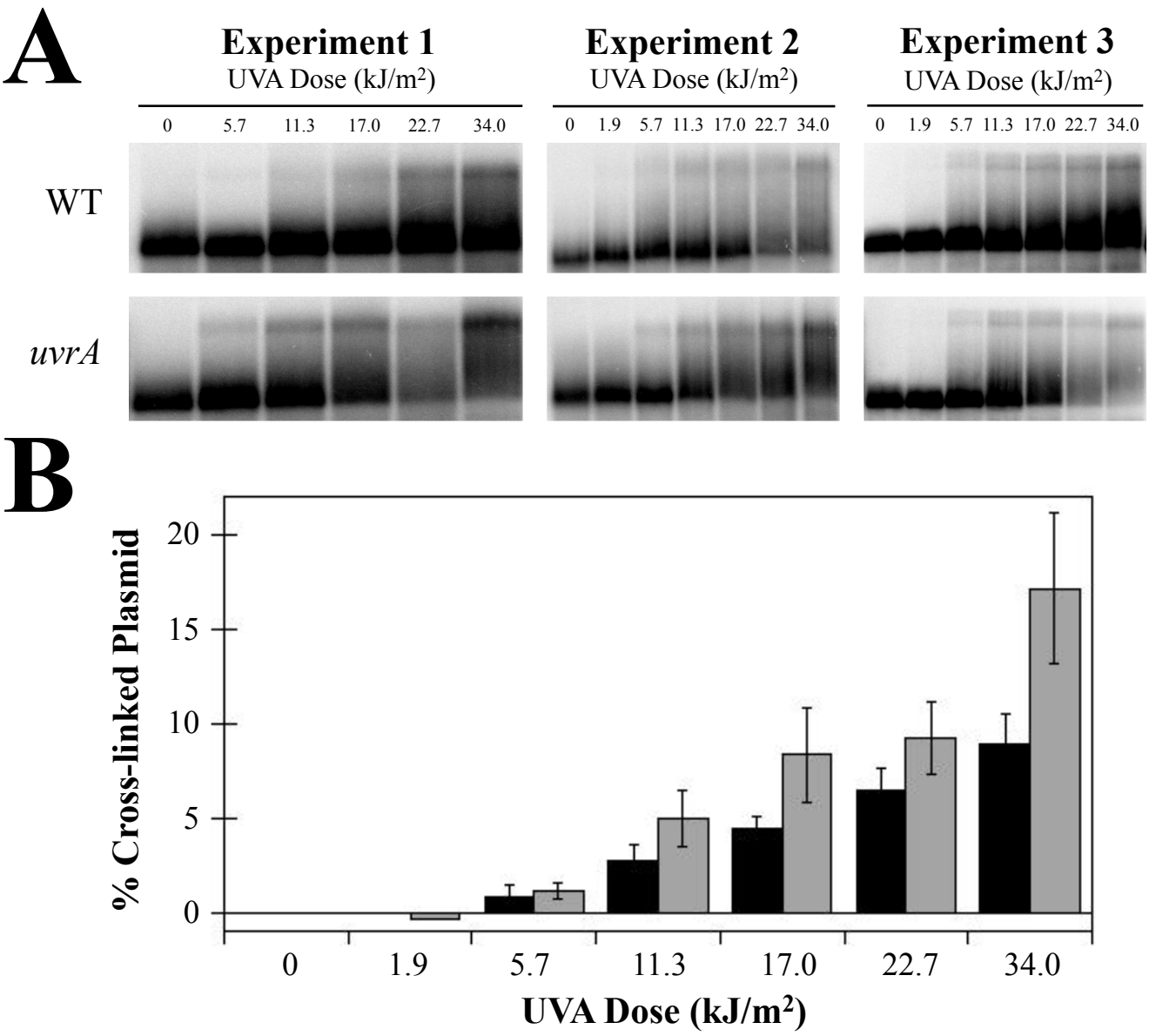

Figure S3. Dose response of wild type and uvrA cultures for interstrand cross-link formation in vivo. A) DNA interstrand cross-links increase with dose. Three independent experiments of wild type and uvrA mutants containing plasmid pBR322 were UVA-irradiated at the indicated dose in the presence of 10 µg/mL of 8-methoxypsoarlen. DNA from cultures were then immediately purified and analyzed as in Fig 3 to observe the interstrand cross-links formed at each dose. B) The percent of cross-links formed in 4.3-kb plasmids at each dose is plotted. Plots represent the average of 3 experiments. Error bars represent standard error of the mean.

figS3

fig S4

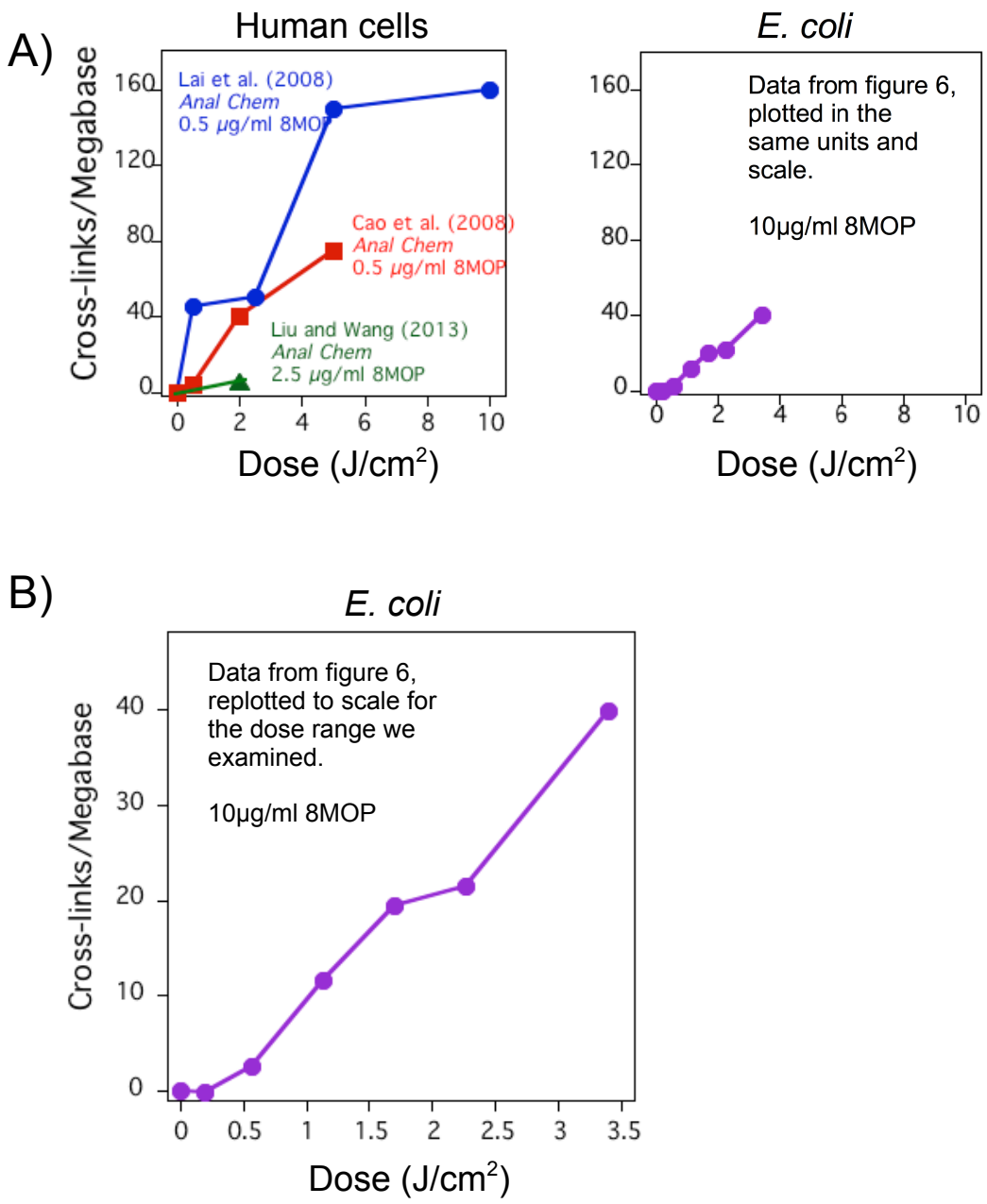

Figure S4. Comparison of our data with those of three previous studies which utilized LC-MS approaches to quantify the UVA dose-dependent induction of interstrand cross-links. A) Several recent studies, primarily in human cells, have used LC-MS approaches to quantify cross-links as a function of 8-methoxypsoralen concentration and UVA dose. The estimates from three of these studies are plotted (left). Cao et al. 2008, red squares; Lai et al. 2008, blue circles; Liu and Wang 2013 green triangles. For context, the results from Figure 6, is replotted as cross-links/megabase and on the same scale as that for the studies in human cells (right), purple circles. While these plots provide context for our quantifications, we would emphasize that differences in the cell type and media used in these experiments prohibit them from being compared directly. B) The data from Figure 6, plotted as cross-links/megabase DNA, on a scale highlighting the dose range we examined.

Figure S5.

Calculation of the number of interstrand cross-links/genome that is lethal in *E. coli.*

The lethal dose for wild-type cells was 1.9 kJ/m^2 (Fig 6A).

The best fit line for y, the fraction of interstrand cross-link-free plasmids was $y = e^{-(m)x} + (m)xe^{-(m)x}$, where under our irradiation conditions, m = 0.023, x = 1.9 kJ/m^2 (Fig 6C).

At the lethal dose, the fraction of interstrand cross-link-free plasmids was equal to y = 0.9990

The fraction of plasmids containing an interstrand cross-link at the lethal dose was 1-y, or 0.001, which corresponds to 1 interstrand cross-link / 1000(4.3 kb plasmids) or 1 interstrand cross-link / 4300kb of DNA.

1 interstrand cross-link/4300kb of DNA corresponds to 1.07 cross-links/4600kb genome.

fig S5

TableS1

	8-methoxypsoralen Survival (%)						Angelicin Survival (%)					
UVA Dose (kJ/m^2)	WT	*recA*	*uvrA*	*uvrD*	*recN*	*polB, dinB, umuDC*	WT	*recA*	*uvrA*	*uvrD*	*recN*	*polB, dinB, umuDC*
0	100	100	100	100	100	100	100	100	100	100	100	100
0.19		97.7 ± 9.8										
0.25									**12.3 ± 7.0**			
0.38		74.3 ± 10.5	56.5 ± 8.2					**2.8 ± 0.9**				
0.50									1.5 ± 1.1			
0.57		**10.3 ± 3.6**										
0.76	116.2 ± 16.2	0.4 ± 0.2	**2.8 ± 0.6**	39.4 ± 8.9	97.5 ± 39.9	80.1 ± 5.9		0.9 ± 0.4	0.5 ± 0.4	**1.1 ± 0.3**		
0.95		0.0 ± 0.0										
1.01									0.1 ± 0.1			
1.13			0.1 ± 0.0					0.5 ± 0.3				
1.26									0.0 ± 0.0			
1.51	66.1 ± 8.9		0.0 ± 0.0	**5.2 ± 1.6**	**12.5 ± 7.0**	**30.0 ± 2.3**		0.1 ± 0.1		0.05 ± 0.0		
1.89								0.0 ± 0.0				
2.27	**11.9 ± 3.5**			0.6 ± 0.2	0.7 ± 0.5	1.2 ± 0.8				0.0 ± 0.0		
3.02	0.3 ± 0.1			0.2 ± 0.1	0.0 ± 0.0	0.1 ± 0.0				0.0 ± 0.0		
3.78	0.0 ± 0.0			0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	56.2 ± 7.2				**22.6 ± 10.4**	**21.4 ± 10.5**
7.56							**5.8 ± 1.7**				0.4 ± 0.2	1.1 ± 0.5
11.34							0.4 ± 0.2				0.0 ± 0.0	0.0 ± 0.0
15.12							0.1 ± 0.0				0.0 ± 0.0	0.0 ± 0.0
18.90							0.0 ± 0.0				0.0 ± 0.0	0.0 ± 0.0